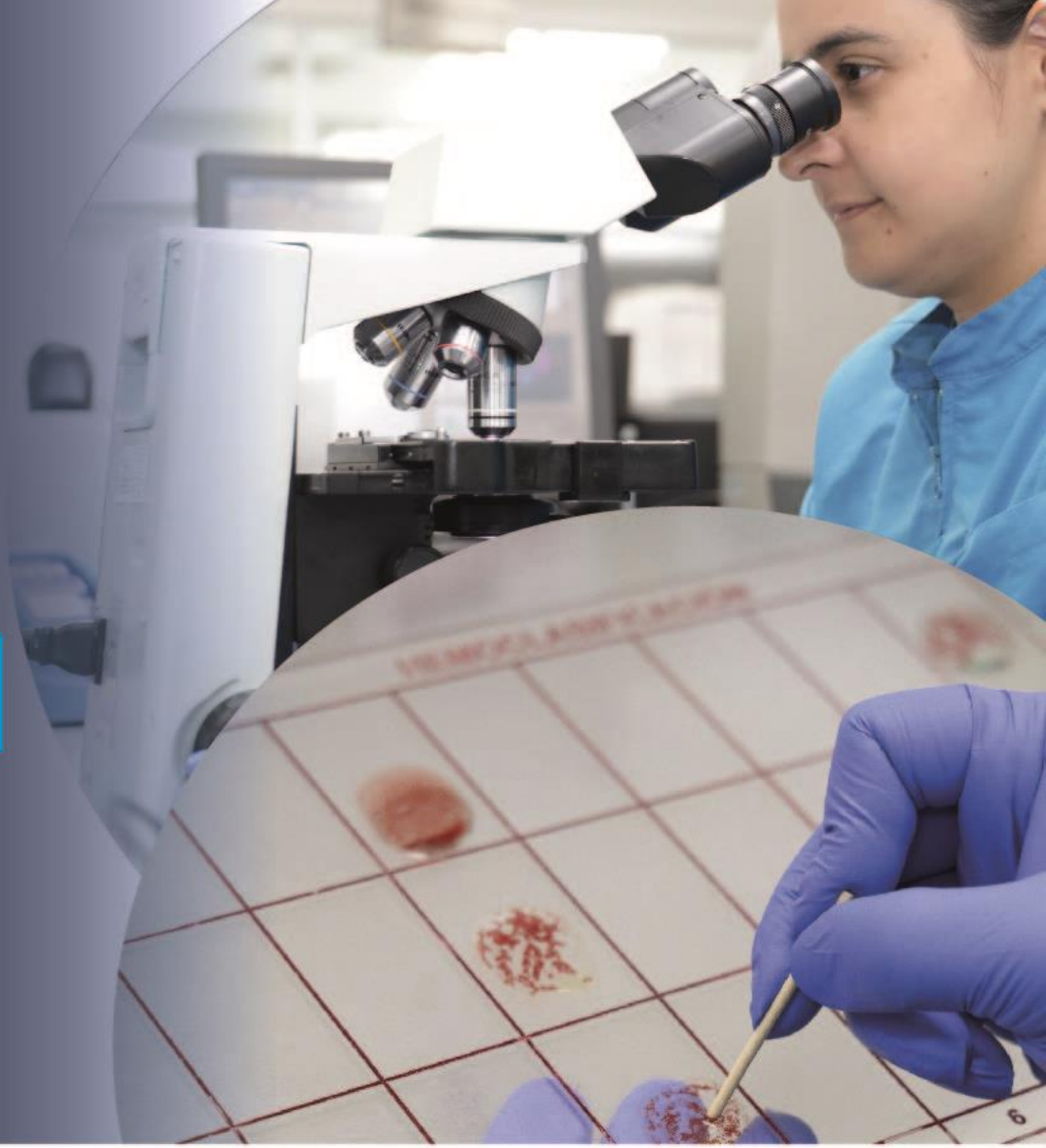
I Simposio en Optimización del uso de Antimicrobianos

Experiencias en PROA



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Consumo racional de antimicrobianos en pacientes hematológicos, experiencia en PROA

Pablo A. Moncada, M.D
Medicina interna, infectología

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1ER PUESTO EN COLOMBIA 2016 merco SALUD

Consumo racional de antimicrobianos en pacientes hematológicos, experiencia en PROA

Pablo A. Moncada V.
Medicina Interna Infectología
Fundación Valle de Lili
Cali, Colombia

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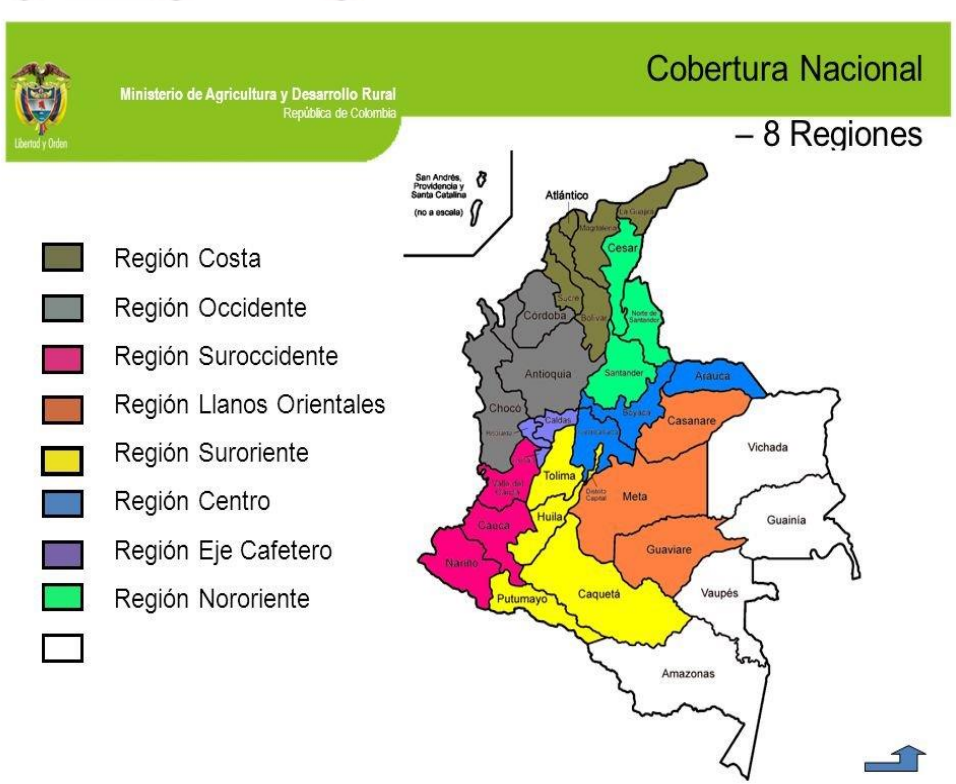
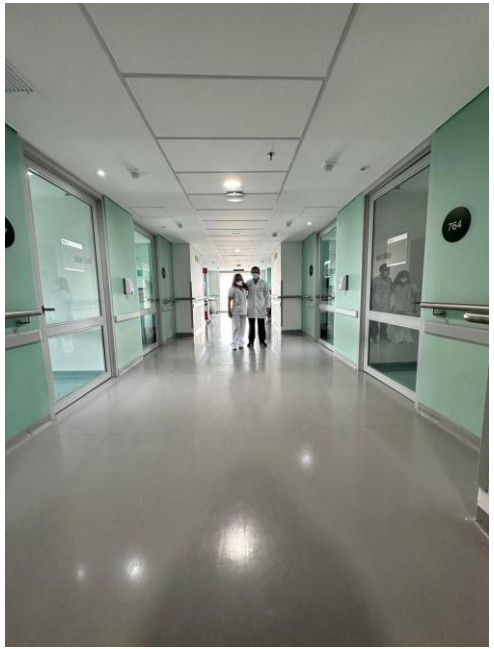
Conflicto de intereses

- Recibido honorarios relacionados
  - Biomerieux
- Recibido honorarios no relacionados.
  - MSD
  - Knight

Fundación Valle de Lili



- Centro medico de alta complejidad
  - Suroccidente Colombiano
    - 550
    - 2 sedes
  - Hematológico
    - TMO
      - 14 camas
    - UCI
      - 20 camas
    - Hospitalización
      - 100 camas



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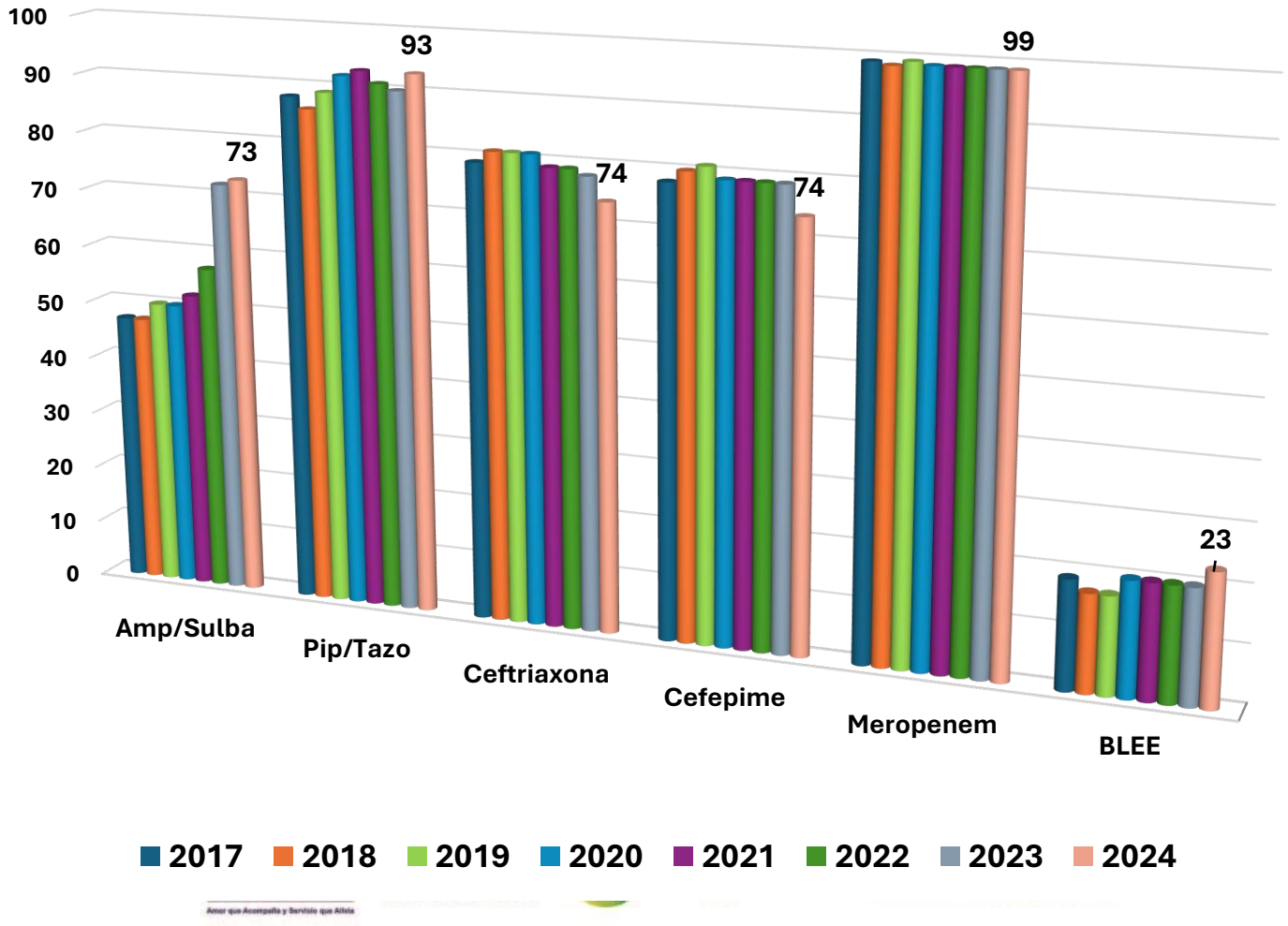
Infecciones urinarias:

- Presencia de uropatógenos (bacterias, hongos, virus) afectando cualquier parte del tracto urinario.
  - Es uno de los diagnósticos infecciosos más frecuentes en la atención sanitaria.
  - Más comunes en mujeres menores de 70 años; la incidencia en hombres y mujeres se iguala más después de esta edad.
  - **Las ITU son frecuentemente mal diagnosticadas,**
    - **Aumentando el uso de antimicrobianos en todos los entornos de atención.**

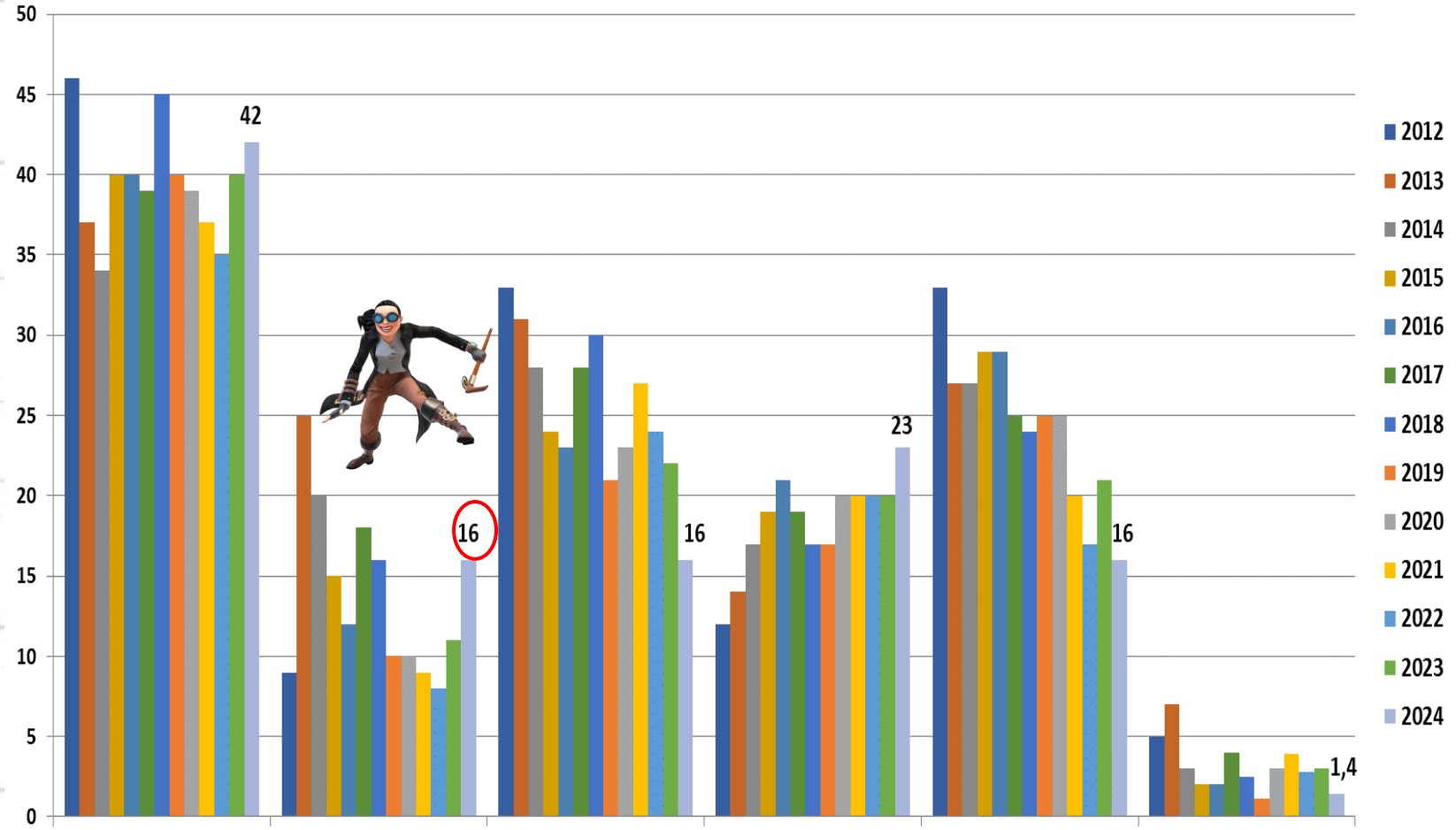
Drekonja, D. M. (2024). Urinary Tract Infection in Male Patients. *Infectious Disease Clinics of North America*, *38*(2), 311–323. doi: 10.1016/j.idc.2024.03.009

Porcentaje de Sensibilidad β Lactámicos

Escherichia coli 2017-2024



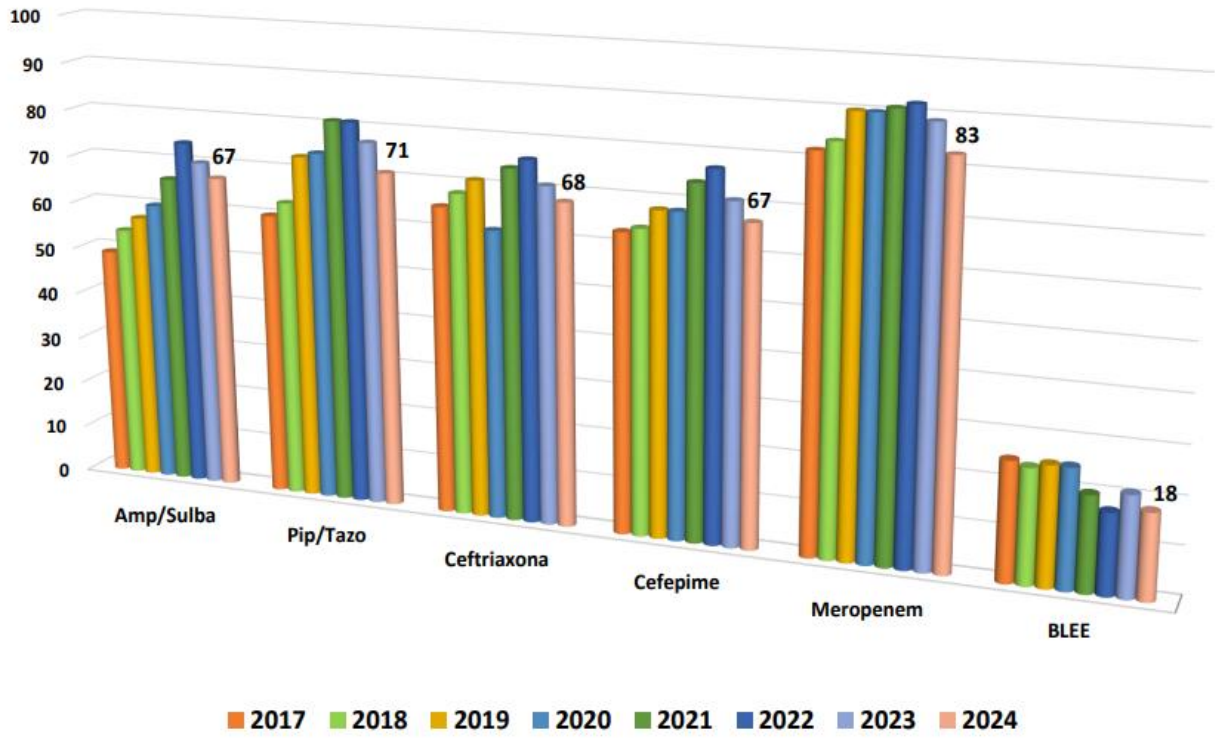
Microorganismos Marcadores de Resistencia 2012 - 2024



Porcentaje de Sensibilidad β Lactámicos

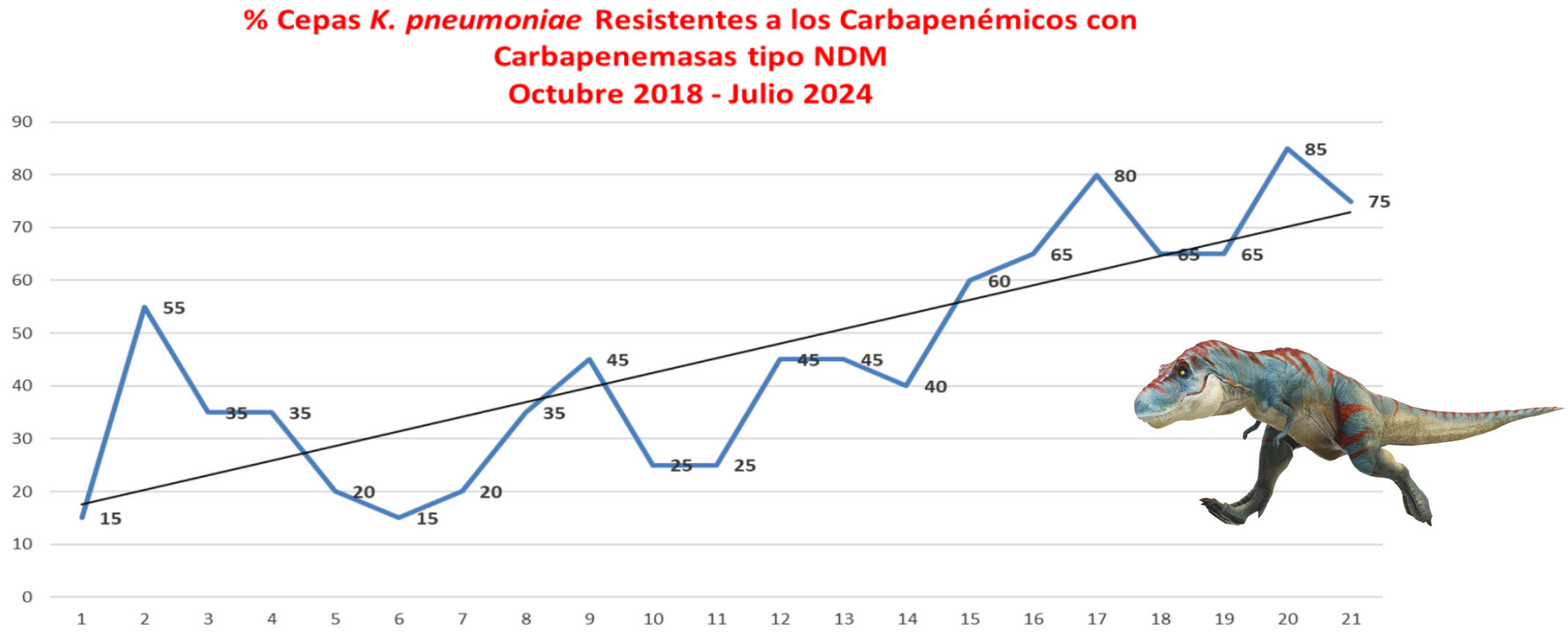
Klebsiella pneumoniae

2017-2024

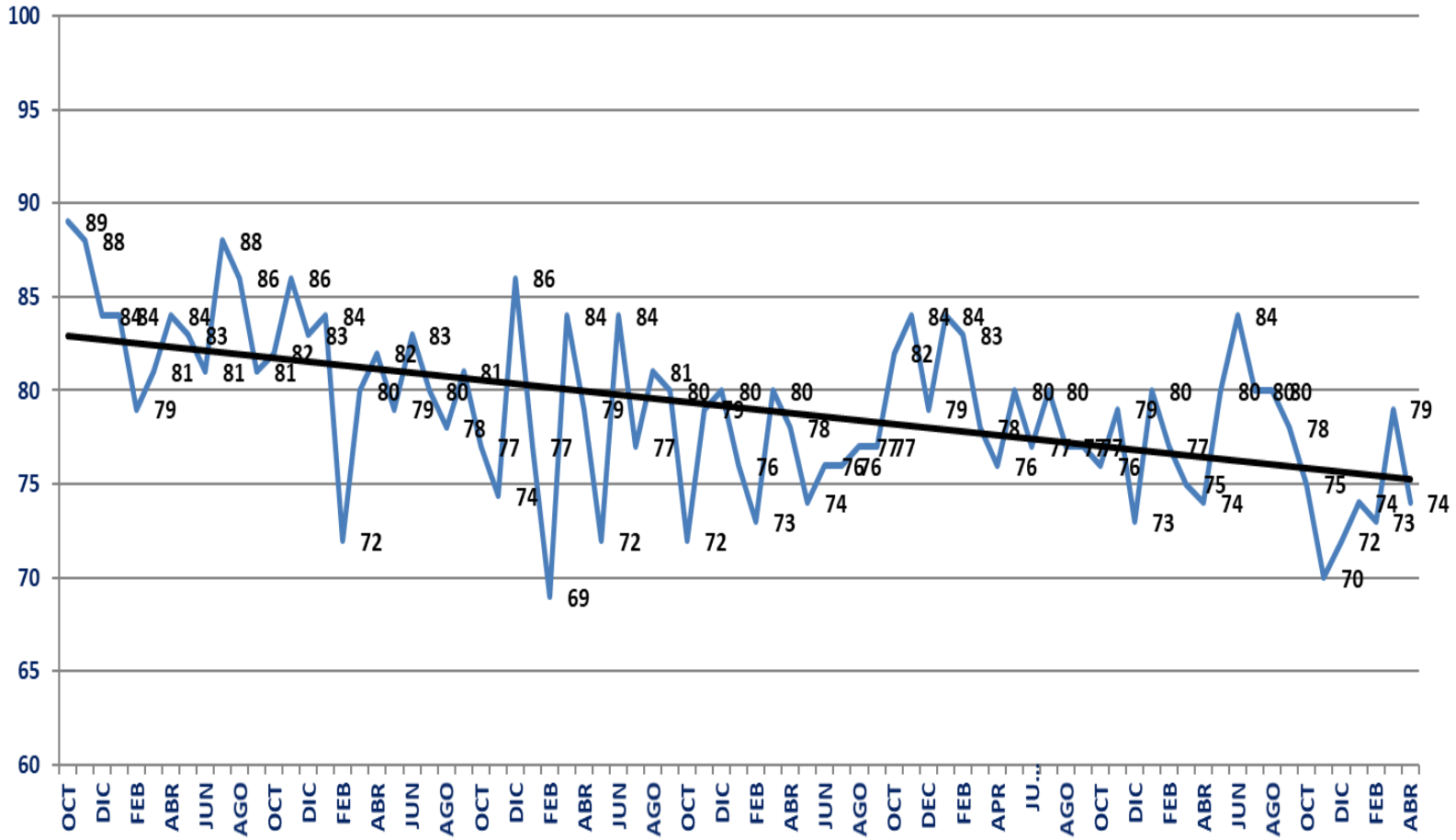


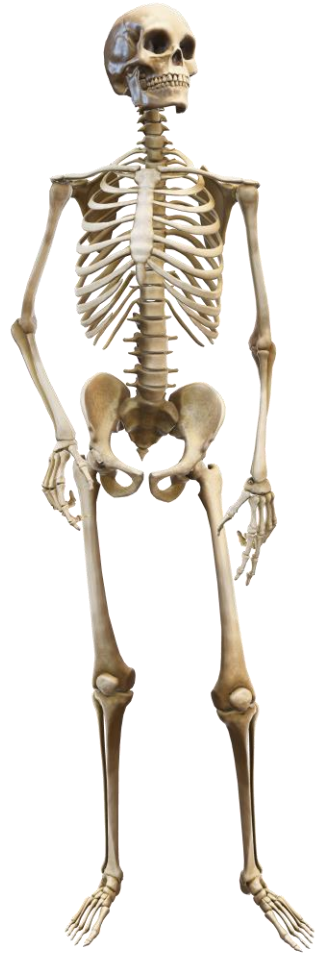
CARBAPENEMASAS

420 Cepas



Porcentaje Sensibilidad Antibiótico Empírico
Hemocultivos
Octubre 2017 - Abril 2024



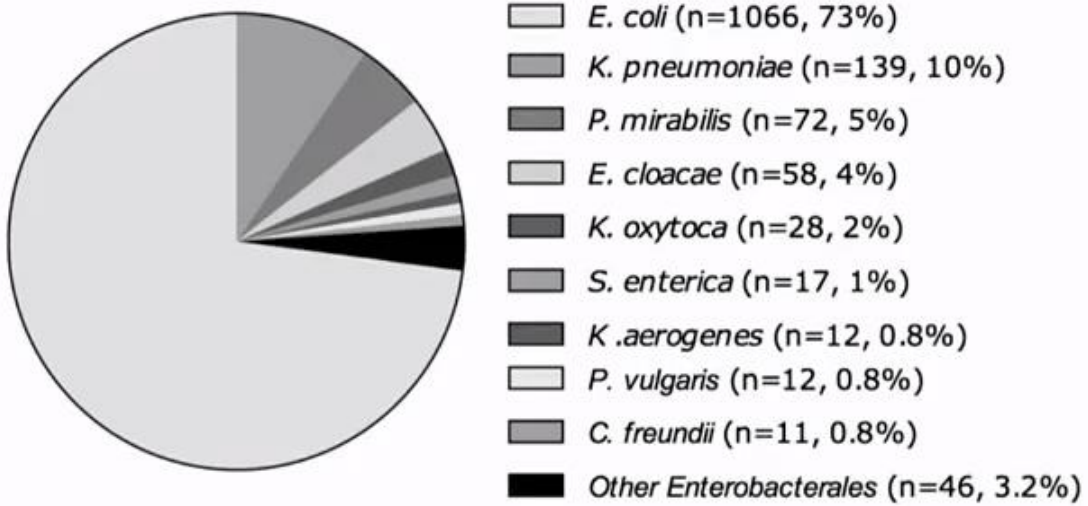


El Rosario · GERMEN · BIOMERIEUX · Labmedico Laboratorio Médico de Referencia

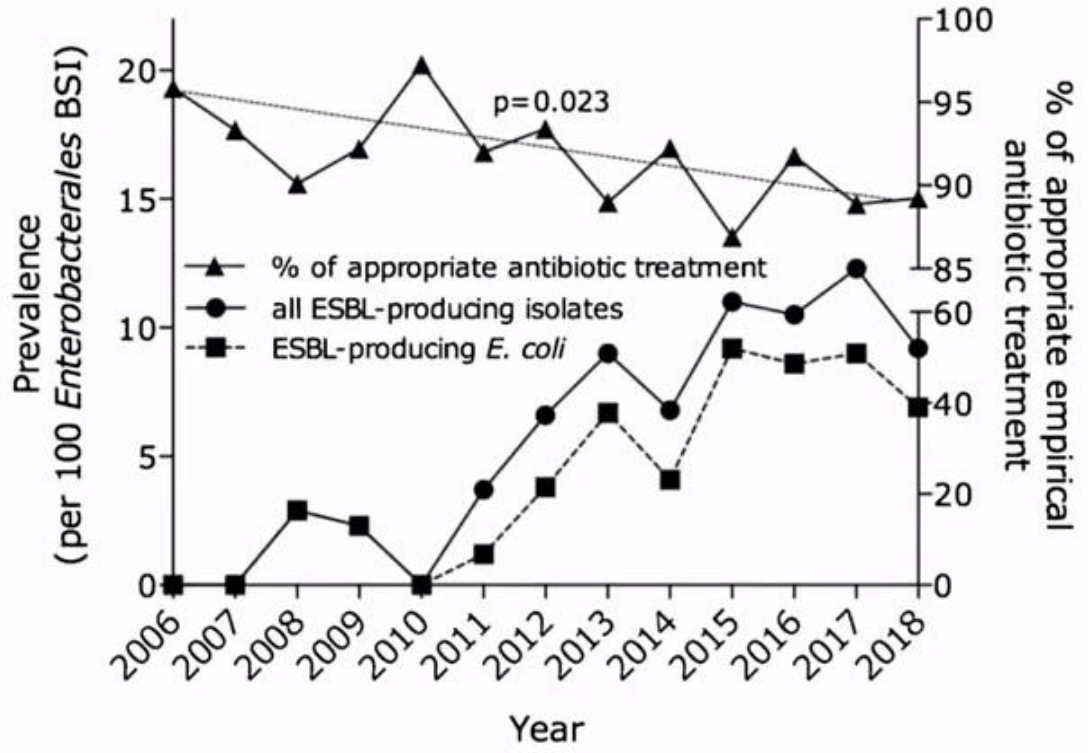
Distribución especialidad y tipo de infección

TIPO DE INFECCION POR ESPECIALIDAD	Infección de Sitio Quirúrgico	Bacteremia	Neumonía /NAV	Infección Catéter Central	Ojos, Oidos Nariz Y Garganta	Infección de Tracto Urinario	Infección de Tracto Gastrointestinal	Infección Catéter Periferico	Piel , Tejido Subcutaneo y tejidos blandos.	Infeccion del sistema nervioso central	Infección ósea y articular	Infección de Tracto Reproductivo	Infección Tracto Respiratorio bajo	Infección del sistema cardiovascular	Total general	%
Otras especialidades < 2%																
Hematologia		25	8	6	4	2	6	1							52	10%
Hemato - Oncología Pediátrica																
Hemato Oncología																
Neonatologia																
Pediatría																
Medicina Interna																
Neurocirugia																
Gastroenterología Pediátrica																
Cirugia General																
Ortopedia Y Traumatología																
Total general	130	98	80	64	55	26	24	12	9	3	3	1	1	1	507	100%
%	26%	19%	16%	13%	11%	5%	5%	2%	2%	1%	1%	0,2%	0,2%	0,2%	100%	

Inappropriate EAT for BSI and prevalence of MDR



Species distribution among 1461 *Enterobacterales* isolates from 1369 blood cultures collected in the emergency department between 2006 and 2018



The prevalence of ESBL+ increased from 0 to 9.2/100 *Enterobacterales* BSI cases ($p < 0.001$), mainly *Escherichia coli* (6.9 cases/100 BSI in 2018*)*.
The rate of appropriate EAT decreased from 95.8 to 89.2% (p = 0.023).
Among IAET, 45% concerned 3GC, with 74.6% of them attributable to ESBL production.

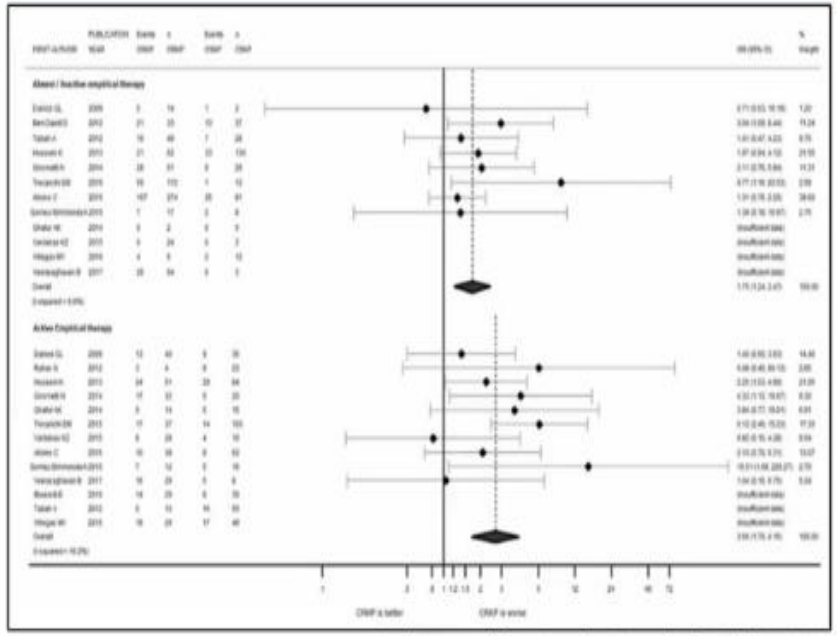
Clemenceaue M Eur J Clin Microbiol Infect Dis 2022

Table. Pooled unadjusted odds ratio for the association between antimicrobial resistance and lethality by type of resistance, Latin America*

Type of resistance	OR (95% CI)	I^2
Carbapenem-resistance	2.86 (2.07–3.95)	61%
Extended-spectrum β-lactamase	1.28 (0.95–1.74)	38%
Methicillin-resistance	1.78 (1.29–2.45)	63%
MDRO†	1.64 (1.16–2.30)	68%
Azol-resistant	1.41 (0.59–3.35)	-
Vancomycin-resistant	4.09 (2.40–6.97)	0%
Random effect model	1.86 (1.55–2.23)	71%

*MDRO, multidrug-resistant organisms; OR, pooled odds ratio.
†Multidrug-resistant organisms include methicillin-resistant *Staphylococcus aureus*, Vancomycin-resistant *Enterococcus* spp, extended-spectrum β-lactamase producing Enterobacterales, carbapenem-resistant Enterobacterales (including *Klebsiella, Enterobacter, Escherichia coli, Proteus, Serratia*), carbapenem-resistant *Pseudomonas aeruginosa*, carbapenem-resistant *Acinetobacter baumannii* and azole/echinocandin-resistant *Candida* spp.

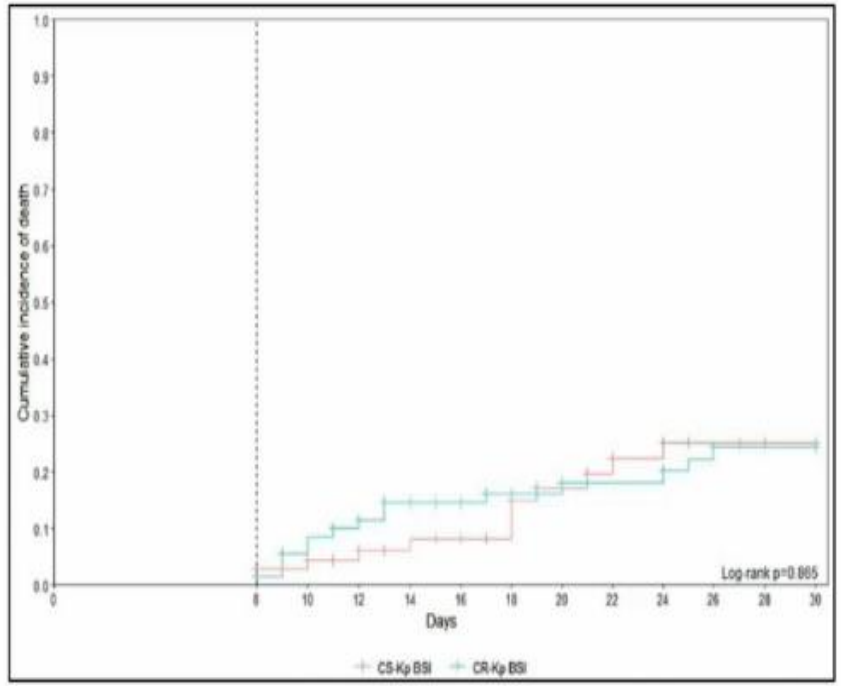
The impact of carbapenem resistance on mortality in patients with *Klebsiella pneumoniae* bloodstream infection: an individual patient data meta-analysis of 1952 patients[1]



Graph extracted from Maraolo AE, *et al*. Infect Dis Ther. 2021.

Study period	Empiric treatment given for CR-Kp
2004–2016	Colistin 61.8%[1]

Mortality in KPC-producing *Klebsiella pneumoniae* bloodstream infections: a changing landscape[2]



Graph extracted from Giacobbe DR, *et al*. J Antimicrob Chemother. 2023.

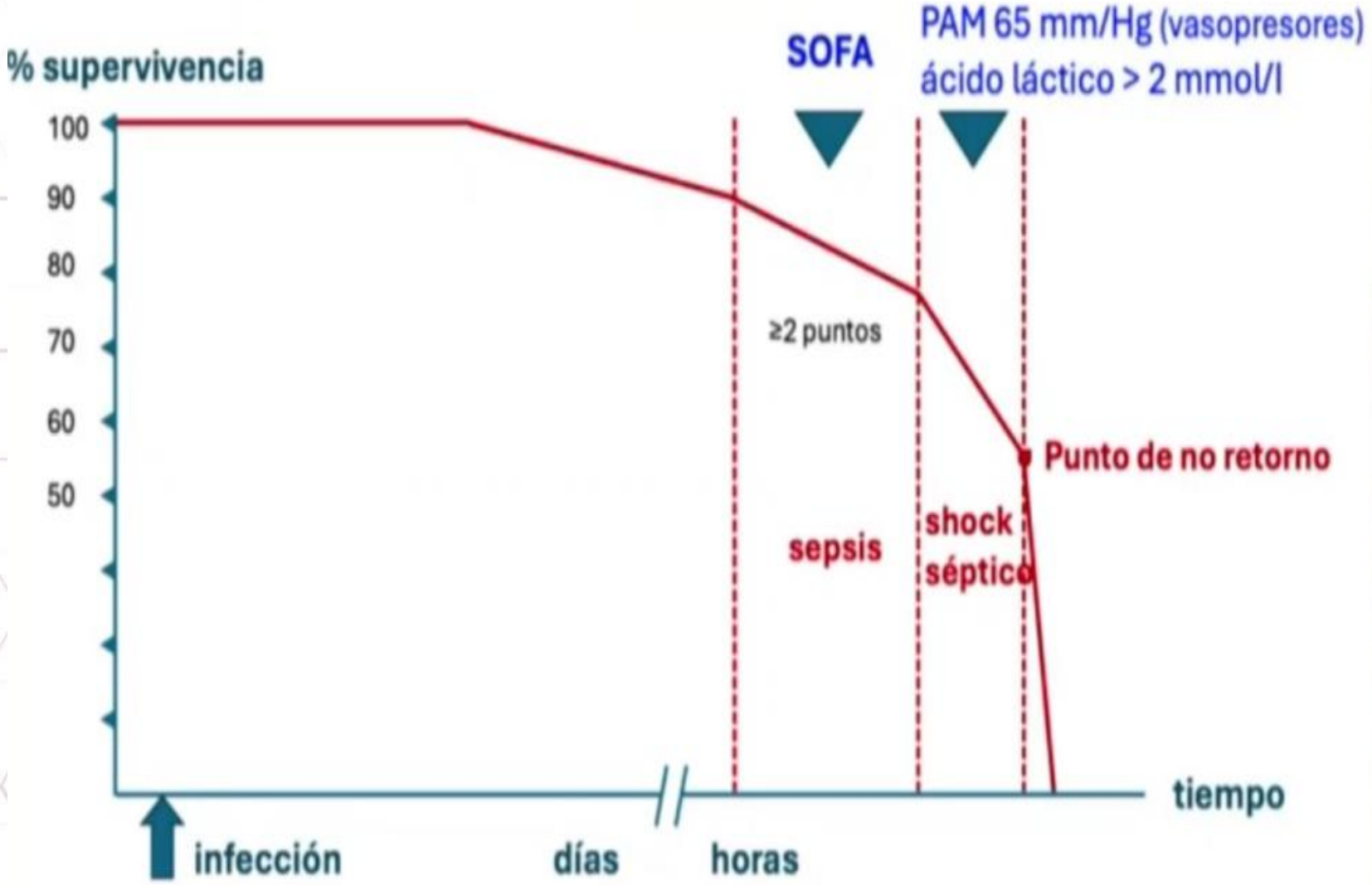
Study period	Empiric treatment given for CR-Kp
2020	Ceftazidime–avibactam* 74.7%[2]

*Ceftazidime–avibactam is the property of Pfizer. Current SmPC available for attendees at the end of the deck.

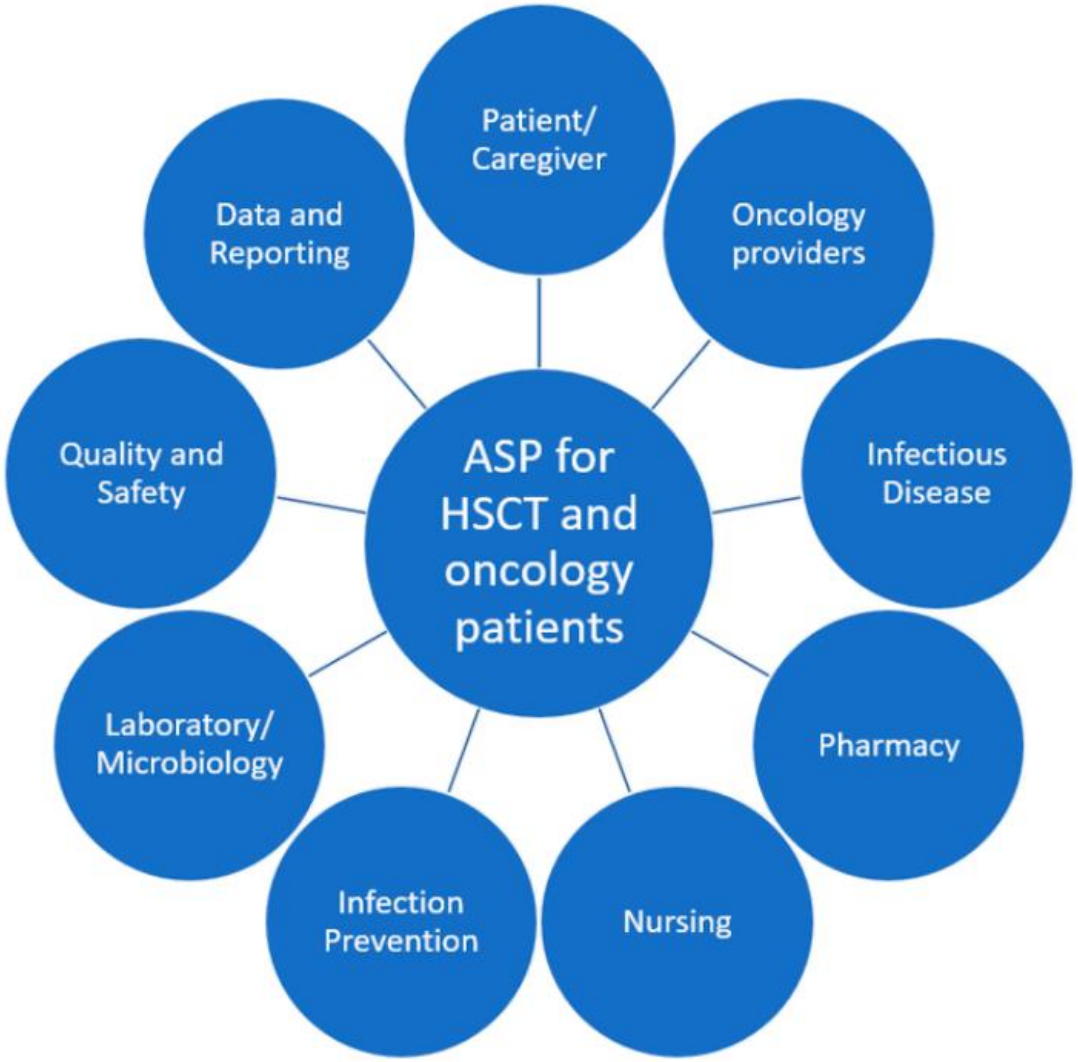
BSI, bloodstream infection; CI, confidence interval; CR, carbapenem-resistant; CS, carbapenem-susceptible; HR, hazard ratio; Kp, *Klebsiella pneumoniae*; KPC, *Klebsiella pneumoniae* carbapenemase; OR, odds ratio; SOFA, Sequential Organ Failure Assessment.

1. Maraolo AE, *et al*. The impact of carbapenem resistance on mortality in patients with *Klebsiella pneumoniae* bloodstream infection: an individual patient data meta-analysis of 1952 patients. Infect Dis Ther. 2021:10(1);541–558; 2. Giacobbe DR, *et al*. Mortality in KPC-producing *Klebsiella pneumoniae* bloodstream infections: a changing landscape. J Antimicrob Chemother. 2023;78(10):2505–2514.

PP-ZVA-ESP-0603; Abril 2024



Mensa J. et al. Rev Esp Quimioter. 2021 Oct;34(5):511-524.



Abbreviations: ASP = Antimicrobial stewardship program, HSCT = hematopoietic stem cell transplant.

Farmacia HOSPITALARIA
Órgano oficial de expresión científica de la Sociedad Española de Farmacia Hospitalaria

ORIGINALES
Artículo bilingüe inglés/español

Impact of an antimicrobial stewardship program on critical haematological patients

Impacto de un programa de optimización de antimicrobianos sobre el paciente crítico hematológico

Jesús Ruiz-Ramos[1], Juan Frasquet[2], José Luis Poveda-Andrés[3], Eva Romá[3], Miguel Salavert-Lleti[4], Álvaro Castellanos[5], Paula Ramírez[5]

[1]Pharmacy Unit. La Fe Healthcare Research Institute (IIS). Hospital Universitario y Politécnico La Fe, Valencia. [2]Microbiology Unit. Hospital Universitario y Politécnico La Fe, Valencia. [3]Pharmacy Unit. Hospital Universitario y Politécnico La Fe, Valencia. [4]Infectious Disease Unit. Hospital Universitario y Politécnico La Fe, Valencia. [5]Intensive Care Unit. Hospital Universitario y Politécnico La Fe, Valencia. Spain.

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Recibido el 26 de noviembre de 2016;
aceptado el 3 de febrero de 2017.
DOI: 10.7399/fh.2017.41.4.10709

Abstract

Objective: Antimicrobial Stewardship Programs (ASPs) have appeared as very useful tools in order to improve the use of antimicrobial agents. The objective of this study is to assess the impact of an ASP on haematological patients hospitalized in an Intensive Care Unit (ICU).
Methods: A quasi-experimental pre-post intervention study, which included haematological patients admitted to an ICU and assessed by the ASP program during 3 years. The impact of the program on patient evolution was assessed by comparison between the previous period and the intervention period in terms of mortality, mean stay, number of re-hospitalizations, and duration of mechanical ventilation for intubated patients.
Results: The ASP team assessed 324 antimicrobial agents in 169 patients; they recommended 121 modifications, including 55 treatment discontinuations. Compared with the pre-intervention period, there were no significant differences in the variables assessed. No variation was observed in colonization by multi-resistant bacteria.
Conclusions: The implementation of an APS on critical haematological patients will lead to a relevant number of treatment modifications, without any impact on the clinical evolution of patients.

Resumen

Objetivo: Los programas de optimización de antimicrobianos (PROA) han surgido como herramientas de gran utilidad para mejorar el uso de estos. El objetivo del presente estudio es evaluar el impacto de un PROA sobre pacientes hematológicos ingresados en una unidad de pacientes críticos.
Métodos: Estudio cuasi-experimental pre-post intervención. Se incluyeron pacientes hematológicos ingresados en una unidad de críticos evaluados por el equipo PROA durante 3 años. El impacto del programa sobre la evolución de los pacientes se evaluó mediante la comparación entre el periodo previo y de intervención de la mortalidad, estancia media, número de reingresos y duración de ventilación mecánica en los pacientes intubados.
Resultados: 324 antimicrobianos de 169 pacientes fueron evaluaron por el equipo PROA, recomendando un total de 121 modificaciones, incluyendo 55 suspensiones de tratamiento. Comparados con el periodo pre-intervención, no se observaron diferencias significativas en las variables consideradas. No se observó variación en la colonización por bacterias multirresistentes.
Conclusiones: La implantación de un PROA sobre el paciente crítico hematológico conduce a un número relevante de modificaciones en el tratamiento, sin afectar la evolución clínica de los pacientes.

RESEARCH Open Access

Efficacy of an antimicrobial stewardship intervention for early adaptation of antibiotic therapy in high-risk neutropenic patients

Claire Durand[1*], Karine Risso[1], Michael Loschi[2,3], Nicolas Retur[4], Audrey Emery[5], Johan Courjon[1,3], Thomas Cluzeau[2,3] and Michel Carles[1,3]

Abstract

Background The 4th European Conference on Infections in Leukemia recommends early adaptation of empirical antibiotic therapy (EAT) for febrile neutropenia in stable patients.

Objectives To assess the efficacy of an antimicrobial stewardship (AMS) intervention promoting early de-escalation and discontinuation of EAT in high-risk neutropenic patients.

Methods This before-after study was conducted in the hematology department of the University Hospital of Nice, France. The AMS intervention included the development of clinical decision support algorithms, a twice-weekly face-to-face review of all antibiotic prescriptions and monthly feedback on the intervention. The primary endpoint was overall antibiotic consumption during hospital stay, expressed as days of therapy (DOT).

Results A total of 113 admissions were included: 56 during the pre-intervention period and 57 during the intervention period. Induction chemotherapy and conditioning for allogeneic stem cell transplantation were the most frequent reasons for admission. In the intervention period, there was a significant decrease in overall antibiotic consumption (median DOT 20 vs. 28 days, $p=0.006$), carbapenem consumption (median DOT 5.5 vs. 9 days, $p=0.017$) and anti-resistant Gram-positive agents consumption (median DOT 8 vs. 11.5 days, $p=0.017$). We found no statistical difference in the rates of intensive care unit admission (9% in each period) and 30-day mortality (5% vs. 0%, $p=0.243$). Compliance with de-escalation and discontinuation strategies was significantly higher in the intervention period (77% vs. 8%, $p<0.001$).

Conclusion A multifaceted AMS intervention led to high compliance with early de-escalation and discontinuation of EAT and lower overall antibiotic consumption, without negatively affecting clinical outcomes.

Keywords Antibiotic, Antimicrobial stewardship, Hematology, Febrile neutropenia

Grouping of Microbial Taxa

Gram Negative

Enterobacteriaceae

- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Klebsiella oxytoca*
- *Enterobacter* spp.
- *Citrobacter* spp.
- *Serratia* spp.
- *Proteus* spp.

Non-Glucose Fermenters

- *Pseudomonas aeruginosa*
- *Acinetobacter baumannii*
- *Stenotrophomonas maltophilia*
- *Burkholderia* spp.

Gram Positive

Staphylococcus aureus

Enterococci

- *Enterococcus faecium*
- *Enterococcus fecalis*

Streptococci

- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*

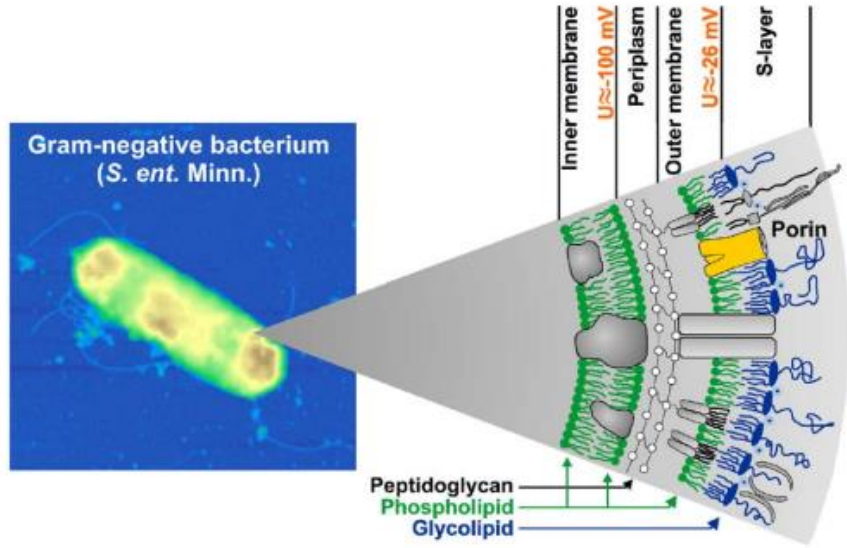


Fig. 1. Cell envelope of Gram-negative bacteria.

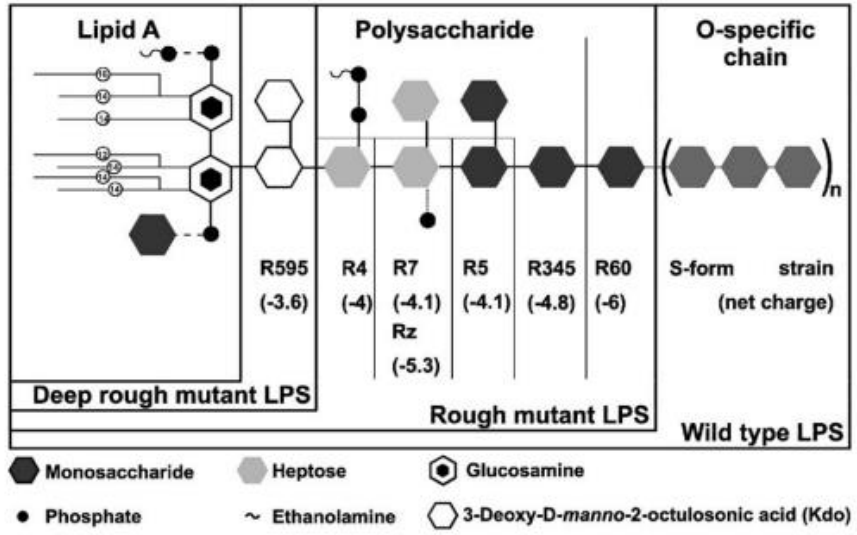
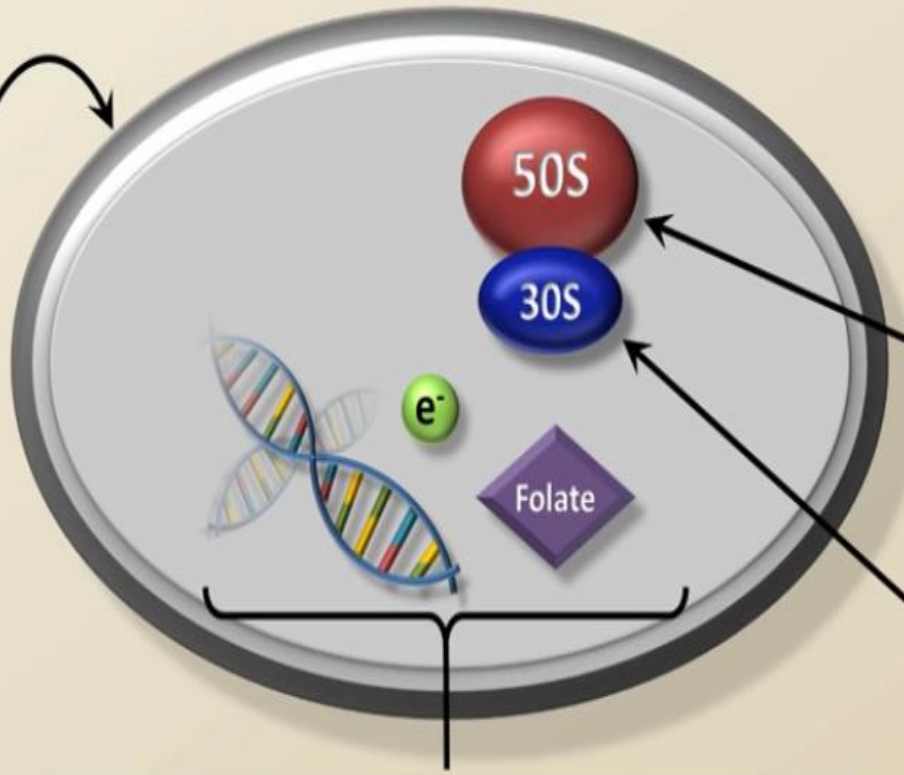


Fig. 2. Schematic representation of the architecture of *Salmonella enterica* serovar Minnesota *S. ent.* Minn. LPS, an enterobacterial wild-type LPS. Substituents may be present in non-stoichiometric amounts. The net charges of the respective chemotypes were calculated according to mass spectrometric data and are given in parentheses.

Mechanisms of Antibiotics



Inhibit Cell Wall Synthesis or Function

- **Beta Lactams**
  - Penicillins
  - Cephalosporins
  - Carbapenems
  - Monobactams
- Vancomycin
- Daptomycin
- Polypeptides

Inhibit Protein Synthesis

- **Inhibit 50S subunit**
  - Macrolides
  - Clindamycin
  - Linezolid
  - Streptogramins
  - Chloramphenicol
- **Inhibit 30S Subunit**
  - Aminoglycosides
  - Tetracyclines
  - Tigecycline

Inhibit Nucleic Acid Synthesis or Function

Inhibit DNA Gyrase +/- Topoisomerase IV: Quinolones

Inhibits Folate Synthesis: Trimethoprim / Sulfamethoxazole

Create Free Radicals: Metronidazole, Nitrofurantoin

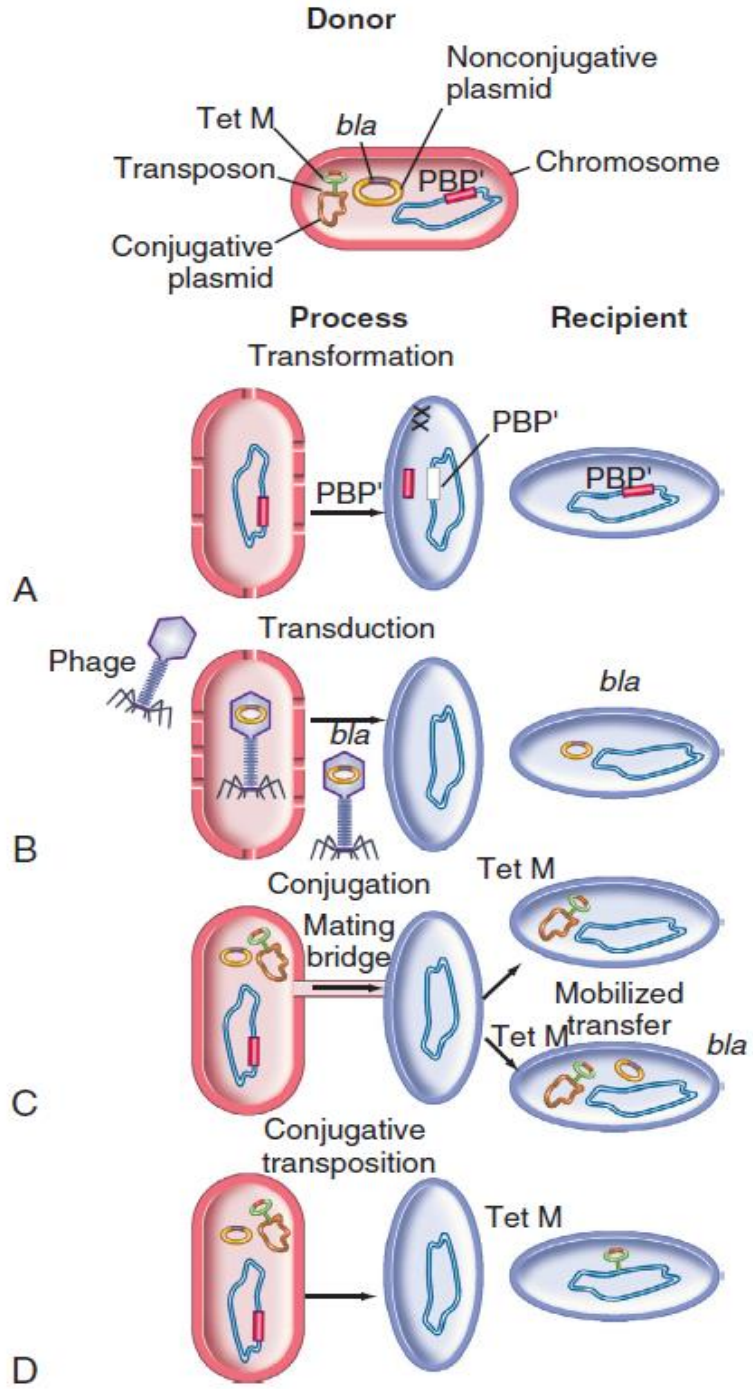
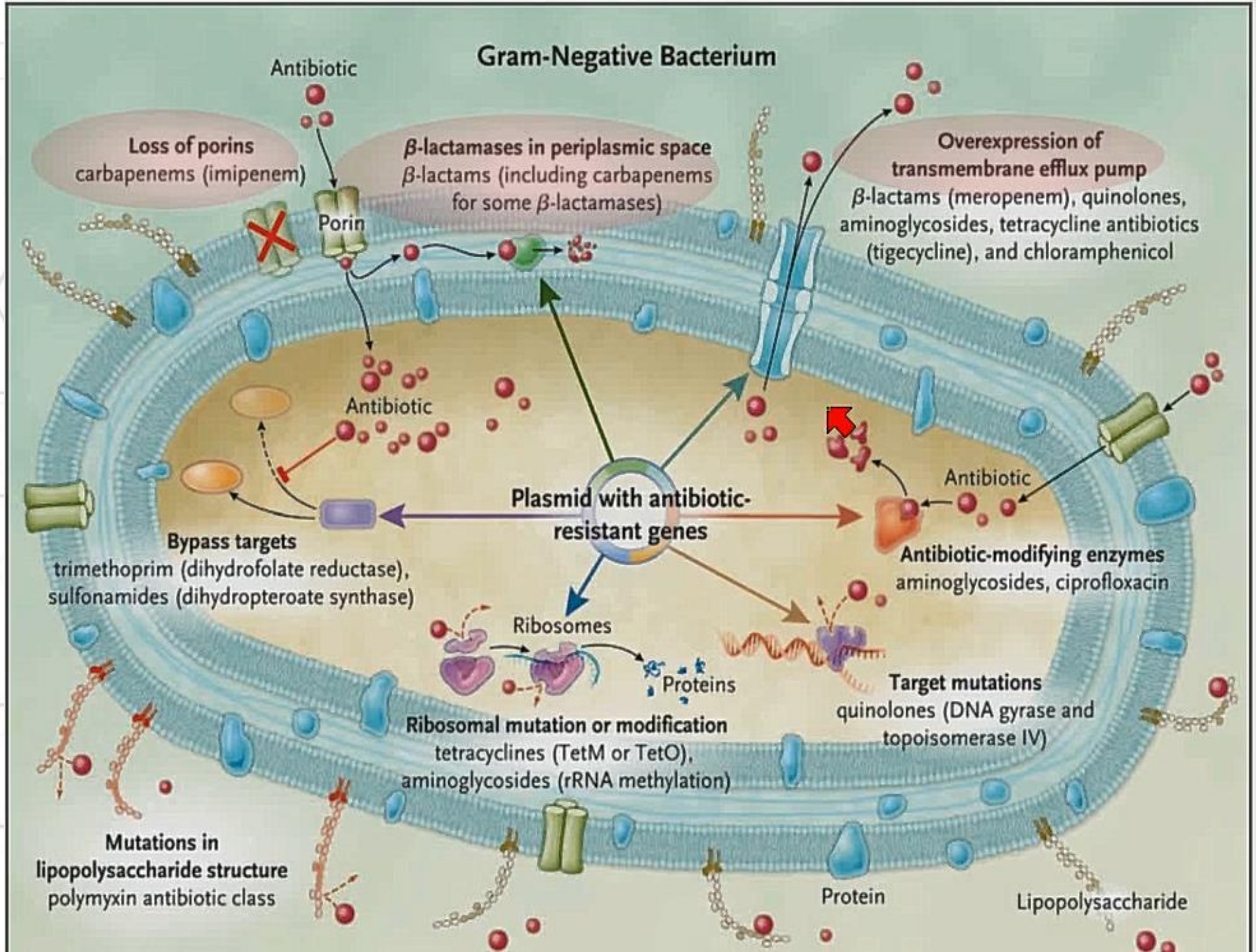
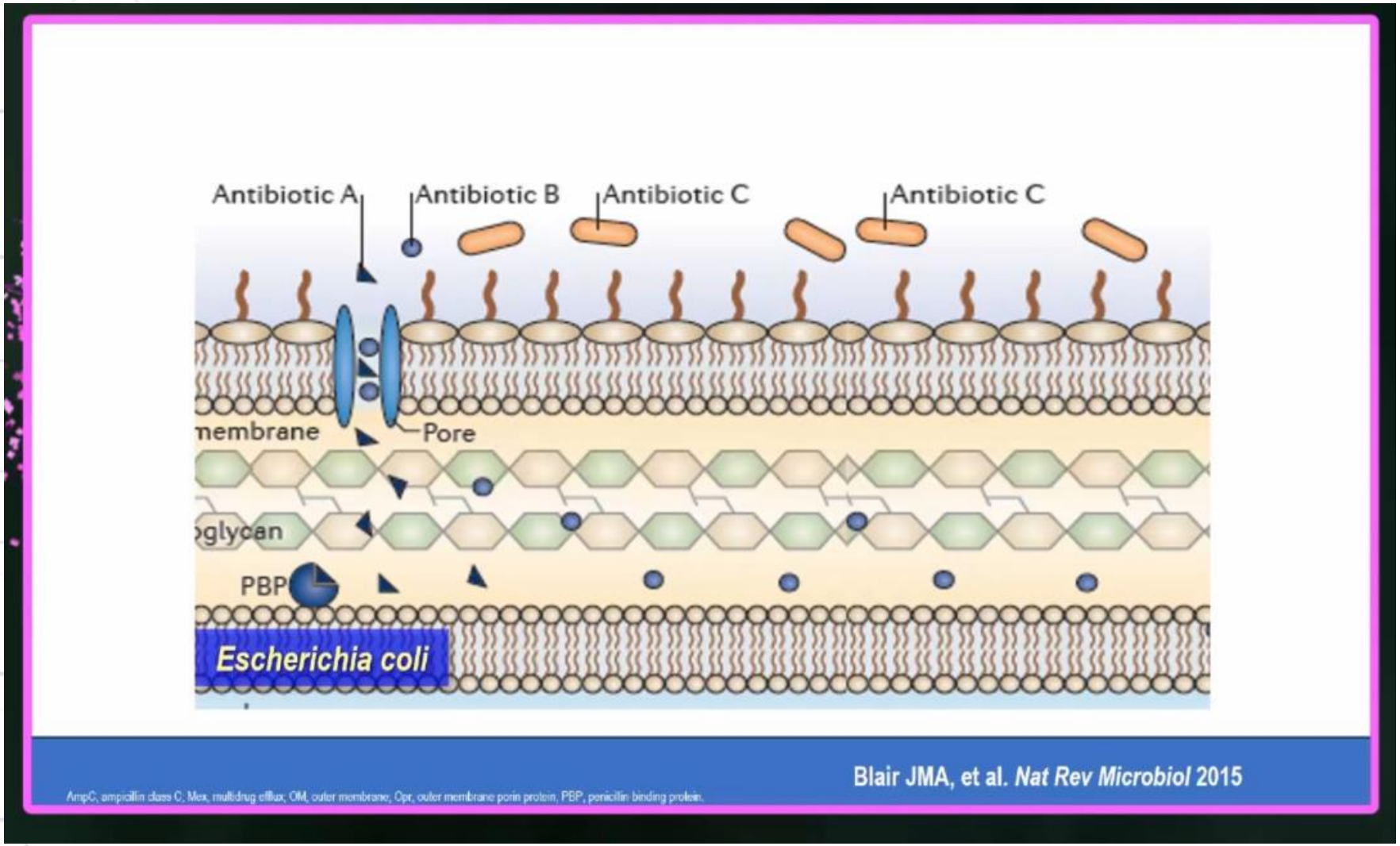
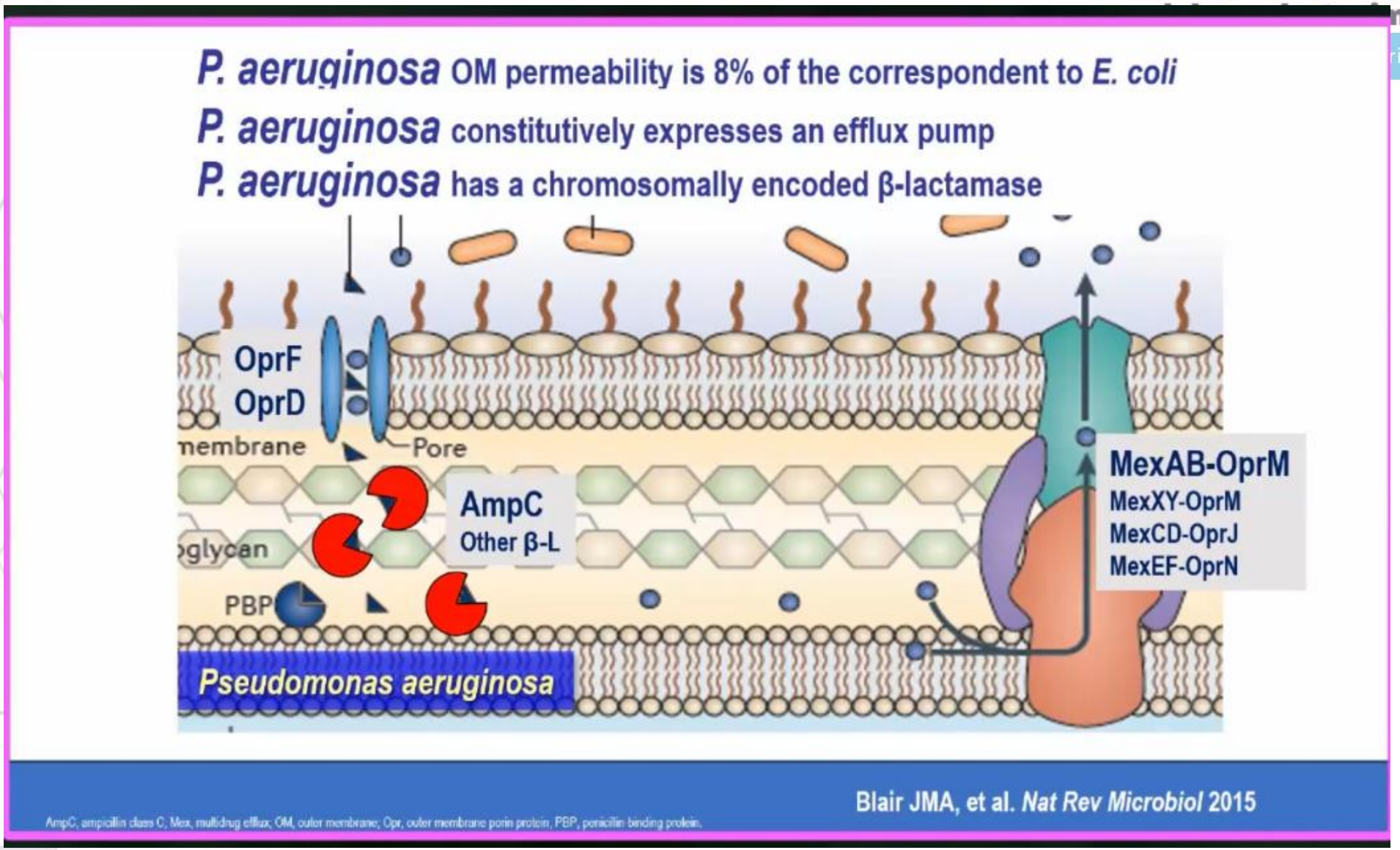


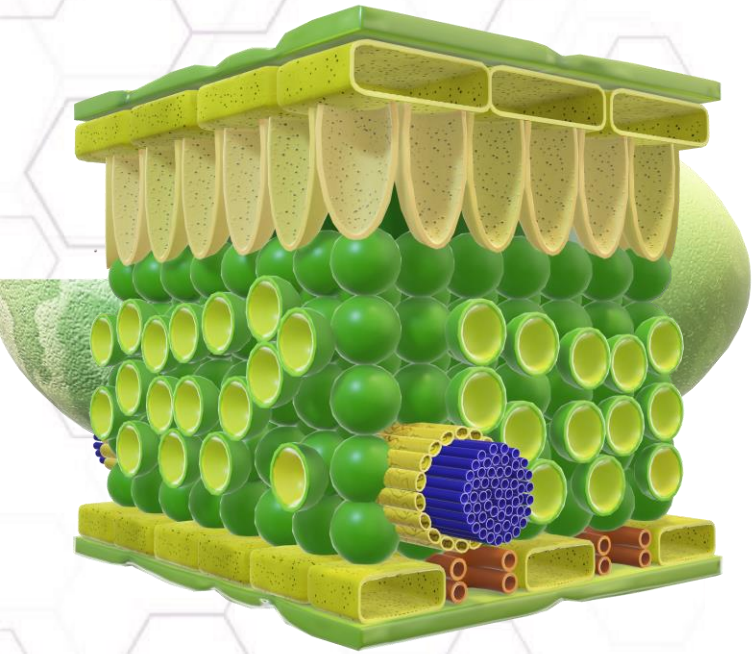
FIGURE 18-1 Examples of recombination events and molecular spread of antibiotic-resistance genes. The donor organism depicted here has three antibiotic-resistance genes: the first on the chromosome, designated as *PBP'*, a low-affinity penicillin-binding protein; the second (a β-lactamase gene labeled *bla*) on a small nonconjugative plasmid; and the third (Tet M, a tetracycline resistance determinant) on a transposon residing on a large self-conjugative plasmid. **A,** Genetic exchange may occur by transformation (naked DNA transfer for dying bacteria to a competent recipient). This generally results in transfer of homologous genes located on the chromosome by recombination enzymes (RecA). **B,** Transduction also may transfer antibiotic-resistance genes (usually from small plasmids) by imprecise packaging of nucleic acids by transducing bacteriophages. **C,** Conjugation is an efficient method of gene transfer, requiring physical contact between donor and recipient. Self-transferable plasmids mediate direct contact by forming a mating bridge between cells. Smaller nonconjugative plasmids might be mobilized in this mating process and be transported into the recipient. **D,** Transposons are specialized sequences of DNA that possess their own recombination enzymes (transposases), allowing transposition ("hopping") from one location to another, independent of the recombination enzymes of the host (RecA-independent). They may transpose to nonhomologous sequences of DNA and spread antibiotic-resistance genes to multiple plasmids or genomic locations throughout the host. Some transposons possess the ability to move directly from a donor to a recipient, independent of other gene transfer events (conjugative transposons or integrative and conjugative elements).



ptimización
nicrobianos:
riencias en PROA


Antibiotic A
Antibiotic B
Antibiotic C
Antibiotic C
nembrane
Pore
oglycan
PBP
Escherichia coli
Blair JMA, et al. Nat Rev Microbiol 2015
AmpC, ampicillin class C; Mex, multidrug efflux; OM, outer membrane; Opr, outer membrane porin protein; PBP, penicillin binding protein.


P. aeruginosa OM permeability is 8% of the correspondent to E. coli
P. aeruginosa constitutively expresses an efflux pump
P. aeruginosa has a chromosomally encoded β-lactamase
OprF
OprD
membrane
Pore
AmpC
Other β-L
glycan
PBP
MexAB-OprM
MexXY-OprM
MexCD-OprJ
MexEF-OprN
Pseudomonas aeruginosa
Blair JMA, et al. Nat Rev Microbiol 2015
AmpC, ampicillin class C; Mex, multidrug efflux; OM, outer membrane; Opr, outer membrane porin protein; PBP, penicillin binding protein.



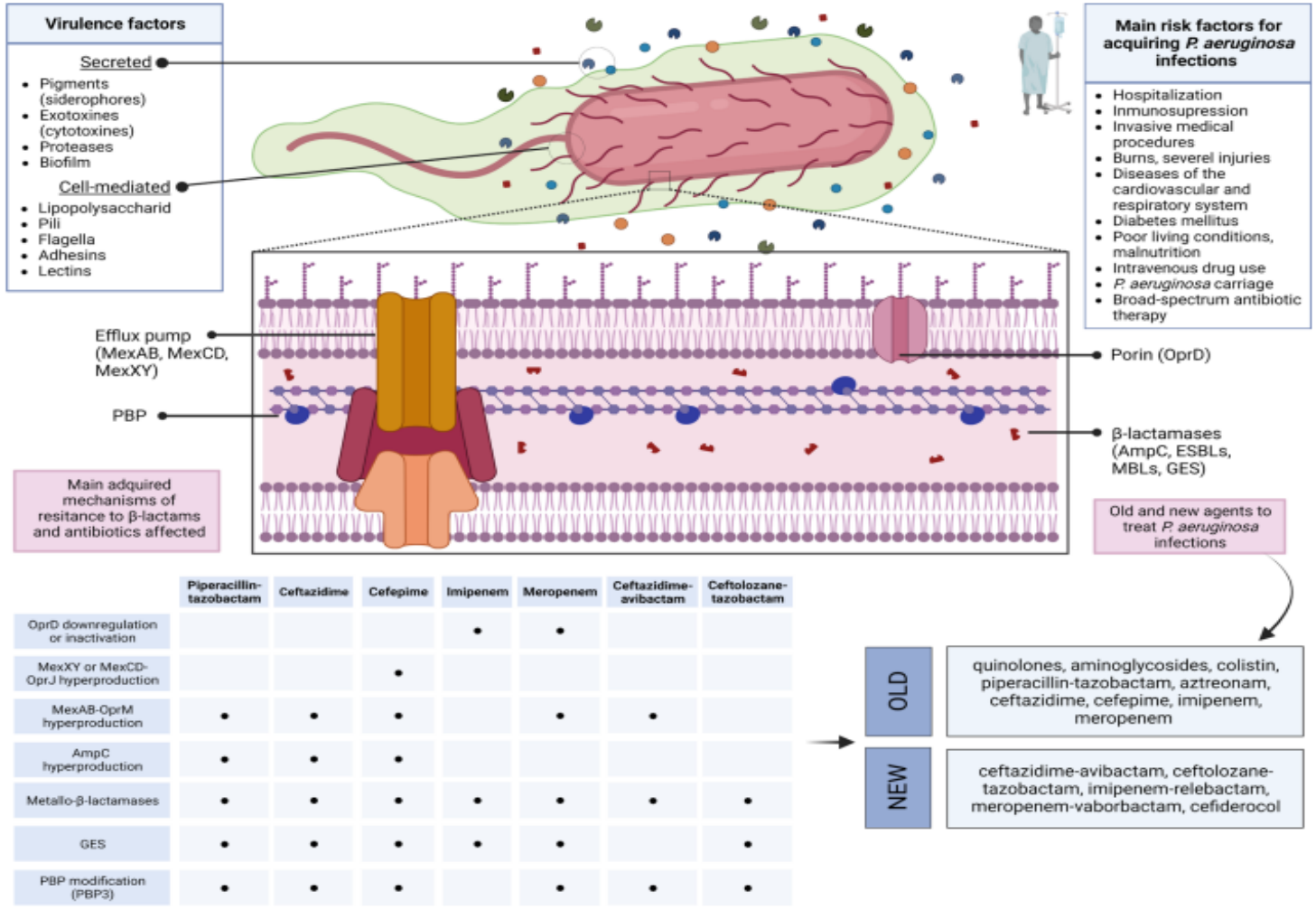
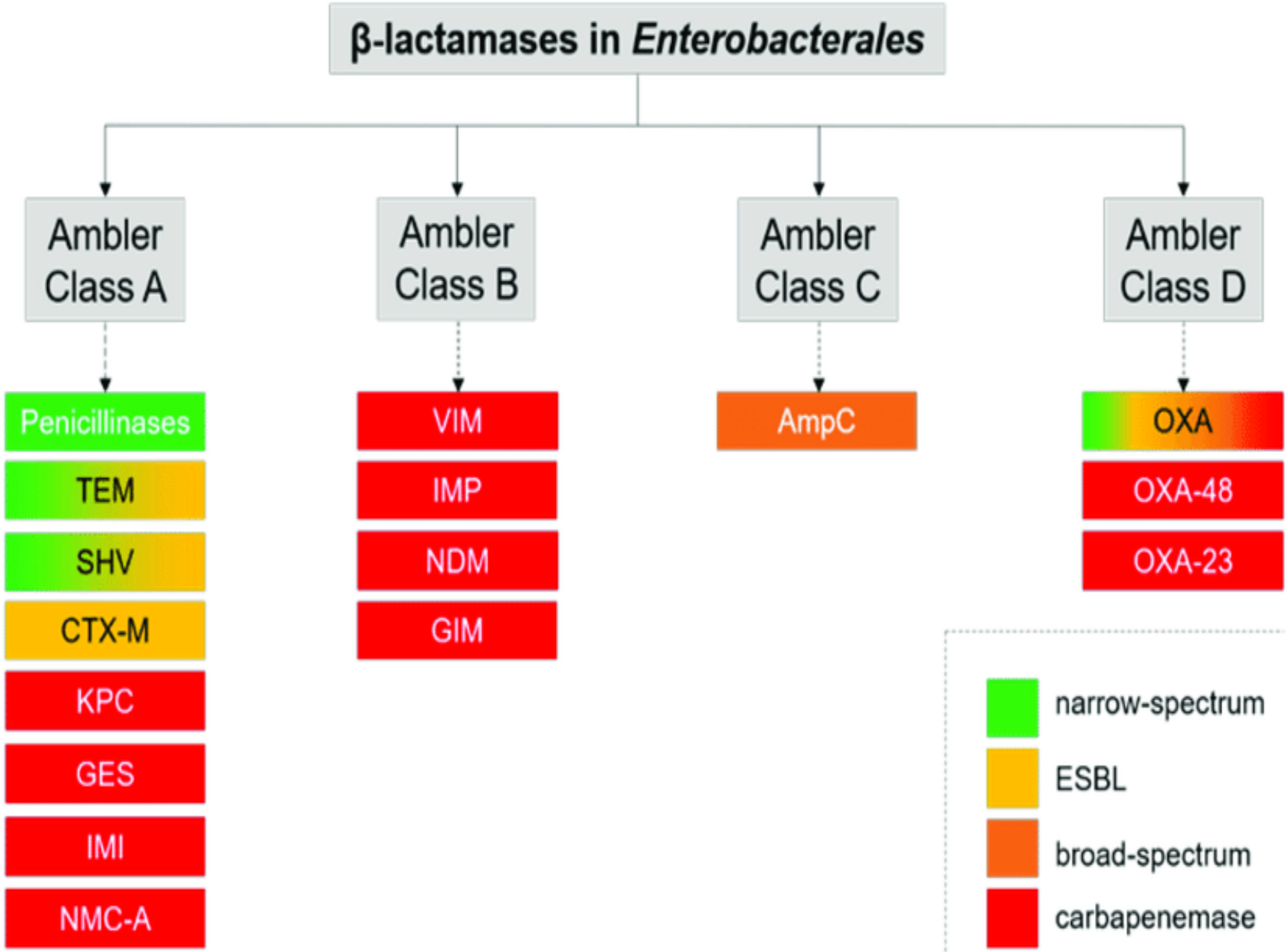
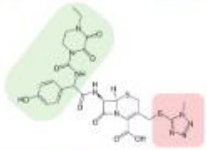
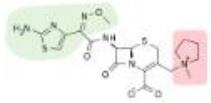
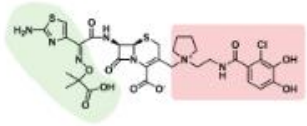


Figure 1 | **Virulence factors, risk factors for acquiring infection, scheme of β-lactam resistance mechanisms and agents to treat *Pseudomonas aeruginosa* infections.**

ESBLs: extended-spectrum β-lactamases, MBLs: metallo-β-lactamases, GES: Guiana extended-spectrum β-lactamase. Created with BioRender.com



Cefalosporinas anti Pseudomonas *aeruginosa*

Anti-pseudomonal cephalosporins	R1	R2	Characteristics
Cefoperazone Approved: 1981			• Good activity against *P. aeruginosa* • Gram-positive activity • Notable side effect: hypothrombinemia
Cefpirome Approved: 1983			• Improved activity against *P. aeruginosa* • Less affected by porin defects and by AmpC hyperproduction • Gram-positive activity
Ceftazidime Approved: 1984 Ceftazidime + avibactam Approved: 2015			• Improved spectrum of activity • Stability against broad-spectrum beta-lactamases • Good activity against *P. aeruginosa* • Avibactam: inhibitory activity against Class C beta-lactamases, Class A and some Class D carbapenemases
Cefepime Approved: 1994			• Broader spectrum of activity • Higher stability against beta-lactamases • Good activity against *P. aeruginosa* • Less affected by porin defects and by AmpC hyperproduction • Reduced potential of resistance development versus ceftazidime
Ceftolozane + tazobactam Approved: 2014–2015			• Increased stability against AmpC-hyperproducing *P. aeruginosa* • Reduced potential of resistance development versus ceftazidime • Limited Gram-positive activity • Tazobactam: inhibitory effect of ESBLs
Cefiderocol Approved: 2019–2020			• Iron chelation and active transport • Improved antibacterial activity • No activity against Gram-positives or anaerobes • Increased stability against serine-beta-lactamases, including ESBLs, and metallo-beta-lactamases • Activity extends to *Acinetobacter* spp. and other non-fermenters (*S. maltophilia, A. xylosoxidans, Burkholderia* spp.)

Graft-versus-host-disease:	Acute →	Chronic →	
Day 0	Day 15–45	Day 100	Day 365 and onwards
	Phase I: Pre-engraftment. (Neutropenia, barrier breakdown (mucositis, central venous access devices))	Phase II: Post-engraftment. (Impaired cellular and humoral immunity; NK cells recover first, increased CD8 T-cells but restricted T-cell repertoire)	Phase III: Late phase. (Impaired cellular and humoral immunity; B-cell and CD4 T-cell numbers recover slowly and repertoire diversifies)	Examples of prevention strategies for decreased incidence
BACTERIAL	Gram-negative bacilli			• Consider LVQ for antibacterial prophylaxis during neutropenia [1] • Penicillin for pneumococcal prophylaxis [1]
BACTERIAL	Gram-positive organisms		Encapsulated bacteria [a]	
BACTERIAL	GI *Streptococci* species			
VIRAL	Herpes simplex virus			• For HSV/VZV: valacyclovir, acyclovir • For CMV-seropositive recipient: letermovir through day 100 post-HSCT [2]
VIRAL		Cytomegalovirus		
VIRAL			Varicella Zoster virus	
VIRAL	Respiratory and enteric viruses (seasonal/intermittent) [b]			Supportive care
VIRAL		Other viruses e.g., HHV-6		
VIRAL			EBV PTLD	Monitor symptoms, EBV monitoring
FUNGAL		*Aspergillus* species		• Voriconazole, posaconazole, isavuconazole, or AMB prophylaxis during neutropenia +/– further risk period (category 2B) [1]
FUNGAL	*Candida* species			
FUNGAL			*Pneumocystis*	• TMP/SMX and alternative agents (category 1) [1]

Abbreviations: AMB = amphotericin B, CMV = cytomegalovirus, EBV = Epstein-Barr virus, GI = gastrointestinal, HHV-6 = Human Herpesvirus 6, HSCT = hematopoietic stem cell transplant, HSV = herpes simplex virus, LVQ = levofloxacin, PTLD = post-transplant lymphoproliferative disorder, VZV = varicella zoster virus.

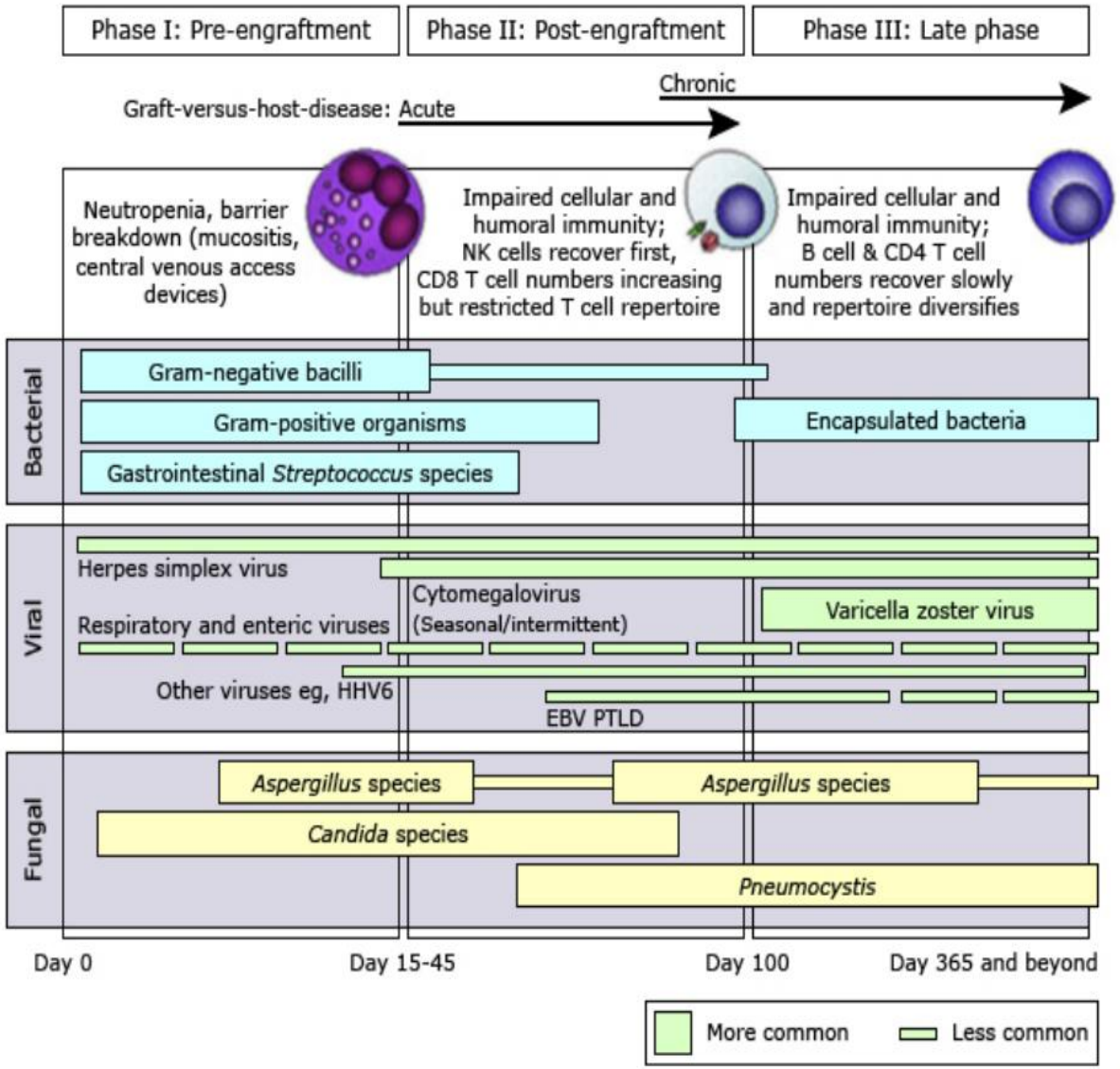
Footnotes:

a: Encapsulated bacteria include: *Streptococcus pneumoniae, Haemophilus influenzae, Neisseria meningitidis*.

b: Respiratory viruses include: respiratory syncytial virus, influenza, etc. Enteric viruses include norovirus, rotavirus.

Figure 1. Phases of opportunistic infections among allogeneic HSCT recipients and examples of prevention strategies—Adapted with permission from Ref. [23]. Copyright 2016, Elsevier. [1] Reference [11]. [2] Reference [24].

Infections after *allogeneic* HSCT



Tomblyn, BBMT 2009

Manifestations of Infection And Neutrophil Count

Signs and Symptoms	% of Patients Who Had a Neutrophil Count/mm³ of <100	101-1000	>1000
Fever	98	90	76
Fluctuance	6	36	52
Fissure or ulceration	21	42	54
Exudate	11	64	91
Purulent sputum	8	67	84
Pyuria	11	63	97

Sickles, et al. *Arch. Int. Med.* 1975

Table 1
Infectious risk of treatment regimens by disease

Disease	Treatment Regimen	Infectious Risk[a]			Types of Infection
		Low	Medium	High	
AML	AML induction and consolidation			X	High risk for bacteremia, IFI, HSV, and VZV reactivation
	Azacitidine, decitabine			X	High risk for IFI, HSV, and VZV reactivation
	Venetoclax + azacitidine			X	High risk for IFI, HSV, and VZV reactivation
ALL	ALL induction and consolidation			X	High risk for bacteremia, IFI, HSV, and VZV reactivation
	ALL induction and consolidation + imatinib/dasatinib			X	High risk for bacteremia, IFI, HSV, and VZV reactivation
	Imatinib + steroids		X		High risk for IFI, PCP
	Dasatinib + steroids		X		High risk for IFI, PCP
	Blinatumomab			X	
	CD19 CAR-T			X	High risk for bacteremia, IFI, HSV, and VZV reactivation
MDS	Azacitidine, decitabine		X		
CLL	Purine analogues (FCR)			X	High risk for bacteremia, HSV, and VZV reactivation, HBV reactivation
	Chlorambucil + rituximab		X		HBV reactivation risk
	BR			X	High risk for bacteremia, HBV reactivation risk
	Ibrutinib			X	Rare PCP, aspergillosis
	Venetoclax			X	High risk for respiratory viruses, HSV reactivation, OI, including PCP
	Idelalisib			X	High risk for PCP
	Alemtuzumab			X	High risk for IFI, all viral infections, including CMV reactivation

(*continued on next page*)

Table 1
(*continued*)

Disease	Treatment Regimen	Infectious Risk[a] Low	Medium	High	Types of Infection
CML	Imatinib			X	HBV reactivation risk
	Dasatinib			X	HBV reactivation risk
High-grade non-Hodgkin lymphomas	R-CHOP/CHOP		X[b]		HBV reactivation risk
	R-DHAP, R-ICE			X	High risk for bacteremia, HBV reactivation
	DA-R-EPOCH			X	High risk for bacteremia, HBV reactivation
	R-HyperCVAD			X	High risk for bacteremia, HBV reactivation
	CD19 CAR-T			X	High risk for bacteremia, IFI, HSV, and VZV reactivation
	Ibrutinib			X	Rare PCP
Hodgkin	ABVD		X		
	A-AVD (Brentuximab + AVD)			X	High risk for bacteremia
	Escalated BEACOPP			X	High risk for bacteremia
	Brentuximab			X	Rare CMV reactivation
	Nivolumab/pembrolizumab		X		Rare TB reactivation risk
Low-grade non-Hodgkin lymphomas	Rituximab monotherapy		X		HBV reactivation risk
	R-CVP		X		HBV reactivation risk
	BR			X	
Myeloma	RD		X		
	RVD/KRD		X		VZV reactivation risk
	Lenalidomide maintenance		X		
	Bortezomib maintenance		X		VZV reactivation risk
	Daratumumab			X	
	VDT-PACE			X	High risk for bacteremia
MPN	Ruxolitinib	X			VZV reactivation, HBV, and EBV reactivation, rare OI

Abbreviations: IFI, invasive fungal infection; KRD, carfilzomib, lenalidomide, and dexamethasone; OI, opportunistic infections; PCP, *Pneumocystis jirovecii* pneumonia; RVD, lenalidomide, bortezomib, dexamethasone.

[a] Infectious risk defined as low (neutropenic fever <10%), medium (neutropenic fever 10%–20%), or high (neutropenic fever >20%).

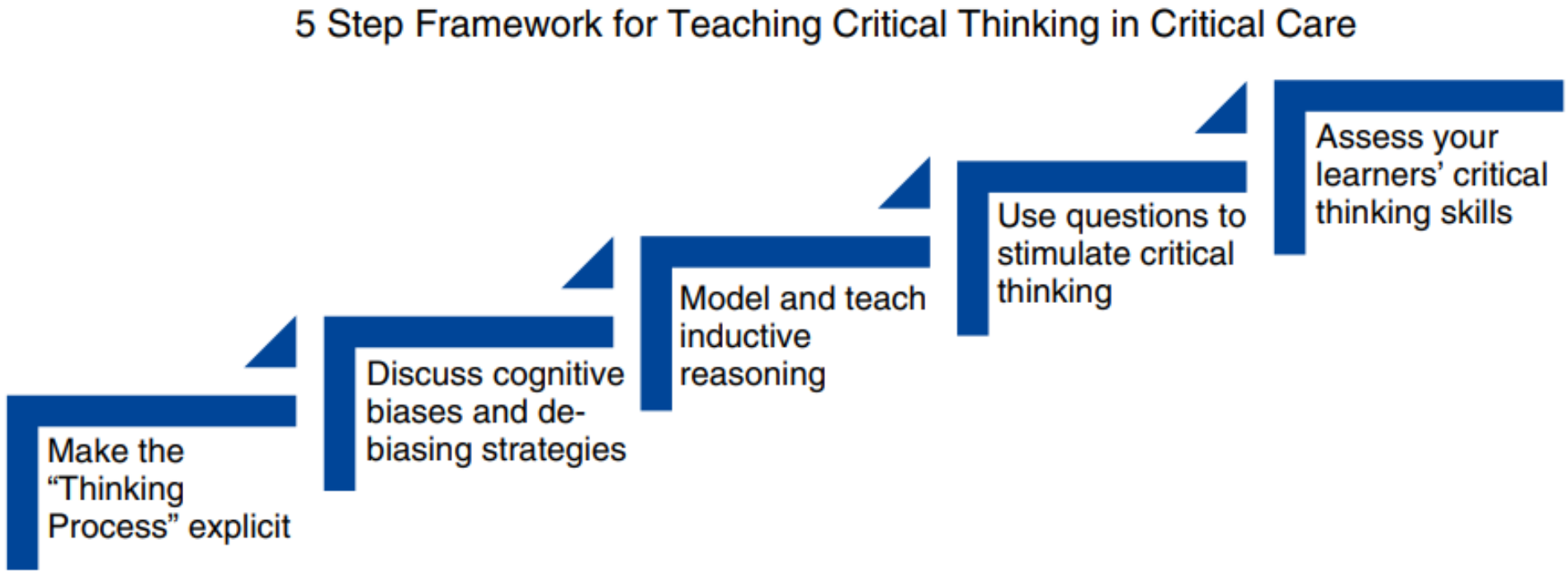
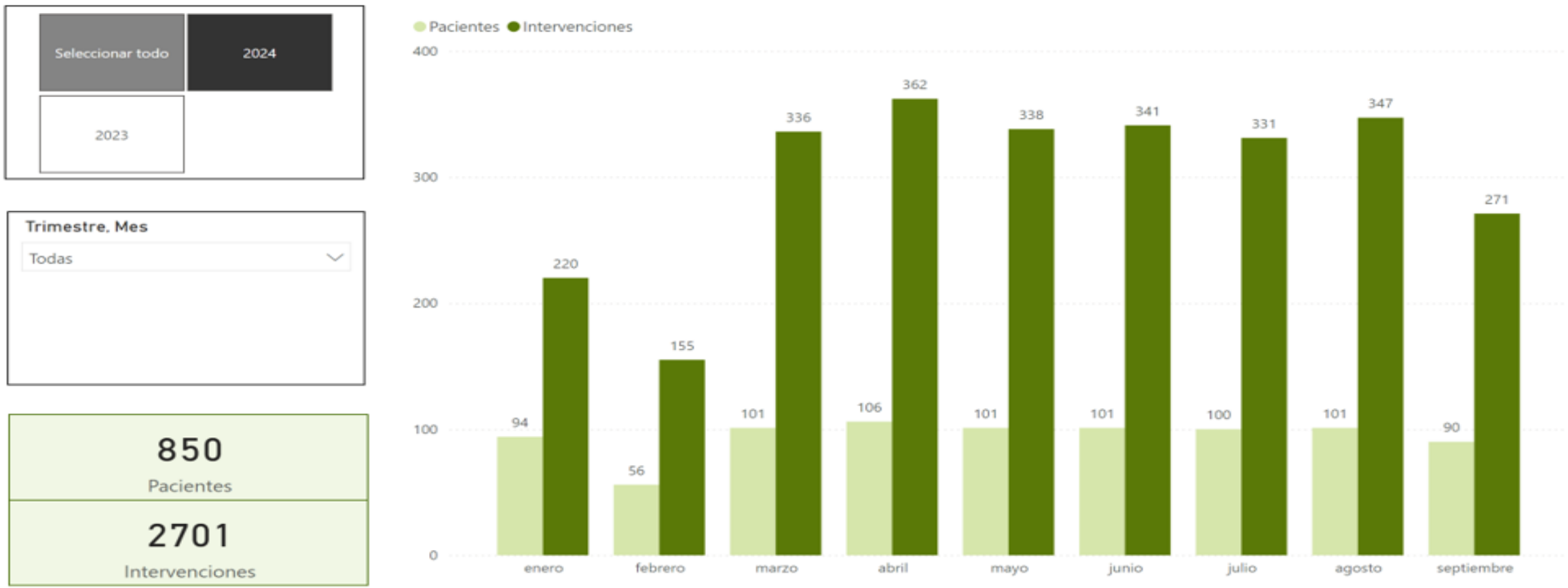


Figure 1. Five strategies to teach critical thinking skills in a critical care environment.

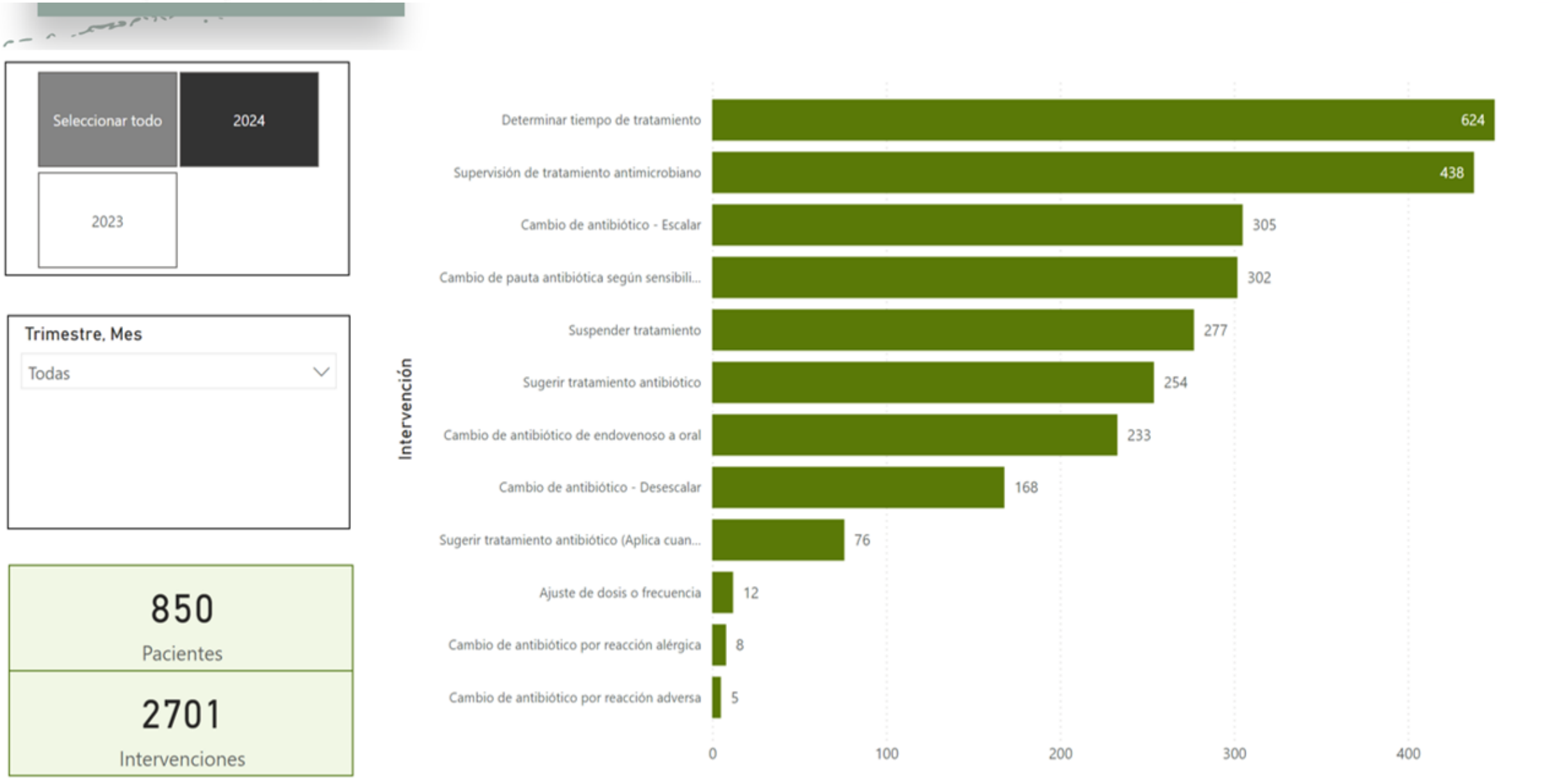
5. Resultados por Sedes institucionales: Sede Principal

5.1. Intervenciones Programa de Regulación y Optimización de Antimicrobianos

Durante el primer semestre y tercer trimestre del 2024, el programa de regulación y optimización del uso de antimicrobianos realizó 2701 intervenciones a 850 pacientes hospitalizados en la sede Principal



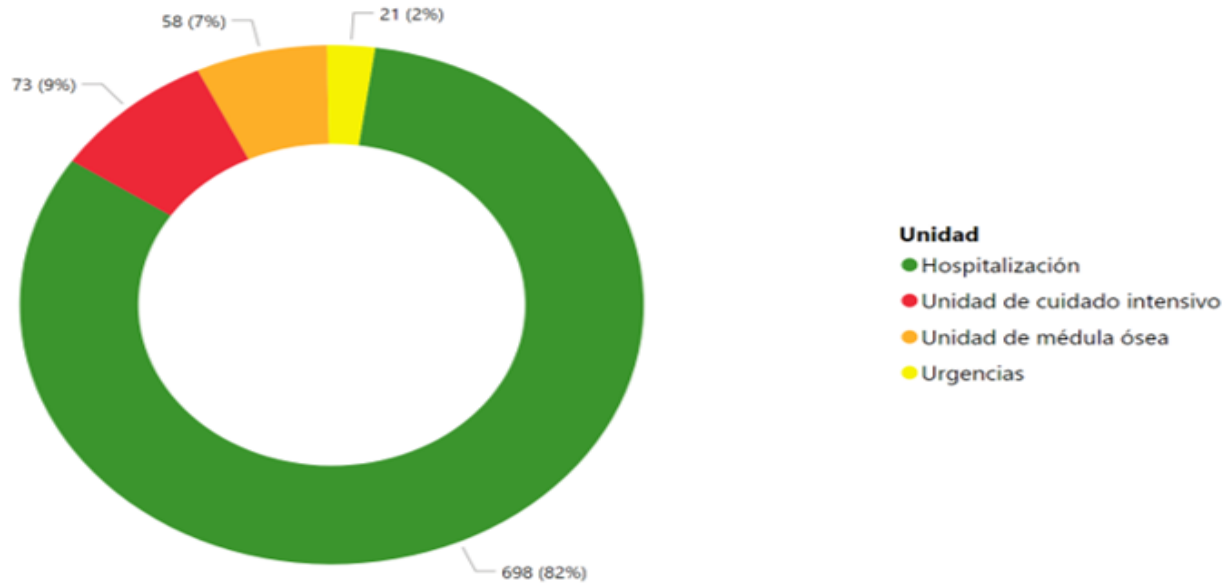
Gráfica 44. Número de intervenciones realizadas por el Programa de Regulación y Optimización del uso de Antimicrobianos. Sede Principal. Fundación Valle del Lili. Enero - Septiembre 2024.



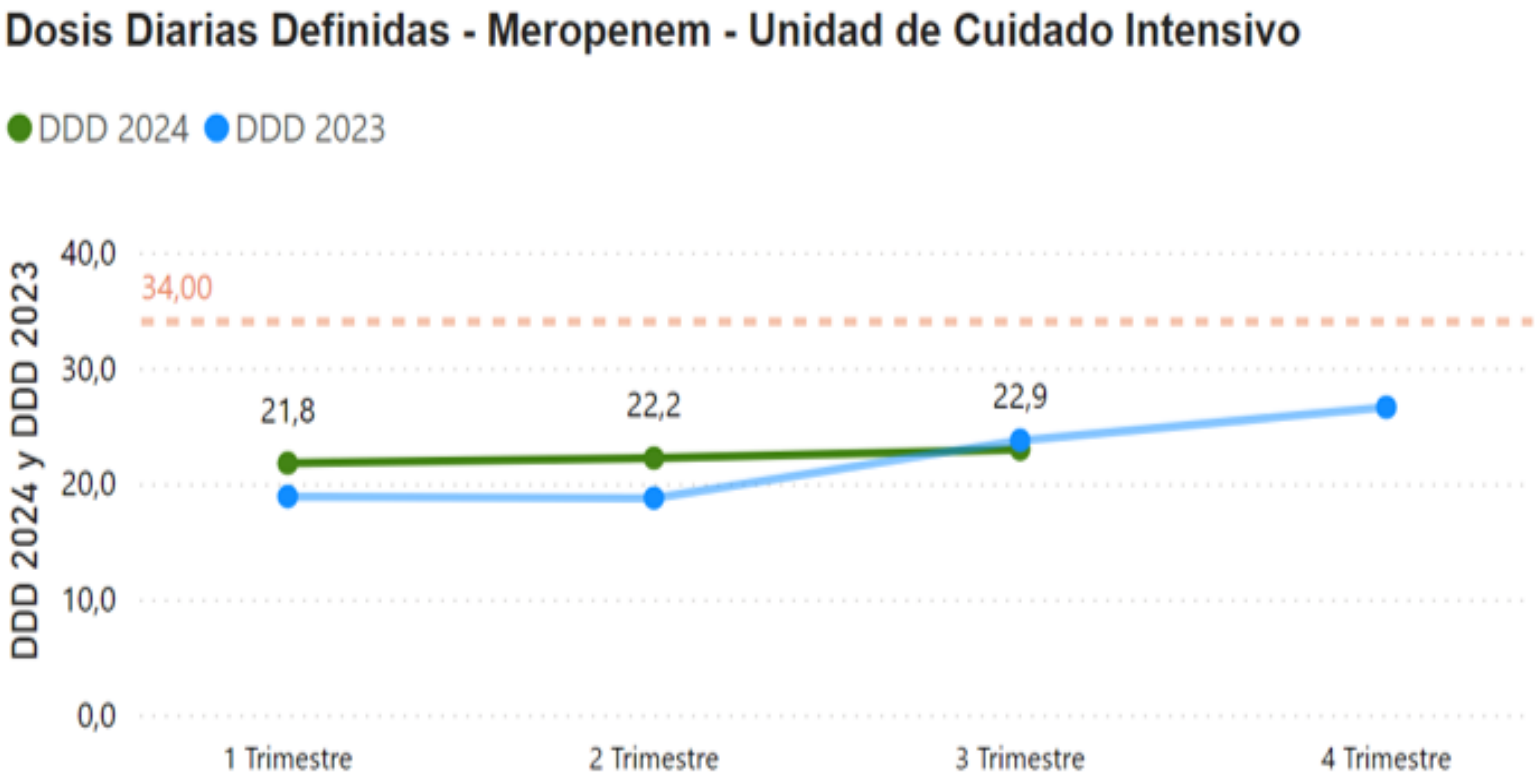
Gráfica 45. Tipo de intervenciones realizadas por el Programa de Regulación y Optimización del uso de Antimicrobianos. Sede Principal. Fundación Valle del Lili. Enero - Septiembre 2024.

5.3. Resultados por Unidades

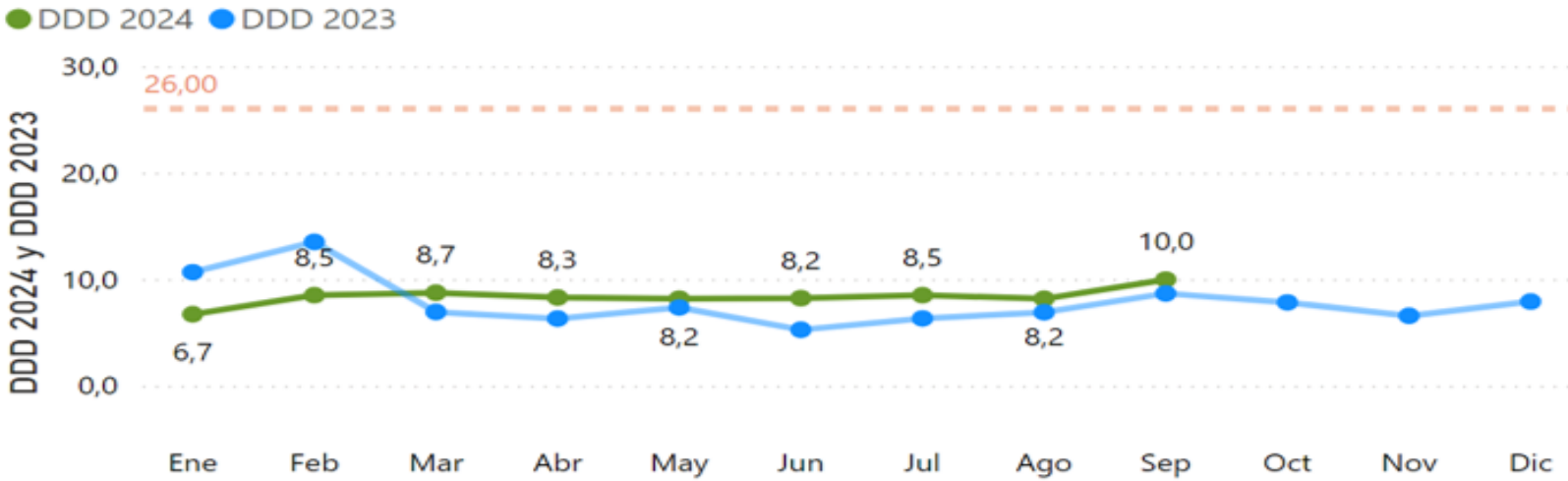
Durante el primer semestre y tercer trimestre del año 2024, en la sede Principal se realizaron 2701 intervenciones, distribuidas de la siguiente la manera; 698 [82%] de los pacientes intervenidos se encontraban internados en la unidad de hospitalización, 73 [9%] en la unidad de cuidado intensivo, 58 [7%] en la unidad de médula ósea y 21 [2%] en urgencias.



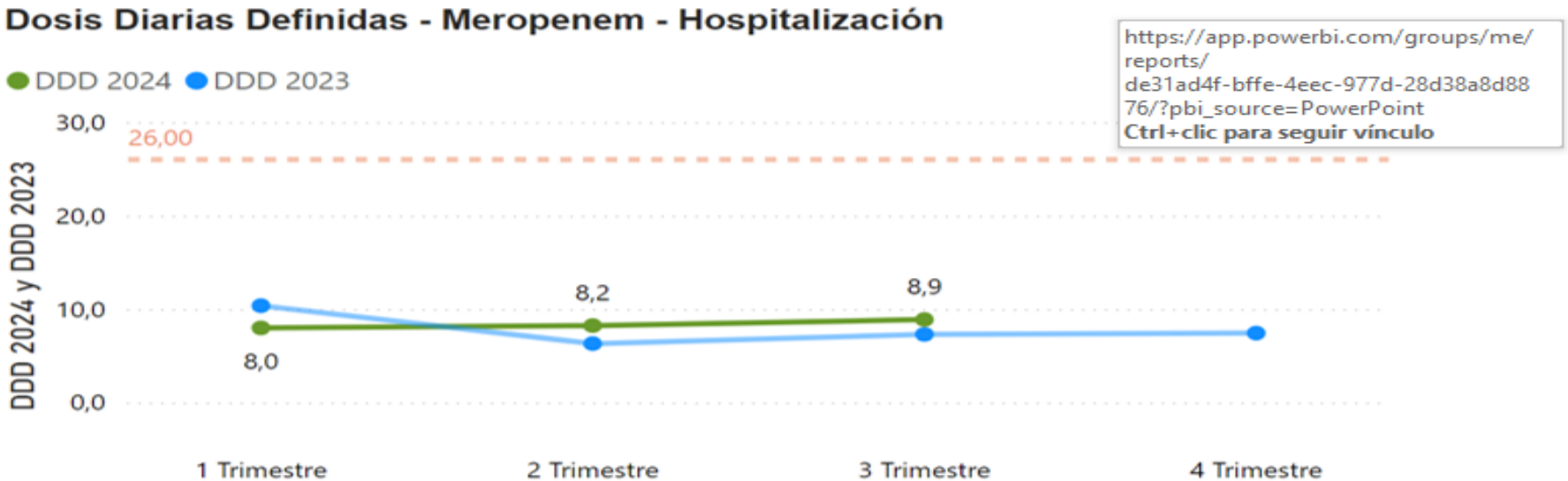
Gráfica 58: Frecuencia intervenciones por unidades. Programa de Regulación y Optimización del uso de Antimicrobianos. Sede Principal. Fundación Valle del Lili. Enero – Septiembre 2024.



Gráfica 68: Dosis diaria definida – Meropenem. Unidad de cuidado intensivo. Fundación Valle del Lili, Sede Principal. Evaluación por trimestres 2024.



Gráfica 87: Dosis diaria definida – Meropenem. Hospitalización. Fundación Valle del Lili, Sede Principal. Enero - Septiembre 2024.

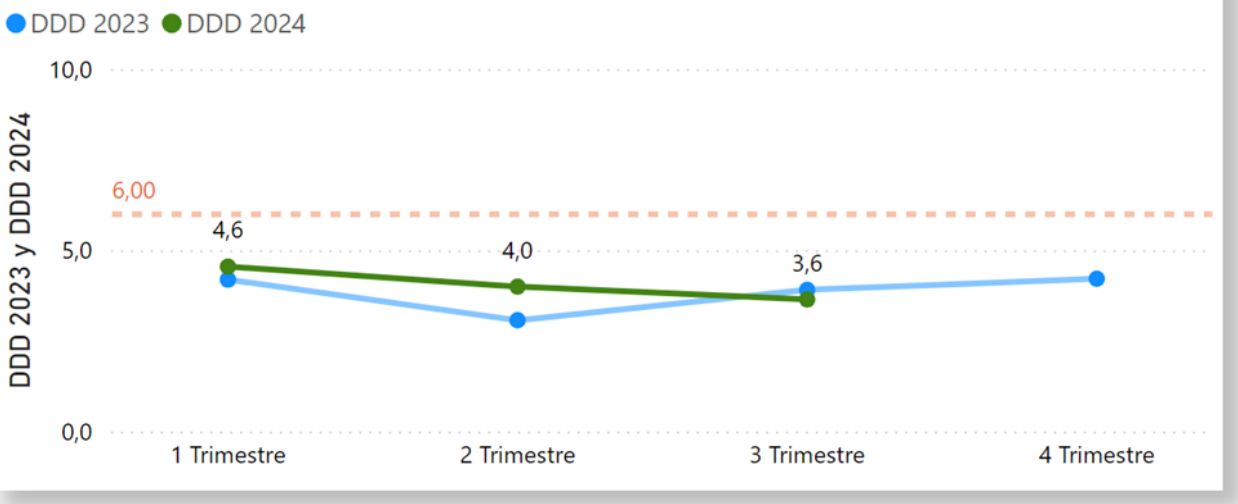


Gráfica 88: Dosis diaria definida – Meropenem. Hospitalización. Fundación Valle del Lili, Sede Principal. Evaluación por trimestres 2024.

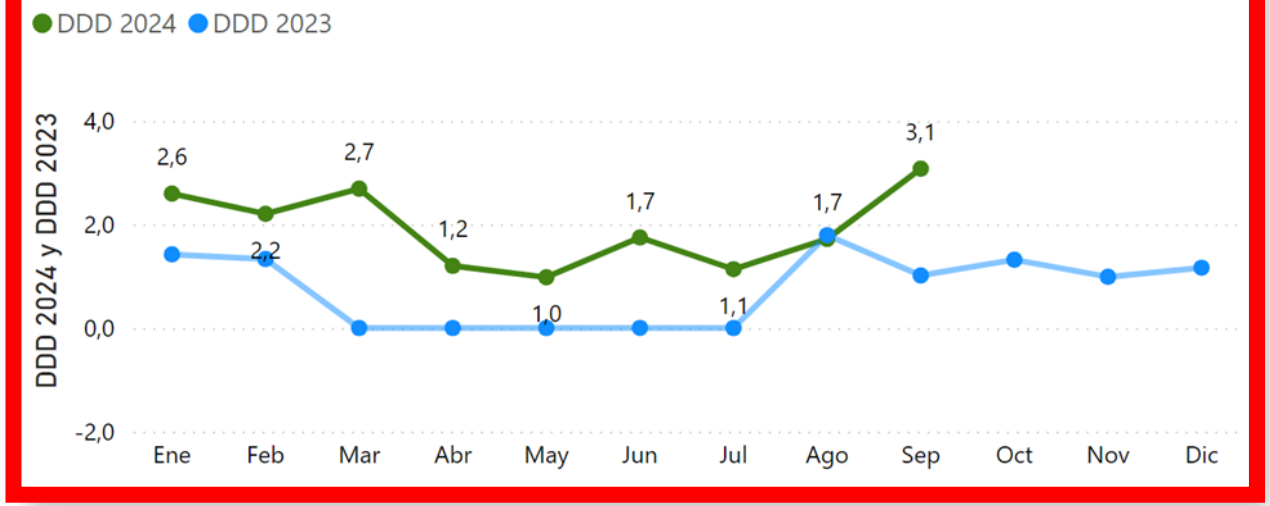
DDD - Hospitalización

Año, Trimestre
Todas

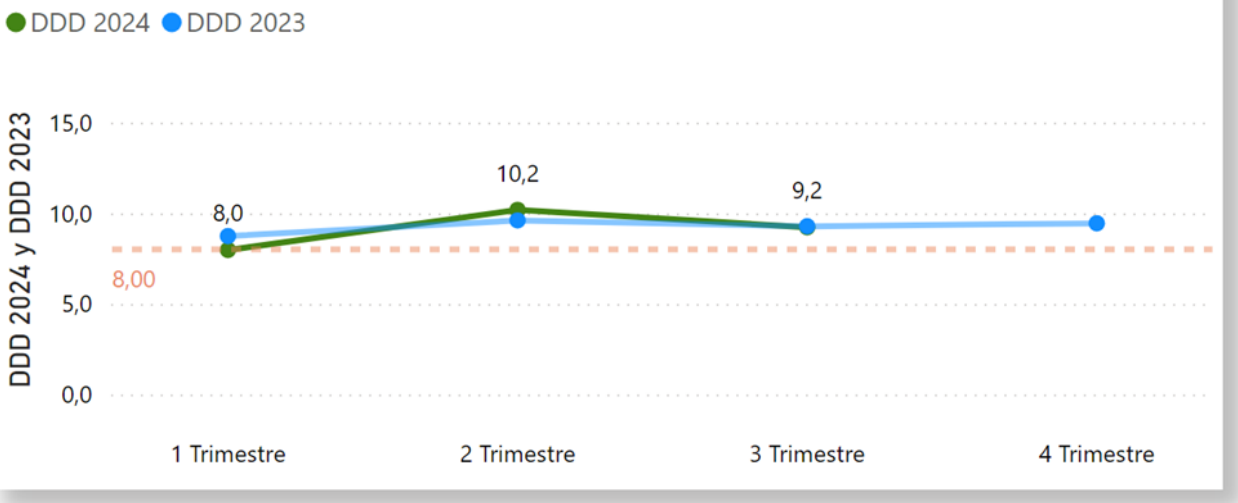
Dosis Diarias Definidas - Cefepime - Hospitalización



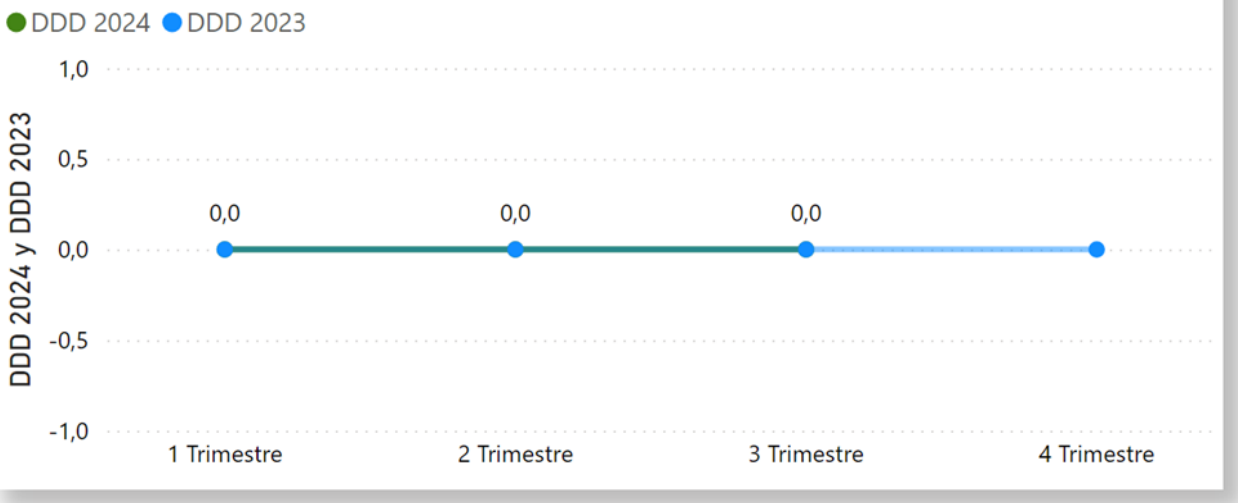
Dosis Diarias Definidas - Ceftazidima/Avibactam - Hospitalización

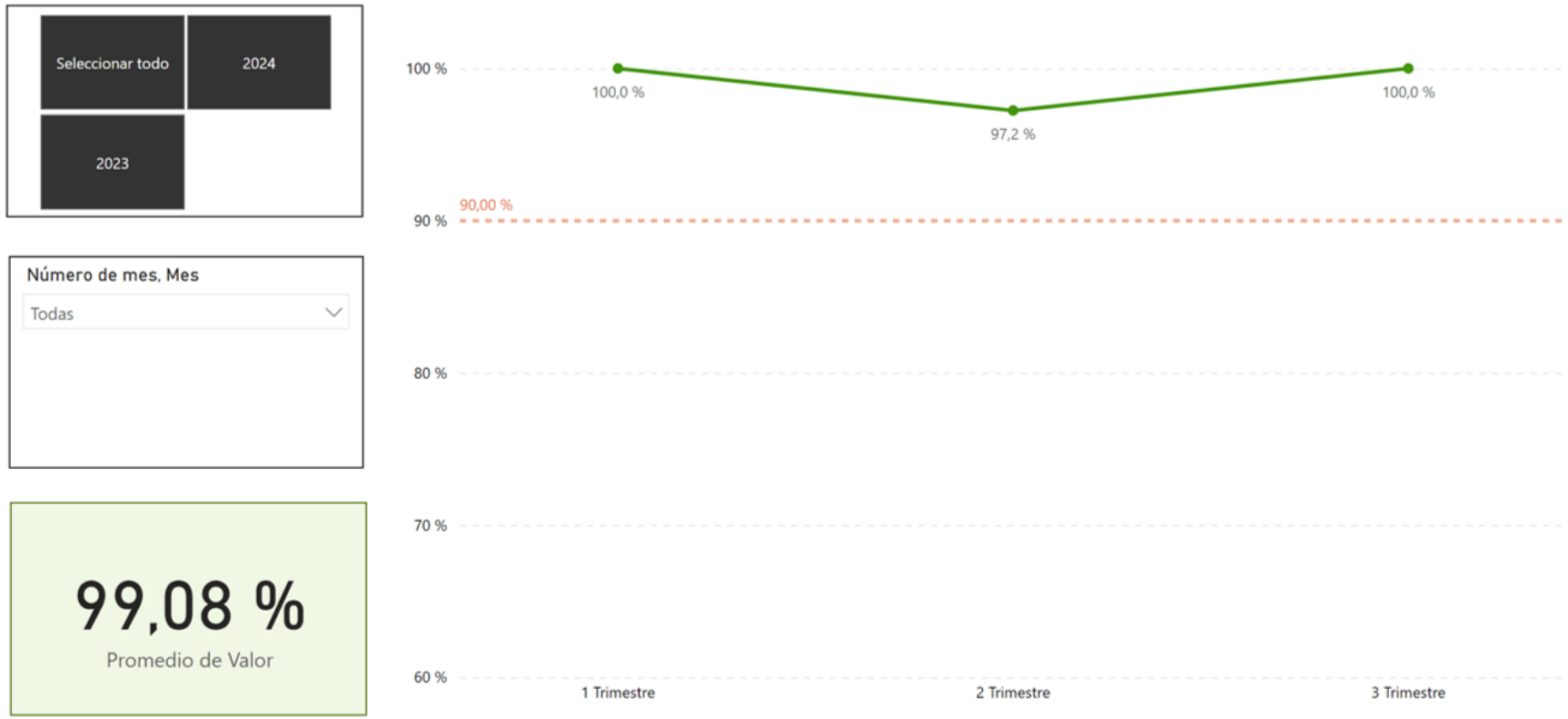


Dosis Diarias Definidas - Ceftriaxona - Hospitalización



Dosis Diarias Definidas - Doripenem - Hospitalización





Gráfica 57: Indicador de proporción de pacientes con neutropenia febril hospitalizados en la unidad de cuidado intensivo con valoración por infectología. Sede Principal. Programa de Regulación y Optimización del uso de Antimicrobianos. Fundación Valle del Lili. Evaluación por trimestres 2024.

Table 2
Suggested prophylaxis by treatment regimen

Disease	Treatment Regimen	Prophylaxis Recommended?				
		Bacterial	CMV	HSV/VZV	IFI	PCP
AML	AML induction and consolidation	■		■	■	▒
	Azacitidine, Decitabine	▒		▒	■	▒
	Venetoclax + Azacitidine	■		▒	■	▒
ALL	ALL induction and consolidation	■		■	■	■
	ALL induction and consolidation + TKI	■		■	■	■
	Imatinib + steroids	▒		▒	■	■
	Dasatinib + steroids	▒		▒	■	
	Blinatumomab	▒		▒	■	
	CD19 CAR-T	■		■	■	
MDS	Azacitidine, Decitabine	▒		▒	▒	
CLL	Purine analogues (FCR)	▒		■		■
	Chlorambucil + Rituximab					
	Bendamustine + Rituximab					
	Ibrutinib			■		■
	Venetoclax			▒	▒	▒
	Idelalisib	▒	[b]			■
	Alemtuzumab	■	[b]	■		■
CML	Imatinib			▒		
	Dasatinib			▒		
High Grade Non- Hodgkin Lymphomas	R-CHOP/CHOP	▒				
	R-DHAP, R-ICE	▒				
	DA-R-EPOCH	▒				
	R-HyperCVAD	▒				
	CD19 CAR-T	■		■		
	Ibrutinib			■		■
Hodgkin	ABVD	▒				
	A-AVD (Brentuximab + AVD)	▒				■
	Escalated BEACOPP	▒				
	Brentuximab	▒	[a]			[a]
	Nivolumab/Pembrolizumab	▒				
Low Grade Non- Hodgkin Lymphomas	Rituximab monotherapy					
	R-CVP	▒				
	BR	▒				
Myeloma	RD	▒				▒
	RVD/KRD	▒		■		▒
	Lenalidomide maintenance	▒	[a]			[a]
	Bortezomib maintenance	▒	[a]	■		[a]
	Daratumumab	▒				▒
	VDT-PACE	▒				▒
MPN	Ruxolitinib			■		

■	▒	
Recommended	Consider for multiply relapsed disease or susceptible host[c] during periods of neutropenia	Not recommended

[a] Prophylaxis recommended for maintenance post–auto-HCT in seropositive patients.
[b] Monitoring recommended.
[c] Susceptible host includes older age, poor nutrition, indwelling catheters or mucositis, prior chemotherapy-induced febrile neutropenia.

- Profilaxis
  - Ivermectina 1,3,14
    - Universal
  - Aciclovir/Valaciclovir
    - Universal
  - Letermovir
    - No implementada
  - Quinolona
    - Suspendida
      - Clorhexidina
  - Azoles
    - Posaconazol
    - Fluconazol
    - Isavuconazol****

FQR infections associated with worse outcomes

280/2306 (12%) had GNR BSI within 100 days of alloSCT

Single-center study with institutional levofloxacin ppx

Followed 2003-2012: BSI rates increased until peak in 2009, then decreased

88/255 (35%) with AST had FQ-R

By organism: 72% *E coli*, 37% *K pneumoniae*, and 42% PsA were FQR

30d mortality: 21% FQR vs. 10% FQS:
Adjusted* HR 2.1, 95% CI 1.1 to 4.2

*Age, severity of illness, conditioning

Possible explanations:
-Delayed effective antibiotics
-More PsA in the FQR group
-Residual confounding

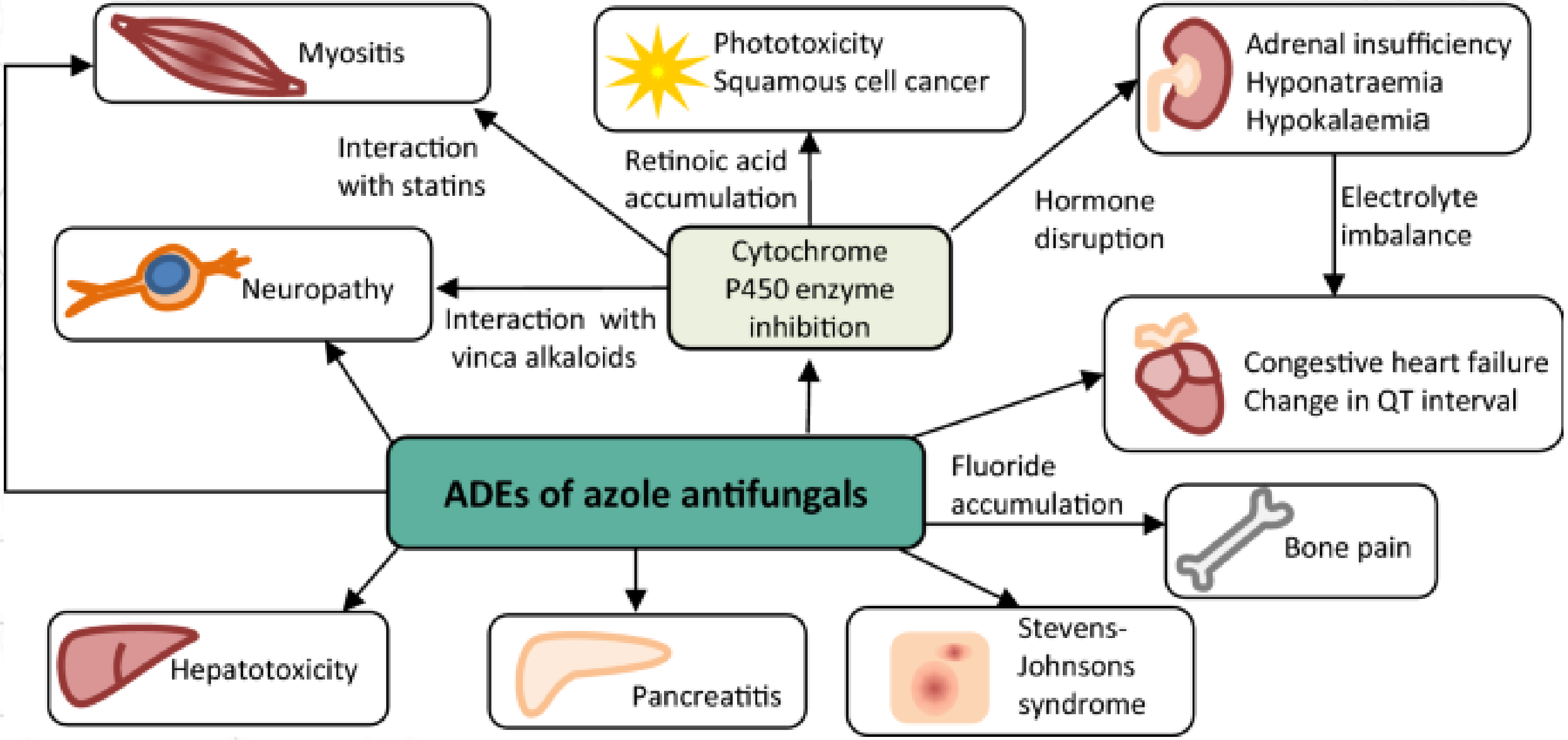
Miles-Jay A et al. 2015

UCSF

DDI:

- Aumento de aprobaciones de medicamentos oncológicos → aumento de interacciones medicamentosas, interacciones medicamentos-alimentos y medicamentos-herbales.
- Cada medicamento aumenta el riesgo de interacciones en un 40%.
- Otros factores: edad avanzada, múltiples comorbilidades y la farmacogenómica.

DeRemer, PharmD, Bcop, Fccp, Fhopa, D. (2022). Clinically Relevant Drug Interactions in the Cancer Setting. *Journal of the Advanced Practitioner in Oncology*.



Causes of Persistent or New Neutropenic Fever

1. Resistant occult new bacterial infection (e.g., VRE, ESBL)
2. Failure of antibiotics/antifungals given for prior infection
3. Chemo-induced mucosal injury (endotoxemia)
4. Non-bacterial infection (virus, AFB, toxoplasmosis)
5. Malignancy-related fevers, Sweet syndrome
6. Superinfection with MDR fungi
7. Drug fever
8. Cytokine release syndrome (CARTT)
9. Engraftment syndromes, acute GvHD
10. HLH
11. Transfusion fever
12. Other uncommon, including combinations of the above

- Fiebre.....
  - Estadificación riesgo
  - Cuantificación CAN
    - Tiempo neutropenia
    - Profilaxis
    - Colonización
    - Comorbilidades
    - Evaluación clínica
- Estudios diagnósticos
  - Valoración dinámica
    - GA, Acido láctico
    - Pruebas moleculares
    - Descalonamiento;
      - Terapia dirigida

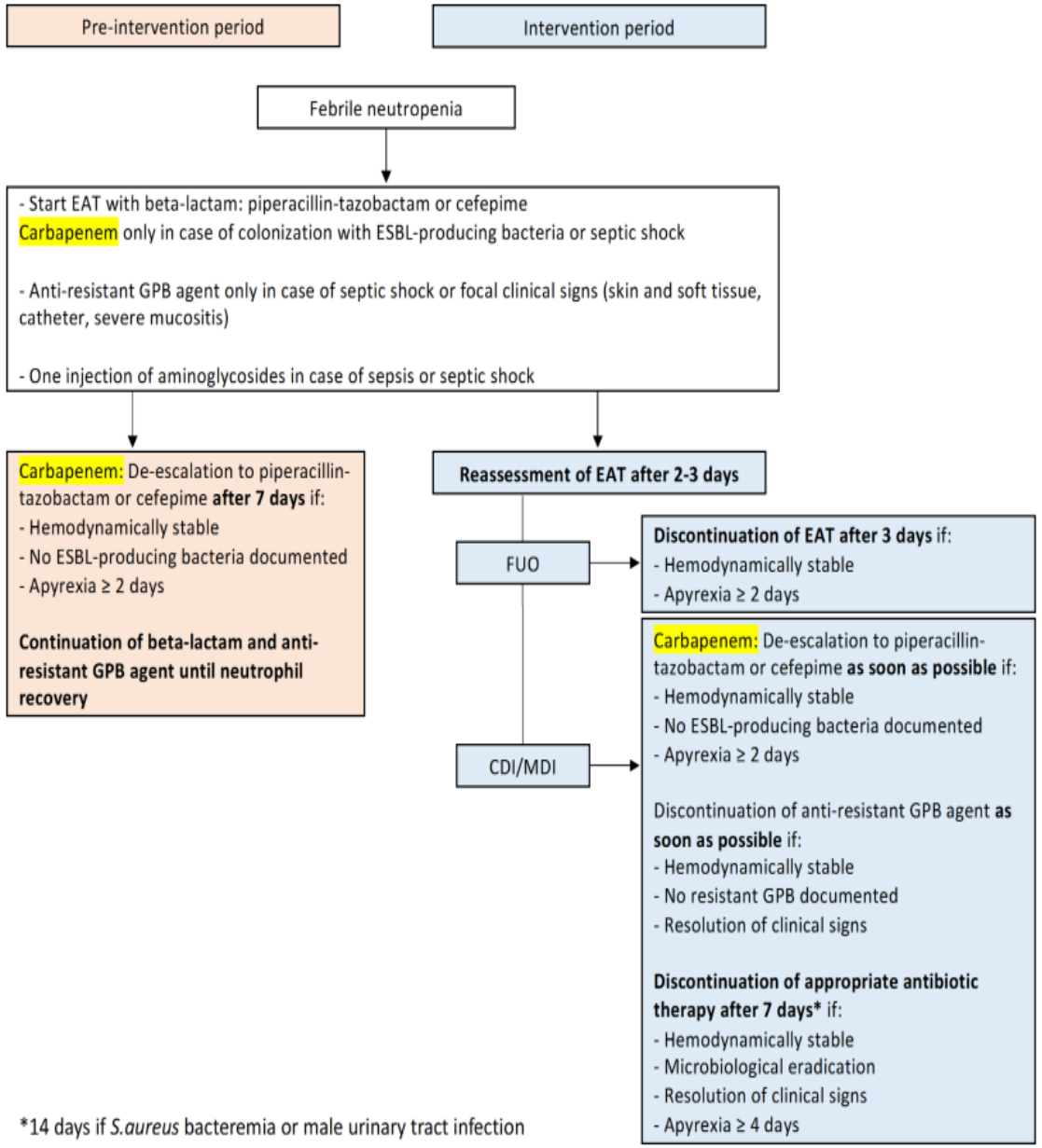


Fig. 1 Summary of febrile neutropenia guidelines during the pre-intervention and the intervention periods. *Abbreviations*: EAT: Empirical antibiotic therapy; ESBL: Extended-spectrum beta-lactamase; GPB: Gram-positive bacteria

Stewardship Challenges for Molecular Infectious Disease Diagnostics

- Detection of nucleic acid ≠ presence of viable pathogen ≠ etiology of disease.
  - Asymptomatic colonization (eg: *C. difficile*, Group A Strep)
  - Prolonged shedding (eg: rhinoviruses, *Mycoplasma*)
  - Reactivation (eg: EBV, CMV)
  - Chromosomal integration (eg: HHV-6)
  - Contamination (eg: dirty catch urine cx, skin contam of blood cx)

Stewardship Challenges for Syndromic Multiplex Testing

- Golden Rules of Diagnostics Stewardship:
  - Only send the test if the result will change clinical management
  - Only send the test if you know what to do with the result
- But what about multiplex panels…?

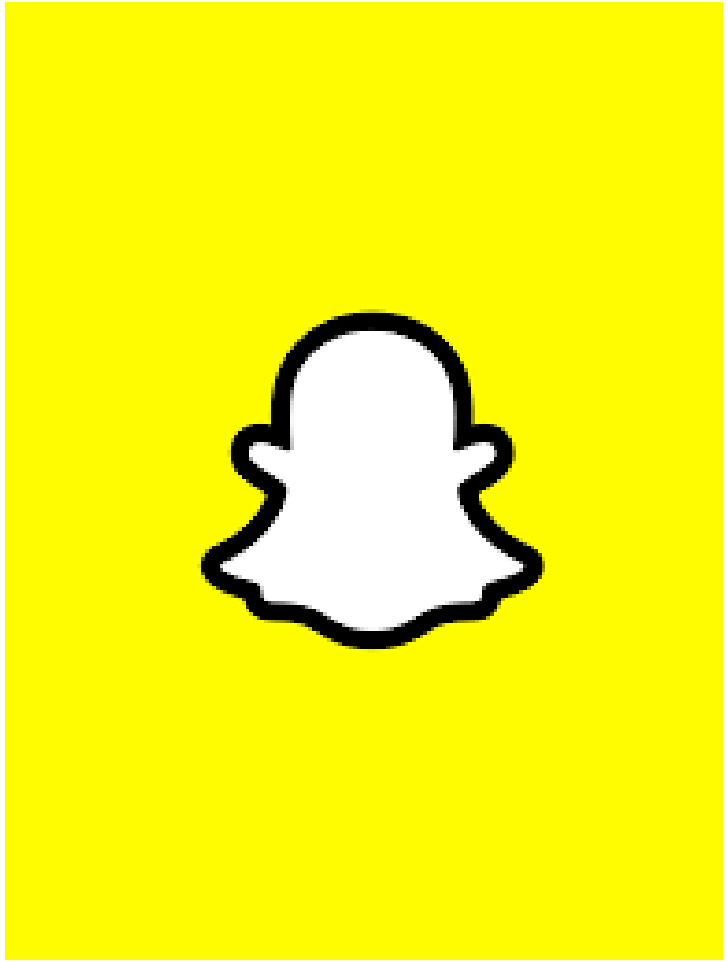
Vs.

- **Beware the detection of a target on a panel you would not have otherwise tested for or that does not fit the clinical scenario**
  - Incidentally detected target with low pre-test probability may be more likely to be a false positive and act as a red herring

Panel FilmArray Biofire Hemocultivos; guías institucionales

Indicaciones
- Paciente con un hemocultivo positivo para bacilos Gram negativos, dos hemocultivos positivos para cocos Gram positivos con MENOS DE 18 HORAS DE INCUBACION o un hemocultivo positivo para levaduras en estado de sepsis o choque séptico - Bacteriemia o fungemia con foco intraabdominal o desconocido - Paciente sin mejoría a pesar de haber iniciado el tratamiento antimicrobiano empírico inicial - Paciente inmunocomprometido ESPECIALMENTE NEUTROPENICO CON SIGNOS DE INESTABILIDAD CLINICA - Varias morfologías visibles en la coloración de Gram. Se procesa el panel molecular a partir de la primera botella positiva. - Otras condiciones no incluidas en este apartado, tomar la decisión en conjunto con el servicio de Infectología - PACIENTES COLONIZADOS POR GERMENES RESISTENTES CON INESTABILIDAD HEMODINAMICA A PESAR DE RECIBIR MEROPENEM
Exclusiones
- Hemocultivos con preliminaries negativos - Hemocultivos positivos desde hace más de 24 horas. - Botellas positivas que fueron refrigeradas o congeladas. - Botellas positivas, sembradas a partir de otros líquidos estériles.

Pacientes hematológicos	Pacientes hematológicos colonizados	Pacientes hematológicos con bacteriemia	Pacientes hematológicos colonizados con bacteriemia; KPC
21	2	5	1



Caso clínico

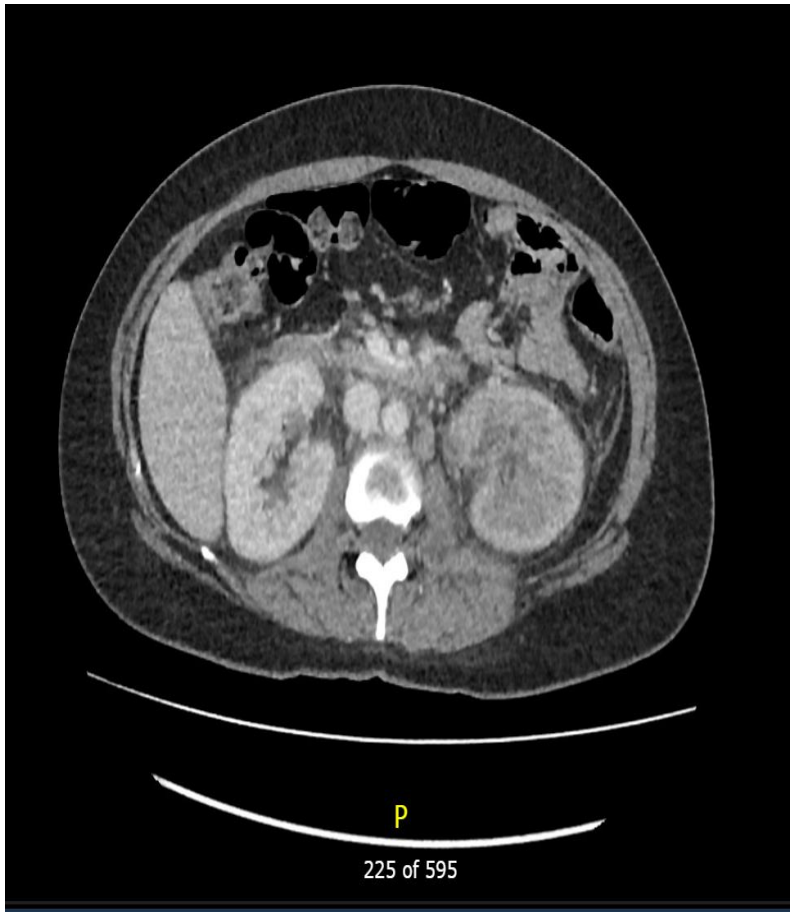
Paciente femenina 41 años

- Antecedentes:
  - cáncer de tiroides
  - trastorno de ansiedad trastorno limítrofe

- DX
  - LEUCEMIA MONOBLASTICA/MONOCITICA AGUDA - SARCOMA MIELOIDE
    - PROTOCOLO 7+3 + Midostaurina por mutación FLT3 ITD
    - Inducción: 11.05.2024

Caso clínico

- 04.05.2024
  - Pielonefritis ?
  - Cefepime
    - El riñón izquierdo se encuentra aumentado de tamaño
      - Disminución difuso en su patrón de realce.
      - Realce urotelial
        - » estriación y aumento en la densidad de la grasa perinéfrica



EXPOSICIÓN

- alta prevalencia de BGNMR:
  - ingreso actual en centro de agudos > 5d
  - hospitalización previa (3m) > 5d
  - residencia
- procedimientos invasivos (catéteres)

INMUNIDAD DE COLONIZACIÓN

- exposición previa a ATB >3 d (past 3m)
- paciente frágil (Charlson)
- stress agudo (pancreatitis, politra, cir mayor)
- Quimio & radioterapia

SELECIÓN

- tratamiento antibiótico actual

⬇

- común a todos los BGN-MR
- reducido VPP

Factores que determinan la colonización por BGN-MR

El factor de riesgo más importante de INFECCIÓN por un BGN-MR es la colonización intestinal de alto grado = alto VPN

Soriano A. 2023

Klebsiella pneumoniae ssp pneumoniae

Microorganismo productor de betalactamasas de espectro extendido (BLEE)..

Antibiograma	CMI	
Amicacina	<=1	Sensible
Ampicilina-Sulbactam	>=32	Resistente
Aztreonam	16	Resistente
BLEES	Positivo	Pos
Cefepime	>=32	Resistente
Ceftazidima	32	Resistente
Ciprofloxacina	1	Resistente
Ertapenem	<=0,12	Sensible
Imipenem	<=0,25	Sensible
Meropenem	<=0,25	Sensible
Piperacilina/Tazobactam	<=4	Sensible
TIGECICLINA	<=0,5	Sensible
Ceftazidima/Avibactam	0,25	Sensible
Ceftalozano/Tazobactam	<=0,25	Sensible

Caso clínico

- 28.05.2024 paciente presenta estado de choque séptico y bacteriemia por BGN en presencia de Meropenem

HEMOCULTIVO

INFORME PRELIMINAR HEMOCULTIVO	*	27/may/2024 14:23	28/may/2024 02:23

Tipo de muestra: SANGRE SET

Método de Recolección: venopunción MSD
Hemocultivo positivo para bacilos Gram negativos, a las 9 horas y 55 minutos de incubación.

HEMOCULTIVO 2

INFORME PRELIMINAR HEMOCULTIVO 2	*	27/may/2024 14:23	28/may/2024 01:52

Tipo de muestra: SANGRE SET

Método de Recolección: CVC subclavio derecho
Hemocultivo positivo para bacilos Gram negativos, a las 9 horas y 34 minutos de incubación.

Profesional responsable: Yasneira Castro Saya c.c. 1053796916

Analito/Examen Test Name	Resultado Result	Unidades Units	Valor de Ref. Ref. Value	Muestra: Sample:	Validado en: Reported:
	MICROBIOLOGIA MOLECULAR				
Klebsiella oxytoca	No Detectado			28/may/2024 07:46	28/may/2024 09:04
Grupo Klebsiella pneumoniae	* Detectado			28/may/2024 07:46	28/may/2024 09:04
Proteus	No Detectado			28/may/2024 07:46	28/may/2024 09:04
Salmonella spp	No Detectado			28/may/2024 07:46	28/may/2024 09:04
Serratia marcescens	No Detectado			28/may/2024 07:46	28/may/2024 09:04
Genes de resistencia:					
CTX M BLEE Clase A	No Detectado			28/may/2024 07:46	28/may/2024 09:04
KPC: resistencia a carbapenemicos	* Detectado			28/may/2024 07:46	28/may/2024 09:04
NDM	* Detectado			28/may/2024 07:46	28/may/2024 09:04
IMP	No Detectado			28/may/2024 07:46	28/may/2024 09:04
OXA48	No Detectado			28/may/2024 07:46	28/may/2024 09:04
VIM	No Detectado			28/may/2024 07:46	28/may/2024 09:04
mcr1 Resistencia Colistina	No Detectado			28/may/2024 07:46	28/may/2024 09:04
mecA resistencia a meticilina	No Aplica			28/may/2024 07:46	28/may/2024 09:04
mecA/C y MREJ (MRSA)	No Aplica			28/may/2024 07:46	28/may/2024 09:04
vanA/B: resistencia a vancomicina	No Aplica			28/may/2024 07:46	28/may/2024 09:04
Levaduras:					
Candida albicans	No Detectado			28/may/2024 07:46	28/may/2024 09:04
Candida glabrata	No Detectado			28/may/2024 07:46	28/may/2024 09:04
Candida krusei	No Detectado			28/may/2024 07:46	28/may/2024 09:04
Candida parapsilosis	No Detectado			28/may/2024 07:46	28/may/2024 09:04
Candida tropicalis	No Detectado			28/may/2024 07:46	28/may/2024 09:04
Candida auris	No Detectado			28/may/2024 07:46	28/may/2024 09:04
Cryptococcus neoformans/gatti	No Detectado			28/may/2024 07:46	28/may/2024 09:04

SE SOLICITA PANEL MOLECULAR DE SEPSIS y se escala a Ceftazidima-Avibactam + Aztreonam

FUNDACIÓN VALLE DEL LILI
Excelencia en Salud al servicio de la comunidad

INFORME FINAL HEMOCULTIVO *

Tipo de muestra: SANGRE SET Sitio Anatómico:

Detección tipo carbapenemasa en panel molecular: KPC y NDM

Klebsiella pneumoniae

Antibiograma	CMI	
Amicacina	32	Resistente
Ampicilina-Sulbactam	>=32	Resistente
Aztreonam	>=64	Resistente
BLEES	Negativo	Neg
Cefepime	>=32	Resistente
Ceftazidima	>=64	Resistente
Ciprofloxacina	>=4	Resistente
Ertapenem	>=8	Resistente
Imipenem	>=16	Resistente
Meropenem	>=16	Resistente
Piperacilina/Tazobactam	>=128	Resistente
TIGECICLINA	1	Sensible
-		
Ceftazidima/Avibactam	>=16	Resistente
Ceftalozano/Tazobactam	>=32	Resistente

HEMOCULTIVO 2

INFORME PRELIMINAR HEMOCULTIVO 2 *

Tipo de muestra: SANGRE SET Sitio Anatómico:

Método de Recolección: CVC subclavio derecho
Hemocultivo positivo para bacilos Gram negativos, a las 9 horas y 34 minutos de incubación.

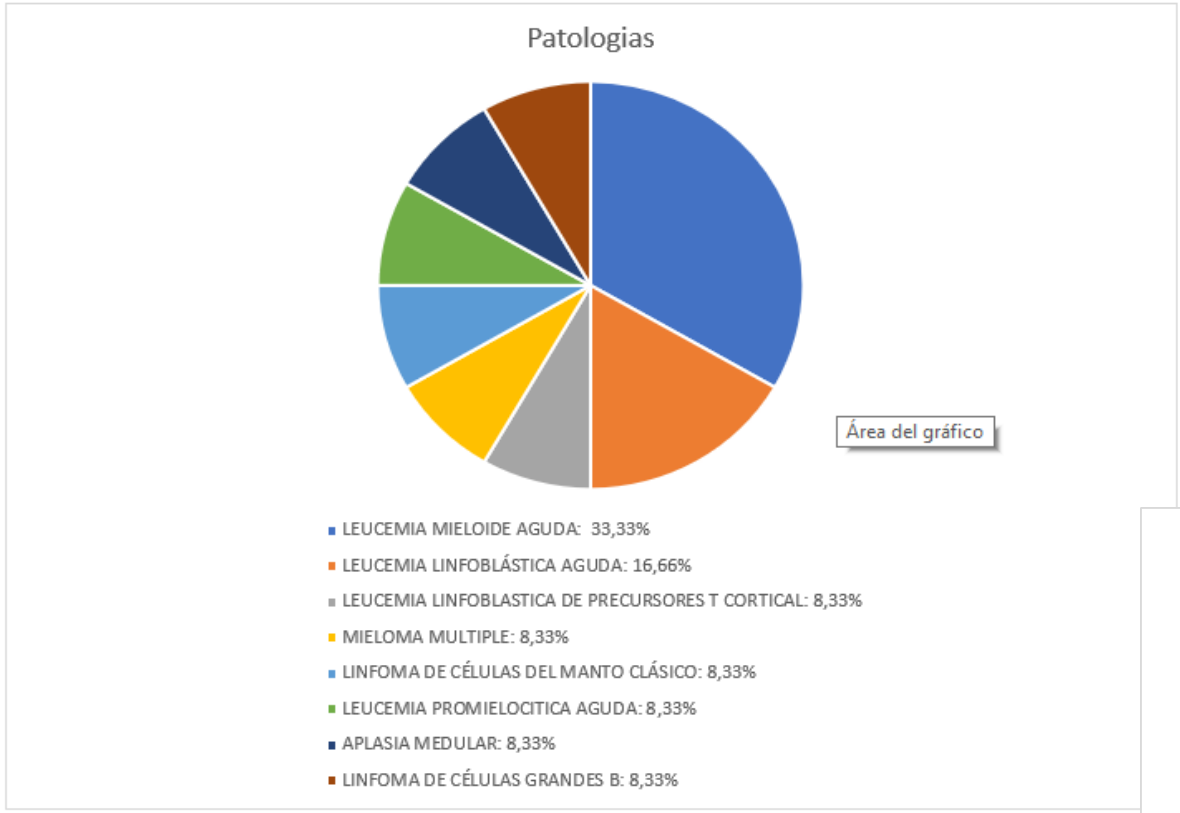
INFORME FINAL HEMOCULTIVO 2

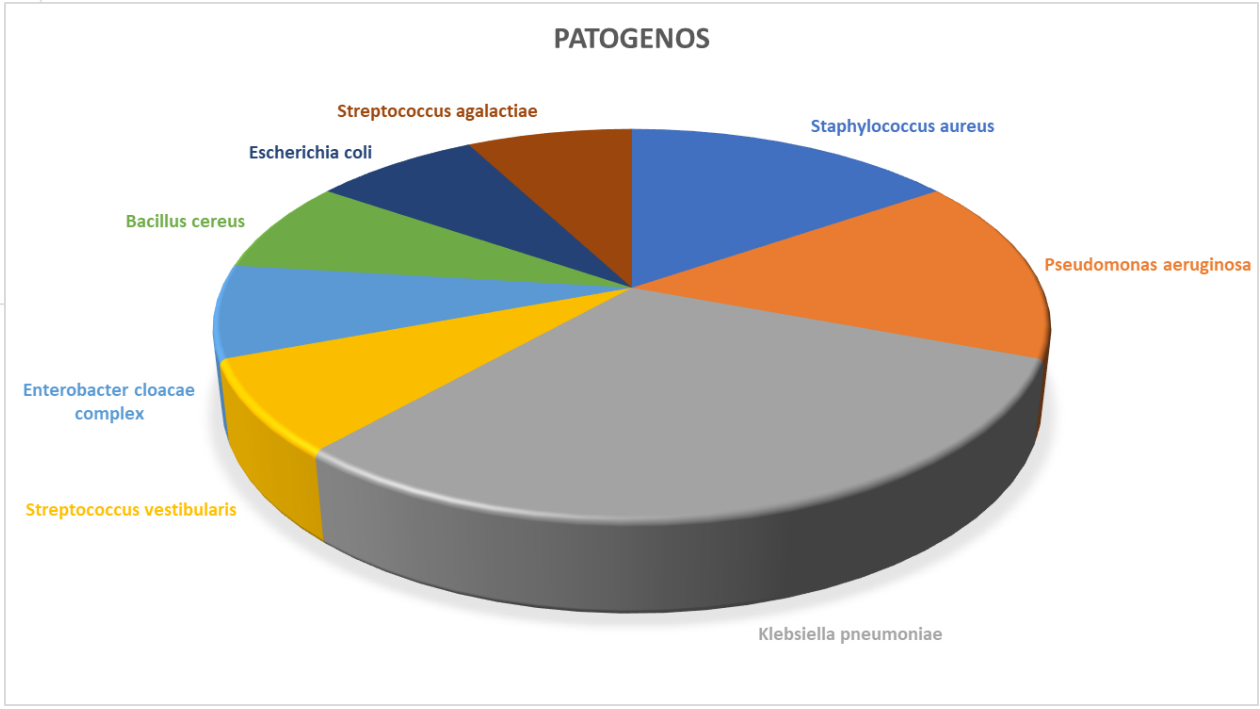
Tipo de muestra: SANGRE SET Sitio Anatómico:

El resultado de la prueba de sensibilidad puede consultarse en el resultado del otro hemocultivo positivo.

PACIENTES HEMATOLÓGICOS VALORADOS ÚLTIMOS 20 DIAS SERVICIO DE INFECTOLOGIA

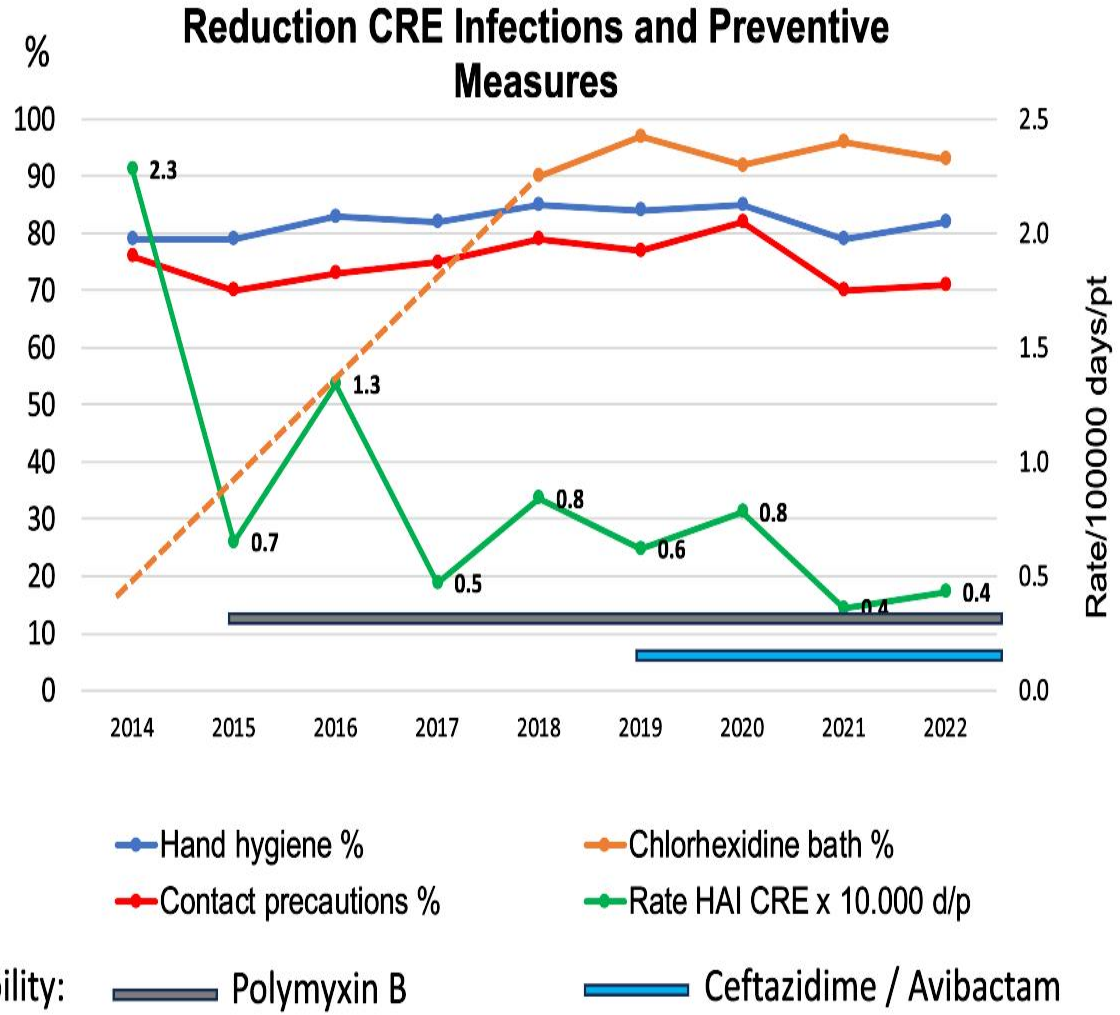
- Total: 12 Pacientes





FUNDACIÓN VALLE DEL LILI

RESULTS



Spearman's rank correlation test, reduction HAI CRE		
	Coef.	P value
Hand Hygiene	-0,24	0,533
Chlorexidine Bath	-0,67	0,048
Contact precautions	0,21	0,579

Rate HAI

Year	Rate x 10000 días pac	Decrease	p Value
2014	2,28		
2015	0,65	-1,63	0,015
2016	1,34	-0,94	1,000
2017	0,47	-1,82	0,003
2018	0,84	-1,44	0,061
2019	0,62	-1,67	0,011
2020	0,78	-1,51	0,037
2021	0,36	-1,92	0,001
2022	0,43	-1,85	0,003

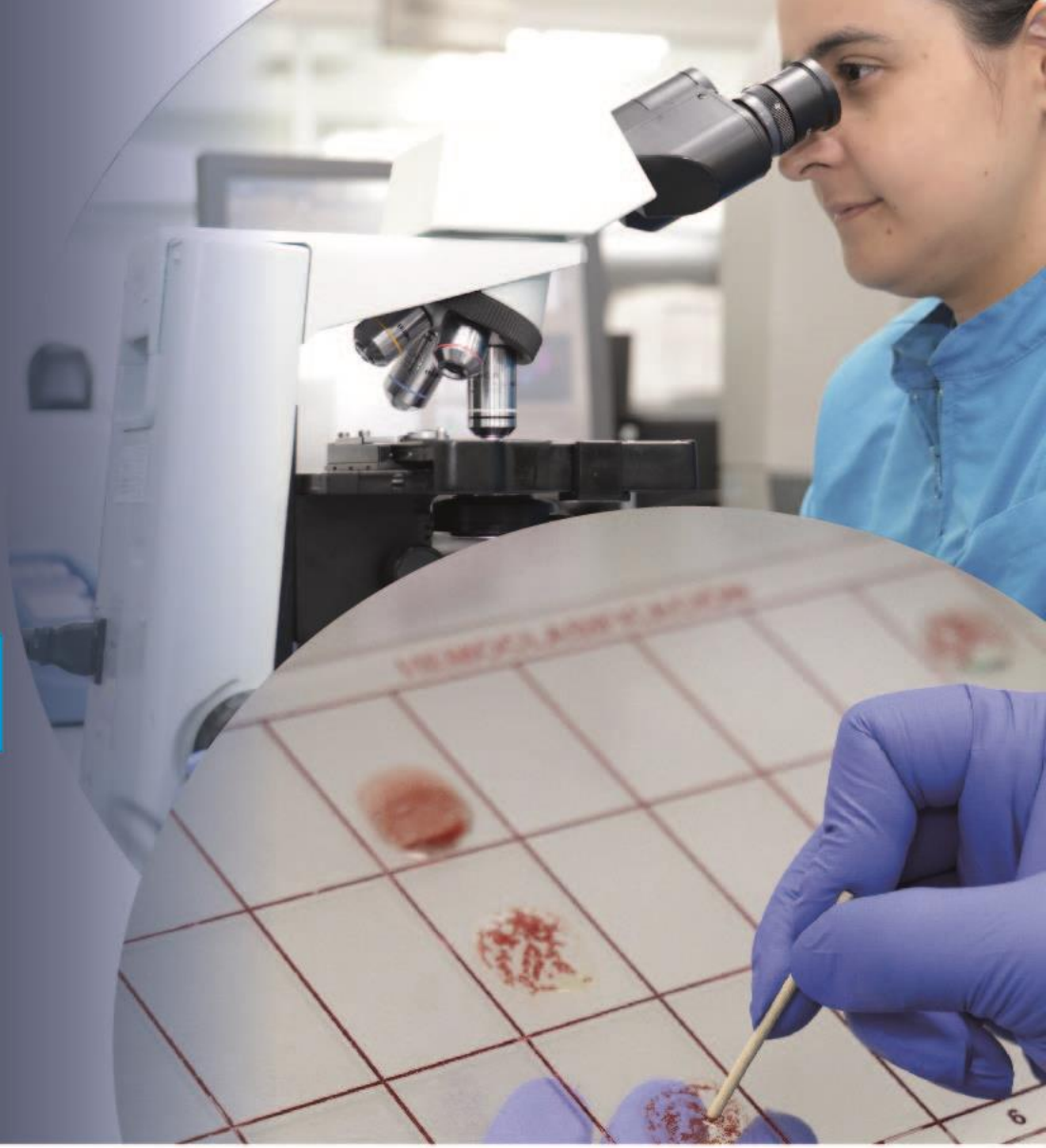
Registro neutropenias – TMO

- **Protocolo:** Eventos infecciosos de pacientes adultos con neutropenia absoluta receptores de trasplante de células hematopoyéticas en una clínica de alta complejidad en Colombia
- 2012 – 2022
- 221 Variables
- **850 Pacientes filtrados hasta la fecha**
  - Base de datos: **BD CLINIC**
  - **Subestudios hasta la fecha:** Real-world effectiveness of Posaconazole prophylaxis in preventing invasive fungal infections in recipients of allogeneic stem cell transplantation

Gracias

I Simposio en Optimización del uso de Antimicrobianos

Experiencias en PROA



Clínica El Rosario
Amor que Acompaña y Servicio que Alivia

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