



INFECTIONS RESPIRATOIRES BASSES: Doit-on changer notre pratique?

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Chef de service de Pneumologie
Hôpital militaire de Tunis
AFMP 2022 Le Caire 03/06/22



INTRODUCTION

- les infections des voies respiratoires dont la pneumonie communautaire (PAC), = principale cause de prescription d'antibiotiques.
- Epidémiologie changeante de la PAC dans le monde avec une population vieillissante croissante avec des comorbidités.
- Pathogènes bactériens courants particuliers selon les zones
- Résistance est en augmentation constante.
- Les diagnostics rapides : thérapie ciblée sur les agents étiologiques.



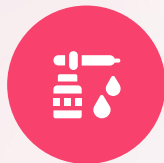
Type

PAC, exacerbation, BA



Origine

Hopital, communauté...
Type de germes



Terrain

BPCO DDB Tr neuro
KBP

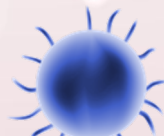
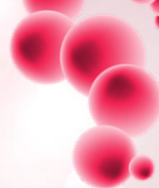
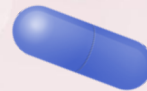


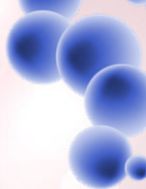
Score de gravité

En fonction de ces
facteurs et de la clinique



**Regles de
prescription:**





INFECTIONS RESPIRATOIRES BASSES

01

PAC bactérienne

Pneumopathie aigue
communautaire

02

Pneumopathies nosocomiales

Rea et VM ++

03

Exacerbations

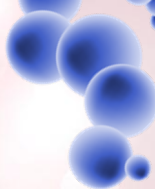
BPCO ASTHME DDB MUCO

04

Pneumonies virales

You can describe the topic of
the section here





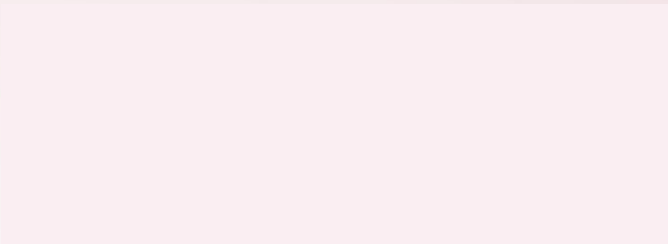
INFECTIONS RESPIRATOIRES BASSES

.....

01

PAC bactérienne

Pneumopathie aigue
communautaire



03

Exacerbations

BPCO ASTHME DDB MUCO

04

Pneumonies virales

You can describe the topic of
the section here



Paramètres de l'épidémiologie microbienne :



Endroit:

Communauté, Ephad,
Hôpital, USI...



Comorbidité:

Le terrain , age patho
neurologique DDB
BPCO...



Facteur saisonnier

Les épidémies
saisonnières , les périodes
de pèlerinage...

3 problèmes majeurs

Sur-
consommation
d'ATB



Resistance
Bacterienne

Absence de
nouvelles
molécules

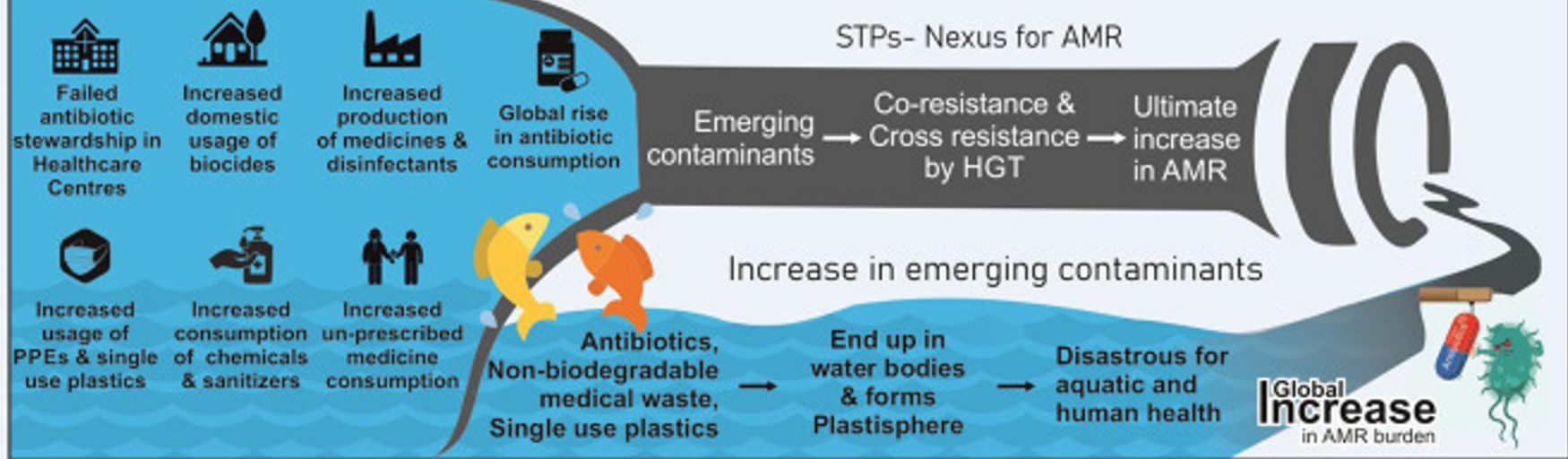


Surconsommation



SARS-CoV-2

COVID-19 has crashed antibiotic stewardship and single-handedly increased the antibiotics, PPE, and biocide usage, causing a ripple effect in the global AMR problem.







Antibiotic Abuse &
unprescribed Drug
sales

Hospital & health
center

Environmental
Stress

Bioaccumulation

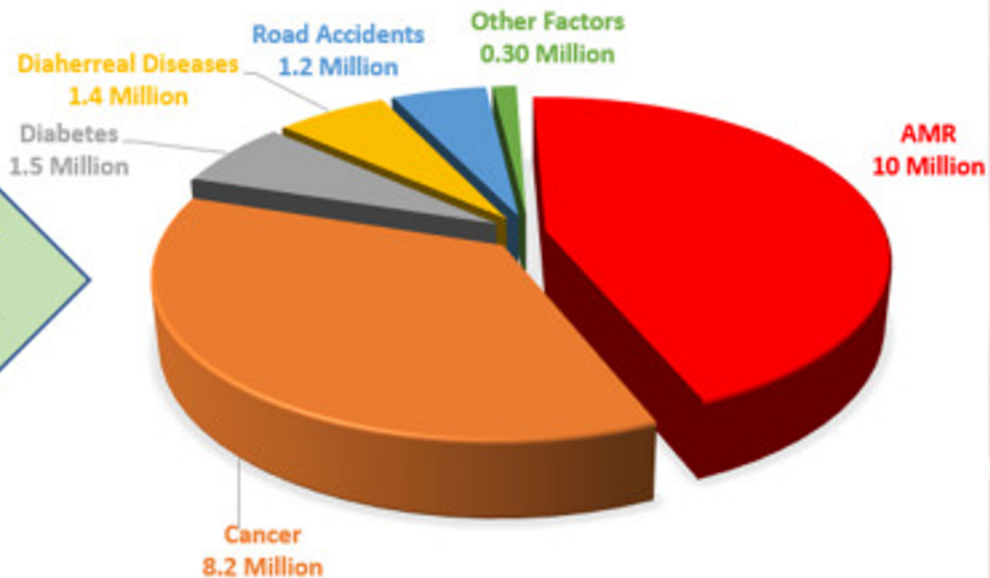
Sewage Treatment
Plants

Horizontal Gene
Transfer

Animal Husbandry,
Veterinary &
Agriculture

Antibiotic Resistance

PROJECTED DEATH COUNT





Antibioresistance

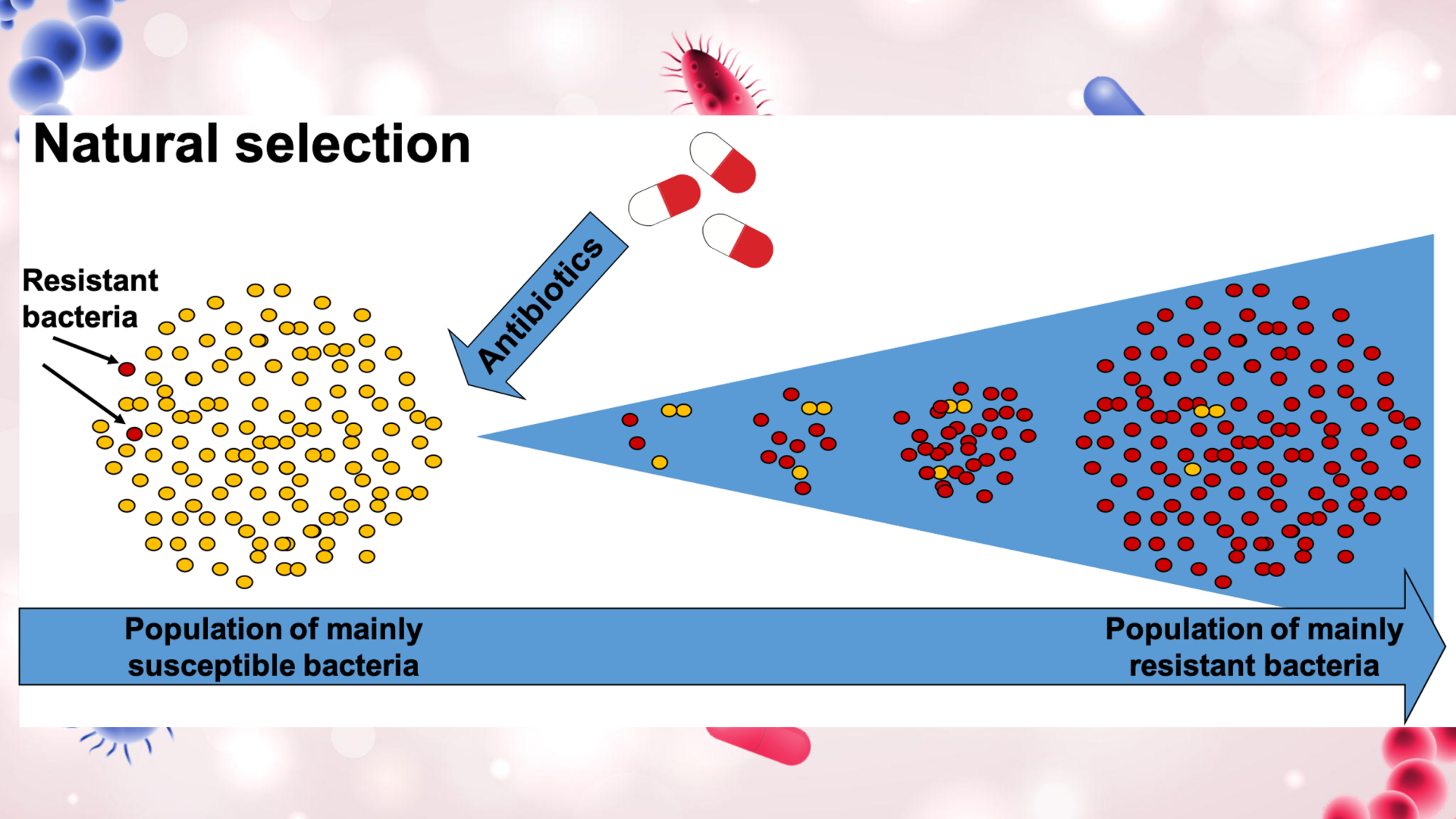
Natural selection

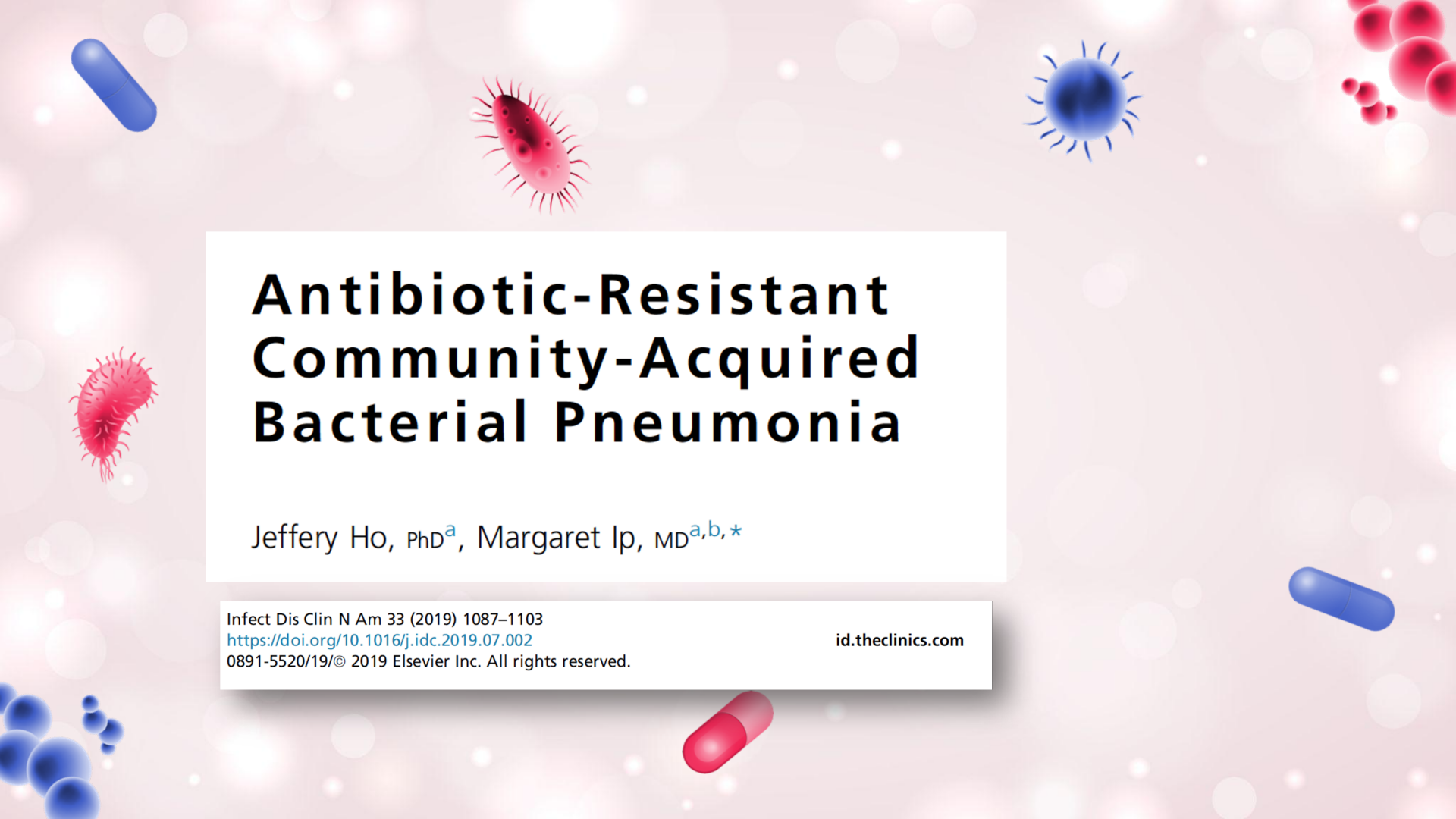
Resistant
bacteria

Antibiotics

Population of mainly
susceptible bacteria

Population of mainly
resistant bacteria





Antibiotic-Resistant Community-Acquired Bacterial Pneumonia

Jeffery Ho, PhD^a, Margaret Ip, MD^{a,b,*}

Infect Dis Clin N Am 33 (2019) 1087–1103
<https://doi.org/10.1016/j.idc.2019.07.002>
0891-5520/19/© 2019 Elsevier Inc. All rights reserved.

id.theclinics.com

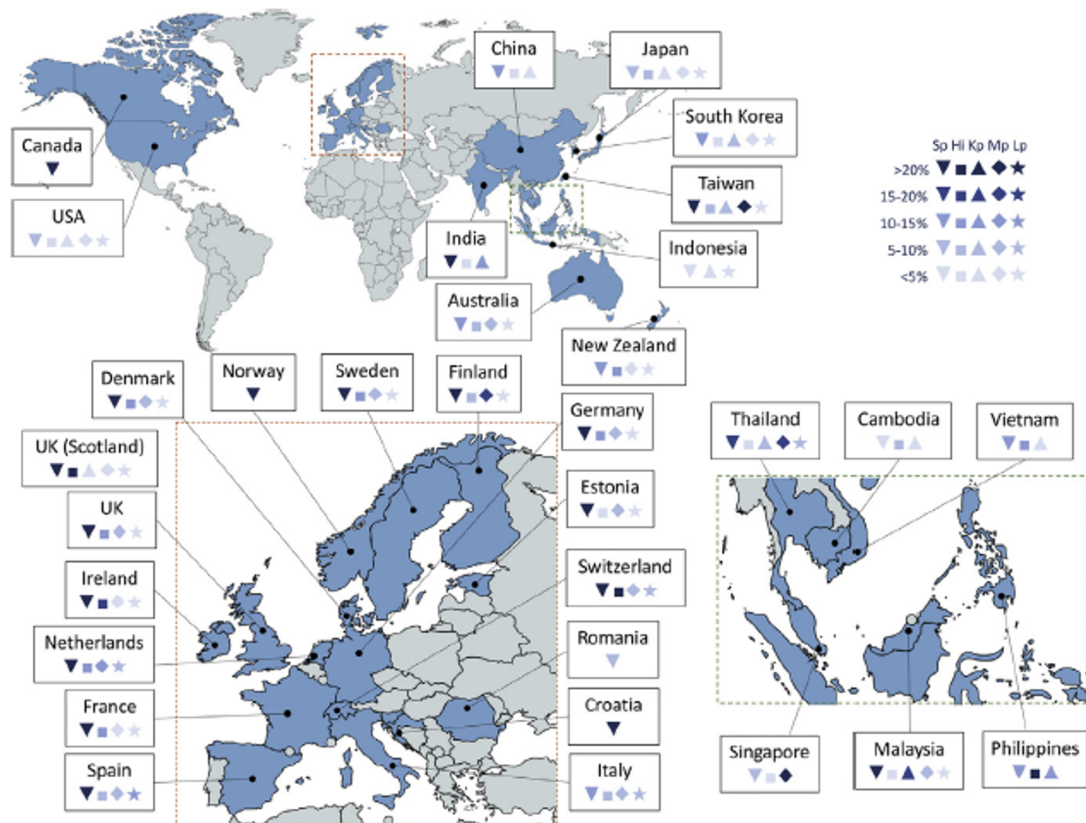


Fig. 1. Geographic distribution of etiologic agents responsible for CAP cases requiring hospitalization.^{4,19,24-26} The shape of the marker represents a bacterial species, whereas its blue color shading denotes the percentage of the etiologic agent. Data are not available in countries shaded in gray. Hi, *H. influenzae*; Kp, *K. pneumoniae*; Lp, *L. pneumophila*; Mp, *M. pneumoniae*; Sp, *S. pneumoniae*.

Table 1
(continued)

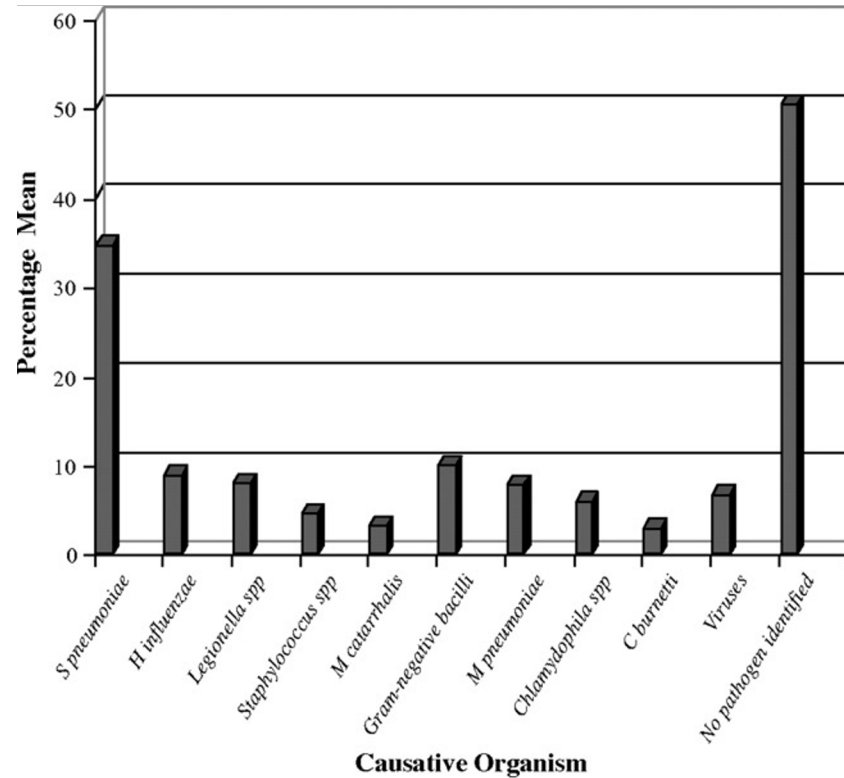
Organism	Resistance Phenotype	Known Common Mechanism of Resistance	Antimicrobial Agents with Potential In Vitro Activity	Remarks (Reference)
Enterobacteriaceae (for example, <i>E coli</i> , <i>K pneumoniae</i>)	Resistance to penicillins, oxyimino-cephalosporins, and monobactams	ESBLs	Carbapenems β-Lactam and/or β-lactamase inhibitors, for example, ceftolozane–tazobactam	Durante-Mangoni et al, ⁷⁷ 2019
	Carbapenem resistance and resistance to other β-lactam antibiotics	Carbapenemases Ambler class A: serine β-lactamases, for example, KPC and penicillinases; B: metallo-β-lactamases, for example, KPC NDM; D: oxacillinases, for example, OXA-48	Aminoglycosides Polymyxins Tigecycline Meropenem-vaborbactam (active against KPC) Ceftazidime-avibactam (active against class A and class D β-lactamases, not active against metallo-β-lactamases, eg, NDM) Two-to-three drug combination regimens	
	Resistance to most β-lactam antibiotics, including carbapenems	AmpC β-lactamases, cell wall porin mutations, efflux pumps		
	Fluoroquinolone resistance	Mutations at QRDR sites of <i>gyrA</i> and <i>parC</i> genes Plasmid mediated (<i>qnr</i> genes)		

Abbreviations: ABC-F, ATP-binding cassette-F; KPC, *Klebsiella pneumoniae* carbapenemase; MFS, major facilitator superfamily; NA, not applicable; NDM, New Delhi metallo-β-lactamase; OMPs, outer membrane porins; QRDR, quinolone-resistant determining region; rRNA, ribosomal RNA.

<i>M pneumoniae</i>	Macrolide resistance	Domain V of 23S rRNA mutation(s) A-to-G/C at 2063 or 2064 positions	Tetracyclines, fluoroquinolones	
<i>C pneumoniae</i>	NA		Tetracyclines, Fluoroquinolones, macrolides	
<i>L pneumophila</i>	Macrolide resistance	L4, L22 mutations, and domain V of 23S rRNA mutations Efflux pump encoded by lpeAB genes	Macrolides, for example, clarithromycin Fluoroquinolones Rifampicin	Descours et al, ⁷⁰ 2017; Massip et al, ⁷¹ 2017; Vandewalle-Capo et al, ⁶⁸ 2017
	Fluoroquinolone resistance	Mutations with a.a. substitutions of gyrA gene		Hennebique et al, ⁷³ 2017
	Rifampicin resistance	Mutations of rpoB gene		Nielsen et al, ⁶⁷ 2000
<i>S aureus</i>	Methicillin resistance	PBP2a (mecA)	Linezolid	
	Reduced susceptibility or resistance to vancomycin	Alterations in cell wall peptidoglycan (vanA), and/or of regulatory genes agr	Tigecycline Ceftaroline	
	Macrolide resistance	Erm genes encoding 23S rRNA methylases Ribosome protection via ABC-F proteins msrA and mefA genes encoding efflux pump (MFS) transporter mphC phosphotransferase gene or ereA, ereB esterase genes		
	Fluoroquinolone resistance	Multiple mutations at QRDR with a.a. substitutions of parC and gyrA genes		

Organism	Resistance Phenotype	Known Common Mechanism of Resistance	Antimicrobial Agents with Potential In Vitro Activity	Remarks (Reference)
Enterobacteriaceae (for example, <i>E coli</i> , <i>K pneumoniae</i>)	Resistance to penicillins, oxyimino-cephalosporins, and monobactams	ESBLs	Carbapenems β -Lactam and/or β -lactamase inhibitors, for example, ceftolozane-tazobactam	Durante-Mangoni et al, ⁷⁷ 2019
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	Resistance to most β -lactam antibiotics, including carbapenems Fluoroquinolone resistance	AmpC β -lactamases, cell wall porin mutations, efflux pumps Mutations at QRDR sites of <i>gyrA</i> and <i>parC</i> genes Plasmid mediated (<i>qnr</i> genes)		

Frequency of causative organisms of community-acquired pneumonia (CAP) in Europe.



T Welte et al. Thorax 2012;67:71-79



Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis



Antimicrobial Resistance Collaborators*



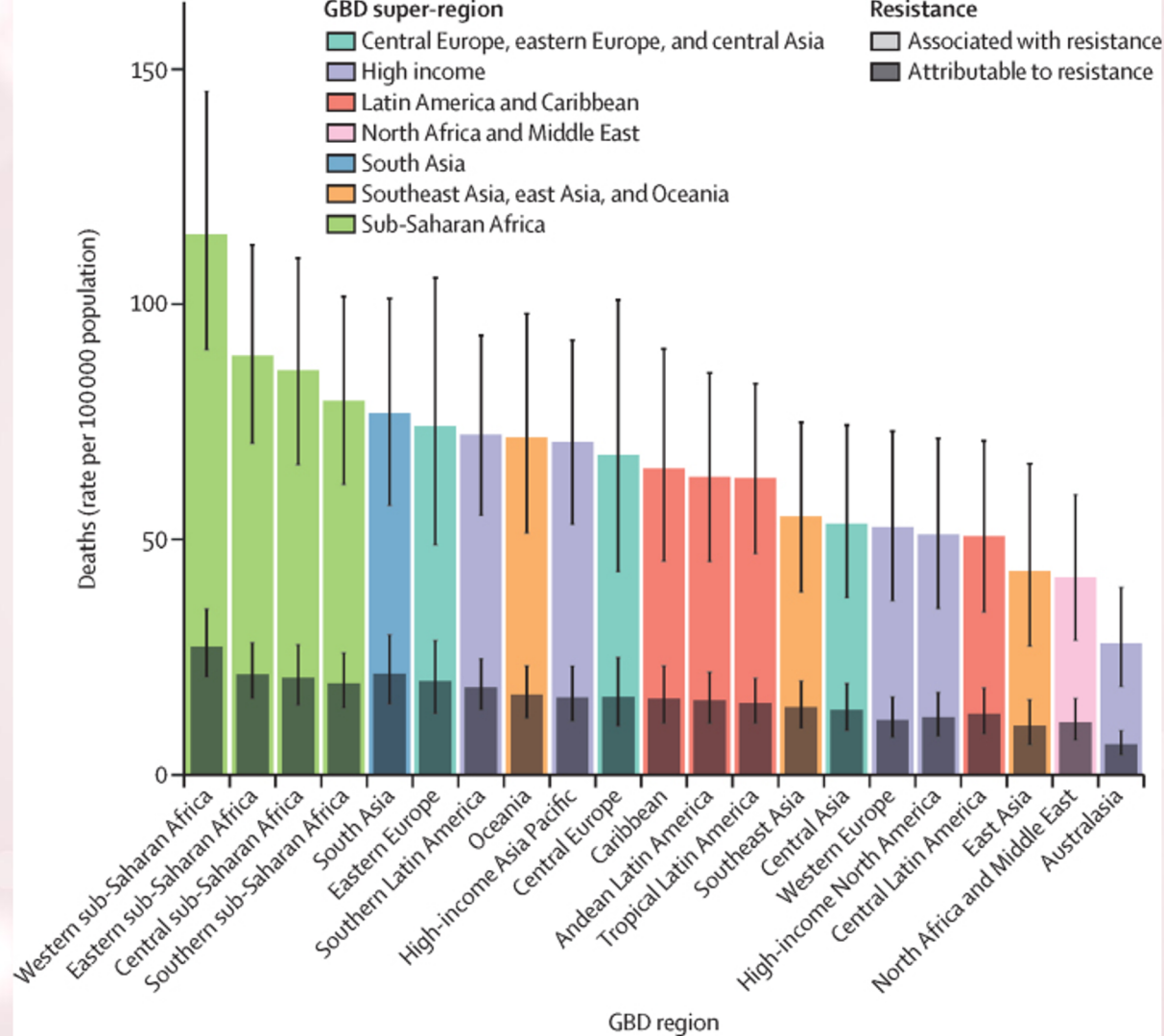
Summary

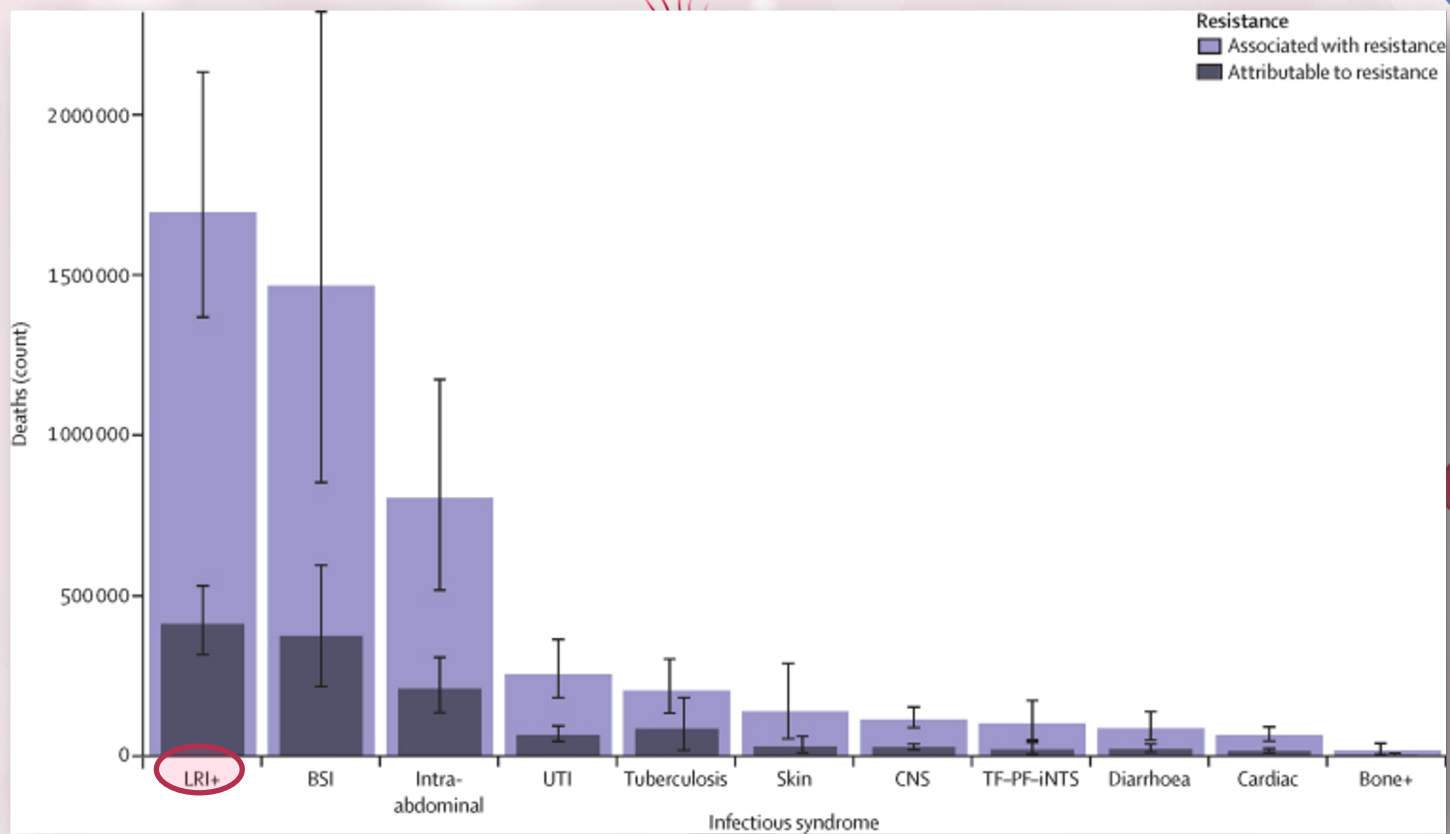
Background Antimicrobial resistance (AMR) poses a major threat to human health around the world. Previous publications have estimated the effect of AMR on incidence, deaths, hospital length of stay, and health-care costs for specific pathogen–drug combinations in select locations. To our knowledge, this study presents the most comprehensive estimates of AMR burden to date.

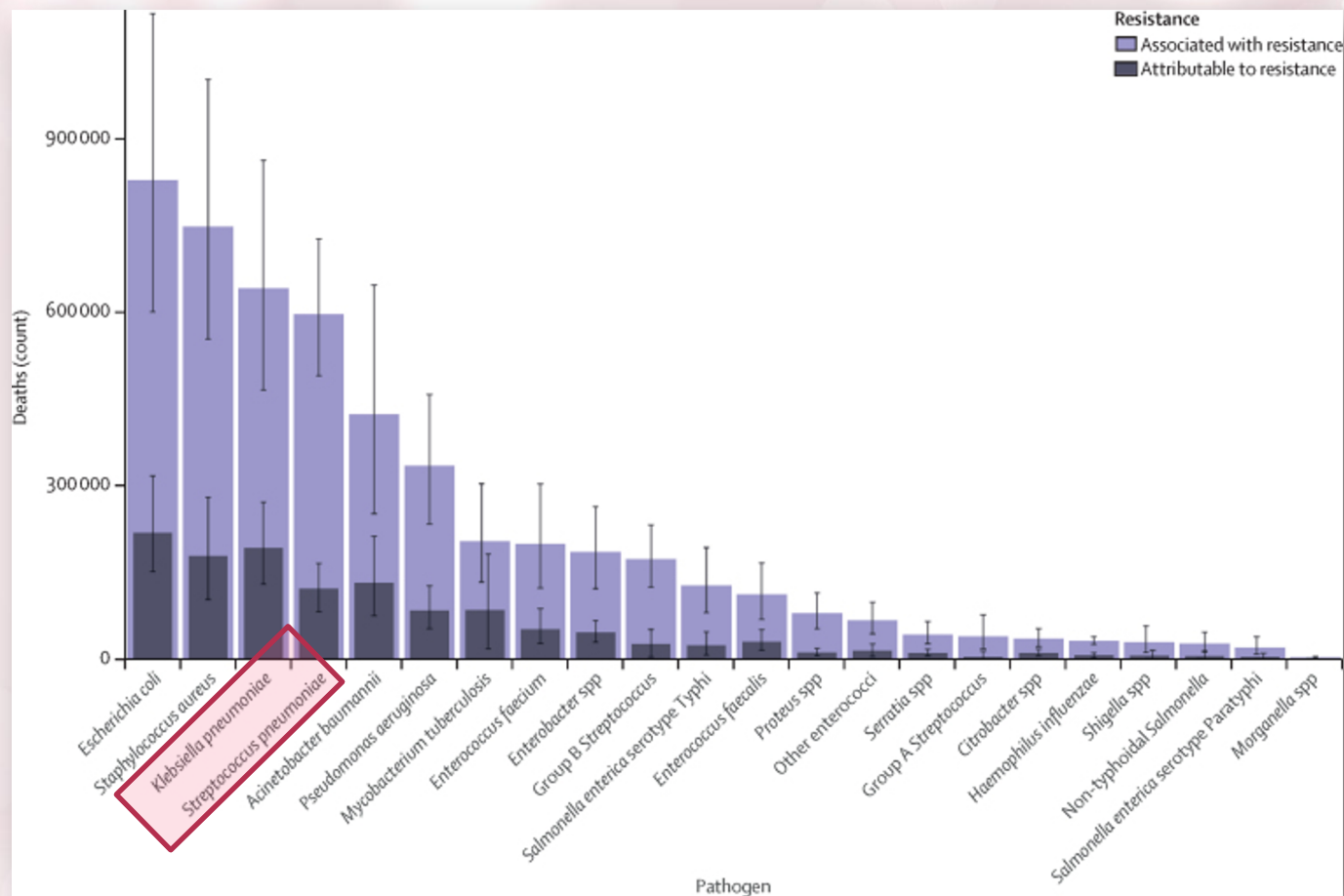
Lancet 2022; 399: 629–55

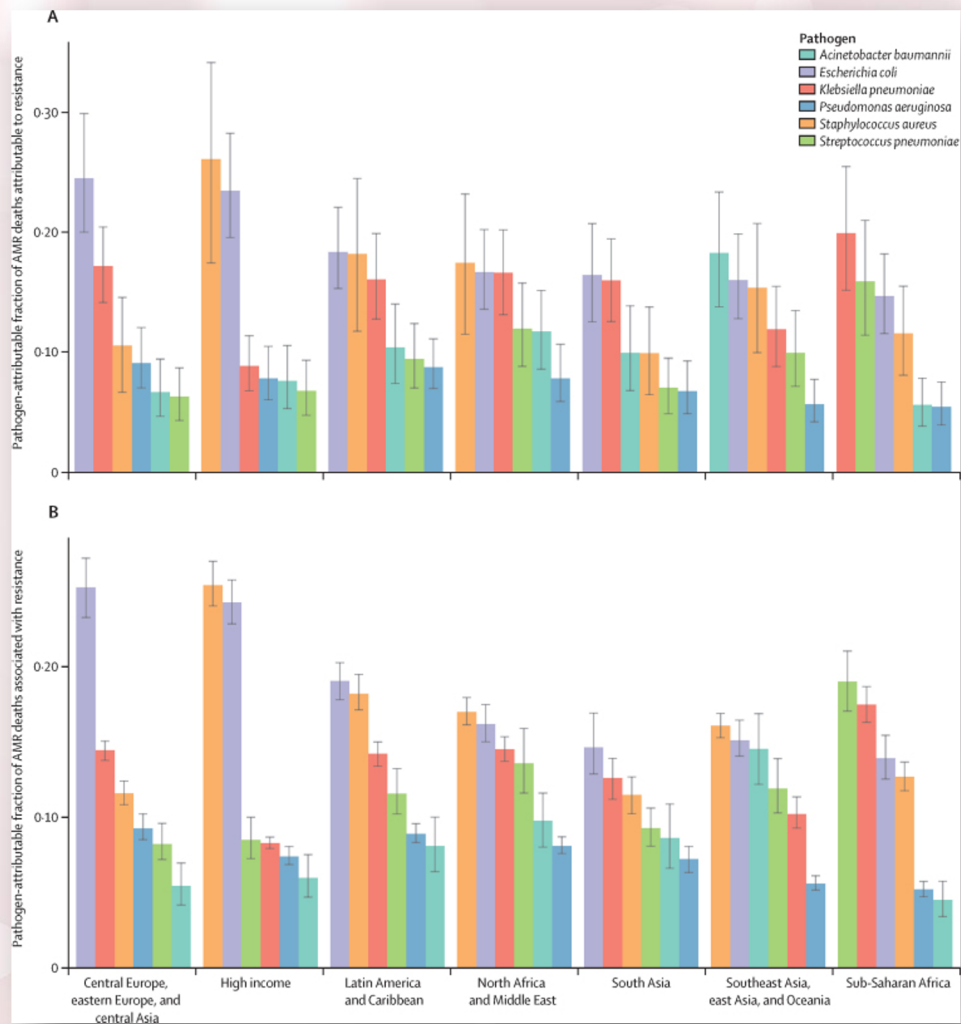
Published Online
January 20, 2022
[https://doi.org/10.1016/S0140-6736\(21\)02724-0](https://doi.org/10.1016/S0140-6736(21)02724-0)





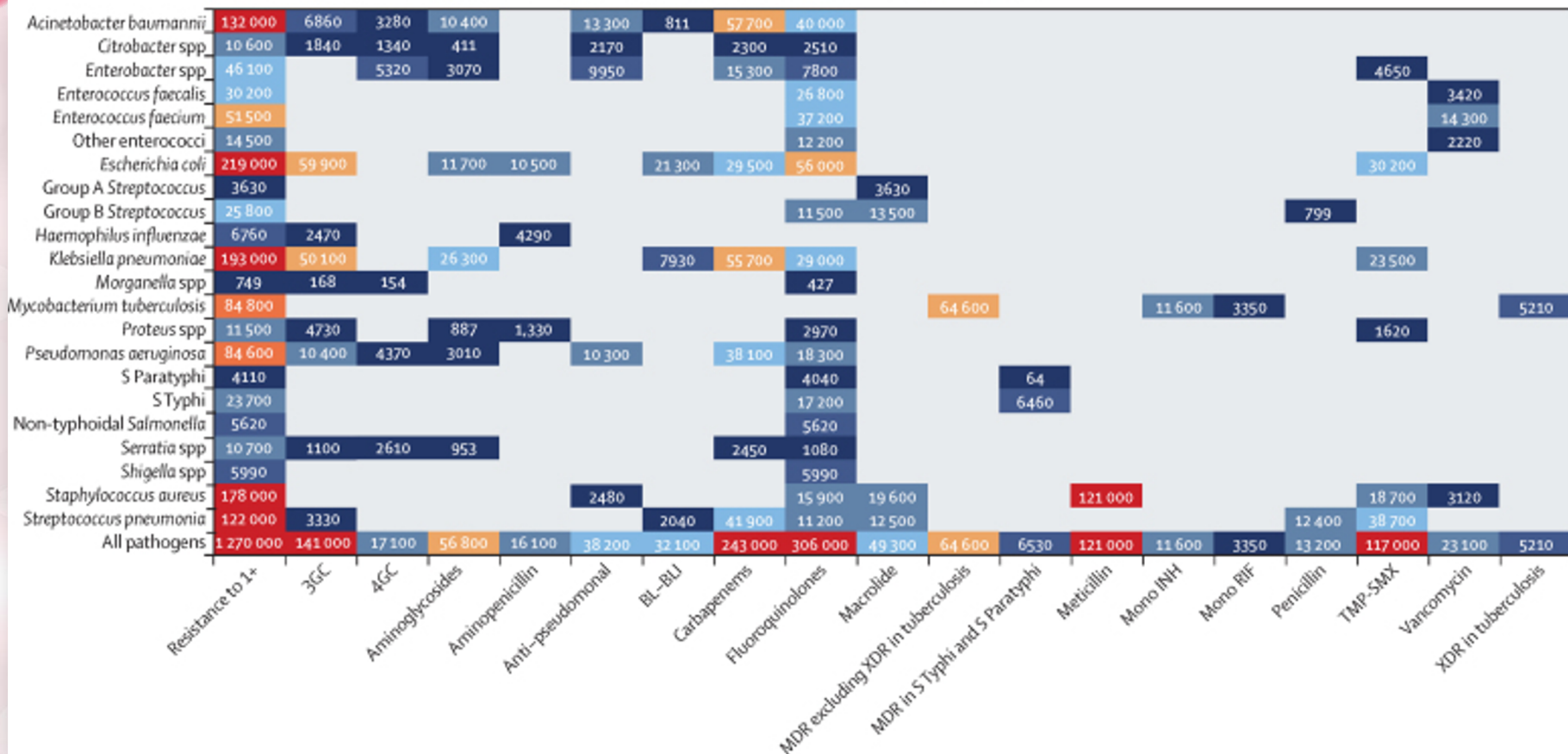


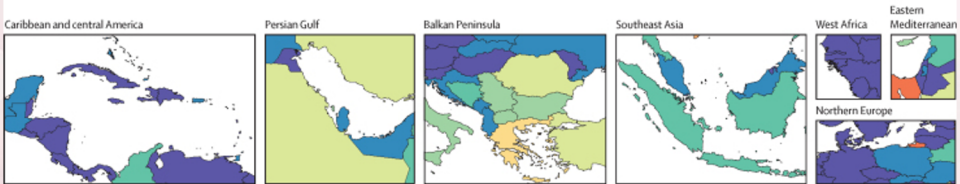
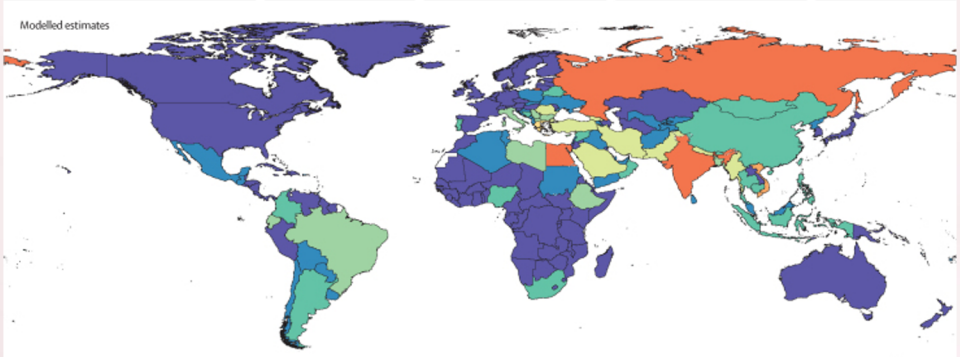
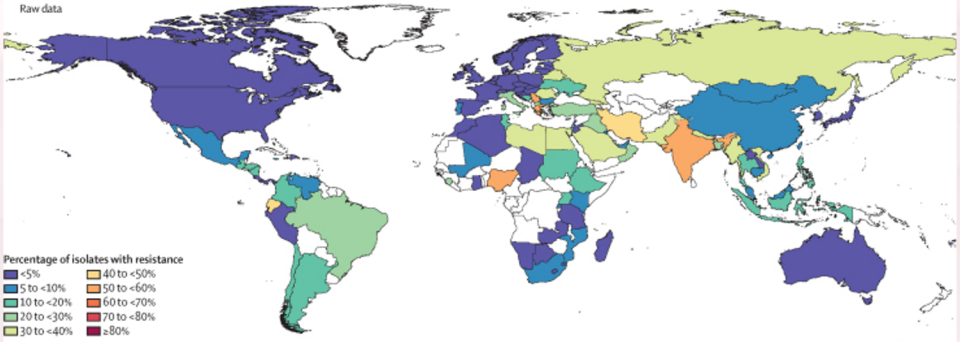




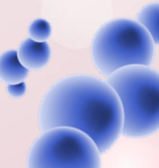
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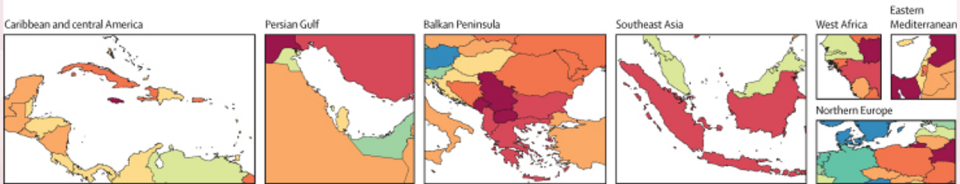
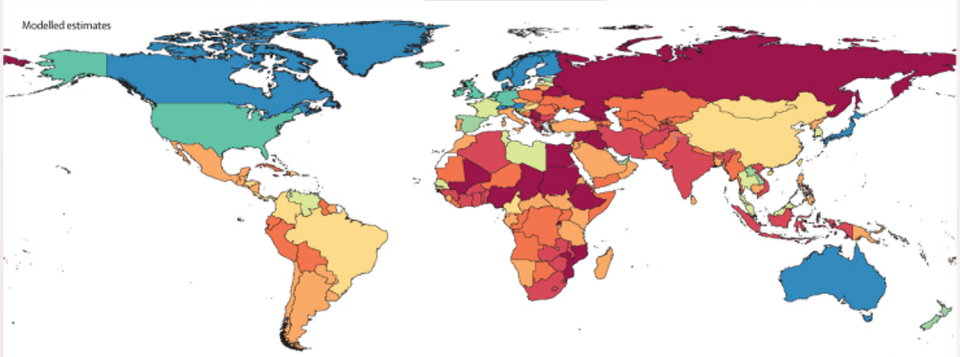
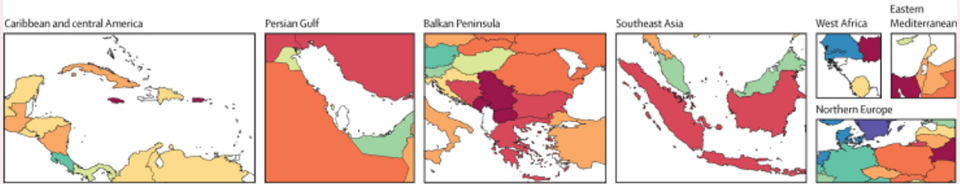
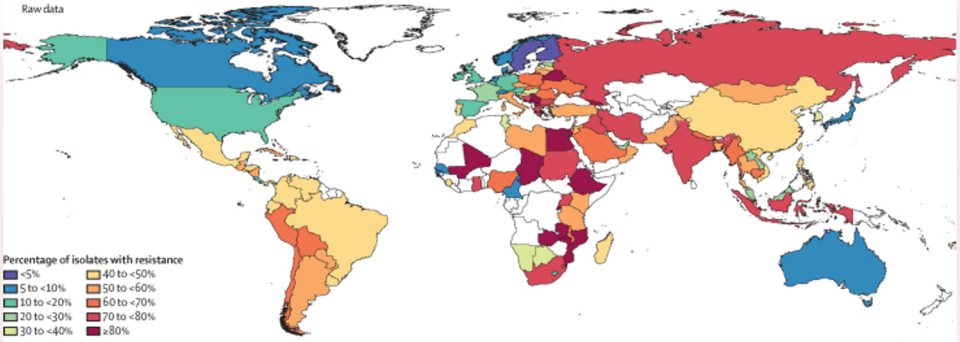
■ ≥100
 ■ 75 to <100
 ■ 50 to <75
 ■ 25 to <50
 ■ 10 to <25
 ■ 5 to <10
 ■ <5
 NA



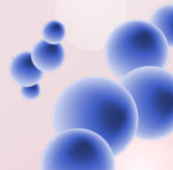


Klebsiella et carbapeneme





Klebsiella et
C3G



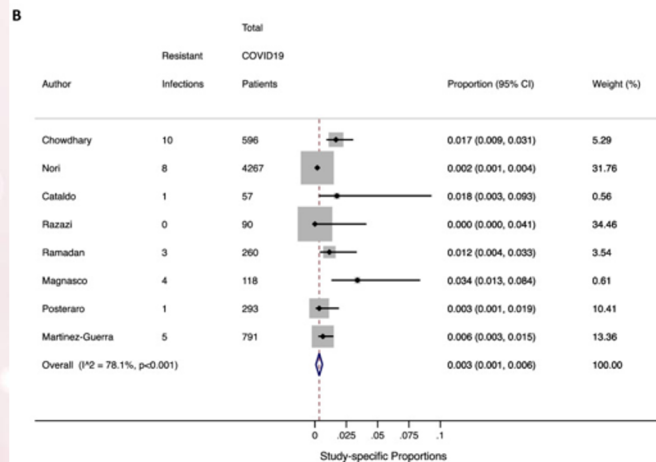
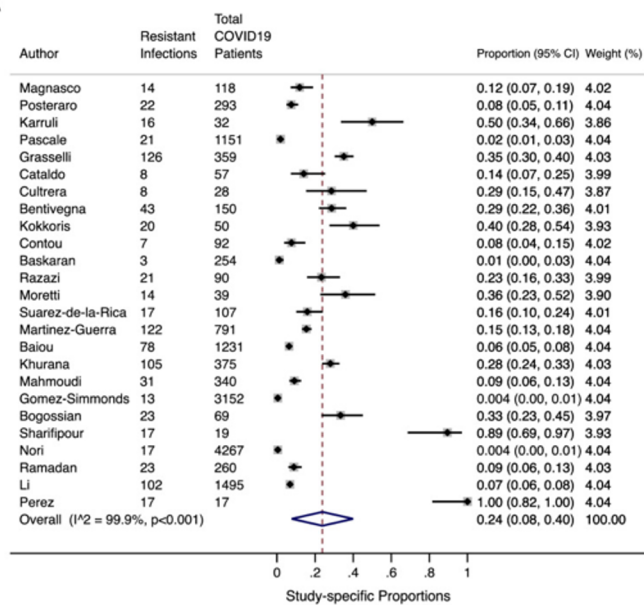
RESEARCH

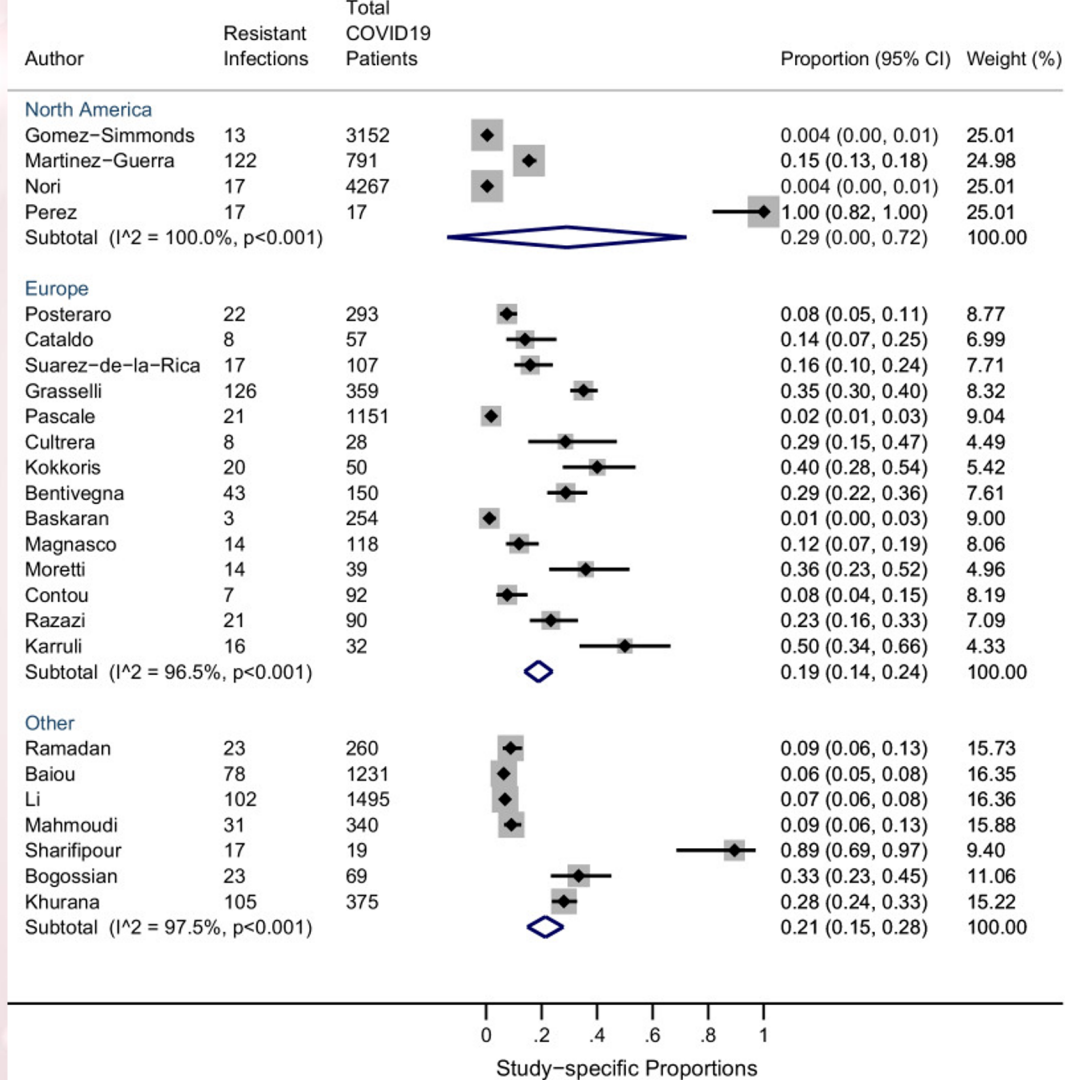
Open Access

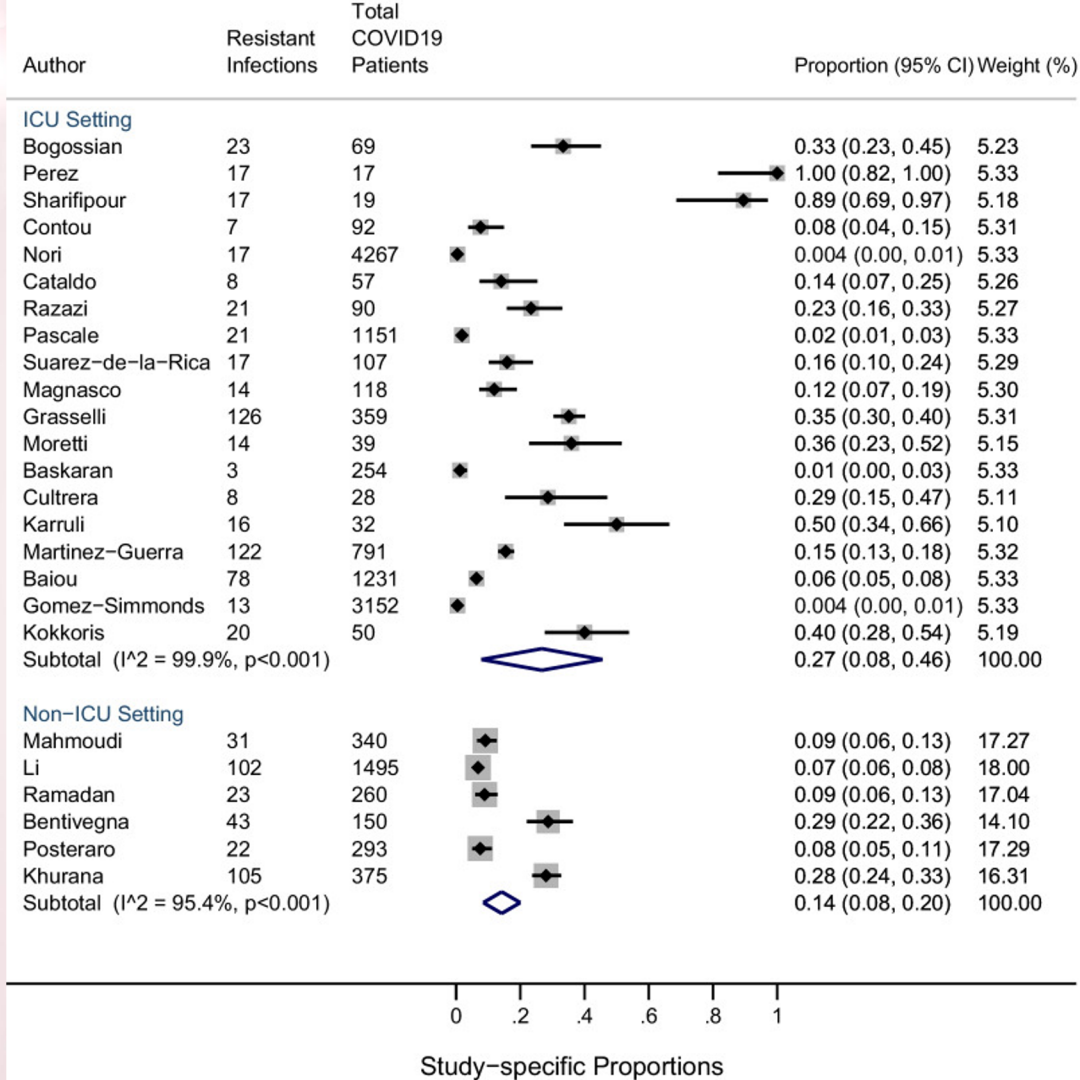
Antimicrobial resistance (AMR) in COVID-19 patients: a systematic review and meta-analysis (November 2019–June 2021)



Ruwandi M. Kariyawasam^{1,2,3}, Danielle A. Julien¹, Dana C. Jelinski¹, Samantha L. Larose¹, Elissa Rennert-May^{1,4}, John M. Conly^{1,5}, Tanis C. Dingle^{1,2,3}, Justin Z. Chen^{1,6}, Gregory J. Tyrrell^{1,2,3}, Paul E. Ronksley^{1,7} and Herman W. Barkema^{1,8*} 









Contents lists available at [ScienceDirect](#)

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv



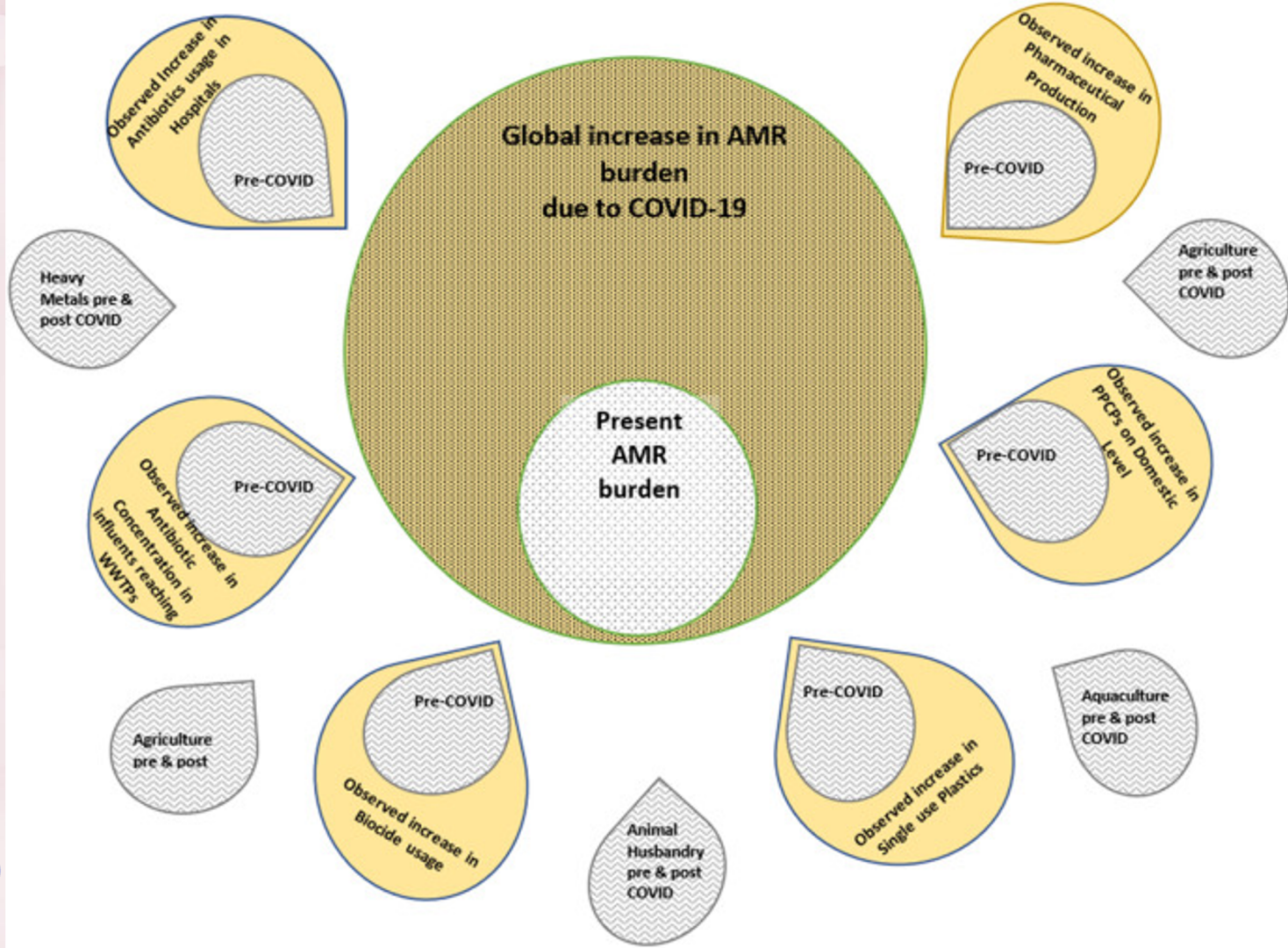
Review

COVID-19 and antimicrobial resistance: A cross-study

Sidra Ghazali Rizvi ^a, Shaikh Ziauddin Ahammad ^{b,*}

^a Indian Institute of Technology-Delhi, Hauz Khas, New Delhi 110016, India

^b Block I, Room # 135, Department of Biochemical Engineering & Biotechnology, Indian Institute of Technology Delhi, Hauz Khas, New Delhi 110016, India





Nouveautés ?



Etudes comparatives

1. Que les 3 principales familles étudiées
2. Pas d'étude Vs Placebo
3. Peu d'études randomisées
4. Principalement PAC en hospitalisation

Empiric antibiotic coverage of atypical pathogens for community-acquired pneumonia in hospitalized adults (Review)

Eliakim-Raz N, Robenshtok E, Shefet D, Gafter-Gvili A, Vidal L, Paul M, Leibovici L



**THE COCHRANE
COLLABORATION®**

SYSTEMATIC REVIEW

Beta-lactam plus macrolides or beta-lactam alone for community-acquired pneumonia: A systematic review and meta-analysis

NOBUYUKI HORITA,¹ TATSUYA OTSUKA,² SHUSAKU HARANAGA,³ HO NAMKOONG,⁴ MAKOTO MIKI,⁵
NAOYUKI MIYASHITA,⁶ FUTOSHI HIGA,⁷ HIROSHI TAKAHASHI,⁸ MASAHIRO YOSHIDA,⁹
SHIGERU KOHNO¹⁰ AND TAKESHI KANEKO¹



Nouvelles molécules

1. Céphalosporine 5eme Gen Ceftobiprol Ceftraoline
2. Macrolide 4eme gen Solithromycine
3. Omdacycline
4. Fluoroquinolone Delafloxacin (approuvé FDA pour les PAC), Nemonoxacin Zabofloxacin
5. Lefamuline : nouvelle famille les pleuromutiline (approuvé FDA pour les PAC)

The background is a light blue surface with several white and blue capsules scattered around. One capsule in the center is broken, with white powder spilling out. There are also several red and blue pills floating in the air. In the corners, there are stylized illustrations of viruses or bacteria: a blue one in the top left, a red one in the top right, a blue one in the bottom left, and a red one in the bottom right.

3 Propositions



Durée de l'antibiothérapie

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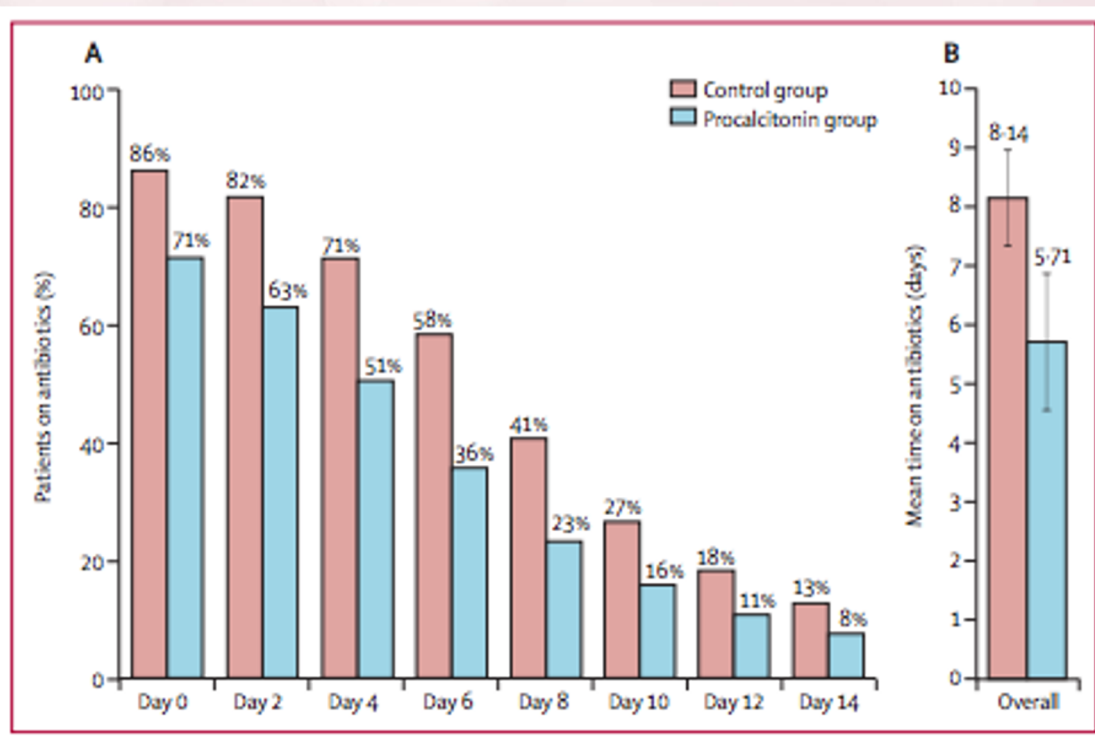
Spectre le plus étroit sur la durée la plus courte..

Effect of procalcitonin-guided antibiotic treatment on mortality in acute respiratory infections: a patient level meta-analysis



Philipp Schuetz*, Yannick Wirz*, Ramon Sager*, Mirjam Christ-Crain, Daiana Stolz, Michael Tamm, Lila Bouadma, Charles E Luyt, Michel Wolff, Jean Chastre, Florence Tubach, Kristina B Kristoffersen, Olaf Burkhardt, Tobias Welte, Stefan Schroeder, Vandack Nobre, Long Wei, Heiner C Bucher, Djillali Annane, Konrad Reinhart, Ann R Falsey, Angela Branche, Pierre Damas, Maarten Nijsten, Dylan W de Lange, Rodrigo O Deliberato, Carolina F Oliveira, Vera Maravić-Stojković, Alessia Verduri, Bianca Beghé, Bin Cao, Yahya Shehabi, Jens-Ulrik S Jensen, Caspar Corti, Jos A H van Oers, Albertus Beishuizen, Armand R J Girbes, Evelien de Jong, Matthias Briel*, Beat Mueller

www.thelancet.com/infection Vol 18 January 2018



Effectiveness of discontinuing antibiotic treatment after three days versus eight days in mild to moderate-severe community acquired pneumonia: randomised, double blind study

Rachida el Moussaoui, Corianne A J M de Borgie, Peterhans van den Broek, Willem N Hustinx, Paul Bresser, Guido E L van den Berk, Jan-Werner Poley, Bob van den Berg, Frans H Krouwels, Marc J M Bonten, Carla Weenink, Patrick M M Bossuyt, Peter Speelman, Brent C Opmeer, Jan M Prins

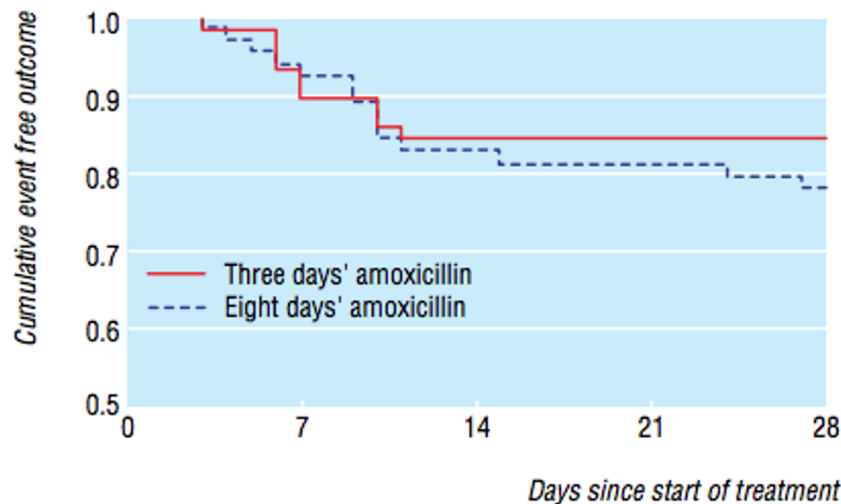


Fig 3 Proportion of patients considered clinical successes in intention to treat population. Day 3=day of randomisation

What is already known on this topic

Recommended duration of antibiotic treatment in adults with community acquired pneumonia is not supported by scientific evidence

Three days' treatment with amoxicillin is as effective as the standard longer course in children with non-severe pneumonia

What this study adds

Discontinuing amoxicillin treatment after three days is not inferior to discontinuing it after eight days in adults with mild to moderate-severe community acquired pneumonia who have substantially improved after an initial three days' treatment

A shorter duration of treatment can help contain the growing resistance rates among respiratory pathogens

JAMA Internal Medicine | [Original Investigation](#) | LESS IS MORE

Duration of Antibiotic Treatment in Community-Acquired Pneumonia A Multicenter Randomized Clinical Trial

Ane Uranga, MD; Pedro P. España, MD; Amaia Bilbao, MSc, PhD; Jose María Quintana, MD, PhD;
Ignacio Arriaga, MD; Maider Intxausti, MD; Jose Luis Lobo, MD, PhD; Laura Tomás, MD; Jesus Camino, MD;
Juan Nuñez, MD; Alberto Capelastegui, MD, PhD

Table 2. Results for the Primary Study Outcomes

Outcome	Control Group	Intervention Group	P Value
Intent-to-Treat Analysis			
Total No. of participants	150	162	
Clinical success, No. (%) ^a			
At day 10	71 (48.6)	90 (56.3)	.18
At day 30	132 (88.6)	147 (91.9)	.33
CAP symptom questionnaire score, mean (SD) ^b			
At day 5	24.7 (11.4)	27.2 (12.5)	.10
At day 10	18.6 (9.0)	17.9 (7.6)	.69
Per-Protocol Analysis			
Total No. of participants	137	146	
Clinical success, No. (%) ^a			
At day 10	67 (50.4)	86 (59.7)	.12
At day 30	126 (92.7)	136 (94.4)	.54
CAP symptom questionnaire score, mean (SD) ^b			
At day 5	24.3 (11.4)	26.6 (12.1)	.16
At day 10	18.1 (8.5)	17.6 (7.4)	.81

Abbreviation: CAP, community-acquired pneumonia.

^a Percentages exclude patients with missing data. In the intent-to-treat population, the percentage of missing data for each variable was as follows: clinical success at day 10, 1.9%; clinical success at day 30, 0.9%; CAP symptom questionnaire score at day 5, 3.8%; and CAP symptom questionnaire score at day 10, 4.4%. In the per-protocol population, the percentage of missing data

was as follows: clinical success at day 10, 2.1%; clinical success at day 30, 1.0%; CAP symptom questionnaire score at day 5, 3.1%; and CAP symptom questionnaire score at day 10, 3.8%.

^b On the CAP symptom questionnaire, which is a specific and validated patient-reported outcome measure based on 18 items, higher scores indicated more severe CAP-related symptoms (range, 0-90).

Key Points

Question How long should antibiotic treatment last for patients with community-acquired pneumonia?

Findings In this randomized clinical trial that included 312 patients, the clinical success rate was 50.4% in controls and 59.7% in the intervention group at day 10 and 92.6% in controls and 94.4% in the intervention group at day 30 without significant differences. The community-acquired pneumonia symptom questionnaire scores at days 5 and 10 were similar between the groups.

Meaning Basing antibiotic treatment duration on clinical stability criteria leads to a significant reduction in treatment duration without increasing the rate of adverse outcomes.



🔑 Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

 Joshua P. Metlay *,  Grant W. Waterer *, Ann C. Long,  Antonio Anzueto ,  Jan Brozek ,  Kristina Crothers ,  Laura A. Cooley ,  Nathan C. Dean ,  Michael J. Fine ,  Scott A. Flanders ,  Marie R. Griffin , [Show All...](#)



Table 3. Initial Treatment Strategies for Outpatients with Community-acquired Pneumonia

	Standard Regimen
No comorbidities or risk factors for MRSA or <i>Pseudomonas aeruginosa</i> [*]	Amoxicillin or
	doxycycline or
	macrolide (if local pneumococcal resistance is <25%) [†]
With comorbidities [‡]	Combination therapy with
	amoxicillin/clavulanate or cephalosporin
	AND
	macrolide or doxycycline [§]
	OR
	monotherapy with respiratory fluoroquinolone .

Definition of abbreviations: ER = extended release; MRSA = methicillin-resistant *Staphylococcus aureus*.

^{*}Risk factors include prior respiratory isolation of MRSA or *P. aeruginosa* or recent hospitalization AND receipt of parenteral antibiotics (in the last 90 d).

[†]Amoxicillin 1 g three times daily, doxycycline 100 mg twice daily, azithromycin 500 mg on first day then 250 mg daily, clarithromycin 500 mg twice daily, or clarithromycin ER 1,000 mg daily.

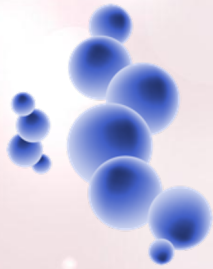
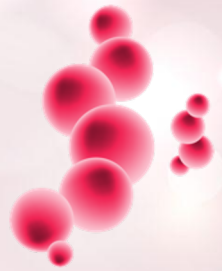
[‡]Comorbidities include chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancy; or asplenia.

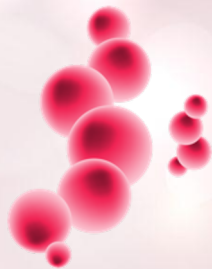
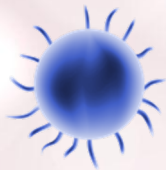
[§]Amoxicillin/clavulanate 500 mg/125 mg three times daily, amoxicillin/clavulanate 875 mg/125 mg twice daily, 2,000 mg/125 mg twice daily, cefpodoxime 200 mg twice daily, or cefuroxime 500 mg twice daily; AND azithromycin 500 mg on first day then 250 mg daily, clarithromycin 500 mg twice daily, clarithromycin ER 1,000 mg daily, or doxycycline 100 mg twice daily.

^{||}Levofloxacin 750 mg daily, moxifloxacin 400 mg daily, or gemifloxacin 320 mg daily.

Table 4. Initial Treatment Strategies for Inpatients with Community-acquired Pneumonia by Level of Severity and Risk for Drug Resistance

	Standard Regimen	Prior Respiratory Isolation of MRSA	Prior Respiratory Isolation of <i>Pseudomonas aeruginosa</i>	Recent Hospitalization and Parenteral Antibiotics and Locally Validated Risk Factors for MRSA	Recent Hospitalization and Parenteral Antibiotics and Locally Validated Risk Factors for <i>P. aeruginosa</i>
Nonsevere inpatient pneumonia*	β -Lactam + macrolide [‡] or respiratory fluoroquinolone [‡]	Add MRSA coverage [§] and obtain cultures/nasal PCR to allow deescalation or confirmation of need for continued therapy	Add coverage for <i>P. aeruginosa</i> and obtain cultures to allow deescalation or confirmation of need for continued therapy	Obtain cultures but withhold MRSA coverage unless culture results are positive. If rapid nasal PCR is available, withhold additional empiric therapy against MRSA if rapid testing is negative or add coverage if PCR is positive and obtain cultures	Obtain cultures but initiate coverage for <i>P. aeruginosa</i> only if culture results are positive
Severe inpatient pneumonia*	β -Lactam + macrolide [‡] or β -lactam + fluoroquinolone [‡]	Add MRSA coverage [§] and obtain cultures/nasal PCR to allow deescalation or confirmation of need for continued therapy	Add coverage for <i>P. aeruginosa</i> and obtain cultures to allow deescalation or confirmation of need for continued therapy	Add MRSA coverage [§] and obtain nasal PCR and cultures to allow deescalation or confirmation of need for continued therapy	Add coverage for <i>P. aeruginosa</i> and obtain cultures to allow deescalation or confirmation of need for continued therapy

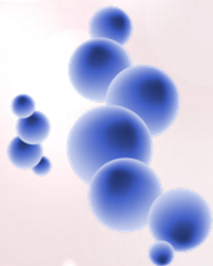




Question 15: In Outpatient and Inpatient Adults with CAP Who Are Improving, What Is the Appropriate Duration of Antibiotic Treatment?

Recommendation

We recommend that the duration of antibiotic therapy should be guided by a validated measure of clinical stability (resolution of vital sign abnormalities [heart rate, respiratory rate, blood pressure, oxygen saturation, and temperature], ability to eat, and normal mentation), and antibiotic therapy should be continued until the patient achieves stability and for no less than a total of 5 days (strong recommendation, moderate quality of evidence).





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Duration of Antibiotic Use Among Adults With Uncomplicated Community-Acquired Pneumonia Requiring Hospitalization in the United States

Sarah H. Yi, Kelly M. Hatfield, James Baggs, Lauri A. Hicks, Arjun Srinivasan, Sujan Reddy, and John A. Jernigan

Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia

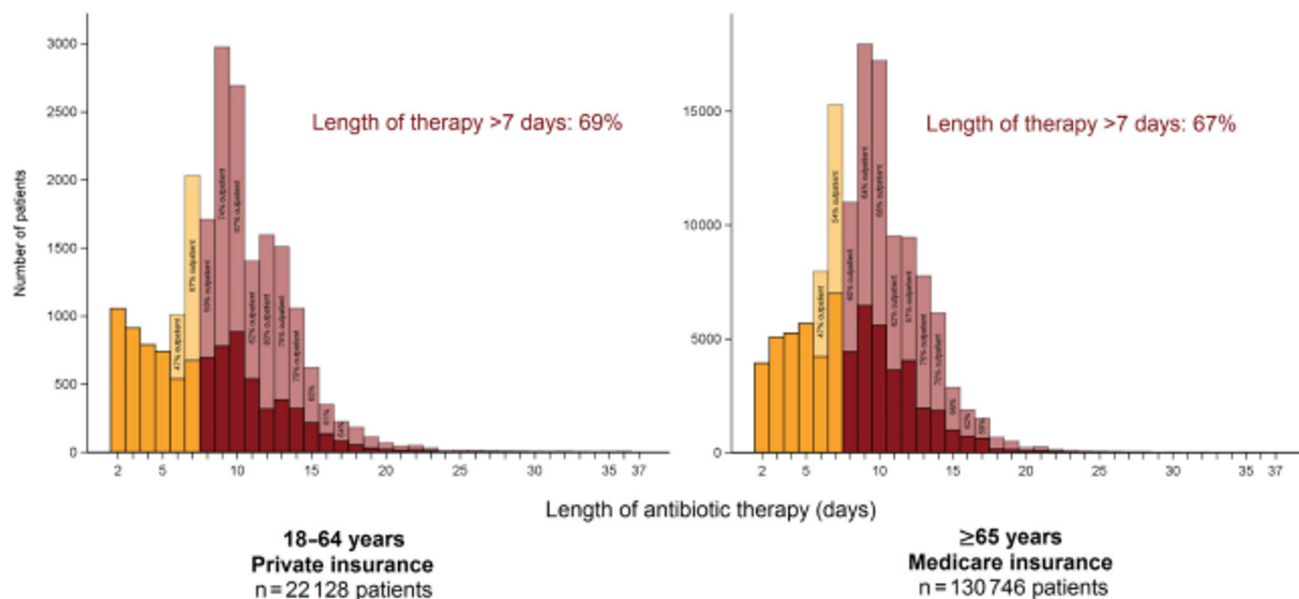
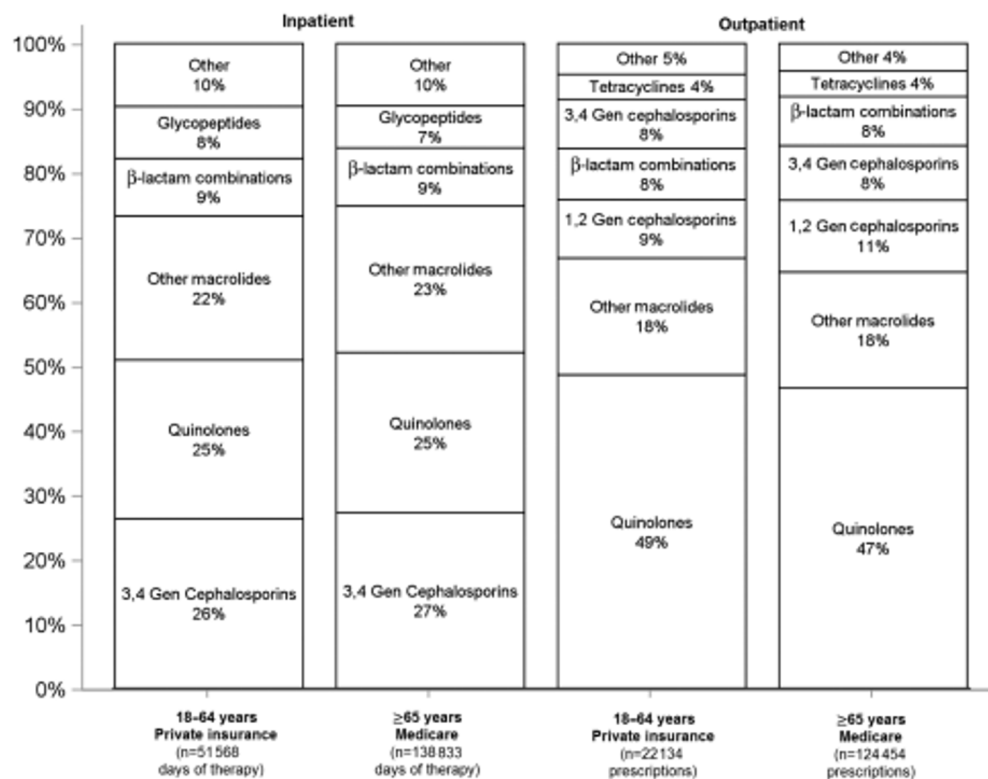


Figure 3.
Total length of antibiotic therapy of adults hospitalized for community-acquired pneumonia.





Traitement des exacerbation des BPCO

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ATB systématique ?

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C-reactive protein point-of-care testing for safely reducing antibiotics for acute exacerbations of chronic obstructive pulmonary disease: the PACE RCT

*Nick A Francis, David Gillespie, Patrick White, Janine Bates, Rachel Lowe,
Bernadette Sewell, Rhiannon Phillips, Helen Stanton, Nigel Kirby, Mandy Wootton,
Emma Thomas-Jones, Kerenza Hood, Carl Llor, Jochen Cals, Hasse Melbye,
Gurudutt Naik, Micaela Gal, Deborah Fitzsimmons, Mohammed Fasihul Alam,
Evgenia Riga, Ann Cochrane and Christopher C Butler*

RESEARCH ARTICLE

2-Day versus C-reactive protein guided antibiotherapy with levofloxacin in acute COPD exacerbation: A randomized controlled trial

Msolli Mohamed Amine^{1,2}, Messous Selma², Sekma Adel^{1,2}, Bel haj ali Khaoula^{1,2}



Colonisation bactérienne

L'éradication nécessaire ?



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Non cystic fibrosis bronchiectasis: A longitudinal retrospective observational cohort study of Pseudomonas persistence and resistance



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Outcomes of *Pseudomonas* eradication therapy in patients with non-cystic fibrosis bronchiectasis

Laura White, Ghazi Mirrani, Mark Grover, Judith Rollason, Adam Malin, Jay Suntharalingam*

Conclusion

**Recherche
de nouvelles
molécules**

Laboratoires



**Durée des
cures et
spectre**

Sociétés savantes



**Traitement
des
exacerbations**

Pneumologues

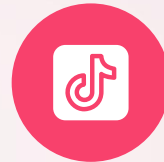


**Colonisation
bactérienne**

MG



THANKS!



Do you have any questions?
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