TOXICITAT PER ANTIMICROBIANS EN EL PACIENT FRÀGIL

SOCIETAT CATALANA DE GERIATRIA I GERONTOLOGIA

Parc Sanitari Pere Virgili

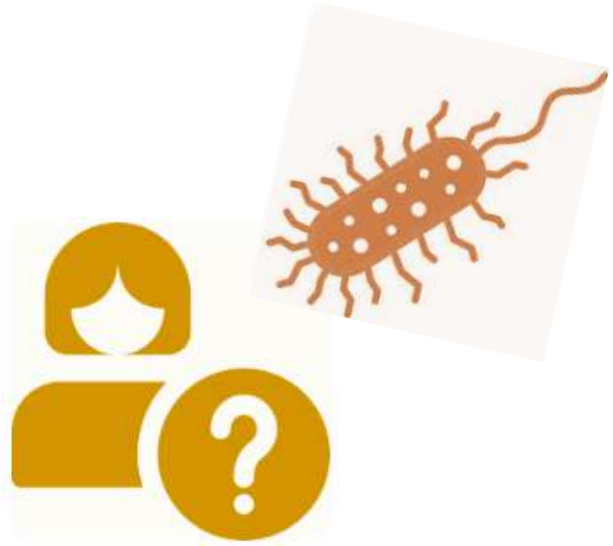
Daniel Sevilla-Sánchez, *PharmD*
Servei de Farmàcia. Comissió d'Infeccions
Parc Sanitari Pere Virgili

01 IMPACTE DEL PK-PD DELS ANTIBIÒTICS i LA SEVA TOXICITAT

02 TOXICITAT EN L'ECOLOGIA i MICROBIOMA DELS ANTIBIÒTICS

03 TOXICITAT ORGÀNICA DELS ANTIBIÒTICS

04 ESTRATÈGIES PER A LA PREVENCIÓ i MANEIG DE LA TOXICITAT DELS ANTIBIÒTICS



Drugs & Aging
https://doi.org/10.1007/s40266-023-01076-8

SYSTEMATIC REVIEW

Prevalence of and Risk Factors for Drug-Related Readmissions in Older Adults: A Systematic Review and Meta-Analysis

Narisha Prasad[1] · Edward C. Y. Lau[1] · Ilsa Wojt[1] · Jonathan Penm[1,2] · Zhaoli Dai[1,3] · Edwin C. K. Tan[1,4]

Table 5 Most implicated drug classes associated with ADR-related readmissions ($n = 2$)

Drug class	Study	No. of cases (% of total drug-related readmissions)	ADR-related readmission cause/clinical presentation (number of cases)	Implicated medications (number of cases)
Anticoagulants	Ekerstad et al., 2017	2 (15.4)	GI bleeding (1), abdominal pain (1)	Warfarin (2)
	Hauviller et al., 2016	12 (13.8)	GI bleeding (10), hematoma (3), anaemia (2), epistaxis (1)	Fluindione (4), heparin (4), enoxaparin (3), warfarin (1)
Antibiotics	Ekerstad et al., 2017	1 (7.7)	Fever and diarrhoea (1), diarrhoea (1), dyspnoea (2)	Clindamycin (1)
	Hauviller et al., 2016	4 (4.6)	–	Cotrimoxazole (1), norfloxacin (1), ceftazidime (1), linezolid (1)
Psychotropics	Ekerstad et al., 2017	3 (23.1)	Constipation (1), fall (2)	Citalopram (1), carbamazepine (1), duloxetine (1)
	Hauviller et al., 2016	6 (6.9)	–	Valproate sodium (1), bromazepam (1), tramadol (1), loxapine (1), benserazide (1), levodopa (1)
Chemotherapy agents	Hauviller et al., 2016	69 (79.3)	Aplasia, agranulocytosis, polyneuropathy, osteoporosis	–

- El 9% dels reingressos hospitalaris son a causa d'un ADR
- 4 famílies de fàrmacs es consideren de major risc:
  - Anticoagulants
  - Antibiòtics
  - Psicotròpics
  - QMT
- Aproximadament 1 de 4 o 5 es consideren potencialment evitables (22,2%)

Prasad N, et al. Prevalence of and Risk Factors for Drug-Related Readmissions in Older Adults: A Systematic Review and Meta-Analysis. Drugs Aging 2024;41(1): 1-11

SYSTEMATIC REVIEW *Age and Ageing* 2020; 1–11
doi: 10.1093/ageing/afaa188

In-hospital adverse drug reactions in older adults; prevalence, presentation and associated drugs—a systematic review and meta-analysis

EMMA L. M. JENNINGS[1,2], KEVIN D. MURPHY[3], PAUL GALLAGHER[1,2,†], DENIS O'MAHONY[1,2,†]

Table 3. Most frequently reported ADR culprit drugs

Rank	ATC 2nd level therapeutic subgroup	n	% (2385)	Most frequently reported pharmacological subgroup*—chemical subgroup** (drug name/chemical substance***)
1	Diuretics	473	19.83%	High ceiling diuretics 234 (9.81%)—sulfonamides 232 (9.73%) (furosemide 194), (bumetanide 32) Potassium sparing 47 (1.97%) Low ceiling diuretics 27 (1.13%)—thiazides 24 (1.01%), excl. Thiazides 13 (0.55%) Combinations 5 (0.21%)
2	Anti-bacterials for systemic use	354	14.84%	Beta-lactams penicillins 106 (4.44%) Cephalosporins 54 (2.26%) Macrolides, lincosamides and streptogramins 46 (1.93%)—macrolides 43 (1.80%) Quinolones 29 (1.22%)—fluoroquinolones 29 (1.22%) Imidazole derivatives, glycopeptides, polymixins 26 (1.09%) (metronidazole 16) Sulfonamides and trimethoprim 23 (0.96%) Aminoglycosides 6 (0.25%) Tetracyclines 1 (0.04%)
3	Antithrombotic agents	292	12.24%	Vitamin K antagonists 82 (3.44%) Heparin group 84 (3.52%) Platelet aggregation inhibitors 77 (3.23%) Enzymes 3 (0.13%)
4	Analgesics	260	10.90%	Opioids 205 (8.60%) – natural opium alkaloids 44 (1.84%) (Morphine 40), tramadol 28 (1.17%), phenylpiperidine derivatives 6 (0.25%), combination with non-opioid analgesics 4 (0.17%) Other analgesics and antipyretics 55 (2.31%)—anilides 34 (1.43%) (co-codamol 31)

- El 16 % dels pacients *ancians* ingressats pateixen ≥1 ADR significant
- 4 famílies de fàrmacs es consideren de major risc:
  - Diurètics (19,8%)
  - ATB (14,8%)
  - Anticoagulants (12,2%)
  - Analgèsics (10,9%)
- La majoria dels ADR es consideren potencialment prevenible (55 – 95%)

Jennings ELM et al. In-hospital adverse drug reactions in older adults; prevalence, presentation and associated drugs—a systematic review and meta-analysis. Age Ageing 2020; 49(6): 948-958

01 **IMPACTE DEL PK-PD DELS ANTIBIÒTICS i LA SEVA TOXICITAT**

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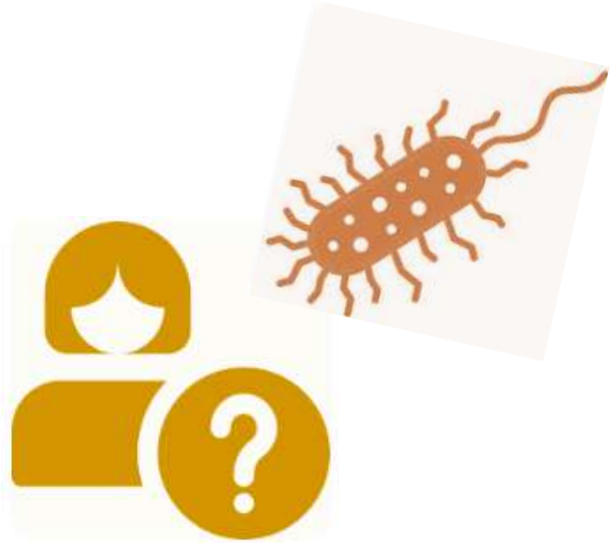
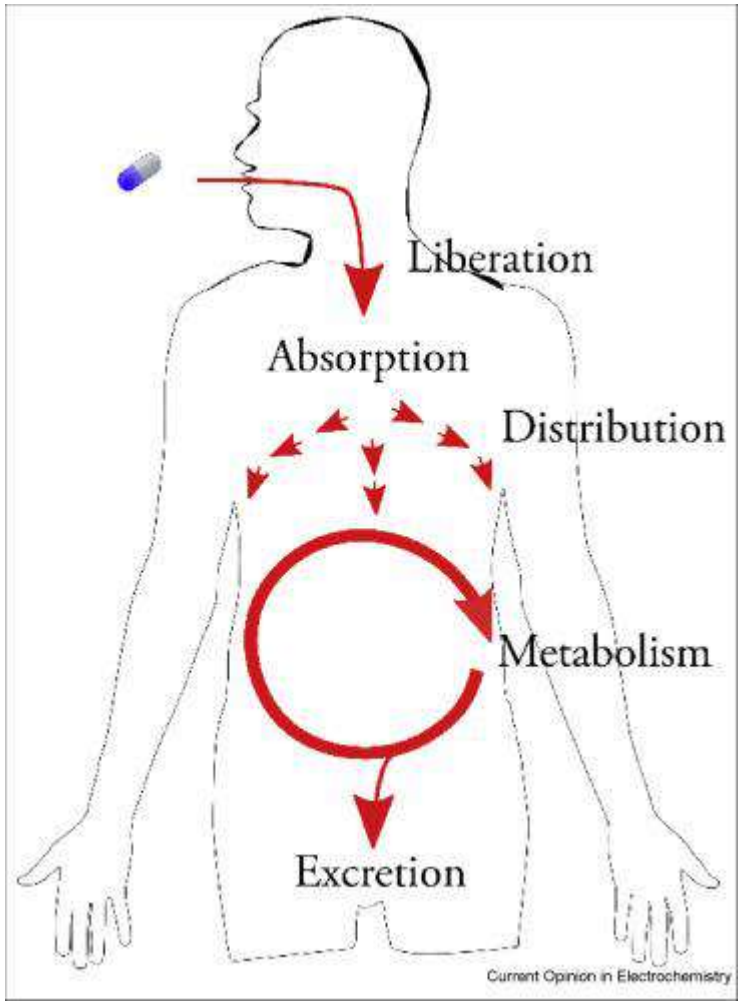




ABSORCIÓ

↓ buidament gàstric ↓ motilitat GI
↓ flux sanguini ↓ transportador GP-P
↓ aclorhídria (IBP, sals Ca^{2+})

↓ BIODISPONIBILITAT / EFICÀCIA

↑ RESISTÈNCIES

METABOLISME

↓tamany-flux-funció hepàtica

↑$T_{1/2}$ ATB elevada extracció hepàtica: macròlids, quinolones, azols

↑ TOXICITAT

DISTRIBUCIÓ

↑ % greix ↓% aigua; Sarcopènia

↑Vd ↑$T_{1/2}$ ATB-liposolubles: quinolones, macròlids, linezolid, antifúngics

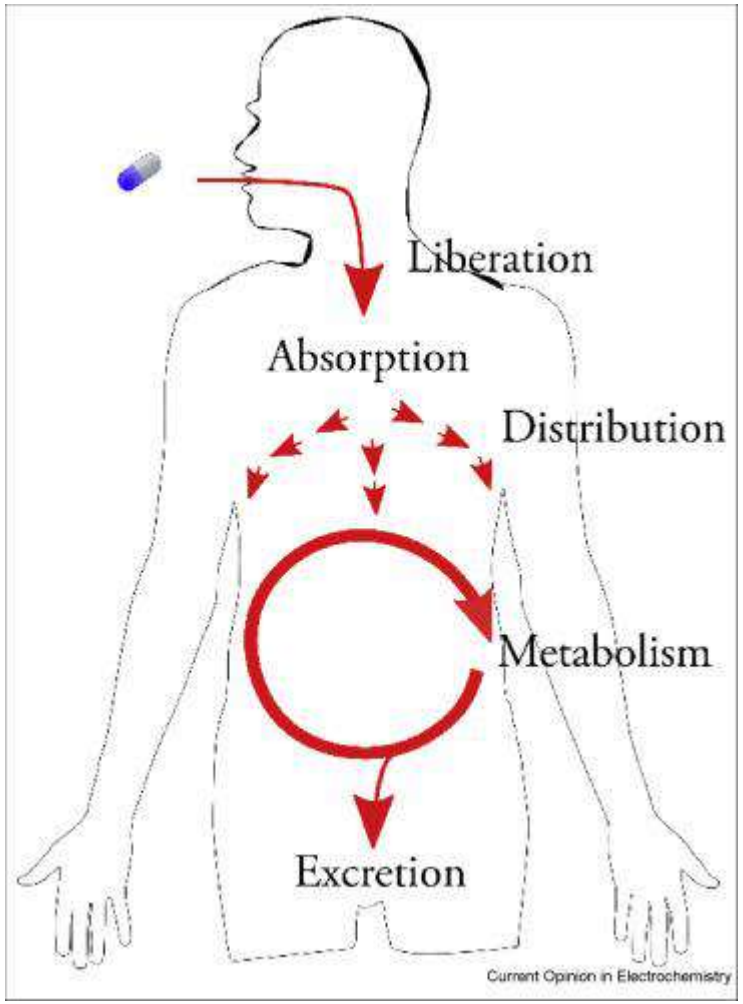
↓ Vd ↑[conc] ATB-hidrosolubles: amino-glicòsids, β-lact, glucopèptids

↓albúmina (desnutrició)

ATB elevada UPP (ceftriaxona, ertapenem) ➔ ↑Fracció lliure

↑ TOXICITAT

Pea F. Pharmacokinetics and drug metabolism of antibiotics in the elderly. Expert Opin Drug Metab Toxicol. 2018;14:1087-100
Giarratano A, et al. Review of antimicrobial use and considerations in the elderly population. Clin Interv Aging. 2018;13:657-6
Faulkner CM, et al. Unique aspects of antimicrobial use in older adults. ClinInfect Dis. 2005;40(7):997-1004



ELIMINACIÓ

↓ Aclariment renal (↓ 8 ml/min/any)
Comorbiditats que potencien la insuficiència renal (DM, ICC, HTA)
Interaccions amb altres fàrmacs que poden ser nefrotòxics

↑$T_{1/2}$ ATB hidròfils amb eliminació renal: β-lactàmics, glucopèptids, aminoglicòsids, daptomicina, quinolones, cotrimoxazol

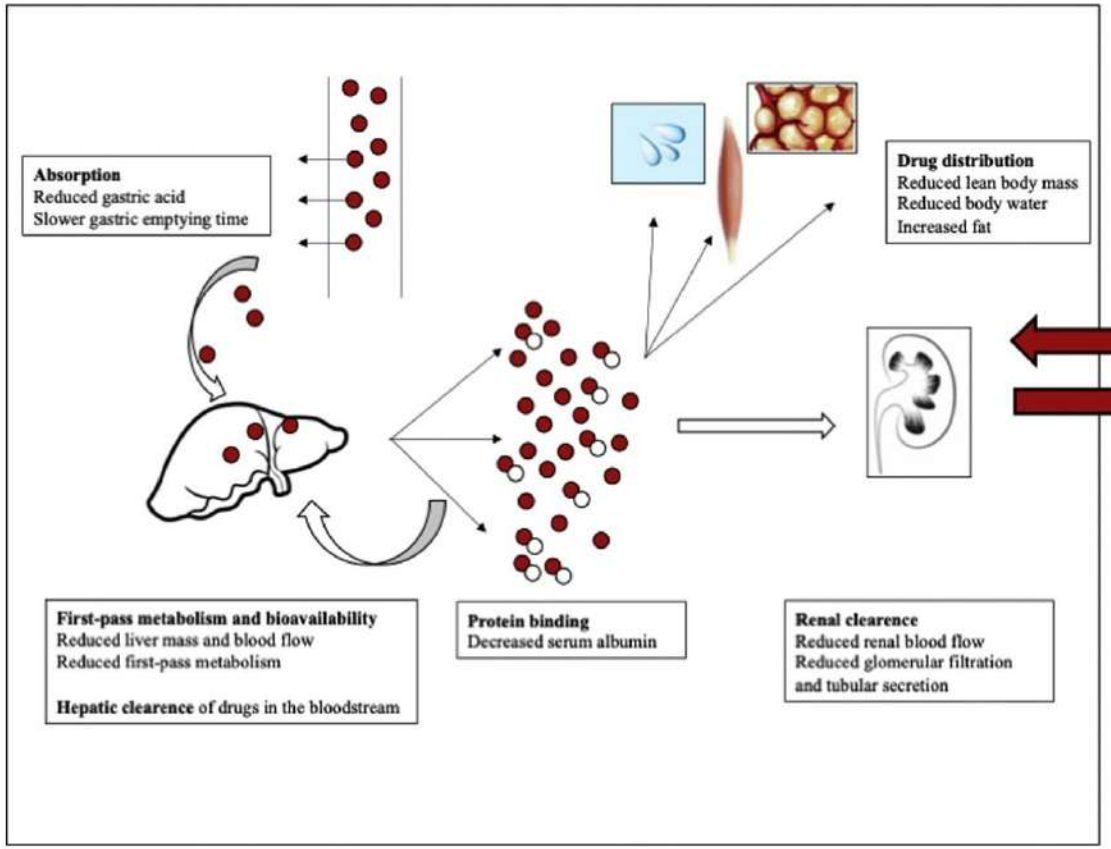
↑ TOXICITAT

Ajust de dosi i pes
Monitorització: clínica + analítica + fàrmac (TDM)

Pea F. Pharmacokinetics and drug metabolism of antibiotics in the elderly. Expert Opin Drug Metab Toxicol. 2018;14:1087-100
Giarratano A, et al. Review of antimicrobial use and considerations in the elderly population. Clin Interv Aging. 2018;13:657-6
Faulkner CM, et al. Unique aspects of antimicrobial use in older adults. ClinInfect Dis. 2005;40(7):997-1004

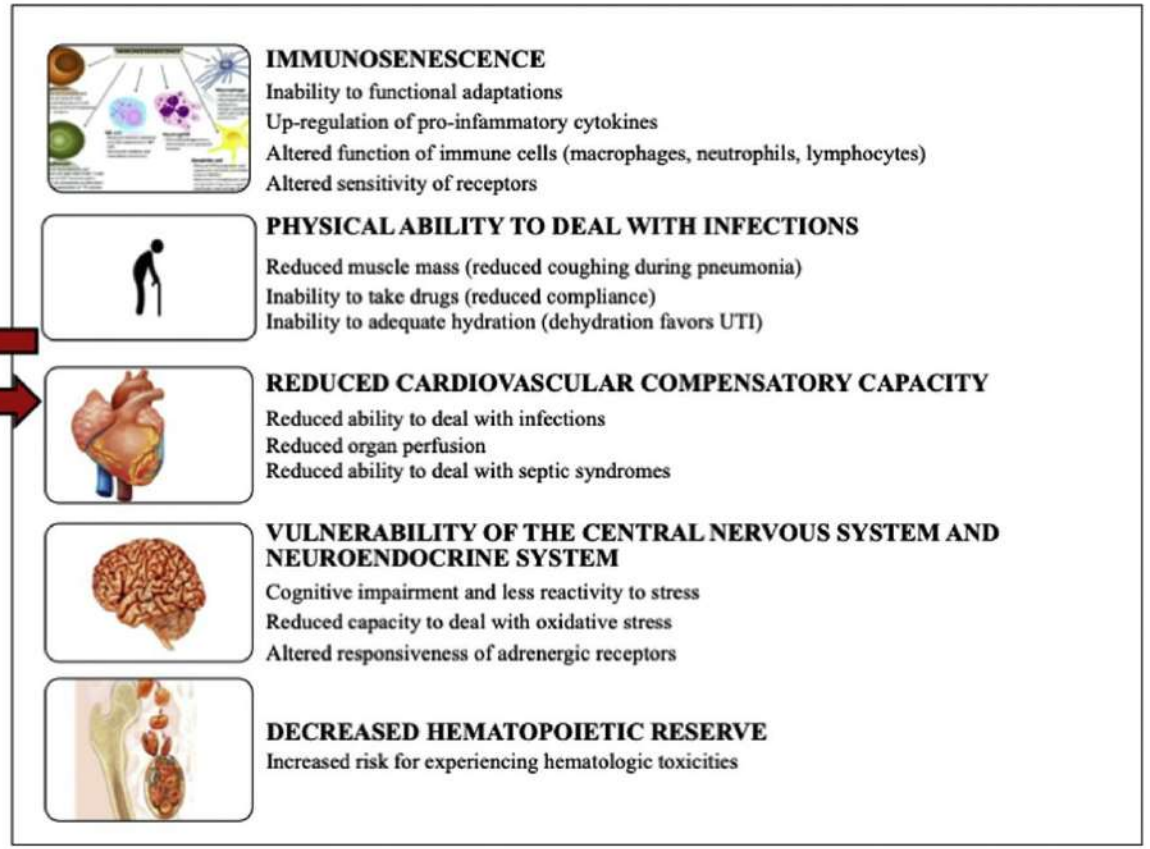
Pharmacokinetics

(concentration and elimination of antibiotics)



Pharmacodynamics

(relationship between the concentration of antibiotics and the clinical effect)



ALTERED SAFETY
ALTERED EFFICACY

Falcone M et al. Considerations for the optimal management of antibiotic therapy in elderly patients. Journ Global Antimicrob Resist 2020; 22: 325-33

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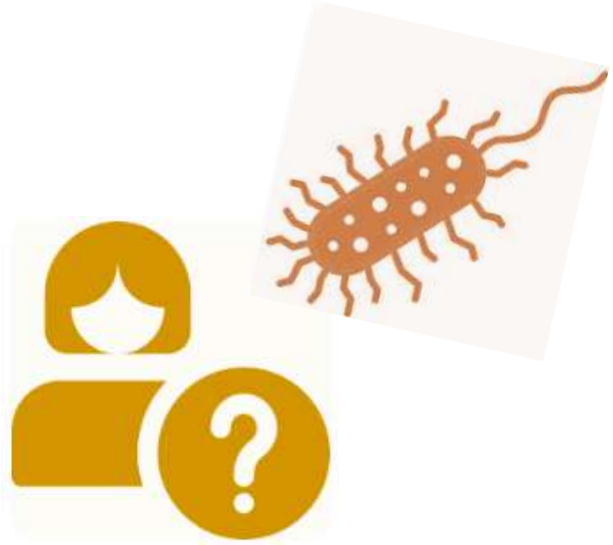
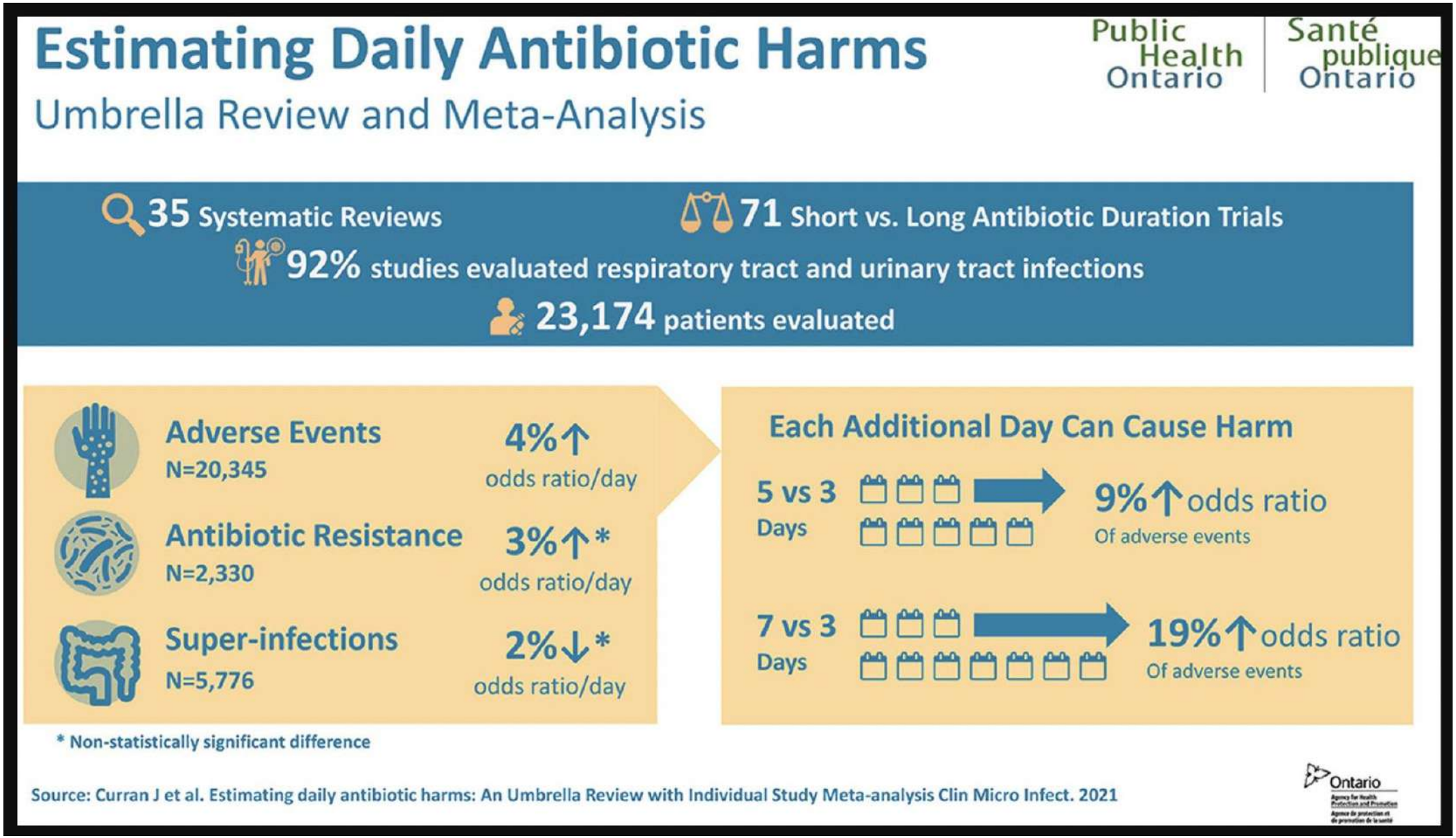


"LI DEIXO L'ANTIBIÒTIC EL CAP DE SETMANA i EL DILLUNS JA HO ATURO"


Estimating Daily Antibiotic Harms
Umbrella Review and Meta-Analysis
Public Health Ontario
Santé publique Ontario
35 Systematic Reviews
71 Short vs. Long Antibiotic Duration Trials
92% studies evaluated respiratory tract and urinary tract infections
23,174 patients evaluated
Adverse Events
N=20,345
4%↑
odds ratio/day
Antibiotic Resistance
N=2,330
3%↑*
odds ratio/day
Super-infections
N=5,776
2%↓*
odds ratio/day
Each Additional Day Can Cause Harm
5 vs 3
Days
9%↑odds ratio
Of adverse events
7 vs 3
Days
19%↑odds ratio
Of adverse events
* Non-statistically significant difference
Source: Curran J et al. Estimating daily antibiotic harms: An Umbrella Review with Individual Study Meta-analysis Clin Micro Infect. 2021
Ontario

Clinical Microbiology and Infection 28 (2022) 479–490

Contents lists available at ScienceDirect

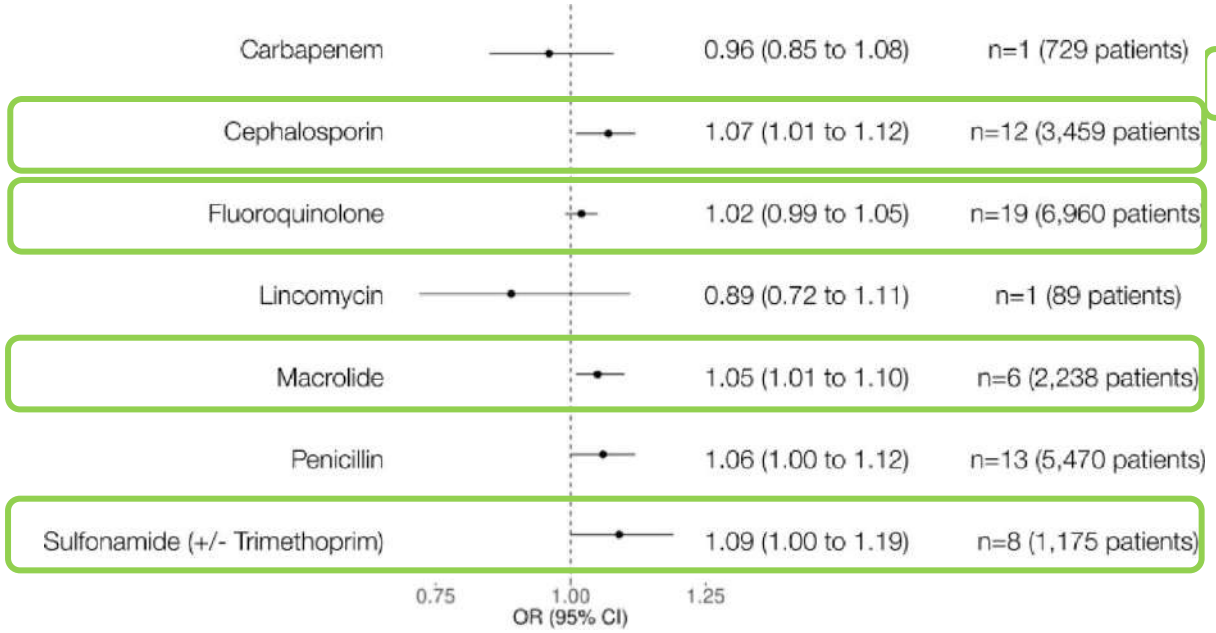
Clinical Microbiology and Infection

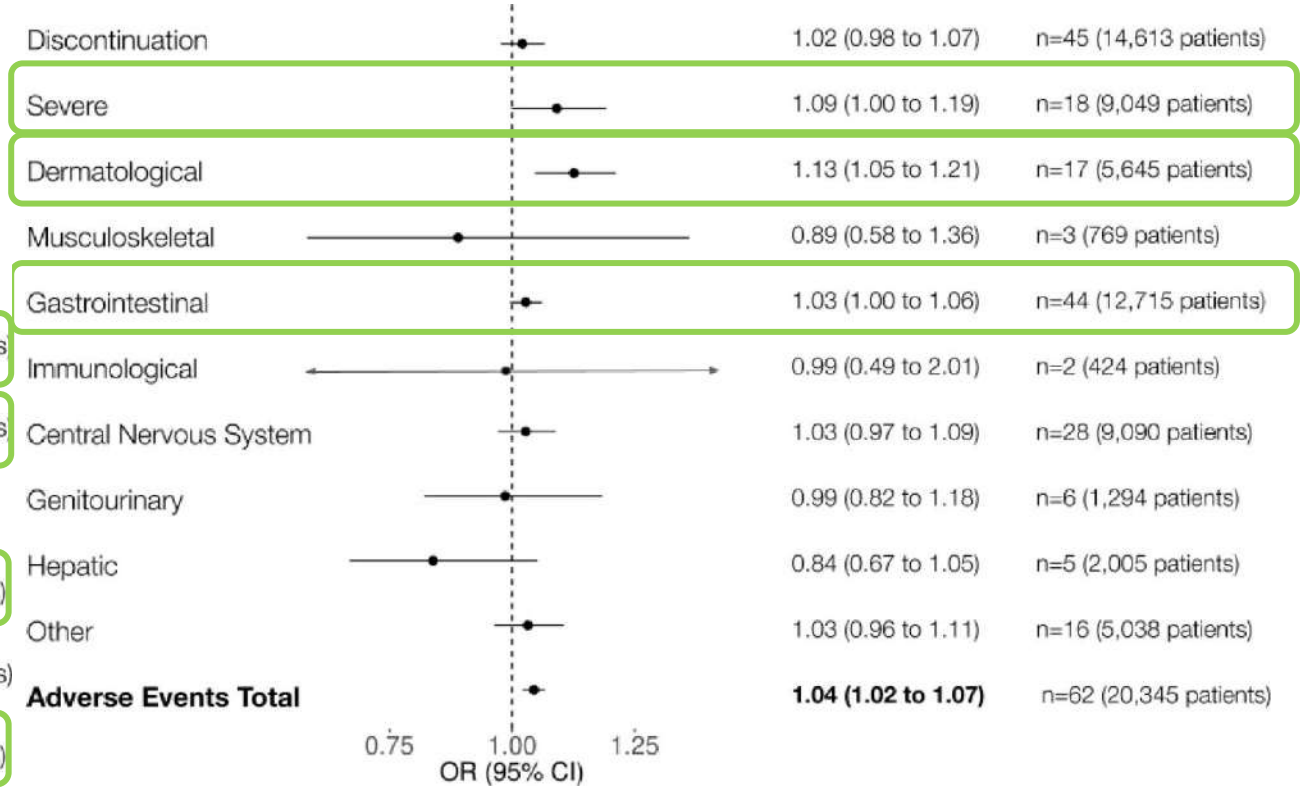
journal homepage: www.clinicalmicrobiologyandinfection.com

Systematic review

Estimating daily antibiotic harms: an umbrella review with individual study meta-analysis

Jennifer Curran [1,*], Jennifer Lo [2], Valerie Leung [3,4], Kevin Brown [3,5], Kevin L. Schwartz [3,5], Nick Daneman [2,3,6,7], Gary Garber [3,8,9], Julie H.C. Wu [3], Bradley J. Langford [3,10]





Curran J et al. Estimating daily antibiotics harms: an umbrella review with individual study meta-analysis. Clin Microb Infect 2022; 28: 479-490

DEADLY DIARRHEA:
C. DIFFICILE CAUSES IMMENSE SUFFERING, DEATH

CS253604

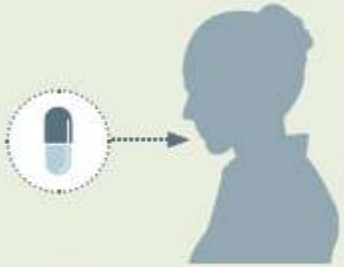
IMPACT

Caused close to half a million illnesses in one year.

Comes back at least once in about 1 in 5 patients who get *C. difficile*.

1 in 11 people 65 and older died within a month of *C. difficile* infection diagnosis.

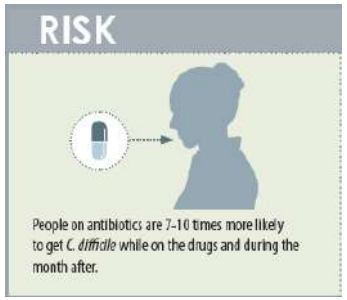
RISK

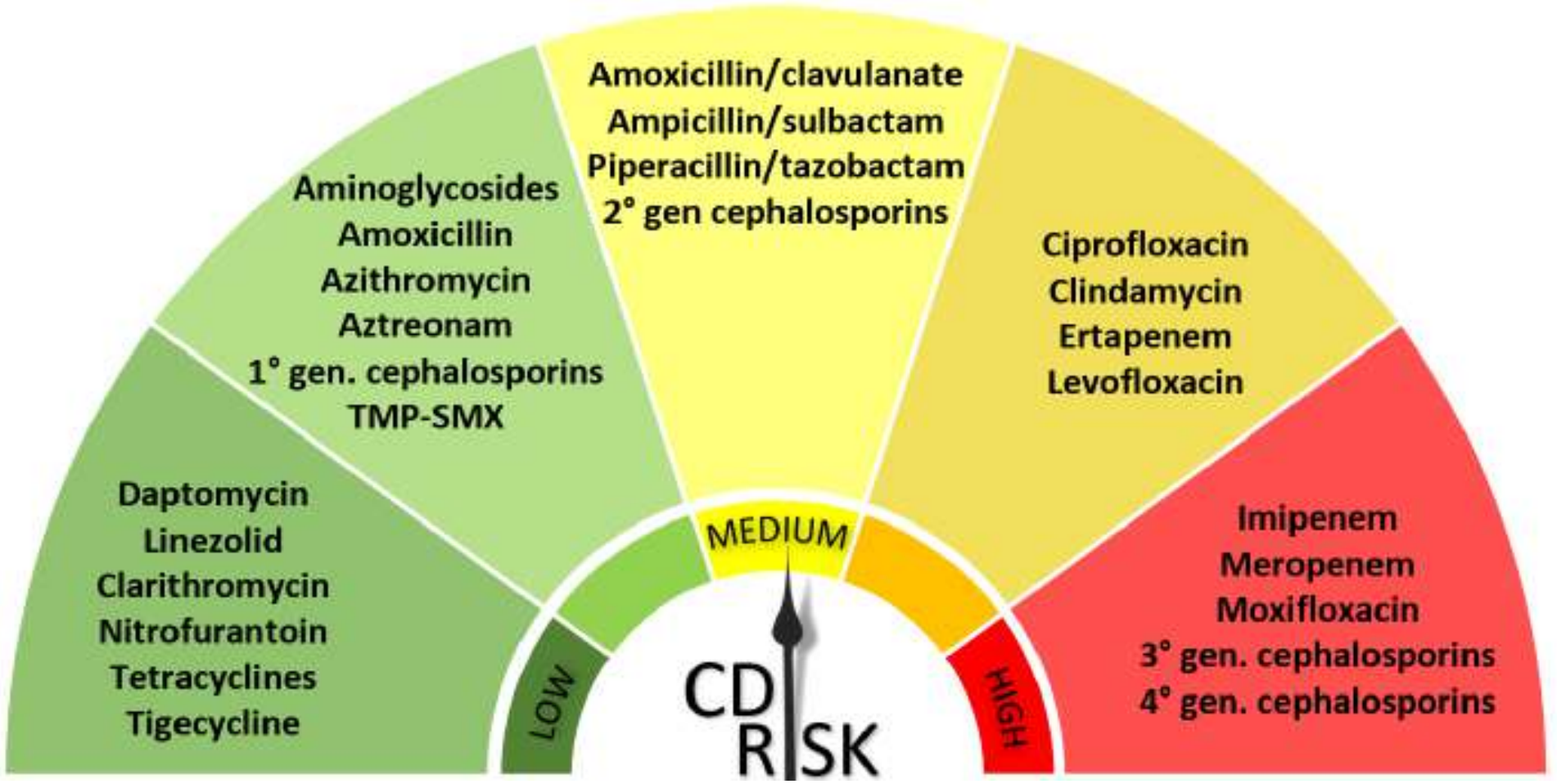


People on antibiotics are 7-10 times more likely to get *C. difficile* while on the drugs and during the month after.

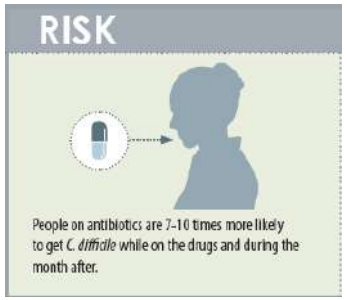
Being in healthcare settings, especially hospitals or nursing homes.

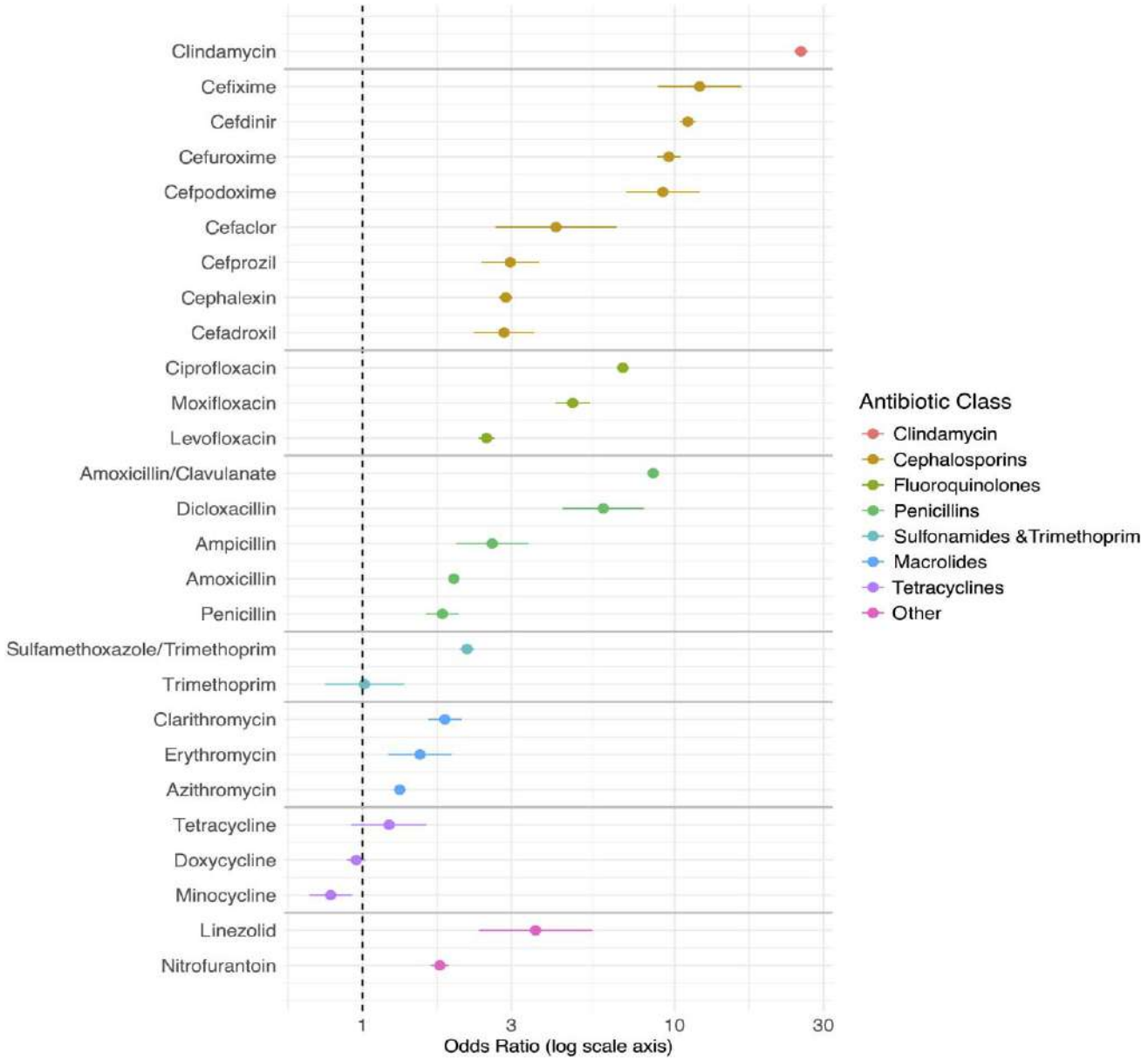
More than 80% of *C. difficile* deaths occurred in people 65 and older.





Di Bella S et al. Clostridioides difficile infection: history, epidemiology, risk factors, prevention, clinical manifestations, treatment, and future options. Clin Microb Rev 2024; 37(2): e0013523





Miller A et al. Comparison of Different Antibiotics and the Risk for Community-Associated Clostridioides difficile Infection: A Case–Control Study. OFID 2023; 10(8): ofad413.

Clinical Infectious Diseases
MAJOR ARTICLE
IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Influence of Antibiotic Exposure Intensity on the Risk of *Clostridioides difficile* Infection

Michael J. Ray,[1,2,●] Luke C. Strnad,[2,3] Kendall J. Tucker,[1] Jon P. Furuno,[1] Eric T. Lofgren,[4] Caitlin M. McCracken,[1] Hiro Park,[1] Jeffrey S. Gerber,[5] and Jessina C. McGregor[1,2]

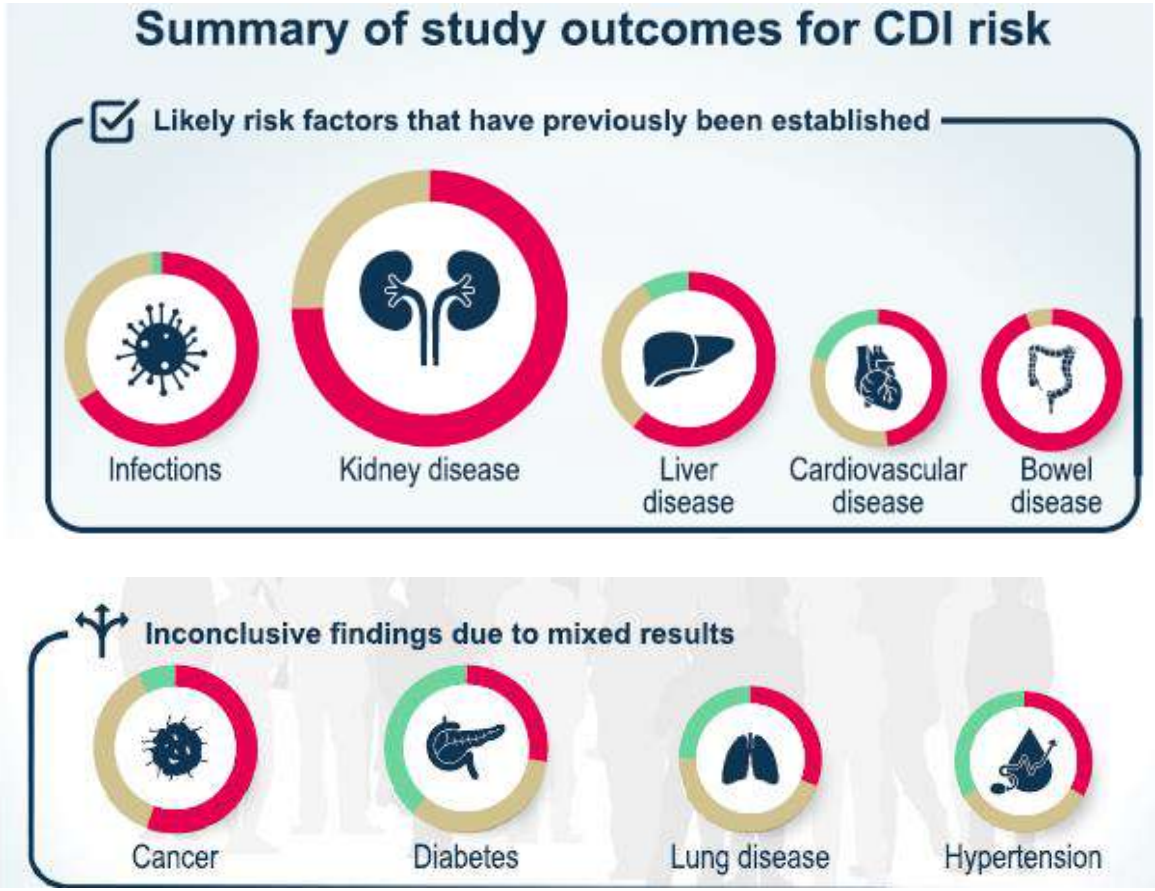
Table 2. Adjusted Relative Risks for Significant CDI Risk Factors Identified in our Final Model

	Relative Risk (95% CI)
ASI per antibiotic day[a]	1.09 (1.06–1.13)
Time at risk[b]	1.007 (.998–1.016)
Number of comorbidities[c]	1.35 (1.22–1.50)
PPI/H2RA	2.53 (1.46–4.39)
NG tube placement	1.76 (1.06–2.93)
GI procedures	2.28 (1.37–3.81)
Chemotherapy	2.02 (1.27–3.22)
Colonization pressure[d]	2.09 (1.92–2.27)

- Les DOT no *capturen* de forma adequada la intensitat de risc de *Cl.difficile*
- ASI (*Antibiotic Spectrum Index*) és una mesura alternativa per valorar la "*intensitat de la teràpia antibiòtica*"
- N = 35457 pacients ingressats ➔ 66% rep ≥ 1 ATB
- Incidència de CDI ➔ 4,1 casos per 10.000 pacients/dia
- Ajustat a factor de confusió:

Cada ↑ d'una unitat d'*ASI* - ATB/dia ➔ ↑ 9% *Cl.Difficile*

Ray M et al. Influence of Antibiotic Exposure Intensity on the Risk of Clostridioides difficile Infection . Clin Infect Dis 2024; 79(5): 1129–35



Eeuwijk Jet al. A Systematic Literature Review on Risk Factors for and Timing of Clostridioides difficile Infection in the United States. Infect Dis Ther 2024; 13: 273-298

Clinical Microbiology and Infection 27 (2021) 697–703

Contents lists available at ScienceDirect

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journal homepage: www.clinicalmicrobiologyandinfection.com

Systematic review

Proton pump inhibitor use and risk for recurrent *Clostridioides difficile* infection: a systematic review and meta-analysis

Kristin M. D'Silva [1,†], Raaj Mehta [2,†], Michael Mitchell [3], Todd C. Lee [4,5], Vibha Singhal [6], Marnie Goodwin Wilson [7,‡], Emily G. McDonald [4,8,*,‡]

Ajustat a anàlisi de sensibilitat, amb seguiment a 56 dies i estudis multivariants:

OR 1.49 (IC 95% 1.12 – 2.00)

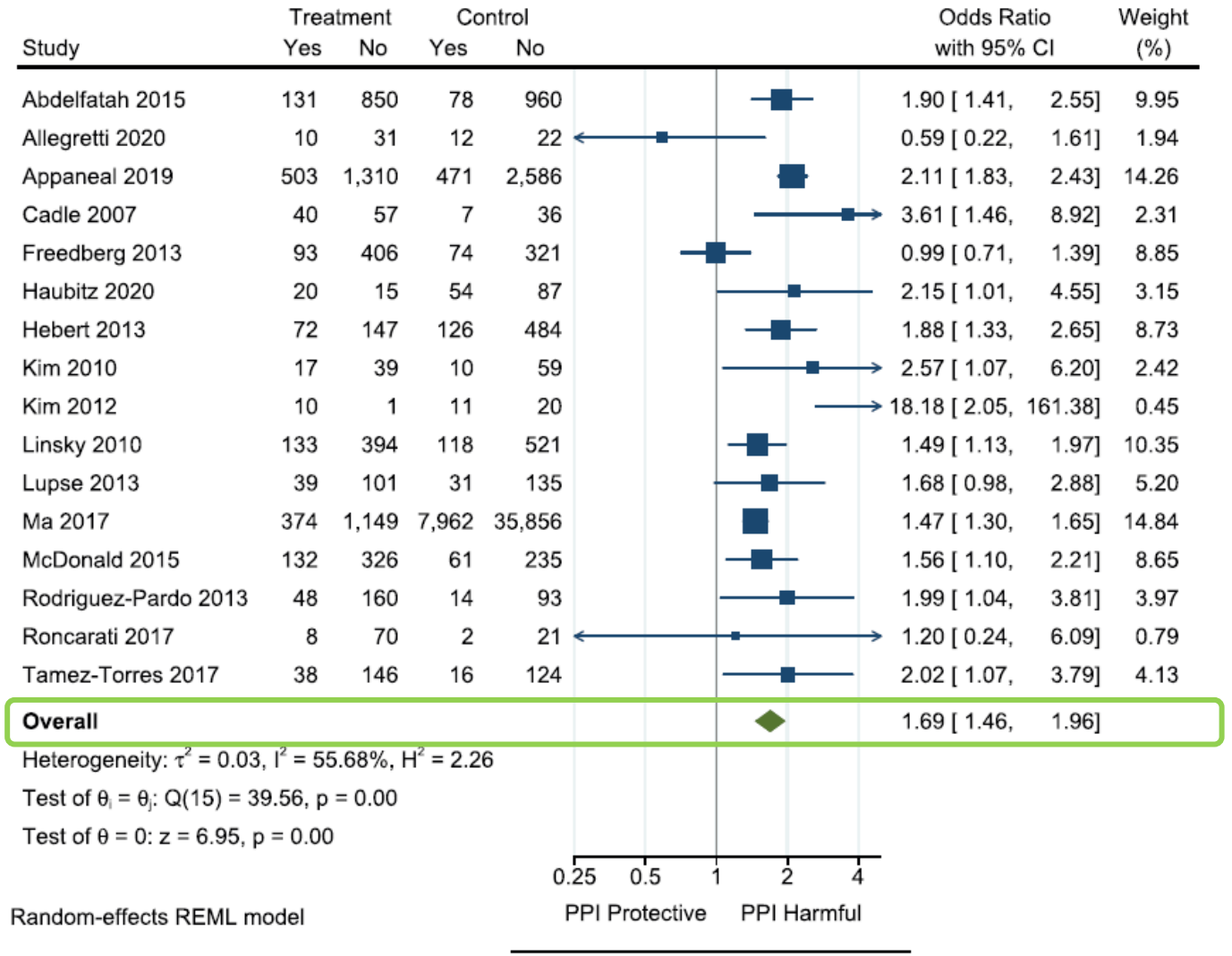
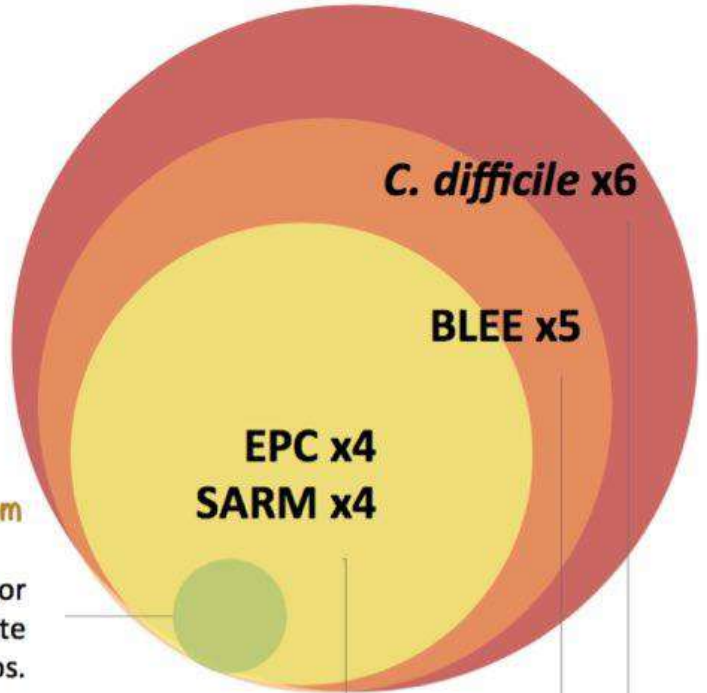


Fig. 2. Meta-analysis of the associated risk of recurrent *Clostridioides difficile* and receipt of a proton pump inhibitor.

D'Silva KM et al. Proton pump inhibitor use and risk for recurrent Clostridioides difficile infection: a systematic review and meta-analysis. Clin Microb Infect 2021; 27: 697-703

LAS QUINOLONAS NO SON ANTIBIÓTICOS 'MENORES'.
Tienen gran capacidad de seleccionar resistencias en tu paciente. Úsalas con juicio.

by @guiaprioam



Este es el riesgo de tener una infección por bacterias resistentes en un paciente que no ha recibido antibióticos.

Este es el incremento de riesgo de tener **infección por SARM o enterobacterias productoras de carbapenemasas** en pacientes que han recibido quinolonas[1-3]

Este es el incremento de riesgo de tener **infección por enterobacterias productoras de BLEE** en pacientes que han recibido quinolonas[4]

Este es el incremento de riesgo de tener **infección por *C. difficile*** en pacientes que han recibido quinolonas[5]

toxicitat dels aïllaments en el benestar dels pacients i la falta de rehabilitació

IMPACTE EMOCIONAL NEGATIU

DEPRESSIÓ | **ANSIETAT** | ***DELIRIUM*** | **SOLETAT** | **POR** | **AVORRIMENT** | **ESTIGMA** | **VERGONYA**

L'AILLAMENT <48 HORES POT <u>NO INFLUIR</u> EN L'ESTAT EMOCIONAL

Alguns poden percebre sensació de PRIVACITAT i DIGNITAT per tenir habitación individual

IMPACTE REHABILITADOR NEGATIU

↓ rehabilitació
Alteració espais a on fer rehabilitació

IMPACTE D'ATENCIÓ NEGATIU

↓ registre constants
↓ cursos clínics
↑ caigudes ↑ úlceres

Abad C et al. Adverse effects of isolation in hospitalised patients: a systematic review. Journ Hosp Infect 2010; 76: 97-102
Wassenberg MWM et al. Psychological impact of short-term isolation measures in hospitalised patients. Journ Hosp Infect 2010; 75: 124-127
Fregonese L et al. Hospital patient experiences of contact isolation for antimicrobial resistant organisms in relation to health care–associated infections: A systematic review and narrative synthesis of the evidence. Amer Journ Infect Contr 2023; 51: 1263-1271

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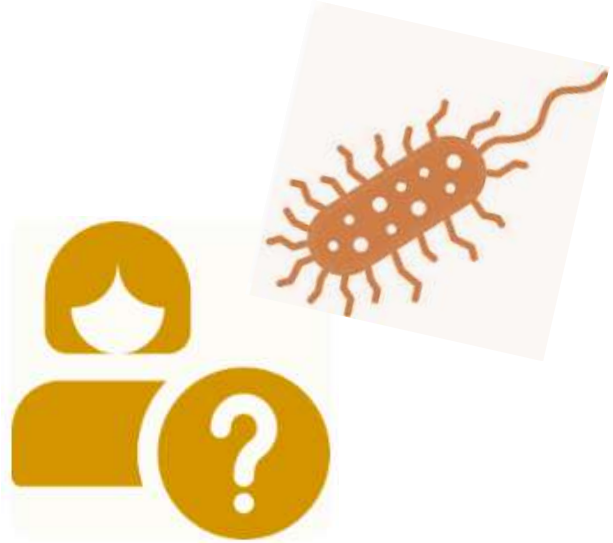
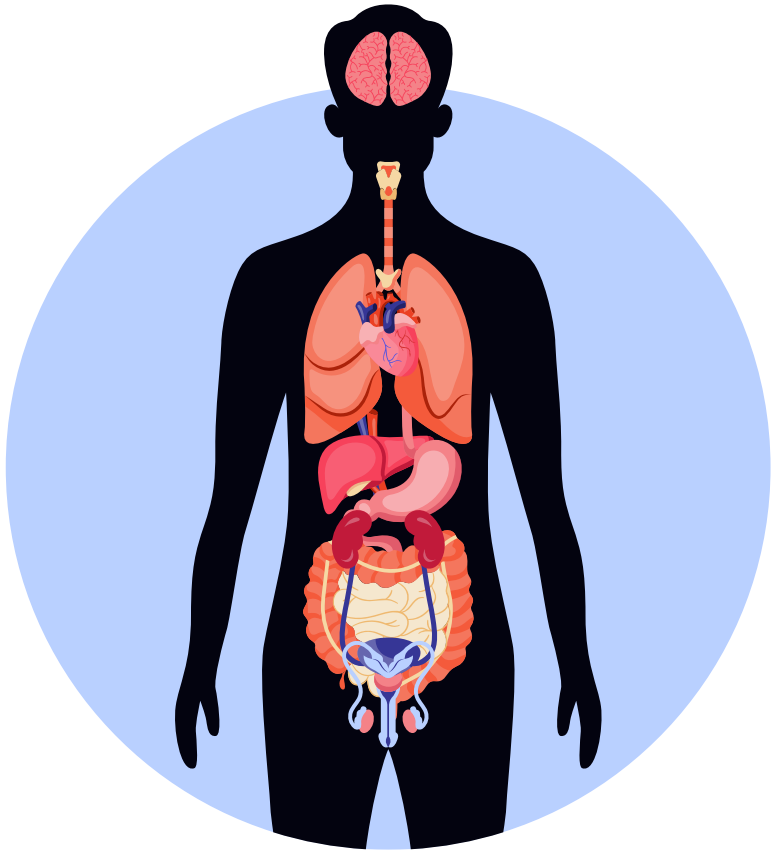
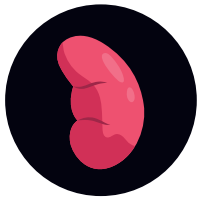




NEUROTOXICITAT



NEFROTOXICITAT

TOXICITAT SISTEMA LOCOMOTOR I OSSI I HEMATOPOIETIC

INTERACCIONS

Soraci L et al. Safety and Tolerability of Antimicrobial Agents in the Older Patient. Drugs Aging 2023; 40: 499-526

NEUROTOXICITAT

Potencial epileptogen dels β-lactàmics

Table 1 Convulsing activity of beta-lactams compared to penicillin G, from [67, 69, 70]

Beta-lactam	Relative pro-convulsive activity (reference: penicillin G = 100)
Cefazolin	294
Cefepime	160
Penicillin G	*100*
Imipenem	71
Aztreonam	42
Ampicillin	21
Ceftazidime	17
Meropenem	16
Ceftriaxone	12
Piperacillin	11
Cefotaxime	8,8
Cefoxitine	1,8

$OR_{carbapenem\ seizure\text{-}risk}$: IMIPENEM: 3,50 (IC95% 2,23 – 5,49)
MEROPENEM: 1,04 (IC95% 0,61 – 1,77)
ERTAPENEM: 1,32 (IC95% 0,22 – 7,74)

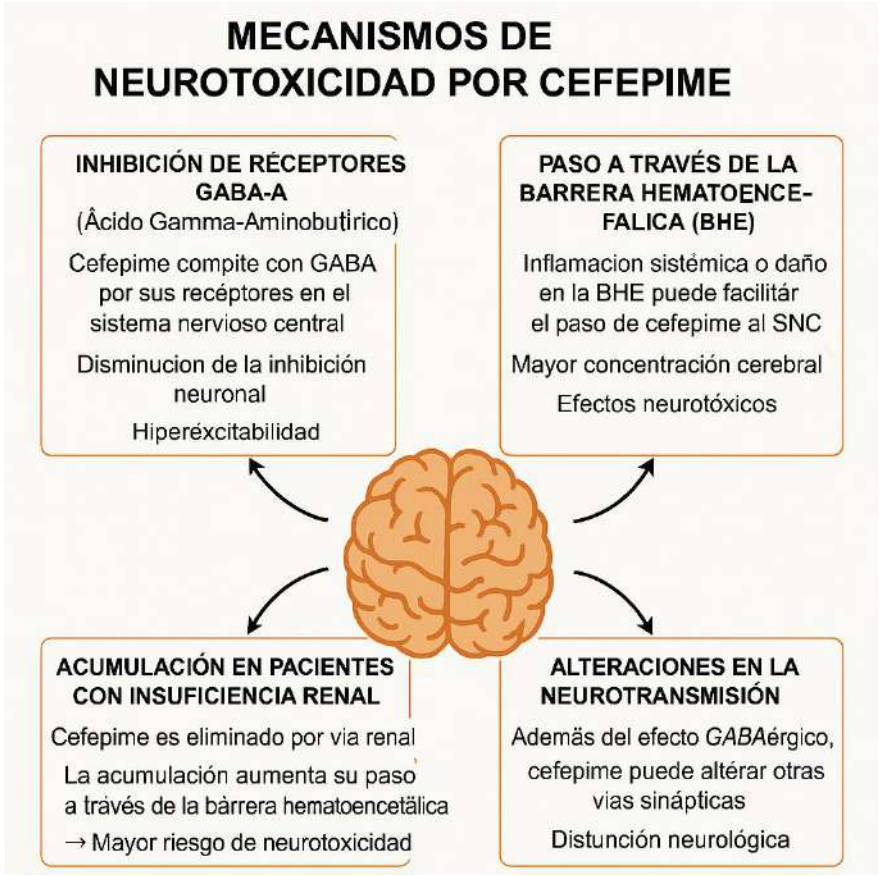
Guilhaumou R et al. Optimization of the treatment with betalactam antibiotics in critically ill patients—guidelines from the French Society of Pharmacology and Therapeutics (Société Française de Pharmacologie et Thérapeutique—SFPT) and the French Society of Anaesthesia and Intensive Care Medicine (Société Française d'Anesthésie et Réanimation—SFAR). Critical Care 2019; 23: 104.

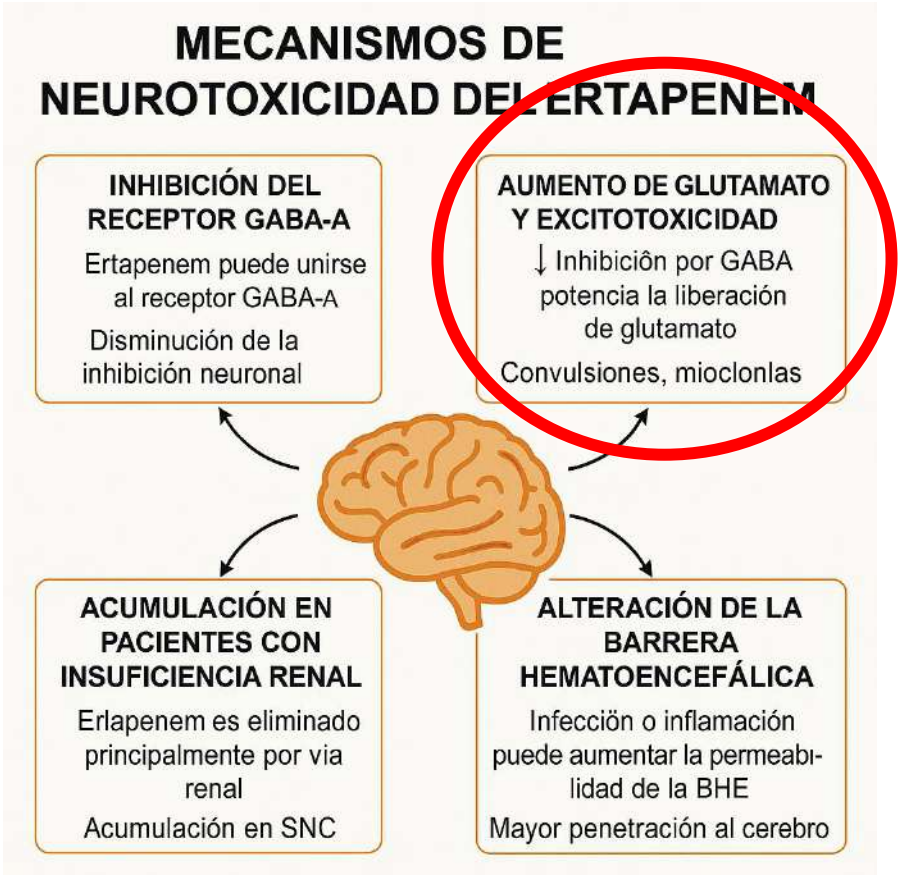
Cannon JP et al. The risk of seizures among the carbapenems: a meta-analysis. J Antimicrob Chemother 2014; 69: 2043-55.

NEUROTOXICITAT

Encefalopatia (mioclònies, tremolors, hiperexcitabilitat, hiperactivitat)

CEFEPIME & ERTAPENEM





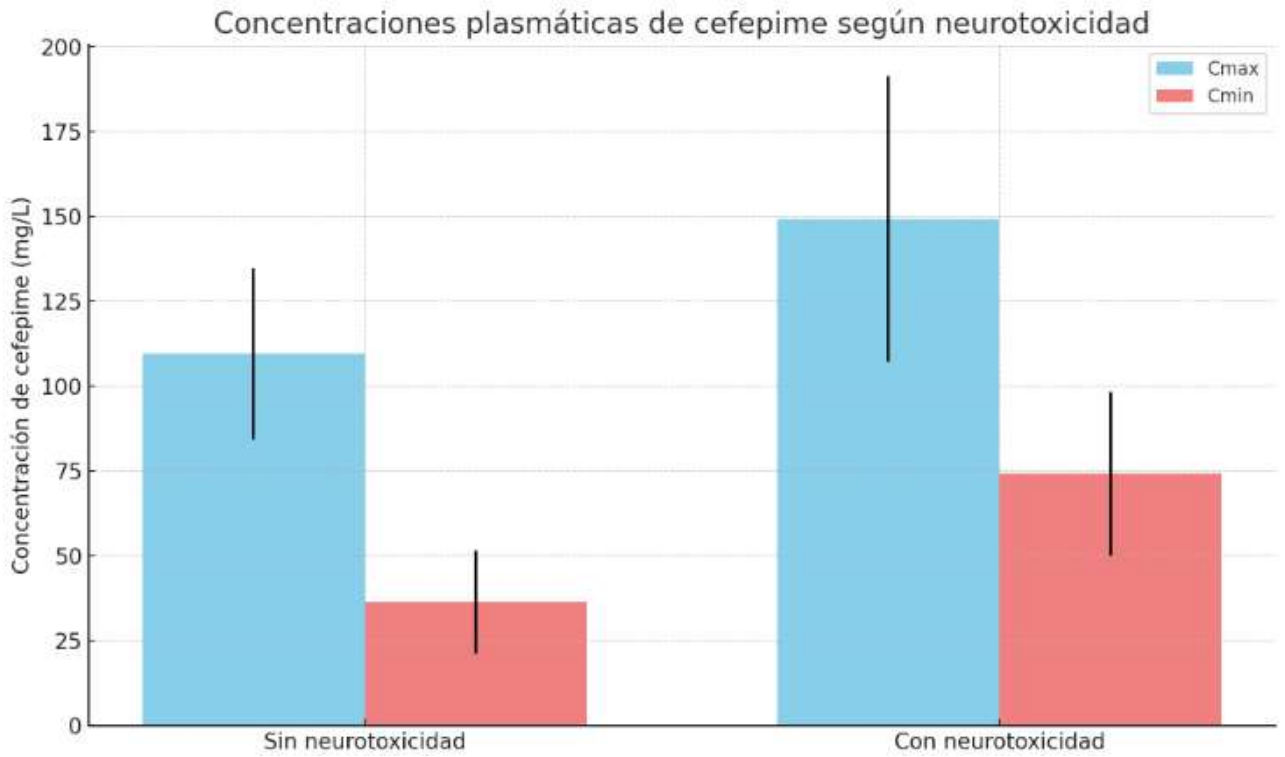
Fins a un 25% dels pacients poden tenir NEUROTOXICITAT tot i una posologia correcta

Payne LE et al. Cefepime-induced neurotoxicity: a systematic review. Crit Care. 2017;21:276.
Deshayes S et al. Neurological Adverse Effects Attributable to b-LactamAntibiotics: A Literature Review. Drug Saf 2017; 40(12): 1171-1198.
Mitaka H et al. Characterizing Ertapenem Neurotoxicity: A Systematic Review and Experience at a Tertiary Medical Center. Open Forum Infect Dis 2024; 11(5): ofae214

NEUROTOXICITAT

Encefalopatia (mioclònies, tremolors, hiperexcitabilitat, hiperactivitat)

CEFEPIME & ERTAPENEM



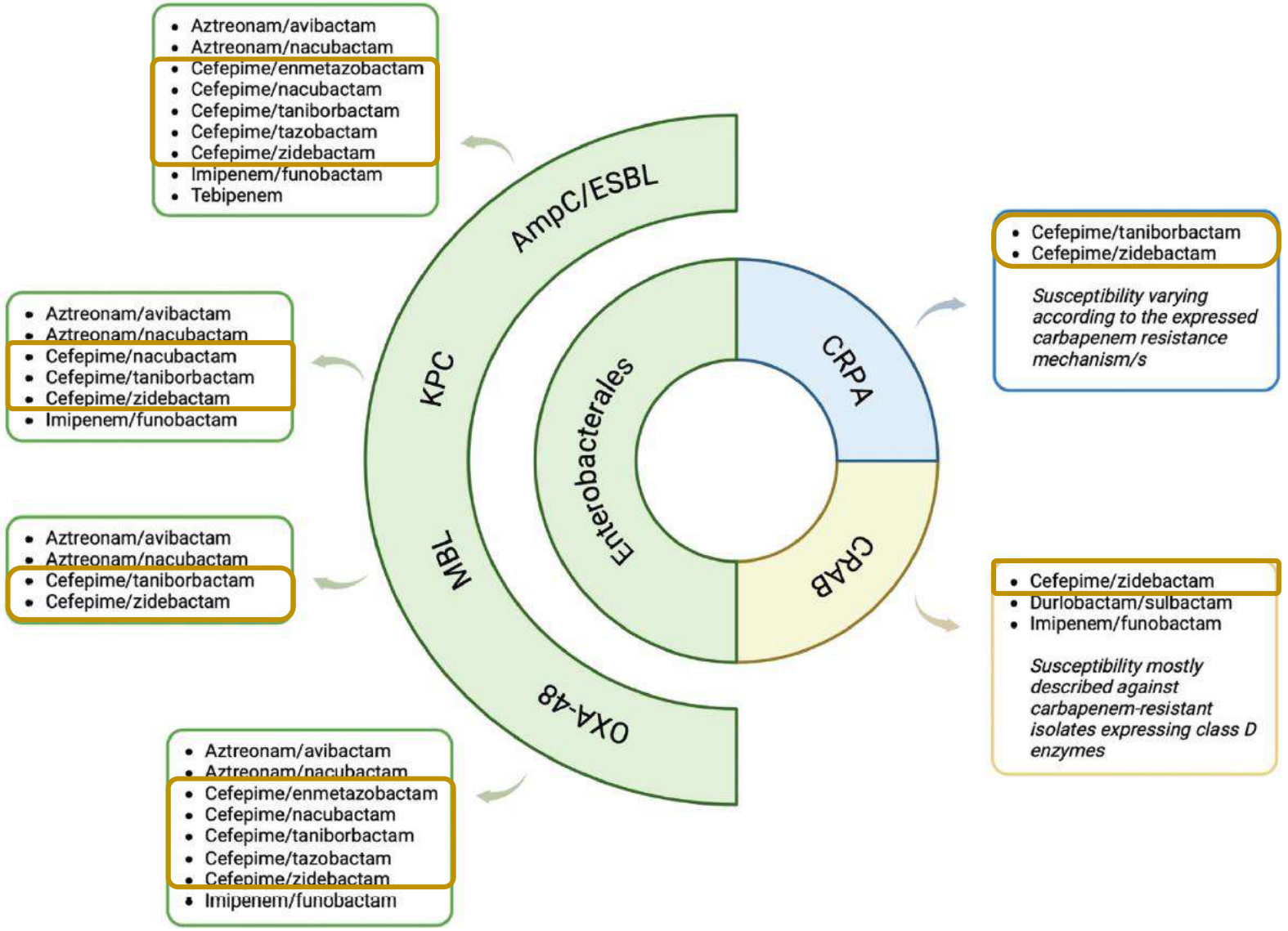
TDM → nivells C_{min}> 49 mg/dL s'estableix com a llindar de toxicitat (estudis previs suggereixen C_{min}> ± 30-35 mg/dL)

Payne LE et al. Cefepime-induced neurotoxicity: a systematic review. Crit Care. 2017;21:276.
Deshayes S et al. Neurological Adverse Effects Attributable to b-LactamAntibiotics: A Literature Review. Drug Saf 2017; 40(12): 1171-1198.
Mitaka H et al. Characterizing Ertapenem Neurotoxicity: A Systematic Review and Experience at a Tertiary Medical Center. Open Forum Infect Dis 2024; 11(5): ofae214

NEUROTOXICITAT

Encefalopatia (mioclònies, tremolors, hiperexcitabilitat, hiperactivitat)

CEFEPIME & ERTAPENEM



Bassetti M et al. Novel agents in development for the treatment of resistant Gram-negative infections. Expert Review of Anti-Infective Therapy, 22(11), 965–976.

NEUROTOXICITAT

Encefalopatia (mioclònies, tremolors, hiperexcitabilitat, hiperactivitat)

NOUS CARBAPENEMS

Sulopenem
Tebipenem

Sulopenem or Ciprofloxacin for the Treatment of Uncomplicated Urinary Tract Infections in Women: A Phase 3, Randomized Trial

Clinical Infectious Diseases® 2023;76(1):66–77

Michael W. Dunne,[1,a,©] Steven I. Aronin,[1] Anita F. Das,[2] Karthik Akinapelli,[1,b] Michael T. Zelasky,[1,c] Sailaja Puttagunta,[1] and Helen W. Boucher[3]

Table 8. Safety Analysis

Variable	Sulopenem Etzadroxil/ Probenecid (N = 833) n (%)	Ciprofloxacin (N= 827) n (%)
Any adverse event		
Any event, no. of patients (%)	208 (25.0)	116 (14.0)
Total no. of events	361	168
Treatment-related adverse event		
Any event, no. of patients (%)	207 (24.8)	115 (13.9)
Total no. of events	223	70
Serious adverse event, no. of patients (%)		
Any event	6 (0.7)	2 (0.2)
Treatment-related event	1 (0.1)	0 (0.0)
Death, no. (%)	1 (0.1)	0 (0.0)
Treatment-limiting adverse event, no. of patients (%)	13 (1.6)	8 (1.0)
Most common treatment-related adverse event, no. of patients (%)		
Diarrhea	103 (12.4)	21 (2.5)
Nausea	32 (3.8)	30 (3.6)
Headache	18 (2.2)	18 (2.2)
Vomiting	13 (1.6)	11 (1.3)
Dizziness	9 (1.1)	5 (0.6)

FDA approves new treatment for uncomplicated urinary tract infections in adult women who have limited or no alternative oral antibiotic treatment options

Content current as of:

10/24/2024

Dunne MW et al. Sulopenem or Ciprofloxacin for the Treatment of Uncomplicated Urinary Tract Infections in Women: A Phase 3, Randomized Trial. Clin Infect Dis 2023; 76(1): 66-77

NEUROTOXICITAT

Encefalopatia (mioclònies, tremolors, hiperexcitabilitat, hiperactivitat)

NOUS CARBAPENEMS

Sulopenem
Tebipenem

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Oral Tebipenem Pivoxil Hydrobromide in Complicated Urinary Tract Infection

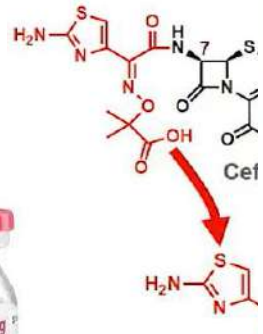
N Engl J Med 2022;386:1327-38.
DOI: 10.1056/NEJMoa2105462

Table 3. Incidence of Adverse Events Occurring during Treatment (Safety Population).*

Event	Tebipenem Pivoxil Hydrobromide (N = 685)	Ertapenem (N = 687)
	number (percent)	
Any adverse event	176 (25.7)	176 (25.6)
Any severe adverse event	10 (1.5)	9 (1.3)
Drug-related adverse event†	64 (9.3)	42 (6.1)
Serious adverse event	9 (1.3)	12 (1.7)
Adverse event leading to drug discontinuation	1 (0.1)	8 (1.2)
Adverse events occurring in >1% of patients, according to preferred term		
Alanine aminotransferase level increase	7 (1.0)	7 (1.0)
Aspartate aminotransferase level increase	7 (1.0)	5 (0.7)
Diarrhea‡	39 (5.7)	30 (4.4)
Edema peripheral	3 (0.4)	7 (1.0)
Headache	26 (3.8)	26 (3.8)
Hypertension	3 (0.4)	7 (1.0)
Nausea	10 (1.5)	6 (0.9)
Vulvovaginal candidiasis	5 (0.7)	7 (1.0)

U.S Food and Drug Administration

Eckburg PB et al. Oral Tebipenem Pivoxil Hydrobromide in Complicated Urinary Tract Infection. N Engl J Med 2022; 386: 1327-38.



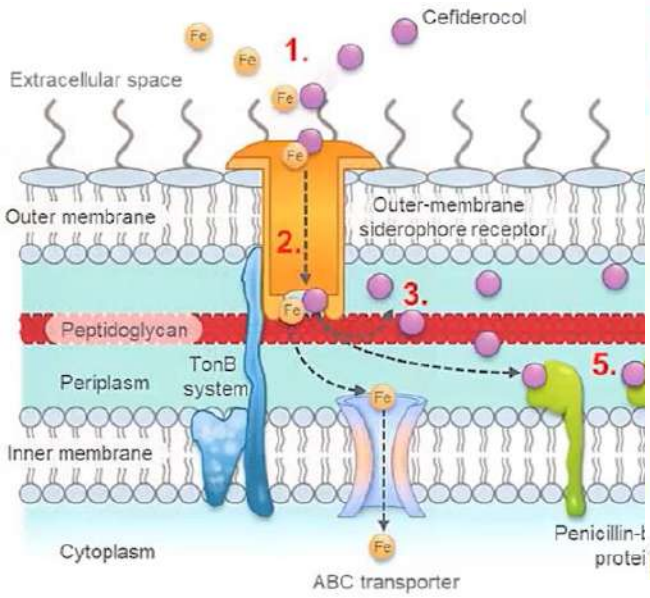


Figure 1. Photographs of urine

Fig. 1. Foley bag demonstrating Purplish Discoloration of Urine.

NEFROTOXICITAT

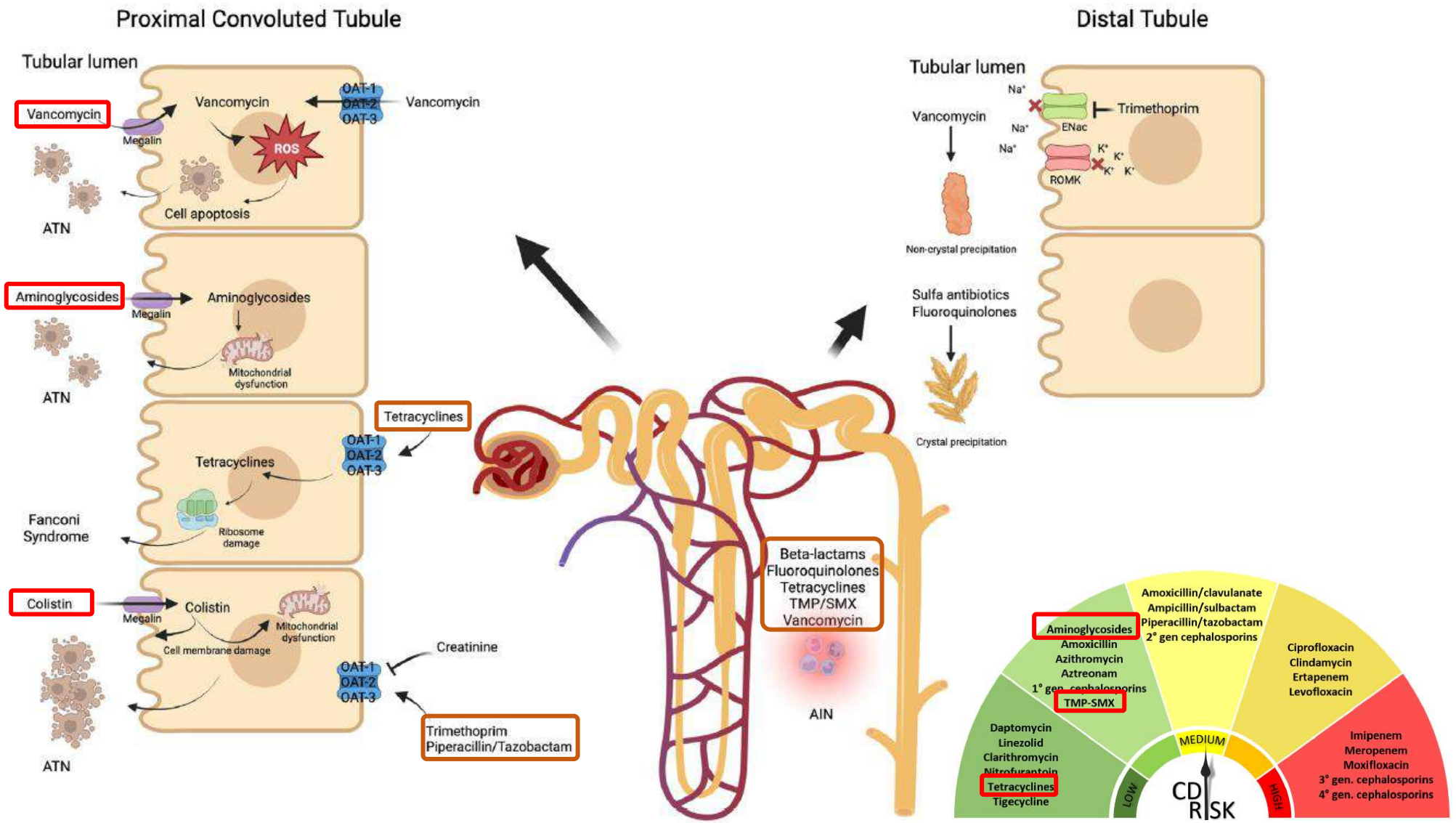


Figure 1. Mechanisms of antibiotic-induced nephrotoxicity. ATN, acute tubular necrosis.

Campbell RE et al. Overview of Antibiotic-Induced Nephrotoxicity. Kidney Int Rep 2023; 8: 2211-2225

NEFROTOXICITAT

💊 Tabla de Nefrotoxicidad de Antibióticos

Grupo de Antibióticos	Incidencia de Nefrotoxicidad	Notas Clínicas
Glucopeptidos (Ej. Vancomicina)	5–43%	Aumenta con dosis altas y uso combinado (ej. con aminoglucósidos o piperacilina-tazobactam)
Aminoglucósidos (Ej. Gentamicina, Amikacina)	10–25%	Reversible si se detecta a tiempo; riesgo aumenta con duración >5 días
Colistina (Polimixinas)	20–60%	Alta toxicidad, dependiente de dosis y duración; más común en pacientes críticos
Tetraciclinas (Ej. Doxiciclina, Tigeciclina)	<2%	Raro, pero puede causar acidosis tubular o insuficiencia renal aguda
Betalactámicos (Ej. Penicilinas, Cefalosporinas)	<1–3%	Generalmente seguros; nefritis intersticial aguda es la complicación típica
Cotrimoxazol (Trimetoprim-Sulfametoxazol)	10–34%	Puede causar hiperpotasemia, aumento de creatinina y nefritis intersticial

Infectious Diseases Society of America 2024 Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections

Pranita D. Tamma,[1] Emily L. Heil,[2] Julie Ann Justo,[3] Amy J. Mathers,[4] Michael J. Satlin,[5] and Robert A. Bonomo[6]

Question 1.1: What Are Preferred Antibiotics for the Treatment of Uncomplicated Cystitis Caused by ESBL-E?

Suggested approach: Nitrofurantoin and TMP-SMX are preferred treatment options for uncomplicated cystitis caused by ESBL-E. Ciprofloxacin, levofloxacin, and carbapenems are alternative agents for uncomplicated cystitis caused by ESBL-E. Although effective, their use is discouraged when nitrofurantoin or TMP-SMX are active. An aminoglycoside (as a single dose) and oral fosfomycin (for *E. coli* only) are also alternative treatments for uncomplicated cystitis caused by ESBL-E.

Question 1.2: What Are Preferred Antibiotics for the Treatment of Pyelonephritis or cUTI Caused by ESBL-E?

Suggested approach: TMP-SMX, ciprofloxacin, or levofloxacin are preferred treatment options for pyelonephritis or cUTIs caused by ESBL-E. Ertapenem, meropenem, and imipenem-cilastatin are preferred agents when resistance or toxicities preclude the use of TMP-SMX or fluoroquinolones. Aminoglycosides are alternative options for the treatment of ESBL-E pyelonephritis or cUTI.

Question 3.1: What Are Preferred Antibiotics for the Treatment of Uncomplicated Cystitis Caused by CRE?

Suggested approach: Nitrofurantoin, TMP-SMX, ciprofloxacin, or levofloxacin are preferred treatment options for uncomplicated cystitis caused by CRE, although the likelihood of susceptibility to any of these agents is low. An aminoglycoside (as a single dose), oral fosfomycin (for *E. coli* only), colistin, ceftazidime-avibactam, meropenem-vaborbactam, imipenem-cilastatin-relebactam, or cefiderocol, are alternative treatment options for uncomplicated cystitis caused by CRE.

Question 3.2: What Are Preferred Antibiotics for the Treatment of Pyelonephritis or cUTI Caused by CRE?

Suggested approach: TMP-SMX, ciprofloxacin, or levofloxacin are preferred treatment options for pyelonephritis or cUTI caused by CRE, if susceptibility is demonstrated. Ceftazidime-avibactam, meropenem-vaborbactam, imipenem-cilastatin-relebactam, and cefiderocol are also preferred treatment options for pyelonephritis or cUTIs. Aminoglycosides are alternative options for the treatment of pyelonephritis or cUTI caused by CRE.

TOXICITAT SISTEMA LOCOMOTOR I OSSI

Fluoroquinolonas de administración sistémica o inhalada: recordatorio sobre las restricciones de uso

Inicio > Comunicación > Notas de seguridad > Fluoroquinolonas de administración sistémica o inhalada: recordatorio sobre las restricciones de uso

Generar pdf

Fecha de publicación: 23 de octubre de 2023

Información para profesionales sanitarios

- Las fluoroquinolonas de uso sistémico o inhalado **no deben prescribirse**:

- Estos medicamentos se deben prescribir con especial precaución a personas de edad avanzada, pacientes con insuficiencia renal, pacientes que hayan recibido un trasplante de órgano sólido o pacientes tratados concomitantemente con corticosteroides, ya que en estos grupos, el riesgo de sufrir tendinitis y rotura tendinosa puede verse aumentado.

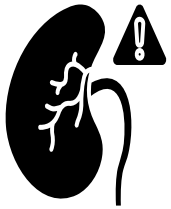
- Indique a los pacientes que interrumpan el tratamiento y acudan al médico ante la aparición de los primeros signos/síntomas sugestivos de una reacción adversa grave, como por ejemplo: tendinitis, rotura tendinosa, mialgia, debilidad muscular, dolor y/o tumefacción articular, neuropatía periférica y efectos sobre el sistema nervioso central.

TOXICITAT SISTEMA HEMATOPOIETIC

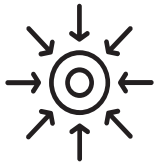
LINEZOLID

PLAQUETOPÈNIA
ANÈMIA
(neuropatia)

↑ Durada (>10 dies)



Insuficiencia Renal

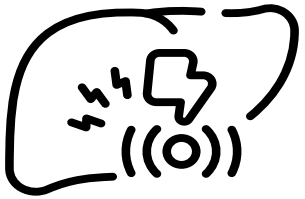


↑ concentració plasmàtica

Edat avançada(>75 anys)

Plaquetopènia basal (<150)

Baix pes

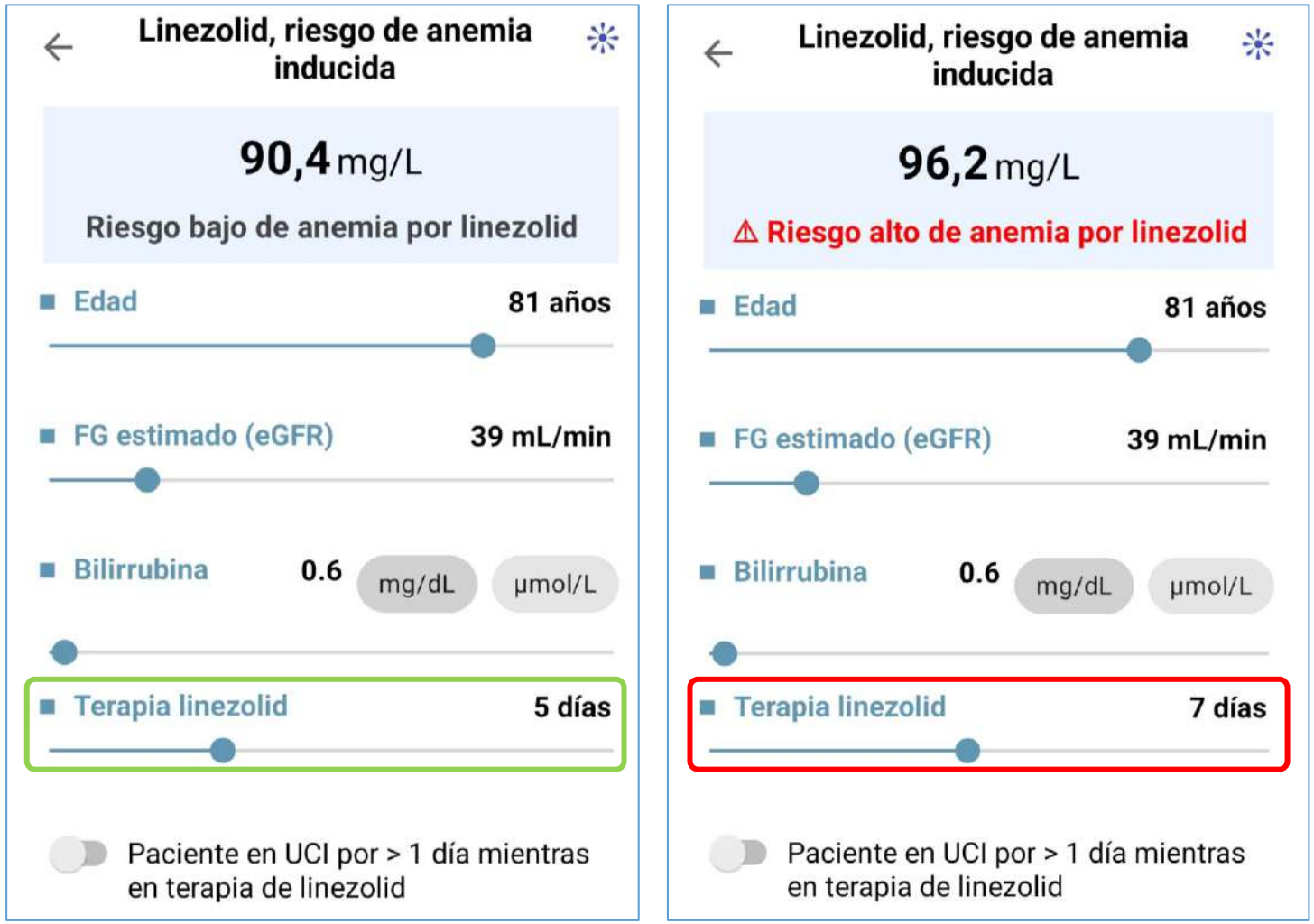


Hepatotoxicitat

TOXICITAT SISTEMA LOCOMOTOR I OSSI

LINEZOLID

PLAQUETOPÈNIA
ANÈMIA
(neuropatia)



**** app Guia Mensa***

Yan Qin et al. A risk factor-based predictive model for linezolid-induced anaemia: a 7-year retrospective study. J Clin Pharm 2021: 46: 1591-99.

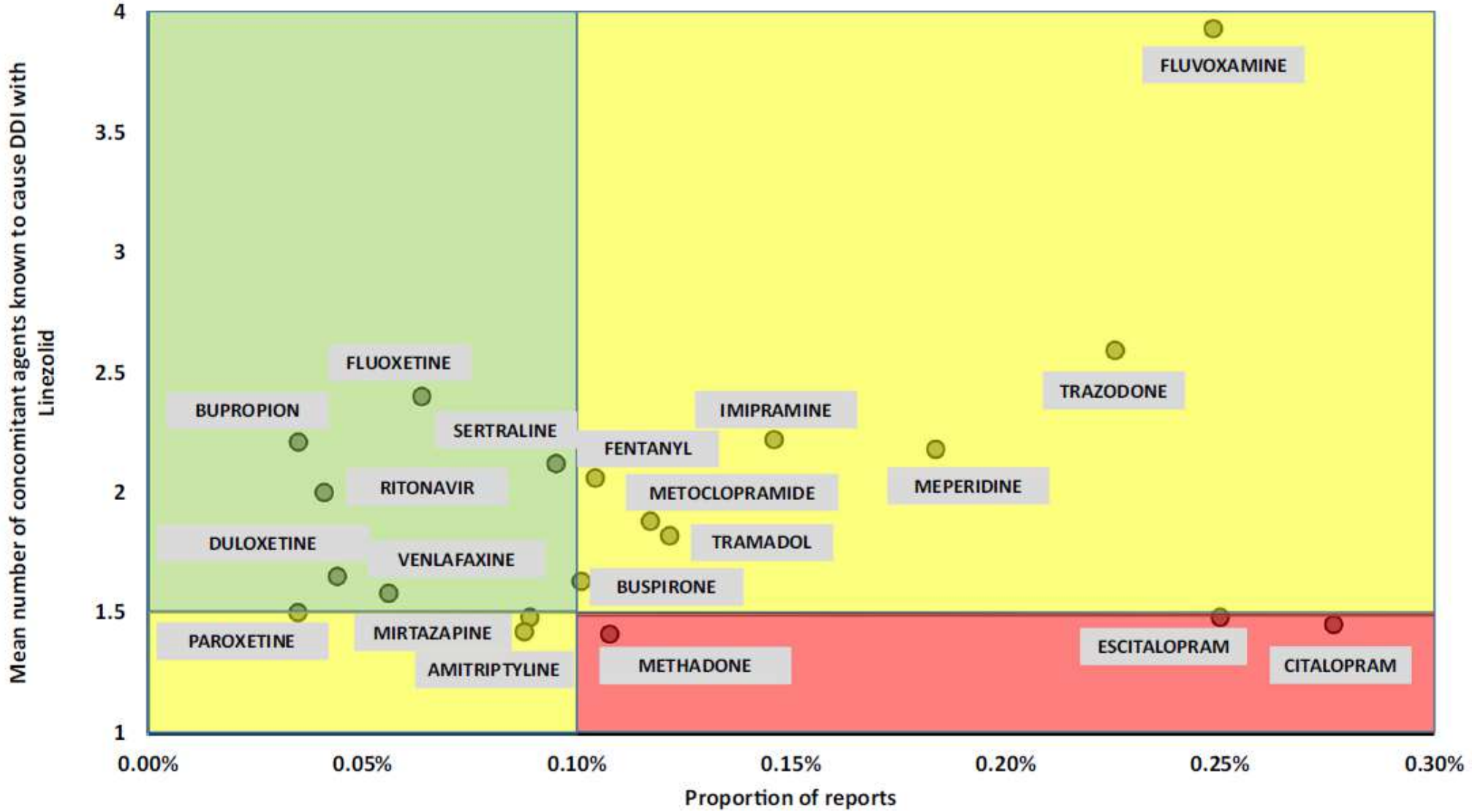
INTERACCIONS

Table 2 Drug–drug interactions

Antimicrobial agent	Interacting drugs → adverse side effect
Aminoglycosides [120]	Amphotericin B, cyclosporin, cisplatin, loop diuretics, tacrolimus, vancomycin → ↑ nephrotoxicity
Amoxicillin, ampicillin [121, 122]	Allopurinol → rash
Fluoroquinolones [123–126]	Medications containing aluminum, iron, magnesium, or zinc; antacids; sucralfate → ↓ absorption of fluoroquinolones
Ciprofloxacin	Antiarrhythmics → ventricular arrhythmias
	Calcium-containing supplements ↓ absorption of ciprofloxacin
	Theophylline → ↑ theophylline concentration
	Warfarin → ↑ bleeding risk
Linezolid [127]	Serotoninergic drugs (MAOIs, TCAs, SSRIs) → serotonin syndrome
Azithromycin [128]	Drugs containing aluminum or magnesium → ↓ azithromycin absorption
Clarithromycin and erythromycin [129–131]	Calcium channel blockers, HMG-Co-A reductase inhibitors, cyclosporine, digoxin, theophylline, and warfarin; DOACs → ↑ concentration of interacting drugs; ↑ concentration of the antibiotic (calcium channel blockers).
Metronidazole [132]	Warfarin → ↑ bleeding risk
	Alcohol → disulfiram-like reaction
Rifampin [133]	Antacids → ↓ rifampin concentration
	Antiarrhythmics, benzodiazepines, calcium channel blockers, corticosteroids, digoxin, enalapril, estrogens and/or progestins, methadone, phenytoin, tamoxifen, theophylline, valproate, voriconazole, warfarin, DOACs → ↓ concentration of the interacting drugs
Tetracyclines [134–138]	Drugs containing aluminum, calcium, iron or magnesium; bismuth subsalicylate → ↓ tetracycline absorption
	Digoxin → ↑ digoxin toxicity
Triazole antifungals [139–141]	Carbamazepine, phenobarbital, phenytoin and rifampin → ↓ concentration of antifungals
	Antiarrhythmics, benzodiazepines, calcium channel blockers, corticosteroids, digoxin, HMG-CoA reductase inhibitors, sulfonylureas, warfarin, DOACs → ↑ concentration of interacting drugs
Itraconazole, ketoconazole	Antacids, H2-receptor antagonists, PPIs → ↓ antifungal absorption
Voriconazole	Phenytoin, PPIs → ↑ concentration of interacting drugs
Trimethoprim-sulfamethoxazole [142]	Phenytoin → ↑ phenytoin concentration
	Sulfonylureas → hypoglycemia
	Warfarin → ↑ bleeding risk
	ACE inhibitors, potassium-sparing diuretics → hyperkalemia

Soraci L et al. Safety and Tolerability of Antimicrobial Agents in the Older Patient. Drugs Aging 2023; 40: 499-526
Anyrs P et al. An international Consensus List of Potentially Clinically Significant Drug-Drug Interactions in older people. JAMDA 2021; 22(10): 2121-2133

INTERACCIONS



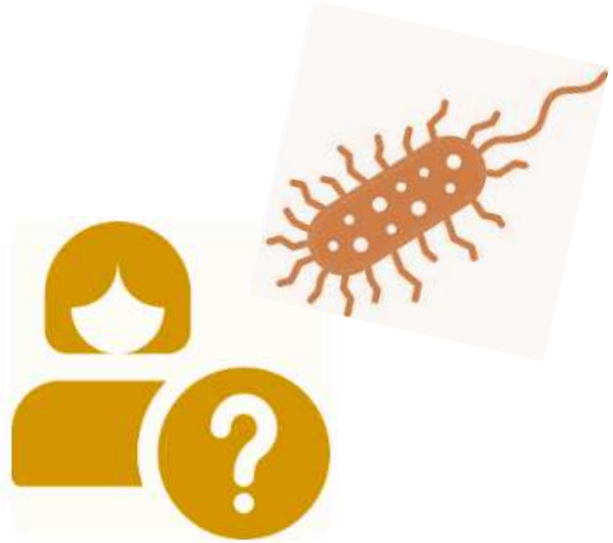
Gatti M et al. Serotonin syndrome by drug interactions with linezolid: clues from pharmacovigilance-pharmacokinetic/pharmacodynamic analysis. Eur Journ Clin Pharmacol 2021; 77: 233-239

01 IMPACTE DEL PK-PD DELS ANTIBIÒTICS i LA SEVA TOXICITAT

02 TOXICITAT EN L'ECOLOGIA i MICROBIOMA DELS ANTIBIÒTICS

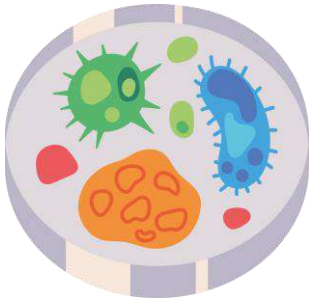
03 TOXICITAT ORGÀNICA DELS ANTIBIÒTICS

04 ESTRATÈGIES PER A LA PREVENCIÓ i MANEIG DE LA TOXICITAT DELS ANTIBIÒTICS

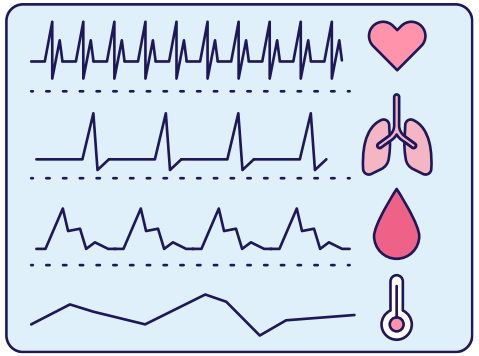


ESTÀ REALMENT INDICAT L'ÚS DE L'ANTIBIÒTIC?

ÉS LA DURADA DEL TRACTAMENT LA CORRECTE?
Shorter is Better



PROGRAMES DE QUALITAT PRODIM + PROA

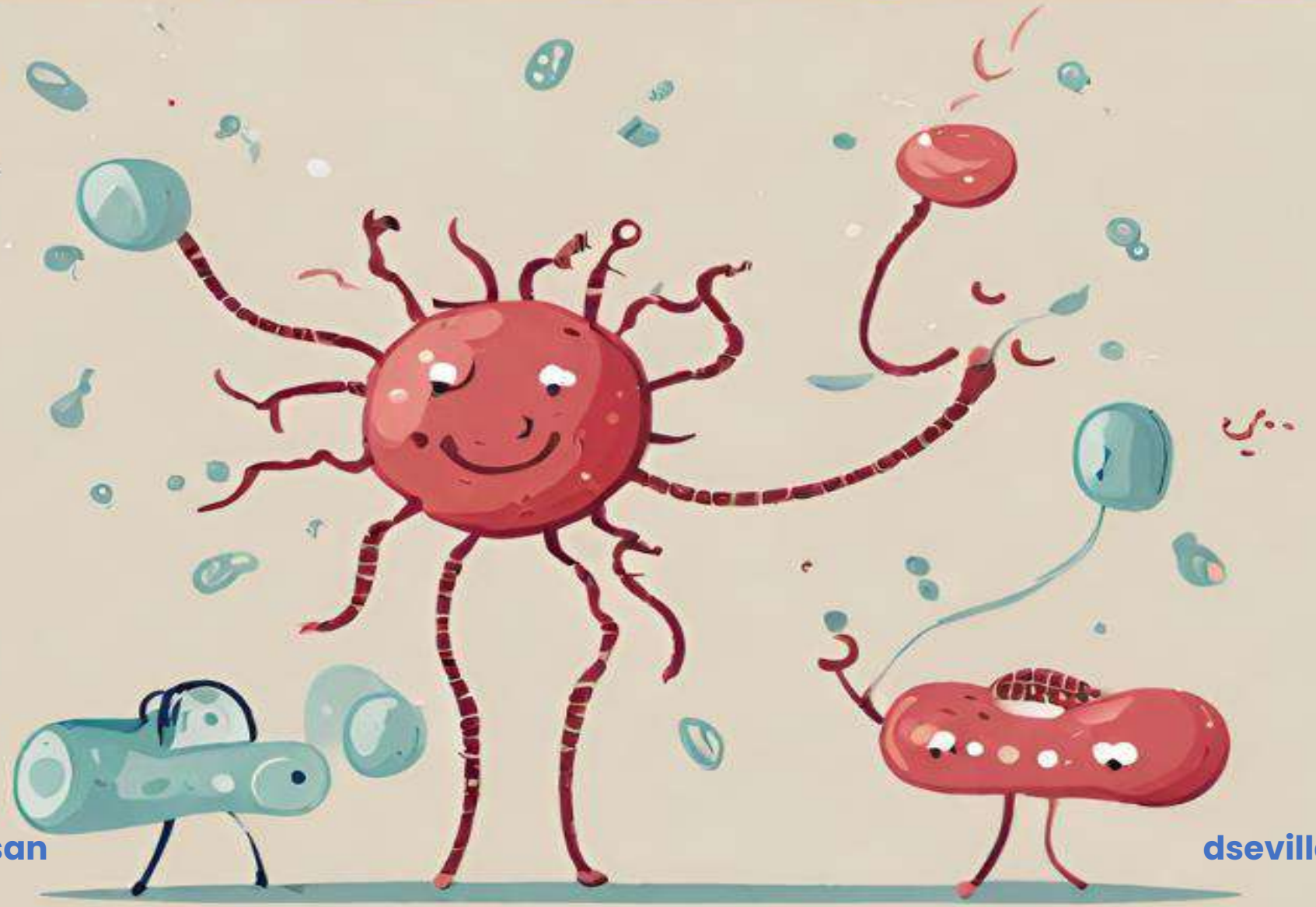


MONITORITZACIÓ PACIENT i BIOMARCADORS

MONITORITZACIÓ FÀRMAC (*TDM*)

PREVENCIÓ + FORMACIÓ + COMUNICACIÓ

THANK YOU!



@danisevisan

dsevilla@perevirgili.cat