Place du Zavicefta (ceftazidime/avibactam) dans le traitement des Pneumonies nosocomiales, Infections des voies urinaires et des Infections intra-abdominales compliquées, chez les adultes

Mabrouk BAHLOUL

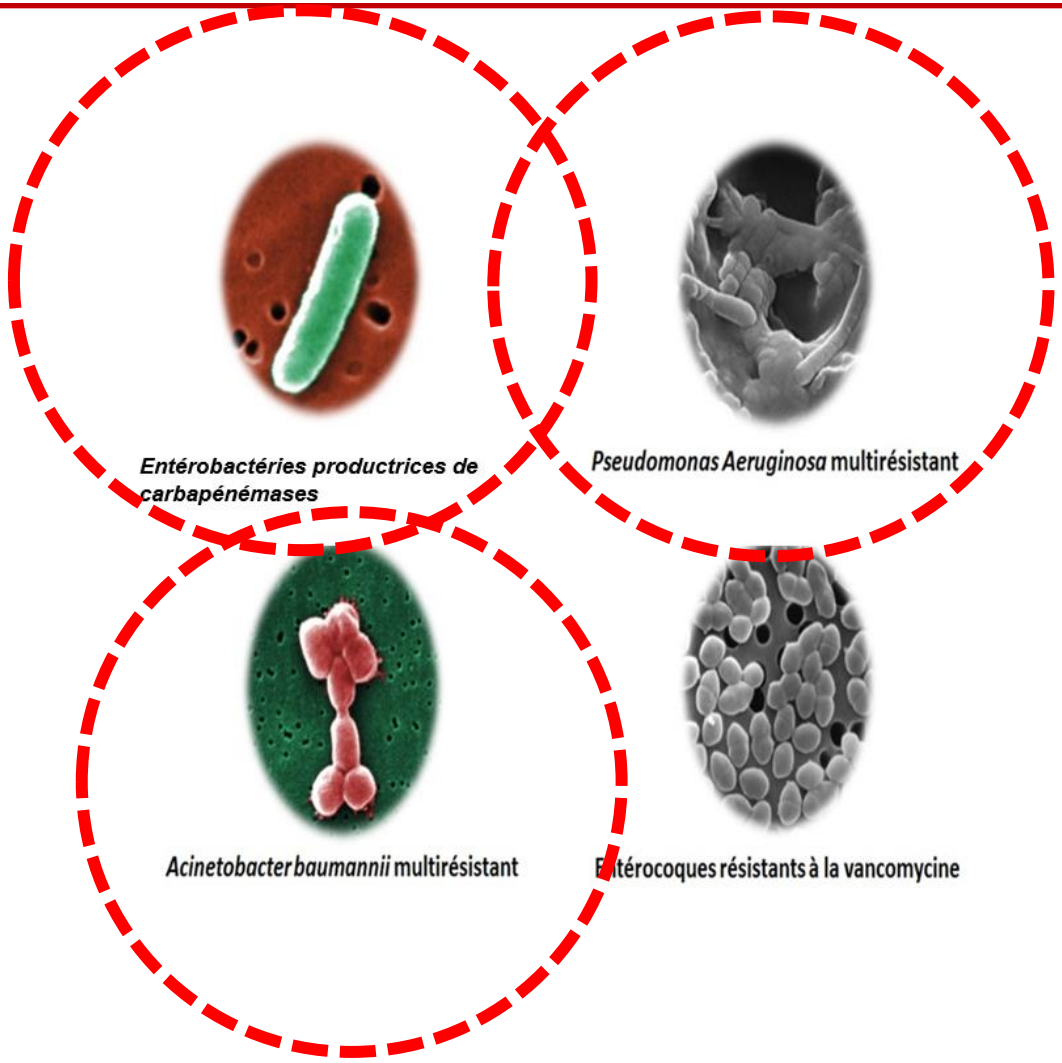
Professor in ICU. Habib Bourguiba University Hospital. Sfax-Tunisia

Email: bahloulmab@yahoo.fr

Samedi 2 décembre 2023

PP-ZVA-TUN-0021

En USI: Bactéries de + en + résistantes



Antibiotics **2022**, *11*, 1009. https://doi.org/10.3390/antibiotics11081009

Introduction

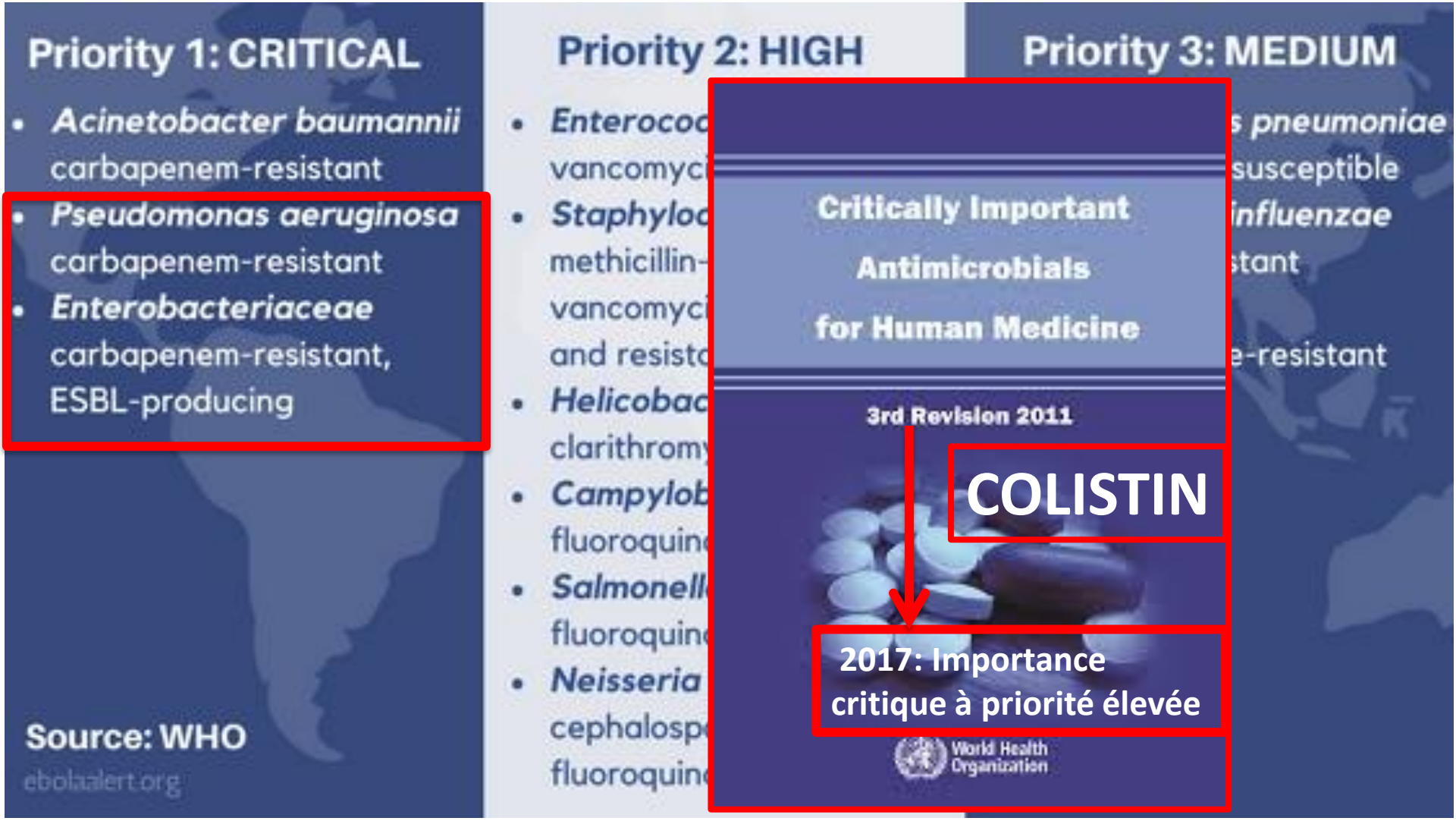
La résistance aux carbapénèmes:

Menace mondiale très sérieuse

Antibiotics **2022**, *11*, 1009. https://doi.org/10.3390/antibiotics11081009

WHO, 2017

liste «d'agents pathogènes prioritaires»

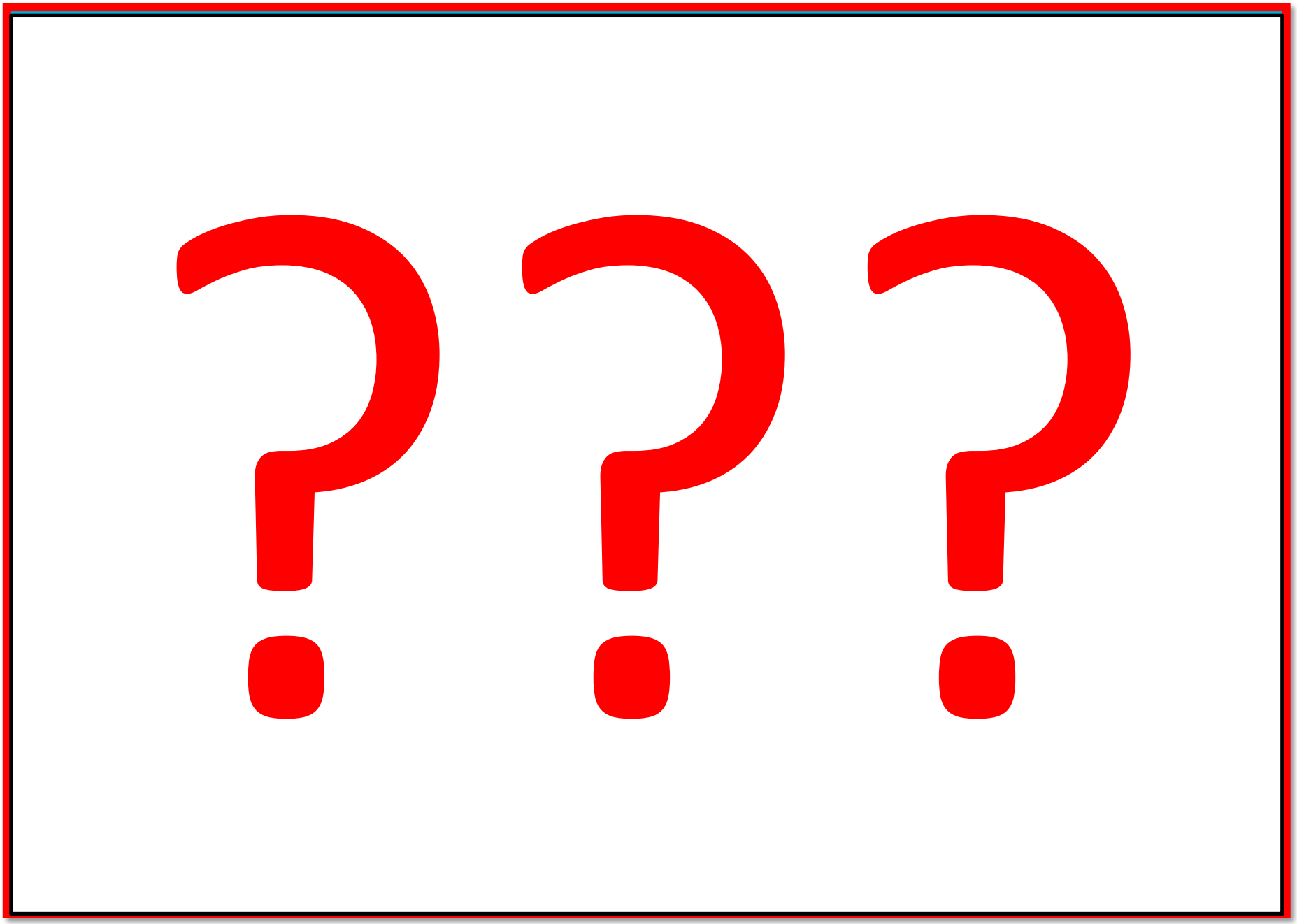


Deaths attributable to AMR every year by 2050: **10 millions**

La résistance aux antimicrobiens constitue une menace croissante pour la santé

Review on Antimicrobial Resistance
Tackling drug-resistant infections globally

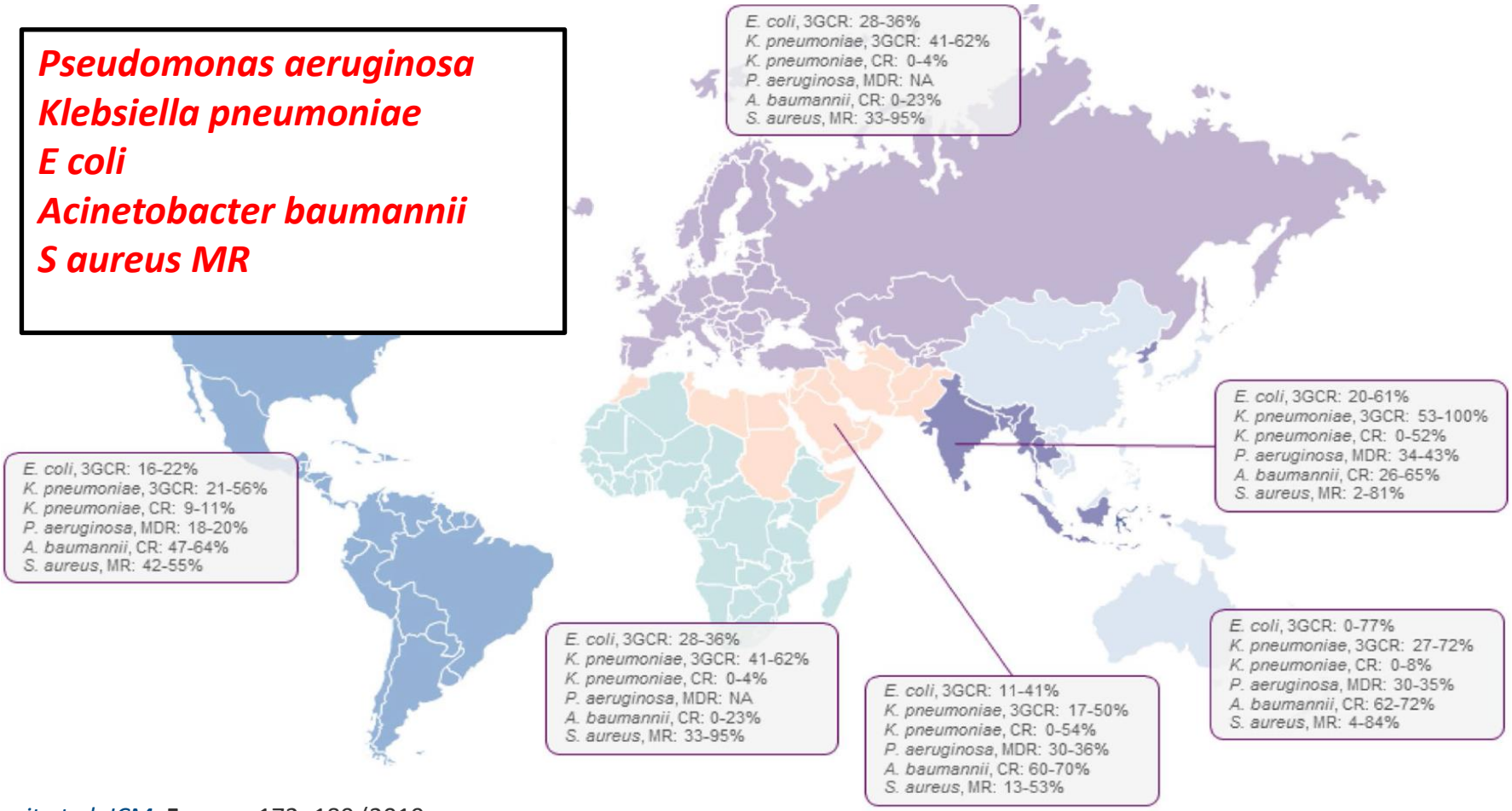
World Health Organization
The Americas



REVIEW

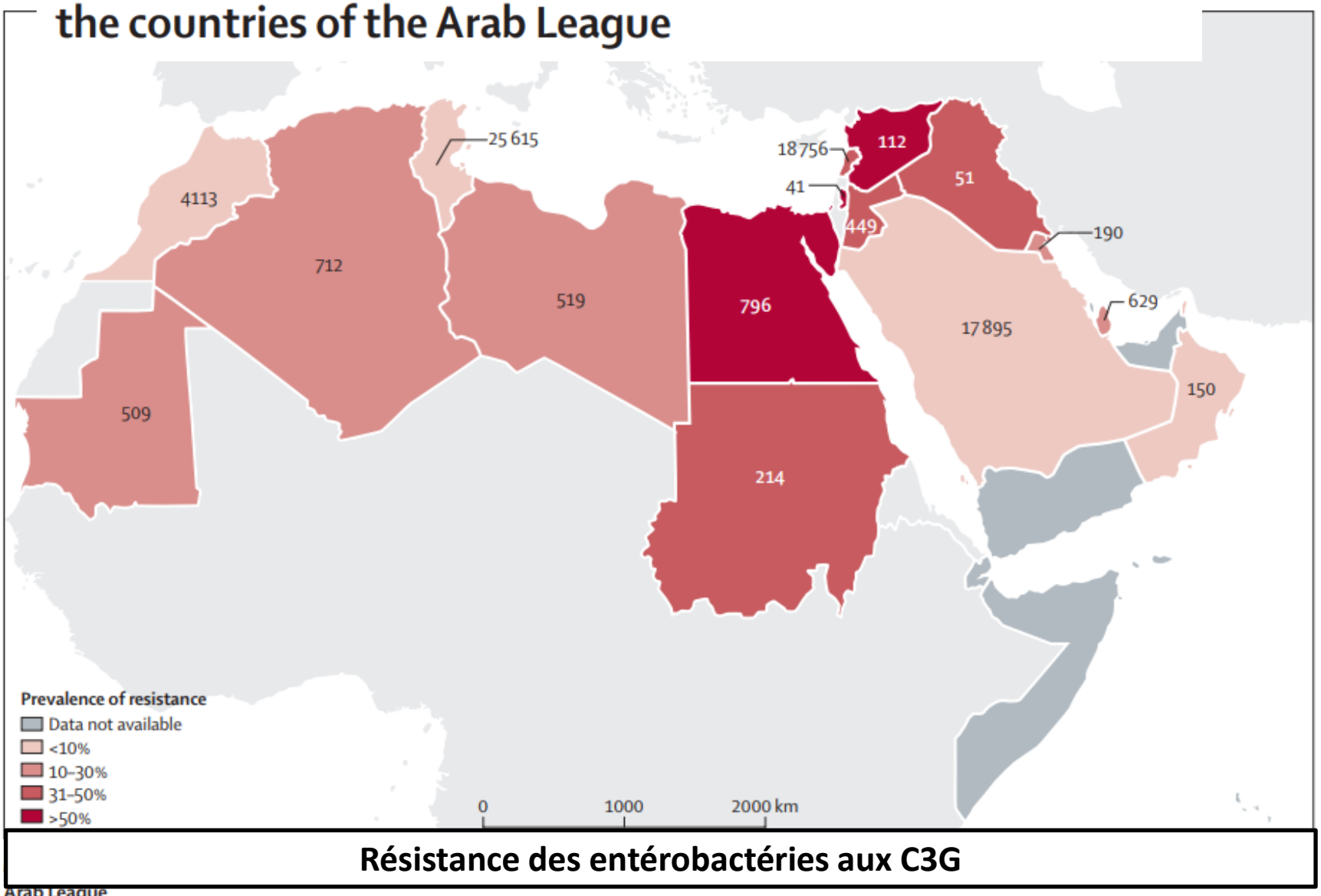
Rationalizing antimicrobial therapy in the ICU: a narrative review

Pseudomonas aeruginosa
Klebsiella pneumoniae
E coli
Acinetobacter baumannii
S aureus MR



Timsit et al; ICM; **5**, pages172–189 (2019

Epidemiology of common resistant bacterial pathogens in the countries of the Arab League

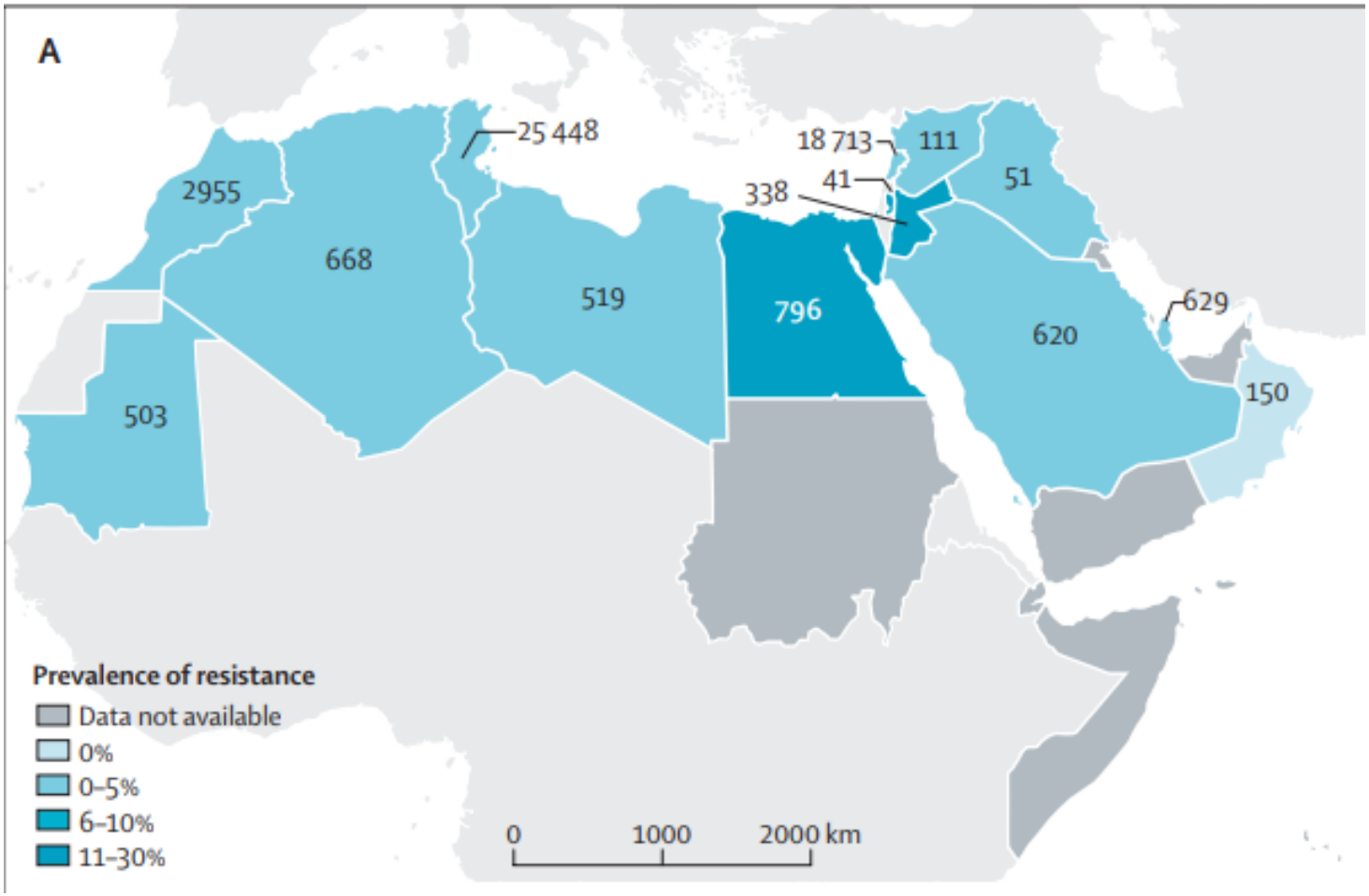


Résistance des entérobactéries aux C3G

Arab League

Lancet Infect Dis. 2018 Dec;18(12):e379-e394. doi: 10.1016/S1473-3099(18)30414-6.

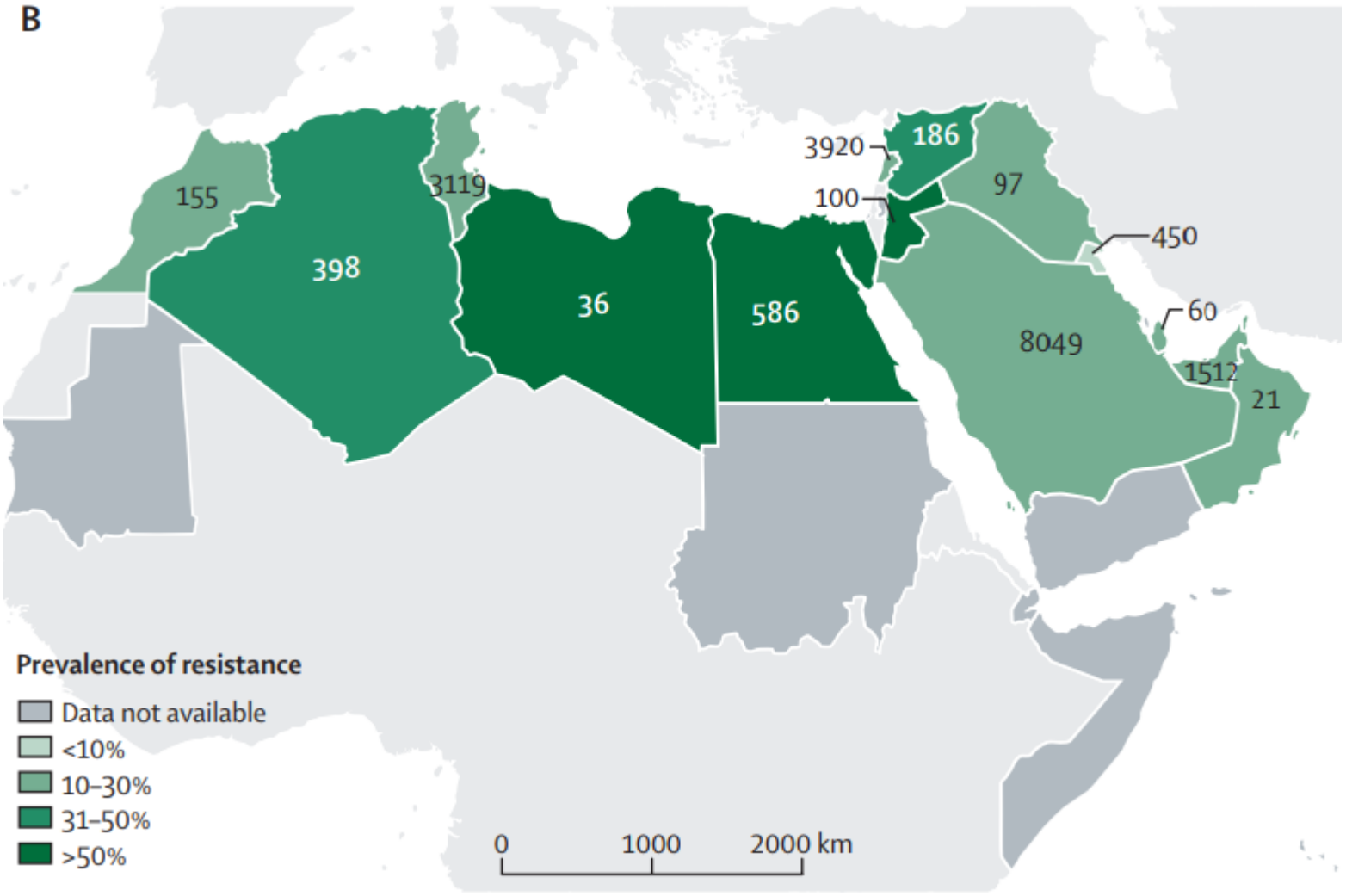
Epidemiology of common resistant bacterial pathogens in the countries of the Arab League



Distribution of carbapenem-resistant Enterobacteriaceae (only Escherichia coli and Klebsiella pneumoniae; A)

Lancet Infect Dis. 2018 Dec;18(12):e379-e394. doi: 10.1016/S1473-3099(18)30414-6

Epidemiology of common resistant bacterial pathogens in the countries of the Arab League



Carbapenem-resistant Pseudomonas aeruginosa (B)

Lancet Infect Dis. 2018 Dec;18(12):e379-e394. doi: 10.1016/S1473-3099(18)30414-6

Epidemiology, risk factors, and clinical outcomes of carbapenem resistant Enterobacterales in Africa: a systematic review

- 169 études (2000 to 2023)
- Afrique du nord: 92 études (54%) **+++**
- **1546 patients**
- **8478/15666 (54%) Entérobactéries Carbapenemase**
  - *Klebsiella spp*: 72%
  - *Escherichia coli*: 13.5%;
  - *Enterobacter* (8.3%).

Journal Pre-proof; Journal of Global Antimicrobial Resistance :https://doi.org/10.1016/j.jgar.2023.10.008

Epidemiology, risk factors, and clinical outcomes of carbapenem resistant Enterobacterales in Africa: a systematic review

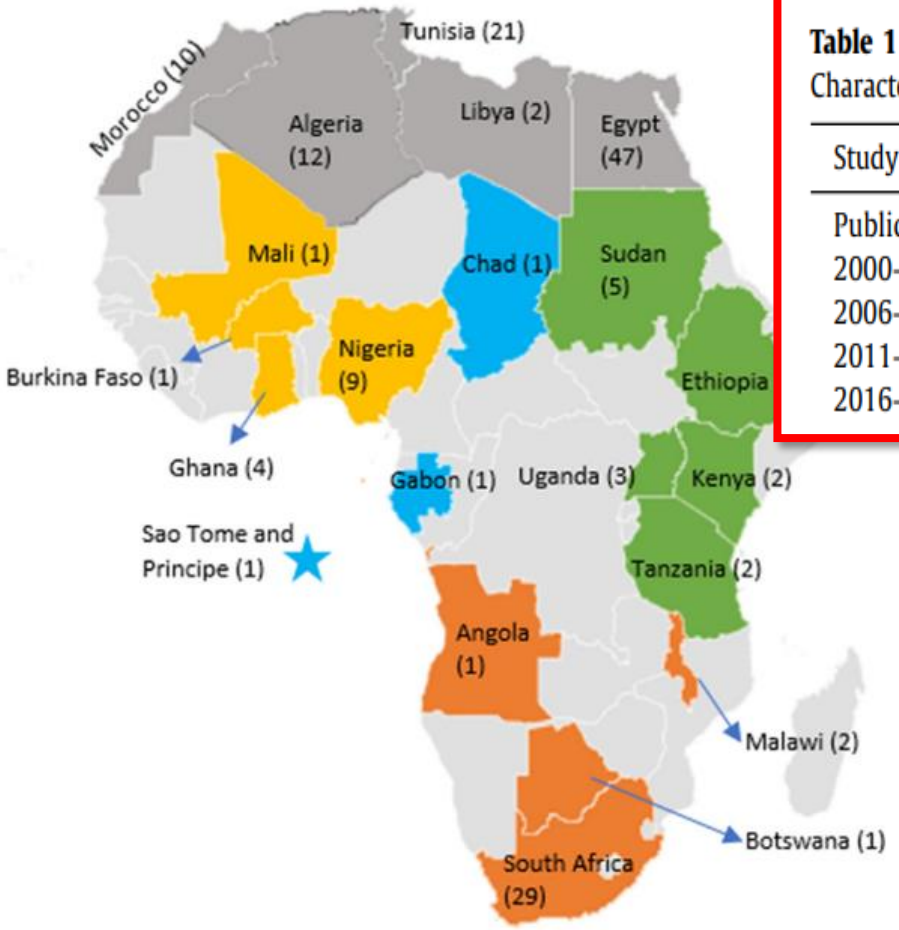


Table 1
Characteristics of articles included in the systematic review.

Study characteristic	Number of studies, n = 169 (%)
Publication year	
2000–2005	0 (0)
2006–2010	2 (1.2%)
2011–2015	29 (17.2%)
2016–2022	138 (81.6%)

Gene de résistance:

- **NDM (43.1%) and**
- **OXA-48-like (42.9%).**

Journal Pre-proof; Journal of Global Antimicrobial Resistance :https://doi.org/10.1016/j.jgar.2023.10.008

Epidemiology, risk factors, and clinical outcomes of carbapenem resistant Enterobacterales in Africa: a systematic review

- **Tunisie: * 21 études**

  *** 986 souches;**

  *** 472 souches CR(47,9%)**

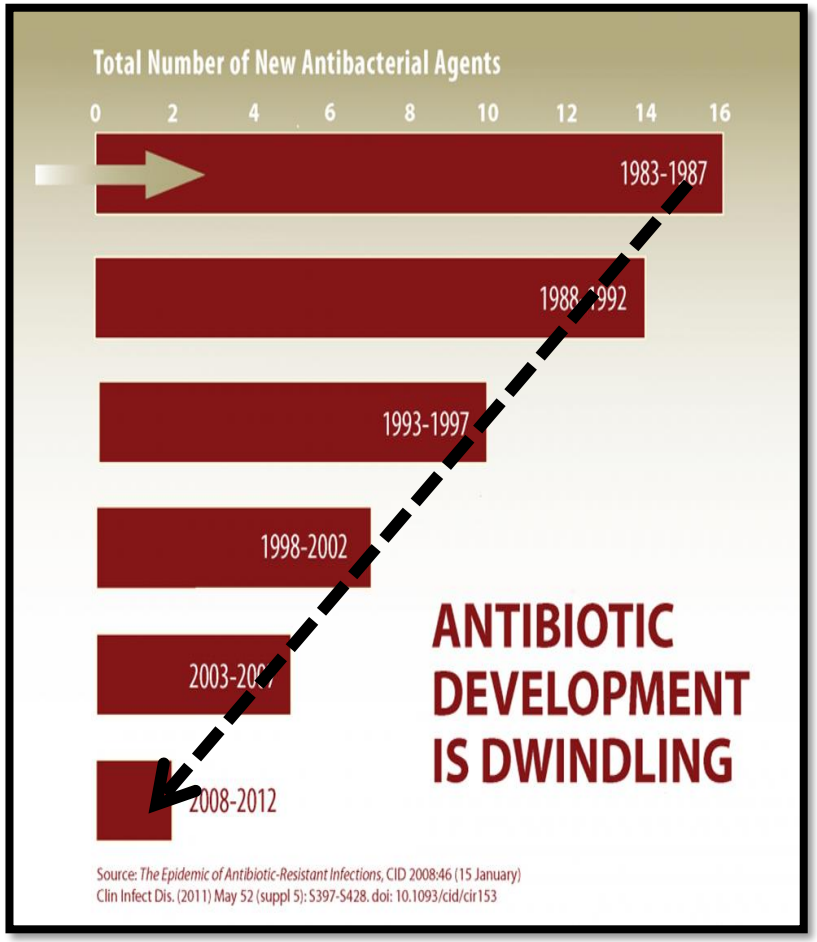
  *** OXA-48-like 370 (78,4%);**

  *** NDM: 96 (20,3%)**

Journal Pre-proof; Journal of Global Antimicrobial Resistance :https://doi.org/10.1016/j.jgar.2023.10.008

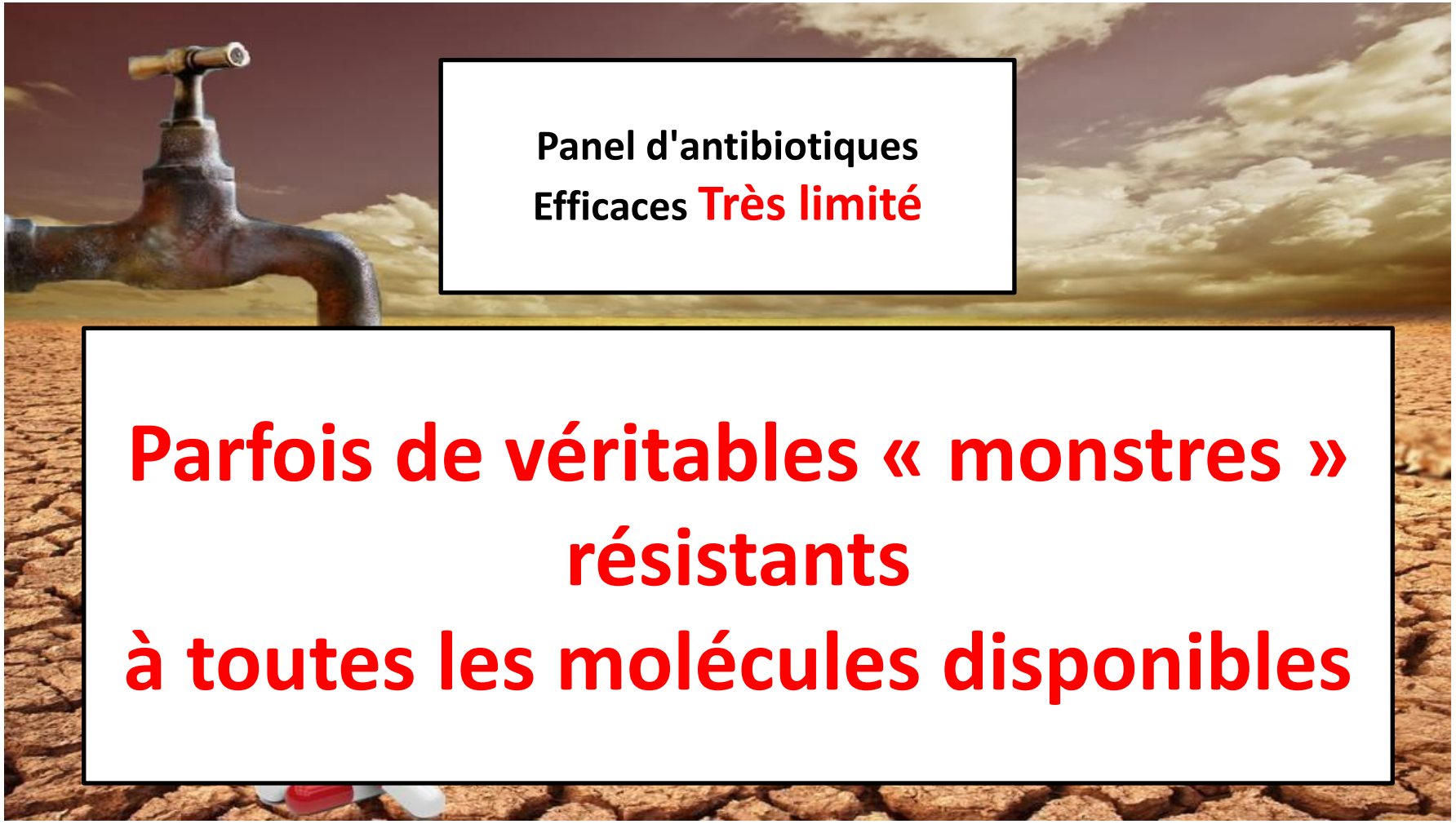
Agents pathogènes

- *Klebsiella pneumoniae*
- *Pseudomonas aeruginosa*
- *Escherichia.coli,*
- *Acinetobacter baumannii*
- ***Staphylococcus aureus***



Antibiotics **2022**, *11*, 1009. https://doi.org/10.3390/antibiotics11081009

Antibiotiques de moins en moins efficaces



Panel d'antibiotiques
Efficaces Très limité

Parfois de véritables « monstres » résistants à toutes les molécules disponibles

Consommation d'antibiotiques en santé animale, projection 2030

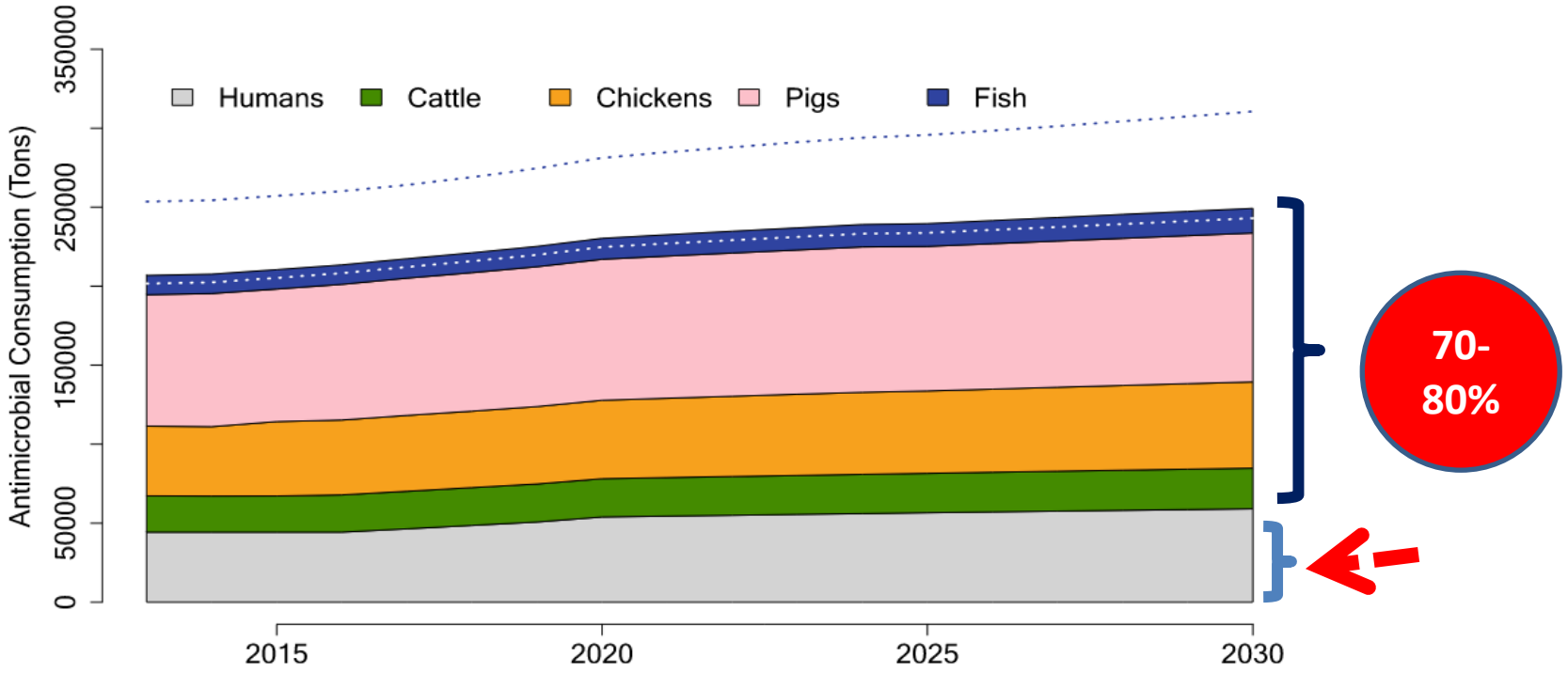


Figure 3. Global antimicrobial consumption, 2013–2030. Dotted lines represent the 95% uncertainty interval for fish.

Scientific Reports | (2020) 10:21878

Les années passent…Les résistances acquises aux ATB augmentent!

- **Pan-drug-résistance (PDR)**

antibiotics

MDPI

•25 pays

• 5 continents.

* Mortalité Associée

40-70%

Agents pathogènes

- *Klebsiella pneumoniae*
- *Pseudomonas aeruginosa*
- *Escherichia.coli,*
- *Acinetobacter baumannii*
- ***Staphylococcus aureus***

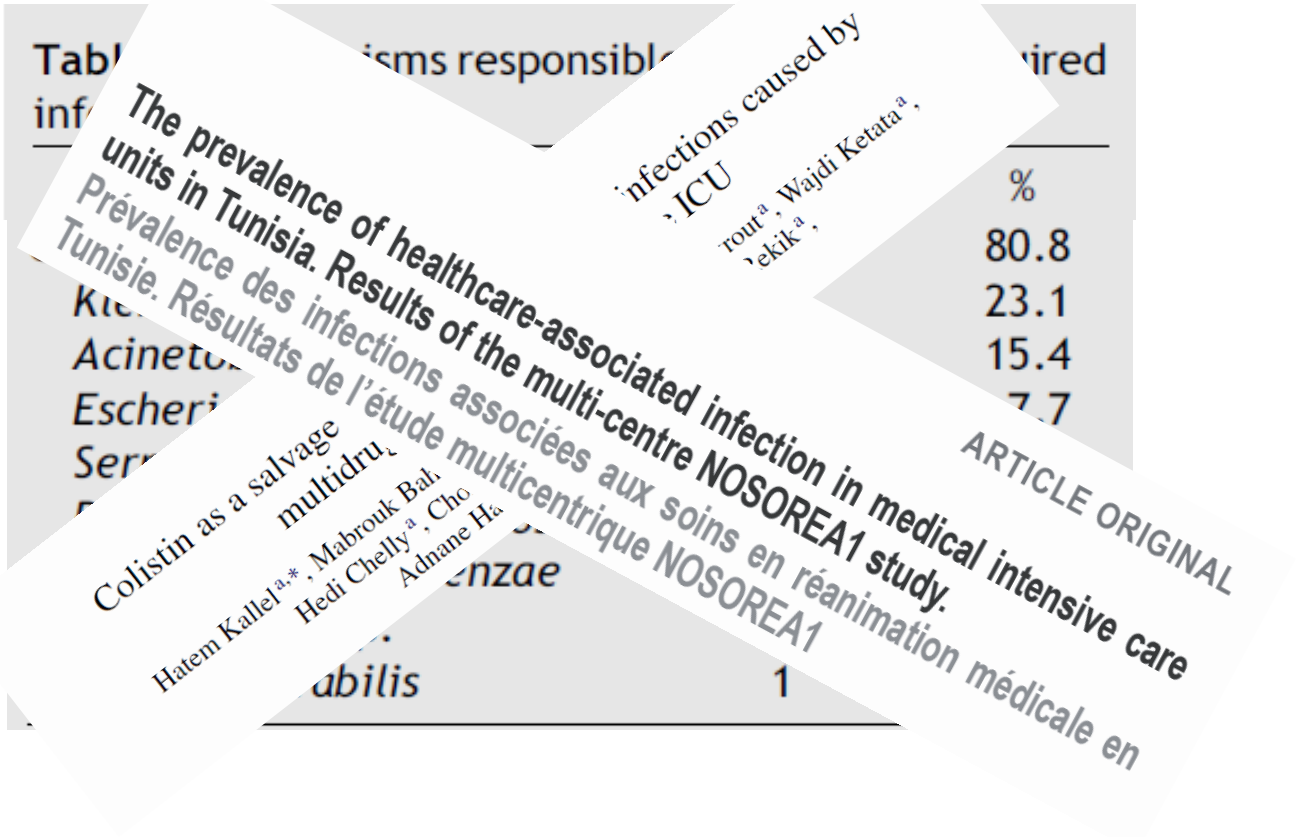
Traitement de sauvetage

Besoin de Nouveaux ATB anti-Gram négatif

En TUNISIE

Prevalence of hospital-acquired infection in a Tunisian hospital

H. Kallel*, M. Bahoul, H. Ksibi, H. Dammak, H. Chelly, C.B. Hamida, A. Chaari, N. Rekik, M. Bouaziz



CONSOMMATION MONDIALE DES ATB PAR PAYS: 2000–2015.

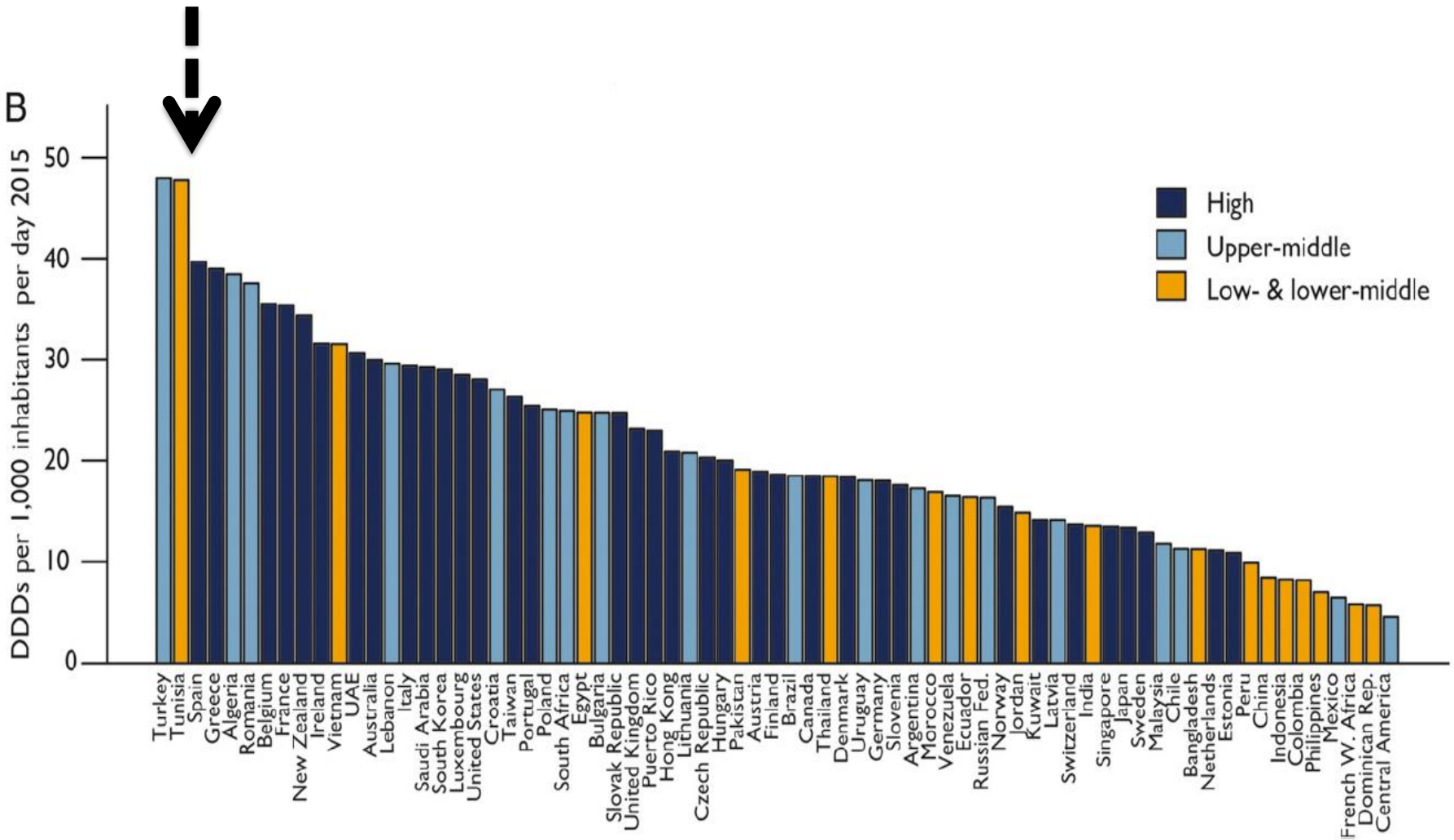
Global increase and geographic convergence in antibiotic consumption between 2000 and 2015

Eili Y. Klein[a,b,c,1], Thomas P. Van Boeckel[d], Elena M. Martinez[a], Suraj Pant[a], Sumanth Gandra[a], Simon A. Levin[e,f,g,1], Herman Goossens[h], and Ramanan Laxminarayan[a,f,i]

[a]Center for Disease Dynamics, Economics & Policy, Washington, DC 20005; [b]Department of Emergency Medicine, Johns Hopkins School of Medicine, Baltimore, MD 21209; [c]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD 21205; [d]Institute of Integrative Biology, ETH Zürich, CH-8006 Zürich, Switzerland; [e]Department of Ecology and Evolutionary Biology, Princeton University, Princeton, NJ 08544; [f]Princeton Environmental Institute, Princeton University, Princeton, NJ 08544; [g]Beijer Institute of Ecological Economics, SE-104 05 Stockholm, Sweden; [h]Laboratory of Medical Microbiology, Vaccine & Infectious Diseases Institute, University of Antwerp, 2610 Antwerp, Belgium; and [i]Department of Global Health, University of Washington, Seattle, WA 98104

Contributed by Simon A. Levin, February 23, 2018 (sent for review October 3, 2017; reviewed by Bruce R. Levin and Dominique L. Monnet)

PNAS | vol. 115 | no. 15 | E3463–E3470


B
DDDs per 1,000 inhabitants per day 2015
0
10
20
30
40
50
High
Upper-middle
Low- & lower-middle
Turkey
Tunisia
Spain
Greece
Algeria
Romania
Belgium
France
New Zealand
Ireland
Vietnam
UAE
Australia
Lebanon
Italy
Saudi Arabia
South Korea
Luxembourg
United States
Croatia
Taiwan
Portugal
Poland
South Africa
Egypt
Bulgaria
Slovak Republic
United Kingdom
Puerto Rico
Hong Kong
Lithuania
Czech Republic
Hungary
Pakistan
Austria
Finland
Brazil
Canada
Thailand
Denmark
Uruguay
Germany
Slovenia
Argentina
Morocco
Venezuela
Ecuador
Russian Fed.
Norway
Jordan
Kuwait
Latvia
Switzerland
India
Singapore
Japan
Sweden
Malaysia
Chile
Bangladesh
Netherlands
Estonia
Peru
China
Indonesia
Colombia
Philippines
Mexico
French W. Africa
Dominican Rep.
Central America

MICROBIAL DRUG RESISTANCE
Volume 00, Number 00, 2019
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DOI: 10.1089/mdr.2019.0138

Research Article

Genetic Background
Multiantimicrobial
Feces of Healthy

Mohamed Sa
Sana Lengli

[1]*Université de Tunis*
Tunis 1006, Tunisia
[2]*Université de Tunis El Mana*
[3]*Department of Botany and*
[4]*Área de Microbiología Mole*
[5]*Environmental Sustainabilit*
Dublin, Ireland

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MICROBIAL DRUG RESISTANCE
Volume 00, Number 00, 2019
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DOI: 10.1089/mdr.2019.0138

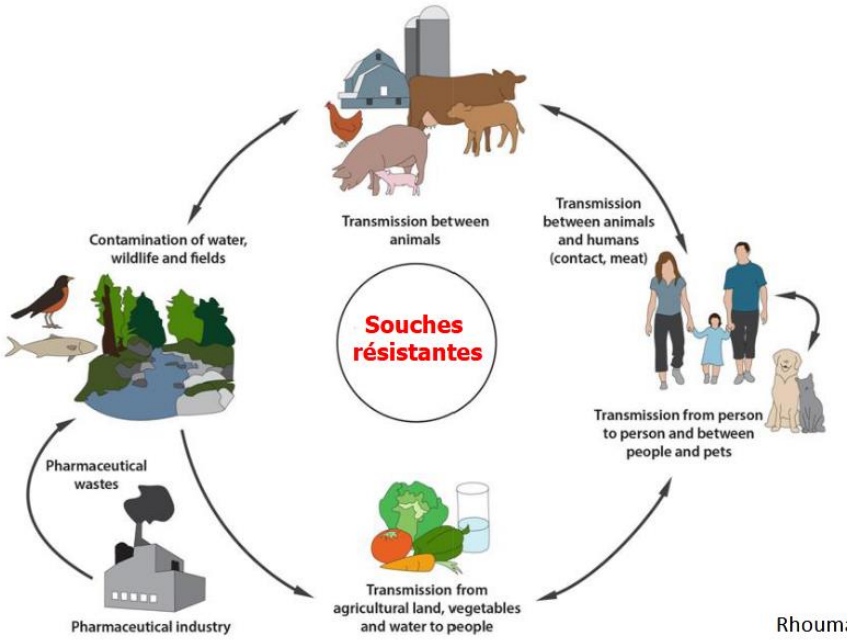
ELSI

Antimicr
enterica se

Rakia Ben Salem[a]
Javier Fernández[c],
María R. Rodicio[c,*]

[a] *Veterinary Research Institute of Tunisia,*
[b] *Faculté des Sciences de Bizerte, Universite*
[c] *Universidad de Oviedo, Departamento de B*
[d] *Regional Center of Veterinary Research, 4000*
[e] *National School of Veterinary Medicine, Depart*

High



Rhouma et coll., 2016

Marie Mo

antibiotics

MDPI

Article

Tunisian Multicenter Study on the Prevalence of Colistin Resistance in Clinical Isolates of Gram Negative Bacilli: Emergence of *Escherichia coli* Harbouring the *mcr-1* Gene

Table 2. Characteristics of colistin-resistant GNB isolates.

	P. aeruginosa (*n* = 28)	*E. coli* (*n* = 7)	*K. pneumoniae* (*n* = 5)	*Enterobacter cloacae* (*n* = 1)	*Raoutella terrigena* (*n* = 1)
Prevalence of colistin resistance, % (90% IC)	9.3 (6.5–12.1)	3 (1.2–4.8)	2.7 (0.8–4.7)	-	-
Colistin MIC [a] range, mg/L	4–128	4–32	32–128	32	32
mcr-1 gene detection, % (90% IC)	0	1.7(0.3–3.1)	0	0	0
ESBL [b], n (encoding genes)	0	3 ($bla_{CTX-M-15}$)	5 ($bla_{CTX-M-15}$)	0	1 ($bla_{CTX-M-15}$)
Carbapenemase, n (encoding genes)	10 (bla_{VIM})	0	5 (bla_{OXA-48})	0	1 (bla_{OXA-48})
Clinical specimen, n (%)					
Urine	2	4	5	1	0
Blood	2	0	0	0	1
Wound	11	3	0	0	0
Sputum	5	0	0	0	0
Others [c]	8	0	0	0	0
Total of isolates (*n* = 836) [d]	301	233	183	25	5

[a] MIC: Minimum Inhibitory Concentrations, [b] ESBL: extended-spectrum-beta-lactamase, Others [c]: [Catheter (*n* = 2), Distal protected aspirate (*n* = 3), pleural fluid (*n* = 3)], Total of isolates (*n* = 836) [d]: include 89 *Acinetobacter baumannii* colistin susceptible isolates.

Antibiotiques de référence : les carbapénèmes

Carbapénèmes = traitement de référence des infections documentées à E-BLSE

Fausse bonne idée

1/ Consommation des carbapénèmes x10

2/ Emergence de résistance aux carbapénèmes (Plusieurs mécanismes)

→ impasse thérapeutique

Carbapénèmases

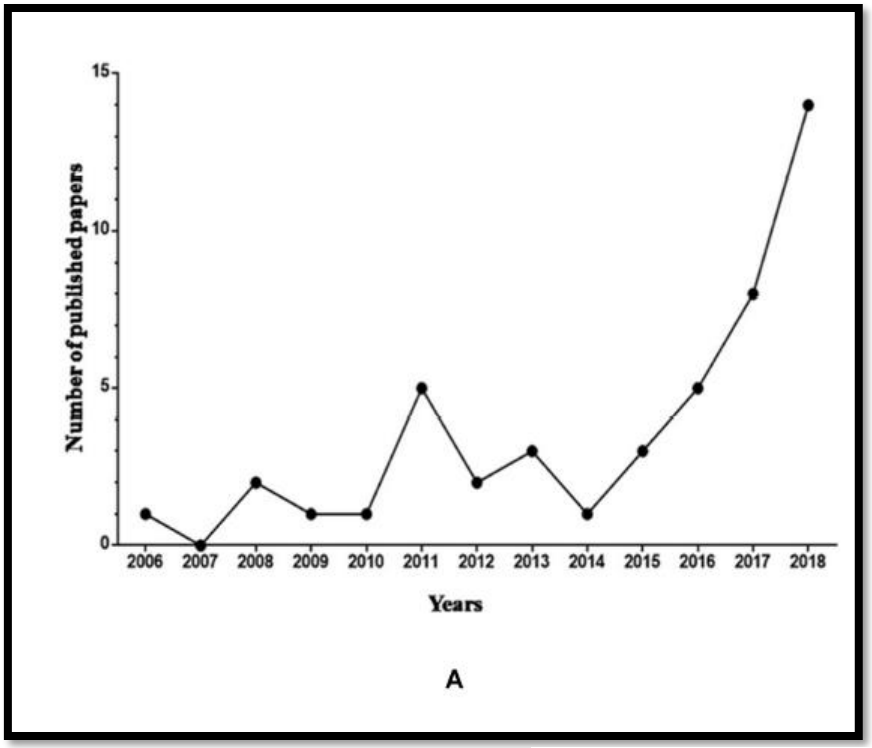
Infection and Drug Resistance

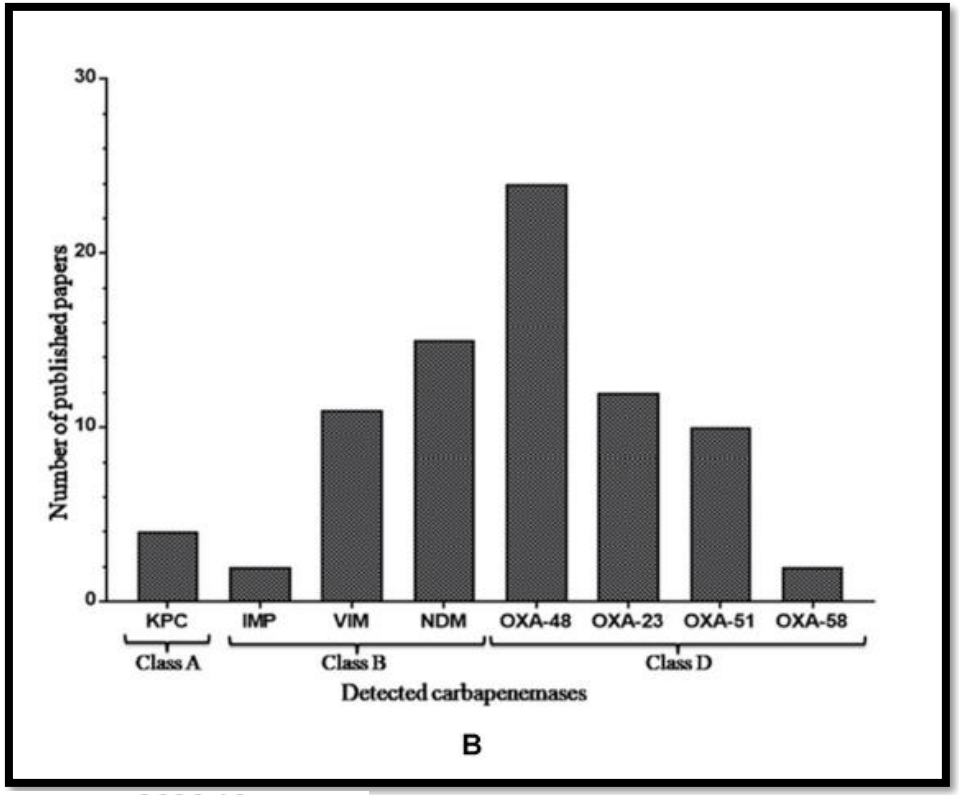
Dovepress
open access to scientific and medical research

Open Access Full Text Article

REVIEW

Carbapenemase Producing Gram-Negative Bacteria in Tunisia: History of Thirteen Years of Challenge





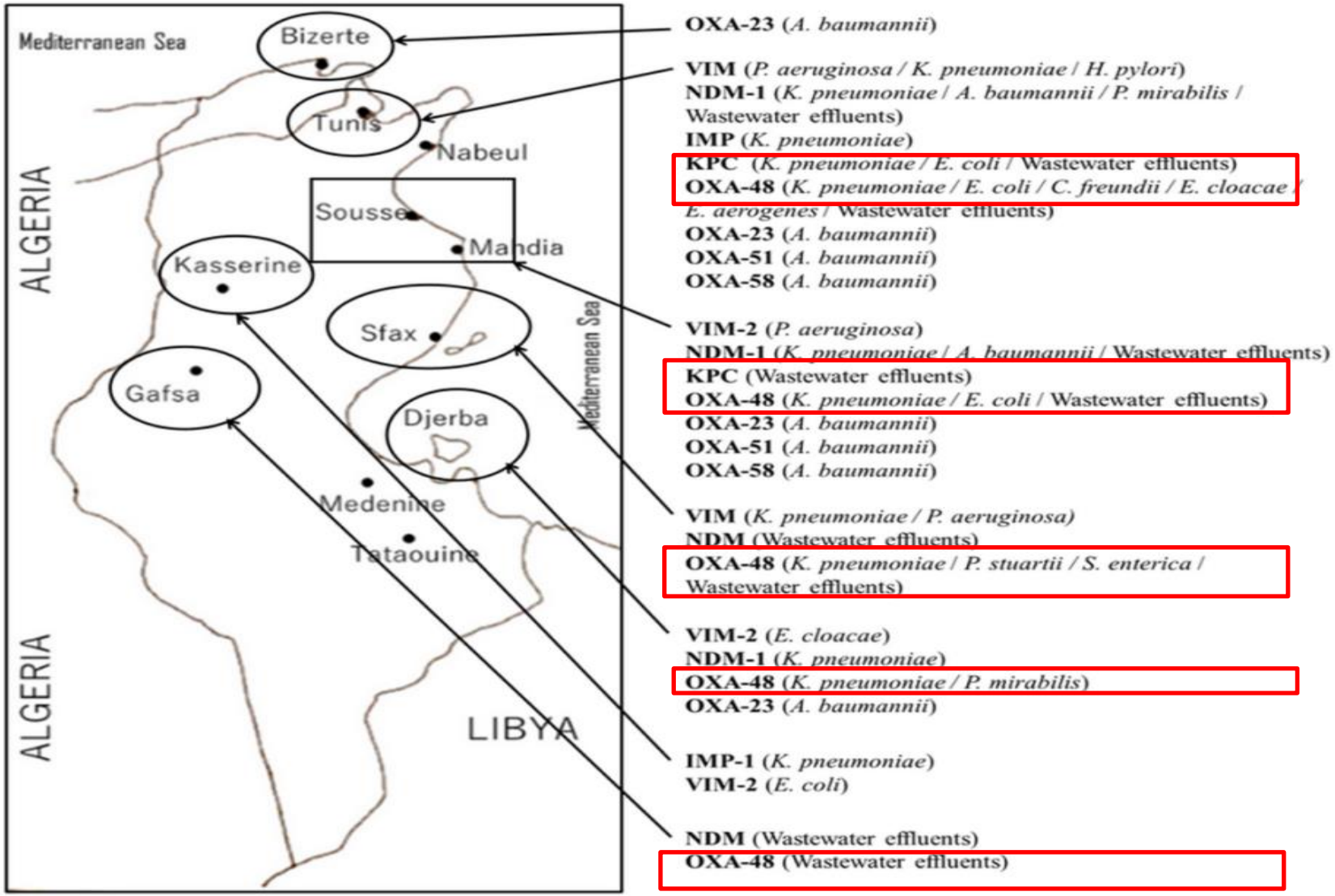


Figure 2 Regional distribution of carbapenemase producing Gram-negative bacteria in Tunisia from 2006 to 2019.

Epidemiology, risk factors, and clinical outcomes of carbapenem resistant Enterobacterales in Africa: a systematic review

Journal Pre-proof; Journal of Global Antimicrobial Resistance :https://doi.org/10.1016/j.jgar.2023.10.008

REA Sfax 2021

	ruginosa
Pipéracilline-Taz	25%
Ceftazidime	25%
Imipénème	29%
Amikacine	10%
Gentamicine	10%
Ciprofloxacine	25%

Antibiotiques Disponibles

Besoin de Nouveaux ATB anti-Gram négatif

Nouveaux ATB anti-Gram négatif

The Novel β-Lactamase Inhibitors

- **Ceftazidime/avibactam**
- Ceftolozane / Tazobactam
- Méropénème-vaborbactam
- Imipénème-cilastatine-relebactam
- Aztréonam-avibactam

https://www.has-sante.fr/jcms/p_3152692/fr/zavicefta-avibactam/-ceftazidime

Ceftazidime C3G

+

Avibactam Inhibiteur non β-lactamine

- Disponible uniquement par voie I.V.
- Action temps-dépendant bactéricide
- Posologie recommandée : 2 g / 500 mg x 3/j sur 2h I.V.

https://www.has-sante.fr/jcms/p_3152692/fr/zavicefta-avibactam/-ceftazidime

Spectre de la Ceftazidime/Avibactam

- **Bactéries à Gram négatif essentiellement :**
- ***Entérobactéries dont E-BLSE et certaines EPC***

- *Classe A : E-BLSE (TEM, SHV, CTX-M), KPC*
- *Classe C : ampC*
- *Certaines Classes D: dont oxa-48*

- ***Pseudomonas aeruginosa***

Spectre de la Ceftazidime/Avibactam

- **Bactéries anaérobies: pas ou peu d'activité**

  inactif sur *Bacteroides spp*.

  inactif sur *Clostridium spp.*

- **Inactif sur :**

❖*S.aureus; E.faecalis; E.faecium*

❖*Stenotrophomonas,*

❖*Acinetobacter*

❖*Carbapénèmases de classe B (NDM1, IMP, VIM) et la plupart des carbapénèmases de classe D*

Indications AMM de ceftazidime / avibactam

1/ Infections intra-abdominales compliquées

2/ Infections des voies urinaires compliquées dont pyélonéphrites

3/ Pneumonies nosocomiales dont les pneumonies nosocomiales acquises sous ventilation mécanique (PAVM)

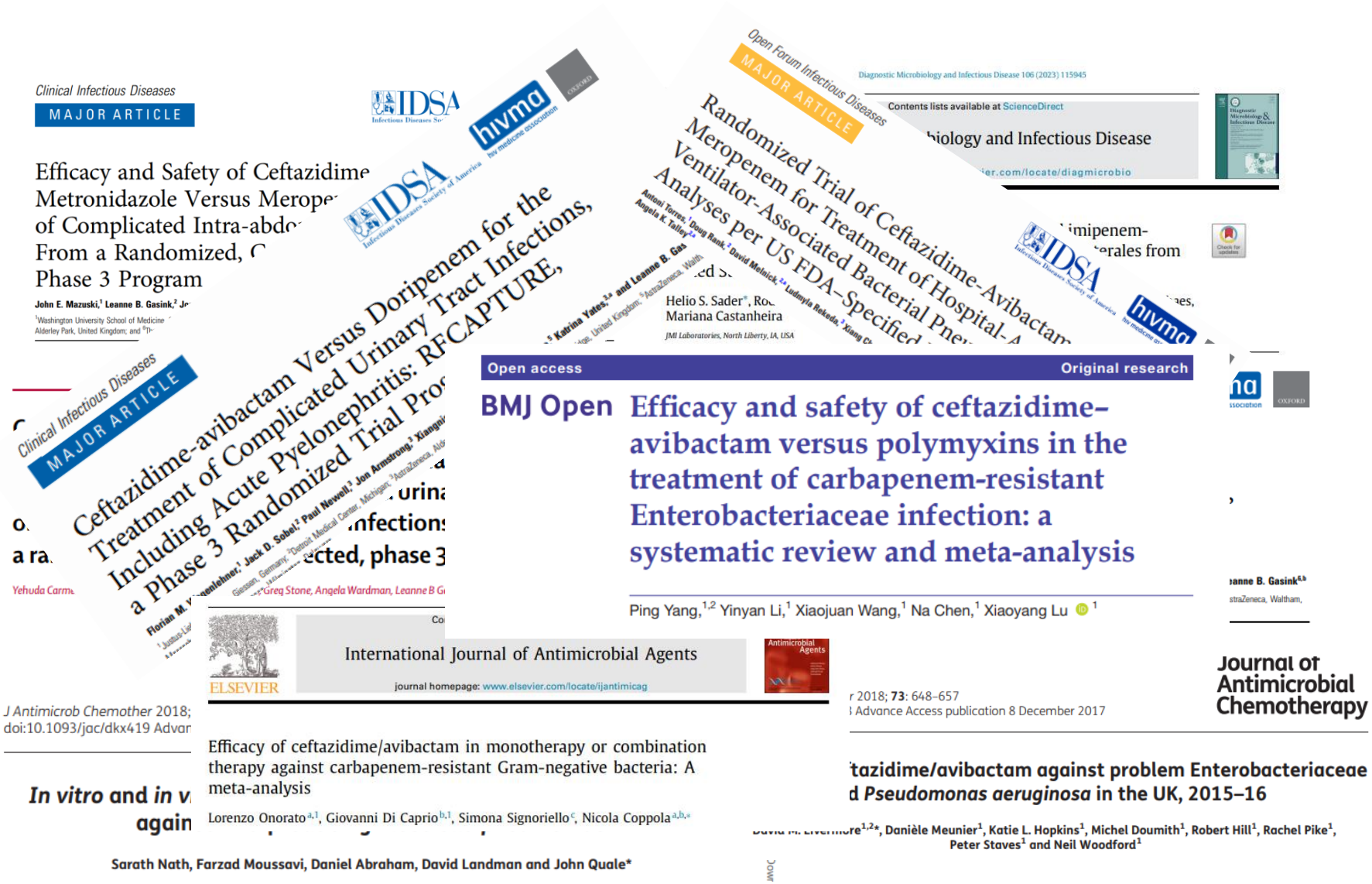
Contre-indications

- Hypersensibilité ceftazidime
- Hypersensibilité avibactam
- Hypersensibilité céphalosporines

Ceftazidime / Avibactam

https://www.has-sante.fr/jcms/p_3152692/fr/zavicefta-avibactam/-ceftazidime

Efficacité: Bien démontrée



Efficacité: Bien démontrée

Frequency and antimicrobial susceptibility of Gram-negative bacteria isolated from patients with pneumonia hospitalized in ICUs of US medical centres (2015–17)

Helio S. Sader*, Mariana Castanheira, Rodrigo E. Mendes and Robert K. Flamm

- 75 US medical centres in 2015–17
- 6091 bacterial isolates
- *Staphylococcus aureus (30.0%),*
- *Pseudomonas aeruginosa* (20.7%), *Klebsiella spp*. (11.8%), *Enterobacter spp*. (8.3%), *Escherichia coli* (7.1%) and *Stenotrophomonas maltophilia* (5.1%).

J Antimicrob Chemother 2018; 73: 3053–3059

Frequency and antimicrobial susceptibility of Gram-negative bacteria isolated from patients with pneumonia hospitalized in ICUs of US medical centres (2015–17)

Helio S. Sader*, Mariana Castanheira, Rodrigo E. Mendes and Robert K. Flamm

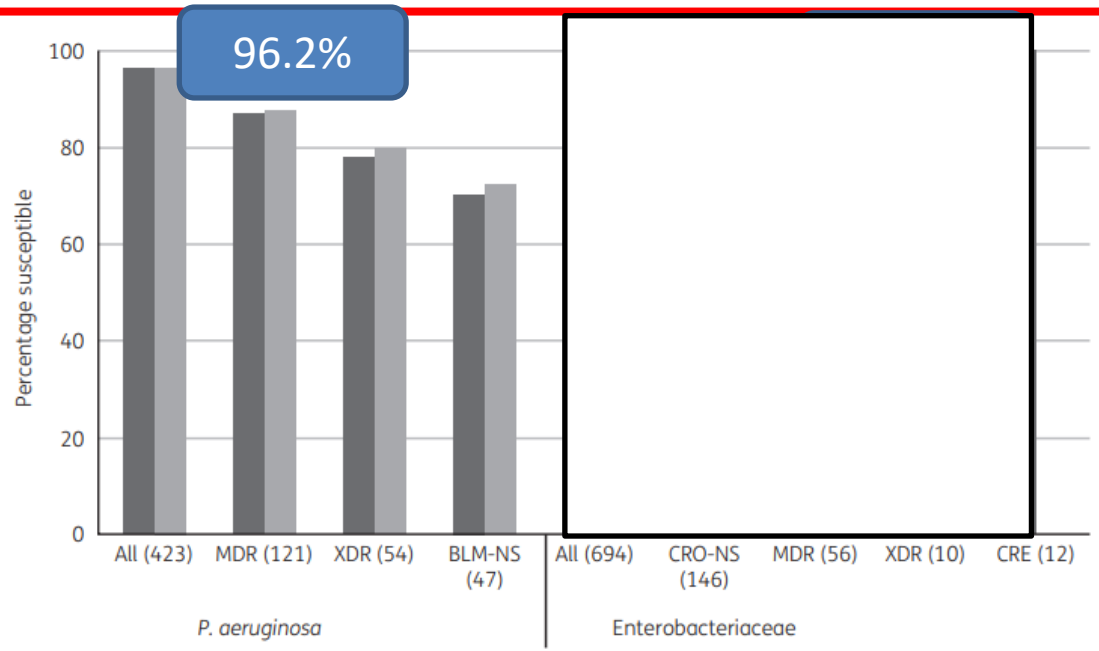


Figure 2. Antimicrobial susceptibility of *P. aeruginosa* and Enterobacteriaceae isolates from 2017 to ceftazidime/avibactam (dark grey bars) and ceftolozane/tazobactam (light grey bars). BLM-NS, β-lactam non-susceptible; i.e. non-susceptible to ceftazidime, meropenem and piperacillin/tazobactam; CRO-NS, ceftriaxone non-susceptible.

J Antimicrob Chemother 2018; 73: 3053–3059

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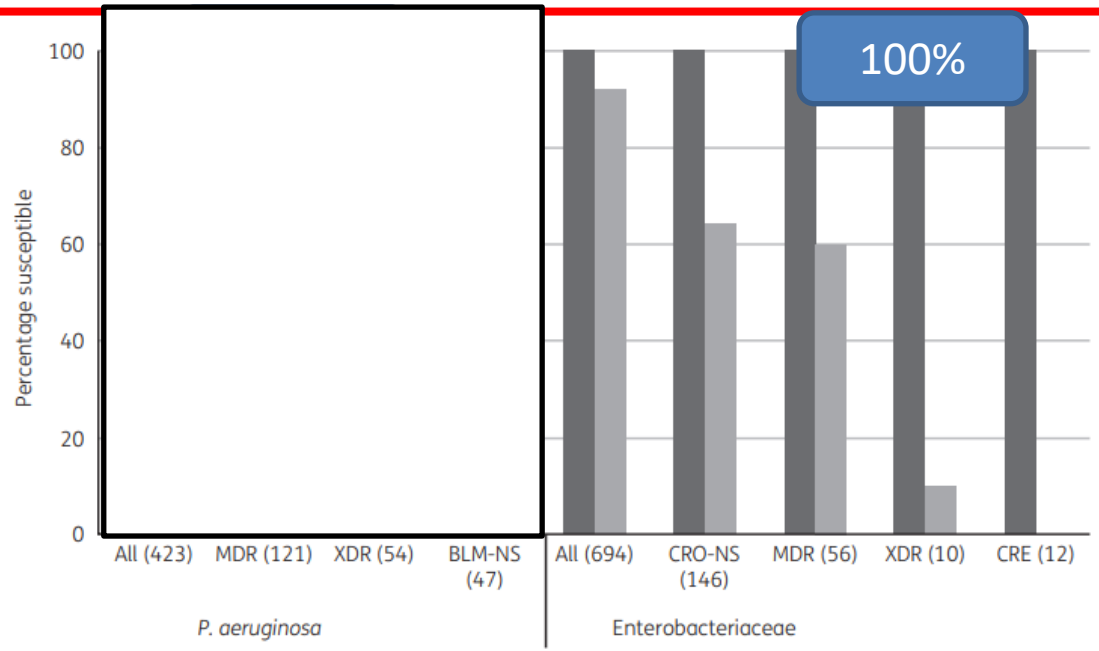

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J Antimicrob Chemother 2018; 73: 3053–3059

Clinical Infectious Diseases
MAJOR ARTICLE

Ceftazidime-avibactam Versus Doripenem for the Treatment of Complicated Urinary Tract Infections, Including Acute Pyelonephritis: RECAPTURE, a Phase 3 Randomized Trial Program

- Étude multicentrique: 25 pays; 160 centres
- 1033 patients: Infection urinaire +/- pyélonéphrite confirmée (223 exclus)
- **810** patients inclus dont 583 (72%) avec PNA
- Deux groupes (1/1):
  - * Ceftazidime/Avibactam :
    - 2,5 g/8heures **(n = 393)**
  - * Doripenem:
    - 500mg x3/j **(n = 417)**

Clinical Infectious Diseases
MAJOR ARTICLE

Ceftazidime-avibactam Versus Doripenem for the Treatment of Complicated Urinary Tract Infections, Including Acute Pyelonephritis: RECAPTURE, a Phase 3 Randomized Trial Program

- Étude multicentrique: 25 pays; 160 centres
- 1033 patients: Infection urinaire +/- pyélonéphrite confirmée (223 exclus)
- 810 patients inclus dont 583 (72%) avec PNA
- Deux groupes (1/1):
  - Ceftazidime/Avibactam : 2,5 g/8heures
  - Doripenem: 500mg x3/j

Durée TTT 10-14 jours

Clinical Infectious Diseases
MAJOR ARTICLE

Ceftazidime-avibactam Versus Doripenem for the Treatment of Complicated Urinary Tract Infections, Including Acute Pyelonephritis: RECAPTURE, a Phase 3 Randomized Trial Program

Germes:

- *Escherichia coli (73,8%)*
- *Klebsiella pneumoniae (12,3%)*
- *P. aeruginosa (4.7%)*
- *P. mirabilis (3.7%)*

Sensible dans 100 % aux traitement prescrit

- **CAZ-AVI (n = 393)**
- **DOR (n = 417)**

Clinical Infectious Diseases
MAJOR ARTICLE

Ceftazidime-avibactam Versus Doripenem for the Treatment of Complicated Urinary Tract Infections, Including Acute Pyelonephritis: RECAPTURE, a Phase 3 Randomized Trial Program

Superiority of Ceftazidime-Avibactam at the 5% significance level

Clinical Infectious Diseases
MAJOR ARTICLE

Efficacy and Safety of Ceftazidime-Avibactam Plus Metronidazole Versus Meropenem in the Treatment of Complicated Intra-abdominal Infection: Results From a Randomized, Controlled, Double-Blind, Phase 3 Program

- 1066 patients avec infection intra-abdominale compliquée
- Ceftazidime-Avibactam + Metronidazole (Groupe 1)
- Meropenem (Groupe 2)
- Critère de jugement principal: guérison clinique 28–35 jours après la randomisation

• CID 2016:62 (1 June) • Mazuski et al

Analysis population	CAZ-AVI + MTZ	MEM	Difference[a]
Réponse Clinique fin TTT			
No. of pts	520	523	
Clinical cure rate[d] (%)	82.5	84.9	− 2.4 (− 6.90 to 2.10)
Réponse Clinique J28–35			
No. of pts	410	416	
Clinical cure rate[d] (%)	91.7	92.5	− 0.8 (− 4.61 to 2.89)
Eradication bacterienne			
No. of pts	413	410	
Clinical cure rate[d] (%)	81.6	85.1	− 3.5 (− 8.64 to 1.58)

Drugs (2018) 78:675–692

• CID 2016:62 (1 June) • Mazuski et al

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Ceftazidime-avibactam for the treatment of complicated intra-abdominal infections

Conclusion: ...

Patients with cIAI known to be infected with *Klebsiella pneumoniae carbapenemase-producing Enterobacteriaceae* would be clear candidates for treatment with this agent, as would patients infected with more common types of extended-spectrum β-lactamase producing Gram-negative pathogens if a carbapenem alternative were desired...

EXPERT OPINION ON PHARMACOTHERAPY, 2016 VOL. 17, NO. 17, 2341–2349, http://dx.doi.org/10.1080/14656566.2016.1249847

Randomized Trial of Ceftazidime-Avibactam vs Meropenem for Treatment of Hospital-Acquired and Ventilator-Associated Bacterial Pneumonia (REPROVE): Analyses per US FDA–Specified End Points

Antoni Torres,[1] Doug Rank,[2] David Melnick,[2,a] Ludmyla Rekeda,[3] Xiang Chen,[3] Todd Riccobene,[4] Ian A. Critchley,[5,a] Hassan D. Lakkis,[3] Dianna Taylor,[6,b] and Angela K. Talley[2,a]

- Etude prospective randomisée,
- **160 centers** in **25** countries
- **Hospital-acquired and ventilator-associated pneumonia**
- 1:1 : **CAZ-AVI** or **meropenem** for 7 to 14 days
- **The primary outcome** was 28-day all-cause mortality
- **Secondary outcomes** included clinical cure at test of cure (TOC) in the ITT and microbiological ITT

Randomized Trial of Ceftazidime-Avibactam vs Meropenem for Treatment of Hospital-Acquired and Ventilator-Associated Bacterial Pneumonia (REPROVE): Analyses per US FDA–Specified End Points

Antoni Torres,[1] Doug Rank,[2] David Melnick,[2,a] Ludmyla Rekeda,[3] Xiang Chen,[3] Todd Riccobene,[4] Ian A. Critchley,[5,a] Hassan D. Lakkis,[3] Dianna Taylor,[6,b] and Angela K. Talley[2,a]

- Résultats:

* 870 patients inclus: (CAZ-AVI = 436; meropenem= 434)

* 2 groupes comparables

Table 1. Patient Demographic and Baseline Clinical Characteristics (ITT Population)

Characteristic	CAZ-AVI (n = 436)	Meropenem (n = 434)	Total (n = 870)
Age, mean (SD), y	62.8 (16.7)	62.8 (17.6)	62.8 (17.2)
<65 y, n (%)	200 (45.9)	201 (46.3)	401 (46.1)
≥75 y, n (%)	129 (29.6)	135 (31.1)	264 (30.3)
Male, n (%)	325 (74.5)	320 (73.7)	645 (74.1)
BMI, mean (SD), kg/m^2	23.8 (6.0)	23.6 (5.2)	23.7 (5.6)
APACHE II score, mean (SD)	14.6 (4.1)	15.0 (4.1)	14.8 (4.1)
APACHE II category, n (%)			
<10	3 (0.7)	2 (0.5)	5 (0.6)
10–19	376 (86.2)	369 (85.0)	745 (85.6)
20–30	57 (13.1)	62 (14.3)	119 (13.7)

2 groupes comparables

Characteristic	CAZ-AVI (n = 436)	Meropenem (n = 434)	Total (n = 870)
VAP	145 (33.3)	145 (33.4)	290 (33%)
Early VAP	36 (8.3)	54 (12.4)	90 (10.3)
Late VAP	109 (25.0)	91 (21.0)	200 (23.0)
Monomicrobial infection	141 (32.3)	141 (32.3)	271 (31.1)
Polymicrobial infection	76 (17.4)	89 (20.5)	165 (19.0)
Prior systemic Gram-negative antibiotic exposure	322 (73.9)	323 (74.4)	645 (74.1)

2 groupes comparables

Pathogen Group/Pathogen	Per-Patient Clinical Cure[b]		Per-Pathogen Microbiological Eradication[c]	
	CAZ-AVI, n/N (%)	Meropenem, n/N (%)	CAZ-AVI, n/N (%)	Meropenem, n/N (%)
Aerobic Gram-negative	126/187 (67.4)	143/195 (73.3)	155/256 (60.5)	174/267 (65.2)
Enterobacteriaceae	92/133 (69.2)	108/147 (73.5)	111/168 (66.1)	126/182 (69.2)
Enterobacter aerogenes	5/8 (62.5)	4/9 (44.4)	5/8 (62.5)	6/9 (66.7)
Enterobacter cloacae	25/29 (86.2)	13/23 (56.5)	22/29 (75.9)	14/23 (60.9)
Escherichia coli	12/22 (54.5)	17/23 (73.9)	14/22 (63.6)	16/23 (69.6)
Klebsiella pneumoniae	44/65 (67.7)	56/75 (74.7)	39/65 (60.0)	54/75 (72.0)
Proteus mirabilis	12/14 (85.7)	9/12 (75.0)	11/14 (78.6)	8/12 (66.7)
Serratia marcescens	11/15 (73.3)	12/13 (92.3)	10/15 (66.7)	8/13 (61.5)
Gram-negative pathogens other than Enterobacteriaceae	54/85 (63.5)	61/84 (72.6)	44/88 (50.0)	48/85 (56.5)
Haemophilus influenzae	13/16 (81.3)	20/25 (80.0)	14/16 (87.5)	23/25 (92.0)
Pseudomonas aeruginosa	38/64 (59.4)	37/51 (72.5)	24/64 (37.5)	20/51 (39.2)
CAZ-NS pathogens[d]	37/49 (75.5)	42/59 (71.2)	35/52 (67.3)	33/64 (51.6)
Enterobacteriaceae	29/36 (80.6)	31/45 (68.9)	31/40 (77.5)	29/47 (61.7)
E. aerogenes	3/4 (75.0)	2/2 (100.0)	3/4 (75.0)	2/2 (100.0)
E. cloacae	6/6 (100.0)	4/6 (66.7)	5/6 (83.3)	5/6 (83.3)
E. coli	4/6 (66.7)	5/8 (62.5)	4/6 (66.7)	4/8 (50.0)
K. pneumoniae	17/22 (77.3)	22/31 (71.0)	17/22 (77.3)	18/31 (58.1)
P. aeruginosa	7/12 (58.3)	13/16 (81.3)	4/12 (33.3)	4/16 (25.0)

Ceftazidime-Avibactam for HAP/VAP • ofid, DOI: 10.1093/ofid/ofz149

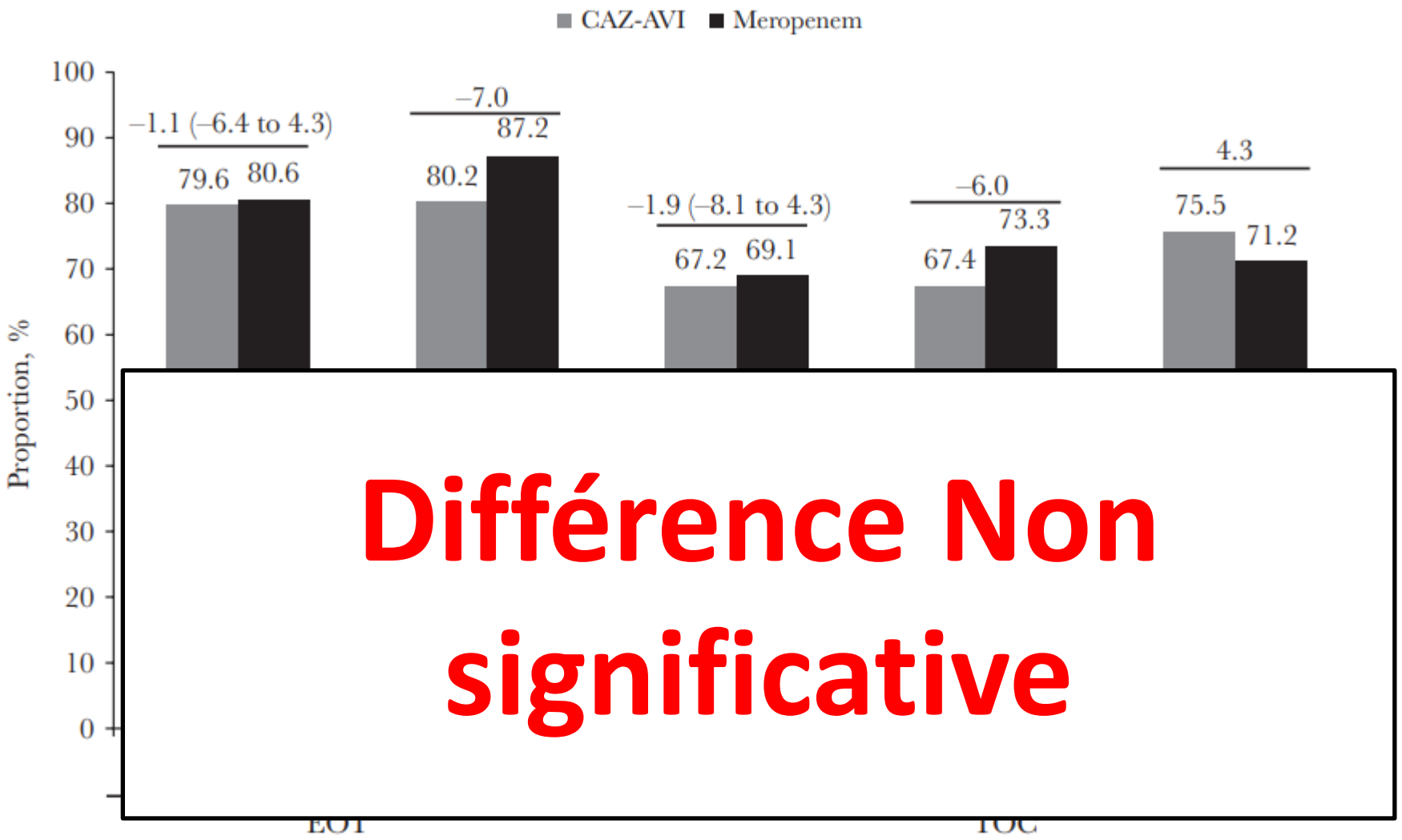
Mortalité à 28 Jours

	Patient Deaths	
Analysis Population	CAZ-AVI, n/N (%) [KM%]	Meropenem, n/N (%) [KM%]
ITT	42/436 (9.6) [9.9]	36/434 (8.3) [8.4]
Micro-ITT	22/187 (11.8)	19/195 (9.7)
CAZ-NS	4/49 (8.2)	5/59 (8.5)

Différence Non significative

Ceftazidime-Avibactam for HAP/VAP • ofid, DOI: 10.1093/ofid/ofz149

Clinical cure rates at EOT and TOC visits



Différence Non significative

Int J Antimicrob Agents. 2019 Dec;54(6):735-740.

Efficacy of ceftazidime/avibactam in monotherapy or combination therapy against carbapenem-resistant Gram-negative bacteria: A meta-analysis

11 études: 396 patients

Outcome (subjects)	No. of studies	Combination therapy [events/total (%)]	Monotherapy [events/total (%)]	Risk ratio (95% CI)
Mortality (all patients)	11 [6–16]	77/202 (38.1)	60/194 (30.9)	1.18 (0.88–1.58)
Microbiological cure (all patients)	7 [6–11,14]	61/94 (64.9)	97/153 (63.4)	1.04 (0.85–1.28)

Efficacité Ceftazidime-Avibactam
En Monothérapie

Open access Original research

BMJ Open

Efficacy and safety of ceftazidime–avibactam versus polymyxins in the treatment of carbapenem-resistant Enterobacteriaceae infection: a systematic review and meta-analysis

Ping Yang,[1,2] Yinyan Li,[1] Xiaojuan Wang,[1] Na Chen,[1] Xiaoyang Lu [1]

The meta-analysis included 11 studies

* 7 retrospective and
* 4 prospective cohort studies
* with 1111 patients enrolled

BMJ Open 2023;13:e070491. doi:10.1136/bmjopen-2022-070491

Mortalité

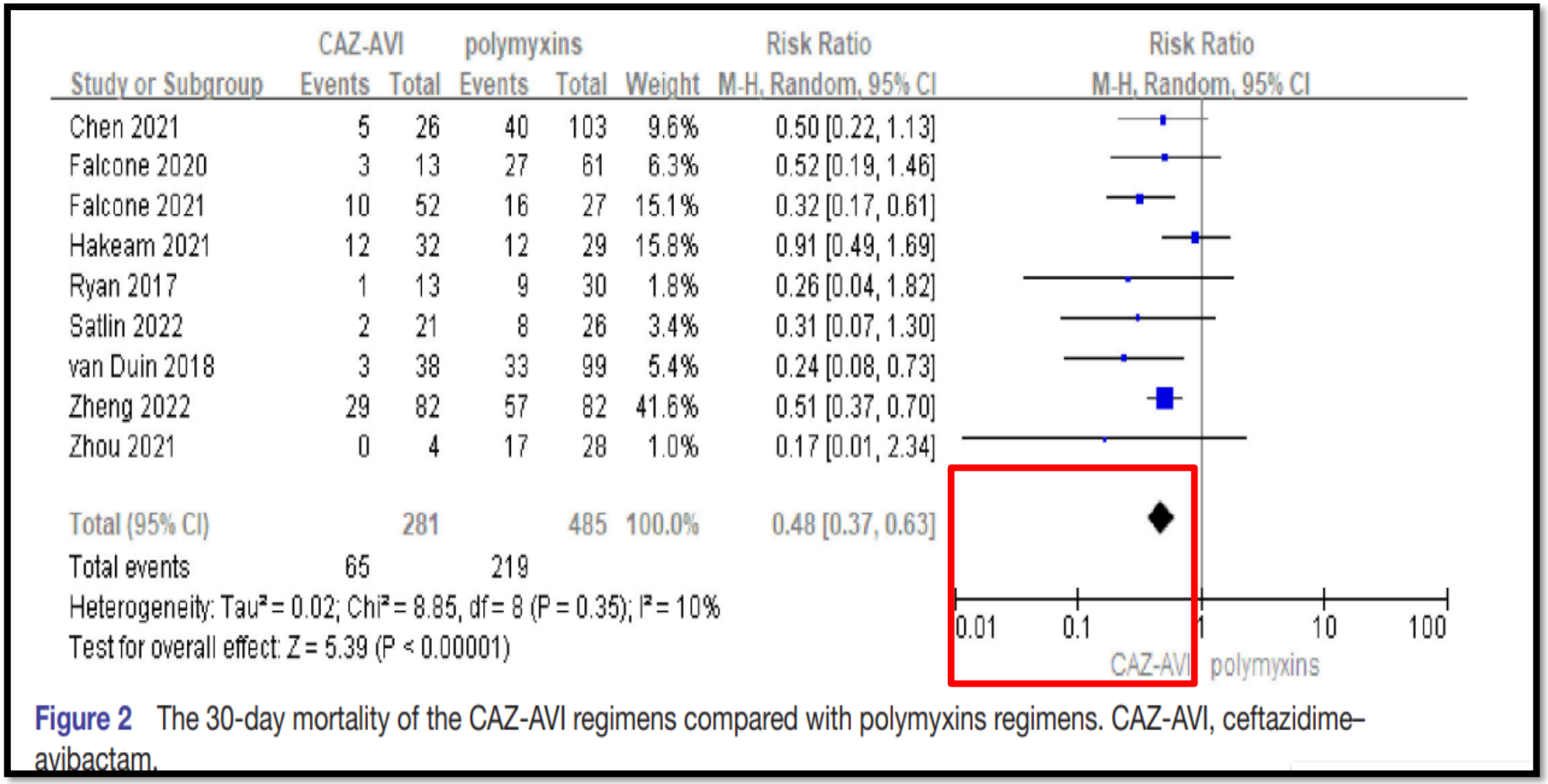


Figure 2 The 30-day mortality of the CAZ-AVI regimens compared with polymyxins regimens. CAZ-AVI, ceftazidime–avibactam.

BMJ Open 2023;13:e070491. doi:10.1136/bmjopen-2022-070491

Nephrotoxicité

Study or Subgroup	CAZ-AVI Events	CAZ-AVI Total	polymyxins Events	polymyxins Total	Weight	Risk Ratio M-H, Random, 95% CI
Almangour 2022	23	149	27	81	34.9%	0.46 [0.28, 0.75]
Falcone 2021	1	52	9	27	7.5%	0.06 [0.01, 0.43]
Hakeam 2021	3	32	3	29	11.7%	0.91 [0.20, 4.14]
Ryan 2017	2	13	13	30	14.1%	0.36 [0.09, 1.35]
Satlin 2022	5	21	7	26	20.4%	0.88 [0.33, 2.39]
van Duin 2018	1	26	6	46	7.2%	0.29 [0.04, 2.32]
Zheng 2022	0	82	7	82	4.1%	0.07 [0.00, 1.15]
Total (95% CI)		375		321	100.0%	0.42 [0.23, 0.77]
Total events	35		72			

Heterogeneity: Tau² = 0.21; Chi² = 9.24, df = 6 (P = 0.16); I² = 35%

Test for overall effect: Z = 2.80 (P = 0.005)

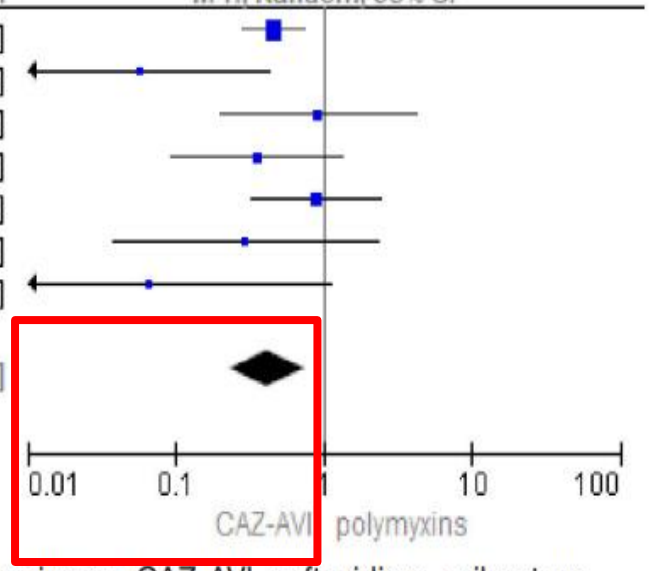


Figure 5 Nephrotoxicity of the CAZ-AVI regimens compared with polymyxins regimens. CAZ-AVI, ceftazidime–avibactam.

BMJ Open 2023;13:e070491. doi:10.1136/bmjopen-2022-070491

Infection
https://doi.org/10.1007/s15010-023-02108-6

REVIEW

Ceftazidime–avibactam versus polymyxins in treating patients with carbapenem-resistant Enterobacteriaceae infections: a systematic review and meta-analysis

Jinglan Chen[1,2,3] · Qin Hu[1,3,6] · Pengxiang Zhou[4,5] · Sheng Deng[1,3]

Received: 17 July 2023 / Accepted: 3 October 2023

- 10 études avec 833 patients
- CAZ-AVI: 325 patients vs
- Polymyxine: 508 patients.

Infection 2023 Oct 25. doi: 10.1007/s15010-023-02108-6. Online ahead of print

Mortalité

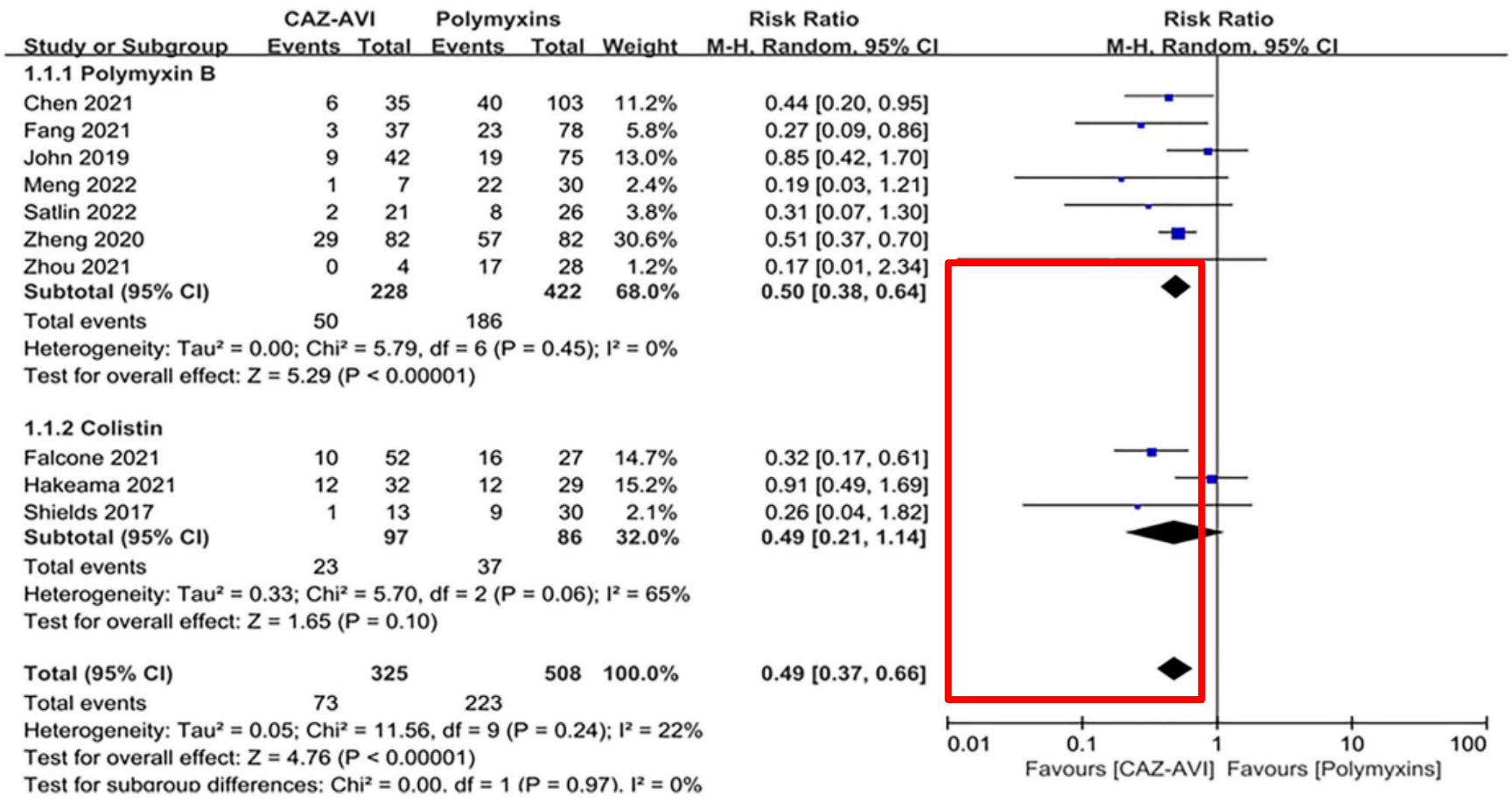


Fig. 2 Thirty-day mortality of the CAZ–AVI-based therapy compared with polymyxin-based therapy in CRE infections

Ceftazidime-avibactam versus polymyxins in treating patients with carbapenem-resistant Enterobacteriaceae infections: a systematic review and meta-analysis

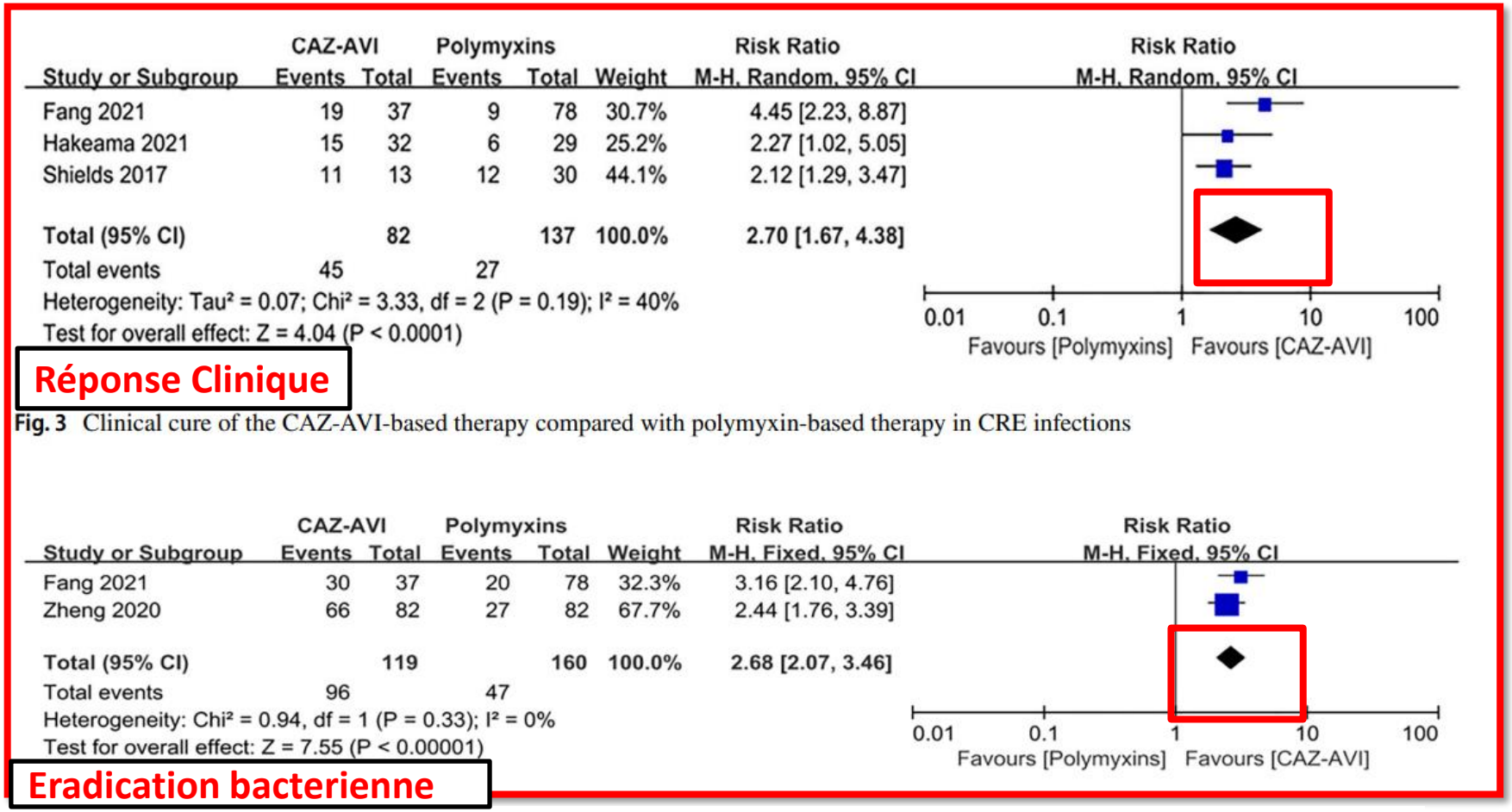


Fig. 3 Clinical cure of the CAZ-AVI-based therapy compared with polymyxin-based therapy in CRE infections

Fig. 4 Microbial clearance of the CAZ-AVI-based therapy compared with polymyxin-based therapy in CRE infections

Infection 2023 Oct 25. doi: 10.1007/s15010-023-02108-6. Online ahead of print

Ceftazidime-avibactam: considérations cliniques dans infections bactériennes à Gram négatif graves

Non actif contre les souches productrices de métallo-blactamase ou la plupart Acinetobacter spp+++

Drugs (2018) 78:675–692

Indications AMM de la **ceftazidime / avibactam**

Infections intra-abdominales compliquées

Infections des voies urinaires compliquées dont pyélonéphrites

Pneumonies nosocomiales dont les pneumonies nosocomiales acquises sous ventilation mécanique **(PAVM)**

Infections dues à des **bactéries aérobies à Gram négatif** chez des patients adultes pour qui les **options thérapeutiques sont limitées**

Zavicefta 2 g/0,5 g (ceftazidime/avibactam) Date : 04/2023. Version : 0.03

Contre-indications +++

- Hypersensibilité ceftazidime
- Hypersensibilité avibactam
- Hypersensibilité céphalosporines

Spectre de la Ceftazidime/Avibactam

- **Bactéries à Gram négatif essentiellement :**
- ***Entérobactéries dont E-BLSE et certaines EPC***

- *Classe A : E-BLSE (TEM, SHV, CTX-M), KPC*
- *Classe C : ampC*
- *Certaines Classes D: dont oxa-48*

- ***Pseudomonas aeruginosa***

Conclusion: Ceftazidime / avibactam: **Quelle Place?**

- **Infection sévère à Entérobactéries C3G R (E-BLSE)**
- **Infection sévère à EPC (Oxa-48, KPC)**
- **Infection à P *aeruginosa* multi-résistantes**
- **Infection sévère à Entérobactéries + P *aeruginosa* multi-résistantes**
- **Place en empirique: ???**

Infection and Drug Resistance

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REVIEW

Carbapenemase Producing Gram-Negative Bacteria in Tunisia: History of Thirteen Years of Challenge

22

Propagation des gènes de résistance

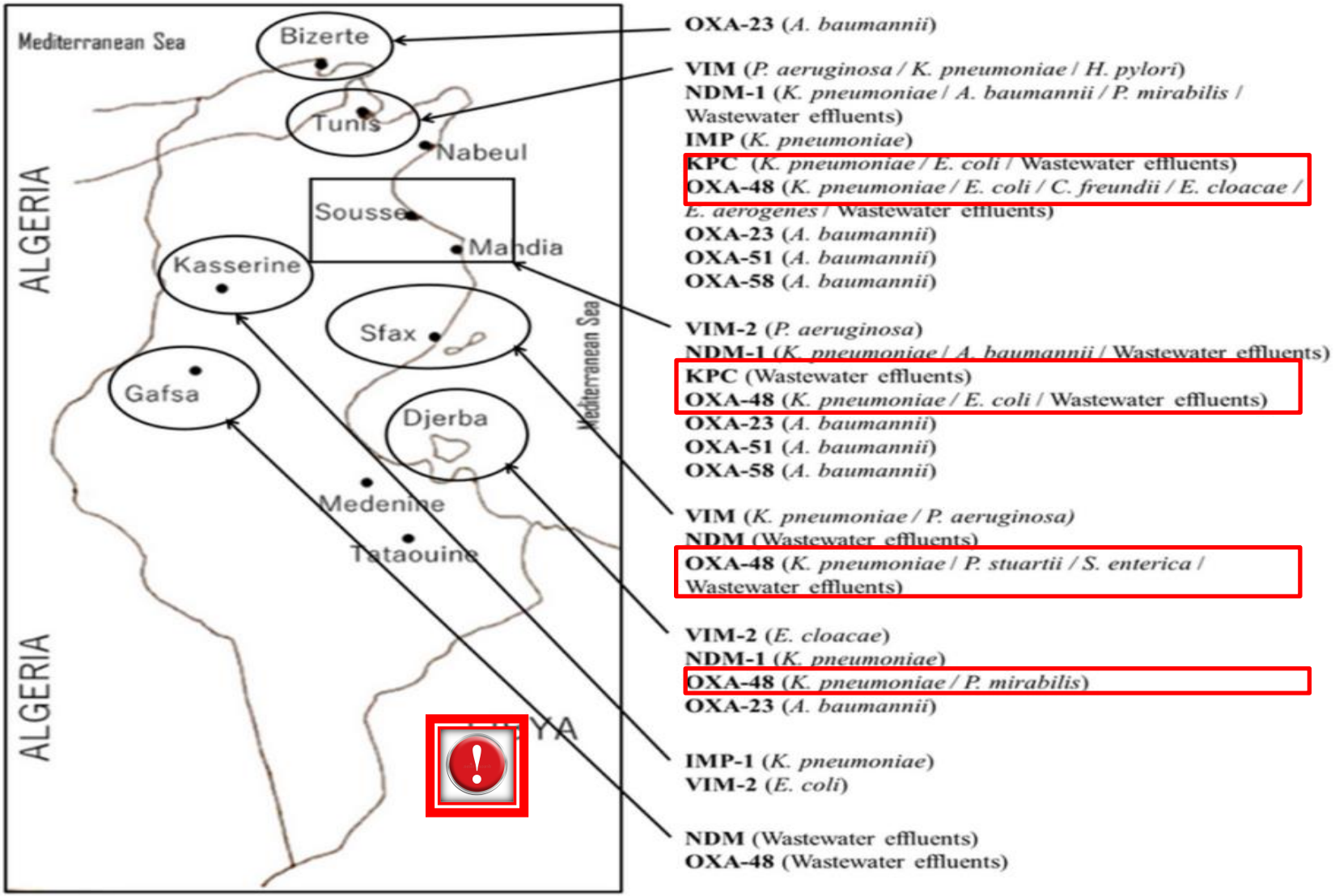

Figure 2 Regional distribution of carbapenemase producing Gram-negative bacteria in Tunisia from 2006 to 2019.

prévention des infections nosocomiales

Conclusion

Ceftazidime / avibactam

Nouveau moyen thérapeutique (Antibiotique) contre

Entérobactéries + P aeruginosa

Multi-résistantes

Merci