



# ANTIMICROBIAL STEWARDSHIP

FROM PRINCIPLES  
TO PRACTICE



BRITISH SOCIETY FOR  
ANTIMICROBIAL  
CHEMOTHERAPY

# THIS E-BOOK HAS BEEN DEVELOPED BY BSAC



BRITISH SOCIETY FOR  
ANTIMICROBIAL  
CHEMOTHERAPY

## IN COLLABORATION WITH ESGAP/ESCMID



**ESGAP**

ESCMID STUDY GROUP  
FOR ANTIMICROBIAL  
STEWARDSHIP

European Society of Clinical Microbiology and Infectious Diseases



**ESCMID**

MANAGING INFECTIONS  
PROMOTING SCIENCE

PLEASE NOTE THAT THE AUTHORS' CHAPTERS DO NOT REFLECT THE OPINION  
OF ANY ORGANISATIONS THEY MAY BE ALIGNED WITH



GLOSSARY OF TERMS

### ACKNOWLEDGEMENT

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PRESIDENT OF BSAC [2015-2018]

## PREFACE

Scientists have known for more than half a century that patients could develop resistance to the drugs used to treat them. Alexander Fleming, who is credited with creating the first antibiotic, penicillin, in 1928, cautioned of the impending crisis while accepting his Nobel prize in 1945: “There is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant.” Since then antibiotics have proved one of the most effective interventions in human medicine. Sadly, the overuse and misuse of this precious resource have brought us to a global crisis of antimicrobial resistance (AMR). To address this crisis nearly seven decades after Fleming’s lecture the first UN general assembly meeting on drug resistance bacteria was convened in September 2017.

It is only the fourth time the general assembly has held a high-level meeting for a health issue. The UN secretary general, Ban Ki-moon, said antimicrobial resistance is a “fundamental threat” to global health and safety. He went on to say “If we fail to address this problem quickly and comprehensively, antimicrobial resistance will make providing high-quality universal healthcare coverage more difficult if not impossible. It will undermine sustainable food production and put the sustainable development goals in jeopardy.” Just before world leaders convened for the meeting, all 193 member states agreed in a declaration to combat the proliferation of antibiotic resistance.

The need for the solution to AMR requiring a “One Health” approach is well accepted. The importance of reducing overuse and misuse of antibiotics by promoting prudent use is one fundamental component of this solution - the concept of antimicrobial stewardship. In the human population, ensuring prudent prescribing across different communities and settings, in different patient populations, in diverse geographies, resources and cultures requires a truly innovative, flexible, collaborative and cross-disciplinary approach. As a global community only by innovating and adapting and adopting the resources we have available to us can we effect true transformational change in prescribing practice.

Those of you who wish to seek an overview of global stewardship may wish to access the plenary presentation on the subject at ESCMID in 2017:

The importance of education to support the development of knowledge and skill sets across the professions is a key objective of the WHO and national action plans for AMR. The development of relevant educational content and its cost-effective and sustainable delivery globally is also a major challenge. The need to combine traditional and modern methods to deliver this are increasingly relevant to ensure better awareness and penetration into health care systems and communities. This e-book offers a more blended or hybrid approach to stewardship education that builds on the success of the massive open on line stewardship course launched in 2015, reaching over 40,000 learners.

[VISIT MOOC SITE](#)

The ebook also compliments new on line learning resources from WHO

[VISIT WHO SITE](#)

which provides a more traditional approach to simple prudent prescribing competencies and how they can be applied to common clinical scenarios, and the CDC programme

[VISIT CDC PROGRAMME SITE](#)

and ESGAP.

[VISIT ESGAP SITE](#)

[VIEW SLIDE SET](#)



This educational resource is complimented by the availability of news items and literature in relation to stewardship from CIDRAP.

 VISIT CIDRAP WEBSITE

This book provides significantly expanded content and experience in relation to a broader stewardship context- for example, stewardship in specific populations, different countries as well as the role of different professions in stewardship to political and media engagement. We hope this book has something to offer everyone practicing in this area.

Therefore, The British Society for Antimicrobial Chemotherapy [BSAC] in collaboration with ESGAP are very pleased to present this e-book on Global Antimicrobial Stewardship that is relevant to health care professions working in preventing and managing infection across the healthcare communities and health care facilities. It aims to support health care professionals, or teams, or policy makers interested in learning about bringing the principles of stewardship to the bed side.

---

**DILIP NATHWANI OBE**

Editor in Chief

Physician and Educator

President of BSAC [2015-2018]





INTRODUCTORY VIDEO  
BY PROFESSOR DAME  
SALLY DAVIES

 WATCH VIDEO

This e-book does not aim to provide a comprehensive traditional textbook of stewardship nor a comprehensive state of the art review of the literature supporting stewardship. Instead, the focus is on application to clinical practice with illustrations of good practice articulated through case studies, stories, videos, podcasts, presentations, practical narratives and self -assessment exercises. We hope you find it informative, engaging and enjoyable. Above all we hope it supports your practice.

# SOLUTIONS

KEY ANTIMICROBIAL STEWARDSHIP SOLUTIONS WHICH  
WILL BE A RECURRING THEME IN THIS BOOK

-  Regulation and legislation
-  Accreditation
-  Surveillance - resistance and consumption
-  Stewardship
  - Structures + processes = outcomes [S+P=O]
  - Implementation [changing systems and organisations, understanding context, cultures and behaviours]
  - Evaluation using data for improvement and scrutiny [metrics]
  - Feedback, education and action
  - Reflect/review/renew
  - Sustainability and further change/innovation

# CHAPTER 1

 AUTHOR: **DILIP NATHWANI**

## OVERVIEW OF AMR

### THE AIM OF THIS INTRODUCTORY CHAPTER IS TO:

Define antimicrobial and antibiotic resistance in the human population.

Describe the core reasons for why it occurs.

Outline the global epidemiology of key antibiotic resistant bacteria, antimicrobial consumption in humans and current limitations of the data.

Outline the clinical and economic impact of drug resistant infections and impact of health care acquired infections.

### THE CHAPTER WILL ALSO DEFINE

Core strategies to combat AMR.

Antimicrobial stewardship and its goals in the context of the “real world” setting.

Introduce the concept through use of a fictional outbreak of a multi-drug resistant infection and the role of individuals and healthcare professional in meeting this challenge.

*Learning outcomes are statements of what a student is expected to know, understand and/or be able to demonstrate after completion of a process of learning*

## LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- define and explain the differences between antimicrobial and antibiotic resistance
- outline the drivers for resistance
- outline the global epidemiology of key antibiotic resistant pathogens and antibiotic consumption
- explain the clinical and economic impact of drug resistant infections and health care acquired infections
- list some definitions of antimicrobial stewardship and goals of stewardship programmes
- identify and communicate the core elements of infection control and stewardship practice in the context of a fictitious outbreak of a drug resistant health care acquired infection
- reflect of the relevance of these elements to their practice

## DEFINE ANTIMICROBIAL AND ANTIBIOTIC RESISTANCE IN THE HUMAN POPULATION

There are many different compounds that can inhibit the growth of microorganisms, and many terms that are used to categorize such compounds. ‘Antimicrobials’, ‘antibacterials’ and ‘antibiotics’ are commonly used terms that can sometimes be used interchangeably, but there are important differences between these words

Antimicrobial is derived from the Greek words anti (against), mikros (little) and bios (life) and refers to all agents that act against microbial organisms, i.e. bacteria, viruses, parasites and fungi.

Antibiotics is derived from the Greek word anti (against) and biotikos (concerning life). The word “antibiotic” refers to substances produced by microorganisms that act against another microorganism. Strictly speaking, antibiotics do not include agents that are produced by chemical or biochemical synthesis. However for simplicity, synthetic or semi-synthetic variants (such as quinolones) are usually included under the term antibiotics. In this book the term antibiotic is used for naturally produced and synthetic compounds that are active against bacteria, mainly those that have been approved for treatment of bacterial infections in humans and/or animals.

In contrast, the term “antimicrobials” include all agents that act against all types of microorganisms – bacteria (antibacterial), viruses (antiviral), fungi (antifungal) and parasites such as protozoa and helminths (antiparasitics)

## WHAT IS ANTIMICROBIAL RESISTANCE?

Antimicrobial resistance is resistance of a microorganism to an antimicrobial drug that was originally effective for treatment of infections caused by it.

Resistant microorganisms (including bacteria, fungi, viruses and parasites) are able to withstand attack by antimicrobial drugs, such as antibacterial drugs (e.g. antibiotics), antifungals, antivirals, and antimalarials, so that standard treatments become ineffective and infections persist, increasing the risk of spread to others.

## WHAT IS THE DIFFERENCE BETWEEN ANTIBIOTIC AND ANTIMICROBIAL RESISTANCE?

Antibiotic resistance refers specifically to the resistance to antibiotics that occurs in common bacteria that cause infections. Antimicrobial resistance is a broader term, encompassing resistance to drugs to treat infections caused by other microbes as well, such as parasites (e.g. malaria), viruses (e.g. HIV) and fungi (e.g. *Candida*).

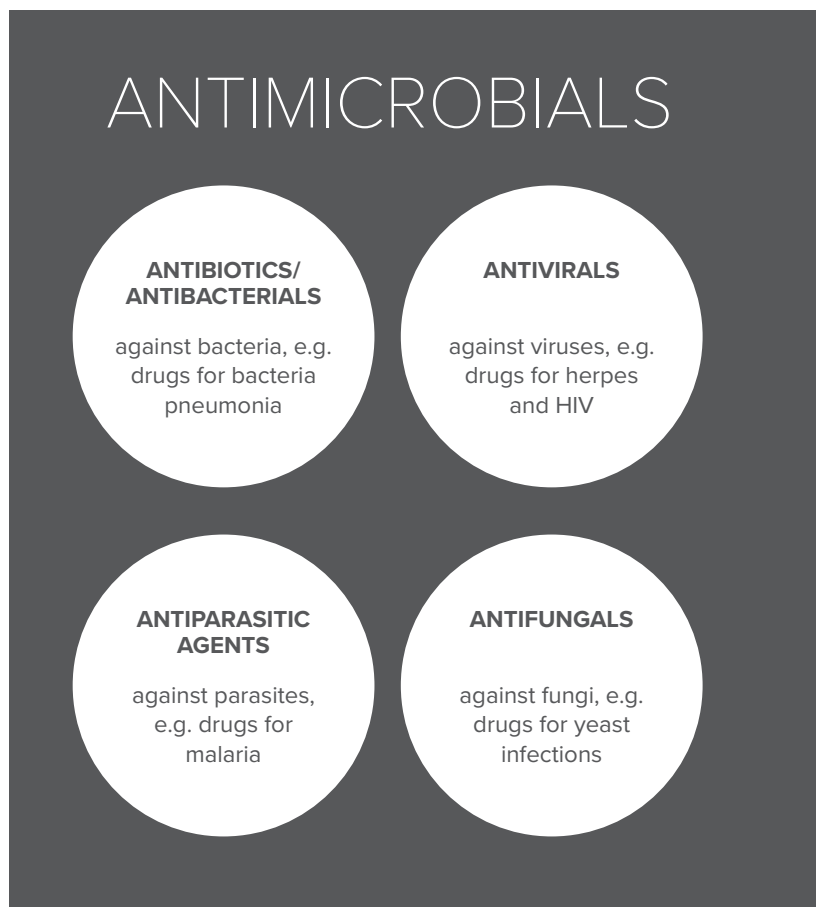


FIGURE 1  
Adapted from Source: <http://www.reactgroup.org/toolbox/category/understand/antibiotics/what-are-antibiotics/>


## ANTIBIOTIC RESISTANCE IS A NATURAL AND ACQUIRED PROBLEM

The evolution of resistant strains is a natural phenomenon that occurs when microorganisms replicate themselves erroneously or when resistant traits are exchanged between them. The pathways to synthesize antibiotics have been around for millions of years. For example, some microorganisms in the environment produce antibiotics naturally and they are used for communication and to compete with other organisms in their environment for space and resources. The organisms that produce natural antibiotics of course have to be able to protect themselves against the action of that antibiotic, and often carry resistance mechanisms.


Other organisms in the same environment will also evolve over time and resistant variants may be selected since they can survive nearby the antibiotic-producing organisms. Therefore, even before the introduction of antibiotics as medicines, antibiotic resistance mechanisms could be found

## TOOLKIT RESOURCE

A SUMMARY OF ANTIBIOTIC RESISTANCE DEFINITIONS, IMPACT AT AN INDIVIDUAL, POPULATION LEVEL IS SUMMARISED BELOW

 **Antimicrobial resistance and consumption factsheet for health professionals**

FOR ADDITIONAL INFORMATION ABOUT RESISTANCE AND USE OF ANTIBIOTICS IN ANIMALS AND AGRICULTURE AND THE ENVIRONMENT:

 **Review on Antimicrobial Resistance: Antimicrobial in agriculture and the environment: reducing unnecessary use and waste**

in environmental bacteria and as protective measures in antibiotic producing microbes.

Antibiotic resistance is not common in pathogenic bacteria. During the eight decades or so that humans have used antibiotics, antibiotic resistance has become prevalent in environmental and pathogenic bacteria alike. Massive use of antibiotics within the health care, veterinary and agricultural sectors has and continues to be prevalent creating a strong selection pressure for resistant bacteria. Selective pressure is any phenomena which alters the behaviour and fitness of living organisms within a given environment. It is the driving force of evolution and natural selection.

Human use of antibiotics has also resulted in an accumulation of these drugs in many environments, where antibiotic resistant bacteria can flourish. This has also resulted in selection and spread of bacteria that are resistant to several different antibiotics.

Adapted from: <http://www.reactgroup.org/toolbox/category/understand/how-did-we-end-up-here-understand/abr-is-a-natural-phenomenon/>

## HOW DO ANTIBIOTICS WORK?

Antibiotics function by disrupting essential processes or structures in the bacterial cell. This either kills the bacterium or slows down bacterial growth. Depending on these effects an antibiotic is said to be bactericidal or bacteriostatic. A bactericidal antibiotic kills the bacteria while the bacteriostatic antibiotics stops bacterial growth but does not kill the bacteria. The human immune system is then needed to clear the infection.

There are several different classes of antibiotics. These can have completely different bacterial targets or act on the same target but at a different site. In principal, there are three main antibiotic targets in bacteria [See toolkit resource] :

- The cell wall or membranes that surrounds the bacterial cell
- The machineries that synthesizes the nucleic acids DNA and RNA
- The machinery that synthesizes proteins (the ribosome and associated proteins)

These targets are absent or different in the cells of humans and other mammals, which means that the antibiotics usually do not harm our human cells but are specific for bacteria. Different antibiotics and how they work are illustrated in this video.

## ANTIBIOTICS MECHANISMS OF ACTION

 WATCH VIDEO

### ▶ WHERE DOES RESISTANCE OCCUR AND HOW DOES RESISTANCE HAPPEN?

The emergence of resistance occurs in our microbiota and is a unique phenomenon associated with antimicrobials.

The term gut microbiota refers to the aggregate of all microorganisms that colonise the gastrointestinal tract including bacteria, viruses, and eukaryotes. The collective genome of the gut microbiota, the microbiome, is estimated to contain more than 3-5 million different genes exceeding the genome of the human body approximately more than a hundred-fold. The human gut microbiota is a host-specific ecosystem, which is, to some extent inherited, critically matures in early childhood and affects central physiological and pathophysiological mechanisms in the host. It is well known that antibiotics even if taken appropriately can shift the gut microbiota to a state termed dysbiosis characterised by many things including loss of diversity, changes in metabolic capacity and reduced colonisation resistance against invading pathogens. Excessive and inappropriate use, for example use of broad spectrum agents, will have a greater impact on dysbiosis which will promote the horizontal transfer of resistance genes and fuels the evolution of drug-resistant pathogens and the spread of antibiotic resistance. Carriage of resistant bacteria in our microbiota can persist for many months, and the risk of prolonged carriage is increased by further antibiotic use.

Antibiotic resistance is how bacteria protect themselves against the effects of an antibiotic. Two common ways are by pumping the antibiotic out of the bacterial cell or by producing molecules that can destroy the antibiotic. Other methods are discussed in video below.

### ▶ WATCH VIDEO ON THE MECHANISMS OF ANTIMICROBIAL RESISTANCE

In the presence of the antibiotic, only non-susceptible i.e. resistant bacteria will survive or at least multiply faster than susceptible bacteria and increase in numbers.

Clinical resistance means that a bacterium can grow in the antibiotic concentrations reached in the body during treatment leading to likely treatment failure.

Bacteria have two alternative pathways to acquire all types of resistance:

- Random changes in the bacterial DNA (mutations) may provide resistance by chance

- Alternatively, they can receive resistance genes from other bacteria nearby.

This process is called horizontal gene transfer.

If a resistance mechanism [mechanisms of resistance outlined in the video below] gives an advantage to the bacterium it may be maintained, and will be passed on to coming generations as the bacterium divides, or be passed along by horizontal transfer by human contact, in food and water, sometimes by respiratory droplet, and across borders through travel and trade.

### ▶ WHAT ARE THE DRIVERS FOR RESISTANCE AND POTENTIAL APPROACHES TO TACKLE RESISTANCE?

At the beginning of the 21st century, antimicrobial resistance is common, has developed against every class of antimicrobial drug, and appears to be spreading into new clinical niches. The determinants that are likely to influence the future epidemiology and health impact of antimicrobial resistant infections are many and include:

the excessive use and misuse of antimicrobial drugs accelerates the emergence of drug-resistant strains, poor infection control practices, inadequate sanitary conditions and inappropriate food-handling, poverty, lack of or inadequate diagnostics tests, use and misuse of antibiotics in agriculture and the environment, travel and other factors encourage the emergence and further spread of antimicrobial resistance. Recognising and understanding these factors [See toolkit resource] will ultimately optimize preventive strategies for an unpredictable future. Some of these determinants have informed the schematic that highlights 10 key interventions needed to tackle AMR: [figure 2].

The video below provides a simple but engaging animated narrative of how resistance has come about, spread, the lack of new antibiotic development and how current and future antibiotics they may be preserved- the concept of stewardship.

### ▶ WATCH ANIMATED VIDEO

## TOOLKIT RESOURCE

### PDF ARTICLE



Antimicrobial Resistance determinants and future control  
Harbarth and Samore Emerging Infectious Diseases



# TACKLING ANTIMICROBIAL RESISTANCE ON TEN FRONTS



Review on Antimicrobial Resistance

FIGURE 2  
From <http://amr-review.org/file/437>

**WHAT ARE THE DRIVERS FOR THE USE AND MISUSE OF ANTIBIOTICS?**

Since this e-book is primarily concerned about the role of antibiotic use and misuse in AMR it is useful to briefly understand the antimicrobial prescribing determinants across the healthcare communities [e.g. ICU, hospitals, community etc.] and different geographical and resourced settings.

For example, in the ICU several factors drive excessive and misuse of antibiotics. These are outlined in figure 3.

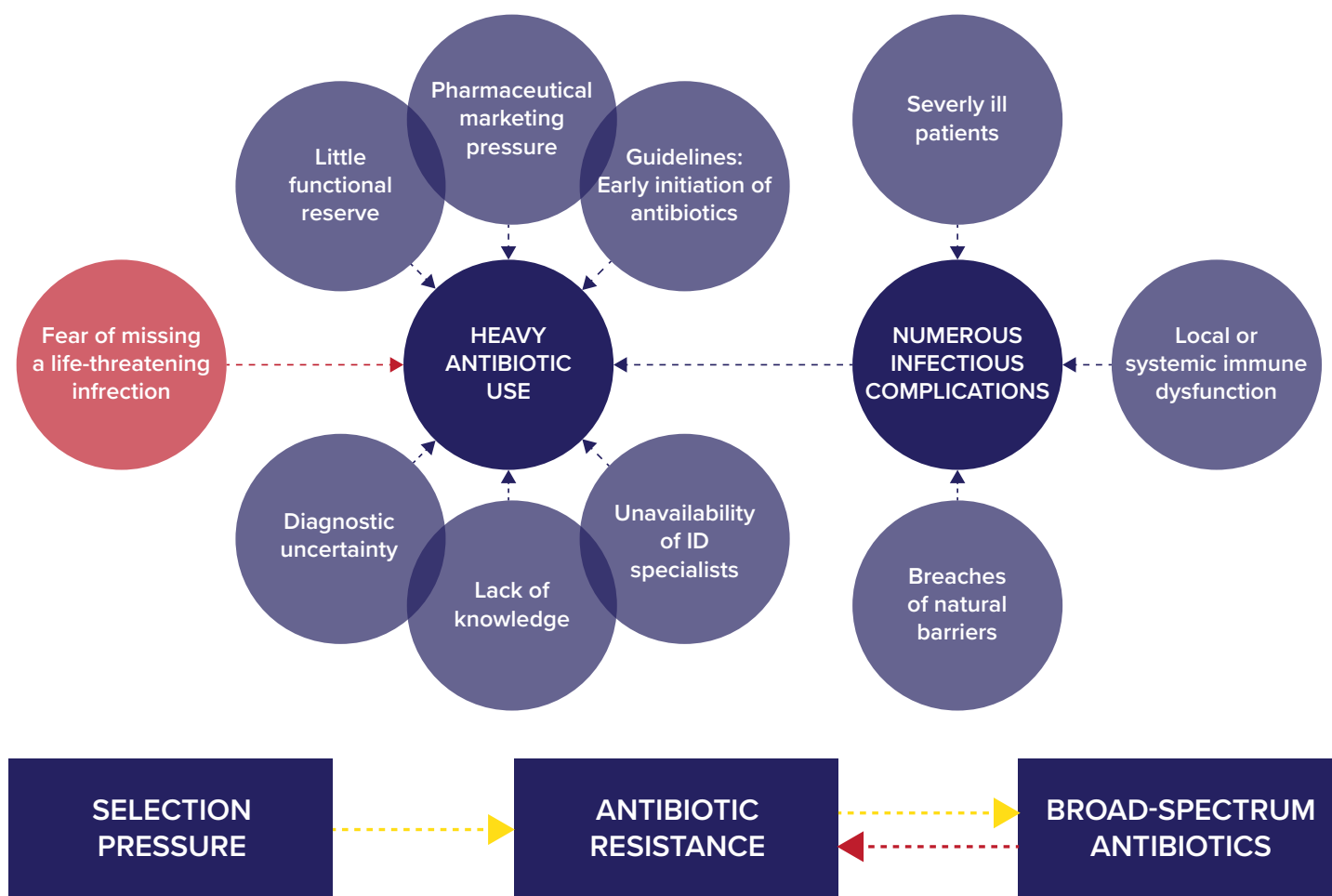


FIGURE 3

Intensive Care Med  
 DOI 10.1007/s00134-015-3978-8  
 Causes and consequences of heavy antibiotic use  
 in the intensive care unit. ID infectious diseases

The drivers for prescribing in the community and outpatient setting are outlined in a brief video by Professor Stephan Harbarth.

The determinants of prescribing in lower income countries, from a prescriber [See toolkit resource], dispenser and

community setting perspective are important as 80% of all human antibiotic prescribing occurs here. Understanding these drivers is critical to developing and effective implementation of stewardship interventions. These are summarized in figure 4.

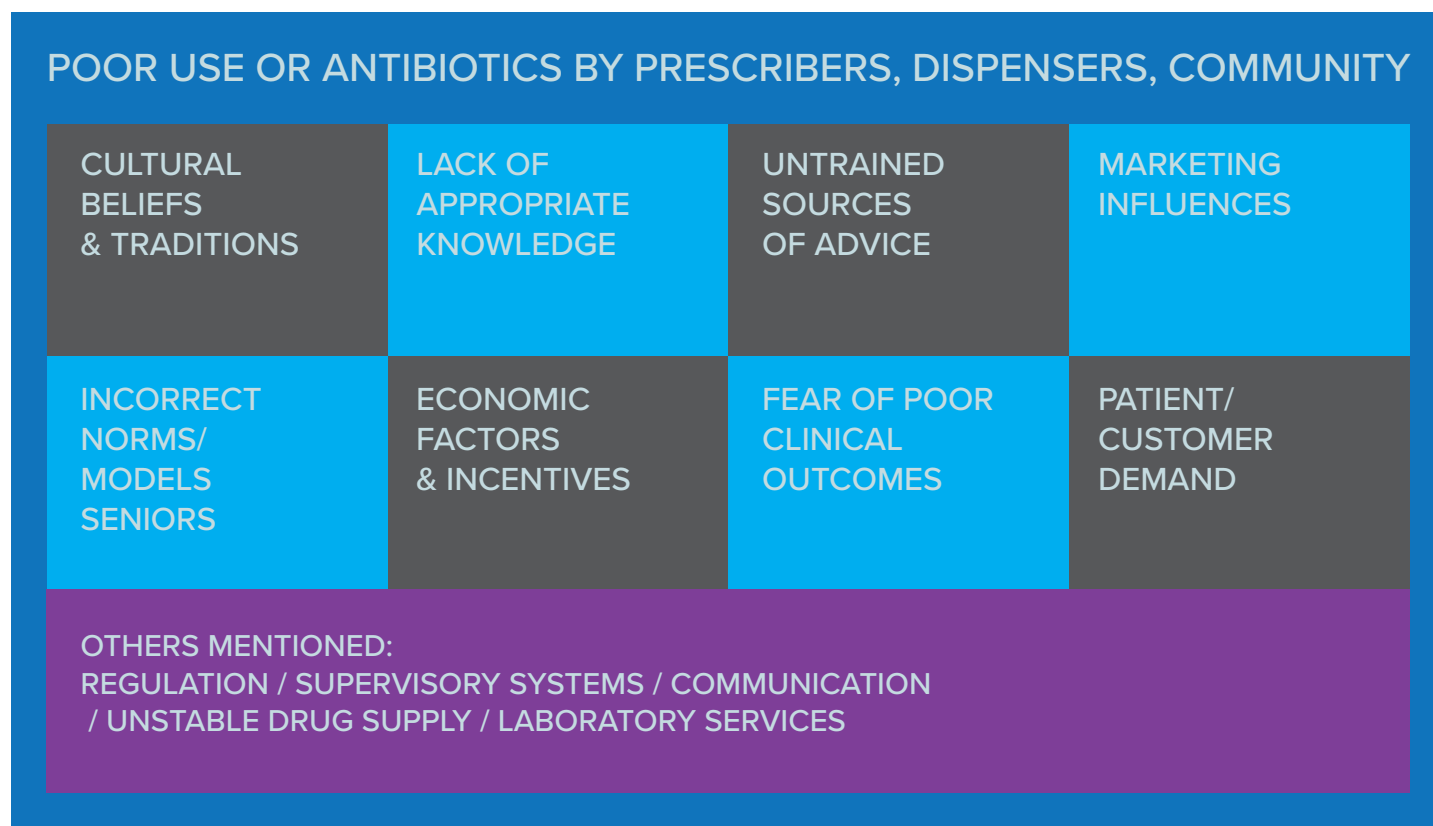


FIGURE 4

Adapted from Soc. Sci. Med 2003; 57:733-44

DRIVERS OF ANTIBIOTIC MISUSE AND ABUSE IN THE OUTPATIENT SETTING: VIDEO INTERVIEW WITH PROFESSOR STEPHAN HARBARTH



## TOOLKIT RESOURCE

PDF ARTICLE



the evidence to support the determinants of prescribing in low income countries

## THE GLOBAL EPIDEMIOLOGY OF ANTIBIOTIC RESISTANCE AND CONSUMPTION IN HUMANS

The global epidemiology of antibiotic consumption and resistance through surveillance is patchily delineated

Data from resource rich settings and hospitals is generally better compared to that in the community and resource limited settings. Investment in better surveillance in all settings has been identified as a priority for improving AMR. However, it is accepted that the overall global burden of AMR is greater in the community as opposed to the hospital setting.

The link between resistance and antimicrobial consumption has been well established [See toolkit resource #1].

A recent state of the world report [See toolkit resource #2] on antibiotic resistance and consumption provides a detailed and global review of the subject. However, good quality surveillance of both is critical and a significant limitation in many parts of the world as recognized in the WHO Global Action Plan [See toolkit resource #3].




Whereas such reports are very valuable in providing insight into resistance and prescribing the introduction of novel and interactive resistance map [See toolkit resource #4] that allows interactive exploration of antimicrobial resistance and consumption will facilitate the presentation of more detailed and up to date information that will support clinicians and policy makers to analyse resistance and consumption patterns. These and locally collected data should be the basis for informing clinical practice, guidance & policy. An example is illustrated below.

The current global position on the availability of data that is of good quality and consistent with other datasets is suboptimal and one of the key recommendations of the Conscience of Antimicrobial Resistance Accountability [CARA] declaration. CARA: The conscience of antimicrobial resistance accountability The Center For Disease Dynamics, Economics & Policy (2016);


 VISIT SITE

## TOOLKIT RESOURCE

### PDF ARTICLES

-  Systematic review and meta-analysis of the effects of antibiotic consumption on antibiotic resistance
-  State of the World's antibiotics 2015 report
-  WHO Global Action Plan

### SITE LINK

-  Resistance Map – Interactive map of resistance and consumption.

## WHAT ARE THE CLINICAL AND ECONOMIC IMPACT OF DRUG RESISTANT INFECTIONS AND IMPACT ON HEALTH CARE ACQUIRED INFECTIONS?

Drug resistance in the context of antibiotics is when the effectiveness of an antibiotic is reduced against a bacterium. A drug resistant infection is one that does not respond to the antibiotic treatment due to the presence of antibiotic resistance

Drug resistant infections were previously associated predominantly with hospitals and care settings, but over the last decade resistant infections have been seen in the wider community too, including long-term care facilities for elderly people. With resistance on the rise, we stand to lose the immense ground we have gained in the last century. This includes: 1) our fight against life threatening infectious diseases such as pneumonia, 2) our battle against conditions such as cancer, where antibiotics are crucial in helping chemotherapy patients avoid and fight infection; and 3) huge advances in surgical procedures like organ transplants and caesarean sections, which have now become routine and relatively low risk, thanks to our ability to effectively stave off or treat acute infections with antibiotics.

When looking at the impact of drug resistant infections a number of outcomes need to be considered . Such analysis is complex and to ensure robustness of quality the methodological considerations require particular attention. These are outlined in figure 5.

The impact on the individual patient, including those in the community, is salutary and influential in articulating the impact even non-life threatening infections to practitioners. This is illustrated by in figure 5 and the overall subject is reviewed in a presentation. See resource toolkit.

At an individual patient level there is emerging evidence of the impact of antibiotic resistance. For example, for simple uncomplicated urinary tract infection laboratory reported urinary resistant isolated has the following impact : Adapted from McNulty et al. *J. Antimicrob. Chemother.* (2006) 58 (5): 1000-1008

	PATIENTS WITH		P-VALUE
	RESISTANT UTI	SUSCEPTIBLE UTI	
Median time to symptom resolution	7 days	3 days	0.0002
Symptom resolution at 5 days	28%	68%	0.0002
Re-consultation in first week or less	17 / 39%	17 / 6%	<0.0001
Significant bacteriuria at one month	8 / 42%	23 / 20%	0.04

## TOOLKIT RESOURCE

SITE LINK



Celine Pulcini – BSAC workshop

### POINTS TO CONSIDER WHEN READING ANTIMICROBIAL RESISTANCE OUTCOME STUDIES

#### TYPE OF OUTCOME

Mortality	In-hospital only	Perspective of study	Hospital	Hospital morbidity, morality and cost	
	In-hospital and after discharge		Third-party payer	In and out-of-hospital health care costs	
	All-cause		Patient	Decreased functional status, loss of work and decreased availability of antibiotic therapy	
Attributable to infection	Length of stay Intensive care unit admission Need for surgery or other procedures Activity level at discharge Loss of functional time (missed work and activities)	Society	Comparison group	Total health care costs and loss of classes of antibiotics	
				Not infected	Interpret as impact of added infection
				Infected with susceptible strain	Interpret as impact of resistance
				Colonised with resistant strain	Interpret as the impact of progressing from colonisation to infection
Economic	Hospital cost Hospital charges Resource utilisation Health care costs	Factors that improve quality		Adjustment for variables, including length of stay, severity of illness and complications before infection	

FIGURE 5

Adapted from George M. Ellopoulos et al. *Clin Infect Dis.* 2003;36:1433-1437



**> WHAT IS THE ECONOMIC IMPACT OF AMR?**

A review of Global Risk by the world economic forum

**> ACCESS FORUM**

provides a global snapshot of the costs, impacts and burden of antibiotic-resistant bacteria across the globe. This illustrates the current burden. Future death and economic burden has been forecasted through modelling studies.

**> VIEW TACKLING DRUG-RESISTANT INFECTIONS DOCUMENT**

These powerful data underline the significant burden of these infections, often to the most vulnerable and least resourced populations of the world. For example, fig 6 provides a global snapshot of the mortality and economic impact on GDP of antibiotic-resistant bacteria across the globe.

The fact that 2-3.5% of the global GDP would fall in 2050 because of inaction is a sobering thought that should inform, global action through investment. The economic impact of specific and common drug resistant infections as opposed to susceptible infections has suggested increased costs outlined in Figure 7. The impact of these infections on mortality, length of stay and cost is outlined in Figure 8. These data, supported by local data, are helpful for justification of the value of clinical stewardship programmes and should inform business cases. See toolkit resource.

**TOOLKIT RESOURCE**

SITE LINK

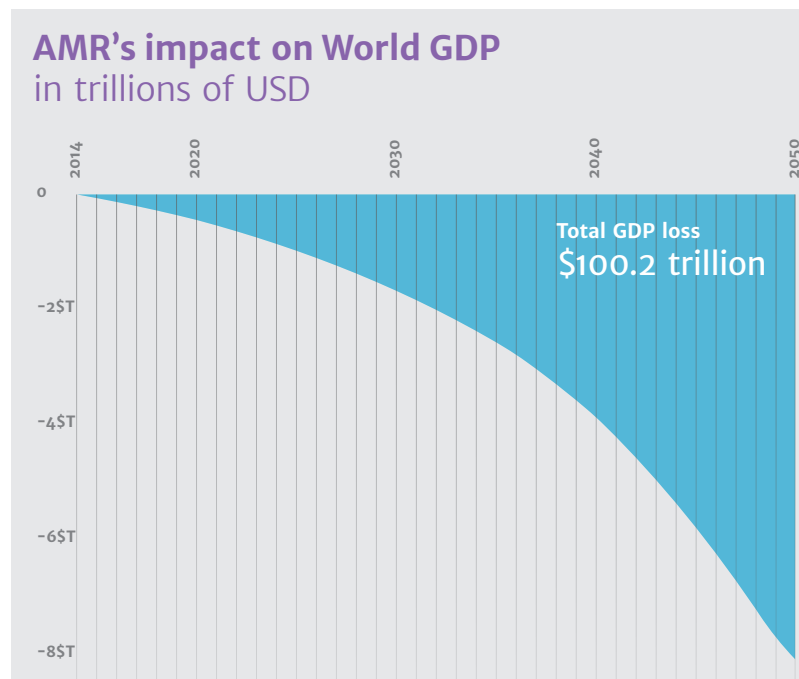
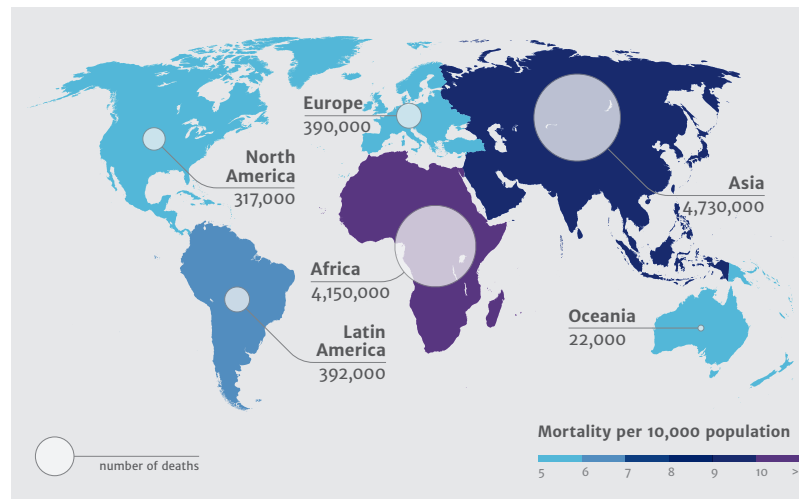


FIGURE 6  
From <http://amr-review.org/file/437>

**EXCESS COSTS ATTRIBUTABLE TO INFECTIONS WITH RESISTANT ORGANISMS VS. INFECTIONS WITH SUSCEPTIBLE ORGANISMS**

RESISTANT ORGANISM	CONTROL	RANGE OF EXCESS COST*
Methicillin-resistant <i>Staphylococcus aureus</i>	Methicillin-susceptible <i>S.aureus</i>	\$695-\$29 030 [21,22,24-36]
Vancomycin-resistant <i>Enterococcus</i>	Vancomycin-susceptible <i>Enterococcus</i>	\$16 711-\$60 988 [40-47]
Resistant <i>Pseudomonas aeruginosa</i>	Susceptible <i>P. aeruginosa</i>	\$627-\$45 256 [48-49]
Resistant <i>Acinetobacter baumannii</i>	Susceptible <i>A. baumannii</i>	\$5336-\$126 856 [23,50-52]
Multiple organisms	Susceptible	\$9372-\$18 990 [12,53,54]
ESBL-producing <i>Enterobacteriaceae</i>	Non-ESBL-producing <i>Enterobacteriaceae</i>	\$3658-\$4892 [56,57]

ESBL, extended-spectrum β-lactamase.

\* Includes both adjusted and unadjusted estimates; includes only studies reporting cost in US dollars.

FIGURE 7  
Adapted from CMI 2014; 20:973-979

**IMPACT OF ANTIMICROBIAL RESISTANCE ON STACKHOLDERS RELATED TO HEALTH**

PATIENT, HOSPITAL AND CLINICIAN ALL ADVERSELY AFFECTED

PATIENT PAYS MORE. HOSPITALS LOSES ON REVENUE FROM NEW PATIENT

PATIENT / PAYER PAYS MORE. HOSPITALS SPENDS MORE ON ANTIBIOTICS

**IMPACT OF ANTIBIOTIC RESISTANCE ON PATIENT MORTALITY, LENGTH OF HOSPITAL STAY**

INFECTION AND CAUSATIVE ORGANISM	INCREASED RISK OF DEATH (OR)	ATTRIBUTABLE LENGTH OF STAY (DAYS)
MRSA bacteremia	1.9	2.2
MRSA surgical infection	3.4	2.6
VRE infection	2.1	6.2
Resistant <i>Pseudomonas aeruginosa</i> infection	1.8 - 5.4	5.7 - 6.5
Resistant <i>Enterobacter</i> infection	5.0	9.0
Resistant <i>Acinetobacter</i> infection	2.4 - 6.2	5 - 13
ESBL-producing or KPC-producing <i>Escherichia coli</i> or <i>Klebsiella</i> infection	3.6	1.6-fold increase

ESBL, extended-spectrum β-lactamase; KPC, *Klebsiella pneumoniae* carbapenemase; MRSA, methicillin-resistant *Staphylococcus aureus*; OR, odds ratio; VRE, vancomycin-resistant enterococci.

FIGURE 8  
Clin Microbiol Infect 2014; 20: 973-979

## STEWARDSHIP AS A SOLUTION TO COMBAT AMR

The graphic below helpfully introduces stewardship as one of the six core strategies to combat AMR

An excellent overview of AMR outlining the drivers for AMR, impact and potential solutions is provided within this video. A state of the art review of the global solutions to AMR is also available. See toolkit resource.

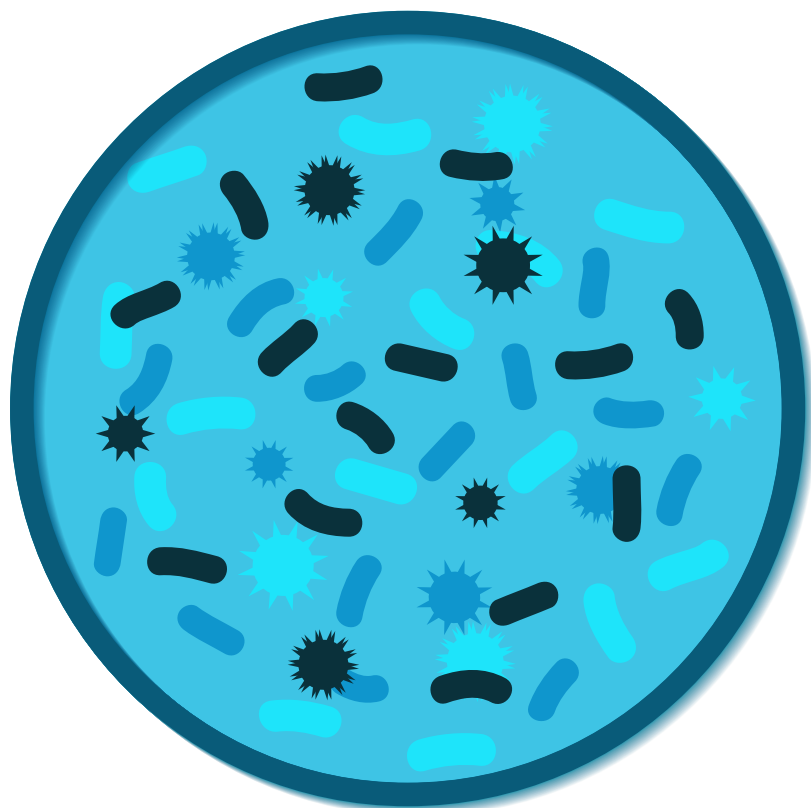
AN OVERVIEW OF AMR, ITS IMPACT AND POTENTIAL SOLUTIONS ARE OUTLINED IN THIS VIDEO

WATCH VIDEO

## TOOLKIT RESOURCE

PDF ARTICLE

State of the art review of global solutions for AMT



### REDUCE

the need for antibiotics through improved water, sanitation and immunization



### IMPROVE

hospital infection control and antibiotic stewardship



### CHANGE

incentives that encourage antibiotic overuse and misuse to incentives that encourage antibiotic stewardship



### REDUCE

and eventually phase out subtherapeutic antibiotic use in agriculture



### EDUCATE

health professionals, policy makers and the public on sustainable antibiotic use



### ENSURE

political commitment to meet the threat of antibiotic resistance

FIGURE 9

### WHAT IS ANTIMICROBIAL STEWARDSHIP AND WHAT ARE ITS GOALS?

The definitions of stewardship are discussed and the goals of stewardship are outlined in the schematic below. Understanding and measuring any unintended consequences of stewardship, especially harm, is also an important goal.

A number of definitions of antimicrobial stewardship exist. The following two definitions provide a means of articulating their meaning to patient care and infection practice and the other the focus is on the need for organizational and systems change. The need to articulate clear goals and their emphasis depending on the target audience is also important.

Antimicrobial stewardship has been defined as

*“the optimal selection, dosage, and duration of antimicrobial treatment that results in the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patient and minimal impact on subsequent resistance.”*

It also can be defined as an

*“organisational or healthcare system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness.”*

More details of both of these definitions, the UK and US guidelines and others are available in the toolkit resource PDF Articles #1, #2, #3. An easy pocket guide to these principles as well as implementation are also available. See toolkit resource PDF Article #4.

## TOOLKIT RESOURCE

### PDF ARTICLES



UK Guideline from NICE



US Guideline from the IDSA



Other country specific or generic guidance



Booklet on antimicrobial stewardship in the hospital setting

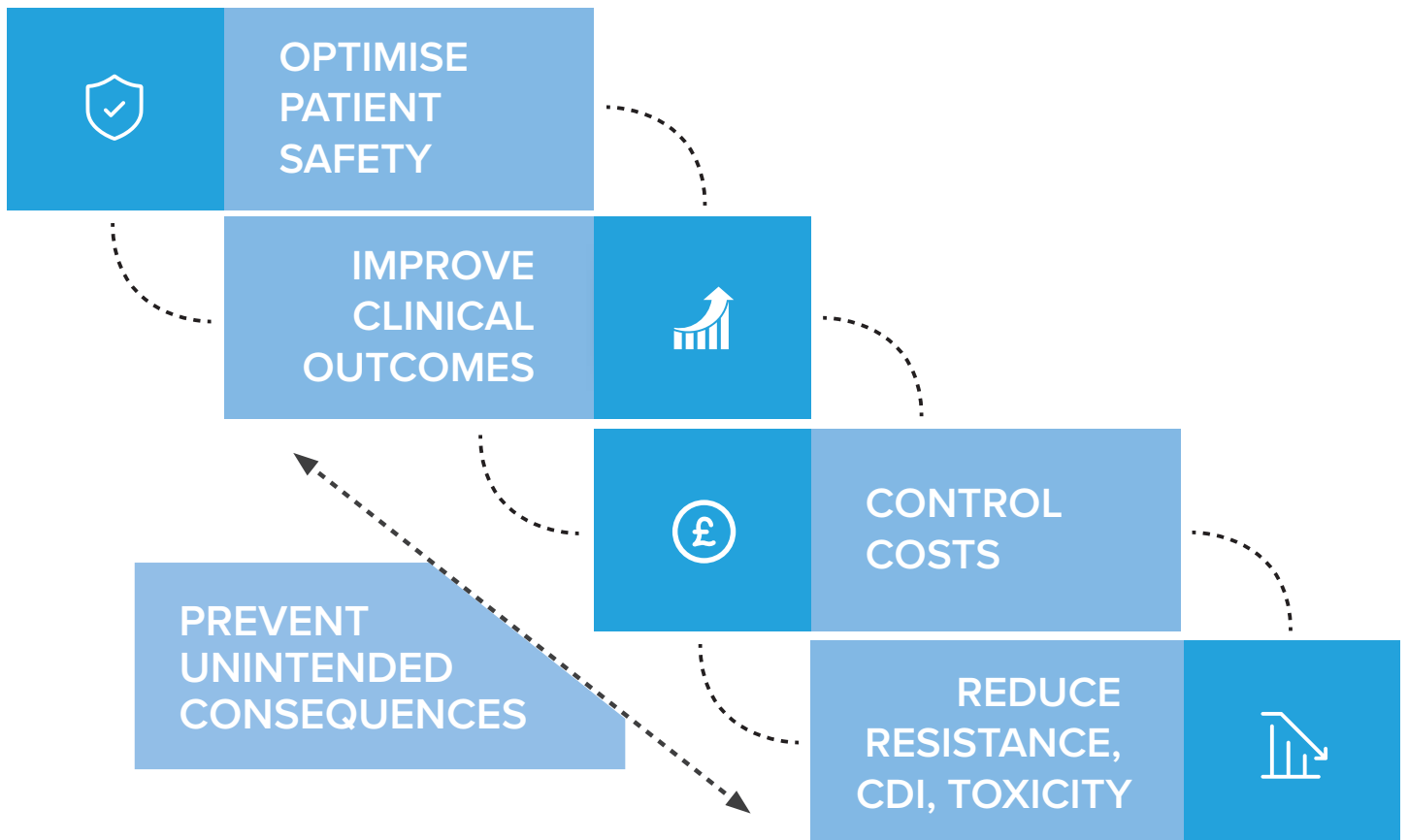


FIGURE 10

A more clinical definition that perhaps is practical and an engaging message for clinicians is:

**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**

FIGURE 11  
Adapted from <http://www.cdc.gov/getsmart/healthcare/inpatient-stewardship>



### HOW DOES THIS LOOK IN PRACTICE?

To illustrate an example of AMR, infection control and stewardship you may wish to watch the following 2 videos. They aim to encourage you to consider key drivers for AMR and identify good and suboptimal practice. This reflection will prepare you for the more detailed learning in the remainder of this book.

For your first activity you are asked to watch this video, which runs for 8 minutes and tells the story of two patients, Bill & Fred, and how they are affected by an infection with a resistant organism.

As you watch the video consider the following:

- What deficiencies in infection control and clinical practice are depicted in the video?
- What are the key drivers for resistance?
- What are the key prescribing issues worthy of investigation in this video?

Now watch part two of our scenario. The video runs for 10 minutes and shows the response to the outbreak by the hospital team.

\*Consider the strengths and weaknesses of the incident management team. Think particularly about how they tried to engage clinicians and their attempts at measuring compliance with good practice. The prescribing issues that may be worthy of investigation and the strengths and weaknesses of the response to the outbreak.

\*Were there any deficiencies in infection control and clinical practice, and drivers for resistance.

*[DISCLAIMER - All characters appearing in this work, both parts 1 & 2, are fictitious. Any resemblance to real persons, living or dead, is purely coincidental]*

BILL & FRED - HOW THEY ARE  
AFFECTED BY AN INFECTION  
WITH A RESISTANT ORGANISM

 WATCH VIDEO

RESPONSE TO THE OUTBREAK  
BY THE HOSPITAL TEAM

 WATCH VIDEO

# CHAPTER 2

 AUTHOR: MARGARET DUGUID

## ANTIBIOTIC USE AND MISUSE ACROSS THE RANGE OF HEALTHCARE COMMUNITIES AND THE DRIVERS/ DETERMINANTS OF MISUSE

### THE AIM OF THIS CHAPTER IS TO:

To consider antibiotic consumption and prevalence of use-in primary and secondary care

- Global consumption of antibiotics
- Antibiotic use in the community setting
  - Prevalence of use
  - Prescribers
  - Antibiotic consumption
  - Common indications for use in the community
  - Patterns of use
- Antibiotic use in the hospital setting
  - Prevalence of use
  - Hospital consumption
  - Trends in hospital antibiotic use
  - Variation in use
  - Indications for use
  - Intensive care units
- Long-term care

The misuse of antibiotics

- What misuse includes
- Inappropriate use in community
- Inappropriate use in hospital
- Inappropriate use in intensive care units
- Non-prescription use of antibiotics

Determinants of antibiotic prescribing and misuse

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Explain changes in the use of antibiotics globally and the drivers of the changes
- Describe the prevalence and volume of antibiotic use in community, hospitals and long-term care aged care settings
- List the most common antibiotic agents prescribed in community and hospital settings
- Describe trends in antibiotic use in hospital settings
- Define misuse of antibiotics
- List common indications where antibiotics are inappropriately prescribed/used.
- List the key drivers/determinants of antibiotic use
- Reflect on the relevance of these elements to their practice

### ANTIBIOTIC CONSUMPTION AND PREVALENCE OF USE IN PRIMARY AND SECONDARY CARE

Measuring and monitoring antibiotic use is an important component of efforts to control the emergence of antimicrobial resistance (AMR) and can be used to:

- identify areas where rates of consumption per person is high and the potential for development of resistance greatest;
- inform initiatives to preserve the efficacy of antibiotics; and
- provide a baseline from which to assess effectiveness of

efforts to reduce antibiotic consumption.

Many countries:

- have systems to measure national antibiotic use at both community and hospital levels and several countries produce annual reports of AMR and antimicrobial (mainly antibiotic) use
- contribute to multi-country antimicrobial use data collections/networks e.g.:

- o European Surveillance of antimicrobial Consumption Network  
<https://ecdc.europa.eu/en/publications-data/antimicrobial-consumption-database-esac-net>




and

- o the Organisation for Economic Co-operation and Development (OECD)  
<http://www.oecd.org/els/health-systems/antimicrobial-resistance.htm>


Most systems report combined paediatric and adult data. See chapter 22 for specific information on paediatric data.

## TOOLKIT RESOURCE


### SITE LINK

-  Antibiotic consumption levels in OECD countries.
-  Center for Disease Dynamics, Economics & Policy. The state of the world's antibiotics.2015.
-  Interactive Map on antibiotic consumption at a country and global level. Center for Disease Dynamics, Economics and Policy.

### PDF ARTICLE

-  European Centre for Disease Prevention and Control. ESAC-Net Surveillance data 2016

### ARTICLE

-  Country reports on antimicrobial use resistance surveillance

## GLOBAL CONSUMPTION OF ANTIBIOTICS

The systems mentioned provide useful data on the volume (rate of consumption) of antibiotic use. They show that antibiotic use has been increasing globally - over the period 2000-2010 overall use is estimated to have increased by 35%. This increase has been greater in low and middle-income countries. India, China and the US used the most antibiotics over all. Five countries (Brazil, Russia, India, China and South Africa) accounted for 76% of the increase in global consumption. This increase has been driven by factors such as economic growth and increased access to antibiotics. High income countries use more antibiotics on a per capita basis.

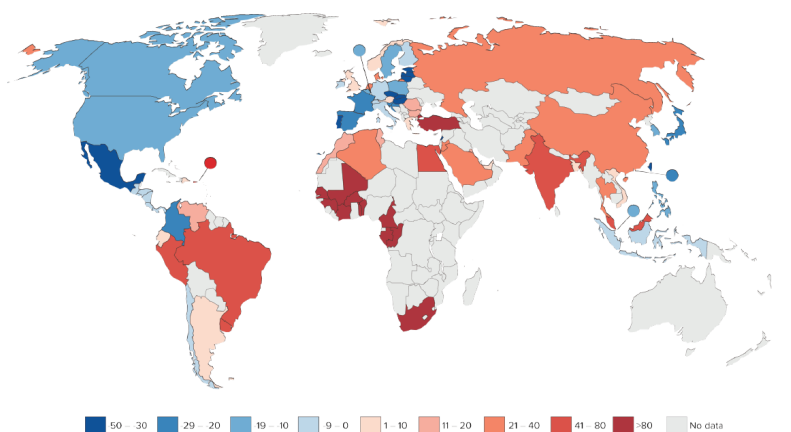
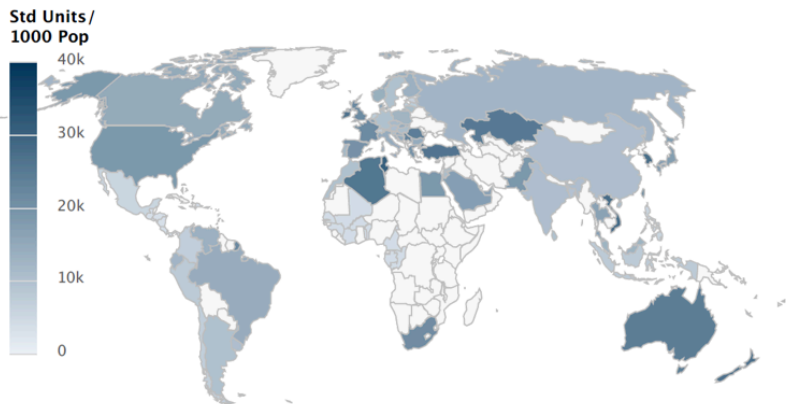


FIGURE 1  
Percentage change in antibiotic consumption per capita 2000-2010

Penicillins and cephalosporins account for around 60% of total global antibiotic consumption. Between 2000-2010 their usage increased by around 40% as did carbapenems, a reserve group of antibiotics. This increase in carbapenem use along with a 13% increase in the last resort agents polymyxins (e.g. colistin) and a doubling of glycopeptide (e.g. vancomycin) use is attributed to the rising rates of antibiotic resistance and development of multi drug resistant organisms.

### Use of All Antibiotics in 2015

Source: IMS Health



Center for Disease Dynamics, Economics & Policy (cddep.org)

FIGURE 2  
Centre for Disease Dynamics, Economics & Policy Interactive Resistance Map. <https://resistancemap.cddep.org/>

If you would like to know more watch this PPT presentation “Global Antibiotic Consumption” by Margaret Duguid,

 **DOWNLOAD SLIDE SET**

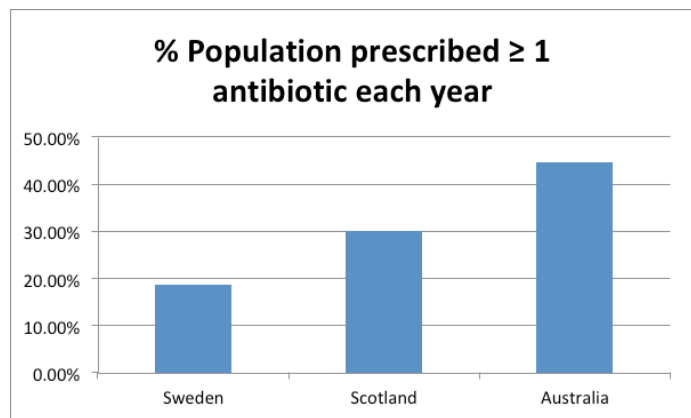


FIGURE 3  
SWEDRES/SVARM 2016 Consumption of antibiotics and occurrence of antibiotic resistance in Sweden, Scottish antimicrobial resistance and use in humans 2015, AURA 2017 - Second Australian report on antimicrobial use and resistance in human health

## ANTIBIOTIC USE IN THE COMMUNITY SETTING

The majority of antibiotic use, around 80%, occurs in the community, prescribed in settings such as outpatient clinics, health posts and general practice.

### Prevalence of use

Prevalence of antibiotic use in the community varies between countries from less than 20% to over 40% of the population dispensed at least one antibiotic each year.

### Prescribers

In Europe, Australia and Canada general practitioners prescribe the majority of antibiotics in the community, dentists account for 3 -10% and nurses and other health professionals < 6%. In the US general practitioners prescribe the most outpatient prescriptions (22%in 2014) closely followed by physician assistants and nurse practitioners (20%), then a range of medical specialists. Dentists are 5th highest prescribers at 9%.

Outside Northern Europe, US and Australasia 19% to 100% of antibiotics are supplied without prescription.

### Antibiotic consumption

Standardised units of measure are used to compare antibiotic use.

Common units of measure of antimicrobial consumption	
Units	Limitations
The most common unit is the World Health Organisation’s (WHO) defined daily dose (DDD). Defined as the assumed average maintenance dose per day for a drug used for its main indication in adults. DDDs allow standardised comparisons between drugs and can be used in community and hospital settings	DDD’s are not suitable for determining antimicrobial use in children.  Doses used for some agents (e.g. penicillins) may vary between countries and may differ from WHO defined DDD’s.
Community measures DDD per 1000 inhabitants Prescriptions or packs dispensed per 1000 inhabitants.	Packs per 1000 inhabitants does not take into account dosage information

<p>Hospitals measures</p> <p>DDD per 100 or 1000 bed days</p> <p>DDD per 1000 admissions (or discharges)</p>	<p>DDD per1000 patient days do not take into account the case mix or infection rates in hospitals.</p> <p>DDD per admission (or discharge) is useful where length of stay is short</p> <p>DDDs per bed-days is more useful in units where lengths of stay are longer</p>
--	--

## ASP METRICS EXAMPLES

- Amongst the OECD countries the average consumption of antibiotics in 2014 was around 20.5 DDDs per 1000 inhabitants.
- There is significant variation in consumption rates across countries– up to a 4.4 fold difference.

[VIEW FIGURE](#)

Human antimicrobial consumption in OECD countries 2005 and 2014

Within countries there are significant regional differences in prescribing rates for antibiotics with some regions prescribing over 2 times that of other regions. These differences cannot be explained by disease incidence alone.

Use in the community is highest in the very young (0-9 years) and the elderly (65+ years).

### Common indications for use in the community

In developed countries, the majority of the use of antibiotics in the community is for respiratory infections (accounting for 90% of antibiotic sales in Swedish children), urinary tract infections and soft tissue infections.

### Seasonal use

Use peaks in winter months, coinciding with season for colds and influenza, indicating use in upper respiratory tract infections where infections are mainly viral and antibiotics are not indicated.

### Patterns of use

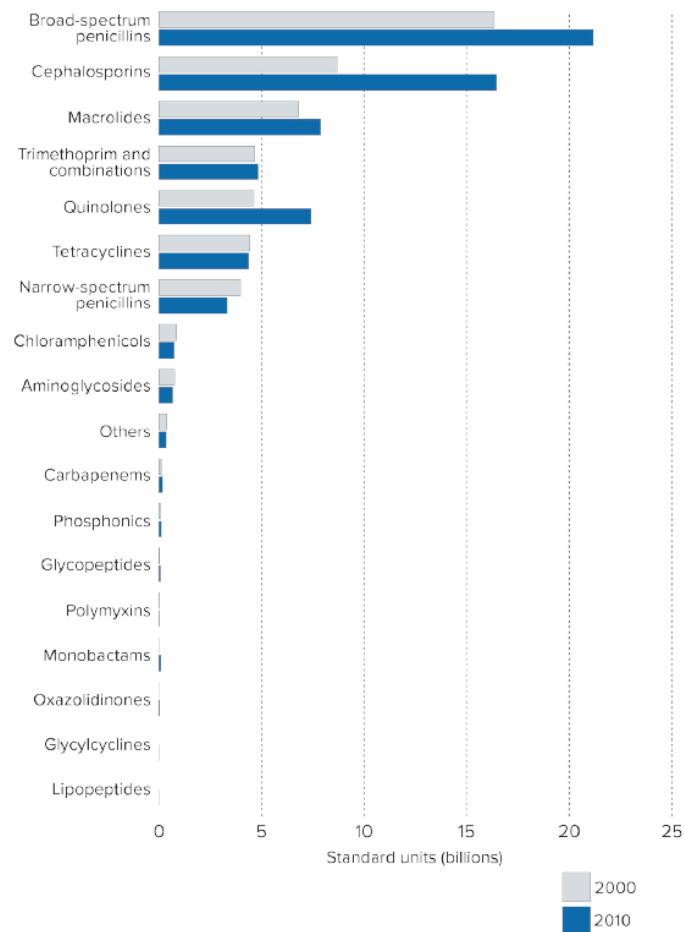


FIGURE 4 Center for Disease Dynamics, Economics & Policy. The state of the world’s antibiotics.2015

Whilst penicillins are the most frequently used antibiotics with 30 to 60% of use, the pattern of use of other antibiotic groups varies considerably between countries. For example, cephalosporins and other beta lactams (including carbapenems) account for 0.2% of total community antibiotic use in Denmark compared to 22% in Germany, and quinolones, 2% of total community antibiotic use in UK compared to 16% in Hungary.

If you would like to know more watch this PPT presentation “Antibiotic Consumption in the Community” by Margaret Duguid,

DOWNLOAD SLIDE SET




## TOOLKIT RESOURCE


### SITE LINK

 Center for Disease Dynamics, Economics & Policy. The state of the world's antibiotics.2015.

 Australian Commission on Safety and Quality in Health Care. AURA: Antimicrobial Use and Resistance in Australia

 Center for Diseases Control. Report on Antibiotic Use in the United States, 2017: Progress and Opportunities

### PDF ARTICLE

 European Centre for Disease Prevention and Control. ESAC-Net Surveillance data 2016

## ▶ ANTIBIOTIC USE IN THE HOSPITAL SETTING

There are substantial variations in use between countries in terms of volume of antibiotics used and the patterns of use.

In 2015 the consumption of systemic antibiotics in European acute hospitals ranged from 1.0 DDD per 1000 inhabitants per day in the Netherlands to 2.9 DDD per 1000 inhabitants per day in Malta.

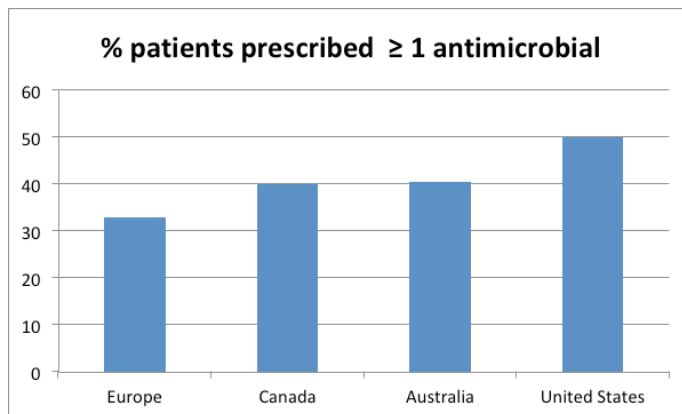
### Prevalence of use

On any one day in hospital 22% to 55% of patients in European hospitals and 50% in US hospitals received one or more antibiotics.

In the US patients 50% of these patients received 2 or more antibiotics compared with 30% in Europe.

VIDEO INTERVIEW WITH DR SHELLEY MAGILL. ALMOST HALF OF PATIENTS RECEIVE AT LEAST ONE ANTIBIOTIC WHILST HOSPITALISED

 WATCH VIDEO



Europe – Mean 33%, Range 22 – 55%

### FIGURE 5

Source: ECDC. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals 2011-2012

Taylor et al Can J Infect Dis Med Microbiol. 2015 Mar-Apr; 26(2): 85–89.

Magill et al JAMA 2014 vol. 312, no. 14, pp. 1438-1446

Antimicrobial prescribing practice in Australian hospitals. Results of 2015 National Prescribing Survey

### Hospital consumption

The data in this section is drawn from surveillance data and point prevalence studies conducted in European, US and Australian hospitals.

### Trends in hospital antibiotic use

- Most high-income countries have not reported a significant change in overall inpatient antibiotic consumption in the last decade.
- Penicillins are the most frequently prescribed antibiotic subgroup in many countries followed by other  $\beta$  lactams (cephalosporins, monobactams, carbapenems) and quinolones.
- There is the shift towards a greater use of broad spectrum agents in many countries with increases in 3rd and 4th generation cephalosporins, beta lactam/beta-lactam inhibitor combinations and carbapenem use.
- Penicillin –  $\beta$  lactam inhibitor combination products and extended spectrum penicillins accounted for 82% of penicillin use in European hospitals in 2015.
- Percentage patients receiving carbapenems varies from <1% to >5% between countries

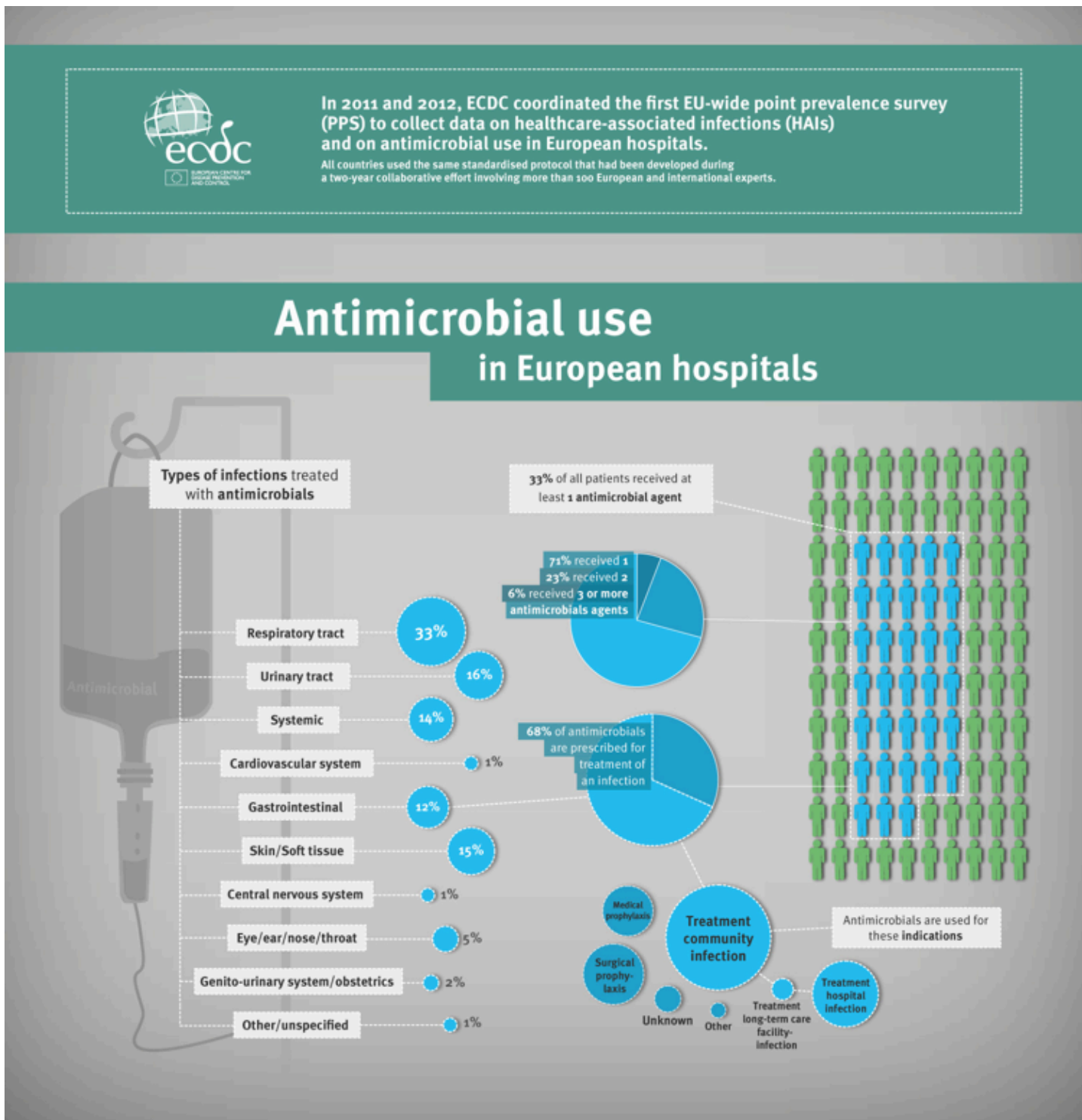


FIGURE 6  
 ECDC <https://ecdc.europa.eu/en/publications-data/antimicrobial-use-european-hospitals>

## PODCAST: DR ARJUN SRINIVASAN ON NATIONAL TRENDS IN INPATIENT ANTIBIOTIC USE AMONG US HOSPITALS.



### Variation in use

This is significant for some agents. For example:

- Percent of cephalosporins and other beta-lactams (including carbapenems) prescribed ranges from 7% in UK to 54% in Bulgaria and in some countries have over taken penicillins as the most frequently prescribed antibiotic class. See FigureX
- Quinolone use ranges from 4% in UK and Australia to 19% in Malta.

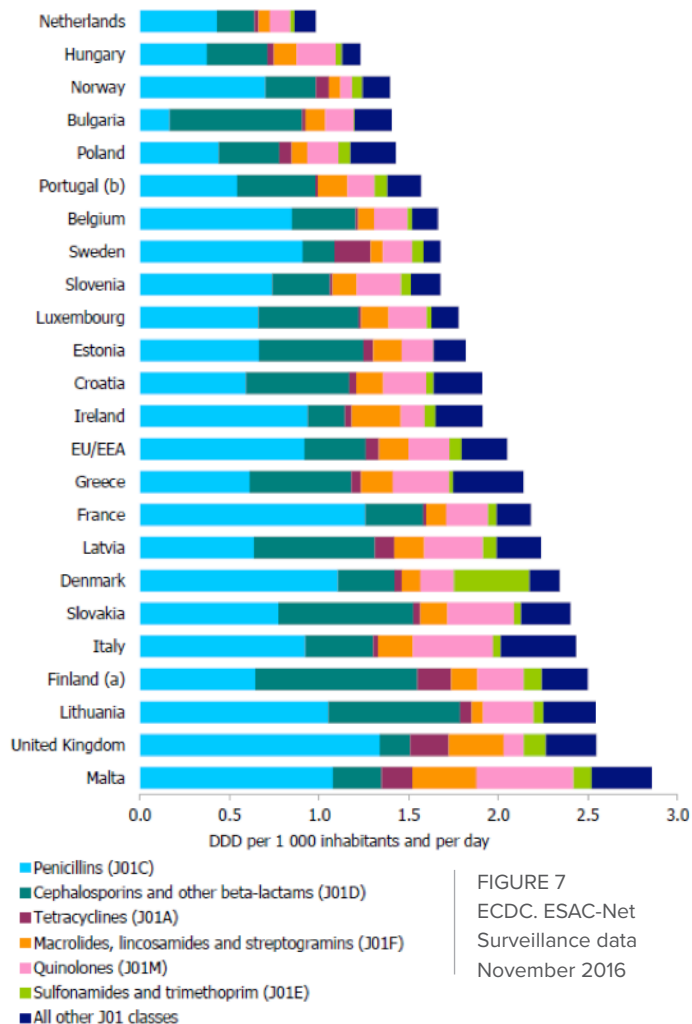


FIGURE 7  
ECDC. ESAC-Net  
Surveillance data  
November 2016

### Indications for use

- Most antibiotics are prescribed for treatment of infections (68% in European and 78% in US hospitals), surgical prophylaxis accounts for around 12% - 19% of inpatient prescriptions and medical prophylaxis around 8% to 11%.

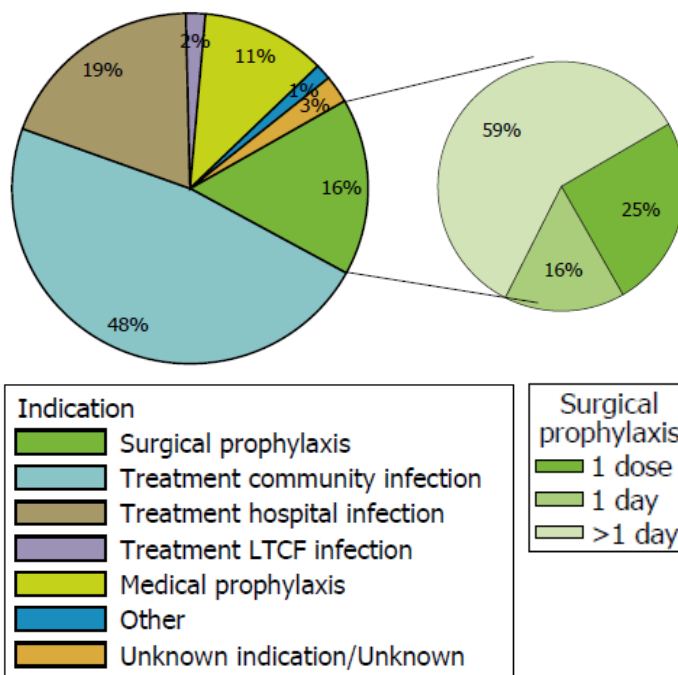


FIGURE 8  
Indications for antimicrobial use in European acute care hospitals  
Source: ECDC PPS 2011-2012  
LTCF = long term care facility

- Lower respiratory tract infections are the most common treatment indications followed by urinary tract infections and skin and soft tissue in higher income countries.
- In lower income countries infections such as lower respiratory tract infections, malaria and gastrointestinal tract infections are more prevalent.

### Intensive care units

Use of antibiotics is higher in ICUs compared with general wards as the prevalence of infection in ICUs is higher.

57% of ICU patients in US and European hospitals were prescribed at least one antimicrobial during their ICU stay.

**ALL OF HOSPITAL****916 DDD/1000  
BED DAYS****SOURCE**

Antimicrobial use in Australian Hospitals. 2015 Report. <https://www.safetyandquality.gov.au/antimicrobial-use-and-resistance-in-australia/>

NB These figures are for adult patients

The increasing presence of multidrug-resistant and extensively drug resistant organisms in ICU units is driving the use of glycopeptides and broad spectrum agents such as piperacillin and tazobactam, 3rd and 4th generation cephalosporins, cabapenems and agents of last resort such as colistin.

The main drivers for antibiotic use in ICU units have been described by Albrich and Harbath. (see chapter 1)

If you would like to know more watch this PPT presentation “Antibiotic Consumption in Hospitals” by Margaret Duguid,

**DOWNLOAD SLIDE SET****LONG TERM CARE**

The prevalence of use of antibiotics in long term facilities such as aged care homes is very high and as much as 75% of use estimated to be inappropriate.

**ICU****1479 DDD/1000  
BED DAYS****TOOLKIT RESOURCE****SITE LINK**

ECDC. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals 2011-2012



Australian Commission on Safety and Quality in Health Care. AURA: Antimicrobial Use and Resistance in Australia



Center for Diseases Control. Report on Antibiotic Use in the United States, 2017: Progress and Opportunities

**PDF ARTICLE**

European Centre for Disease Prevention and Control. ESAC-Net Surveillance data 2016

**ARTICLES**

Baggs J, Fridkin SK, Pollack LA, Srinivasan A, Jernigan JA 2016, ‘Estimating National Trends in Inpatient Antibiotic Use among US Hospitals from 2006 to 2012’, JAMA Intern Med, vol 176, no.11, pp1639-1648

Magill SS, Edwards JR, Beldavs ZG, Dumyati G, Janelle SJ et al 2014 ‘Prevalence of antimicrobial use in US acute care hospitals May to September 2011’. JAMA, vo

**AGED CARE (NURSING) HOMES****PREVALENCE OF ANTIMICROBIAL USE**

Use is generally higher than in the community

- 50 – 80% of aged care residents receive at least one course of systemic antibiotics each year
- antibiotics are prescribed for around 75–90% of all infectious episodes
- antibiotics account for almost 40% systemic drugs prescribed
- More than 1 in 10 residents receive an antimicrobial at any one time

**COMMON INDICATIONS FOR USE**

- urinary tract infections
- skin and soft tissue infections; and

- respiratory tract infections

**VARIATION IN USE**

- Consumption rates vary between countries
- 5.9 DDD/1000 residents per day in Germany to 135.7/1000 residents per day in Northern Ireland
- Patterns of use vary across different countries and are influenced by national and regional guidelines
- Use of parenteral administration ranges from <1% to 7-9%

**APPROPRIATENESS OF USE**

- 40 – 75% or antibiotic use is claimed to be inappropriate
- 30% prescriptions prescribed for > 6 months

## TOOLKIT RESOURCE

### SITE LINK



Australian Commission on Safety and Quality in Health Care. AURA: Antimicrobial Use and Resistance in Australia



Center for Diseases Control. Report on Antibiotic Use in the United States, 2017: Progress and Opportunities

### PDF ARTICLE



ECDC Point Prevalence Study of Healthcare Associated Infection and Antimicrobial Use in European Long-term Care Facilities 2013

### ARTICLES

van Buul LW, van der Steen JT, Veenhuizen RB, Achterberg WP, Schellevis FG, Essink RT, et al. 2012. "Antibiotic use and resistance in long term care facilities". *J Am Med Dir Assoc*, vol.13, no. 6, pp. 568.e1-13.

Lim CJ, Kong DCM, Stuart RL. 2014;" Reducing inappropriate antibiotic prescribing in the residential care setting: current perspectives". *Clin Interv Aging*, vol. 9, pp 1-13

- iv route when oral can be used
- dose is too high or too low compared to what is indicated for that patient
- duration is too long or too short
- duration is > 24 hours for surgical prophylaxis, (except where guidelines endorse longer duration)
- treatment is not streamlined or changed when microbiological culture data become available
- prescription of agent for patients with a known allergy to the agent,
- drug-drug interaction
- poor patient adherence to the prescribed treatment.

If you would like to find out more watch this PPT by Margaret Duguid Insert power point presentation Misuse of antibiotics



DOWNLOAD SLIDE SET

### Inappropriate use in community

Much of the inappropriate prescribing of antibiotics in the community is for infections not caused by bacteria such as colds and influenza and other viral infections, and, in low income countries, for diarrhoea, malaria.

- over 50% of antibiotics may be prescribed unnecessarily in the community for upper respiratory tract infections
- as many as 30% of residents in aged care facilities are prescribed antibiotics when not indicated for asymptomatic urinary tract infections.

Few countries assess appropriateness of antibiotic use at a national level and consumption data is often used to indicate overuse or inappropriate use. For example, in the community or outpatient setting:

- A high seasonal variation of total or specific antibiotic consumption indicates an unnecessary use of antibiotics for treatment of viral upper respiratory tract infections.
- variation in consumption and patterns of use across practices, regional areas or countries can suggest overuse, inappropriate use or use not concordant with guidelines.



## MISUSE OF ANTIBIOTICS


Misuse includes:

- underuse- this is quite frequent in LMIC due to a lack of access to healthcare services
- unnecessary use – where an antimicrobial is not indicated and there is no health benefit for the patient (e.g. treatment of an upper respiratory infection caused by a virus or an antibiotic is not recommended)
- inappropriate (or suboptimal) use – where timing, antimicrobial choice, dose, route, frequency of administration or duration of treatment is incorrect. For example:
  - delayed administration in a critically ill patient,
  - choice of an antibiotic with an unnecessarily broad spectrum or too narrow a spectrum
  - drug-bug mismatch

## TOOLKIT RESOURCE

### SITE LINK

 Australian Commission on Safety and Quality in Health Care. AURA: Antimicrobial Use and Resistance in Australia

 Center for Diseases Control. Report on Antibiotic Use in the United States, 2017: Progress and Opportunities

 Dr Katherine Fleming-Dutra, Improving antibiotic prescribing in outpatient setting podcast

### PDF ARTICLE

 Organisation for Economic Co-operation and Development. Antimicrobial resistance.2016 'Policy Insights'

### ARTICLE

Fleming-Dutra KE, Hersh AL, Shapiro DJ, Bartocoes M, Enns EA et al 2016, 'Prevalence of inappropriate antibiotic prescriptions among US ambulatory Care Visits, 2010-2011', JAMA, Vol. 315, no. 17, pp1864-1873

### Inappropriate use in hospital

**25% - 50% INPATIENT USE IS UNNECESSARY OR INAPPROPRIATE**

Non-adherence to guidelines is similarly high.

Common reasons for inappropriate prescribing include: antibiotic not indicated; spectrum too broad (including continuation of initial therapy with broad spectrum agents after results of susceptibility tests are known), incorrect duration, and incorrect dose and frequency.

Doctors in some hospitals prescribed 3 times as many antibiotics as doctors in other [hospitals](#).

Indications where antibiotics are commonly prescribed inappropriately or guidelines not followed:

- surgical prophylaxis
- respiratory infections (community acquired pneumonia,

bronchitis, COPD infective exacerbations) urinary tract infections

- skin and soft tissue infections.

Surgical prophylaxis regimens are commonly prescribed inappropriately:

- Choice, dose, timing or duration of therapy is suboptimal
- \* Rates of patients receiving prophylaxis for > 24 hours range from 10% to 90%. Best practice is < 5%
- In low income countries antibiotics are often prescribed after surgical procedures, using 7 times more antibiotics.

### Inappropriate use in ICU


**30 - 60% ANTIBIOTIC PRESCRIBING IN ICU UNNECESSARY OR INAPPROPRIATE**

Suboptimal prescribing in ICU includes: poor choice of antibiotic (including inadequate first line empirical therapy), use of redundant combinations of agents, failure to de-escalate therapy and excessive duration of therapy.


## TOOLKIT RESOURCE

### SITE LINK

 Center for Disease Dynamics, Economics & Policy. The state of the world's antibiotics.2015

 ECDC. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals 2011-2012

### PDF ARTICLE

 European Centre for Disease Prevention and Control. ESAC-Net Surveillance data 2016

### ARTICLE

Magill SS, Edwards JR, Beldavs ZG, Dumyati G, Janelle SJ et al 2014 'Prevalence of antimicrobial use in US acute care hospitals May to September 2011'. JAMA, vol 312, no. 14, pp. 1438-1446



## NON-PRESCRIPTION USE OF ANTIBIOTICS

Whilst many countries have regulations limiting antibiotic prescribing to registered health practitioners these laws are not enforced in most LMICs and some high-income countries. In much of the world antibiotics are sold without prescription. Non-prescription use:

- accounts for 19% - 100% of antimicrobial use outside northern Europe, Australasia and the US.
- Is associated with very short courses (driven by financial situation), inappropriate antimicrobial and dose choices
- Is driven by poor access to health care

In some countries substandard or counterfeit antibiotics also contribute to antibiotic use with little or no benefit. In South Africa 1 in 5 medicines are estimated to be counterfeit.

- A lack of knowledge of local antimicrobial resistance, gaps in antibiotic knowledge and/or awareness of available evidence or local or national prescribing guidelines.
- Diagnostic uncertainty and fear of poor clinical outcomes - leading to increased use of broad spectrum agents or unnecessary prescription of antibiotics e.g. for viral infections.
- Sociocultural factors such as patients' expectation of receiving an antibiotic and the health professions perception of that expectation
- Socioeconomic factors such as reimbursement systems and marketing by the pharmaceutical industry.
- Inadequate or poorly regulated supply of antibiotics

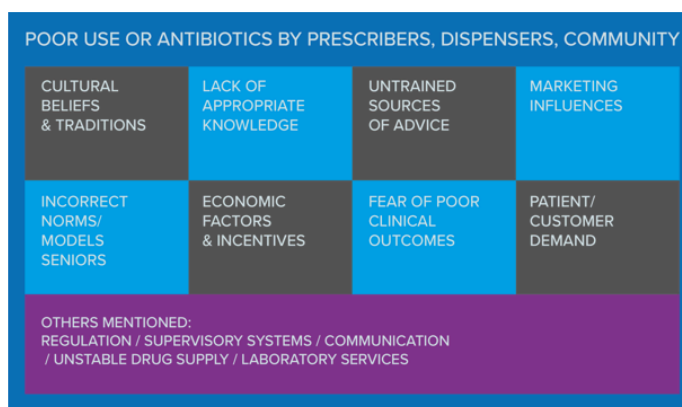


FIGURE 9  
Source: Adapted from Soc. Sci. Med 2003;57:733-44

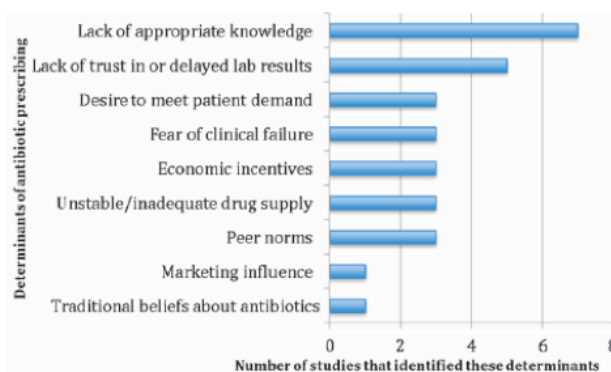


FIGURE 10  
Source: Adapted from Soc. Sci. Med 2003;57:733-44



FIGURE 11  
Source: Adapted from Soc. Sci. Med 2003;57:733-44

## TOOLKIT RESOURCE

### SITE LINK



Center for Disease Dynamics, Economics & Policy.  
The state of the world's antibiotics.2015

### ARTICLE

Morgan DJ, Okeke IN, Laxminarayan R, Perencevich, Weisenburg S. 2011, 'Non-prescription antimicrobial use worldwide: a systemic review' Lancet Infectious Diseases, vol. 11, no. 9, pp.692-701. Doi:10.1016/S1473-3099(11)70054-8

## DETERMINANTS OF ANTIBIOTIC PRESCRIBING AND USE

There are many factors that can influence antibiotic use and negatively affect prescribing behaviour. These are listed in the diagram below and include:

- psychosocial determinants such as attitudes, beliefs and social norms. In hospitals there is a culture and "etiquette" around prescribing set by senior medical staff that is rooted in the autonomy of decision making and a culture of medical hierarchy. Health professionals are often reluctant to question prescribing decisions of colleagues and in some sectors, such as private hospitals, senior prescribers have complete autonomy in deciding what antibiotic to use, how much to use and for how long.
- Resistance is not seen as a problem important in prescriber's own daily practice

Drivers of antibiotic prescribing in hospitals differ from those in the community.

## DR STEPHEN HARBARTH. DRIVERS OF ANTIBIOTIC MISUSE IN OUTPATIENT SETTINGS



Cultural differences in attitudes and expectations, along with regulation and the accessibility of antibiotics and diagnostic testing may explain the variation in antibiotic use between countries. Cultural factors, (patient, practitioner and organisational) may also contribute to the 2 to 3 times variation in prescribing within countries and across institutions. The local drivers of antibiotic use need to be assessed as part of any local efforts to improve antibiotic use.

## TOOLKIT RESOURCE

### PDF ARTICLE



Radyowijati A & Haak H. Improving antibiotic use in low-income countries: An overview of evidence on determinants.

### ARTICLES

Hulscher ME, Grol RPTM, van der Meer JWM 2010, 'Antibiotic prescribing in hospitals a social and behavioural scientific approach', *Lancet Infect Dis*, vol.10, pp.167-75

Touboul-Lundgren P, Jensen S, Draai J, Lindbaek M 2015 'Identification of cultural determinants of antibiotic use cited in primary care in Europe: a mixed research synthesis study of integrated design 'Culture is all around us', *BMC Public Health*, vol. 15 :908

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Canadian Antimicrobial Resistance Surveillance System Report 2016

Center for Diseases Control. Report on Antibiotic Use in the United States, 2017: Progress and Opportunities.

Magill SS, Edwards JR, Beldavs ZG, Dumyati G, Janelle SJ et al 2014, "Prevalence of antimicrobial use in US acute care hospitals May to September 2011". JAMA, Vol.312, no. 14, pp 1438-1446

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Yoon YK, Park GC, An H, Chun BC, Sohn JW 2015, 'Trends in antibiotic consumption in Korea according to national reimbursement data'. Medicine, vol. 94, no. 46 e2100

van Buul LW, van der Steen JT, Veenhuizen RB, Achterberg WP, Schellevis FG, Essink RT, et al. 2012. "Antibiotic use and resistance in long term care facilities". J Am Med Dir Assoc, vol.13, no. 6, pp. 568.e1-13.

Lim CJ, Kong DCM, Stuart RL. 2014;" Reducing inappropriate antibiotic prescribing in the residential care setting: current perspectives". Clin Interv Aging, vol. 9, pp 1-13.

National Centre for Antimicrobial Stewardship and Australian Commission on Safety and Quality in Health Care. Antimicrobial prescribing and infections in Australian residential aged care facilities; Results of the 2015 aged care National Antimicrobial Prescribing Survey pilot.

Fleming-Dutra KE, Hersh AL, Shapiro DJ, Bartocoes M, Enns EA et al 2016, 'Prevalence of inappropriate antibiotic prescriptions among US ambulatory Care Visits, 2010-2011', JAMA, Vol. 315, no. 17, pp1864-1873

National Centre for Antimicrobial Stewardship and Australian Commission on Safety and Quality in Health Care. Antimicrobial prescribing practice in Australian hospitals. Results of 2015 National Prescribing Survey.

Morgan DJ, Okeke IN, Laxminarayan R, Perencevich, Weisenburg S. 2011, 'Non-prescription antimicrobial use worldwide: a systemic review'. Lancet Infectious Diseases, Vol.11, n.9, pp 692-701. Doi:10.1016/S1473-3099(11)70054-8

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Touboul-Lundgren P, Jensen S, Drai J, Lindbaek M 2015 'Identification of cultural determinants of antibiotic use cited in primary care in Europe: a mixed research synthesis study of integrated design 'Culture is all around us ', BMC Public Health, vol. 15 :908

Radyowijati A and Haak H 2003, 'Improving antibiotic use in low-income countries: An overview of evidence on determinants'. Soc Sci Med, Vol. 57, no. 4, pp 733-44.

# CHAPTER 3

 AUTHORS: **ELIZA DOLLARD & LILIAN M ABBO**

## WHAT IS ANTIMICROBIAL STEWARDSHIP?

### THE AIM OF THIS INTRODUCTORY CHAPTER IS TO:

Define key principles of prudent antimicrobial prescribing.

Outline goals of antimicrobial stewardship (AMS).

Discuss possible unintended consequences of antimicrobial stewardship.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Appraise what is antimicrobial stewardship and what is prudent antimicrobial prescribing
- Explore opportunities for implementing antimicrobial stewardship programs in acute care hospitals
- Discuss possible unintended consequences of antimicrobial stewardship
- Apply key principles of prudent antimicrobial prescribing in acute care hospital scenarios

### WHAT IS ANTIMICROBIAL STEWARDSHIP AND WHY IS IT IMPORTANT?

In this YouTube video animation you will:

UNDERSTAND WHY IS ANTIMICROBIAL STEWARDSHIP IMPORTANT FOR YOUR INDIVIDUAL PATIENT AND THE GLOBAL COMMUNITY

 WATCH VIDEO

### Case Scenario

A 54 years old female teacher, had a root canal and was prescribed clindamycin to treat a dental abscess. After 48 hours, she started to feel tired and was not able to go to work that day. Four days later she started to have watery diarrhoea and abdominal pain and thought that she had a stomach virus from one of the kids in school.

Within 6 days she was admitted to the hospital in septic shock where she was diagnosed with severe *Clostridium difficile* colitis complicated with a toxic megacolon requiring total colectomy. She consequently developed short gut syndrome dependent on total parenteral nutrition. She subsequently underwent intestinal transplantation and on post-operative day

12, became febrile, septic with intra-abdominal collections, acute pancreatitis and bacteremia with 4/4 blood cultures growing gram negative rods. All cultures from blood an abdomen grew *Klebsiella pneumoniae*:

Klebsiella pneumoniae	
	MIC Interp
Amikacin	Resistant
Cefazolin	Resistant
Cefepime	Resistant
Ceftazidime	Resistant
Ceftriaxone	Resistant
Gentamicin	Resistant
Levofloxacin	Resistant
Meropenem	Resistant
Piperacillin/Tazobactam	Resistant
Tetracycline	Resistant
Tobramycin	Resistant
Trimethoprim/Sulfa	Resistant

**KLEBSIELLA PNEUMONIAE CARBAPENAMASE PRODUCER  
COLISTIN E TEST = 12uG/ML**

*Is this a frightening scenario? Yes, indeed.*

Antibiotic resistance not only happens in acute hospitalised patients but can start in the community. In this case, an antibiotic prescribed in the outpatient setting by a dentist lead to significant complications and possible mortality.

Perhaps you will be the next healthcare provider caring for a patient with a multidrug resistant infection or, worse (depending on one's perspective), you yourself could contract a multidrug resistant organism for which there is no effective antimicrobial therapy available. Unfortunately, this is not science fiction, or a new unknown infection from an exotic land. Antibiotic resistance is a serious problem worldwide. We use this terms as resistance to bacteria is common and the focus of this chapter. There are very limited new options to treat multidrug resistant gram-negative bacteria, with very few antibiotics in the development pipeline. Development of new antimicrobials for multidrug resistant organisms has to be a public health priority; nonetheless, "The development of new antibiotics without having mechanisms to insure their appropriate use is much like supplying your alcoholic patients with a finer brandy." (Dennis Maki, IDSA meeting, 1998)

## ▶ IMPACT OF ANTIMICROBIAL STEWARDSHIP (AMS) PROGRAMS

In chapter 1 you learnt about the overall clinical, microbial and economic impact of infections with drug resistant bacteria. AMS programs have been shown to have significant beneficial impact on many of these outcomes and include appropriate antibiotic prescribing, reduction in overall prescribing in some cases, length of antibiotic therapy, decrease length of stay, reduced morbidity and mortality and overall a reduction in healthcare costs. A recent systematic review showed benefits of AMS on microbial outcomes, the impact for example GNB infections, an important and key challenge globally is illustrated in Fig.1 Strategies for AMS programs and evidence for the impact of process and outcome measures will be summarised in this eBook.

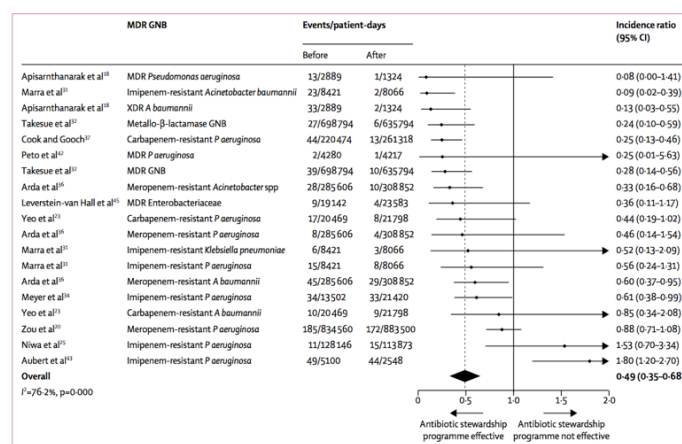


Figure 2: Forest plot of the incidence ratios for studies of the effect of antibiotic stewardship on the incidence of MDR GNB. GNB=Gram-negative bacteria. MDR=multidrug-resistant. XDR=extensively drug-resistant.

**Lancet Infect Dis 2017**  
**Published Online**  
**June 16, 2017**  
[http://dx.doi.org/10.1016/S1473-3099\(17\)30325-0](http://dx.doi.org/10.1016/S1473-3099(17)30325-0)

FIGURE 1  
[http://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(17\)30325-0/fulltext](http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(17)30325-0/fulltext)

## KEY PRINCIPLES OF PRUDENT ANTIMICROBIAL PRESCRIBING

Modern medicine would not be possible without antibiotics (Figure 2). These amazing drugs have revolutionised how we care for patients in the 21st century. We are able to care for premature babies, critically ill patients with sepsis, transplant solid organs and provide chemotherapy to patients with cancer among other miracles. Unfortunately, the appropriate and inappropriate use of these drugs has consequences.

As global rates of antibiotic resistant infections increase antibiotic research and development has been dwindling, resulting in a catastrophic lack of weapons to use in this public health crisis. In response to this challenge, healthcare workers on the front lines have been tasked with minimizing unnecessary and inappropriate prescribing of antibiotics in order to prevent development of resistance while maintaining or improving patient outcomes.

Antimicrobial stewardship is defined (as previously presented in Chapter 1) as ensuring that every provider selects **“The right antibiotic, for the right indication (right diagnosis), the right patient, at the right time, with the right dose and route, causing the least harm to the patient and future patients.”** This definition outlines the key principles of antibiotic prescribing. If followed strictly, these principles ensure that providers only prescribe antibiotics for non-self-limiting bacterial infections. Figure 3 provides more detail to each principle as relates it to clinical evaluation.

### Modern Medicine Is Not Possible Without Antibiotics

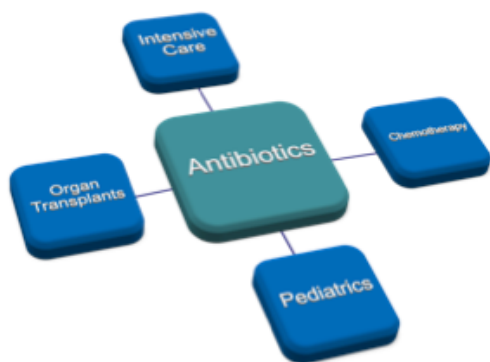


FIGURE 2

The goals of stewardship have been outlined in Chapter 1: Introduction to AMR. This chapter will provide more detail to each of the five goals.

Table 1. Overview of different outcome measures and some general remarks.

Outcome measures	Remarks
<b>Clinical</b>	
Mortality	Important, but less suitable for mild infections (e.g. uncomplicated UTI)
LOS	General or ward-specific (e.g. ICU stay); easy to obtain, but highly sensitive to biases
Complications	Complications such as IV catheter-related problems and phlebitis
<i>Clostridium difficile</i>	Also indirect measure for antimicrobial use
Readmission rates	Due to relapse, but important to consider effect of neighboring institutions
Toxicity (systemic)	Most frequently in renal function and liver
Other complications	For example, IV catheter-related thrombosis and noninfective phlebitis
<b>Microbiological</b>	
Resistance levels	Difficult to measure due to generally long time frame (months to years)
<b>Antimicrobial consumption</b>	
Total use	Often measured in DDDs; however, discrepancies are known due to generalization
IV/PO ratio	Of interest with an active IV-to-PO switch program
Broad/narrow ratio	Potentially relevant with regard to resistance development
Appropriateness of therapy	Labor intensive and possibly subjective, but of importance
<b>Financial</b>	
Cost-benefit ratio	Preferably done as cost-effectiveness study, including all costs and benefits (at least at hospital level, but preferably at societal level)

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

TABLE 1  
Overview of Different outcome measures in antibiotic stewardship  
From: Jan-Willem, et al. Expert Review of Anti-infective Therapy, 14:6, 569-575

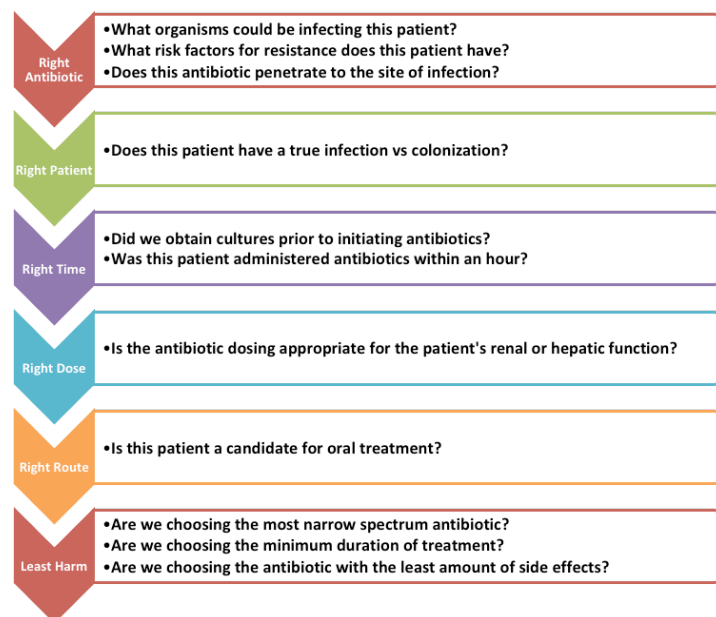


FIGURE 3  
Principles of Prudent Antimicrobial Prescribing



## ANTIMICROBIAL STEWARDSHIP GOALS

Depending on the clinical setting AMS programs will target their goals and outcomes based on available resources and current short, mid and long-term opportunities. However, the overarching goals fall under the following categories (Figure 4):

- 1) improve patient care and outcomes
- 2) reduce collateral damage and
- 3) impact costs.

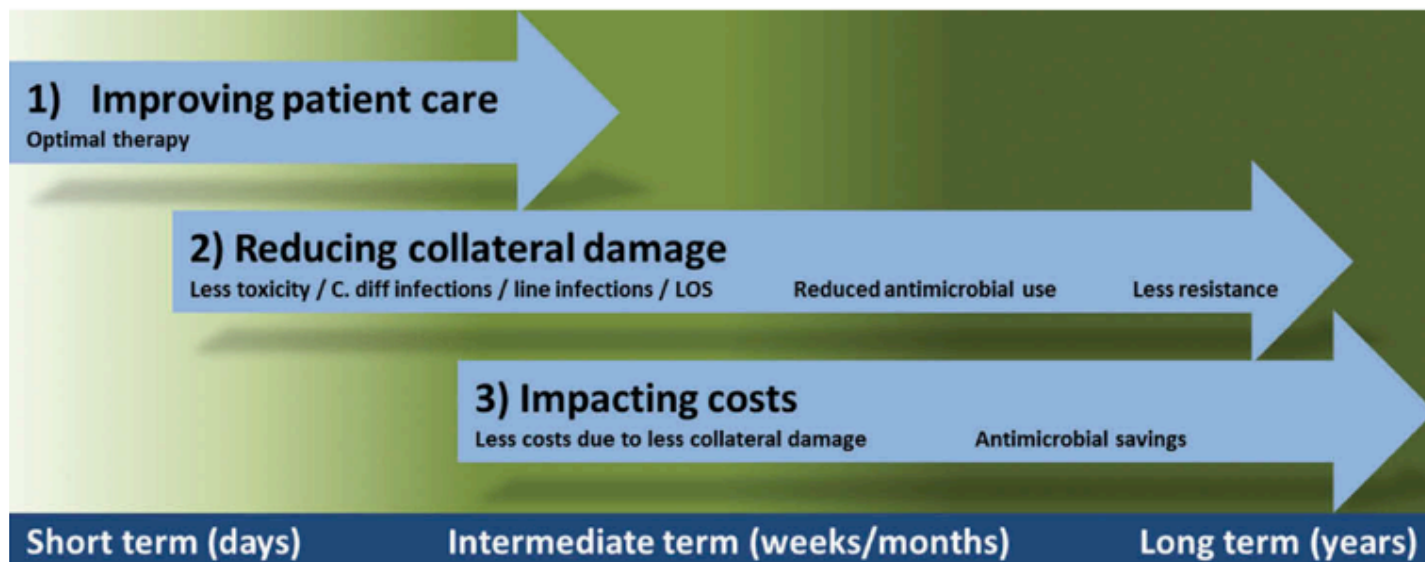


FIGURE 4  
From: Jan-Willem, et al. Expert Review of Anti-infective Therapy, 14:6, 569-575

## IMPROVE PATIENT OUTCOMES

Antibiotics cause dysbiosis or disruption in the normally “diverse” intestinal flora or gut microbiome.

One of the goals of antimicrobial stewardship is to minimise or prevent unnecessary changes in the gut biome to prevent the development and transmission of antimicrobial resistance among our commensal biome. Reducing antibiotic exposure will minimise the duration and extend of disruption of the microbiome thereby ultimately reducing collateral damage and improving patient outcomes.

Antimicrobial stewardship programs have a direct responsibility to ensure prudent antibiotic prescribing. Multiple studies have shown that antibiotics are prescribed unnecessarily in around one third to half of the patients, and that they are prescribed inappropriately (timing, molecule, dose, route, duration) in the same proportions. Inadequate initiation of antibiotics can increase mortality by up to 50%.

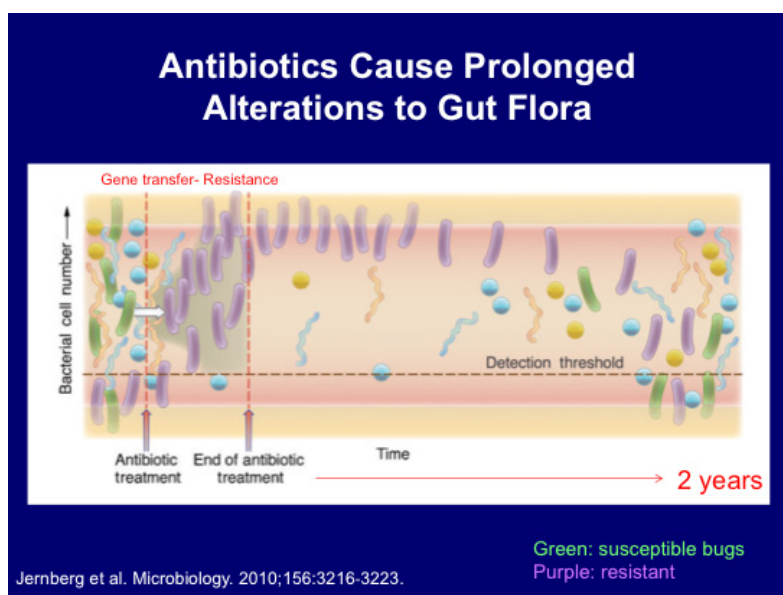


FIGURE 5  
Antibiotics Cause prolonged alterations to Gut Microbiome

Inadequate therapy can refer to initiating therapy to which the organism is resistant or initiating therapy with no coverage for the organism present (e.g. spectrum that is too narrow).

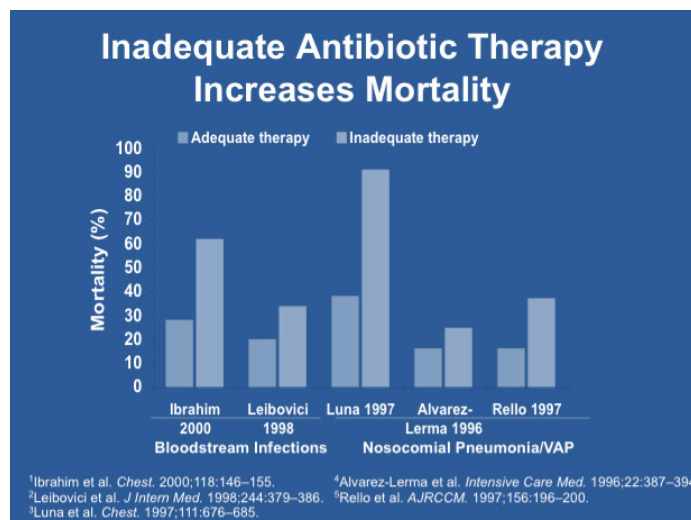


FIGURE 6  
Inadequate antibiotic therapy increases mortality

In addition, prolonged courses of antibiotics increase the risk of colonisation with multidrug resistant organisms. Therefore, the chain of transmission (in particular within healthcare settings) increases the risk of horizontally infecting more than one patient. Interrupting the chain is as important as preventing the development of resistance. Reducing unintended consequences by practicing prudent prescribing and limiting the duration of therapy to appropriate treat each infection with the safest, effective course of antibiotics is an important stewardship goal.

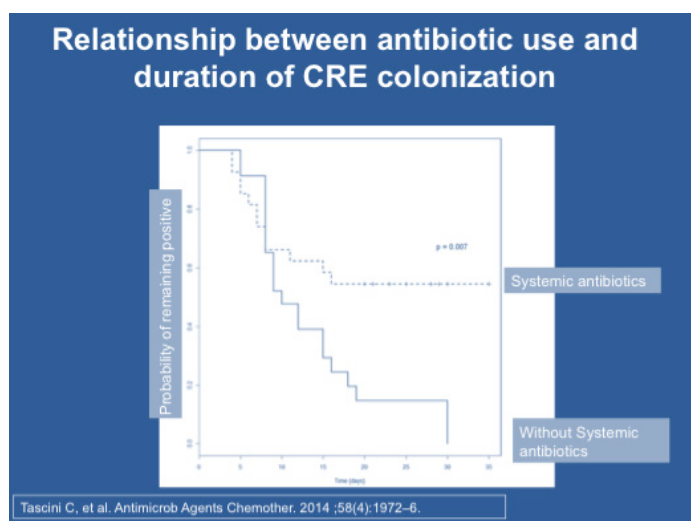



FIGURE 7  
Relationship between antibiotic use and duration of Carbapenem Resistance colonization

There are many ways that a stewardship program may ensure timely and appropriate antibiotic initiation. One way is to create clinical pathways that direct prescribers toward appropriate antibiotics for specific disease states. These clinical pathways can either be built into the medical record software at the time of prescribing, or can be available to prescribers via a manual or internet portal.

In addition to timely and appropriate antibiotic initiation, stewardship programs may minimise risk for adverse events by implementing interventions for timely review or renal dose adjustment. Timely de-escalation (being part of the review of antibiotic prescriptions) will minimize patient exposure to broad spectrum antimicrobials and therefore reduce their risk for associated events such as resistance or *C. difficile* infection. Renal dose adjustments will ensure patients are not over- or under-dosed which may increase their risk for adverse effects, infection relapse, or development of resistance.

**Surgical Prophylaxis**

Antibiotic Stewardship programs may become involved with standardising surgical prophylaxis to avoid unnecessary broad-spectrum antibiotic use and reduce rates of surgical site infections (SSIs) using evidence-based therapies. Surgical site infections are among the most common healthcare-associated infections globally and have been associated with increased post-operative hospital days, additional surgical procedures, and often higher mortality. The 2014 Annual Epidemiological Report by the European Center for Disease Prevention and Control (ECDC) reported that the cumulative incidence of SSIs ranged from 0.5% up to 9.7%, with the highest rates in colon surgery (European Centre for Disease Prevention and Control. Annual epidemiological report 2014 Antimicrobial resistance and healthcare-associated infections. 2015.). The ECDC has published a systematic review and evidence-based guideline on perioperative antibiotic prophylaxis (PAP) to standardize administration, dosing, and duration of exposure

 [VIEW GUIDANCE DOCUMENT](#)

Stewardship programs have an opportunity for intervention by ensuring intuitions are following these guidelines to minimise infections and patient exposure to unnecessary antibiotics. Europe has seen a statistically significant decrease in surgical site infections between 2009 and 2012 in the areas of cesarean section ( $p < 0.001$ ) and laminectomy ( $p < 0.01$ ). Conversely, a statistically significant increasing trend was noted for colorectal surgery ( $p < 0.05$ ) (Figure 8).

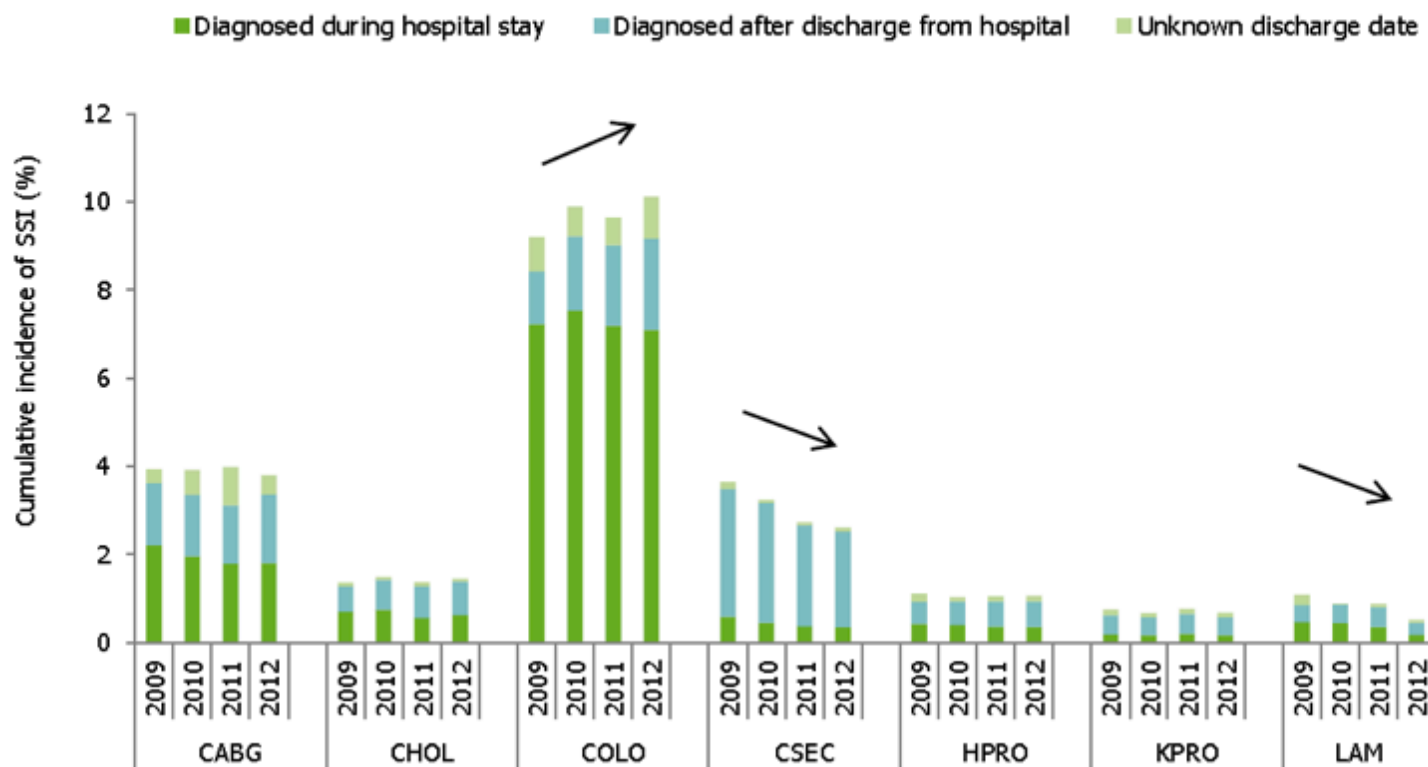


FIGURE 8  
Cumulative incidence of surgical site reported infections by year and operation type, EU/EAA, 2009-2012

## TOOLKIT RESOURCE

Additional resources on antibiotic selection based on surgical procedures have been provided by the Society for Healthcare Epidemiology of America (SHEA). (Anderson DJ, Podgorny K, Berríos-Torres SI, Bratzler DW, Dellinger EP, Greene L, Nyquist AC, Saiman L, Yokoe DS, Maragakis LL, Kaye KS. Strategies to prevent surgical site infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol.* 2014;35(6):605.)

## LEARNING OUTCOME REDUCE COLLATERAL DAMAGE

Reduce *C. difficile* colonisation or infection by controlling “high risk” antibiotics. *C. difficile* is the leading cause of hospital-acquired gastrointestinal illness and has been associated with increased length of stay, morbidity, and mortality. The most significant risk factors for *C. difficile* infection (CDI) are exposure to antibiotics and exposure to the organism. In hospitals and long-term care facilities, *C. difficile* may be spread on contact surfaces throughout the hospital and on the hands of healthcare workers. Any antibiotic can cause CDI and is particularly important that we limit antibiotic use to the right drug and duration to minimise alterations in the intestinal microbiome that allow *C.difficile* spores to germinate and cause colonisation and infection.

## REDUCE ANTIBIOTIC CONSUMPTION AND COSTS WITHOUT INCREASING MORTALITY OR INFECTION-RELATED RE-ADMISSIONS

In order to reduce antibiotic consumption and costs without increasing mortality or infection-related re-admissions, an accurate diagnosis at the time of prescribing is key. AMS programs may assist in accurate diagnosis by providing clinical pathways which quickly summarise guidelines, or by ensuring access to rapid diagnostic options (e.g. rapid influenza or strep tests). If positive, rapid influenza tests may decrease antibiotic consumption as patient has a clear diagnosis of viral infection. If negative, they may reduce anti-viral agent prescribing or inpatient isolation costs.

Once a provider has determined that a patient truly has a non-self-limiting bacterial infection, an effort must be made to choose the narrowest spectrum agent that is appropriate for the disease state.

AMS programs may help providers by identifying infections with the highest risk of over-prescribing and targeting those patient populations whether they practice in a clinic or ambulatory healthcare setting, an acute care hospital or a long-term care facility antimicrobial stewardship programs may also focus on length of therapy to ensure that patients are treated for the minimum duration supported by the literature.

Lastly, comprehensive AMS programs would ensure access to transitions of care services.

## OPTIMISE HEALTHCARE COSTS

Various types of antimicrobial stewardship interventions have been published with associated cost savings. Table 1 shows a small sampling of some of these interventions. The most common cost outcomes evaluated in stewardship studies have included drug cost, laboratory costs, and length of stay. These cost saving studies have been used to validate further investment into stewardship infrastructure and expansion.

Study	Intervention	Impact
Seligman SJ et al.	Restriction	Total reduction in antibiotic costs by 29%
Britton HL et al.	Clinical guidelines	Total purchases of cephalosporins decreased by \$55,715 or 46.2%
Briceland LL et al.	De-escalation	Total cost savings of \$38,920.95 during intervention period
Avorn J et al.	Clinical Pathway	Savings of \$76,000 annually
McGregor JC et al.	Computerized monitoring software	Savings of 84,188 compared to control arm over 3 months

TABLE 2  
Examples of documented cost savings associated with stewardship interventions  
Source : <https://www.cdc.gov/getsmart/healthcare/evidence/asp-int-costs.htm>

More recently, a Cochrane review of 221 studies reviewed outcomes associated with AMS programs. In the review, duration of antibiotic treatment decreased by 1.95 days (95% CI 2.22 to 1.67; 3318 participants; high-certainty evidence) with a similar risk of death. There was also moderate-certainty evidence of a decreased length of stay. Both of these outcomes directly impact overall healthcare costs and can be used to validate further efforts for AMS program expansion.

## TOOLKIT RESOURCE

PDF ARTICLE

 CDI IDSA Guidelines 2018

## TOOLKIT RESOURCE

SITE LINK

 The full Cochrane review can be found here

### **LEARNING OUTCOME** EVALUATE CORE ELEMENTS OF ANTIMICROBIAL STEWARDSHIP AND DISCUSS OPPORTUNITIES TO IMPLEMENT CORE ELEMENTS IN YOUR PRACTICE SETTING

The U.S. Centers for Disease Control and Prevention have established core elements necessary for developing a successful antimicrobial stewardship program. These core elements are as follows:

- **Leadership Commitment:** Dedicating necessary human, financial and information technology resources.
- **Accountability:** Appointing a single leader responsible for program outcomes. Experience with successful programs show that a physician leader is effective
- **Drug Expertise:** Appointing a single pharmacist leader responsible for working to improve antibiotic use.
- **Action:** Implementing at least one recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (i.e. “antibiotic time out” after 48 hours), IV to PO programs, prospective audit and feedback, antibiotic restrictions, etc.
- **Tracking:** Monitoring antibiotic prescribing and resistance patterns
- **Reporting:** Regular reporting information on antibiotic use and resistance to doctors, nurses and relevant staff
- **Education:** Educating clinicians about resistance and optimal prescribing

It is extremely important that healthcare providers recognise the need for and the value of ASPs and support their existence in healthcare facilities. The optimal structure and components of ASPs will vary according to the specific institution’s needs. However, a successful program requires the involvement of well trained and enthusiastic physicians and pharmacists and the strong support of the healthcare administration and medical staff. Interested physicians and pharmacists can usually demonstrate to institutions that an ASP can pay for itself in short order by reducing pharmacy costs and reducing length of stays.

In summary, we need to use our resources wisely; “to widen access to appropriate medications to encompass all people – regardless of race, gender, or socio-economic status – while at the same time reserving these precious compounds to treat only those diseases for which they are specifically required.”  
Our grandparents lived during an age without antibiotics.

The potential of drug resistance to catapult us all back into a world of premature death and chronic illness is all too real. As we age and ponder the inevitable entry into the age demographic in which our risk of hospitalisation is not negligible, it is worth us thinking about how we might react to acquiring an infection with carbapenemase-producing *Klebsiella* or a multidrug resistant *Pseudomonas* for which there are no available antibiotics to use.

We must all recognise the seriousness of this problem and commit ourselves to using these precious resources wisely. ASPs can help us identify such situations and avoid inappropriate antimicrobial use. We have the means to ensure that our antimicrobial armoury remains effective and that we preserve the effectiveness of future antimicrobials in the pipeline.

### **LEARNING OUTCOME** PATIENT CASES: APPLY KEY PRINCIPLES OF PRUDENT ANTIMICROBIAL PRESCRIBING TO THE FOLLOWING SCENARIOS

1. A 35-yo woman presents with 2 days of burning on urination and today noticed some blood in her urine. You diagnose acute uncomplicated cystitis. What is a 2010 IDSA Guideline first line recommended agent for treatment of AUC?
  - a. No antibiotics and reassurance
  - b. Cranberry juice
  - c. Ampicillin
  - d. Ciprofloxacin
  - e. Nitrofurantoin

#### **ANSWER: E**

First-line agents for acute uncomplicated cystitis include trimethoprim-sulfamethoxazole, nitrofurantoin, or fosfomycin. Fluoroquinolones are reserved as second-line therapy due to high prevalence of in-vitro resistance. Ensuring that patients are started on the correct guideline-based therapy can prevent further fluoroquinolone resistance from developing due to overuse with inappropriate prescribing.



2. A 58-year-old female with end stage renal disease has fever (Tmax 101.9 F) during hemodialysis. Three sets of blood cultures are taken and patient is empirically started on vancomycin and cefepime. At 72 hours cultures report a methicillin susceptible *S. aureus* (MSSA). Using stewardship principles, what alterations in antibiotic therapy should be recommended?

- a. Discontinue cefepime and continue vancomycin
- b. Discontinue cefepime and vancomycin, initiate cefazolin
- c. Discontinue cefepime and vancomycin, initiate ceftaroline
- d. Replace the hemodialysis catheter and discontinue all antibiotics

**ANSWER: B**

Beta-lactam antibiotics are preferred over vancomycin for treatment of MSSA. The appropriate course of action is to discontinue antibiotics that are no longer necessary (e.g. cefepime for gram negative coverage), and de-escalate the vancomycin to a narrow-spectrum beta-lactam, such as cefazolin or oxacillin.

the system. The following chart provides examples of possible unintended consequences that should be tracked and reported concurrently with the primary outcomes.





Stewardship Goals	Possible Unintended Consequences
Reducing length of stay	Increasing rates of readmission
Reducing duration of surgical prophylaxis	Increasing rates of surgical site infections
Restricting or limiting specific antimicrobials to reduce inappropriate use	Increasing use of non-restricted antimicrobials (e.g. "squeezing the balloon")
	Delaying doses of antimicrobials due to restriction processes

**SOURCE**

[http://www.idsociety.org/Guidelines/Patient\\_Care/IDSA\\_Practice\\_Guidelines/Antimicrobial\\_Agent\\_Use/Implementing\\_an\\_Antibiotic\\_Stewardship\\_Program/](http://www.idsociety.org/Guidelines/Patient_Care/IDSA_Practice_Guidelines/Antimicrobial_Agent_Use/Implementing_an_Antibiotic_Stewardship_Program/)



## TOOLKIT RESOURCE

### SITE LINKS

-  Alliance for the prudent use of antibiotics "APUA" Clinical Scenarios "Test Target Treat"
-  Managed Healthcare: 4 Case Studies
-  Stewardship Program Examples: US CDC
-  BSAC Gram Negative MOOC: Online course on antimicrobial stewardship and management of Gram negative Infections

## TOOLKIT RESOURCE

### SITE LINKS

-  Hughes J, Huo X, Falk L, Hurford A, Lan K, et al. (2017) Benefits and unintended consequences of antimicrobial de-escalation: Implications for stewardship programs. PLOS ONE 12(2): e0171218
-  Benefits and unintended consequences of antimicrobial de-escalation: Implications for stewardship programs

## POSSIBLE UNINTENDED CONSEQUENCES OF ANTIMICROBIAL STEWARDSHIP

The performance management of any stewardship program is measured primarily through structural and process measures with various measurable outcomes according to the literature. Nonetheless, balancing measures to detect unintended negative consequences of these interventions are fundamental to ensure that antibiotic stewardship programs are safe. Healthcare systems, clinicians and patients should be confident of the results and value of the interventions.

Balancing measures (looking at a system from different directions) measure the effects of changes designed to improve one part of the system causing new problems in other parts of

*References:*

1. Hassoun A, Huff MD, Asis E, Chahal K, Azarbal A, Lu S. Effect of target-enriched multiplex polymerase chain reaction on patient outcomes and costs during the 2013-14 influenza season. *J Hosp Infect.* 2017 Apr 21. pii: S0195-6701(17)30196-2).
2. Bratzler DW, H. P., & Surgical Infection Prevention Guideline Writers Workgroup. (2005). *Antimicrobial prophylaxis for surgery: An advisory statement from the national surgicalinfection prevention project.* *Am J Surg,* 189(4), 395. doi:10.1016/j.amjsurg.2005.01.015).
3. *Surveillance of surgical site infections in Europe 2010-2011.* ECDC Surveillance Report. 2011.)
4. Surawicz CM1, Brandt LJ, Binion DG, Ananthakrishnan AN, Curry SR, Gilligan PH, McFarland LV, Mellow M, Zuckerbraun BS. Guidelines for diagnosis, treatment, and prevention of clostridium difficile infections. *Am J Gastroenterol.* 2013;4(108):478.)

# CHAPTER 4

 AUTHOR: **CONOR JAMIESON**

## KEY STEPS IN DEVELOPING AN ANTIMICROBIAL STEWARDSHIP PROGRAMME

### THE AIM OF THIS CHAPTER IS TO:

Identify a range of stewardship activities that are applicable to a broad range of healthcare settings.

Identify the key personnel who need to be involved.

Describe the developmental stages in the processes.

Outline some of the potential barriers to these stages and suggest solutions to overcome them.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Describe key steps in developing an antimicrobial stewardship programme
- Identify the key personnel who need to be involved in the programme
- Outline some key activities to be carried out by the stewardship programme
- Describe some output measures that can be monitored for the programme (financial, guideline compliance, outcomes - decreased length of stay, etc.)

### INTRODUCTION

The goals of antimicrobial stewardship and a range of definitions of stewardship were outlined in Chapter 1. An antimicrobial stewardship programme is a systematic approach to implement a range of activities to achieve those goals. These can be as basic or as complex as resources allow - a range of relatively simple interventions can produce measurable changes in antimicrobial use, but if the ultimate aim is to drive improvements in the quality of prescribing with improved patient outcomes, then a mix of activities will be required, involving a range of healthcare professionals.

A stewardship programme can only be successful in an organisation or healthcare setting if the following criteria are met:

- Motivation to improve outcomes for patients with infections, prevent avoidable harm related to antimicrobial prescribing and a recognition of the potential and actual impact of antimicrobial resistance; this motivation needs to be present at many levels in an organisation – both from healthcare professionals but also shared by the senior executive team, those with the power to implement/support/fund the scheme, or capable of being persuaded of the benefit of the scheme (whether in terms of the benefits listed above, or purely financial/operational benefits);
- The stewardship programme is established with clear lines of accountability and there is a structure within the organisation/setting that can allow the implementation of a stewardship programme to take place, support the scheme, monitor its performance and hold it to account for performance and outcome measures;




- There needs to be both clinical and executive leadership provided to and by the scheme – it needs to have high level support and input from a senior management team, as well as clinical supporters/champions. These are essential to overcome any organisational and professional barriers that might hamper the activities of the programme.

The core components of a stewardship programme have been outlined by CDC and are listed below:

## TOOLKIT RESOURCE

### SITE LINK

 Sinai Health System – University Health Network Antimicrobial Stewardship Program (SHS-UHN ASP).

### VIDEO

Sinai Health System – University Health Network Antimicrobial Stewardship Program (SHS-UHN ASP).

 WATCH VIDEO

**Table 1. Core Elements of Hospital Antibiotic Stewardship Programs**

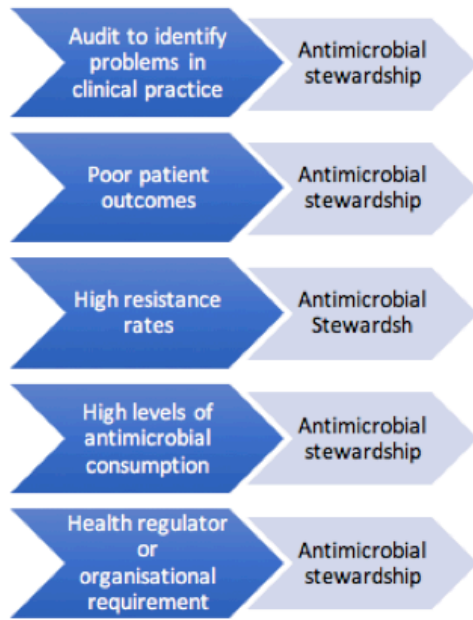
Leadership commitment	Dedicating necessary human, financial, and information technology resources
Accountability	Appointing a single leader responsible for program outcomes and accountable to an executive-level or patient quality-focused hospital committee. Experience with successful programs shows that a physician or pharmacist leader is effective
Drug expertise	Appointing a single pharmacist leader responsible for working to improve antibiotic use
Action	Implementing at least 1 recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (ie, antibiotic "time-out" after 48 h)
Tracking	Monitoring process measures (eg, adherence to facility-specific guidelines, time to initiation or de-escalation), impact on patients (eg, <i>Clostridium difficile</i> infections, antibiotic-related adverse effects and toxicity), antibiotic use and resistance
Reporting	Regular reporting of the above information to doctors, nurses, and relevant staff
Education	Educating clinicians about disease state management, resistance, and optimal prescribing

Source: Centers for Disease Control and Prevention [4].

| <https://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html>

Identifying the need for an antimicrobial stewardship may come from a number of drivers:

- Local audit which identifies problems in clinical practice (e.g. poor adherence to guidelines)
- Poor patient outcomes, or evidence of avoidable harm (e.g. high rates of surgical site infections, *Clostridium difficile* infections)
- High resistance rates in pathogens of clinical significance in the healthcare setting and the local environment
- High levels of antimicrobial consumption (and associated costs), perhaps compared to relevant regional or national benchmarks
- A need to implement a stewardship programme, driven by local health regulators or other similar organisations having such a programme in place.



## BUSINESS CASE

For the fortunate few, once the need has been identified, it may be possible that there is funding and support identified to move onto the next step of setting up the programme, but for many settings it is likely that a business case for funding the programme will be required. Those who control the budgets for funding initiatives like a stewardship programme may have to be persuaded of the benefits of such a scheme, in the face of competing priorities for funding.




In this context, there may be a number of metrics that are known which can help support a business case for a stewardship programme:

Operational	Financial	Clinical
Reduction in length of stay for hospital inpatients	Reduced expenditure on antimicrobials	No increase in mortality
No increase in ICU length of stay	Reduced consumption of broad spectrum antibiotics	Reduced incidence of infections due to key multi-resistant organisms

This business case should outline any initial and ongoing education and training requirements that might need to be funded to further develop the individuals or staff groups recruited/redeployed to stewardship activities – these could include attending training days, courses or conferences. Examples of how business cases may be developed are provided in the resource box. Many examples stem from a US perspective but could be adapted to geographical, healthcare system and resource context.

## TOOLKIT RESOURCE


### PDF ARTICLES

-  A sample antimicrobial stewardship programme proposal
-  Development of a business case for an inpatient Antimicrobial Stewardship Program
-  How to pitch an Antibiotic Stewardship Program to the Hospital C-Suite

### ARTICLE

Karanika et al. Systematic review and meta-analysis of clinical and economic outcomes from the implementation of hospital-based antimicrobial stewardship programs. *AAC*, 2016; 60:4840-4852

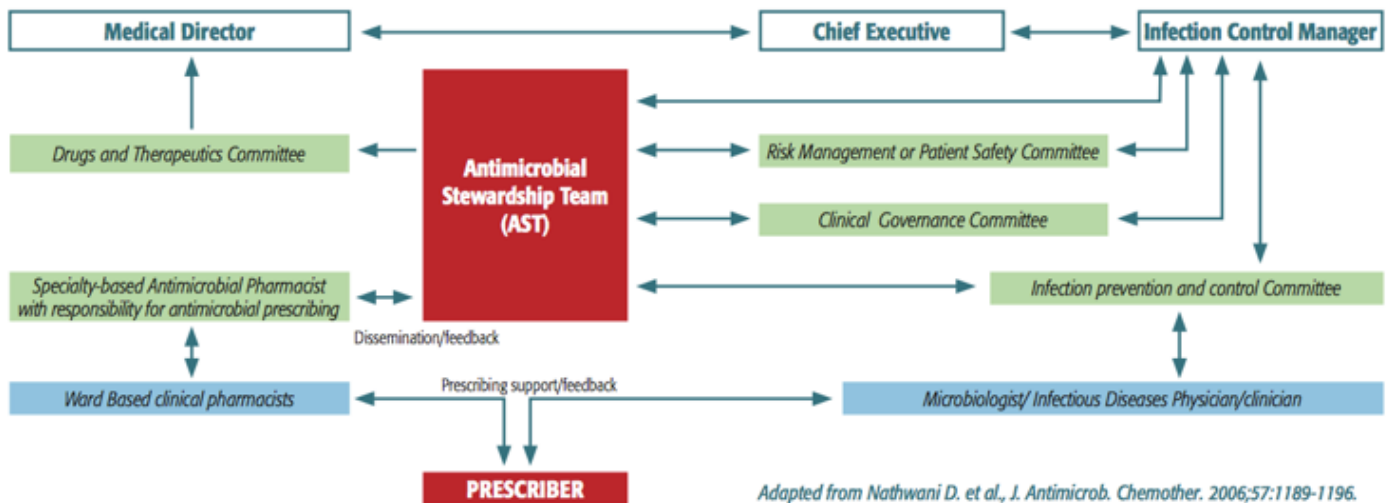
### SITE LINK

-  Pulcini et al, Commentary: Human resources estimates and funding for antibiotic stewardship teams are urgently needed, *Clinical Microbiology and Infection*, <https://doi.org/10.1016/j.cmi.2017.07.013>

## ANTIMICROBIAL STEWARDSHIP COMMITTEE

A stewardship committee is fundamental to any stewardship scheme as it will provide the strategic direction, guidance, manpower, intelligence, resources etc. for any stewardship activities.

It may be a stand-alone group or it may be a sub-committee or part of a larger group such as an infection prevention and control committee or a drugs and therapeutics committee. If it is a stand-alone group, it should be integrated into the governance structure of the organisation so that it is accountable. The diagram below outlines how such a committee might fit in a hospital setting.



Taken from BSAC 'Practical Guide to Antimicrobial Stewardship in Hospitals' by Dilip Nathwani and Jacqui Sneddon

**Composition of a stewardship committee:**

A successful committee will be one which includes representatives of key staff groups involved in antimicrobial prescribing, and which is representative of the organisation it is a part of. One of the biggest challenges for the committee will be getting the required members to attend, and the time commitment from busy healthcare professionals should not be underestimated. In primary care, it may be difficult to access the specialist expertise that is usually available in secondary care, such as infection specialists.

Staff member	Key Benefits/Rationale
Medical microbiologist	In depth microbiology knowledge, laboratory knowledge, clinical knowledge
Infectious diseases physician	Clinical knowledge, infectious diseases knowledge
Antibiotic pharmacist	In depth knowledge of antibiotics, PK/PD, formulary maintenance, clinical pharmacy knowledge
Infection control nurse	Input into infection control agenda, liaison with Infection Prevention and Control committee
Consultant physician and consultant surgeon	Clinical knowledge, representation of consultant physician staff group, 'shop floor' experience

Nurse	Input from and representation of nursing staff; key staff group who can have a major impact on stewardship; often provide patient's perspective
Junior doctor representative	Insight from the 'shop floor' of the organisation; liaison with other junior medical staff; feedback
Pharmacy representative	Additional insight from pharmacy staff
Primary care representatives (for secondary care committees)	
Secondary/tertiary care representatives (for primary care committees)	
Data analyst	Support for data analysis, IT skills

Of these, there will be a core team of individuals who are involved in the day to day activities of implementing, delivering and monitoring the stewardship scheme. These usually include infectious disease physicians, medical microbiologists and specialist pharmacists, in hospital settings, but the composition of the core team may vary from one place to another.

**Identifying the expertise**

It is likely that any organisation will already have some of the key members of a stewardship team in place, but it is also likely that there may be a need to recruit some expertise, or else train/up skill existing employees to take on or be involved in a stewardship role.

Part of the remit of the group should be to recruit the experience and expertise it needs to be able to deliver the remit outlined in the terms of reference of the group, if this is not in place when the group is formed.

In resource limited situations, it may not be possible to access the expertise required to implement a fully developed antimicrobial stewardship programme in house; in these situations, it may be necessary to rely on non-expert staff groups to implement elements of a stewardship programme that are practical and feasible (see chapter 16), sometimes within a distant mentorship programme. Even a limited stewardship programme can bring benefits in terms of reducing antimicrobial consumption.

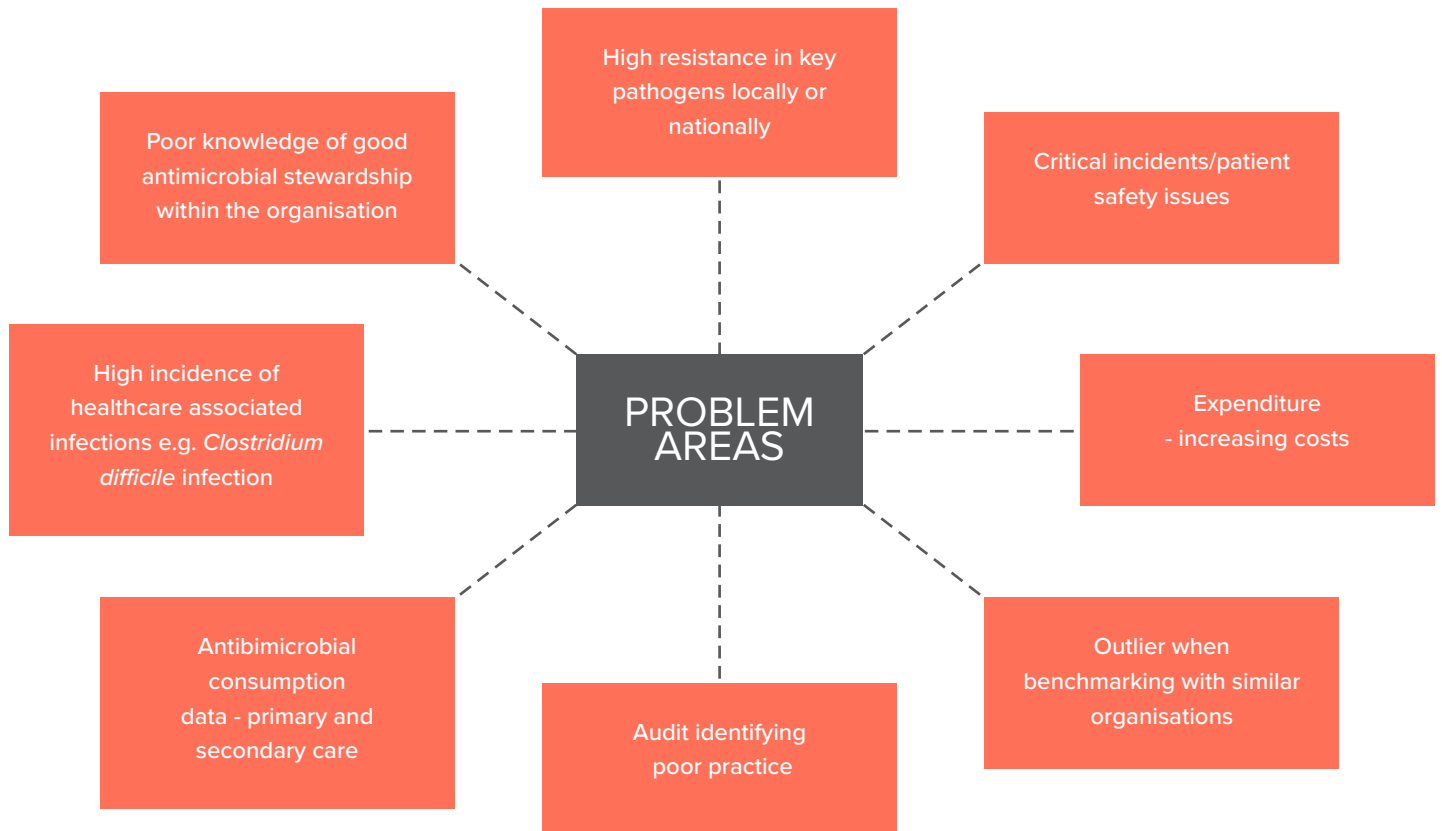
**Champions and supporters outside of the stewardship committee:**

While it is important to have expertise within the group, it is also vital to have supporters and champions who will promote and support the work of the group in the wider organisation. In addition, the group should be able to promote the benefits of its activities in terms of patient safety, reduced harm, reduced length of stay, reduced morbidity.

**Identifying priorities for the group:**

Once a group has been formed and staffed/supported appropriately, the next step is to develop an action plan for the group – either surveying the organisation to identify key priorities, or using prior knowledge to identify the priorities for the group.

There are a number of potential indicators of problem areas or areas needing intervention within an organisation or healthcare setting, and the diagram below lists some, but is not exhaustive.



**High resistance in key pathogens locally or nationally**

identified from resistance surveillance, local antibiograms, high use of broad spectrum agents, information from national surveillance programmes.

**Critical incidents/patient safety issues**

organisation may have reporting system for patient safety incidents; monitor for incidents relating to antimicrobial use; audits of door to needle times for sepsis; high rate of surgical site infections indicating poor practice in antimicrobial prophylaxis; Morbidity and Mortality meetings, Root Cause Analysis of critical incidents.

**Outlier when benchmarking with similar organisations**

it may be possible in some countries to benchmark local performance with certain indicators to other similar organisations, or a national average

**Audit identifying poor practice**

e.g. poor compliance with prescribing guidelines, poor patient outcomes in specific infections (c.f. critical incidents); excessive durations of antimicrobial therapy

**Antimicrobial consumption**

evidence of increasing antimicrobial consumption; consumption higher than similar organisations or locations (c.f. benchmarking)

**High incidence of healthcare associated infections**

e.g. healthcare associated *Clostridium difficile* infections; surgical site infections; outbreaks

**Poor knowledge of antimicrobial stewardship guidelines**

perhaps do not exist in the organisation; poor compliance with guidelines identified from audit, stewardship rounds etc.

Once this has been done, develop an action plan to address issues. The scale of the task may seem overwhelming, so might be best to tackle the easy wins first – for more complex tasks, using quality improvement and implementation science techniques see chapter 11. The table below provides examples of stewardship activities that may be relevant, with an approximation of the timescales involved in implementing any activity and the level of input required to implement and maintain it going forward.

Level of intervention	Timescale		
	Short	Medium	Long term
Low	Formulary restriction; Selective reporting of microbiology results	Pre- or post-authorisation programmes for restricted antibiotics	Controlling access of new antimicrobials onto formulary; Dedicated antibiotic prescribing section on drug chart
Medium to high	Guideline development, dissemination and implementation; Point prevalence surveys;	Audit programme Audit and feedback Dose optimisation/ PK-PD/ Therapeutic drug monitoring service	Referral systems Resistance surveillance Antimicrobial consumption Behaviour change techniques; Academic detailing; Stewardship rounds; Education and training; Quality improvement projects; Computerised decision support in electronic prescribing systems

TOOLKIT RESOURCE

SITE LINKS

 PHE Fingertips website

 ESAC Antimicrobial resistance data

 ECDC

 CDDEP Resistance map

## DEVELOPING ANTIMICROBIAL PRESCRIBING GUIDELINES

It is unusual for no guidance on antimicrobial prescribing to be available to prescribers in most healthcare settings, but there will undoubtedly be some situations where this is the case. In such situations, the time and effort required to develop guidelines from scratch may be considerable, and it may be a more cost-effective initial step to borrow and adapt other guidelines that are relevant to the local situation, or implement national guidelines where these are available. These can then be modified to suit the local situation – for example, recommending appropriate drugs which are available locally and are included on the local formulary.

Where this is done, it is important to sense check the guidelines and ensure that local resistance profiles don't undermine the empiric recommendations.

Once this is done, there should be a plan to review these on a regular basis to ensure that they remain relevant and current.

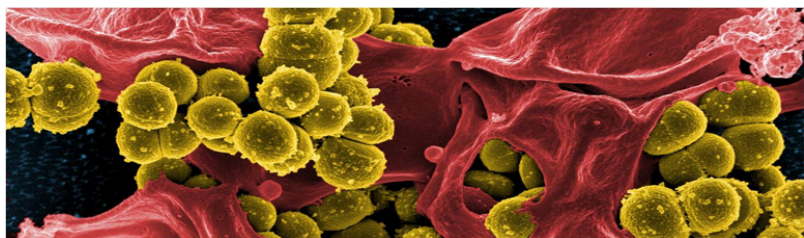
This article, published in 2002 provides a very good summary of the steps involved in developing, disseminating and implementing antibiotic guidelines.

## EDUCATE AND TRAIN

Education is a key part of antimicrobial stewardship, but it can be extremely time consuming, especially when the sheer number of healthcare professionals who need to be educated is considered.

Developing educational resources can be challenging, especially in resource limited settings. In these situations, making use of existing resources can be the most effective strategy.

Internet or web based educational resources [e-learning resources] are likely to be the most cost-effective method of reaching large groups of staff, where the infrastructure exists to allow this – see the BSAC MOOCs on Antimicrobial Stewardship and Gram-negative infections.



## VIEW GUIDELINES ARTICLE

### TOOLKIT RESOURCE

#### PDF ARTICLE



WHO guideline development article

#### SITE LINK



A Quick Win from India – The Impact of Policy Guidelines on Hospital Antibiotic Use over a Decade: A segmented time series analysis Chandy et al, 2014

Face to face education can be very effective, but consideration must be given to the practicality of this – large groups of staff, time consuming to develop education and deliver it, and frequently changing/rotating staff mean the task can seem endless.

Opportunistic educational interventions can occur on stewardship ward rounds and can be helpful in highlighting poor practice or reinforcing good practice, explaining a particular learning point or putting knowledge into clinical context.

A one size fits all model does not work when there are different professional groups who need to be educated, or there are differing levels of knowledge within a professional group.

### TOOLKIT RESOURCE

#### SITE LINKS



BSAC Antimicrobial Stewardship MOOC



Gram negative infections MOOC



**Day to day activities:**

The core team involved in antimicrobial stewardship activities (see above) will probably do many of the following activities on a daily basis:

- Providing consults for specific patients, at the request of clinicians – providing guidance on appropriate investigations and sampling, initiation of empiric therapy, streamlining to directed therapy, recommendations for referral to other specialties for imaging, surgery or other investigations or management;
- Reviewing prescriptions for antimicrobial agents – checking for appropriateness, guideline compliance, monitoring use of restricted agents or agents which require specific authorisation from ID or microbiology;
- Providing advice on optimisation of antimicrobial therapy – e.g. therapeutic drug monitoring for narrow therapeutic index agents, modifying doses in renal or hepatic impairment, advising on alternative therapy in cases of clinically significant drug interactions with existing medication
- Promoting conversion from IV medication to oral options
- Providing education – formal teaching session, ad hoc education on ward rounds
- Gathering data – e.g. point prevalence surveys, audit data, quality improvement data collection, primary care prescribing data
- Maintenance and update of existing guidelines
- Managing an outpatient parenteral antimicrobial therapy service
- Academic detailing e.g. in primary care physician practices
- Horizon scanning – monitoring the availability of new antimicrobial agents and their impact on practice, financial monitoring of expenditure on antimicrobials, assessment of new evidence or national guidance on local practice; dealing with drug shortages; reviewing local resistance profiles for key pathogens;
- Implementing and monitoring compliance with national quality standards or quality initiatives (e.g. CQUIN or Quality Premium targets in UK, NSQHS3 in Australia, CMMS scheme in USA).

For medical professionals, these activities will take place in the context of a number of competing priorities including managing individual patients under the ID team, running clinics, running the clinical microbiology laboratory service, authorising microbiology results and so on. For pharmacy professionals, they may also be required to provide general clinical pharmacy services on wards or in the pharmacy department. This serves to underline the

importance of having protected time to carry out antimicrobial stewardship activities, something which should be addressed in any business case.

**Measuring success or progress:**

Careful consideration should be given to how the achievement of the priorities, or progress with achieving them, can be measured. This should be planned from the very beginning.

**Questions to ask:**

What does success look like – what are we trying to achieve? For example, reduction of empirical broad spectrum antibiotic use in a specific clinical area.

How will success be identified? What will we measure to know that we have reduced this?

Does everyone know what we are trying to achieve, and why? Often we forget to involve front line staff in the understanding of the need for change, and fail to take account of their needs and priorities when trying to implement change

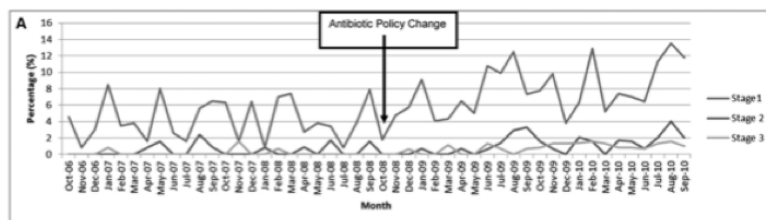
How long will it take to measure? How often do we need to measure? Is our planned measurement process feasible, can it be carried out within existing time constraints? Is the frequency of measurement achievable?

How will we know if we have failed or if the change is causing harm or increasing risk?

For example, a policy change to switch from using cephalosporins for surgical prophylaxis in orthopaedic surgery to using gentamicin led to a 94% increase in acute kidney injury (AKI) in a Scottish hospital. Bell et al, JASN 2014;25:2625-2632



**Increase in percentage of AKI (adjusted) stages 1, 2, and 3 for each month following policy change.**





Within an antimicrobial stewardship programme, there is often a mix of measurement processes going on – continuous background monitoring of simple to collect data (often collated by someone outside of the ASP team) such as financial expenditure, volumes of antibiotics dispensed, length of stay – as well as more targeted measurements of quality such as point prevalence surveys and localised quality improvement initiatives. Monitoring of local adverse incident reporting systems, where they exist, is also important. Chapters 10 and 11 have more detailed information on measuring antimicrobial use and quality.

**Barriers:**

In an ideal world, there would be sufficient resources available to develop an antimicrobial stewardship programme in any given healthcare setting, which would be welcomed by administrators and clinicians alike, with full engagement with its various initiatives. In reality, there are always a number of barriers to implementing any programme and these vary depending on the local situation.

A global survey of antimicrobial stewardship was conducted in 2011, and it also gathered information on the barriers that prevent the implementation and delivery of antimicrobial stewardship programmes. The table below lists the most commonly reported barriers.

	Barriers to delivering a functional and effective AMS programme					
	Lack of personnel or funding, n (%)	Other higher priority initiatives, n (%)	Administration not aware of AMS programme, n (%)	Opposition from prescribers, n (%)	Lack of information technology support and/or ability to get data, n (%)	No barriers, n (%)
Current AMS programme (763)	219 (29)	118 (15)	68 (9)	128 (17)	175 (23)	55 (7)
Planned AMS programme (348)	100 (29)	69 (20)	48 (14)	43 (12)	57 (16)	31 (9)

| Howard et al. JAC 2015; 70: 1245-1255

However, the table below illustrates how these barriers may be overcome:

Barriers	Potential solution
Lack of personnel/funding	Use/train staff with broad skills sets e.g. align infection control and stewardship skill sets; develop a business case to recruit staff.
Educational challenges – limited teaching in medical education; up-skilling pharmacy and nursing staff to be involved; sheer volume of healthcare professionals involved; access to educational events or courses for key staff	BSAC MOOC ( <a href="https://www.futurelearn.com/courses/antimicrobial-stewardship/">https://www.futurelearn.com/courses/antimicrobial-stewardship/</a> ), online courses such as those for nursing staff ( <a href="http://www.nes.nhsscotland.com/education-and-training/by-theme-initiative/healthcare-associated-infections/training-resources/antimicrobial-stewardship-workbook.aspx">http://www.nes.nhsscotland.com/education-and-training/by-theme-initiative/healthcare-associated-infections/training-resources/antimicrobial-stewardship-workbook.aspx</a> ), pharmacy staff ( <a href="http://nwapg.co.uk">http://nwapg.co.uk</a> ); Health Education England ( <a href="https://www.e-lfh.org.uk/programmes/antimicrobial-resistance/">https://www.e-lfh.org.uk/programmes/antimicrobial-resistance/</a> ).  See chapter 13 for more information on education and competencies, including examples from other countries.
Geographic – multi-site, on and off-site provision of services, out of hours advice/information	Using IT where possible – electronic referral systems, apps for mobile phones to access guidelines etc. Telecommunications can be used to overcome geographic barriers, and the increasing availability of internet based conferencing may be a solution
Infrastructure – may be basic/limited and may not be opportunities to implement structural changes which could have a big impact – e.g. electronic prescribing, amending drug charts, no internet or other IT systems	Look at low-tech solutions for providing advice or information; <a href="#">posters or leaflets</a> in clinics or on wards; use of apps that don't require internet access

<p>Getting buy-in from medical/surgical staff, especially in areas where professional boundaries are maintained and inter-professional working is not established.</p>	<p>Promotion of benefits of scheme, including need for all healthcare professionals to be involved; may need profession specific messages and interventions; recruit champions to help break down professional barriers <a href="https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-016-1290-0">https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-016-1290-0</a></p>
<p>Resistance to getting project started</p>	<p>Sell the benefits – costs, bed days, outcomes; focus on quick wins to build confidence and support, such as monthly spend for certain antibiotics reducing as part of the stewardship scheme.</p>
<p>Breaking down the view that the stewardship team are the ‘police’ and developing co-operative working to improve patient care.</p>	<p>Sell the benefits, and highlight the threats; promote the positive effect on patient outcomes with lack of evidence of harm where appropriate; have a consistent message that antibiotic stewardship is about improving prescribing, not about restricting antibiotics or reducing costs.</p>
<p>Working in areas where there is no clinical pharmacy service, or no medical microbiologists, or no ID physicians; nursing staff roles not evolved; no access to microbiology services or results.</p>	<p>Up skill the existing staff groups to understand and implement basic antimicrobial stewardship initiatives; make use of staff with related skill sets; use regional and partnership models for stewardship – see this example from Denmark <a href="http://qualitysafety.bmj.com/content/22/11/907">http://qualitysafety.bmj.com/content/22/11/907</a></p>

# CHAPTER 5

 AUTHOR: **PAUL POTTINGER**

## ASSESSING THE NEED AND MOTIVATION


### THE AIM OF THIS CHAPTER IS TO:

Learners will prepare to implement new antimicrobial stewardship initiatives - either from scratch or to add new features to existing programs - by first understanding the current state of affairs at their center.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Develop strategies for measuring the process and outcomes of your centre's current stewardship activities.
- Clarify the organisational structure and accountability of your centre's current stewardship activities.
- Explore and document your center's motivation to improve antimicrobial stewardship in terms of its leadership and dedication to the cause (measured in human and financial capital).

 *The secret of change is to focus all of your energy, not on fighting the old, but on building the new.*

—Dan Millman

### INTRODUCTION

Congratulations. If you've made it this far in the book, you understand the importance of antimicrobial stewardship: It enhances individual patient outcomes and improves public health. Antimicrobial stewardship is wonderful! But... you sense that your centre could be doing more. Where to start?

Understanding the current state of affairs is essential. You may be surprised to learn of good work that is already being done at your hospital or clinic. If so, wonderful! But perhaps with a specific resource or structural modification, even more remarkable things could be accomplished! Or, you may be disheartened to find that virtually no stewardship program exists. If so, take heart: that is an opportunity for change, and you may be the one to take the lead.

Many centres have stewardship efforts that lie somewhere between these extremes.

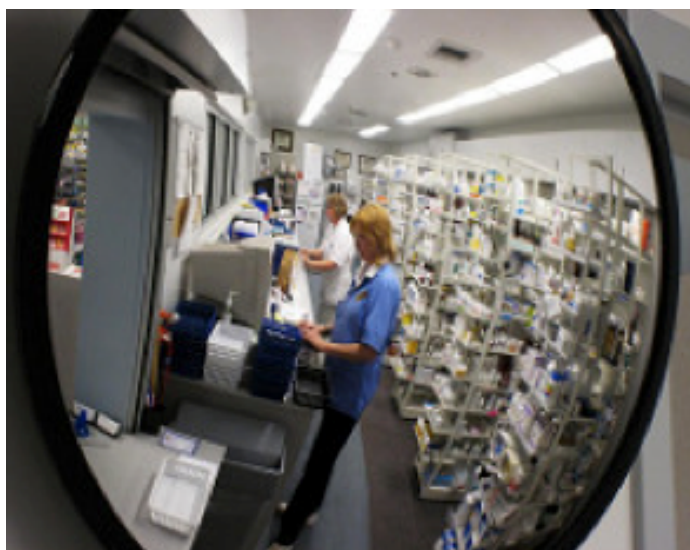


## RESOURCES

The word “resources” is often used as a euphemism for “money.” Certainly, funding is an important consideration. However, the situation is more complicated. Think of resources as “human” and “technical.”

### Human Resources:

Antimicrobial stewardship starts with people: That is why it’s fun! And... that is why it’s challenging. Technology is key, and some processes can be automated, but impactful stewardship remains a handcrafted discipline. Thus, the most important feature of your assessment will be identifying the key stakeholders and understanding their needs and expectations.



"Pharmaceutical (296)" flickr photo by Doug Waldron  
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Effective stewardship programs are led by pharmacists and physicians, preferably in full partnership. Each leader’s time should be protected for stewardship activities. This work requires dedicated time and attention, and should never be added to a full plate. The proper amount of protected time varies by circumstance and setting. In large centres, stewardship may be a full-time job, whereas in smaller hospitals a reduced fraction of effort may be appropriate. The best stewards are clinically active and visible to front-line providers; this earns trust and paves the way for acceptance of their recommendations. But, because clinical medicine requires tremendous time and energy, these questions require clear answers: Will stewardship leaders be paid for their time, or will they have to apply for grants to support their wages? What other duties are expected?

The ideal ratio of stewards to patients is uncertain, and likely depends on the setting (for example, inpatient versus ambulatory). A finite number of charts can be reviewed—and

interventions proposed—by any single individual. As a rough start, one pharmacist should probably be hired for at least every hospital 500 beds. But, if the level of patient complexity is high, this may be insufficient. Some estimates and funding requirements have been recently suggested and provide helpful steer in relation to human resourcing.

## TOOLKIT RESOURCE

### PDF ARTICLE



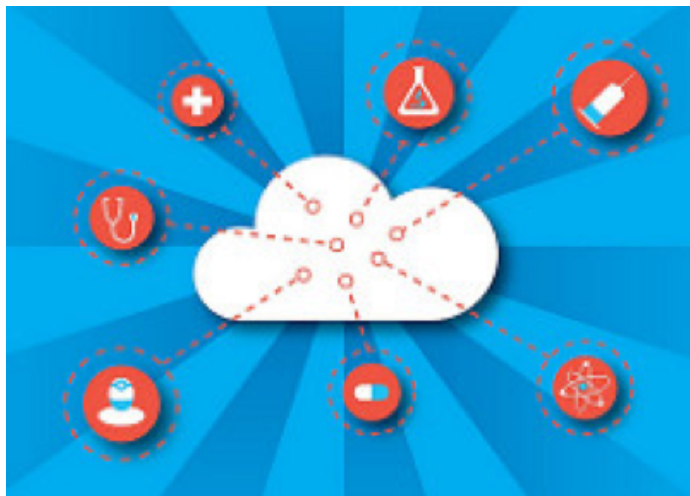
Human resources estimates and funding for antibiotic stewardship teams are urgently needed

Other human resources should be assured. Microbiologists are also important partners, and there should be a plan for robust collaboration between stewardship and the clinical laboratory. Micro lab directors can provide antibiotic resistance data, guide providers at the point of care with savvy messaging, and implement rapid diagnostic testing to facilitate prompt de-escalation of empiric therapy. Nurses and Clinical Officers are front-line partners in care, and may have a large impact upon the success or failure of stewardship programs. Understanding their needs and securing their partnership should be a top priority.

Information technology (IT) specialists abstract data, generate reports, and build interfaces. These activities require expertise, and asking the stewardship leaders to take this on may negatively impact their productivity. Are these individuals available for consultation on a regular basis? Do they have financial and professional incentive to collaborate? Finally, is there assistance for the stewards in arranging meetings, tracking projects, and staying organised? Administrative assistance can make all the difference between effective stewardship and failure.

### Technical Resources:

The modern practice of medicine generates epic floods of data: prescriptions, laboratory results, imaging, vital signs... charts bristle with information. This provides antimicrobial stewards with rich opportunities to support decisions in real time, mine data, and understand trends. But, only if they have access to the information.



"Health and Medical Cloud" flickr photo by perspec\_photo88  
<https://flickr.com/photos/111692634@N04/15855652400>  
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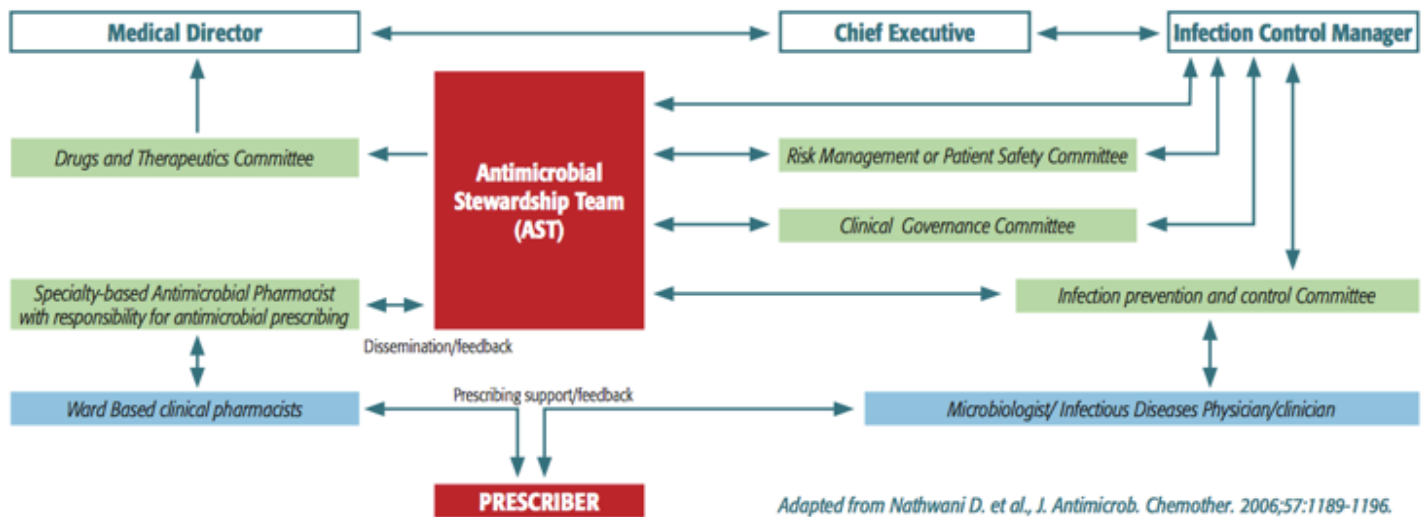
Does your centre embrace computerised order entry? Is the medical record electronic, and if so is it searchable? Is the pharmacy database online, and if so can reports be generated which facilitate tracking antibiotic use? If so, does it track antibiotic orders or actual administrations, for instance via patient barcode administration? Is there a system to alert the stewards in real time if restricted medications are prescribed? If the electronic medical record is a mosaic of different systems, can it be tamed by a third-party solution—and, if so, is there a commitment from the executive sponsors to pay for it, and from the IT department to support it? These technical resources do not surpass the human factors outlined above, but they can make the steward's job much easier if they are available. If these resources are not available, work can still proceed at a slower pace, but they may be worth negotiating for as part of a startup package, or may become a longer-term goal to aim for.

### LEADERSHIP STRUCTURE AND ACCOUNTABILITY

If one word could encapsulate antimicrobial stewardship, it would probably be “teamwork,” because so many stakeholders are involved. Partnership between pharmacist and physician leaders is essential, and both should understand their roles and responsibilities from the beginning. For instance, if the physician thinks of the pharmacist as an “assistant” or subordinate, then the pharmacist's job satisfaction may be reduced. If the pharmacist expects the physician to review every intervention, then progress may be painfully slow. This relationship should be structured in the most equitable and efficient way possible.

How will the stewardship program fit into existing leadership structures? Will the stewards be nested within the infection prevention team, or will they be considered a separate entity? Will they be held accountable for their work, and if so, what criteria will be used to determine accountability? Hospital executives are important stakeholders, but because stewardship touches so many lives in so many ways, it may be difficult for non-clinicians to grasp the program's tremendous importance. The pharmacist and physician stewardship leaders should know precisely what their supervisors want and expect to hear regarding progress and impact. How often will reports be required, what form should they take, and what information should they contain? Executive sponsors need to know that they are getting a good return on their investment, so they may focus on cost savings as measured by pharmacy expenditure, days of therapy, and length of stay. These are fine metrics, as described below... although tracking them can be a chore. If arbitrary goals are set, the stewards should know what the implications are if they are missed.





| Taken from BSAC 'Practical Guide to Antimicrobial Stewardship in Hospitals' by Dilip Nathwani and Jacqui Sneddon

## PROCESS

If stewardship efforts are already underway, you must understand how the program currently operates.



"doctor-researching" flickr photo by Taylorlight  
<https://flickr.com/photos/141311777@N02/26912273309>  
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One daily activity model emphasises formulary restriction, in which orders for certain "high value" antimicrobials require stewardship approval. This approach has been demonstrated to reduce inappropriate antimicrobial prescribing. But, if this is a prominent feature of the program, who will field the calls?

A common alternative to formulary restriction involves prospective audit and feedback. Here, prescribers may write for high-value antimicrobials, but as clinical data accrues in the coming days the stewards will reach out to guide them,

especially regarding de-escalation or dose adjustments. If so, how will these cases be identified? When will the stewards discuss them internally, and when will they reach out to the primary teams with recommendations?

Most programs employ a combination of prospective audit with feedback and formulary restriction. Regardless of the balance between these techniques, how is the stewards' advice communicated and recorded? Written recommendations may improve recommendation acceptance, but getting those notes into the chart takes time. Is this feasible in every case, or in select clinical circumstances?

If a separate infectious diseases consultant practices in the hospital, is that person informed of recommendations being made by the stewardship team, to ensure a coordinated effort and consistent messaging?

When does stewardship happen? Do protocols differ overnight, on weekends, or during holidays? If so, what arrangements are made? If trainees cover these duties, have they been properly trained and are they able to obtain support when needed?

Finally, how are periodic outcomes reviews accommodated in light of the very busy daily workflow (see below)? Is time allotted for data abstraction, analysis, and presentation? How often will the team update order sets? When will new antimicrobial agents be reviewed for consideration of addition to the formulary? Are educational efforts scheduled on a regular basis?

## OUTCOMES

Successful antimicrobial stewardship programs measure the impact of their interventions in a variety of ways. Ask how the stewards know whether they are doing a good job. A range of outcome metrics have been recommended to evaluate stewardship programmes.



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### Common metrics include:

#### *Antimicrobial consumption*

Pharmacy expenditures are easily tracked, and management considers this an important number to follow. But, cost is only one measurement of antimicrobial consumption, and it may not tell the whole story. For instance, if a few patients have appropriately received long courses of expensive drugs, then it may not have been possible to cut the budget safely. And antimicrobial expenses should be compared with the total pharmacy budget over time. Tracking actual antibiotic orders may be more illuminating. Measuring days of therapy (DOT) is quite popular, because of ease of measurement: Every day that a patient spends in the hospital and receives even a single dose of the drug in question is considered a day of therapy. This metric does not distinguish between single doses (for instance if given for surgical prophylaxis) and treatment doses. Thus, another metric can also be used: The defined daily dose (DDD) which is the assumed average maintenance dose per day for a drug used for its main indication in adults. The DDD allows for standardized comparisons across centers, health systems, or entire nations. However, some hospital pharmacy systems may not provide this information easily, thus making DOT an attractive alternative.

#### *Antimicrobial Resistance*

Reducing, or at least delaying, the emergence of antimicrobial resistance is a key goal of stewardship efforts. Can your program demonstrate stability—if not improvement—in resistance rates for key pathogens over time? Patience is a virtue here, because the antibiogram tends to change slowly, and because many specimens are collected at the time of admission, when the microbial ecology may already be influenced by outside selective pressures. But, this is an important yardstick to follow.

#### *Guideline Compliance*

If the stewardship team has published guidelines for antimicrobial use, or created order sets for common infections, how frequently are they being followed? And, are there actionable trends regarding guideline compliance? For instance, if a particular service rarely adheres to the guidelines, have they been consulted to determine the issue at hand? A related metric is time to effective therapy: How long does it take teams to get their septic patients onto the appropriate antimicrobial spectrum? Do patients with *S. aureus* bacteremia always receive the bundle of best practices such as undergoing echocardiography? Are providers willing to convert from IV to PO route of administration when appropriate?

#### *Clostridium Difficile Rates*

*C. diff* is a bacterium that may cause serious infection during or after antimicrobial therapy. Virtually any antibiotic may precipitate *C. diff* infection, but risk rises with duration of therapy and breadth of spectrum. And, it causes misery—if not true peril—for everyone involved. Thus, whether fair or not, its incidence is frequently interpreted as a surrogate for stewardship effectiveness.

#### *Harm Avoidance*

Studying bad outcomes that do not happen is a stiff challenge. *C. difficile* infection, mentioned above, is one example of patient harm. Other adverse events that can be prevented with vigilance include nephrotoxicity or ototoxicity due to aminoglycosides, central venous catheter complications among patients who might have received oral therapy, and serious drug-drug interactions. Even one of these events will harm the patient and place the hospital at risk. Effective antimicrobial stewards warn frontline providers about these possibilities and offer risk reduction strategies. And, the stewards should be given credit for preventing these events.

## TOOLKIT RESOURCE

PDF ARTICLE



Metrics



## > MOTIVATION

Ultimately, your needs assessment should yield a measurement of the center's eagerness to embrace change. Along with leadership, the creation of stewardship structures, and good communication, motivation is pivotal to driving change. The greatest measure of motivation is a demonstrated commitment to effective antimicrobial stewardship. A hospital lacking the essential components above may still be fully committed to revving up stewardship, but there should be evidence for this commitment—both tangible and intangible.



### *Tangible Commitment*

A written document such as a charter or declaration of intent should be agreed upon. This serves two purposes. First, it clarifies important details of the program, especially the financial and logistical support for stewardship personnel. Second, it signals to everyone in the organization that leadership takes stewardship seriously. A public vote of confidence may be important for the new team in winning the hearts and minds of reluctant front-line providers.



"Businessmen shaking hands" flickr photo by reynernmedia  
<https://flickr.com/photos/89228431@N06/11220931254>  
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### *Intangible Commitment*

Equally important—if not more so—is evidence that your efforts will be welcome. This information may seem difficult to obtain, but it is worth pursuing. The easiest way forward is to talk with people... lots of people. Physicians, pharmacists, nurses, microbiologists, IT specialists, executives... all the stakeholders who would be impacted by your work should be consulted. Is this the first time stewardship is being organized at the center? If so, is there a groundswell of interest and enthusiasm among frontline providers? Or, is this seen as a “top-down” initiative that threatens physician autonomy? Has stewardship been attempted there before? If so, what went wrong? Do healthcare workers already have an unfavorable opinion of stewards? Regardless of the backstory, pursuing intangible factors involves friendly dialogue with stakeholders, which sets the stage for successful implementation and long lasting collaborations.

## > CONCLUSION

In this chapter we have learned the importance of assessment—assessment of the centre's antimicrobial stewardship needs, and its commitment to make change. This is essential to accomplish before beginning the implementation of a new program. Antimicrobial stewardship is serious business, and it is challenging. If it were easy, everyone would do it! Invest the time necessary to create a program that is impactful, sustainable, and fun to direct.

## **DELIVERABLE: ASSESSMENT REPORT**

### **ASSEMBLE A REPORT INCLUDING THE FOLLOWING ELEMENTS:**

#### **Resources**

- Team members (Is there a physician director, pharmacist director, microbiologist, data analyst, administrative supporter?)
- Information technology (Is there infrastructure to obtain microbiological and medication data in a timely fashion, and to generate summative reports as necessary?)
- Frontline provider support (Are order sets embedded in computer-order-entry, or within easy reach of manual order entry? Is there protected time for ongoing provider education?)

#### **Leadership Structure and Accountability**

- Team member support (Executive championship to advocate for new resources?)
- Reporting structure (Clarity regarding expectations and timeline?)

#### **Process**

- Daily work flow (Prospective audit with feedback? Formulary restriction?)
- Committee involvement (Active participation in stakeholder groups such as infection control, order set development, pharmacy & therapeutics?)
- Periodic reporting (Access to aggregate data periodically to assess progress?)

#### **Outcomes**

- Antimicrobial use (DOT or DDD measured?)
- Antimicrobial cost (Medications ordered, or administered, or purchased?)
- Antimicrobial resistance (Tracking changes to susceptibility of major pathogens to representative classes of antimicrobials over time?)
- Compliance (Provide use of empiric guidelines, willingness to accept ASP recommendations?)
- Safety (Harm avoidance measured?)

#### **Commitment**

- Recognition of importance of ASP (Written charter or program declaration?)
- Financial support (Salary guaranteed for at least several years regardless of short-term outcome measurements?)
- Groundswell of enthusiasm (General enthusiasm for ASP or palpable resistance?)

### TOOLKIT RESOURCE

#### SITE LINK



Barlam TF 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*, Volume 62, Issue 10, 15 May 2016, Pages e51–e77,



National Quality Partners Playbook: Antibiotic Stewardship in Acute Care. National Quality Forum, National Quality Partners, Antibiotic Stewardship Action Team. (2016)



CDC Antimicrobial Stewardship Implementation Resources.

#### ARTICLE

Cosgrove SE et al. Guidance for the knowledge and skills required for antimicrobial stewardship leaders. *Infection Control and Hospital Epidemiology*. 35(12): 1444-1451. (2014)

#### PDF ARTICLE



Jump Start Stewardship Implementing Stewardship in a Small, Rural Hospital. (2016)



Measuring the impact of antimicrobial stewardship programs Dik et al



### SUMMARY OF LEARNING OUTCOMES

1. Develop strategies for measuring the process and outcomes of your centre's current stewardship activities.
2. Clarify the organisational structure and accountability of your centre's current stewardship activities.
3. Explore and document your center's motivation to improve antimicrobial stewardship in terms of its leadership and dedication to the cause (measured in human and financial capital).

# CHAPTER 6

▶ AUTHORS: **RAHEELAH AHMAD & ALISON HOLMES**

## EXPERTISE, STRUCTURES AND ORGANISATION

### THE AIM OF THIS CHAPTER IS TO:

Be able to critically analyse the structure and organisation of antimicrobial stewardship programmes at the organisational and national level for improved implementation. While this chapter will be of interest to all readers, AMS pharmacists, AMS committees where they exist, and local authority level managers who are planning new programmes will find this of particular interest.

*traditional, alternative and innovative models for enhanced and broad clinical engagement in stewardship*

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Map within their own organisation where Antimicrobial Stewardship (AMS) programmes are situated
- Identify the concepts of expertise, structures and organisation in the national context (using their country national action plan) and reflect on how this may help or hinder broad clinical engagement
- Understand the different ways in which other countries are involving professional groups in the delivery of AMS programmes
- Take a view across the healthcare sector and reflect on a framework to assess the level of integration of approaches to AMS

### ▶ DEFINING YOUR ORGANISATION AND HEALTHCARE SECTOR

Health care is organised differently between countries and sometimes within countries (for example federal and state level care). But the way health care is organised has implications for the way AMS is organised, financed and monitored and hence on outcomes. As you work through this chapter a series of short activities is recommended so that the concepts remain relevant to your context. You may need to look at other resources or talk to others within or outside of your organisation to fill in the gaps once you have had a go. When we talk about the concepts of structures (what goes into a system) and processes (what we do with these inputs) it is useful to look at these structures in some detail, how programmes are formally organised and also the expertise available. Understanding and critiquing some of the facilitators for and barriers hindering AMS improvement through the way AMS is organised can help move away all the focus from individual behaviour change. This is not to say that individual behaviour change is not important or effective, but if we pause and look at structures and organisation this should then provide another mechanism for enhanced behaviours, optimal clinical practice and patient experience.

**Activity A:** Consider briefly the type of service organisation you work within including where your patients come from, if they can access you directly or must be referred. Are you described as a primary care, secondary, acute care (or other) organisation? Thinking very broadly do these factors have any implications for the way AMS is organised within your organisation?

**Activity B:** Now complete the table below, again for your own healthcare organisation. If you are not based in one single organisation then select one that you have working knowledge of.

	Finances come from	Staff are deployed from	Accountability for AMS outcomes
Federal level			
State level			
Locally (at the level of organisation)			
Add here any exceptions – so if it's different for certain professional groups or certain indicators add it here			

**Activity C:** Reflecting on the descriptions in activity A and B which (if any) in your experience have acted as facilitators for improving AMS or indeed barriers? Are there any mis-matches in terms of lines of accountability which hinder effective AMS?

### SITUATING ANTIMICROBIAL STEWARDSHIP WITHIN THE ORGANISATION

This section looks at how AMS programmes are placed within the organisation. Is AMS and Infection Prevention and Control (IPC) integrated? Does AMS come under the umbrella of patient safety or quality improvement? Understanding where AMS programmes are positioned within the organisational structural and process charts helps understand how performance of AMS is captured (which is picked up in chapters 10 and 12). Two examples are provided below (Figure 1 & 2).

The distinction between AMS, IPC and quality improvement is historical in many cases. Though many of the desired outcomes are consistent across these three functions they sometimes appear as dis-jointed and distinct because of the way they are organised. Simply by examining the structure and organisation in your organisation can open up a conversation with colleagues about aims of programmes. Whilst these programmes may be aligned at strategic level, this alignment does not always transfer to the day to day operational life of the organisation. (Figures 1 & 2)

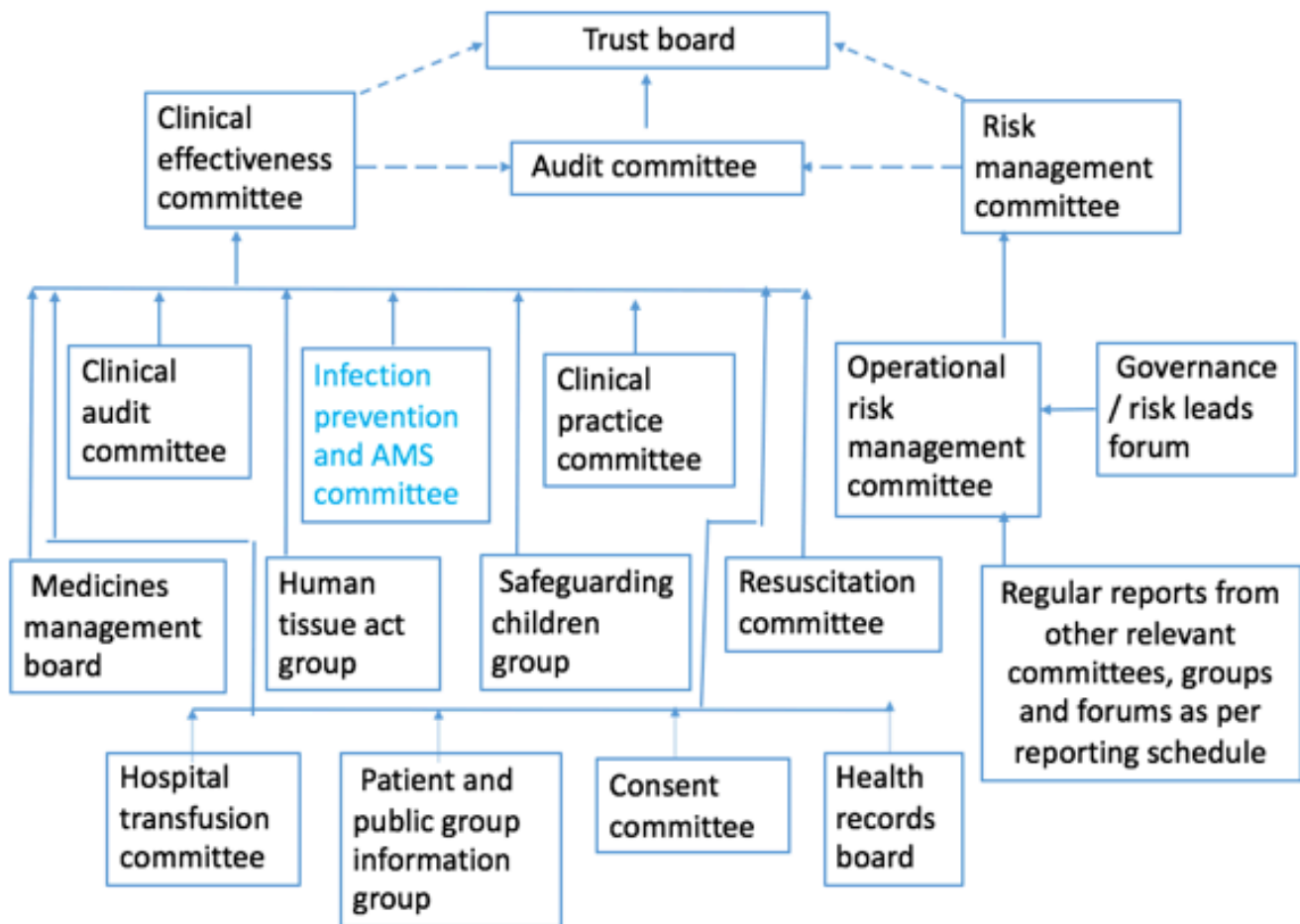


FIGURE 1  
Example governance structure

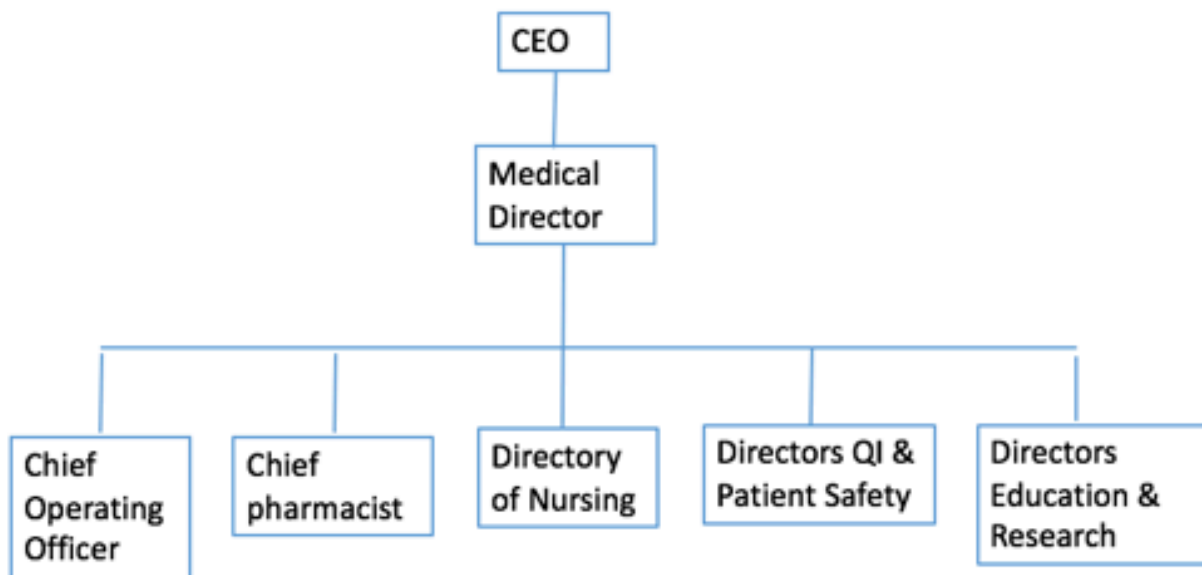


FIGURE 2  
Example organisational structure

## NATIONAL ACTION PLANS

Many countries are in the process of developing National Action Plans. Those countries which have a strategy in place will be thinking about execution and implementation. The next activity asks you to extend the assessments made above to your own national action plan. Readers are encouraged to also look at plans of countries which are of contextual relevance due to health system organisation, culture, epidemiology, policy or another factor which may be comparable.

**Activity D:** The following link provides the library of National Action Plans

<http://www.who.int/antimicrobial-resistance/national-action-plans/library/en/>

Do these plans (your own country and one other selection as suggested above) propose alternative and innovative models for stewardship? Do they promote broad clinical engagement? Do they suggest how this can be done? How?

## EXAMINING WORKFORCE ENGAGEMENT ACROSS PROFESSIONAL GROUPS

On the specific aim of assuring wider workforce engagement, there are limited published examples and almost all are from higher income countries. This does not mean that such models do not exist in low and middle income countries, but that they have not been shared in the international literature. Assessing the extent of workforce engagement is particularly relevant when planning new programmes or expanding existing programmes. Two examples of such an assessment are provided below (Table 1). Engagement is considered in two main domains. For a given programme: Who is the target audience? Who is involved in the delivery of the programme? The issue of roles of the wider workforce are also discussed in chapter 25 and 26

TARGET	Primary care clinician	Nurses	Community pharmacy	Long-term institutional care	Hospital staff	Public health body	Public/patients	Other
Antibiotics toolkit, England 6								
Who is the target audience	✓						✓	Royal College of General Practitioners
Who is involved in the delivery of the programme	✓		✓		✓*			

\* microbiologists, pharmacists

TABLE 1  
Target and delivery of AMS initiative

## TOWARDS INTEGRATED MODELS OF AMS

Looking back at section one of this chapter where you were asked about the part of the health sector in which you work and at how the organisation may act as a barrier or facilitator, we now look at using a more comprehensive framework for this assessment. Healthcare organisations are composite parts of health systems which are required to deliver best outcomes efficiently, whilst facing the challenges of macroeconomic constraints, technology costs, and increasing public need and demand. Models which achieve integration of care across primary, secondary, tertiary and long-term care are needed to achieve this and particularly for AMS<sup>1</sup>. Much AMS activity

has concentrated in hospital settings. This has been a helpful and practical place to start but the hospital physical structure is something of an ‘artificial’ boundary, which neglects bi-directional influences between hospital and community care services. Antimicrobial use in the community and long-term care facilities are associated with the development of AMR in and outside hospitals<sup>3</sup>. The way people access health care varies in different countries and has evolved. For example, the availability of blended care and complex patient care pathways in some countries allows for care which would traditionally have been delivered in hospitals to now be carried out on a day case basis as well as in primary and community care or in the



patient's home. This evolution is both patient-centred and allows for more rational use of services. But with this comes the need for AMS approaches which are truly integrated across service providers and sectors. The availability of antimicrobials without a prescription in some countries, and increasing availability of online pharmacies transcending country boundaries provides an additional challenge for AMS 4. Fundamentally, AMS is lagging behind the advances made in health service delivery and patient behaviours by remaining sector-based. It is even important that where resources are scarce the approaches suggested here for integrated models of care be considered at planning stages. So it's really important to think about integration NOW whether planning or evaluating your AMS programme or initiative.

So how can we assess integration of AMS across services and sectors? The general healthcare literature offers a number of theoretical integrated care models, however, AMS is not explicit in any of these wider health system integration models.

Using a model first developed for looking at programmes to address infectious diseases (Malaria, TB and HIV), Table 2 sets out a comprehensive framework based on the six facets of critical health system function 5. This framework can be used to assess the extent of integration and identify potential strengths and weaknesses of multi-sectoral AMS.

Facets of critical health systems function	Elements of integration adapted for AMS initiatives
Stewardship and governance	Regulatory mechanism Accountability framework
Financing	Pooling of funds Provider payment methods Funding source Cross-programme use of funds
Planning	Planning
Service delivery	Human resources for delivery of AMS Physical infrastructure for laboratory testing
Monitoring and evaluation	Data collection and recording Data analysis Reporting systems Performance management system
Demand generation	Financial incentives Information, education and communication
<p><b>Definition of full and partial integration:</b></p> <p>An element is classed as <b>fully or predominantly integrated (green)</b> across the health system if it is exclusively under the management and control of the general healthcare system. An element is classed as <b>partially integrated (amber)</b> if some but not all cases are managed and controlled both by the general healthcare system and a specific programme-related structure. A dimension is <b>not integrated</b> if it is exclusively under the management and control of a specific programme-related structure (which is distinct from the general healthcare system).</p>	

Extension activity E: This activity is recommended for the AMS (or equivalent) committee or working group at organisational or regional level. Using a RAG rating (red - not integrated; amber - partially integrated; green - fully integrated) assess the extent to which your programme is integrated using the definitions provided in above Table 2).

## TOOLKIT RESOURCE

### EXCEL DOCUMENT



You may like to refer to the worked examples in the literature or use the template provided here

# CHAPTER 7

 AUTHOR: **NICK BROWN**

## THE ROLE OF LABORATORY AND RAPID DIAGNOSTICS/ BIO-MARKERS IN STEWARDSHIP

### THE AIM OF THIS CHAPTER IS TO:

Define empirical antimicrobial prescribing and discuss its limitations.

Describe the core reasons for why it is used.

Review the time points in the patient's overall treatment where diagnostic test results can lead to interventions to improve antimicrobial therapy.

Describe how the laboratory can contribute to antimicrobial stewardship initiatives.

Introduce some newer technologies within the laboratory and show how they are changing the way in which diagnostic tests are performed.

Describe the critical role of the clinician in making best use of diagnostic tests.

Describe acute phase proteins as bio-markers for infection and their use in antimicrobial stewardship.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Explain what empirical prescribing is and understand why it is currently part of normal day-to-day practice.
- Understand why empirical prescribing is not ideal and why improvement in the diagnosis of infection are needed
- Explain how the laboratory can support antimicrobial stewardship activities
- Explain why the clinician needs to understand optimal use of diagnostic tests and how the results could otherwise be misleading
- Understand what rapid bio-marker tests are (e.g. C-reactive protein and procalcitonin) and how their use could help support antimicrobial prescribing decisions

### INTRODUCTION TO EMPIRICAL PRESCRIBING

In most healthcare settings, and especially in the community, the majority of people with infections are treated without the use of any diagnostic tests. That is, a clinical diagnosis is made using the patient history and physical examination and a treatment, which may include an antimicrobial agent, is prescribed on the basis of a clinical judgement as to the cause of the infection and what treatment it will respond to. Thus, a mild purulent skin infection is assumed to be most likely either staphylococcal or streptococcal and an appropriate antibiotic, such as flucloxacillin, or similar, is prescribed. This is empirical, or 'best guess' prescribing.

For many decades, such practice has worked well and this is particularly the case where the clinical diagnosis is easy and reliable and susceptibility to the prescribed antimicrobial agents is very high. Clearly, it is the only practical option where there is no easy access to laboratory tests or where the costs of testing are not affordable. However, response to empirical treatment cannot be guaranteed. Key risks associated with this practice include:

OVER- OR UNNECESSARY TREATMENT OF CONDITIONS WHERE THE CLINICAL FEATURES OF BACTERIAL AND VIRAL INFECTIONS ARE SIMILAR (E.G. SORE THROAT, COUGH, EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE, OTITIS MEDIA)

PRESCRIPTION OF ANTIBIOTICS WITHOUT KNOWING WHAT ORGANISM IS CAUSING THE INFECTION, LEADING TO UNNECESSARILY BROAD SPECTRUM TREATMENT TO COVER ALL POSSIBILITIES AND A LIKELIHOOD OF TREATMENT FAILURE IF THE WRONG ORGANISM IS TARGETED

PRESCRIPTION OF ANTIBIOTICS WITHOUT KNOWING WHETHER-OR-NOT THE ORGANISM CAUSING THE INFECTION IS SENSITIVE OR RESISTANT TO THAT ANTIBIOTIC WITH AN EVER INCREASING RISK THAT IT IS RESISTANT

INCREASED LIKELIHOOD THAT THE PATIENT WILL RETURN FOR ANOTHER CONSULTATION AND A FURTHER EMPIRICAL ANTIBIOTIC PRESCRIPTION WILL BE GIVEN

Therefore, it is possible that some patients with persistent or recurrent infections could be treated with repeated courses of antibiotics without the prescriber ever having a confirmed diagnosis.

The situation is slightly different for hospital in-patients, in that there is easier access to laboratory diagnostic tests. A patient with a suspected infection is more likely to have a range of tests performed and these will include general investigations (such as blood count, electrolytes) as well as specific tests to diagnose the cause of infection (for example, by culture of urine in suspected cystitis, or blood cultures in the more unwell patient with suspected sepsis). Indeed, it has been stated that approximately 70% clinical diagnoses in hospital are made on the basis of a pathology test. However, the turnaround time for most of these specific tests is too long to be of immediate practical help for the clinician and this is because most tests for bacterial infection still rely on prolonged incubation to grow bacteria on culture media. Serological tests rely on the detection of antibodies to the infection and these may not appear for at least 10-14 days after the onset of the infection. Molecular tests,

such as those using the polymerase chain reaction (PCR), are more useful for viral infections than bacterial infections, although this is changing. Therefore, even in hospital, most antibiotic prescribing remains empirical. It is more likely in hospital than in the community that a confirmed diagnosis will be made eventually, even if this takes several days, but this is too late to influence the initial antibiotic prescription.

The issue of empiric antibiotic prescribing was a major component of the report from the recent UK Antimicrobial Resistance (AMR) Review, chaired by Lord O'Neill. Here, one recommendation was that diagnostic tests should be developed to enable the correct treatment to be moved earlier in the patient pathway and ultimately aim for a situation where the initial prescription is an informed prescription. That is, treatment of what the patient has, rather than what they might have. Some of the tests we need to achieve this would be described as disruptive technologies. This term is used to describe new developments that require a new way of thinking about or managing a process.

A variety of different initiatives have been launched to help facilitate this. The Longitude Prize is a £10m prize fund that will reward the development of a rapid, affordable and easy to use point-of-care (point-of-care) diagnostic test that will help improve the immediate diagnosis of infection (and thereby conserve antibiotics and reduce the selection pressure on the emergence and spread of resistance) (<https://longitudeprize.org/>).

## THE USE OF CURRENTLY AVAILABLE DIAGNOSTIC TESTS TO INFORM THE OPTIMAL USE OF ANTIBIOTICS

While initiatives such as the O'Neill review will influence the development of new diagnostic tests, even now, various laboratory methodological strategies to improve the utility of current tests have been, or are being introduced.

The laboratory can have a key role in the identification and management of patients with infection and therefore help guide antimicrobial prescribing. This can facilitate antibiotic stewardship initiatives at a number of different time points in the patient management pathway.

### Initial patient consultation


Diagnostic tests can be valuable to help rule in or rule out the presence of an infection at the first point of contact with a clinician. Ruling out infection may be as useful, and sometimes more useful, than ruling it in. Tests with a high negative predictive value can be used to identify patients who do not need treatment with an antibiotic or who may be suitable for a delayed treatment prescription. An example would be the use of a urine dipstick test in a young woman with symptoms of possible urinary tract infection, but who was not particularly unwell.

The ability to distinguish between viral and bacterial infection is also useful, since patients with viral infections may be able to be managed without antibiotics. An example would be the use of point-of-care molecular tests for respiratory tract viruses, such as influenza, respiratory syncytial virus (RSV) and rhinovirus.

Ideally, diagnostic tests used in this situation should have a very quick turnaround time (optimally available at point-of-care), since a result is needed in a very short time frame to be able to influence the immediate treatment decision. However, currently, many of the available tests have problems with test performance (sensitivity, specificity, negative- and positive-predictive values) and cost. These are discussed further below.


## TOOLKIT RESOURCE

### SITE LINK


 **Rapid diagnostics: stopping unnecessary use of antibiotics. The Review on Antimicrobial Resistance. Chaired by Jim O'Neill. October 2015.**  
<https://amr-review.org/>

The complete review is made up of several reports, many of which will be of interest to the participant. However, here we concentrate particularly on the report relating to the use of diagnostic tests:

### PDF ARTICLE

 This report provides an overview of how diagnostics can play an important role in the fight against antimicrobial resistance, by reducing unnecessary use. It addresses how we can improve innovation as well as encourage the uptake of diagnostics.

### PDF ARTICLE

 A Pluddemann, I Onakpoya, S Harrison, B Shinkins, B Shinkins, A Tompson, R Davis, CP Price and C Heneghan. Position Paper on Anti-Microbial Resistance Diagnostics – Centre for Evidence-Based Medicine, University of Oxford June 2015.

### Antibiotic treatment review at 48-72 hours

If diagnostic tests are performed at the time of the initial presentation of the patient, it is likely that results will begin to be available after 48-72 hours, depending on the investigations performed. While this is too late to alter the immediate treatment, it does offer the opportunity for the treatment to be reviewed and amended as appropriate. This is the basis for the 'Start Smart then Focus' strategy promoted in the UK ([https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/417032/Start\\_Smart\\_Then\\_Focus\\_FINAL.PDF](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/417032/Start_Smart_Then_Focus_FINAL.PDF)). The initiation of prompt antibiotic therapy in a septic patient is recognition that delay is associated with a poor outcome in sepsis. However, this therapy can then be tailored to the specific microorganism identified and its antibiotic susceptibility. Various options for treatment modifications at 48-72 h are available (for example, discontinue antibiotics, continue the same antibiotics, review the dose or route of administration, or de-escalate to a narrower spectrum agent).

## End of treatment

Many patients are currently treated with defined courses of antibiotics (for example, 5 days, 7 days, 10-14 days), but there is little evidence to support the choice of treatment duration in most situations and these durations are often arbitrary. Indicators of the inflammatory or acute phase response, such as the C-reactive protein and procalcitonin, have been proposed as tests that could be used to provide assurance that a patient has recovered from an infection and that antimicrobial therapy can be stopped. This is elaborated further below.

## THE ROLE OF THE LABORATORY IN STEWARDSHIP

The microbiology laboratory can have a significant role in facilitating many of the activities that optimise antimicrobial use. Although the structure of the antimicrobial stewardship team itself may vary in detail from one country to another, often a medical microbiologist is a key member and their close day-to-day working relationship with the laboratory means that many activities are intertwined. These include procedures for reporting significant results, giving advice about best use of the laboratory, recommending antimicrobial treatment regimens, developing guidelines and participation in audit. The laboratory also participates in surveillance, both at a local and higher level. This aids the development of local resistance profiles to guide the choice of empirical therapy and also feeds into regional, national and international surveillance.

Laboratories can optimise the information that they provide to clinical teams in a number of ways. Firstly, they can assure the quality of the results they provide by complying with national and international guidance on laboratory test methods. In the UK, these include the Standard Methods for Investigation. There are laboratory accreditation requirements, such as those run by the UK Accreditation Service (UKAS) designed to assess compliance with the ISO15189 standard. These may be mandatory or form part of the healthcare commissioning process. Laboratories also participate in internal and external quality assurance schemes.

Considering the specific areas of interest for stewardship, laboratories can often optimise their service by liaising with their users to tailor what they do to meet the demands of the clinical service. Timeliness of reporting is one simple example of this. Ideally, reports should be available to clinicians at the time that they want them to make clinical decisions. Often, relatively straight forward enhancements to the laboratory service can make a large difference. An example would be extended laboratory opening hours, 7 day per week working and reporting to meet deadlines of ward rounds or patient review.

These issues could all be considered to be general best practice to enhance the output of the laboratory and ensure that it is

of maximum benefit to patient care. There are also specific technological advances that aim to improve the service further.

Microbiology laboratories have only recently been automated to any significant extent. While analysers have been widely used for specific indications for many years, for example, for serological analysis or incubating blood cultures, routine bacterial culture is still a very manual process requiring a relatively large number of staff compared to some other laboratory specialties. However, in the past decade, there have been major advances in microbiology automation, which are now in widespread use. While many of these developments have been designed to enable higher laboratory throughput of specimens at lower cost, they can also have positive benefit for stewardship activities. As well as improving laboratory turnaround times, automation can provide greater consistency of culture between samples and, in some cases, improve the yield of organisms from cultured samples.

Newer technologies, such as matrix assisted laser desorption ionisation time of flight (MALDI TOF) mass spectroscopy, have been utilised in the last few years to identify bacteria to species level much more rapidly and cheaply than was possible before. It has become possible to identify isolates from blood cultures within hours of the cultures signalling positive, which means that tailored antimicrobial therapy can be given.

Antimicrobial susceptibility testing is a key area of laboratory practice that has a major impact on antibiotic prescribing. The intention of susceptibility testing is to give the clinician an indication as to whether-or-not an infection is likely to respond to a specific antibiotic or not. This is often done by attributing a label of 'sensitive' or 'resistant' to the report. As knowledge of antimicrobial resistance and its detection has become more sophisticated, the information that is given has become much more reliable. The cut off, or breakpoint, between sensitive and resistant can now be calculated scientifically when compared to the somewhat arbitrary thresholds that were used historically. Much work has been done by the two major scientific bodies in this area, the Committee for Laboratory Science and Investigation (CLSI) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST), to harmonise breakpoints and make sure that laboratory susceptibility testing is more informed and consistent than previously.

There are automated susceptibility testing methods in use in many laboratories, such as provided by VITEK™ or Phoenix™ machines, amongst others. These are able to give the species identification of the bacterium as well as the minimum inhibitory concentration (MIC) for a variety of different antimicrobials. Again, these are useful for standardisation of reporting.

They are, however, more expensive than some other testing methods.

Restrictive reporting of the results of antimicrobial susceptibility testing is one stewardship activity that varies from laboratory to laboratory and, perhaps, may be underused. Within the UK, it is common practice for the reporting of susceptibility results to be limited to those antibiotics that the medical microbiologist wants the clinician to prescribe. That is, results for agents that fall outside the local prescribing formulary or are inappropriate for the particular infection can be hidden from view. Such a restrictive reporting practice has been shown to influence clinician prescribing behaviour. Indeed, even the order in which the antibiotic susceptibility results are presented can change prescribing, with those agents put at the top of the list more likely to be prescribed.

An important growth area is the use of whole genome sequencing. This has been made possible by the development of new technologies that can provide sequence data in a timescale that is clinically useful and at an ever decreasing cost. Sequencing has been used to create a genetic 'fingerprint' of organisms for epidemiological purposes. The sequence may also provide species identification information and, usefully, also indicate the presence or absence of genes encoding resistance mechanisms. A recent EUCAST consultation has discussed the uses and current limitations of this information. However, for some infections, most notably tuberculosis, sequencing is being used routinely to guide treatment options and has the capability to provide information much more quickly than traditional mycobacterial culture techniques.

## ROLE OF THE CLINICIAN IN LABORATORY TESTING

The value of a laboratory test is dependent on several factors, including the performance characteristics of the test (sensitivity, specificity, positive- and negative-predictive value). Some factors are influenced by the clinician requesting the test, such as how the sample has been taken and then transported to the laboratory and what clinical information is provided with the request. However, how the test is used in clinical practice is also key. In the wrong setting, a test result may not only be unreliable, but often frankly misleading. Clearly, in these circumstances there may be an adverse impact on antimicrobial prescribing. It is crucial that clinicians understand these limitations of the tests they order and help the laboratory perform the correct investigations and produce a meaningful result.

Many pathogenic microorganisms may be found as part of the normal commensal flora. Isolation of these organisms may not necessarily indicate infection. Likewise, many body sites have

## TOOLKIT RESOURCE

### SITE LINK



UK Standard Methods for Investigation



European Committee on Antimicrobial Susceptibility Testing (EUCAST)

These two websites are examples of guidance for laboratories on how to perform existing diagnostics tests in a standardised manner and to the optimal quality

### PDF ARTICLE



Consultation on Report from the European Committee on Antimicrobial Susceptibility Testing (EUCAST) Subcommittee on the Role of Whole Genome Sequencing (WGS) in Antimicrobial Susceptibility Testing of Bacteria. European Committee on Antimicrobial Susceptibility Testing. 2016

### VIDEOS

Podcasts from the British Society for Antimicrobial Chemotherapy (BSAC) Antimicrobial Resistance Roundtable series 5 Feb 2015 – lectures on diagnostic tests and antimicrobial stewardship by:

Peter Hawkey



WATCH VIDEO

Alex Van Belkum



WATCH VIDEO

### SITE LINK



Examples of educational activities to improve the use of urine dipsticks in the 'To Dip or Not to Dip' initiative

This slide resource aims to educate healthcare professionals on the correct use of urine dipsticks and thereby reduce inappropriate antibiotic prescribing in elderly patients who do not have genuine urine infections



a normal commensal flora and samples sent to the laboratory in the absence of signs or symptoms of infection may be difficult to interpret. Therefore, the clinician must understand the limitations of testing and result interpretation and be able to put these into clinical context rather than simply take a result at face value.

A common mistake is to send a sample for a wide range of diagnostic tests when the likelihood that the patient has the conditions concerned is low. This is particularly the case in the community, where often the pre-test probability that a patient has the condition that is being tested is low. This often means that a positive test result is more likely to be a false-positive result than a genuine result. Again, the implication of this is that a patient may be given an incorrect diagnosis and be treated for something that they do not have. Equally important, they are not treated for whatever it is that they do have.

A blood culture can easily be contaminated with skin organisms at the time that the sample is being taken. Historically, up to 10% blood cultures were contaminated in this way, although with better aseptic sampling techniques, contamination rates can be 3% or lower – much improved, but still significant. Patients with contaminated blood cultures are often commenced on unnecessary antimicrobial therapy while the issue is being investigated. They may also have other investigations to investigate an infection that they haven't got.

An important example of a laboratory test being interpreted incorrectly is the overuse of urine dipsticks in the diagnosis of urinary tract infection. These are widely seen as a simple test that can be used at point-of-care to detect patients with urinary tract infections that require antibiotic treatment. However, their value depends critically on the patient group in which they are being used. In the elderly, asymptomatic bacteriuria is very common and a positive dipstick test does not necessarily mean that the patient needs treatment. Overall, this may represent one of the largest areas of antibiotic overtreatment and quality improvement programmes to educate users about appropriate use and interpretation of dipsticks are part of many stewardship activities. Conversely, in very young infants, not only are good urine samples more difficult to obtain, but dipsticks may lack the sensitivity to detect all urine infections.

## ACUTE PHASE PROTEINS AND OTHER BIOMARKERS

For many years it has been recognised that bacterial sepsis is accompanied by an inflammatory response, the acute phase response, and that various biomarkers increase in concentration in the blood as a result. At its most general level, an increase in fibrinogen levels in blood increases plasma viscosity and this can be measured easily and cheaply as the erythrocyte sedimentation rate (ESR). However, although the ESR is a useful

marker of various inflammatory conditions, it is not specific for infection and is slow to respond to an infective stimulus.

Many other indicators of the acute phase response have been described and these include various cytokines and plasma proteins, including albumin and ferritin. However, most of these have not been shown to be clinically useful in the acute management of infection.

C reactive protein (CRP) is produced by the liver in response to the release of pro-inflammatory cytokines. It rises and falls more quickly than ESR and therefore can be used to indicate the onset of an inflammatory process in the body and monitor its progress. It is not specific to infection, but can be useful to differentiate between a bacterial and a viral infection and therefore has potential to be used to guide initiation of antimicrobial therapy.

Procalcitonin (PCT), a precursor of calcitonin, is synthesised by various tissues in response to inflammation and appears to be more specific for bacterial infection. Hence there has been considerable interest in its potential use for antimicrobial stewardship. Specific areas that have been investigated include the use of PCT as a guide to the diagnosis of sepsis and the duration of antimicrobial therapy, predominantly in the critical care setting.

Many factors influence the value of biomarkers in antimicrobial stewardship. Logistic issues, such as transport of samples to wherever the test is being performed, play a big part, as they are critical to the turnaround time. Whatever test is performed, if it not available at the time a prescribing decision is being made, it cannot be clinically useful. This is why point-of-care testing is so appealing as a concept. However, point-of-care testing can often be more expensive than testing on a larger scale in a central laboratory and, given that the same standardisation issues apply to point-of-care testing as to laboratory testing, there can be problems with training, quality assurance and hence test performance. Nevertheless, NICE guidance for the management of lower respiratory tract infection in the community recommends the use of CRP as a point-of-care test in the GP surgery. Fundamental to the success or failure of biomarkers in stewardship are data to demonstrate that patient outcomes are improved in order to justify the increased cost.

## TOOLKIT RESOURCE

### SITE LINK



Podcast from the Federation of Infection Societies (FIS) annual conference '2013 – Action on Infection' – Matthew Dryden lecture on diagnostics in stewardship and procalcitonin (PCT) 'Does smarter testing improve patient outcomes?'

# CHAPTER 8

▶ AUTHORS: **ALASDAIR MACGOWAN & MELISSA BAXTER**

## OPTIMISING STEWARDSHIP THROUGH BETTER PK-PD

### THE AIM OF THIS CHAPTER IS TO:

The aim of this chapter is to provide a basic understanding of the principles of pharmacokinetics and pharmacodynamics underpinning antimicrobial use. Such an understanding will allow optimal use of antimicrobials for individual patients and in so doing, aid in antimicrobial stewardship by optimizing clinical outcomes, reducing antimicrobial resistance and adverse events.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Become familiar with terms pertaining to PK-PD
- Appreciate the complexities of PK-PD of antibiotics.
- Appreciate the clinical circumstances that might demand altered antimicrobial dosing/regimens
- Understand the rationale behind bespoke dosing regimens.
- Appreciate the benefits to antimicrobial stewardship of understanding drug exposure response relationships and optimizing PK-PD

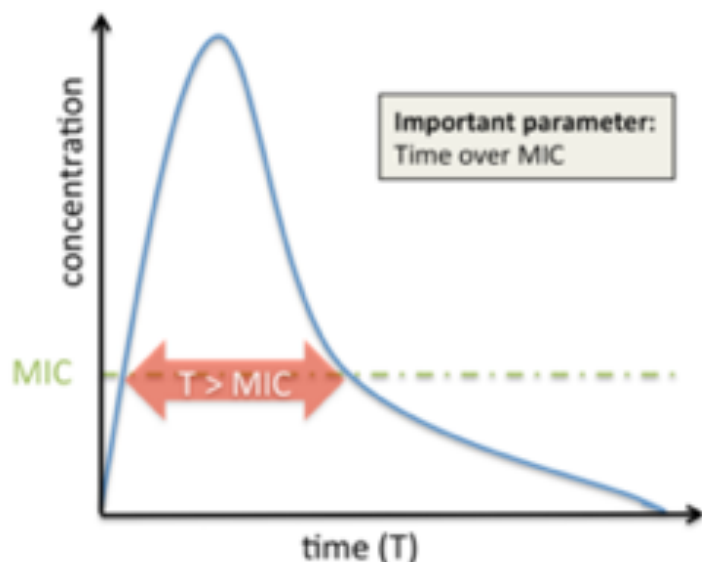
### ▶ PHARMACOKINETICS AND PHARMACODYNAMICS (PK-PD)

Definitions of pharmacokinetic and pharmacodynamic properties

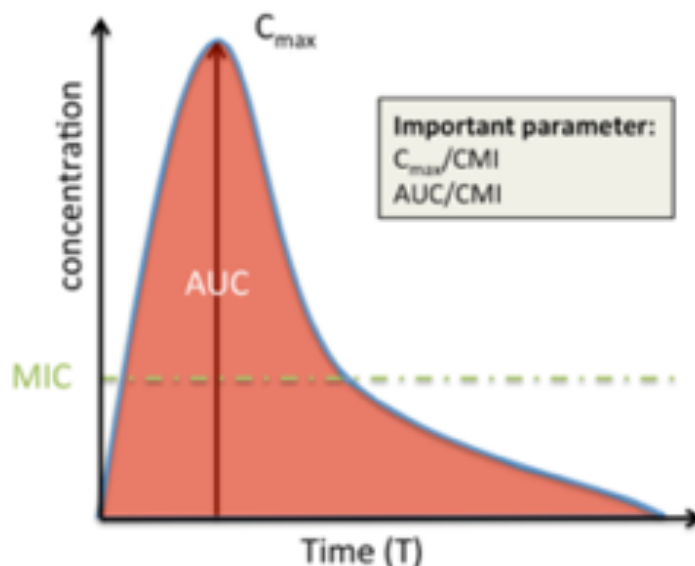
PK	Pharmacokinetics - How a drug moves through the body
PD	Pharmacodynamics- concentration effect relationship - the effect may be related to the infecting agent (kill or resistance) or host (adverse events)
MIC	Minimum inhibitory concentration
MBC	Minimum bactericidal concentration
Cmax	Peak antibiotic concentration
AUC	Area under the plasma concentration curve
Concentration dependent killing	Greater killing as the ratio of drug concentration to MIC increases in the therapeutic range
Time dependent killing	Effect depends on duration unbound drug is at concentrations exceeding the MIC
Volume of distribution	Virtual space into which a drug distributes assuming uniform concentrations
Bacteriostatic	Inhibits microbial growth and replication
Bacteriocidal	Causes bacterial death
Post antibiotic effect (PAE)	Maintained suppression of bacterial growth following exposure to an antibiotic

ASPECTS OF PK-PD

Time dependent antibiotics  
(eg  $\beta$ -lactams)



Concentration dependent antibiotics  
(eg aminoglycosides)



MIC: minimum inhibitory concentration  
 $C_{max}$ : peak concentration  
 AUC: area under the curve

PHARMACODYNAMIC PARAMETERS PREDICTIVE OF OUTCOME

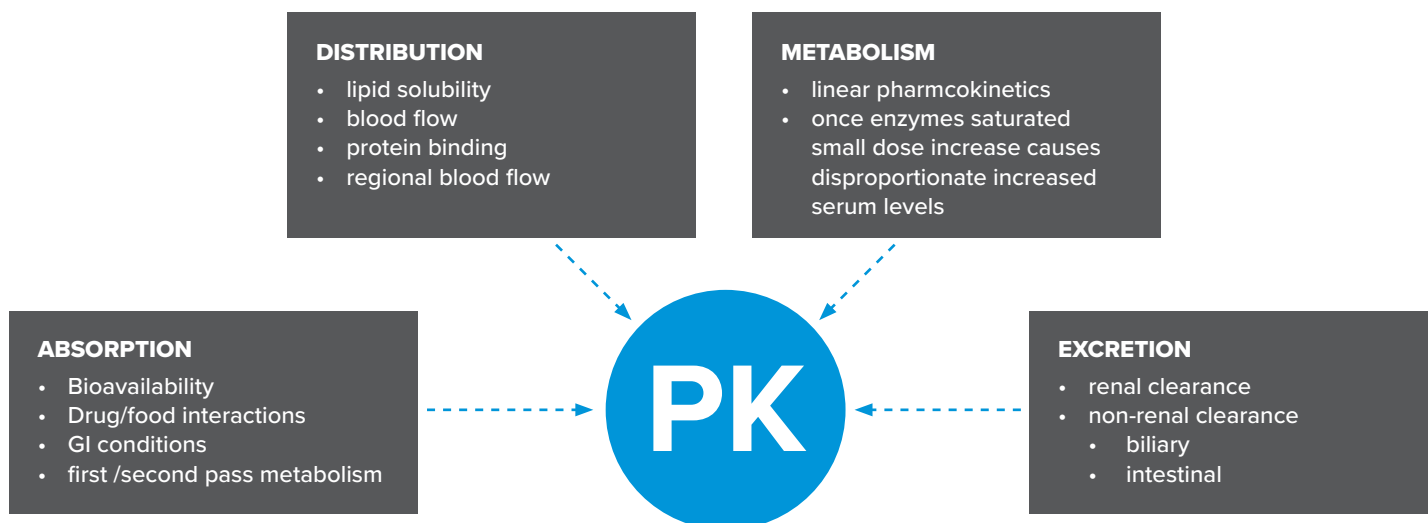
$T > MIC$	Duration of time drug concentration is above the MIC
$C_{max}:MIC$	Ratio of maximal drug concentration to MIC
$AUC_{0-24}:MIC$	Ratio of 24 hour area under the plasma concentration time curve to MIC

COMMONLY USED ANTIMICROBIAL PHARMACODYNAMIC PARAMETERS

Antimicrobials differ in their pharmacokinetic and pharmacodynamic (PK-PD) behaviour. The PK-PD measure that correlates with efficacy depends on the bactericidal activity and duration of persistent effects of the agent. For time dependent agents, the rate of bacterial killing is maximised at a low multiple of the MIC and achieving higher concentrations does not result in greater killing. For concentration dependent agents there is greater killing as the ratio of  $C_{max}: MIC$  increases within pharmacologically relevant concentrations. Altering the dose primarily affects  $C_{max}: MIC$  and  $AUC: MIC$ , whereas altering the

dosing interval affects AUC: MIC and  $T>MIC$ . For concentration dependent agents an increase in volume of distribution will reduce the ability for a standard dose to achieve a high  $C_{max}$ . Hydrophilic agents (beta-lactams, glycopeptides, aminoglycosides) are unable to passively diffuse through the cytoplasmic membrane and are inactive against intracellular organisms. They have a limited extracellular distribution and are often excreted renally. Conversely lipophilic agents (macrolides, tetracyclines, fluoroquinolones) freely cross membranes and therefore have activity against intracellular organisms, wide distribution, and intracellular accumulation and often undergo hepatic metabolism.

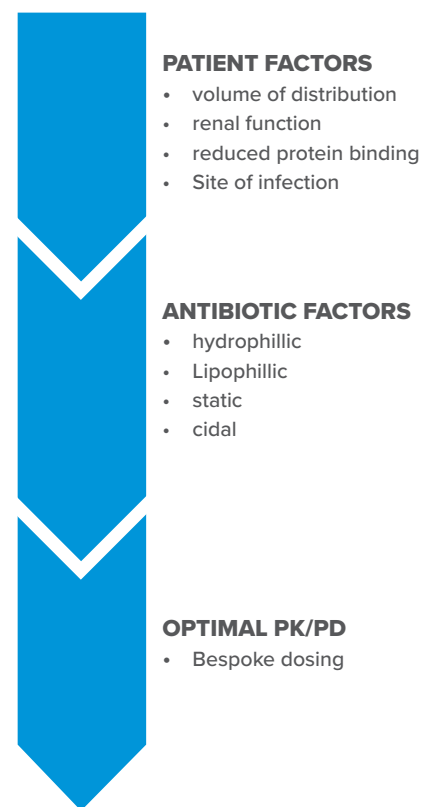
In setting a susceptibility breakpoint, resistance mechanisms, site of infection and dosing regimen must be considered. Furthermore, serum concentrations may not absolutely predict clinical outcome - the concentrations at the site of infection may be more important.



**> WHEN IS PK/PD CLINICALLY RELEVANT?**

	Potential altered PK/PD	Example
Obesity	Reduced tissue penetration	Quinolones
	Shorter mean $T_{1/2}$ *	Vancomycin
	Increased Vd**	Aminoglycosides
	Increased clearance	Aminoglycosides
Renal insufficiency	Decreased clearance	Aminoglycosides
Neonates	Decreased clearance	Aminoglycosides Glycopeptides
Children	Increased clearance	Aminoglycosides
Critical illness	Increased Vd	Aminoglycosides Beta lactams Glycopeptides Colistin
	Increased clearance	Beta lactams
Pregnancy	Increased clearance	Aminoglycosides Cefuroxime
	Increased Vd	Hydrophilic agents
Cystic fibrosis	Increased clearance	Aminoglycosides

\* $T_{1/2}$  half life, \*\*Vd volume of distribution)



CLASS	EXAMPLE	EFFECT	DISTRIBUTION	EXCRETION	PRIMARY PD PARAMETER	PAE	TDM
Beta Lactams	Amoxicillin	Bactericidal	Low protein binding and hydrophilic	Renal	T>MIC	Short or no PAE	Not routine
Glycopeptides	Vancomycin	Bactericidal	Hydrophilic	Renal	AUC:MIC	Short PAE	Recommended for all patients
Aminoglycosides	Gentamicin	Bactericidal	Hydrophilic	Renal	C <sub>MAX</sub> :MIC & AUC:MIC	Significant	Recommended for all patients
Fluoroquinolones	Ciprofloxacin	Bactericidal	Lipophilic wide distribution	Renal & hepatobiliary	C <sub>MAX</sub> :MIC & AUC:MIC	Significant	Not recommended
Macrolides	Azithromycin	Bacteriostatic	Lipophilic wide distribution	Hepatobiliary	T>MIC & AUC:MIC	Significant	Not recommended
Tetracyclines	Doxycycline	Bacteriostatic	Lipophilic wide distribution	Hepatobiliary	AUC:MIC	Significant	Not recommended
Lincosamide	Clindamycin	Bacteriostatic	Lipophilic wide distribution	Hepatobiliary	AUC:MIC	Demonstrated in <i>S.aureus</i>	Not recommended
Oxazolidinone	Linezolid	Bacteriostatic	Lipophilic wide distribution	Renal	AUC:MIC	Short	CF, ESRF, neonates, burns, MIC >2mg/l interacting meds
Lipopeptide	Daptomycin	Bactericidal	Highly protein bound hydrophilic	Renal	C <sub>MAX</sub> :MIC & AUC:MIC	Significant	dosing >6mg/kg, renal impairment
Polymyxin	Colistin (colistimethate sodium)	Bactericidal	Hydrophilic and lipophilic properties	Renal	AUC:MIC	Significant	Recommended for all patients

## CLINICAL APPLICATION OF PK/PD IN SPECIAL CIRCUMSTANCES

### Critical illness

Multi-organ failure can result in alterations to the absorption, distribution, metabolism and excretion of a drug. Under dosing is associated with insufficient treatment and increased risk of resistance, and overdosing with toxicity.

Alterations in protein binding, fluid shifts into the interstitium and pH affect drug distribution. These are most relevant for hydrophilic drugs that have a relatively low Vd. Similar concentration-time profiles are observed with lipophilic agents in critically ill and non-critically ill patients.

With respect to protein binding, only the unbound portion is active. Higher proportions of unbound drug due to low serum protein concentrations result in temporarily high drug concentrations but as hypoalbuminaemia is associated with

increased Vd, the free drug is diluted over the total body water. In severe hypoalbuminaemic states increased loading and maintenance doses may be necessary when using highly bound hydrophilic antibiotics.

Augmented renal clearance risks subtherapeutic concentrations with time dependent antimicrobials. Where patients have acute kidney injury the impact of altered PK depends on the proportion of antimicrobial that is renally excreted. In general it is better to prolong the dosing interval for concentration dependent agents, while maintaining an unmodified dose to maximize C<sub>max</sub>: MIC: for time dependent agents dose reduction while maintaining the dosing interval maximizes T>MIC.

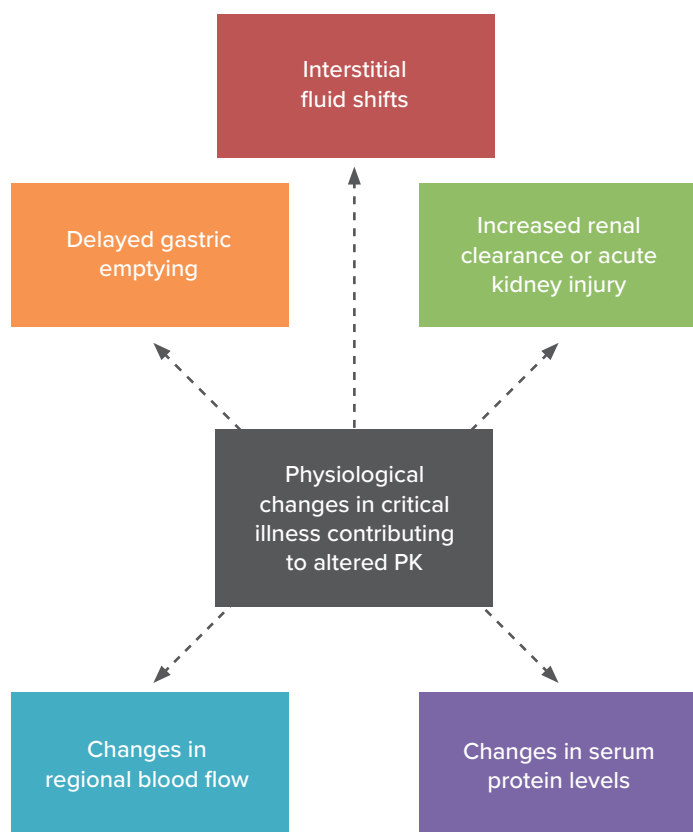
### Ventilator associated pneumonia (VAP)

With VAP there can be a large microbial load resulting in a population of resistant organisms present on initiation of treatment. Killing the susceptible population can allow for

amplification of the non-susceptible sub population and emergence of resistance during treatment. Considering drug exposure at the site of infection, it is suggested that optimal pharmacodynamic exposures in the epithelial lining fluid (ELF) are a better predictor of appropriate pneumonia treatment for extracellular pathogens than plasma. This is however unvalidated by clinical studies.

**Cerebrospinal fluid (CSF)**

Penetration to the CSF and extracellular space of the brain is dependent on molecular size, lipophilicity, plasma protein binding (only the unbound fraction can freely penetrate). Concentration of antibiotics in the CSF is also dependent on their affinity for transport systems responsible for the removal of toxic compounds from the CNS. Infection of the CNS causes an increase in permeability of the blood-CSF/ Blood-brain barrier and decrease in CSF flow leading to an increase in drug concentrations during inflammation. The most important determinant of efficacy in meningitis is the relationship between antibiotic concentration in the CSF and the MBC of the organism. Intraventricular administration of antibiotics in addition to systemic therapy is used for antimicrobials with poor penetration into the CSF and/or high systemic toxicity such as aminoglycosides, vancomycin and polymyxins.



**Physiological changes in critical illness affecting PK**

**Pregnancy**

Several physiological changes in pregnancy can impact on PK including:

- Increased maternal fat and total body water
- Reduced plasma protein levels
- Delayed gastric emptying
- Increased gastric pH
- Increased cardiac output and renal blood flow
- Altered activity of hepatic metabolizing enzymes.

Serum levels of many drugs are lower in pregnancy largely due to the increased renal clearance and expanded intravascular volume.

Antibiotic	Standard dose	Dose alteration in Pregnancy	FDA category*	Notes
Ceftriaxone	2g Once daily IV (non CNS infection)	Not required	B	
Cefuroxime	750mg TDS IV	Increase dose suggested	B	Lower serum levels and shorter T <sub>1/2</sub>
Metronidazole	4500mg TDS PO	Not required	B	Avoid 1 <sup>st</sup> Trimester
Penicillin V	500mg -1g QDS PO	Shorter dosing interval or increase dose suggested	B	Lower serum levels
Gentamicin	5mg/kg IBW	5mg/kg ABW	C	
Erythromycin	250-500mg QDS	No dose alteration recommended	B	High variability in serum levels
Vancomycin	Dose based on renal function	Monitor TDM	B	

TABLE 2  
Suggested dosing of commonly used antimicrobials in pregnancy based of PKPD

\* FDA categories: A – well controlled studies failed to demonstrate risk in first trimester. B – animal reproduction studies failed to demonstrate risk C – animal reproduction studies have shown an adverse effect on the foetus



**Neonates**

Newborns have drug clearances that differ from children and adults and immature renal function in neonates requires antibiotic dosing adjustment. Aminoglycosides are commonly given neonates, their pharmacokinetic parameters differ among neonates and the gestational age is an important factor in determining variability. Gentamicin has a long T1/2 and large Vd especially in premature infants that increases with sepsis, when the Vd is large a dose of 5 mg/kg is optimal. Clinically, renal function is the most important factor for elimination. Gentamicin trough concentration >2 mg/l is associated with toxicity, and peak <5 mg/l associated with reduced efficacy. Late onset sepsis caused by coagulase negative staphylococci or methicillin resistant Staphylococcus aureus (MRSA) has resulted in an increased administration of vancomycin in neonates. As with gentamicin, vancomycin pharmacokinetics are different in neonates due to higher extracellular fluid volume and limited renal elimination capacity and the vancomycin PK is significantly altered as neonates mature. Risk factors for developing nephrotoxicity related to vancomycin treatment are trough concentrations greater than 10 mg/l, concomitant treatment with an aminoglycoside and treatment beyond 21 days, others include high peak concentrations, high total dose, pre-existing renal failure, and concurrent treatment with amphotericin or furosemide.

As well as increased percentage of fat per kg of bodyweight, obese individuals have a larger absolute lean body mass (LBM), with lean components accounting for 20-40% of excess body weight.

Loading doses are based on Vd, and should be based on ideal body weight (IBW) when the distribution of a drug is restricted to lean tissues. For drugs distributed mostly in lean mass and partly fat tissue a calculation of loading dose should be performed with IBW plus a percentage of EBW and loading dose for drugs equally distributed in fat tissues should be TBW.

Hydrophilic antibiotics distribute well in water but not adipose tissue. As the water content of adipose tissue approximates 30%, the Vd for hydrophilic drugs may be only 0.3 of the Vd in other tissues. This distribution into the water component of adipose tissue may warrant increasing the dose in proportion to the excess body weight using the dosing weight correction factor (DWCF)

Weight measure	Calculation M	Calculation F	Notes
Total (actual) body weight (TBW)	Patient weight in kgs		Dose used for lipophilic agents when renal clearance is normal
IBW (devine formula - surrogate marker of lean body mass)	50 + (2.3 x height in inches over 60")	45 + (2.3 x height in inches over 60")	Several variations on this equation have emerged
Excess body weight	EBW = TBW - IBW		See DWCF
Dosing weight correction factor (DWCF)/ adjusted bodt weight (ABW)	Dosing weight - DWCF (TBW-IBW) + IBW		Corrects for additional water content of adipose tissue - for use with hydrophilic agents, DWCF value varies depending on the agent

TABLE 3  
Definitins of weight measures and suggested use

TOOLKIT RESOURCE

ARTICLES

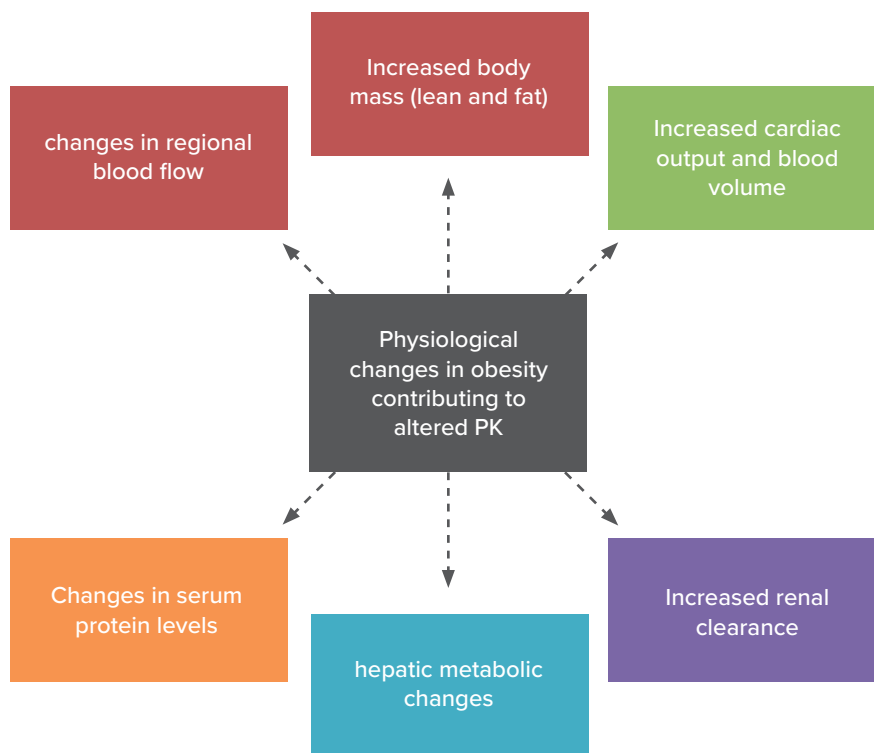
Neonatal TDM and dosing

National Institute for Health and Care Excellence (NICE) (2012) Neonatal infection (early onset): antibiotics for prevention and treatment. NICE clinical guideline CG149

Ku LC, Smith PB. Dosing in neonates: special considerations in physiology and trial design. Pediatric research. 2014. Doi:10.1038/pr.2014.143

**Obesity**

Pathophysiological alterations in obesity can cause changes in PK-PD necessitating weight related dosage adjustments for antimicrobials. Fixed regimens can lead to under dosing or total body weight based dosing to overdosing and toxicity. Blood flow in fat is poor and accounts for 5% of cardiac output compared to 22% in the lean tissue.



**Physiological changes in obesity contributing to altered PK**

Drug	Obesity dosing	Comments
Beta lactams	Consider larger doses	Higher doses may be necessary in obesity to achieve adequate [ ]
Vancomycin	TBW	Reduced $T_{1/2}$ allows more frequent maintenance dosing to avoid large peak [ ] with larger doses and overcome increased clearance
Linezolid	Unchanged	Diminished serum levels in obese patients but clinical cure achieved with standard dosing.
Gentamicin	BNF: IBW 40% addition of EBW (TBW-IBW) to IBW	Early TDM essential
Daptomycin	TBW	Data suggests outcomes similar with IBW dosing but may be MIC and organism specific. TDM recommended
Ciprofloxacin	ABW to achieve adequate tissue penetration	Higher plasma peak [ ] required to give the same tissue penetration in obese vs. non obese.

TABLE 4  
Suggested dose alterations in obesity

## TOOLKIT RESOURCE

## SITE LINKS



UKMI dosing in obesity

## Dosing in Obesity

Wurtz R, Itokazu G, Rodvold K. Antimicrobial dosing in obese patients. *Clin Infect Dis*. 1997;25(1):112–8



Medicines Q &As. How should antibiotics be dosed in Obesity?



Drug dosing in extremes of body weight in critically ill patients. 1st edn (V1.0). 2013

**Burns**

Pharmacokinetics of antibiotics can be significantly altered in burns patients. The factors affecting PK include the area and depth of the burn, presence of sepsis, degree of hydration, serum protein concentrations, age, creatinine clearance and time after injury. In the acute phase of burn injury (lasting approximately 48 hours) altered capillary permeability results in loss of protein rich fluid from the vascular system. Resultant hypovolaemia can lead to reduced cardiac output, tissue hypoperfusion and reduced renal blood flow and function. Beyond 48 hours of injury, the second, hypermetabolic phase is characterized by an increase in cardiac output with and increased blood flow to kidneys and liver. Creatinine clearance may become significantly elevated.

**Renal failure**

Renal function is especially important for hydrophilic antimicrobials that are almost entirely renally excreted, lower doses are needed with impaired renal function.

In patients with moderate to severe chronic kidney disease (CKD) the Vd is increased due to reduced protein binding, increased tissue binding or fluid overload.

Where renal replacement therapy is necessary a variety of methods from peritoneal dialysis, intermittent hemodialysis and continuous renal replacement therapy (CRRT) all vary in efficiency of solute removal.

Access to the peritoneal cavity for dialysis allows for local and systemic drug delivery. As the rate of clearance is low (~10ml/min) peritoneal dialysis does not enhance drug removal to the degree that requires dose modification, therefore recommendations are as for those with eGFR or creatinine clearance <15 ml/min.

The impact of haemodialysis on drug therapy depends on molecular weight, degree of protein binding and Vd of the drug. CRRT is a generic term encompassing various modalities of continuous haemodialysis or haemofiltration commonly used to support critically ill patients with acute or chronic renal failure. Rate of drug clearance during CRRT can be highly variable in critically ill patients.

Following dialysis, supplemental dosing should be considered. Serum trough levels of antibiotics such as gentamicin and vancomycin should be measured immediately after dialysis to determine the need for ongoing doses.

## TOOLKIT RESOURCE

## PDF ARTICLE

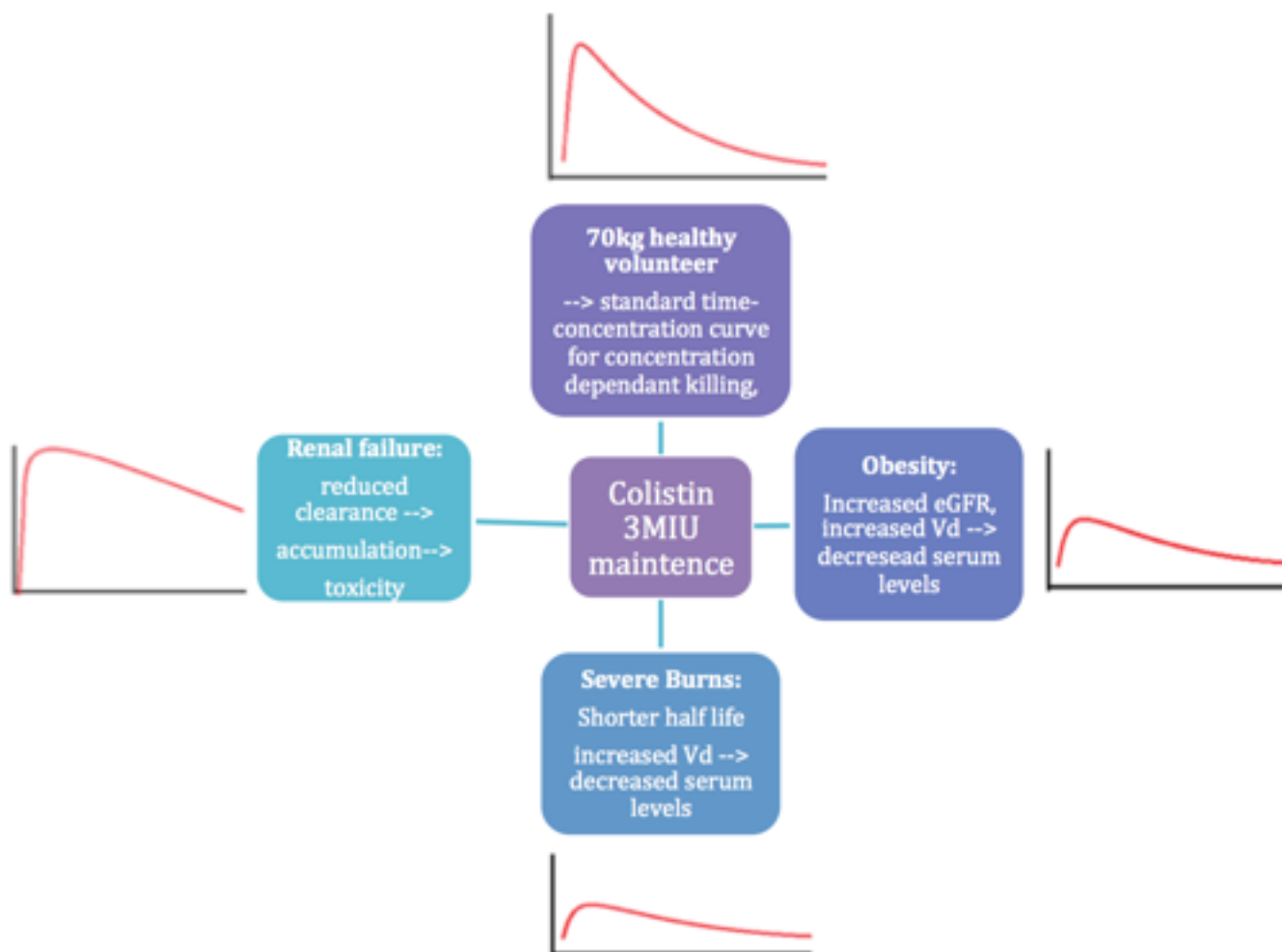
## Dosing in Renal failure

Matzke GR, Aronoff GR, Atkinson Jr AJ, Bennett WM, Decker BS, Eckardt K-U, et al. Drug dosing consideration in patients with acute and chronic kidney disease—a clinical update from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int*. 2011;80:1122–37

**Where can PK/PD be suboptimal? Worked example with Colistin dosing**

The standard dose of colistin (9 Megaunits loading followed by 3 megaunits three times per day maintenance) is administered. For each scenario the effect on the time-concentration curve is demonstrated.

The emergence of multi drug resistant Gram-negative bacteria has led to a revival of the polymyxins. Polymyxin E – colistin is used frequently as salvage therapy for nosocomial infections caused by *Pseudomonas aeruginosa*, *Acinetobacter* sp and carbapenemase producing Enterobacteriaceae. Use of colistin had largely been abandoned due to frequent toxicity, namely dose dependent nephrotoxicity and neurotoxicity. Colistin exists in two forms; colistin sulfate used for bowel decontamination and topical treatment and the intravenous form of the prodrug colistimethate sodium.



**> INTERACTIVE CASE STUDY**

A 58-year-old female is transferred to your hospital following a road traffic accident whilst holidaying in Turkey. Amongst her injuries she sustained a fractured femur that required insertion of a femoral nail. You are contacted by the clinical team as the patient has been spiking temperatures above 38°C for several days with raised inflammatory markers CRP 130mg/L and WCC 15.6 x10<sup>9</sup>. She has deteriorated today and is now rigoring, tachycardic and requiring fluid boluses to maintain her blood pressure. The wound appears erythematous and is leaking serous fluid. Empiric meropenem 1g tds is commenced. The following day blood cultures are positive with Gram-negative rods on microscopy. Swabs of the surgical site have provisionally isolated *Klebsiella pneumoniae*.

**What are your immediate actions?**

1. Inform the surgeons that washout is necessary to control sepsis.
2. Check CPE screen results.
3. Infection control precautions as CPE positive until proven otherwise.

4. Review the patients clinical progress.
5. All of the above

**> SEE ANSWER**

The following day the blood culture report reads as follows:  
Isolated after 27 hours incubation in Aerobic and anaerobic bottles

*Klebsiella pneumoniae*:

Amikacin	R
Aztreonam	R
Ceftriaxone	R
Ceftazidime	R
Ciprofloxacin	R

Co-amoxiclav	R
Cotrimoxazole	R
Ertapenem	R
Gentamicin	R
Meropenem	R
Piperacillin/tazobactam	R

ESBL: Detected

Meropenem, ertapenem, aztreonam, tigecycline, colistin, fosfomycin MIC to follow

Disc testing for carbapenemase production to follow

**Which of the following PK-PD factors will influence your recommended treatment?**

1. Meropenem and Ertapenem MIC
2. Renal function
3. Site of infection
4. Allergies
5. Weight



Despite CPEs being able to hydrolyse carbapenems outcomes are improved when a carbapenem is added to the regimen. Renal function must be taken into account as large doses of carbapenems are indicated given the higher MICs of CPEs as well as nephrotoxic agents such as colistin and aminoglycosides being used in combination. Site of infection is of importance as it is necessary to understand how likely it is to achieve therapeutic antimicrobial levels in certain compartments, and here the aim is to penetrate bone. Patient weight is also an important factor in determining the ability to attain high antimicrobial levels in the target area. Allergy is important for all antimicrobial prescriptions but is not a PK or PD parameter.

Further sensitivities are available:

Meropenem MIC 8 mg/l	R
Ertapenem MIC 32mg/l	R
Aztreonam MIC 16mg/l	R
Tigecycline MIC 0.12mg/l	S
Fosfomycin MIC 1024 mg/l	R
Colistin MIC 0.25 mg/l	S

Disc testing: Carbapenemase detected.

Referred to reference laboratory for confirmation of mechanism.

**Which treatment options should be considered?**

1. Meropenem monotherapy
2. Meropenem plus colistin
3. Meropenem plus aztreonam
4. Colistin monotherapy
5. Meropenem plus fosfomycin plus colistin



The optimal treatment regimen for CPE infection is yet to be defined. In general combination therapy is preferred and outcomes are improved when a carbapenem is added to the regimen. Colistin monotherapy has been associated with treatment failure. Aztreonam retains activity against some carbapenemase enzymes (metallobeta-lactamases) but it is inactivated by the ESBL, depending on the type of carbapenemase produced meropenem and aztreonam may be a useful combination in that the ESBL can be inhibited by meropenem and the carbapenemase by aztreonam. Fosfomycin has shown activity against KPC producing enterobacteriaceae but its use has been associated with relapse and emergence of resistance amongst susceptible isolates in vivo.

**CONTINUOUS INFUSIONS OF BETA-LACTAM ANTIBIOTICS**

In attempt to mediate the risk of subtherapeutic serum levels and potential treatment failure with antimicrobials time dependent antimicrobials there is debate over whether these should be administered as standard doses, as an intermittent bolus or as continuous infusion and is focused on beta lactams. It is suggested that therapeutic targets for continuous infusion therapy should be a steady state concentration  $C_{ss}$  that is 4x the MIC.

Where bacteria have low MICs and are in the susceptible range there may be little benefit to continuous infusion over intermittent bolus, however the latter may fail with pathogens with a higher MIC. Where there is renal impairment the utility of continuous infusion is less relevant as beta lactam clearance will be impaired. Several meta-analyses and double blinded randomized controlled trials have reported results trending towards improved clinical outcomes but the lack of standardisation amongst studies with regards to dosing, PK/PD parameters, patient population has made the therapeutic PD benefit less clear.

## THERAPEUTIC DRUG MONITORING (TDM)

TDM is used to optimise antibiotic use with the overall aims of improving exposure and outcomes, minimizing toxicity and ultimately reduce antimicrobial resistance. It is most commonly employed for drugs with a narrow therapeutic range and is likely to be beneficial in populations where there is profound PK variability such as critical illness. TDM is used to ensure that target exposures are being achieved, as previously discussed certain patient populations may be expected to have altered PK such that the recommended dose from the drug manufacturer may not be sufficient to achieve therapeutic targets. The MIC of the organism can also impact on the dose necessary to achieve target concentrations. For certain antimicrobials the outcomes of certain infections correlate with the AUC: MIC ratio which in turn correlates with serum trough levels, such that the trough level is a surrogate PK measure. For example when treating MRSA infections with vancomycin a trough concentration of 15 mg/l will result in an AUC: MIC ratio of >400 and is therefore a suitable target for therapy.

## COMBINATION THERAPY

Optimising combination treatment is vital for difficult to treat organisms such as *Pseudomonas aeruginosa*, *Acinetobacter* sp and multi-drug resistant *Enterobacteriaceae* owing to single or multiple resistance mechanisms.

There are several reasons to combine antimicrobial therapy; to broaden spectrum, achieve improved activity/synergy and to suppress the emergence of resistance. With regard to MDR *Enterobacteriaceae* such as KPC (*Klebsiella pneumoniae* carbapenemase) reduced risk of death with bacteraemia has been observed when antimicrobial regimens include more than one drug with in vitro activity against the organism and enhanced efficacy is observed when a carbapenem is used.

Treatment of severe infections by *P. aeruginosa* is challenging. Limited by the few anti-pseudomonal antibiotics available and its ability to acquire resistance by several mechanisms (degrading enzymes, reduced permeability, active efflux and target modification). Multidrug resistance, defined as resistance to carbapenems, aminoglycosides and fluoroquinolones is frequent and isolates resistant to all antipseudomonal antibiotics increasingly common. Combination therapy has been more controversial in treating *P. aeruginosa*, failing to improve survival in bacteremia or affect outcome in VAP. The nature of the resistance mechanism may undermine the use of combination therapy in *P. aeruginosa* infections, such as single efflux mutations affecting both beta lactams and fluoroquinolones. When resistance is mutational meropenem and tobramycin are most likely to retain activity for the beta lactam and aminoglycoside classes. For multi-drug resistant

strains combination therapy is the cornerstone of therapy on the basis that singularly resistant and inactive antibiotics can obtain a synergistic or additive effect. Therapy for multi-drug resistant and pan-resistant strains of *P. aeruginosa* depends on the mechanism of resistance but largely encompasses colistin in combination with an antipseudomonal carbapenem

## RESISTANCE SUPPRESSION

Subpopulations with reduced antibiotic susceptibility are a normal feature of dense populations especially *P. aeruginosa* and *Staphylococcus aureus*. The likelihood of antibiotic treatment provoking the emergence of resistant subpopulations depends on the propensity for resistance within the population (spontaneous mutation rate), host defenses controlling the growth of the resistant subpopulation and antibiotic drug levels at the site of infection. It is suggested that drug levels should at least exceed 8-10 times the MIC to prevent emergence of resistant subpopulations. As drug exposures increase, the selective pressure increases causing more injury to the fully susceptible population of bacteria relative to the less-susceptible population causing their amplification. Once a sufficient exposure is then achieved resistance suppression is achieved. However there has been little focus on the impact of dosing and probability of resistance emergence. Strains with MICs close to the clinical breakpoint are at risk of emergence of resistance when treated with monotherapy.

## TOXICODYNAMICS

Toxic side effects can occur as plasma and tissue drug concentrations increase that may be a result of accumulation if kidney and liver function has deteriorated. Toxicodynamic modeling can be used to estimate the concentrations associated with probable toxicity.

Antibiotic	Dose dependent toxicity	Manifestation
Colistin (colistimethate sodium)	Nephrotoxicity	Increased serum urea and creatinine Dizziness, weakness, paraesthesia, vertigo, visual disturbance, confusion, ataxia, neuromuscular blockade
	Neurotoxicity	
Penicilin	Neurotoxicity	Twitching, seizures
Imipenem/cilastatin	Neurotoxicity	Seizures



Linezolid	Bone marrow suppression Lactic acidosis  Peripheral/Optic neuropathy	Anaemia, leucopenia, pancytopenia, thrombocytopenia Nausea, vomiting, abdominal pain, hyperventilation, low bicarbonate. Change to acuity, colour vision, field defect, blurred vision
Co-trimoxazole	Bone marrow suppression	Leukopenia, neutropenia, thrombocytopenia, agranulocytosis
Chloramphenicol	Reversible bone marrow suppression (Aplastic anaemia is dose independent)	Leukopenia, reticulocytopenia, thrombocytopenia, anaemia
Aminoglycosides	Nephrotoxicity Ototoxicity	Increased serum urea and creatinine Hearing impairment, vestibular disturbance
Fluoroquinolones	Neurotoxicity	Seizures
Daptomycin	Muscular toxicity	Raised CPK, Myalgia, muscle weakness

PK- PD of new agents

There are many issues surrounding the introduction of new antimicrobials into clinical use. They are often being used in salvage therapy and multi-drug resistant infections, for which they may be being used out with their license. If being used in areas such as critical care where altered PK is to be expected, then there may be little or no evidence to guide optimal dosing - which is where there is a reliance on PKPD in vitro data to guide dosing. Matters are complicated further by patients on renal replacement therapy where variable amounts of drug may be removed depending on drug factors and the method of renal replacement. In this situation TDM will guide dosing but this is hampered by the need to develop an accurate, validated assay method having obtained from PKPD data expected targets and toxicities.

 OPTIMISING PK/PD FOR ANTIMICROBIAL STEWARDSHIP

Many pathogens have demonstrated high-grade resistance to a range of antibiotics such that multidrug resistance is recognized as a global problem and major public health concern.

In light of this, coupled with the declining rate of antimicrobial drug discovery, the utility of PK-PD relationships to optimise drug exposure is increasingly recognised to ensure clinical outcomes while suppressing the emergence of antimicrobial resistance. Suboptimal antimicrobial concentrations trigger development of multidrug resistance. Improving outcomes from infection requires understanding of the interactions between the drug, host and infecting pathogen. Antimicrobial stewardship employs the clinical application of PK-PD principles while providing the narrowest coverage for the infection by optimizing the agent, dose and duration with the aim of the best control of infection whilst maintaining minimal impact on resistance selection.

TOOLKIT RESOURCE


ARTICLES


**PK-PD.** Levison ME. Pharmacodynamics of antimicrobial drugs. *Infect Dis Clin North Am.* 2004;18(3):451–65.  
MacGowan AP. Role of Pharmacokinetics and Pharmacodynamics: Does the Dose Matter? *Clin Infect Dis* 2001 33(s3):S238–9.

**Emergence of Resistanc.** Drusano GL, Louie A, Macgowan A, Hope W. Suppression of Emergence of Resistance in Pathogenic Bacteria: Keeping Our Powder Dry, Part 1 *Antimicrob Agents Chemother* 2016;60(3):1183-1193

Drusano GL, Hope W, MacGowan A, Louie A. Suppression of Emergence of Resistance in Pathogenic Bacteria: Keeping Our Powder Dry, Part 2. *Antimicrob Agents* 2015;60(3):1194–201.

SITE LINKS

 **Carbapenemase producing organisms**  
Acute trust toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae Public Health England. 2013.

 PHE, UK Standards for Microbiology Investigations. Detection of bacteria with carbapenem hydrolysing  $\beta$ -lactamases (carbapenemases).

 INTERACTIVE CASE STUDY ANSWERS**What are your immediate actions?**

1. Inform the surgeons that washout is necessary to control sepsis.
2. Check CPE screen results.
3. Infection control precautions as CPE positive until proven otherwise.
4. Review the patients clinical progress.
5. All of the above

**Answer 5.**

At this point the concern is that the patient might be infected with a carbapenemase producing *Klebsiella pneumoniae*. With infection of orthopaedic devices antibiotic treatment alone is unlikely to suffice for anything other than superficial wound infection. Antibiotics should be given alongside surgical intervention that may include washout and debridement or implant removal. As the patient has been an inpatient in a hospital abroad they should be considered at risk of colonisation with a CPE as per public health England guidance. This patient should have been admitted to a side room and local infection control guidance followed regarding contact precautions and screening for CPE. It is important not to assume meropenem would suffice, as there is concern of carbapenemase production.

**Which of the following PK-PD factors will influence your recommended treatment?**

1. Meropenem and Ertapenem MIC
2. Renal function
3. Site of infection
4. Allergies
5. Weight

**Answer 1,2,3,5****Which treatment options should be considered?**

1. Meropenem monotherapy
2. Meropenem plus colistin
3. Meropenem plus aztreonam
4. Colistin monotherapy
5. Meropenem plus fosfomycin plus colistin

**Answer 2,3,5** BACK TO QUESTIONS

# CHAPTER 9

▶ AUTHORS: **MARK GILCHRIST & ORLA GEOGHEGAN**

## THE STEWARDSHIP TOOLKIT

### THE AIM OF THIS CHAPTER IS TO:

Gain an understanding of the different antimicrobial stewardship interventions that can be deployed as part of an effective stewardship programme.

Identify specific stewardship interventions that can be applied in your healthcare setting.

Understand the ways in which stewardship interventions can be communicated to engage clinicians.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Be aware of the tools available to carry out a baseline analysis of antimicrobial stewardship within your organisation.
- Recognise key personnel who should be included in antimicrobial stewardship groups.
- Understand where antimicrobial stewardship groups fit within organisational structures.
- Know how to identify areas where antimicrobial stewardship programs should be focused.
- Define core and additional interventions which can be employed in antimicrobial stewardship programs.
- Be able to identify measures to assess the effectiveness of antimicrobial stewardship programs.
- Recognise different routes of communication which may be used within an antimicrobial stewardship program

### ▶ HOW TO IMPLEMENT A SUCCESSFUL ANTIMICROBIAL STEWARDSHIP PROGRAMME

It is recommended that you use a baseline checklist to assess current Antimicrobial Stewardship (AMS) within the hospital. This can provide a useful gap analysis prior to implementing an Antimicrobial Stewardship Programme (ASP). Baseline checklists are available from [CDC](#) or [NICE](#). You may find the Measurement for Improvement Toolkit from the Australian Commission on Safety and Quality in Health Care resources useful in the design of an ASP; you can access the toolkit [here](#).

A proposed approach to implementing a successful ASP within an organisation is outlined in figure 1.



FIGURE 1  
Proposed approach for implementing a successful ASP within an organisation

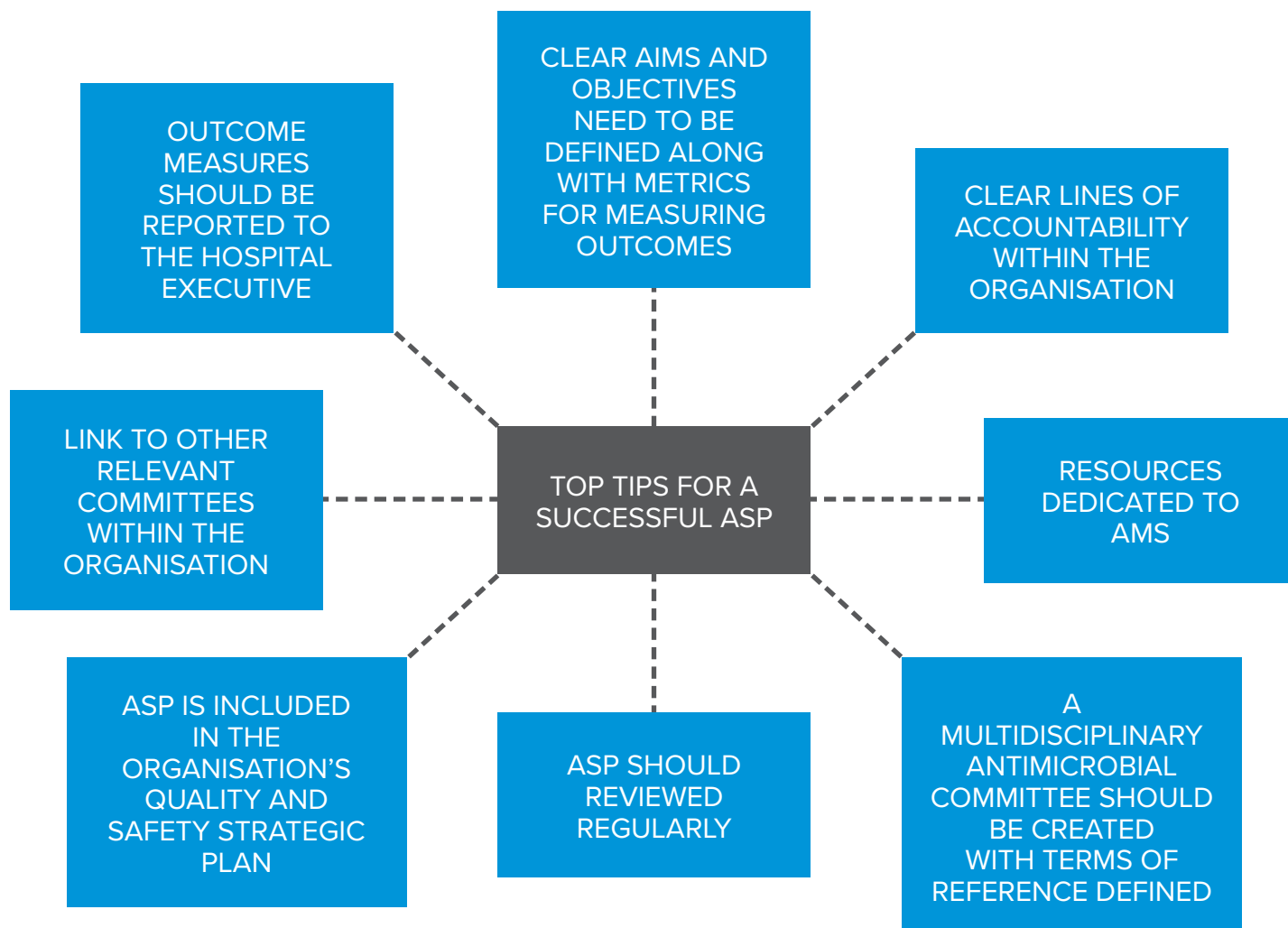


FIGURE 2  
Top tips for a successful ASP

### ▶ PROPOSED MEMBERS OF ANTIMICROBIAL STEWARDSHIP GROUPS

A successful antimicrobial stewardship group needs to include the core members of the AMS team in addition to representatives from clinical specialities within the organisation. Proposed members of antimicrobial stewardship groups are detailed in figure 3.

### PROPOSED MEMBERS OF ANTIMICROBIAL STEWARDSHIP GROUPS

- A senior leader who has experience of implementing change
- Infectious diseases physician
- Microbiologist
- Antimicrobial pharmacist
- Representatives from clinical specialities
- Infection control representative
- Drug and Therapeutics committee representative
- Nurse representative
- Primary care representative

FIGURE 3  
Proposed members of antimicrobial stewardship groups

**POSITION OF ANTIMICROBIAL STEWARDSHIP GROUPS WITHIN THE ORGANISATION**

One of the key elements of implementing a successful ASP is establishing where the antimicrobial stewardship group sits within the organisation. There must be clear lines of accountability to the executive team and governing bodies as well as other relevant committees within the organisation.

Figure 4 shows an example of where the antimicrobial stewardship group lies within the organisational structure in Imperial College Healthcare NHS Trust, a large multi-site teaching hospital in London, England.

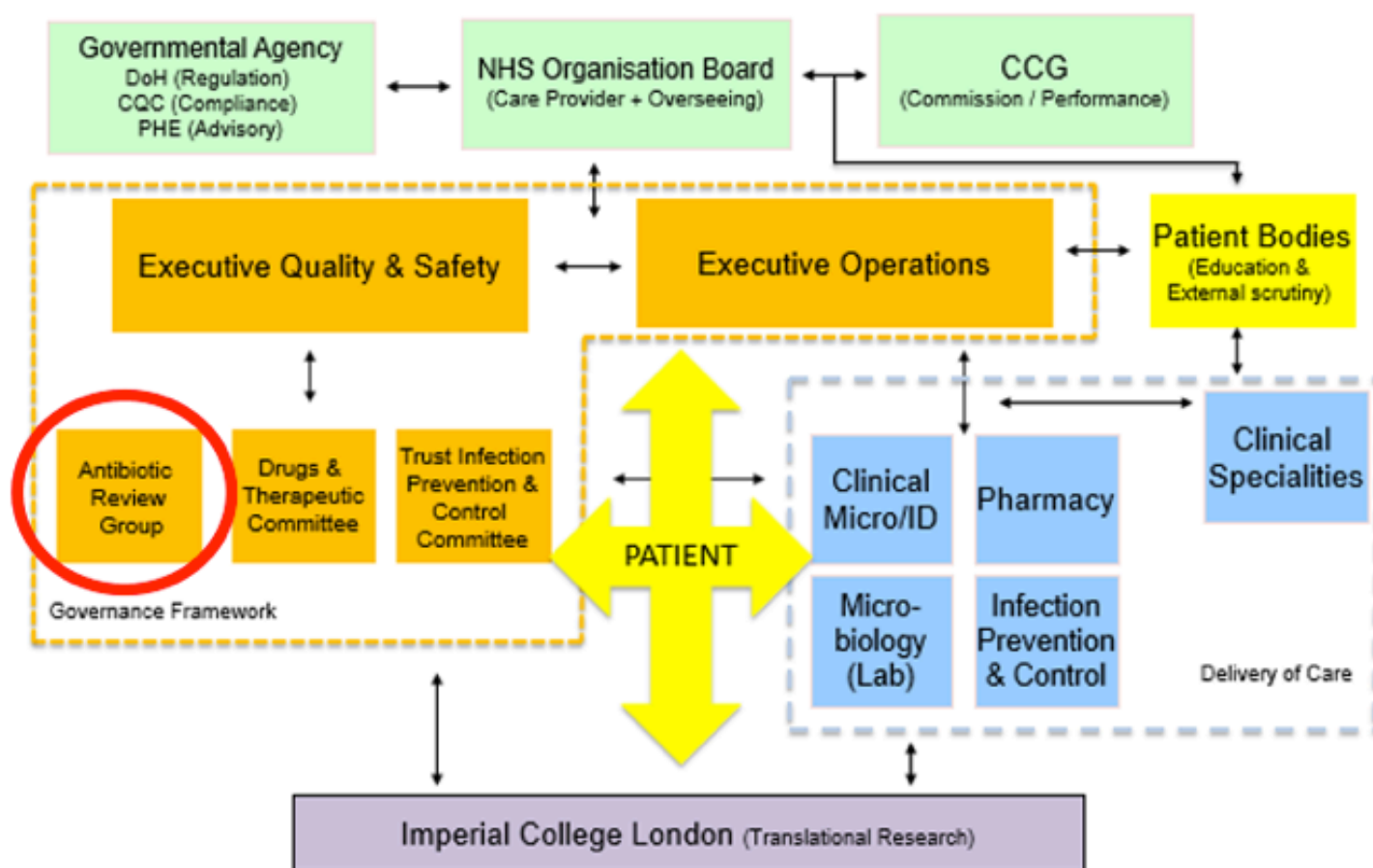


FIGURE 4 An example of where the antimicrobial stewardship group lies within the organisational structure in Imperial College Healthcare NHS Trust



**> HOW TO IDENTIFY PRIORITY AREAS IN WHICH TO FOCUS ASP**

ASP would cover the whole of the organisation, however many centres are limited by the AMS resources available. In such settings, priority areas for ASP should be identified and targeted. Figure 5 provides suggested priority areas for targeting ASP.

Successful ASPs are continually reviewed and adjusted according to changes in priority over time. Point prevalence surveys, surveillance of AMR, surveillance of antimicrobial use and benchmarking with peers are useful tools to review priorities within an established ASP.

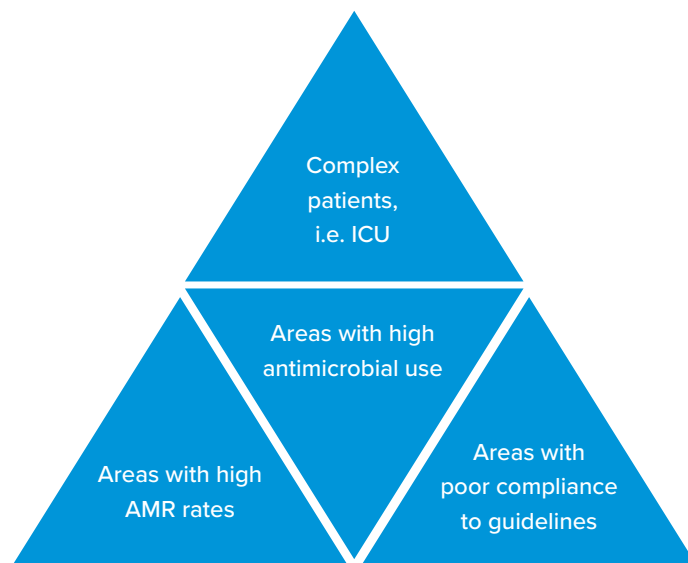


FIGURE 5  
Suggested priority areas for targeting ASP

Click on the icons in figure 6 to hear how teams have implemented ASPs across the world



FIGURE 6  
Examples of implementation of stewardship from around the world

- Videos:
- 1 & 2 Dr Adrian Brink (S Africa)
  - 3 Angeliki Messina (S Africa)
  - 4 Dr James Hatcher (England)
  - 5 Dr Sylvia Hinrichsen (Brazil)

## THE ASP TOOLKIT

A successful ASP should include clinical leadership and corporate responsibility. There is no “one size fits all” approach to ASPs and programmes will vary according to the size and specialities provided within your organisation. A global survey of ASP found that there were many different AMS interventions in use in different organisations (see figure 7).

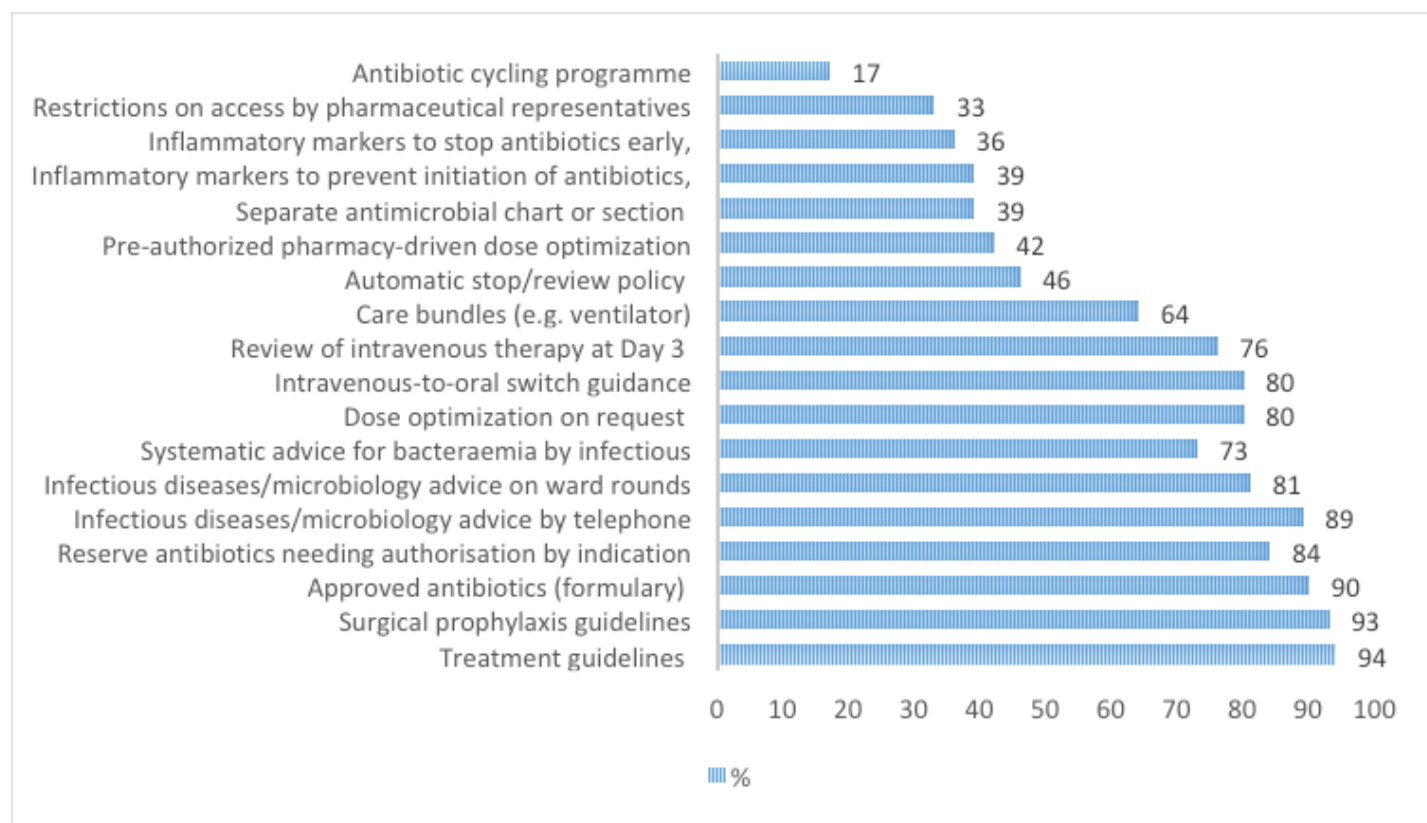


FIGURE 7  
Results of a global survey on types of AMS interventions employed as part of an ASP

For an AMS programme to be effective a range of interventions are required. The interventions implemented should reflect both the needs and resources of the organisation. Listen to Professor Peter Davey discuss interventions to improve antibiotic prescribing in hospitals by [clicking here](#).

To provide the foundations for a successful ASP it is suggested that core AMS interventions are implemented initially. Once the ASP has been successfully established additional interventions can be added as appropriate. Core and additional AMS interventions as defined by the IDSA are shown in figure 8(2).

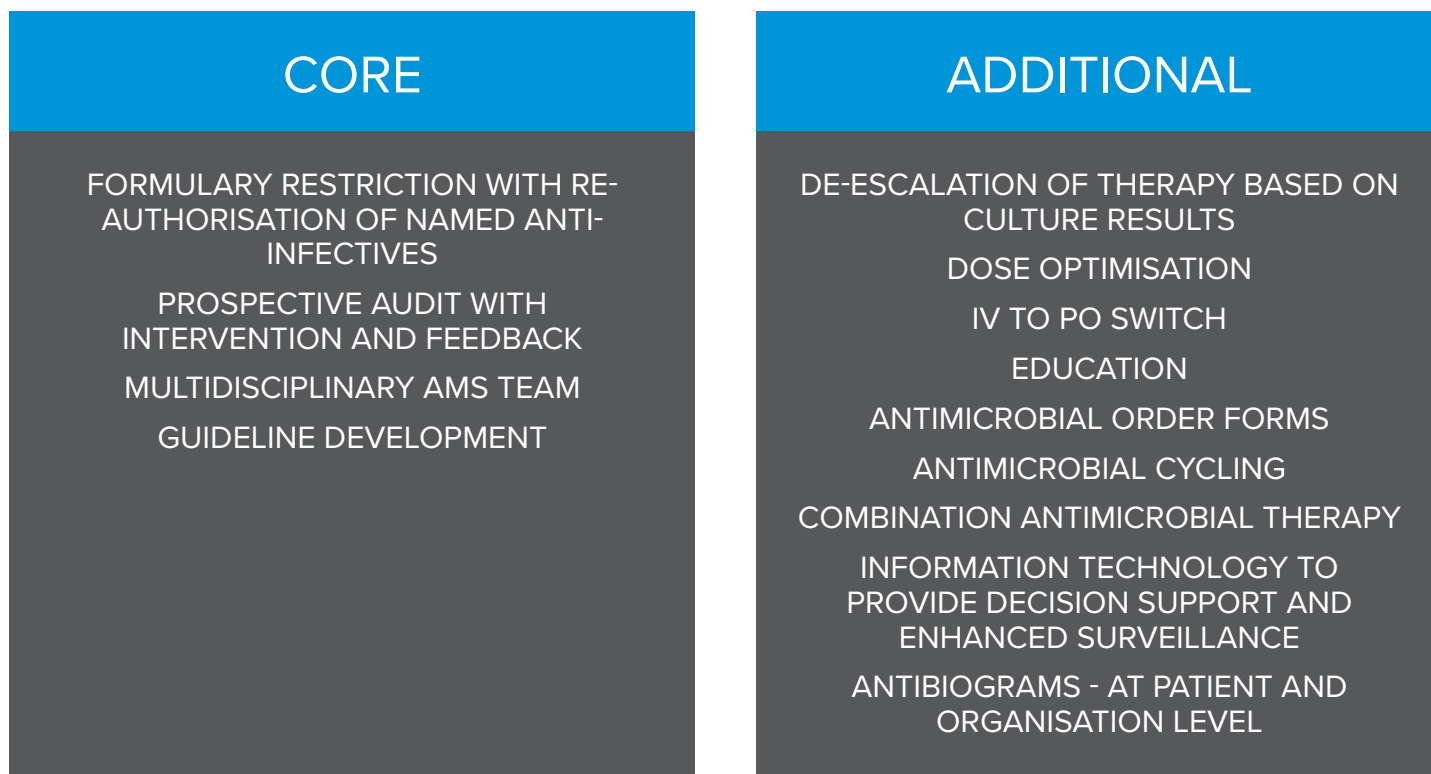


FIGURE 8  
Core and additional AMS interventions

### ➤ CORE INTERVENTIONS

It is recommended that organisations choose either pre-authorisation of restricted antimicrobial agents or prospective audit and feedback, or a combination of both. These are sometimes referred to as front-end and back-end strategies and are discussed further in figure 9.

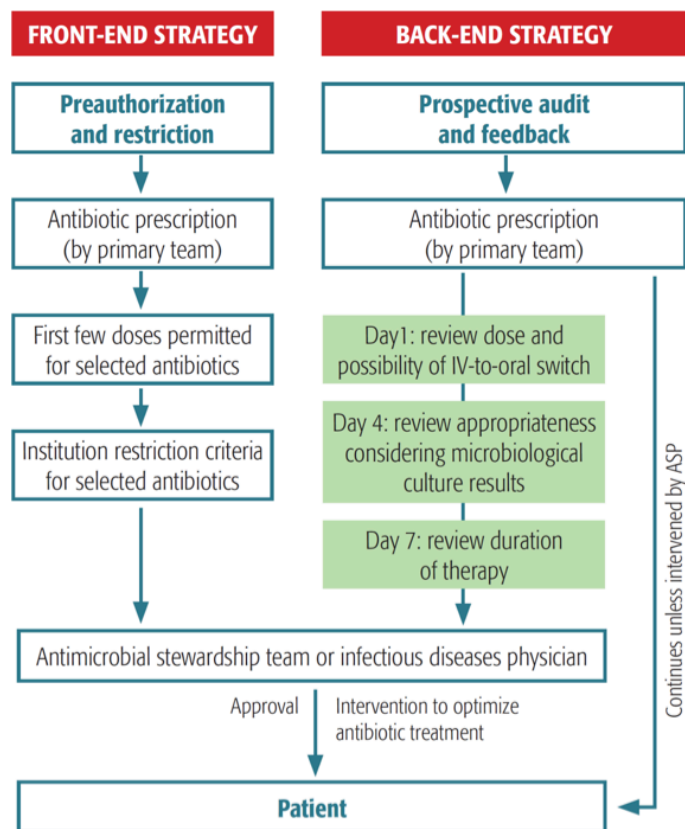
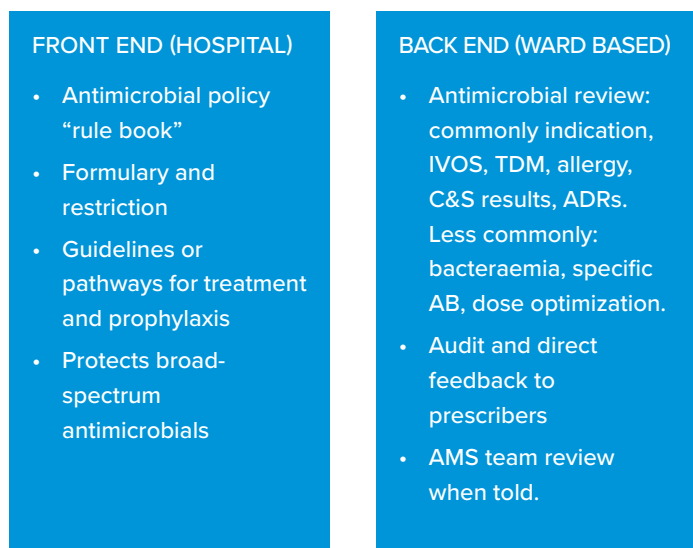


FIGURE 9  
How pre-authorisation of restricted antimicrobial agents and prospective audit and feedback can be used as part of an ASP(3).  
Figure adapted from Chung GW et al. Virulence 2013;4(2):151–157

## CHAPTER 9 - THE STEWARDSHIP TOOLKIT

The advantages and disadvantages of pre-authorisation of restricted antimicrobial agents or prospective audit and feedback are discussed in table 1.

Pre-authorisation	Prospective audit and feedback
<b>Advantages</b>	
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
Potential to decrease antibiotic expenditure	Facilitates prescriber education
Facilitates a rapid response to antibiotic shortages	Accommodates review of extended antimicrobial therapy
Gives Infection Team direct control over antibiotic use	Allows for de-escalation of antibiotics once sensitivities available
<b>Disadvantages</b>	
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
Potential for variation in advice depending on the team member consulted	Can be difficult to de-escalate if patient is responding
Real-time resource intensive	IT support needed to identify patients to target
Potential for incorrect / omitted details in an attempt to bias antibiotic choice	Reductions in targeted antibiotic use may not be immediate

TABLE 1

Comparison of pre-authorisation versus prospective audit and feedback of restricted antimicrobials(2)

AMS team members should have clearly defined roles and responsibilities and receive adequate training and resources to allow them to fulfil their duties. Often there will be much overlap in roles between the core members of the AMS team. Suggested roles for core AMS team members are included in figure 10(1):

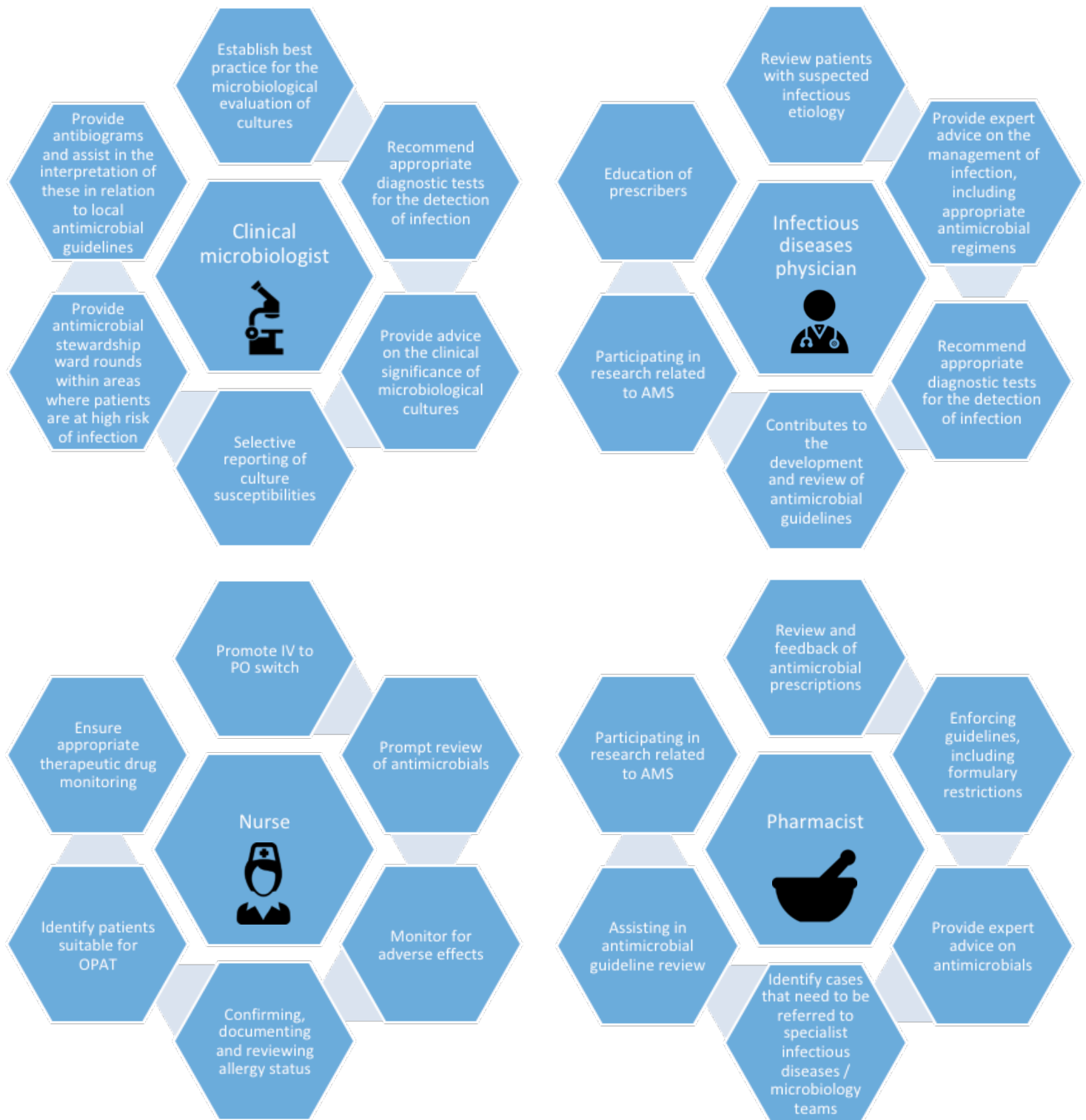


FIGURE 10

Suggested roles for core members of the AMS team. Images courtesy of Vishal Marotkar, IconTrack, Creative Stall and Jeff from Noun Project

## GUIDELINE DEVELOPMENT

Organisations should have comprehensive, evidence based guidelines relevant to the local population freely available at the point of prescribing. Antimicrobial agents should be chosen based on local microbiology and susceptibility patterns, with guidelines reviewed annually with local antibiograms.

Guidelines should include recommendations on antimicrobial agent, route, dose and duration. The UK Specialist Advisory Committee on Antimicrobial Resistance recommends a minimum standard for empirical treatment guidelines and prophylaxis guidelines which are displayed in table 2.

Table 2: UK Specialist Advisory Committee on Antimicrobial Resistance minimum standards for empirical treatment guidelines and prophylaxis guidelines(4)

Empirical treatment guidelines	Prophylaxis guidelines
<ul style="list-style-type: none"> <li>• Sepsis of unknown origin</li> <li>• Upper respiratory tract infections</li> <li>• Lower respiratory tract infections including:                             <ul style="list-style-type: none"> <li>- community acquired pneumonia</li> <li>- hospital acquired pneumonia</li> <li>- exacerbations of chronic obstructive pulmonary disease</li> </ul> </li> <li>• Urinary tract infections</li> <li>• Skin and soft tissue infections including:                             <ul style="list-style-type: none"> <li>- cellulitis</li> <li>- chronic ulcers</li> <li>- necrotizing fasciitis</li> <li>- injuries or bites</li> </ul> </li> <li>• Gastro-intestinal infections including:                             <ul style="list-style-type: none"> <li>- food poisoning</li> <li>- intra-abdominal sepsis</li> </ul> </li> <li>• Eye, ear, nose and throat infections</li> <li>• Central nervous system infections including:                             <ul style="list-style-type: none"> <li>- bacterial meningitis</li> <li>- viral encephalitis</li> </ul> </li> <li>• Genital tract infections</li> <li>• Blood stream infections</li> <li>• Endocarditis</li> </ul>	<ul style="list-style-type: none"> <li>• Bacterial endocarditis prophylaxis including procedure-specific criteria to identify which patients should be offered prophylaxis</li> <li>• Endoscopic procedures including procedure-specific criteria to identify which high-risk patients should be offered prophylaxis</li> <li>• Surgical prophylaxis recommendations for common surgical interventions within the organisation including:                             <ul style="list-style-type: none"> <li>- timing of initial dose</li> <li>- single dose where possible</li> <li>- criteria for repeat doses</li> </ul> </li> <li>• Splenectomy immunization and antimicrobial prophylaxis</li> </ul>

<ul style="list-style-type: none"> <li>• Specific confirmed infections including:                             <ul style="list-style-type: none"> <li>- <i>Staphylococcus aureus</i></li> <li>- <i>Clostridium difficile</i></li> <li>- Tuberculosis</li> </ul> </li> </ul>	
--	--

SA health has a comprehensive section on antimicrobial guideline development which was developed by the South Australian expert Advisory Group on Antimicrobial Resistance (SAAGAR). This includes a guideline on the principles of antimicrobial prescribing, a range of surgical prophylaxis guidelines and guidelines for the prescribing and monitoring of aminoglycosides and vancomycin.

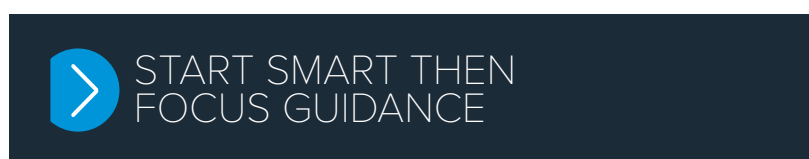


You may also find John Hopkins Medicine’s Antibiotic Guidelines useful.



These guidelines contain recommendations on formulary restriction, the treatment of specific organisms and infections, allergy and therapeutic drug monitoring.

Guidelines should include recommendations on documentation, 48-72 hour review, and intravenous to oral switch. The principles of “Start Smart Then Focus” are a useful reference when developing antimicrobial guidelines.



Prescribing principles from “Start Smart Then Focus” for empirical therapy and surgical prophylaxis are shown in figures 11 and 12 respectively.



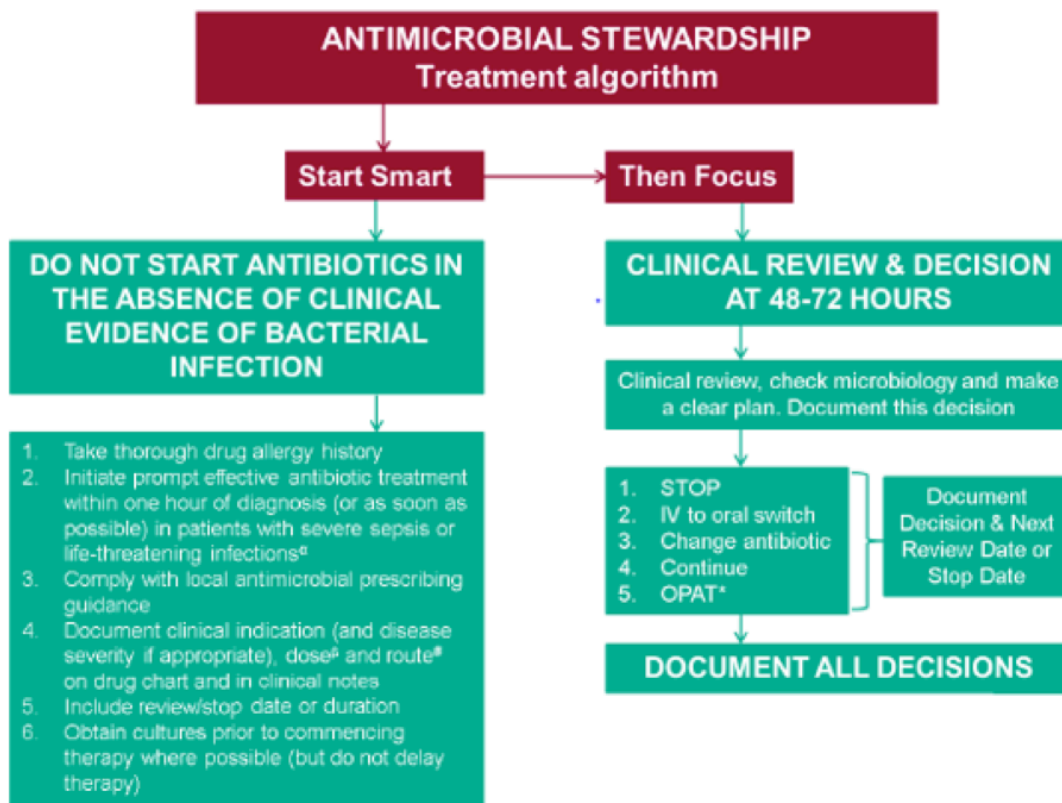


FIGURE 11 Prescribing principles for empirical antimicrobial therapy from “Start Smart Then Focus”

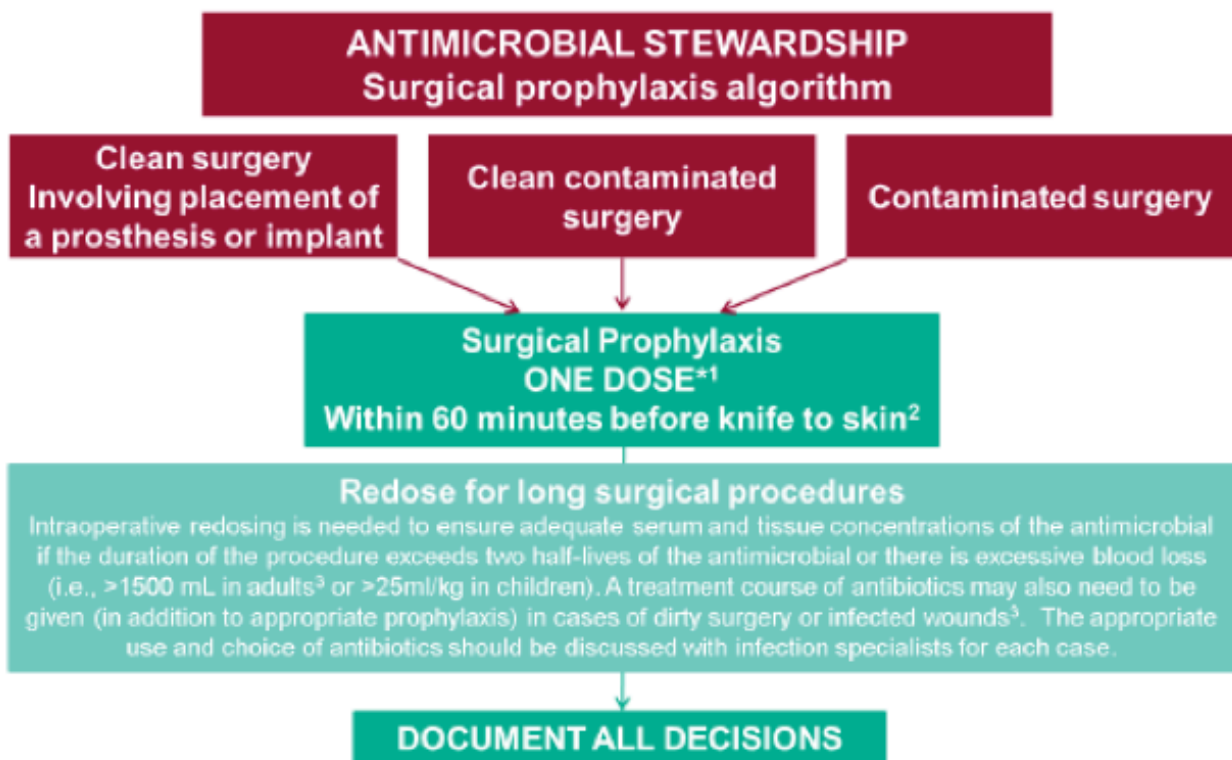


FIGURE 12 Prescribing principles for surgical prophylaxis from “Start Smart Then Focus”

## ADDITIONAL INTERVENTIONS

### De-escalation of therapy based on culture results

The need to take microbiology cultures where appropriate should be incorporated into empirical treatment guidelines. Antimicrobial prescriptions should be reviewed at 48-72 hours and de-escalated to a narrow-spectrum agent or escalated in line with available microbiology culture and susceptibility results. The prescribing outcome should be documented in the medical notes.

Electronic prescribing systems may be utilised to remind prescribers of the need for a review of antimicrobial therapy at 48-72 hours and an alert for mismatches between microbiological culture results and antibiotic therapy may be available.

### Dose optimisation

Dose optimisation is needed to ensure antimicrobial therapy is effective whilst minimising the possibility of adverse effects.

Standard antimicrobial doses should be included in empirical therapy guidelines and optimised according to renal function, hepatic function, severity of infection and therapeutic drug monitoring. Pharmacists are a key resource in dose optimisation, especially in the interpretation of therapeutic drug monitoring and complicated pharmacokinetics.

### IV to PO switch

Criteria for switching from intravenous to oral therapy should be readily available to prescribers. Oral prescribing should be used wherever possible. The benefits of oral prescribing are shown in figure 13. Recommended intravenous to oral switch criteria are shown in figure 14.

### BENEFITS OF ORAL PRESCRIBING

- lower treatment costs
- decreased nursing time
- reduced risk of infection from intravenous catheters
- reduced length of stay
- higher patient satisfaction

FIGURE 13 Benefits of prescribing oral antimicrobials(1)

### AN INTRAVENOUS TO ORAL SWITCH SHOULD BE CONSIDERED WHEN A PATIENT MEETS ALL OF THE FOLLOWING CRITERIA:

- Temperature <38°C for the previous improving 24 hours
- Signs & symptoms of infection improved or resolved
- Oral / nasogastric intake tolerated & absorbed
- No specific indication for prolonged intravenous therapy e.g. meningitis, febrile neutropenia, bacteraemia, endocarditis, osteomyelitis
- Availability of a suitable oral agent
- Patient likely to be adherent with oral therapy
  - In children consideration needs to be given to the palatability of oral agents

FIGURE 14 Suggested criteria for switching antimicrobial therapy from the intravenous to oral route(1)

### Education

Education of healthcare professionals is a crucial part of an effective antimicrobial stewardship programme. Unlike other medications where prescribing is restricted to specialists, for example cytotoxic agents, antibiotics are widely prescribed by clinicians at all stages of their career, in many cases without regulation. Healthcare professionals should receive education on induction and mandatory updates every 3 years(5). The role of an antimicrobial stewardship programme within a wider educational programme for healthcare professionals and the general public is shown in figure 15 below(6).

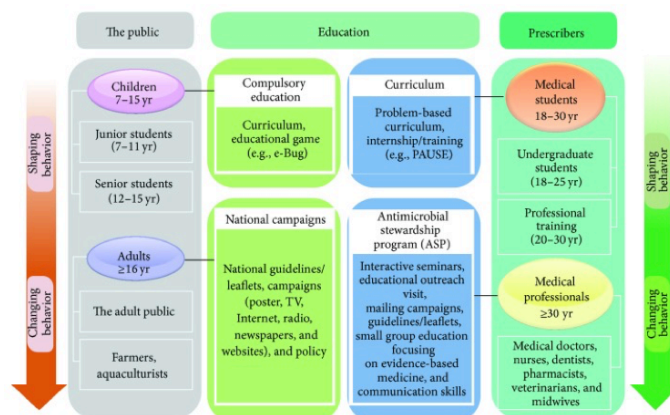


FIGURE 15 How education of prescribers via curriculum and an ASP fits into educational proposals for the wider population.

Continual education is key. In the United Kingdom (UK) it is recommended that defined antimicrobial prescribing and stewardship competencies are incorporated into appraisals for prescribers. These competencies can also be used to inform educational sessions for prescribers.

**> ACCESS THE ARHAI ANTIMICROBIAL PRESCRIBING AND STEWARDSHIP COMPETENCIES**

You can access a free online learning module by the University of Dundee and British Society of Antimicrobial Chemotherapy here:

**> ACCESS MODULE**

The Stanford Center for Continuing Professional Education provides a free online learning course on managing infections in the outpatient setting.

**> ACCESS LEARNING COURSE**

**Antimicrobial order forms**

Sections specifically may be built into paper drug charts to encourage best practice when prescribing and reviewing antimicrobial agents as shown in figure 16.

**> UPDATING THE DRUG CHART**

Click above to read about how updating the drug chart improved antimicrobial stewardship at a large teaching hospital in England

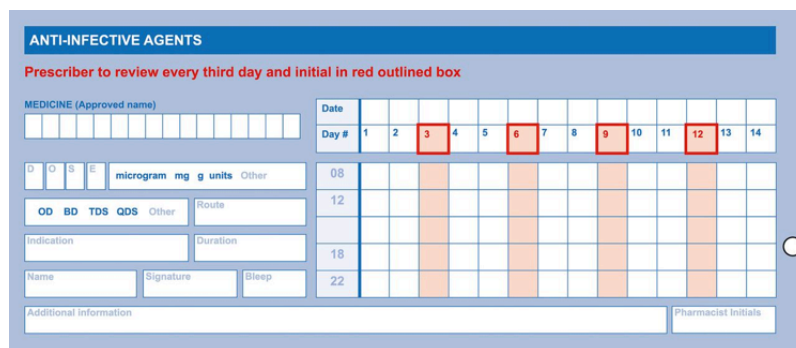


FIGURE 16 Example of an antimicrobial section in a paper drug chart(7)

**Antimicrobial cycling**

Antimicrobial cycling involves the substitution of some classes of antimicrobials from use within an organisation for a defined period of time. The original antimicrobial is then reintroduced at a later date. The aim of this intervention is to limit the selection of antimicrobial resistance to the cycled antimicrobials. Although early studies favoured this approach, subsequent mathematical modelling studies suggest that antimicrobial cycling is unlikely to be effective in the control of AMR.

**Combination antimicrobial therapy**

Combination antimicrobial therapy, for example the addition of an aminoglycoside to a beta-lactam, may be an effective way of reducing the prescribing of broader-spectrum antimicrobials. The inclusion of combination therapy in empirical guidelines must be based on local susceptibility data. Recent national susceptibility data in England has highlighted this as a useful AMS intervention as shown in figure 17, click below to read the full ESPAUR report.

**> ESPAUR REPORT**

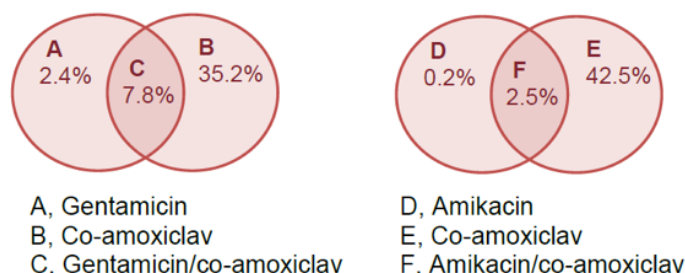


FIGURE 17 Susceptibility of E. coli blood culture isolates within England to combination therapy with co-amoxiclav and an aminoglycoside(8)

**Information technology to provide decision support and enhanced surveillance**

Electronic decision support tools have a potential role in assisting AMS programmes if they are integrated into prescribing workflow. However the implementation of such systems is resource intensive and requires the ongoing support of the AMS team. Such systems could provide data useful for audit and surveillance of antimicrobial consumption at both a patient and organisational level.

In hospitals with electronic prescribing, order sets may be incorporated into the system to promote adherence to guidelines and increase convenience for prescribers. Prescriptions generated from order sets can then be used to generate reports for use in ASPs and audits.

Mobile apps are now common and can be useful for providing antibiotic guidelines at the point of care. There is also an opportunity to include educational messages or specialist prescribing information such as safety of antibiotics in pregnancy and breastfeeding. Dose calculators can be included for antimicrobials with a narrow therapeutic window. However there is a need for patient education as to why clinicians need to use mobile devices at the bedside.

Some apps are Trust specific whilst others are designed to use across wider areas such as that provided by NHS Scotland which is illustrated in figure 18.

**Surveillance**

Surveillance structures should be in place at local and national levels to assess antimicrobial usage and AMR over time; data can be used to inform ASPs. Surveillance can improve outcomes at local, national and global levels as is shown in figure 19.

**Mobile Decision Support App for Antimicrobial Prescribing** NHS SCOTLAND

This mobile app will be available from iTunes and Google Play app stores from 1 August 2016.

**What does it do?**  
It provides all healthcare staff across Scotland with free access to:

- ✓ Gentamicin and vancomycin dosage calculators
- ✓ A decision aid for managing urinary tract infections in older people
- ✓ Primary Care Guidance on antimicrobial prescribing
- ✓ Secondary Care Guidance on antimicrobial prescribing – Some Boards have already added their guidance; others will incorporate theirs over time.
- ✓ An audit tool to support collation of data for antimicrobial quality indicators.

**Why is this important?**  
Improving antibiotic prescribing is a top NHS priority, with the potential to reduce waste, variation and harm in caring for patients, and to improve population health by minimising the spread of antimicrobial resistance. This mobile decision support app is an important new tool which clinicians can use to help make antimicrobial prescribing equally safe and effective across hospital, primary care and community settings.

**How can I be confident in the quality of this app?**  
This app has been developed by the Scottish Antimicrobial Prescribing Group, part of Healthcare Improvement Scotland and NHS Education for Scotland with support from the Scottish Government Chief Pharmacist's Office. The app is registered as a medical device with the Medicines and Healthcare products Regulatory Agency and has CE marking to indicate that it meets their quality requirements.

Scottish Antimicrobial Prescribing Group | Healthcare Improvement Scotland | NHS Education for Scotland

FIGURE 18  
An example of an antimicrobial app used within NHS Scotland

LISTEN TO DR ARJUN SRINIVASAN DISCUSSING HIS WORK USING SURVEILLANCE TO IMPROVE ANTIBIOTIC PRESCRIBING PRACTICES



# HOW SURVEILLANCE CAN IMPROVE HEALTH OUTCOMES

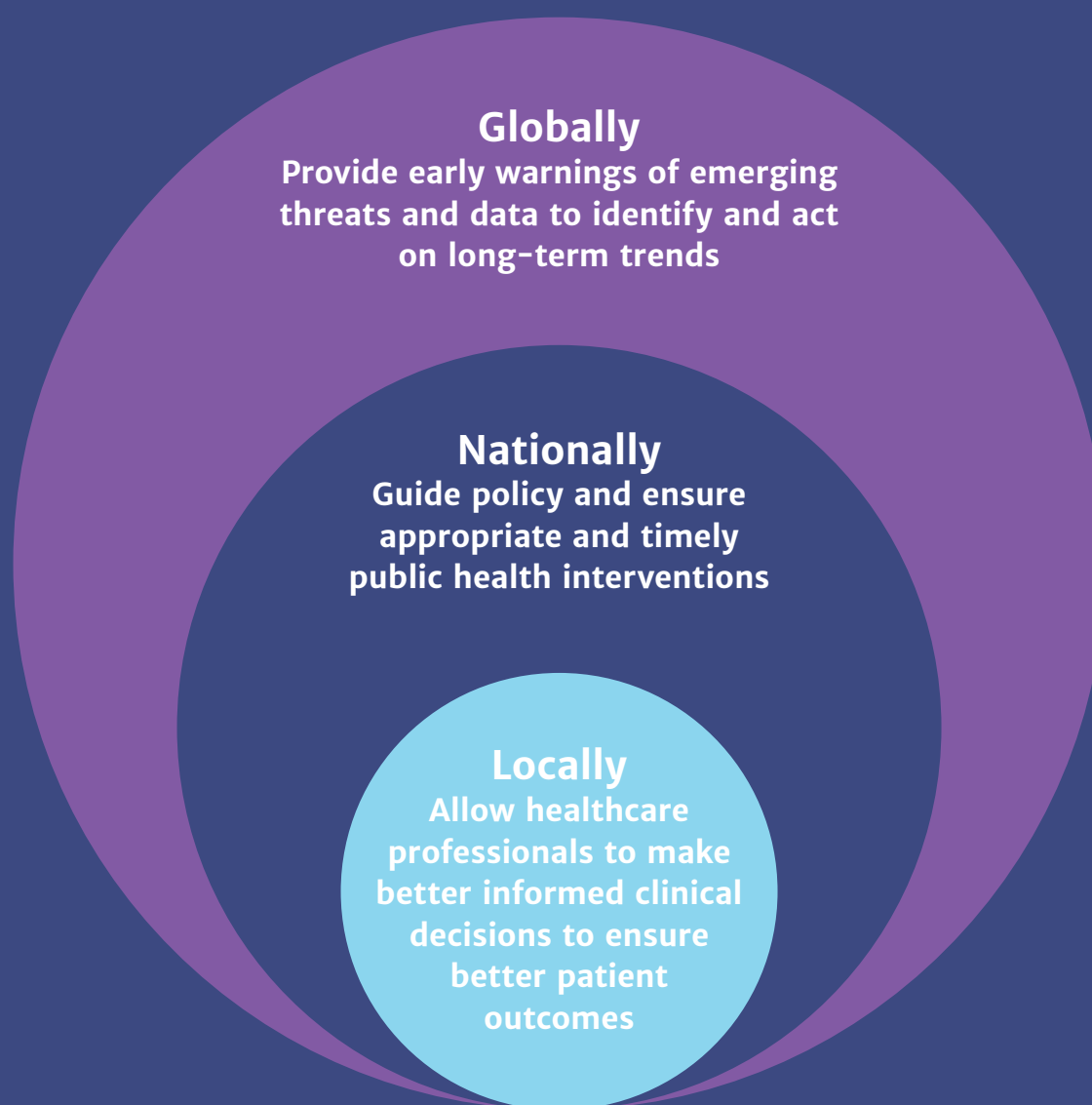


FIGURE 19

How surveillance can improve health outcomes. Image courtesy of Review on Antimicrobial Resistance(9)



The CDC recommends the use of DOTs in preference to DDDs to measure antimicrobial consumption. However many organisations do not have the ability to capture DOTs and DDDs are used in surveillance, including in the UK. Antimicrobial usage data and AMR are reported nationally in many countries, with the ability to generate reports to benchmark against similar institutions:

**NAUSP:**

Reports antimicrobial use and AMR in Australian hospitals on a bimonthly basis. Australian hospitals can register here.



**PHE fingertips:**

Reports on AMR, antibiotic consumption, healthcare associated infection rates, infection prevention and control and antimicrobial stewardship in English primary and secondary care as shown in figure 20. Click below to access the data.

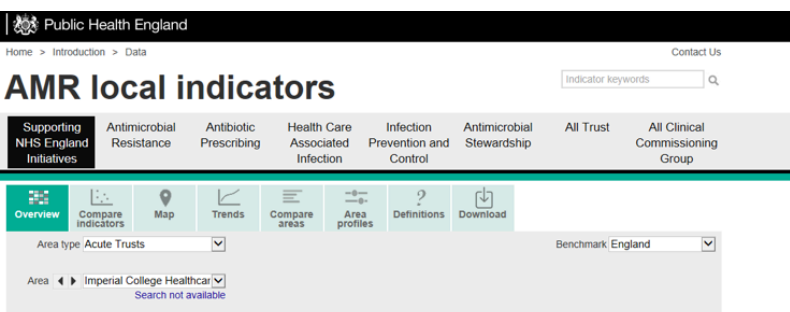


FIGURE 20  
PHE fingertips AMR local indicators

**CDDEP:**

Allows global comparison of AMR and antimicrobial consumption from contributing countries as shown in the example in figure 21. Allows for comparisons between countries. Access the data below.



**Antibiotic Resistance of *Klebsiella pneumoniae* in Thailand**

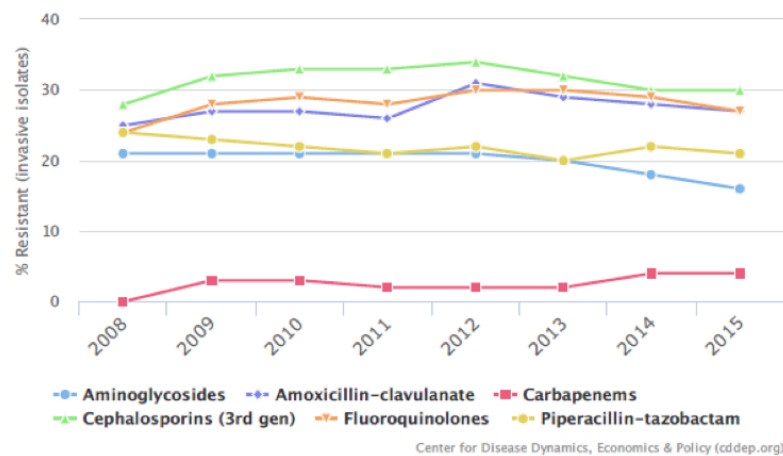


FIGURE 21  
AMR data on *Klebsiella pneumoniae* from Thailand

**HOW DO I ASSESS THE EFFECTIVENESS OF AN ANTIMICROBIAL STEWARDSHIP PROGRAMME?**

There are many ways to assess the effectiveness of an ASP, including:

- Audit of compliance with guidelines
- Audit documentation – e.g. indication, stop/review date, 48-72 hour review
- Audit time to 1st dose of antibiotic in sepsis
- Monitor antibiotic consumption data, including benchmarking to similar institutions
- Monitor antibiotic expenditure data
- Monitor stewardship interventions and acceptance rates
- Review adverse events in relation to antimicrobials

Defined outcome measures should be defined as part of an organisations ASP strategy. Metrics that can be used to evaluate interventions made as part of an ASP in patients with specific infectious syndromes are shown in figure 22.





FIGURE 22 Metrics that can be used to evaluate interventions made as part of an ASP(10)(1)

**Point prevalence surveys**

Local point prevalence surveys (PPS) are recommended on a bi-annual or annual basis(5) as a tool to assess compliance with antimicrobial guidelines. Results of PPS should be shared with the executive team and disseminated to specialities who are responsible for developing action plans within their area. Key metrics which should be included in PPS are shown in figure 23.

Learn more about Point Prevalence surveys by taking the “Challenges in Antibiotic Resistance: Point Prevalence Surveys” course from Future Learn and BSAC.



FIGURE 23 Suggested key metrics for PPS

 ACCESS COURSE

Organisations should be encouraged to take part in national and global PPS surveys to provide data on variation in prescribing practice and AMR. Further information on such studies is available:

 ECDC PPS STUDY

## COMMUNICATION

Within an ASP there are a number of key areas which will need to be disseminated to staff, for example ASP vision, updates to guidelines, PPS results, AMR rates, infection outbreaks and antimicrobial shortages.

Routes of communication to all staff members within the organisation must be established within an ASP. When planning communication the proposed audience must be considered; what works in one setting may not work in another. Proposed communication routes are suggested in figure 24.

### PROPOSED COMMUNICATION ROUTES

- Posters in clinical areas / staffrooms
- Use of hospital intranet
- Organisational newsletter
- AMS newsletter
- Hospital-wide email
- Notifications via electronic prescribing programme or app
- Discussion at relevant hospital committees
- Screensaver / background on computers within the organisation
- Email to divisional leads for dissemination in clinical areas
- Social media

FIGURE 24  
Suggested communication routes which may be used within an ASP

Some useful infographics which could be adapted locally can be found on the NCAS website.

 VIEW INFOGRAPHICS

See figure 25 for an example from New Zealand where educational messages are given about an antibiotic or class of antibiotics on a monthly basis.



### Piperacillin/tazobactam or Tazocin® - did you know?

- Piperacillin/tazobactam is a broad-spectrum **penicillin** antibiotic. Broad spectrum antibiotics are not a substitute for rational thought
- Fever is not a sign of Tazocin® deficiency
- It is a restricted antibiotic and can only be used under advice from Infection Services or for significantly unwell patients with indications named in the PML Antibiotic Guidelines. If started empirically, ongoing use must be reviewed and a rationale documented at day 2 to continue
- Its spectrum of activity isn't actually very different to Augmentin (amoxicillin-clavulanate). Its main advantage is it that it also targets *Pseudomonas* spp.
- It does not cover MRSA, ESBLs or some intracellular pathogens such as *Legionella* spp.
- It is less effective than amoxicillin against *Enterococcus* spp.
- It has excellent anaerobic cover so DO NOT co-prescribe metronidazole with it
- The usual dose is 4.5g four times a day in severe infections
- It may need to be reduced to three times daily if eGFR is below 40mls/min and twice daily if below 20mls/min. If necessary please contact your ward Pharmacist for advice
- It can only be given intravenously and should be given by intermittent infusion over 20 to 30 minutes
- It can reduce the excretion of methotrexate and enhance the action of vecuronium and similar neuromuscular agents
- Each 4.5g dose contains 260mg or 11.3mmol of sodium (almost three times more than ceftazidime and meropenem). Be aware of this when using in patients with fluid overload

This information is brought to you by the 3DHB Antimicrobial Stewardship Committees. If you have questions or concerns about antibiotic use, please contact: CCDHB ID pharmacist (#6114) or HVDHB ID pharmacist (027 405 615).

FIGURE 25  
Antibiotic of the month newsletter (courtesy of Chris Little, Capital and Coast District Health Board and Emma Henderson, Hutt Valley District Health Board, New Zealand)

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# CHAPTER 10

▶ AUTHOR: **WILLIAM MALCOLM**

## WHAT IS MEASUREMENT AND WHY IS IT IMPORTANT?

### THE AIM OF THIS CHAPTER IS TO:

Outline the importance of measurement within antimicrobial stewardship programmes.

Describe the main types of measures used in surveillance of antimicrobial use programmes.

Outline the importance of sharing data with clinicians.

### THE CHAPTER WILL ALSO DEFINE:

The concept of defined daily doses (DDD) as a measure of antibiotic use quantity.

The use of point prevalence surveys (PPS) to provide information on qualitative use of antibiotics.

The concept of data visualisation to maximise the impact of data on antibiotic use.

## LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

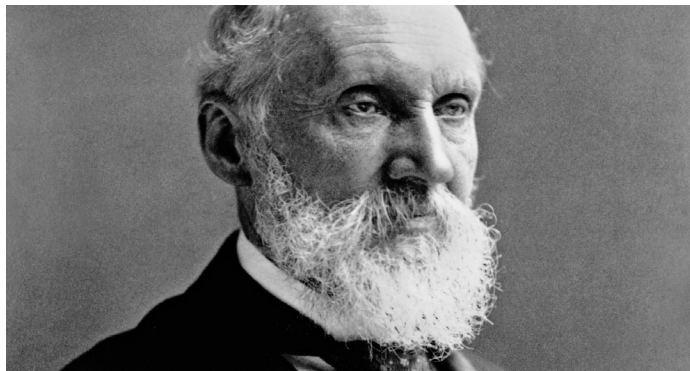
- Outline why measurement is a core element of antimicrobial stewardship programmes.
- Define and explain the differences between quantitative and qualitative measurement of antibiotic use.
- Explain the advantages, disadvantages and alternatives to defined daily doses as a measure of antibiotic use.
- List the types of data collected in point prevalence surveys.
- Give examples of ways information on antibiotic use can be presented and shared to drive improvement.
- Reflect on how to apply learning from this chapter to their own practice.

Measurement is part of our everyday lives. Have you ever thought am I gaining or losing weight or is my child getting taller? The only way to find out the answer is to measure something. In these examples you would measure your weight or the child's height. In any antimicrobial stewardship programme, one of the key components will be the measurement of antimicrobial use with antibiotics being the commonest agents used. We use this term through this chapter.

A dictionary definition of measurement is:

“ The act or process of ascertaining the extent, dimensions, or quantity of something ”

Lord Kelvin was a famous mathematician and physicist. He is best remembered for having the absolute temperature scale - the Kelvin scale-- named in his honour. Kelvin died before Sir Alexander Fleming made his miraculous discovery of penicillin. So what has Kelvin to do with antimicrobial stewardship? The answer is that Kelvin knew about the importance of measurement. Kelvin said:



“ *To measure is to know*

What Kelvin meant is how can we possibly know something, unless we measure it? In terms of antibiotic use: How can we possibly know about antibiotic prescribing unless we measure it?

On the importance of measurement Kelvin went further when he said:

“ *When you can measure something and express it in numbers, you know something about it. But when you cannot express it in numbers, your knowledge is of a meagre and unsatisfactory kind*

The most important quote attributed to Kelvin on measurement is:

“ *If you cannot measure it, you cannot improve it*

The principle that you need to understand the baseline - the point from which you're starting - in order to know if you are improving is now a fundamental part of improvement science and as stewardship is quality improvement based, this principle is fundamental to antimicrobial stewardship programmes.

TAKE A FEW MINUTES TO CONSIDER THE WAY ANTIBIOTICS ARE USED IN THE CLINICAL AREA WHERE YOU WORK. WHAT DO YOU KNOW?

IS ANTIBIOTIC USE INCREASING OR DECREASING?

ARE THERE ANTIBIOTIC PRESCRIBING POLICIES IN PLACE?

IF SO, HOW WELL DO YOU FOLLOW THEM?

HOW WELL DO OTHER PRESCRIBERS FOLLOW THEM?

The only way to determine if antibiotic use is improving is through measurement. Measurement firstly to set the baseline and then repeated measurement to check if things are improving. As Kelvin said, "To measure is to know."

The next chapter in this e-book will consider in detail the quality improvement approach to antimicrobial stewardship and will reinforce the importance of measurement. When measurement is being planned consideration needs to be given to the specific reason for collecting data as this will inform the type and quality of data to be collected.

So in antimicrobial stewardship programmes there are three main types of measures:

- Quantity of antimicrobial use
- Quality of antimicrobial use
- Antimicrobial stewardship measures

The rest of this chapter will look at quantitative and qualitative measurement of antimicrobial use. The use of structure, process and outcome measures will be considered in more detail in chapter 11.

## ▶ QUANTITY OF ANTIMICROBIAL USE

If your hospital has electronic prescribing of medicines, data on antibiotic use will be available in the information system. In the many hospitals without electronic prescribing the hospital pharmacy system can provide information on antimicrobials supplied to wards and other clinical areas. These data can be used as a proxy for antimicrobials given to patients. In the community data on antimicrobial use may come from medicine sales data or from national medicines use surveillance programmes.

### Introducing defined daily doses (DDDs) as a measure

Clinicians involved in prescribing, supplying or administering antibiotics will be familiar with their doses. However, within an antimicrobial stewardship programme, when it comes to measuring and expressing antibiotic use in numerical terms (remembering Kelvin's wise words!) a standardised measure is required. The most common, standardised measure is defined daily doses (DDD). The World Health Organisation (WHO) has assigned DDDs to antibiotics.

## ▶ VISIT WHO SITE ON DDD

The basic definition for a DDD is the:

*Assumed **average maintenance dose per day for a drug used for its main indication in adults***

In simple terms, the DDD is the amount of antibiotic that a typical adult patient will receive each day for treatment of an infection. Remember the DDD is a technical measurement - a dose used to measure drug use. It is not a clinical dose. The DDD calculated by the WHO is often a compromise based upon information on doses used in different countries and it often differs from those doses recommended for clinical use because the doses for individual patients will be based on patient characteristics, such as age, weight, and pharmacokinetic considerations, such as renal function.

DDDs are used for monitoring trends of antibiotic use over time (e.g. is use going up or down) in a ward, hospital or group of hospitals. This is called '**surveillance of antibiotic use**'. DDD measurements may be undertaken on a monthly or quarterly basis depending on the setting and the antibiotics included. To calculate the total DDDs for a period, the total number of grams of each antibiotic used in a ward (or whole hospital) during a defined period is divided by the WHO assigned DDD value for

that antibiotic.

In summary, front line clinicians are unlikely to use DDDs as they are not useful for informing the clinical care of individual patients. However, DDDs are a commonly used standardised metric in surveillance programmes. A metric is a quantifiable measure that is used to track and assess the status of a specific process, in this case quantity of antibiotic prescribing. Antibiotic use expressed in DDDs enables comparison of patterns of antibiotic use over time, between locations and after improvement interventions, thereby identifying areas for further investigation using audit and quality improvement methods.

### Are DDDs a perfect measure of antibiotic use in stewardship programmes?

DDDs were never developed specifically to monitor the impact of antimicrobial stewardship interventions. It is not a perfect measure. The table below shows some advantages and disadvantages of DDD as a metric.

#### What are alternatives to DDDs?

An alternative is the Days of Therapy (DOT). One DOT represents the administration of a single antibiotic on a given day regardless of the number of doses administered or dosage strength e.g. administration of cefuroxime as a single 1.5g dose or as three 750mg doses eight hours apart would both represent 1.0 DOT. The use of DOT may overcome some of the disadvantages of DDDs. The main disadvantage is they are relatively more difficult to measure as they require patient level information.

Other ways of expressing antibiotic use are:

**Prescribed Daily Dose** - The Prescribed Daily Dose (PDD) can be determined from prescription studies, medical or pharmacy records and patient interviews. It is important to relate the PDD to the infection for which the antibiotic is required. There can be differences in the PDD between countries based on national treatment guidelines.

**Number of prescription items** – In community settings the number of prescription items dispensed may be used. These data will give an indication of the number of times antibiotics were used.

**Cost** - These data are easy to obtain and are generally easily understood by administrators but price differences between different products and changes over time limit their usefulness.

**Volume** - Common physical units such as grams are easy to obtain and can be used to produce DDD.

#### The importance of a denominator

When measuring antibiotic use it is helpful to review the raw DDD data to get an indication of whether it is changing over time. In simple terms plot the dots and see what is going on i.e.



## ADVANTAGES

INTERNATIONALLY RECOGNISED AS ASSIGNED AND PUBLISHED BY WHO.

ONCE SET BY WHO A DDD IS NOT OFTEN CHANGED - THIS ALLOWS ASSESSMENT OF PRESCRIBING OVER TIME.

EASY TO PRODUCE INFORMATION ON ANTIBIOTIC USE EXPRESSED IN DDD FOR WARD, UNIT OR HOSPITAL.

ABILITY TO COMPARE ANTIBIOTIC USE IN A STANDARDISED WAY BETWEEN WARDS, HOSPITALS, REGIONS OR COUNTRIES

## DISADVANTAGES

UNSUITABLE FOR PAEDIATRIC SETTINGS AS DDD DEFINED AS AVERAGE DOSE IN ADULTS.

CAN OVER OR UNDERESTIMATE ANTIBIOTIC USE AS DO NOT ACCOUNT FOR ALTERNATIVE DOSING REGIMES DUE TO RENAL DYSFUNCTION, OBESITY ETC.

BIAS AGAINST COMBINATION THERAPY - USE OF THREE NARROW SPECTRUM ANTIBIOTICS RATHER THAN ONE BROAD SPECTRUM ANTIBIOTIC WILL RESULT IN THREE TIMES AS MANY DDD BEING USED FOR THE SAME INFECTION.

MAY NOT REFLECT DOSE USED FOR A PARTICULAR INFECTION.

is use increasing or decreasing? The quantitative measurement of antibiotic use is usually presented as a rate with the number of DDD as the numerator and a denominator that takes account of changes in the population of interest over time. A denominator will be needed to enable the measurement of use over time and between geographical regions such as hospitals, regions or countries to become meaningful.

In the community setting the simplest denominator is the number of inhabitants in the population. The most common measure is DDD per 1000 inhabitants per day (often called DID). Other more complex denominators may take into account characteristics of the population such as age and gender and relative comorbidity.

In hospitals changes in the patient census may impact on the quantity of antimicrobial use. Normalising antibiotic use and presenting it as a rate will help account for fluctuations in hospital activity such as the number of patients in hospital and their length of stay. One of the most commonly used denominators in hospital programmes is the number of patient days or occupied bed days. This requires information on bed utilisation. The landmark guidance on antimicrobial stewardship

by the Infectious Disease Society of America and Society for Healthcare Epidemiology of America recommends DDD/1000 patient days as a metric for hospital based antimicrobial stewardship programmes.



[VIEW IMPLEMENTING AN ANTIBIOTIC STEWARDSHIP ARTICLE](#)



[VIEW GUIDELINES FOR DEVELOPING AN INSTITUTIONAL PROGRAM TO ENHANCE ANTIMICROBIAL STEWARDSHIP ARTICLE](#)

When comparing antibiotic use between hospitals also remember that total antibiotic use defined as DDD will be influenced by specialty mix within and between hospitals: hospitals with specialist units such as intensive care units may have higher use of antibiotics than a local non-specialised hospital.

SO DESPITE THE INHERENT DISADVANTAGES, THE DDD HAS BECOME ESTABLISHED AS THE COMMON, STANDARDISED METRIC FOR THE SURVEILLANCE OF ANTIBIOTIC USE.

HOWEVER, DDDS WILL NOT TELL THE WHOLE STORY, OTHER TYPES OF MEASUREMENT ARE NEEDED.....

## ➤ QUALITY OF ANTIMICROBIAL USE

The key disadvantage of the quantitative approach is whether it really reflects the quality of antibiotic prescribing. A quantitative approach will tell you about the volume of total antibiotic use or of particular antibiotics; is it increasing or decreasing, but does this really reflect the quality of antibiotic prescribing?

A qualitative approach is required to provide information on which patients are being given which antibiotics, their indication, which antibiotics are being used for treatment of particular infections and whether the antibiotics prescribed are in accordance with local prescribing guidelines. Remembering the principle that we need to measure to improve, then, the use of **Point Prevalence Surveys (PPS)** enables assessment of the quality of antibiotic use and identification of targets for quality improvement. Electronic prescribing and routine data linkage is not available in most hospitals and so PPS has become a key approach to planning and assessing the impact of antimicrobial stewardship interventions. A good course for those interested in learning more about this is available:

➤ [VIEW PPS COURSE](#)

A common definition for **point prevalence** is the amount of people with a particular characteristic at a certain **point** in time. It is determined by taking the total of the people with the characteristic divided by the total of people in the population of interest. So a PPS of antibiotic use will measure the number of people taking antibiotics at a given point in time.

### Why undertake a PPS?

- Identify and monitor rates of antibiotic prescribing in hospitalised patients (adults, children and neonates)
- Identify differences between prescribing rates between hospital departments, hospitals, regions and countries
- Determine variation in antibiotics, dose and indication across different locations

Depending on the way the PPS is set up and the data collected there can be wealth of information:

- Use of broad or narrow spectrum antibiotics
- Indications for antibiotics - community or hospital acquired infections, medical or surgical prophylaxis
- Which antibiotics are being used for particular infections?
- Are they prescribed in line with local guidelines?
- What is the duration of antibiotics for surgical prophylaxis?
- Has a clear duration of treatment or stop date been recorded?
- Has the treatment been changed in light of microbiology results?

Furthermore, PPS can help to identify targets for quality improvement in antibiotic prescribing, identify interventions to promote better stewardship of antibiotics to assist the fight against antimicrobial resistance and assess the effectiveness of interventions through repeated surveys.

### What data needs to be collected in a PPS?

#### Ward or denominator data

This will be information about the ward in which the PPS is being undertaken, including the type of ward, the number of patients present on the study day.

## Patient or numerator data

For each patient prescribed any of the specified antimicrobials the following types of data will be recorded:

DATA ELEMENT	DATA OPTIONS
Name of drug	From filtered WHO Drug List
Route	Parenteral, Oral, Rectal, Inhalation
Unit dose	Grams or NU, to three decimal places
Dosage frequency	1-12 per day, every (18, 36, 48) hours, twice per week, three times per week, continuous infusion
Indication	Coded list of indications
Indication group	Indication group
Prophylaxis	Surgical, medical
Diagnosis	Coded list of diagnosis
Day of therapy	1-28, 29+, Long Term, Unknown
Is Review/Stop date documented	y/n/unknown
Reason in notes	y/n/unknown
Complies with (local) guidelines	y/n/unknown
Date start indication	DD/MM/YY (the date fir antimicrobial was prescribed for indication)

## Examples of PPS tools

The use of PPS within local or national antimicrobial stewardship or surveillance programmes has become more common in recent years. Between 2006 and 2009, the European Surveillance of Antimicrobial Consumption (ESAC) programme developed a standardised PPS dataset. In 2011, ESAC was integrated into the work of the European Centre for Disease Prevention and Control (ECDC). The dataset used by ESAC was adapted for a combined PPS on healthcare associated infection and antimicrobial use in 2011 and 2016. More information on this ECDC Point Prevalence Survey in European acute care hospitals is available [here](#).

Antimicrobial resistance is a global problem. Therefore, the Global PPS of Antimicrobial Consumption and Resistance has been developed. The Global-PPS is an ambitious project collecting data at a global level to monitor rates and quality of antimicrobial prescribing combined with microbiology and resistance data in hospitalised patients. It has established a global network for PPS and aims to include as many hospitals from as many countries from all continents. The Global-PPS creates global awareness about antibiotic use and resistance and will be instrumental in planning and supporting national and local stewardship interventions in a range of resource and geographical settings. [Watch this presentation](#) on the aims and








benefits of the Global-PPS from Ann Versporten, Global-PPS coordinator, University of Antwerp, Belgium

WHY NOT TRY USING THE GLOBAL PPS FORM TO COLLECT DATA ON A SINGLE PATIENT (PAGE 3) OR YOUR WARD (PAGE 2) TO HELP YOU, HAVE A LOOK AT AN [EXAMPLE OF A COMPLETED FORM](#) TO HELP YOU GET STARTED.

IF YOU HAVE NOT PARTICIPATED IN A PPS BEFORE YOU MAY FIND IT USEFUL TO TRY COLLECTING DATA FOR A FEW PATIENTS TO SEE HOW IT FEELS TO COLLECT THIS DATA OR YOU COULD COLLECT DATA FOR ALL PATIENTS IN YOUR WARD. IT MAY LOOK LIKE A LARGE TASK TO COLLECT THIS DATA SET FOR ALL PATIENTS ON ANTIBIOTICS, BUT SEVERAL STUDIES FROM VARIOUS COUNTRIES HAVE SHOWN THAT ON AVERAGE ONE-THIRD OF PATIENTS IN A WARD WILL BE PRESCRIBED AN ANTIBIOTIC ON A GIVEN DAY. SO THAT MEANS, FOR A 30-BEDDED WARD, THERE WILL BE TEN PATIENTS RECEIVING AN ANTIBIOTIC FOR WHOM YOU WOULD COLLECT DATA

Are you now thinking about collecting data in your own setting? [Watch this presentation](#) which outlines the factors you will need to consider when planning for a PPS for the first time. Most of these will be relevant whether you are planning a small-scale survey in a small number of wards or a hospital-wide PPS.

PPS is a well-established stewardship tool in some parts of the world, but in other countries clinicians have just begun to explore how to use PPS. Read testimonials from clinicians from around the world who have undertaken a PPS:

-  Australia
-  India
-  Japan
-  Malta
-  Singapore
-  South Africa
-  USA

## USING DATA TO IMPROVE ANTIMICROBIAL STEWARDSHIP

The how and why of measurement in antimicrobial stewardship is important but more important is that once you have gone to the effort to collect and analyse the data that you use it, that you share it with front-line clinicians to enable them to reflect on their practice and change their prescribing behaviour to improve patient outcomes and minimise resistance and other harm.

It is important to share data in as near real time as possible. Timely feedback of data means that it is more likely that the clinicians seeing the data were responsible through their prescribing behaviours for the results. Engagement with clinicians is crucial to change their prescribing behaviours.

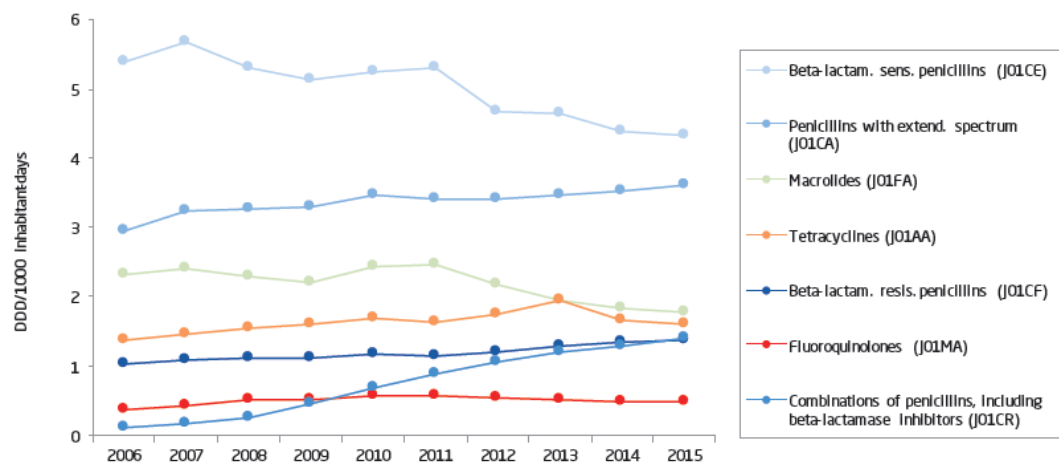
Quantitative and qualitative data can be feedback in a variety of ways. The method will be driven by the intended audience and whether the data are being used for improvement, accountability or research.

To encourage a whole team approach it is beneficial to share data at multi-professional meetings and this can be done informally at ward meetings or via hospital or directorate level audit meetings or in a community setting with all staff in a clinic. It is useful to show comparisons with peers (e.g. between wards within the same hospital or with other nearby hospitals as useful enabler to facilitate change. Similarly identifying outliers is also a useful technique. When providing a benchmark it is important that the benchmark is meaningful. A useful benchmark is to use the 'best in class' approach which recognizes that variation exists and sets the target at the 25th percentile i.e. the level of performance that the best quarter of prescribers can achieve.

It is always important to highlight success as well as identify areas for improvement and encourage discussion of how changing ward processes may help to improve prescribing. Common methods of sharing data are published reports, benchmarking and run charts.

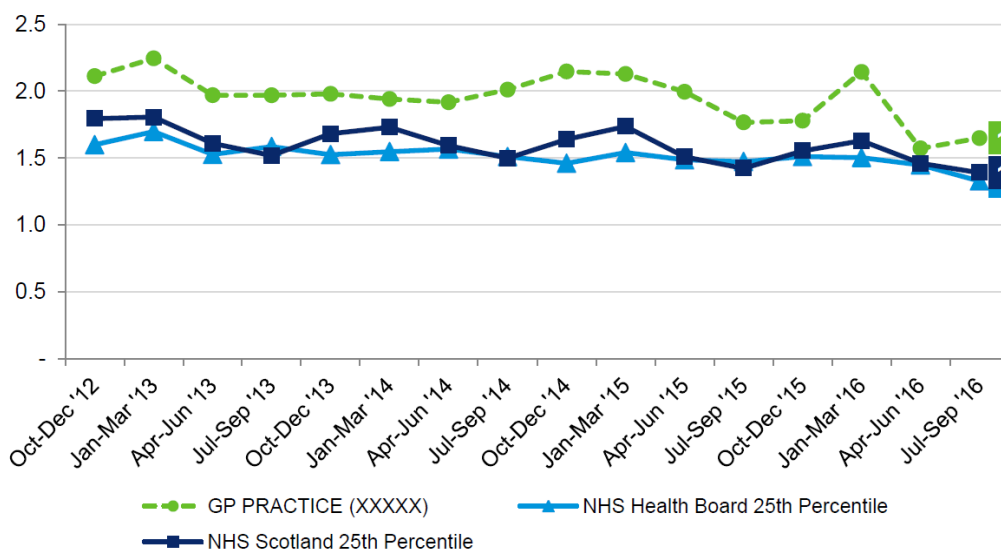
Here are some examples of the ways antibiotic use data can be presented.

Figure 5.2. Consumption of leading antimicrobial groups for systemic use in primary health care, Denmark DANMAP 2015



This example from Denmark shows the change in use of different antibiotic groups at national level over a 10 year period.

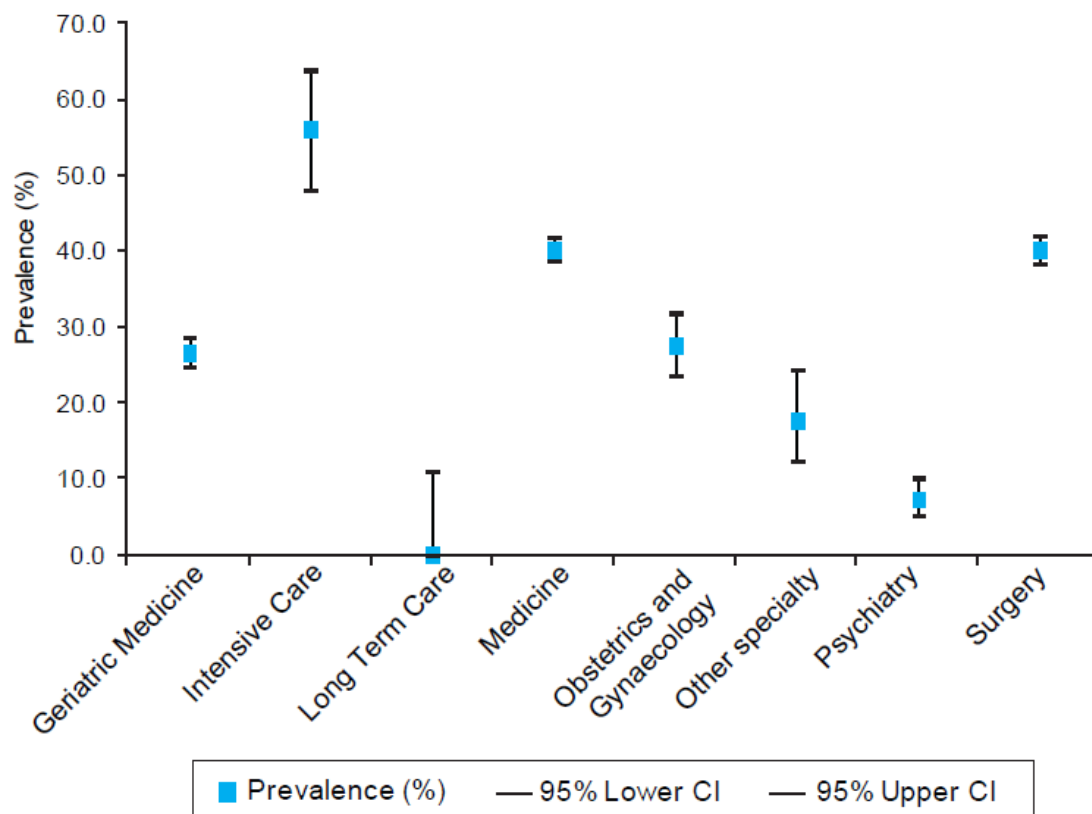
Number of Antibiotic Prescriptions Dispensed per 1,000 Patients per Day



Here is an example of a report issued to GP practices in Scotland which shows their prescribing data versus benchmarks. These benchmarks are the 25th percentile i.e. the antibiotic prescribing rate achieved or bettered by the quarter of practices with the lowest prescribing rate in the local NHS board and across Scotland as a whole.

The figure below is taken from the national PPS of healthcare associated infection and antimicrobial prescribing 2016 published by Health Protection Scotland and shows how the prevalence of antibiotic prescribing varied by specialty. The highest prevalence of patients receiving one or more antibiotics was reported in intensive care patients. –figure 20

**Figure 20: Prevalence of antimicrobial prescribing by specialty in acute adult inpatients (including independent hospital inpatients) in 2016**



### WHAT ABOUT DATA VISUALISATION?

A priority for antimicrobial stewardship programmes is to support learning health systems through maximising the use of current and emerging data. For the data to have its greatest impact it must be easily accessible, visualised well and meaningful to clinicians and managers. The information will then be a catalyst for quality improvement by enabling continuous monitoring of the impact of infection prevention and treatment interventions on antibiotic use together with intended and unintended patient outcomes.

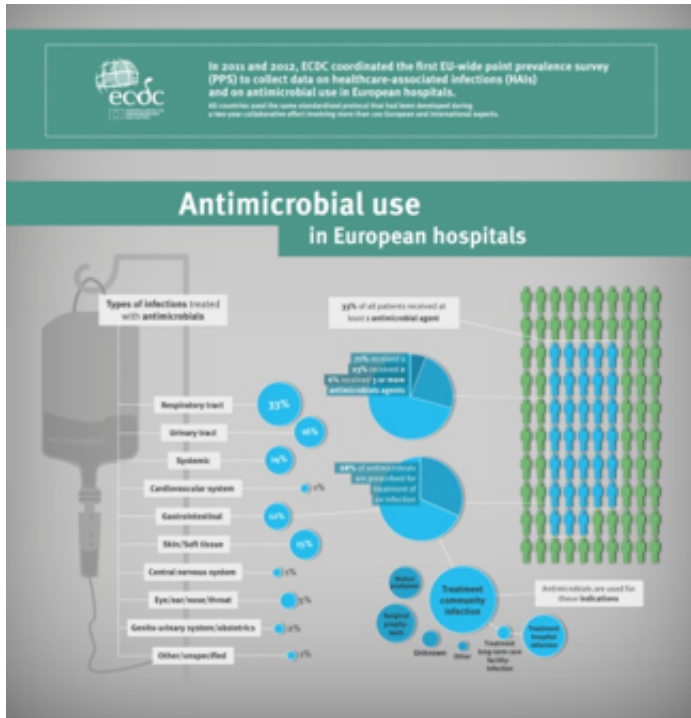
Data visualisation is the presentation of data in a pictorial or graphical format. It enables decision makers to see analytics presented visually, so they can grasp difficult concepts or identify new patterns. It is increasing being used to feedback data to

clinicians who may be reluctant to read detailed text heavy reports.

A good example of data visualisation and benchmarking is the use of AMR indicators within the Fingertips application developed by Public Health England. This system presents information in a publicly accessible website showing data on AMR indicators which can be viewed in format selected by the user which show temporal trends and comparison with benchmarks.

When producing published reports the use of data visualisation techniques are also being employed more frequently to summarise the key information.

Here is an example of an infographic showing antimicrobial use in European hospitals produced by ECDC from PPS data.



In summary measurement important. Think about what data you need, who and how it will be collected, how the data will be used to generate intelligence and most importantly how it will be quickly fed back to drive improvement.

*To measure is to know*



# CHAPTER 11

 AUTHOR: **JACQUELINE SNEDDON**

## METHODS FOR IMPROVING THE QUALITY OF ANTIMICROBIAL PRESCRIBING USING LOCAL DATA

### THE AIM OF THIS CHAPTER IS TO:

Describe the simple interventions that can improve antimicrobial use within a ward or hospital.

Outline the improvement methodologies that can support stewardship.

Describe the types of measures that can be used and their utility.

Outline methods of feeding back data to drive improvements in practice.

### THE CHAPTER WILL ALSO DEFINE:

The model for improvement and PDSA cycles.

Goals for quality improvement interventions.

Concepts behind action and evaluation planning.

## LEARNING OUTCOMES

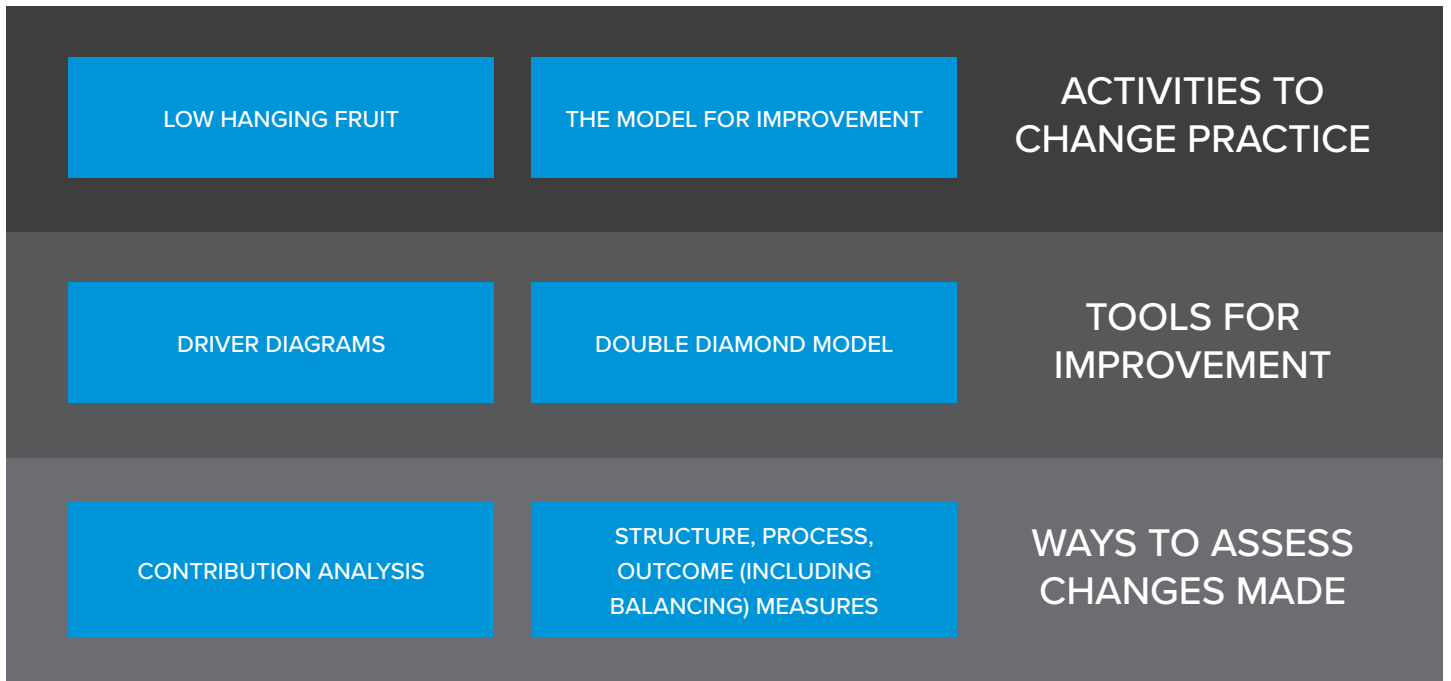
On completion of this chapter, the participant should be able to:

- List some quick wins to improve antimicrobial use
- Outline how a quality improvement approach can be applied to antimicrobial use
- Identify suitable formats for sharing data with various audiences
- Reflect on how to apply learning from this chapter to their own setting

### INTRODUCTION

The previous chapter covered why measurement is important within any stewardship programme and how both quantitative and qualitative measurement can be used to provide useful information about antimicrobial use within a hospital. While this type of information is extremely useful it cannot provide sufficient detail about the prescribing process to identify where changes can be made to improve clinical practice. Small scale data collection at individual ward level can be used to inform improvements in practice through changing behaviours of clinical staff. Various interventions based on audit of clinical practice can be easily achieved in any setting without the need for complex IT systems. Common methodologies include prospective audit and feedback, various quality improvement approaches and systems to restrict the use of specific antibiotics. Collecting, analysing and most importantly sharing data from these interventions can drive improvements in prescribing behaviours, increase compliance with local policies and ultimately optimise antibiotic therapy at individual patient level. This chapter will consider the evidence supporting various interventions, provide practical advice on using various methodologies and also provide information about models for planning interventions as well as measures for evaluating the outcomes of interventions.

Some new concepts and terminology that will be considered include:



**▶ GETTING STARTED WITH IMPROVING ANTIMICROBIAL PRESCRIBING**

When resources are scarce or when you require to demonstrate that a new project or idea will deliver benefits that have a positive impact on patient care it is often helpful to target ‘quick wins’. This means that with a small amount of effort over a short period of time something truly useful can be achieved. By using this approach investment in a programme of work can be secured or it can be used to generate enthusiasm amongst fellow clinicians to get involved. Interventions that provide quick wins often involve targeting things that are easy to achieve referred to as ‘low hanging fruit’. Low Hanging Fruit is a metaphor commonly used for undertaking the easiest and simpler tasks first and is based on the concept that when farmers are harvesting fruit or when animals are grazing on fruit they would tend to take the low hanging fruit first as it is easiest to reach. There are good examples from the literature about targeting low hanging fruit to achieve success in stewardship programmes. Initiatives including intravenous-to-oral switch, batching of intravenous antimicrobials, therapeutic substitution, and formulary restriction, can result in early successes and significant cost savings.

Prospective audit and feedback of data collected on antibiotic prescribing targeted at wards or problem areas of practice is also useful as a quick win. An example of this type of approach is shown in a study from Canada. [Audit and Feedback to Reduce Broad-Spectrum Antibiotic Use among Intensive Care Unit.](#)

Data from antimicrobial consumption or from point prevalence surveys can be used to identify areas for improvement. These can then be captured in a simple audit form (see example below) that can be used to look at issues in more detail.

Patient ID	
Name of drug	
Route	
Unit dose	
Dosage frequency	
Indication	
Complies with (local) guidance	

Such an initiative utilising audit and feedback across hospitals in South Africa delivered improvements in several aspects of antimicrobial prescribing. This involved pharmacists used 5 targeted measures to inform interventions to improve both the quality and quantity of antibiotic use.

**▶ VIEW LOW HANGING FRUIT ARTICLE**

**▶ VIEW DOCUMENT**

## QUALITY IMPROVEMENT (QI) APPROACH

### Introduction to QI

The use of quality improvement methodology within healthcare has expanded rapidly over the past ten years. This started in the United States with several healthcare providers addressing deficiencies in their systems which were leading to high litigation costs, supported by the Institute for Healthcare Improvement (IHI).



Quality improvement in healthcare is now widespread across Europe, North America, Canada, Australia and is emerging as a valuable tool in lower and middle income countries. Much of the experience and the tools used in quality improvement originated in the manufacturing and aviation industries which have radically improved safety during the past 25 years.

Before starting to collect data within a clinical setting it is important to think carefully about the specific reasons for collecting it as this will inform the type and quantity of data to collect.

There are 3 reasons for collecting data:

- Research to generate evidence
- Accountability - judgement or scrutiny of performance
- Quality improvement

This table compares the important factors in deciding which type of data we need:

	IMPROVEMENT	ACCOUNTABILITY	RESEARCH
Purpose	Understanding of Process Evaluation of change To bring new knowledge into daily practice	Comparison Reassurance	To discover new knowledge
Data	Gather just enough data to learn and complete another cycle	Large amounts of data on ongoing basis	Gather as much data as possible 'just in case'

Duration	Short period of time – weeks, months Small 'tests of change' accelerates the rate of improvement	Medium – long duration Longitudinal trends and historic data	Can take long periods of time to obtain results
Analysis	Run charts or statistical process control charts	League tables/ benchmarking achievement of target	Traditional statistical tests

Quality improvement methodology involves changing practice and there are 3 elements which are necessary for improvement to be successful:

### NECESSARY FOR IMPROVEMENT TO BE SUCCESSFUL



#### WILL TO CHANGE

CONVINCING PEOPLE THAT CHANGE IS BENEFICIAL



#### IDEAS TO EFFECT CHANGE

HOW TO MAKE PROCESSES AND OUTCOMES BETTER



#### EXECUTION OF THE IDEAS

TOOLS AND TECHNIQUES ALONG WITH THE CAPACITY AND CAPABILITY AMONGST STAFF WHO WILL PUT THE IDEAS INTO PRACTICE

**Applying QI to antimicrobial stewardship**

QI interventions within infection management are typically directed at managing invasive medical devices and increasing compliance with local policies for infection control and antimicrobial prescribing. There are several quality improvement methodologies used in healthcare e.g. the Model for Improvement, LEAN, Six Sigma but all use similar components.

 **VIEW QUALITY IMPROVEMENT APPROACHES ARTICLE**

The Model for Improvement provides a simple yet powerful tool for accelerating improvement based on three fundamental questions:

- What are we trying to achieve? A clear aim – what, how much, by when?
- How will we know that change is an improvement? Measuring processes and outcomes
- What changes can we make that will result in an improvement? What do we want to test? What can we learn as we go along?

The Model uses PDSA (PLAN, DO, STUDY, ACT) cycles to test changes which may result in improvement. It is useful to consider PDSA as an ongoing process as shown in this diagram.



When using a quality improvement approach such as the Model for Improvement it is important to identify data to demonstrate

what is happening and these are usually process measures which are easy to collect.

If trying to improve compliance with the local antibiotic policy within a ward some potential process measures that could be collected daily over a short time period might be:

- How many of the clinical staff on the unit/ward are aware of the local antibiotic policy and able to access it at the point of care?
- How many patients have received the correct antibiotic as specified in the local policy?

However, outcome measures which measure the impact of changes on patients are more valuable but also more difficult to collect e.g. Are the policy antibiotics effectively treating a specific infection? – clinical cure rate/ mortality/ ICU admission.

In the following example the Model for improvement and a PDSA cycle is applied to a common scenario in clinical practice: a recent audit has identified that patients undergoing vascular surgery received a range of antibiotics as surgical prophylaxis and in many cases antibiotic choice did not follow the local policy.

AIM	Within 2 weeks all patients undergoing vascular surgery will receive the correct antibiotic for surgical prophylaxis as defined in the local policy.
MEASURES	<p>Availability of antibiotic policy in vascular surgery ward and in all theatres where vascular surgery is performed.</p> <p>Ward staff, surgeons, anaesthetists and other theatre staff aware of antibiotic policy and can access it.</p> <p>Adequate stock of the policy antibiotic is available in all theatres used for vascular surgery.</p> <p>Patients undergoing vascular surgery are prescribed and administered the policy antibiotic at the correct time prior to the procedure.</p>
TESTS	<p>Display/locate policy in ward and all relevant theatre areas and check still available daily.</p> <p>Engage with all staff to ensure they are aware of the policy and know where to find it in ward and theatre – test methods of communication e.g. email, face-to-face, phone call, clinical meetings.</p> <p>Stock of antibiotics checked by theatre staff daily/weekly or topped up by Pharmacy staff daily/weekly.</p> <p>Audit antibiotic prescription and administration documentation in patient medication chart/ notes.</p>

In the above example the suggested measures are all process measures but a potential longer term outcome measure would be surgical site infection rate for patients undergoing vascular surgery – review data before and after the intervention.

To ensure that your improvement will be successful test each change with one member of staff initially then expand to several staff ensuring each change is tested in all staff groups and in all theatres.

This is the tried and tested method for implementing sustainable change but it is important to remember that some tests will fail and not have the desired outcome. However, this is still useful learning and helps to think of new tests to improve practice. Failed tests may also give us useful information about potential ‘balancing measures’ to help assess unintended outcomes of changes in practice. This will be discussed further in the next section.

Improvement, like science, is about learning what works so there are no ‘bad results’. Some of the greatest scientific achievements were preceded by failure!



"Light bulb" flickr photo by NikonFilm35 <https://flickr.com/photos/nikonfilm35/4209619566> shared under a Creative Commons (BY-ND) license

*“I did not fail one thousand times; I found one thousand ways how not to make a light bulb.”*

- Thomas Eddison

Now watch this short video which may help to understand the importance of clinical engagement and making quality improvement everyone’s business:

INTERVIEW WITH DR BRIAN ROBSON (CLINICAL DIRECTOR OF HEALTHCARE IMPROVEMENT SCOTLAND AND IHI FELLOW) DISCUSSING WHY MEASUREMENT IS IMPORTANT TO IMPROVE SAFETY IN HEALTH CARE AND WHY EVERYONE NEEDS TO GET INVOLVED

 WATCH VIDEO

#### Breakthrough series collaborative

It can be helpful to collaborate with other clinical teams working on improvement within the same area of practice to share learning, ideas and what has been successful. This can be done formally as a breakthrough series collaborative

 VIEW COLLABORATIVE HEALTH-CARE ARTICLE

and there is evidence supporting this approach to achieve changes in a variety of areas .

 VISIT NCBI SITE

By working in this way it is possible to achieve greater gains and achieve greater clinical engagement through identifying a common area for improvement and working together to optimise outcomes.

**Use of Indicators****STRUCTURAL INDICATORS**

MEASURE WHETHER GOVERNANCE STRUCTURES ARE IN PLACE FOR STEWARDSHIP SUCH AS: DOES A HOSPITAL HAVE AN ANTIMICROBIAL TEAM WHICH MEETS REGULARLY, REPORTS TO SENIOR MANAGEMENT AND HAS AN ACTION PLAN

**PROCESS INDICATORS**

MEASURE SYSTEMS IN PLACE FOR STEWARDSHIP SUCH AS A SURVEILLANCE PROGRAMME FOR ANTIBIOTIC USE, A PROGRAMME OF AUDITS, EDUCATION FOR HEALTHCARE STAFF

**OUTCOME INDICATORS**

MEASURE THE IMPACT OF A STEWARDSHIP PROGRAMME AND SHOULD INCLUDE BOTH INTENDED AND UNINTENDED OUTCOMES SUCH AS REDUCED USE OF RESTRICTED ANTIBIOTICS (INTENDED) AND INCREASE IN RESISTANCE TO RECOMMENDED ANTIBIOTICS (UNINTENDED).

**Quality Indicators**

We can use measures called Quality Indicators on an ongoing basis to monitor quality improvement in both governance of and use of medicines. Antimicrobial prescribing indicators are explicitly defined measurable items of antibiotic use giving a possible indication on the level of quality. They can allow trends

to be measures across time, between locations and before/ after interventions. There are three main types of indicators – structural, process and outcome.

Outcome indicators should also include some balancing measures which reflect how a change in practice may impact on other parts of the system. A good example of a balancing measure is illustrated in a study where a change of policy for surgical prophylaxis in orthopaedic patients to a gentamicin-based regimen resulted in an increase in acute kidney injury.



[VIEW JOURNAL ARTICLE](#)

Suitable indicators for stewardship along with some examples from hospitals across the UK are included within the Public Health England Start Smart Then Focus publication already discussed in chapter 10.



[VIEW START SMART THEN FOCUS PUBLICATION](#)

Another example of simple measures collected from a small sample of patients each week is the 5 x 5 audit developed in Australia. As well as collecting data about prescriptions it also encourages dialogue with clinical teams to influence prescribing behaviour.



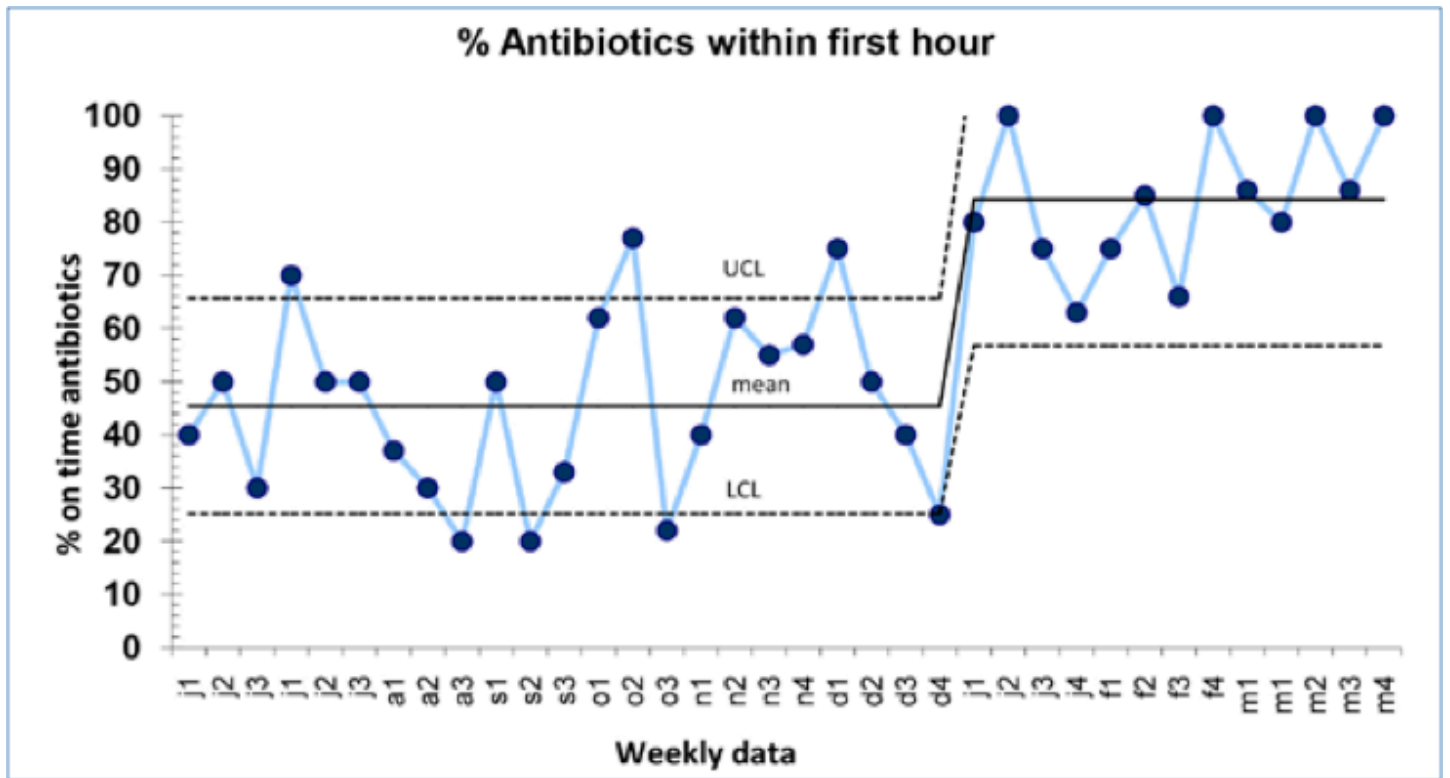
[VIEW ANTIMICROBIAL AUDIT ARTICLE](#)

**Sharing data to improve practice**

For all types of audit and quality improvement initiatives, regular and timely feedback is essential to drive improvements in practice. Sharing prescribing data in real time with front line clinicians is the most effective way to allow them to reflect on their practice and encourage them to change their prescribing behaviours. Comparison with peers and identification of prescribers who are outliers are useful techniques to change behaviour.

Ideally clinical teams (medical, pharmacy and nursing staff) should collect audit data within their ward or department to give ownership. This is also important because they are the ones that understand the system most so are best placed to suggest how improvements could be made.





SPSP Acute Adult End of Phase Report August 2016  
<http://www.scottishpatientsafetyprogramme.scot.nhs.uk/programmes/acute-adult>

Many methods can be used for feeding back data depending on the audience and whether the data is being used for scrutiny e.g. targets or for quality improvement. Published reports, run charts and benchmarking tables are examples of feedback outputs.

**Run charts**

These simple charts plotting performance against a target over time are a good way to present improvement data in a visual way that is easily understood by both healthcare staff and patients/visitors. These charts have been widely used within many improvement initiatives to share data and are often displayed on the wall within a ward/unit.

An example of a run chart which focused on one element of the Sepsis 6 work, timely administration of antibiotics, in a region of Scotland is shown on the next page:

Run charts can be used to set Upper and Lower Control limits as in the one above (UCL and LCL) which indicate that something unusual is happening and alert staff to investigate. They can also be annotated with text to indicate improvement initiatives such as training, new documentation or reasons why performance may be poor e.g. extreme staff shortage.

**Benchmarking**

Comparing your own data with that of other clinical teams is a good way to drive improvement as clinicians can often be motivated to make changes if their peers are shown to be performing better than they are.

The Fingertips AMR portal developed by Public Health England is a good example of how benchmarking has been used to compare practice across hospital and community services.



Fingertips demonstrates how modern IT packages can be used to create infographics as an engaging method of displaying healthcare data that is meaningful to both staff, patients and the public.

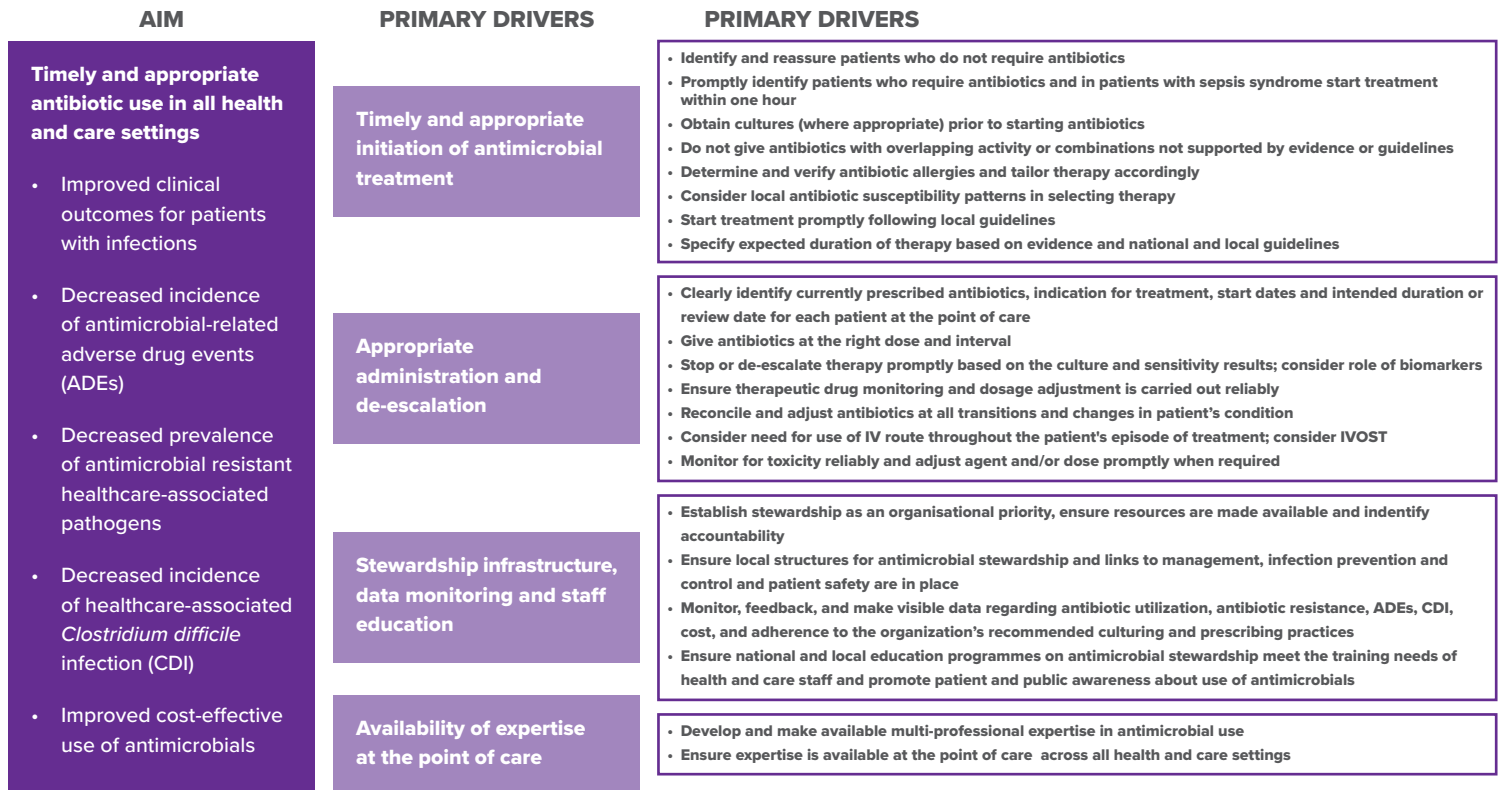
**Planning tools for action and evaluation**

A variety of tools are available to map out what antimicrobial stewardship programmes and individual interventions are trying to achieve. The reason for using such tools is to ensure that you are clear about your objectives and on how you will measure progress.

**Driver diagrams**

Driver diagrams are commonly used within QI programmes to provide an overall aim then document how this will be achieved through primary drivers, secondary drivers and actions. An example of a driver diagram for antimicrobial stewardship is shown below:

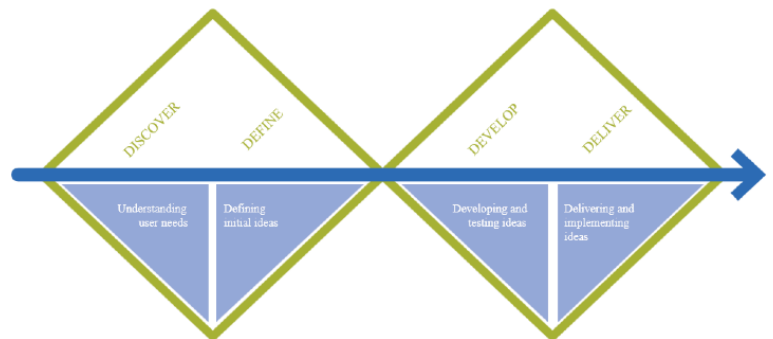
A summary of the key aims of the national stewardship programme in Scotland are shown in the following Antimicrobial stewardship driver diagram:



Based on the CDC/IHI Antimicrobial stewardship Driver Diagram [https://www.cdc.gov/getsmart/healthcare/pdfs/Antibiotic\\_Stewardship\\_Driver\\_Diagram\\_10\\_30\\_12.pdf](https://www.cdc.gov/getsmart/healthcare/pdfs/Antibiotic_Stewardship_Driver_Diagram_10_30_12.pdf)

**Double diamond model**

The Double Diamond model is another approach to plan QI initiatives which is based on behavioural science. This model is useful for small scale changes within a single ward or department and is informed by considering 4 key phases. A key feature of this model is the need for engagement of staff throughout.



This article from the Design Council explains more about this model:

 VIEW DESIGN COUNCIL ARTICLE

Planning how you will undertake QI is important before getting started with data collection but it is also important to think about how to evaluate impact and this is best done at the start. There are various models which can be used to do this and these focus on short, medium and long term outcomes of your overall stewardship programme and/or a specific QI initiative.

The **logic model** is a tool that can be used to monitor and evaluate short-, medium- and long-term outcomes that are linked to the key activities of a programme of work. They are commonly used to evaluate public health interventions and useful further information is available including templates.

 VIEW LOGIC MODELS

The **outcome evaluation framework**, sometimes also called ‘Contribution analysis’, is a similar model and seeks to detail activities, outputs and outcomes together with measures of impact at various points in time. This type of approach acknowledges the complexities of healthcare and does not assume that outcomes are solely due to the interventions described but that the interventions contribute to the eventual outcome which is trying to be achieved. The tables opposite illustrates how this framework may be applied to development and implementation of antimicrobial guidance.

 HOW TO GET STARTED WITH IMPROVING ANTIMICROBIAL PRESCRIBING

Hopefully this chapter has provided information and practical advice about how to get started with some small scale data collection to inform some local improvement work. To conclude here is a summary of what to consider in your own setting.

Direct control	
Input	Outputs and activities
Resources – funding, ideas, Antimicrobial Team staff time	Antimicrobial prescribing guidance document in various formats

Direct influence Short term outcomes	
Reach and reaction	Capacity and capability
Clinicians access the guidance Clinicians report they find the guidance useful	Increased knowledge and skills in prescribing antimicrobials Change in behaviour in prescribing antimicrobials

Indirect influence Medium and long term outcomes	
Decisions and practice	Patient and service
Individual clinicians report improved behaviour in antimicrobial prescribing in line with guidance Spread of effective prescribing across team(s)	Improved patient safety Increased compliance with guidance and optimal outcomes for patients with infections

<b>People – who to involve</b>	Colleagues, clinical teams in wards/departments where improvement work will take place, managers (clinical directors, risk committee, safety committee). Remember to think about what improvement will mean for each staff group – why should they want to get involved? Will it make their job easier? Consider the question “what’s in it for me?”
<b>Problems – how to identify</b>	Engage with ward staff – what do they think are issues, what existing local data sources could help to assess the problem and be used to demonstrate improvements?
<b>Aims – how to test changes</b>	What is the key objective or problem that you wish to solve? Start small, collect some data over short time period, review it and discuss with clinical team, suggest changes and see if they work as expected.
<b>Tools to support improvement</b>	There are many resources available to support improvement. Some have been referenced within this chapter. It’s also helpful to network with colleagues working in antimicrobial stewardship via professional organisations and conferences to learn what has worked for others.

# CHAPTER 12

 AUTHORS: **ESMITA CHARANI & PETER DAVEY**

## ANTIMICROBIAL STEWARDSHIP AND BEHAVIOUR CHANGE

### THE AIM OF THIS CHAPTER IS TO:

This chapter aims to describe the cultural and contextual determinants of antibiotic prescribing behaviours in secondary care.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- How culture and context determine antibiotic prescribing behaviours
- Why the influence of culture on antibiotic prescribing behaviours need to be investigated and included in initiatives to optimise antibiotic use in secondary care.
- the key components of quality improvement in healthcare and how this links to behaviour change science

### THE NEED TO OPTIMISE ANTIBIOTIC PRESCRIBING

With the continued widespread use of antibiotics, despite alarming increase in the development and spread of resistant pathogens, organisations have focused their efforts on getting the bug-drug-patient combination right to ensure their effectiveness (1). Interventions to optimise antibiotic use in hospitals range from the restrictive to persuasive and include use of technologies such as electronic prescribing systems, smartphone apps and clinical decision support systems. In the last decade there has been increased efforts to address the rise of antibiotic resistance on a global scale with the WHO and national governmental organisations contributing to the debate.

Antibiotic therapy remains an area of medicine that requires knowledge and expertise, however due to the ubiquitous nature of infectious diseases and healthcare acquired infections, all healthcare professionals will treat patients with an infection. Worldwide, diagnosis and treatment of infections is being undertaken by healthcare professionals in all specialties and yet it is estimated that up to one third of hospital antibiotic prescriptions are inappropriate. Trying to explain the concept of collateral damage caused by inappropriate antibiotic use to healthcare professionals remains a challenge.

Clearly optimisation of antibiotic prescribing requires healthcare professionals (HCPs) to change their practices. Therefore, antibiotic interventions are all concerned with behaviour change.

Culture plays a role in this subject, but to date has been largely neglected and left out of the equation with most research in antibiotic stewardship, focused on the easily tangible and measurable for example producing policy and guidelines, measuring resistance, and measuring prescribing, with some education and training mainly for junior doctors. As one

of the core goals of antimicrobial stewardship is to improve patient safety a report on the importance of a patient safety culture is very pertinent.

A recent Cochrane review found that interventions were more effective if they were designed to enable prescribers by increasing their capability or opportunity to follow policies. This finding applied to restrictive interventions as well as to educational or persuasive interventions. However, few interventions used the most effective enablement techniques of goal setting and feedback combined with action planning.

 VISIT SITE

 THE ROLE OF BEHAVIOUR AND CULTURE IN ANTIBIOTIC PRESCRIBING

There is increasing qualitative evidence, indicating antibiotic prescribing to be more complex than a simple case of following guidelines (3). In the field of antibiotic stewardship, evidence points to the influence of culture as a key determinant of antibiotic prescribing behaviours.

Culture can be defined in many ways. We use the definition of culture by Spradley:

Culture, he defines, is the acquired knowledge people use to interpret, experience and generate behaviour.

It refers to how people learn and moderate their behaviours as members of a team. Culture does not have to underpin everything we do. But we use it as a cognitive map, a GPS to navigate our behaviours with.

But why is culture important in this field? As mentioned before if all antibiotic stewardship programmes have behaviour change as an outcome, and in view the definition of culture by Spradley, then all antibiotic stewardship programmes are concerned with the culture within healthcare. We avoid culture at our peril. It has been said that “culture eats strategy for breakfast”. So, we want to use some evidence from literature to see if this saying holds true.

In a study in three primary care GP surgeries over two years, Gabbay and colleagues used ethnography methods to investigate how GPs access evidence based guidelines. Ethnography is a study of people in the context of their social and physical environment, and includes observations, face to face interviews and documentary analysis. What they found, and defined as mindlines, was really culture at work (2). In their two years of observing doctors and nurses they discovered that

TOOLKIT RESOURCE

VIDEOS

Talk by Professor Mary Dixon Woods on what we know and what we need to improve about quality and safety in hospitals

 WATCH VIDEO

Lecture on Social determinants of Health

 WATCH VIDEO

DOWNLOAD SLIDE SET

 E Charani MOOC slides

SITE LINK

 Importance culture patient safety

healthcare professionals rarely refer to explicit guidelines, rather, they used collectively reinforced internalised tacit mindlines that were structured from personal and colleagues’ experiences, and interactions with opinion leaders. HCPs they found, used socially constructed knowledge. In secondary care, culture can be a key determinant of behaviours. Mary Dixon Woods and colleagues conducted an ethnographic study across 200 intensive care units in England. These units had implemented the Matching Michigan programme to reduce central line infections. The common trait of successful units was that they had made efforts to develop an understanding of the context in which the interventions were being implemented. As a result, any hierarchies were removed and local leaders were involved in the decision-making process. Unsuccessful units, had not engaged with senior consultants as part of the implementation process of the programme. This study reinforced the need account for local cultures and context in the development and implementation process of clinical interventions that aim to change behaviours of healthcare staff. Engaging with clinical leaders and recognising local champions acknowledges the hierarchies which dominate healthcare.

 VIEW IMPROVEMENT PROGRAMMES DOCUMENT

Culture has also been studied across different specialties of medicine and surgery in order to describe the observed variation in antibiotic prescribing behaviours.

Ethnography has also been used to describe the influence of culture and team dynamics on the antibiotic prescribing behaviours of surgical teams in a study conducted across 6 surgical teams in a large teaching hospital in London. The surgeons in this study were inclined to see themselves as ‘interventionist’ whose primary responsibility is the surgical intervention. In this context, antibiotic decision making was commonly delegated to others. This study provided a platform for an international research collaboration investigating antibiotic prescribing in the surgical pathway in low and middle income countries.

## HIERARCHIES

Medical practice is historically hierarchical where knowledge, experience and expertise are highly prized. Tribalism in medicine has been described and discussed in the literature. Further evidence of the conflict between the behaviours of individuals, the medical hierarchy and guidelines and policy can be found in a qualitative study where 39 healthcare professionals from nursing, medical and pharmacy professions across three hospitals in a large teaching NHS Trust in London were interviewed. The study explored their perceived self-reported determinants on antibiotic prescribing. What was identified was the existence of tacit rules governing prescribing. Hierarchy and prescribing etiquette overruled policy and guidelines: Senior clinicians wielded significant influence on the prescribing choices and decisions of junior doctors.

In another study conducted at Imperial amongst the medical specialty, doctors perceived that the de-escalation and stopping of antibiotics was the responsibility of senior doctors. The junior doctors also reported a lack of feedback on their prescribing decisions. The study called for a need to improve the communication and feedback to junior prescribers in order to help them develop optimised antibiotic prescribing behaviours.

Is the impact of hierarchy the same everywhere? When the qualitative study design conducted at Imperial (Charani et al CID 2013) was replicated in Norway it was interesting to find differing results with hierarchy not emerging as a key determinant. This may be because Norway, being a more egalitarian society with efforts made to flatten visible hierarchies (eg. all hospital staff wearing the same white uniform), have inadvertently overcome some barriers which still exist in many other healthcare organisations globally.


In Norway, geographical access to laboratories was a more pressing barrier to effective antibiotic prescribing and stewardship:

[VIEW ARTICLE](#)

Internationally however, the influence of culture and senior colleague influence on decision making remain powerful determinants of antibiotic decision making. In a survey of the week five participants of the MOOC course the 505 respondents (from 53 countries) overwhelmingly ranked the opinion of senior colleagues above the recommendations in policy and guidelines in relation to antibiotic decision making (ECCMID 2017 abstracts).

## TOOLKIT RESOURCE


### SITE LINKS

 Charani E, Castro-Sanchez E, Sevdalis N, et al. Understanding the determinants of antibiotic prescribing within hospitals: The role of “prescribing etiquette.” Clin Infect Dis. 2013;57(2):188-196.

 Graphic


 Audio file

### PDF ARTICLE

 A literature review of behavioural analysis of behavior change and antimicrobial prescribing in healthcare settings

### SITE LINK

 NCDI

 Should surgeons be allowed to prescribe

 NCDI



 VISIT ESCMID SITE

 BEHAVIOUR CHANGE AS QUALITY IMPROVEMENT

Clearly there is evidence that there is a need to employ methods from outside the fields of microbiology and drug discovery, and hospital policy to implement effective antibiotic stewardship programmes.

Quality improvement interventions take many forms. As we have seen in the earlier chapters understanding through measurement, what is happening in your location is key to change and improvement. In its widest sense quality improvement is the combined and unceasing efforts of everyone to make changes that will lead to better patient outcomes, better system performance (care) and better professional development.

Change making should become an intrinsic part of everyone's job, every day, in all parts of the system.

Changing systems is only part of the improvement arsenal – behaviours also need to be improved. In relation to antibiotic prescribing what behaviours need to change and how?

Despite existing policies and guidelines, antibiotic use in hospitals continues to be suboptimal, in the face of rising resistance. Evidence from social sciences can help develop more sustainable and context driven stewardship interventions. To help develop more contextually driven interventions we can learn from existing behavior change techniques employed in other fields.

Some behaviour change techniques (BCTs):

COM-B Model (Capability, Opportunity, Motivation – Behaviour)

This technique is based on the premise that for any change in behavior, a person must:

- Be physically and psychologically capable of performing the necessary actions
- Have physical and social opportunity to change their behaviour
- Have more motivation to adopt the new behaviour, rather than the old behaviour.

 VISIT BEHAVIOUR CHANGE SITE

There are specific actions that have been proven to lead to successful behaviour change across an array of topics:

Goal setting and Action Planning

Goal setting includes agreeing on a defined “how good by when” goal in terms of the behaviour to be achieved. Action planning involves prompt planning of performance of the behaviour.

Goal setting and Action Planning are widely used behavior change techniques, particularly for motivating individuals to change behaviours directly impacting themselves such as smoking cessation, and for people with chronic conditions. Though effective to and essential to bringing about behavior change there is less evidence of their use in antibiotic stewardship interventions.

Audit and Feedback

Audit and feedback, which has been tried in stewardship interventions, is the monitoring and feedback provision on outcomes of behaviour to the people whose behaviour is expected to change. A summary of all the behaviour change techniques that are applicable to antibiotic stewardship are in the references below:

 VISIT SCIENCE DIRECT SITE

 VISIT NICE SITE

There is an emerging body of evidence supporting the right methods for applying behavior change techniques such as audit and feedback. A Cochrane review on audit and feedback and its effect on healthcare professional behaviours has been published. In it the authors identify the key steps to successful and effective audit and feedback as:

- 1) utilising multimodal approach to delivery of the feedback (e.g. textual and graphic);
- 2) providing more than once (i.e. up to monthly, repeated feedback);
- 3) being delivered by a trusted colleague or supervisor;
- 4) targeting behaviours where there is significant room for improvement (i.e. baseline performance is low); and
- 5) being accompanied by explicit recommendations for changing practice (i.e. goals and action plans)

The British Society for Antimicrobial Chemotherapy (BSAC) has led the Cochrane systematic review of interventions to improve antibiotic prescribing to hospital inpatients. Working with Professor Susan Michie, Director of the Centre for Behaviour Change at University College London, data extraction sheets were designed that identified BCTs in the 214 papers in the review. In this power point slide Prof Peter Davey leads you through the review process and highlights the key points.

## TOOLKIT RESOURCE

### SLIDESHET



Behaviours and BCTs - Peter Davey

## ▶ EXAMPLES OF SUCCESSFUL APPLICATION OF BEHAVIOUR CHANGE THEORY TO ANTIMICROBIAL STEWARDSHIP RESEARCH

Despite the emerging evidence indicating the strong influence of culture and team dynamics, it is disappointing to see so few new papers emerging which attempt to incorporate better social science into antibiotic stewardship programmes as it has an important role to play to improve the implementation of antimicrobial stewardship. We can learn from existing examples of interventions where social science and behavior change science can be applied to produce more effective outcomes. There are several examples of using behavior change and social science research to inform antibiotic prescribing interventions. These are summarised in two recent invited reviews in JAC:

1. Toma M, Davey P, Marwick C, Guthrie B. A framework for ensuring a balanced accounting of the impact of antimicrobial stewardship interventions. *J Antimicrob Chemother* 2017;72(12):3223-31
2. Driving sustainable change in antimicrobial prescribing practice – How can social and behavioural sciences help? Fabiana Lorenzatto, Esmira Charani, Nick Sevdalis, Carolyn Tarrant & Peter Davey. *JAC* 2018 in press (hopefully!)

As the evidence in this chapter has demonstrated social science research can address a key gap in antibiotic stewardship programmes by helping healthcare professionals develop contextually driven interventions that are sustainable.

### References and additional materials

1. Davey P, Marwick CA, Scott C, Charani E, McNeil K, Brown E, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev* 2017. 2017;(2).
2. Gabbay J, LeMay A. Practice-Based Evidence for Healthcare: Clinical Mindlines. In: *PRACTICE-BASED EVIDENCE FOR HEALTHCARE: CLINICAL MINDLINES*. 2011. p. 1–269.
3. Charani E, Edwards R, Sevdalis N, Alexandrou B, Sibley E, Mullett D, et al. Behavior change strategies to influence antimicrobial prescribing in acute care: A systematic review. Vol. 53, *Clinical Infectious Diseases*. 2011. p. 651–62.

### Reading resources:

1. Skodvin B, Aase K, Charani E, Holmes A and Smith I. An antibiotic stewardship program initiative: A qualitative study on prescribing practices among hospital doctors. *ARIC* under review. <http://www.ncbi.nlm.nih.gov/pubmed/26075065>
2. Davey P, Peden C, Charani E, Marwick C, Michie S. Time for Action: Improving Design and Reporting of Behaviour Change Interventions for Antibiotic Stewardship in Hospitals; Early Findings from a Systematic Review *International Journal of Antibiotic Agents*. 2015 Mar;45(3):203-212. doi: 10.1016/j.ijantimicag.2014.11.014. <http://www.ncbi.nlm.nih.gov/pubmed/25630430>
3. Gabbay J, May A. Evidence based guidelines or collectively constructed “mindlines?”. *Ethnographic study of knowledge management in primary care*. *BMJ*. 2004;329:1013. doi:10.1136/bmj.329.7473.1013. <http://www.ncbi.nlm.nih.gov/pubmed/15514347>
4. Dixon-Woods M, Leslie M, Tarrant C, Bion J. Explaining Matching Michigan: an ethnographic study of a patient safety program. *Implement Sci*. 2013;8(1):70. doi:10.1186/1748-5908-8-70. <http://www.ncbi.nlm.nih.gov/pubmed/23786847>
5. Rawson TMM, Charani E, Moore LSPS, et al. Mapping the decision pathways of acute infection management in secondary care among UK medical physicians: A qualitative study. *BMC Med*. 2016;14(1):208. doi:10.1186/s12916-016-0751-y.
6. Charani E, Tarrant C, Moorthy K, Sevdalis N, Brennan L, Holmes AHH. Understanding antibiotic decision making in surgery – a qualitative analysis. *Clin. Microbiol. Infect*. 2017;23(10):752-760. doi:http://dx.doi.org/10.1016/j.cmi.2017.03.013.

# CHAPTER 13

 AUTHOR: **DIANE ASHIRU-OREDOPE**

## KNOWLEDGE AND PRACTICE IN STEWARDSHIP: EDUCATIONAL COMPETENCIES FOR PRUDENT PRESCRIBING

### THE AIM OF THIS CHAPTER IS TO:

highlight the current landscape and development of educational competences for prudent prescribing.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Understand the current landscape of educational competencies globally
- Describe the educational strategies available for AS
- Describe the process for developing competencies
- List published competencies for prudent prescribing
- Consider which educational resources could be useful in their location

### INTRODUCTION

Increasing knowledge and improving prescribing practice through education is considered an important and core persuasive AMS intervention, in comparison to restrictive interventions such as formulary restrictions.

Educational strategies can be either passive or active. Examples of passive and active education strategies include:

- Printed antimicrobial prescribing guidelines, prescribing guidelines on organisation's website, posters, handouts, conference attendance, staff/teaching sessions with minimal interactive sessions (passive strategies)
- Focus groups for consensus-building, workshops, one-on-one targeted sessions e.g. via academic detailing or educational outreach by clinical educators (eg ID physician/microbiologist or pharmacist) (active strategies)

Whilst increasing knowledge is an essential step in improving antimicrobial stewardship, education alone has been shown to be only marginally effective in changing prescribing practices and has not been shown to have a sustained effect.

Face-to-face educational visits have been shown to have greater and longer lasting effects on changing prescribing behaviour than printed material or group interactions alone.<sup>1</sup>

The technique has been cited the most likely effective single method for changing prescribing behaviour. However it is resource intensive.

In this chapter, the current landscape of knowledge and practice is highlighted as well developing educational competencies for prudent prescribing.

In the context of this chapter, all healthcare professionals and health students are considered, including doctors, pharmacists, nurses, dentists and other allied healthcare professionals. In many countries only doctors and dentists can prescribe antimicrobials, but increasingly, nurses and pharmacists can independently prescribe medicines including antimicrobials. Other allied healthcare professionals such as podiatrists and physiotherapists may also have a key role in influencing referrals of patients with infections which require antimicrobials.

The importance of improving awareness, understanding of antimicrobial resistance through effective communication, education and training is indeed the first objective of the WHO Global Action Plan on Antimicrobial Resistance. In particular, the need to make AMR a core component of professional education, training, certification and CPD (Figure 1).


*“Steps need to be taken immediately in order to raise awareness of antimicrobial resistance and promote behavioural change, through public communication programmes that target different audiences in human health, animal health and agricultural practice as well as consumers. Inclusion of the use of antimicrobial agents and resistance in school curricula will promote better understanding and awareness from an early age.”*

*“Making antimicrobial resistance a core component of professional education, training, certification, continuing education and development in the health and veterinary sectors and agricultural practice will help to ensure proper understanding and awareness among professionals.”*

WHO Global Action Plan 2015<sup>2</sup>

FIGURE 1  
WHO Global Action Plan - objective 1 on education and training

## WHY IS ANTIBIOTIC RESISTANCE EDUCATION SO IMPORTANT FOR HCPS AND THE PUBLIC?

 WATCH VIDEO

Responses to this call for AMR as a core component of education is the development of educational resources such Massive Open On-line Courses with global reach

### CURRENT LANDSCAPE: NATIONAL STRATEGIES TO IMPROVE AMS KNOWLEDGE AND PRACTICE

There are a number of steps that governments, educational establishments, professional bodies have taken to implement objective 1 of the global action plan. The first open survey of countries' national action plan preparedness on Antimicrobial Resistance (AMR) at the 70th World Health Assembly highlights the progress made so far by countries across the world.

147 governments representing 95% of the world's population responded (Figure 2 and Table 1.)

	Total	%
A. No training for health workers on AMR	12	8.2
B. Ad hoc training courses in some health-related disciplines.	44	29.9
C. AMR is covered in some pre-service training and/or some special courses for health workers.	48	32.7
D. Continuing professional development (CPD) opportunities are available nationwide for health workers on AMR and implications for antimicrobial use & infection prevention.	36	24.5
E. AMR is systematically incorporated in pre-service training curricula for all relevant health cadres. Regular CPD on AMR reaches relevant groups for human health nationwide, in public and private sectors.	5	3.4
No response provided	2	1.4

TABLE 1  
Steps countries have taken on the question Training and professional education on AMR in the human health sector

The survey highlights progress made:

- 77 countries having multi sectoral plans
- 57 in the process of developing one.
- 37 reported having no formal plan.

High income countries generally reported having more capacity in all aspects of responding to the challenge of tackling AMR, but significant challenges with low-middle income countries and especially fragile states.

Tackling AMR in human health systems is progressing better than animal health, this is perhaps most evident for training where only 12 countries have no training in the human health sector compared to 33 countries in the veterinary sector (Table 1).

The five countries that selected option E were Belarus, Norway, United Kingdom (EURO region), Haiti (AMRO) and Lebanon (EMRO). Majority of the countries that have no training for health workers on AMR are in the African (6), WHO South-East Asia (2), Western Pacific (4) regions (Figure 1).

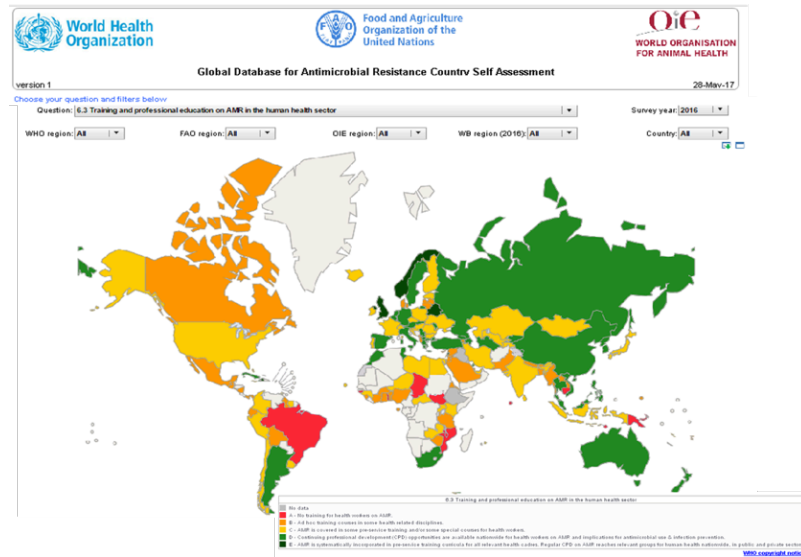


FIGURE 3 Global map of answers on actions on AMR training for healthworkers<sup>3</sup>

Steps that governments have taken to implement objective 1 of the global action plan (as reported to WHO) n=147

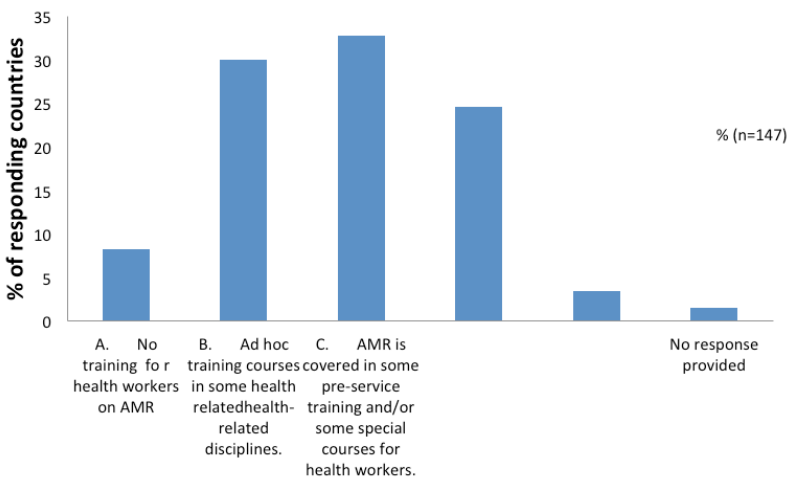


FIGURE 2 Steps that governments have taken to implement objective 1 of the global action plan

## TOOLKIT RESOURCE

### SITE LINKS

- 1 Avorn J, Soumerai S. Improving drug-therapy decisions through educational outreach: a randomised controlled trial of academically based 'detailing'. *New England Journal of Medicine* 1983;308:1457–1461
- 3 WHO 2015. Global action plan on antimicrobial resistance
- 4 WHO HQ Reports

### ARTICLE

- 2 Dartnell J. *Understanding, Influencing and Evaluating Drug Use*. North Melbourne, Victoria: Therapeutic Guidelines Ltd, 2001

## ▶ EXAMPLES OF HOW COUNTRIES HAVE IMPLEMENTED OBJECTIVE 1 OF THE GLOBAL AMR ACTION PLAN

Table 2: provides a summary of antibiotic awareness/ education and training strategies as written in national antimicrobial resistance action plans.

Below we provide examples of how these have been implemented

### UK

In the UK, the Health and Social Care Act: code of practice on the prevention and control of infections and related guidance (DH 2015)<sup>4</sup> states that healthcare providers should ensure that all prescribers receive induction and training in prudent antimicrobial use and are familiar with the antimicrobial resistance and stewardship competencies.

There are also recommendations in national guidance that there should be mandatory core training in prudent antibiotic use for doctors, pharmacists and nurses, in addition to an introductory session on each induction programme and that this should be repeated every three years, with particular emphasis on those antibiotics that provoke *C. difficile* infection (CDI) (PHE & DH 2008<sup>5</sup>; PHE 2011<sup>6</sup>).

Finally in 2013, the national action plan on antimicrobial resistance specified actions required to improve professional education and training and public engagement

The first national antimicrobial prescribing and stewardship competences to be developed anywhere in the world were published in 2013 by the United Kingdom. The antimicrobial prescribing and stewardship competences complement in the UK generic competency framework<sup>7</sup> for all prescribers (2016) which expects prescribers to understand antimicrobial resistance and the roles of infection prevention and antimicrobial stewardship.

Since then the implementation of the competences have been assessed in undergraduate curricular as well as the educational approaches to improving the knowledge of prescribers

- Educational approaches to improve knowledge of antimicrobial prescribing

A national survey to identify what learning materials and resources are currently available to support prescribers with learning and education around AMR and antimicrobial prescribing highlighted that

- In 61% of responding organisations, all prescribers receive induction and training in prudent antimicrobial use.
- 40% confirmed prescribers are familiar with and/or given the PHE/ARHA antimicrobial resistance and stewardship competencies.

- The most popular formats of resources were training workshops.
- More than 75% of the resources were targeted towards the training of medical prescribers (of all grades in both primary and secondary care including dentists)

The national survey highlighted the general approaches at a local/regional level to education and training (Figure 3):

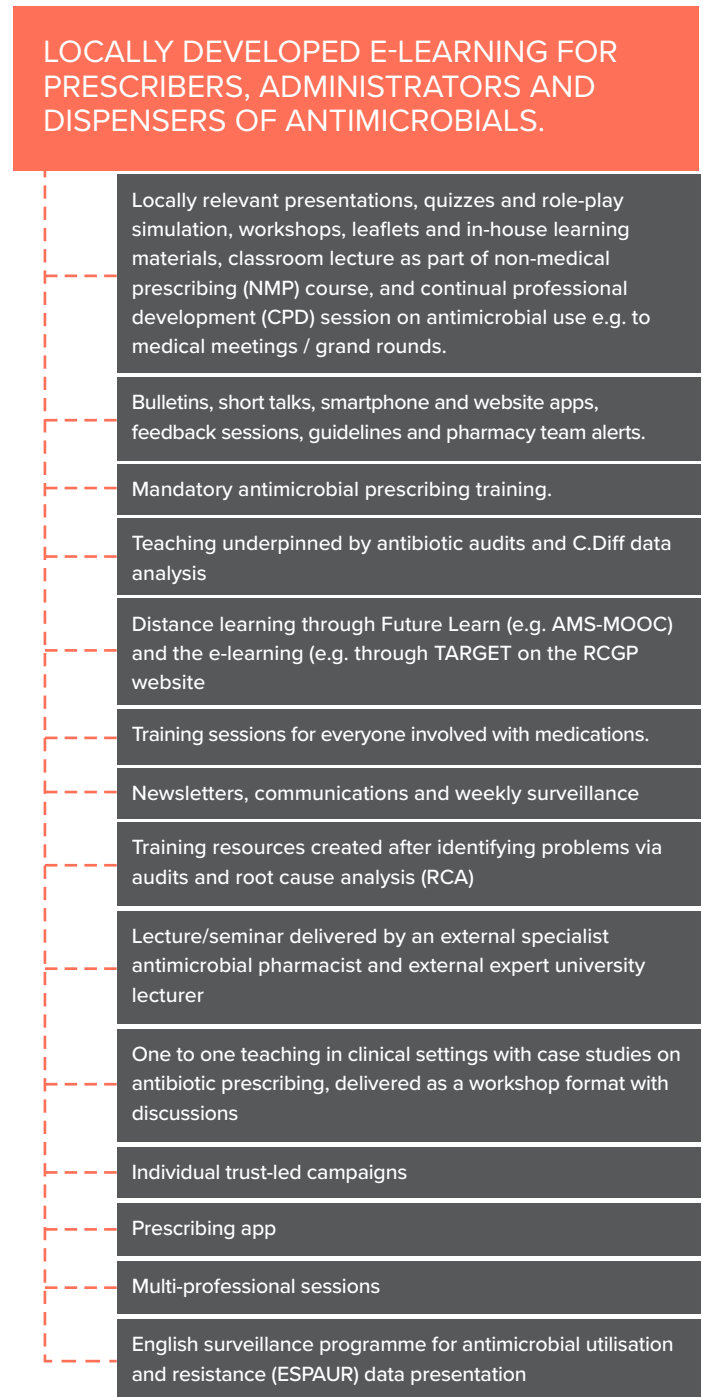


FIGURE 4 general approaches at a local/regional level to education and training



**Australia****Antimicrobial Stewardship in Australian Hospitals 2011**

In Australia, it is recommended that prescribers are taught to prescribe according to the Therapeutic Guidelines on Antibiotics at undergraduate, postgraduate and professional development programmes. Hospitals are highlighted as responsible for educating clinical staff about local AMS programmes (Figure 4).

[VIEW AMS DOCUMENT](#)

**Ghana**

As part of developing its national action plan on AMR, Ghana conducted baseline assessment of knowledge, attitudes, beliefs and practices of not only healthcare professionals but also Civil Society Organisations in health<sup>8</sup>. Following this a training programme for media practitioners, pharmacists, nurses, traditional rulers and civil society organisations/non governmental organisations was implemented from 2015<sup>9</sup>

## Reports, Training Manuals, Educational materials



From a presentation given by Director of Pharmaceutical Services  
Ministry of Health Ghana - Martha Gyansa

**China**

Following a survey in 2016, educators in Chinese medical schools have recognised the importance of developing AMR education and training programmes. Three AMR education and training programmes were designed following a national project: (1) a programme for undergraduate students in medical schools has been approved and launched at Peking University as an optional course open to all undergraduate students; (2) a training programme for chief pharmacists on antimicrobial stewardship has launched its pilot projects in five provinces across China; (3) the programme for students in clinical medical students have been approved to be launched at Peking University from 2017.

**India**

Strategic priority 1 of India's AMR action plan 2017 – 2021, focuses on improving awareness and understanding of AMR through effective communication, education and training, and has 2 focus areas – first is communications and information, education, communication (IEC) resources to raise awareness amongst all stakeholders, and second focus area is education and training to improve the knowledge and behaviour of professionals in all sectors.

[VIEW AMR DOCUMENT](#)

**South Africa**

In South Africa as part of implementing the national AMR action plan, an antibiotic prescribing license to be awarded following an antibiotic prescribing course is being developed in collaboration with the Health Professions Council of South Africa and providers of health. It was envisaged that it would be a biennial, renewable, web-based qualification.

In addition,

- there are two national training centres which rapidly train prescriber-pharmacist-hospital manager teams from provincial hospitals throughout SA to promote the initiation of ASPs in their hospitals and in turn train local practitioners in stewardship

and

- An open learning free course on Clinical Antibiotic Stewardship for which a certificate of completion is awarded for practitioners who complete the course,

[VIEW CLINICAL ANTIBIOTIC STEWARDSHIP ARTICLE](#)

## CLINICAL ANTIBIOTIC STEWARDSHIP FOR SOUTH AFRICA

 WATCH VIDEO

## FREE WORLDWIDE ACCESS TO AMS TRAINING

Free worldwide access to AMS training is available through Massive Open Online content (MOOCs) are available from the universities of Uppsala (Sweden)<sup>10</sup> and Dundee (UK)<sup>11</sup>.

FIGURE 5

Antimicrobial Stewardship: Managing Antibiotic Resistance by University of Dundee and British Society for Antimicrobial Chemotherapy

ONLINE COURSE

### Antimicrobial Stewardship: Managing Antibiotic Resistance

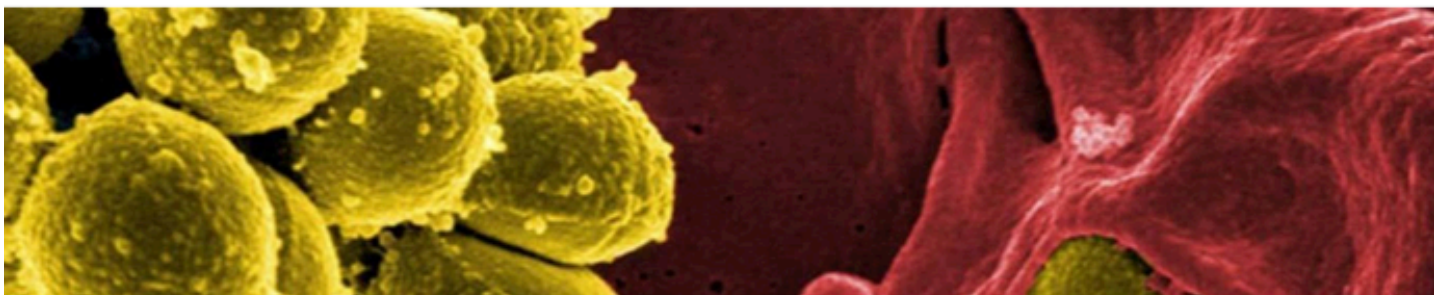
Understand antibiotic resistance, and how antimicrobial stewardship can slow down or reduce it, with this free online course



Join free

Upgrade - £59

What's the difference?



ONLINE COURSE

### Antibiotic Resistance: the Silent Tsunami

Understand antibiotic resistance and what actions are needed to address this increasingly serious global health threat



Register interest




COUNTRY	ACTIONS RELATING TO GLOBAL ACTION PLAN OBJECTIVE 1	STRATEGIES TO IMPROVE ANTIBIOTIC PRESCRIBING/ STEWARDSHIP PRACTICES
Australia	<ul style="list-style-type: none"> <li>Develop public campaigns across sectors to increase antibiotic resistance awareness through education and training.</li> </ul>	<ul style="list-style-type: none"> <li>A National AMS network to co-ordinate national projects aimed at producing a consistent approach to AMS.</li> <li>Develop resources to support the implementation of AMS. Existing accreditation and quality assurance programmes to be reviewed to ensure compliance with AMS practices.</li> </ul>
Canada	<ul style="list-style-type: none"> <li>Increase promotion of appropriate use of antimicrobials in human and animal medicine using AMR awareness campaigns.</li> </ul>	<ul style="list-style-type: none"> <li>Support research and dissemination of results regarding research on stewardship measures.</li> </ul>
Germany	<ul style="list-style-type: none"> <li>Increasing education and awareness of AMR aimed at the public.</li> <li>Developing a training programme for continuing professional development (CPD) and determining whether CPD in AMR could be enforced.</li> </ul>	<ul style="list-style-type: none"> <li>Creating a checklist approach for developing communication strategies for doctor/patient discussions regarding the use of antibiotics.</li> <li>Developing an online forum for healthcare professionals.</li> <li>Certain hospitals to contribute towards quality reports.</li> </ul>
Norway	<ul style="list-style-type: none"> <li>Improve the level of understanding of AMR amongst the general population by implementing mass media campaigns.</li> <li>Set up infection control conferences for healthcare personnel which focus on antibiotic guidelines.</li> </ul>	<ul style="list-style-type: none"> <li>Develop the Prescription Register to incorporate a diagnostic code on all antibiotic prescriptions for humans to allow antibiotic use to be recorded.</li> <li>Review the possibility of setting up a feedback system for GP prescribing and offer peer review assessments of antibiotic prescribing.</li> </ul>
Spain	<ul style="list-style-type: none"> <li>Developing a national awareness campaign aimed at all healthcare workers and public and a strategic plan for education and training.</li> <li>An ongoing training programme will be set up for healthcare professionals regarding AMR.</li> </ul>	<ul style="list-style-type: none"> <li>The self-evaluation of prescribers will be developed and encouraged.</li> </ul>
South Africa	<ul style="list-style-type: none"> <li>AMR public awareness campaigns to be introduced, including vaccination awareness.</li> <li>Core curricula for AMR will be implemented.</li> </ul>	<ul style="list-style-type: none"> <li>Provide leadership and guidance to develop effective AMS at all levels.</li> <li>Incorporate AMS activities into job descriptions, performance appraisals and CPD activities.</li> <li>A series of AMS interventions are being implemented (for example, AMS ward rounds and a dedicated antibiotic section in drug charts).</li> </ul>
UK	<ul style="list-style-type: none"> <li>Embed infection prevention practices into all education programmes for healthcare workers.</li> <li>Ensure adherence to local guidelines.</li> <li>Audit local prescribing to determine the outcome of antimicrobial stewardship practices.</li> <li>Increase public engagement focusing on the appropriate use of antimicrobials.</li> </ul>	<ul style="list-style-type: none"> <li>Work with Royal Colleges and professional bodies to identify how to use appraisal and revalidation systems to reinforce AMS.</li> </ul>
USA	<ul style="list-style-type: none"> <li>Implement public health programmes. By 2020, set up antimicrobial stewardship programmes in all acute hospitals.</li> </ul>	<ul style="list-style-type: none"> <li>Support other countries to develop and implement national plans and strategies to enhance AMS.</li> <li>Develop appropriate metrics to determine the success of AMS effort.</li> </ul>

TABLE 2

A summary of antibiotic awareness/ education and training strategies in national antimicrobial resistance action plans<sup>12</sup>

## TOOLKIT RESOURCE


### SITE LINKS

 5 <https://www.gov.uk/government/publications/the-health-and-social-care-act-2008-code-of-practice-on-the-prevention-and-control-of-infections-and-related-guidance>


 6 <https://www.gov.uk/government/publications/clostridium-difficile-infection-how-to-deal-with-the-problem>

 7 <https://www.gov.uk/government/publications/antimicrobial-stewardship-start-smart-then-focus>

 8 <https://www.rpharms.com/resources/frameworks/prescribers-competency-framework>

 9 <http://ghndp.org/reactcso/index.php/ghana-cso-reports/144-report-assessment-of-the-knowledge-attitudes-beliefs-and-practices-of-civil-society-organisations-in-health-on-antibiotic-use-and-resistance>

 10 <http://ghndp.org/reactcso/index.php>

 11 <https://www.futurelearn.com/courses/antibiotic-resistance>

 12 <https://www.futurelearn.com/courses/antimicrobial-stewardship>

13 Adapted from: Sadak M, Cramp E, Ashiru-Oredope D. Current Treatment Options in Infectious Diseases 8 (2) 57–712 <https://www.futurelearn.com/courses/antimicrobial-stewardship>

## SUMMARY

Whilst national AMR action plans include education and training, currently the global picture of implementation is mixed, highlighting more work and coordination is required.

## WHAT ARE COMPETENCES FOR ANTIMICROBIAL PRESCRIBING AND STEWARDSHIP

Competences, or a competency framework, are sets of behaviours that are instrumental in the delivery of desired results.<sup>13 14</sup> These behaviours support individuals and an organisation in the attainment of organisational set objectives.

Why are competencies important?

Competences can be used by prescribers to help develop their prescribing practice at any point in their professional development in relation to prescribing antimicrobials and can be used to plan continuing professional development in order to maintain and improve their competence.

In addition to the individual benefits of competences, competences can also provide clarity for regulators, education providers and professional bodies to inform standards, guidance and the development of training.

To understand the level of competence, it is necessary for individuals to undertake an honest assessment of their current level of knowledge and skills and their ability to apply them in practice. The help of others (e.g. colleagues, peers and/or manager) can be sought in this assessment. Once there is a realistic assessment of knowledge, skills and competence, learning needs and how these can be met can be determined. It will be important to revisit the competences and ensure continuous assessment to identify progress in achieving all of the competences.<sup>15</sup> It is important that developed competences should align with relevant national/international guidance and resources

## WHO SHOULD THE COMPETENCES BE INTENDED FOR?

Antimicrobial Prescribing and Stewardship competences should be developed for all healthcare workers but in particular for

Independent prescribers:

- **A primary care/family medicine doctor**
- **Physicians**
- **Surgeon**
- A medicine **trainee**
- A **first year graduate** from medical school who can write and sign antimicrobial prescriptions
- A **nurse or pharmacist prescriber** who can prescribe a range of antimicrobials for a range of clinical conditions, without supervision.
- A **dentist** who can prescribe several different antimicrobials

As well as non-independent prescribers (where relevant) including:

- Nurse or pharmacist prescribers who can only prescribe specific antimicrobials (e.g. trimethoprim) in specific circumstances (e.g. urinary tract infections)
- **Final year medical students** who are encouraged to write prescriptions, but need a qualified doctor to sign the prescription

## TOOLKIT RESOURCE

### ARTICLES

14 Whiddett S, Hollyforde S. The Competencies Handbook. London: Institute of Personnel and Development, 1999.

15 Bartram D, Robertson I, Callinan M. Introduction: a framework for examining organisational effectiveness. In: Robertson IT, Callinan M, Bartram D, eds. Organisational Effectiveness: The Role of Psychology. Chichester: Wiley, 2002; 1–12.

## DEVELOPING COMPETENCES

Competences should be developed using an evidence-based approach. One example of a step-wise approach taken to develop competences is:



## CURRENT LANDSCAPE: DEVELOPED COMPETENCES ACROSS THE WORLD: UK - NATIONAL COMPETENCES

### DEVELOPMENT OF THE FIRST NATIONAL ANTIMICROBIAL STEWARDSHIP COMPETENCES

#### WATCH VIDEO

The UK antimicrobial prescribing and stewardship competences consists of five dimensions, each of which includes statements that describe the activity and outcomes that prescribers should be able to demonstrate

- Educating the public and clinicians in the prudent use of antimicrobials as part of an antimicrobial stewardship programme is of paramount importance to control AMR. Improving surveillance, and infection prevention and control are other key strategies.
- Using current available evidence, regulatory documents and national antimicrobial stewardship guidance for primary and secondary care, **five competency dimensions (31 statements)** for antimicrobial prescribing and stewardship competences were developed in England (table 1).
- The competences are designed to complement the United Kingdom's Generic prescribing competency framework for all prescribers
- The five dimensions of competencies are shown in the table with one example of a competency statement for each category
- All competencies can be found on the UK Department of Health's website

#### VISIT DEPARTMENT OF HEALTH SITE



Five Dimensions	No of Statements	Illustrative example of competency statements
1) Infection prevention and control: all independent prescribers must understand the principles and demonstrate competence in preventing and controlling infections	5 statements	Understand how current vaccines can benefit prescribing practices, including reducing the need for prescribing antimicrobials and decreasing resistant antimicrobial resistant strains e.g. of <i>S. pneumoniae</i> .
2) Antimicrobial resistance and antimicrobials: including modes of action and spectrum of activities of antimicrobials and the mechanisms of resistance	6 statements	Knowledgeable in the appropriate use of antimicrobial agents for: <ul style="list-style-type: none"> <li>• prophylaxis to minimise the risk of infection</li> <li>• treatment of infections</li> </ul>
3) Prescribing antimicrobials: including the key elements in prescribing appropriate antimicrobial agents for prophylaxis and treatment	8 statements	Competent in AM prescribing by demonstrating knowledge of when not to prescribe antimicrobials, and use of alternatives, such as the removal of invasive devices, e.g intravenous or urinary catheters and incision and drainage of abscesses.
4) Antimicrobial stewardship: demonstrating an understanding and including antimicrobial stewardship in day to day practice	8 statements	Demonstrate clinical competence and understand the importance of Appropriately choosing one of the five antimicrobial prescribing decisions 48 hours after initiating antimicrobial treatment (ARHAI Guidance – Start Smart – then Focus)
5) Monitoring and learning: all independent prescribers must demonstrate continuing professional development in antimicrobial prescribing and stewardship	4 statements	Demonstrate CPD in AMS by using locally agreed process measures of quality (eg compliance with guidance), outcome and balancing measures, such as unintended adverse events or complications.

## EXPERT PROFESSIONAL CURRICULUM FOR ANTIMICROBIAL PHARMACISTS IN THE UK

Additionally in the UK, expert professional curriculum has been developed for antimicrobial pharmacists who mainly lead antimicrobial stewardship activities in hospitals.

The curriculum was developed by the UK Clinical Pharmacy Association Pharmacy Infection Network and endorsed by the Royal Pharmaceutical Society as a tool to support pharmacists in meeting the requirements for joining the Royal Pharmaceutical Society Faculty. The aim of the curriculum was to support antimicrobial pharmacists in delivery of antimicrobial stewardship. The curriculum is available to view via <http://bsac.org.uk/ukcpa-expert-professional-curriculum-for-antimicrobial-pharmacists/>

The curriculum covers five areas and within each area there are three levels of competency that cover professional practice from being new to the specialty (Advanced stage I), through gaining experience of complex issues (Advanced stage II) to working at national level (Mastery).

1. Infection and antimicrobial stewardship in context: awareness and interpretation of local and national antimicrobial usage and resistance data, national and international policy pertaining to antimicrobial stewardship and global issues in AMR.
2. Clinical microbiology: theory, laboratory tests and their interpretation, clinical principles of infection and principles of AMR.
3. Antimicrobials: therapeutic drug monitoring, pharmacology, pharmacokinetics and pharmacodynamics, and antimicrobial use in special populations.
4. Management of clinical syndromes: organized by bodily system.
5. Principles of an antimicrobial stewardship plan: role of the stewardship team and key components of hospital and primary care stewardship programmes.

Examples of the knowledge and behaviours expected at different levels are given within the document

A Syllabus for Infection and Antimicrobial Stewardship is also suggested.



## GUIDANCE FOR THE KNOWLEDGE AND SKILLS REQUIRED FOR ANTIMICROBIAL STEWARDSHIP LEADERS (USA)<sup>16</sup>

In the USA, the Society for Healthcare Epidemiology of America partnered with other leaders in advancing the field of antimicrobial stewardship, to develop a summary description of the core knowledge and skills required for antimicrobial stewardship professionals engaged with building, leading, and evaluating Antimicrobial Stewardship Programmes (). The categories included were:

- General principles of antimicrobial stewardship
- Approaches to stewardship interventions
- Antimicrobials
- Microbiology and laboratory diagnostics
- Measurement and analysis
- Informatics/IT Program building and leadership
- Special populations and non-acute hospital settings
- Infection control

## AN ANTIBIOTIC STEWARDSHIP CURRICULUM FOR MEDICAL STUDENTS<sup>17</sup>

A curriculum intended for use in U.S. medical schools. It is comprised of: three didactic lectures with facilitator notes and audio recordings, nine corresponding exam questions (available on request), and five small group activities with facilitator guides. The didactic lectures are geared toward medical students in the pre-clinical years whilst the small group activities are geared toward medical students on clinical clerkships

## EUROPE

*A European consensus: ESCMID generic competencies in antimicrobial prescribing and stewardship*

Currently, European Society of Clinical Microbiology and Infectious Diseases is developing a Europe-wide consensus-based set of generic competencies in antimicrobial prescribing and stewardship that is relevant for all independent prescribers across Europe.


No published competences have been located for any country Africa or in Australia, India, China or South Africa.

## TOOLKIT RESOURCE

### ARTICLES

17 Cosgrove, S., Hermsen, E., Rybak, M., File, T., Parker, S., & Barlam, T. (2014). Guidance for the Knowledge and Skills Required for Antimicrobial Stewardship Leaders. *Infection Control and Hospital Epidemiology*, 35(12), 1444-1451. doi:10.1086/678592

### SITE LINK

 18 <https://www.cdc.gov/getsmart/community/for-hcp/continuing-education.html>

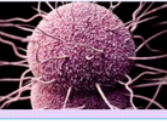
## EDUCATIONAL RESOURCES

### Reducing Antimicrobial Resistance level 1 e-learning

was developed in England to support all health and social care staff – both clinical and non-clinical - in a variety of settings to understand the threats posed by antimicrobial resistance, and ways they can help to tackle this major health issue.

## Reducing Antimicrobial Resistance

An e-learning package to support staff in understanding the threats posed by antimicrobial resistance



**Menu**

- Antimicrobial Resistance
- Resources for all staff working in health and social care
- Resources for all staff working in primary care (including GPs)
- Meet the team
- Open access session
- How to access

**Antimicrobial Resistance**

The Antimicrobial Resistance programme has been designed to support all health and social care staff – both clinical and non-clinical - in a variety of settings to understand the threats posed by antimicrobial resistance, and ways they can help to tackle this major health issue. This programme has been developed by Health Education England in collaboration with Public Health England and NHS England.

Antibiotic (antimicrobial) resistance poses a major threat to everyday life and modern day medicine where lives could be lost as a result of antibiotics not working as they should. All health and social care staff, as well as the public, have a very important role in preserving the power of antibiotics and in controlling and preventing the spread of infections.

This programme consists of an [e-learning session](#) entitled 'Reducing Antimicrobial Resistance: An Introduction' aimed at all health and social care staff, and a myriad of resources to support awareness and education of clinical staff on antimicrobial resistance in different care settings.

The aims of these resources are to help health and social care staff:

- Discuss why there is such a concern about misuse of antibiotics and antimicrobial resistance.
- List the key risks for development of antimicrobial resistance.
- Identify their role in tackling antimicrobial resistance.

There is also a [guide for GPs](#) and a short informative [animation](#) which is aimed at the public and has been produced in partnership with Public Health England to help all

In partnership with



 VISIT SITE

**CDC: Get Smart about Antibiotics**

Get Smart: Know When Antibiotics Work in Doctor's Offices

Get Smart Home CDC > Get Smart Home

About + For Healthcare Professionals

For Patients +

For Healthcare Professionals -

Outpatient Healthcare Professionals +

Inpatient Healthcare Professionals +

Community Pharmacists +

Continuing Education & Curriculum Opportunities +

Improving Prescribing +

Program Development and Evaluation +

Programs and Measurement +

Partners +

Materials and References +

CDC's Get Smart program has resources for healthcare professionals working in outpatient and inpatient healthcare settings, as well as community pharmacies.

**OUTPATIENT HEALTHCARE PROFESSIONALS**  
Adult and pediatric treatment guidelines, materials to use with patients in the outpatient setting...

**INPATIENT HEALTHCARE PROFESSIONALS**  
Resources to implement antibiotic stewardship programs in an inpatient setting, success stories...

**COMMUNITY PHARMACISTS**  
Materials to use with your patients...

**CONTINUING EDUCATION AND CURRICULUM OPPORTUNITIES**  
Opportunities for healthcare professionals to learn more about antibiotic resistance and appropriate antibiotic prescribing practices...

 VISIT SITE

**TARGET toolkit for primary care**

TARGET (Treat Antibiotics Responsibly, Guidance, Education, Tools) resources aim to help influence health-workers, prescribers' in primary care and patients' personal attitudes, social norms and perceived barriers to optimal antibiotic prescribing. It includes a range of resources that can each be used to support health-workers, prescribers' and patients' responsible antibiotic use, helping to fulfil CPD and revalidation requirements. The training resources are available for free and can be accessed online by different health professionals, GPs, trainee GPs, medical students, GP trainers, physician assistants, practice nurses and non-medical prescribers.

**TARGET Antibiotics toolkit**



[Training resources](#)   [Patient information leaflets](#)   [Self assessment checklist and audit](#)


[Resources for clinicians](#)   [Antibiotic management guidance](#)   [External clinical resources](#)



 VISIT SITE

**A GP guide to antimicrobial resistance**

A SHORT EDUCATIONAL VIDEO FOR GENERAL PRACTITIONERS

 WATCH VIDEO

**Antimicrobial stewardship workbook for nurses:**



**Antimicrobial Stewardship**



**Educational Workbook**

**WORKBOOK CONTENTS**

Contents	Page	Section 3: Bacteria, Resistance and Antibiotics	Section 5: Considerations for Hospital Practice
Target Audience	3		
How to Use the Workbook	4	Bacteria, Resistance and Antibiotics – The Basics	Considerations for Hospital Practice
NMC Revalidation	5	Different Types of Bacteria	IV to Oral Switch Therapy (IVOST)
KSF Mapping	6	Where Do We Find Microbes and Microbial Infection?	Sign 104 guidelines – Antibiotic Prophylaxis in Surgery
<b>Section 1: Introduction to Antimicrobial Stewardship</b>		Antimicrobial Resistance	Gentamicin and Vancomycin
Introduction to Antimicrobial Stewardship	7	How Does Antimicrobial Resistance Develop?	Sepsis Management
Antimicrobial Prescribing and Stewardship Videos	8	Antibiotics and How They Work	Resources and Reading List
Role of the nurse in Antimicrobial Stewardship Video	8	Antibiotics and How They Work: Common side effects	Acknowledgements
<b>Section 2: Antimicrobial Stewardship in Practice</b>		<b>Section 4: Diagnosis and Assessment of Infection</b>	Evaluation and Written Reflective Account
Antimicrobial Stewardship in Practice	9	Microbiology Investigations	Certificate of Achievement
Antimicrobial Stewardship in Scotland	9	Avoiding Contamination of Blood Cultures	
HAI Standards	10	Testing for Antimicrobial Susceptibility	
Antimicrobial Management Teams (AMT)	11	Antimicrobial Prescribing Practice	
Scottish Patient Safety Programme (SPSP) Responsibility and Accountability	12	Local Antimicrobial Prescribing Policy	
The Role of the Nurse in Antimicrobial Management	14	Patient Education, Awareness and Involvement	
		Review of Antimicrobial Prescriptions	

 VISIT SITE

**Antibiotic Guardian**

an educational and behaviour change intervention resource which asks health and social care professionals, leaders, students, educators and members of the public to choose one of the available tailored pledges on how they plan to contribute to tackling AMR.



Antibiotic Guardian was developed as part of UK activities for European Antibiotic Awareness Day (EAAD), and in support of the UK 5-year AMR strategy.

**Process** and **outcome** evaluations for the Antibiotic Guardian (AG) campaign performed and published in peer review publications (BMC Public Health and Journal of Public Health) in 2016 showed the wide reach of the campaign and its success in increasing commitment to tackling AMR in both healthcare professionals and members of the public as well as leading to increased knowledge and changed behaviours (self-reported

 VISIT SITE

**The prescribing simulator**

is an online training environment that provides the opportunity for prescribers to practice in a simulated online environment at any time or place. Users are presented with clinical scenarios that require a prescription on a certain prescription form. The prescription is then automatically scored and feedback is provided to guide the user as to where future improvements can be made.

 VISIT SITE

**The Prescribing Safety Assessment (PSA)**

The Prescribing Safety Assessment (PSA) is an assessment required of all foundation medical trainees who have studied in UK medical schools or overseas. Over 40,000 students and doctors have now benefited from taking part in both the assessment and associated training materials. Currently 400 question items out of a total of around 3,000 (13%) cover antimicrobial drugs and their usage.

 VISIT SITE

PRESCRIBING SKILLS FOR  
THE PSA EXAM FROM ELSEVIER  
AND PODMEDICS

 WATCH VIDEO

**The ScRAP Programme**

an educational toolkit for primary to help prescribers to reduce unnecessary prescribing of antibiotics. It consists of: - A pre-recorded presentation that can be streamed online - Icebreaker video - Patient Consultation video

 VISIT SITE

**NICE**

developed a free e-learning session on antimicrobial stewardship targeted at commissioning and provider organisations, service managers and local decision-making groups, to ensure that effective antimicrobial stewardship programmes are in place, and that prescribers are supported to make changes to their use of antimicrobials where necessary

 VISIT SITE

**AMSportal**

is a free online forum collaboratively developed by The Royal Pharmaceutical Society and the University College London and funded by Health Education England North Central and East London, that signposts viewer's to resources and information to promote learning about microbiology and antimicrobial stewardship.



**BSAC AMR Portal**

The antimicrobial resource centre (ARC) was developed by the British Society of Antimicrobial Chemotherapy as a global repository of information for all people interested in the effective management of infectious diseases



**CANADA**

The CPhA provides resources on the roles pharmacists can play in antimicrobial stewardship, a webinar on stewardship for common infections, and links to Canadian stewardship initiatives.



Antibiotic Stewardship Open Virtual Learning Committee (European Society for Clinical Microbiology and Infectious Diseases) - AS-OVLC is an open-access web-based resource that has been created to provide information and tools to foster antimicrobial stewardship among healthcare professionals. (Twitter: @ESGAP\_ABS)



Do Bugs Need Drugs? (DBND) is a community education program about handwashing and responsible use of antibiotics. Materials are available for healthcare professionals and the public that explain why antibiotic resistance is an issue and steps to prevent antibiotic resistance from developing.



Antimicrobial Resistance Learning Site for Veterinarians open-source teaching modules are designed for integration into existing veterinary school courses regarding: Pharmacology, Microbiology, Public Health, and Species-specific medicine.



## Antibiotic Prescribing Game



“On call: antibiotics”, an electronic prescribing game to support and encourage the prudent use of antimicrobials in acute care was developed by researchers and clinicians at Imperial college. “On call: antibiotics” allows doctors, nurses and pharmacists to manage a series of virtual patients attending a simulated hospital. Racing against the clock and the increasing workload, players receive information about the symptoms experienced by patients and have to diagnose and manage the cases. To be successful, players have to make optimal use of antibiotics and antibiotic prescribing behaviours.

The game provides immediate feedback on players’ performance and decisions, considering clinical accuracy and the impact on other professionals and the wider hospital environment.

# CHAPTER 14

▶ AUTHOR: **MARC MENDELSON**

## ANTIBIOTIC STEWARDSHIP EDUCATION IN LOW RESOURCE SETTINGS

### THE AIM OF THIS CHAPTER IS TO:

To review the educational resources predominately developed by, and applicable to, low and middle-income countries.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Learners will assess the available educational resources in their setting and the need to expand their concept of who delivers antibiotic stewardship education in countries with a lack of infection specialists.

#### ▶ RECOGNISING A PROBLEM

Studies of knowledge, attitude and practice in undergraduate health students from high resource settings relating to antibiotic resistance (ABR) and antibiotic stewardship (ABS) have repeatedly demonstrated that the prescribers of tomorrow are inadequately prepared to prescribe and optimally administer antibiotics. The few similar studies from low- and middle-income countries (LMIC) concur; In South Africa, only one third of final-year medical students from 3 of the country's top medical schools felt confident to prescribe antibiotics, and 95% recognised their need for better education in ABR/ABS (Wasserman 2017). Similarly, only one third of final-year South African pharmacy students remembered having had formal stewardship teaching, yet 90% desired it (Burger 2016). Postgraduate education too, needs improving; almost all of those questioned in a Brazilian study, believed ABR was an important problem, only 3% felt that practicing stewardship was important (Guerra). All too often, ABR is seen as someone else's problem, and hence understanding of the need to become better educated in stewardship, is lost.

#### ▶ THE CHALLENGE

Staffing shortages, fragmented health systems, and lack of infection specialists across the health professions who can teach stewardship, impose significant challenges on delivering antibiotic stewardship education in LMICs. Furthermore, due to stretched service delivery, apportioning time for stewardship education for postgraduate health care professionals can cause further tension in the system.

#### ▶ MAKING THE MOST OF WHAT IS ALREADY OUT THERE

In view of these challenges, LMICs need to make use of what is already out there, especially online educational opportunities which have become increasingly accessible through developments in global information and communications technology (Figure 1).



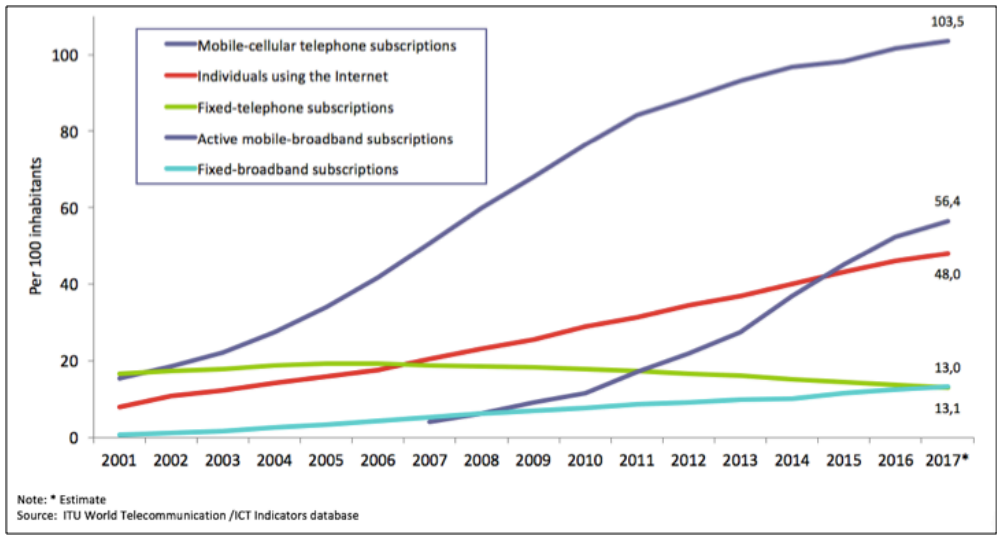


FIGURE 1  
Global trends in mobile cellular telephone subscriptions and internet usage  
Image by kind permission International Telecommunications Union

With the massive scale of social media and other content creation that happens on the web every minute (Figure 2), there are clearly huge opportunities for online learning.

(There are also ‘one-stop-shop’ websites providing literature, social media-based tools and twitter chats such as the University of Minnesota’s Center for Infectious Diseases Research and Policy (CIDRAP) website

 VISIT SITE

 VISIT CIDRAP SITE

Opportunities include access to comprehensive stewardship courses either developed in high income settings but applicable globally, such as:

or The ReAct toolbox,

BSAC’S MASSIVE ONLINE OPEN COURSE

 WATCH VIDEO

 VISIT ReACT SITE

which contains a number of educational videos highlighting why stewardship is important.

or those developed in, and specifically directed towards, the LMIC-setting, such as the South African Antibiotic Stewardship Programme (SAASP) Open Learning course:

ReAct toolbox

 WATCH VIDEO

 VIEW SLIDE SET

The World Health Organisation too, is developing an active Community of Practice, to support a discussion forum around development of national action plans, which will include educational resources. Further stewardship educational programs developed in low resource settings, which are freely available are outlined in Table 1.

PROGRAMME	LEAD ORGANISATION	COUNTRY	TARGET AUDIENCE	DESCRIPTION
<a href="#">Clinical Antibiotic Stewardship for South Africa</a>	South African Antibiotic Stewardship Programme	South Africa	Medical Students Physicians	Free, self-paced online course introducing AMS, describes how to implement ASPs, & provide guidance for prescribing and interpreting clinical results, and teach about IPC.
<a href="#">South African Antibiotic Stewardship Prescribing Guidelines for Adults</a>	South African Antibiotic Stewardship Programme	South Africa	Medical Students Physicians Pharmacists	Free algorithmic antibiotic prescribing guidelines App, hosted on the Essential Medical Guidance (EMG) platform. Includes training on stewardship principles & approach, as well as guidelines for specific infections
<a href="#">Distance Learning Course in Antimicrobial Stewardship for Africa</a>	Infection Control Africa Network	Africa	Physicians, Pharmacists Microbiologists Nurses	3.5-month online distance learning course - 5 modules relating to infectious diseases; one focused on AMS. Lectures, reading materials, & discussion forums to engage with tutors & other students. Free for African participants.
<a href="#">Online Rational Medicines Use module</a>	University of Western Cape	South Africa	Health Care Professionals	Single semester online course with weekly tasks, discussion forums & written assignments
<a href="#">Antibiotics Smart Use</a>	AMR Containment Program in Thailand	Thailand	Health Care Professionals, Patients, Public	Country-wide education campaign for prescribers. Shared experiences, treatment guidelines, diagnostic tools, patient education tools (DVDs, pamphlets & other materials)
<a href="#">ASPIC (Antibiotic Stewardship, Prevention of Infection &amp; Control)</a>	Indian Council of Medical Research	India	Pharmacists Microbiologists	5-day workshop of lectures, site visits, practical training focusing on IPC, implementation of antimicrobial policy guidelines, conducting research projects in antibiotic policy
<a href="#">Dept of Health Manual of procedures for implementing AMS in hospitals</a>	Philippines Dept of Health & WHO	Philippines	Physicians	Operational guide and reference for developing training programs and materials
<a href="#">Training-of-Trainers Workshop on AMS Advocacy Training</a>	Philippines Dept of Health & WHO	Philippines	Health Care Professionals	Interactive session on current initiatives & challenges of each hospital in relation to IPC, rational use of antimicrobials and surveillance of AMR. Also included was a consultation on draft AMS pilot program implementation.
<a href="#">Training-workshop for government Level III hospitals on the implementation of the AMS</a>	Philippines Dept of Health & WHO Corazon Locsin Montelibano Memorial Regional Hospital	Philippines	Physicians	AMS program with an educational component piloted at Philippine General Hospital and Corazon Locsin Montelibano Memorial Regional Hospital, now scaled up to provide training at all Dept of Health level III hospitals

TABLE 1

Antimicrobial stewardship educational programmes developed by low-and middle-income countries. AMS – Antimicrobial Stewardship; ASP – Antimicrobial Stewardship Program; IPC – Infection Prevention & Control. Adapted from Susan Rogers Van Katwyk; Sara L Jones; Steven J Hoffman. Mapping educational opportunities for healthcare workers on antimicrobial resistance and stewardship around the world. Human Resources for Health (In Press).

**▶ EDUCATING HEALTH CARE PROFESSIONALS IN LOW RESOURCE SETTINGS – A HOSPITAL-BASED APPROACH**

It is generally accepted that education programmes should be combined with strong stewardship interventions for maximal effect, and not be delivered in isolation. Developing postgraduate education programmes for health care professionals in LMICs must take into account how stewardship will be delivered in a low resource setting with few trained infection specialists and will need to adapt the traditional concept of who the opinion leaders are that can influence adoption of good prescribing practice in low resource setting. While multidisciplinary hospital teams led by infectious diseases specialists, microbiologists, infectious diseases pharmacists and infection prevention control specialists may be achievable in high income countries and few individual hospitals in LMICs that have trained staff

it needs to be adapted in settings deprived of infection specialists. This is being done in South Africa, where two national training centres provide tools

**▶ VIEW SLIDE SET**

and practical training programmes for non-infection specialist teams from hospitals throughout the country. A team of a prescriber-pharmacist-nurse manager from each hospital, receive practical education on how to perform stewardship rounds in a variety of settings (wards, intensive care units, academic and district-level hospitals), diagnostic stewardship taught on laboratory rounds, and small group sessions (Figure 3) to cover essential pharmacology, and optimising use. These non-specialist teams then set up antibiotic stewardship programmes in their hospitals, and receive ongoing mentorship from their National Training Centre.

**▶ VIEW DOCUMENT**



**FIGURE 3**  
South African National Antibiotic Stewardship Training Course comprises practical stewardship ward and intensive care unit rounds, small group discussions, and laboratory teaching

An equally successful, sustainable reduction in antibiotic use has been achieved across a South African private hospital group employing non-specialist pharmacists trained in a simple stewardship intervention targeting 4, low-hanging fruit changes in prescribing.



VIEW DOCUMENT

A collaborative programme of mentorship of South African pharmacists by U.S. Infectious Diseases specialist pharmacists has been instrumental in developing pharmacists as valued antibiotic stewards in South Africa, and serves as an example of the value of collaborative educational programmes and partnerships between LMICs and high-income countries.



VIEW DOCUMENT

Developing nurse- and community health worker-led models of care in LMICs would further expand the potential models of stewardship and the needs for these cadres to receive role-specific education and training. Successful task shifting of antiretroviral management from doctors to primary health clinic nurses (Fairall et al.) is a good example of how nurses in low resource settings can play a greater role in stewardship.

## TOOLKIT RESOURCE

### ARTICLE

Guerra CM, Pereira CA, Neves Neto AR, Cardo DM, Correa L. Physicians' perceptions, beliefs, attitudes, and knowledge concerning antimicrobial resistance in a Brazilian teaching hospital. *Infect Control Hosp Epidemiol* 2007;28(12):1411-1414

### SITE LINK



Wasserman S, Potgieter S, Shoul E, Constant D, Stewart A, Mendelson M, Boyles TH. South African medical students' perceptions and knowledge about antibiotic resistance and appropriate prescribing: Are we providing adequate training to future prescribers? *S Afr Med J*. 2017 Apr 25;107(5):405-410. doi: 10.7196/SAMJ.2017.v107i5.12370. PMID: 28492121



Burger M, Fourie J, Loots D, Mnisi T, Schellack N, Bezuidenhout S, and Meyer JC. Knowledge and perceptions of antimicrobial stewardship concepts among final year pharmacy students in pharmacy schools across South Africa. *Southern African Journal of Infectious Diseases* 2016; 31(3):84–90



Fairall L, Bachmann MO, Lombard C, et al. Task shifting of antiretroviral treatment from doctors to primary-care nurses in South Africa (STRETCH): a pragmatic, parallel, cluster-randomised trial. *Lancet*. 2012 Sep 8;380(9845):889-98.

# CHAPTER 15

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## STEWARDSHIP IN DEVELOPED COUNTRIES

### THE AIM OF THIS CHAPTER IS TO:

To provide 2 examples of successful stewardship initiatives from a large academic medical center in North America.

To present an overview of interesting and successful stewardship initiatives in European countries.

To describe the current status of antimicrobial stewardship programs, challenges & opportunities in Gulf Cooperation State Countries (GCC).

To share success stories of implementing stewardship in the Gulf region.

To present an overview of national surveillance programs and stewardship in Australia.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Explain the pharmacists' role in the use of rapid diagnostic tests in the hospital setting
- Define interventions by a pharmacist in the management of *S. aureus* bacteremia
- Demonstrate basic awareness of stewardship initiatives running in European countries.
- Demonstrate skills for initiating prospective audit with intervention and feedback and preauthorization in limited resources setting
- Demonstrate awareness of surveillance programs and stewardship initiatives in Australia

### ▶ NORTH AMERICA

#### **Example 1: Role of Pharmacist in Management of Patients with *S. aureus* bacteremia**

Ideally, every stewardship program should employ an ID pharmacist with formal ID training gained through completion of an accredited post-graduate residency or fellowship in ID. In the United States there are only about 400 pharmacists with formal post graduate ID training. With more than 5,000 hospitals the reality of having an ID-trained pharmacist at every hospital is a challenge. Therefore it is necessary for antimicrobial stewardship programs (ASP) to utilize the talent of all pharmacists.

An established ASP in a 1,400 bed teaching hospital with ID pharmacists implemented a program utilizing all pharmacists to assist in the management of patients with *Staphylococcus aureus* bacteremia (SAB) 24 hours a day 7 days a week. Based on previous internal data, all patients with SAB were not being optimally managed, therefore ASP proposed a study to implement a pharmacist driven bundle approach. After obtaining support from the Division of ID and approval by the Pharmacy and Therapeutics committee the proposal became hospital policy.

When a blood culture turned positive and the rapid diagnostic test identified SAB, pharmacists were alerted via the electronic medical record 24/7. They would evaluate compliance with 4 components in the SAB bundle and make interventions if necessary.

To illustrate an example of pharmacists using a bundle approach to manage patients with *Staphylococcus aureus* bacteremia (SAB) you may wish to listen to this podcast. As you listen to the podcast consider the following



- What are the four metrics that make up the bundle?
- What was the impact on mortality of the pharmacist driven management of SAB bundle?
- How could you apply this program at your hospital to help improve the management of patients with SAB?

 VIEW SLIDE SET


**Example 2: Role of Pharmacists in Rapid Diagnostic Tests**

A pharmacist has multiple roles in an antibiotic stewardship program. One of the key roles can be helping to implement a rapid diagnostic test (RDT). A RDT without ASP can be a waste of money when the physician does not act on the results rapidly. The pharmacist can use the RDT result to make sure the patient is on the most effective antibiotic based on local hospital guidelines. For example if the RDT identifies methicillin susceptible *S. aureus* and the patient is on vancomycin, the pharmacist can recommend switching vancomycin to cefazolin or nafcillin. The ASP metric to collect for this intervention is time to effective therapy.


Several studies have show that a RDT with ASP involvement shortens the time to effective antibiotic therapy. Some studies have also shown a mortality benefit. The key to successful implementation within a hospital is to make sure the microbiologist and ASP pharmacist work together. This infographic demonstrates the 4 steps to implementing a RDT and how a pharmacist provides an important role in the process.


TOOLKIT RESOURCE


SITE LINK


 [An Automated, Pharmacist-Driven Initiative Improves Quality of Care for \*Staphylococcus aureus\* Bacteremia](#)

THESE STUDIES PROVIDE EXAMPLES OF PHARMACISTS USING RDT

 [Controversies in Antimicrobial Stewardship: Focus on New Rapid Diagnostic Technologies and Antimicrobials](#)

 [Review of Rapid Diagnostic Tests Used by Antimicrobial Stewardship](#)

 [Impact of rapid identification of \*Acinetobacter Baumannii\* via matrix-assisted laser desorption ionization time-of-flight mass spectrometry combined with antimicrobial stewardship in patients with pneumonia and/or bacteremia](#)

 [An Antimicrobial Stewardship Program’s Impact with Rapid Polymerase Chain Reaction Methicillin-Resistant \*Staphylococcus aureus\*/\*S. aureus\* Blood Culture Test in Patients with \*S. aureus\* Bacteremia](#)

Antibiotic Stewardship

Rapid Diagnostic Tests



#1

Microbiologist assesses the test



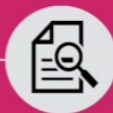
#2

ASP assesses potential impact



#3

ASP educates physicians



#4

ASP makes interventions/collects data

1. The microbiologist can identify and evaluate new RDT. They need to make sure the instrument can be incorporated in the current work flow within the lab.
2. The ASP pharmacist can evaluate the potential impact of the RDT on patient care. For example, if SAB RDT is being considered the first step is to identify how many patients at your hospital have SAB. The microbiologist can provide this data. Next the pharmacist should identify the “time to effective antibiotic therapy”. In hospitals using standard culture methods without a RDT, the time to effective therapy can be as long as 3-4 days.
3. Once the ASP team has decided to implement a RDT, the pharmacist should work with the microbiologist to provide education to the medical staff. Just sending an email or posting an announcement in a new letter is often not enough.
4. The ASP pharmacist can make interventions and collect data such as time to effective antibiotic therapy to document the impact on patient care.



### EUROPE

Europe is a great resource for antimicrobial stewardship, and it offers a huge diversity in culture and health systems. Most stewardship initiatives were started more than 20 years ago. Being aware of stewardship programmes in Europe can then be a source of inspiration.

#### **Stewardship initiatives at the European level**

##### *ESGAP*

ESGAP is the ESCMID (European Society of Clinical Microbiology and Infectious Diseases) Study Group for Antimicrobial stewardship (<https://www.escmid.org/index.php?id=140>). A summary of ESGAP activities is presented here:

 VIEW SLIDE SET

##### *ECDC*

The European Centre for Disease Prevention and Control (<http://ecdc.europa.eu/en/Pages/home.aspx>) has relentlessly worked to combat antimicrobial resistance (AMR). A selection of ECDC most prominent stewardship actions is detailed here:

 VIEW SLIDE SET

##### *European Commission*

The European Commission has issued a number of reports and guidance documents, and has done much to curb antimicrobial resistance, with a second 2017 European action plan on AMR :

 VISIT SITE

 VIEW AMR ACTION PLAN DOCUMENT

and 2017 EU guidelines on prudent use of antimicrobials in humans:

 VIEW PRUDENT USE OF ANTIMICROBIALS DOCUMENT

Other useful documents summarising the progress made in European countries:

 VIEW AMR REPORT DOCUMENT

 VIEW BEST PRACTICE ARTICLE

##### *WHO-Europe*

WHO regional office for Europe includes EU member states as well as many other European countries. It has done much to improve antibiotic use : useful resources, promotion of the World Antibiotic Awareness Week, country visits and educational courses, publications...

More information is available here:

 VISIT SITE

##### *E-Bug programme*

E-Bug has developed wonderful (free access) teaching resources about microbes and antibiotics, initially developed to teach children and teenagers, but the scope has expanded over the years : <http://www.e-bug.eu>

 VISIT SITE



**Examples of successes at national level**

A few national or regional initiatives are cited below as examples to illustrate a specific stewardship intervention. This is far from being exhaustive.

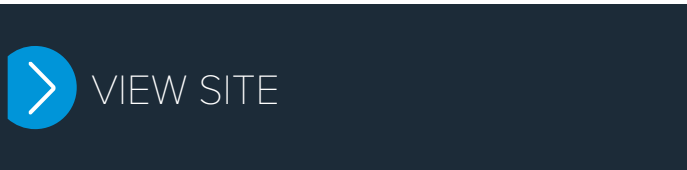
**1. Interventions at the health system level**

*Antibiotic stewardship cross-sectoral networks*

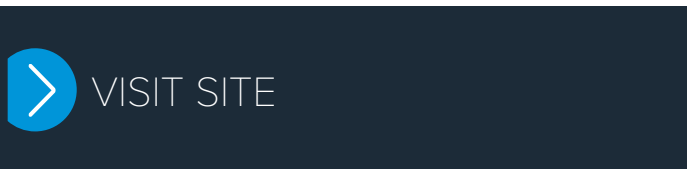
In some countries, such as Sweden;



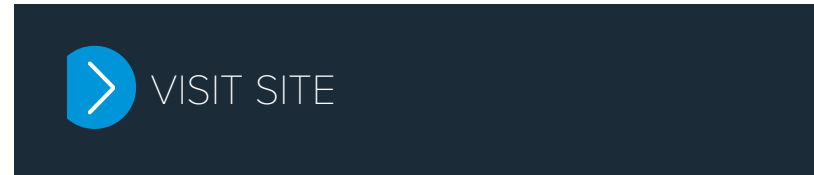
or France;



antibiotic stewardship programmes are implemented in different settings (hospital, primary care, long-term care facilities) and at local, regional and national levels. This is also done at a regional level in Andalusia in Spain;



or in Scotland in the UK

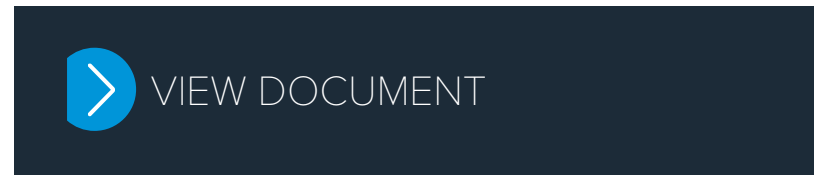


*Restrictive measures*

Restrictions on antibiotic prescribing are commonplace in hospitals, but are quite rare in primary care. In Slovenia, co-amoxiclav, fluoroquinolones, oral 3rd generation cephalosporins and macrolides' prescriptions are audited in the outpatient setting, and prescribers are fined if their prescriptions do not comply with national guidelines.

*Accreditation/Certification of hospitals*

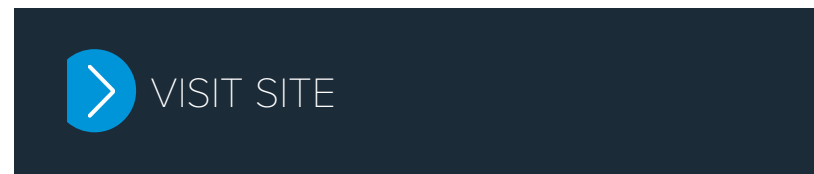
For example in France, implementation of an antibiotic stewardship programme (assessed using a composite indicator,



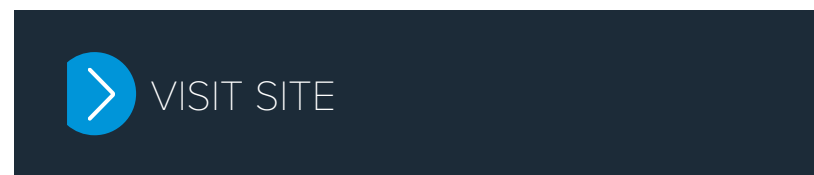
is mandatory in hospitals to get accredited.

*Pay-for-performance*

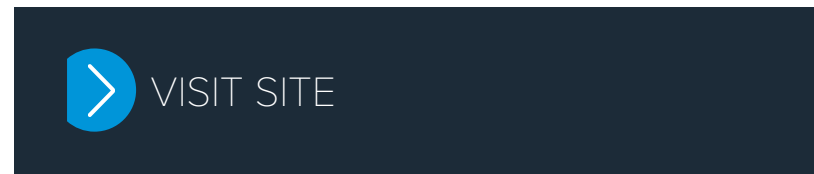
Some countries, such as France



or the UK in hospitals



and in primary care:



have introduced pay-for-performance systems linked to antibiotic use targets, and this has led to a decrease in antibiotic use.

## Public reporting

In England, the data on antibiotic consumption and resistance for both hospitals and primary care are publicly available on a website:



## 2. Interventions targeting healthcare professionals

### Education

Many educational resources are available. Let us cite the Massive Online Open Course on Antimicrobial Stewardship produced by the British Society for Antimicrobial Chemotherapy



In Germany, a 4-week training programme to become a certified 'ABS-expert' has been running for some years, and an ABS-network facilitates exchange of experience among antimicrobial stewards.



### Guidelines

Guidelines helping prescribers choosing the best antibiotic regimen exist in almost all countries. In the Netherlands, SWAB (The Dutch Working Party on Antibiotic Policy) introduced an electronic national antibiotic guide 'SWAB-ID' for the antibiotic treatment and prophylaxis of common infectious diseases in hospitals;



Every hospital in the Netherlands has been offered the opportunity to adapt this version to local circumstances and resources and distribute it through an independent website. At present, approximately 60 % of Dutch hospitals uses a local, customised version of SWAB-ID.



## Public commitment

In France, prescribers are encouraged to show their public commitment to prescribe antibiotics responsibly, by displaying a poster in the waiting room



## Practical tools for antimicrobial stewardship teams

Most countries are now sharing these at national level, such as in France;



or in the Netherlands;



The University of Antwerp (Belgium) has developed practical tools (with a free e-learning module) for point-prevalence surveys.



## 3. Interventions targeting the general public

### Public awareness and information campaigns

A recent review has been published:



Information documents

- Non-prescription pads in France

 VIEW DOCUMENT

or in the UK

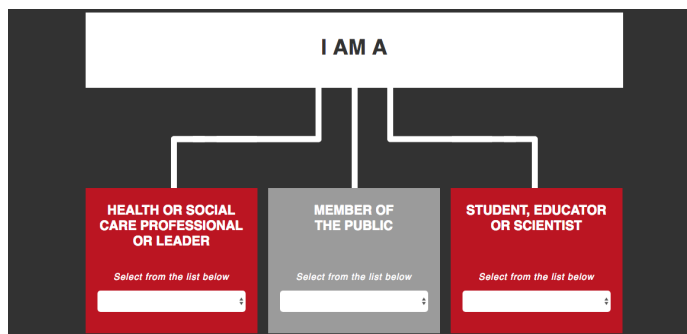
 VIEW DOCUMENT

- Lots of other information documents have been developed in many countries, for example in the UK

 VISIT SITE

Other interventions

The Antibiotic Guardian campaign was launched in 2014 in the UK (<http://antibioticguardian.com>). It encourages everyone to become an antibiotic guardian, and to choose a pledge to demonstrate his/her public commitment to responsible antibiotic use.







 VISIT SITE

TABLE 1 - Objectives of ASP in GCC |

TOOLKIT RESOURCE

SITE LINK

-  ECDC
-  French ID society
-  Dutch Ateams
-  ReACT Group
-  BSAC ARC

 GULF COOPERATION STATES

Antibiotic misuse is a major determining factor of Antimicrobial Resistance (AMR), occurring in around 50% of prescribing (CDC report, antibiotic resistance threats in the United States 2013). Gulf Cooperation States (GCC) countries are facing challenges of emerging antimicrobial resistance. The examples listed below are practical interventions undertaken to try and address this issue.

**GCC Point Prevalence Survey to understand ASP Practices**

A web-based survey was conducted in 2015 addressed to GCC countries namely, Saudi Arabia, UAE, Bahrain, Oman, Qatar, and Kuwait. There were a total of 44 responses from 4 GCC countries as follows: Saudi Arabia 38/47 (80.9%), UAE, Oman, & Bahrain 6/47 (19.1%)

Twenty-nine out of the participating hospitals (66 %) had ASP in place; the majority of these were tertiary care teaching hospitals with 200-800 bed capacity. Of the 44 responses the top three objectives were to reduce resistance, improve clinical outcome and reduce costs (Table 1). Preauthorisation and restricted list of antimicrobial agents appeared to be the core stewardship strategy practiced in GCC countries (Figure 1).

SETS OF OBJECTIVES OF ASP	FREQUENCY (44 RESPONSES)
Improve clinical outcome	75%
Minimise or stabilize resistance	77%
Reduce cost	47.7%
Reduce <i>C.difficile</i> infection	13.6%
Reduce length of stay	2.3%

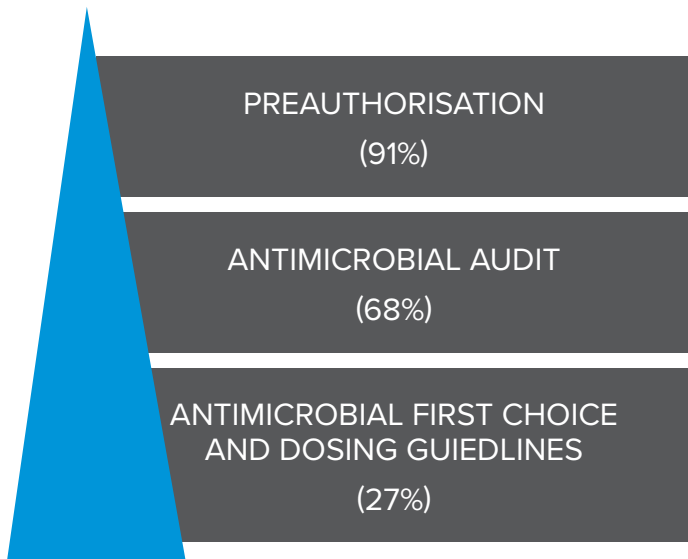


FIGURE 1  
Top three strategies of ASP in GCC (out of 44 responses)

A noticeable finding of GCC survey was the reported favourable impact on patients and hospitals after initiation of ASP; these were around reduction in healthcare-associated infection, inappropriate antibiotic prescribing, length of stay or mortality metrics and antimicrobial resistance, Figure 2.

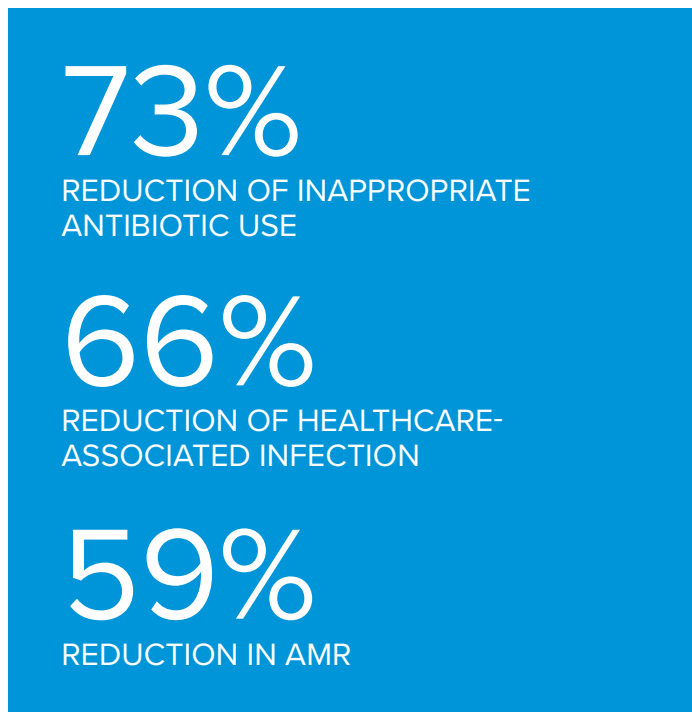


FIGURE 2

In some hospitals, barriers to ASP were identified these are shown in Table 2.

BARRIERS	PREVALENCE
Hospital administration not aware	9%
Lack of personnel or funding	23%
Multiple factors	52%
Obstruction from prescribers	11%
Others	11%

TABLE 2  
Barriers to effective antimicrobial Stewardship (out of 44 responses)



READ THE FULL PAPER

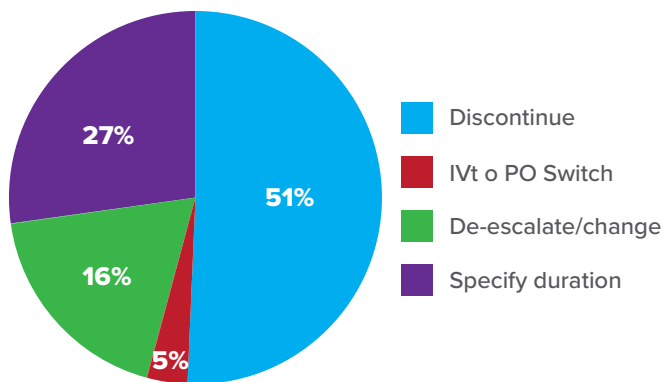


[CLICK HERE FOR A COPY OF THE DATA COLLECTION SHEET](#)

**Saudi Arabia Experience**

*Example 1 (above): Prospective audit with intervention and feedback in Adult Medical & Surgical Wards at King Fahad Medical City*

A total of 602 patients on antibiotics were reviewed with 310 requiring the following interventions Figure 3.



These interventions resulted in a

- Behavioural change & better prescriber’s awareness of the need to specify the antimicrobial duration from the time of prescription, which has subsequently reduced the cost of top 3 prescribed antibiotics (piperacillin-tazobactam, ceftriaxone, & carbapenem) by 360,000 Saudi Riyals per year.
- Education opportunity to avoiding antibiotics when the evidence of bacterial infection is lacking.

- Communication opportunities to increase effective dialogue between the primary team & antimicrobial stewardship team, which has developed a culture of trust.

Within the first 3 months of implementing the antimicrobial stewardship programme compliance to ASP recommendations improved from 12 to 43% with documentation of duration further improving by 46%.

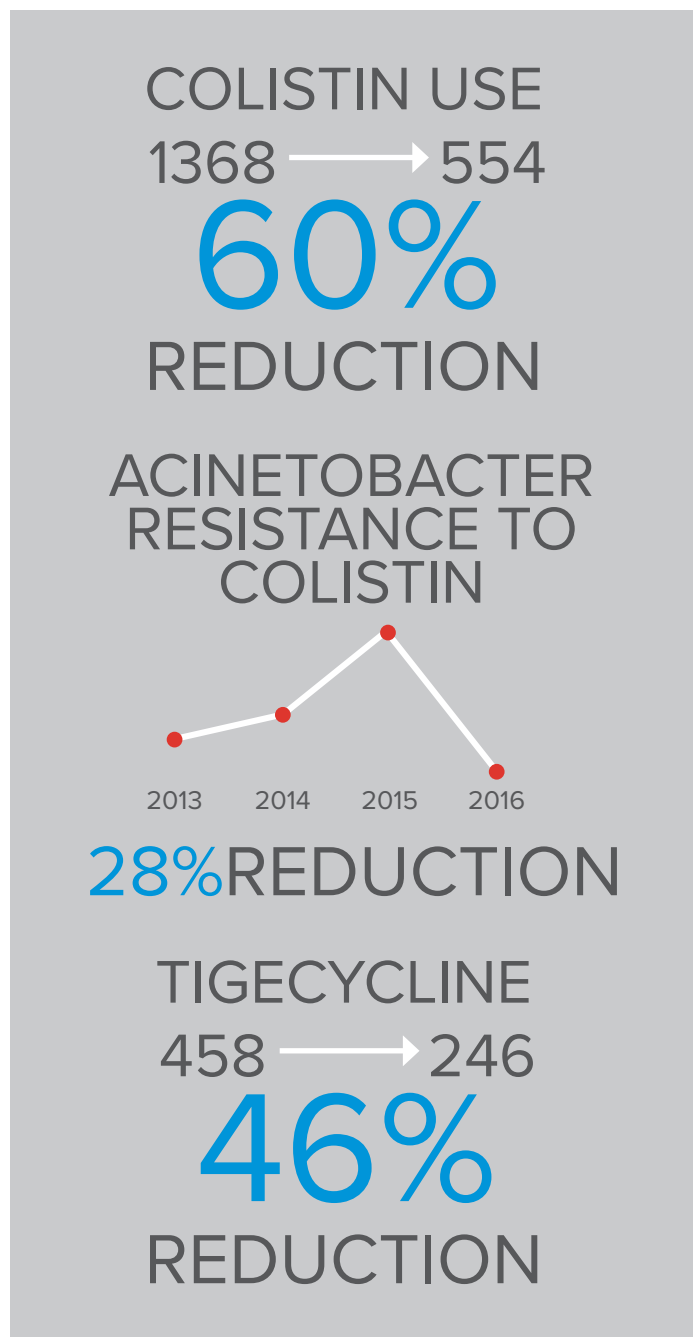
*Example 2: Implementing pre-authorization to reduce key antibiotic agents*

In a tertiary medical center in Saudi Arabia, there were several challenges around managing the treatment of gram negative bacteria. These included the wide spread use of colistin and tigecycline, a lack of ASP policies and minimal infection specialists. The hospital invited an ID pharmacist trained in ASP to help create an AS programme initially looking at a restriction system around key antibiotics and selective microbiology reporting. Four ID assistant consultants were hired to help the primary ID consultant and pharmacist. Click here to listen to the challenges faced and interventions deployed.

[DOWNLOAD SLIDE SET](#)

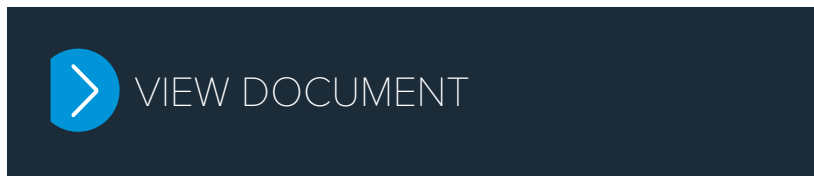


Colistin and tigecycline were switched from being widely available to being under restriction. Colistin use decreased by 60% and it was associated with significant reduction in Acinetobacter resistance from 31% to 3% in a year. Tigecycline use decreased by 46%, while carbapenem use and associated resistance stayed the same, which could be attributed to switching from colistin.



*Example 3: Saudi Arabian Ministry of Health initiative*

As per the directive of his Excellency the Saudi Minister of Health, the General Directorate of Infection Prevention and control has formulated a national AMR committee to meet the global action plan to combat microbial resistance. Five technical committees reporting to the national AMR have completed the national road map to combat AMR.



Among the ambitious objectives of stewardship committee is mandating antimicrobial stewardship education in medical, nursing, & allied sciences' curricula to improve knowledge, skills, and attitudes toward antimicrobial prescribing. This document was further been incorporated into a wider WHO report of Saudi Arabia;

**TOOLKIT RESOURCE**

ARTICLES

Alawi MM, Darwesh BM. A stepwise introduction of a successful antimicrobial stewardship program. Experience from a tertiary care university hospital in Western, Saudi Arabia. Saudi Med J. 2016;37(12):1350-1358

Enani M, The Antimicrobial Stewardship Program in Gulf Cooperation Council (GCC) States: Insights from a regional survey Journal of Infection Prevention, Oct 2015: 1-5

Amer MR, Akhras NS, Mahmood WA, Al-Jazairi AS. Antimicrobial stewardship program implementation in a medical intensive care unit at a tertiary care hospital in Saudi Arabia. Ann Saudi Med. 2013;33(6):547-54.

**Bahrain Experience**

The Ministry of Health covers 80% of health services in Bahrain. Antimicrobial stewardship was introduced within Bahrain in 2010 in Al-Salmanyia Medical Centre.

To view the challenges and opportunities of Bahrain's antimicrobial stewardship programme:



### Acknowledgement

Hail Al Abdely, DG of infection prevention & control, chair, Saudi national AMR committee, Ministry of Health;

Areej Malhani, Clinical Pharmacist & Stewardship committee coordinator, KFMC;

Maha Alawi, Infectious diseases & Stewardship leader in KAUH, Jeddah;

Jameela Al Salman, Infectious Diseases Consultant & Stewardship leader in Bahrain

### AUSTRALIA

Australia has been an early adopter of antimicrobial stewardship, with some areas of demonstrated success.

- One key area of success has been the development and implementation of national antimicrobial prescribing guidelines, called [Therapeutic Guidelines: Antibiotic](#) (available since 1978). They cover hospital and community prescribing, and are well respected and widely endorsed.
- In 2015, the importance of these guidelines was further augmented by their inclusion in both the [National Standards for Hospital Accreditation](#) and the [Clinical Care Standards for Antimicrobial Stewardship](#).
- In 2011, the Australian Commission on Safety and Quality in Healthcare (ACSQHC) published recommendations for what was expected of programs for [AMS in Australian hospitals](#), and, in 2013, for the first time, evaluation of the quality of the AMS programs was included in accreditation standards for hospitals.
- Hospitals were required to show that they had antimicrobial prescribing policies in place (usually incorporating a formulary with restrictions), and that auditing was occurring and clinical improvement activities were taking place.

Most larger hospitals now have established AMS committees to oversee the hospital's AMS activities.

- Established AMS programs at Australian tertiary hospitals are multifaceted and use a multi-pronged approach, combining elements such as formulary control; the use of decision-support and approval systems; post-prescription review; clinical consult rounds; education and workforce training; and auditing with feedback.

- Most tertiary hospitals have dedicated staff resources for AMS. These members of staff, often called 'AMS teams', tend to do the day-to-day work of prescription review, education and auditing.
- AMS teams at the bigger hospitals are primarily led by infectious diseases physicians and clinical pharmacists. At smaller sites, non-ID-expert medical, pharmacy and nursing staff are leading programs. There is growing awareness of the importance of building [capacity](#) and involving all healthcare staff in AMS as part of everyday work.

A [number of studies](#) have evaluated and demonstrated the impact of AMS programs in Australian hospitals.

Auditing is clearly necessary for monitoring adherence to recommendations, identifying areas that need intervention and driving improvement.

- In Australia, surveillance of antimicrobial consumption in hospitals has been undertaken since 2004 through the National Antimicrobial Utilisation Surveillance Program (NAUSP). This program has allowed the tracking of changes in consumption over time and some limited comparisons between hospitals. However, it is important to note that participation is voluntary, and adjustment of data according to hospital case-mix is not available, so analysis and comparisons must be undertaken with caution. Involvement in NAUSP increased after the new accreditation standards were released. In 2014, 129 hospitals contributed data (representing 82% of beds from hospitals of greater than 50-bed size). The [NAUSP data](#) have demonstrated a small decline in hospital antimicrobial consumption (-6.2% DDD/1000 OBD) from its peak in 2010. Consumption measured by defined daily doses per 1000 occupied bed days appears to be higher than Sweden and on par with Denmark.
- In addition, there is a program called the [National Antimicrobial Prescribing Survey \(NAPS\)](#). This is a comprehensive program that was first developed in 2011, and in 2016 involved >400 hospitals (with >25,000 prescriptions). The annual audit activity is a point prevalence survey of antimicrobial use across inpatients in hospitals. The audit assesses both concordance with guidelines and appropriateness of prescribing. The rollout of this audit has been accompanied by extensive training to enable auditors to assess appropriateness in a consistent manner, and the use of appropriateness as a measure has been important in gaining clinicians' acceptance of the findings (appreciating that guidelines do not always apply to individual patients).

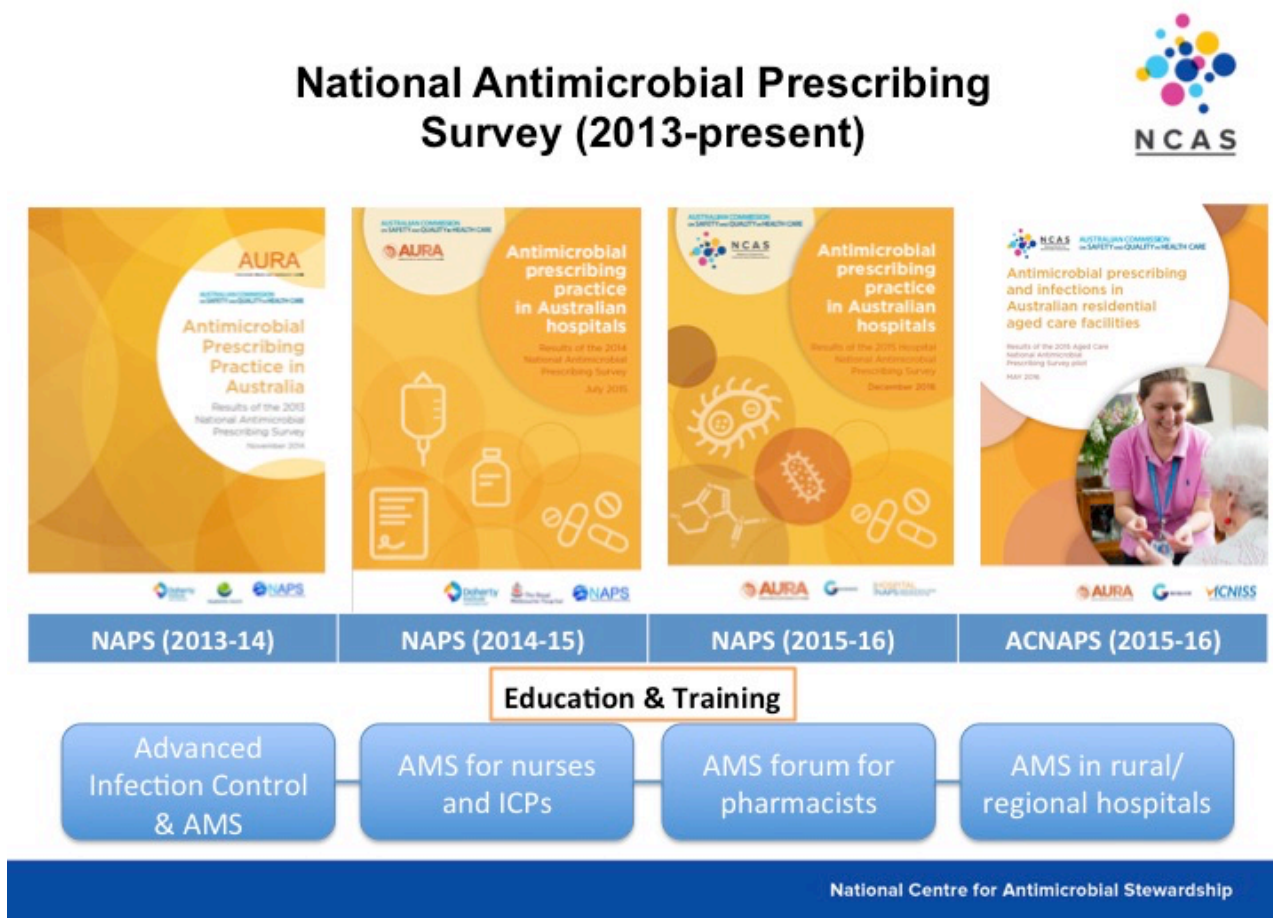


FIGURE Examples of the National Antimicrobial Prescribing Survey (NAPS) reports (image credit: Australian Commission on Safety and Quality in Health Care [ACSQHC]), and education and training activities undertaken by the National Centre for Antimicrobial Stewardship (NCAS).

Participation in the NAPS audit has become part of hospitals' training and education for staff, with experts within the NAPS program routinely providing clinical information and assessment support to hospital auditors. The program's focus on appropriateness of prescribing has required and facilitated the dissemination of key information and assessment skills to these critical personnel, thereby directly informing clinical improvement activities in hospitals. The NAPS also enables hospitals to instantaneously generate their hospital-specific report and benchmarking (comparison with peer-group hospitals) report following data-entry. This facilitates the quick utilisation of data for quality improvement activities.

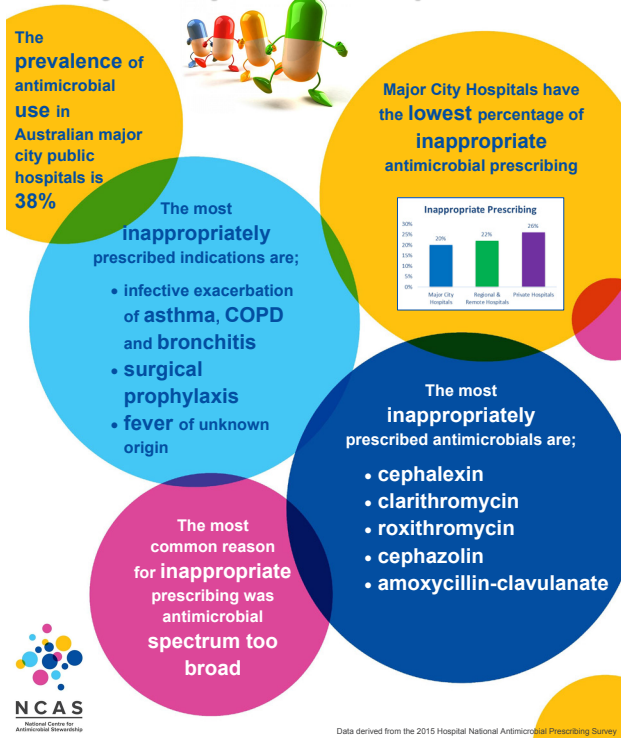
Areas of problematic prescribing in hospitals have been identified over the years, leading to more focused activities. The [NAPS 2015 report](#) provides the latest published results as well as an overview of the previous years' findings. Importantly, the NAPS program is unique in that it assesses concordance with guidelines and appropriateness of prescribing on a national scale. Drawing on the annual surveys' findings, additional

modules focused on target areas, such as the Surgical NAPS and the Hospital-in-the-Home (HITH) NAPS, have also been developed and deployed.

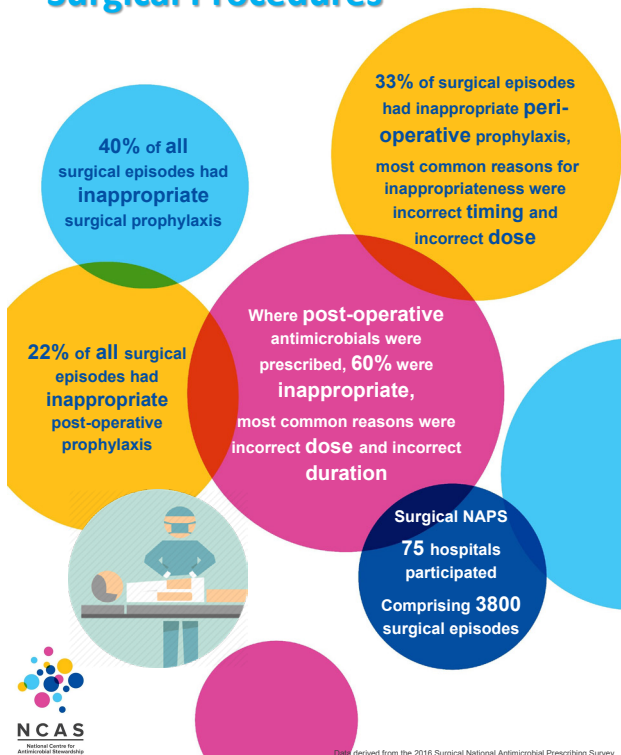
The [Clinical Care Standards for Antimicrobial Stewardship](#) were developed by the ACSQHC in 2016 and are intended to describe appropriate practice at an individual patient level. They are a powerful description of what 'good care' should look like in relation to safe, high quality antimicrobial drug use.

Activity around AMS in the community has arguably lagged behind activity in hospitals. Australia is a [high consumer of antibiotics in the community](#) relative to other OECD countries. Data on antimicrobial use in the community largely come from the [Pharmaceutical Benefits Scheme \(PBS\)](#). This is a program through which the Commonwealth government subsidises medication costs in the community. It governs the reimbursement of costs for a specified list of drugs and indications, and thus functions as a formulary with restrictions (restricting access to fluoroquinolones, for example).

## Antimicrobial Prescribing in Major City Public Hospitals



## Antimicrobial Prescribing in Surgical Procedures



The **NPS MedicineWise** program has been funded by the Commonwealth government to support education for general practitioners, and provides evidence-based information free from the influence of pharmaceutical companies. It is likely that there is much scope to further develop AMS activities in the community to address the high consumption rates and poor concordance with evidence-based recommendations that have been described in [some studies](#).

Auditing of antimicrobial use in the community has been somewhat limited by an inability to link the indication for use to the individual prescription. Early data are emerging from a program called **MedicineInsight**, in which data are electronically extracted from medical records.

Data from primary care settings are suggesting that usage is **poorly compliant with recommendations**, particularly for respiratory infections. Studies focused on appropriateness of antimicrobial prescribing in the community as well as prescriber knowledge and perceptions are being piloted.

One area where detailed information is emerging is the residential aged care sector. In 2015, an **aged care NAPS** (acNAPS) was conducted across 186 residential aged care facilities (RACFs), and was able to identify several key areas of inappropriate prescribing.

- A high level of antibiotic use among residents was noted, with a significant proportion (22%) of antimicrobials prescribed for prophylaxis.
- It was found that prescriptions were often continuing beyond 6 months.
- Urinary infections and skin and soft tissue infections figured most highly amongst the indications for prescription.

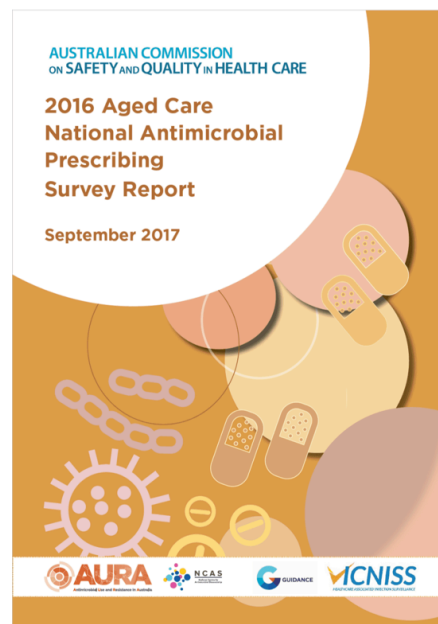
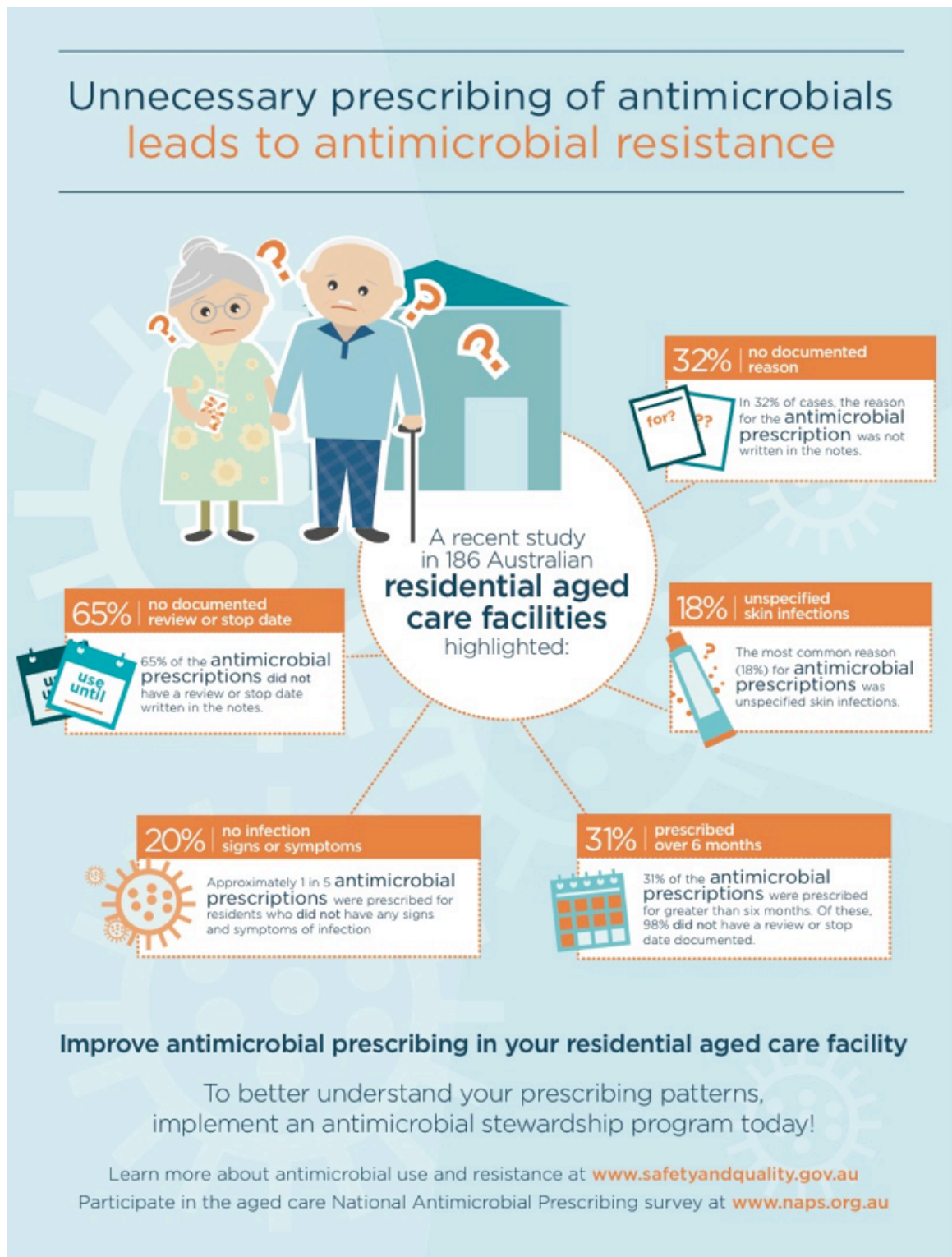


FIGURE Aged Care National Antimicrobial Prescribing Survey (2016). Image credit: ACSQHC





AUSTRALIAN COMMISSION  
ON SAFETY AND QUALITY IN HEALTH CARE



AIS-AC  
ANTIMICROBIAL STewardship IN Aged Care

FIGURE  
Poster highlighting data from the Aged Care National Antimicrobial Prescribing Survey (2015). Image credit: ACSQHC.

In 2013, the ACSQHC began a program called [AURA](#), which focused on collating data from cross-sectoral surveillance of antimicrobial usage and resistance. The 2016 and 2017 [AURA reports](#) drew on existing programs (NAUSP and NAPS) as well as enhanced laboratory surveillance data to produce useful snapshots of the current state of play.

It has been recognised that surveillance must be accompanied by action to address the problems that are identified. Australia's first [National Strategy](#) to address antimicrobial resistance was released in 2015, and, importantly, took a “one health” approach, incorporating animal and human health. This was followed by an [implementation plan](#) that detailed activities for the coming years.

Some elements of this plan build on existing initiatives that have successfully driven improvement.

- In hospitals, one example has been the use of computerised workflow-based tools to support AMS programs. Australian hospitals have been early adopters of these tools, and [independent evaluations](#) have suggested good uptake and an association with improved prescribing.
- Workflows that incorporate both pre-prescription approval and post-prescription review by multidisciplinary AMS teams are now common in tertiary hospitals.
- Workforce capacity building has been undertaken by groups such as the [National Centre for Antimicrobial Stewardship](#) through education and training. This same group conducts the NAPS and has undertaken research on sustainable interventions to improve prescribing behaviours.

In the Australasian region, New Zealand is another country where initiatives to tackle AMR have made some progress.

- In 2017, the [Health Quality & Safety Commission](#) commenced the development of a national action plan for AMR.
- Antimicrobial consumption in the community has been assessed by some [studies](#), and the use of extended-spectrum penicillins (particularly among children and Pacific communities) and topical antibiotics appears to be high.
- A few New Zealand hospitals participate in the Australian NAPS, generating hospital-specific reports rather than contributing to Australia's national surveillance program.
- No AMS-specific accreditation standards currently exist but clinical groups have been progressing plans in this area.

While Pacific nations currently do not have surveillance systems in place to monitor antimicrobial use and AMR, initiatives to develop national action plans have commenced with the support of the World Health Organisation's Western Pacific Regional Office. Fiji launched its national action plan in 2015, and, in the absence of active surveillance programs, has focused on the dissemination of messages about appropriate antibiotic use.



### AURA 2017

Second Australian report on antimicrobial use and resistance in human health



FIGURE  
Antimicrobial Use and Resistance in Australia Report (2017). Image credit: ACSQHC.



# CHAPTER 16

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## STEWARDSHIP IN THE RESOURCE LIMITED SETTINGS - EXAMPLES OF GLOBAL SUCCESS STORIES

### THE AIM OF THIS CHAPTER IS TO:

To assess the role of prescription auditing & focused group discussions in antimicrobial stewardship.

To ascertain the effect of antibiotic consumption and development of antimicrobial resistance in a tertiary care hospital.

Understand how non-specialised pharmacists without Infectious Diseases expertise can contribute to stewardship initiatives within a hospital or within a hospital network

Understand how to implement a pharmacist-driven prospective audit and feedback model to initiate and maintain AMS programs in single or multiple non-academic urban and rural institutions:

- Reducing excessive prescribing by targeting basic antibiotic processes (“low-hanging fruit”)
- Improving time from antimicrobial prescription to infusion (“Hang-time”)
- Improving adherence to peri-operative antibiotic prophylaxis guidelines to enable a reduction in surgical site infections

To understand how regulatory intervention is relevant for the AMS goal of improving patient safety by curbing self-medication practices and reducing antibiotic consumption at the community level.

To understand the process of developing antibiotic sales regulation in resource limited settings, where problems on access to antibiotics, and excess in their use coexist.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Reflect how non-specialised pharmacists can coordinate interdisciplinary engagement
- Outline how to effect change utilizing a formal model of step-wise change management and quality improvement principles
- Using such a model, outline the design, implementation and maintenance of a prospective pharmacist-driven audit and feedback stewardship intervention in a variety of geographical and socio-economic settings
- Outline the apparent skills beyond those of infectious diseases and microbiology that are critical in starting and maintaining a sustainable AMS program, and as such the participants should be able to:
  - Define the important determinants of a collaborative model to achieve breakthrough in improvement
  - Define how effective behaviour change techniques (BCTs) are used in the model, such as self-monitoring, feedback combined with goal setting and action plans
- Outline the methods to monitor and evaluate the impact of regulating antibiotic sales.
- Reflect on the importance of managing the political sphere during the process of introducing antibiotic sales regulation.
- Understand how to prepare an antibiogram for their hospital as well as for the community
- Understand how to collect antibiotic consumption data through prescription auditing.
- Understand how to carry out focus group discussions with their clinical colleagues in different specialties.

## INTRODUCTION

Although developing and implementing a successful AMS program is a challenge in any healthcare setting, there are unique challenges to smaller and rural hospitals with limited resources which may hamper the ability to implement ideal sustainable AMS strategies (Figure 1). Thus, there is a need for alternative stewardship models that use available organisational infrastructure and resources. Furthermore, contextual aspects in resource-limited settings also place a challenge to develop AMS programmes at the community level. To illustrate, this chapter describes the experiences of five countries with different AMS approaches but with successful outcomes.

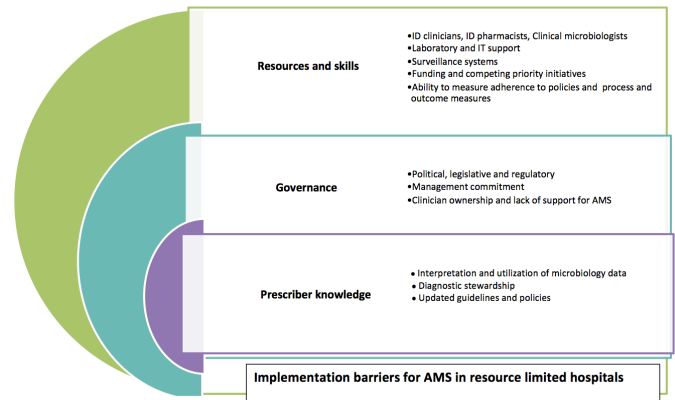


FIGURE 1  
Barriers to implementation of AMS



## SOUTH AFRICA

### GLOBAL SUCCESS STORY: ANTIMICROBIAL STEWARDSHIP MODEL TO REDUCE EXCESSIVE PRESCRIBING

The aims of this model were to promote collaborative action utilising existing resources and the concept of “low hanging fruit”, across a diverse group of 47 urban and rural private SA hospitals (Netcare Ltd), with regard to both implementation of an AMS program, and to achieve a sustainable reduction in overall antibiotic consumption. The reasons for utilizing pharmacists is explained in following video:

THE REASONS FOR IMPLEMENTING AMS IN THIS WAY AND WHY PHARMACISTS WERE USED.

VIDEO INTERVIEW WITH DR DENA VAN DEN BERGH, QUALITY IMPROVEMENT DIRECTOR, NETCARE LTD (LTD)

WATCH VIDEO

### PROCESS MEASURES INVOLVING “LOW-HANGING FRUIT” FOR PHARMACIST AUDIT DURING DEDICATED ANTIBIOTIC ROUNDS (ALL PATIENTS ON ANTIBIOTICS)

The primary metric was overall reduction in consumption by focusing initially on “low-hanging” fruit in reference to AMS. This refers to selecting the most obtainable audit targets with limited resources. In addition, such simple interventions as opposed to more complex strategies are ideal to initiate an initial AMS program if stewardship has not started yet. The reasons are further elucidated in video 2

THE REASONS FOR CHOOSING “LOW-HANGING AMS FRUIT” FOR PHARMACIST AUDIT

VIDEO INTERVIEW WITH DR DENA VAN DEN BERGH, QUALITY IMPROVEMENT DIRECTOR, NETCARE LTD (LTD)

WATCH VIDEO

	PROCESS MEASURES <sup>A</sup>	DEFINITION
1	Cultures not done prior to commencement of empiric antibiotics	Patients started on empiric antibiotics and no cultures performed within 48 hours prior to or on initiation of treatment.
2	More than 7-days of antibiotic treatment	Prolonged duration of treatment included therapy which continued for between 8-14 days (inclusive) i.e. antibiotic therapy exceeding the duration deemed longer than appropriate for effective treatment of that particular agent or condition, according to local guidelines.
3	More than 14-days of antibiotic treatment	Prolonged duration of treatment included therapy which continued beyond 14 days i.e. antibiotic therapy which exceeds the duration deemed longer than appropriate for effective treatment of that particular agent or condition, according to local guidelines.
4	More than 4 antibiotics at the same time	The unintentional overprescribing and concurrent systemic use of 4 or more antimicrobials in a given patient on the same calendar day for at least two consecutive days.
5	Concurrent “double” or redundant antibiotic coverage	The intentional concurrent administration of two or more antibiotics with overlapping or duplicate spectra in terms of Gram-negative, Gram-positive and anaerobic cover, on the same calendar day for at least two consecutive days.
5.1	Redundant Gram-negative coverage	Defined as the concurrent administration of two or more of any of the following agents in or between groups: cephalosporins (cefuroxime, ceftriaxone, ceftazidime, cefotaxime, cefepime); fluoroquinolones (ciprofloxacin, levofloxacin); penicillin/ $\beta$ -lactamase-inhibitor combinations (amoxicillin/clavulanate, piperacillin/tazobactam); aminoglycosides (amikacin, gentamycin, tobramycin); carbapenems (meropenem, ertapenem, doripenem or imipenem) and tigecycline.
5.2	Redundant Gram-positive coverage	Defined as the concurrent administration of two or more of any of the following agents in or between groups: $\beta$ -lactams (amoxicillin, amoxicillin-clavulanate, cefazolin, cloxacillin), tigecycline, clindamycin, linezolid and glycopeptides (vancomycin, teicoplanin).
5.3	Redundant anaerobe coverage	Defined as the concurrent administration of two or more of any of the following agents in or between groups: metronidazole, penicillin/ $\beta$ -lactamase-inhibitor combinations (amoxicillin/clavulanate, or piperacillin/tazobactam), carbapenems (meropenem, ertapenem, doripenem or imipenem), moxifloxacin, clindamycin, ceftioxin, or tigecycline.

TABLE 1

Defining the process measures for audit. Reproduced with permission Lancet ID

<sup>A</sup> For all of these audit measures, doctors were consulted by the pharmacist before any changes were effected (face-to-face, verbal or mobile phone messages).

## AMS “BREAKTHROUGH SERIES COLLABORATIVE” MODEL FOR IMPLEMENTATION AND MONITORING PROCESS

The AMS model, a Netcare adaptation of the “Institute for Healthcare Improvement (IHI) Model” (PDSA cycles) and the “Breakthrough Series Collaborative” was implemented in a step-wise manner (Figure 2).

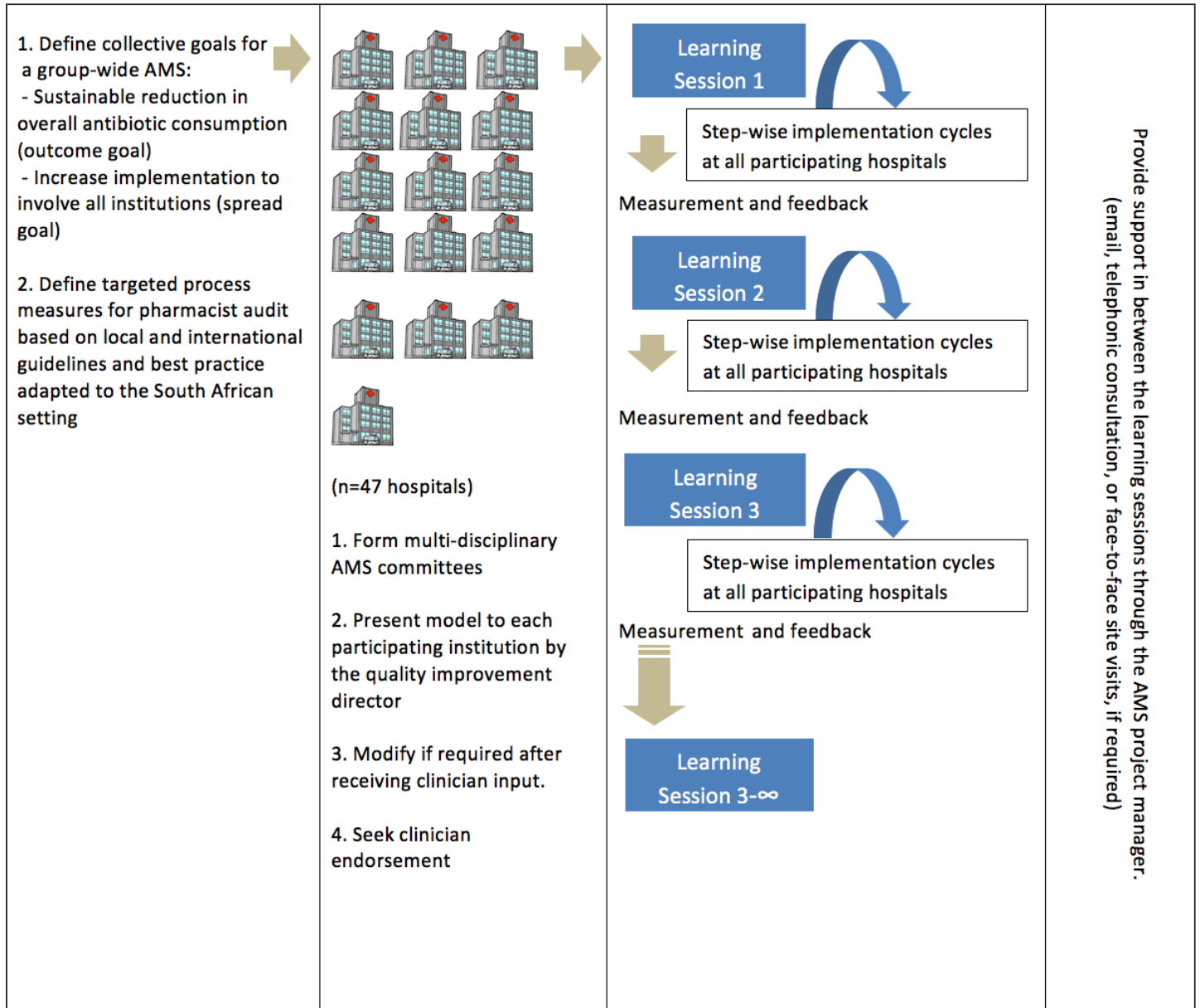


FIGURE 2  
 Figure 2 Netcare AMS model for implementation

The “Breakthrough Series Collaborative” requires adherence to fundamental tenets (Video 3)

THE MODEL FOR IMPROVEMENT REQUIRES COLLABORATIVE PHARMACIST TEAMS TO ASK THREE QUESTIONS

VIDEO INTERVIEW WITH DR DENA VAN DEN BERGH, QUALITY IMPROVEMENT DIRECTOR, NETCARE LTY (LTD)



## ▶ THE IMPORTANCE OF COLLABORATIVE LEARNING SESSIONS AND STANDARDISED MEASUREMENT

Initial training for the five interventions was provided through face-to-face regional learning sessions with pharmacists as well as to pharmacy managers, clinicians, nurses and infection prevention practitioners (Learning session 1). In line with the breakthrough series model, each pharmacist was then required to undertake an implementation process in their hospital including collection of audit data on a standardised template (.xls). Following Learning session 1, conference calls were held every 6-8 weeks with pharmacists nationally, hosted by the QI director and AMS project manager (Learning session 2 - ∞). In between the learning sessions support was provided by the project manager.

Aims of the joint learning cycles (sessions)

- Collaborative learning between hospitals
- Clarify requirements of AMS implementation
- Brainstorming of ideas to overcome obstacles to implementation
- Sharing of success
- Evaluation of accuracy and consistency of data
- Comparative feedback on progress and improvements or otherwise

## AIMS OF THE LEARNING CYCLES AND IMPORTANCE OF STANDARDISED MEASUREMENT

VIDEO INTERVIEW WITH MS ANGELIKI MESSINA, AMS PROJECT MANAGER, NETCARE LTD (LTD)



At all participating sites data was collected weekly on a standardised measurement tool (Figure 3) during pharmacist AMS ward rounds conducted initially in intensive care and high care units followed by audits in wards. Audits did not occur for established extended treatment syndromes such as infective endocarditis and other deep-seated infections (e.g. osteo-myelitis. Mandatory monthly submission of audit data using the measurement tool was sent via email to the AMS project manager.

## ▶ THE IMPORTANCE OF FEEDBACK TO FACILITATE ADJUSTMENTS TO HOSPITAL ACTION PLANS FOLLOWING SELF-MONITORING

Improvements in the five interventions were measured by the project manager via quality improvement run charts (Figure 4) and hospital feedback provided monthly via email and during learning cycles. A summary of the model is depicted in Figure 5.

### Netcare Group (n=47 hospitals) weekly run chart: Antibiotic duration > 7 days

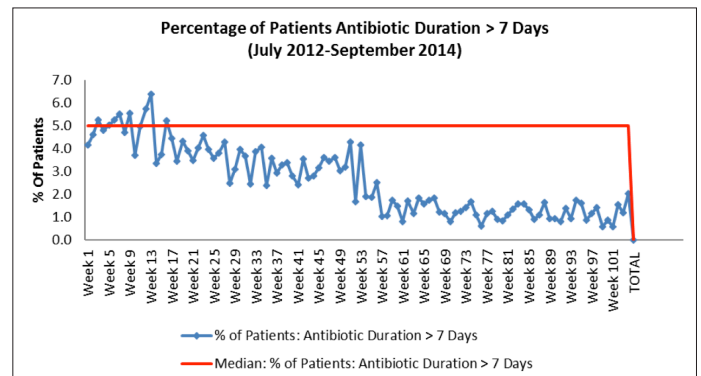


FIGURE 4 Example of a run chart for one of the audited measures (antibiotics prescribed for > 7 days)

Aims of feedback by the project manager to the hospitals:

- Provide monthly feedback to pharmacists and their managers, specifically regarding:
  - Improvements in compliance with the measures (or otherwise)
  - Improvements in antibiotic consumption data measured in DDDs/100 bed days (or otherwise)
  - Individualized goals
- The pharmacists in turn provided verbal and/or written feedback (1-3 monthly) to doctors, hospital management and AMS committee's including IPPs of each hospital.
- Following goal setting and hospital self-monitoring, action plans were adapted to:
  - Incorporate how much time pharmacists spent performing daily auditing activities
  - How many of the targeted interventions had been implemented?
  - What improvements had taken place?
  - What the impact on individual hospital antibiotic consumption had been?

Week	Denominator	Numerator	% Compliance
	Total number of patients on antibiotics reviewed during dedicated stewardship rounds	Total number of patients where the particular “low-hanging-fruit” intervention was implemented with the doctor’s permission	
Week 1	17	13	76.5
Week 2	27	19	70.4
Week 3	19	15	78.9
Week 4	29	19	65.5
Week 5	36	19	52.8
Week 6	26	21	80.8
Week 7	20	15	75.0
Week 8	15	10	66.7
Week 9	10	10	100.0
Week 10	16	14	87.5
Week 11	20	19	95.0
Week 12	13	10	76.9
Week 13	10	7	70.0
Week 14	11	9	81.8
Week 15	23	19	82.6
Week 16	10	6	60.0
Week 17	19	14	73.7
Week 18	21	19	90.5
Week 19	32	24	75.0
Week 20	13	9	69.2
Week 21	13	8	61.5
Week 22	21	18	85.7
Week 23	21	20	95.2
Week 24	22	21	95.5
Week 25	17	14	82.4
Week 26	22	16	72.7
Week 27	25	17	68.0
Week 28	18	17	94.4

FIGURE 3  
Example of a standardised measurement tool

 DOWNLOAD DATA  
COLLECTION TEMPLATE



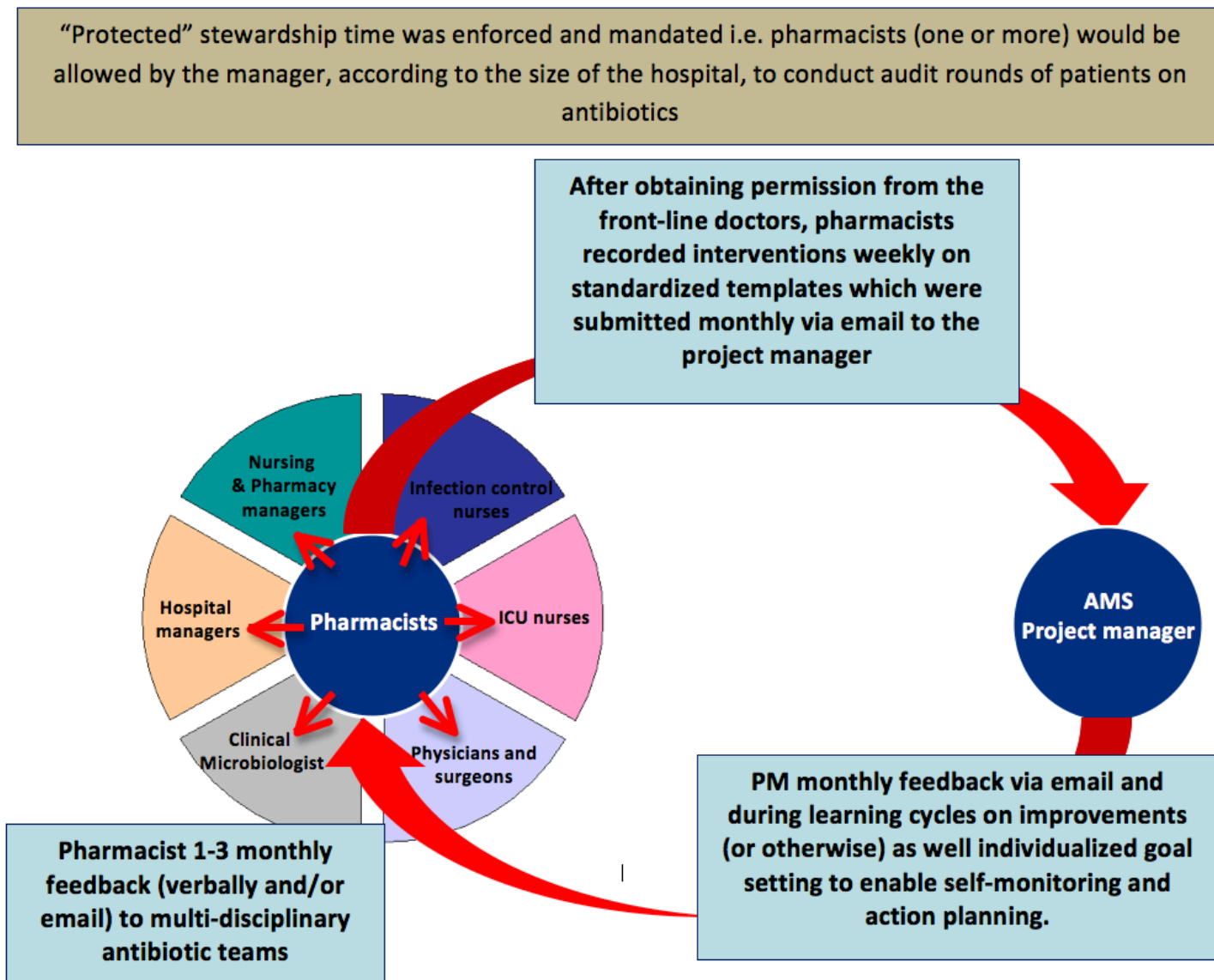


FIGURE 5  
Graphic summary pharmacist-driven audit and feedback model

## IMPACT OF THE AMS MODEL

Fifty-three learning cycles were held. For 104 weeks of standardized measurement and feedback, 116 662 patients on antibiotics were reviewed, with 7 934 interventions recorded for the five designated examples of “low-hanging fruit”, indicating that almost one in 15 prescriptions required pharmacist intervention. 39% (3316) of 7934 pharmacist interventions were for excessive duration. The model had a significant impact on antibiotic consumption, with a lowering of 18.35 in mean antibiotic DDD/100 bed days from 101.40 (95% CI 91.19 – 111.61) to 83.04 (95% CI 76.33 – 89.76) in the pre-and post-implementation phases, respectively, representing an 18.1% reduction in overall consumption ( $p < 0.001$ ). (Figure 6)

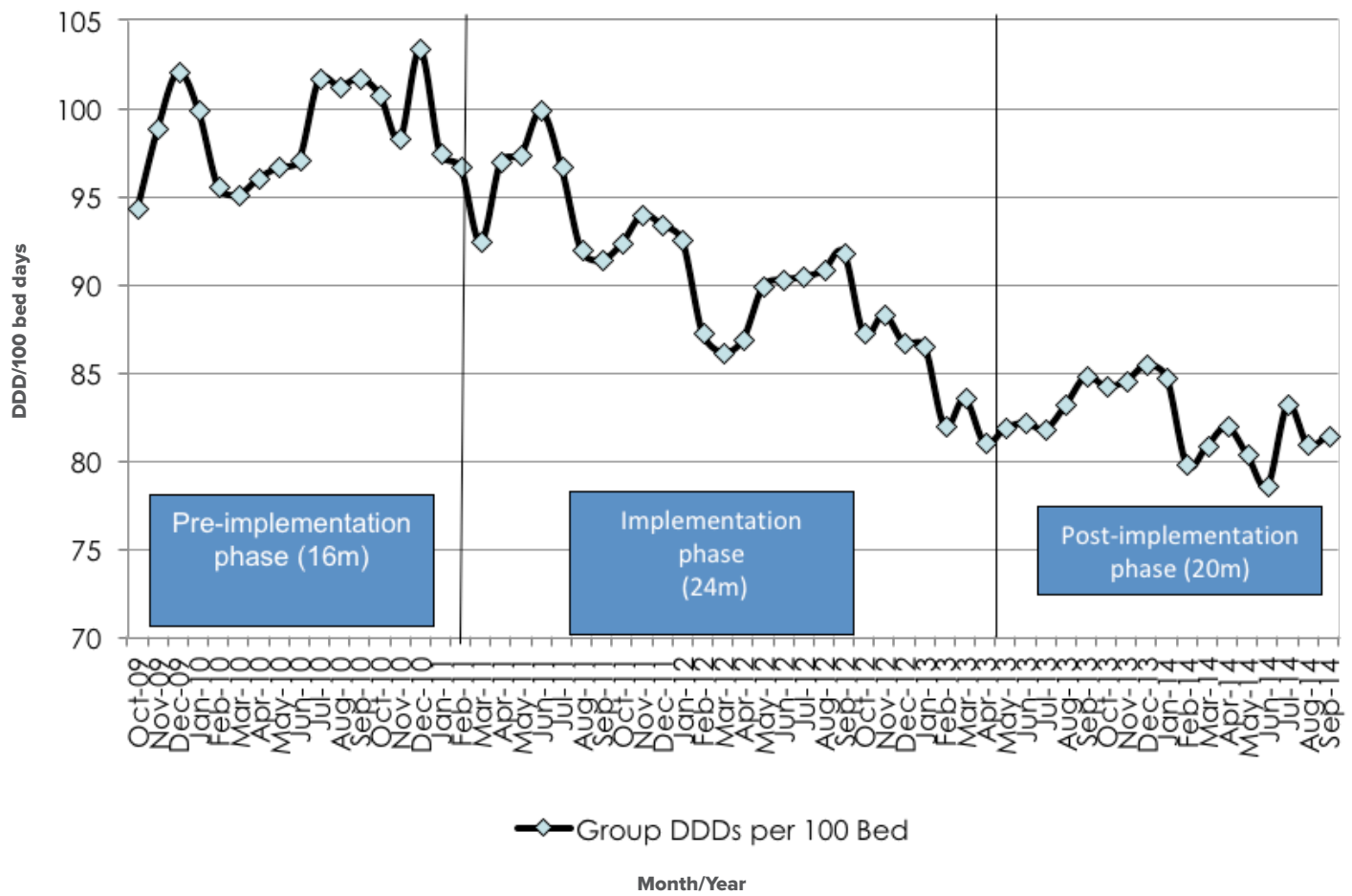


FIGURE 6 Mean antibiotic consumption for three phases of the Netcare antimicrobial stewardship model (n=47 hospitals) (Oct 2009-September 2014)

To illustrate how this pharmacist-driven model can be used as a stewardship strategy to target other interventions, you may wish to watch the following slideshow:

Slideshow lecture briefly outlining use of the same audit and feedback ams model to improve antibiotic “hangtime” and to improve compliance with a peri-operative antibiotic prophylaxis guideline.

[VIEW SLIDE SET](#)

## TOOLKIT RESOURCE

### ARTICLES

#### ANTIBIOTIC “HANG-TIME”

Messina et al. *Infect Dis Ther* (2015) 4 (Suppl 1):S5-S

#### PERIOPERATIVE ANTIBIOTIC PROPHYLAXIS

Brink et al. *J Antimicrob Chemother* 2017; 72: 1227-1234



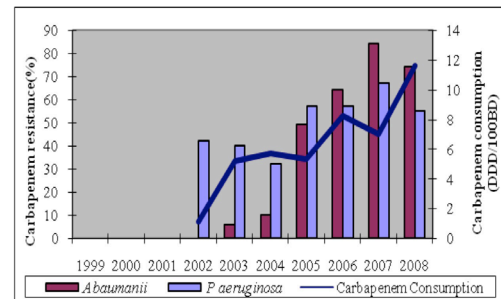
## INDIA

High burden of infection results in over and inappropriate use of antimicrobials in low and middle-income countries in Asia. There is no active AMSP program in most of their health care facilities. Considering this it is imperative that a tool kit is made which can be readily available as a web resource.

### DEVELOPMENT OF DRUG RESISTANCE

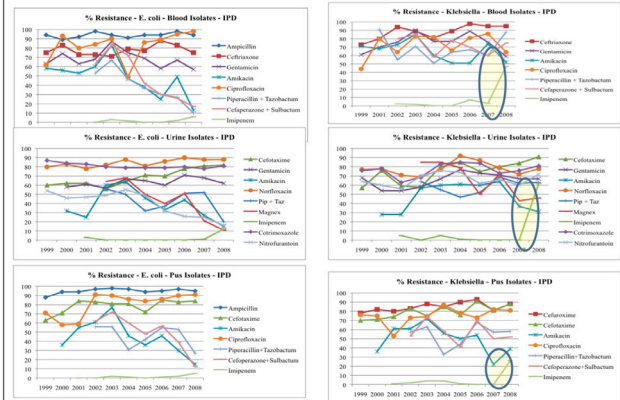
There is a well-established association at the population level between antibiotic consumption and antimicrobial resistance. A 10-year (1999-2008) trend analysis of antimicrobial consumption and development of resistance in non-fermenters, in Sir Ganga Ram Hospital, established the association between increase in consumption of carbapenems and the associated development of resistance in *A. baumannii*. Another study on 10-year analysis of multi-drug resistant blood stream infections caused by enterobacteriaceae also established the association between resistance and consumption of carbapenem and piperacillin/tazobactam in *K. pneumoniae*.

### Association between carbapenem consumption and resistance in *P. aeruginosa* and *A. baumannii* (SGRH)



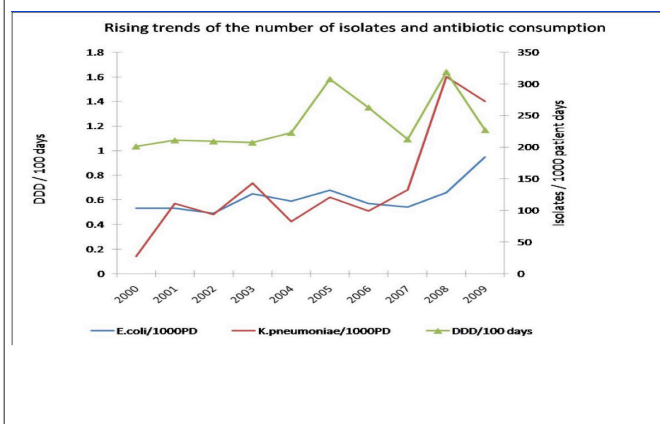
Goel N, Wattal C et al. J Antimicrob Chemother 2011;66(7):1625-1630

### Detection of new drug resistance pattern



Antibiotic trend analysis at SGRH 1999-2008

### Ten years trends at SGRH (2000-2009)



## STORY 1: MAKING & UTILISATION OF AN ANTI BIOGRAM: BUGS VS DRUGS

Understanding the epidemiology and emerging resistance trends at an institutional level is essential for choosing appropriate empiric therapy, monitoring resistance trends over time (within an institution & across institutions), infection control activities & resistance containment strategies.

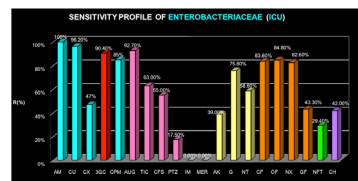
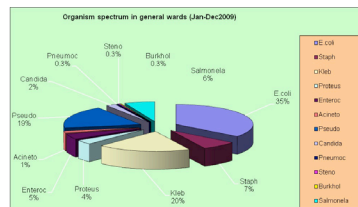
**Antibiogram helps in formulating optimum antibiotic policy and appropriate presumptive therapy**

### Making of an antibiogram

#### Step:1

1. Compile Local Hospital data
2. Based on site of infection

1. Geographic Variations (ICUs / Wards / OPD etc.)
2. % Distribution of Bugs
3. % Susceptibility of antibiotics



#### Step 2:

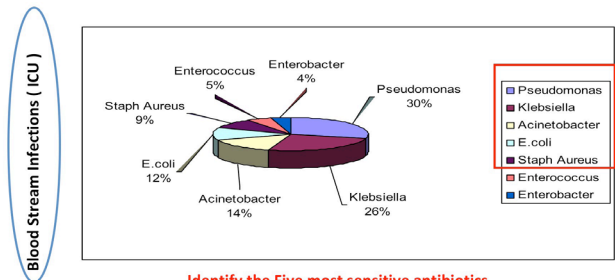
Put the data in given template:

1. Site of Infection, Type of Infection.
2. Causative pathogens.
3. Recent 12 month data.
4. Capture pathogens contributing to 80-90% of infections.
5. Capture the susceptibility of antimicrobials from highest to lowest.
  1. BSI
  2. UTI
  3. Respiratory
  4. SSTI

- User Friendly Tool kit to put in data based on Site of Infection
- Tool kit will be separate for OPD, Ward and ICU isolates
- Tool kit contains 5 most common pathogens, and the antibiotics in their decreasing order of sensitivity
- Tool kit will also contain the Validity period

Hospital surveillance data (Jan-16 till Dec-16)			Validity of these data: Dec 2016		
S. No	Most common pathogens	% prevalence	S. No.	Most sensitive antibiotics pathogens in descending order.	
1			1		
2			2		
3			3		
4			4		
5			5		

#### Identify the Five most common pathogens

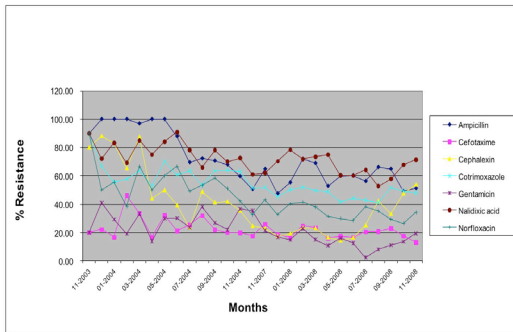


#### Identify the Five most sensitive antibiotics

Pathogen	Antibiogram for Blood Stream Infections(BSI) - ICU												
	Antibiotic sensitivity%												
Pseudomonas	Pipazo	Imipenem	Ertapenem	CefSul	Ceftazidim	Ceftrovan	Amikacin	Ciprofloxacin	Colistin	Vancomycin	Clindamycin	Gentamicin	Oxacillin
Pseudomonas	62	85	-	79	45	-	57	23	98	-	-	-	44
Klebsiella	65	93	92	76	40	45	65	59	-	-	-	-	43
Acinetobacter	43	62	-	85	20	-	32	33	0	-	-	-	32
E. coli	67	95	94	79	45	50	70	65	98	-	-	-	56
St aureus	69	68	70	70	50	50	-	56	-	97	54	-	59

But antimicrobial resistance is currently found almost as frequently in the community as well. Since there was very little data available on antimicrobial resistance in community especially in developing countries, we tried to establish a new methodology for surveillance of antimicrobial resistance in low-resource setting in the community. This was a project in collaboration with WHO and antimicrobial use was also being monitored simultaneously during a period of 2004 to 2008.

### Time series analysis of antibiotic resistance



Wattal C et al... Journal of Applied Therapeutic research, 2009;7(2): 37-45

### Trends in antibiotic use

Table 2. Trends in antibiotic use for the period January–December 2004 (Patient Exit Interview Data).

Antibiotic Name	DDD/ 1000 patients
<b>Cephalosporins J01DA</b>	
Cefixime	4289
Cefuroxime	2273
Cephalexin	1826
Cladaxoxil	1750
Cefepime Proxetil	1198
<b>Fluoroquinolones J01MA</b>	
Levofloxacin	8792
Ciprofloxacin	6164
Ofloxacin	4899
Gatifloxacin	4438
Norfloxacin	2444
Ciprofloxacin+Tinidazole	2257
<b>Macrolides J01FA</b>	
Roxithromycin	5879
Azithromycin	3664
Clarithromycin	887
<b>Nalidixic Acid J01MB02</b>	
Nalidixic Acid	1
<b>Penicillins J01C</b>	
Amoxicillin+Clavulanate	5663
Amoxicillin	5380
Amoxicillin+Clavacillin	3101
<b>Sulfonamides, Trimethoprim J01E</b>	
Cotrimoxazole	95
<b>Tetracycline J01A</b>	
Doxycycline	4483
Tetracycline	208
<b>Urinary Anti-infective</b>	
Nitrofurantoin J01X01	49

Table 1. Trends in antibiotic use for the period January–December 2004 (Bulk purchase data).

Antibiotic	DDD/1000 population
<b>Cephalosporins J01DA</b>	
Cefuroxime	114
Cefixime	85
Cephalexin	58
Cefacloroxil	41
Cefepodoxime Proxetil	38
<b>Fluoroquinolones J01MA</b>	
Levofloxacin	418
Ciprofloxacin	242
Ofloxacin	202
Ciprofloxacin+Tinidazole	176
Gatifloxacin	111
Norfloxacin	100
<b>Macrolides J01FA</b>	
Roxithromycin	151
Azithromycin	131
Clarithromycin	26
<b>Penicillins J01C</b>	
Amoxicillin+Clavulanate	158
Amoxicillin	147
Amoxicillin+Clavacillin	77
<b>Sulfonamides, Trimethoprim J01E</b>	
Cotrimoxazole	39
<b>Tetracycline J01A</b>	
Doxycycline	251
Tetracycline	6

Wattal C et al... Journal of Applied Therapeutic research, 2009;7(2): 37-45

### STORY 2: PRESCRIPTION AUDITING AS A CONCEPT AND INTERPRETATION

A study was done in our hospital which is a 675-bedded tertiary care hospital in New Delhi, between August 2010 and June 2011, to evaluate if the feedback to clinicians of their own antibiotic prescribing data result in any change in their antibiotic prescribing habits. The antibiotic prescribing rates measured as daily defined doses/100 bed days (DDD/100BD) on hospital based prescribers. The high antibiotic prescribing units of the hospital were divided into 2:

1. In the intervention arm, information on resistance rates and antibiotic-prescribing patterns were provided to all doctors. Comparison information with peer units within the specialty (without disclosing the identity of the units) and the rest of the hospital was also distributed.
2. In the control arm, only information on resistance rates was provided every month.

### Calculation of Daily Defined Doses

- Calculated by dividing the total grams of the antimicrobial agent used, by the numbers of grams in an average daily dose of the agent given to an adult patient.

$$\text{Aggregated DDD} = \frac{\text{Total antibiotic in grams}}{\text{Daily dose (ABC cal)}^1}$$

- Total ABS in grams data:  
Pharmacy records (purchase)  
HIS records (consumption)

1. European Society of Clinical Microbiology and Infectious Diseases (ESCMID)

The following achievements were noted:

1. The information gathered was useful to start locally relevant interventions.
2. Established a methodology to study antimicrobial use and resistance in communities in resource poor settings.
3. Involving several types of health-care facility at the community level for data collection increased awareness of the issue of growing resistance to antimicrobial therapy and its relation to antimicrobial use.

### • Calculation of bed days

$$\text{Bed Day/year} = \frac{\text{Total number of beds} \times \text{occupancy index} \times 365}{}$$

### • Calculation of Antibiotic consumption Rate

$$\text{(DDD/100 BD): } \frac{\text{DDD} \times 100}{\text{Bed days}}$$



**EXERCISE**

Calculate the DDD/100 BD for imipenem of a 600 bedded hospital with occupancy index of 85% if pharmacy reports consumption of 1000 ampoules (500 mg) of imipenem in 1 year.

Imipenem (J01DHJ1)

Daily dose of imipenem= 2g

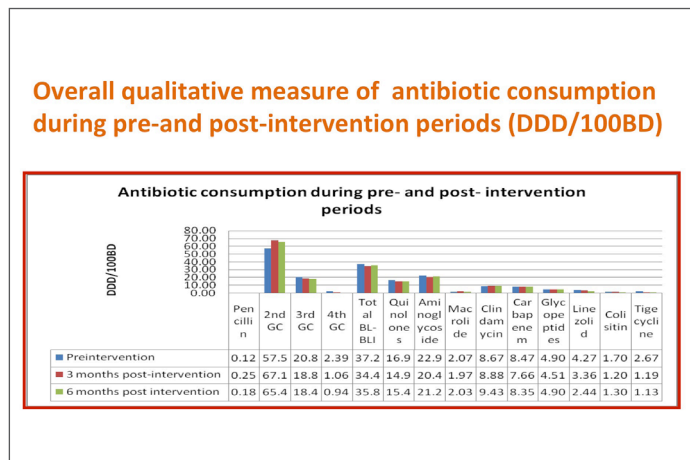
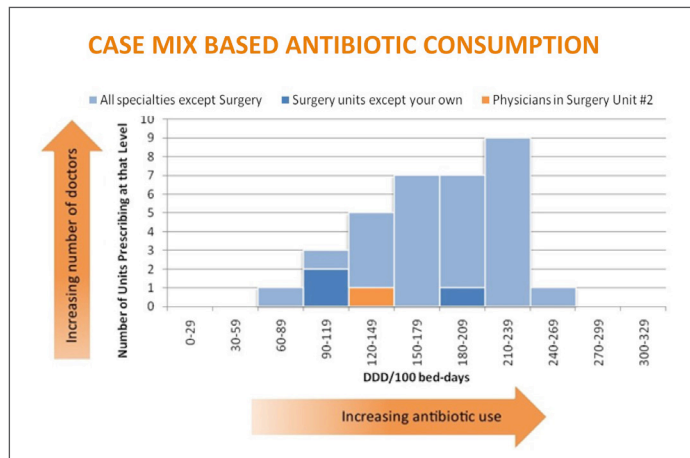
DDD : Total antibiotic in grams/Daily dose

DDD= 1000 x 0.5 g/2= 250

Total BD= No of beds x occupancy index x duration  
600 x 0.85 x 365 = 186150

DDD/100 BD= DDD x 100/BD  
250x 100/186150= 0.13DDD/100BD

Any significant behaviour changes in the two groups were assessed by comparing baseline (pre-intervention) antibiotic-prescribing rates with post-intervention antibiotic-prescribing rates.



In our study, providing doctors with information on how their antibiotic-prescribing rates compared to those of their peers showed no change in prescribing patterns, even among high prescribers. It has been shown, in developed countries, that prospective audit of antimicrobial use with direct interaction and feedback to the prescriber can result in reduced inappropriate use of antimicrobials. Such studies are seldom done in resource poor settings. This study was the first from India on the effectiveness of intervention program through feedback to the physicians of their own prescription habits in a hospital setting. The result of this study was suggestive that passive intervention only did not elicit desirable behavioural change in the physicians whereas the possibility of direct interaction with the prescribers to reduce antimicrobial consumption may be more effective at least in our setting.

TOOLKIT RESOURCE

SITE LINK



[http://www.cochrane.org/CD000259/EPOC\\_audit-and-feedback-effects-on-professional-practice-and-patient-outcomes](http://www.cochrane.org/CD000259/EPOC_audit-and-feedback-effects-on-professional-practice-and-patient-outcomes)

STORY 3: FOCUS GROUP DISCUSSIONS

With the knowledge we gained from the previous study, we moved on to our next venture, focus group discussions (FGDs). Persuasive intervention in the form of monthly prescription auditing and feedback on antimicrobial prescribing, dissemination of educational resources and reminders were continued, but in addition, FGDs were performed. The aim of this study was to evaluate the impact of FGD as an adjunct intervention to the feedback strategy on antibiotic prescribing rates on hospital based prescribers before and after the FGD. The doctors of 45 surgical units of the hospital were included in the study which extended from June 2013 to August 2015. Every month FGD was conducted with one specialty to cover all specialties included in the study on turnkey basis. Method, significance of measuring antibiotic consumption, the possible reasons for high antibiotic prescription of a particular unit and adherence to the antibiotic policy were discussed.



<b>Antibiotic consumption data</b>	<ul style="list-style-type: none"> <li>Retrieved electronically by speedminer software (Petaling Jaya, Malaysia), part of the Hospital Information System (Intersystem Cambridge, MA, USA) expressed in DDD/100BD</li> </ul>
<b>Passive intervention</b> (Monthly feedback sheets distributed electronically and hard copy)	<ul style="list-style-type: none"> <li>Respective units' prescription pattern</li> <li>Unit's percentile score and the median antibiotic prescribing across all units in the hospital</li> </ul>
<b>Persuasive intervention (FGD)</b> (On a turn key basis with each unit)	<ul style="list-style-type: none"> <li>Regarding their prescription behavior</li> <li>Changes that could have been done to reduce antibiotic use in the respective units</li> </ul>

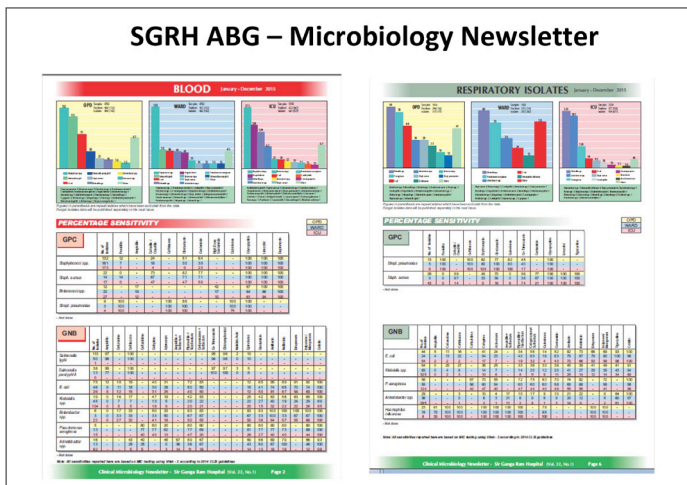
- Primary outcome measure** : Total systemic (oral or parenteral) antimicrobial use in each unit measured in DDD/100 bed days
- Statistical analysis** : Assessed by segmented regression analysis of interrupted time series for pre-intervention and 3 and 6 months post-intervention data

to 31.42% at 6 months of intervention. Although previous intervention studies from the west have demonstrated successful strategies for altering prescribers' behaviour, most have focused on discouraging use of specific drugs rather than reducing overall antibiotic prescriptions. The study throws up the challenge at the sustainability of the intervention as the effects did not persist for more than 3 months irrespective of the surgical speciality.

## TOOLKIT RESOURCE

SITE LINK

<http://www.health.org.uk/publication/path-sustainability>



### ➤ OTHER CONTRIBUTORY FACTORS

We organised ASPs and devoted time on education process and expected significant changes in prescribing habits. But, our experience in the field suggest that there are certain other factors like infection control activity play a significant role in amplifying & disseminating bacterial resistance which consequently influences the prescribing habits. The increasing number of invasive measures and interventions as well as existing poor hygiene standards play a significant role in determining bacterial resistance in LMICs. The best approach in settings with a high prevalence of MDR pathogens probably involves hand hygiene plus careful assessment of the institutions circumstances and application of more aggressive measures such as patient isolation, staff cohorting, and active surveillance cultures.

At the end, consensus recommendations were made with the aim to reduce their antibiotic prescription rate. To assess the impact and sustainability of FGD, pre-intervention antibiotic consumption data was compared with the prospective or post intervention data of the respective units 3 and 6 months' post FGD.

Overall antibiotic prescription reduced from 190.68 DDD/100BDs to 185.88 DDD/100 BDs (-2.5%) and 187.14 DDD/100 BDs (-1.88%) in 3 and 6 months' period post-intervention, respectively. Increase in the use of penicillin, 2nd generation cephalosporins and clindamycin was associated with decrease in use of 3rd & 4th generation cephalosporins, β lactam inhibitors, quinolones, macrolides, aminoglycosides, carbapenems, glycopeptides, linezolid, colistin and tigecycline.

This study highlighted two important facts. First, the meagre reduction (-1.88%) in antibiotic consumption post intervention and second, poor sustainability of the impact shown by initial (post 3 months of intervention) reduction of antibiotic prescription seen in 42.8% of the units which further reduced

In conclusion, antimicrobial resistance has reached dangerous levels & prescribing practices have to change in order to combat this problem. Newer antibiotics may not offer a solution on their own as they are likely to be expensive and unaffordable in the developing world. More importantly, the newer drugs will also eventually lose their potency. We will continue the cycle unless we change our approach towards antibiotic usage. Adherence to evidence based practice is essential which includes improved diagnostic services & availability of antimicrobial resistance surveillance data. Educating public in correct use of antimicrobials could go a long way towards curbing resistance. In addition to the above measures, to reduce antimicrobial resistance and consequent antimicrobial consumption in hospitals, it is necessary to have a good ASP combined with optimal adherence to infection control measures. It is a challenge to bring this change in developing countries.

## SOUTH AMERICA

### STORY 1: THE PROBLEMS: INAPPROPRIATE ANTIBIOTIC USE AND ANTIBIOTIC RESISTANCE IN LATIN AMERICAN COUNTRIES

During the late 1990's, leading Latin American infectious disease specialists warned: "The giant is awakening", urging to raise awareness and act upon the increasing bacterial resistance in the region. The Pan American Conference on Antimicrobial Resistance, organised by PAHO and the Pan American Infectious Disease Association (API) in 1998, called for action to identify priority problems and required interventions. Since then, a series of studies were undertaken aiming to: a) assess antibiotic consumption levels, using sales data converted into defined daily dose per 1000 inhabitants per day (DDD/TID); b) identify antibiotic prescription, dispensing and consumption patterns through household, pharmacies and healthcare setting surveys.

These studies identified the problem of inappropriate antibiotic use in the region as twofold: 1) unjustified antibiotic prescription by health care professionals, especially with broad spectrum antibiotics; and 2) self-medication with antibiotics. With regard to this second problem, a revision of pharmacy legislation in Latin American countries conducted by PAHO concluded that antibiotics were actually considered as prescription-only medicines by all national legislations. However, law was not enforced due contextual factors including: insufficient health care coverage and access to public services and medicines; within governmental institutions, scarce awareness about the problem of antibiotic misuse, and regulatory weaknesses, which led to scarce inspection and sanctions to pharmacies; and within the community, strong cultural beliefs with regard to antibiotics use. These factors led to a high demand for antibiotics and an ample offer in private pharmacies.

This situation was especially sensitive in Mexico, where up to 40% of all antibiotics were obtained without medical prescription in private pharmacies and where they were sold by undertrained clerks –not dispensed by pharmacists. This country had had the highest level of consumption in the region, although it showed a decreasing trend. However, consumption of quinolones and new macrolides (such as azithromycin) rose sharply, as in other countries in the region (Figure 7).

### STORY 2: THE PROCESS AND IMPACT OF INTRODUCING REGULATIONS FOR ANTIBIOTIC SALES IN CHILE, BRAZIL AND MEXICO

Following concern with the problems of bacterial resistance, high levels of consumption and self-medication with antibiotics in Latin America, several countries have introduced regulatory measures to restrict antibiotic sales, either at the national or sub-national level. The experiences of Chile, Mexico and Brazil offer a good example of the challenges and opportunities for introducing this regulation, as well as to understand its impact.

#### Chile

Chile regulated antibiotic sales only with medical prescription in 1999. Governmental attention was facilitated by available indicators on antibiotic consumption and antibiotic resistance. Infectious-disease specialists acted as policy entrepreneurs calling the attention of health officials to these problems and to PAHO recommendations. The feasibility of the regulation of antibiotic sales was further facilitated by a positive previous experience in regulating benzodiazepine sales. The introduction of the regulation was accompanied by extensive media coverage, public information campaign and involvement of community pharmacies.

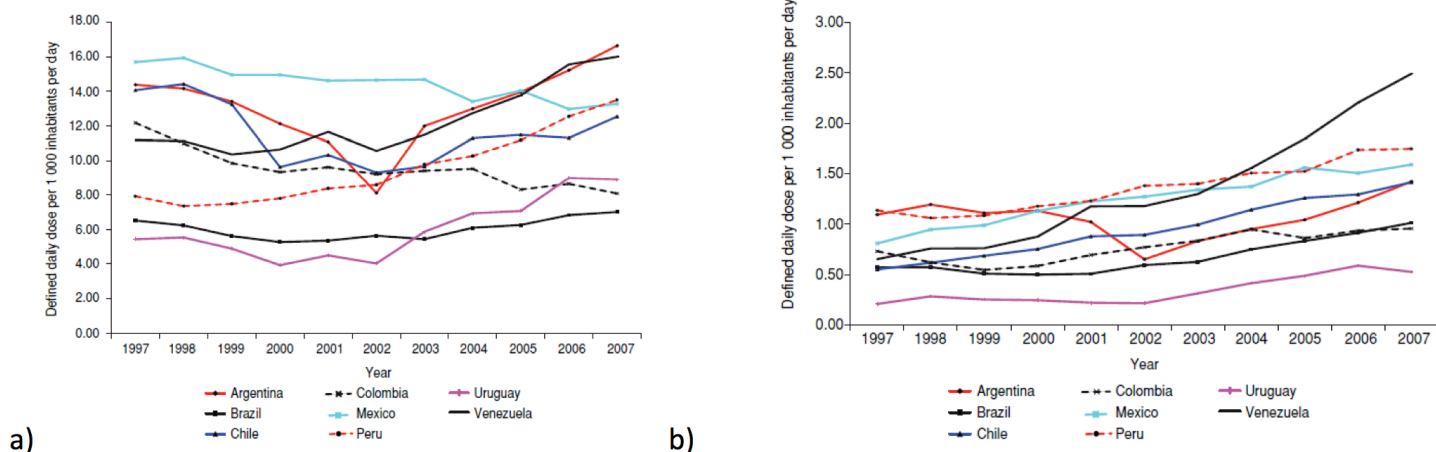


FIGURE 7 Trends in a) Overall antibiotic utilization, and b) Quinolone utilization in eight Latin American countries, 1997-2007. Source: Wirtz VJ, Dreser A and Gonzales R (2010). Trends in antibiotic utilization in eight Latin American countries, 1997–2007. Rev Panam Salud Pública 27: 219–225

An initial 30% overall decrease on antibiotic consumption was attained, which affected mainly those antibiotics that were previously sold without prescription (penicillins and cotrimoxazole). The initial dramatic success of this regulation was short-lived: as campaigns were not sustained, three years later antibiotic consumption levels rose again; however, consumption remained below the pre-intervention level (Figure 8).

**Slide presentation:**

Impact of regulatory measures on antibiotic sales in Chile



VIEW SLIDE SET

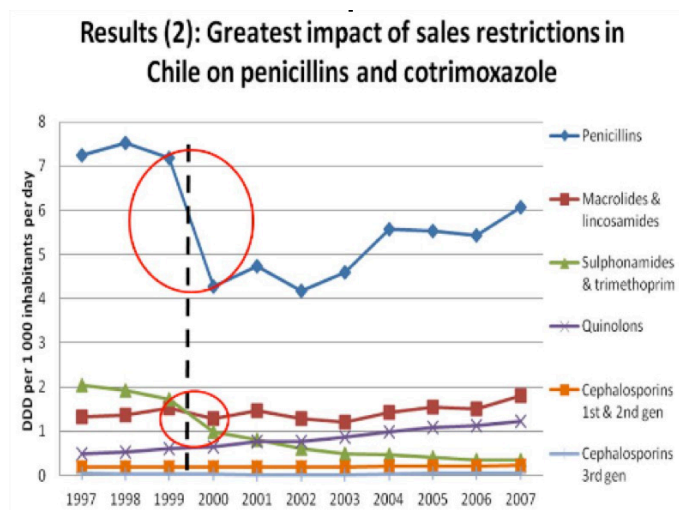


FIGURE 8

Impact of antibiotic sales regulation in Chile. Source: Herrera-Patiño J, Santa-Ana-Tellez Y, Dreser A, Gonzalez R, Wirtz VJ. Consumption of antibiotics before and after sales regulations in Chile, Colombia and Venezuela. In: <http://slideplayer.com/slide/8478401/>

**Slide presentation:**

Consumption of antibiotics before and after sales regulations in Chile, Colombia and Venezuela



VIEW SLIDE SET

**Brazil**

The Brazilian National Health Surveillance Agency (ANVISA) had been discussing the need to improve the control of antibiotic sales since 2009. However, it was the spread of the multi-resistant KPC bacteria and related deaths during 2010 – followed widely by the media– which speeded up the regulation process. The regulation was implemented since November 2010, establishing that antibiotics were to be sold only with prescription, which was to be retained in pharmacies. The resolution was supported mainly by medical groups, but faced the opposition of pharmacy and commerce associations. Arguing the social impact of the regulation (e.g. insufficient infrastructure of public medical services, scarce access to medical care in rural areas, and the risk of triggering a parallel black market of antibiotics) these associations sought to withdraw the resolution. Nevertheless, the resolution was implemented. An interrupted time series analysis using the DDD/TID unit concluded that, two years after the regulation, antibiotic consumption in the private sector decreased by nearly 24% (Figure 9). Aiming to overcome problems with pharmacies' compliance, a stricter regulation was introduced in April 2013, incorporating antibiotics into the ANVISA national system for management of controlled substances.

**Mexico**

The problems of antibiotic use had remained low in the health policy agenda of Mexico, where attaining access to medicines has been top priority. However, in 2009, in the midst of the influenza A H1N1 pandemic, self-medication with antibiotics was associated with delayed medical care and high influenza mortality in the country. This created an unprecedented public debate. Infectious disease specialists, public health and veterinary experts saw this as open window of opportunity to propose to the government priority actions to improve antimicrobial use and mitigate resistance. The Ministry of Health enacted a decree effective as of August 2010, which enforced the regulation of antibiotic sales only with medical prescription; additionally it required prescriptions to be retained and registered in pharmacies, and imposed high penalties for non-compliance. Pharmacy associations opposed to the regulation, arguing economic losses and logistical difficulties for the pharmacies, as well as the negative health and economic effects on poor populations with scarce access to healthcare. Bigger pharmacy chains developed a different strategy, by opening medical clinics adjacent to pharmacies. Between 2010 and 2013, the number of these pharmacy clinics, offering cheap or even free consultation (and antibiotic prescriptions), tripled in the country –buffering the impact of the regulation.

**Slide presentation:**

Regulation of antibiotic sales in Mexico: process and impact



An interrupted time series analysis using the DDD/TID unit to assess the impact of the regulation concluded that there was an overall 12% decrease (around 1 DDD/TID) on antibiotic consumption, largely because penicillins; no shift toward use of other classes of antibiotics, such as quinolones, was observed. A clear reduction on the seasonal variation on amoxicillin (34%) and ampicillin (93%) consumption (which were best-seller medicines in the country), as well as an increase in the use of some symptomatic medicines (as substitute products) was also documented. Another study concluded that, after the regulation, there was no increment in hospital admissions related to bacterial infections, a feared side-effect of the intervention. This body of evidence points to the success of the regulatory intervention on curbing unnecessary antibiotic use by self-medication in the country. Monitoring and improving medical prescription, especially on the emerging pharmacy clinics, remain an important challenge.

# TOOLKIT RESOURCE

## ARTICLES

Bavestrello, L. and Cabello, Á. (2011). Community antibiotic consumption in Chile, 2000-2008. *Rev Chil Infect*, 28(2), 107-112.

Dresler, A., Vázquez-Vélez, E., Treviño, S. and Wirtz, V.J. (2012). Regulation of antibiotic sales in Mexico: an analysis of printed media coverage and stakeholder participation. *BMC Public Health*, 12, 1051.

Santa-Ana-Tellez, Y., Mantel-Teeuwisse, A. K., Leufkens, H. G. M., & Wirtz, V. J. (2015). Seasonal Variation in Penicillin Use in Mexico and Brazil: Analysis of the Impact of Over-the-Counter Restrictions. *Antimicrobial Agents and Chemotherapy*, 59(1), 105–110.

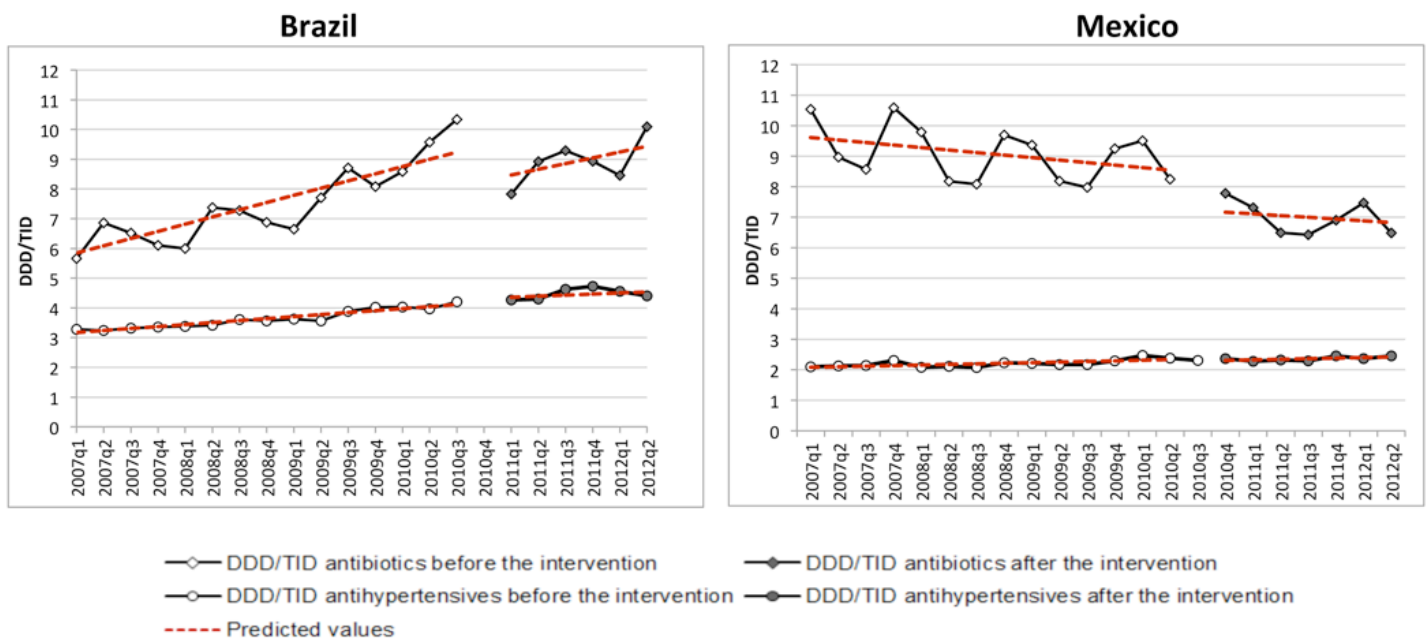


FIGURE 9 Trends in antibiotic consumption for Brazil and Mexico (2007–2012), and impact of the 2010 regulation on antibiotic sales. Source: Santa-Ana-Tellez Y, Mantel-Teeuwisse AK, Dresler A, Leufkens HGM, Wirtz VJ (2013) Impact of Over-the-Counter Restrictions on Antibiotic Consumption in Brazil and Mexico” PLOS ONE, 2013; 8; 10 ; e75550-e75550)



## CONCLUSIONS

Taken together, the cases of these Latin American countries show that regulating antibiotic sales can be very politically sensitive issue in resource limited settings, because insufficient access to health care, and because economic interests are affected. However, media attention, together with the efforts of concerned researchers, public health and infectious disease specialists can draw political will. Using a standard methodology, it was possible to prove that these regulatory interventions were successful in curbing self-medication practices and reducing antibiotic consumption in the community. The remaining challenge for the region in years to come is to improve the quality of medical antibiotic prescription, both in hospital and ambulatory care. A number of interesting AMS programmes are now being developed in Latin American hospitals --particularly in Colombia. The processes and impact related to their implementation have to be well documented in order to gain valuable lessons for the region.

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# CHAPTER 17

▶ AUTHOR: **AOIFE FLEMING**

## STEWARDSHIP IN LONG TERM CARE FACILITIES

### THE AIM OF THIS CHAPTER IS TO:

Outline the factors impacting on antimicrobial prescribing in Long Term Care Facilities (LTCFs).

Describe the prevalence of infection, antimicrobial prescribing and antimicrobial resistance in LTCFs.

Describe the impact of antimicrobial stewardship in this setting.

### THIS CHAPTER WILL ALSO OUTLINE:

Strategies to combat AMR in LTCFs.

Outline case scenarios and examples of how to implement AMS initiatives at a local level.

## LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Explain the unique factors impacting on AMR and AMS in LTCF
- To understand the factors influencing the prescribing of antimicrobials in LTCF
- Identify and communicate the core goals of a LTCF AMS strategy
- Reflect on their own practice and how to introduce AMS in LTCF

### ▶ LONG TERM CARE FACILITY SETTING FACTORS

Antimicrobial stewardship is vitally important in Long term care facilities (LTCFs). Over any given year, up to 70% of LTCF residents are prescribed an antimicrobial with studies suggesting that a large proportion of these prescriptions are inappropriate. Point prevalence studies have indicated that between 3% and 15% of LTCF residents are prescribed antimicrobials at any given time. The CDC factsheet below outlines the scale of antimicrobial prescribing in the United States of America.



Risk factors for Healthcare associated Infections (HCAIs) in LTCFs:

- co-morbidities, age related immune decline
- shared facilities (communal areas, toileting facilities, bedrooms) and minimal isolation facilities for residents with infections
- invasive medical devices e.g. urinary and vascular catheters, gastrostomy tubes
- wound management

A meta-synthesis of studies investigating the factors influencing antimicrobial prescribing in LTCF developed the conceptual model as outlined in Figure 1.

 [VIEW DOCUMENT](#)



| FIGURE 1

*The challenges of diagnosing and managing HCAs are compounded by the following;*



## TOOLKIT RESOURCE

### ARTICLES

Crnich C et al. Optimizing antibiotic stewardship in nursing homes: a narrative review and recommendations for improvement. *Drugs Aging* 2015;32:699-716

Dyar O.J et al. Strategies and challenges of antimicrobial stewardship in long-term care facilities. *Clinical Microbiology and Infection* 2015;21:10-19

## > ANTIMICROBIAL PRESCRIBING PRACTICES

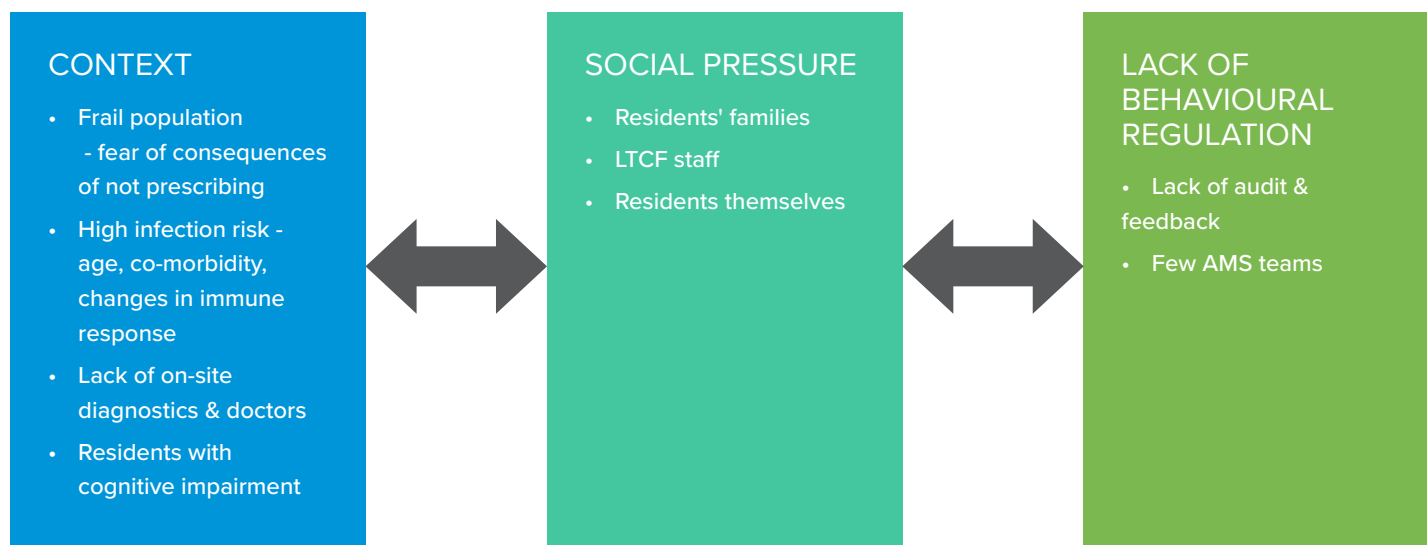
Antimicrobials are most frequently prescribed in LTCFs for Urinary tract infections (UTIs), Respiratory tract infections (RTIs) and Skin and Soft tissue infections.

There is significant variability in antimicrobial prescribing practices between LTCFs, as seen in large point prevalence studies.

Antimicrobial prescribing in LTCFs is variable between and within LTCFs due to the following factors:

- Medical care delivered in different structures e.g. one medical group practice, one general practitioner, several general practitioners from different practices or doctors from adjunctive hospital/secondary care settings, on-call doctor cover
- Not all LTCFs have doctor visits on a daily basis and access to Infectious Diseases Consultants or specialist ID/ Antimicrobial Pharmacists is limited
- Doctors reliant on nursing staff to assess and communicate information – frequent telephone ordering of antimicrobial prescriptions without patient bedside consultation

Qualitative research investigating the factors influencing antimicrobial prescribing in LTCFs has found that drivers of antimicrobial prescribing in this setting are listed in the following figure:



## IMPACT OF ANTIMICROBIAL RESISTANCE

There is a lack of local antimicrobial resistance data available to guide prudent prescribing in the LTCF setting.

Subsequently, the rate of multidrug resistant organism (MDRO) infections in LTCFs is not well recorded.

A study evaluating Centers for Medicaid and Medicare Services Long Term Care Minimum Data Set (MDS) found a rate of MDRO infections of 4.2% among nursing home residents across the USA (range 1.9% to 11.4% in individual states).

LTCF residents are commonly colonised by bacteria, which makes the interpretation of microbiology samples complicated, with colonisation often judged as infection when the reports are read. This can lead to unnecessary antimicrobial prescribing.

Colonisation with MDROs is common – especially with Methicillin Resistant *Staphylococcus aureus* (MRSA). Studies have found colonisation rates up to 50% in LTCFs, much higher than that 5-10% among hospitalised patients.

The prevalence of Vancomycin Resistant Enterococci (VRE) ranges from 4-16% and is on the increase, as is the prevalence of colonisation with Extended Spectrum beta-lactamase (ESBL) and Carbapenem Resistant Enterococci (CRE). These are areas of concern as the eradication of colonisation can be difficult and

often leads to infection.

The risk of colonisation is driven higher by the following factors:

- recent antimicrobial use (within the last 4 months)
- high resident dependency levels
- urinary or vascular catheters,
- ulcers/wounds
- urinary or faecal incontinence

Risk factors for colonisation with *Clostridium difficile* in LTCFs include:


- previous history of *C.difficile* infection
- antimicrobial use with the last 3 months
- recent hospitalisation.


LTCFs have been termed “reservoirs” for MDROs and *C.difficile*. Case clusters of MDRO or *C.difficile* outbreaks in LTCFs in regional LTCFs and acute hospitals have been published. The close proximity of residents in either shared bedrooms or communal areas (bathrooms, dining etc.) contributes to the horizontal transmission of pathogens in LTCFs.

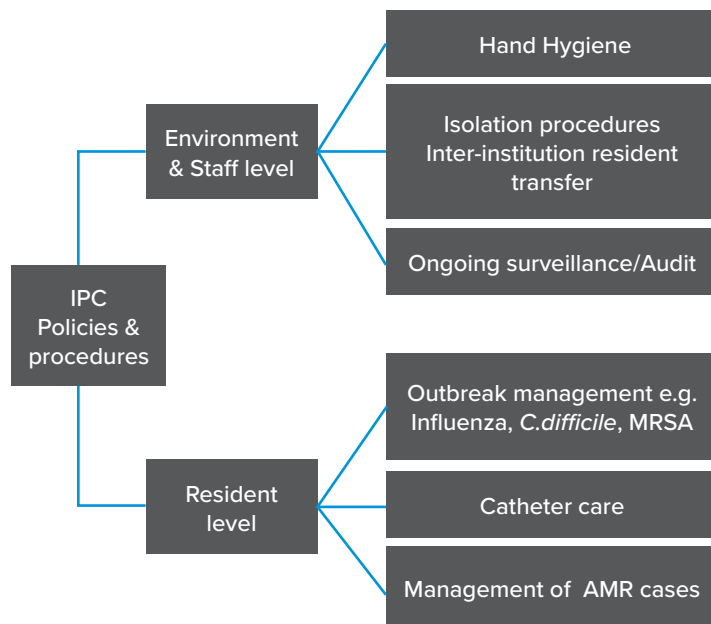
Evidence supports that there is a higher rate of AMR in the LTCF population.

## TOOLKIT RESOURCE

### SITE LINK

 Fleming A et al. Eur J Public Health. 2017 Apr 1;27(2):307-312. doi: 10.1093/eurpub/ckw138. Antimicrobial susceptibility of long term care facility and general practice urine samples in patients 65 years and older: an observational study.

 Examining the relationship between multidrug-resistant organism acquisition and exposure to antimicrobials in long-term care populations: a review. Michele L. Shaffer, PhDa, b, , Erika M.C. D'Agata, MD, MPHc, Daniel Habtemariam, BAd, Susan L. Mitchell, MD, MPHc, d Annals of Epidemiology Volume 26, Issue 11, November 2016, Pages 810–815



The importance of robust infection prevention and control systems in LTCF cannot be highlighted enough. As already mentioned, the transmission of pathogens, which could be potentially resistant, is a contributing factor to the development of infectious outbreaks such as influenza. LTCF should follow national/regional protocols on IPC in practice.

Guidance on IPC is available on the CDC webpage:

 VISIT SITE

The main features of an IPC policy and practice initiative in LTCFs should include the above Figure.

#### Case Scenario:

Mr Henry is a resident of Forest Glen nursing home and is 79 years of age. He has a history of COPD, hypertension and atrial fibrillation. The doctor is called to review the patient as he is unwell and his family have become concerned and do not want him to be transferred to the nearby acute hospital. Mr Henry routinely takes rampril, atorvastatin, tiotropium inhaler, fluticasone/salmeterol inhaler and salbutamol nebulas prn. There is no x-ray machine in the LTCF and the family ask the doctor to prescribe an antimicrobial co-amoxiclav which Mr Henry responded to 4 weeks ago. However, on review of the resident (fever >38°C, chills, sweating, headache, sore throat, extreme fatigue) the doctor takes a throat swab and sends it

for testing to the local microbiology laboratory as she suspects influenza. The family are not happy about this and request that the doctor prescribes co-amoxiclav.

#### What should the doctor do next?

- The doctor should take time to discuss with the family and the nurse that the presenting signs and symptoms are suggestive of influenza and not a COPD exacerbation. He should outline that COPD has increased Mr Henry's risk of influenza and that there have been cases in the locality in recent days.
- The doctor should examine the patient and ensure that there is no secondary bacterial infection in the respiratory system (check for consolidation, check breathing, type of cough, CURB score);

 VISIT SITE

- Mr Henry has presented with uncomplicated Influenza (no signs of lower RTI or CNS involvement or significant exacerbation of his COPD); therefore no hospital admission is required at this point. However, the family should be made aware that this situation could change and if transfer is needed over the coming days they should be prepared for this in Mr Henry's best interests.

- An anti-viral agent such as Oseltamivir 75mg bd po should be started as soon as possible without waiting for laboratory confirmation. (Note that Mr Henry does not have renal impairment, dose adjustment may be needed depending on the degree of renal impairment).
- A risk assessment should be conducted, as well as contacting the local public health office to notify them of the infection, anti-viral chemoprophylaxis should be prescribed to other residents at risk as per local guidance.
- Influenza vaccination status of all residents and staff should be recorded, and non-vaccinated cases should be contacted for vaccination. Remember it takes two weeks for the vaccine to take effect.
- Close the LTCF to visitors to reduce the spread of Influenza around the LTCF and into the community.

### SURVEILLANCE OF HEALTHCARE ACQUIRED INFECTIONS AND ANTIMICROBIAL PRESCRIBING

Several initiatives have been implemented over recent years to record, by means of point prevalence studies (PPS), the prevalence of HCAI and antimicrobial prescribing at a given point in time in LTCFs.

In Europe the European Centre for Disease Prevention and Control (ECDC) has conducted a Point Prevalence Survey of Healthcare-Associated Infections and Antimicrobial use in Long-Term Care Facilities (HALT) has been conducted in 2010, 2013 and 2016.

### VIEW PPS ARTICLE

The objectives of this PPS are to facilitate ECDC surveillance of Healthcare-associated Infections (HAIs) and antimicrobial use in LTCFs. The most recent HALT study European level report has not been published yet. The 2013 HALT report is available here:

### VIEW REPORT

This report included 1181 LTCFs (77,264 residents) in 19 countries. Data were collected on a single day and preparation involved training LTCF staff to collect and submit the data. The crude prevalence of residents receiving at least one antimicrobial

was 4.4% (n = 3,367 of 77,264) and this ranged from 1.0% in Hungary to 12.2% in Greece. Antimicrobials were most frequently prescribed for the treatment of infection (72.8%), with RTIs (39.0%), UTIs (35.1%) and skin/wound infections (16.0%) being the most commonly treated infections.

The 2016 Irish national report has been published and included data from 10,044 residents in 224 Irish LTCFs.

### VIEW REPORT

The national report provides detailed information on the types of LTCFs included and the prevalence of HAIs and enables countries to benchmark their performance against the European average. Of particular interest from an AMS perspective is the detail on antimicrobial prescribing; the national crude prevalence in Ireland in 2016 was 9.8% compared to the European average in 2013 of 4.4%. The indications for antimicrobial prescriptions are well detailed. Also, due to Ireland's participation in HALT since 2010, the Irish HALT Steering Group have identified a number of key priorities for implementation which will be discussed further later on the Chapter.

### ANTIMICROBIAL STEWARDSHIP

A challenge for conducting AMS in LTCFs is that, compared to acute care settings, many of the key stakeholders to drive this agenda are based off site (e.g. medical physicians, pharmacists, specialist public health/infection prevention & control nurses). LTCFs have minimal in-house diagnostic facilities and the turnaround time for microbiological and blood sample results can be several days.

In order to support LTCF to implement AMS initiatives the CDC has published a very useful resource and more information is available here;

### WATCH VIDEO

### WATCH VIDEO



Key areas to focus on for LTCF AMS:

**ANTIMICROBIAL PRESCRIBING**

- follow local/national guidelines
- choose correct antimicrobial for indication, correct dose & frequency, follow up on microbiology investigations, review duration

**URINARY DIPSTICK**

- Reduce inappropriate testing
- Correct interpretation & follow up with urine sample testing to confirm presence and/or susceptibility

**URINARY CATHETERS**

- reduce inappropriate antimicrobial prescribing for asymptomatic bacteriuria

**IPC**

- Reduce colonisation and infection risk
- focus on MDRO, Influenza, *C.difficile*

It is important to consider that AMS initiatives in LTCFs require tailored approaches suitable for the local context and supportive organisational commitment.

A pilot cluster randomised controlled in the United Kingdom evaluated the implementation of a paper-form in LTCFs that required documentation of antimicrobial prescribing practices. The form required the recording of clinical signs & symptoms, physician evaluation, indication for the antimicrobial, appropriate diagnostic evaluation, clinical re-evaluation, and review of diagnostic tests within 48-72 hours, and duration of treatment. The 12 week pilot study showed a significant decrease in antimicrobial use of 4.9% in the intervention group (p=0.02) compared with baseline, and a significant increase of 5.1% in the control group (p=0.04).

<http://www.leedscommunityhealthcare.nhs.uk/seecmsfile/?id=2322>

**TOOLKIT RESOURCE**  
 SITE LINK  
 [ncbi.nlm.nih.gov](http://ncbi.nlm.nih.gov)

	ESAC Europe n = 260	HALT Europe n = 117	Donlon et al Ireland n = 69	Van Schooneveld et al. Nebraska USA n = 37
Antimicrobial stewardship committee	8%	16%	16%	36%
Therapeutic formulary	16%	57%	23%	19%
Antimicrobial guidelines	50%	45%	28%	27%
Data about antimicrobial consumption	-	33%	16%	81%
Data about local antimicrobial resistance profiles	9%	17%	12%	76%
Regular training of prescribers on antimicrobial use	16%	22%	7%	8%
Individual antimicrobial prescribing profiles	-	27%	10%	11%
Pharmacist advice on antimicrobial use	-	19%	36%	-
Regular audits assessing antimicrobial use	-	-	-	81%

TABLE

Cross-sectional surveys of antimicrobial stewardship programmes in long-term care facilities. Ref. Dyar et al Clinical Microbiology and Infection 2015;21:10-19.

An important development in the United States has been the Centers for Medicare and Medicaid requirement for all LTCF to have an antibiotic stewardship program by November 28 2017.

 [VIEW ARTICLE](#)

In order to support LTCF in the implementation of an antibiotic stewardship policy a comprehensive template was published by Jump et al.

 [VIEW TEMPLATE](#)

### FOCUS ON UTI AND CAUTI IN LTCF

LTCF residents are at increased risk of antimicrobial prescribing for UTI and CAUTI (Catheter associated UTI). Some initial clinical presentations may warrant an antimicrobial prescription – but many do not. In order to improve the diagnosis of UTI in this setting a structured and evidence based approach should be followed. Many public health organisations have introduced at local and/or national level guidance to improve the diagnosis and treatment of UTI. It is important to note that the most relevant guidance to a LTCF is that which has been based on AMR data and evidence from that region.

Key points which are present across the guidelines are:

- Take care when interpreting urine dip sticks as false positive results are often given due to the presence of asymptomatic bacteriuria, especially in residents with a catheter
- A positive dipstick result in an asymptomatic patient is not indicative of a UTI and should not be treated
- If a patient is treated empirically with antimicrobials, a urine sample should be sent for microbiological investigation before the antimicrobial is given, to guide antimicrobial susceptibility
- Positive microbiological urine sample results, without symptoms, is not indicative of infection. Catheterised patients often have elevated white blood cells in the urine due to the presence of the catheter.
- Empiric antimicrobial prescribing should be guided by local guidance and AMR patterns.

Public Health England has published the following quick reference guide with specific points on diagnosis for patients >65 years:

 [VIEW GUIDELINE DOCUMENT](#)

In Ireland, the following guidance for the diagnosis and management of UTI in LTCF residents >65 years has been available with several years:

 [VIEW GUIDELINE DOCUMENT](#)

 [VIEW INFORMATION FOR CARE HOMES ARTICLE](#)

The importance of tailoring antimicrobial prescriptions cannot be highlighted enough and the Start Smart then Focus campaign should be adopted and adhered to in LTCFs should an antimicrobial be prescribed. This initiative was developed in the United Kingdom and has since been used widespread. See Figure on the next page for the Irish Start Smart then Focus Antibiotic Bundle for hospitals, the principles of which should guide LTCF antimicrobial prescribing also.

# Start Smart, Then Focus

## An Antibiotic Care Bundle for Hospitals



### Day 1: Start Smart...

1. Start antibiotics only if there is clinical evidence of bacterial infection
  - If there is evidence of bacterial infection, prescribe in accordance with your local antibiotic guidelines and appropriately for the individual patient (see notes below)
2. Obtain appropriate cultures before starting antibiotics
3. Document in both the drug chart and medical notes:
  - Treatment indication
  - Drug name, dose, frequency and route
  - Treatment duration (or review date)
4. Ensure antibiotics are given within four hours of prescription
  - Within 1 hour for severe sepsis or neutropenic sepsis

When deciding on the most appropriate antibiotic(s) to prescribe, consider the following factors:

- History of drug allergy (document allergy type: minor (rash only) or major (anaphylaxis, angioedema))
- Recent culture results (e.g. is patient colonised with a multiple-resistant bacteria?)
- Recent antibiotic treatment
- Potential drug interactions
- Potential adverse effects (e.g. C. difficile infection is more likely with broad spectrum antibiotics)
- Some antibiotics are considered unsafe in pregnancy or young children
- Dose adjustment may be required for renal or hepatic failure

Consider removal of any foreign body/indwelling device, drainage of pus, or other surgical intervention

For advice on appropriate investigation and management of infections, consult your local infection specialist(s) (microbiologist, infectious disease physician and/or antimicrobial pharmacist)

### ...then Focus (Day 2 onwards)

At 24-48 hours after starting antibiotics, make an **Antimicrobial Prescribing Decision**

- Review the clinical diagnosis
- Review laboratory/radiology results
- Choose one of the five options below
- Document this decision

#### Options

1. Stop antibiotic(s)
  - no evidence of bacterial infection, or infection resolved
2. Switch from intravenous to oral antibiotic(s)
  - if patient meets criteria for oral switch
3. Change antibiotic(s)
  - narrower spectrum, if possible;
  - broader spectrum, if indicated
4. Continue current antibiotic(s)
  - review again after further 24 hours
5. Outpatient parenteral antibiotic therapy
  - consult with local OPAT team

Adapted from the RCSI Hospital Antimicrobials Stewardship Working Group (2011) 'Start Smart, Then Focus' antibiotic stewardship programme

'Start Smart then Focus' antibiotic bundle Ref. Royal College of Physicians Ireland.

LTCF residents with urinary catheters are at increased risk of inappropriate antimicrobial prescribing. The figure on the next page outlines guidance from Leeds Community Healthcare for the prevention of catheter associated UTIs in LTCF and this rational approach should form an important part of a LTCF antimicrobial stewardship strategy. Reducing the number of unnecessary urine cultures is crucial to reduce the inappropriate diagnosis of CAUTI and inappropriate antimicrobial use. Further information is available on:



VIEW ANTIBIOTIC STEWARDSHIP FAQs DOCUMENT

#### Case Scenario:

Mrs Jones, an 82 year old resident at Riverside nursing home presents with symptoms of confusion and is disoriented. She has a background of mild dementia, has limited mobility and takes medication for hypertension, atrial fibrillation and hyperlipidaemia. She has had 6 UTI over the last 12 months. The nurse conducts a urine dipstick which is positive. The nurse has contacted the on-call doctor as it is the weekend and requests a prescription for ciprofloxacin.

What steps should be taken by the doctor?

- The doctor should visit the resident gather more clinical information from the nurse regarding the patients signs and symptoms; is there dysuria, urinary frequency/urgency, new onset incontinence, fever >38°C, suprapubic tenderness, haematuria, pain/tenderness?
- If none of the above are present, it is unlikely to be an infection and 'watchful waiting' should be implemented for the next few days, as well as ensuring that the patient is well hydrated.

- Any differential diagnoses should be investigated.
- The positive dipstick is not an indicator of infection
- If a UTI is suspected with the presence of clinical signs and symptoms, previous microbiology results of UTI samples from recent infections should be reviewed and a mid-stream urine sample should be sent before any antimicrobial is prescribed.
- The previous results may indicate which antimicrobial the causative organism would be susceptible too; however, the prescription should be informed by the microbiology results once available over the coming days.



Leeds Community Healthcare **NHS**  
NHS Trust

## Has your patient got signs and symptoms of a catheter associated urinary tract infection (CAUTI)?

**Diagnosis of a CAUTI must always involve assessing for clinical signs and symptoms compatible with a CAUTI.**  
Signs and symptoms include:

- Fever
- Rigors, shivering, shaking
- New onset or worsening confusion / delirium
- Malaise / lethargy with no other identified cause
- Back pain
- Pelvic discomfort / pain
- Acute haematuria



**Dip stick testing of urine must NOT be used to diagnose a CAUTI, because:**

- Patients with a urinary catheter are likely to always have non visible haematuria due to ongoing trauma of the catheter
- Patients with a urinary catheter are likely to have bacterial colonisation of their urine due to the presence of the catheter
- These can all be normal findings in a catheterised patient and in isolation does not indicate infection



**When to take a catheter sample of urine (CSU)**

- A CSU should only be obtained when a diagnosis of CAUTI has been made
- Obtain the CSU before the patient commences antibiotics
- The CSU will help guide antimicrobial treatment but does not help in establishing the diagnosis
- Obtaining a CSU when there is no clinical evidence of a CAUTI may lead to a false positive result and unnecessary treatment with antibiotics

**How to obtain a CSU:**

- Obtain the specimen aseptically via the drainage bag needle free sampling port
- Clean the sampling port with a 70% isopropyl alcohol swab and allow to dry
- CSUs may also be obtained aseptically during catheterisation
- The sample should normally be sent in a red -topped (boric acid containing) sterile container and filled to the line
- A false negative culture result can occur with a small urine volume

**Changing the catheter:**

- Patients who have a diagnosis of a CAUTI should have their catheter changed with appropriate antibiotic cover\*
- Change the catheter after the patient has commenced antibiotics for the CAUTI



Prescribing antibiotics when there is no clinical evidence of a CAUTI should not be done and may increase patient's multi-resistance to antibiotics.

**References:**

Urinary Catheterisation: Adults and Children's (Urethral, Supra Pubic and Intermittent) Policy and Standard Operating Procedures. Leeds Community Healthcare NHS Trust 2015  
\*Guideline for antimicrobial prophylaxis during urinary catheterisation in adults. Leeds Teaching Hospitals NHS Trust 2010

Catheter associated urinary tract infections (CAUTI). Management of infection guidance for primary care. Leeds Teaching Hospitals NHS Trust 2011  
Catheter associated urinary tract infections (CAUTI) in adults (>16 years of age) - Guideline for the management of in secondary care). Leeds Teaching Hospitals NHS Trust 2013

© Leeds Community Healthcare NHS Trust, March 2015 ref: 1265

[www.leedscommunityhealthcare.nhs.uk](http://www.leedscommunityhealthcare.nhs.uk)

### SEPSIS IN LTCF

There is an increasing focus on the early treatment of Sepsis in LTCFs with the introduction of LTCF specific early warning score tools/checklists being introduced to support the treatment of sepsis in LTCF and reduce the need for resident transfer to acute care setting.

 [VIEW UK SEPSIS RESOURCE ARTICLE](#)

### ANTIMICROBIAL STEWARDSHIP IN LTCFS

#### Goals and outcomes

Antimicrobial Stewardship in LTCF Goals:

1. Introduce a culture to support AMS in your LTCF
2. Consider strategies that are tailored and appropriate for your setting
3. Have a LTCF AMS Champion to lead the strategy and garner support
4. Introduce strategies one by one in feasible steps.
5. Benchmark against other, similar LTCF in your region locally and nationally
6. Improve communication between key stakeholders on the AMS team and with healthcare providers at points of resident transfer (e.g. acute hospital – LTCF interface)
7. Give positive and constructive feedback

#### Measuring AMS in LTCFs:

The CDC Core Elements of Antibiotic Stewardship for Nursing Homes advises that nursing homes work in a step-wise fashion and implementing AMS strategies one by one and gradually adding to the overall strategy over time.

#### Audit and Feedback:

- Identify key priority areas and focus on them one by one e.g. conditions accounting for largest proportion of antimicrobial prescribing such as UTI
- Measure the timeliness of interventions on an Early Warning Sepsis score
- Conduct audits of antimicrobial prescribing and compare the results to regional/national LTCF antimicrobial prescribing guidelines


The availability of electronic data on antimicrobial prescriptions can facilitate detailed audits in LTCF, especially if the prescription data is linked to medical clinical records and/or microbiology test results.

The aforementioned supportive paper for the implementation of the CMS requirements provides useful information on the monitoring of antimicrobial consumption and AMR trends.

 [VIEW DOCUMENT](#)

## TOOLKIT RESOURCE

### PDF ARTICLE

 [CDC Checklist of core elements for antibiotic stewardship programs in nursing homes](#)

 [Measures of antibiotic prescribing use and outcomes](#)

This checklist recommends the following components for examining antibiotic prescribing in LTCF:

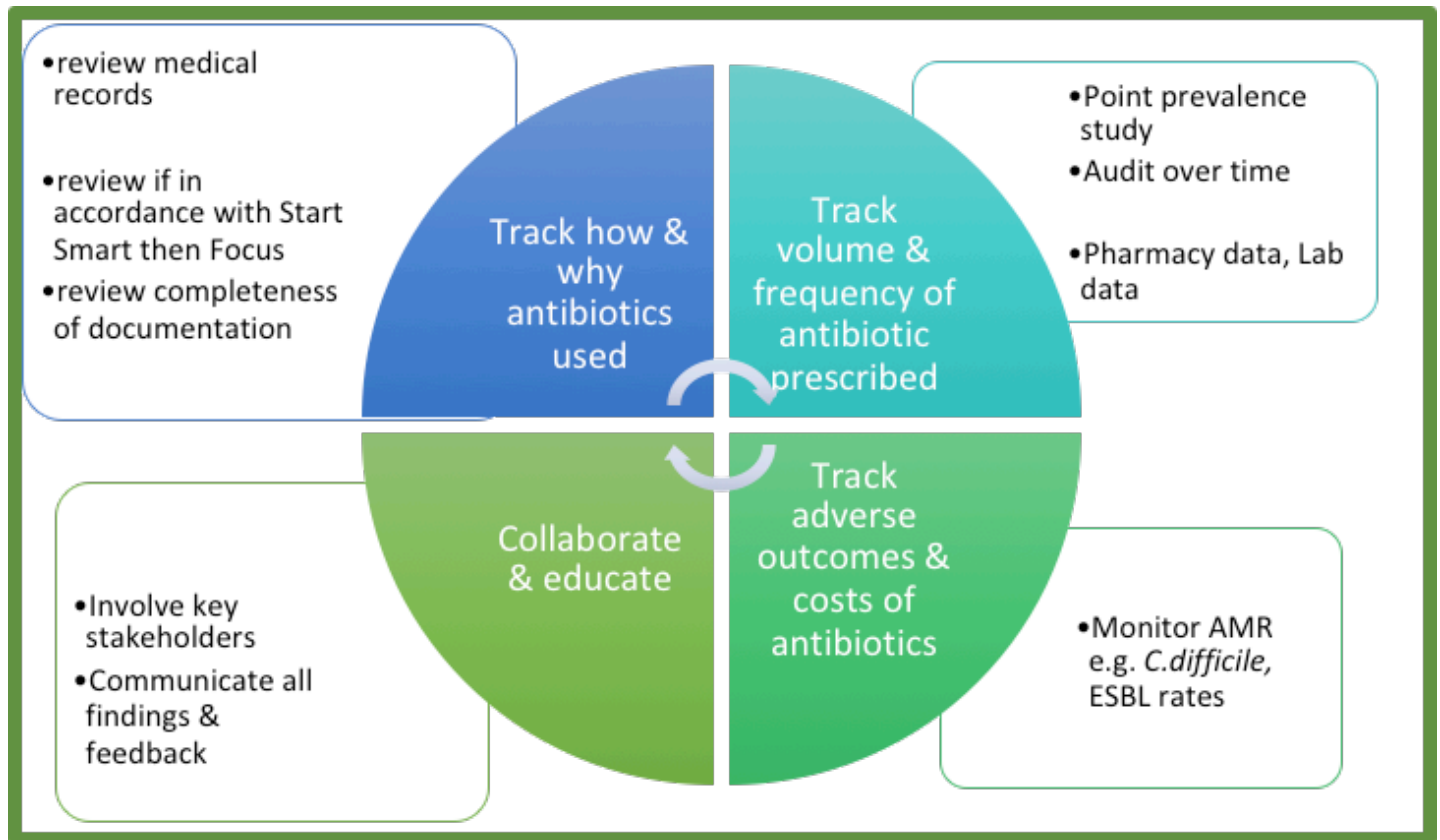


Figure. Measures of antibiotic prescribing. (adapted from the CDC guideline available from <https://www.cdc.gov/longtermcare/pdfs/core-elements-antibiotic-stewardship-appendix-b.pdf>)



# CHAPTER 18

 AUTHOR: **ANDREW M. MORRIS**

## STEWARDSHIP IN THE INTENSIVE CARE UNIT

### THE AIM OF THIS CHAPTER IS TO:

Highlight the importance and opportunities for antimicrobial stewardship in ICUs.

Outline the structures needed for successful antimicrobial stewardship in the ICUs.

Describe interventions that are best suited to antimicrobial stewardship in ICUs.

Review metrics to reflect effectiveness and safety of ICU antimicrobial stewardship.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Importance and opportunities of ICU Antimicrobial Stewardship
- Structures needed for Antimicrobial Stewardship in the ICU
- The best interventions to steward antimicrobials in the ICU
- ICU Antimicrobial Stewardship outcome measures

### INTRODUCTION

Approximately half of intensive care unit (ICU) patients are believed to be infected. The risk of infection increases with disease severity.

These infected patients have an increased risk of death, so the use of antimicrobial agents is widespread in ICUs, with about three quarters of patients receiving antimicrobials at any time. Because most of these antimicrobials are parenteral, broad-spectrum, and often relatively new, ICU antimicrobial expenditures usually dwarf similar expenditures elsewhere in the hospital. Antimicrobial use in ICUs is also associated with increasing antimicrobial resistance, likely in a complex and multifactorial way. Juxtaposing antimicrobial adverse consequences including drug-resistant and *C. difficile* infections with rising antimicrobial costs and limited discovery of new antimicrobial agents, has resulted in strong calls for antimicrobial stewardship (AMS) in ICUs.

Despite this, evidence supporting AMS—especially in ICUs—is limited. The greatest benefits of hospital-based AMS programs appear to be in critical care, but systematic reviews of AMS programs in ICUs only identified single-centre studies of short duration. Multi-centre long-term studies are thus a major existing gap in evidence. A Cochrane review on AMS interventions in hospitals suggests favourable outcomes from enabling over restrictive interventions.

In this chapter, AMS in ICUs will be considered in terms of program structure, possible interventions, and outcomes.

## TOOLKIT RESOURCE

## SITE LINKS



Expert Rev Clin Pharmacol. 2017 Apr;10(4):457-465. doi: 10.1080/17512433.2017.1293520. Epub 2017 Mar 2.



Collaborative approach of individual participant data of prospective studies of de-escalation in non-immunosuppressed critically ill patients with sepsis.



Gutiérrez-Pizarraya A1, Leone M2, Garnacho-Montero J3, Martin C2, Martin-Loeches I4.



Emerg Med Clin North Am. 2017 Feb;35(1):199-217. doi: 10.1016/j.emc.2016.09.007.



Antimicrobial Stewardship in the Management of Sepsis. Pulia MS1, Redwood R2, Sharp B3. (this one is from ED but has some very good key points applicable to ICUs like rapid diagnostics, order sets to guide therapy and stewardship of diagnostic testing)

AMS programs in ICUs, however, are believed to have unique needs: patients generally have a higher acuity of illness (with a higher mortality), pathogens are more often nosocomial and have higher resistance rates, per-patient antimicrobial utilization is higher and costlier, and opportunities for interprofessionalism have been realized in ICUs more rapidly than in many other healthcare settings. Accordingly, AMS programs require careful design and consideration.

**ICU AMS Team Membership**

Teams should be interprofessional and multidisciplinary.



Traditionally, discussion around choice of antimicrobial therapy has been a collaboration between intensivist and either a microbiologist or infectious diseases physician.

Over time, the opportunities for broader collaboration and perspectives have grown to include ICU pharmacists and AMS pharmacists. Some programs have started to also include infection preventionists, nurses, and even patients or their advocates (e.g. family, guardians, etc.) Broadening the team poses early challenges (as there are perceived threats to autonomy, challenges with logistics and communication methods), but over time prove beneficial. An obvious additional challenge for team membership relates to funding the various positions (which is beyond the scope of this chapter). In my experience, although some ICU teams may feel capable of “self-stewarding”, proper antimicrobial stewardship requires an external person or team to provide a different perspective.

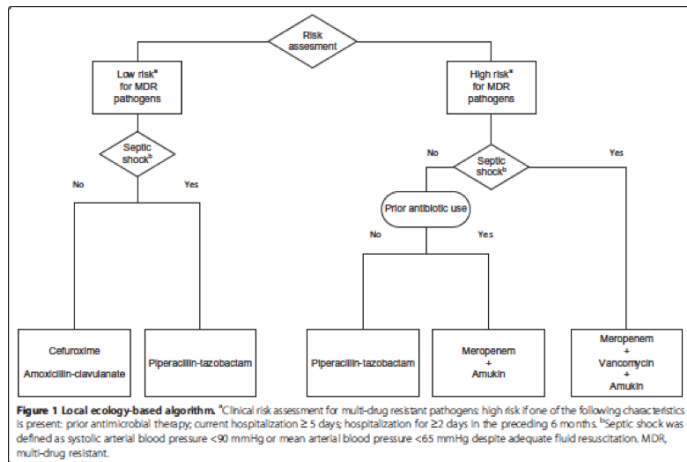
**> PROGRAM STRUCTURE**

ICUs and their staff are supportive of AMS. A recent Canadian survey found that intensivists were overwhelmingly in support of AMS, and felt that AMS improved patient care. Despite this, AMS programs are not well established in ICUs. The Canadian study showed that few ICUs had a full complement of interventions aimed at improving antimicrobial prescribing. A recent study in Germany was consistent with this finding, with only a small minority of hospitals even employing an infectious diseases specialist.

There are several available resources for general structuring of AMS programs. These include guidance documents from the Infectious Diseases Society of America and the Society for Hospital Epidemiology of America, National Stewardship Guidance from Scotland, as well as standards set out by an increasing number of organizations, including The Joint Commission, the Centers for Disease Control and Prevention, Accreditation Canada, and the Australian Commission on Safety and Quality in Health Care.

**ICU Antimicrobial Stewardship Structural Supports**

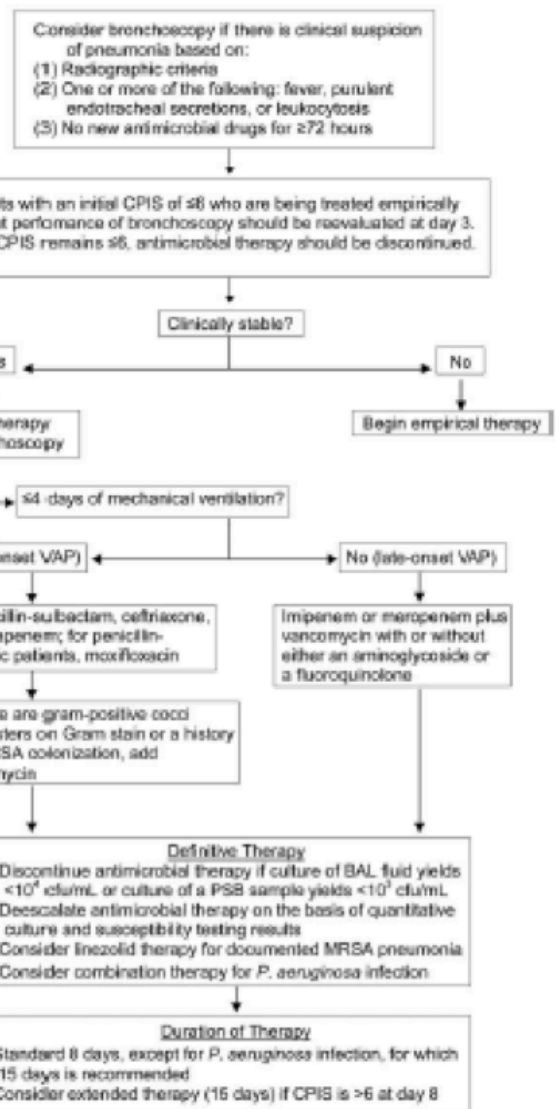
Because of patient complexity and acuity, ICU AMS requires information optimisation. Empiric therapy should be guided by recent, accurate antibiograms that are specific to the local community (for community-acquired infections) and the ICU (for nosocomial infections). ICUs should also have standardised approaches to management of common scenarios, that account for local resistance rates.



De Bus L, Saerens L, Gadeyne B, et al. Development of antibiotic treatment algorithms based on local ecology and respiratory surveillance cultures to restrict the use of broad-spectrum antimicrobial drugs in the treatment of hospital-acquired pneumonia in the intensive care unit: a retrospective analysis. *Crit Care*. 2014;18(4):R152.

Dellit TH, Chan JD, Skerrett SJ, Nathens AB. Development of a guideline for the management of ventilator-associated pneumonia based on local microbiologic findings and impact of the guideline on antimicrobial use practices. *Infect Control Hosp Epidemiol*. 2008;29(6):525-533

Sepsis ventilator-associated pneumonia, intra-abdominal infections, central line-associated bloodstream infections, and candidemia are just some common scenarios that should be protocolised.



**FIGURE 1.** Algorithm for the management of ventilator-associated pneumonia (VAP) used in the study. BAL, bronchoalveolar lavage; cfu, colony-forming units; CPIS, clinical pulmonary infection score; MRSA, methicillin-resistant *Staphylococcus aureus*; PSB, protected specimen brush.

In hospitals and ICUs with computerised physician order entry (CPOE), electronic order sets can facilitate standardising antimicrobial practice.

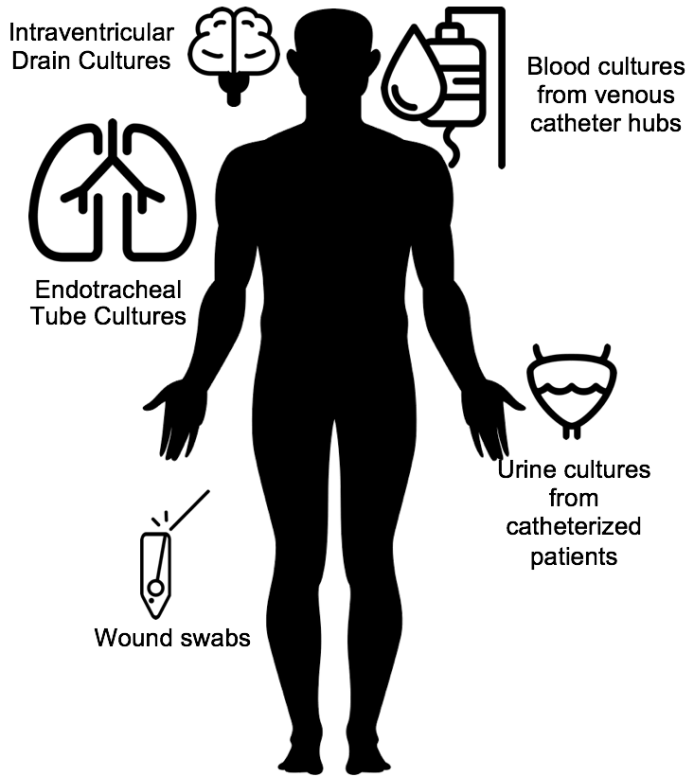
Ideally, when ICU teams are reviewing patients, they can have a temporal snapshot of the patients' infectious disease history: their colonisation status, their prior and current antimicrobial therapy, and prior and current microbiology results. Computerised decision support to do this has been available for many years, but carries considerable expense and so is not routinely used in ICUs at present.

VIDEOS ON THESE TOPICS



**> INTERVENTIONS**

**Diagnostic Stewardship**

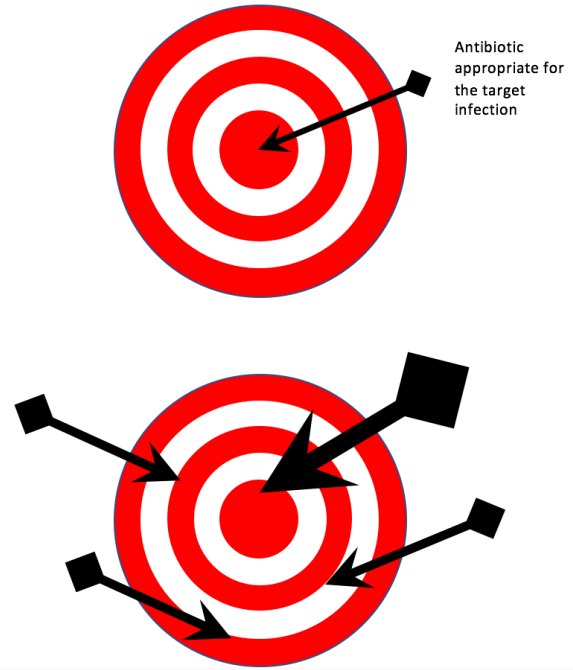


Diagnostic Stewardship Opportunities in Intensive Care Units: Causes of False Positive Results Driving Unnecessary Antimicrobial Use

With the complexities of care in the ICU, treatment decisions can be influenced by a variety of factors. Positive microbiologic results from urine cultures (in asymptomatic, catheterised patients), sputum or endotracheal aspirate cultures, or blood cultures drawn through central venous catheters are all likely to lead to unnecessary antimicrobial prescribing. By limiting microbiologic testing to foci or organ systems that are likely infected, false positive test results (and subsequent antimicrobial therapy) will be minimised. Methods to steward diagnostics are beyond the scope of this chapter.

**Guidance of Empiric Therapy**

Figure: Empiric therapy in the ICU. Bull's eye represents causative organism. Ideally, we want a single arrow shot (antibiotic), hitting the target (top). Unfortunately, most treatment in ICUs represents broad-spectrum antibiotics and/or multiple antibiotics (bottom).



Most of antimicrobial prescribing in ICUs is empiric. Accordingly, intensivists require guidance on empiric therapy. The most common conditions where intensivists prescribe antimicrobials are community-acquired and ventilator-associated pneumonia, intra-abdominal infection, undifferentiated sepsis, and candidemia.

**VIDEOS ON THIS TOPIC**

**> WATCH VIDEOS**

Guidelines can help, although most guidelines do not account for local resistance patterns, which may change rapidly. Accordingly, it is best to at least have up-to-date ICU-specific antibiograms.

**> VIEW DOCUMENT**

Antibiograms according to source (e.g. blood, respiratory tract, etc.) are recommended, however, the weighted-incidence syndromic antibiogram (WISCA) has recently been advocated. WISCAs consider the various organisms causing clinical syndromes, and then list the agents or combinations of agents that cover the infection. Intensivists should also have access to community-based antibiograms, to guide management of patients being admitted through the emergency department, either from independent living, or from long-term care.



### Coaching

Antimicrobial stewardship generally requires a variety of behaviour change techniques. AMS in the ICU is no different. An increasingly adopted behaviour change technique involves feedback and monitoring, often referred to as prospective audit and feedback. These are types of coaching. In the ICU, coaching can involve routinely scheduled meeting with the ICU team (ideally 3-5 times per week), or meeting with the prescriber when a new prescription or antimicrobial order is written. Some programs have focused on “priority” antimicrobials (recently referred to as reserve antibiotics by the World Health Organization). AMS will involve reviewing whether the use of each antibiotic is “appropriate” or not. Appropriateness is not always objective in empiric therapy, so feedback should discuss whether the need for antibiotics is consistent with the clinical picture, and whether the choice, route, dose, frequency, and duration is appropriate.

### TIPS FOR COACHING DURING AUDIT AND FEEDBACK

- **Come prepared**  
*Have the list of patients, and try to have as much current information (esp. up-to-date microbiology and antimicrobial therapy) as possible.*
- **Start off with introductions, if necessary**  
*Make sure names and roles are clear for everyone present*
- **Allow prescribing team to discuss first**  
*“Tell me about Ms. X in bed 1”*
- **Early in the relationship, don’t try to make too many recommendations**  
*Perhaps focus on less contentious issues (e.g. dosing). Coaching requires a relationship to develop prior to establishing trust.*
- **Consider setting durations as another relatively easier target**  
*There are published trials on shortened durations (e.g. ventilator-associated pneumonia, intra-abdominal sepsis, etc.)*
- **Streamlining therapy for infections with microbiological confirmation is usually straightforward**  
*When a patient is growing penicillin-susceptible *Streptococcus pneumoniae*, stepping down to penicillin should not be contentious*
- **Accept that risk tolerance varies between healthcare providers**  
*Rather than trying to change risk tolerance, try and characterize a prescriber’s risk. If a prescriber is unwilling to discontinue empiric coverage for, say, *Pseudomonas aeruginosa*, it is far more useful to first ask what probability he/she would tolerate for *Pseudomonas* being the causative agent.*
- **Make sure each encounter is a learning one**  
*Even mentioning, say, some information on pharmacokinetics, or mechanisms of resistance may be enough to provide added value to the coaching session.*
- **Be patient**  
*Behaviour change takes time.*
- **Don’t sweat any single antimicrobial**  
*Although tempting to argue at length over stepping down from meropenem to, say, cefazolin for *S. aureus* bacteremia, arguments over any single patient’s management is more likely to be harmful than helpful.*



**Restrictive Methods**

Authorisation (requiring approval for an antimicrobial prior to its use or for future use after a first dose is given) is ill-advised for antimicrobial stewardship in the ICU. Because the stakes are high, any intervention that obstructs workflow and timely patient care is likely to be met with resistance. Additionally, critically ill patients often have multiple consultants involved, and approaches using authorisation do not lend themselves to a collaborative model that ICUs increasingly employ.

**Evolving Approaches***Selective oropharyngeal and digestive decontamination*

“Decontaminating” the digestive tract in critically ill patients has been extensively studied, albeit in settings with low antimicrobial resistance. In meta-analyses, and in a large multicentre cluster randomised trial, it was associated with clinical benefit and low levels of antibiotic resistance. Compared with selective oropharyngeal decontamination (where antibiotics are only topically applied in the mouth), selective digestive decontamination (involving intravenous and enteral non-absorbable antibiotics) is associated with lower mortality, reduced length of stay, and lower rates of ICU-acquired bacteremia and candidemia. Concerns of antimicrobial resistance in settings with higher prevalence of antimicrobial resistance have prevented widespread adoption of this approach.

*Biomarker-guided therapy*

Biomarkers are measurable substances that reflect a physiologic or pathologic process. Procalcitonin and, to a lesser extent, C-reactive protein are two biomarkers that hold the most potential for guiding antimicrobial therapy in critically ill patients. When used—usually using an appreciable decline in biomarker level from the start of therapy or a single value below a threshold value—biomarkers appear to facilitate safe discontinuation of antimicrobial therapy. Unfortunately, clinicians seem reluctant to follow biomarker guidance on many patients—probably because of well-founded concerns regarding biomarkers’ abilities to definitively rule out active infection.

 **OUTCOME MEASURES**
**Appropriateness****Categorization of Antimicrobial Prescribing Appropriateness in Critical Care:**

The following statements collectively define *APPROPRIATE* antimicrobial prescribing:

(i) Patient has a proven or probable infection and the antimicrobial therapy covers an antimicrobial spectrum that is neither too narrow nor too broad.

**TOOLKIT RESOURCE**

## ARTICLES

Dresser LD, Bell CM, Steinberg M, Ferguson ND, Lapinsky S, Lazar N, et al. Use of a structured panel process to define antimicrobial prescribing appropriateness in critical care. *J Antimicrob Chemother.* 2017. doi: 10.1093/jac/dkx341

Hebert C, Ridgway J, Vekhter B, Brown EC, Weber SG, Robicsek A. Demonstration of the weighted-incidence syndromic combination antibiogram: an empiric prescribing decision aid. *Infect Control Hosp Epidemiol.* 2012;33(4):381-8.

Spellberg B. The New Antibiotic Mantra—“Shorter Is Better”. *JAMA Internal Medicine.* 2016;176:1254-5. doi: 10.1001/jamainternmed.2016.3646.

van den Bosch CM, Hulscher ME, Natsch S, Gyssens IC, Prins JM, Geerlings SE, et al. Development of quality indicators for antimicrobial treatment in adults with sepsis. *BMC Infect Dis.* 2014;14:345.

- (ii) Patient has a proven or probable infection and the antimicrobial therapy is not included in the patient’s allergy history with clear contraindications.
- (iii) Patient has a proven or probable infection and the antimicrobial therapy has no clear and obvious contraindications.
- (iv) Patient has a proven or probable infection and the antimicrobial therapy is administered via a route best suited to the infection and clinical status of the patient.
- (v) Patient has a proven or probable infection and the antimicrobial therapy is dosed (dose and frequency) sufficiently to treat the infection.
- (vi) Patient has a proven or probable infection and the antimicrobial therapy is expected to reach the target site(s).
- (vii) Patient has a proven or probable infection and the current antimicrobial therapy duration does not exceed evidence-based (or accepted) lengths of therapy.

ANY of the following statements define *EFFECTIVE BUT UNNECESSARY* antimicrobial prescribing:

- (i) Patient has a probable infection and the empirical antimicrobial therapy covers an antimicrobial spectrum that is too broad OR has a proven infection and the antimicrobial therapy targets the identified organism(s) but is too broad.



*(ii) Patient has a proven infection and the antimicrobial therapy includes double coverage for an identified organism where double coverage is not known or not generally accepted to be superior.*

*(iii) Patient has a proven or probable infection and the antimicrobial therapy is administered by a parenteral route when an enteral route is possible and expected to be equally effective.*

*(iv) Patient has an infection and the antimicrobial therapy is dosed too high and/or too frequently to treat the proven or probable infection.*

*(v) Patient has a proven or probable infection and the current antimicrobial therapy duration exceeds evidence-based (or accepted) lengths of therapy.*

*ANY of the following statements define INAPPROPRIATE antimicrobial prescribing:*

*(i) Patient does not have an infection and has no clear indication for the prescribed antimicrobial therapy.*

*(ii) Patient had suspected infection but has no objective evidence of active infection AND has not objectively responded to a reasonable (at least 3 days) empirical course of antimicrobial therapy.*

*(iii) Patient is receiving antimicrobial therapy for prophylaxis or pre-emptive treatment without evidence to support the practice and the risk and severity of anticipated infection is expected or known to be low.*

*(iv) Patient has a proven or probable infection but is prescribed a drug for which there is a clear, life-threatening contraindication.*

*ANY of the following statements define UNDER-TREATMENT in antimicrobial prescribing:*

*(i) Patient has a proven or probable infection but the prescribed antimicrobial therapy has insufficient activity to treat the identified or anticipated organism(s).*

*(ii) Patient has a proven or probable infection but the prescribed antimicrobial therapy is not administered via a route best suited to treat the infection.*

*(iii) Patient has a proven or probable infection but the prescribed antimicrobial therapy is dosed too low or infrequently to treat the infection.*

*(iv) Patient has a proven or probable infection but the prescribed antimicrobial therapy is not expected to reach the target site(s).*

*(v) Patient has a proven or probable infection but the prescribed antimicrobial therapy was discontinued prior to completing a course that is evidence-based (or accepted to be sufficient).*

*(vi) Patient has a proven infection and requires antimicrobial therapy but is not prescribed antimicrobial therapy and the*

*patient is not deemed palliative.*

*(vii) Patient has clear indications for antimicrobial prophylaxis but is not prescribed prophylactic antimicrobial therapy.*

Antimicrobial stewardship, ideally, guides the appropriate use of antimicrobials. However, appropriateness is inherently subjective, and changes over time as new research better defines the role of empiric and definitive antimicrobial therapy. Recently, using Delphi consensus-based methodology, criteria and categories of appropriateness of antimicrobial therapy in ICUs was developed. The authors categorised antimicrobial therapy in the ICU as “appropriate”, “effective but unnecessary”, “inappropriate”, and “under-treatment”.

### **Quality Indicators**

One way to improve the use of antimicrobials in the ICU, is to ensure that overall care of infectious diseases is of a high quality. Process measures can help guide therapy. A Dutch group recently published quality indicators for antimicrobial therapy in sepsis: obtain cultures;

prescribe empirical antimicrobial therapy according to the national guideline; start

intravenous drug therapy; start antimicrobial treatment within one hour; and streamline

antimicrobial therapy. Similar indicators have not been published for other relevant conditions seen in the ICU, but modifications could likely be developed on a local level.

### **Antimicrobial Use**

Antimicrobial use measures are generally useful for trending and benchmarking purposes, but lack clinical relevance. For example, an ICU with a large number of neutropenic patients and high levels of antimicrobial use and cost may be more appropriate in their prescribing than a cardiac ICU (with primarily patients with heart failure and acute coronary syndromes) who use 20% fewer antimicrobials. This is why appropriateness is the ideal single measure. Regardless, all measures of antimicrobial use should be standardized according to patient volume, usually per 1000 patient-days. Below are different means of measuring use.

### **Defined Daily Doses (DDD)**

These are relatively easy to collect and provide a good indication of overall antimicrobial use. Often, ASPs will focus on “reserve” antibiotics, such as carbapenems. A concern with DDDs relates to dosing modifications in the ICU, where some DDDs will underestimate drug exposure (e.g. in the setting of dosage adjustment for dialysis) and some others will overestimate drug exposure (e.g. in the bariatric population, or those with central nervous system infection).

### Days of Therapy (DOT)

These tend to be more difficult to collect than DDDs, capture a similar measurement, and largely avoid issues related to dosing modifications seen with DDDs.

### Cost

Cost does not correlate well with appropriateness of most other measures of antimicrobial quality. It marginally reflects how broad-spectrum an antibiotic is.

### Antimicrobial Resistance

At this point in time, the magnitude of measurable benefit for reducing antimicrobial resistance and antimicrobial resistant organisms (AROs) is uncertain. Although reducing or controlling AROs is an oft-cited justification for antimicrobial stewardship, the evidence that measurable improvements can be seen in ICUs is weak at present. Regardless, I always recommend following *C. difficile* and candidemia rates, supplemented by antibiogram monitoring of common non-fermenting Gram negative bacteria such as *Pseudomonas aeruginosa*, and *Acinetobacter* species.

### Balancing Measures

The literature is rather consistent that antimicrobial stewardship is safe. Nevertheless, introducing stewardship into ICUs may result in hesitant clinicians who are concerned about patient outcomes. Tracking mortality, length of stay, ventilation days, and other markers of patient safety are recommended. Using severity metrics (e.g. APACHE-2 scores) is also recommended, to ensure that mortality risk doesn't change over time.

## SUMMARY

The ICU is, in many ways, the perfect setting for antimicrobial stewardship: substantial drug-resistance, prevalent antimicrobial use, and a geographically-confined interprofessional patient care setting. By taking a methodical approach to antimicrobial stewardship—focusing on diagnostic stewardship, guiding empiric therapy based on local data and best available evidence, and coaching—antimicrobial use can be optimised. The most important outcome to measure is appropriateness, although it remains a challenge to do this reliably.

# CHAPTER 19

▶ AUTHOR: HAIFA LYSTER

## STEWARDSHIP IN THE IMMUNOCOMPROMISED PATIENT SETTING

### THE AIM OF THIS CHAPTER IS TO:

Describe the challenges to Antimicrobial Stewardship (AMS) in the immunocompromised host.

Outline the opportunities for AMS in the immunocompromised patient setting.

### THE CHAPTER WILL ALSO DEFINE:

The concept of 'Net state of immunosuppression' as a guide to differential treatment options.

The challenges to diagnosing and treating infections in this special patient population.

## LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Define an immunocompromised host
- Evaluate the role of net immunosuppression in mediating the risk of infections in susceptible hosts
- Describe barriers to antimicrobial stewardship (AMS) in the immunocompromised patient setting
- Identify the opportunities for AMS in immunocompromised hosts
- Discuss the role of multi-disciplinary working in delivering AMS in this setting
- List considerations for antimicrobial treatment in this special patient population

### ▶ INTRODUCTION

Antimicrobial stewardship (AMS) in the immunocompromised is a little more challenging as patients have a reduced ability to immunologically respond (if at all) to an infection. A wide-range of conditions can result in immune-compromise including primary immunodeficiency, diseases such as advanced diabetes and HIV, severe malnutrition and drug-induced immune compromise, such as during the treatment of cancer, inflammatory conditions or post-transplantation. Advances in the management of cancer, solid organ transplantation (SOT) and hematopoietic stem-cell transplantation (HSCT) have improved patient survival, but the subsequent immunocompromised state, regardless of the mechanism, means that these patients are at increased risk of infection.

There are a number of challenges to diagnosing and treating infections in this patient group:

- Patients are susceptible to a broad spectrum of infections, including to pathogens with normally low pathogenic potential (opportunistic pathogens), which can progress rapidly
- Timely active anti-infective therapy is required for good outcomes, but can be complicated by delays in processes of care and, for example, drug-drug interactions
- The physiological parameters used to guide, for example, the starting and stopping of antibiotic therapy in immunocompetent patients do not apply

- Invasive diagnostic (e.g. bronchoscopy) and/or less commonly used blood tests (e.g. CMV PCR, cryptococcal antigen, galactomannan) may be required to confirm infection
- The required length of antimicrobial therapy is even more poorly defined in immunocompromised patients than in the immune-competent
- Multidrug-resistant organisms (MDROs) such as *Clostridium difficile*, vancomycin-resistant enterococci (VRE) and carbapenem-resistant Enterobacteriaceae (CRE) are common due to repeated and prolonged broad-spectrum antimicrobial courses.

HOW ARE ANTIBIOTIC STEWARDSHIP EFFORTS DIFFERENT FOR IMMUNOCOMPROMISED PATIENTS? INTERVIEW



Broad-spectrum antimicrobial agents are commonly used in areas of the hospital where immunocompromised patients are managed, such as haematology and oncology units, and often account for a high proportion of overall hospital use (Fig. 1). Such areas are clearly excellent ‘targets’ for AMS and should be prioritised.

Implementation of AMS programs have been associated with lower mortality rates in cancer patients (Fig. 2) and reduced medication errors in hospitalised HIV patients. There are currently no AMS guidelines in SOT patients.

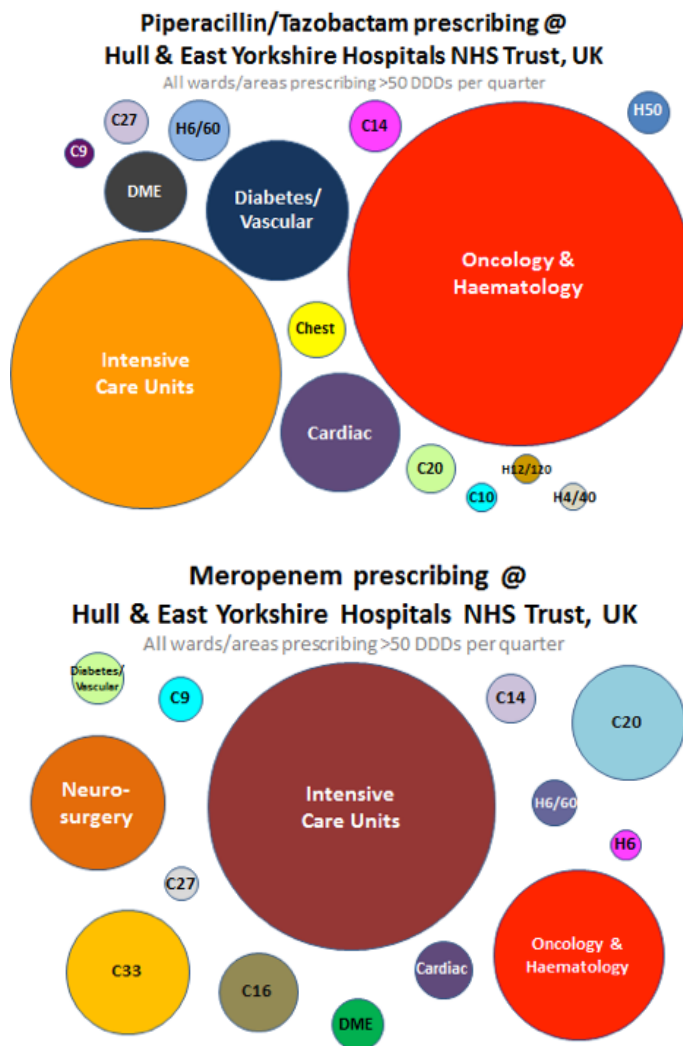
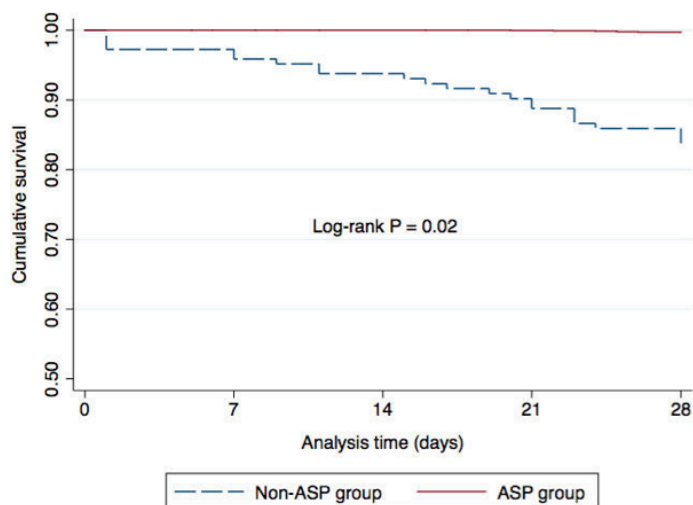


FIGURE 1 Diagrammatic representations of broad-spectrum antibiotic use in Haematology & Oncology compared to other wards at a UK teaching hospital

FIGURE 2 Kaplan–Meier curves of 28-day mortality according to adherence to ASP

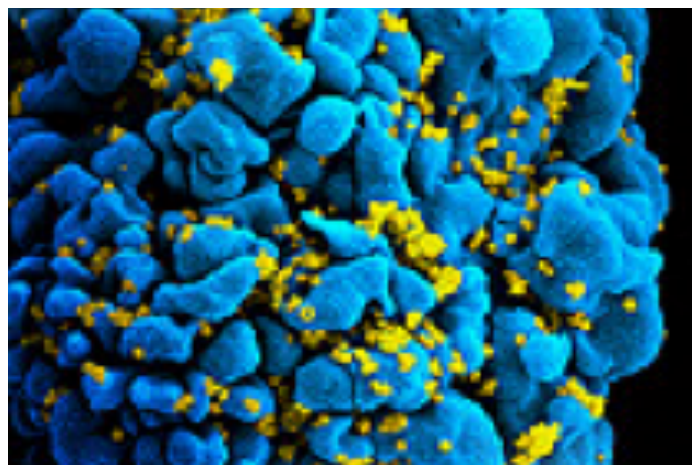
From: Rosa RG, Goldani LZ, dos Santos RP. Association between adherence to an antimicrobial stewardship program and mortality among hospitalised cancer patients with febrile neutropaenia: a prospective cohort study. BMC infectious diseases. 2014;14:286.

<https://bmcinfectdis.biomedcentral.com/articles/10.1186/1471-2334-14-286>

**Fungi and viruses**

While AMS usually refers to antibacterial agents, in immunosuppressed patients AMS should also include antifungal and antiviral therapies, which are commonly empirically used in the management of, for example, non-resolving neutropenic sepsis. There is a high mortality and morbidity associated with invasive fungal infections such as *Candida* species, aspergillosis and cryptococcus, coupled with diagnostic difficulties, which often results in overuse of antifungal agents, combination therapies and prolonged treatment duration (see e-book chapter on antifungal stewardship). There are a number of opportunistic viral infections; the most common is cytomegalovirus (CMV), where appropriate antiviral strategies are important to improve outcomes. Also, community-acquired respiratory viruses e.g. respiratory syncytial virus (RSV), adenovirus, human metapneumovirus are associated with poor outcome in immunocompromised patients, however, consensus guidelines on their management is lacking.

**AMS IN THE IMMUNOCOMPROMISED NOT JUST ANTIBACTERIALS**



"HIV-infected T cell" flickr photo by NIAID <https://flickr.com/photos/niaid/6813384933> shared under a Creative Commons (BY) license

**Net state of immunosuppression**

Immunosuppressed patients are not all the same. The concept of a 'net state of immunosuppression' is complex and is based on clinically synthesising a combination of factors that may impact on the patient's current immune status, such as immunosuppressive agents, neutropenia, malnutrition and comorbidities, as well as infections with immunomodulating viruses (e.g. HIV). The net state of immunosuppression can vary considerably between patients and there is intra-patient variability over time. For example, transplant patients take multi-drug regimens of immunosuppressants with higher doses during the early period post-SOT when the risk of rejection,

and therefore infection, is greatest. The changing timeline of infection after SOT can guide prophylactic and treatment strategies; during periods of augmented immunosuppression, for example, for the treatment of rejection (cellular- or antibody-mediated), the infection risk 'clock' resets to the initial transplant time-point. Although assessing a patient's net state of immunosuppression can be challenging, it is useful in assessing what infections the patient may be at risk of and what level of investigation and antimicrobial intervention is therefore justified (see Fig. 3). Scoring systems such as the MASCC score for febrile neutropenia have been developed and are recommended in some guidelines to identify lower risk patients who can be treated, for example, with an early switch from IV to oral antibiotics or on an outpatient basis with either oral or IV therapy, although clinical judgement remains of primacy.

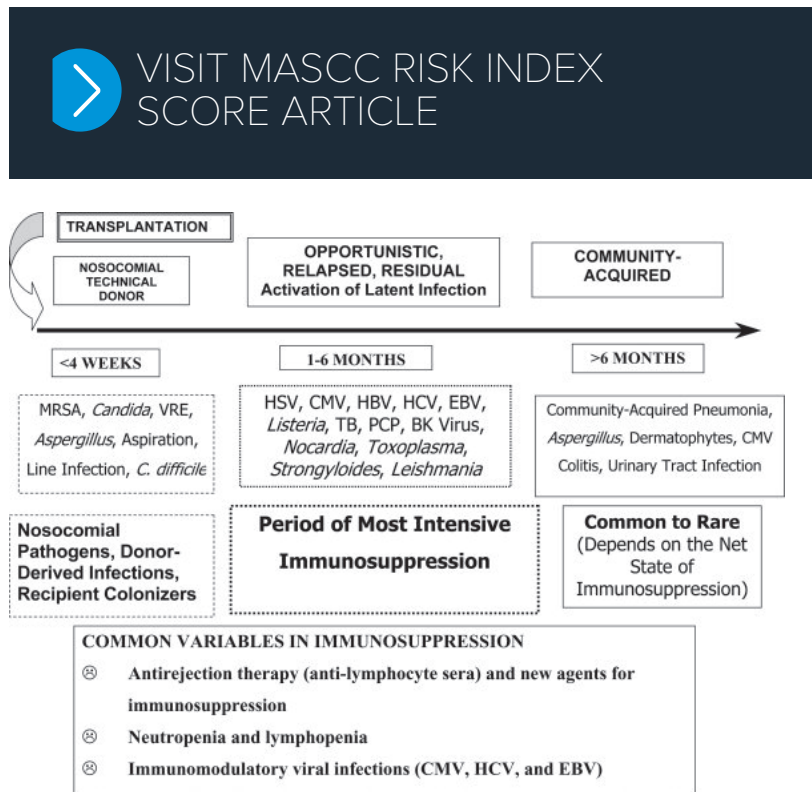


FIGURE 3  
Timeline of post-transplant infections  
From: Fishman JA1. Infections in immunocompromised hosts and organ transplant recipients: essentials.  
Liver Transpl. 2011 Nov;17 Suppl 3:S34-7. doi: 10.1002/lt.22378  
<http://onlinelibrary.wiley.com/doi/10.1002/lt.22378/full>



## CHALLENGES TO AMS IN THE IMMUNOCOMPROMISED

### Broad spectrum of potential infections

Infections remain a major source of morbidity and mortality in immunocompromised patients, which can be due to common pathogens, but there are also a large number of opportunistic organisms. However, the suspicion of certain infections is higher at different time points; accurate diagnosis is clearly important in guiding appropriate therapy. There are a number of opportunistic infections requiring an effective strategy for prophylactic or pre-emptive antimicrobials; e.g. bacteria such as *Mycobacterium jiroveci* (PJP) and viruses such as CMV and hepatitis B. It is also of note that there are specific types of infections associated with sub-groups of immuno-compromised patients; e.g. BK virus and renal transplant recipients and cryptococcal infection and HIV.

Awareness of whether new chemotherapeutic agents, immunosuppressants and other immunomodulatory agents are associated with particular infections (e.g. hepatitis B reactivation with rituximab, viral infections (in particular CMV) with alemtuzumab, and bacterial and fungal infections with sirolimus) is important and can help guide pre-emptive management and AMS (e.g. knowing when something is not required).

### Antimicrobial resistance

CRE are an emerging global public health concern with mortality rates of 40% in SOT recipients and 65% in patients with haematologic malignancies. Antibiotics with activity against CRE have a number of limitations in terms of either adverse effects or pharmacokinetics, and combination antimicrobial therapy is often used. The rapid administration of active antibacterial agents against Gram-negative bacteria is clearly important in immunocompromised patients (e.g. neutropenic sepsis); however, in many countries 'traditional' empiric regimens may not be active against CRE or extended-spectrum beta-lactamase (ESBL) producers. Although modern molecular methods are shortening the time to identification of pathogens in well-resourced hospitals, and of antibiotic sensitivity testing, in many centres, even in the developed world, this can still take 2 to 3 days. Whether guideline-based empiric regimens provide cover for highly resistant bacteria depends on the local epidemiology of such infections, emphasising the importance of surveillance specific to immunocompromised patient groups.

## INCIDENCE OF CRE

0.4% TO 26.3%

IN SOT

## CRE ASSOCIATED MORTALITY

33% TO 100%

IN HSCT/HAEMATOLOGICAL MALIGNANCY

Created from: Stephanie M. Pouch & Michael J. Satlin (2017) Carbapenem-resistant

Enterobacteriaceae in special populations: Solid organ transplant recipients, stem cell


transplant recipients, and patients with hematologic malignancies, *Virulence*, 8:4, 391-402, DOI:


10.1080/21505594.2016.1213472

<http://dx.doi.org/10.1080/21505594.2016.1213472>

## TOOLKIT RESOURCE


### SUGGESTED READING

 The role of antibiotic stewardship in limiting antibacterial resistance among hematology patients. Gyssens IC, Kern WV, Livermore DM; ECIL-4, a joint venture of EBMT, EORTC, ICHS and ESGICH of ESCMID. *Haematologica*. 2013 Dec;98(12):1821-5

 The global challenge of carbapenem-resistant Enterobacteriaceae in transplant recipients and patients with hematologic malignancies. Satlin MJ, Jenkins SG, Walsh TJ. *Clin Infect Dis*. 2014 May;58(9):1274-83

## TOOLKIT RESOURCE

### SITE LINK

 Public Health England Carbapenemase-producing Enterobacteriaceae toolkit



**Diagnostics**

Obtaining diagnostic certainty of infection is further complicated since patients may present with more than one pathogen simultaneously. Colonisation by a number of pathogens is a genuine risk and needs to be accurately differentiated from active or invasive disease in order to avoid unnecessary prescribing.

Facilitating rapid and accurate diagnostics would lead to early, targeted antimicrobial therapies and support AMS. However, microbiology laboratories often outsource tests infrequently used with a consequent lag time to the results; teams caring for immunocompromised patients often disproportionately request these tests resulting in delay and impact on clinical decisions and AMS. Diagnostic uncertainty and turnaround delay have been cited as barriers for AMS in immunocompromised patients (Fig. 4); tests for the diagnosis of respiratory virus or invasive fungal infections were deemed the most useful for guiding treatment.

**Figure 1: Availability of molecular and non-molecular diagnostic tests and azole levels for transplant patients**

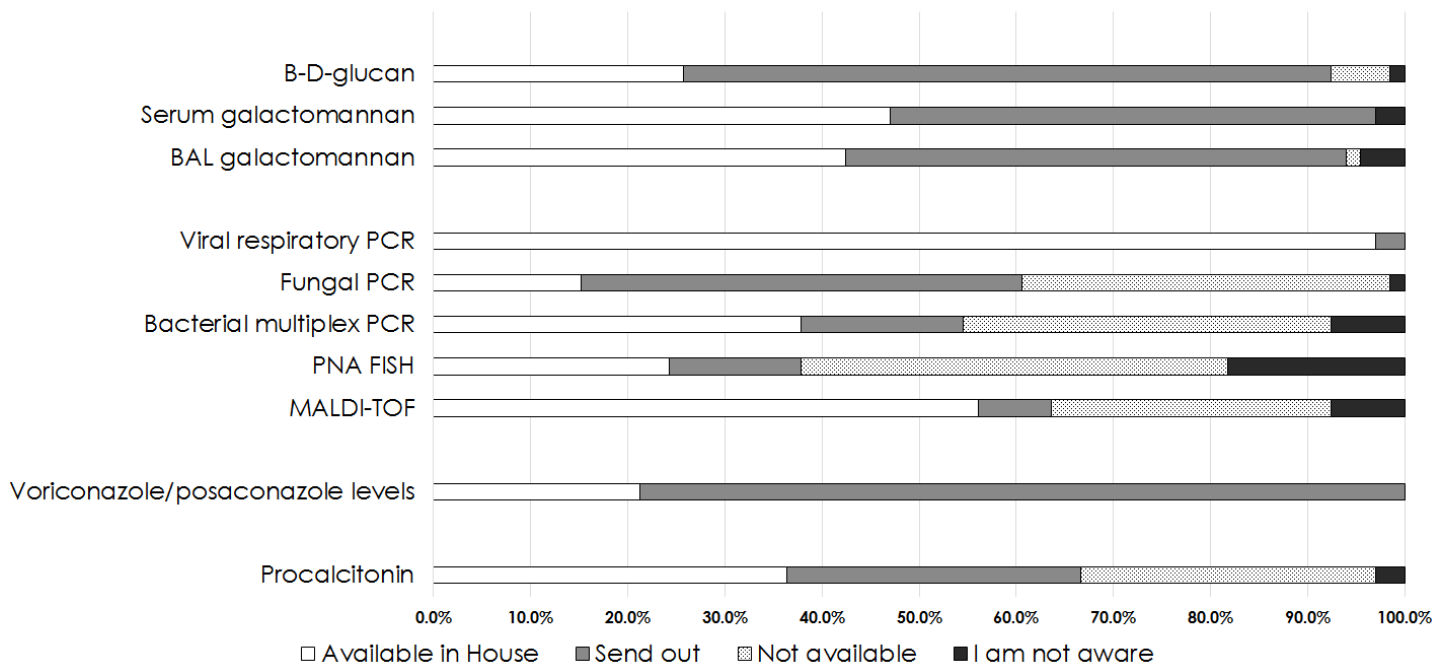


FIGURE 4  
Availability of novel diagnostics and azole levels for transplant patients

From: Seo, S., Lo, K., & Abbo, L. (2016). Current State of Antimicrobial Stewardship at Solid Organ and Hematopoietic Cell Transplant Centers in the United States. *Infection Control & Hospital Epidemiology*, 37(10), 1195-1200. doi:10.1017/ice.2016.149 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5466005/>

**Prescriber opposition**

An important factor in successful AMS in the immunocompromised is the perceptions and attitudes of the team of physicians and healthcare professionals looking after these patients. To encourage a change in prescribing behaviour, it is important to understand and address any existing negative beliefs. A survey conducted in a teaching hospital assessed the knowledge of and attitudes about antimicrobial use and resistance amongst physicians. The risk of missing an infection, and whether a patient was critically ill or immunosuppressed, were factors felt to most influence antibiotic prescribing. Interestingly, while most agreed that antibiotics were overused and were concerned about resistance, they felt that others, not themselves, overprescribed antibiotics. Most wanted more education about antibiotics and feedback about their own practice.

As a preventative measure, broad-spectrum antimicrobials are often prescribed as a catchall for extended periods, resulting in increased costs, antimicrobial resistance and drug toxicity. De-escalation and discontinuation of antimicrobials is often resisted by clinicians as these patients are deemed 'sicker' and/or 'special-cases' compared to immune-competent patients. Junior team members are not empowered or do not have sufficient confidence or clinical support to discontinue antimicrobial therapy, hence engagement with, and involvement of, senior clinical colleagues is essential.

## CRITICAL ILLNESS AND/OR IMMUNOCOMPROMISED STATE

# FOR >80% OF DOCTORS

OFTEN OR ALWAYS INFLUENCES PRESCRIBING

Created from: Lilian Abbo, Ronda Sinkowitz-Cochran, Laura Smith, Ella Ariza-Heredia, Orlando Gómez-Marín, Arjun Srinivasan, Thomas M. Hooton. Faculty and Resident Physicians' Attitudes, Perceptions, and Knowledge about Antimicrobial Use and Resistance *Infect Control Hosp Epidemiol* 2011;32(7):714-718

[https://www.researchgate.net/publication/51212778\\_Faculty\\_and\\_Resident\\_Physicians%27\\_Attitudes\\_Perceptions\\_and\\_Knowledge\\_about\\_Antimicrobial\\_Use\\_and\\_Resistance](https://www.researchgate.net/publication/51212778_Faculty_and_Resident_Physicians%27_Attitudes_Perceptions_and_Knowledge_about_Antimicrobial_Use_and_Resistance)

**The golden hour**

Neutropenia remains the predominant predisposing factor for infection in most cancer patients, and neutropenic sepsis is a life threatening complication. A new gold standard 'door-to-needle' time of 1 hour for the administration of intravenous antibiotics, similar to that in the Surviving Sepsis Campaign, has been introduced. An audit across the United Kingdom highlighted only 26% of patients achieved this standard, citing numerous reasons for the delay, the most common being that antibiotics were prescribed by a doctor, but their administration delayed by a nurse or until the patient was transferred to the specialist ward followed by a prolonged time to assessment by a junior doctor. Patient group directives allowing the first dose of empiric antibiotics recommended in local guidelines to be administered by an advanced nursing practitioner can help to reduce such delays, but can potentially lead to over-prescribing in patients who are subsequently shown not to have neutropenic sepsis or severe infection. Interventions to improve 'door-to-needle' time and optimise AMS in immunocompromised patients are not mutually exclusive and should synthesise to improve both.

## TOOLKIT RESOURCE

### SITE LINK



Antibiotic stewardship in the Cancer Patient, Dr Rod Quiltz, PharmD – video presentation - discussed the importance of antibiotic stewardship in the immunocompromised cancer

**Drug allergy labelling**

Inaccuracy with antibiotic allergy labelling can drive inappropriate or inferior anti-infective agent selection or increased use of broad-spectrum agents. The impact of this may be compounded in immunocompromised patients once, for example, potential drug-drug interactions are accounted for.

## ▶ OPPORTUNITIES FOR AMS IN THE IMMUNOCOMPROMISED

There are considerable opportunities for AMS in immunocompromised patients (Fig 5). A recent survey assessing the extent of AMS programs at SOT and hematopoietic stem cell transplant (HSCT) centres in the United States found that the top 5 AMS activities that included immunocompromised patients were: formulary restriction, guideline development, prospective audit and feedback, education and dose optimisation<sup>8</sup>.

### Opportunities for antimicrobial stewardship in immunocompromised hosts

- Produce and distribute to health care providers updated antimicrobial susceptibility trends for common organisms
- Formulary review
- Preprescription authorization
- Postprescription review and feedback
  - Monitoring drug interactions
  - Renal dosing optimization
  - Streamlining and discontinuation of unnecessary antimicrobials
- Antifungal stewardship
- Antiviral stewardship
- Develop multidisciplinary protocols, algorithms, and guidelines for the diagnosis, management, and prophylaxis of common infections
- Discuss microbiology, antibiotic use, and infection-related outcome data in multidisciplinary committees

#### FIGURE 5


From: Antimicrobial stewardship in immunocompromised hosts. Abbo LM, Ariza-Heredia EJ. *Infect Dis Clin North Am*. 2014 Jun;28(2):263-79

[https://www.researchgate.net/publication/262491931\\_Antimicrobial\\_Stewardship\\_in\\_Immunocompromised\\_Hosts](https://www.researchgate.net/publication/262491931_Antimicrobial_Stewardship_in_Immunocompromised_Hosts)


## TOOLKIT RESOURCE

### SUGGESTED READING

 Antimicrobial stewardship in immunocompromised hosts. Abbo LM, Ariza-Heredia EJ. *Infect Dis Clin North Am*. 2014 Jun;28(2):263-79

 Current State of Antimicrobial Stewardship at Solid Organ and Hematopoietic Cell Transplant Centers in the United States. Seo SK, Lo K, Abbo LM. *Infect Control Hosp Epidemiol*. 2016 Oct;37(10):1195-200

### VIDEO

 Antibiotic Stewardship in Oncologic Care  
-- Aliyah Baluch, MD video presentation

### Formulary review and restriction

Limiting access to antimicrobials is essential to minimise unnecessary broad-spectrum antimicrobial use and subsequent resistance. Regular formulary review should not only consider cost, but also spectrum coverage as per local epidemiology, therapeutic efficacy, how access to certain antimicrobials is controlled (e.g. carbapenems) without negatively impacting patient access and outcome, and include agents required for both prevention and treatment of common infections in this patient group (e.g. CMV, fungal, and Gram-negative bacterial infections). Close working relationships with pharmacy for contingency planning during drug supply shortages is crucial.

### Guidelines

Developing clinical guidelines in collaboration with the cancer and transplant teams is a core function of AMS occurring in 76% and 71% of HSCT and SOT centres, respectively<sup>8</sup>. Regular review of guidelines taking into account patients' common co-morbidities (e.g. renal impairment and bone marrow suppression) will simplify clinical decision-making; implementation has been shown to improve outcomes even with partial adherence<sup>14</sup>.

Neutropenic sepsis: prevention and management in people with cancer. UK National Institute for clinical Excellence (NICE) Clinical guideline [CG151]

 VISIT NICE ARTICLE

 VIEW GUIDELINES

### Prospective Audit and Feedback (PAF) / Pre-authorisation

PAF is at the heart of AMS and in the immunocompromised host is preferred to pre-authorisation in order to prevent any delay in therapy in serious infection<sup>8</sup>. PAF facilitates the re-evaluation of empiric treatment when further test results are available and has more potential for educational opportunities, which can include de-escalation and intravenous to oral conversion. A study in oncology and HSCT patients utilising PAF was associated with decreased antimicrobial use and cost without causing harm.<sup>15</sup>

### Antimicrobial dose-optimisation - using pharmacokinetic(PK) and pharmacodynamics (PD) principles

Optimal antimicrobial dosing requires an understanding of the relationship between its concentration in the body (PK) and its clinical response (PD). Because immunocompromised patients

with sepsis may have increased volume of distribution and altered drug clearance pathways, traditional dosing regimens may not be appropriate. PK-PD optimised dosing regimens can be extrapolated from critically ill patients<sup>16-18</sup>; the issues are similar in haematological malignancy patients<sup>19-21</sup>.

## IMIPENEM 500MG EVERY 6 HOURS IN FEBRILE NEUTROPENIA

53%

PROBABILITY OF ADEQUATE COVER FOR COMMON BACTERIAL PATHOGENS

Created from: Reassessment of recommended imipenem doses in febrile neutropenic patients with hematological malignancies. Lamoth F, Buclin T, Csajka C, Pascual A, Calandra T, Marchetti O. *Antimicrob Agents Chemother.* 2009 Feb;53(2):785-7. doi: 10.1128/AAC.00891-08. Epub 2008 Dec 1.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2630622/>

The use of therapeutic drug monitoring can be very useful to guide individualised dosing; this practice is established with regards to a number of antibacterial agents (e.g. aminoglycosides) with increasing utilisation in optimising the newer azole antifungals (e.g. voriconazole, posaconazole) and, in some centres, for other antibacterials such as beta-lactams.

Highly active antiretroviral therapy (HAART) and immunosuppressants are also associated with significant drug-drug interactions; multidisciplinary stewardship efforts can reduce medication errors in these patients with pharmacists playing a major role<sup>2,22</sup>

### Multi-disciplinary team working

AMS is a multidisciplinary team approach; to work effectively there should be close collaboration between the AMS team and the HIV, cancer or transplant teams with a shared appreciation of the complexities of caring for these patients. Successful implementation requires an open MDT approach that fits well with the way HIV, cancer and transplant teams generally work. A consistent AMS team with regular rounds and MDT attendance is important to increase compliance and acceptance, and develop trust.

### ➤ SUMMARY

Applying various AMS strategies in this challenging patient population is both feasible and essential to optimise treatment outcomes whilst minimising antimicrobial resistance at a time when there is a paucity of novel anti-infectives in the development pipeline. Many challenges remain so it is important that centres share their experiences and that collaborative research opportunities are explored.

“

*So, it's a little different than doing stewardship in other populations, but it's doable, it just takes a little more time*

Lilian Abbo

## TOOLKIT RESOURCE

### SUGGESTED READING



Pharmacokinetic and pharmacodynamics issues for antimicrobial therapy in patients with cancer Theuretzbacher U. *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America* 2012;54(12):1785-1792

# CHAPTER 20

➤ AUTHOR: **SANJEEV SINGH**

## SURGICAL PROPHYLAXIS

### THE AIM OF THIS CHAPTER IS TO:

To understand the importance and prevention of surgical site infection.

To understand the pharmacokinetics and pharmacodynamics of antibiotics used for surgical prophylaxis.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

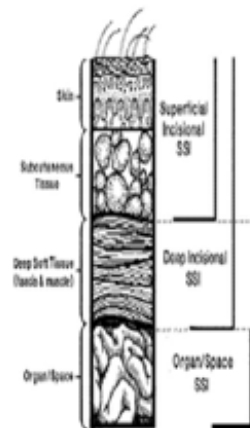
- Ensure rational prescription of prophylaxis
- Ensure complete adherence to guidelines on surgical prophylaxis
- Understand pharmacokinetics and pharmacodynamics of recommended antibiotics for surgical prophylaxis
- Understand Surgical Site Infection versus surgical prophylaxis

### ➤ BACKGROUND

Surgical Site infection is one of the most common healthcare associated infections. SSI leads to additional hospital stay of 6.5 days at a cost 3,246 Pounds. SSI is an important outcome measure for surgical procedures.

### Pathogenesis of Surgical Site Infection (SSI)

- $\text{Dose} \times \text{virulence}$   
Resistance of Host  
= risk of SSI
- $\geq 10^5$  / gm tissue  $\uparrow$  risk; with foreign body only 100/gm is needed to cause SSI
- Pathogens:  
*Endogenous* – flora normally contained  
*Exogenous* – healthcare personnel, environment, devices/materials used

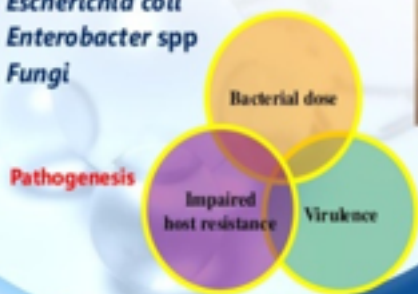


### ➤ DEFINITION

Surgical antibiotic prophylaxis is defined as the use of antibiotics before, during, or after a diagnostic, therapeutic or surgical procedure to prevent infectious complications. This term is used to describe antimicrobial therapy prescribed to clear infection by an organism or to clear an organism that is colonising a patient but is not causing infection.

## Surgical site infections

- 20% *Staphylococcus aureus*
- 16% *Pseudomonas spp*
- 15% *Staphylococci* (coagulase-negative)
- <10% *Enterococcus spp*
- <10% *Escherichia coli*
- <10% *Enterobacter spp*
- <10% *Fungi*

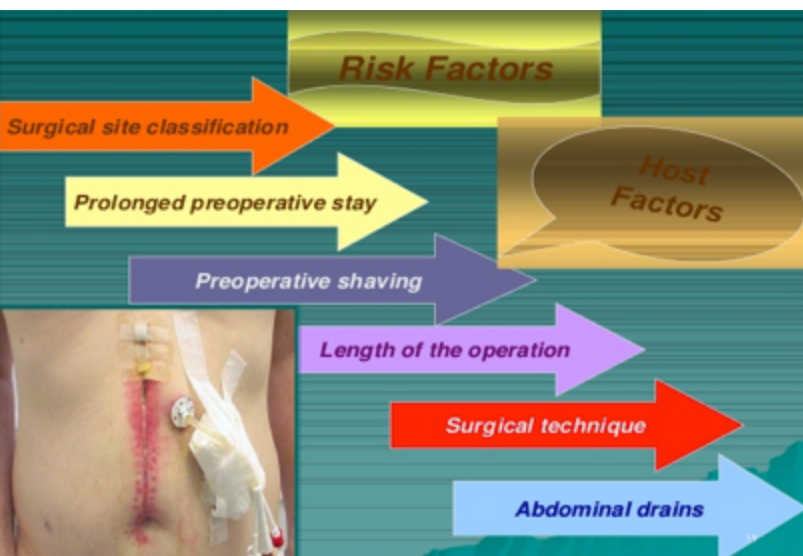


### IMPORTANCE

1. World Health Organisation (WHO) Clean Care is safer Care programme shows that surgical site infection (SSI) is the most surveyed and frequent type HAI in LMICs and affects up to one third of patients who have undergone a surgical procedure. In LMICs, the pooled incidence of SSI was 11.8 per 100 surgical procedures (range 1.2 to 23.6)<sup>1,2</sup>. Although SSI incidence is much lower in high-income countries, it remains the second most frequent type of HAI. The European Centre for Disease Prevention and Control (ECDC) reported data on SSI surveillance for 2010-2011.

### RANKING

The highest cumulative incidence was for colon surgery with 9.5% episodes per 100 operations, followed by 3.5% for coronary artery bypass graft, 2.9% for caesarean section, 1.4% for cholecystectomy, 1.0% for hip prosthesis, 0.8% for laminectomy and 0.75% for knee prosthesis<sup>3</sup>



### RATIONALE

Surgical Site infection is used to encompass the surgical wound and infections involving the body cavity, organs, which may or may not be associated with implants or prosthetic devices. Prophylactic administration of antibiotics inhibits growth of contaminating bacteria, and their adherence to prosthetic implants, thus reducing the risk of infection.

## TOOLKIT RESOURCE

### PDF ARTICLES

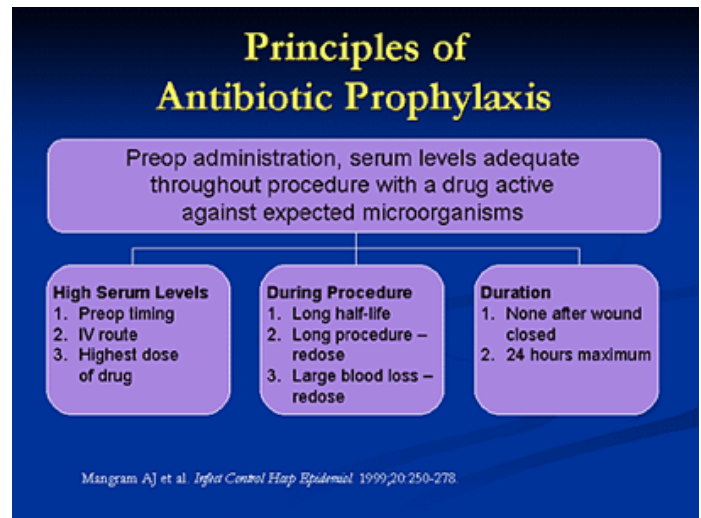
- 1 Allegranzi B, Bagheri Nejad S, Combescure C, Graafmans W, Attar H, Donaldson L, et al. Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. *Lancet*. 2011;377(9761):228-41.
- 2 Report on the burden of endemic health-care-associated infection worldwide. A systematic review of the literature. Geneva: World Health Organization; 2011.
- 3 Surveillance of surgical site infections in Europe 2010–2011. Stockholm: European Centre for Disease Prevention and Control 2013

### VIEW SLIDE SET

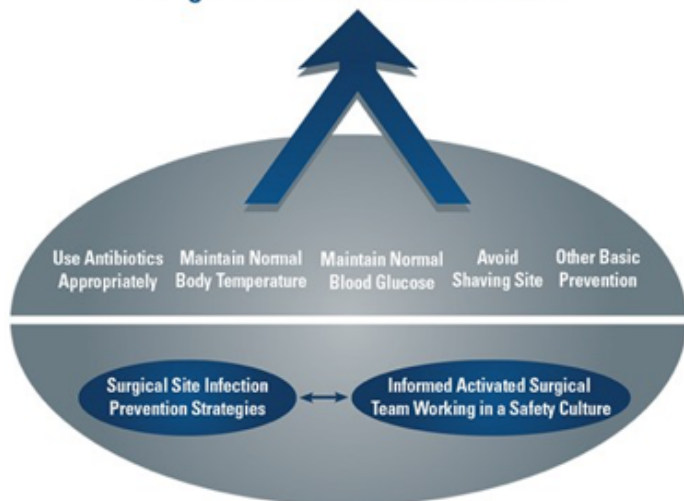


**REQUIREMENT/PRE REQUISITE TO PREVENT SSI**

- Pre OP bath with Triclosan with contact time of 2-3mts a day prior and on the day of surgery
- Use of Clippers
- Fasting Blood Sugar
- Normo-thermia
- Pre op preparation with PVP (7.5%) or Chlorhexidine (2%)
- Appropriate sterilisation practices in OR
- Surgical asepsis
- Disinfection practices in recovery area and wards
- Wound Care

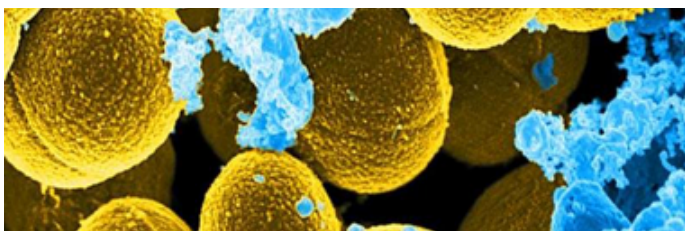


**Surgical Site Infection Prevention**



**SELECTION OF ANTIMICROBIAL AGENT FOR SURGICAL PROPHYLAXIS**

1. Characteristics of the ideal agent
2. The comparative efficacy of the antimicrobial agent for the procedure
3. The safety profile
4. The patient’s medication allergies



**Salient Features for Surgical Prophylaxis:**

- Usually, a single first-generation cephalosporin for operations not expected to encounter anaerobes or a single second-generation cephalosporin with anaerobic operations based on local susceptibility patterns is sufficient.
- For clean operations on the skin and subcutaneous tissues that do not involve any portion of the gastrointestinal tract, a semi synthetic penicillin resistant to penicillinases, such as oxacillin or cloxacillin, is probably effective, although there are limited published data to support this recommendation.
- Administration of antibiotics that are active against enteric anaerobes for procedures involving the lower gastrointestinal tract should be considered routine.
- Procedures on the upper gastrointestinal tract should involve use of antibiotics with activity against Gram-positive cocci and common Gram-negative organisms but which are not active against anaerobes.
- Procedures that do not enter any portion of the intestinal or genitourinary tract are sufficiently covered with antibiotics that are primarily active against Gram-Positive cocci.
- β-Lactam allergies are often cited as a contraindication for antibiotic prophylaxis
- For operations in which the risk is primarily from skin organisms vancomycin or teicoplanin is a common choice for patients allergic to β-Lactam. If local susceptibility patterns are favourable, clindamycin can be used.
- First-generation cephalosporins are the most commonly used agents for prophylaxis in caesarean section. Concern about neonatal exposure to antibiotics and the effect on neonatal sepsis have led to delays in administering antibiotics until after the umbilical cord has been clamped.

RECOMMENDATIONS

TOPICS	WHO 2016	SHEA/IDSA 2014	CDC (unpublished draft) 2014	NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE 2008/2013	ROYAL COLLEGE OF SURGEONS IN IRELAND 2012
Surgical antibiotic prophylaxis	Yes Strong recommendation, low quality of evidence When indicated (depending on the type of operation), surgical antibiotic prophylaxis should be administered prior to the surgical incision..	I Administer only when indicated. I Administer within 1 hour of incision to maximize tissue concentration	Yes: 1B Administer a preoperative antimicrobial agent only when indicated, i.e. based on published clinical practice guidelines and timed so that a bactericidal concentration of the agent is established in the serum and tissues when the incision is made.	Yes Antibiotic prophylaxis should not be used routinely for clean non-prosthetic uncomplicated surgery. When antibiotic prophylaxis is needed, a single dose of antibiotic intravenously on starting anaesthesia should be considered. However, prophylaxis should be given earlier for operations in which a tourniquet is used.	Yes: 1A Single dose only unless otherwise indicated. Give an additional dose of antibiotic if the surgical procedure is prolonged or there is major intraoperative blood loss (>1.5 L in adults or 25mL/kg in children). Ensure that the antibiotic is given at induction (within 60 minutes before

 LISTEN TO AUDIO

 TIME OF ADMINISTRATION

Antimicrobial prophylaxis should be administered only when indicated based on published clinical practice guidelines and timed such that a bactericidal concentration of the agents is established in the serum and tissues when the incision is made.<sup>12</sup>

- Antimicrobial therapy should be initiated within the 60 minutes prior to surgical incision to optimize adequate drug tissue levels at the time of initial incision.<sup>4</sup>
- The half-life of the antibiotic should be considered:<sup>5</sup> administration of Vanomycin or a fluroquinolone should begin within 120 minutes before surgical incision because of the prolonged infusion times requires for these drugs




**> REPEAT DOSING**


- To ensure adequate antimicrobial serum and tissue concentrations, repeat intraoperative dosing is warranted for procedures that exceed two half-lives of the drug and for procedures in which there is excessive blood loss(>1500ml)(4)
- Redosing may also be warranted in the setting of factors that shorten antimicrobial half-life,such as extensive burns.
- The dosing interval should be measured from the time of the preoperative dose(not from the beginning of the procedure)
- Redosing may not be warranted for patients in whom the antimicrobial half-life is prolonged,such as renal insufficiency.
- For clean and clean-contaminated procedures, additionalprophylactic antimicrobial agent doses should not be administered after the surgical incision(12)is closed in the operating room, even in the presence of a drain

Clindamycin	6
Ertapenem	NA
Fluconazole	NA
Gentamicin	NA
Levofloxacin	NA
Metronidazole	NA
Moxifloxacin	NA
Piperacillin–tazobactam	2
Vancomycin	NA
Oral antibiotics for colorectal surgery prophylaxis (used in conjunction with a mechanical bowel preparation)	
Erythromycin base	NA
Metronidazole	NA
Neomycin	NA

**TOOLKIT RESOURCE**

SITE LINKS

 4 Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt) 2013; 14:73.

 12 Sandra , Berríos, Craig et al. Centers for Disease Control and Prevention Guidelinefor the Prevention of Surgical Site Infection, 2017. JAMA Surg. 2017;152(8):784-791

**> DURATION**

- For surgeries less than 4hrs: Single dose
- For surgeries greater then 4hrs: 3 doses
- In general, repeat antimicrobial dosing following wound closure is not necessary and may increase the risk for the development of antimicrobial resistance.<sup>6-11</sup>

Antimicrobial	Recommended Redosing Interval (From Initiation of Preoperative Dose)
Ampicillin–sulbactam	2
Ampicillin	2
Aztreonam	4
Cefazolin	4
Cefuroxime	4
Cefotaxime	3
Cefoxitin	2
Cefotetan	6
Ceftriaxone	NA
Ciprofloxacin	NA

## TOOLKIT RESOURCE

### SITE LINKS

- 6 Antimicrobial prophylaxis for surgery. Treat Guidel Med Lett 2012; 10:73.
- 7 Goldmann DA, Hopkins CC, Karchmer AW, et al. Cephalothin prophylaxis in cardiac valve surgery. A prospective, double-blind comparison of two-day and six-day regimens. J Thorac Cardiovasc Surg 1977; 73:470.
- 8 McDonald M, Grabsch E, Marshall C, Forbes A. Single- versus multiple-dose antimicrobial prophylaxis for major surgery: a systematic review. Aust N Z J Surg 1998; 68:388.
- 9 Conte JE Jr, Cohen SN, Roe BB, Elashoff RM. Antibiotic prophylaxis and cardiac surgery. A prospective double-blind comparison of single-dose versus multiple-dose regimens. Ann Intern Med 1972; 76:943.
- 11 Harbarth S, Samore MH, Lichtenberg D, Carmeli Y. Prolonged antibiotic prophylaxis after cardiovascular surgery and its effect on surgical site infections and antimicrobial resistance. Circulation 2000; 101:2916.

### ARTICLE

- 10 Pollard JP, Hughes SP, Scott JE, et al. Antibiotic prophylaxis in total hip replacement. Br Med J 1979; 1:707.

## TOPICAL ADMINISTRATION OF IRRIGATIONS, PASTES, AND WASHES

Limited high-quality data are available regarding the use of antimicrobial irrigations, pastes, and washes that are administered topically. Additional high quality data on the safety and efficacy of topical antimicrobial administration as an adjunct to i.v administration are needed to determine the role of tropical antimicrobial prophylaxis of every 100 hospitalized patients at any given time, seven in developed and 15 in developing countries will acquire at least one HAI. The endemic burden of HAI is also significantly (at least 2-3 times) higher in low-and middle –income countries (LMICs) than in high-income nations, particularly in patients admitted to intensive care units, and neonates

## CONTRIBUTORY FACTORS IN SURGICAL SITE INFECTION

1. Nutritional status
2. Tobacco use
3. The intraoperative technique
4. Correct selection, timing and dosing of antibiotics
5. Age
6. Gender
7. Clean vs. clean/ contaminated surgery
8. Blood loss

### Ready Reckoner for Surgical Prophylaxis:(based on ASHP, IDSA and SHEA report 2013)

Procedure	1 <sup>ST</sup> Line agents	Alternative Agents in Pts With b-Lactam Allergy
Colorectal	Cefazolin + metronidazole, cefoxitin, cefotetan, ampicillin sulbactam,h ceftriaxone + metronidazole,n ertapenem	Clindamycin + aminoglycosideg or aztreonam or fluoroquinoloneh-j, metronidazole + aminoglycosideg or fluoroquinolone
Hysterectomy	Cefazolin, cefotetan, cefoxitin, ampicillin–sulbactamh	Clindamycin or vancomycin + aminoglycosideg or aztreonam or fluoroquinoloneh-j Metronidazole + aminoglycosideg or fluoroquinoloneh-j
Vascular and cardiac surgery	Cefazolin	Clindamycin,d vancomycind
Liver transplantationq,t	Piperacillin–tazobactam, cefotaxime + ampicillin	Clindamycin or vancomycin + aminoglycosideg or aztreonam or fluoroquinolone
Total joint replacement	Cefazolin	Clindamycin,d vancomycind

 VIEW DOCUMENT

## ▶ SUMMARY

- Surgical Site infection is one of the most common healthcare associated infections.
- Pre requisite to prevent SSI includes pre OP bath with Triclosan with contact time of 2-3mts a day prior and on the day of surgery, use of clippers, Fasting Blood Sugar, normo-thermia etc
- The ideal surgical prophylaxis antimicrobial would be one that is most appropriate for the procedure and safe for the patient.
- Antibiotics that require prolonged infusion should be administered 120 mins prior to surgical incision. Others should be administered 60 mins prior to surgical incision.
- Redosing is not recommended for surgeries that last less than 4 hours.



### References

1. Allegranzi B, Bagheri Nejad S, Combescure C, Graafmans W, Attar H, Donaldson L, et al. Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. *Lancet*. 2011;377(9761):228-41.
2. Report on the burden of endemic health-care-associated infection worldwide. A systematic review of the literature. Geneva: World Health Organization; 2011.
3. Surveillance of surgical site infections in Europe 2010–2011. Stockholm: European Centre for Disease Prevention and Control; 2013 ([http://ecdc.europa.eu/en/publications/Publications/SSI-\(in-europe-2010-2011\).pdf](http://ecdc.europa.eu/en/publications/Publications/SSI-(in-europe-2010-2011).pdf), accessed 13 July 2016).
4. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Surg Infect (Larchmt)* 2013; 14:73.
5. Global guidelines for the prevention of surgical site infection. World Health Organization 2016 <http://www.who.int/gpsc/global-guidelines-web.pdf?ua=1> (Accessed on November 08, 2016).
6. Antimicrobial prophylaxis for surgery. *Treat Guidel Med Lett* 2012; 10:73.
7. Goldman DA, Hopkins CC, Karchmer AW, et al. Cephalothin prophylaxis in cardiac valve surgery. A prospective, double-blind comparison of two-day and six-day regimens. *J Thorac Cardiovasc Surg* 1977; 73:470.
8. McDonald M, Grabsch E, Marshall C, Forbes A. Single- versus multiple-dose antimicrobial prophylaxis for major surgery: a systematic review. *Aust N Z J Surg* 1998; 68:388.
9. Conte JE Jr, Cohen SN, Roe BB, Elashoff RM. Antibiotic prophylaxis and cardiac surgery. A prospective double-blind comparison of single-dose versus multiple-dose regimens. *Ann Intern Med* 1972; 76:943.
10. Pollard JP, Hughes SP, Scott JE, et al. Antibiotic prophylaxis in total hip replacement. *Br Med J* 1979; 1:707.
11. Harbarth S, Samore MH, Lichtenberg D, Carmeli Y. Prolonged antibiotic prophylaxis after cardiovascular surgery and its effect on surgical site infections and antimicrobial resistance. *Circulation* 2000; 101:2916.
12. Sandra, Berríos, Craig et al. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. *JAMA Surg*. 2017;152(8):784-791.



# CHAPTER 21

› AUTHORS: **DAVID ENOCH & LAURA WHITNEY**

## ANTIFUNGAL STEWARDSHIP

### THE AIM OF THIS CHAPTER IS TO:

Describe what Antifungal Stewardship (AFS) is.

Outline the very basic principles medical mycology.

Describe the different ways antifungals are used.

Outline the advantages and disadvantages of AFS.

Outline how to start an AFS programme.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Explain what antifungal stewardship is
- Outline the aims of AFS
- Outline the advantages and disadvantages of AFS
- Describe the differences between AFS and AMS
- Understand more about diagnosing fungal infections
- Understand more about antifungal resistance
- Describe how to do it
- Describe ways to start
- Describe some of the challenges
- Describe who you need
- Describe what you need
- Describe how you continue
- Describe how you expand
- Reflect the relevance of these elements to their practice

### › INTRODUCTION

Invasive fungal infections are associated with significant morbidity and mortality. Patients who develop invasive fungal infections often have highly complex underlying conditions and this, coupled with poor diagnostic tests, often leads to unnecessary and inappropriate prescribing of antifungal agents.

Antifungal agents are often not as well tolerated as antibacterial agents and many are extremely expensive. A number of antifungal drugs also have significant drug-drug interactions with other medication (especially the triazole drugs). One of the principle drivers of antimicrobial stewardship has been the rise in antibacterial resistance. Until recently, this has been of less concern with fungi. There is now increasing resistance to a number of antifungal agents and *Candida auris*, which has a relatively high level of resistance to antifungals, has recently been identified as an emerging problem.

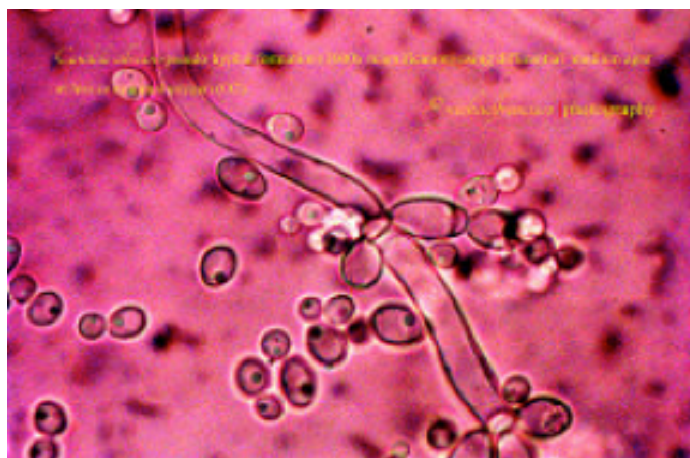


PUBLIC HEALTH ENGLAND *CANDIDA AURIS* PAGE



**SOME BASIC MYCOLOGY**

Medically important fungi capable of causing invasive fungal infection can be broadly split into three categories. They include yeasts (e.g. *Candida* spp. and *Cryptococcus* spp.), moulds (e.g. *Aspergillus* spp. and the zygomycetes) and dimorphic fungi (e.g. *Histoplasma* spp.). The dermatophytes (e.g. *Microsporum* spp.), whilst capable of causing superficial infections, rarely cause invasive infections



"Candida albicans (1000X magnification)" flickr photo by MichaelFrancisco <https://flickr.com/photos/micodude/6500725393> shared under a Creative Commons (BY) license

*Candida albicans* is the most commonly isolated strain of *Candida*. Invasive candidiasis is the most common fungal disease among hospitalized patients in the developed world. Invasive candidiasis consists of deep-seated tissue candidiasis (*Candida* in a sterile site) and candidaemia (*Candida* in the bloodstream). Deep-seated candidiasis may be a consequence of either direct inoculation or haematogenous spread. Risk factors for invasive candidiasis are described in table 1

Invasive aspergillosis is a major cause of invasive mould infection which tends to affect the immunocompromised. Risk factors include haematological malignancy, solid organ transplant recipients, haematopoietic stem cell transplant (HSCT) recipients, solid tumours, HIV/AIDS, an inherited immunodeficiency or presence on an ITU.

**Antifungal resistance**

Fluconazole resistance (See Fig. 1) has been recognized for several years, especially in *C. glabrata* (dose dependent) and *C. krusei* (intrinsically resistant to fluconazole). Azole resistance has also been seen in *C. parapsilosis* and *C. auris*. Predictors associated with fluconazole resistant *Candida* spp. include neutropenia, chronic renal disease, and previous fluconazole exposure. Echinocandin resistance is increasingly recognized.

Resistance is mediated primarily through mutations in hot-spot regions of FKS genes, which encode the echinocandin target enzyme (1,3-β-D-glucan synthase). Resistance can emerge on therapy.

Azole resistance has also been demonstrated in *Aspergillus fumigatus*. Fungal biofilm associated infections are recognised as an escalating clinical problem and are frequently refractory to conventional therapy because of resistance. Studies of fungi using in-vitro and in-vivo biofilm models have demonstrated less susceptibility to antimicrobial therapy than planktonic free floating cells.

Risk factors for invasive candidiasis	Risk factors for invasive candidiasis	Risk factors for invasive candidiasis on ITU
Critical illness	Y	Y
Abdominal surgery, with particular risk among patients who have anastomotic leakage or have had repeat laparotomies	Y	Y
Acute necrotising pancreatitis	Y	
Haematological malignancy	Y	
Neutropenia		Y
Solid organ transplantation	Y	
Solid organ tumours	Y	
Neonates, particularly low birth weight	Y	Y
Broad spectrum antibiotics	Y	
Central venous catheter	Y	Y
Total parenteral nutrition	Y	Y
Haemodialysis	Y	Y
Urinary catheter		Y
Glucocorticoid therapy	Y	
Fungal colonisation		Y
Infection or sepsis		Y
Mechanical ventilation		Y
Diabetes		Y
Acute Physiology and Chronic Health Evaluation II (APACHE II) * or APACHE III score		Y
Gastrointestinal bleed		Y
Age		Y

TABLE 1  
Risk factors for invasive candidiasis.  
\* APACHE: Acute Physiology and Chronic Health Evaluation

## % Resistance to Fluconazole in Candidaemia, England, 2012-16

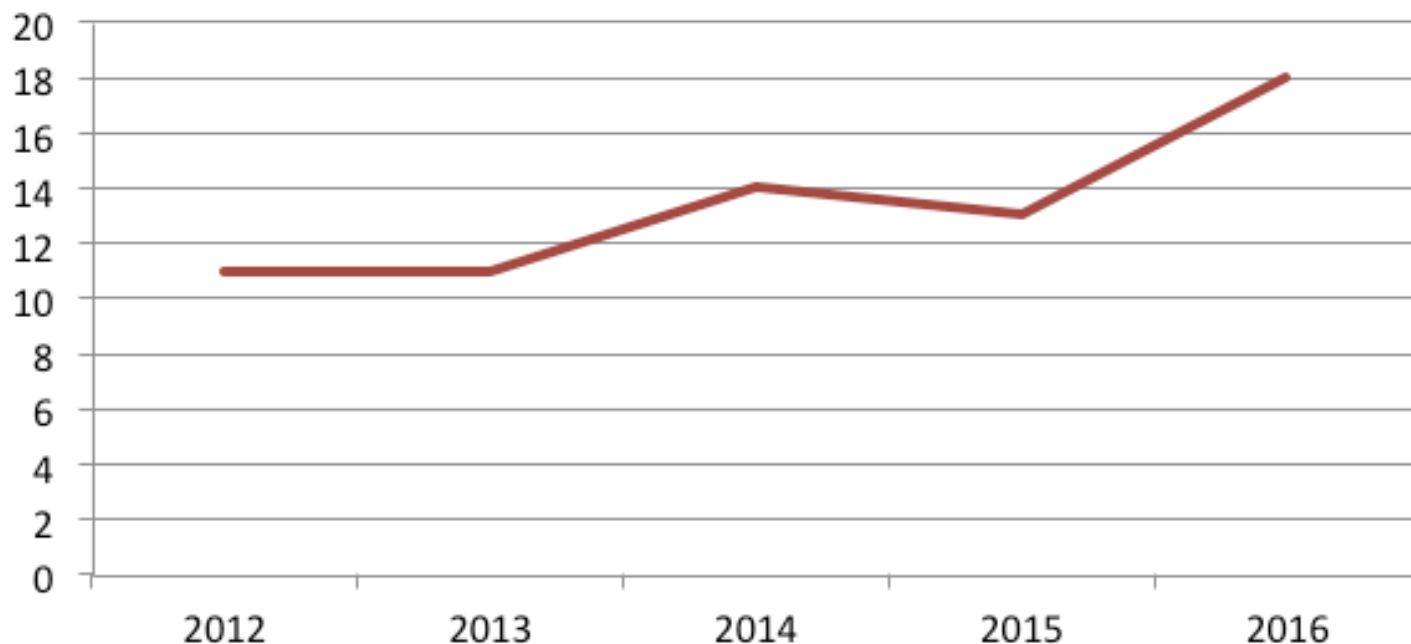


FIGURE 1

Adapted from: Laboratory surveillance of Candidaemia in England, Wales and Northern Ireland: 2016 Health Protection Report Volume 11 Number 32  
[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/645312/hpr3217\\_cnddmia2016.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/645312/hpr3217_cnddmia2016.pdf)

### WHAT IS ANTIFUNGAL STEWARDSHIP (AFS)?

Antimicrobial stewardship has previously been defined in chapter 3. Antimicrobial stewardship in immunocompromised patients is also discussed in chapter 19. Antifungal stewardship can be defined in the same way as ‘the optimal selection, dosage, and duration of antifungal treatment that results in the best clinical outcome for the treatment or prevention of infection with minimal toxicity to the patient and minimal impact on subsequent resistance’ (Box 2).

#### BOX 2: DEFINITION OF AFS

The right antifungal  
 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

### AIMS OF AFS PROGRAMME

The aims of AFS programmes include:

- Improved patient outcome
- Maximising drug efficacy
- Minimise drug toxicity
- Prevent the emergence of breakthrough infections
- Minimise the development of resistance
- Minimise or mitigate the effects of drug-drug interactions
- Maximise cost efficiency

### WHAT ARE THE BENEFITS OF AFS?

A number of research papers describe the financial benefits of commencing AFS programmes; reducing inappropriate antifungal use can lead to significant cost savings due to the high cost of many of the drugs.

More recently, papers have described benefits in terms of improved outcome (e.g. mortality; adherence to guidelines). With the emergence and rise of antifungal resistance in recent

years, it is becoming imperative that AFS is used in order to reduce antifungal resistance.

### ▶ WHAT ARE THE DISADVANTAGES OF AFS?

The main disadvantage is one of resources. AFS takes time. Importantly, the people who perform AFS need knowledge, experience and confidence of dealing with the highly complex patients who typically suffer from invasive fungal infections. Many studies of successfully implemented AFS programmes describe using a multidisciplinary approach (e.g. antimicrobial pharmacist plus an infection specialist) which increases the resources required.

### ▶ WHAT ARE THE DIFFERENCES BETWEEN ANTIFUNGAL STEWARDSHIP AND ANTIMICROBIAL STEWARDSHIP (AMS)?

There are a number of differences between AFS and AMS.

- There are fewer diagnostic and monitoring tests available for fungal infections than for bacterial infections and staff are generally less confident in interpreting results. Fungal diagnostics may be unavailable in some hospitals or the turnaround time may be so long as to render them ineffective, leading to empirical treatment of infections. Rational prescribing relies on being able to accurately characterise the infection.
- There is a greater wealth of experience with bacterial infections compared to fungal infections. This can make the choosing of antifungal agents for protocols difficult for those involved in approval and implementation of such protocols and formulary submissions.
- Staff are less familiar with fungal infections and their treatments compared with bacterial infections. This is a reflection of the fact that they may not have received in-depth education on treating fungal infections as it is not regularly an area of focus for medical school curricula. Furthermore, fungal infections are rarer than bacterial infections so the majority of healthcare professionals will not have as much experience in managing them.
- Patients requiring antifungal therapy are often on complex medication regimens and therefore toxicity and drug-drug interactions seem to be more of an issue than when treating bacterial infections.
- Fungi are structurally similar to human cells, meaning that drugs used to target them can often have side effects and interactions.
- AFS is almost exclusive to secondary care; the majority of prescribing is within this sector, with most antifungals being restricted to hospital use only. Although systemic antifungals

(fluconazole) are available over the counter in pharmacies for certain indications.

- Fungal prophylaxis/ treatment courses are often more prolonged than for antibacterials.
- Antibacterial resistance has a significantly higher profile, being described as a global emergency, compared to antifungal resistance, which is less well defined and discussed, particularly at international levels.



"Money" flickr photo by Got Credit <https://flickr.com/photos/gotcredit/33810597472> shared under a Creative Commons (BY) license

### ▶ FUNDING OF ANTIFUNGALS AND ITS EFFECTS ON AFS

Due to their high costs the majority of antifungal agents (liposomal amphotericin B, voriconazole, posaconazole, isavuconazole and the echinocandins) are not included within treatment tariffs in England. The exception is for patients within 100 days of a bone marrow transplant and those on ITU, where treatment tariffs are considered to be sufficient to fund any antifungal agents required. Some specialist tariffs exist for management of patient groups (for example at the national aspergillosis centre in Manchester). Usage of these drugs is reported to NHS England on a monthly basis through SLAM (Stop, Look, Assess, Manage) reporting and any expenditure refunded in full. When cheaper generic drugs become available this does not automatically change their status to within tariff.

Thus, there is little incentive for English hospitals to fund resources for antifungal stewardship, which as described above is complex and time consuming and to exert its maximal effect requires the introduction of specialist diagnostics, which add to the cost. Some interventions may reduce costs in in-tariff drug use so may be worth pursuing, but most antifungal use occurs outside tariff.

In Scotland, Wales and Northern Ireland there is not a purchaser-provider split. Health Boards are responsible for the cost of all

medicines supplied from their annual budgets so the Health Board benefits from any efficiency savings resulting from stewardship directly.

Health services outside the UK may have different funding systems. It can be useful to try and understand the system you use.

## ➤ TYPES OF ANTIFUNGAL USE

Antifungal agents are used in a wide variety of ways in different populations. There is also great variability of use between different patient groups. This is most likely to be due to differences in patient populations, risk factors, environmental considerations and prior antibacterial and antifungal use.

Antifungal agents are used to prevent infections in some susceptible patients (i.e. **prophylaxis**).

They can be used **empirically**, i.e. an antifungal agent is used in a susceptible patient who has clinical evidence of infection and is not improving with an antibacterial agent, so is presumed to have a fungal infection (but there is no actual clinical or pathological evidence of fungal infection).

For a diagnosis of **proven IFI**, specimens must be obtained by a sterile technique from a normally sterile site. Invasive mould infection is proven if hyphae are seen in a histological or cytological specimen (with evidence of tissue damage seen either in the biopsy material or “unequivocally” by imaging) or a mould is grown in culture from that specimen with clinical or radiological evidence of infection at the site from which the specimen was taken. Systemic yeast infection would be proven on the same evidence as above or if the yeast was grown in a blood culture. A diagnosis of **probable IFI** requires a combination of host factors and microbiological and clinical criteria, whereas a diagnosis of **possible IFI** requires host factors and clinical features.

Treatment decisions therefore depend on:

- Host factors
- Clinical features
- Microbiology results
  - **Host factors**
    - Factors that render a patient susceptible to IFI include:
      - Neutropenia
      - Allogeneic HSCT recipient
      - T-cell immunosuppression
      - Prolonged corticosteroids (>3 weeks)
      - Inherited severe inherited immunodeficiency
  - **Clinical features**
    - Clinical features include pyrexia, cough and sinus pain etc. They also include radiological features (particularly CT changes).
  - **Microbiology tests**
    - These are discussed later in the chapter.

## BOX 3: DEFINITIONS OF INVASIVE FUNGAL DISEASE (IFD) (EORTC-MSG CRITERIA)

**Possible:** Those cases with appropriate host factors and sufficient clinical evidence consistent with IFD, but for which there was no mycological support

**Probable:** Those cases with a host factor, clinical features, and mycological evidence of IFD

**Proven:** Those cases in which fungal elements in diseased tissue are demonstrated for most conditions

From: Revised Definitions of Invasive Fungal Disease from the European Organization for Research and Treatment of Cancer/ Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group <https://academic.oup.com/cid/article/46/12/1813/297334/Revised-Definitions-of-Invasive-Fungal-Disease>

## ➤ DIAGNOSING FUNGAL INFECTIONS

As described above, diagnosing fungal infections can be difficult.

Access to timely diagnostics is essential. The British Society for Medical Mycology has provided guidelines / best practice recommendations for microbiology laboratories (and histopathology and radiology; Schelenz et al 2015). Whilst not all tests need to be performed locally, a short turnaround time is essential to affect patient management. Unfortunately, these guidelines do not make recommendations as to acceptable turnaround times. However, a turnaround time of <48 hours would be ideal for serological and molecular tests.

The diagnostics (and how to interpret them) required include:

- Galactomannan screening of serum (two times per week) from patients with haematological malignancies at high risk of invasive aspergillosis should be considered in those not receiving mould-active prophylaxis; optical density (OD) index threshold of 0.5 has a high negative predictive value, enabling invasive aspergillosis to be excluded
- Galactomannan testing of BAL from patients at high risk of invasive aspergillosis should be considered, although the current OD index cut-off of 0.5 might change. Some centres use a cut-off of between one and three.
- $\beta$ -D-glucan screening of serum from patients at high risk of invasive fungal disease should be considered; a negative result has a high negative predictive value, enabling invasive fungal disease to be excluded. These high-risk categories include immunosuppressed patients and intensive care patients.
- PCR screening of serum for aspergillus from patients at high



risk of invasive fungal disease should be considered; a negative result has a high negative predictive value, enabling invasive fungal disease to be excluded

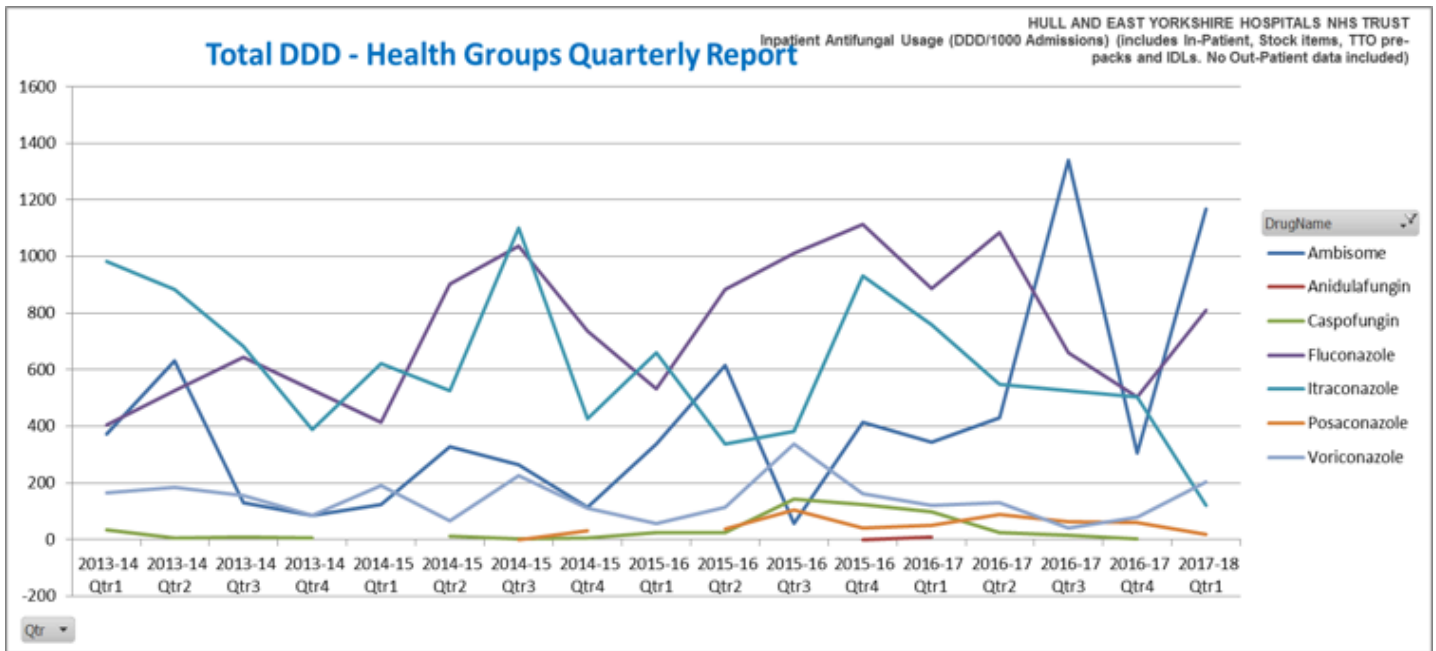
- Combination testing with aspergillus PCR plus another antigen test improves the positive predictive value and diagnosis of invasive fungal disease

**➤ AFS: HOW DO YOU DO IT?**

*How do you start?*

Initially it is important to understand antifungal use in your patient population. Audit and surveillance (Fig. 2) can be helpful, both to identify particular challenges to address or to identify poor practice to modify. It can also be used to persuade clinical and managerial colleagues of the need for a stewardship programme and provide some useful data to assess the efficacy of your interventions.

a) Haematology, infectious diseases and oncology healthcare group



b) Surgery healthcare group

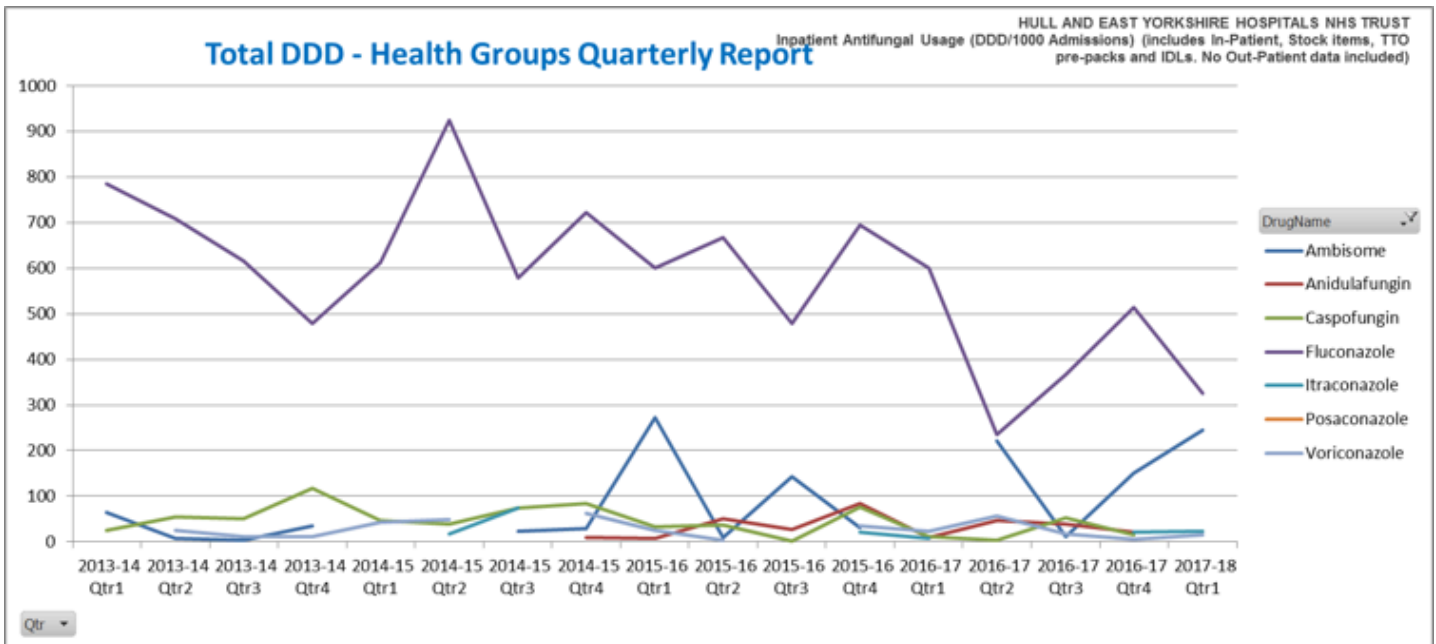




FIGURE 2  
 Example of surveillance of anti-fungal defined daily doses at a UK teaching hospital, 2013-2018


## TOOLKIT RESOURCE


## SITE LINK - UK

 Ashbee HR, Barnes RA, Johnson EM, Richardson MD, Gorton R, Hope WW. Therapeutic drug monitoring (TDM) of antifungal agents: guidelines from the British Society for Medical Mycology. *J Antimicrob Chemother.* 2014; 69: 1162-76


 Schelenz S, Barnes RA, Barton RC, Cleverley JR, Lucas SB, Kibbler CC, Denning DW; British Society for Medical Mycology. British Society for Medical Mycology best practice recommendations for the diagnosis of serious fungal diseases. *Lancet Infect Dis.* 2015; 15: 461-74. [http://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(15\)70006-X/fulltext](http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(15)70006-X/fulltext)


## SITE LINK - EUROPE

 European Conference on Infections in Leukaemia (ECIL) guidelines page

 European Society Clinical Microbiology and Infectious Diseases (ESCMID) guidelines page

## SITE LINK - NORTH AMERICA

 Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, Reboli AC, Schuster MG, Vazquez JA, Walsh TJ, Zaoutis TE, Sobel JD. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2016 Feb 15;62(4):e1-50

 Patterson TF, Thompson GR 3rd, Denning DW, Fishman JA, Hadley S, Herbrecht R, Kontoyiannis DP, Marr KA, Morrison VA, Nguyen MH, Segal BH, Steinbach WJ, Stevens DA, Walsh TJ, Wingard JR, Young JA, Bennett JE. Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2016 Aug 15;63(4):e1-e60

Freifeld AG, Bow EJ, Sepkowitz KA, Boeckh MJ, Ito JI, Mullen CA, Raad II, Rolston KV, Young JA, Wingard JR; Infectious Diseases Society of America. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the infectious diseases society of america. *Clin Infect Dis.* 2011 Feb 15;52(4):e56-93. doi: 10.1093/cid/cir073.

A good starting point is to create or review guidelines and clinical pathways in line with local epidemiology (especially for invasive candidiasis) and patient population. Guidelines that are available already that can be adapted are provided in resource toolkit. The availability and turn-around-time of diagnostics should be considered within this process.

Ideally funding for the service should be agreed prior to commencing the programme and resourced from those expecting to see reductions in expenditure (usually commissioners in England).

Aim to start small by choosing a particular clinical area or a small group of drugs. Building relationships and knowledge and influencing prescribing can be easier if you dedicate your time to working with a small group of colleagues and patients. Haematology and intensive care units are typically good places to start, usually being the biggest users of antifungals. Specialist centres may also find transplant and upper gastrointestinal surgery to be heavy users of antifungal agents. Another option is to use audit data or local knowledge to identify areas of antifungal use that require optimisation. Interventions may be addressed incrementally according to resources, risk levels, or ease of implementation

### EXAMPLES OF AFS THAT WORK INCLUDE:

- Reviewing all patients on voriconazole to ensure TDM is undertaken and results outside therapeutic range are acted upon could be implemented relatively easily and with a limited stewardship team (i.e. with just a pharmacist). A summary of the need for TDM is provided in table 2
- Reviewing all candidaemia patients and ensuring all patients complete all aspects of the care bundle (Gouliouris et al 2016):
  - Adequate empirical therapy
  - timely treatment
  - lines reviewed
  - echocardiography
  - repeat blood cultures
  - rationalised antifungal therapy
- Managing patients with candidaemia can be reviewed by watching the following link



WATCH VIDEO



- Prospectively collect data on your stewardship activities – design a database. Or collaborate with a centre that already has one! Previous AFS programmes have collected the following data: patient demographics; antifungal drug; indication for therapy; site of infection; causative organism, if identified; interventions made during stewardship activities (including whether these were accepted); length of stay and in-hospital mortality. Monitoring antifungal consumption and expenditure and candida epidemiology is also key

Antifungal	GRADE quality of evidence and strength of recommendation	Prophylaxis	Treatment	Toxicity
Itraconazole	Evidence quality recommendation	Moderate Strong	Moderate Strong	Moderate Weak
Voriconazole	Evidence quality recommendation	Low Weak	High Strong	High Strong
Posaconazole	Evidence quality recommendation	Moderate Strong	Moderate Strong	High Strong against
Fluconazole	Evidence quality recommendation	High Strong against	High Strong against	High Strong against
Flucytosine	Evidence quality recommendation	NA	Low Weak	Moderate Strong
Echinocandins	Evidence quality recommendation	High Strong against	High Strong against	High Strong against
Polyenes	Evidence quality recommendation	High Strong against	High Strong against	High Strong against

TABLE

summary of need for therapeutic drug monitoring when using antifungal agents (based on Ashbee et al)

## > AFS: WHAT ARE THE CHALLENGES?

**Funding** – getting this from the commissioners (who will be the ones who see the cost benefits) can be difficult. NHS England is currently looking at how to incentivise AFS. In the meantime, Trusts could initiate programmes focusing on in tariff use.

**Time** – AFS is more time consuming compared to antibacterial stewardship. The MDT need dedicated time in job plans and consideration of how work will be covered during annual leave/sickness absences.

**Expertise** – try to link with centres with embedded stewardship programmes and learn from them

**Persuasive ability** – it is often difficult to stop/modify antimicrobials in critically ill immunocompromised patients

## > WHO DO YOU NEED TO INVOLVE?

*Who are the stakeholders?*

These include Commissioners, Trust managers/financial officers, clinicians in high risk areas (e.g. haematology, oncology, ITU, respiratory, transplant), microbiology, infectious diseases, pharmacy, and patients.



"Tools" flickr photo by Kimberlie Kohler <https://flickr.com/photos/bbbellezza/5542980497> shared under a Creative Commons (BY-SA) license

## WHAT DO YOU NEED?

### Guidelines

For diagnosis of infections and prophylaxis and treatment in groups of patients frequently seen in your setting. Audit standards should be set within guidelines ideally.

### Diagnostics

Rapid turn-around time (TAT) is essential. It is likely to be necessary to work with clusters of local labs as cost can be prohibitive if small sample numbers. Good NPV of beta-D-glucan and GM (particularly from BAL) can be useful for stopping empiric therapy.

### TDM

Need to have rapid TAT and easy availability. Taking levels in high income clinical countries is easy with guidance available;

## VIEW TDM OF ANTIFUNGAL AGENTS GUIDELINES

from the British Society for Medical Mycology

However, knowing how to amend doses if levels are outside therapeutic range is more complex. Voriconazole dose response in adults is non-linear. Small incremental dose increases/reductions are recommended. Posaconazole has more linear pharmacokinetics. The newer tablet formulation is associated with less variability in absorption so should reduce the need for dose modification and possibly TDM too. TDM for isavuconazole

is currently not recommended by the manufacturer though it is available. TDM is not required for amphotericin B or the echinocandins. Flucytosine monitoring is recommended for all patients receiving treatment.

### Surveillance

Numbers and types of infections seen (proven/probable/possible) and species if known, candidaemia epidemiology – proportion of albicans/non-albicans, with a particular eye on more difficult to treat species – *C. auris*, *C. glabrata*, *C. krusei*. Monitor the proportion of candidaemias susceptible to fluconazole and echinocandins, preferably looking at MIC data and reporting mode MIC.

### Outcome data

These can include: length of stay, in-patient mortality, costs of program versus costs saved, in-tariff costs versus outside tariff. Intervention rates, types and acceptance. Quality indicator data – guideline compliance, IV-PO switch, proportion of empiric prescriptions stopped within a week if no IFI diagnosed, TDM done when indicated – results within range or acted upon if outside.

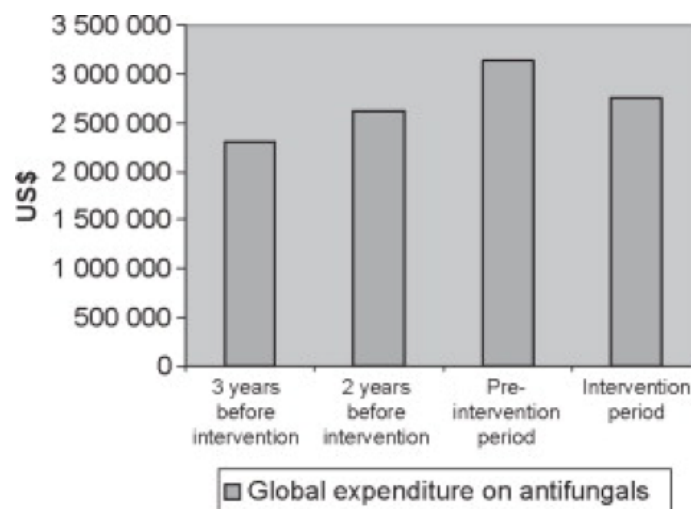


FIGURE 3  
Antifungal costs before and after a stewardship intervention  
From: López-Medrano F, San Juan R, Lizasoain M, et al. A non-compulsory stewardship programme for the management of antifungals in a university-affiliated hospital. *Clin Microbiol Infect.* 2013; 19: 56-61.  
[http://www.clinicalmicrobiologyandinfection.com/article/S1198-743X\(14\)60309-8/fulltext](http://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(14)60309-8/fulltext)

### Persuasive champions/on ward presence



"Continue Key" flickr photo by Got Credit <https://flickr.com/photos/gotcredit/33716130276> shared under a Creative Commons (BY) license

## > HOW DO YOU CONTINUE?

- How do you embed it into practice?

Have regular time in job plans with cover for leave. It is also possible to get AFS embedded in departments by appointing department champions. In this model the clinical team has responsibility for AFS and the AFS team advises them. This model is similar to that employed in some hospitals for infection control and antibacterial stewardships. AFS is included in the job plans of clinicians; they are the experts in their fields after all!

- How do you expand?


Only expand once the service is up and running and working well. Options include:


- Increase scope of practice
- Expand into out-patients
- Set up clinics
- Link with other hospitals to do collaborative work


## TOOLKIT RESOURCE


WHAT AFS INITIATIVES HAVE OTHER GROUPS DONE?


SITE LINK


 Apisarnthanarak A, Yatraserit A, Mundy LM; Thammasat University Antimicrobial Stewardship Team. Impact of education and an antifungal stewardship program for candidiasis at a Thai tertiary care center. *Infect Control Hosp Epidemiol.* 2010; 31: 722-7

 Gouliouris T, Micallef C, Yang H, Aliyu SH, Kildonaviute K, Enoch DA. Impact of a candidaemia care bundle on patient care at a large teaching hospital in England. *J Infect.* 2016; 72: 501-3


 López-Medrano F, San Juan R, Lizasoain M, et al. A non-compulsory stewardship programme for the management of antifungals in a university-affiliated hospital. *Clin Microbiol Infect.* 2013; 19: 56-61

 Micallef C, Aliyu SH, Santos R, Brown NM, Rosembert D, Enoch DA Introduction of an antifungal stewardship programme targeting high-cost antifungals at a tertiary hospital in Cambridge, England. *J Antimicrob Chemother.* 2015; 70: 1908-11


 Standiford HC, Chan S, Tripoli M, et al. Antimicrobial stewardship at a large tertiary care academic medical center: cost analysis before, during, and after a 7-year program. *Infect Control Hosp Epidemiol.* 2012; 33: 338-45.

 Valerio M, Rodriguez-Gonzalez CG, Muñoz P. et al. Evaluation of antifungal use in a tertiary care institution: antifungal stewardship urgently needed. *J Antimicrob Chemother.* 2014; 69: 1993-9

PDF ARTICLE

 Mondain V, Lieutier F, Hasseine L, et al. A 6-year antifungal stewardship programme in a teaching hospital. *Infection.* 2013; 41: 621-8

VIDEOS

 Prof Patricia Munoz at Fungal Update 2016

 Prof Adilia Warris at Fungal Update 2016

 David Denning - BSAC workshop

# CHAPTER 22

▶ AUTHOR: **SANJAY PATEL**

## STEWARDSHIP IN PAEDIATRICS

### THE AIM OF THIS CHAPTER IS TO:

To explain the reasons why clinicians prescribe antibiotics to children.

To explain the reasons why parents take their child with fever to see a healthcare professional.

To demonstrate that the duration and severity of symptoms is rarely improved with antibiotics in the majority of children with respiratory tract infections.

To provide strategies for clinicians to better negotiate antibiotic decisions with parents.

To provide strategies to effectively steward antimicrobial use in hospitalised children.

### LEARNING OUTCOMES

On completion of this chapter, the participant should understand:

- The aetiology and duration of symptoms differs considerably between adults and children with respiratory tract infections.
- It is extremely difficult for clinicians to reliably distinguish bacterial and viral respiratory tract infections and there are few reliable diagnostic tests available in community based settings. Unfortunately, this uncertainty often results in clinicians prescribing “just in case”, despite the availability of good evidence demonstrating that antibiotics make little or no difference to the speed of symptoms resolution in most children with bacterial RTIs
- Decisions about whether to prescribe antibiotics in children with RTIs should be made using evidence based guidelines. Inconsistent prescribing practices impact on future health seeking behaviour and antibiotic expectations.
- Discussing antibiotic decisions with parents in terms of severe versus non-severe infections is likely to be more effective than an explanation based on distinguishing bacterial and viral infections.
- In children with uncomplicated sore throats, ear, sinus and chest infections, the pros and cons of antibiotics should be discussed with parents before prescribing. Clinicians and parents should consider the relatively small benefits of antibiotics versus the risk of adverse effects, antibiotic resistant infections in the future, and the impact on parental anxiety and future health seeking behaviour.
- Parent satisfaction remains high, even when no prescribing or delayed prescribing approaches are adopted, as long as parental concerns have been addressed during the consultation.
- Antimicrobial stewardship is an extremely effective way of improving antibiotic prescribing within hospital settings. Although there is currently no standardized measure of antibiotic prescribing in children, days of therapy (DOT) is likely to be a useful measure for benchmarking

### ▶ INTRODUCTION

The majority of children with fever and/or infective symptoms who are taken by their parents/ carers for a consultation are looked after by community based healthcare professionals. This explains why 80% of paediatric antibiotic prescribing occurs in community settings.

### WHO IS PRESCRIBING?



General practice

11%



Hospital inpatients

7%



Hospital outpatients

5%



Dental practices

3%



Other community settings

<https://www.gov.uk/government/publications/health-matters-antimicrobial-resistance/health-matters-antimicrobial-resistance>

Respiratory tract infections make up more than 50% of these presentations (Figure 1) and of these, approximately 60% are prescribed antibiotics, although there is good evidence to suggest that the majority of these children gain little or no benefit from them.<sup>1</sup>

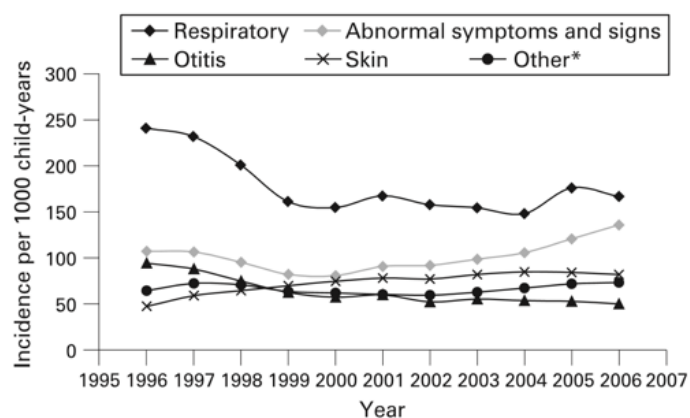


FIGURE 1  
From Thompson PL et al. *ADC* 2009  
Thompson PL, Spyridis N, Sharland M, Gilbert RE, Saxena S, Long PF, et al. Changes in clinical indications for community antibiotic prescribing for children in the UK from 1996 to 2006: will the new NICE prescribing guidance on upper respiratory tract infections just be ignored? *Arch Dis Child*.

Young children are the highest recipients of antibiotics (Figure 2)

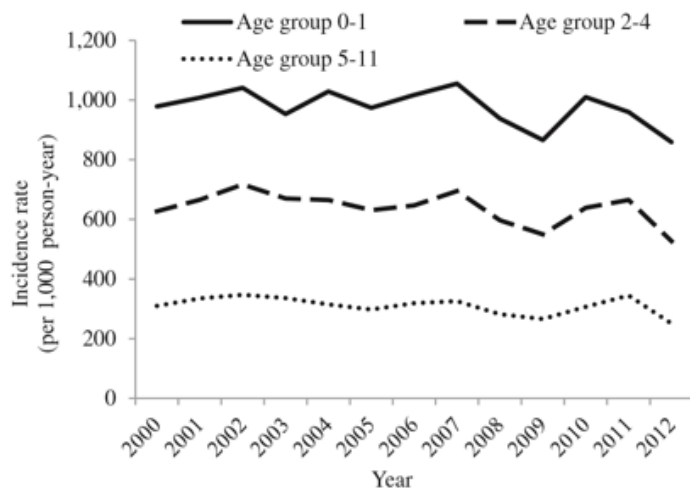
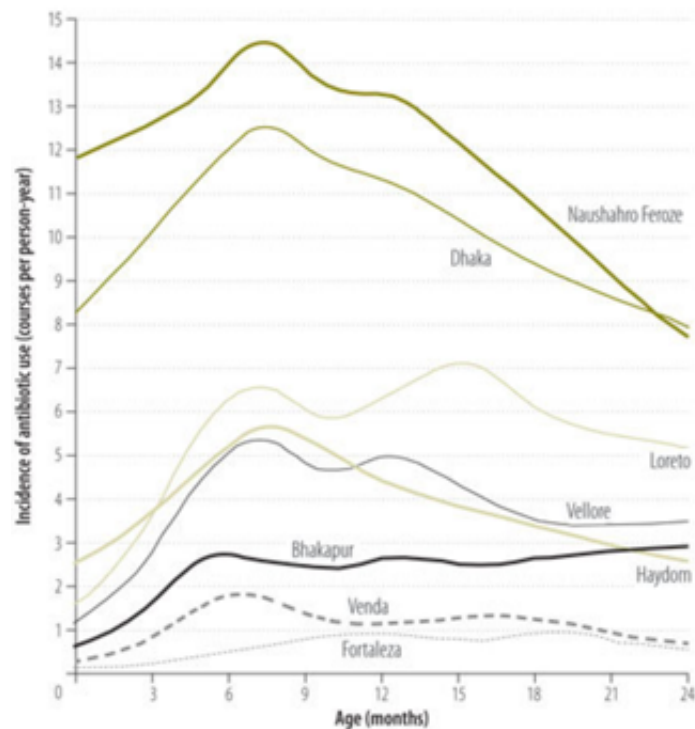


FIGURE 2  
From: Pottegard A, Broe A, Aabenhus R, Bjerrum L, Hallas J, Damkier P. Use of antibiotics in children: a Danish nationwide drug utilization study. *Pediatr Infect Dis J*. 2015; 34(2): e16-22

Rates of antibiotic use in children are considerably higher in low-income countries:



Antibiotic use in children under 2 years of age from sites in eight different countries: Dhaka (Bangladesh), Fortaleza (Brazil), Vellore (India), Bhaktapur (Nepal), Naushahro Feroze (Pakistan), Loreto (Peru), Venda (South Africa) and Haydom (United Republic of Tanzania). Rogawski TE et al. *Bull World Health Organ*. 2017 Jan 1; 95(1): 49–61.

## TOOLKIT RESOURCE

### PDF ARTICLE



Thompson PL, Spyridis N, Sharland M, Gilbert RE, Saxena S, Long PF, et al. Changes in clinical indications for community antibiotic prescribing for children in the UK from 1996 to 2006: will the new NICE prescribing guidance on upper respiratory tract infections just be ignored? *Arch Dis Child*

### SITE LINK



Pottegard A, Broe A, Aabenhus R, Bjerrum L, Hallas J, Damkier P. Use of antibiotics in children: a Danish nationwide drug utilization study. *Pediatr Infect Dis J*. 2015; 34(2): e16-22



This chapter will initially focus on antibiotic prescribing in community based settings, exploring the drivers for prescribing and strategies to address these. Antibiotic stewardship strategies for children with severe infections managed within hospital settings will then be discussed.

## ANTIBIOTIC PRESCRIBING FOR CHILDREN IN COMMUNITY BASED SETTING

### a) Why do clinicians prescribe antibiotics for children?<sup>2</sup>

- Perceived vulnerability of children, especially young children
- Seeking safety in the face of uncertainty (especially if re-presentation)
  - Uncertainty is driven by the difficulty in distinguishing bacterial and viral infections
  - Perceived risk of suppurative complications from an untreated bacterial respiratory tract infection, especially in young children
- Repercussions of “missing something” in a child
  - The media are inclined to pick up on any cases where significant morbidity/death in a child has resulted from a healthcare professional ‘missing’ a severe infection
  - Staff with little experience of seeing unwell children are less confident at ruling out severe infection

### b) Epidemiology of serious infections in children

*Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B are the most common infectious agents responsible for bacterial meningitis and sepsis in children. The introduction of conjugate vaccines against these agents has resulted in a marked reduction in their prevalence in children (Figures 3 to 5, respectively), explaining the significant reduction in rate of serious infections in children over recent years.

### c) Does the natural history of infections in children and adults differ?

One of the reasons that parents request antibiotics is the persistence of symptoms during an infective episode. However, the natural history of respiratory tract infections differs considerably between adults and children, with children often experiencing a considerably longer duration of symptoms following viral infections. Following a rhinovirus infection, 20% of adults remain symptomatic at 10 days, compared to 73% of children. Cough occurs in 40% of adults, with only 20% still affected by day 10, compared to 70% of children experiencing

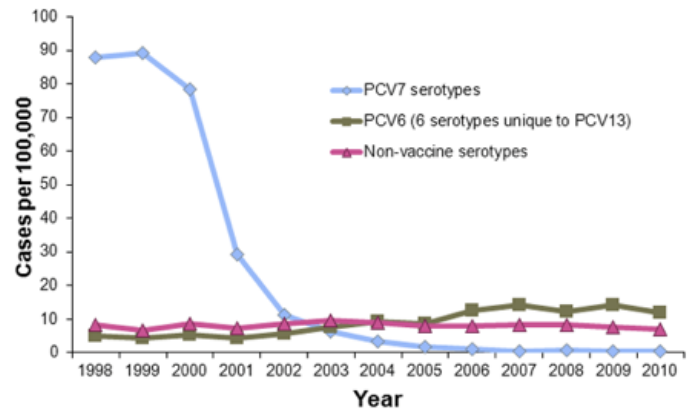


FIGURE 3 Rates of invasive pneumococcal disease among children aged <5 years, 1998-2010, USA <https://www.cdc.gov/vaccines/pubs/surv-manual/chpt11-pneumo.html>

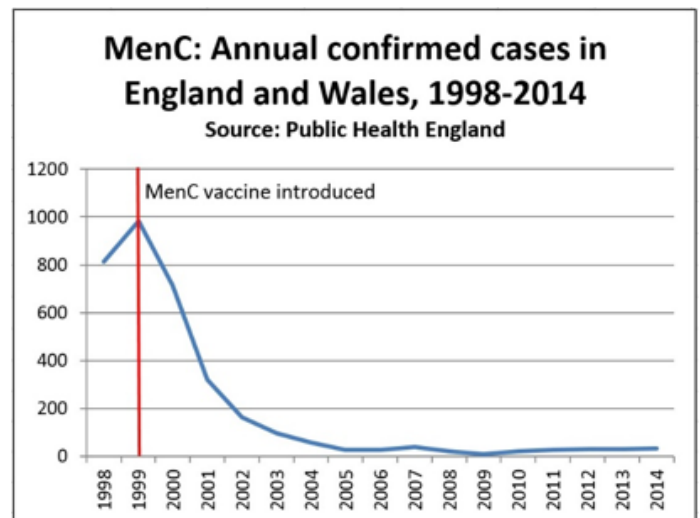


FIGURE 4

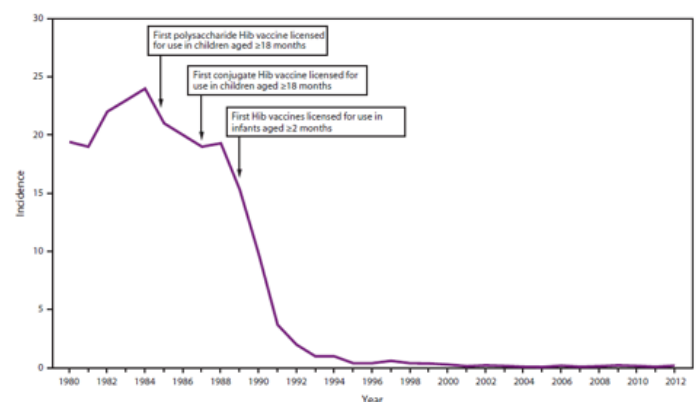


FIGURE 5 Incidence per 100,000 population of invasive *Haemophilus influenzae* type b (Hib) disease in children aged <5 years, 1980-2012, USA <https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6301a1.htm>



cough, with it persisting at day 10 in over 40%. (Cotton et al. S Afr Fam Pract (2004) . 2008 ; 50(2): 6–12).

The aetiology of respiratory tract infections also varies markedly between adults and children. A study of children admitted with lower respiratory tract infections (RTI) demonstrated that a viral cause was responsible in the vast majority (77%). There is even variation within the paediatric population; RTI in young children are more likely to be of viral aetiology than in older children. The prevalence of throat swabs positive for Group A streptococcus is far lower in younger children with acute pharyngitis than in older children (Figure 6).

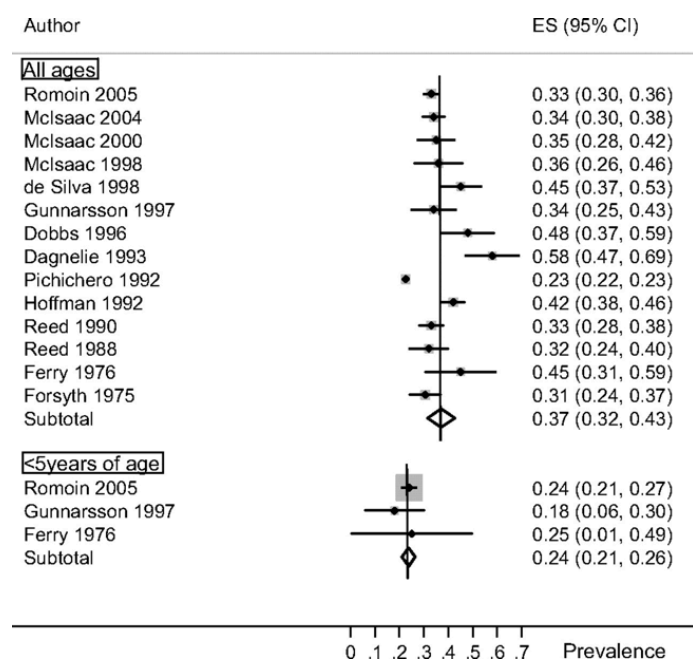


FIGURE 6  
<http://pediatrics.aappublications.org/content/pediatrics/126/3/e557.full.pdf> Shaikh N, Leonard E, Martin JM. Prevalence of streptococcal pharyngitis and streptococcal carriage in children: a meta-analysis. Pediatrics. 2010; 126(3): e557-64.

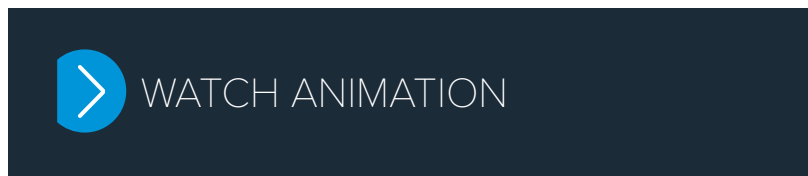
**d) Common misconceptions**

**i) “Parents bringing their child to a GP / ED with a fever usually expect antibiotics”**

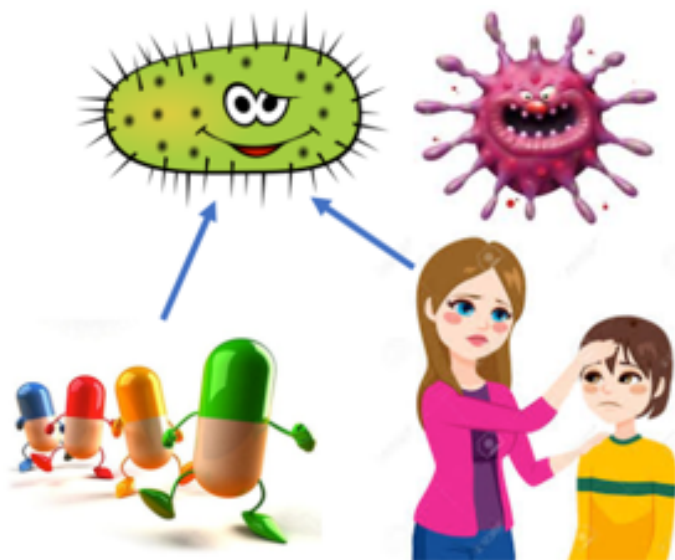
**NOT TRUE** - parents do not generally expect antibiotics when they seek a consultation:<sup>2</sup>

- Parents seek a consultation because:-
  - It provides a proper ‘health-check’ and in their opinion, removes any ‘health-threat’
- Parents lack confidence to distinguish self-limiting illnesses from serious ones but believe that clinicians can

- They want advice on how to manage their child’s symptoms



**ii) “If a parent expects antibiotics, it is because they think that their child has a bacterial infection”**



**NOT TRUE** – parents often feel that antibiotics are required to treat ‘severe’ infections rather than to treat bacterial infections:<sup>3</sup>

- parents often believe that features suggesting a severe infection include high fever, prolonged duration of symptoms and degree of impact on the child (sleep / school)
- Parents perception of susceptibility also plays a role in their expectation for antibiotics (younger, underlying health issues)

**iii) “Withholding antibiotics simply makes parents re-present later / present elsewhere”**

**NOT TRUE** – not prescribing does not increase the rate of representations. Parents are extremely reassured when a shared decision making approach is used to discuss their child’s illness, even when antibiotics are subsequently not prescribed. If anything, parents are less likely to represent during that illness and are often empowered to self-manage future illnesses.<sup>1</sup>

**iv) “If antibiotics are not prescribed, parents are more likely to complain”**

**NOT TRUE** – adopting a shared decision making approach with the parents when managing a child with an infection results in extremely high levels of satisfaction, even when antibiotics are not prescribed.<sup>4</sup>

**v) “Young children are more susceptible to suppurative complications following a respiratory tract infection than older children”**

**NOT TRUE** – young children have far lower rates of suppurative complications than older children, even when antibiotics are not prescribed:<sup>5</sup>

- Rate of mastoiditis following otitis media (age 0-4 years versus 5-15 years): 1.33 vs 2.39 per 10,000
- Rate of quinsy after tonsillitis (age 0-4 years versus 5-15 years): 1.59 vs 5.99 per 10,000

**vi) “Children with infected eczema require antibiotic treatment”**

**NOT TRUE** – Children with skin and soft tissue infections (SSTI) make up an increasing proportion of patients started on antibiotics. There is evidence to suggest that oral and topical antibiotics have no effect (and potentially a harmful effect), on subjective eczema severity in children with clinically infected eczema in the community (Figure 7).

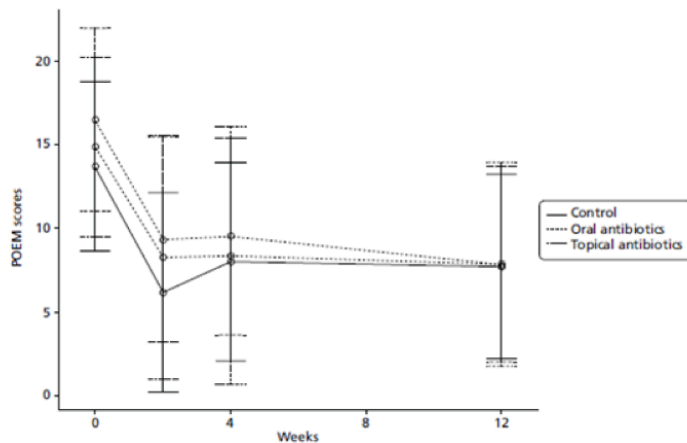


FIGURE 7 FROM: Francis NA, Ridd MJ, Thomas-Jones E, Shepherd V, Butler CC, Hood K, et al. A randomised placebo-controlled trial of oral and topical antibiotics for children with clinically infected eczema in the community: the ChildRen with Eczema, Antibiotic Management (CREAM) study. Health Technol Assess. 2016; 20(19): i-xxiv, 1-84. <https://www.journalslibrary.nihr.ac.uk/hta/hta20190/#/abstract>

**e) What’s the best way to negotiate antibiotic decisions with parents?**

By assuming that parents expect antibiotics when their child is unwell, there is a risk that this becomes the focus of the consultation, with the clinician trying to justify their decision not to prescribe antibiotics. This approach also commonly results in clinicians explaining illness in terms of bacterial and viral infections. Unfortunately, parents rarely seek antibiotics because they think their child has a bacterial illness; instead their opinions about antibiotic need are based on their perception of severity of illness in their child, including factors such as impaired sleep, height of fever and prolonged duration of symptoms.<sup>3</sup>

**Bacteria versus virus?**



**Severe versus non-severe?**

A more effective approach to achieving a successful consultation involves focusing on the reasons the parent sought a consultation. It is important to reassure the family that although their child has an infection that is having an impact on their sleep/feeding, their symptoms are not indicative of a severe infection in terms of objective parameters / ‘red-flags’. Parents should also be provided with information about the likely duration of symptoms and advice on how to manage them. Most importantly, one must clearly explain the symptoms that parents should look out for and the actions required if they were to occur. All this information should ideally be provided both verbally and in writing. Using such a shared decision making decision approach results in marked reductions in antibiotic prescribing.<sup>4</sup>

Another effective strategy that can be used in conjunction with the approaches outlined above is the use of delayed prescribing, where an antibiotic prescription can be collected at the parents’ discretion after 72 hours if they feel that their child still not improving. Parents are often extremely reassured when such an approach is adopted and the overall use of antibiotics is reduced by up to 80% in some studies.<sup>1</sup>

**f) Do all children with bacterial respiratory tract infections require treatment with antibiotics?**

One of the major challenges facing clinicians is distinguishing whether a child presenting with an RTI has a bacterial or viral infection. It is often extremely difficult to make this decision clinically and there are few reliable diagnostic tests that can assist in a community based setting. This uncertainty often results in clinicians prescribing “just in case”. However, there is an increasing body of evidence to show that antibiotics do not significantly reduce severity or duration of symptoms in the majority of children with RTIs, irrespective of the aetiology: -

i) Acute otitis media (AOM)

A systematic review of 13 RCTs (3401 children and 3938 AOM episodes) from high-income countries demonstrated that antibiotics have no early effect on pain, a slight effect on pain in the days following and only a modest effect on the number of children with tympanic perforations, contralateral otitis episodes and abnormal tympanometry findings at two to four weeks and at six to eight weeks compared with placebo. This suggests that in high-income countries, most cases of AOM spontaneously remit without complications.

Even in children with AOM under 2 years of age, there is evidence to suggest that antibiotics make very little difference to the severity of symptoms in the majority of children (Figure 8):

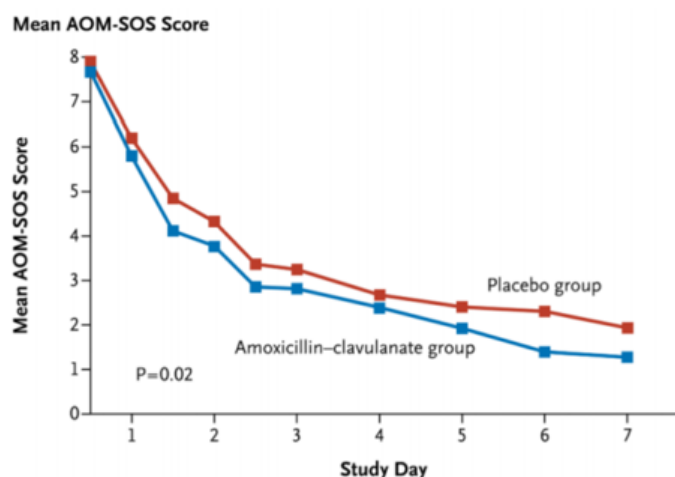


FIGURE 8 Resolution of symptoms in children under 2 years of age with AOM Hoberman A et al. Treatment of acute otitis media in children under 2 years of age. N Engl J Med. 2011 Jan; 364(2):105-115 Copyright © (notice year) Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society

ii) Tonsillitis

There is data, albeit limited, to suggest that antibiotics have little or no impact in reducing the severity of symptoms in the majority of children with acute tonsillitis:

Study or subgroup	Antibiotics n/N	Placebo n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
I Symptom of fever on day 3: children					
Krober 1985	0/15	0/11			Not estimable
Nelson 1984	12/17	10/18		36.0 %	1.27 [ 0.76, 2.13 ]
<b>Subtotal (95% CI)</b>	<b>32</b>	<b>29</b>		<b>36.0 %</b>	<b>1.27 [ 0.76, 2.13 ]</b>

From Spinks at al: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000023.pub4/full>

Spinks A, Glasziou PP, Del Mar CB. Antibiotics for sore throat. Cochrane Database Syst Rev. 2013; (11): CD000023

iii) Lower respiratory tract infections (LRTIs)

The lack of evidence around the benefits of antibiotics in children with LRTIs is suggested by the fact that there is currently a randomised controlled trial recruiting children between 6 months and 12 years of age presenting with an acute uncomplicated lower respiratory infection (LRTI), defined as an acute cough as the predominant symptom, judged to be infective in origin, lasting <21 days. Patients will be randomised to either an antibiotic arm (amoxicillin) or a placebo arm for 7 days and the primary outcome being evaluated is the duration of significant symptoms

g) So which children with RTIs should we be treating with antibiotics?

i) Acute otitis media

Consider starting oral antibiotics only if any of the following criteria are met in a child presenting with AOM (bulging ear drum or discharge):-

- Symptoms for 4 days or more
- Purulent discharge from ear canal (not due to otitis externa)
- Systemically unwell
- Under 6 months of age with presumed AOM
- In children 6 months - 2 years old:-
  - Bilateral OM
  - Unilateral OM and symptom score of >8 in children 6 months - 2 years old (0=no symptoms, 1=a little, 2=a lot) for the following criteria:-
    - fever (>39°C = score of 2)
    - tugging ears

- crying more
- irritability
- difficulty sleeping
- less playful
- eating less

### ii) Tonsillitis

Base decision to treat on FeverPAIN score (Fever, Purulence, Attend within 3 days of onset or less, severely Inflamed tonsils, No cough or coryza)

### SEE SCORE

- score 0-1 = 18% streptococci: use no antibiotics
- score 2-3: 34-40% streptococci, use back up/delayed antibiotic
- score  $\geq 4$ : 62-65% streptococci, use immediate antibiotic

This score is validated in children aged 3 years and older. However, younger children are less likely to have a bacterial aetiology and are less likely to develop complications.

### iii) LRTIs

There is a paucity of evidence to guide antibiotic prescribing decisions in children and most national guidelines tend to focus on LRTIs in adults. Prior to the results of the ARTIC PC study being made available,

### VISIT SITE

a pragmatic approach seems most appropriate, with consideration of antibiotics if persistent/recurrent fever over preceding 24-48 hours with chest wall recession and tachypnoea.

### h) Educational strategies

Clinicians should be provided with up to date information on antimicrobial stewardship and the management of paediatric infections within robust education programmes. Priority should be placed on ensuring that consistent management approaches are adopted across community settings and front of house hospital settings (emergency department/paediatric assessment

unit). Inconsistent prescribing practices impact on health seeking behaviour and antibiotics expectations during future infective episodes.

## TARGET ANTIBIOTIC WEBINAR SERIES - ANTIBIOTICS FOR CHILDREN



## TOOLKIT RESOURCE

### PDF ARTICLES



Shaikh N, Leonard E, Martin JM. Prevalence of streptococcal pharyngitis and streptococcal carriage in children: a meta-analysis. *Pediatrics*. 2010; 126(3): e557-64



Hoberman A et al. Treatment of acute otitis media in children under 2 years of age. *N Engl J Med*. 2011 Jan; 364(2):105-115 Copyright © (notice year) Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society

### SITE LINKS



<https://www.cdc.gov/vaccines/pubs/surv-manual/chpt11-pneumo.html>



<https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6301a1.htm>



Cotton et al. *S Afr Fam Pract* (2004) . 2008 ; 50(2): 6-12





Francis NA, Ridd MJ, Thomas-Jones E, Shepherd V, Butler CC, Hood K, et al. A randomised placebo-controlled trial of oral and topical antibiotics for children with clinically infected eczema in the community: the ChildRen with Eczema, Antibiotic Management (CREAM) study. *Health Technol Assess*. 2016; 20(19): i-xxiv, 1-84

## TOOLKIT RESOURCE

## SITE LINKS

 <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000023.pub4/full>

 Spinks A, Glasziou PP, Del Mar CB. Antibiotics for sore throat. *Cochrane Database Syst Rev.* 2013; (11): CD000023

 Antibiotics for Lower Respiratory Tract Infection in Children presenting in Primary Care

## ANTIBIOTIC PRESCRIBING FOR CHILDREN IN HOSPITAL SETTINGS

Over 35% of paediatric inpatients receive at least one antimicrobial on any given day. An even greater percentage of children are on antimicrobials in tertiary centres. Parenteral administration is very common in Asia (88%), Latin America (81%) and Europe (67%) and critically important antibiotics for hospital-acquired infections are used more commonly in neonates than in children (34.9% versus 28.3%). Table 2 outlines the most-commonly recorded reasons for prescribing antibiotics in children and neonates in hospital.<sup>16</sup> A significant proportion of neonates and children are receiving these antimicrobials inappropriately.

Top 10 most-recorded reasons to treat children ( $\geq 1$  month) and neonates ( $\leq 30$  days)

Reason to treat (children)	%	Reason to treat (neonates)	%
Bacterial lower respiratory tract infection	18.7	sepsis	36.4
Prophylaxis for medical problems	15.1	prophylaxis for maternal risk factors	12.2
Prophylaxis for surgical disease	9.9	prophylaxis for newborn risk factors	11.3
Sepsis	9.0	lower respiratory tract infection	8.7
Treatment for surgical disease	6.1	prophylaxis for surgical disease	5.4
Urinary tract infection (upper and lower)	5.6	prophylaxis for medical problems	5.1
Febrile neutropenia/fever in oncologic patients	4.8	catheter-related bloodstream infection	3.4
Upper respiratory tract infection	4.6	CNS infections	3.2
Skin/soft tissue infections	4.4	treatment for surgical disease	2.6
Viral lower respiratory tract infection	3.7	skin/soft tissue infections	2.6

TABLE 2

From Versporten et al: <https://academic.oup.com/jac/article-lookup/doi/10.1093/jac/dkv418> Include link to article in Toolkit Resource [Versporten A, Bielicki J, Drapier N, Sharland M, Goossens H. The Worldwide Antibiotic Resistance and Prescribing in European Children (ARPEC) point prevalence survey: developing hospital-quality indicators of antibiotic prescribing for children. *J Antimicrob Chemother.* 2016; 71(4): 1106-17.]

### a) Antimicrobial stewardship in hospitalised children

Although far fewer children receive antibiotics in hospital settings than in community based settings, the impact of injudicious prescribing in hospitals can be catastrophic, including outbreaks of highly resistant infections resulting in significant mortality and morbidity.

Active surveillance of antimicrobial prescribing (antimicrobial stewardship) is more easily performed in hospital than in community based settings. The principles of antimicrobial stewardship (prospective audit with intervention and feedback +/- formulary restriction and preauthorisation) apply equally to children as they do to adults (Table 1). In paediatric patients, as in adults, the successful implementation of stewardship strategies have a significant impact on reducing overall antimicrobial use, broad spectrum intravenous antibiotic use, and reducing rates of resistance, along with delivering substantial cost savings. There are some unique challenges in paediatrics, however, including a paucity of data on optimal antimicrobial strategies,<sup>7</sup> a relative lack of local microbiological data to guide empirical antibiotic choices and limited human resources available for stewardship activities. Clinical challenges include:

- Severe childhood infection often presenting with non-specific symptoms and signs, especially in infants and neonates
- Young infants (<3 months of age) being at considerably higher risk of early and late-onset sepsis due to invasive infection
- Commonly used investigations such as C-reactive protein and blood cultures lacking sensitivity in young children



**TABLE 1. Key Principles of Pediatric Antimicrobial Stewardship**

Area Addressed	Principles	Strategies in Highly Regulated, Structured Healthcare Setting	Strategies in Poorly Regulated, Minimally Structured Healthcare Setting	Examples of Key Professionals Involved in Implementation of Context-specific Strategies
Timely antibiotic management <b>Who? When?</b>	<ul style="list-style-type: none"> <li>- Prompt initiation of AM therapy if bacterial infection suspected</li> <li>- Avoid using AMs when not indicated (eg, upper respiratory tract infection)</li> <li>- Inclusion of guidance on clinical syndromes that do and do not require AM therapy in clinical guidelines and algorithms</li> </ul>	<ul style="list-style-type: none"> <li>Use care bundles supported by electronic prescribing and automated algorithms</li> <li>Use strategies such as delayed prescribing for patients unlikely to benefit from immediate antibiotic treatment</li> </ul>	<ul style="list-style-type: none"> <li>Develop regulatory approaches to deal with counterfeit or poor-quality antibiotics</li> <li>Train community pharmacists and community and hospital health workers on rational antibiotic dispensing including alternative pharmacological treatments for minor illnesses</li> </ul>	<ul style="list-style-type: none"> <li>- First contact AM prescribers (community and hospital)</li> <li>- Pharmacists (community and hospital)</li> <li>- Regulators</li> <li>- Public health practitioners and organizations</li> </ul>
Appropriate selection of antibiotics <b>What?</b>	<ul style="list-style-type: none"> <li>- Selection of appropriate AM regimens</li> <li>- Selection of AMs on basis of local antibiograms and guidelines with preference given to AMs less likely to promote the emergence of resistance</li> </ul>	<ul style="list-style-type: none"> <li>Develop and use rapid microbiological diagnostics and biomarkers</li> <li>Regular automated review of local microbiology resistance data to update empiric AM prescribing guidelines</li> </ul>	<ul style="list-style-type: none"> <li>Specify responsibility for and mechanisms to ensure guidelines are available, relevant to context and up to date</li> <li>Establish surveillance activities to collect regional or local microbiological data</li> </ul>	<ul style="list-style-type: none"> <li>- First contact AM prescribers (community and hospital)</li> <li>- AM experts, eg, infectious diseases specialists</li> <li>- Pharmacists (community and hospital)</li> <li>- Microbiologists</li> <li>- Epidemiologists and public health practitioners</li> </ul>
Appropriate administration and de-escalation of antibiotics <b>How?</b>	<ul style="list-style-type: none"> <li>- Optimize dosing (ie, never use "low dose")</li> <li>- Review microbiology and clinical status at 48–72 h to decide: stop, switch, continue, modify</li> <li>- Administer short antibiotic courses as appropriate</li> <li>- Therapeutic drug monitoring</li> <li>- Appropriate prophylactic use of AMs</li> </ul>	<ul style="list-style-type: none"> <li>Restrict formulary for empiric treatment at 48h for inpatients to encourage review of prescriptions and de-escalation</li> <li>Include recommendations for iv to oral switching and outpatient parenteral antibiotic therapy in guidelines</li> </ul>	<ul style="list-style-type: none"> <li>Ensure availability of pediatric formulations to overcome need for manipulation of AMs, eg, solid forms, and to ensure appropriate dosing</li> <li>Use antimicrobial batching to maximize use of antimicrobials for a specific duration and at a specific dose</li> </ul>	<ul style="list-style-type: none"> <li>- Pharmacists (community and hospital)</li> <li>- First contact AB prescribers (community and hospital)</li> <li>- AB champions who can provide AS interventions</li> <li>- AM experts, eg, infectious diseases specialists</li> <li>- Microbiologists</li> <li>- Pharmaceutical companies (including generics manufacturers)</li> </ul>
Use of expertise and resources <b>Resources</b>	<ul style="list-style-type: none"> <li>- Establishment of AS teams/committees and identification of AS champions</li> <li>- Administrative and leadership support</li> <li>- Collaboration with manufacturers</li> </ul>	<ul style="list-style-type: none"> <li>Form stewardship teams building on locally available expertise and with support from regulatory and management bodies</li> </ul>	<ul style="list-style-type: none"> <li>Identify local antibiotic champion and provide training ("knowledge brokers")</li> </ul>	<ul style="list-style-type: none"> <li>- AB champions as lead</li> <li>- All of the above</li> <li>- Healthcare managers, administrators and funders</li> </ul>
Continuous and transparent monitoring of antibiotic use and antimicrobial resistance <b>Information</b>	<ul style="list-style-type: none"> <li>- Audit and feedback</li> <li>- Education</li> <li>- Prospective monitoring of relevant outcomes</li> <li>- Benchmarking</li> </ul>	<ul style="list-style-type: none"> <li>Ensure ongoing, prospective and openly accessible (at local or higher level) monitoring of key parameters to identify areas for intervention</li> <li>Involve prescribers in the development and implementation of benchmarking activities including strategies for case-mix adjustment</li> </ul>	<ul style="list-style-type: none"> <li>Use run charts and other simple devices to provide immediate feedback on the success of implementing key stewardship activities</li> <li>Foster co-operation and data sharing between different providers as a means of strengthening stewardship networks</li> </ul>	<ul style="list-style-type: none"> <li>- Microbiologists</li> <li>- Pharmacists (community and hospital)</li> <li>- Epidemiologists</li> <li>- Public health practitioners</li> <li>- Regulatory bodies</li> </ul>

From Bielicki et al. PIDJ 2015 [http://journals.lww.com/pidj/fulltext/2015/03000/Antimicrobial\\_Stewardship\\_for\\_Neonates\\_and.29.aspx](http://journals.lww.com/pidj/fulltext/2015/03000/Antimicrobial_Stewardship_for_Neonates_and.29.aspx)



Although the majority of hospitals have local prescribing guidelines for common infections, formal paediatric antimicrobial stewardship remains rather rudimentary in the majority of paediatric and neonatal in-patient settings.

## i) Children with co-morbidities

Children with co-morbidities post challenges in terms of antimicrobial stewardship: -

- their potential for rapid deterioration often results in a lower threshold for commencing antibiotics
- they are often vulnerable in terms of impaired immunity and the presence of indwelling devices, meaning that empirical antibiotic choices need to take account of a wider range of potential pathogens and pathologies
- they are more likely to be colonised with resistant organisms, which often results in broader spectrum antibiotics being used empirically

## ii) Hospital acquired infections

Bloodstream infections account for a particularly high proportion of paediatric hospital acquired infections compared with all other medical specialities. Not only are clear guidelines required for the management of these infections, including information on the timely removal of central lines, but more importantly, robust infection control measures must be in place, including central line care bundles to avoid unnecessary exposure to long courses of IV antibiotics and increased mortality and morbidity.



## EVALUATING THE QUALITY OF ANTIBIOTIC PRESCRIBING IN CHILDREN

Collecting data on antibiotic prescribing allows the quality of prescribing and the effectiveness of stewardship activities to be evaluated. In addition, providing feedback to clinicians about their prescribing is an important way to obtain 'buy-in' and is likely to be an effective driver for sustaining behaviour change.

However, a major challenge is quantifying the volume of antibiotics prescribed to children. The most commonly used measure in adults is the defined daily dose (DDD; the assumed average maintenance dose per day for a drug used for its main indication in adults). Weight variation in children means that DDD has a very limited role in accurately quantifying paediatric antibiotic prescribing and is a poor marker for benchmarking. Although there is currently no standardized measure of antibiotic prescribing in children, days of therapy (DOT) is likely to be a far more useful measure (Figure 9).

Metrics for benchmarking include:

- Total antibiotic use (DOT)
- Total parenteral antibiotic use (DOT)
- Total oral antibiotic use (DOT)
- Broad-spectrum parenteral antibiotic use (DOT)
- Combination parenteral antibiotic use (DOT)
- Total oral antibiotic use in respiratory tract infections (DOT)
- Broad spectrum oral antibiotic use in respiratory tract infections (DOT)
- Antibiotic use for surgical prophylaxis (DOT)
- Antibiotic use for medical prophylaxis (DOT)

## TOOLKIT RESOURCE

### SITE LINKS



Versporten A, Bielicki J, Drapier N, Sharland M, Goossens H. The Worldwide Antibiotic Resistance and Prescribing in European Children (ARPEC) point prevalence survey: developing hospital-quality indicators of antibiotic prescribing for children. *J Antimicrob Chemother.* 2016; 71(4): 1106-17.



Bielicki J, Lundin R, Patel S, Paulus S. Antimicrobial stewardship for neonates and children: a global approach. *Pediatr Infect Dis J.* 2015; 34(3): 311-3.

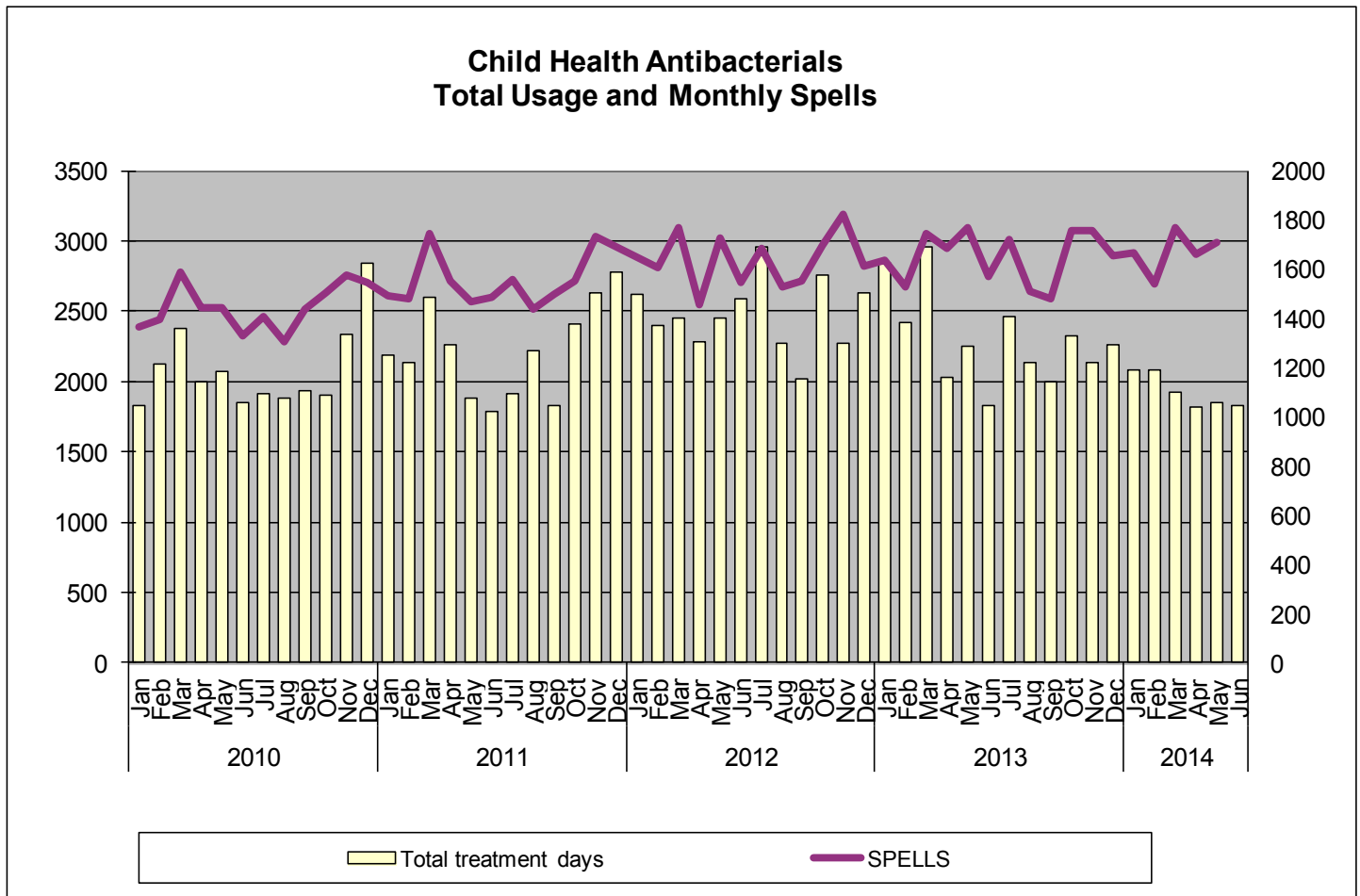


FIGURE 9 Example of paediatric antibiotic surveillance and impact of thrice weekly paediatric stewardship rounds at University Hospitals Southampton, UK

In addition to measuring the quantity of antimicrobial prescribing, it is important to measure the quality of prescribing, including:

- Documentation of the reason for antimicrobial prescribing
- Adherence to local prescribing guidelines
- Dosing as per local prescribing guidelines

The implementation of a paediatric antimicrobial stewardship programme over several years at a Children’s hospital in the USA has been evaluated:

Although the collection of high quality data in community settings is often challenging, it is essential that metrics on antibiotic prescribing in these children are collected in order to evaluate the impact of community based interventions to improve prescribing and to facilitate benchmarking between clinicians and centres.



## SUMMARY

The vast majority of paediatric antibiotic prescribing occurs in community settings. Although extremely challenging, focusing interventions on this cohort of children is likely to have the greatest impact on population level prescribing. However, it is often difficult to collect high quality prescribing data on this cohort of children and antibiotic stewardship strategies used to improve antibiotic prescribing in hospital setting are often hard to implement in community based settings. Prioritising data collection is essential for getting buy-in from clinicians and is likely to be an effective driver for behaviour change.

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# CHAPTER 23

› AUTHOR: **PRIYA NORI**

## ANTIMICROBIAL STEWARDSHIP AND OPAT

### THE AIM OF THIS CHAPTER IS TO:

To describe the core elements of OPAT care bundles and their relationship to antimicrobial stewardship.

To define distinct models of OPAT delivery and their ideal settings.

To identify potential conflicts between core stewardship principles and feasibility of OPAT.

To highlight the individual roles of the stewardship pharmacist and physician in improving OPAT care.

To identify unique challenges to OPAT in various countries.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Describe key elements of a multi-disciplinary OPAT bundle
- Outline distinct models of OPAT care delivery
- Describe unique challenges to OPAT in different parts of the world
- List examples of challenges central to the OPAT-stewardship dilemma, such as antibiotic spectrum versus convenience of dosing

### CLINICAL VIGNETTE:

A 75-YEAR-OLD FEMALE WITH HISTORY OF OBESITY AND DIABETES IS ADMITTED TO THE HOSPITAL WITH 3 WEEKS OF RIGHT KNEE PAIN, SWELLING, AND WARMTH. SHE HAS HISTORY OF PRIOR BILATERAL TOTAL KNEE ARTHROPLASTY 10 YEARS AGO. PHYSICAL EXAM REVEALS DEHISCENCE OF PRIOR SURGICAL WOUND WITH PURULENT DRAINAGE. SHE UNDERGOES DEBRIDEMENT OF RIGHT KNEE INFECTION WITH EXPLANT OF OLD PROSTHESIS AND PLACEMENT OF AN ANTIBIOTIC IMPREGNATED SPACER. SYNOVIAL TISSUE CULTURES REVEAL METHICILLIN SUSCEPTIBLE STAPHYLOCOCCUS AUREUS. SHE IS TREATED WITH IV CEFAZOLIN 2G EVERY 8 HOURS INITIALLY, THEN DISCHARGED HOME ON IV CEFTRIAZONE 2G DAILY TO COMPLETE A 6-WEEK COURSE

**> INTRODUCTION**

Outpatient parenteral antibiotic therapy (OPAT) is a well-established, cost-effective solution to prolonged hospitalisation for management of complex infections<sup>1</sup>. The goal of OPAT is the provision of high quality anti-infective therapy accessible across a multitude of patient care settings. Over 3 decades of North American and European OPAT experience attests to the success and sustainability of OPAT programs<sup>2,3</sup>. Care of OPAT patients is a coordinated, multidisciplinary effort at each stage: <sup>1</sup>) initial presentation to the acute care setting, <sup>2</sup>) inpatient convalescence, <sup>3</sup>) transition of care to home or skilled nursing facility, and finally, <sup>4</sup>) post-acute care by the OPAT team<sup>4</sup>. Reductions in hospital lengths of stay, readmission rates, antibiotic utilisation, and optimisation of patient outcomes are goals central to OPAT, hospital administration, and antimicrobial stewardship.

In 2013, Muldoon et al. proposed a bundle of OPAT program best practices including appropriate patient selection, infectious diseases consultation, patient/caregiver education, discharge planning, outpatient monitoring/tracking, and a program outcomes review for quality assurance<sup>5</sup>

Several of the proposed bundle elements align with the expertise of antimicrobial stewardship programs and represent core stewardship functions discussed in chapters 2 and 3 (see figure 2):

- 1 Initial selection of the appropriate antimicrobial regimen for a given indication, dose, route, and projected treatment duration by the infectious diseases (ID) consultative service (clinicians and pharmacists)
- 2 Monitoring for clinical response, antimicrobial tolerability, and adjustment of regimens based on alterations in laboratory parameters
- 3 Selection of the most appropriate, tolerable, and feasible discharge regimen considering factors such as antimicrobial cost, drug stability in the outpatient setting, and compatibility with selected IV access
- 4 Appropriateness and timing of IV to PO switch considering penetration at the site of infection <sup>5</sup>.
- 5 Education and counselling on risk factors for infection recurrence, infection prevention, and treatment goals and expectations <sup>4,6</sup>.

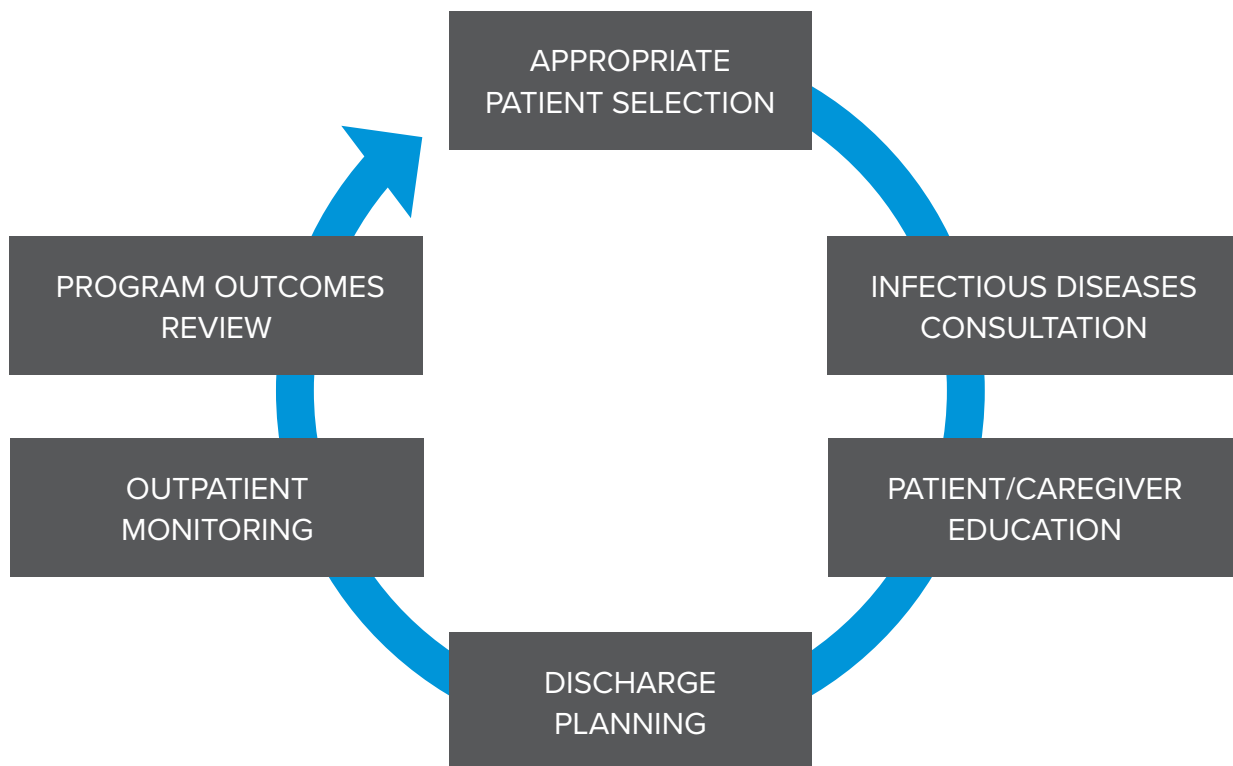








FIGURE 1  
OPAT Bundle for Patient Care Optimisation<sup>5</sup>

# TOOLKIT RESOURCE

## SITE LINK

-  Financial impact of a home intravenous antibiotic program on a medicare managed care program.
-  Good practice recommendations for outpatient parenteral antimicrobial therapy (OPAT) in adults in the UK: a consensus statement
-  Practice guidelines for outpatient parenteral antimicrobial therapy. IDSA guidelines
-  Bundle in the Bronx: Impact of a Transition-of-Care Outpatient Parenteral Antibiotic Therapy Bundle on All-Cause 30-Day Hospital Readmissions
-  Are we ready for an outpatient parenteral antimicrobial therapy bundle? A critical appraisal of the evidence
-  Outpatient parenteral antimicrobial therapy and antimicrobial stewardship: challenges and checklists

6 Input on cessation of antibiotics at clinical cure or clinical failure, if the later is due to surgical disease such as retained prosthesis or necrotic bone

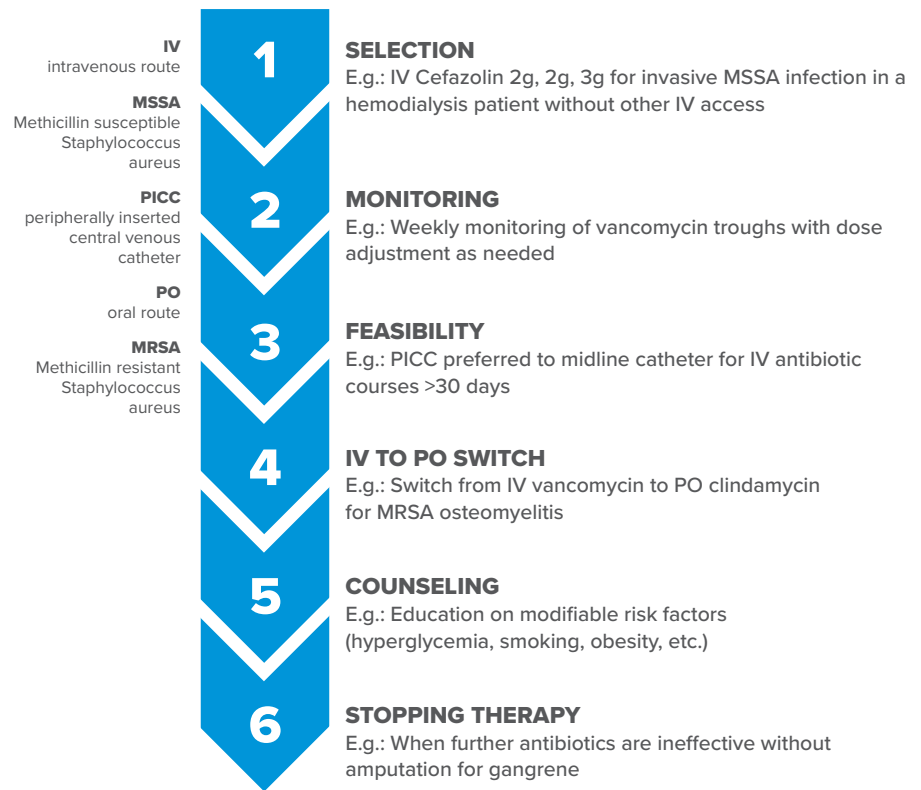


FIGURE 2 Continuum of Stewardship Core Activities within OPAT Programs

## TRANSITIONS OF CARE FROM ACUTE TO POST-ACUTE OPAT CARE SETTINGS

A transition-of-care OPAT service coordinating both inpatient and outpatient aspects of management may potentially impact outcomes and processes of care. In 2013, Keller and colleagues reported results of a controlled, quasi-experimental study of a newly implemented infectious diseases transition service (IDTS) for OPAT patients discharged from the Hospital of the University of Pennsylvania, most of whom received OPAT from a home health agency. Primary outcomes included readmissions and ED visits within 60 days of discharge, while secondary outcomes included process of care measures (e.g. antimicrobial therapy errors, laboratory test receipt, outpatient follow-up) and non-readmission clinical outcomes (mortality within 60 days of discharge, *Clostridium difficile* infections, adverse antimicrobial events, and catheter complications). After adjusting for covariates, no significant difference in primary outcome was observed between intervention arm and control arm patients (adjusted odds ratio [OR] = 0.48; 95% CI 0.13-1.79), however, implementation of the IDTS was associated with fewer antimicrobial therapy errors (OR = 0.062; 95% CI = 0.015-0.262) increased laboratory test receipt (OR 27.85; 95% CI 12.93-59.99), an improved outpatient follow-up (OR = 2.44; 95% CI 1.50-3.97). A significant difference in use of penicillins and cephalosporins was observed between intervention and control arm patients, but the impact of this difference on outcomes is not known (together, these drug classes accounted for over 50% of antimicrobials used in the study)<sup>7</sup>.



## ▶ OPAT PATIENT DIVERSITY AND DISTINCT OPAT CARE MODELS

OPAT patients share comorbidities (diabetes mellitus, chronic kidney dysfunction, vascular disease, etc.), and all require extended antibiotic courses for moderate to severe, often chronic or recurrent infections<sup>4</sup>. However, they hail from diverse socioeconomic backgrounds and geographic settings (e.g. urban versus suburban or rural populations; community residents versus skilled nursing or long term care residents). Variable health insurance coverage of costly antimicrobials and skilled nursing services is challenge unique to OPAT patients in countries with a substantial mix of private and government insurance plans. These factors may influence the selection of the OPAT regimen by the ID consultative team. Upon transition of patient care to the post-acute care setting, home infusion therapy versus placement in a skilled nursing facility for receipt of OPAT is also influenced by insurance coverage, patient functional status and need for additional skilled nursing services.

In the United States, Medicare part D may cover the cost of intravenous (IV) antibiotics but may not cover infusion-related nursing services and supplies associated with in home administration of OPAT<sup>8</sup>. For instance, while generic daptomycin has been available in the United States since 2016, extended courses utilised in the treatment of complex or refractory methicillin resistant *Staphylococcus aureus* (MRSA) infections are associated with a significant cost, with a 500mg vial costing roughly \$360 to \$382 USD<sup>9</sup>. Therefore, OPAT utilisation of daptomycin remains limited, especially in economically disadvantaged areas of the US. However, in the UK, there are multiple reports of successful daptomycin use for OPAT, perhaps due to fewer financial barriers, ease of administration, and patient tolerance (once daily dosing and short infusion times)<sup>10</sup>.





### DISTINCT OPAT MODELS CAN BE INDIVIDUALISED TO AVAILABLE RESOURCES, PATIENT DEMOGRAPHICS, GEOGRAPHY, AND ACCESS TO SPECIALTY SERVICES:

- Centralised OPAT at ambulatory infusion centers (office or hospital-based)
- Home-based OPAT via licensed infusion and skilled nursing agencies, or
- OPAT within skilled nursing facilities

 PDF ARTICLE

## TOOLKIT RESOURCE

### SITE LINKS



-  7. The Impact of an Infectious Diseases Transition Service on the Care of Outpatients on Parenteral Antimicrobial Therapy
-  8. <https://www.medicare.gov/part-d/coverage/part-d-coverage.html>. Accessed July 1, 2017
-  9. <https://www.drugs.com/price-guide/daptomycin>. Accessed July 1, 2017
-  10. Developments in outpatient parenteral antimicrobial therapy (OPAT) for Gram-positive infections in Europe, and the potential impact of daptomycin

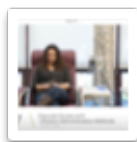
In all models, infectious diseases specialists serve as OPAT leaders coordinating patient care and clinically monitoring patients at outpatient follow up visits. However, comprehensive OPAT management (patient outreach, IV access care, monitoring of labs, education, and counseling) is multidisciplinary endeavor of trained nurses, pharmacists, and outreach coordinators<sup>4</sup>. Ambulatory infusion centres are best suited to populous urban areas where patients are not required to travel far distances for their infusions, and OPAT programs are financially sustainable due to high patient volume and revenue generated<sup>11</sup>.

In rural or remote regions, home infusion therapy may be preferred due to patient convenience and distance from infusion clinics. For instance, in Canada, the prevalence of existing OPAT programs is not well understood, but availability of OPAT services varies based on province, geography, and access to clinics<sup>12</sup>.

## TOOLKIT RESOURCE

### SITE LINKS

- A 1-year retrospective review of outcomes of an informal OPAT program in Toronto identified readmissions and repeat emergency department visits in nearly 50% of patients. This led to the allocation of resources for a coordinated and structured OPAT program
-  11. Legal and Reimbursement Issues in OPAT. IDSA OPAT-ebook
  -  12. Patient Characteristics and Outcomes of Outpatient Parenteral Antimicrobial Therapy: A Retrospective Study



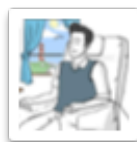
**AMBULATORY  
INFUSION  
CENTER**

**Pros:**

- Well-monitored setting
- Staff on site to troubleshoot problems
- Clinical care and infusion therapy centralised

**Cons:**

- More feasible in urban or suburban settings
- Success relies on patient adherence to visits



**HOME INFUSION BY  
PATIENT, CAREGIVER  
OR NURSE**

**Pros:**

- Patient independence
- Comfortable setting
- Regular nursing visits to monitor and troubleshoot problems
- Feasible in rural settings

**Cons:**

- Regular physician visits necessary
- Success relies on high-functioning patient or caregiver and adherence to treatment plan



**SKILLED  
NURSING  
FACILITY**

**Pros:**

- Well-monitored setting with additional therapeutic services (physical therapy, wound care, etc.)
- Feasible in rural, urban, or suburban settings
- On site physician visits and nursing care

- Success less dependent on patient adherence

**Cons:**

- Loss of independence
- Unfamiliar setting

FIGURE 3  
Pros and Cons of Distinct OPAT Models

**THE PHYSICIAN STEWARD AND OPAT CARE IN THE UNDERSERVED**

Like other urban centers, New York City (NYC) presents a unique opportunity for OPAT given that patients are often medically complex, socioeconomically disadvantaged, or have limited functional status requiring intensive nursing care. Antimicrobial stewardship (selection of the most tolerable and narrow-spectrum OPAT regimen for the appropriate duration), stewardship of microbiologic testing and resource allocation is of particular concern in this setting. With the emergence of rapid molecular diagnostics in microbiology such as MALDI-ToF, the role of stewardship has expanded to ensure that new technologies function to preserve rather than consume healthcare resources and meaningfully impact patient care<sup>13</sup>.

Despite well-coordinated OPAT, emergency department (ED) utilisation and readmissions resulting in repeated microbiologic testing, repeated antibiotic courses for treatment failures and infection recurrences remain problematic in OPAT patients<sup>14-16</sup>




A PREDICTION MODEL FOR 30-DAY HOSPITAL READMISSIONS IN OPAT PATIENTS INCLUDES AGE (ODDS RATIO [OR], 1.09 PER DECADE; 95% CONFIDENCE INTERVAL [CI] 0.99-1.210), AMINOGLYCOSIDE USE (OR, 2.33; 95% CI 1.17-4.57) RESISTANT ORGANISMS (OR, 1.57; 95% CI 1.03-2.36), AND NUMBER OF PRIOR HOSPITAL DISCHARGES IN THE PAST 12 MONTHS WITHOUT IV ANTIBIOTICS (OR, 1.2 PER PRIOR ADMISSION; 95% CI 1.09-1.32).

- 26% (207/782) of OPAT patients were readmitted within 30 days consistent with prior studies.
- 8% of readmitted patients and 4% of non-readmitted patients were prescribed aminoglycosides at initial discharge (p=0.03)
- The study highlights the importance of stewardship in the selection of alternative, safer OPAT regimens

 PDF ARTICLE

## TOOLKIT RESOURCE

### SITE LINKS

-  13. Implementation of Rapid Molecular Infectious Disease Diagnostics: The Role of Diagnostic and Antimicrobial Stewardship
-  14. Patients with prosthetic joint infection on IV antibiotics are at high risk for readmission
- 15. Association of laboratory test result availability and re-hospitalizations in an outpatient parenteral antimicrobial therapy programme
-  16. Predictors of hospital readmission in patients receiving outpatient parenteral antimicrobial therapy. Pharmacotherapy

ED utilisation is frequent in disadvantaged settings, particularly in the Bronx, where approximately 30% of its 1.4 million residents live below the federal poverty level<sup>17,18</sup>. Without coordinated care, such patients discharged on long-term IV antibiotics experience loss to follow up and treatment failures. Poor outcomes in patients discharged on IV antibiotics from the Montefiore Health System in the Bronx, NY catalysed the development of a transition-of-care OPAT program in 2015. A nurse coordinator was essential to patient outreach, appointment reminders, and trouble shooting of patient concerns by phone. Infusion services were provided to patients at home by licensed pharmacy and nursing agencies, or at skilled nursing facilities. OPAT physicians served as antimicrobial stewards by reviewing weekly laboratory results and contacting infusion teams and skilled nursing staff with necessary therapeutic adjustments (e.g. drug level-based vancomycin dose adjustment for MRSA infections). Compared to the prior standard care, patients enrolled in the Montefiore OPAT program after 2015 had significantly lower 30-day readmissions (13.0% vs. 26.1%,  $P < .01$ )<sup>4</sup>

OPAT in Asia represents another potentially unharnessed opportunity to improve the care of underserved populations. A 2017 study by Fisher and colleagues sought to characterize OPAT in Asia, a setting not previously well described. They surveyed 171 different healthcare facilities in 17 Asian countries, including India, Singapore, China, Japan, and Australia. Interestingly, 57% of facilities administer OPAT but only 3% of facilities outside of Singapore reported comprehensive OPAT services overseen by specialists. Coordinated efforts to standardize “unchecked” OPAT in Asia is a priority of the international Infectious Diseases and Stewardship community,

which is best achieved by harnessing local champions and identifying local incentives and needs<sup>20</sup>.

### OPAT-STEWARDSHIP DILEMMA





While OPAT programs have emerged across myriad settings, promotion of judicious antimicrobial use through stewardship is now embedded in regulatory standards for healthcare accreditation in the United States<sup>21</sup>. Often, targeted antibiotic selection for a given infection may conflict with practical aspects of OPAT care, including convenience and feasibility of long term treatment. “Collateral damage” of OPAT may include emergence of drug resistance, development of healthcare associated infections such as *Clostridium difficile*, and antibiotic associated toxicities. Thus the “antimicrobial stewardship-OPAT dilemma” described by Gilchrist and colleagues referring to the critical balance of prolonged antibiotic therapy with antibiotic adverse effects<sup>6</sup> as shown in Figure 4.

**COMMON OPAT-STEWARDSHIP CHALLENGES:**  
 1) LACK OF PUBLISHED DRUG STABILITY DATA FOR CERTAIN NARROW SPECTRUM AGENTS, 2) LACK OF NARROW-SPECTRUM AGENTS WITH CONVENIENT DOSING SCHEDULES, 3) LONG INFUSION TIMES FOR CERTAIN AGENTS (E.G. IV VANCOMYCIN), 4) OVERLY BROAD SPECTRUM COVERAGE OF AVAILABLE ONCE-DAILY AGENTS (E.G. CEFTRIAXONE, DAPTOMYCIN, ERTAPENEM, ETC.)

 PDF ARTICLE

## TOOLKIT RESOURCE

### SITE LINKS

-  17. Quick Facts Bronx County, New York. United States Census Bureau, 2010–2015.
-  18. Research, Statistics, Data & Systems. Centers for Medicaid and Medicare Services. 2013.
-  19. Medicaid Regional Data Compendium. The Medicaid Institute at United Hospital Fund. 2014.
-  20. Outpatient parenteral antibiotic therapy (OPAT) in Asia: missing an opportunity

## TOOLKIT RESOURCE

### SITE LINKS



21. New Societal Approaches to Empowering Antibiotic Stewardship

IN A STUDY OF 1212 UNIQUE EPISODES OF DIABETIC FOOT ULCER, MRSA INFECTIONS ACCOUNTED FOR 57% OF ALL INVASIVE INFECTIONS AND WERE ASSOCIATED WITH INCREASED MORTALITY RISK (HAZARD RATIO 1.987; 95% CI 1.106-3.568) (CHEN SY ET AL. INVASIVE SYSTEMIC INFECTION AFTER HOSPITAL TREATMENT FOR DIABETIC FOOT ULCER: RISK OF OCCURRENCE AND EFFECT ON SURVIVAL. CLIN INFECT DIS. 2017; 64 (3): 326-334. DOI: 10.1093/CID/CIW736.)



PDF ARTICLE

A frequent indication for OPAT is the costly diabetic foot infection complicated by devascularised bone and osteomyelitis. Patients with uncontrolled diabetes frequently have underlying vascular disease and renal dysfunction, which affects antibiotic dosing and route of administration. These comorbidities complicate wound healing and predispose to recurrent infection<sup>22;23</sup>. In addition, site invasive systemic infection cause significant morbidity and mortality even after initial hospitalization and treatment.

## TOOLKIT RESOURCE

### SITE LINKS



22. David G. Armstrong, Andrew J.M. Boulton, and Sicco A. Diabetic Foot Ulcers and Their Recurrence. N Engl J Med 2017; 376:2367-2375. June 15, 2017DOI



23. Microbiology of diabetic foot infections: from Louis Pasteur to “crime scene investigation.”



24. Systemic Antibiotic Therapy for Chronic Osteomyelitis in Adults

Osteomyelitis associated with chronic diabetic foot ulcers is often polymicrobial (*Staphylococcus aureus*, *Streptococci*, *Pseudomonas*, *Enterobacteriaceae*, anaerobes, skin flora, yeast, etc.)<sup>24</sup>. Selection of targeted antibiotic regimens for diabetic osteomyelitis feasibly administered for 4-6 weeks is challenging. Since several oral antibiotic classes achieve bone levels exceeding minimum inhibitory concentrations (MICs) of pathogens, prolonged courses of oral agents alone or in combination represents a viable and cost saving alternative to OPAT, avoiding the need for durable IV access<sup>25</sup>. Use of outpatient oral regimens with high bioavailability can potentially avert hospital admissions unless treatment failures occur with optimal oral therapy.

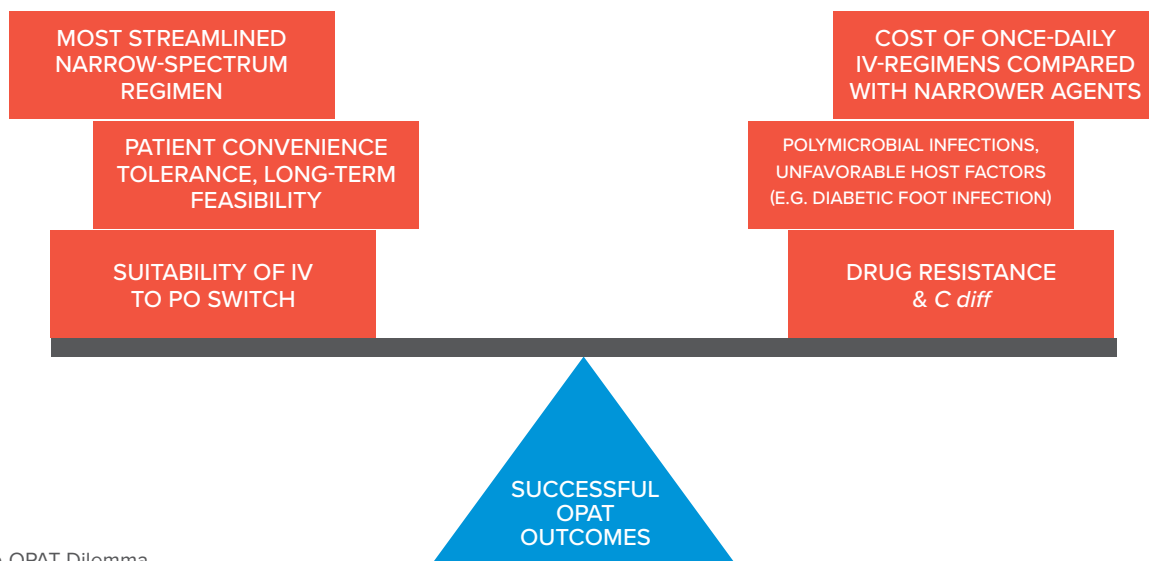


FIGURE 4  
Stewardship-OPAT Dilemma

**EXPANDED ROLE OF THE STEWARDSHIP PHARMACIST IN OPAT**

The 2012 UK consensus guidelines on OPAT best practices endorse the clinical antimicrobial pharmacist as a potential co-director of a comprehensive OPAT team<sup>2</sup>. Several fundamental stewardship principles are incorporated into the proposed OPAT-stewardship framework of Gilchrist et al.,

namely, IV to PO switch, protocols for laboratory monitoring and reporting of adverse antimicrobial events, and tracking of antimicrobial resistance data<sup>6</sup>. An antimicrobial stewardship pharmacist has the training and expertise to assume leadership of these functions, while the physician and nursing leaders coordinate OPAT patient clinical care.

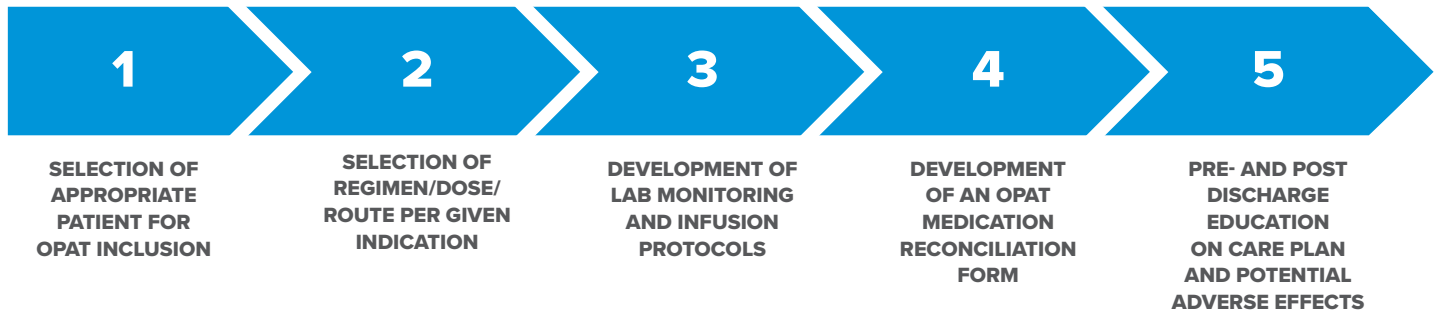



FIGURE 5  
Expanded Stewardship Pharmacist Role in OPAT

A PHARMACIST-LEAD OPAT SERVICE AT A 316-BED SAFETY NET HOSPITAL IN INDIANA PROVIDES OPAT CARE TO UNINSURED OR UNDERINSURED PATIENTS. PRIOR TO PROGRAM IMPLEMENTATION IN 2008 SEVERAL DEVIATIONS FROM OPAT STANDARDS OF CARE WERE NOTED. AFTER IMPLEMENTATION, CLINICAL CURE AT THE END OF TREATMENT WAS OBSERVED IN 93% OF PATIENTS. AUTHORS CONCLUDED THAT A PHARMACY-DRIVEN OPAT INTERVENTION IS SAFE, EFFECTIVE, AND ADAPTABLE TO OTHER SETTINGS

 PDF ARTICLE

TOOLKIT RESOURCE

SITE LINKS

 25. European Surveillance of Antimicrobial Consumption (ESAC): Outpatient Parenteral Antibiotic Treatment in Europe

Several antibiotic classes with good oral bioavailability can achieve tissue levels exceeding pathogen MICs. A 2012 review of antibiotic therapy for chronic osteomyelitis reported that fluoroquinolones, linezolid, fosfomycin, and trimethoprim-sulfamethoxazole achieve bone concentrations at approximately 50% of serum, and metronidazole penetrates bone at concentrations approximating those in serum. Both doxycycline and clindamycin are viable oral options for MRSA osteomyelitis but doxycycline has variable bone concentrations depending on site. Rifampin also demonstrates bone concentrations approximating those in serum and is suggested for combination therapy particularly in the setting of infected prostheses. At this time, superiority of bactericidal versus bacteriostatic treatment of osteomyelitis remains uncertain<sup>24</sup>.

## CONCLUSION

OPAT and antimicrobial stewardship are unified by the mutual objective of selecting the most effective, well tolerated, and streamlined regimen individualized to the host and site of infection. Often pathogen-directed once daily regimens are appropriate for OPAT (e.g. IV vancomycin for an invasive MRSA infection in an elderly patient). At other times, once daily regimens are prescribed preferentially due to convenience of dosing and likelihood of patient adherence to prolonged antibiotic courses. In the later case, regimens may be too broad for a given indication (e.g. once daily ertapenem for an intra-abdominal infection with a susceptible strain of Enterobacter).

An OPAT program design adapted from an antimicrobial stewardship paradigm can ensure appropriate selection of long-term antibiotic regimens, dose adjustments per renal and hepatic function, therapeutic drug monitoring, and ongoing patient education and counseling on risk factor mitigation, infection prevention, and expected treatment outcomes. Antimicrobial stewards (pharmacists and physicians) are integral to the multidisciplinary OPAT team. Mounting evidence in favor of oral antibiotic therapy for bone and joint infections supports early stewardship intervention, including IV to PO conversion and potential de-escalation from empiric broad-spectrum IV therapy to targeted PO therapy.

A 2009 COCHRANE REVIEW DID NOT DEMONSTRATE A CLEAR BENEFIT OF IV VERSUS PO THERAPY, AND IDSA PROSTHETIC JOINT INFECTION GUIDELINES SUGGEST THAT HIGHLY BIOAVAILABLE ORAL ANTIBIOTICS MAY BE AN APPROPRIATE ALTERNATIVE TO PROLONGED IV THERAPY. THE OVIVA NON-INFERIORITY 5-YEAR TRIAL WILL ULTIMATELY REPORT RESULTS OF 1054 PATIENTS RANDOMIZED TO 6 WEEKS OF ORAL VERSUS IV THERAPY FOR TREATMENT OF BONE AND JOINT INFECTIONS IN THE UK (CONTERNO LO ET AL. ANTIBIOTICS FOR TREATING CHRONIC OSTEOMYELITIS IN ADULTS. COCHRANE DATABASE SYST REV. 2009; 8(3):CD004439



PDF ARTICLE

OSMON DR, ET AL. DIAGNOSIS AND MANAGEMENT OF PROSTHETIC JOINT INFECTION: CLINICAL PRACTICE GUIDELINES BY THE INFECTIOUS DISEASES SOCIETY OF AMERICA. CLIN INFECT DIS. 2013;56(1):E1-25.; LI, HK ET AL.



PDF ARTICLE

ORAL VERSUS INTRAVENOUS ANTIBIOTIC TREATMENT FOR BONE AND JOINT INFECTIONS (OVIVA): STUDY PROTOCOL FOR A RANDOMISED CONTROLLED TRIAL. TRIALS. 2015; 16: 583. DOI: 10.1186/S13063-015-1098-Y)



PDF ARTICLE



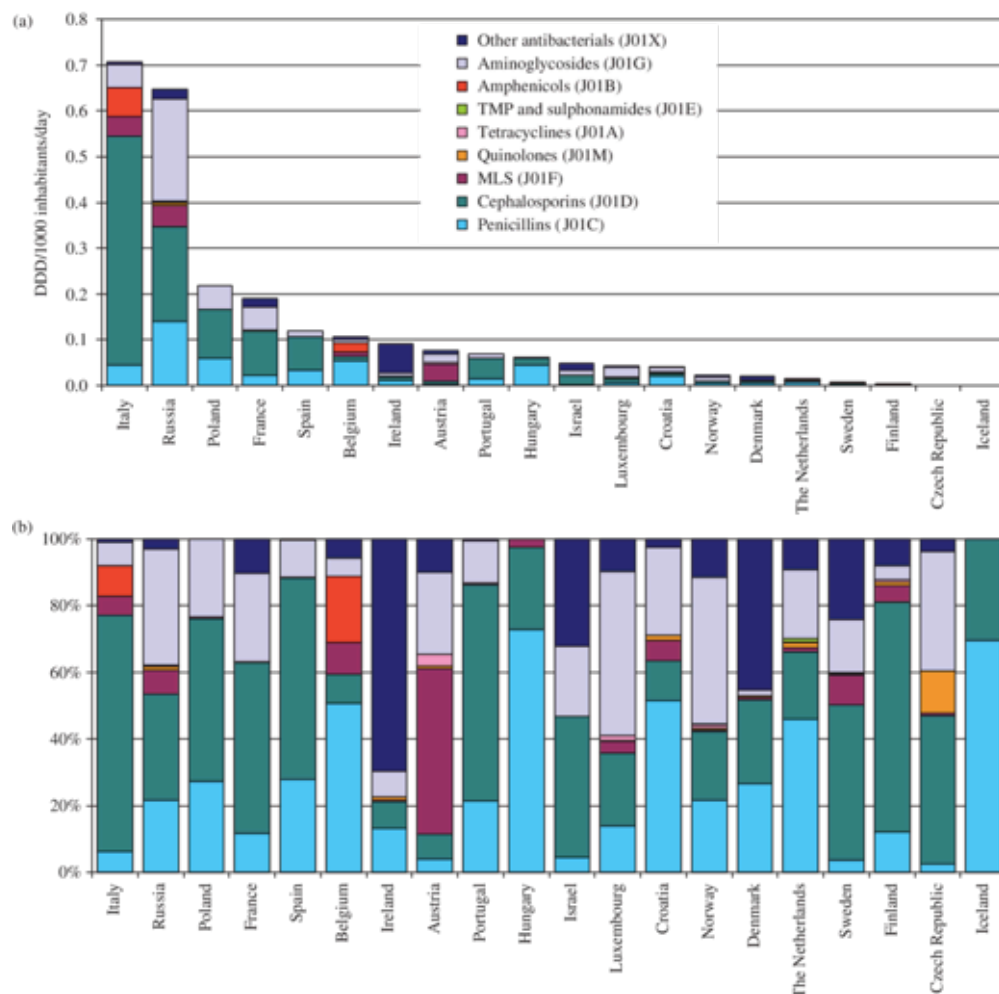


FIGURE 6  
European Surveillance of Antimicrobial  
Consumption, OPAT Distribution,  
2006<sup>25</sup>

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# CHAPTER 24

 AUTHOR: **KARIN THURSKY & ARJUN RAJKHOWA**

## THE USE OF INFORMATION TECHNOLOGY TO SUPPORT ANTIMICROBIAL STEWARDSHIP

### THE AIM OF THIS CHAPTER IS TO:

Delineate the factors and variables involved in prescribers' decision-making around antimicrobials.

Outline the uses and significance of computerised decision support systems (CDSSs) in AMS programs.

Describe different kinds of CDSSs, and evaluate and present evidence of their impact on prescribing.

Understand the factors that influence successful implementation of CDSSs.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Discuss reasons why CDSSs are required both for prescribers and for AMS programs.
- Describe the features of CDSSs that support antimicrobial prescribing.
- Compare and contrast the different types of CDSSs.
- To discuss the issues that may impact on the uptake of these systems into clinical practice.

### OVERVIEW

Antimicrobial stewardship (AMS) refers to activities that optimise prescribing, enhance treatment outcomes and potentially help mitigate the impact of the selection of pathogens with antimicrobial resistance. At the patient level in hospitals, prescribing involves and is underpinned by a complex range of decisions that are frequently based on poorly structured information. Clinicians need to consider a multitude of factors that will influence the quality of prescribing. Diagnostic criteria, disease severity, availability of microbiology results and susceptibility data, availability of antimicrobials, and patient factors all determine and contribute to the prescriber's decision-making, and impact on whether the right drug is prescribed at the right time and for the right duration.

Decision-making is necessarily contingent and complex, and variable levels of adherence to guidelines, where local or national guidelines are available, can be observed among clinicians. There are multiple stakeholders as well as existing prescribing hierarchies involved in decision making. (Figure 1) Senior clinicians with experience demonstrate an increased ability to reduce the complexity of decisions around antibiotic prescribing, and patients who go through infectious diseases consultations have better outcomes. For clinicians with heavy workloads, less experienced or junior clinicians and clinicians working in hospitals that do not have comprehensive infectious diseases support, access to information technology (including computerised decision support) can be beneficial.

# DEFINITION OF COMPUTERISED DECISION SUPPORT

*“THE PROVISION OF CLINICAL  
KNOWLEDGE, INTELLIGENTLY  
FILTERED AND PRESENTED  
AT APPROPRIATE TIMES, TO  
ENHANCE PATIENT CARE”*

Purcell GP. What makes a good clinical decision support system. BMJ 2005;.

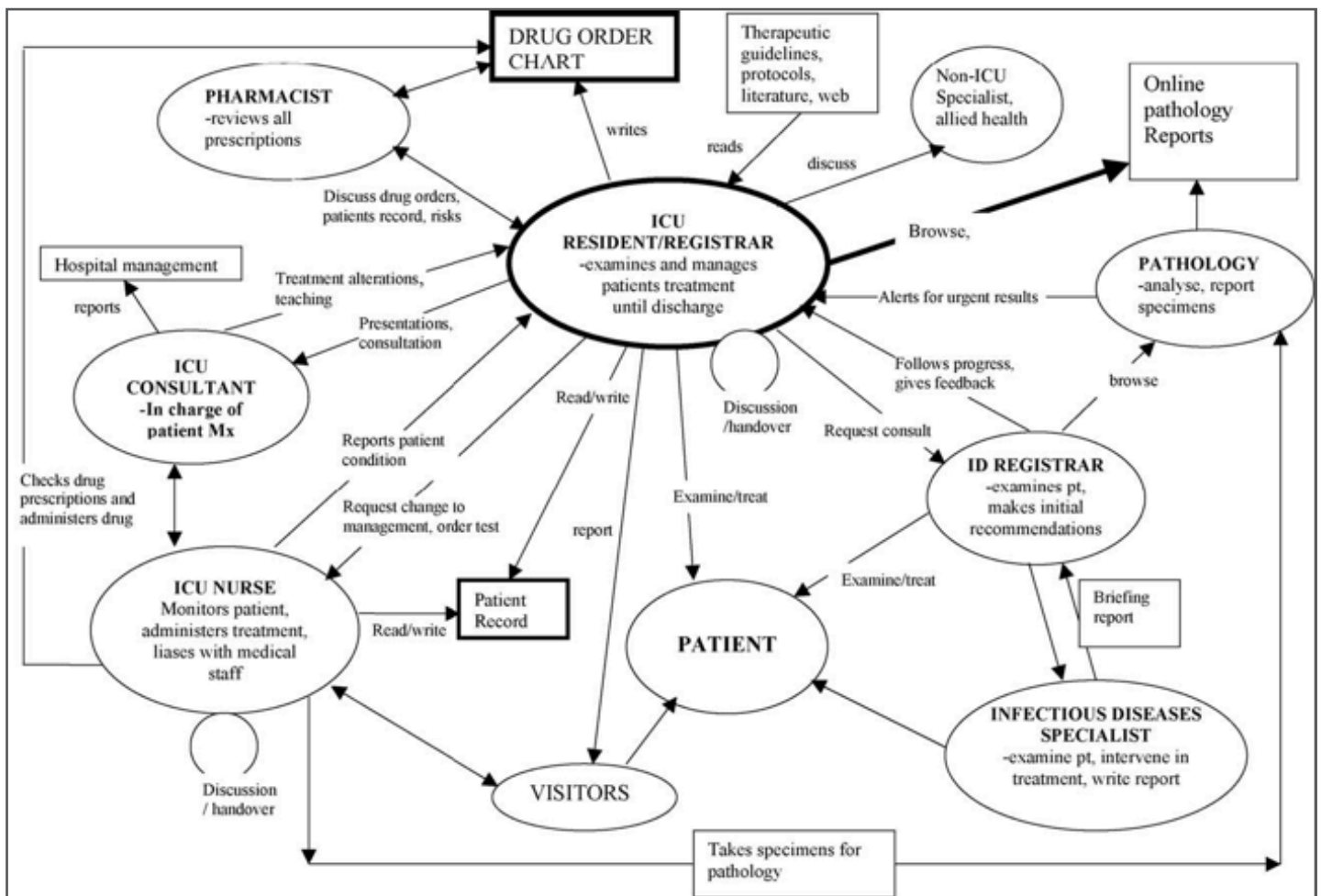


FIGURE 1 This figure describes the complex flow of information related to antimicrobial prescribing in a tertiary hospital intensive care unit. In this consolidated flow chart, there are multiple stakeholders, multiple sources of information, and multiple users of this information. (Thursky KA, Mahemoff M. User-centered design techniques for a computerised antibiotic decision support system in an intensive care unit. Int J Med Inform. 2007;76(10):760-8)

Decision support involves “the provision of clinical knowledge, intelligently filtered and presented at appropriate times, to enhance patient care”. Computerised decision support thus refers to the provision of electronically stored information that enhances and optimises clinicians’ decision-making at the point of care.

It is important to recognise that a computerised decision support system (CDSS) cannot replace infectious diseases consultation and expert decision-making, but it can optimise and enhance decisions at the point of care by bringing together and synthesising patient-specific data, clinical guidelines and information from other sources. CDSSs have the potential to reduce the complexity of decision-making, improve the quality of decisions and increase the appropriateness of prescribing.

Importantly, in light of the challenges associated with drug-resistant infections and risks posed by the inappropriate use of antimicrobials, CDSSs with post-prescription review and auditing features can help health care providers keep track of prescribing patterns within their units. Auditing and feedback from CDSSs can guide internal quality control processes as well as contribute to local and national surveillance of antimicrobial use, thus informing AMS initiatives and interventions at various levels. Key infectious diseases bodies support the use of CDSSs in AMS programs, and have highlighted its potential to support quality improvement initiatives.

sources. IT systems can thus support AMS programs in three important ways – by providing decision support, recording and facilitating the informational workflow, and enabling auditing.

Computerised decision support systems in antimicrobial stewardship are usually targeted at the prescriber or the AMS team (or, in some cases, both). (Figure 2). The various types of CDSSs are discussed below.

**1. The prescriber**

Antimicrobial prescribing can be influenced by the use of formulary restriction and antimicrobial approval processes, rules and alerts. These are conceptualised as being part of restrictive approaches to AMS, whereas persuasive approaches include the use of clinical guidelines and pathways. CDSSs may be implemented as stand-alone systems or integrated with other hospital systems, including EMM/EMR systems. Use of the CDSS may be forced (or mandatory) or voluntary (generally through education, and hospital procedure and policy).

**2. The AMS team**

A key role of the AMS team is to undertake post-prescription review. This may be facilitated by systems that identify patients for clinical review (e.g., approval systems and EMM or pharmacy dispensing systems). There are many ‘back-end’ systems that link patient data from multiple systems (pharmacy and microbiology). Antimicrobial stewardship programs must undertake surveillance of antimicrobial use and drug-resistant infections to monitor and measure the impact of the programs. This requires the collection and synthesis of large amounts of data, including records of indications (if available), and prescribed agents, doses and durations.

TOOLKIT RESOURCE

ARTICLES

Thursky K. Use of computerized decision support systems to improve antibiotic prescribing. *Expert Rev Anti Infect Ther.* 2006;4(3):491-507.

Sintchenko V, Coiera E, Gilbert GL. Decision support systems for antibiotic prescribing. *Curr Opin Infect Dis.* 2008;21(6):573-9

▶ USING INFORMATION TECHNOLOGY TO SUPPORT ANTIMICROBIAL STEWARDSHIP

A large amount of information (ideally presented in a timely manner) about patients, likely pathogens, treatment options, and potential drug interactions, contraindications and adverse reactions needs to be considered by clinicians at the point of care. Decision-making can be optimised by the intelligent and effective presentation of clinical guidelines, rules and alerts for antimicrobials, or even computation of information from multiples

The role of CDSS in hospitals

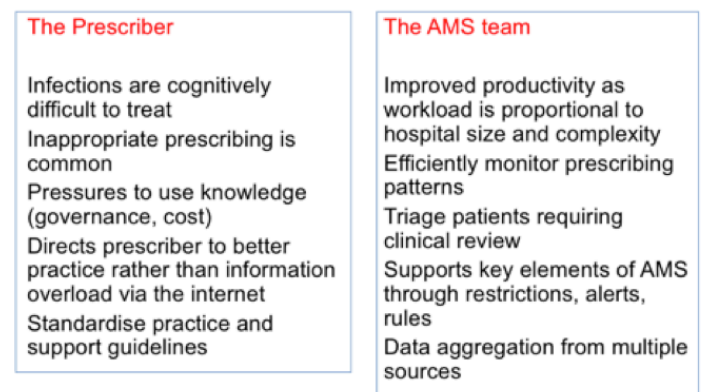


FIGURE 2 Usefulness of CDSSs in AMS programs



## ▶ ARE ANTIMICROBIAL CDSSs EFFECTIVE?

Studies evaluating CDSSs have demonstrated that they can improve the quality and reduce the costs of antimicrobial prescribing.

- Outcomes associated with qualitative improvement such as increased appropriateness of prescribing, reduced medication and dosing errors, and reduced incidence of healthcare-associated infections have been observed.
- From a cost perspective, CDSSs have been associated with significant cost avoidance or minimisation, with the literature reporting savings in antimicrobial expenditure per patient or for the hospital, and reductions in total medical expenditure and length of stay.

## TOOLKIT RESOURCE

### ARTICLES

Baysari MT, Lehnbohm EC, Li L, Hargreaves A, Day RO, Westbrook JI. The effectiveness of information technology to improve antimicrobial prescribing in hospitals: A systematic review and meta-analysis. *Int J Med Inform.* 2016;92:15-34.

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## ▶ TYPES OF ANTIMICROBIAL CDSSs

(See PDF Toolkit resources 1,3,4,5,6)

A range of CDSSs are available, and hospitals need to carefully consider their requirements and local capacity for implementation. (Figure 3 and Figure 4)

A CDSS can be as simple as an online portal containing guidelines and formulary restrictions. Passive decision support through electronic access to guidelines (on the Internet, hospital

intranet or mobile applications) can easily be incorporated into the clinical workflow and used at various entry points in hospital systems. More complex CDSSs can be integrated with other applications such as EMM systems, and can include advanced decision support. Hospitals can have more than one tool to support their AMS program.

Currently, the most commonly used CDSSs for AMS are:

- electronic guidelines and mobile applications;
- electronic antimicrobial approval systems;
- electronic infection prevention and surveillance systems; and
- e-prescribing and EMM systems.

## Examples of Antibiotic Decision Support

- **Passive:** Intranet/internet guidelines/apps
  - E.g., Smart phone apps
- **Pharmacy-based (back-end)**
  - E.g., Aminoglycoside monitoring, redundant antibiotic combinations, therapeutic mismatches
- **Approval systems**
  - E.g., Guidance MS (Royal Melbourne Hospital)
- **Computerised physician order entry/Electronic Medication Management (EMM) system**
- **Advanced CDSS with/without order entry**
  - E.g., Antibiotic assistant/Theradoc (Hospira), TREAT (Tel-Aviv), Antimicrobial Resistance Utilization and Surveillance Control (ARUS-C) (Singapore)

Thursky, K (2006). Use of computerized decision support systems to improve antibiotic prescribing. *Expert Rev Anti Infect Ther*; 4:491-507. Sintchenko, V., et al. Decision support systems for antibiotic prescribing. *Curr Opin Infect Dis* 21, (2008). Cresswell K et al. A systematic assessment of review to promoting the appropriate use of antibiotics through hospital electronic prescribing systems. *Int J Pharm Pract.* 2016.

FIGURE 3  
Examples of decision support

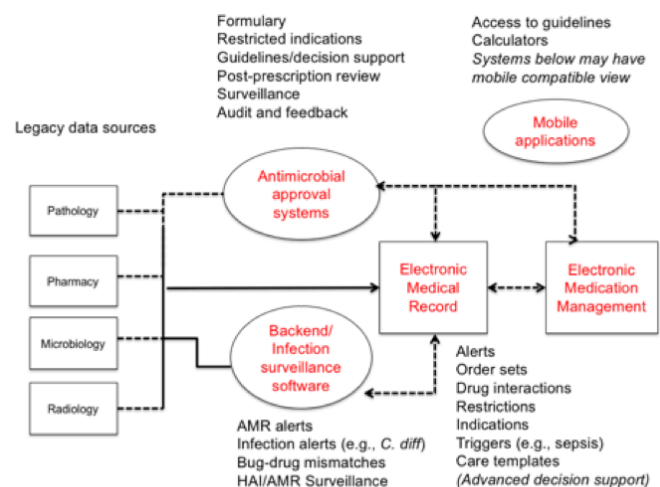


FIGURE 4  
There are multiple options for introducing decision support for AMS programs



### Mobile applications

Clinical portals, including those containing guidelines, are increasingly becoming mobile device-compatible, ensuring that with increased smartphone use among clinicians, passive decision support becomes more accessible at the point of care.

- In addition to traditional resources such as pocket guides, reference handbooks and computer desktop-accessible portals, mobile apps and mobile browser-compatible portals can serve as suitable platforms for the dissemination of clinical practice guidelines, and are likely to be consulted more frequently due to their accessibility and availability at the bedside.
- AMS opportunities include disease- or drug-based guidelines, calculators and dissemination of data such as antibiograms.
- Importantly, these platforms allow guidelines and other supplementary information to be updated more easily.

The following table provides some examples of mobile applications that have been used for AMS:

Imperial College Antibiotic Prescribing Policy App (IAPP)	Imperial college, London <a href="http://www.imperial.ac.uk/medicine/hpru-amr/applications-and-tools/imperial-antibiotic-prescribing-policy-iapp/">http://www.imperial.ac.uk/medicine/hpru-amr/applications-and-tools/imperial-antibiotic-prescribing-policy-iapp/</a>
Sanford Guide Online	Sanford Guide <a href="https://www.sanfordguide.com/">https://www.sanfordguide.com/</a>
John Hopkins Antibiotic Guide	Johns Hopkins Medicine <a href="http://www.hopkinsmedicine.org/apps/all-apps/johns-hopkins-abx-guide-2017">http://www.hopkinsmedicine.org/apps/all-apps/johns-hopkins-abx-guide-2017</a>
Microguide	Horizon Strategic Partners, UK <a href="https://itunes.apple.com/gb/app/microguide/id447171786?mt=8">https://itunes.apple.com/gb/app/microguide/id447171786?mt=8</a>
015 EMRA Antibiotic Guide	Emergency Medicines Residents Association, US <a href="https://itunes.apple.com/us/app/2017-emra-antibiotic-guide/id1164251928?mt=8">https://itunes.apple.com/us/app/2017-emra-antibiotic-guide/id1164251928?mt=8</a>
UptoDate Online	<a href="https://www.uptodate.com/home/product">https://www.uptodate.com/home/product</a>

Antibiotic Pocket	Borm Bruckmeier Publishing, LLC Medica <a href="https://itunes.apple.com/us/app/antibiotics-pocket/id434810841?mt=8">https://itunes.apple.com/us/app/antibiotics-pocket/id434810841?mt=8</a>
Spectrum MD - Localized Antimicrobial Stewardship	<a href="https://play.google.com/store/apps/details?id=com.spectrum&amp;hl=en_GB">https://play.google.com/store/apps/details?id=com.spectrum&amp;hl=en_GB</a>
Impact	Infection Control Branch, Centre for Health Protection, Department of Health, Hong Kong <a href="http://www.chp.gov.hk/en/static/40563.html">http://www.chp.gov.hk/en/static/40563.html</a>
CBR-based Imperial Antibiotic Prescribing Policy (ENIAPP) smartphone app	Imperial College London <a href="http://www.imperial.ac.uk/medicine/hpru-amr/applications-and-tools/imperial-antibiotic-prescribing-policy-iapp/">http://www.imperial.ac.uk/medicine/hpru-amr/applications-and-tools/imperial-antibiotic-prescribing-policy-iapp/</a>

A few points about the effectiveness of apps need to be considered.

- While third-party apps are also available, these may not support or be compliant with local practices or clinical guidelines, although the option of local customisation is offered by some apps.
- A potential cause for concern is the fact that users must generate updates on their own devices, which could lead to problems with version control.
- Further, as they provide passive decision support, there is some uncertainty about the impact of mobile apps.
- It is unclear whether these tools lead to sustained change in prescribing behaviour. One reason may be that key decisions are often made on the ward round by a senior consultant or fellow. Passive apps provide less incentive than systems that are able to provide patient-specific information.

## TOOLKIT RESOURCE

### ARTICLES

Goff DA. iPhones, iPads, and medical applications for antimicrobial stewardship. *Pharmacotherapy*. 2012;32(7):657-61

### Electronic antimicrobial approval systems

Antimicrobial authorisation and approval systems that support formulary control and indication restrictions can underpin and form part of restrictive and persuasive AMS strategies.

- Approval systems, either integrated with hospital EPS/EMM systems, or implemented autonomously in the absence of these systems, are being adopted by several institutions around the world.
- The core function of an electronic approval system is to support the local antimicrobial formulary (through customisation of algorithms for 'restricted' antimicrobials and approved indications) and provide an approval process for prescribers and pharmacists. It can do this by generating alerts that require the AMS team to act (by undertaking post-prescription review, for example).
- To ensure approval systems fit comfortably into the workflow, the AMS team can determine locally-relevant criteria for the generation of alerts and thus customise the approval process.

Implementation experience indicates that approval systems cannot be proposed as a replacement for expert decision-making but can improve the quality of prescribing by helping direct the attention of expert prescribers and the AMS team to prescriptions that require review.

Importantly, an electronic approval system enables auditing of antimicrobial use, and facilitates feedback to individual prescribers and AMS teams within units (the persuasive component of AMS). This necessitates collaboration among staff and units.

- For the successful implementation of an approval system, it will be essential to expedite, secure and maintain ongoing collaboration between pharmacy, microbiology and infectious diseases staff, and staff in individual hospital units.
- As part of this process, local customisation of the formulary and indications for use, as determined by the AMS team or therapeutics team, may also be required.

As approval systems have been implemented at several institutions, there is now considerable research focused on evaluation of their impacts. Approval systems have been found to be very effective in reducing consumption of targeted antimicrobials as well as medicine costs.

Any system that requests an indication (e.g., an approval system or EPS) is open to 'gaming' by prescribers, as indications can be erroneously or deliberately selected to provide access to particular antimicrobials.

### CASE STUDY: ANTIMICROBIAL RESTRICTION AND APPROVALS

Guidance MS™ (Royal Melbourne Hospital, Australia) is used in 70 Australian hospitals, including public, private, metropolitan and regional hospitals. The program supports a number of AMS interventions, including formulary control; restriction of indications for target antimicrobials; access to national guidelines; alerts for non-standard indications; administration alerts by pharmacists when medications are given without approval; and targeted post-prescription review, feedback and reporting. This system has been associated with:

- reduced consumption of targeted or 'restricted' antimicrobials (e.g., third-generation cephalosporins) and increased consumption of narrow spectrum antimicrobials (e.g., benzylpenicillin, doxycycline and aminopenicillins);
- improved resistance patterns in some Gram-negative isolates in intensive care units. (REF 2)

A network of 5 hospitals using Guidance as a centrally-deployed CDSS (and operating coordinated AMS programs on the basis of a 'hub and spoke' model) witnessed improved antimicrobial use, reduced costs and better treatment outcomes. (REF 1) Data from the Australian National Antimicrobial Prescribing Survey, a program contributing to national surveillance of antimicrobial use in Australia, showed that hospitals using Guidance had a higher mean appropriateness of antimicrobial prescribing (in 2014, 82.2%, n=1518 prescriptions) compared to the national average in Peer Group A hospitals (74.4%, n=10,955 prescriptions).

## TOOLKIT RESOURCE

### ARTICLES

Buising KL, Thursky KA, Robertson MB, Black JF, Street AC, Richards MJ, et al. Electronic antibiotic stewardship—reduced consumption of broad-spectrum antibiotics using a computerized antimicrobial approval system in a hospital setting. *J Antimicrob Chemother.* 2008

## TOOLKIT RESOURCE

### ARTICLES

Bond, S. E., Chubaty, A. J., Adhikari, S., Miyakis, S., Boutlis, C. S., Yeo, W. W., Batterham, M.J., Dickson, C., McMullan, B.J., Mostaghim, M. & Li-Yan Hui, S. (2017). Outcomes of multisite antimicrobial stewardship programme implementation with a shared clinical decision support system. *Journal of Antimicrobial Chemotherapy*, 72(7), 2110-2118

### Infection prevention and surveillance systems

Infection prevention systems can provide decision support to AMS teams based on the integration of data from pharmacy dispensing and laboratory systems, diagnostic imaging systems and the EHR. These systems work at the 'back-end' and require dedicated staff to review the reports and alerts that are generated and then to act on them. The type of interventions that can be undertaken include:

- Rules-based alerts for bug-drug mismatches (e.g., a prescription for an antimicrobial in a setting of known resistance), redundant anaerobic coverage, positive blood cultures, etc.

The benefits of infection prevention systems include:

- They can help identify patients at risk of developing nosocomial infections, monitor antimicrobial resistance, and assist with routine surveillance activities, including reporting and generating antibiograms.
- They can help improve antimicrobial dosing and monitoring.

The following table provides examples of commercial electronic infection prevention systems:

Safety Surveillor	Premier HealthCare, Charlotte, North Carolina <a href="https://www.premierinc.com/transforming-healthcare/healthcare-performance-improvement/patient-safety/">https://www.premierinc.com/transforming-healthcare/healthcare-performance-improvement/patient-safety/</a>
Theradoc	Premier HealthCare, Charlotte, North Carolina <a href="http://www.theradoc.com/">http://www.theradoc.com/</a>
MedMined	CareFusion, BD, New Jersey <a href="https://www.bd.com/en-us/offerings/brands/medmined">https://www.bd.com/en-us/offerings/brands/medmined</a>

Sentri7	Wolters Kluwer <a href="http://www.pharmacyonesource.com/products/sentri7/">http://www.pharmacyonesource.com/products/sentri7/</a>
ICNET	ICNET systems, Illinois <a href="http://www.icnetplc.com/">http://www.icnetplc.com/</a>
RL Solutions	RL, Ontario, Canada <a href="http://www.rlsolutions.com/rl-products/infection-surveillance">http://www.rlsolutions.com/rl-products/infection-surveillance</a>
QC Pathfinder	Vecna Technologies, Cambridge, Massachusetts <a href="https://www.vecna.com/vecna-medical-launches-qc-pathfinder-version-6-0-with-updated-nhsn-reporting-capabilities-and-pharmacy-intervention-tracking/">https://www.vecna.com/vecna-medical-launches-qc-pathfinder-version-6-0-with-updated-nhsn-reporting-capabilities-and-pharmacy-intervention-tracking/</a>

A number of factors relating to the implementation of infection prevention systems need to be considered.

- Infrastructure and implementation issues, such as the lack of interoperability between legacy pathology and pharmacy systems, and lack of adequate support for integration, may prevent facilities from adopting third-party infection prevention systems.
- Like approval systems, infection prevention systems require a clinical workforce to monitor and act on alerts, and generate reports and feedback.
- The level of sophistication of the reports provided by these systems depends on the level of integration with pathology and pharmacology. Many will provide real-time run charts of target pathogens (e.g., *Staphylococcus aureus bacteremia*) or clinical conditions (e.g., hospital acquired pneumonia).
- Infection prevention programs should be differentiated from hospital microbiology systems. Hospital microbiology programs can also support AMS by providing recommendations about the clinical significance of a result (e.g., *Candida* in sputum is rarely a pathogen), as well as limiting the presentation of antibiotics that the pathogen is susceptible to to avoid broad spectrum use (known as cascade reporting).

### Electronic prescribing, medication management systems: developing antibiograms; tracking DOTs or DDDs/ 1000 patient days; developing ad hoc reports to monitor AMS team interventions

EPS/EMM systems are information systems that allow clinicians to generate electronic medication prescriptions. EMM systems encompass the following functions:

- computerised entry of physician orders (e-prescribing);
- medication review;
- dispensing;
- recording of medicines administration; and
- decision support (optional).

Most commercial EPSs have features associated with front-end decision support that can be support AMS.

- These include attributes such as default values, routes of administration, doses and frequencies.
- These may also include allergy alerts and drug interaction alerts.
- EMM systems can support a bundle of interventions, including antimicrobial restriction, dosing recommendations, rules-based alerts and order sets for disease conditions.
- An important advantage of these systems is that they can capture all the details of the antimicrobials prescribed and administered to the patient. This enables reporting of days of therapy (DOT) per 1000 patient days rather than the standard approach of defined daily doses (DDDs). Defined daily doses are less meaningful and cannot be used for paediatric patients.

Studies have shown that EMM systems can have an impact on prescribing and patient outcomes:

- Cost-effectiveness studies have demonstrated that EMM systems, particularly those with decision-support functionality, can lead to long-term savings due to reductions in adverse drug events, readmissions and healthcare costs.
- There are a few well-designed studies that have demonstrated reduction in mortality, length of stay and readmission for patients admitted with community-acquired pneumonia and sepsis.

However, a few implementation-related concerns need to be considered. Poor implementation of systems and lack of decision-support (e.g., error checking) can lead to patient harm. It is critically important that the AMS team is involved during the implementation of these systems to ensure that rules-based alerts and knowledge bases are locally applicable. Significant resources are required for local customisation of pre-set content. Studies evaluating EMM systems have highlighted features, outcomes and procedural issues that could negatively impact antimicrobial prescribing:

- large numbers of drug and dosing combinations;
- erroneous auto-complete directions that contradict intended orders;

- untimely transmission of discontinuation orders from the prescriber to the pharmacy;
- high order override rates (>90%) arising from inconsistent decision support mechanisms; and
- pre-set, off-the-shelf drug databases that are not amenable to local customisation.

Many of these systems are focused on 'front-end' decision support. They are effective in reducing transcription errors and improving the quality of the prescription. However, they are less effective in identifying the wrong choice of drug, which points to the need for post-prescription review.

Some systems provide dedicated AMS modules that identify patients that would benefit from AMS review. These might include patients with blood stream infections, or other pathogens (e.g., *C.difficile*), patients prescribed particular target antimicrobials (criteria may include cost, toxicity or spectrum, or non-guideline approved drugs), patients suitable for IV-to-oral switch or dose optimisation, including therapeutic dose monitoring.

These systems may have the ability to provide ad-hoc reports or formatted reports to monitor the AMS team's interventions

## TOOLKIT RESOURCE

### ARTICLES

Forrest GN, Van Schooneveld TC, Kullar R, Schulz LT, Duong P and Postelnick M. Use of electronic health records and clinical decision support systems for antimicrobial stewardship. *Clin Infect Dis.* 2014; 59 Suppl 3: S122-33

Schiff GD, Amato MG, Egual T, Boehne JJ, Wright A, Koppel R, et al. Computerised physician order entry-related medication errors: analysis of reported errors and vulnerability testing of current systems. *BMJ Qual Saf.* 2015;24(4):264-71

## DISCUSSION OF ISSUES AROUND ALERT FATIGUE IN EMRS



WATCH VIDEO

A recent poster presented at ID Week in 2017 described the impact of the Epic® Antimicrobial Stewardship Module in an 805-bed US metropolitan hospital. The program significantly improved the efficiency of the ASP, increasing the number of antimicrobials reviewed by 5442 to 8288 in a 12-month period before and after the implementation (from ~14 to 22 prescriptions per day). The proportion of interventions increased from 36% to 89% of prescriptions, mainly in optimisation of therapy (dose and alternative therapy) and safety/monitoring (TDM, bug-drug mismatch review, recommendation for follow-up cultures, request for additional sensitivities, and ophthalmology consult for candidemia). The program did not lead to improvements in de-escalation and cost-savings.

N.Pettit et al. *Open Forum Infectious Diseases*, Volume 4, Issue suppl\_1, 1 October 2017, Pages S263–S264, <https://doi.org/10.1093/ofid/ofx163.580>

### Advanced decision support systems

Advanced decision support systems use complex logic, mathematical modelling or case-based probabilities to provide patient-specific recommendations. They can provide decision support by helping identify potential infections, pathogens and treatment options based on inputs about patient symptoms, for example. A few systems have been successfully trialled and implemented.

- TREAT (Treat Systems, Denmark) is a CDSS that uses mathematical models to predict sites of infection and specific pathogens. A cluster-randomised trial across three wards in three countries demonstrated that the system was associated with improved appropriateness of empirical antimicrobial therapy and patient outcomes.
- The Antimicrobial Assistant system, developed by the Latter-Day Saints Hospital in Utah, was an early leader in advanced decision support. It used predictive models for infection control and surveillance, and its impacts were evaluated in

studies relating to AMS, surgical prophylaxis and adverse drug events.

Nascent machine learning and text-mining mechanisms, such as those deployed by one tool that can predict invasive pulmonary fungal infection from computed tomography (CT) reports, have the potential to be incorporated into AMS systems. For example, a Canadian CDSS was augmented with machine-learning capabilities to identify inappropriate prescriptions and recommend changes (including dose and dosing frequency adjustments, discontinuation of therapy, early switch from intravenous to oral therapy, and changes relating to redundant antimicrobial spectrum).

Advanced CDSSs also have a potential role in the detection and management of sepsis in hospitals with EHRs. A system that generated early sepsis alerts using data from disparate clinical portals was associated with improved care and patient outcomes. However, a recent systematic review of eight studies has found sepsis alerts systems to have limited predictive value for individual patients.

## TOOLKIT RESOURCE

### ARTICLES

Paul, M., Andreassen, S., Tacconelli, E., Nielsen, A. D., Almanasreh, N., Frank, U., Cauda, R. & Leibovici, L. (2006). Improving empirical antibiotic treatment using TREAT, a computerized decision support system: cluster randomized trial. *Journal of Antimicrobial Chemotherapy*, 58 (6), 1238-1245

Evans RS, Pestotnik SL, Classen DC, Clemmer TP, Weaver LK, Orme JF, et al. A computer-assisted management program for antibiotics and other antiinfective agents. *N Engl J Med*. 1998;338:232-8



## WHAT ARE THE FACTORS THAT ARE LIKELY TO RESULT IN SUCCESSFUL IMPLEMENTATION OF A CDSS?

There are factors intrinsic to the proposed software that will influence uptake by clinicians, and these should be considered when deciding on the choice of CDSS.

Implementation of new technology into the clinical workflow requires very careful planning that needs to be started many months in advance. (See Figure 5)

Cultural factors, such as institutional dynamics, capacity for collaboration between hospital units, and support for interventions and initiatives, can play a critical role in determining the success of AMS programs (even without information technology). For CDSS-supported AMS programs to be successful, technical readiness (e.g., strong IT infrastructure and server, and dedicated IT resources), administrative readiness (e.g., executive support), and an appropriately trained project officer (often a clinical pharmacist) to oversee the implementation and training are necessary. (See Figure 6)

It is really important for AMS team members to be formally engaged in all CDSS implementation activities, from scoping and developing functional specifications through to the final deployment. The development or local customisation of content for these systems is time-consuming. Introduction of antimicrobial restrictions (for example) needs to be discussed with each hospital unit, and appropriate training organised for clinical staff. Measuring user acceptance after implementation and continually monitoring uptake and usage is essential.

While the consolidation of data using CDSSs provides enormous opportunity for AMS programs, it is important to consider both the quality and volume of the alerts. One hospital's experience with one of these systems found that of a total of 8,571 alerts that were generated for 791 patients over a five-month period, only 284 interventions were made. 2–3 hours per day were required for review, and 1–2 hours per day for intervention and documentation. Data overload and alert fatigue is a very important issue for AMS programs, highlighting the importance of triaging workflow.

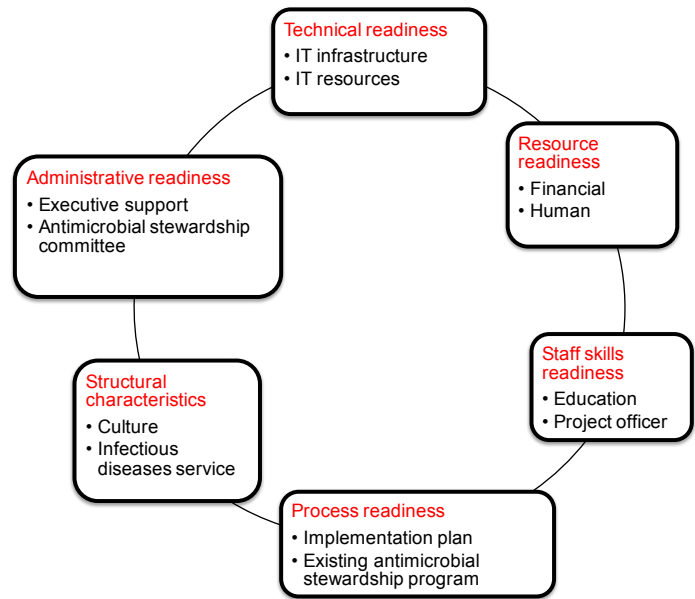


FIGURE 5 Factors influencing organisational readiness and resources required for implementation of a CDSS as part of an AMS program

### Features of CDSSs and factors that are likely to increase clinician uptake

- Speed
- Usability (ease of use, usefulness)
- Integration into workflow
- Promote action rather than inaction (i.e provide alternatives)
- Simple interventions work best
- Evidence/justification should be provided
- Impact should be monitored and feedback given to clinicians
- Incentives for use (printouts, calculations etc)
- Local adaptation of guidelines and local development

(Bates 2003, Kawamoto 2005, Moxey 2010)

FIGURE 6 Features of CDSSs and factors that are likely to increase clinician uptake.

## TOOLKIT RESOURCE

### ARTICLE

Bates DW, Kuperman GJ, Wang S, Gandhi T, Kittler A, Volk L, et al. Ten commandments for effective clinical decision support: making the practice of evidence-based medicine a reality. *J Am Med Inform Assoc.* 2003;10(6):523-30



## ▶ SUMMARY

- CDSSs are useful tools in AMS programs. A range of CDSS options, based on different approaches to decision support, are available, including mobile applications, approval systems, surveillance programs and EMR/EMM systems.
- CDSSs are simply assistive tools and cannot replace expert decision-making. They may support the prescriber or the AMS program, or both.
- Organisational and workflow factors can determine the effectiveness of a CDSS. There should be an established AMS program in place prior to implementation.
- AMS teams should consider existing and planned IT infrastructure when adopting a CDSS, and aim for the integration of systems where possible.
- Integration of CDSSs with existing hospital systems usually requires customisation and modification to ensure interoperability.

CDSS	TYPE	INTERVENTION OPPORTUNITIES	ADVANTAGES AND DISADVANTAGES
Smartphone applications	Passive	Dissemination of guidelines <ul style="list-style-type: none"> <li>• Disease-based</li> <li>• Drug-based</li> </ul> Calculators (dosing) Antibiograms	Rapid dissemination Useful for hospitals with poor IT infrastructure Not usually integrated with hospital systems Uncontrolled use, including version control May not influence prescribing of senior clinicians
Infection Prevention Surveillance Systems	Back-end (Asynchronous)	Pharmacy +/- laboratory integration Rule based alerts: <ul style="list-style-type: none"> <li>• Drug-bug mismatches</li> <li>• Double coverage</li> </ul> Monitor restricted drug usage Surveillance - real-time alerts	Support an organisational approach Can be integrated with an EMR Requires substantial resources to review reports and to determine clinically relevant alerts that need action Requires dedicated EFT to support Commercial systems can be expensive
Approval systems (standalone)	Front-end	Enforce formulary May be pre-prescription or post-prescription (after dispensing) Enforce approved indications by drug Educational opportunity for the prescriber Can include clinical decision support Reports and feedback	Can work well in the absence of EHR or EPS Support an organisational approach to AMS Best combined with an antimicrobial team to review patients at a time period post approval 24-48 hours

<p>CPOE/EMR EMR</p>	<p>Front-end Front end</p>	<p>Error alerts - allergy, dosing, medicine-medicine interactions</p> <p>Chart abstraction tools to screen and identify patients at risk for sepsis, or collate information for AMS (medicines, results)</p> <p>Pre-prescription restriction rules</p> <p>Record AMS recommendations and interventions</p> <p>Support order sets for syndromes (e.g., community-acquired pneumonia, sepsis)</p> <p>Alerts and triggers to identify patients suitable for intravenous-to-oral switch</p> <p>AMS review care protocols (templates or phased order sets)</p>	<p>Will reduce transcription errors but incorrect choice or indication may not be impacted</p> <p>Best combined with CDSS</p> <p>Real time interventions and alerts possible but alert fatigue is very common</p> <p>Allows for retrieval of data for research</p> <p>Patient-centred rather than organisational</p> <p>Requires additional resources to develop customised AMS reports</p> <p>Significant time required by hospital IT and investment by the institution to create the tools</p> <p>Eliminates the cost of external vendor</p> <p>Templates must be incorporated into EMR at each site</p> <p>Less responsive to change</p>
<p>Advanced CDSS</p>		<p>Causal probabilistic network approach to identification of pathogens, by specimen type or underlying conditions of patient</p> <p>Case-based probability</p> <p>Machine learning algorithms</p> <p>Pathogen prediction</p>	<p>Complex, usually 'home-grown' systems</p> <p>Currently in early phase of adoption.</p>

# CHAPTER 25

▶ AUTHOR: ENRIQUE CASTRO SANCHEZ

## THE ROLE OF THE NURSE IN STEWARDSHIP

### THE AIM OF THIS CHAPTER IS TO:

This chapter justifies the participation of nurses in antimicrobial stewardship and the benefits of including them as core components of stewardship teams. Different drivers encouraging the participation of nurses, such as operational and organisational factors are discussed.

Following that, some of the clinical tasks and roles that can be readily assumed by nurses in hospitals and community settings are discussed, including prescribing. The chapter presents some ideas about the importance of integrating non-clinical nursing staff, such as executives and managers, into stewardship efforts and with other healthcare professionals.

Finally, the chapter briefly reviews some of the experiences already published reporting on nurse-led or nurse-focused interventions, concluding with some of the remaining barriers to be addressed before participation of nurses in stewardship programmes can be extended and scaled-up.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

#### 1 Why should nurses be involved in antimicrobial stewardship?

- Describe drivers for participation of nurses in antimicrobial stewardship activities.

#### 2 Expanding the participation of nurses in antimicrobial stewardship

- Identify how antimicrobial documents and policies consider nursing participation in stewardship.
- Explain antimicrobial stewardship clinical tasks that could be adopted by nurses.
- Consider the impact in antimicrobial usage of advanced nursing roles such as prescribing.

#### 3 Public health and community nursing contribution to stewardship

- Critically argue some public health nursing behaviours that could be embedded within antimicrobial stewardship frameworks.
- Reflect on emerging activities in nursing homes and long-term care facilities that would benefit antimicrobial stewardship initiatives.

#### 4 Integration between nursing roles and activities in AMR and other professionals

- Understand the areas for antimicrobial stewardship synergy and integration between nurses and other professionals.

#### 5 Stewardship, a target for nurses in executive and directive positions.

- Discuss how nurses in executive and directive positions can contribute to and strengthen antimicrobial stewardship programmes.

#### 6 Nurse-focused interventions in antimicrobial stewardship

- Reflect upon some existing nurse-centred stewardship interventions.

#### 7 Barriers to resolve the participation of nurses in stewardship

- Examine some of the barriers to increased involvement of nurses in stewardship.
- Evaluate existing initiatives implemented to address barriers to nurse involvement.

**WHY SHOULD NURSES BE INVOLVED IN STEWARDSHIP?**

Due to the size of the challenge posed by drug-resistance infections worldwide, there have been calls to increase the number of health care workers involved in optimal antimicrobial stewardship (AMS) interventions

*“Governments, healthcare system leaders, and private actors should expand funding opportunities to increase the essential health workers on the frontline of fighting resistance”*

Tackling drug-resistant infections globally: final report and recommendations the review on antimicrobial resistance chaired by jim o'neill may 2016. [https://amr-review.Org/sites/default/files/160525\\_final%20paper\\_with%20cover.Pdf](https://amr-review.Org/sites/default/files/160525_final%20paper_with%20cover.Pdf)

However, by 2035 healthcare systems around the world will face a shortage of just under 13 million professionals (WHO, A universal truth: No health without a workforce, 2014). Successful AMS programmes will therefore have to strengthen existing cadres of professionals involved, whilst increasing the general stewardship workforce.

Developing nursing-based interventions and fostering the interest and participation of nurses in stewardship makes sense for many reasons. Nurses are the largest and most consistent healthcare workforce, with 19.3 million nurses worldwide (World Health Organization's World Health Statistics Report, 2011). All healthcare systems around the world have nurses: for example, there were ~100,000 doctors in the UK in 2017, but just under 300,000 registered nurses (<http://www.nhsconfed.org/resources/key-statistics-on-the-nhs>); in the US, just over 4 million nurses were professionally active in 2017 (<http://www.kff.org/other/state-indicator/total-registered-nurses/>); and in India, there are approximately 1.5 million nursing professionals (WHO, World Health Statistics Report 2011).

WHY SHOULD NURSES BE INVOLVED IN STEWARDSHIP PROGRAMS?

**> WATCH VIDEO**

Additionally, in many settings around the world the relative availability of nurses may help address the chronic undersupply of medically trained healthcare professionals. Thus, tasks and roles traditionally carried out by physicians and surgeons may need to be performed by nurses, with adequate support, training and supervision.

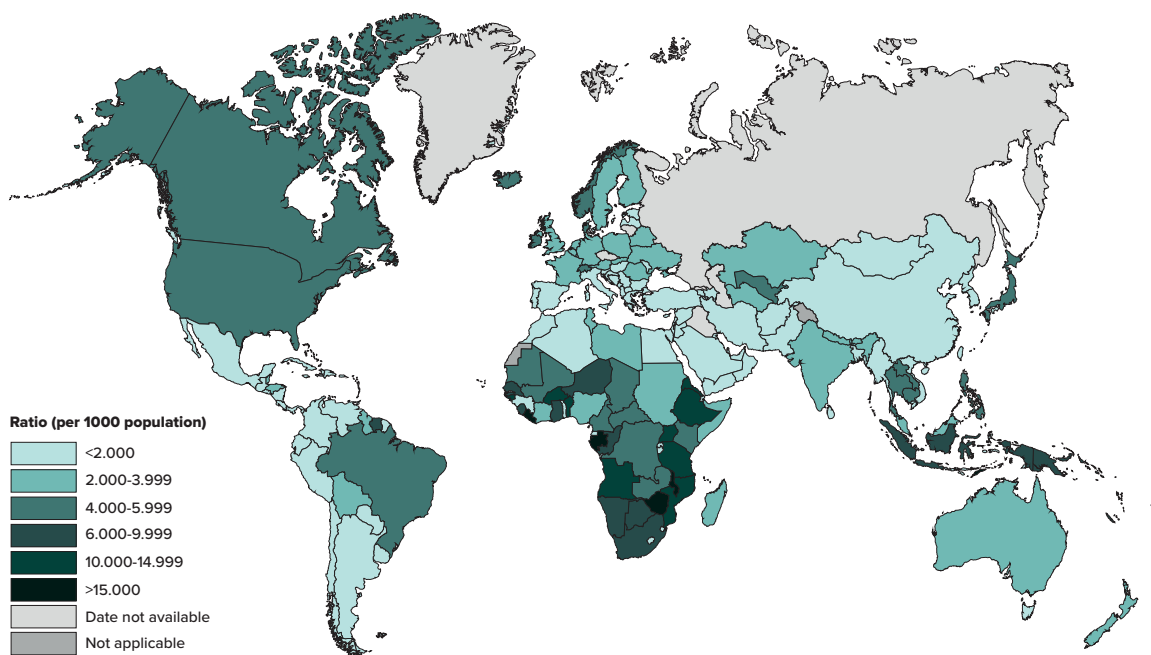
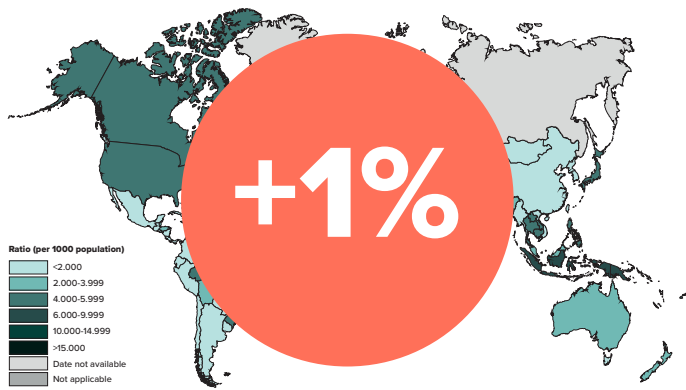


FIGURE 1  
Ratio of nurses & midwives to physicians, worldwide

Increasing stewardship capacity by adding a proportion of the nursing workforce (say, 1%) to AMS interventions could therefore be a powerful antimicrobial quality improvement measure.



### EXPANDING THE PARTICIPATION OF NURSES IN ANTIMICROBIAL STEWARDSHIP

Many authors have already proposed that antimicrobial efforts should consciously include nursing participation (Charani et al, 2013; Edwards et al, 2011), a gradual shift from earlier views about the optimal composition of antimicrobial stewardship teams (IDSA, 1997). These initial ideas did not offer much scope to nurses, unlike more recent perspectives that endorse 'interprofessional efforts across the continuum of care' and recognize a typical team core comprised of:

## PROPOSED CORE COMPOSITION OF ANTIMICROBIAL STEWARDSHIP TEAMS

- INFECTIOUS DISEASES PHYSICIAN
- CLINICAL MICROBIOLOGIST
- CLINICAL PHARMACIST WITH EXPERTISE IN INFECTION
- OTHER MEMBERS COULD BE SPECIALIST NURSES, FOR EXAMPLE INFECTION PREVENTION OR STEWARDSHIP NURSES...

(Nathwani, 2012)

In fact, some authors argue that the participation of nurses in stewardship may be extensive but 'unrecognised' (Olans et al, 2016). Some roles that appear naturally linked to stewardship activities are presented in Figure 2.

Table 1. Overlap of Nursing Activities With Function Attribution in Current Antimicrobial Stewardship Models

	Nursing	Microbiology	Case Management	Pharmacy	Infectious Diseases	Infection Control	Inpatient Physician	Administration
<b>Patient admission</b>								
Triage and appropriate isolation	*					*		
Accurate allergy history	*			*	*		*	
Early and appropriate cultures	*			*	*		*	
Timely antibiotic initiation	*			*	*		*	*
Medication reconciliation	*			*	*		*	
<b>Daily(24 h) clinical progress monitoring</b>								
Progress monitor and report	*		*	*	*		*	
Preliminary micro results and antibiotic adjustment	*	*		*	*		*	
Antibiotic dosing and de-escalation	*			*	*		*	
<b>Patient safety &amp; quality monitoring</b>								
Adverse events	*			*	*		*	
Change in patient condition	*			*	*		*	
Final culture report and antibiotic adjustment	*	*		*	*		*	
Antibiotic resistance identification	*	*		*	*		*	
<b>Clinical progress/patient education/discharge</b>								
IV to PO antibiotic, outpatient antibiotic therapy	*		*	*	*		*	
Patient education	*			*	*		*	
Length of stay	*		*	*	*		*	*
Outpatient management, long-term care, re-admission	*		*	*	*		*	*

Abbreviations: IV, intravenous; PO, per os (oral).

FIGURE 2 Nursing input in AMS across the clinical pathway (Olans, 2015)

## TOOLKIT RESOURCE

SITE LINK



Charani E, Holmes AH. Antimicrobial stewardship programmes: the need for wider engagement. *BMJ Qual Saf.* 2013;22:885-887

ARTICLE

Edwards R, Drumright L, Kiernan M, Holmes A. Covering more Territory to Fight Resistance: Considering Nurses' Role in Antimicrobial Stewardship. *J Infect Prev.* 2011;12(1):6-10. doi:10.1177/1757177410389627

## ROLE OF NURSES IN ANTIMICROBIAL STEWARDSHIP PROGRAMS




## WHAT CAN NURSES DO TO COMBAT ANTIMICROBIAL RESISTANCE?




## TOOLKIT RESOURCE

### SITE LINK

 Olans RN, Olans RD, DeMaria A. The Critical Role of the Staff Nurse in Antimicrobial Stewardship—Unrecognized, but Already There. *Clin Infect Dis.* 2016; 62(1): 84–89

### PDF ARTICLE

 Nathwani D. (2012) Practical Guide to Antimicrobial Stewardship in Hospitals

Nurses could ensure that:

- Adequate microbiological samples for culture and sensitivity are obtained prior to instigation of any antimicrobial therapy, if allowed by the patient's clinical condition (i.e., if the patient has sepsis and is not catheterised, it is inappropriate to wait for a urine specimen, although it is nearly always possible to perform a blood culture prior to antibiotic commencement).
- Laboratory results are communicated in a timely manner and consideration given to the impact of results on existing therapeutic decisions.
- Prescribed antimicrobials reflect local and national guidelines, as relevant.
- Antimicrobial doses are not missed and are administered according to optimal dose intervals.

- Antimicrobial administration is adapted to clinical needs as well as patient condition (i.e., evaluating oral routes if clinically appropriate).
- Improvements in the patient condition inform clinical decisions (e.g. to stop antibiotics).
- Patients and healthcare professionals are informed and educated about optimal antimicrobial use.
- Audits of antimicrobial use are supported by nurses.

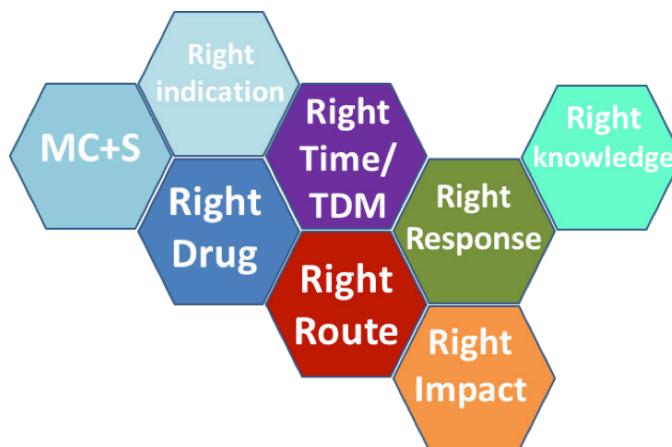


FIGURE 3  
Some clinical nursing roles in antimicrobial stewardship  
Key: MC&S = Microscopy, culture and sensitivity; TDM = therapeutic drug monitoring (e.g. gentamicin, vancomycin)



Depending on the setting and local scope of practice, nurses may be able to perform advanced roles, managing patients autonomously by, for example, prescribing antibiotics. For these cadres, it has been suggested that capacity-building, consulting and supporting others to use antimicrobials optimally may be as crucial as clinical aspects (Manning, 2014).

Videos from Castro-Sanchez:





## SUGGESTED ANTIMICROBIAL STEWARDSHIP ACTIONS FOR NURSES IN ADVANCED PRACTICE ROLES

- ADVANCE OWN KNOWLEDGE ABOUT ANTIBIOTICS
- OPTIMIZE ANTIBIOTIC PRESCRIBING PERFORMANCE AND PRACTICE
- ADVOCATE ADOPTION OF ANTIMICROBIAL STEWARDSHIP RECOMMENDED ACTIONS IN PRACTICE SETTING
- REACH OUT AND CONNECT WITH LOCAL NURSES IN ADVANCED PRACTICE ROLES

(Manning, 2014)

The impact on antimicrobial use of the growing number of nurse prescribers worldwide will require increased attention. Recent data suggests that in Scotland nurses were responsible for more than 5% of antimicrobials prescribed in the community (Figure 4).

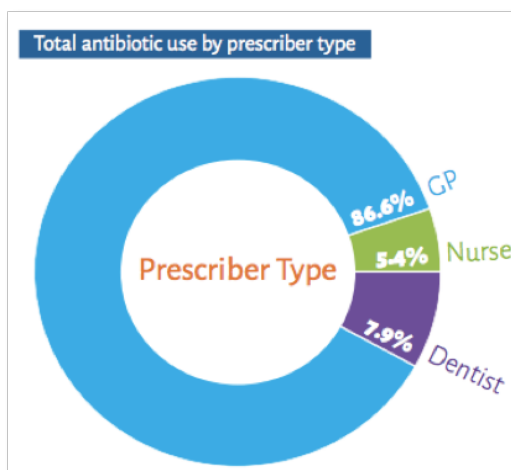


FIGURE 4  
Scottish Antimicrobial use and resistance in humans (2015)  
<https://www.isdscotland.org/Health-Topics/Prescribing-and-Medicines/Publications/2016-08-30/2016-08-30-SAPG-2015-Report.pdf?25829714537>

Should this trend in prescribing continue, in the near future community-based nurse prescribers may be responsible for more antimicrobial prescriptions than the volume issued in hospitals.

Additionally, in the last five years, prescribing of antimicrobials by nurses appears to represent a growing proportion of all nurse prescriptions (Figure 5).

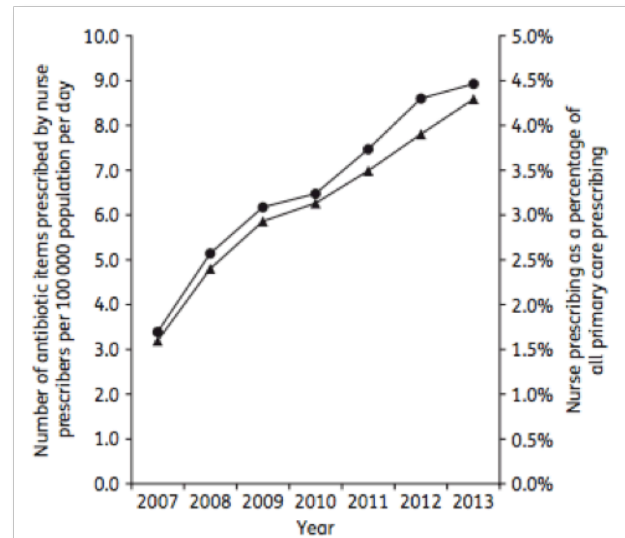


Figure 1. Number of antibiotic items prescribed by nurse prescribers per 100,000 population per day (circles) and nurse prescribing as a percentage of all primary care prescribing (triangles) in Scotland.

FIGURE 5

From: Ness V, Malcolm W, McGivern G, Reilly J. Growth in nurse prescribing of antibiotics: the Scottish experience 2007–13. *J Antimicrob Chemother* 2015; 70: 3384–3389  
<https://academic.oup.com/jac/article-lookup/doi/10.1093/jac/dkv255>

### PUBLIC HEALTH AND COMMUNITY NURSING CONTRIBUTION TO ANTIMICROBIAL STEWARDSHIP

The largest proportion of antimicrobials is prescribed in community settings, where nurses can potentially influence decisions. Further, there is an increased recognition of wider public health determinants of antimicrobial exposure that offer opportunities for nurses to act. For example, and in recognition of those determinants, the Royal College of Nursing in the UK launched in 2014 a statement about antimicrobial resistance that highlighted the crucial role of nurses to:


- Reducing demand for antibiotics.
- Influencing public and patient knowledge and expectations of antibiotic prescribing through their societal contacts.
- Leading and implementing immunisation programmes across all age groups to prevent avoidable infection and associated morbidity and mortality.

- Leading and implementing public health strategies to support the public to 'live well' and prevent or reduce the burden of long term conditions such as diabetes, liver disease, obesity.

Equally, nurses could be instrumental in leading, supporting, implementing and evaluating antimicrobial improvement initiatives in nursing homes or long-term care facilities

[VISIT SITE](#)

TOOLKIT RESOURCE  
SITE LINK

 CDC. 2017. The Core Elements of Antibiotic Stewardship for Nursing Homes

In these settings, skilled nurses should balance the increased vulnerability and frailty of patients with the careful use of screening and diagnostic tests as well as the meticulous management of invasive devices. For example, avoiding measures that have limited or no clinical benefit yet can trigger antimicrobial prescriptions, such as routine urine sampling, could be led, implemented and evaluated by nurses (Health Protection Agency, 2017)

- AMS and Nursing Homes - how can nurses make a difference?

[VIEW DOCUMENT](#)

## INTEGRATION BETWEEN NURSING ROLES AND ACTIVITIES IN AMR AND OTHER PROFESSIONALS

Whilst encouraging the participation of nurses in AMS activities can be beneficial on many levels, including new professional cadres and increasing the AMS-related interventions of existing professionals can have unintended consequences or lead to inefficiencies, if the process is not mapped, supported and audited.

Whilst obviously some responsibilities such as establishing a diagnosis and carrying out a comprehensive medical assessment are to be carried out by doctors, other responsibilities could be shared, or integrated, among the components of the healthcare team. For example, establishing the allergy status of a patient; timely initiation of antimicrobials; monitoring therapeutic drug levels; adhering to optimal infection prevention and control practice, etc., could be collaborative roles (Castro-Sanchez et al, 2017).



FIGURE 6  
Integration of nursing, medicine and pharmacy stewardship interventions (Castro-Sánchez et al, 2017)

## STEWARDSHIP, A TARGET FOR NURSES IN EXECUTIVE AND DIRECTIVE POSITIONS

In addition to fostering new clinical roles related to AMS, organisations would benefit from raising the awareness of antimicrobial resistance at nursing executive and board levels. It is likely that engaged board members and managers could have an impact on stewardship initiatives similar to that achieved in hand hygiene and infection prevention and control programmes. Further, demonstrating and developing a link to those programmes as well as patient safety and quality improvement interventions may be useful starting points to engage with hospital executives.

Recommendations from the American Nurses Association/ Centers for Disease Control and Prevention Workgroup on the Role of Registered Nurses in Hospital Antibiotic Stewardship Practices

[VIEW DOCUMENT](#)

**NURSE-FOCUSED INTERVENTIONS IN ANTIMICROBIAL STEWARDSHIP**

An Australian study (Gillespie, 2013) emphasised the opportunity for nurses and nurse education to influence the intravenous-to-oral switch decision, as a collaborative exercise between pharmacists, nurses, and doctors (Figure 9). Following education there was an increase in instances where nurses said they would question the need for intravenous antibiotics from 14% to 42% (P<.001).

**28% ↑**  
**IN DISCUSSIONS**  
**ABOUT IV TO PO SWITCH**

**TOOLKIT RESOURCE**

SITE LINK



Gillespie E, Rodrigues A, Wright L, Williams N, Stuart RL. Improving antibiotic stewardship by involving nurses. *Am J Infect Control.* 2013 Apr;41(4):365-7. doi: 10.1016/j.ajic.2012.04.336.

Similar improvements were seen in care homes where an online educational intervention was implemented (Wilson et al, 2017). The course improved knowledge, beliefs and attitudes of nurses towards AMS and was associated with an increased participation in stewardship activities.

**CONFIDENCE RELATED TO LEARNING OBJECTIVE FOR EACH MODULE**

**ATTITUDES TOWARD CLINICAL ASSESSMENT OF RESIDENTS**

**ATTITUDES REGARDING ROLE IN ANTIMICROBIAL STEWARDSHIP**

**ATTITUDES ABOUT ANTIMICROBIAL STEWARDSHIP**

**BELIEFS ABOUT ANTIMICROBIAL STEWARDSHIP AND INFECTION CONTROL AND PREVENTION**

(Wilson, 2017)

**Table 1**  
 Results of the questionnaire

Question	% (95% confidence interval)		P
	Pre-education	Post-education	
Duration of working, y	920	827	
Unable to state what antibiotics patient is on	27 (17.8-35.3)	15 (7.2-23.1)	.07
Able to state the duration the patient will be on antibiotics	50	60	.11
Would consider if the antibiotic was required before administering	14 (7.2-20.8)	43 (32.1-54.0)	.001
Understands what the switch to oral program is about (one site only)	24	94	<.001
Would question a patients antibiotic order if you thought it was inappropriate	92	97	.11
Have previously questioned a patents antibiotic order	71 (62.1-80.0)	91 (86.6-98.2)	<.001
Use of antibiotics can aid the development of resistance	59 (49.4-68.7)	79 (70.9-88.6)	.003
Use of antibiotics can increase the risk of VRE	5 (0.7-9.3)	23 (13.5-32)	.004
Use of IV antibiotics increases the risk of IV line associated bacteraemias	38 (28.5-47.5)	70 (60.9-80.9)	<.001

FIGURE 7  
 Effect of an educational intervention on nursing knowledge about antimicrobial resistance (Gillespie, 2013) Improving antibiotic stewardship by involving nurses <http://www.sciencedirect.com/science/article/pii/S0196655312008188>

**TOOLKIT RESOURCE**

SITE LINK



Wilson BM, Shick S, Carter RR, et al. An online course improves nurses' awareness of their role as antimicrobial stewards in nursing homes. *Am J Infect Control,* 2017

Interesting experiences led and managed by nurses have also been reported in low- and middle-income countries; an increasing response and activity by nurses in these settings is likely to be vital in the global response to AMR.

Broad Spectrum Coverage: Cross-Professional Engagement to fight antimicrobial resistance in South Africa:

**VIEW PRESENTATION**

## CHAPTER 25 - THE ROLE OF THE NURSE IN STEWARDSHIP

For example, a study by Du Toit et al in a South African hospital reported on a nurse-led intervention implementing a checklist. The intervention decreased excessive antibiotic duration, increased compliance with cultures before antibiotics, and optimised device removal (Figures 8, 9).

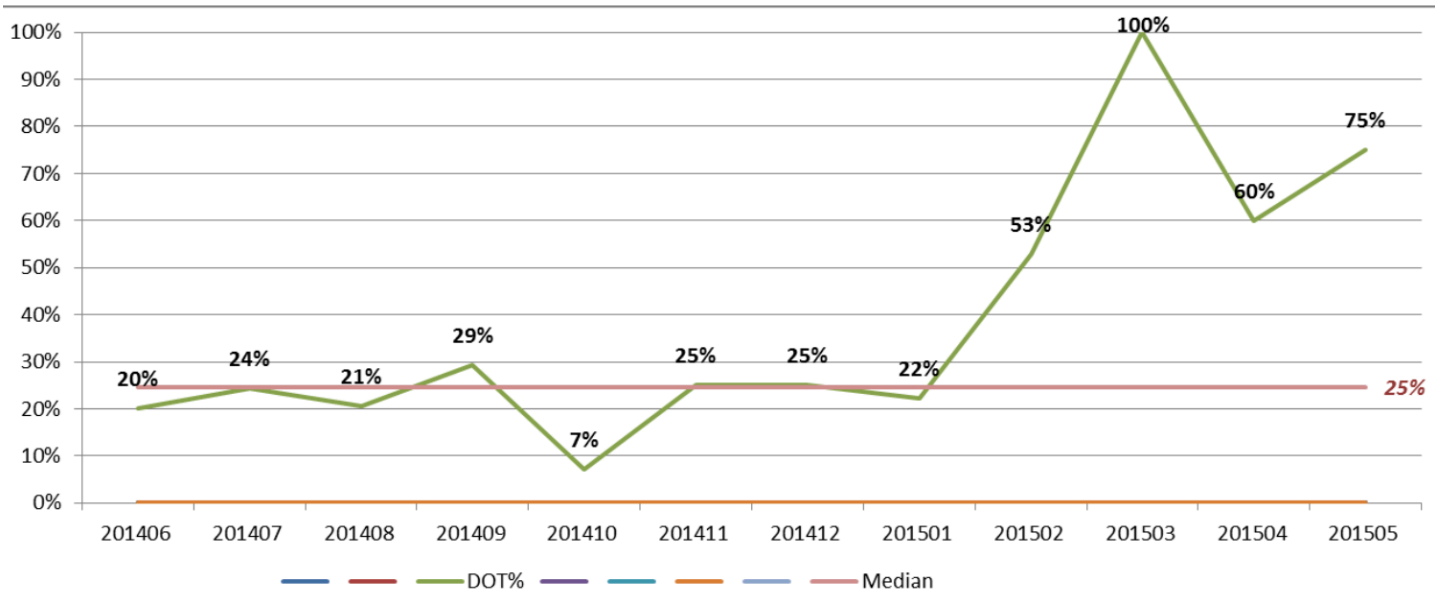


FIGURE 8  
Improvement in compliance with “duration of therapy”

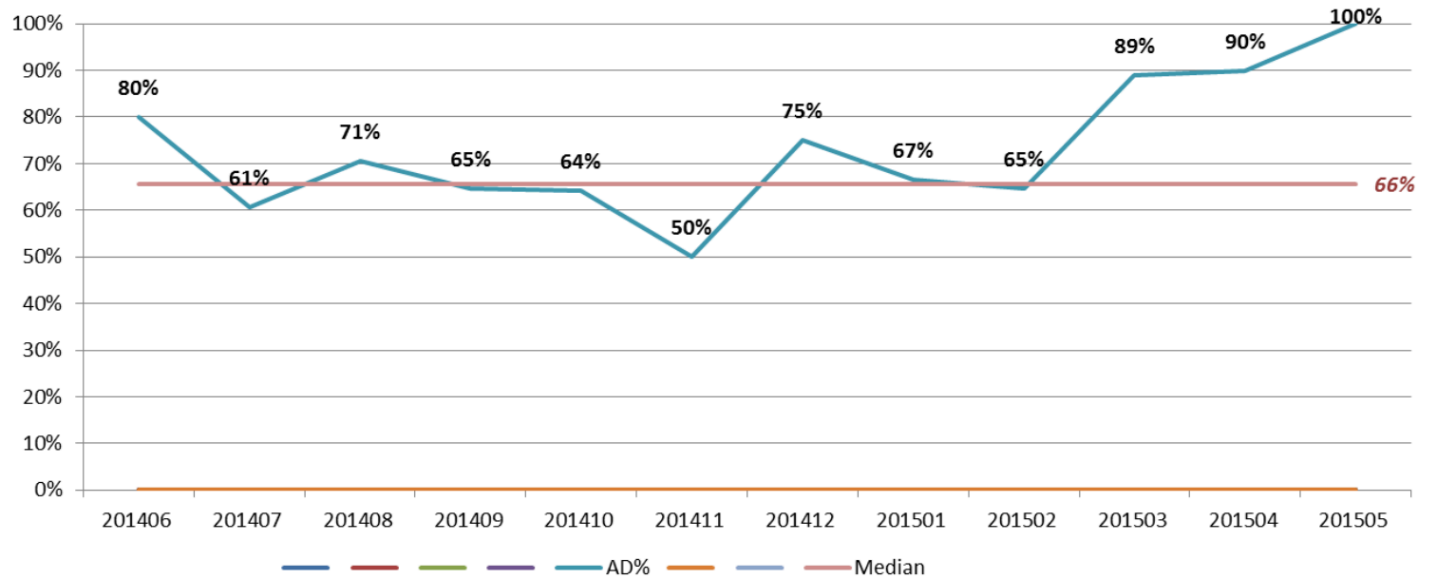


FIGURE 9  
Improvement in compliance with device removal

From: Du Toit, Briette (2015). The role of the critical care nurse in the implementation of an antimicrobial stewardship programme in a resource-limited country. Thesis (MSc) --Stellenbosch University, 2015. <http://hdl.handle.net/10019.1/98036>

**BARRIERS TO RESOLVE THE PARTICIPATION OF NURSES IN STEWARDSHIP**

Several barriers can affect the development, implementation and scale-up of antimicrobial stewardship roles for nurses. Among these barriers we find:

**a) Ownership/'branding'**

Despite the growing interest in the participation of nurses in stewardship, frequently nurses do not recognise the potential impact of their role in antimicrobial stewardship. If stewardship is suggested, it is possible that nurses express concern for the tasks and care left undone due to staff shortages or workloads of increased complexity. As such, nurses may also consider that stewardship refers to appropriate prescribing, rather than appropriate management of antimicrobials. Such ideas may drive perceptions of inappropriateness and foster an unwillingness to participate in AMS activities (Cotta, 2014).

	Heard about AMS	Willing to participate in AMS
Anaesthetists	38%	51%
Pharmacists	80%	100%
Physicians	64%	55%
Surgeons	37%	48%
<b>Nurses</b>	<b>22%</b>	<b>43%</b>

However, examining the recommended antimicrobial management principles included in clinical guidelines such as 'Start Smart Then Focus' (PHE, 2015) is helpful to identify elements easily embedded in routine optimal care.

- 01** Minimise unnecessary prescribing of antimicrobials
- 02** Ensure adequate timing of antimicrobial administration
- 03** Adopt necessary infection prevention and control measures
- 04** Obtain samples for microscopy, culture and sensitivity testing
- 05** Therapeutic drug monitoring, following adequate and/or adjusted dosing
- 06** IV administration only in severely ill, unable to tolerate oral treatment
- 07** Review microbiology results daily, de-escalate to narrow-spectrum
- 08** Review IV treatment daily, switch to oral route promptly
- 09** Require single dose surgical prophylaxis regimens as appropriate

FIGURE 9  
Optimal antimicrobial management principles

**TOOLKIT RESOURCE**

PDF ARTICLE

 Public Health England. 2015. Start Smart Then Focus'

In fact, some authors have proposed that 'Good nursing care is good stewardship, and good stewardship is good nursing care'

**CHA ANTIMICROBIAL STEWARDSHIP: GOOD NURSING IS GOOD STEWARDSHIP**

 WATCH VIDEO

*'Good nursing care is good stewardship, and good stewardship is good nursing care'*

**b) Educational barriers**

Probably, nurses have difficulty identifying their role and involvement within stewardship due to the inadequate education they receive on the topic at undergraduate level (Castro-Sánchez et al, 2016). In essence, nurses do not know what they should do as stewards and stewardship processes that are often less well conducted (e.g. single-dose surgical prophylaxis or intravenous-to-oral switch) appear to be even less frequently included in course curricula.

This theory-practice gap is being resolved by implementing education interventions targeting different settings. For example, increased undergraduate nursing education about antimicrobials in Scotland led to significant knowledge and attitude improvements, which are likely to translate into positive clinical, health and fiscal outcomes for patients and the health service.

 WATCH VIDEO

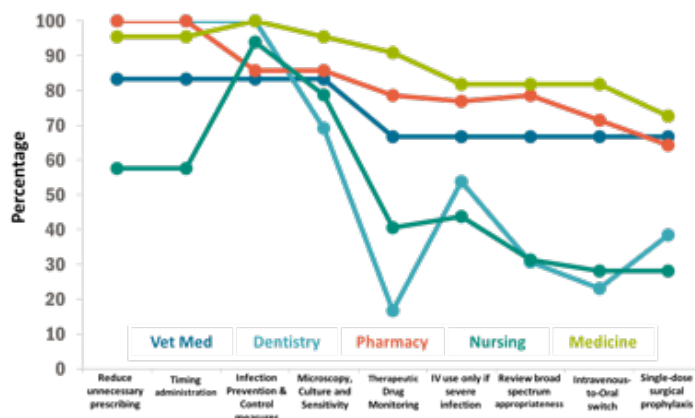
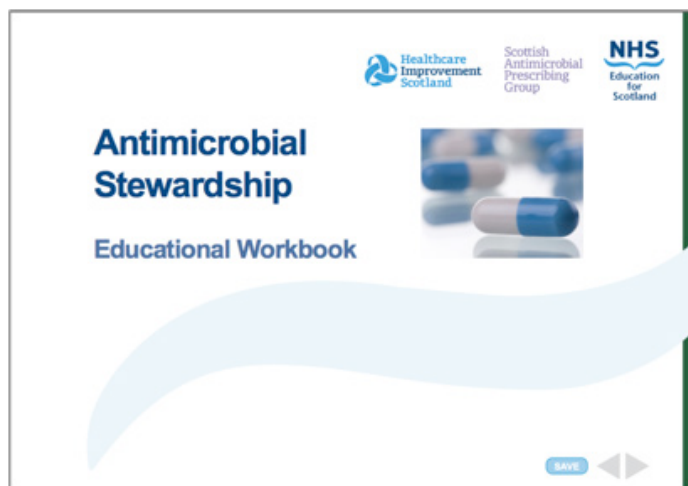


FIGURE 10 Antimicrobial stewardship principles by undergraduate discipline, UK courses, 2013  
 From: Castro-Sánchez E, Drumright LN, Gharbi M, Farrell S, Holmes AH (2016) Mapping Antimicrobial Stewardship in Undergraduate Medical, Dental, Pharmacy, Nursing and Veterinary Education in the United Kingdom. PLoS ONE 11(2): e0150056. <https://doi.org/10.1371/journal.pone.0150056>


Finally, efforts to develop formal educational packages for nurses have already crystallised into resources such as clinical workbooks that aim to provide learning about antimicrobial stewardship and support practice in this area (NES Scot, 2015).



Other initiatives have taken advantage of new technologies such as smartphone applications ('apps') and, in collaboration with end-user nurses, have co-designed nurse-specific guidelines that reflect nurse interests and work requirements to increase participation in stewardship (Wentzel et al, 2014). The impact and sustainability of such approaches is yet to be established, recognising that its use may not be feasible worldwide.

## TOOLKIT RESOURCE

### SITE LINKS

 Castro-Sánchez E, Drumright LN, Gharbi M, Farrell S, Holmes AH (2016) Mapping Antimicrobial Stewardship in Undergraduate Medical, Dental, Pharmacy, Nursing and Veterinary Education in the United Kingdom. PLoS ONE 11(2): e0150056

### PDF ARTICLE

 NHS Education for Scotland (2015) Antimicrobial Stewardship Educational Workbook

**Antibiotic Information App** Jobs Log out

Find an antibiotic:

Search within this antibiotic:

Application	Dose	Preparation	Administration			
Precautions, details	Details	Acute responses	Side effects	Compatibility	Interactions	Contraindications
About this antibiotic	Properties	Available products	Indication	Extra checks		
Safety, checks	Your own safety	Protocols	Overdose			
Medical information, other	Pharmacokinetics	Renal failure	Contact			

Recent updates: Version: 30-01-2013 Versie 1.2



### c) Leadership

Whilst clinical nursing roles in stewardship appear to be increasing, there is still a need to engage with nurse leaders so they recognise the importance of the nursing contribution towards stewardship efforts. Encouragingly, some nursing leaders are galvanising the debate about antimicrobial resistance and AMS



READ VIV BENNET'S  
BLOG ENTRY



READ JO BOSANQUET'S  
BLOG ENTRY

Building leadership capacity among stewardship nurses and increasing the awareness about the threat of antimicrobial resistance among nursing leaders has also been proposed as a useful approach to ensure that nursing efforts in stewardship are continued and effective.



VIEW IMPERIAL EVENT



FIGURE 11

1st International Nursing Summit on Antimicrobial Stewardship, National Institute for Health Research in Healthcare Associated Infection and Antimicrobial Resistance at Imperial College London



### CONCLUSION

Optimal antimicrobial stewardship efforts demand multidisciplinary approaches to retain impact and sustainability. Although the participation of nurses in stewardship initiatives remains limited and focused on clinical aspects, there are emerging opportunities to expand these roles and involve executives, leaders and policy-makers.

Learning from existing experiences from around the world will help address some of the challenges associated with the implementation of this new sphere of practice for nursing professionals.

## CHAPTER 25 - THE ROLE OF THE NURSE IN STEWARDSHIP

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# CHAPTER 26

 AUTHORS: **DEBRA A GOFF & TIMOTHY GAUTHIER**

## THE ROLE OF THE PHARMACIST IN STEWARDSHIP

### THE AIM OF THIS CHAPTER IS TO:

Define the role of an antibiotic stewardship pharmacist.

Describe eight key roles of a stewardship pharmacist.

Provide examples of how pharmacists perform each role.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- Explain how to work with a microbiologist to implement a rapid diagnostic test in the hospital setting
- List some ways a pharmacist can provide advocacy for the responsible use of antibiotics
- Define the different roles of the pharmacist in antibiotic stewardship



A pharmacist has multiple roles in an antibiotic stewardship program. The Society of Infectious Diseases Pharmacists (SIDP) and the American Society of Health-System Pharmacists (ASHP) in the United State published a position paper highlighting the importance of pharmacists with training in antimicrobial stewardship in an effective antimicrobial stewardship program (ASP). Ideally, every ASP pharmacist should have formal infectious diseases (ID) training and maintain their ID skills through continuing education and professional development. The reality of having an ID-trained pharmacist at every hospital presents a challenge. Certificate programs, online courses, and eBooks are highly encouraged if more formal training is not possible.

The Centers for Disease Control (CDC) Core Elements document states successful stewardship programs must have not only physician leadership and accountability but also drug expertise from a pharmacist leader. We describe 8 core roles of an ASP pharmacist and provide real-world examples from successful ASPs.

## PATIENT CARE




### Managing Drug Interactions





In the hospital setting, pharmacists working from a centralised pharmacy can make interventions such as IV to PO conversion, renal dosage adjustments, therapeutic drug level monitoring and review antibiotic durations of therapy. Pharmacists who participate in patient care rounds are able to perform these tasks as well and are able to provide more advanced interventions including PK/PD optimisation based upon patient-specific factors and MIC of the organism and rapid de-escalation of therapy.

## TOOLKIT RESOURCE

### PDF ARTICLE

-  Checklist for Core Elements of Hospital Antibiotic Stewardship Programs
-  Core Elements of Antibiotic Stewardship in Nursing Homes
-  The Essential Role of Pharmacists in Antimicrobial Stewardship

### SITE LINK



-  Core Elements of Outpatient Antimicrobial Stewardship
-  Goff DA., Kullar R., Goldstein E et al. Lancet Inf Dis 2017 Feb;17(2):e56-e63. doi: 10.1016/S1473-3099(16)30386-3. A global call from five countries to collaborate in antibiotic stewardship: united we succeed, divided we might fail.

## TOOLKIT RESOURCE

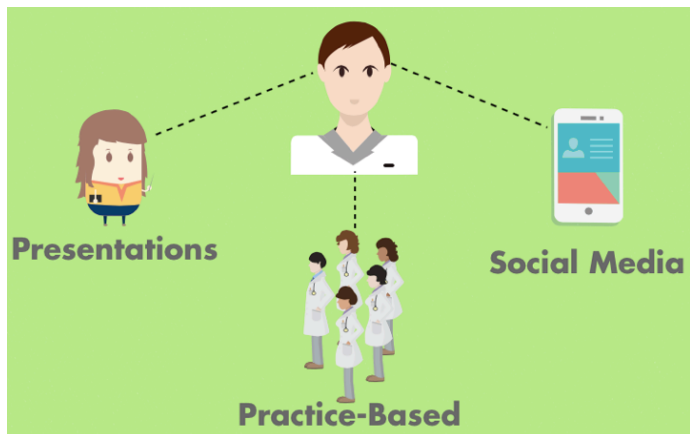
### PDF ARTICLE

-  IV to PO Conversion: Quick Reference Guide for Hospital Pharmacists

### SITE LINK

-  Pharmacokinetics and Pharmacodynamics for antibiotics: back to basics
-  Insights and Resources: Antibiotic renal dose adjustments

➤ EDUCATOR



Pharmacists provide education on antimicrobial stewardship by sharing drug expertise knowledge within and external to the pharmacy profession. Let's look further into three categories of education...

A. Presentations

Within the classroom setting a common lecture for pharmacists to give is on “bugs and drugs”, which focuses on clinical infectious diseases pharmacotherapy.

B. Practice-based education

Teaching in the field is an important component in the learning process. Pharmacists serve to cultivate drug knowledge for trainees and providers. Since all specialties in healthcare prescribe antibiotics, the role of the pharmacist in providing education on the responsible use of antibiotics is critical.

C. Social Media for education

Social media is one forum that has attracted much attention as a non-traditional mechanism for education. This includes platforms such as Facebook, Instagram, Twitter, Figure1, and Youtube. In these spaces pharmacists can connect with an audience in a unique way, while providing meaningful resources or information.

One example comes from the @IDstewardship on Instagram, authored by an infectious diseases PharmD with several years of experience leading antimicrobial stewardship. His writing consists of practical information for real-world use of antibiotics, interviews with thought leaders, and fundamentals of infectious diseases pharmacotherapy

➤ WATCH VIDEO



**idstewardship** Got #cefazolin? The hospital pharmacy does!... Cefazolin (Ancef) is a 🍌 first-generation #cephalosporin and beta-lactam antibiotic. It is most commonly employed for its Gram positive activity, which includes 🦠 MSSA and Streptococcus pyogenes (both common skin and soft tissue infection pathogens)... Cefazolin can cover some limited Gram negatives and the acronym 🦠 "PEcK" is used to help remember Proteus, E. coli, Klebsiella... ❌ Cefazolin does not have any noteworthy anaerobic coverage... Cefazolin is used at great frequency in the 🏠 operating room for #surgical prophylaxis. . #Pharmacy #PharmacySchool #PharmSchool #Medicine #MedSchool #NursingSchool #PASchool #ARNPschool #RNscool #pharmacotherapy

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## TOOLKIT RESOURCE


### PDF ARTICLE

 [Practical Guide to Antimicrobial Stewardship in Hospitals](#)

### SITE LINK

 [Antimicrobial Stewardship Online Training Course \(British Society for Antimicrobial Chemotherapy and University of Dundee\)](#)

 [Development of Antimicrobial Competencies and Training for Staff Hospital Pharmacists \[open-access\]](#)

 [Review of Twitter for Infectious Diseases Clinicians: Useful or a Waste of Time? \[open-access\]](#)


 [Instagram and Clinical Infectious Diseases \[open-access\]](#)


## TOOLKIT RESOURCE


### PDF ARTICLE

 [PDF of IDSA 2018 guideline \[open access\]](#)

### SITE LINK

 [Wenzler E, Wang F, Goff DA et al. An Automated, Pharmacist-Driven Initiative Improves Quality of Care for Staphylococcus aureus Bacteremia. Clin Infect Dis. 2017 Apr 4. doi: 10.1093/cid/cix315. \[Epub ahead of print\]](#)

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## RESEARCH

Research is an important component of antibiotic stewardship. The Infectious Diseases Society of America (IDSA) guidelines suggest ASPs implement interventions to improve antibiotic use and clinical outcomes that target patients with specific infectious diseases syndromes. This approach allows the message to be focused, reinforces hospital specific guidelines, and is sustainable. Performing antimicrobial stewardship without collecting outcome metrics is a weakness of some ASPs. It is imperative to determine if ASP interventions provide meaningful impact on antimicrobial use, resistance rates, and patient outcomes. Pharmacist initiated ASP research can be done collaboratively with the physicians, nurses, and microbiologists. Some examples of pharmacist initiated ASP studies include

- Disease based stewardship: An Automated, Pharmacist-Driven Initiative Improves Quality of Care for Staphylococcus aureus Bacteremia.
- Evaluating a specific antibiotic: Evaluation of Minocycline for Multidrug-Resistant Acinetobacter baumannii Infections
- Pharmacokinetic-Pharmacodynamic dose optimization: Extended-infusion cefepime reduces mortality in patients with Pseudomonas aeruginosa infections.


## RAPID DIAGNOSTIC TESTS


Rapid diagnostic tests (RDT) are game changing in the management of patients with infectious diseases. Several studies have shown that a RDT with ASP involvement shortens the time to effective antibiotic therapy. Some studies have also shown a mortality benefit. The key to successful implementation within a hospital is to make sure the microbiologist works with ASP. Studies have shown that when a RDT is made available without ASP, the results are not acted upon rapidly. This is a waste of financial resources and does not improve patient care. Pharmacists should work with the microbiologist to develop a strategy to receive the RDT result prior to implementation. In a paper chart system where significant delays can occur, the lab may need to page, text or phone the pharmacist. Hospitals with electronic records need to determine the most efficient way to alert the pharmacist with the test result. The toolkit provides a RDT review article and several studies that show how RDT plus ASP improves patient care.





## TOOLKIT RESOURCE

## SITE LINK

 Wenzler E, Wong J, Goff DA et al . Controversies in Antimicrobial Stewardship: Focus on New Rapid Diagnostic Technologies and Antimicrobials. *Antibiotics (Basel)*. 2016 Jan 14;5(1). pii: E6. doi: 10.3390/antibiotics5010006.

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## DRUG THERAPY EXPERT

**Pharmacokinetic/ Pharmacodynamic (Pk/PD) optimization:** As drug therapy experts, pharmacists are able to develop treatment plans that optimise PK/PD parameters. An important example of where this comes into play is for beta-lactam infusions. The longer the period of time the concentration of drug is above the bacteria's minimum inhibitory concentration (MIC) at the site of infection, the more bacterial killing. Through administering an intravenous beta-lactam (e.g., cefepime) over 3 hours or 4 hours (rather than the standard 30 minutes), the amount of time the concentration is above the MIC can be increased, thus improving bacterial killing. This can positively impact the chances for a successful outcome.

**Therapeutic drug monitoring:** Many antibiotics require therapeutic drug monitoring (e.g., vancomycin, aminoglycosides, voriconazole). In these instances the pharmacist's familiarity with the medications plus their understanding of complex drug interactions can be invaluable.


**Formulary decisions:** Pharmacists play a part in hospital antimicrobial formulary management. They help to decide which antibiotics should be on “protected status” to assure they are used appropriately with ASP oversight

HERE IS A BRIEF TEDX TALK ABOUT HOW PHARMACISTS ARE THE NEW “DISRUPTORS” IN HEALTHCARE, BECAUSE OF THEIR ROLE AS THE DRUG THERAPY EXPERT


 WATCH VIDEO

## TOOLKIT RESOURCE

## PDF ARTICLE

 Extended-Infusion Cefepime Reduces Mortality in Patients with *Pseudomonas aeruginosa* infection. [open access]

## SITE LINK

 Antimicrobial Stewardship Programs: A Review for the Formulary Decision Maker [open access]

## PATIENT SAFETY

Through individual action and by participating on inter-professional teams, pharmacists are working to impact patient safety in the area of antimicrobial use.


In improving patient safety, pharmacists can be involved in:

- Reporting medication errors
- Evaluating data from reported errors
- Participating in root-cause analysis
- Developing and implementing system-wide changes to improve practices
- Participating in hospital committee work




Pharmacists are patient safety leaders and with antimicrobial stewardship, their role extends from the medication management arena into other realms, such as infection control. One key example of this is with *Clostridium difficile* infection. In preventing and controlling this important pathogen, a combination of infection control and prudent antimicrobial use is warranted.

## TOOLKIT RESOURCE

### PDF ARTICLE

 **Patient Safety Movement. Actionable Patient Safety Solution (APSS) #3A: Antimicrobial Stewardship. The Role of Pharmacy and the Microbiology Lab in Patient Safety [open access]**

### SITE LINK

-  [Institute for Safe Medication Practices Tools and Resources](#)
-  [Institute for Safe Medication Practices Canada. Ontario Antimicrobial Stewardship Project. Preserving Antibiotics for Future Generations](#)
-  [Five Medication-Related Interventions Every Pharmacist Should Know about \*Clostridium difficile\*](#)

## QUALITY CARE

Achieving quality in care aligns with antimicrobial stewardship goals and some antimicrobial stewardship pharmacists are even employees of the hospital quality department rather than the hospital pharmacy department.

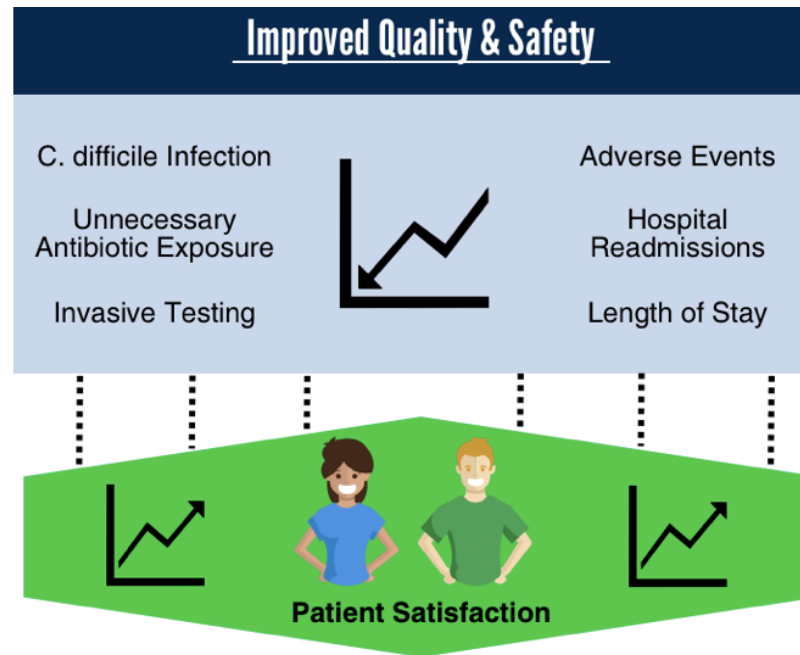
As new antimicrobial stewardship processes or services are developed, continuous quality improvement monitoring may be necessary. Through these monitors, enhancements can be identified for further enhancing quality of care. As data from monitors is produced, it can be reported to administration to demonstrate the value of antimicrobial stewardship programs.

One study showed one in five inpatients treated with antibiotics are harmed.

Internationally, antimicrobial stewardship standards are becoming a component of quality measures. As this trend persists, the pharmacists must engage quality officers to ensure compliance.

## ADVOCACY

Pharmacists play an important role in advocating the responsible use of antibiotics to healthcare providers, patients and consumers. Advocacy can occur at **Anytime**, to **Anyone**, **Anywhere**. Remember the 3A's when you think of antibiotic advocacy. This 5 minute podcast provides real-world examples for pharmacists on how to advocate for the responsible use of antibiotics.



## 1 in 5 inpatients treated with antibiotics is harmed

Retrospective cohort study of 5,579 adult internal medicine inpatients at Johns Hopkins Hospital

- 27% received antibiotics
- 20% developed at least 1 adverse antibiotic event
- 19% of antibiotic regimens not clinically indicated



### 324 antibiotic adverse events:

GI 41%	MDRO infection 26%	Renal 14%
Heme 9%	Hepatobiliary 4%	Neuro 4%

Tamma PD et al. JAMA Intern Med 2017; 177:1308-15.

This #VisualAbstract was created by Michael Edmond / @Mike\_Edmond

## Advocacy for Responsible Use of Antibiotics

**Anytime**



**Anyone**



**Anywhere**



## TOOLKIT RESOURCE

## PDF ARTICLE



Antimicrobial Stewardship Across 47 South African Hospitals: an Implementation Study [open access]

## SITE LINK



National Quality Partners Playbook: Antibiotic Stewardship in Acute Care



A Review of Quality Measures for Assessing the Impact of Antimicrobial Stewardship Programs in Hospitals [open access]



Australian Commission on Safety and Quality in Healthcare: Antimicrobial Stewardship Initiative



Association of Adverse Events With Antibiotic Use in Hospitalized Patients. Tamma et al



Website with daily updates on antibiotic global news, literature, meetings, research, article links, and podcasts



IDSA Guideline Implementing an Antibiotic Stewardship Program



## DOWNLOAD SLIDE SET

To illustrate an example of a pharmacist advocating for the responsible use of antibiotics you may wish to watch the following 2 videos. Video one is from a TEDx talk by Debra Goff PharmD titled “Antibiotics: just-in-case” As you watch the video consider the following

- What is the predicted numbers of deaths from antibiotic resistant infection by 2050 if we just stay the course?
- What percent of antibiotics prescribed by doctors in US hospital have errors such as the wrong dose, wrong duration, or even the wrong drug?
- How can a patient be an antibiotic steward while they are hospitalised?

## TEDX TALK



## WATCH VIDEO

This short 1 minute animated video with voice over, provides an easy quick way to engage not only healthcare providers in antibiotic stewardship but also consumers and patients. It provides the user with a 1-minute elevator pitch on the responsible use of antibiotics. As you watch the video think of the following:

- After a colleague, patient, or friend watches the video what type of discussion would you have with them?
- What are the key take aways from the video?

## ANIMATED VIDEO



## WATCH VIDEO

# CHAPTER 27

 AUTHOR: MICHAEL CORLEY

## INFORMING & INFLUENCING: STEWARDSHIP, POLITICIANS & THE MEDIA

### THE AIM OF THIS CHAPTER IS TO:

Outline the benefits of engaging with politicians and mainstream media on issues relating to antimicrobial resistance (AMR) and antimicrobial stewardship (AMS).

Argue that a culture of transparency and public accountability can help to drive the creation and maintenance of a dynamic community of research and practice in AMR and AMS.

Demonstrate that the need for public engagement on AMR and AMS has never been more urgent.

Point to the challenges of communicating clearly and responsibly to non-specialists on AMR and AMS.

Signpost to a few resources that can aid clearer and more responsible communication.

Offer several ways in which healthcare professionals and scientists can engage with mainstream media, new media, politicians, and the policymaking process.

### LEARNING OUTCOMES

On completion of this chapter, the participant should be able to:

- understand why engaging with politicians and journalists is so important to raising awareness of AMS
- appreciate the link between a dynamic community of research and practice and a culture of transparency and accountability
- articulate why the need for public engagement has never been more urgent
- outline the challenges of communicating clearly and responsibly
- list some of the resources that can aid clear and responsible communication
- engage confidently with a range of politicians and journalists

*“Never doubt that a small group of thoughtful committed citizens can change the world. Indeed, it is the only thing that ever has.”*

Margaret Mead, US Anthropologist (1901 to 1978)

*Though much of the information in this chapter can be applied universally, many of the references are to UK-based bodies and practices. This is only because it would have been impractical to try to account for differences between every media outlet, voting chamber, or system of government. Instead, it is hoped that readers will adopt and adapt the content to suit their own circumstances.*

## GOING PUBLIC

### **Bringing about positive and sustainable change**

Whether you call it campaigning, influencing, advocating, networking, or giving voice, this chapter is focused on some of the ways that we – both individually and collectively – can bring about positive and sustainable change by engaging with mainstream media and politicians.

Like the first principle of open justice, good AMS must not only be done; it must also be seen to be done. How else can best practice be extended and sustained if it is not first acknowledged, and a high value given to it by the public, politicians, and the media?

This principle also underpins the culture of transparency – which is essential for learning, improving, and making each other accountable for the actions we take. Engaging with the media and politicians, then, can help to raise good stewardship to a level of consciousness that can drive the creation and maintenance of a dynamic community of practice and research.

### **Responding to the urgent need**

And yet despite the undeniable benefits of raised awareness almost all of the evidence suggests that the need for public engagement on AMR has never been more urgent.

A 2015 survey by the World Health Organization across 12 countries highlighted the lack of familiarity with the language of antibiotic resistance.

pointed to several dominant, but competing, discourses on the subject: ‘AMR as healthcare’, ‘AMR as development’, ‘AMR as innovation’, ‘AMR as security’ and ‘AMR as One Health’. Each has its own scientific origin, conception of the problem, and method to prioritise action. Alone, they cannot account for the total complexity of the challenge.

### **Getting the story straight**

Wedded to the complexity of several competing discourses is the phenomenon that more and more people want to involve themselves in the creation and delivery of the campaigns they support. This is understandable, and mostly desirable. But it stands to reason that for each of us to be helped in our efforts we must all tap into an approach that is essentially coherent and cohesive. One of the quickest and easiest ways to do this is for each of us to think about our audience when:

- Defining the problem
- Outlining practical solutions
- Describing the part we play (or would like to play)
- Deciding what language to use (e.g. technical, conversational, rhetorical)
- Bringing what we say to life with examples and illustrations
- Linking our story to recent or forthcoming events or developments
- Issuing a clearly-defined ‘call to action’

### **Case study**

Did the many headlines and discussions that followed the BMJ’s publication (July 2017) of Llewellyn et al’s opinion piece on when it is appropriate to stop taking antibiotics, help or hinder the public’s understanding of AMR and AMS?

 VISIT SITE

A study by Wellcome Trust in the same year also found people in the UK have little awareness of what ‘antibiotic resistance’ means and how it might affect their health.

 VISIT SITE

Even among healthcare professionals, AMR can mean different things to different people. An article published by Wernli et al in the BMJ in 2017

 VIEW ARTICLE

 VIEW PUBLICATION





Rule that patients must finish antibiotics course is wrong, study says

Experts suggest patients should stop taking the drugs when they feel better rather than completing their prescription

It is, of course, a question of perspective. Debate is to be welcomed – but what if it leads to more confusion than clarity? BSAC’s take on the situation was published in the Guardian soon afterwards.

*BSAC’s reply, published in the Guardian (July 2017), to ‘The antibiotics course has had its day’ article*

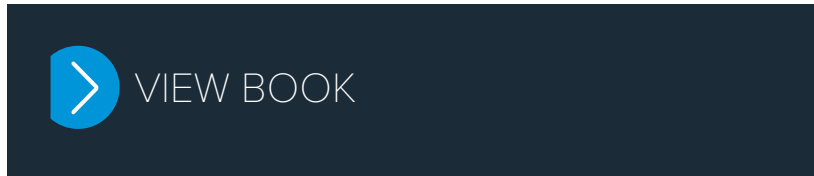
Follow professional advice on antibiotics

The idea that patients should stop taking antibiotics ‘when they feel better’ is too subjective, say representatives of the British Society for Antimicrobial Chemotherapy



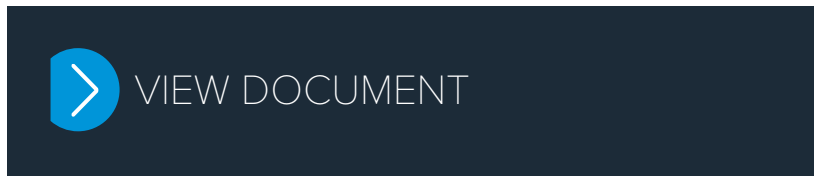
Communicating clearly and responsibly

As Ben Goldacre points out in his book Bad Science,



many mainstream journalists do not have a scientific background. Consequently, we must all take some responsibility for working with newsgathering organisations to inform debate and to report developments accurately and proportionately.

If you want to communicate research results to the public, you might like to consider The Royal Society’s excellent guidance on the subject: ‘Science and the public interest: Communicating the results of new scientific research to the public’.





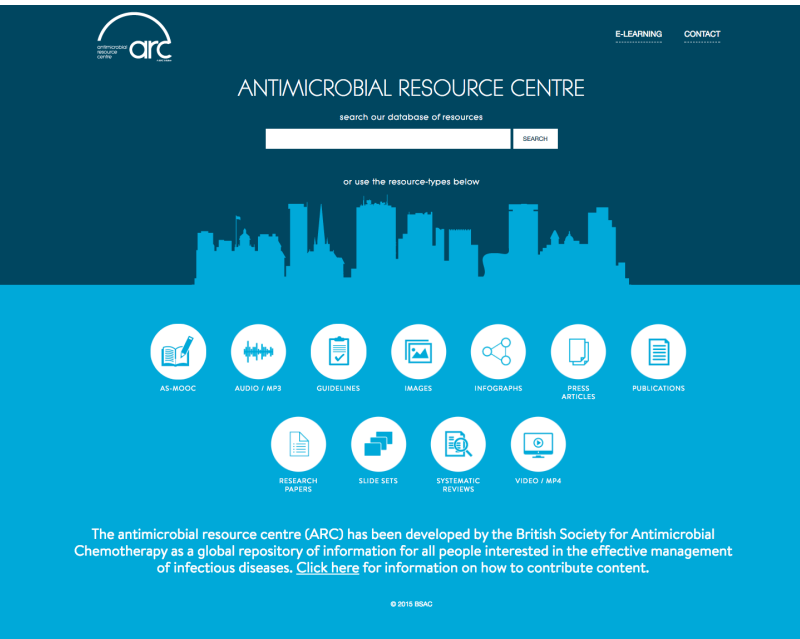
**Accessing free information and educational resources**

In addition to your own research, there is a wealth of existing resources for you to draw upon when seeking to inform and influence people outside of your own profession. The Antimicrobial Resource Centre (ARC) was developed by BSAC as a global repository of information for anyone interested in the effective management of infectious diseases.



It includes a wide range of materials: videos, podcasts, infographics, guidelines, images, press articles, publications, research papers, slide sets, and systematic reviews.

As well as accessing content, users are encouraged to contribute it, so that we can all help to build a huge library that is free to use anywhere in the world.



**Joining forces with others**

The power of cooperation and collaboration is nowhere more evident than through the membership of a professional body like the British Society for Antimicrobial Chemotherapy (BSAC),



the support of a campaign like Antibiotic Action (the public engagement arm of BSAC),



or in the pledge to act as an Antibiotic Guardian. Politicians and journalists rarely underestimate strength in numbers.



To demonstrate the importance of cooperation, BSAC produced a mini-manifesto, “Making Resistance Futile: Moving Antimicrobial Resistance Policy into Action”, that outlines why authorities must find ways to engage learned societies and other professional bodies, in local, national and international efforts to combat resistance. Learned societies are a fundamental part of the research, policy, service, and education landscape, providing substantial intellectual, public and reputational benefit at a negligible cost to the public purse.



## MAINSTREAM MEDIA

### Establishing contact with journalists

Whether you choose to work with others or alone, there are always opportunities to promote an event or a development via print and/or broadcast news. If you are keen on securing your own coverage, the Media Trust has produced a short introduction to writing a public relations plan.

## VISIT RESOURCE HUB

If you intend to offer a story or yourself (as a spokesperson) start by identifying all relevant health, science, and general news, reporters. A scan of articles published on AMR should yield a number of the names you need. Any good search engine will help you to do this.

### Using case studies

Most journalists are trained to tell stories through the impact they have on people. As such, it will pay for you to put lives at the heart of whatever it is you choose to say. Evidence can then be used to show how typical or likely any given experience was.

Do you know anyone who has been directly affected by the effects of AMR and who is prepared to share their experience in a bid to educate or support others? Do you know of any innovative practices that are having, or could have, a dramatic impact in the lab or a healthcare setting?

### Writing a letter to the editor

The subject matter of letters to the editor varies widely. However, the most common topics include:

- Supporting or opposing a stance taken by the publication in its editorial, or responding to another writer's letter to the editor
- Commenting on a current issue being debated by a governing body – local, regional or national depending on the publication's circulation. Often, the writer will urge elected officials to make their decision based on his/her viewpoint
- Remarking on materials (such as a news story) that have appeared in a previous edition. Such letters may either be critical or praising
- Correcting a perceived error or misrepresentation.

### Issuing an open letter

These are intended to be read by a wide audience, or a letter intended for an individual, but that is nonetheless widely

distributed intentionally. Open letters usually take the form of a letter addressed to an individual but provided to the public through newspapers and other media, such as a letter to the editor or blog. Especially common are critical open letters addressed to political leaders.

## NEW MEDIA

### Popularising the subject

Think of the success of high-profile scientists like Alice Roberts, Brian Cox, and Robert Winston, in communicating complex ideas simply and powerfully. Many of these figures make the most of new media to talk to people outside of the world of science.

### Blogging, vlogging and podcasts

Many new media outlets welcome ideas for blogs, vlogs, podcasts, and news articles. Here are just some of them for you to consider subscribing and/or contributing to:

HuffPost

## VISIT SITE

The Conversation

## VISIT SITE

BuzzFeed

## VISIT SITE

'Comment is Free' in the online Guardian

## VISIT SITE

Reflections on Infection Prevention and Control

## VISIT SITE

BSAC's blog



**Meeting up, listening in, speaking out**

There is a growing network of like-minded people who stage open events (of varying sizes and levels of formality) to demonstrate the appeal and relevance of science to the wider world. They offer great opportunities to educate, inform, debate – and even entertain – in a range of settings.

Why not search online for details of events in your area. Among the most active networks in the UK are (nota bene: this list is by no means exhaustive):

Café Scientifique is a place where, for the price of a cup of coffee or a glass of wine, anyone can come to explore the latest ideas in science and technology. Meetings take place in cafes, bars, restaurants and even theatres, but always outside a traditional academic context.



Soapbox Science is a novel public outreach platform for promoting women scientists and the science they do. Its events transform public areas into an arena for public learning and scientific debate.



STEM Learning is the largest provider of STEM (science, technology, engineering, and mathematics) education and careers support to schools, colleges and other groups working with young people across the UK. Through partnership with Government, charitable trusts and employers, the Network is dedicated to increasing the number of young people engaged in STEM-related studies and careers.



TED is a non-profit initiative devoted to spreading ideas, usually in the form of short, powerful talks (18 minutes or less). It covers almost all topics in more than 100 languages. Meanwhile, independently-run TEDx events help share ideas in communities around the world.



**POLITICIANS**

**Lobbying public servants**

Wherever you live, start by engaging your own elected representative(s). If you are based in his or her constituency they have an obligation to respond to you.

In the UK, you can find who represents you by visiting WriteToThem. As the name suggests, this site also provides an electronic letter-writing tool, with clear advice on how best to win the attention of the people who were elected to serve.



WHY HEALTHCARE PROFESSIONALS SHOULD ENGAGE WITH POLITICIANS AND THE POLICYMAKING PROCESS - KEVIN HOLLINRAKE MP



**Case study**

Do not assume that all politicians and/or policymakers are aware of the challenges wrought by AMR. Much can be achieved by simply offering to discuss your work with an elected representative(s). For example, the UK's Shadow Health Minister, Julie Cooper, was deeply affected by a visit to the microbiology team in a nearby hospital. She referred to this visit during a Westminster Hall Debate to mark World Antibiotic Awareness Week 2017.



*“I recently met with microbiologists at the Royal Blackburn Hospital and they were clear that urgent action is needed to prevent the inappropriate use of antibiotics. They were adamant: if we fail to address this issue we are fast approaching a situation where even the simplest routine operations will not be possible as we lose the fight against infection.”*

*“Concerns about AMR are shared by MPs on all sides of the House and together we have a responsibility to press the Government to act. The question is not whether we can afford to act but whether we can afford not to.”*

Julie Cooper MP for Burnley, Shadow Health Minister

## WHAT CAN MPS DO TO RAISE AN ISSUE IN UK PARLIAMENT?

MPs will have personal preferences on what methods they use to raise a matter in the House. You can find more information about each of the methods below at [www.parliament.uk](http://www.parliament.uk) or by requesting the relevant factsheet from the House of Commons Information Office. MPs can:

- Ask a Parliamentary Question of a particular Minister, either written or oral
- Apply for an Adjournment Debate, during which a Minister must give a response
- Introduce a Private Members' Bill
- Present a petition
- Table or sign an Early Day Motion (EDM)

### Linking up with All-Party Parliamentary Groups (APPGs)

APPGs are informal cross-party groups that have no official status within Parliament. They are run by and for Members of the Commons and Lords, though many choose to involve individuals and organisations from outside Parliament in their administration and activities.

The benefits of these groups are listed as follows by Parliament's website:

- A forum for cross-party interaction which is not controlled by the whips
- A forum for interaction between parliamentarians in both Houses
- A forum for parliamentarians, academics, business people, the third sector and other interested parties
- A time and space for policy discussion and debate
- A means for parliamentarians to set the policy agenda, which is normally dictated by the front benches and in particular, by the Government's legislative priorities.

Here is a selection of APPGs that might be considered most relevant to our work:

Antibiotics (BSAC provides the secretariat for this Group)

 VISIT SITE

Future Generations



Personalised Medicine



Global Health



Pharmacy



Health



Primary Care and Public Health



Health in All Policies



Scientific



Life Sciences



Sepsis



Malaria and Neglected Tropical Diseases



**Staging an event**

Holding an event can be a good way to launch a campaign or to raise awareness of the work you are undertaking. If you would like to invite an MP to your event – or ask him or her to sponsor an event in the Palace of Westminster – think carefully about your aims.

- What value will they add to your event, and what would you like to gain from their attendance?
- What will their role be?
- What will they get out of the event?
- How does this fit with their specialist interests?
- Is this the best event to invite them to, or are you planning another which might be more appropriate?

Patient Safety



### Checking the record

Anyone can search Parliament's publications and records. This portal includes open access to Hansard, which is the edited verbatim report of proceedings in both House. You can find out who said what and when, by searching these pages.



### Following Select Committee inquiries

Select Committees work in both Houses of Parliament. They check and report on areas ranging from the work of government departments to economic affairs. The results of these inquiries are public and many require a response from the government.

Here are some of the Select Committees that could be considered most relevant to our work:

Education (Commons)



Environment, Food and Rural Affairs (Commons)



Health (Commons)



Science and Technology (Commons)



Science and Technology (Lords)



### Contacting representatives in the devolved administrations

If you live in Scotland, Wales, Northern Ireland or London, you also have at least one elected representative working on devolved issues. In Scotland, Members of the Scottish Parliament (MSPs) represent local or regional constituencies, as do Welsh Assembly Members in Wales and London Assembly Members in London. In Northern Ireland, you have one Northern Ireland Assembly Member to represent you. You can find out more by visiting: [www.scottish.parliament.uk](http://www.scottish.parliament.uk), [www.assemblywales.org](http://www.assemblywales.org), [www.niassembly.gov.uk](http://www.niassembly.gov.uk) or [www.london.gov.uk](http://www.london.gov.uk).

### Monitoring the work of think tanks

A think tank, policy institute, or research institute is an organisation that undertakes research and advocacy on topics such as social policy, political strategy, economics, military, technology, and culture. Most policy institutes are non-profit organisations. Other think tanks are funded by governments, advocacy groups, or businesses, or derive revenue from consulting or research work related to their projects.

Here is just a selection of UK-based think tanks that specialise in health and science policies:

2020health.org Grass roots independent think tank for health and technology. Based in Westminster.



Institute for Public Policy Research The Institute for Public Policy Research is the UK's leading progressive think tank, producing cutting edge research and innovative policy ideas for a just, democratic and sustainable world.



Overseas Development Institute (ODI) ODI is Britain's leading independent think tank on international development and humanitarian issues. ODI offers a fellowship scheme for postgraduate economists to work in the public sectors of developing countries in Africa





Reform Suggests improvements in the delivery of public services and economic prosperity. Produce research of outstanding quality on the core issues of the economy, health, education and law and order. Based in Westminster.



The Bow Group Develops policy, publishes research, and stimulates debate within the Conservative Party.



### **Responding to public consultations**

Public consultations are part of a regulatory process by which the public's input on matters affecting them is sought. Its main goals are to improve the efficiency, transparency and public involvement in large-scale projects or laws and policies. As the title would suggest, anyone can respond.

You can search all UK Government consultations by keywords, publication type, policy area, department, document status, location, and publication date.



### **Signing up for Parliamentary alerts**

Keep updated with political developments by signing up for Parliamentary alerts via email. Simply select your areas of interest when subscribing.



# CHAPTER 1

## OUTCOME 1: UNDERSTANDING BROADLY WHAT ANTIBIOTICS ARE, HOW THEY WORK AND THE BASIC MECHANISMS OF RESISTANCE

Antibiotics act against bacteria. They function by disrupting essential processes or structures in the bacterial cell. This either kills the bacterium or slows down bacterial growth. Depending on these effects an antibiotic is said to be bactericidal or bacteriostatic.

Antimicrobial resistance is resistance of a microorganism to an antimicrobial drug that was originally effective for treatment of infections caused by it.

In principal, there are three main antibiotic targets in bacteria:

- The cell wall or membranes that surrounds the bacterial cell
- The machineries that synthesizes the nucleic acids DNA and RNA
- The machinery that synthesizes proteins (the ribosome and associated proteins)

Bacteria have two alternative pathways to acquire all types of resistance:

- Random changes in the bacterial DNA (mutations) may provide resistance by chance
- Alternatively, they can receive resistance genes from other bacteria nearby. This process is called horizontal gene transfer.

## OUTCOME 2: OUTLINE THE DRIVERS FOR RESISTANCE

The excessive use and misuse of antimicrobial drugs accelerates the emergence of drug-resistant strains, poor infection control practices, inadequate sanitary conditions and inappropriate food-handling, poverty, lack or inadequate diagnostics tests, use and misuse of antibiotics in agriculture and the environment, travel and other factors encourage the emergence and further spread of antimicrobial resistance

## OUTCOME 3: OUTLINE THE GLOBAL EPIDEMIOLOGY OF KEY ANTIBIOTIC RESISTANT PATHOGENS AND ANTIBIOTIC CONSUMPTION

The global epidemiology of antibiotic consumption and resistance through surveillance is patchy, not consistent or uniform and not adequately delineated across the healthcare settings. Areas of good practice are emerging.

In the EU, the annual costs to society was Euro 1.56 billion and 600 million days of lost productivity

The impact of drug resistance infections compared to susceptible infection led to increased attributable cost, length of stay, mortality and morbidity.

## OUTCOME 4: EXPLAIN THE CLINICAL AND ECONOMIC IMPACT OF DRUG RESISTANT INFECTIONS AND IMPACT ON HEALTH CARE ACQUIRED INFECTIONS

In the USA majority of the 99,000 deaths due to health care acquired infections were due to drug resistant infections

In the EU, the annual costs to society was Euro 1.56 billion and 600 million days of lost productivity

The impact of drug resistance infections compared to susceptible infection led to increased attributable cost, length of stay, mortality and morbidity.

## OUTCOME 5: LIST SOME DEFINITIONS OF ANTIMICROBIAL STEWARDSHIP AND GOALS OF STEWARDSHIP PROGRAMMES

Antimicrobial stewardship has been defined as “the optimal selection, dosage, and duration of antimicrobial treatment that results in the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patient and minimal impact on subsequent resistance.” It also can be defined as an “organizational or healthcare system wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness.

The goals of stewardship are to improve patient’s outcomes, increase patient safety, reduce resistance and optimise costs. Understanding and measuring any unintended consequences of stewardship, especially harm, is also an important goal.

## OUTCOME 6: IDENTIFY THE CORE ELEMENTS OF INFECTION CONTROL AND STEWARDSHIP PRACTICE AND THEN CONSIDER THEM IN THE CONTEXT OF A FICTITIOUS OUTBREAK OF A DRUG RESISTANT HEALTH CARE ACQUIRED INFECTION.

For the core components of an infection control and prevention programme visit the following:

<https://www.reactgroup.org/toolbox/prevent-infection/health-care/core-components/>

For the core components of an antimicrobial stewardship programme visit the following <https://www.reactgroup.org/toolbox/prevent-infection/health-care/core-components/>

# CHAPTER 2

## OUTCOME 1: EXPLAIN CHANGES IN THE USE OF ANTIBIOTICS GLOBALLY AND WHAT IS DRIVING THIS CHANGE

Antibiotic use has been increasing globally. Over the period 2000-2010 overall use is estimated to have increased by 35% with broad spectrum penicillins and cephalosporins (the most commonly supplied antibiotics) increasing by 40%. This increase has mainly been driven by factors such as economic growth, increased expenditure on health and increased access to antibiotics in middle income countries. Although high income countries continue to use the most antibiotics per capita. Rising rates of antibiotic resistance and development of multi drug resistant organisms is leading to increases in use of glycopeptides and reserve and last resort agents such as carbapenems and polymyxins (e.g. colistin).

## OUTCOME 2: DESCRIBE THE PREVALENCE AND VOLUME OF ANTIBIOTIC USE IN COMMUNITY, HOSPITALS AND LONG-TERM CARE AGED CARE SETTINGS

The majority of antibiotic use, around 80%, occurs in the community where the percentage of the population prescribed an antibiotic use varies between countries. There is a four-fold difference in volume of antibiotics used amongst OECD countries. Use is highest in the young and the old, and is higher in winter months where use is associated with inappropriate treatment upper respiratory tract infections.

There is a three-fold difference in volume of antibiotics used in hospitals between high and low using countries in Europe with 22% to 55% of inpatients prescribed one or more antibiotics. More patients are prescribed antibiotics in ICUs and the rate of use is higher.

Antibiotic use in nursing homes is high and during the period of a year 50 – 80% of residents will receive at least one course of systemic antibiotics.

## OUTCOME 3: LIST THE MOST COMMON ANTIBIOTIC AGENTS PRESCRIBED IN COMMUNITY AND HOSPITAL SETTINGS

Penicillins are the most frequently used antibiotics in the community (making up 30 - 60% of use). Followed by cephalosporins, macrolides and quinolones with proportion and volume of use varying considerably between countries.

In some countries cephalosporins and other beta lactams (including carbapenem) are now prescribed more commonly in hospitals than penicillins (including penicillin-  $\beta$  lactam inhibitor combinations) followed by quinolones.

## OUTCOME 4: DESCRIBE TRENDS IN ANTIBIOTIC USE IN HOSPITAL SETTINGS

Around two thirds to three quarters of antibiotic use in high income countries is for the treatment of infections and up to one fifth for surgical prophylaxis.

There is a shift towards a greater use of broad spectrum agents with increases in 3rd and 4th generation cephalosporins, penicillin -  $\beta$  lactam inhibitor combinations and carbapenem use. In 2015 penicillin-  $\beta$  lactam inhibitor combinations and extended spectrum penicillins accounted for around 80% of penicillin use in European hospitals.

The increasing presence of multidrug-resistant and extensively drug resistant organisms in ICU units is driving the use of glycopeptides and broad spectrum agents such as piperacillin and tazobactam, 3rd and 4th generation cephalosporins, cabapenems and agents of last resort such as colistin.

## OUTCOME 5: DESCRIBE MISUSE OF ANTIBIOTIC AGENTS

There are three areas of misuse

underuse- mostly associated with lack of access to healthcare services in low income countries

unnecessary use – an infection is not caused by a bacterium e.g. a viral infection, or where an antibiotic is not needed

inappropriate (or suboptimal) use – where timing, antimicrobial choice, dose, route, frequency of administration or duration of treatment is incorrect.

## OUTCOME 6: LIST COMMON INDICATIONS WHERE ANTIBIOTICS ARE INAPPROPRIATELY PRESCRIBED/USED

In the community antibiotics are inappropriately prescribed for upper respiratory tract infections where over 50% of antibiotics prescribed may be unnecessary. Up to 30% antibiotics use for asymptomatic bacteruria in nursing homes residents is not indicated.

In low income countries, antibiotics are often used inappropriately for diarrhoea and malaria.

In hospitals indications where antibiotics are commonly prescribed inappropriately include: surgical prophylaxis (especially excessive duration), respiratory infections (community acquired pneumonia, bronchitis) and urinary tract infections

# CHAPTER 2

## OUTCOME 7: LIST THE KEY DRIVERS/ DETERMINANTS OF ANTIBIOTIC USE

- Attitudes, beliefs and social norms of the prescriber
- The organisational culture including the prescribing “etiquette” set by senior medical staff based on autonomy of decision making and a culture of medical hierarchy.
- Resistance not seen as a problem important in prescriber’s own daily practice
- A lack of knowledge of local antimicrobial resistance, gaps in antibiotic knowledge and/or awareness of local or national prescribing guidelines.
- Diagnostic uncertainty
- Patients’ expectation of receiving an antibiotic and the prescriber’s/suppliers perception of that expectation
- Reimbursement systems and marketing by the pharmaceutical industry.
- Regulation of the supply of antibiotics

# CHAPTER 3

## OUTCOME 1: APPRAISE WHAT IS ANTIMICROBIAL STEWARDSHIP AND WHAT IS PRUDENT ANTIMICROBIAL PRESCRIBING

Antimicrobial stewardship is defined (as previously presented in Chapter 1) as ensuring that every provider selects “The right antibiotic, for the right indication (right diagnosis), the right patient, at the right time, with the right dose and route, causing the least harm to the patient and future patients.” This definition outlines the key principles of antibiotic prescribing. These principles ensure that providers only prescribe antibiotics for non-self-limiting bacterial infections. Antimicrobial stewardship programs create processes that promote prescribing that aligns with the above definition. Additionally, the stewardship program takes responsibility for tracking and reporting prescribing and resistance trends over time.

Prudent antimicrobial prescribing ultimately leads to improved patient safety, better clinical outcomes, cost-effective treatment, reduction in toxicity and adverse events. There are many ways that a stewardship program may ensure timely and appropriate antibiotic initiation. One way is to create clinical pathways that direct prescribers toward appropriate antibiotics for specific disease states. These clinical pathways can either be built into the medical record software at the time of prescribing, or can be available to prescribers via a manual or internet portal.

In addition to timely and appropriate antibiotic initiation, stewardship programs may minimise risk for adverse events by implementing interventions for timely review or renal dose adjustment. Timely de-escalation (being part of the review of antibiotic prescriptions) will minimize patient exposure to broad spectrum antimicrobials and therefore reduce their risk for associated events such as resistance or *C. difficile* infection. Renal dose adjustments will ensure patients are not over- or under-dosed which may increase their risk for adverse effects, infection relapse, or development of resistance.

## OUTCOME 2: EXPLORE OPPORTUNITIES FOR IMPLEMENTING ANTIMICROBIAL STEWARDSHIP PROGRAMS IN ACUTE CARE HOSPITALS

This chapter has described opportunities to implement antimicrobial stewardship interventions such as

- Optimal use of antibiotics for surgical prophylaxis (selection and duration)
- Reduce antibiotic consumption and costs without increasing mortality or infection-related re-admissions
- Pertinent studies that demonstrate how stewardship programs can optimise healthcare costs
- Describe the core elements of antimicrobial stewardship programs with examples of areas where interventions could be successfully implemented

The U.S. Centers for Disease Control and Prevention have established core elements necessary for developing a successful antimicrobial stewardship program. These core elements are as follows:

- **Leadership Commitment:** Dedicating necessary human, financial and information technology resources.
- **Accountability:** Appointing a single leader responsible for program outcomes. Experience with successful programs show that a physician leader is effective
- **Drug Expertise:** Appointing a single pharmacist leader responsible for working to improve antibiotic use.
- **Action:** Implementing at least one recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (i.e. “antibiotic time out” after 48 hours), IV to PO programs, prospective audit and feedback, antibiotic restrictions, etc.
- **Tracking:** Monitoring antibiotic prescribing and resistance patterns
- **Reporting:** Regular reporting information on antibiotic use and resistance to doctors, nurses and relevant staff
- **Education:** Educating clinicians about resistance and optimal prescribing

# CHAPTER 3

## OUTCOME 3: APPLY KEY PRINCIPLES OF PRUDENT ANTIMICROBIAL PRESCRIBING IN ACUTE CARE HOSPITAL SCENARIOS

Two clinical scenarios are presented to demonstrate how antimicrobial stewardship programs can aid in prudent prescribing. The toolkit has additional resources.

## OUTCOME 4: DISCUSS POSSIBLE UNINTENDED CONSEQUENCES OF ANTIMICROBIAL STEWARDSHIP

Process, outcomes and balancing measures are needed to appropriately appraise the value and consequences of antimicrobial stewardship. Balancing measures in particular are needed to detect unintended negative consequences of these interventions are fundamental to ensure that antibiotic stewardship programs are safe. Healthcare systems, clinicians and patients should be confident of the results and value of the interventions.

In summary, this chapter highlights that we need to use our resources wisely; “to widen access to appropriate medications to encompass all people – regardless of race, gender, or socio-economic status – while at the same time reserving these precious compounds to treat only those diseases for which they are specifically required.” We must all recognise the seriousness of this problem and commit ourselves to using these precious resources wisely balancing unintended consequences. ASPs can help us identify such situations and avoid inappropriate antimicrobial use. We have the means to ensure that our antimicrobial armoury remains effective and that we preserve the effectiveness of future antimicrobials in the pipeline



# CHAPTER 4

## OUTCOME 1: DESCRIBE KEY STEPS IN DEVELOPING AN ANTIMICROBIAL STEWARDSHIP PROGRAMME

A successful stewardship requires motivation, accountability and leadership.

## OUTCOME 2: IDENTIFY THE KEY PERSONNEL WHO NEED TO BE INVOLVED IN THE PROGRAMME

These include medical and pharmacy staff, but also nursing staff and other specialties.

## OUTCOME 3: OUTLINE SOME KEY ACTIVITIES TO BE CARRIED OUT BY THE STEWARDSHIP PROGRAMME

A business case may be necessary to get these staff into service.

Every organisation will have barriers that will need to be overcome to get a stewardship programme up and running.

## OUTCOME 4: DESCRIBE SOME OUTPUT MEASURES THAT CAN BE MONITORED FOR THE PROGRAMME (FINANCIAL, GUIDELINE COMPLIANCE, OUTCOMES - DECREASED LENGTH OF STAY, ETC.)

The programme should have short, medium and long-term goals and have governance and reporting/monitoring processes built in – both to measure success and avoid harm.

# CHAPTER 5

## KEY MESSAGES FROM THIS CHAPTER

1. Develop strategies for measuring the process and outcomes of your centre's current stewardship activities.
2. Clarify the organisational structure and accountability of your centre's current stewardship activities.
3. Explore and document your center's motivation to improve antimicrobial stewardship in terms of its leadership and dedication to the cause (measured in human and financial capital).

# CHAPTER 6

## KEY MESSAGES FROM THIS CHAPTER

- If AMS programmes are 'invisible' in the organisational structure in terms of programme implementation it is not clear which resources are then available for these activities.
- In terms of governance, clear lines of accountability within an organisation are critical. These accountability pathways may be part of wider quality improvement or dedicated to infection control and AMS. Either way these should be identifiable.
- At the national level, action plans must identify the scope and relevance of the various stakeholders, including capacity building that may be required. Depending on the maturity of the national action plan, a ground up approach can also be employed by assessing this workforce and public engagement at the programme level.
- Finally, by taking a view across the healthcare sector, use of a framework to assess the level of integration of approaches to AMS ensures that our strategies are line with patient pathways as a well as the journey of organisms.

# CHAPTER 7

## OUTCOME 1: EXPLAIN WHAT EMPIRICAL PRESCRIBING IS AND UNDERSTAND WHY IT IS CURRENTLY PART OF NORMAL DAY-TO-DAY PRACTICE

Empirical prescribing is where a prescription (in this case for an antibiotic) is written before the cause of the illness is fully understood and is therefore a 'best guess' to cover the most likely causes. Current diagnostic tests have a turn around time that is too slow. Clinicians usually cannot or do not want to wait until results are back before offering treatment.

## OUTCOME 2: UNDERSTAND WHY EMPIRICAL PRESCRIBING IS NOT IDEAL AND WHY IMPROVEMENT IN THE DIAGNOSIS OF INFECTION ARE NEEDED

Empirical prescribing means that patients get the prompt antibiotic treatment that they need if they have a serious infection. However, it also means that they may receive unnecessary treatment if they do not have an infection, or may receive an inappropriate antibiotic for the infection they have.

Improvements to diagnostic tests are required to reduce turn around times and, ideally, make each antibiotic prescription an informed prescription.

## OUTCOME 3: EXPLAIN HOW THE LABORATORY CAN SUPPORT ANTIMICROBIAL STEWARDSHIP ACTIVITIES

Existing laboratory practices can facilitate antimicrobial stewardship activities by providing results to clinicians in a clinically useful timeframe. Laboratory accreditation and other quality assurance activities make sure that results are fit for purpose.

The introduction of laboratory automation and updated working practices can make results available sooner. Newer technologies, such as matrix assisted laser desorption ionisation time of flight (MALDI TOF) mass spectroscopy to identify bacteria, whole genome sequencing to interrogate the core genome of the organism and internationally standardised antibiotic susceptibility methodology to identify antibiotic resistance are all changing diagnostic services dramatically.

## OUTCOME 4: EXPLAIN WHY THE CLINICIAN NEEDS TO UNDERSTAND OPTIMAL USE OF DIAGNOSTIC TESTS AND HOW THE RESULTS COULD OTHERWISE BE MISLEADING

The value of any diagnostic test is dependent on it being used in the right way. The correct test must be performed in the correct context. Otherwise, the result might be misinterpreted and lead to the wrong diagnosis and/or treatment. An example is the use of urine dipsticks (used for the diagnosis of urinary tract infection) in elderly patients, who are likely to have positive results even in the absence of true infection.

## OUTCOME 5: UNDERSTAND WHAT RAPID BIOMARKER TESTS ARE (E.G. C-REACTIVE PROTEIN AND PROCALCITONIN) AND HOW THEIR USE COULD HELP SUPPORT ANTIMICROBIAL PRESCRIBING DECISIONS

C-reactive protein (CRP) and procalcitonin (PCT) are examples of acute phase proteins. Test values rise in the presence of an inflammatory response and they have reasonable specificity for bacterial infections.

These tests can be used to differentiate between bacterial and viral infection and therefore identify some patients who might not need any antibiotic treatment at all. They can also be used to monitor progress with treatment and help support a decision to stop antibiotics.

# CHAPTER 8

## KEY MESSAGES FROM THIS CHAPTER

- Be familiar with common terminology pertaining to PKPD underpinning antimicrobial use. This is most relevant to the characteristics of the time-concentration curve and properties of antimicrobials that dictate their killing action.
- Be aware of clinical situations that may dictate optimization of dosing strategies out with standard dosing regimens. Examples include critical illness, neonates, pregnancy and obesity.
- Understand the complex issues of treating multi-drug resistant bacteria, where PKPD properties are manipulated by using combination therapy and altered drug dosing.
- Appreciate how PKPD can be applied to antimicrobial stewardship, aiming to achieve optimal outcomes while limiting the emergence of resistance and overuse of antimicrobials.

# CHAPTER 9

## OUTCOME 1: BE AWARE OF THE TOOLS AVAILABLE TO CARRY OUT A BASELINE ANALYSIS OF ANTIMICROBIAL STEWARDSHIP WITHIN YOUR ORGANISATION

Baseline checklists to assess current Antimicrobial Stewardship (AMS) practices can provide a useful gap analysis prior to implementing an Antimicrobial Stewardship Programme (ASP). Useful resources are baseline checklists from CDC or NICE and the Measurement for Improvement Toolkit from the Australian Commission on Safety and Quality in Health Care.

A proposed approach to implementing a successful ASP is:

- Collect baseline data within the organisation.
- Survey the AMS culture within the organisation.
- Assess the resources available to support an ASP.
- Review existing antimicrobial guidelines and policies.
- Review communication within the organisation.

## OUTCOME 2: RECOGNISE KEY PERSONNEL WHO SHOULD BE INCLUDED IN ANTIMICROBIAL STEWARDSHIP GROUPS

A successful antimicrobial stewardship group needs to include the core members of the AMS team in addition to representatives from clinical specialities within the organisation, for example:

- A senior leader who has experience of implementing change
- Infectious diseases physician
- Antimicrobial pharmacist
- Microbiologist
- Nurse representatives
- Representatives from clinical specialities
- Infection control representative
- Drug and Therapeutics committee representative
- Primary care representative

## OUTCOME 3: UNDERSTAND WHERE ANTIMICROBIAL STEWARDSHIP GROUPS FIT WITHIN ORGANISATIONAL STRUCTURES

A successful ASP should include clinical leadership and corporate responsibility. Clear lines of accountability to the executive team and governing bodies as well as other relevant committees within the organisation need to be established in the development of an ASP. An example of where the antimicrobial stewardship group lies within the organisational structure in a large multi-site teaching hospital is provided.

## OUTCOME 4: KNOW HOW TO IDENTIFY AREAS WHERE ANTIMICROBIAL STEWARDSHIP PROGRAMS SHOULD BE FOCUSED

There is no “one size fits all” approach to ASPs and programmes will vary according to the size and specialities provided within the organisation. ASP should cover the whole of the organisation, however many centres are limited by the AMS resources available. In such settings, priority areas for ASP should be identified and targeted. Suggested priority areas are:

- Complex patients, i.e. ICU or acute admissions
- Areas with high antimicrobial use
- Areas with high AMR rates
- Areas with poor compliance to guidelines

Point prevalence surveys, surveillance of AMR, surveillance of antimicrobial use and benchmarking with peers should be used to review priorities within an established ASP.



# CHAPTER 9

## OUTCOME 5: DEFINE CORE AND ADDITIONAL INTERVENTIONS WHICH CAN BE EMPLOYED IN ANTIMICROBIAL STEWARDSHIP PROGRAMS

Core interventions should form the basis of an ASP. Core interventions include:

- Formulary restriction with re-authorisation of named anti-infectives
- Prospective audit with intervention and feedback
- Multidisciplinary AMS team
- Guideline development

Additional interventions should then be considered for inclusion in an ASP as resources allow with accordance with what is appropriate within the individual healthcare setting. Additional interventions include:

- De-escalation of therapy based on culture results
- Dose optimisation
- Intravenous to oral switch
- Education
- Antibigrams - at patient and organisation level
- Information technology to provide decision support and enhanced surveillance
- Antimicrobial order forms
- Antimicrobial cycling
- Combination antimicrobial therapy

## OUTCOME 6: BE ABLE TO IDENTIFY MEASURES TO ASSESS THE EFFECTIVENESS OF ANTIMICROBIAL STEWARDSHIP PROGRAMS

Defined outcome measures should be defined as part of an organisations ASP strategy and used to assess the effectiveness of the ASP. Suggested outcome measures include:

- Audit of compliance with guidelines.
- Audit documentation – e.g. indication, stop/review date, 48-72-hour review.
- Audit time to 1st dose of antibiotic in sepsis.
- Monitor antibiotic consumption data, including benchmarking to similar institutions.
- Monitor antibiotic expenditure data.
- Monitor stewardship interventions and acceptance rates.
- Review adverse events in relation to antimicrobials.

## OUTCOME 7: RECOGNISE DIFFERENT ROUTES OF COMMUNICATION WHICH MAY BE USED WITHIN AN ANTIMICROBIAL STEWARDSHIP PROGRAM

There needs to be a clear plan on how to disseminate important ASP messages to staff, for example ASP vision, updates to guidelines, PPS results, AMR rates, infection outbreaks and antimicrobial shortages. The proposed audience must be considered; what works in one setting may not work in another. Proposed communication routes include:

- Posters in clinical areas / staffrooms
- Use of hospital intranet
- Organisational newsletter
- AMS newsletter
- Hospital-wide email
- Notifications via electronic prescribing programme or app
- Discussion at relevant hospital committees
- Screensaver / background on computers within the organisation
- Email to divisional leads for dissemination in clinical areas
- Social media

# CHAPTER 10

## KEY MESSAGES FROM THIS CHAPTER

- Measurement is central to antimicrobial stewardship
- Through measurement you can plan and prioritise stewardship interventions.
- Measurement is essential to evaluate the impact of stewardship interventions on clinical practice and demonstrate benefits for patients.
- Measurement of the quantity and the quality of antibiotic use are both needed.
- Focusing on data visualisation will enhance understanding and engagement with the data.
- Without information feedback measurement alone will not drive improvement.

# CHAPTER 11

## KEY MESSAGES FROM THIS CHAPTER

- There are some easy 'quick wins' that can be implemented in any setting to improve antimicrobial use – start by looking for 'low hanging fruit'.
- Quality improvement methodology can be used to effect change quickly on a small scale. There are many models but all use key principles of having Will, Ideas and Execution.
- When applying quality improvement methods to antimicrobial prescribing remember you need a clear aim and both process and outcome measures.
- Collaborating with others working on stewardship through a breakthrough collaborative can be helpful to share ideas and learn from each other.
- Prescribing indicators are a simple tool for ongoing assessment of antimicrobial use to monitor trends over time and evaluate the impact of interventions, both intended and unintended.
- Sharing local improvement data is the most important step in the process to engage the clinical team and support behaviour change.
- There are a variety of planning tools available to support development and evaluation of stewardship interventions and larger multi-faceted programmes.

# CHAPTER 12

## KEY MESSAGES FROM THIS CHAPTER

- Interventions designed to optimise antibiotic prescribing in hospitals are more effective if they are designed to enable prescribers by increasing their capability or opportunity to follow policies.
- Currently few interventions use the most effective enablement techniques of goal setting and feedback combined with action planning.
- A better understanding of the contextual and social determinants of antibiotic decision making in secondary care is required in order to develop tailored interventions that enable prescribers to optimise their decision making.
- To do this, we need to utilise the knowledge from social science and improvement science research to try and understand the context in which interventions work to develop sustainable behaviour change.

# CHAPTER 13

## OUTCOME 1: UNDERSTAND THE CURRENT LANDSCAPE OF EDUCATIONAL COMPETENCES FOR PRUDENT ANTIMICROBIAL PRESCRIBING

Of 145 countries responding to WHO's questionnaire on development and implementation of a national AMR action plan, only 12 countries did not have any training for their health workers.

## OUTCOME 2: DESCRIBE THE EDUCATIONAL STRATEGIES AVAILABLE FOR ANTIMICROBIAL STEWARDSHIP

Educational strategies for antimicrobial stewardship can be passive or active. Examples of passive strategies include distribution of printed antimicrobial prescribing guidelines, prescribing guidelines on organisation's website, posters, handouts, conference attendance, staff/teaching sessions with minimal interactive sessions. Whilst active strategies include focus groups for consensus-building, workshops, one-on-one targeted sessions e.g. via academic detailing or educational outreach by clinical educators (eg ID physician/microbiologist or pharmacist).

## OUTCOME 3: DESCRIBE THE PROCESS FOR DEVELOPING COMPETENCIES

Competences should be developed using an evidence-based approach. One example of a step-wise approach taken to develop competences is:

- Defining the target group/audience
- Review of the literature
- Review of existing competences and published curricula/training objectives
- Synthesis of new competences
- Expert panel review and competency refinement using eg Delphi methodology/expert consensus/workshop

## OUTCOME 4: BE AWARE OF THE CORE COMPONENTS OF EDUCATIONAL COMPETENCES FOR PRUDENT PRESCRIBING AND WHICH EDUCATIONAL RESOURCES COULD BE USEFUL IN THEIR LOCATION

- Infection and antimicrobial stewardship in context: awareness and interpretation of local and national antimicrobial usage and resistance data, national and international policy pertaining to antimicrobial stewardship and global issues in AMR.
- Clinical microbiology: theory, laboratory tests and their interpretation, clinical principles of infection and principles of AMR.
- Antimicrobials: therapeutic drug monitoring, pharmacology, pharmacokinetics and pharmacodynamics, and antimicrobial use in special populations.
- Management of clinical syndromes: organized by bodily system.
- Principles of an antimicrobial stewardship plan: role of the stewardship team and key components of hospital and primary care stewardship programmes.

Several educational resources available from around the world have been provided in this chapter. They are not meant to be a comprehensive list.

# CHAPTER 14

## KEY MESSAGES FROM THIS CHAPTER

- The prescribers and antibiotic stewards of tomorrow are poorly prepared for the task and require better education and training through improved undergraduate curriculae in LMICs.
- Much of the educational material developed by high income countries and already in the public domain through the internet is applicable to LMICs, but there is an increasing amount of online material and tools available, which have been developed in LMICs, that is directly applicable to low resource settings.
- The high-income model of multidisciplinary antibiotic stewardship teams of infection specialists needs to be adapted and the essentials taught to non-specialist prescribers, pharmacists, nurses and community health workers.
- Different models of stewardship, which put pharmacists, nurses and community health workers at the heart of the stewardship response need to be developed in low resource settings, in line with the health systems of those countries.



# CHAPTER 15

## KEY MESSAGES FROM THIS CHAPTER

- In the US, pharmacists have an important role in applying the results from a rapid diagnostic test to help improve the time to effective antibiotic therapy in the management of patients with *S. aureus* bacteremia.
- In Europe, antimicrobial stewardship initiatives have been implemented for more than a decade in most countries, and have used a variety of strategies.
- In GCC, Antimicrobial resistance is a global public health threat. A strategic solution to stabilize or reduce microbial resistance is implementing Antimicrobial Stewardship Programs in healthcare settings. Gulf Cooperation States are joining WHO global action plan in combatting resistance
- In Australia, comprehensive national guidelines, coordinated national audit activities, and strong policy drivers have been integral to the success of AMS programs.

# CHAPTER 16

## KEY MESSAGES FROM THIS CHAPTER

### South Africa

- Successful stewardship programs can be implemented in a variety of geographical and socio-economic settings by health-care workers without formal ID training.
- Skills beyond infectious diseases are critical in initiating and maintaining AMS programs.
- By focusing on a “vital few” antibiotic process measures such as excessive antibiotic duration (> 7 or >14 days) or prescription of antibiotics with overlapping or duplicate spectra, can yield significant returns with the least effort.
- The creation of such alternative models for stewardship that can be embedded within existing systems are dependent on local context and resources but are key to success across diverse settings
- Integral to success is collaborative cross-disciplinary shared learning

### India

- Sharing of hospital antibiogram & prescription auditing data with prescribers results in a change in their prescribing pattern, but the effect did not last for long
- For sustainable behavioural changes among prescribers, continuous efforts in the form of prescription auditing along with periodic focus group discussions would be a more effective approach.

### South America

- AMS involves healthcare system-wide approaches promoting the judicious use of antimicrobials; this includes addressing the regulatory environment. Despite the social and political challenges, regulating over-the-counter sales has proven effective in curbing self-medication with antibiotics. However, efforts have to be sustained over time.
- Assessing antibiotic consumption levels, using sales data converted into defined daily dose per 1000 inhabitants per day (DDD/TID), is useful to raise leverage about addressing the problem of antibiotic consumption in outpatient settings, as well as to guide the implementation and evaluation of interventions

# CHAPTER 17

## OUTCOME 1: EXPLAIN THE UNIQUE FACTORS IMPACTING ON AMR AND AMS IN LTCF

Antimicrobial resistance patterns in LTCF are showing an increase in the rates of multidrug resistant organisms such as VRE, CRE and ESBLs. The nature of this setting, where isolation facilities are often not available, contributes to this.

The elderly LTCF population are at increased risk of infection, with sometimes serious consequences, which can drive high rates of antimicrobial prescribing.

Unlike the secondary care setting, LTCFs often do not have an AMS strategy due to lack of on-site multidisciplinary teams to drive this agenda.

## OUTCOME 2: TO UNDERSTAND THE FACTORS INFLUENCING THE PRESCRIBING OF ANTIMICROBIALS IN LTCF

Antimicrobial prescribing in LTCF is influenced by many factors unique to the setting, especially the frail population, the lack of on-site diagnostic and microbiological resources, and doctors are primarily off-site.

Misinterpretation of urine dipsticks can lead to overprescribing of antibiotics for urinary tract infections.

## OUTCOME 3: IDENTIFY AND COMMUNICATE THE CORE GOALS OF A LTCF AMS STRATEGY

Antimicrobial stewardship in LTCF must be developed and implemented with a locally appropriate and relevant strategy.

The strategy must examine on the rate of antimicrobial prescribing and also the choices of antimicrobials prescribed, with a focus on local or national prescribing guidelines.

The strategy must also examine the interpretation of urinary dipsticks and urinary catheter care.

Infection Prevention and Control policies and procedures must adhere to national standards to prevent the spread of infection or outbreaks.

The strategy should be feasible, using readily accessible data to benchmark antimicrobial resistance and prescribing data against local or national data.

## OUTCOME 4: REFLECT ON THEIR OWN PRACTICE AND HOW TO INTRODUCE AMS IN LTCF

For the core components of introducing AMS in your LTCF visit the following:

<https://www.cdc.gov/longtermcare/pdfs/core-elements-antibiotic-stewardship-appendix-b.pdf>

# CHAPTER 18

## OUTCOME 1: IMPORTANCE AND OPPORTUNITIES OF ICU ANTIMICROBIAL STEWARDSHIP

- An overwhelming majority of patients in ICUs receive antimicrobials, with high associated costs.
- ICUs environments often contain drug-resistant infections.
- Optimizing use of antimicrobials addressed antimicrobial use and costs, minimizing antimicrobial selection pressure.

## OUTCOME 2: STRUCTURES NEEDED FOR ANTIMICROBIAL STEWARDSHIP IN THE ICU

- ICU ASPs require external “coaches”, preferably with infectious diseases expertise (i.e. infectious diseases physician or pharmacist, or a microbiologist).
- An interprofessional team will bring the most varied and holistic approach to antimicrobial stewardship.
- Optimising antimicrobials in the ICU requires timely and reliable information:
- Antibigrams – preferably ward-specific, and weighted-incidence syndromic antibiograms (WISCA)
- Accurate, up-to-date report of patient’s clinical status, microbiology information, and recent and current antimicrobial therapy

## OUTCOME 3: THE BEST INTERVENTIONS TO STEWARDSHIP ANTIMICROBIALS IN THE ICU

- Coaching, or prospective audit with feedback, appears to be the best approach to stewarding antimicrobials in the ICU.
- Ensuring diagnostic tests for infection are necessary, valid and reliable (diagnostic stewardship) will reduce unnecessary antibiotic treatment.
- ICU prescribers benefit from antimicrobial guidance directed to empiric therapy, preferably based on local resistance patterns.
- De-escalation or simplifying antibiotics is another way ICU prescribers can benefit from stewardship

## OUTCOME 4: ICU ANTIMICROBIAL STEWARDSHIP OUTCOME MEASURES

- Ascertaining and reporting on “appropriateness” of therapy holds the greatest promise for evaluating antimicrobial stewardship interventions.
- De-escalation and patient outcomes?
- Consumption and cost metrics are useful secondary measures, but lack the clinical context of “appropriateness”.
- Balancing measures and antimicrobial resistance are important considerations in evaluating antimicrobial stewardship in the ICU.

# CHAPTER 19

## OUTCOME 1: DEFINE AN IMMUNOCOMPROMISED HOST

A wide-range of conditions can result in immune-compromise including primary immunodeficiency, diseases such as advanced diabetes and HIV, severe malnutrition and drug-induced immune compromise, such as during the treatment of cancer, inflammatory conditions or post-transplantation.

These patients have a reduced ability to immunologically respond (or at all) to an infection.

## OUTCOME 2: EVALUATE THE ROLE OF NET IMMUNOSUPPRESSION IN MEDIATING THE RISK OF INFECTIONS IN SUSCEPTIBLE HOSTS

The net state of immunosuppression can vary considerably between patients and there is intra-patient variability over time. Although assessing a patient's net state of immunosuppression can be challenging, it is useful in assessing what infections the patient may be at risk of and what level of investigation and antimicrobial intervention is therefore justified.

## OUTCOME 3: DESCRIBE BARRIERS TO AMS IN THE IMMUNOCOMPROMISED PATIENT SETTING

- Difficult to diagnose infections – invasive diagnostics and less commonly used blood tests may be required to confirm infection
- Broad spectrum of infections: Need to differentiate between colonisation and active infection; MDROs are common due to repeated and prolonged broad-spectrum antimicrobial courses
- Prescriber perception and attitudes – patients are deemed 'sicker' and / or 'special-cases' compared to immune-competent patients
- Inaccuracy with antibiotic allergy labelling can drive inappropriate agent choice
- Need for timely treatment

## OUTCOME 4: IDENTIFY THE OPPORTUNITIES FOR AMS IN IMMUNOCOMPROMISED HOSTS

The most commonly included AMS activities implemented in this patient setting include:

- Formulary review and restriction
- Guideline development
- Prospective audit and feedback
- Education
- Dose optimisation

## OUTCOME 5: DISCUSS THE ROLE OF MULTI-DISCIPLINARY WORKING IN DELIVERING AMS

To work effectively there should be close collaboration between the AMS team and the HIV, cancer or transplant teams with a shared appreciation of the complexities of caring for these patients. Success requires an open MDT approach and collaborative development of guidelines.

## OUTCOME 6: LIST CONSIDERATIONS FOR ANTIMICROBIAL TREATMENT IN THIS SPECIAL PATIENT POPULATION

- Must be timely: delay in initiation potentially increases mortality
- Appropriate: must cover the suspected pathogen(s) – these may not just be bacteria BUT also viruses and/ or fungi need to be considered
- Administered at optimal dosing – taking consideration of PK-PD and drug-drug interactions
- Prompt de-escalation/ discontinuation when practical

# CHAPTER 20

## OUTCOME 1: RATIONAL ANTIMICROBIAL PRESCRIPTION FOR SURGICAL PROPHYLAXIS

The selection of antimicrobial would depend on the type of surgery. Usually, a single first-generation cephalosporin for operations not expected to encounter anaerobes or a single second-generation cephalosporin with anaerobic operations based on local susceptibility patterns is sufficient. It has to be administered 60 minutes prior to surgery or for antimicrobials like Vancomycin it should be administered 120 minutes. Repeat dose is recommended only for surgeries lasting more than 4 hours.

## OUTCOME 2: ADHERENCE TO GUIDELINES

It is very important to adhere to Institutional surgical prophylaxis guidelines. If the institution doesn't have one, then it is mandatory to comply with International guidelines released by organizations such as WHO, CDC, SHEA etc.

## OUTCOME 3: UNDERSTANDING PHARMACOKINETICS/PHARMACODYNAMICS OF RECOMMENDED SURGICAL PROPHYLAXIS

Understanding basic pharmacokinetics of surgical prophylaxis is very essential. It is especially important because redosing of the antimicrobial depends on a pharmacokinetic parameter named "biological half-life". The biological half-life of a substance is the time it takes for a substance to lose half of its pharmacologic activity. Intra operative redosing is recommended only for procedures that exceed two half-lives of the antimicrobial used for surgical prophylaxis.



# CHAPTER 21

## OUTCOME 1: UNDERSTANDING WHAT AFS IS

Antifungal stewardship can be defined as ‘the optimal selection, dosage, and duration of antifungal treatment that results in the best clinical outcome for the treatment or prevention of infection with minimal toxicity to the patient and minimal impact on subsequent resistance’.

## OUTCOME 2: UNDERSTANDING SOME BASIC MEDICAL MYCOLOGY

Medically important fungi capable of causing invasive fungal infection can be broadly split into three categories; yeasts (e.g. *Candida* spp. and *Cryptococcus* spp.), moulds (e.g. *Aspergillus* spp. and the zygomycetes) and dimorphic fungi (e.g. *Histoplasma* spp.).

*Candida albicans* is the most commonly isolated strain of *Candida*. Invasive candidiasis is the most common fungal disease among hospitalised patients in the developed world. Invasive aspergillosis is a major cause of invasive mould infection and tends to affect the immunocompromised.

Antifungal resistance is well recognized and has been associated with antifungal exposure.

## OUTCOME 3: UNDERSTANDING SOME OF THE BENEFITS OF AFS

AFS programmes have been associated with:

- reducing inappropriate antifungal use
- cost savings due to the high cost of many antifungals
- improved patient outcomes (e.g. mortality)

With the rise of antifungal resistance in recent years, AFS is likely to be important in mitigating further emergence of antifungal resistance.

## OUTCOME 4: UNDERSTANDING THE DIFFERENT WAYS ANTIFUNGALS ARE USED

Antifungal agents are used to prevent infections in some susceptible patients (i.e. prophylaxis).

They can also be used empirically in a susceptible patient who has clinical evidence of infection and is not improving with an antibacterial agent, so is presumed to have a fungal infection.

For a diagnosis of proven IFI, specimens must be obtained by a sterile technique from a normally sterile site. Invasive mould infection is proven if hyphae are seen in a histological or cytological specimen or a mould is grown in culture from that specimen with clinical or radiological evidence of infection at the site from which the specimen was taken. Systemic yeast infection would be proven on the same evidence as above or if the yeast was grown in a blood culture. A diagnosis of probable IFI requires a combination of host factors and microbiological and clinical criteria, whereas a diagnosis of possible IFI requires host factors and clinical features.

Treatment decisions therefore depend on:

- Host factors
- Clinical features
- Microbiology results

## OUTCOME 5: UNDERSTANDING HOW TO START AN AFS PROGRAMME

It is important to understand antifungal use in your patient population. Audit and surveillance can be helpful to identify challenges or poor practice. It can also be used to persuade clinical and managerial colleagues of the need for AFS and provide data to assess the efficacy of future interventions. A good starting point is to create or review guidelines and clinical pathways in line with local epidemiology and patient population. The availability and turn-around-time of diagnostics should be considered within this process.

# CHAPTER 22

## KEY MESSAGES FROM THIS CHAPTER

- Discussing antibiotic decisions with parents in terms of severe versus non-severe infections is more likely to be effective than an explanation based on the distinction between bacterial and viral infections.
- It is extremely difficult for clinicians to reliably distinguish bacterial and viral respiratory tract infections and there are few reliable diagnostic tests available in community based settings. Unfortunately, this uncertainty often results in clinicians prescribing “just in case”, despite the availability of good evidence demonstrating that antibiotics make little or no difference to the speed of symptoms resolution in most children with bacterial RTIs.
- Decisions about whether to prescribe antibiotics in children with RTIs should be made using evidence based guidelines.
- Clinicians should be provided with up to date information on the management of common infections in children within a robust education programme. Priority should be placed on ensuring that consistent approaches to management are adopted across community and front of house hospital settings (emergency department/paediatric assessment unit). Inconsistent prescribing practices impact on future health seeking behaviour and antibiotic expectations.
- Parent satisfaction remains high, even when no prescribing or delayed prescribing approaches are adopted, as long as parent concerns have been addressed during the consultation.
- Antimicrobial stewardship is an extremely effective way of improving antibiotic prescribing within hospital settings.

# CHAPTER 23

## OUTCOME 1: DESCRIBE KEY ELEMENTS OF A MULTI-DISCIPLINARY OPAT BUNDLE

Key elements of a multi-disciplinary OPAT bundle as outlined in figure 1 include the following actions:

- Initial selection of the appropriate antibiotic regimen
- Monitoring for clinical response and tolerability, and adjusting doses as needed
- Selecting the most feasible discharge regimen in terms of cost, drug stability and compatibility with IV access
- Determining the timing of IV to PO switch
- Providing education on infection risk factors, treatment goals and expectations
- Determining when to stop antibiotics at clinical cure or clinical failure, if the later is due to surgical disease

## OUTCOME 2: OUTLINE DISTINCT MODELS OF OPAT CARE DELIVERY

Distinct OPAT care models can be adapted to available resources, staff, geography, and patient access to care. Briefly, these are:

- Centralised, office or hospital-based infusion centres
- Home-based programs utilizing specialized infusion and nursing teams
- OPAT care within skilled-nursing facilities

## OUTCOME 3: DESCRIBE UNIQUE CHALLENGES TO OPAT IN DIFFERENT PARTS OF THE WORLD

- Underserved populations in need of OPAT care exist throughout the world, from the urban poor of New York City to rural communities in Canada
- Studies suggest that standardization of OPAT care delivery in Asia is still needed

## OUTCOME 4: LIST EXAMPLES OF CHALLENGES CENTRAL TO THE OPAT-STEWARDSHIP DILEMMA DESCRIBED BY GILCHRIST AND COLLEAGUES

- It is challenging to select a narrow spectrum OPAT regimen with a convenient dosing schedule, which does not require frequent dose adjustment or laboratory monitoring.
- A prime example is the selection of once daily IV ceftriaxone for methicillin susceptible *S. aureus* (MSSA) treatment rather than IV nafcillin or oxacillin.

# CHAPTER 24

## OUTCOME 1: DISCUSS REASONS WHY CDSSS ARE REQUIRED BOTH FOR PRESCRIBERS AND FOR AMS

Decision support is required for prescribers as antibiotic prescribing decisions are complex, and rely on multiple patient and infection factors. Decision-making around antimicrobial prescribing necessitates review of a large amount of information. Factors to consider include signs and symptoms of infection, likely pathogens, treatment options, and potential drug interactions, contraindications and adverse reactions.

Inappropriate prescribing is common

CDSSs can support better decision making by enabling access to patient information, enforcing compliance with antimicrobial policies and procedures, and driving evidence-based prescribing.

Management and review of large clinical workloads can be streamlined through use of CDSSs. Audit processes can be enhanced through CDSSs. AMS can use CDSSs to provide restrictions and approvals, to monitor prescribing behaviours, to efficiently triage patients who require post-prescription review, and to assist with reporting and feedback.

## OUTCOME 2 & 3: DESCRIBE THE FEATURES OF CDSSS THAT SUPPORT ANTIMICROBIAL PRESCRIBING. COMPARE AND CONTRAST THE DIFFERENT TYPES OF CDSSS

Different types of CDSSs facilitate different functions and operations, and prioritise different kinds of information.

Online clinical portals containing guidelines enable clinicians to access and use recommendations at the point of care.

Antimicrobial approval and authorisations systems support formulary control and indication restrictions facilitate. They facilitate auditing of antimicrobial use (particularly when combined with post-prescription review) and feedback to prescribers.

Infection prevention and surveillance systems can help identify bug-drug mismatches and generate alerts to help identify patients who are at risk of developing nosocomial infections.

Advanced decision support systems can provide decision support by helping identify potential infections, pathogens and treatment options based on inputs about patient symptoms and other information.

## OUTCOME 4: TO DISCUSS THE ISSUES THAT MAY IMPACT ON THE UPTAKE OF THESE SYSTEMS INTO CLINICAL PRACTICE

Data overload and alert fatigue is a potential problem, and the importance of triaging workflow needs to be emphasised.

Successful implementation of CDSSs depends on a number of factors, including the speed and usability of the system; the extent to which it has been successfully integrated into the workflow; the clarity of recommendations and interventions; the availability of evidence and justifications for recommendations; the monitoring of impact and clinician feedback; incentives for use; and local adaptation of guidelines.

# CHAPTER 25

## OUTCOME 1: WHY SHOULD NURSES BE INVOLVED IN ANTIMICROBIAL STEWARDSHIP?

- Describe drivers for participation of nurses in antimicrobial stewardship activities.
- Shortages in human resources worldwide and increased demands on antimicrobial stewardship programmes encourage the involvement of nurses in stewardship.

## OUTCOME 2: EXPANDING THE PARTICIPATION OF NURSES IN ANTIMICROBIAL STEWARDSHIP

- Identify how antimicrobial documents and policies consider nursing participation in stewardship.
- Guidelines such as 'Start Smart Then Focus' or the European Commission Guidelines for the Prudent Use of Antimicrobials in Humans recognises the participation of nurses in antimicrobial stewardship initiatives.

Explain antimicrobial stewardship clinical tasks that could be adopted by nurses.

Typical roles for nurse participation in stewardship include clinical areas such as ensuring that adequate biological samples are obtained before instigation of antimicrobials; evaluation of clinical response and discussion of de-escalation; and patient education, among others.

Consider the impact in antimicrobial usage of advanced nursing roles such as prescribing.

Prescribing nurses are bound by existing prescribing guidelines. The volume of antimicrobials prescribed by nurses around the world continues to increase.

## OUTCOME 3: PUBLIC HEALTH AND COMMUNITY NURSING CONTRIBUTION TO ANTIMICROBIAL STEWARDSHIP

Critically argue some public health nursing behaviours that could be embedded within antimicrobial stewardship frameworks.

- Nurses could reduce the demand for antibiotics in primary care by influencing public and patient knowledge and expectations of antibiotic prescribing through their societal contacts; Leading and implementing immunisation programmes across all age groups to prevent avoidable infection and associated morbidity and mortality; Leading and implementing public health strategies to support the public to 'live well' and prevent or reduce the burden of long term conditions such as diabetes, liver disease, obesity.

Reflect on emerging activities in nursing homes and long-term care facilities that would benefit antimicrobial stewardship initiatives.

- Nurses can avoid measures that have limited or no clinical benefit yet can trigger antimicrobial prescriptions, such as routine urine sampling.

## OUTCOME 4: INTEGRATION BETWEEN NURSING ROLES AND ACTIVITIES IN AMR AND OTHER PROFESSIONALS

Understand the areas for antimicrobial stewardship synergy and integration between nurses and other professionals.

- Establishing the allergy status of a patient; timely initiation of antimicrobials; monitoring therapeutic drug levels; adhering to optimal infection prevention and control practice, etc., could be collaborative roles.

## OUTCOME 5: STEWARDSHIP, A TARGET FOR NURSES IN EXECUTIVE AND DIRECTIVE POSITIONS

Discuss how nurses in executive and directive positions can contribute to and strengthen antimicrobial stewardship programmes.

- Engaged board members and managers could have an impact on stewardship initiatives similar to that achieved in hand hygiene or infection prevention and control programmes, patient safety and quality improvement.

## OUTCOME 6: NURSE-FOCUSED INTERVENTIONS IN ANTIMICROBIAL STEWARDSHIP

Reflect upon some existing nurse-centred stewardship interventions.

- Some studies emphasising nursing education achieved improvements in intravenous-to-oral switches and discussions about the need for continued intravenous antibiotics as well as increased participation in stewardship activities, decreased excessive antibiotic duration, increased compliance with cultures before antibiotics, and optimised device removal.

# CHAPTER 25

## OUTCOME 7: BARRIERS TO RESOLVE THE PARTICIPATION OF NURSES IN STEWARDSHIP

- a. Examine some barriers for increased involvement of nurses in stewardship.
  - Ownership, education and leadership
- b. Evaluate existing initiatives implemented to address barriers to nurse involvement.
  - ‘Good nursing care is good stewardship, and good stewardship is good nursing care’. Education interventions, including resources such as clinical workbooks and new technologies such as smartphone applications (‘apps’), targeting different settings have led to significant knowledge and attitude improvements.
  - Building leadership capacity among stewardship nurses has been the focus of nursing meetings and summits.



# CHAPTER 26

## OUTCOME 1: EXPLAIN HOW TO WORK WITH MICROBIOLOGIST TO IMPLEMENT A RAPID DIAGNOSTIC TEST IN THE HOSPITAL SETTING

Rapid diagnostic tests (RDT) are game changing in the management of patients with infectious diseases. The key to successfully implementing RDT includes good communication between the microbiology lab and the antibiotic stewardship pharmacists or physician.

The stewardship pharmacists should work with the microbiologist to develop a strategy to receive the RDT result prior to implementation of the RDT.

## OUTCOME 2: LIST SOME WAYS A PHARMACIST CAN PROVIDE ADVOCACY FOR THE RESPONSIBLE USE OF ANTIBIOTICS

Pharmacists play a key role in advocacy of appropriate antibiotic use. Advocacy can occur at Anytime, to Anyone, Anywhere.

Pharmacists can engage in a discussion about antibiotics with patients, consumers, and other healthcare professionals. Discussion points should include how antibiotics are societal drugs that impact everyone.

Pharmacists can volunteer to speak about the responsible use of antibiotics to healthcare providers, students, community organizations, and school children.

## OUTCOME 3: DEFINE THE DIFFERENT ROLES OF THE PHARMACIST IN ANTIBIOTIC STEWARDSHIP

Pharmacists have many different roles in different parts of the world. This can vary from the traditional role of drug dispensing (South America) to being credentialed to prescribe antibiotics (US). Pharmacists in all settings can apply their drug expertise to assure patients receive the correct antibiotic at the correct dose and duration and de-escalate when appropriate.

Pharmacists can provide more advanced interventions including PK/PD optimisation based upon patient-specific factors and MIC of the organism.

Rapid diagnostic tests can be implemented with antibiotic stewardship pharmacists intervention to assure time to effective antibiotic therapy is maximized.

Research is an important role for stewardship pharmacists. More data is needed to show the impact of antibiotic stewardship on patient outcomes and antibiotic resistance. Designing stewardship interventions as a study that can be published helps teach the world in addition to advancing the profession of pharmacy.

Pharmacists can help to link antibiotic stewardship interventions to both quality and patient safety.

## CHAPTER 27

## OUTCOME 1: UNDERSTAND WHY ENGAGING WITH POLITICIANS AND JOURNALISTS IS SO IMPORTANT TO RAISING AWARENESS OF AMS

Whether you call it campaigning, influencing, advocating, networking, or giving voice, we can bring about significant and sustainable change by engaging with mainstream media and politicians.

AMS must not only be done; it must also be seen to be done. Best practice will only be extended and sustained if it is acknowledged, and a high value given to it by the public, politicians, and the media.

## OUTCOME 2: APPRECIATE THE LINK BETWEEN A DYNAMIC COMMUNITY OF RESEARCH AND PRACTICE AND A CULTURE OF TRANSPARENCY AND ACCOUNTABILITY

Effective public engagement helps to create a culture of transparency – which is essential for learning, improving, and making each other accountable for the actions we take.

## OUTCOME 3: ARTICULATE WHY THE NEED FOR PUBLIC ENGAGEMENT HAS NEVER BEEN MORE URGENT

- A 2015 survey by the World Health Organization across 12 countries highlighted the lack of familiarity with the language of antibiotic resistance
- A study by Wellcome Trust in the same year also found people in the UK have little awareness of what ‘antibiotic resistance’ means and how it might affect their health
- Even among healthcare professionals, AMR can mean different things to different people. An article published by Wernli et al in the BMJ in 2017 pointed to several dominant, but competing, discourses on the subject: ‘AMR as healthcare’, ‘AMR as development’, ‘AMR as innovation’, ‘AMR as security’ and ‘AMR as One Health’. Each has its own scientific origin, conception of the problem, and method to prioritise action.

## OUTCOME 4: OUTLINE THE CHALLENGES OF COMMUNICATING CLEARLY AND RESPONSIBLY

- AMR is at the heart of several competing discourses
- More and more people want to involve themselves in the creation and delivery of the campaigns they support
- We need to develop a campaigning approach that is essentially coherent and cohesive

- Many mainstream journalists do not have a scientific background.

## OUTCOME 5: LIST SOME OF THE RESOURCES THAT CAN AID CLEAR AND RESPONSIBLE COMMUNICATION

If you want to communicate research results to the public, you might like to consider The Royal Society’s excellent guidance on the subject: ‘Science and the public interest: Communicating the results of new scientific research to the public’.

In addition to your own research, there is a wealth of existing resources for you to draw upon when seeking to inform and influence people outside of your own profession. The Antimicrobial Resource Centre (ARC) was developed by BSAC as a global repository of information for anyone interested in the effective management of infectious diseases. It includes a wide range of materials: videos, podcasts, infographics, guidelines, images, press articles, publications, research papers, slide sets, and systematic reviews.

## OUTCOME 6: ENGAGE CONFIDENTLY WITH A RANGE OF POLITICIANS AND JOURNALISTS

The power of collaboration is nowhere more evident than through the membership of a professional body like the British Society for Antimicrobial Chemotherapy (BSAC), the support of a campaign like Antibiotic Action (the public engagement arm of BSAC), or in the pledge to act as an Antibiotic Guardian. Politicians and journalists rarely underestimate strength in numbers.

There are always opportunities to promote an event or a development via print and/or broadcast news. The Media Trust has produced a short introduction to writing a public relations plan.

Also, think of the success of high-profile scientists like Alice Roberts, Brian Cox, and Robert Winston, in communicating complex ideas simply and powerfully. Many of these figures make the most of new media to talk to people outside of the world of science.

Wherever you are based, start by engaging your own elected representative. If you live in his or her constituency they have an obligation to respond to you. There are many ways in which a public servant can raise issues and/or lobby for change, inside and outside whichever voting chamber and/or system of government they have been elected or appointed to serve.



# DILIP NATHWANI



## Professor DILIP NATHWANI

MB, FRCP (London & Ed), DTM&H, OBE

Co-Director Academic Health Sciences Partnership [AHSP] in Tayside, Consultant Physician in Infectious Diseases and Honorary Professor of Infection, Ninewells Hospital and Medical School, Dundee

Dilip qualified from Aberdeen University in 1984, and has subsequently training in internal medicine/infection/tropical medicine in Aberdeen, Glasgow and Birmingham, UK. Since 2014 he is the Co-Director of the AHSP in Tayside, the first of its kind in Scotland and with the primary aim of enabling innovation across the health and social care sector. He also has been the recent [2008-2017] Chairman of Scottish Government Funded Scottish Antimicrobial Prescribing Group (SAPG). SAPG is a national clinical antimicrobial stewardship programme. Chair of the European Study Group on Antibiotic Policies [ESGAP] from 2011–14 and President of the British Society for Antimicrobial Chemotherapy [BSAC]; Recent National Specialty Adviser for Infectious Diseases to the Scottish Government Health Department; External advisor on Antimicrobial Stewardship & Education Policy to a number of professional societies, governments and non-UK governmental bodies including WHO; Programme director of the first Massive open on line course [MOOC] on Antimicrobial stewardship. In 2015 he was awarded the Order of the British Empire [OBE] by Her Majesty the Queen for outstanding services to the treatment of Infectious Diseases.

Dilip has authored more than 250 peer reviewed publications and has a range of local, national and international contributions to research & innovation in the domains of education, quality improvement, guidelines and policy, particularly in the field of antimicrobial stewardship. He also has been interested in outcomes research and value based healthcare.



# MARGARET DUGUID



Margaret Duguid has over 30 years experience in the quality and safety of medicines use as a pharmaceutical

advisor and hospital pharmacy manager. Most recently Margaret was the Pharmaceutical Advisor at the Australian Commission on Safety and Quality in Health Care (the Commission) where she was involved in national initiatives promoting the safe and quality use of medicines and antimicrobial stewardship. Margaret served on the Commission's Antimicrobial Stewardship Advisory Committee for a number of years and in 2011 she co-edited the commission's publication Antimicrobial Stewardship for Australian Hospitals.



# ELIZA DOLLARD



# LILIAN ABBO

**>** Eliza Dollard received her Doctor of Pharmacy from the University of Connecticut School of Pharmacy in 2014. She completed her Pharmacy Practice and Infectious Diseases residencies at Jackson Memorial Hospital in Miami, Florida. After residency she became the Pediatric Infectious Diseases Clinical Pharmacist at Holtz Children’s Hospital, associated with Jackson Health System, where she resided until 2017. She now lives in Portland, Maine where she serves as the Pediatric Infectious Diseases Clinical Pharmacist for Barbara Bush Children’s Hospital and the Health-System Antimicrobial Stewardship Clinical Pharmacist for MaineHealth.


**>** Dr. Lilian M Abbo, is a board certified infectious diseases physician, expert in the management of transplant associated infections and multidrug resistant organisms, and the Chief for Infection Prevention and Antimicrobial Stewardship at Jackson Health System. Dr. Abbo has direct responsibility and authority for the strategic assessment and implementation of programs to prevent healthcare associated infections and monitor the appropriate use of antimicrobials in an extremely large, complex system that deals with an incredible range of patient populations and clinical conditions. She also frequently works with the hospital system’s communications team to address the local and national news media and community groups about infectious disease, antimicrobial stewardship, and other public health matters.

Dr. Abbo obtained her medical degree from the Universidad Central de Venezuela, “Luis Razetti” Medical School followed by a fellowship in Infectious Diseases at Jackson Memorial Hospital/ University of Miami. She has co-authored over 70 peer-reviewed publications, 3 book chapters and more than 80 abstracts in the fields of antimicrobial stewardship, transplant associated infections and infection prevention. She is a co-author of the 2016 Infectious Disease Society of America (IDSA) Guidelines for the Implementation of Antimicrobial Stewardship Programs in Acute Care Hospitals.

Lilian is a Fellow of the IDSA, she also serves several national and international committees for IDSA, the Society of Healthcare Epidemiology of America and the American Society of Transplantation. She been an invited speaker in more than 35 international and over 100 regional/ local oral conferences. Lilian is the course director for the British Society for Antimicrobial Chemotherapy (BSAC) Massive online education course “Gram negative infections” available in future learn. Her research grants are in the areas of antimicrobial resistance and stewardship. She has received several awards from the University of Miami for her leadership in diversity and for her work in the advancement of women in academia and healthcare.




## CONOR JAMIESON

 Conor Jamieson is the Pharmacy Team Leader for Antimicrobial Therapy at Sandwell and West Birmingham NHS Trust in Birmingham, UK. He graduated from Aston University with a first class honours in Pharmacy in 1996 and was awarded a PhD in Microbiology by the same institution in 2002. Since then he has been working in clinical practice in the NHS in the field of antimicrobial stewardship. He was formerly Honorary Treasurer of the British Society of Antimicrobial Chemotherapy, having previously served as a council member of the Society, and is the current chair of the Drug Stability Testing Working Party for BSAC




## PAUL POTTINGER

 Dr. Pottinger is an Associate Professor of Infectious Diseases at the University of Washington in Seattle, USA. He co-directs the Antimicrobial Stewardship Program at UW Medical Center with Rupali Jain, PharmD. Together, they partner with medical providers to improve the use of anti-infective medications for the complex and heterogeneous patient population there. He directs the hospital's clinical ID section, and the ID & Tropical Medicine Clinic. He is also Associate Director of the ID Training Program, where his efforts focus on optimising the fellows' clinical training experience.



## ALISON HOLMES

 Professor Alison Holmes FMedSci is a Professor of Infectious Diseases at Imperial College London and has a longstanding clinical and research career in the field of infectious diseases with particular interests in antibiotic use, antimicrobial resistance and public health, particularly in the context of acute care.


Alison is Director of the National Institute for Health Research Health Protection Research Unit in Healthcare Associated Infections and Antimicrobial Resistance at Imperial College London and holds various awards as Principal or Co-Principal Investigator on a range of multidisciplinary research programmes.

She leads a large multi professional and multi-disciplinary research group and network, with strong collaborations both nationally and internationally.

Within the NHS, she is Director of Infection Prevention and Control and an Associate Medical Director, as well as a consultant in infectious diseases.




## RAHEELAH AHMAD

 Raheelah Ahmad PhD FHEA FRSPH Health Management Programme Lead within the faculty of Medicine at Imperial College London at the National Institute for Health Research (NIHR) Health Protection Research Unit for Healthcare Associated infections and Antimicrobial Resistance. Raheelah is leading research to evaluate sustained impact of interventions across the healthcare economy to address antimicrobial resistance (NIHR Fellowship in Knowledge Mobilisation). Her research to evaluate public health interventions at the system and organisational level from provider and user perspectives, has attracted consistent funding in the UK and internationally (ESRC, NIHR, World Bank, Global Fund and DIFD). Current research includes investigating antibiotic use along surgical pathways (England, Scotland, Rwanda, India & South Africa). Raheelah completed her Masters in Health Services Management at LSHTM, doctorate in Health Management at Imperial's Business School and BSc (hons) in Mathematics at UCL. She is also Senior Associate Editor for the international peer reviewed journal Public Health.





## NICHOLAS BROWN

 Dr Nicholas Brown MBChB MA MD FRCP  
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Nick Brown is a Consultant Medical Microbiologist at Addenbrooke's Hospital in Cambridge and an Associate Lecturer at the University of Cambridge. He is employed by Public Health England (PHE) and is currently interim Lead Public Health Microbiologist for the East of England. He is the immediate past President of the British Society for Antimicrobial Chemotherapy (BSAC).

Nick has a career long interest in the use of antibiotics and antibiotic resistance. He was recently appointed Director of the Antibiotic Action initiative of the BSAC. He is also a member of various groups working on the implementation of the strategy to combat antibiotic resistance, including diagnostic stewardship.



## ALASDAIR MACGOWAN

 Alasdair MacGowan is Lead Public Health Microbiologist for Public Health England in the South West, Professor of Antimicrobial Therapeutics at the University of Bristol, and Consultant in Infection at North Bristol NHS Trust. He has led a mixed NHS academic research group in the area of antimicrobial chemotherapy for over twenty years, and provides medical input into the National Antibiotic Assay Reference Laboratory at Southmead Hospital. He has a research interest in antibacterial pharmacokinetics/dynamics, rapid diagnostics and antimicrobial resistance in the community. He holds a Programme Grant on management and diagnosis of Blood Stream Infection from NIHR England, has a Research for Patient Benefit Grant on antibiotic optimisation to prevent emergence of resistance, is Work Package Lead in an EU FP7 Programme Grant on resurrecting old antibiotics, and is part of two IMI funded academic consortia involved in various aspects of drug development. At present, active grants total >£20m. He is a former President of the British Society for Antimicrobial Chemotherapy (BSAC), chairs the BSAC Standing Committee on Antimicrobial Resistance Surveillance and is UK representative on European CDC Expert Committee EUCAST.



## MELISSA BAXTER

**>** Melissa qualified from the University of Aberdeen Medical School in 2011, achieving the MBChB degree with honours. Having completed postgraduate foundation rotations in Cornwall she is currently a training registrar in Medical Microbiology and Virology in the Southwest Peninsula Deanery. She enjoys training in all aspects of bacteriology and in particular orthopaedic and soft tissue infections. Interests outside of work include cycling, surfing and kayaking.



## MARK GILCHRIST

**>** Mark Gilchrist MPharm MSc (IPresc) FFRPS FPharmS Mark is Consultant Pharmacist Infectious Diseases & Stewardship at Imperial College Healthcare NHS Trust.

He is a council member of British Society of Antimicrobial Chemotherapy and co-chairs its UK OPAT Initiative. He is an senior honorary lecturer at Imperial College London, together with being a spokesman on antimicrobials and fellow of the Royal Pharmaceutical Society.


Mark has particular interests in antimicrobial stewardship around improving systems and processes that affect local, national and international AMR. His clinical interests include OPAT, tuberculosis and critical care.

Postgraduate education includes an MSc and non-medical independent prescribing status and he was recently awarded the NHS Leadership Academy Nye Bevan Award in executive healthcare leadership. He is immediate past chair of the UK Clinical Pharmacy Association - Pharmacy Infection Network (UKCPA PIN) and was awarded RPS Faculty Fellowship (Infection) in 2013.

He has delivered many lectures and workshops on AMS both at national and international level and has published around his areas of interest. He was a member of the working group that reviewed and developed the 2015 Public Health England "Start Smart then focus" stewardship toolkit and co-authored the UKCPA/RPS Faculty infection curriculum. Mark was a tutor on the global massive open online course on AMS and is an editor for Pharmacotherapy and Journal of Antimicrobial Stewardship.




# ORLA GEOGHEGAN

 Orla Geoghegan is lead pharmacist, infection at Imperial College Healthcare NHS Trust. Her postgraduate qualifications include an MSc in clinical pharmacy and a certificate in independent prescribing. Orla is a member of the Royal Pharmaceutical Society and UK Clinical Pharmacy Association.



# WILLIAM MALCOLM

 William Malcolm is Pharmaceutical Advisor in Health Protection Scotland (HPS), part of NHS National Services Scotland. HPS is responsible for the planning, coordination and delivery of specialist health protection activities to protect all the people of Scotland from infectious and environmental hazards.

As a member of the Scottish Antimicrobial Prescribing Group (SAPG), a national clinical multi-disciplinary forum that leads the national antimicrobial stewardship programme, William leads the national surveillance programme for antibiotic use in humans in Scotland. William is a firm believer in the ability of informatics as a driver for optimization of antibiotic use to improve patient outcomes and minimize harm in patients with and at risk from infection.



## JACQUELINE SNEDDON

Dr Jacqueline Sneddon is Project Lead for the Scottish Antimicrobial Prescribing Group (SAPG), a national clinical multi-disciplinary forum that leads the national antimicrobial stewardship programme. Jacqueline holds a Pharmacy degree from Heriot-Watt University, a PhD in Medicinal Chemistry and MSc in Clinical Pharmacy both from the University of Strathclyde. She is a Fellow of the Faculty of the Royal Pharmaceutical Society (RPS) and Chair of the UK Clinical Pharmacy Association (UKCPA) Pharmacy Infection Network.

Within SAPG Jacqueline has led development of education resources on antimicrobial stewardship, prescribing quality indicators, development of national consensus on antimicrobial policies and initiatives to improve the use of antimicrobials in Care Homes and recently development of a national antimicrobial app. She was a tutor on the global massive open on-line course on Antimicrobial stewardship and was a topic expert for the NICE guideline on Antimicrobial stewardship: changing risk-related behaviours in the general population.




## ESMITA CHARANI

Esmita Charani MPharm, MSc, MRPSGB  
Esmita is the Senior Academic Pharmacist within the faculty of Medicine at Imperial College London at the NIHR Health Protection Research Unit for Healthcare Associated Infections and Antimicrobial Resistance. She is also a visiting Researcher at Haukeland University Hospital, Bergen Norway, where she is involved in helping implement that national antibiotic stewardship programme. She is currently completing her doctoral thesis investigating antimicrobial stewardship across India, Norway, France and England. She is the co-developer of a Massive Open Online Course on antimicrobial stewardship with the University of Dundee and BSAC.

She is the recipient of the RPSGB Galen Pharmacy Research Award for research into antibiotic dosing and obesity and an investigator in a NIHR Invention for Innovation award investigating the development and use of a point of care personalised clinical decision support tool for antimicrobial prescribing. The focus of her research has been behaviour change interventions and the role of mobile health technologies to influence decision making. She is co-investigator on the ESRC award (2017-2021): Optimising antibiotic use along surgical pathways: addressing antimicrobial resistance and improving clinical outcomes (in England, Scotland, Rwanda, India & South Africa). Esmita completed her Masters (MPharm Hons) in Pharmacy at University College London, and her MSc in Infectious Diseases at LSHTM.




## PETER DAVEY

 Peter Davey MD FRCP, Professor, Medical School Lead for Healthcare Improvement, Population Health Sciences Division, Medical School, University of Dundee

Peter is the Medical School Lead for Healthcare Improvement at the University of Dundee. He trained as an Infectious Diseases Physician in Birmingham UK and at the Tufts New England Medical Centre in Boston. He joined the University of Dundee in 1989 on a University Grants Committee Clinical Senior Lectureship to work on record linkage in the fields of antibiotic prescribing and healthcare associated infection. He is past President of the British Society for Antimicrobial Chemotherapy. He was awarded the Garrod Medal by BSAC in 2015 for his contribution to improving prescribing of antibiotics.



## DIANE ASHIRU- OREDOPE

 Dr Diane Ashiru-Oredope is the Lead Pharmacist for the Antimicrobial Resistance Programme at Public Health England.

An antimicrobial pharmacist by background; she started working in public health in 2010 as part of the Health Protection Agency. She has chaired and led the implementation of a range of national toolkits and guidance on antimicrobial stewardship (AMS). Over the last nine years, Diane has led the development, implementation and evaluation of the national AMS toolkit Start Smart then Focus, the national antimicrobial prescribing and stewardship competences as well as the international AMR campaign, Antibiotic Guardian which is underpinned by behavioural science. Currently she is the deputy chair for the English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) and leads the national planning group for World Antibiotic Awareness Week, European Antibiotic Awareness Day and the UK Antibiotic Guardian campaign. Outside of her core role, Diane is on the editorial board for the Journal of Antimicrobial Chemotherapy, honorary Lecturer at UCL School of Pharmacy, volunteer tutor for the People's University which delivers public health Masters courses/modules for healthcare professionals in low and middle income countries, committee member for UKCPA Pharmacy Infection Network, member of Royal Pharmaceutical Society (RPS) Expert Advisory Group for Antimicrobial Resistance and adviser for Commonwealth Pharmacists Association.





## MARC MENDELSON

**>** Marc Mendelson is Professor of Infectious Diseases and Head of the Division of Infectious Diseases & HIV Medicine at Groote Schuur Hospital, University of Cape Town (UCT). He studied Medicine at St Mary's Hospital, London and specialized in Infectious Diseases at Addenbrookes Hospital, Cambridge, where he attained his PhD. He moved to The Rockefeller University, New York in 2001 and subsequently to UCT to work on tuberculosis and innate immunity.

Marc is Chair of the South African Ministerial Advisory Committee on Antimicrobial Resistance, the South African lead for Antimicrobial Resistance on the Global Health Security Agenda, co-chair of the South African Antibiotic Stewardship Programme, and co-author the South African Antimicrobial Strategic Framework. He is on a number of WHO technical advisory panels relating to antibiotic resistance, is a member of the scientific advisory group of the Global Antibiotic Research and Development Partnership (GARDP), and a member of the AMR Core Team of the World Economic Forum/Wellcome Trust collaboration on implementing new models of antibiotic R&D.

He is Past-President of the Federation of Infectious Diseases Societies of Southern Africa, and President-Elect of the International Society for Infectious Diseases.




## ARJUN RAJKHOWA

**>** Dr. Arjun Rajkhowa is the centre manager of the National Centre for Antimicrobial Stewardship, based at the Peter Doherty Institute for Infection and Immunity at the University of Melbourne and Royal Melbourne Hospital in Melbourne, Australia. He is a qualitative researcher whose interests include policy, public health and communications.





## CÉLINE PULCINI


 Céline Pulcini is Full Professor of Infectious Disease in Nancy, France. Her main research interest lies in antimicrobial stewardship and vaccination practices with the aim of preventing the emergence of bacterial resistance to antibiotics.

Professor Pulcini is Secretary of ESGAP, the European Society for Clinical Microbiology and Infectious Diseases (ESCMID) Study Group for Antimicrobial stewardship; she was editor for an ESGAP book on Antimicrobial stewardship.

She is or has recently served also as Expert for the National Antibiotic Plan of the French Ministry of Health, the ECDC and the WHO. As well as serving as an Associate Editor for the journal *Clinical Microbiology and Infection*, Professor Pulcini has also authored or co-authored over 160 international publications. She received in 2017 the ESCMID Young Investigator Award.



## DEBRA GOFF


 Debra A. Goff, Pharm.D., FCCP, Infectious Diseases Specialist. Debra Goff is an Infectious Diseases Specialist and founding member of the Antimicrobial Stewardship Program at The Ohio State University Wexner Medical Center (OSUWMC) in Columbus Ohio. She is the past-Director of the Infectious Diseases Residency program at OSUWMC. She is an Associate Professor at the College of Pharmacy working with the One Health Antibiotic Stewardship team at OSU. Dr. Goff received her Bachelor of Pharmacy and Doctor of Pharmacy degrees from the University of Illinois at Chicago, where she also completed her residency.

Dr. Goff is a 2016 TEDx Columbus speaker on antibiotics “just in case” there’s infection. She is the international advisor to the Federation of Infectious Diseases Society of South Africa (FIDSSA) mentoring South African pharmacists. She received the 2016 OSU Emerging International Outreach and Engagement Award for her work in South Africa. She is the 2017 American College of Clinical Pharmacy (ACCP) recipient of the Global Health Award. She serves as a faculty mentor to young African leaders as part of the Mandela Washington Fellowship Program. Dr. Goff is part of the World Health Organization (WHO) Pathogens Priority List Working Group. She serves on the IDWeek planning committee for the Infectious Disease Society of America (IDSA) and Making a Difference Infectious Diseases (MAD-ID) annual meeting.

Her interests include antimicrobial resistance, the application of rapid diagnostic tests with stewardship interventions, use of Twitter to increase global engagement and cross collaboration with surgeons, oncologists, veterinarians, and patient advocate organizations in antibiotic stewardship. She lectures nationally and internationally as an antimicrobial stewardship advocate and tweets regularly on topics relevant to antibiotic stewardship.



## KHALID ELJAALY

 Khalid Eljaaly, PharmD, CAPPs, MS, BCPS, is an assistant professor and infectious disease/antibiotic stewardship pharmacist in faculty of pharmacy, King Abdulaziz University, Jeddah, Saudi Arabia, and an associate faculty/research fellow in the University of Arizona, Tucson, AZ, USA. He graduated with a PharmD degree from King Abdulaziz University. He completed his PGY1 pharmacy practice residency at a Tuft-University affiliated hospital and his PGY2 infectious disease pharmacy residency at BIDMC, a Harvard Medical School-affiliated hospital in Boston, MA, USA. Then, he completed both infectious disease/antibiotic stewardship pharmacy fellowship and Master of Science in clinical translational sciences at University of Arizona. He is a member of the social media committees of both the Society of Infectious Diseases Pharmacists (SIDP) and the Infectious Diseases Practice and Research Network of the American College of Clinical Pharmacy. He is also a member of the antibiotic stewardship committee of SIDP, a member of the editorial advisory board of Contagion®, a member of the Saudi Ministry of Health stewardship implementation team. His Twitter account is called “Antibiotic Tweets” and his handle is @khalideljaaly.




## KIRSTY BUISING

 Associate Professor Kirsty Buising is an infectious diseases physician working for the Victoria Infectious Diseases Service (VIDS) at the Royal Melbourne Hospital in Melbourne, Australia. She is deputy director of the National Centre for Antimicrobial Stewardship and chief investigator for the Australian National Health and Medical Research Council (NHMRC)-funded Centre for Research Excellence in Antimicrobial Stewardship. Kirsty also holds an appointment as a clinical research physician at VIDS, leading research and development for the Guidance Group. Kirsty serves on advisory groups at state, national and international levels in the areas of antimicrobial stewardship, guideline development and healthcare associated infection.

Kirsty completed her doctorate of medicine on the use of computerised decision support for antimicrobial stewardship, and a Masters of Public Health. Her team have successfully received NHMRC Partnership grants and a Centre for Research Excellence to develop their work in antimicrobial stewardship. She has served as part of the authorship group for Therapeutic Guidelines: Antibiotic, working on national prescribing guidelines. As an advisor to the Australian Commission for Safety and Quality in Healthcare, she has had a role in influencing policy. The National Centre for Antimicrobial Stewardship team have conducted national surveys to gather data on antibiotic use in Australia. The Guidance team have developed electronic tools for antimicrobial stewardship that have been implemented in over 60 Australian hospitals and run national workshops to build capacity amongst doctors, nurses and pharmacists to improve the way we use antibiotics to optimise patient outcomes, and help to tackle antibiotic resistance. Kirsty has taught at international workshops and advised on regional initiatives to improve antimicrobial use.



## MUSHIRA ENANI


 Dr. Mushira Enani, MbChB, FRCPE, FACP, FIDSA Medical Director & Infectious Diseases Consultant, department of Medicine. Assistant Dean of Female Affairs, Assistant Professor of Medicine, King Fahad Medical City, Riyadh Saudi Arabia

Dr. Enani is a graduate of King Abdulaziz University (KAU), faculty of medicine, Jeddah, Saudi Arabia. She joined Internal Medicine residency training program in Riyadh, King Khalid university hospital/ King Saud university where she obtained the regional Arab Board in Internal Medicine & was selected as the best resident in performance as R2. She is a member of the Royal College of Physicians of Edinburgh (MRCPE).

Currently, Dr. Enani works at King Fahad Medical City (KFMC) in Riyadh as ID consultant in the department of Medicine, is Assistant Professor of Medicine, King Saud Bin Abdulaziz University for Health Sciences and Assistant Dean for female Affairs in Faculty of Medicine at KFMC and Medical Director of Main Hospital.



## ADRIAN BRINK

 Clinical Microbiologist, Ampath National Laboratory Services, Milpark hospital, Johannesburg, South Africa and Associate Professor, Division of Infectious Diseases and HIV Medicine, Department of Medicine, Groote Schuur Hospital, University of Cape Town, Cape Town, South Africa.

Dr Adrian Brink gained his MB BCh degree from the University of Pretoria in South Africa in 1984, before completing further medical training including his M Med (Clinical Microbiology) degree, in 1994. He currently works in Johannesburg, South Africa, as Head of Clinical Microbiology at the Ampath National Laboratory Services, Milpark hospital, Johannesburg.

Dr Brink was founding President of the Federation of Infectious Diseases Societies of Southern Africa and is an Executive Member of the latter council. He is currently co-chair of the South African Antibiotic Stewardship Program (SAASP). He has presented at national and international congresses and has authored or co-authored more than 70 papers in peer-reviewed journals, including Lancet Infectious Diseases, the International Journal of Antimicrobial Agents, Emerging Infectious Diseases and the Journal of Antimicrobial Chemotherapy. He is also serves on the editorial boards of several Journals incl. Infectious Diseases in Clinical Practice, Frontiers in Microbiology and the Southern African Journal of Infectious Diseases. Dr Brink is senior author of the Massive Open Online Course on Antimicrobial Stewardship and interactive e-Book of Antimicrobial Stewardship (British Society of Antimicrobial Chemotherapy and University of Dundee, Scotland). He currently serves on the South African Minister of Health's Ministerial Advisory Committee (MAC) on antimicrobial Resistance

Dr Brink's research interests include antibiotic resistance in community-acquired and intensive-care-related infections, the pharmacokinetics and outcome measures of antibiotics in ICU patients including antimicrobial stewardship (AMS) in primary care and in hospitals. In addition, the use of quality improvement models and behaviour change techniques in AMS.



## ANAHI DRESER

**>** Anahí Dreser is a researcher and lecturer in the Centre for Health Systems Research at the Mexican National Institute of Public Health (INSP). She is the co-leader of the research group Medicines in Public Health: Access, use, and antimicrobial resistance. Her research interests include pharmaceutical policies, antibiotic stewardship programmes, medicines consumption, and quality of health care.

Anahí Dreser is a medical doctor, holds a MSc in Control of Infectious Diseases, and is a PhD candidate in Public Health and Policy (LSHTM, UK). Her doctoral investigation analyses the process of developing antibiotic policies in Mexico. Currently, she collaborates with key stakeholders in Mexico as well as with the Pan-American Health Organization in initiatives directed at improving the use of antibiotics and containing antimicrobial resistance.



## REENA RAVEENDRAN

**>** Consultant, Dept of Clinical Microbiology & Immunology, Sir Ganga Ram hospital.

Dr. Reena Raveendran has acquired her MBBS from Govt. Medical College, Kottayam, Kerala in 1998. She then pursued her MD in Clinical Microbiology from Govt. Medical College, Thiruvananthapuram, Kerala in 2003.


She joined Sir Ganga Ram hospital in 2004, as Senior Research Officer, WHO project. She was the key person in the successful completion of the project “Community-based Surveillance of antimicrobial Use and Resistance in Resource Constrained Settings”.

Then onwards she has been working as a consultant with Sir Ganga Ram hospital in various sections and is currently looking after Tuberculosis diagnosis. Areas of her special interests include bacteriology, mycobacteriology, antimicrobial stewardship, quality control and controlling spread of tuberculosis. She has more than 25 publications in reputed national and international journals. She has presented many papers & posters and delivered lectures in various national and regional conferences. She is an integral part of the organization team conducting various National conferences and workshops by Sir Ganga Ram Hospital.

She is an active member of various professional bodies like Indian Association of Medical Microbiologists, Delhi Chapter - Indian Association of Medical Microbiologists, Hospital Infection Control Society and Clinical Infectious Diseases Society. She is also a certified internal auditor by ISO 15189 and NABL 112 as well as NABH. She takes keen interest in various quality control activities of the Dept. of Microbiology as well as the hospital at large.



# CHAND WATTAL

 Prof. (Dr.) Chand Wattal is presently working as Hony. Senior Consultant & Chairman Dept. of Clinical Microbiology, Ganga Ram Institute for P G Education & Research, Sir Ganga Ram Hospital, Rajinder Nagar, New Delhi, India. He did his MD (Medical Microbiology) from PGI, Chandigarh, in Jan 1983; MBBS from GMC, Kashmir 1977 & has a total professional experience of more than 30 years. Dr. Wattal has been a postgraduate teacher and a guide/co-guide of MD since 1985 and for DNB Microbiology since 2003. He is an astute academican. He is an expert to the technical advisory committee, Ministry of Health and Family Welfare, Government of India & is on several Task Forces for Rational Antibiotic Use (DGHS) and its Researchable Areas with ICMR. The Department of Clinical Microbiology, Sir Ganga Ram Hospital (SGRH) which Dr. Wattal is heading; brings out SGRH Microbiology Newsletter twice every year giving the details of the antibiogrammes and other articles of academic interest to the clinicians and clinical microbiologists ever, since 1995 which is also webcast. Dr. Wattal has 90 research & 15 book publications in peer-reviewed journals to his credit out of which, 36 are in International journals; has delivered 220 guest lectures and chaired 94 scientific sessions, which includes publications in Medical Clinics of North America, Lancet Infectious Diseases to name a few, has made contribution in Book Series/Lung Biology in Health and Disease on a topic "Pulmonary Hydatid Diseases in India, Diagnosis and Management" Publisher: Marcel Decker. Inc., USA. His books on "Emergencies in Infectious Diseases: from Head to Toe" was released in April 2009 by Vice Chancellor, Jamia University, Delhi.; Post Transplant Infections was released by Prof K.S. Chugh on 13 Dec 2013 and Hospital Infection Prevention: Principles & Practices (Springer Publication) was released on 20 Jan 2014. He was twice Guest Editor: Journal of International Medical Sciences Academy (JIMSA) Special issue July-Sept. 2004 on 'Advances in Clinical Microbiology and Infections Diseases practice in India' Jan-March 2010 on "Emerging infections: Indian Perspective." He is on the panel of Editorial

Board of Ind J of Paed., J of Lab. Physicians, IJMM AND IJMR In recognition of his academic achievements; he has been assigned the task of Chief Investigator WHO (Geneva) Project on Rational Antibiotic Usage which has finished its Phase I & II. Phase III has been funded by Melinda Bilgates Foundation currently. The findings have got chronicled in the WHO publications, 2010-11 He has participated as guest lecturer and made scientific presentations in 169 National and International Conferences. Dr. Wattal has been the recipient of several awards and brought laurels to his institution through such awards. He has been awarded by the Lt. Governor of Delhi the "Dharma Vira Award for excellence" in his profession for the year 2004; this award is given every year to the best consultant of the hospital and one of his publications was awarded S. Nundy Award as the best publication of the year 2009. Awarded long distinguished service award by Shri J.P.Nadda, Union Health Minister in 2015. Was awarded the best publication of the year in Virology published in IJMM by the Association of The Medical Microbiologists of the country in the year 2012. He has been a valued office bearer of IAMM-DC since 2006. Was re-elected twice as its treasurer and is currently the ex-officio secretary of this society. He has been elected unopposed to the executive council of the National Body of IAMM. He has also been entrusted with the job of running an EQAS program for North and North East of India for the specialty of Clinical Microbiology under the aegis of the National Body of IAMM of the country since Jan 2014. His pioneering contribution to the country and the specialty of Clinical Microbiology has been immense in the field of monitoring of antibiotic resistance and development of antibiotic policy in the country in the capacity of a member of the National Task Force for framing antibiotic policy. In recognition of his outstanding contribution in the field of medicine and service to the mankind Delhi Medical Association conferred upon him "Vishisht Chikitsa Rattan Award on Doctor's Day 10th July 2016. He is a sought after speaker for his specialty in the country and abroad.






## AOIFE FLEMING

 Dr Aoife Fleming is a Lecturer in Clinical Pharmacy at University College Cork, Ireland. She holds a joint appointment with the Pharmacy Department at the Mercy University Hospital as a research Pharmacist since 2016. She graduated with a degree in Pharmacy from Trinity College Dublin in 2004 and completed a Masters in Hospital Pharmacy in 2007 while working at Beaumont Hospital Dublin. She has extensive experience working the hospital and community pharmacy settings. Dr Fleming completed a Health Research Board Doctoral Scholarship in Health Services Research in 2014 at the School of Pharmacy, University College Cork. Her PhD investigated Antimicrobial Stewardship in Ireland with a specific focus on long-term care facilities. Aoife has published and collaborated in the area of antimicrobial stewardship and continues to conduct research in this area.



## ANDREW M. MORRIS

 Dr. Morris obtained his MD (1994) degree from the University of Toronto. He trained in Internal Medicine from 1994 to 1997 at the University of Toronto, where he subsequently completed sub-specialty training in Infectious Diseases in 1999. He went on to complete a Master of Science degree in Epidemiology from the Harvard School of Public Health in 2000, while completing a Bayer Healthcare-Canadian Infectious Diseases Society (now AMMI Canada) research fellowship under the supervision of Professor Allison McGeer.


Dr. Morris spent 6 years with the Department of Medicine at McMaster University and Hamilton Health Sciences as a consultant in infectious diseases and general internal medicine. While there, he helped develop an antimicrobial stewardship program in the Hamilton General Hospital intensive care unit. (This program won the Canadian Healthcare Excellence in Quality Award in 2006.) He returned to the University of Toronto in 2007, where he joined the Division of Infectious Diseases in the Department of Medicine at Mount Sinai Hospital and University Health Network. He is currently Professor, and works as a consultant in Infectious Diseases and General Internal Medicine. Dr. Morris is past Chair of the Specialty Committee of Infectious Diseases with the Royal College of Physicians and Surgeons of Canada, Chair of the Antimicrobial Stewardship and Resistance Committee for the Association of Medical Microbiology and Infectious Diseases Canada, and Chair-elect of the Antimicrobial Stewardship Committee for the Society of Healthcare Epidemiology of America.

He is the founding Director of the SinaiHealth System-University Health Network Antimicrobial Stewardship Program (SHS-UHN ASP), formed in 2009. The SHS-UHN ASP is the first and largest antimicrobial stewardship program in Canada, overseeing antimicrobials in 3 acute care hospitals, 1 cancer hospital, and 3 rehabilitation facilities, and a long-term care facility. He worked with Accreditation Canada to make Canada the first jurisdiction in the world to require antimicrobial stewardship in hospitals. He has authored or co-authored over 100 peer-reviewed publications, with an emphasis on antimicrobial stewardship, critical care, and *Staphylococcus aureus* bacteremia.





## HAIFA LYSTER

 Haifa Lyster FFRPS, FRPharmS  
Consultant Pharmacist in Transplantation & Ventricular Assist Devices (VADs) at The Royal Brompton & Harefield NHS Foundation Trust.


Haifa graduated from the School of Pharmacy, University of Bath in 1992 and continued her studies obtaining a Masters degree at London School of Pharmacy and is a qualified independent non-medical prescriber. She is both a Fellow of the Royal Pharmaceutical Society and of its' Faculty.

Haifa has worked in thoracic transplantation & VADs based at Harefield hospital since 1998 with a leading role in managing VAD and heart and lung transplant patients in all aspects of their pharmaceutical care, particularly in anti-infective and immunosuppression regimens. She is currently undertaking a PhD research doctorate developing PK/PD models of a number of antifungal agents in ECMO patients.

Haifa is the pharmacy lead for NHSE Cardiothoracic Clinical Reference Group and Vice chair of SOTPA (Solid Organ Transplant Pharmacy Association). She is also currently the Vice chair (elect) of the Pharmacy & Pharmacology council for the International Society of Heart & Lung Transplantation (ISHLT).



## SANJEEV SINGH

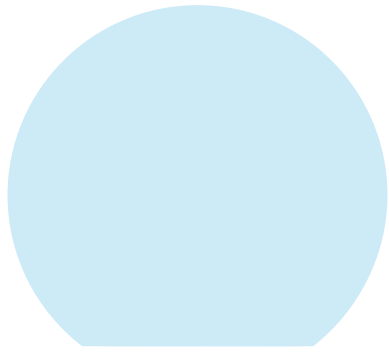
 Dr Sanjeev Singh is a pediatrician by training and did his MPhil in Hospital Management. He completed his PhD in Infection Prevention and Control. He is a Chair of Infection Prevention and Antibiotic Stewardship at Amrita Institute of Medical Sciences at Kochi

He worked as a Regional Coordinator at WHO-India in a Disease eradication program before joining as Sr Medical Superintendent at AIMS, Kochi.

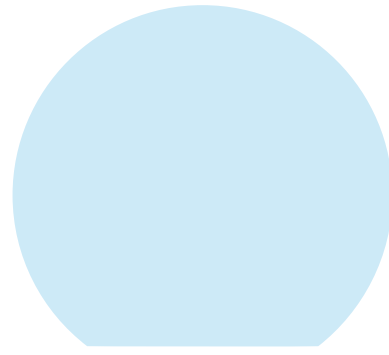
He has gained his fellowship on Healthcare worker Safety from University of Virginia and fellowship on Health Technology Assessment (HTA) from University of Adelaide. He is an Improvement Advisor from Institute of Healthcare Improvement, US.

Dr Sanjeev is also an Ambassador from India to Society of Healthcare Epidemiology of America (SHEA) and has been adjudged as "Heros of Infection Control" by Association of Professionals of Infection Control (APIC), US. He is the International surveyor at International Society for Quality (ISQua). He is presently the Vice Chairman of Research Committee at NABH, Chairman of Technical Committee at AHPI (Association of Healthcare Providers of India) and Health Sector Skills Council of India (GOI), a member of Drug Safety Council (GOI) and member of National Advisory Body on Occupational Exposures. He is also a Principal Assessor for ISO9001:2015 and NABH.


He is an external consultant to WHO, a Technical Advisor to several State government healthcare projects (E learning, reduction of IMR, Antibiotic Stewardship and Infection Control), Technical Expert for University of Antwerp's Point Prevalence Surveillance and Institute of Healthcare Improvement's (US) on Neonatal Collaborative program and a member of Core Working and Technical Advisory Group on Antibiotic Stewardship for the State of Kerala.



DAVID  
ENOCH




LAURA  
WHITNEY

 David is a consultant microbiologist in Cambridge. He trained in London and did medical jobs in London and the South East before training in medical microbiology at the Royal Free Hospital in London and then Cambridge. He was a consultant initially in Peterborough before moving back to Cambridge 5 years ago.



## SANJAY PATEL


 Dr Sanjay Patel is a paediatric infectious diseases and immunology consultant working at Southampton Children's Hospital, England. His main areas of interest are OPAT and antibiotic stewardship.

In 2012, he introduced the first paediatric outpatient parenteral antibiotic therapy (p-OPAT) service in the UK. He chaired the joint BSAC / British Paediatric Allergy, Immunology and Infectious Diseases Group p-OPAT national working group tasked to develop good practice guidelines for the introduction and delivery of p-OPAT services in the UK, which were published in October 2014.

He leads the antimicrobial stewardship service at Southampton Children's Hospital and was a member of the NICE antibiotic stewardship guideline development group which published guidelines in 2015. He is on the BSAC OPAT standing committee and sits on BSAC council. He is co-lead for the module on antimicrobial stewardship for the European Society of Paediatric Infectious Diseases on-line antibiotic management course and runs infectious diseases courses at Imperial College and in Iceland. As project lead of Healthier Together Wessex, he is working with primary care colleagues to improve antibiotic prescribing in community based settings ([www.what0-18.nhs.uk](http://www.what0-18.nhs.uk)).



## PRIYA NORI

 Priya Nori, MD. Medical Director, Antimicrobial Stewardship Program

Co-Director, OPAT Program

Assistant Professor of Clinical Medicine at the Albert Einstein College of Medicine, Montefiore Health System



## KARIN THURSKY

➤ Professor Karin Thursky is the Director of the National Centre for Antimicrobial Stewardship, the Deputy Head of Infectious Diseases at the Peter MacCallum Cancer Centre, and the Director of the Guidance Group at Royal Melbourne Hospital. An infectious diseases physician, she is a leader in the design and implementation of antimicrobial stewardship programs, with a particular expertise in the use of computerised systems to support better antibiotic prescribing. The Guidance program, which supports clinical teams in hospitals to monitor the appropriateness and safety of antibiotic use, is implemented in over 60 hospitals across Australia. The National Antimicrobial Prescribing Survey is a core component of the National Antimicrobial Resistance Strategy. Her multidisciplinary team of clinician and health service researchers is working to establish and implement antimicrobial stewardship programs across animal and human health sectors.



## ENRIQUE CASTRO-SÁNCHEZ


➤ Enrique Castro-Sánchez is currently combining an Early Career Research Fellowship exploring increased participation of nurses in antimicrobial stewardship decision-making and positions as Lead Research Nurse at the Health Protection Research Unit in AMR and HCAI at Imperial College London, working on the theme "Innovations in behaviour change, technology and patient safety to improve infection prevention and antimicrobial use".

He was awarded a PhD cum laude in Nursing at the University of Alicante (Spain) in 2015. He trained in nursing and management of nursing services in Spain, followed by an MSc in Public Health at the London School of Hygiene and Tropical Medicine in 2003. His research interests include health literacy in infectious diseases and healthcare-associated infections; health inequalities on infectious diseases; policy influence on management of infectious diseases.

Enrique has got a broad clinical experience in tropical and infectious diseases including malaria, leprosy, tuberculosis, HIV and sexually transmitted infections. He has consulted to the WHO Global Infection Prevention and Control Unit in Geneva, developing leadership materials to support the new Core Components in Infection Prevention and Control. He sits at BSAC Council, he is a Florence Nightingale Foundation Scholar, member of the European Academy of Nursing Science, and was elected as Emerging Leader in International Infectious Diseases in 2016 by the International Society for Infectious Diseases".




## TIMOTHY GAUTHIER

 Timothy P. Gauthier, Pharm.D., BCPS-AQ ID is a pharmacist with advanced training and experience in the fields of infectious diseases and antimicrobial stewardship. He remains active in teaching, clinical practice, research, and service. You can find him on social media @IDstewardship.



## MICHAEL CORLEY

 Michael joined the British Society for Antimicrobial Chemotherapy as its Senior Policy and Public Affairs Officer in May 2017.


He has previously worked as the Director of Public Affairs for Adoption UK, and as the Head of Communications and Campaigns for the Royal Society for the Prevention of Accidents (RoSPA).

Michael is a qualified Senior Journalist who has worked for both the Coventry Telegraph and the Gloucestershire Echo, where he was the Politics Editor.

He has a Bachelor of Arts degree in History and Politics, and a Master of Arts degree in Modern Literature (which was awarded with distinction).



## GAVIN BARLOW


 Gavin Barlow, MB ChB DTM&H MD FRCP, Consultant in Infection, Hull & East Yorkshire Hospitals NHS Trust, Hon. Senior Clinical Lecturer, Centre for Immunology and Infection, Hull York Medical School and University of York.

GB qualified in Medicine at Leicester University in 1993 and trained in infectious diseases and general internal medicine in Leeds, Sheffield and Dundee, including a two-year research training fellowship at the University of Dundee. GB's main clinical interests are orthopaedic infection, outpatient parenteral antibiotic therapy (OPAT), antimicrobial stewardship, and the management of complex bacterial and healthcare-associated infections.

Research interests are broad, but predominantly focus on the epidemiology and clinical care of infections commonly managed in the NHS. GB was awarded Fellowship of the Royal College of Physicians, London in 2009 and is the British Society for Antimicrobial Chemotherapy (BSAC) Officer for Stewardship and Surveillance.



## TRACEY GUISE

 Tracey Guise is Chief Executive Officer at the BSAC. She is a seasoned senior executive with over 20 years' experience within not for profit organisations including past leadership roles at the Royal College of Paediatrics and Child Health and an early career in the civil service. In her current role Tracey contributes to and supports delivery of the strategic aims of the Society and, most recently, its global education agenda.







SALLY  
BRADLEY



NEIL  
WATSON

 Sally has a background in the quality assurance of medical education and project management of yearly awards to recognise excellence in teaching and innovative teaching initiatives.

Since joining BSAC she is part of the team coordinating, developing and creating eLearning courses for a global audience, including a suite of massive open on-line courses, Webinar based courses for General Practitioners on behalf of Public Health England and this eBook.

 Neil is a Creative Graphic, UI designer and Web Developer based in Cambridgeshire. Neil has worked with the British Society for Antimicrobial Chemotherapy to provide web development and design services for the Society's portfolio of national and international activities and is an integral part of the BSAC team. Neil has over a decade of experience of high level development projects and has collaborated with leading software companies including PlayStation, XBOX, Nintendo, BBFC & UKIE, as well as other charitable bodies including Wembley National Stadium Trust and Animal Health Trust & Wood Green Animal Charity.