



**AMERICAN
UNIVERSITY OF BEIRUT**
FACULTY OF MEDICINE

EXPERIENCE AND PERSPECTIVES FROM IMPLEMENTING AN ANTIMICROBIAL STEWARDSHIP PROGRAM

SEPTEMBER 15, 2023

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I declare no conflict of interest in relation to this presentation



OBJECTIVES

1- ANTIMICROBIAL RESISTANCE- GLOBAL IMPACT

2- AMR – SETTING THE STAGE

3- ANTIMICROBIAL STEWARDSHIP

4- EXPERIENCE AT THE AUBMC

- **ASP AT AUBMC**
- **SUCCESSFUL INTERVENTIONS**
- **DATA AND OUTCOMES**

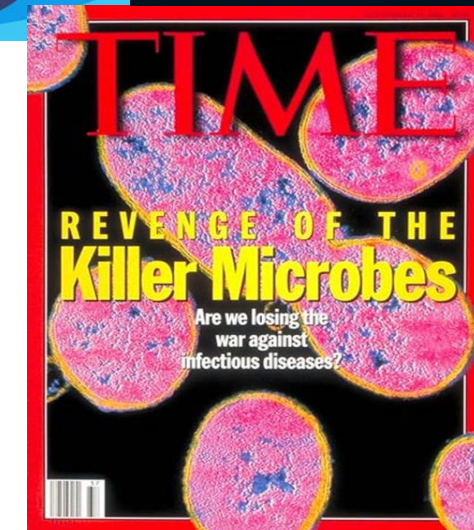
5- COVID-19 at AUBMC

6- CONCLUDING REMARKS

AMR is rising to dangerously high levels in **all parts of the world** and is recognized as a major threat to public health, economy, and security.

Changing world and **climate** disruptions.

New resistance mechanisms are emerging and spreading, threatening our **ability to treat common infectious diseases**.
– such as **pneumonia, tuberculosis, Gonorrhea, and foodborne illnesses.**

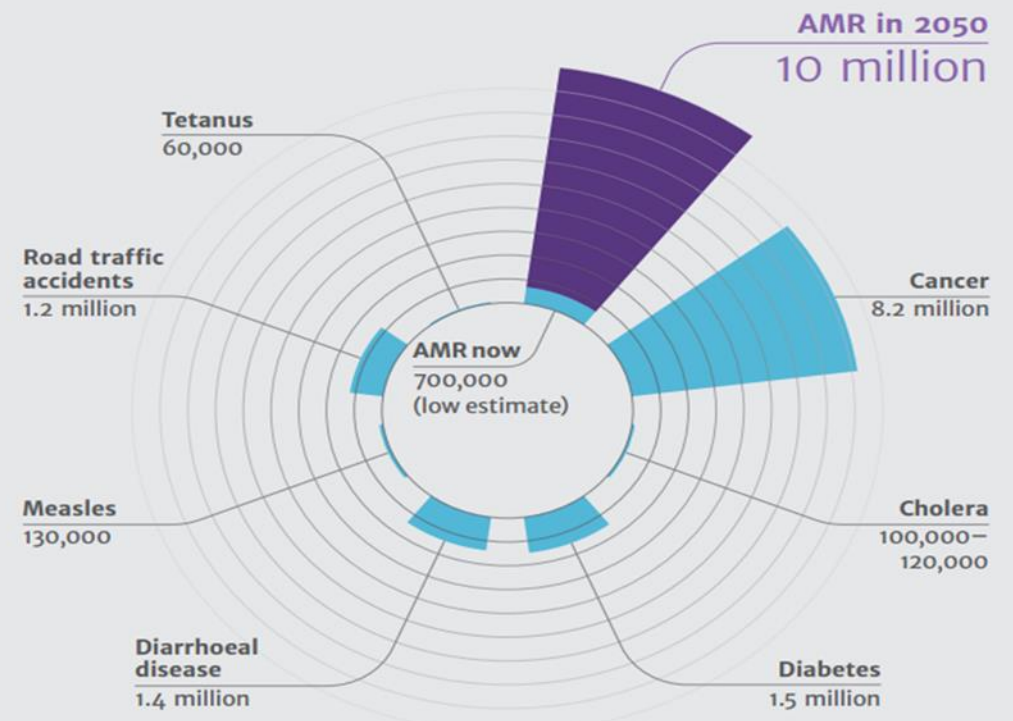




THE MAGNITUDE OF THE THREAT

It is estimated that a continued rise in AMR would lead to **10 million deaths** yearly across the globe by 2050.

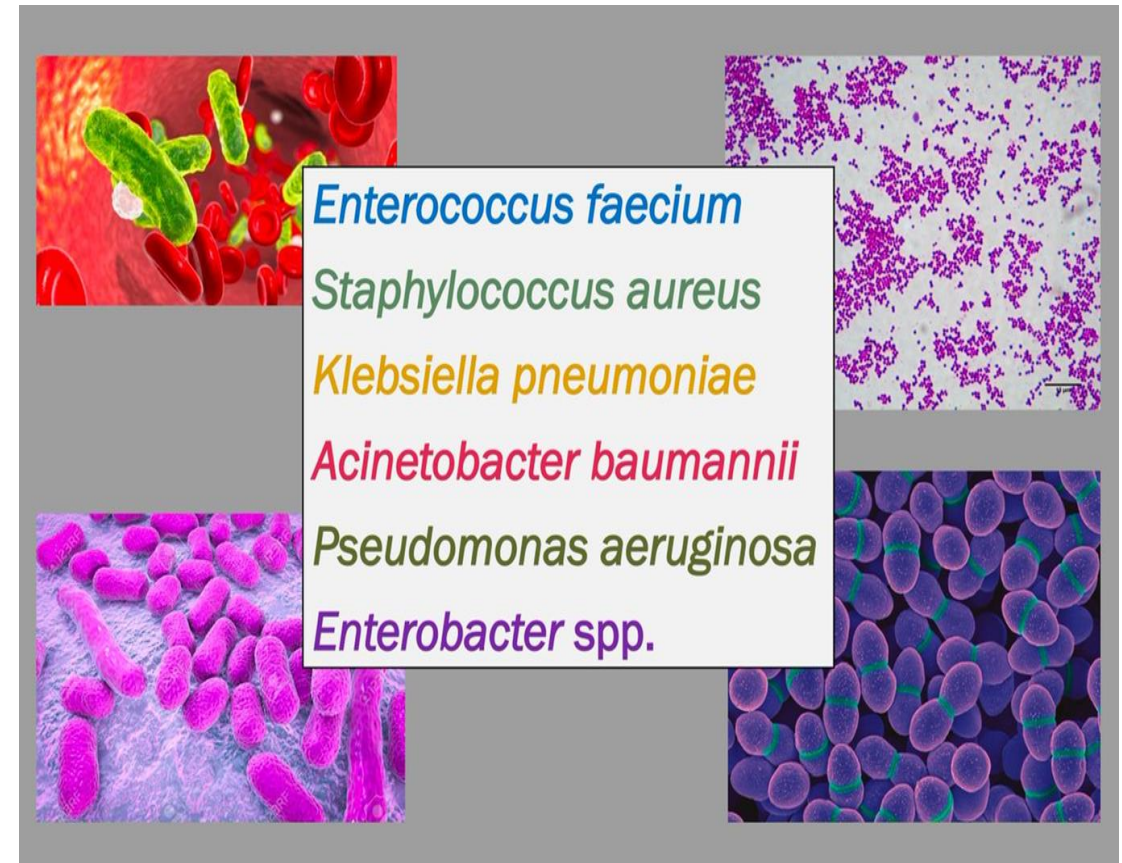
Deaths attributable to AMR every year compared to other major causes of death



THE MAGNITUDE OF THE THREAT

During the last decade, there was a **dramatic rise in AMR**, especially among **Gram-negative bacteria**. Of particular interest is the emergence of multiple resistant strains including **the ESKAPE organisms**.

The ESKAPE pathogens are the leading cause of **nosocomial infections** throughout the world.



THE PIPELINE IS DRY



THE REGIONAL CONTEXT

We are faced with **high rates of antimicrobial resistant organisms** in the Middle East.

Hotspot for infections diseases due to cultural and religious and economic factors.

Some countries have **economic stability and wealth**

- Travel
- Tourism

Other countries suffer from **political instability and conflicts**

- Weaken their health infrastructures
- Displaced millions of people
- Victims of violence and wars





CONSEQUENCES OF AMR

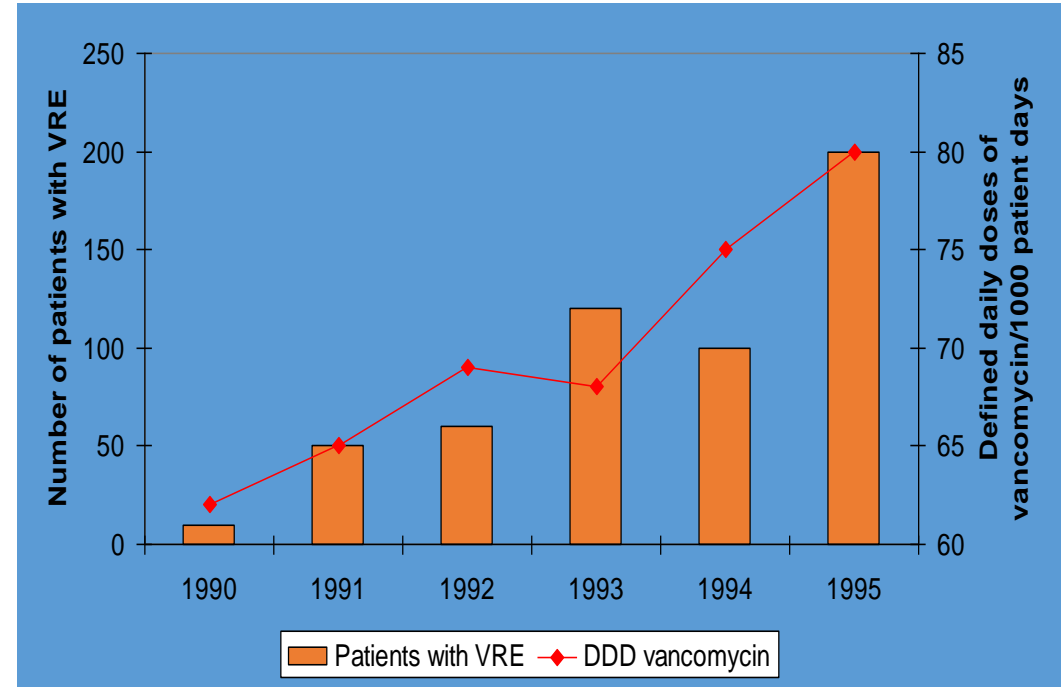
- High morbidity and mortality
- Significant direct and indirect costs
- Prolonged hospitalizations
 - due to antibiotic treatment failures
- Increasing incidence of *C. difficile*
- Toxicity





ANTIBIOTIC EXPOSURE LEADS TO RESISTANCE

- **Exposure to antibiotics** increases the risk of colonization or infection with a resistant organism.
- **Increased Risk**
 - **ESBL producing organisms and Cephalosporins**
 - **Carbapenem Resistant Enterobacterales and Carbapenems**



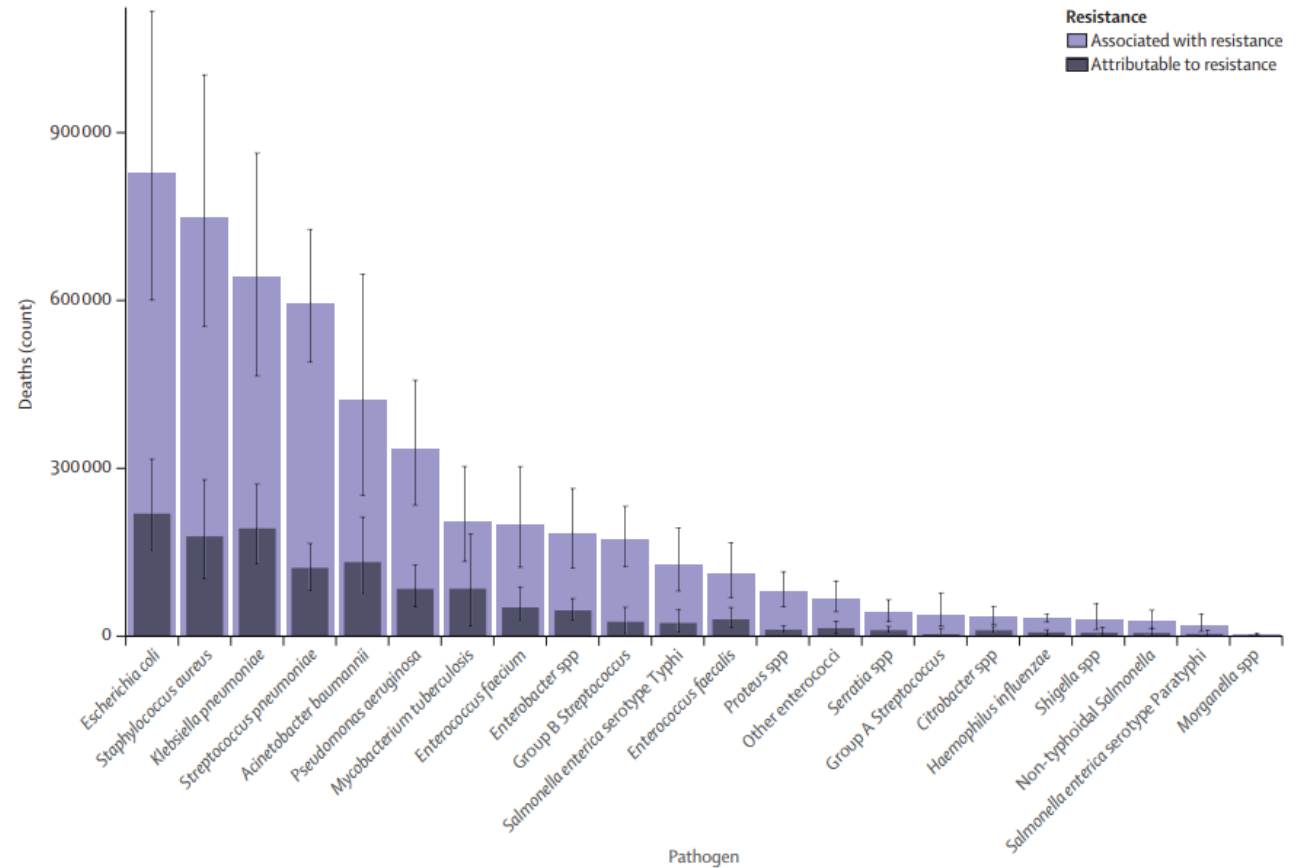
Increasing use of antibiotics increases the prevalence of resistant bacteria in hospitals.



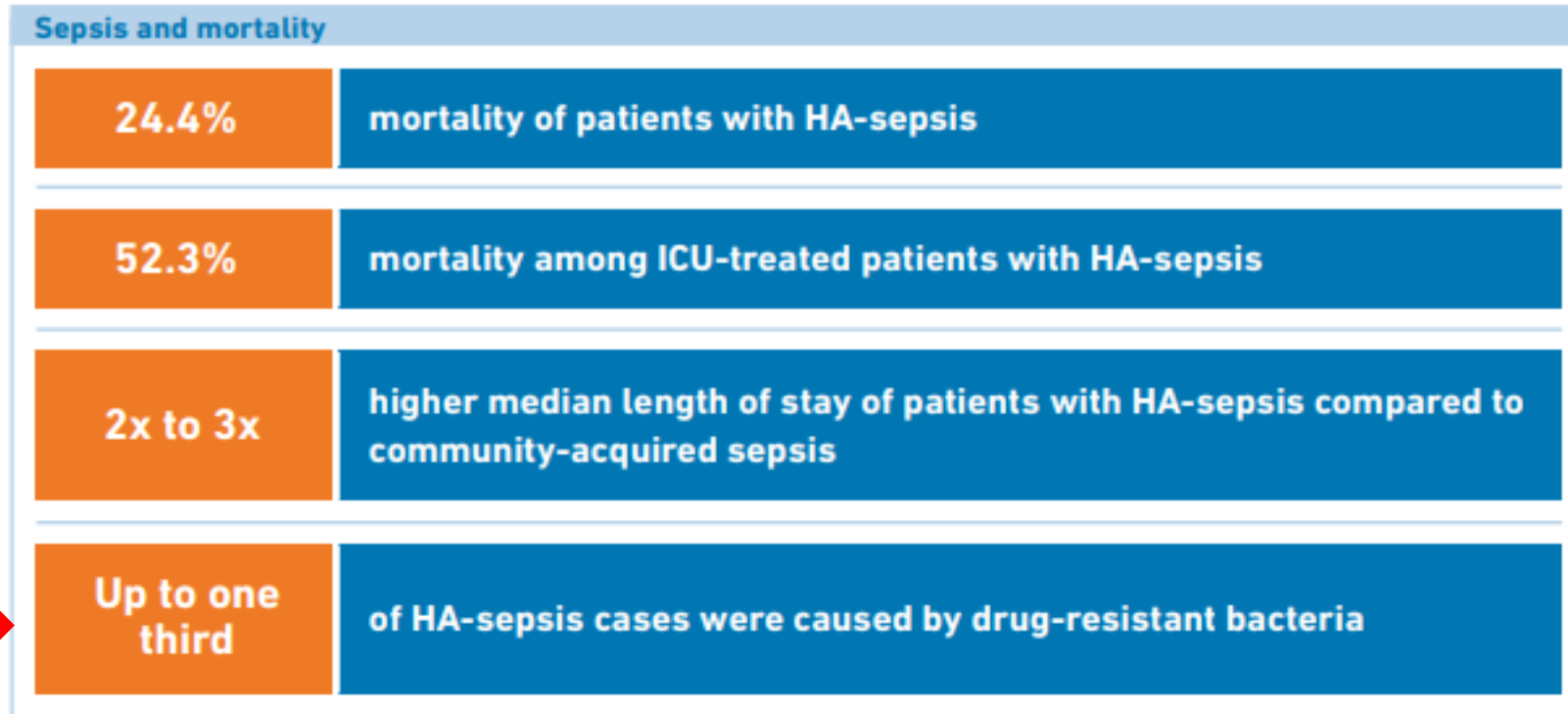
ANTIBIOTIC RESISTANCE INCREASES MORTALITY

In 2019, approximately 5 million deaths were associated with AMR, of which 1.27 million deaths were attributable to AMR.

The six leading pathogens for deaths associated with resistance were **Escherichia coli**, **Staphylococcus aureus**, **Klebsiella pneumoniae**, **Streptococcus pneumoniae**, **Acinetobacter baumannii**, and **Pseudomonas aeruginosa**



MORTALITY FROM SEPSIS/nosocomial



HA-sepsis: health care-associated sepsis. ICU: intensive care unit.

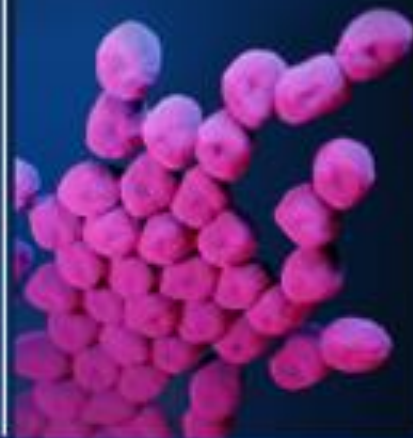
A systematic review published in 2020, which included an analysis of 51 countries (with 21 categorized as low- to middle-income) highlighted the burden of hospital acquired sepsis, particularly in the intensive care unit.

6 of the 18 most alarming **antibiotic resistance threats** cost the U.S. more than **\$4.6 billion annually**



Vancomycin-resistant
Enterococcus
(VRE)

Carbapenem-resistant
Acinetobacter
species
(CRAsp)



Methicillin-resistant
Staphylococcus
aureus (MRSA)



Carbapenem-resistant
Enterobacterales
(CRE)



Extended-spectrum
cephalosporin resistance
in *Enterobacterales*
suggestive of extended-
spectrum β -lactamase
(ESBL) production

Multidrug-resistant (MDR)
Pseudomonas
aeruginosa



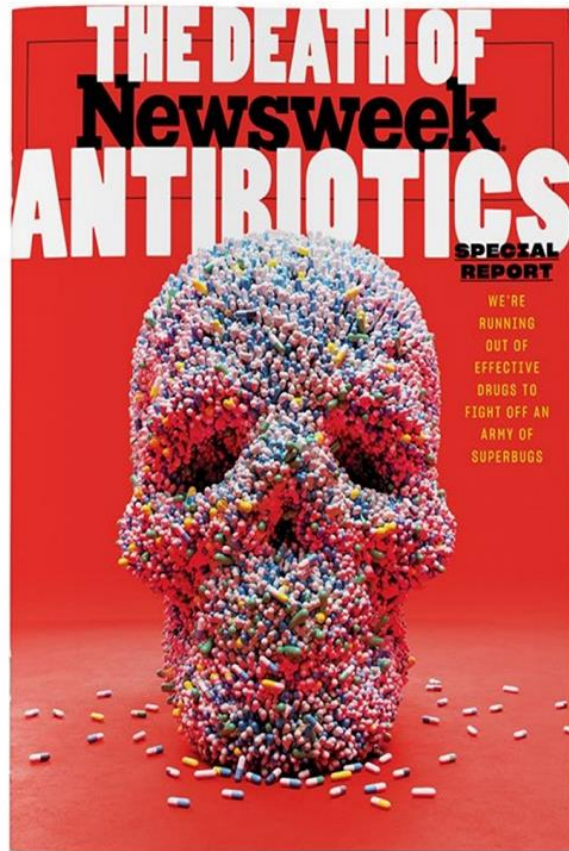
www.cdc.gov/DrugResistance



U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention



DEVELOPING A FRAMEWORK TO TACKLE AMR



THE NEED FOR A REASONABLE AND PRACTICAL APPROACH
ANTIMICROBIAL STEWARDSHIP



ANTIMICROBIAL STEWARDSHIP PROGRAM (ASP)

What is it?

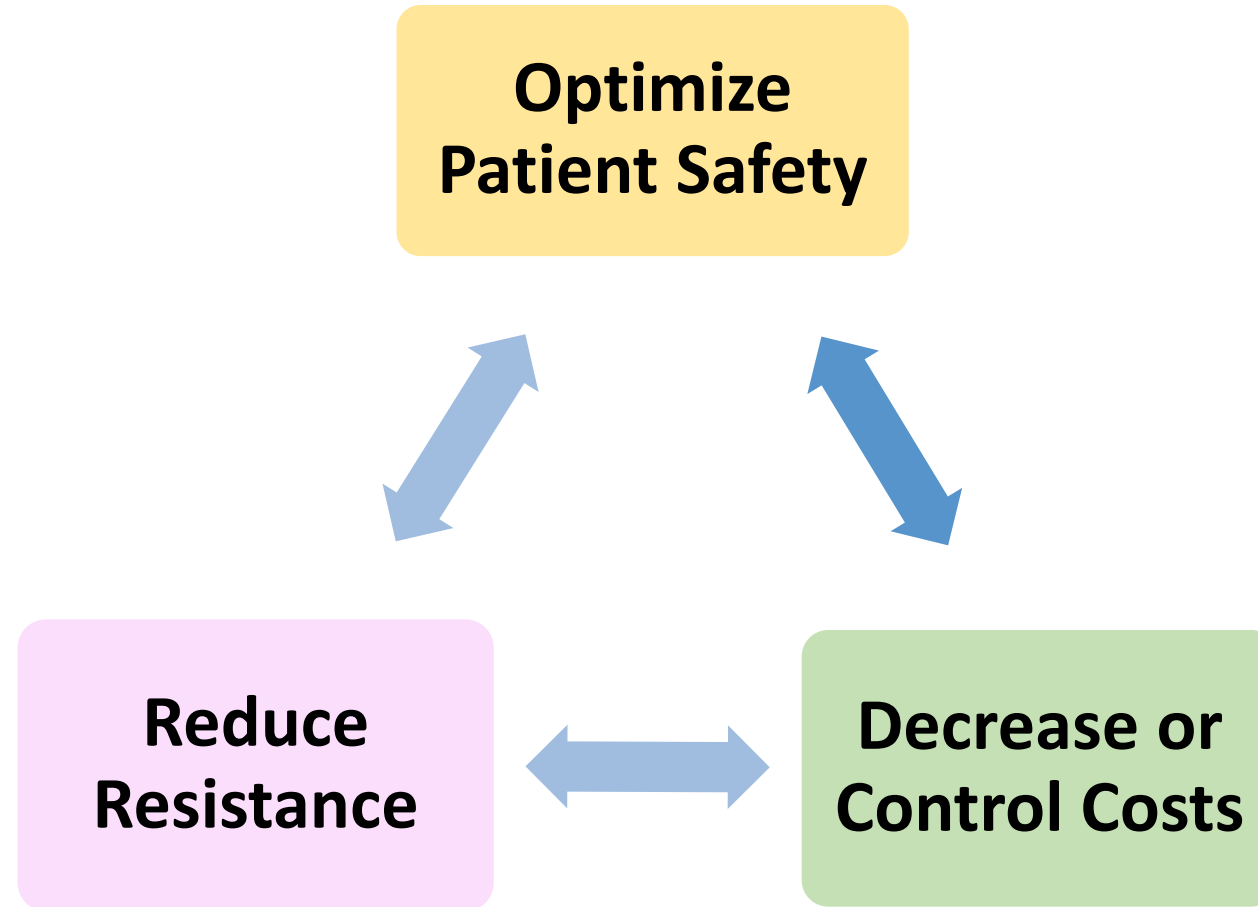
- A comprehensive system of health-care **providers, pathways, guidelines, order sets,** and **informatics** designed to **optimize** antimicrobial utilization

Mission

- To **improve patient outcomes** through **optimization** of antimicrobial therapy and support the education of health-care providers in appropriate antimicrobial use

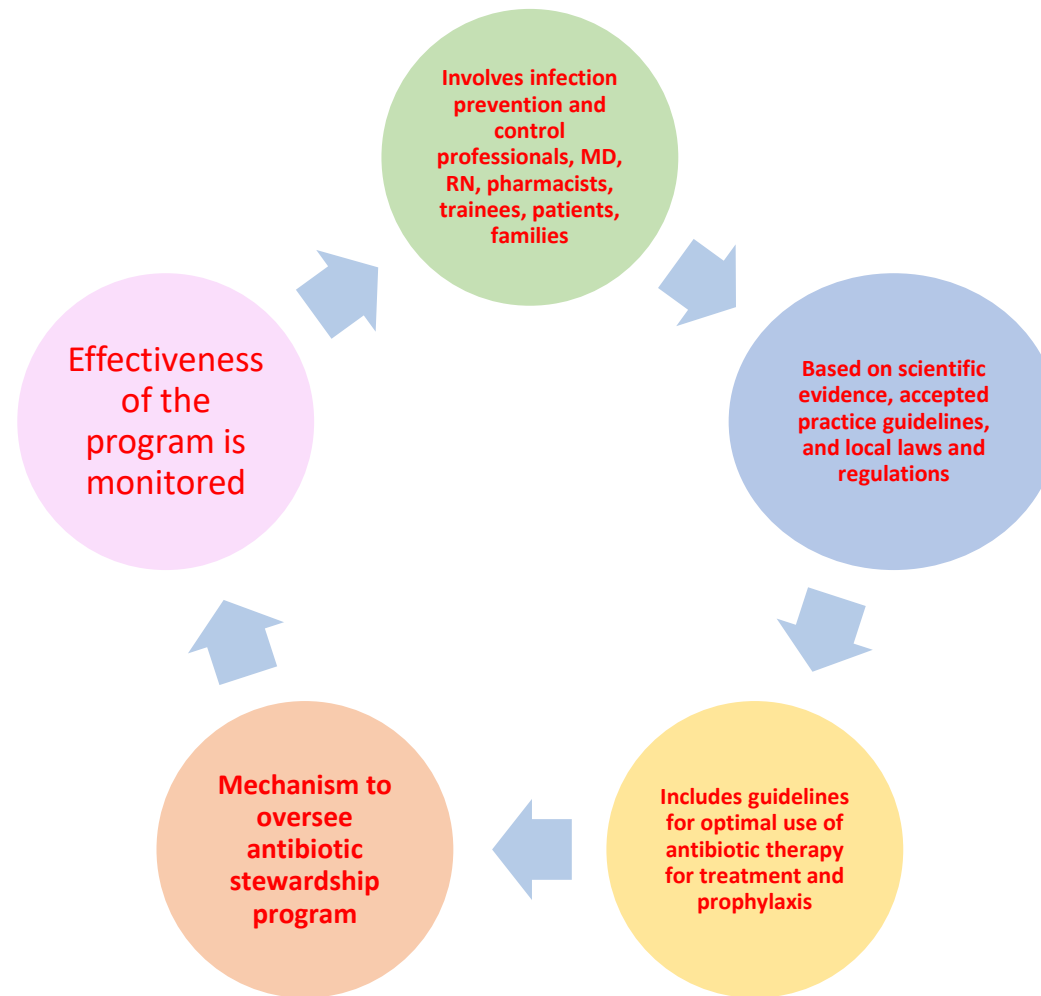


ANTIMICROBIAL STEWARDSHIP





ANTIMICROBIAL STEWARDSHIP



ANTIMICROBIAL STEWARDSHIP HOW?

Antimicrobial stewardship promotes the use of the:

- Right antibiotic
- Right dose
- Right route
- Right duration
- Right time



SMART APPROACH TO ANTIBIOTIC USE

START SMART

Do not start antibiotics unless there is clear evidence of infection.

Take a thorough allergy history.

Obtain cultures before antibiotics.

Initiate antibiotics within 1 hour of diagnosis in patients with severe-sepsis or life threatening infection.

Comply with local antibiotic guidelines.

Document clinical indication on the prescription and in clinical notes.

Include a review date or duration of therapy.

At 48 – 72 hours, review the clinical diagnosis & continued need for antibiotics.
Document a clear plan of action, either:

THEN FOCUS

Stop antibiotics if there is no evidence of infection.

Switch antibiotics from intravenous to oral.

Change antibiotics, ideally to a narrower spectrum (or broader if required) according to the microbiology results if applicable.

Referral for outpatient parenteral antibiotic therapy (OPAT).

Continue and document next review or stop date.



ASP AT THE AUBMC



ASP at AUBMC

LAUNCHING OF THE ANTIMICROBIAL STEWARDSHIP PROGRAM

- Efforts started in 2007
- Official launch of the program : June 2018
- ASP team works under the umbrella of the **ANTIMICROBIAL STEWARDSHIP COMMITTEE**
- Multidisciplinary team approach
 - Collaboration with infection control, infectious diseases adult and pediatric divisions, pharmacy, microbiology laboratory, quality, and various medical/surgical departments

SUMMARY OF ASP ACTIVITIES

- Operates at AUBMC, all nursing units
- Provides support 24/24 hours, 7/7 days
- Reports to the Chief of Staff

ANTIMICROBIAL STEWARDSHIP PROGRAM AT AUBMC

Infection
Control



Director of ASP



Co-Director of ASP

Pharmacy
and Nursing

Microbiology
Lab



Pharmacist

Quality

Medical
Doctors



Pediatric ASP

IT/DATA



PROCESS MEASURES OF THE ASP

Prospective Process Measures

Appropriateness of antibiotic drug regimen
Appropriate duration of therapy
Appropriate antibiotic drug choice post 48-72h of therapy initiation

Retrospective Process Measures

- **Defined Daily Dose (DDD) for antimicrobials**
- **Duration of Therapy (DOT) for carbapenems**
- Restricted antimicrobial usage rate in percentage
- Rate of adherence to guidelines, care bundles, policies
- Appropriateness of time of initiation of pre-operative antibiotic
- Impact Assessment (C diff rates, MDROs...)
- Antibiotic cost per patient-day



KEY ELEMENTS OF AMS HANDSHAKE STEWARDSHIP

- New, specific ASP model
- Involves prospective review of **antimicrobial** ordering
- Includes a compressed “second look” of relevant clinical and historical patient data
- Utilization of the EMR
- **In-person recommendations are then provided directly to the medical team.**





KEY ELEMENTS OF AMS

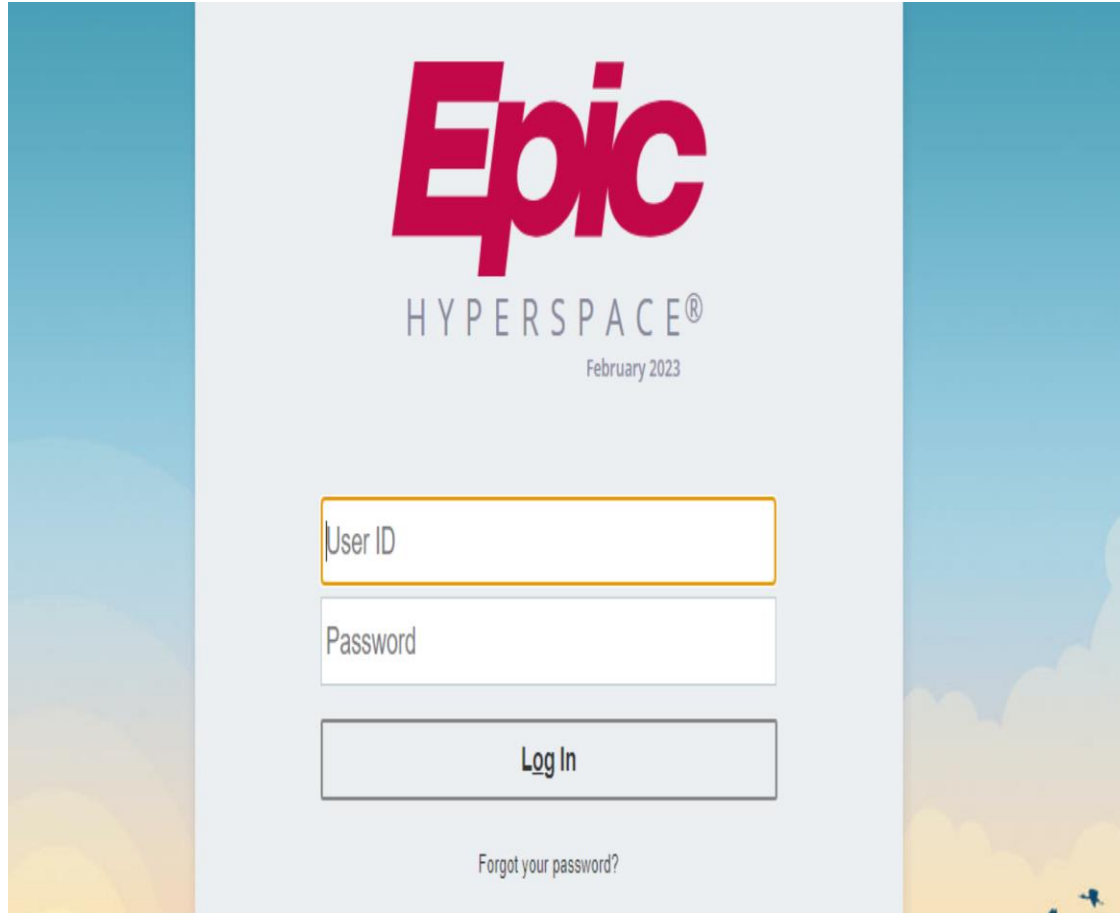
Prospective Audit and Feedback

Re-evaluation of the choice of antibiotics based on diagnostic results

Contact the provider with alternative recommendations if antimicrobial use is **unjustified** based on predetermined criteria.



KEY ELEMENTS OF AMS



ELECTRONIC MEDICAL RECORD

- Antibiotic Time-Outs
- require less direct ASP involvement
- Clinical Pathways and Clinical Decision Support
- Integrated in the EMR to offer alternative antibiotics
- Alerts for inappropriate use based on microbiological data
- **Alerts for toxicities**
- **DDIs**



TYPICAL ANTIMICROBIAL STEWARDSHIP INTERVENTIONS

Directly Related to Antimicrobial Stewardship

- **IV to PO Switch**
- **Therapy De-escalation:** empiric to targeted therapy, or discontinuation if cultures negative
- **Duration of Therapy:** completed targeted or empiric therapy (specific to indication)
- **ID Consult/Follow-up Recommended:** patient on an antimicrobial and needs consult/follow-up
- **Drug-Bug Mismatch:** Antibiotic resistant to culture, or susceptible in vitro but not for specific indication
- **Duplicate Coverage:** Unnecessary duplicate coverage of antimicrobials

Indirectly Related to Antimicrobial Stewardship

- **Dose change:** under-dosing (for specific indication, obese patients, site of infection), overdosing (renal/liver dose adjustment), includes antibiotics that need dose change/extended infusion use to target specific organism.
- **Frequency change:** Same as for dose change.
- **Therapeutic Monitoring:** Applies to aminoglycosides and vancomycin in specific, monitoring of levels, serum creatinine, and other laboratory parameters as applicable



ADDITIONAL STRATEGIES

ASP Rounds/Educational Sessions

- Therapeutic monitoring of antibiotics (core curriculum), pharmacists, ID fellows → Audience: medical residents (core curriculum)
- Introduction to antimicrobial stewardship → Audience: ID fellows
- Updates in antimicrobial stewardship → Audience: ID division, pharmacists

Order Sets

- Febrile Neutropenia
- Perioperative antibiotics
- Continuous/extended infusion of beta-lactams in the critical care areas
- Antibiotic lock therapy



OPTIMIZING ANTIBIOTIC USAGE

Carbapenem sparing strategies

Extended Infusion of beta lactams

Antibiotic Lock Therapy Order Set

Febrile Neutropenia Order Set

Peri-operative order sets including intra-operative re-dosing of antibiotics

COVID-19 protocols and order sets

KEY ELEMENTS OF AMS

ROLE OF INFECTION CONTROL

-Hand hygiene
-PPE
-Limited visitation

Local
epidemiologic
data

Point prevalence
testing

Surveillance
testing

Outbreak
investigations





ANTIMICROBIAL STEWARDSHIP INTERVENTION AT AUBMC

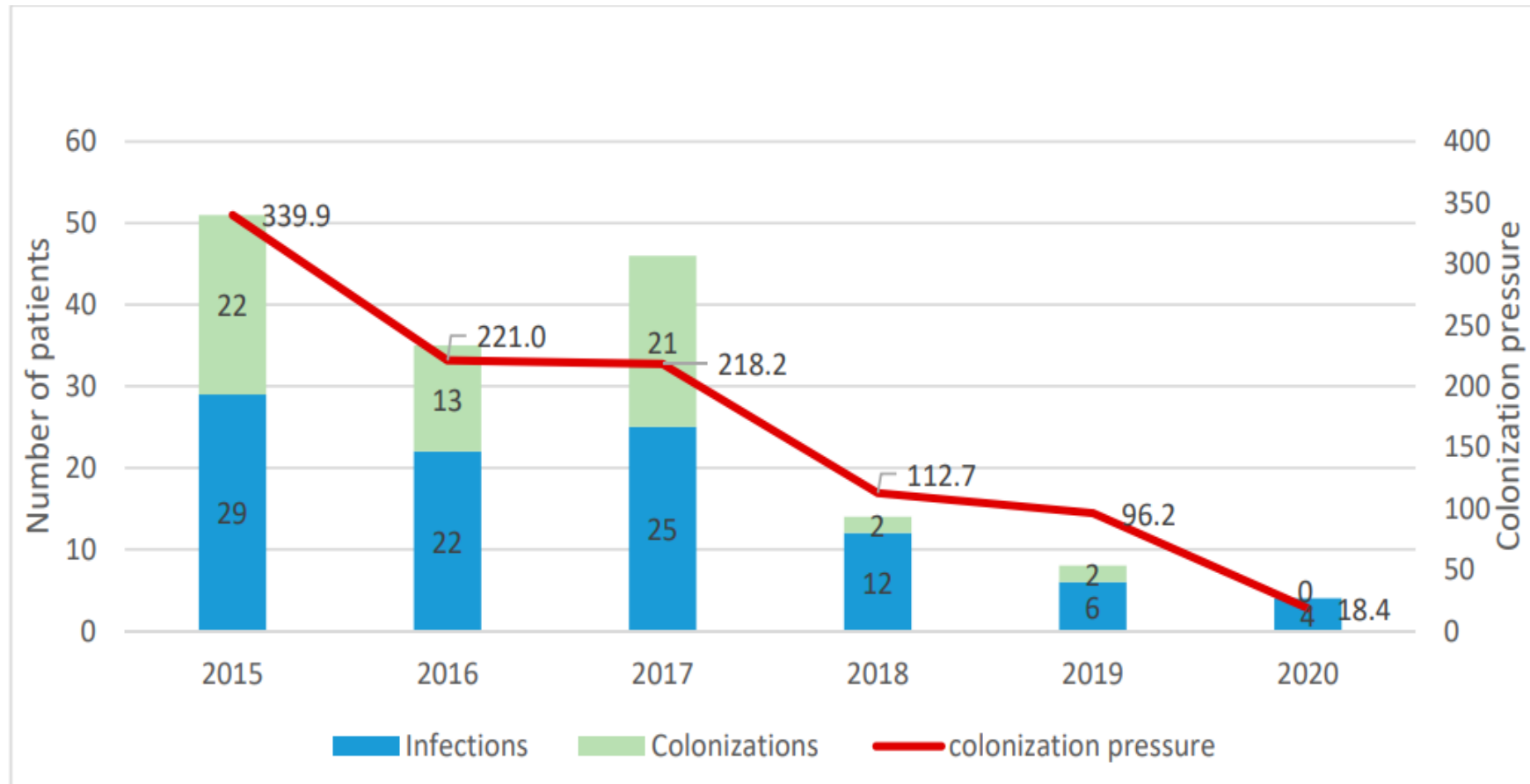
The Impact of Antimicrobial Stewardship and Infection Control Interventions on *Acinetobacter baumannii* Resistance Rates in the ICU of a Tertiary Care Center in Lebanon

Nesrine A. Rizk¹, Nada Zahreddine^{2,†}, Nisrine Haddad^{3,†}, Rihab Ahmadi², Audra Hannun³,
Souad Bou Harb¹, Sara F. Haddad¹, Rony M. Zeenny³ and Souha S. Kanj^{1,*}

Due to the emergence of carbapenem resistance, namely among *Acinetobacter baumannii*, the ASP team introduced, in April 2019, an initiative for carbapenem sparing with the aim of reducing carbapenem consumption and assessing the impact on resistance rates.



ASP and ICP combined intervention at AUBMC



CRAb Colonization Pressure in ICU over 7-year Period by Year



OPTIMIZING ANTIBIOTIC USAGE

Carbapenem sparing strategies

Extended Infusion of beta lactams

Antibiotic Lock Therapy Order Set

Febrile Neutropenia Order Set

Peri-operative order sets including intra-operative re-dosing of antibiotics

COVID-19 protocols and order sets



Extended Infusion Order Set in the ICU

		Identification label	
Extended Infusions of Antibiotics for Adults in Critical Care Units			
Last Name: _____ Unit: _____ First and Middle Name: _____ Weight: _____ Height: _____ Patient Number: _____ Expanded Precautions: <input type="checkbox"/> None <input type="checkbox"/> Airborne Date of Birth: _____ Age: _____ <input type="checkbox"/> Droplet <input type="checkbox"/> Contact <input type="checkbox"/> Contact Plus Gender: <input type="checkbox"/> Male <input type="checkbox"/> Female Other Precautions: _____ Admission Date: _____ Allergy <input type="checkbox"/> No <input type="checkbox"/> Yes (specify reaction): _____ Admitting Physician: _____			
The following abbreviations may not be used to document patient care: U IU QD QOD .X mg X.0 mg MS MSO ₄ MgSO ₄ CC µg mcg <input checked="" type="checkbox"/> Check the Applicable Order		Nurse's Name and Signature _____ Time Notes _____	
<input checked="" type="checkbox"/> Consult Infectious Diseases			
Kindly pick the desired antibiotic and dose based on the patient's creatinine clearance (CrCl).			
<input type="checkbox"/> Cefepime – Continuous Infusion Loading dose (LD): <input type="checkbox"/> Omit LD of Cefepime if a dose was given within the past 8 hours <input type="checkbox"/> CrCl greater than or equal to 10 mL/min: 15 mg/kg IV in 50mL D5W (if total dose ≤1g) or 100mL D5W (if total dose >1g) bolus ____ over 30 min Maintenance dose: Begin immediately after LD <input type="checkbox"/> CrCl greater than or equal to 60 mL/min: 2 gm IV in 100mL D5W over 8 hours every 8 hours <input type="checkbox"/> CrCl between 30 and 59 mL/min: 2 gm IV in 100mL D5W over 12 hours every 12 hours <input type="checkbox"/> CrCl between 10 and 29 mL/min: 2 gm IV in 100mL D5W over 24 hours every 24 hours <input type="checkbox"/> CrCl less than 10 mL/min or on dialysis (HD, PD, or CVVHD): Do not use this order sheet and use adjusted dose for intermittent infusion		<input type="checkbox"/> Piperacillin/Tazobactam – Extended Infusion Loading dose (LD): <input type="checkbox"/> Omit LD of Piperacillin/Tazobactam if a dose was given within the past 6 hours <input type="checkbox"/> Any CrCl level, on HD, or on PD: 4.5 gm IV in 50mL NSS over 30 min Maintenance dose: <input type="checkbox"/> CrCl greater than or equal to 40 mL/min: Start maintenance dose 4 hours after LD. Give 4.5 gm in 50mL NSS over 4 hours every 6 hours <input type="checkbox"/> CrCl between 20 and 39 mL/min: Start maintenance dose 4 hours after LD. Give 3.375 gm in 50mL NSS over 4 hours every 6 hours <input type="checkbox"/> CrCl less than 20 mL/min: Start maintenance dose 8 hours after LD. Give 3.375 gm in 50mL NSS over 4 hours every 12 hours <input type="checkbox"/> On HD or PD: Start maintenance dose 8 hours after LD. Give 3.375 gm in 50mL NSS over 4 hours every 12 hours. Dose after dialysis. <input type="checkbox"/> On CVVHD: Specific dosing regimen tailored to patient's condition	
<input type="checkbox"/> Ceftazidime – Continuous Infusion Loading dose (LD): <input type="checkbox"/> Omit LD of Ceftazidime if a dose was given within the past 8 hours <input type="checkbox"/> CrCl greater than or equal to 10 mL/min: 15 mg/kg IV in 50mL D5W (if total dose ≤1g) or 100mL D5W (if total dose >1g) bolus ____ over 30 min Maintenance dose: Begin immediately after LD <input type="checkbox"/> CrCl greater than or equal to 50 mL/min: 2 gm IV in 100mL D5W over 8 hours every 8 hours <input type="checkbox"/> CrCl between 30 and 49 mL/min: 2 gm IV in 100mL D5W over 12 hours every 12 hours <input type="checkbox"/> CrCl between 10 and 29 mL/min: 2 gm IV in 100mL D5W over 24 hours every 24 hours <input type="checkbox"/> CrCl less than 10 mL/min or on dialysis (HD, PD, or CVVHD): Do not use this order sheet and use adjusted dose for intermittent infusion		<input type="checkbox"/> Meropenem – Extended Infusion Loading dose (LD): <input type="checkbox"/> Omit LD of Meropenem if a dose was given within the past 8 hours <input type="checkbox"/> Any CrCl level, on HD, or on CVVHD: 1 gm IV in 100mL NSS over 30 min Maintenance dose: <input type="checkbox"/> CrCl greater than or equal to 50 mL/min with Meningitis or Cystic Fibrosis: Start maintenance dose 8 hours after LD. Give 2 gm IV in 100mL NSS over 4 hours every 8 hours <input type="checkbox"/> CrCl greater than or equal to 50 mL/min: Start maintenance dose 8 hours after LD. Give 1 gm IV in 100mL NSS over 4 hours every 8 hours <input type="checkbox"/> CrCl between 30 and 49 mL/min: Start maintenance dose 8 hours after LD. Give 1 gm IV in 100mL NSS over 4 hours every 8 hours <input type="checkbox"/> CrCl between 10 and 29 mL/min: Start maintenance dose 12 hours after LD. Give 1 gm IV in 100mL NSS over 4 hours every 12 hours <input type="checkbox"/> CrCl less than 10 mL/min or on HD: Start maintenance dose 24 hours after LD. Give 500 mg in 50mL NSS IV over 4 hours every 24 hours. Dose after dialysis <input type="checkbox"/> On CVVHD: Start maintenance dose 8 hours after LD. Give 1 gm IV in 100mL NSS over 4 hours every 8 hours	
Administration Instructions <input checked="" type="checkbox"/> Contact the pharmacist to help resolve medication scheduling and compatibility issues.			

Extended infusion of beta-lactam antibiotics: optimizing therapy in critically-ill patients in the era of antimicrobial resistance

Nesrine A. Rizk*, Zeina A. Kanafani*, Hussam Z. Tabaja and Souha S. Kanj

Division of Infectious Diseases, Department of Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon

Prolonged infusion is an alternative dosing approach that promises to provide higher fT > MIC necessary for the bactericidal effect of beta-lactam agents. EI/CI is favored in the ICU where the PK/PD of antibiotics are altered and the MICs against isolated pathogens are higher.



ACTIVELY REDUCE ANTIBIOTIC TREATMENT

SHORT-COURSE THERAPY FOR COMMON INFECTIONS

SHORTER IS BETTER LESS IS MORE

Shorter Is Better

Diagnosis	Short (d)	Long (d)	Result	#RCT
CAP	3-5	5-14	Equal	14
Atypical CAP	1	3	Equal	1
Possible PNA in ICU	3	14-21	Equal	1*
VAP	8	15	Equal	2
cUTI/Pyelonephritis	5 or 7	10 or 14	Equal	9**
Intra-abd Infection	4	10	Equal	2
Complex Appendicitis	1-2	5-6	Equal	2
GNB Bacteremia	7	14	Equal	3 [†]
Cellulitis/Wound/Abscess	5-6	10	Equal	4 [‡]
Osteomyelitis	42	84	Equal	2
Osteo Removed Implant	28	42	Equal	1
Debrided Diabetic Osteo	10-21	42-90	Equal	2 ^Φ
Septic Arthritis	14	28	Equal	1
Bacterial Meningitis (peds)	5	10	Equal	1
AECB & Sinusitis	≤5	≥7	Equal	>25
Variceal Bleeding	3	7	Equal	1
Neutropenic Fever	AFx72h/3 d	+ANC>500/9 d	Equal	2
Post Op Prophylaxis	0-1	1-5	Equal	55 ^Ψ
Erythema Migrans (Lyme)	7	14	Equal	1
<i>P. vivax</i> Malaria	7	14	Equal	1

Total: 19 Conditions

>125 RCTs

*Infiltrate on CXR but low CPIS score (≤6), both ventilated and non ventilated, likely CAP, HAP, and VAP combined;
 **2 RCT included males, the smaller one found lower 10-18 d f/up cure in males with 7 days of therapy but no difference at longer follow-up, larger exclusive male study found no diff in cure; [†]GNB bacteremia also in UTI/cIAI RCTs; [‡]3 RCTs equal, 1 (low dose oral flucox) [↑]relapses 2° endpoint; ^Φall patients debrided, in 1 study total bone resection (clean margins); ^ΨIncludes meta-analysis of 52 RCTs; refs at <https://www.bradspellberg.com/shorter-is-better>

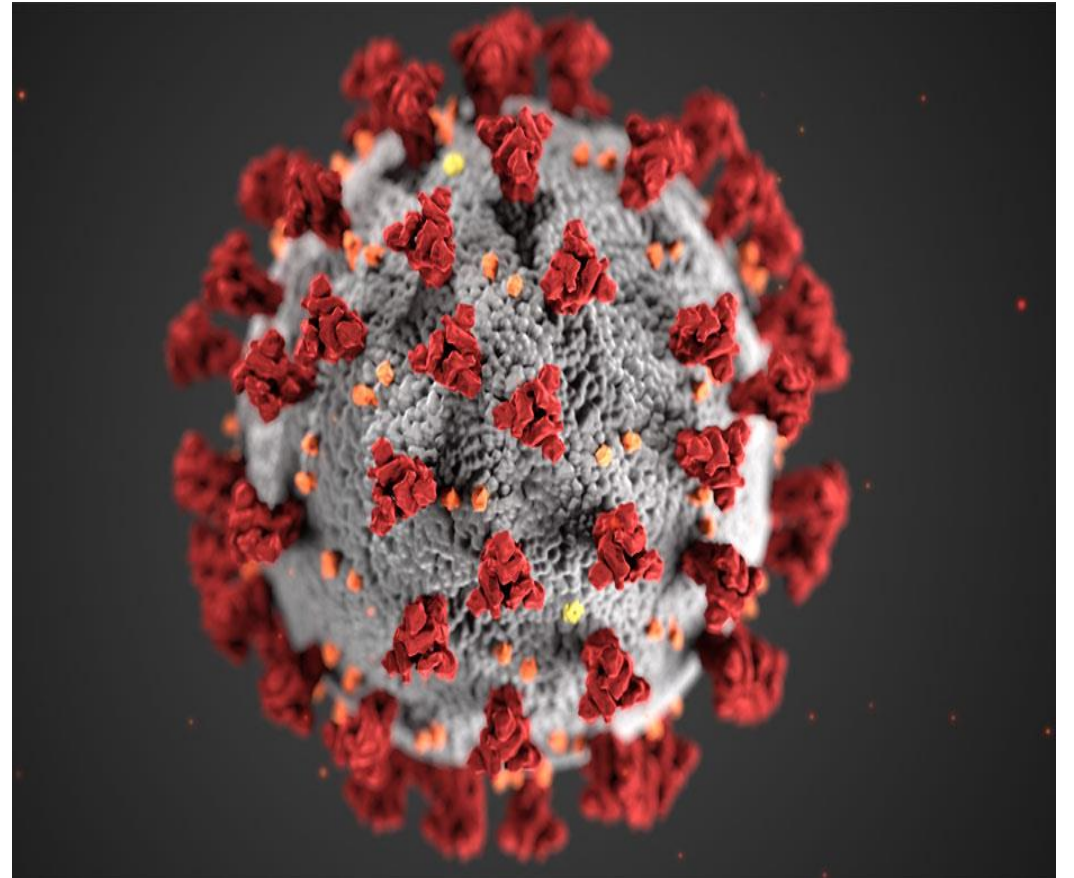


ANTIMICROBIAL STEWARDSHIP STRATEGIES

COMPONENT	IDSA/ SHEA Guideline Strength of Evidence	Implemented at AUBMC
Formulary restriction with audit and feedback	AI	✓
Education	AIII, BII	✓
Guidelines, pathways	AI, AIII	✓
Antimicrobial cycling	CII	No
Antimicrobial order form	BII	✓
Combination therapy	CII	Not routine
De-escalation	AII	✓
Dose optimization	AII	✓
IV to PO Conversion	AII	✓



**COVID-19
CREATED A PERFECT
STORM FOR RESISTANT
INFECTIONS IN
HEALTHCARE SETTINGS**



AMR POST COVID-19

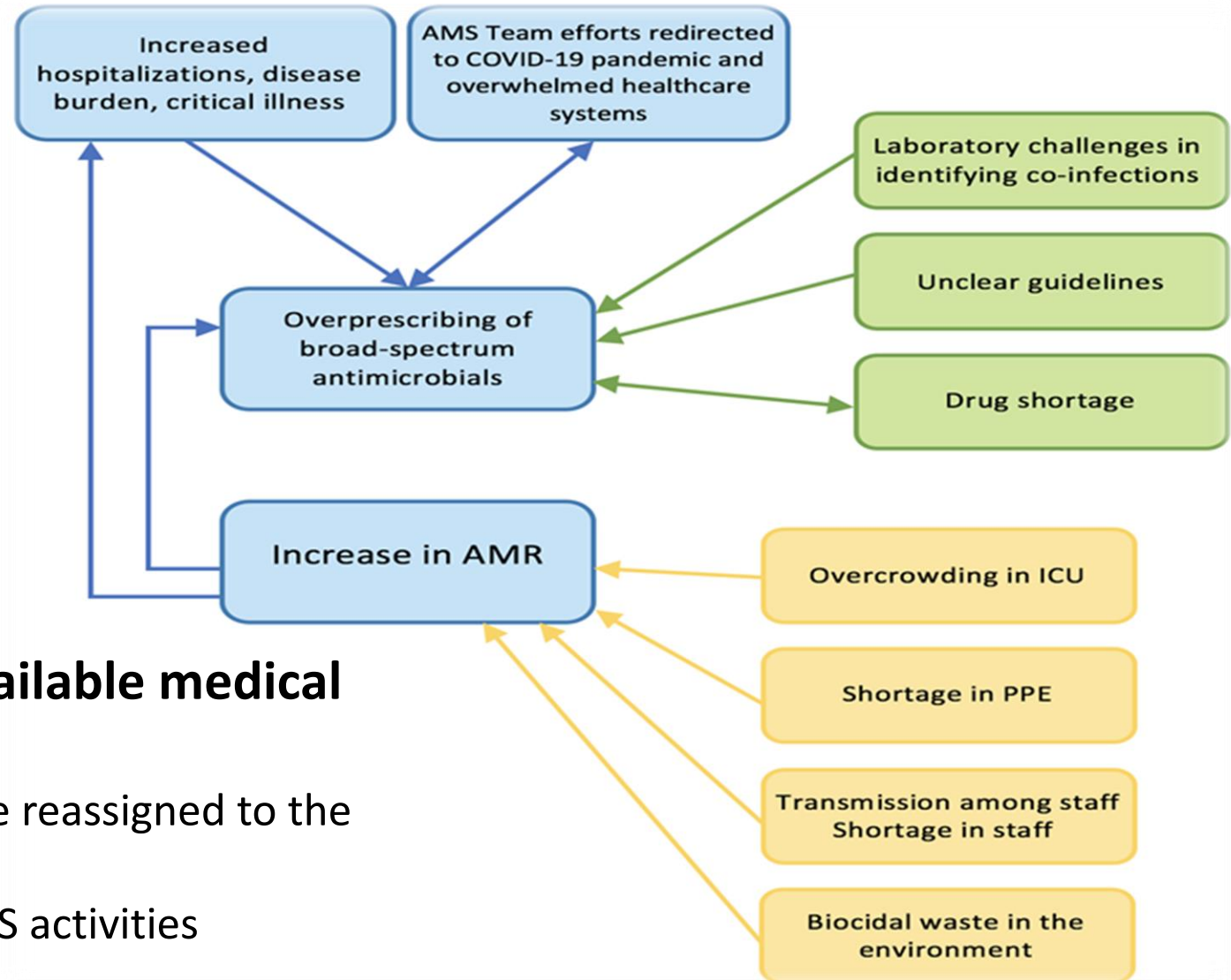


THE COVID-19 RESULTED IN AN UNPRECEDENTED SURGE IN HOSPITAL ADMISSIONS OVERWHELMING HEALTHCARE SYSTEMS ACROSS THE WORLD ESPECIALLY AMONG CRITICALLY ILL



FACTORS CONTRIBUTING TO THE INCREASE IN AMR DURING THE COVID-19 PANDEMIC

- **Associated repurposing of all available medical resources to the response**
 - ID physicians and pharmacists were reassigned to the COVID frontline
 - indirectly leading to decreased AMS activities





SEVERAL CHALLENGES

STAFFING ISSUES

- Our approach is based on a multidisciplinary approach
 - ID Pharmacist role
 - Shortage of clinical pharmacists
 - Nursing team support
 - EPIC team: reports and integrating order sets etc.



SEVERAL OBSTACLES

FINACIAL ISSUES

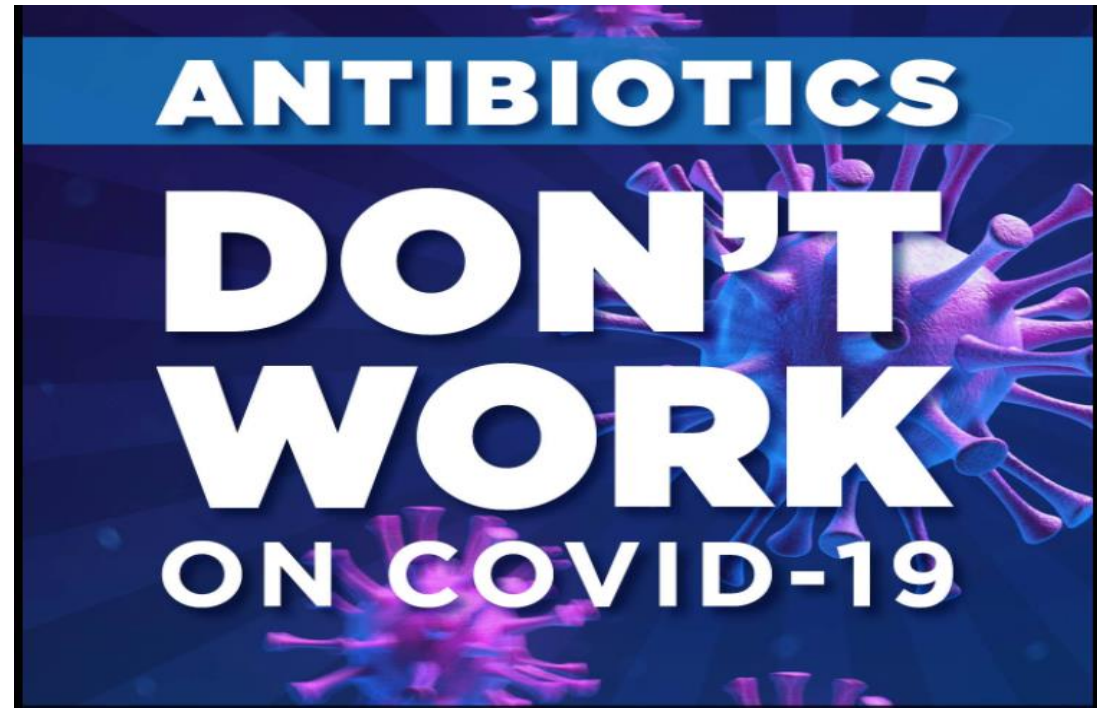
- Medication and antibiotic shortages
- Supplies/equipment
- Performance

WORLD POST COVID-19

- Rise in AMR worldwide and especially in LMICs
- Lingering pandemic, low vaccination rates
- Healthcare restructure ??



COVID-19: IMPACT ON ANTIMICROBIAL CONSUMPTION





ANTIMICROBIAL STEWARDSHIP INTERVENTION AT AUBMC

Evaluate the impact of Antimicrobial Stewardship Program (ASP) interventions on antibiotic consumption and trends of Antimicrobial Resistance (AMR) at a tertiary care center in Beirut before and after the COVID-19 pandemic.



ANTIMICROBIAL STEWARDSHIP INTERVENTION AT AUBMC

ASP team recommendations considered as interventions.

ASP interventions compiled from **January 2019 to December 2021**.

Collected data on antimicrobial consumption, measured as **defined daily dose (DDD)** per 100 patient days, for all anti-infectives and restricted anti-infectives quarterly.

Obtained data on **Multidrug-Resistant Organism (MDRO)** rated from the clinical microbiology laboratory from 2019 to 2022.



REASONS TO ENDORSE STEWARDSHIP

PROPER ANTIBIOTIC USE WITHIN STEWARDSHIP PROGRAMS CAN ENHANCE PATIENT OUTCOMES AND PLAY A ROLE IN FIGHTING INFECTIONS WHILE ALSO REDUCING THE DANGERS OF ANTIMICROBIAL RESISTANCE.





IMPLEMENTATION OF STEWARDSHIP

- **IMPLEMENT ANTIMICROBIAL STEWARDSHIP MEASURES**
- **INCLUDE PATIENT EDUCATION**
- **PROVIDE TRAINING FOR HEALTHCARE PROFESSIONALS**
- **CONDUCT REGULAR AUDITS AND FEEDBACK OF PRESCRIPTION PRACTICES**
- **ENSURE AVAILABILITY OF EFFECTIVE ANTIBIOTICS FOR SEPSIS TREATMENT IN THE LONG-TERM**
- **MINIMIZE UNNECESSARY ANTIBIOTIC USE**



**KEEP
CALM
AND DO**

**ANTIMICROBIAL
STEWARDSHIP**



GRATEFUL SUPPORT

ID DIVISION

CHIEF

FELLOWS

HOUSESTAFF

PHARMACY

NURSE

ICP

MICRO LAB

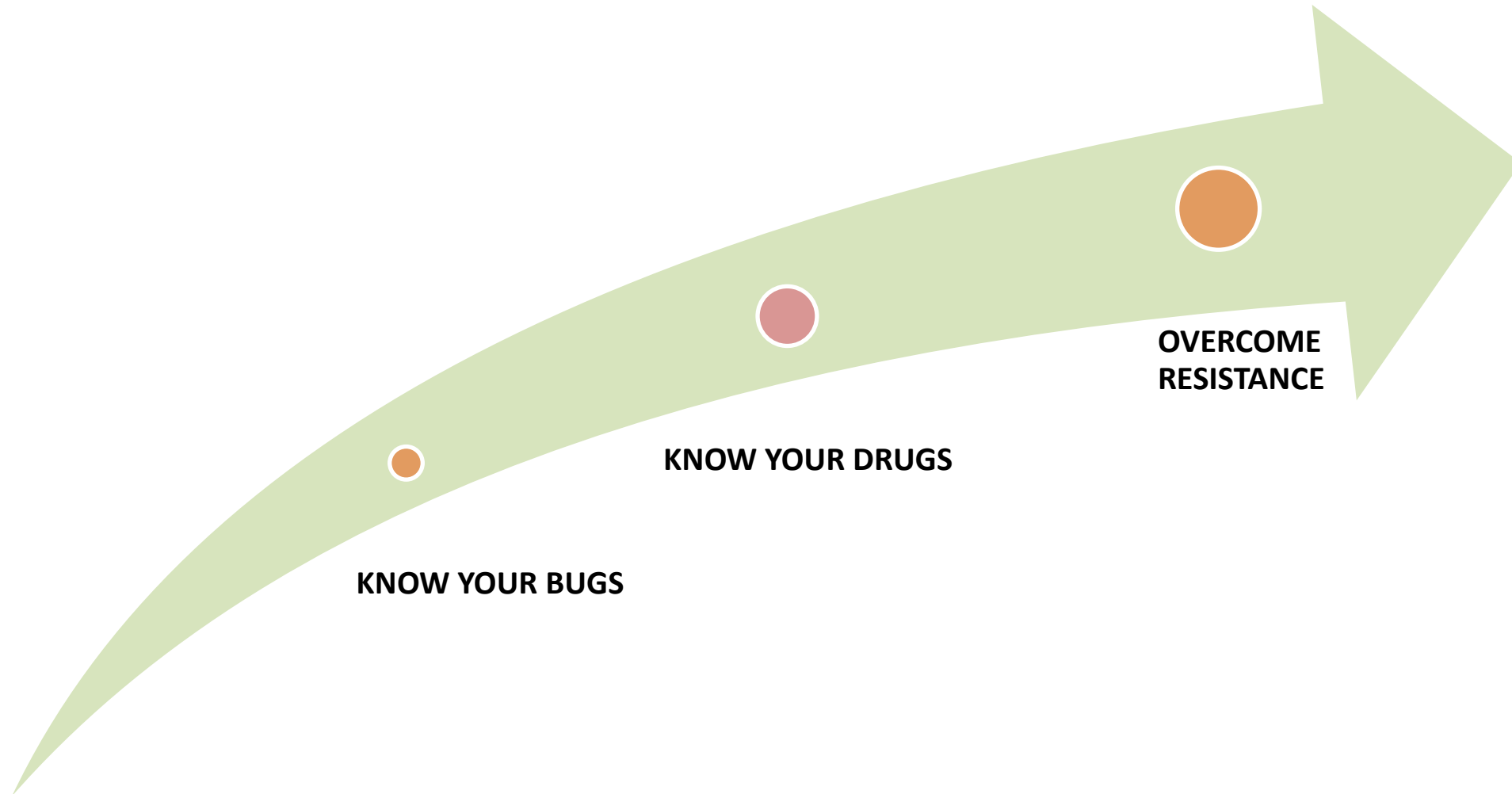


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ANTIMICROBIAL STEWARDSHIP



THANK YOU



ANTIBIOTIC STEWARDSHIP IN YOUR FACILITY WILL



DECREASE

- ANTIBIOTIC RESISTANCE
- C. DIFFICILE INFECTIONS
- COSTS

INCREASE

- GOOD PATIENT OUTCOMES

