Overview of Antimicrobial Resistance
and
Antimicrobial Stewardship in Health Care Settings

Session 4

Module 12

Learning Objectives

By the end of this module the participants should be able to:

- Define antimicrobial resistance (AMR)
- Describe AMR in health care setting
- Describe the interface between infection prevention control (IPC) and AMR
- Identify the strategies to prevent the emergence of AMR
- Describe AMR surveillance
- Define antimicrobial stewardship
- Describe the goals and principles for antimicrobial stewardship

Definition of terms

- **Antibiotics**
  - medicine that inhibit the growth or destroy bacteria
- **Antimicrobials**
  - agents that kills micro organisms or inhibit their growth
- **Antimicrobial resistance** (AMR)
  - ability of a micro organism to resist the effect of an antimicrobial agents that once successfully worked against it
- **Antimicrobial Stewardship**
  - multifaceted approach that healthcare organizations have adopted to optimize prescribing of antimicrobials

Introduction to AMR

Introduction

- Emergence of AMR involves a complex interaction of multiple factors
- Indicates the ability of a microbe strain to survive and/or multiply despite the administration
- and absorption of a drug given in doses equal to or higher than those usually recommended

How Does Resistance Arise?

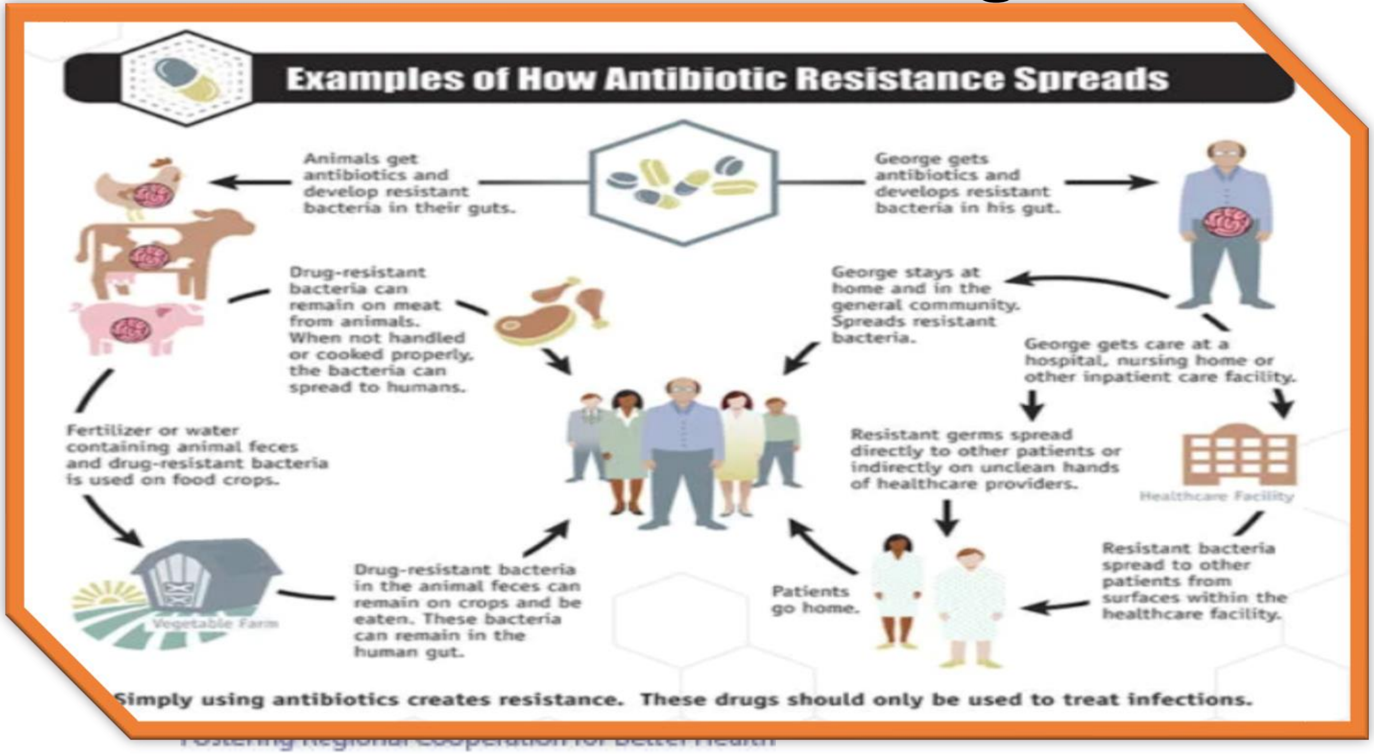
- Microorganisms either have natural resistance to drugs or they can develop it
- Mutations in microbes and selection pressure from antimicrobials use provides a competitive advantage for mutated strains

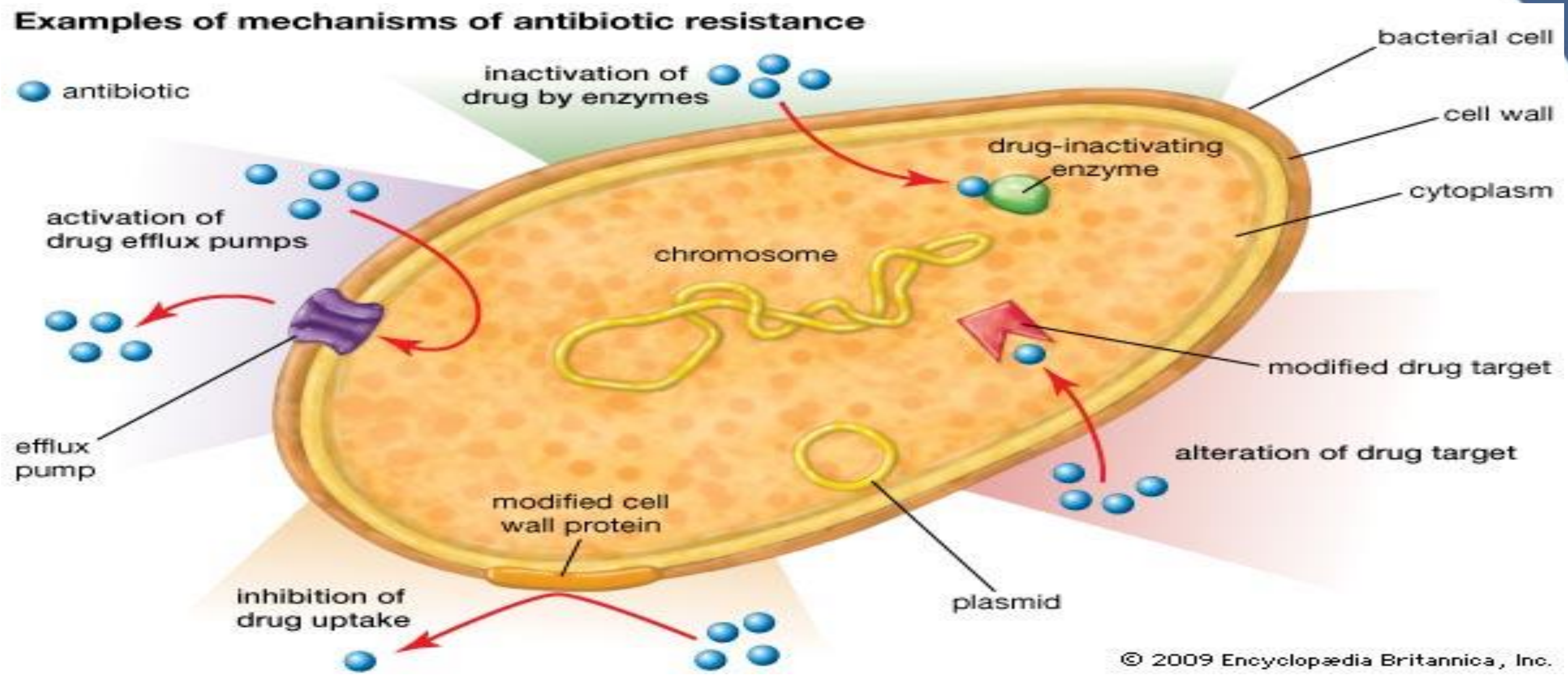
- The presence of antimicrobials in the environment in higher concentrations increases the pressure by natural selection

- Under dosing of antimicrobial agents aid step-wise selection of resistance

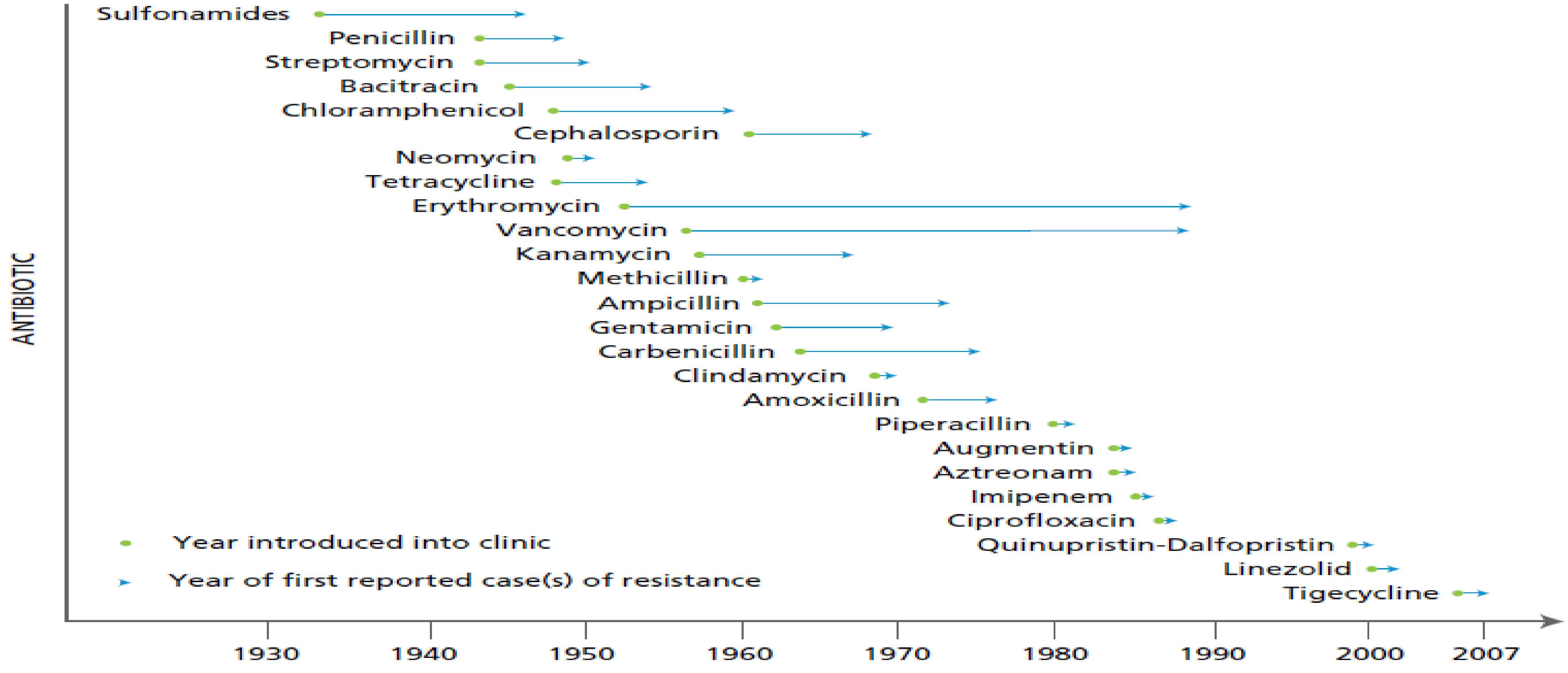
How Does Resistance Arise? (cont.)

- In many cases, resistance to a certain drug from a class leads to resistance to all other drugs in that class




Examples of mechanisms of antibiotic resistance
antibiotic
inactivation of drug by enzymes
bacterial cell
cell wall
drug-inactivating enzyme
cytoplasm
activation of drug efflux pumps
chromosome
modified drug target
efflux pump
alteration of drug target
modified cell wall protein
inhibition of drug uptake
plasmid
© 2009 Encyclopædia Britannica, Inc.

Evolution of Antibiotic Resistance



Note: Some of the dates are estimates only.

Antibiotic-resistance-death-of-a-wonderdrug LA Insight Pharma Reports 2008,

Evolution of Antibiotic Resistance

Antibiotic	Year Deployed	Resistance Observed
Sulphonamides	1930s	1940s
Penicillin	1943	1946
Streptomycin	1943	1959
Chloramphenicol	1947	1959
Tetracycline	1948	1953
Erythromycin	1952	1988
Vancomycin	1956	1988
Methicillin	1960	1961
Ampicillin	1961	1973
Cephalosporins	1960s	Late 1960s

Current AMR Status

- Drug resistance is increasing globally
  - Diseases are becoming resistant to drugs faster than we can develop new treatments
  - Infections that can be managed are transforming to life threatening ones:
    - Malaria
    - TB
    - *Streptococcus pneumoniae*

AMR types

Drug resistance occurrence are observed in all types of microorganisms including bacteria, viruses, parasites and fungi and are subcategorized into two types:

- **Intrinsic _ resistance**
  Intrinsic resistance is the natural or innate resistance of bacteria to a particular antibiotic
- For example, Gram-negative bacteria are naturally resistant to vancomycin; enterococci are resistant to cephalosporins.
- **Acquired_ resistance**
- Acquired resistance is when bacteria become resistant to an antibiotic to which it was previously susceptible.
- This is the most dangerous type of resistance that contributes to the overall spread of antibiotic resistance.

Types of Bacteria posing the greatest threat

Priority 1: Critical

Bacteria	Gram identification
Carbapenem-resistant *Acinetobacter baumannii**	Negative
Carbapenem-resistant *Pseudomonas aeruginosa**	Negative
Carbapenem-resistant and ESBL-producing Enterobacteriaceae*	Negative

Priority 2: High

Bacteria	Gram identification
Vancomycin-resistant *Enterococcus (VRE) faecium**	Positive
Methicillin-resistant *Staphylococcus aureus (MRSA)**	Positive
Clarithromycin-resistant *Helicobacter pylori*	Negative
Fluoroquinolone-resistant *Campylobacter spp.*	Negative
Fluoroquinolone-resistant *Salmonellae*	Negative
Cephalosporin and/or fluoroquinolone-resistant *Neisseria gonorrhoeae*	Negative

Priority 3: Medium

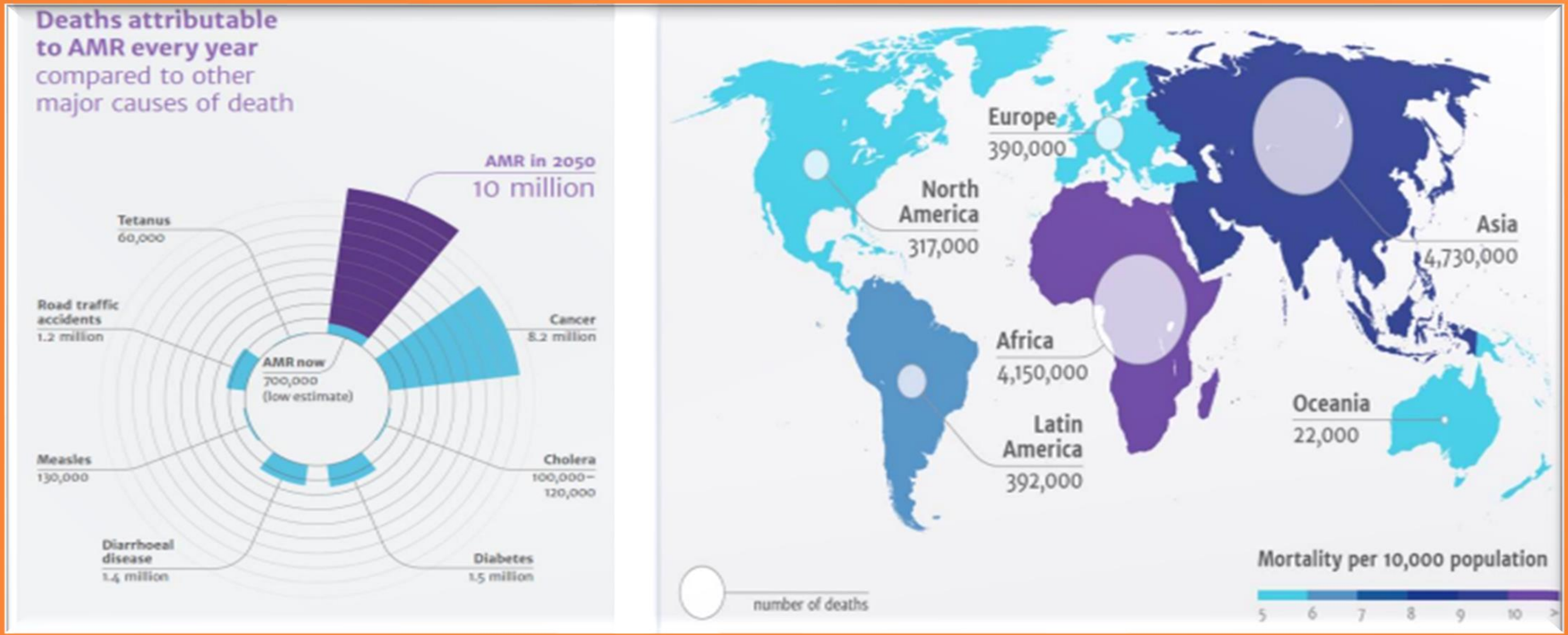
Bacteria	Gram identification
Penicillin—non-susceptible *Streptococcus pneumoniae*	Positive
Ampicillin-resistant *Haemophilus influenzae*	Negative
Fluoroquinolone-resistant *Shigella spp.*	Negative

Bacteria commonly causing infections in hospitals and in the community

Name of bacterium/resistance	Examples of typical diseases	No. out of 194 Member States providing data	No of WHO regions with national reports of 50% resistance or more
E. coli - vs 3rd gen. cephalosporins - vs fluoroquinolones	Urinary tract infections, bloodstream infections	86 92	5/6 5/6
K. pneumoniae - vs 3rd gen. cephalosporins - vs carbapenems	Pneumonia, bloodstream infections, urinary tract infections	87 71	6/6 2/6
S. aureus - vs methicillin "MRSA"	Wound infections, bloodstream infections	85	5/6

Source: WHO Antimicrobial Resistance Surveillance System (GLASS).

Future potential mortality due to AMR



Drivers of AMR

AMR is driven by:

- Prescribers and patient behaviour
- Health System challenges
- Non-human use of antimicrobials
- Technological developments

Behavioral Factors

- Patient
  - Self medication
  - Incomplete dosing
  - Access of medicines from informal dispensers
- Prescriber/providers
  - Lack of information to support drug selection
  - Incentives / influence from marketers

Factors Influencing Prescriptions

- Patient expectation and satisfaction
- Severity of illness
- Duration of illness
- Parents demands
- Concerns about secondary bacterial infection
- Time

Physician Overuse

Physicians

Prescribing unnecessary antibiotics, Prescribing Antibiotics for Viral Infections, 2 or more antibiotics

↓

Kills Resident Bacteria (Normal flora)

↓

Some survive

↓

Antibiotic resistant genes

↓

Passing of these genes to pathogenic bacteria

Antibiotic resistance

↓

Physician Overuse

Physicians

Prescribing unnecessary antibiotics, Prescribing Antibiotics for Viral Infections, 2 or more antibiotics

↓

Kills Resident Bacteria (Normal flora)

↓

Some survive

↓

Antibiotic resistant genes

↓

Passing of these genes to pathogenic bacteria

Antibiotic resistance

↓

Patient Misuse

Patients

↓

Not finishing full course of antibiotics

↓

Misuse

↓

Leaving 1 or 2 doses

↓

Some bacteria not killed

↓

Resistance developed for future antibiotic treatment

Over the counter (OTC) antibiotics

Antibiotics

↓

Available as OTC medicines

↓

Inappropriate use

↓

Overuse or Misuse

↓

Antibiotic resistance

Healthcare workers

Hospital

↓

Healthcare workers

↓

Not following infection control protocols

↓

Resistance transferred by bacteria swapping genes

Hospitalized patients

Hospital

↓

Immunocompromised patients

↓

Exposed to Pathogenic organisms

↓

Increased use of different antibiotics

↓

Rapid development of resistance

Health Systems challenges

- Insufficient or poorly trained health care workers
- Poor drug resistance surveillance
    - Drug resistance data very limited
- Poor infrastructure
- Lack of regulation and enforcement
    - Pharmaceuticals supply chain
    - Drug quality & efficacy / post market surveillance

Use of Antibiotics in Animal Health and Agriculture

Antibiotics are used to:

- Promote rapid growth and earlier marketing
- Reduce incidence of disease thereby cut costs

Examples:

U.S:

- Use of fluoroquinolones in poultry responsible for human resistance (banned 2005)

Netherlands:

- 20% of MRSA infections derived from animal strains

Antibiotics in animal feed now banned in Europe

Non-human use of antimicrobials

Animal feed

↓

Mixed with antibiotics to prevent infections and to promote growth

↓

Resistant organisms in animals

↓

Spread to humans

Non-human use of antimicrobials…cont

Antibiotics in food and water

Antibiotics found in beef cattle, pigs and poultry

↓

Drainage with antibiotics contaminates groundwater

↓

Same antibiotics mixed with municipal water systems

↓

Antibiotics in food and drinking water

↓

Promote bacterial resistance.

Dangers of AMR

- Increased morbidity and mortality
- Hampers infectious diseases control
- Threatens a return to a pre-antibiotic era
- Increases health care costs
- Jeopardizes health-care gains to society
- Threatens health security
- Damages trade and economies

Health and Economic Consequences

- Short term consequences
  - Borne by the patient
    a. Prolonged hospital stay
    b. Morbidity and mortality
- Long term
  - Borne by All
    a. Reduced number of effective drugs
    b. Increased cost of health care delivery

Health Consequences of Resistance

- TB
  - Killed 1.6 million people in 2006
  - Treatment: 4 drugs, 6-9 months
- MDR- and XDR- TB
  - 2007: 50,000 cases were XDR-TB
  - Sept 2009: Cases of XDR-TB recorded in at least 57 countries
  - 2018; MDR cases 2300 in Kenya
- Gonorrhea
  - 78 million people are infected with gonorrhea each year globally
  - 97% of the countries surveyed reported the presence of drug-resistant gonorrhea strains
  - 66 %—in high-income countries reported the emergence of resistance to last-resort drug treatments for the infection

AMR & IPC

Spread of AMR genes is facilitated by:

- Interspecies gene transmission
- Poor sanitation and hygiene
- Appearance of successive resistant clones

AMR Surveillance &Monitoring

- Tracks changes in microbial population
- Permits early detection of resistant strains
- Supports prompt notification and investigation of out breaks

The findings are needed to:

- Inform clinical therapy decisions
- Guide policy recommendations
- Assess impact of resistance containment interventions

Antimicrobial Resistance Surveillance & monitoring(Cont')

- Surveillance of antibiotic resistance and monitoring of IPC practices are crucial in order to understand the local situation and

- put in place appropriate prevention action and develop tailored antimicrobial stewardship strategies

- Monitoring focuses on process and structure such as Hand Hygiene compliance and isolation room capacity

Antimicrobial Resistance Surveillance & monitoring(Cont')

- The IPC programme should conduct surveillance of AMR and HAI outcomes to detect colonized or infected patients and to track the burden of infection and resistance over time in your facility,

- in order to implement the proper vertical IPC practices for the microorganisms identified.

- Surveillance and monitoring complement each other; they should be conducted at the same time.

IPC Strategies to combat against AMR

- **conduct surveillance of antibiotic-resistant bacteria, including screening of high-risk patients;**
- **provide antimicrobial stewardship and monitoring of antibiotic consumption;**
- **put in place triage and identify patients with antibiotic resistance so that we can put contact precautions in place;**
- **practice hand hygiene**
- **clean and disinfect the environment**
- **decontaminate medical devices**
- **train all health care workers on key IPC measure that stop the spread of AMR; and**
- **monitor infrastructure for IPC and IPC practices.**

IPC Strategies to combat against AMR

- Ensuring appropriate patient placement, ideally in a single room with a dedicated toilet
- Perform hand washing and or Hand rubbing hands.
- Ensure proper cleaning of High-touch items and surfaces such as patient room ,door handle, call bell, light switch ,Hallway on patient etc
- Note: Handrubing between 15–30 seconds, is significantly more efficient than hand washing with plain soap and water at reducing bacterial contamination of the

Antimicrobial Stewardship (AMS) in Health Care Settings

Objectives

- Define antimicrobial stewardship
- Describe the goals and principles for antimicrobial stewardship
- Describe the set up of AMS programs

Introduction to AMS

- AMS refers to the multifaceted approach (including policies, guidelines, surveillance, prevalence reports, education and audit of practice) that healthcare organizations have adopted to optimize prescribing
- AMS programs in hospitals seek to optimize antimicrobial prescribing in order to:
    - Improve individual patient care
    - Reduce hospital costs
    - Slow the spread of antimicrobial resistance
- Overarching role is to change and direct antimicrobial use at a health care institution

Goals of AMS

Optimize patient safety

Decrease cost

Slow or reduce emergence of resistance

Benefits of An AMS Program

- Reduction in 20%- 40% of antimicrobial use, with savings of USD 200,000–USD 900,000
  http://www.cdc.gov/getsmart/healthcare/resources/slides/getsmart-healthcare.pdf
- Promotion of patient safety and reduction in mortality
- Minimize drug-related adverse events
- Reduction of HAIs

Benefits of an AMS Program (cont.)

- Reduction of global bacterial resistance
- Provide the infrastructure to preserve antimicrobials
- Can be implemented in any healthcare setting (from the smallest to the largest)

Elements of a Successful Stewardship Program

Comprehensive program includes:

- Active monitoring of resistance

- Fostering of appropriate use
    - Often used as a surrogate marker for impact on resistance

- Collaboration of effective infection control to minimize secondary spread of resistance

Establishing an AMS Program

Core Elements

- Leadership
- Scope
- Ownership
- Location
- Tools
- Implementers
- Review and feedback

Scope of AMS Program

When setting up an AMS program:

- Define what the institution considers appropriate antimicrobial use
- Determine the scope of the program
  - Hospital-wide
  - Departmental
  - Unit
  - Critical care unit

Core Elements of AMS

- **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

Core Elements of AMS (cont.)

- **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)
- **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

Strategies for AMS Programs

- Education and guideline implementation strategies
- Formulary and restriction strategies
- Prospective audit with intervention
- Feedback (review and feedback strategies)

Antimicrobial Stewardship Strategies

5 D's of AMS

- Diagnosis
- Drug Selection
- Dose Optimization
- De-escalation
- Duration of Therapy

Best Practice for Antimicrobial Use

- Appropriate lab investigations are recommended for all infections. These are necessary for diagnosis, treatment and follow up
- Microbiological samples should be collected **before** initiating antimicrobial therapy
- The hospital formulary is to be used while choosing antimicrobial therapy
- Check for factors that will affect drug choice and dose such as renal and hepatic dysfunction, drug interactions and hypersensitivity reactions

Best Practice for Antimicrobial Use (cont.)

- Ensure that appropriate dose is prescribed; if uncertain consult the clinical pharmacist or check in the hospital formulary
- The need for antimicrobial therapy should be reviewed regularly (every 72 hours)
- For most infections 5 to 7 days of antimicrobial therapy is sufficient

Barriers and Possible Solutions to AMS

Barriers to AMS

Description	Barriers	Possible solutions
Human resources	• Poor availability of different specialists to create and maintain a functional AMS team	• Raise awareness of hospital directors/ managers/policy makers about benefits of AMS
	• Available specialists overloaded with other inherent tasks • AMS activities generally are not paid	• Training of relevant medical doctors, clinical microbiologists and pharmacists • Make AMS standard of care and hospital accreditation and foresee remuneration for AMS activities

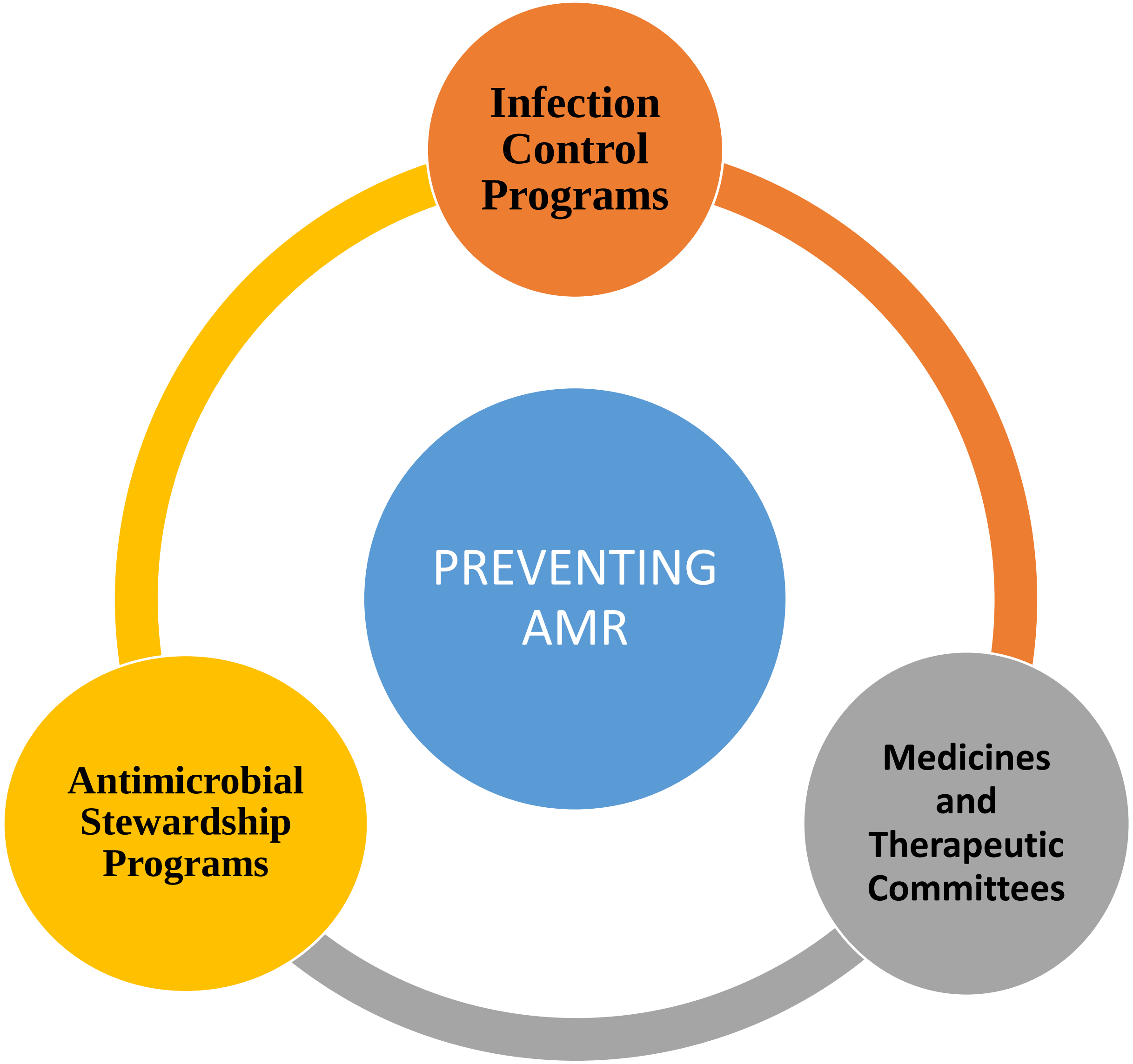
Description	Barriers to AMS (cont.)	Possible solutions
Knowledge/ education of rational antibiotic use among health care professionals	• Suboptimal undergraduate training on microbiologic, ecologic and pharmacologic aspects of antibiotic resistance	• Revision of the curricula related to antibiotic resistance in Schools of Medicine, Pharmacy and others involved
	• Limited continuous medical education programs for physicians, microbiologists and pharmacists	• Provide and update continuous medical education programs certified by respected institutions
	• Many physicians receive medical information mainly from companies • Prescriptions and drug selection often influenced by this information and gifts	• Authorities should control and supervise promotional activities of pharmaceutical companies

Description	Barriers to AMS (cont.)	Possible solution
Prescribing practices	• Therapeutic freedom' is highly valued among many	• Initial training followed by continuous education, audit and feedback
	• Lack of stable drug supply	• Respected essential drugs list, hospital formulary • Generate awareness among prescribers and pharmacists of the importance of stable and consistent drug supply

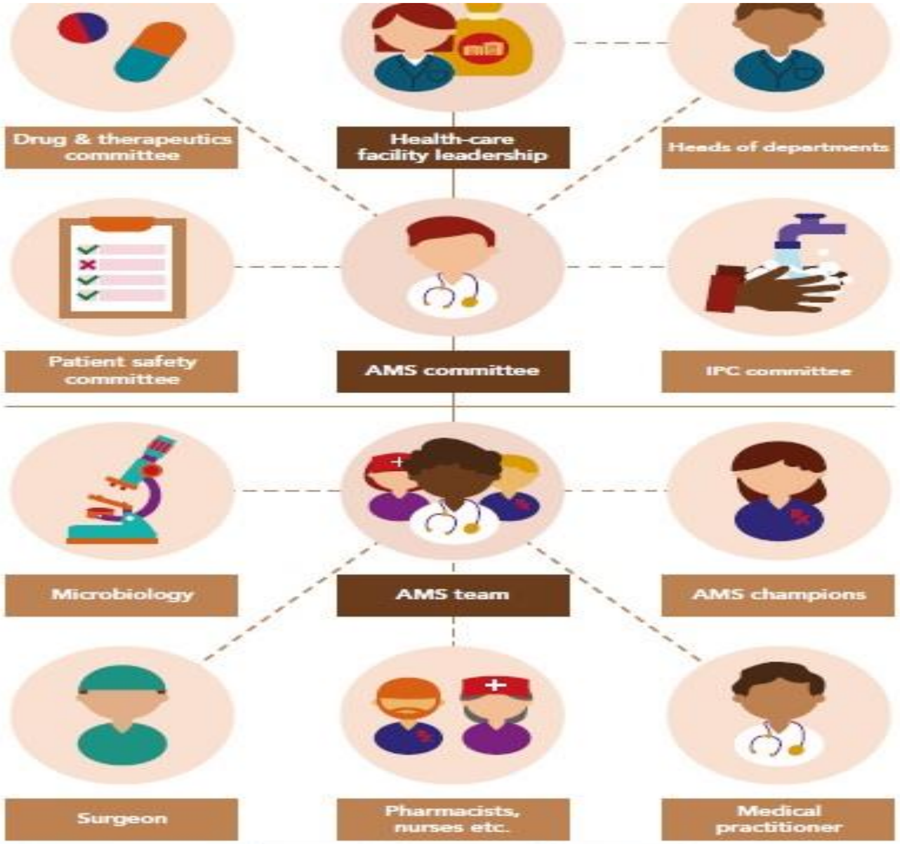
Description	Barriers to AMS (cont.)	Possible solutions
Guidelines and recommendations (clinical decision support)	• Multitude of guidelines present, often outdated or inappropriate • Lack of ownership on local guidelines • Lack of access to up-to-date information	• Selection of guidelines most suitable to the institution and adaption • Revision of local guidelines by the AMS team jointly with opinion leaders among local prescribers • Provide open access templates for common infections that can be locally adapted
	• Suboptimal microbiology laboratory diagnostic tools	• Improvement of laboratory performance • Introduction of relevant near-patient tests • Simple testing guidance for laboratories and quality assurance

Description	Barriers to AMS (cont.)	Possible solutions
Infection prevention and control (IPC)	• Poor availability of medical staff and nurses for IPC team • Poor interest, knowledge and compliance of health care workers basic IC practices	• Education of health care workers and hospital management on healthcare-associated infections (HAIs) and role of IPC activities
	• IPC activities generally have no budget • Structural deficiencies of the institution (i.e. scarcity of isolation rooms, lack of basic supplies for hand hygiene, patient care articles)	• Provision of resources to maintain a fully functional IPC team • Revision and modification of main structural and supply caveats

Collaborative Effort



Multidisciplinary Team



AMS Gorvenance Structure:
Source: Antimicrobial stewardship programmes in health-care facilities in low- and Middle-income countries. A WHO Practical Toolkit

Summary (cont.)

....infection prevention control and prudent use of antimicrobial agents are not only related, but also pivotal steps to stop both selection and dissemination of multi-drug resistant organisms (MDROs)

Key Points

- AMR has critical consequences for individual patients and the healthcare system overall, and increases the cost of healthcare.
- In many cases, resistance to a certain drug from a class leads to resistance to all other drugs in that class.
- AMR is driven by multiple factors including provider and patient behavior, the health system, non-human use of antibiotics, and technology.

Key Points (cont.)

- AMS refers to a multifaceted approach to optimize prescribing.
- An effective AMS program relies on leadership, commitment of resources, accountability, and drug expertise.

Thank you.
Questions?