

Résistance aux antibiotiques dans les pays du Sud: quelles sont les données qui nous manquent?

Martin Vandeputte MD, PhD student



ALLIANCE FRANCOPHONE DES ACTEURS DE SANTÉ CONTRE LE
VIH ET LES INFECTIONS VIRALES CHRONIQUES OU ÉMERGENTES

25/05/2023



**INSTITUTE
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MEDICINE**
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Question

■ Quelle est selon vous la situation actuelle en termes d'antibiorésistance dans les pays « du Sud » (malgré le manque de données)?

■ La majorité des infections sont causées par des germes multiR

■ Mauvaise, avec des taux de R 5x supérieurs à ceux des pays « à hauts revenus » pour certains antibiotiques.

■ Globalement similaire à celle des pays « à hauts revenus »

■ La majorité des morts par infection sont causées par des germes multiR

■ Impossible de se prononcer par manque de données



Question

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■ **Mauvaise, avec des taux de R 5x supérieurs à ceux des pays « à hauts revenus » pour certains antibiotiques**

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■ La majorité des morts par infection sont causées par des germes multiR

■ Impossible de se prononcer par manque de données

Mais...



Cas clinique vécu à Mayotte

- Homme de 45 ans
 - Diabète type NIR
 - HTA
 - IRC
- Admission pour arthrite septique récidivante genou G
 - *MSSA*
 - *P. aeruginosa*
 - *S. maltophilia*
- Multiples lignes d'antibiothérapie
 - Amoxicilline
 - Oxacilline/Clindamycine
 - PipTazo/Cipro
 - Cotrimoxazole/Cipro



Cas clinique vécu à Mayotte

- Retour en salle d'opération pour nouveau drainage
- Dégradation respiratoire après chirurgie < pneumonie LID
- Intubation, amines
- Aspiration trachéo-bronchique:



Cas clinique vécu à Mayotte

PRÉLÈVEMENT BRONCHIQUE PROTÉGÉ	VB			
<u>Aspect macroscopique</u>	VB	Prélèvement limpide		
<u>Leucocytes</u>	VB	Quelques leucocytes		
<u>Hématies</u>	VB	Absence d hématies		
<u>Cellules</u>	VB	Rares cellules épithéliales		
<u>Cellules bronchiques</u>	VB	Absence de cellules bronchiques		
<u>Macrophages</u>	VB	Absence de macrophages		
<u>Coloration de gram</u>	VB	1 ligne		
Absence de Germe visible				
<u>Cultures :</u>	VB	1 ligne		
Entre 10p4 et 10p5 UFC/ml Acinetobacter baumannii				
<u>Culture mycologique :</u>	VB	NEGATIF		
<u>Dossier terminé</u>	VB	OUI		



Cas clinique vécu à Mayotte

RECHERCHE D'ENTEROBACTERIES MULTIRÉSISTANTES	VB		
<u>Recherche d'entérobactéries multirésistantes</u>	VB	POSITIVE	
<u>Cultures :</u>	VB	1 ligne	
Présence de Acinetobacter baumannii BMR : producteur de carbapenemase			
<u>Dossier terminé</u>	VB	OUI	



Cas clinique vécu à Mayotte

10p5 UFC/ml *Acinetobacter baumannii* BMR : producteur de carbapenemase

Antibiogramme

	Diamètre	Résultat	CMI
Ticarcilline		R	?
Ticarcilline/ac. clavulanique		R	?
Pipéracilline		R	?
Pipéracilline/tazobactam		R	?
Aztréonam		R	>256
Céftazidime		R	>512
Céfépime		R	>512
Imipénème		R	>64
Gentamicine		S	?
Tobramycine		S	?
Amikacine		R	32
Ciprofloxacine		R	?
Fosfomycine		R	?
Sulfamides		R	>512
Rifampicine		R	

Genotypage: OXA-23 & NDM-1 CPase



Cas clinique vécu à Mayotte

PUS PROFOND	VB		
<u>Origine du prélèvement</u>	VB	Genou	
<u>Leucocytes</u>	VB	Quelques leucocytes	
<u>Hématies</u>	VB	Nombreuses hématies	
<u>Cellules</u>	VB	Absence de cellules épithéliales	
<u>Coloration de gram</u>	VB	2 lignes	
Flore polymorphe abondante Nombreux Bacilles Gram négatif			
<u>Culture</u>	VB	Culture positive	
<u>Cultures :</u>	VB	2 lignes	
Nombreux Acinetobacter baumannii BMR : producteur de carbapenemase Assez nombreux Stenotrophomonas maltophilia			
<u>Culture mycologique :</u>	VB	NEGATIF	
<u>Dossier terminé</u>	VB	OUI	

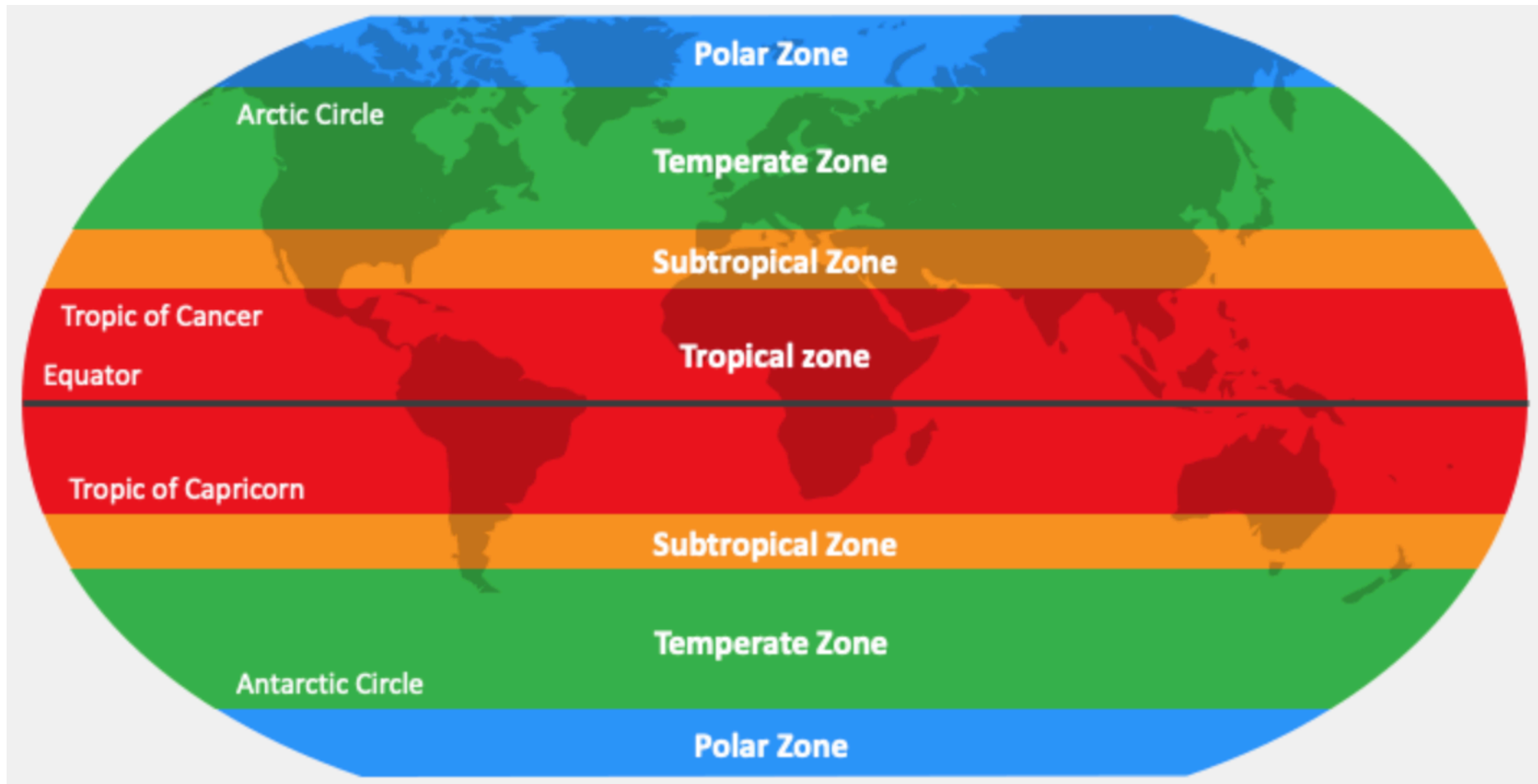


Cas clinique vécu à Mayotte

- Traitement par **Imipenem/Cilastatine** - **Gentamycine** - **Colistine** aerosol
- Evolution rapide vers ARDS
- Décès après 8 jours en réa

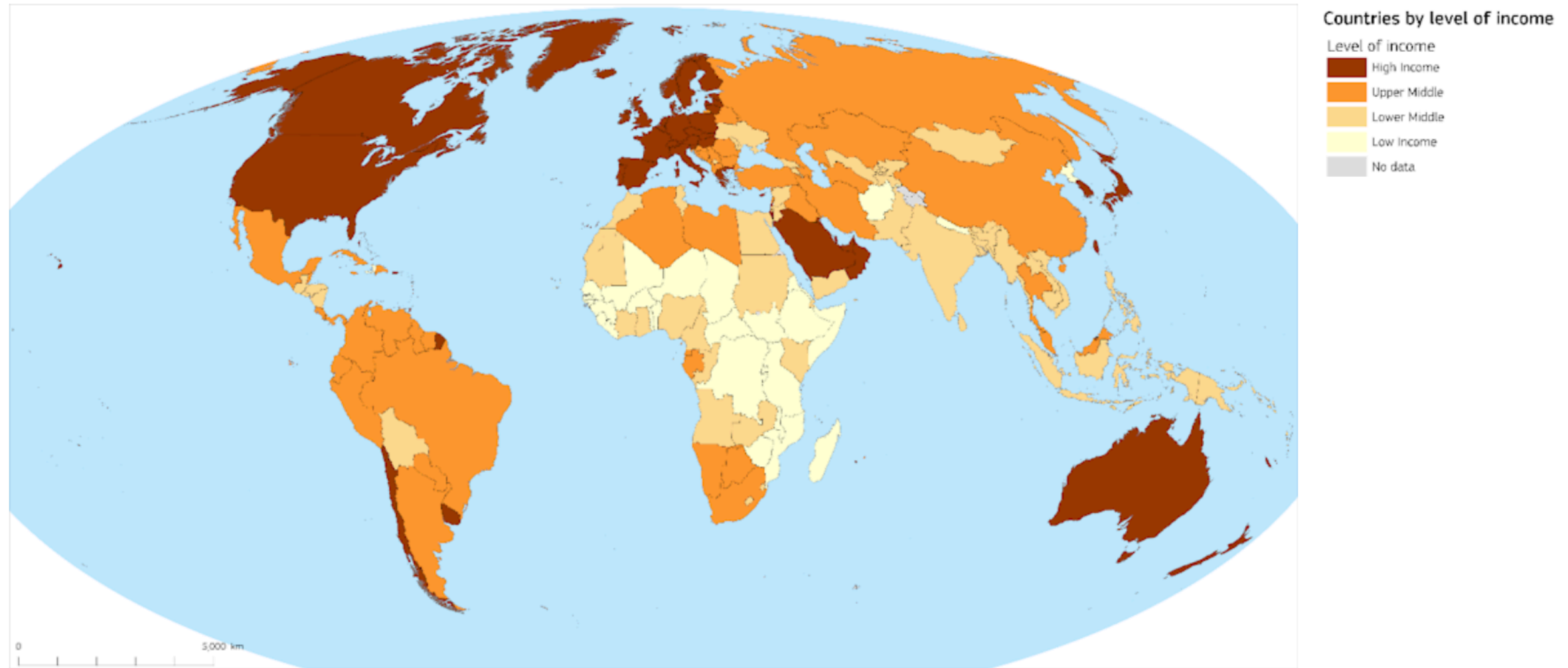


Sud? Tropiques?



Sud? Tropiques? LMIC

Figure 1. **Classification of countries in income classes**



Résistance dans les LMIC



Mapping Antimicrobial Resistance and Antimicrobial Use Partnership



The MAAP project, led by, and for Africans, represents the first time that large quantities of AMR and AMC data are being systematically collected, processed, and evaluated in Africa.

MAAP REVIEWED

819,584

AMR records spanning from 2016 to 2019, from **205 LABORATORIES** across **14 COUNTRIES**.

326 hospital and community pharmacies and **16** national level datasets on antimicrobial consumption.

ONLY 1.3% of the biology laboratories across the 14 countries perform bacteriological testing



Out of the **187,000** samples tested for antimicrobial resistance, **88%** did not include records of patients' clinical profile—the diagnosis, the origin of infection, comorbidities and previous antimicrobial usage—while the remaining **12%** had incomplete information.

Iskandar et al. *Antimicrob Resist Infect Control* (2021) 10:63
<https://doi.org/10.1186/s13756-021-00931-w>

Antimicrobial Resistance
and Infection Control

REVIEW

Open Access



Surveillance of antimicrobial resistance in low- and middle-income countries: a scattered picture

Katia Iskandar^{1,2,3*}, Laurent Molinier⁴, Souheil Hallit^{2,5}, Massimo Sartelli⁶, Timothy Craig Hardcastle^{7,8}, Mainul Haque⁹, Halyna Lugova¹⁰, Sameer Dhingra¹¹, Paras Sharma¹², Salekul Islam¹³, Irfan Mohammed¹⁴, Isa Naina Mohamed¹⁵, Pierre Abi Hanna³, Said El Hajj¹⁶, Nurul Adilla Hayat Jamaluddin¹⁵, Pascale Salameh^{2,16,17†} and Christine Roques^{18,19†}

Obstacles à une surveillance efficace

- Accès limité ou non-disponibilité des réactifs
- Infrastructures du laboratoire insuffisantes
- Personnel labo et clinique limité, en termes de nombre et de formation
- Problèmes de communications labo <-> cliniciens
- Assurance qualité insuffisante - pas de règles
- Dépendance à des financements extérieurs
- Pas de standardisation des AST
- Fragmentation des sources de données



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Global Antimicrobial Resistance and Use Surveillance System (GLASS)



Résistance dans les LMIC



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Table 1 Selected countries AMR National Surveillance Programs

Countries	Bangladesh	Brazil	India	Lebanon	Malaysia	South Africa
Population ^a	163.05 million	211.05 million	1.37 billion	6.86 million	31.95 million	58.56 million
World bank country classification by income ^[66]	LMIC	UMIC	LMIC	UMIC	UMIC	UMIC
GLASS-AMR ^a	Yes	Yes	Yes	Yes	Yes	yes
National action plan ^a	In place	In place	In place	In place	In place	In place
National coordinating center ^a	Established	Established	Established	Established	Established	Established
Number of enrolled national surveillance centers ^a	8	18	130	30	110	353
Number of enrolled hospitals	0	11	65	30	42	350
In patient/ outpatient facilities	8 Inpatient/ Outpatient facilities	7 outpatient facilities	65 outpatient facilities	0	68 outpatient facilities	3 outpatient facilities
AST Standard ^a	CLSI	EUCAST/CLSI	CLSI	EUCAST/CLSI	EUCAST/CLSI	EUCAST/CLSI
National Reference Laboratory ^a	Established	Established	Established	Established	Established	Established
EQA	Provided	Provided	Not provided	Not reported	Provided	Provided
Number of laboratories performing AST ^a	8	11	41	30	43	50

Résistance dans les LMIC

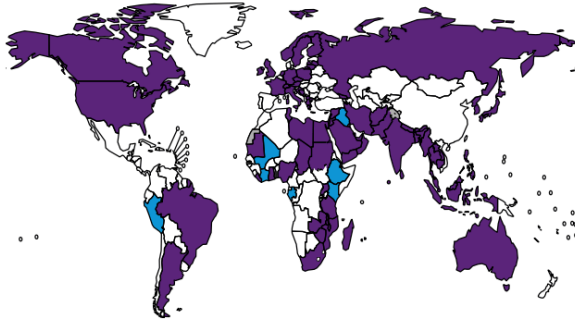


■ Enrolled in GLASS-AMR and GLASS-AMC ■ Enrolled in GLASS-AMR ■ Enrolled in GLASS-AMC □ Not enrolled ■ Not applicable

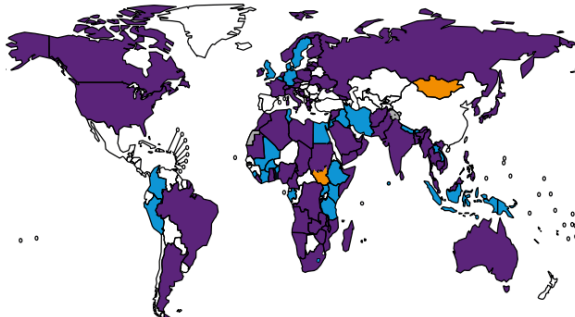
Enrolment status by end of 2017



Enrolment status by end of 2019



Enrolment status by end of 2021



About the GLASS dashboard

Global AMC data

Global AMR data

Glass dashboard

Global AMR data

<https://worldhealthorg.shinyapps.io/glass-dashboard/>



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Résistance dans les LMIC

Données globales

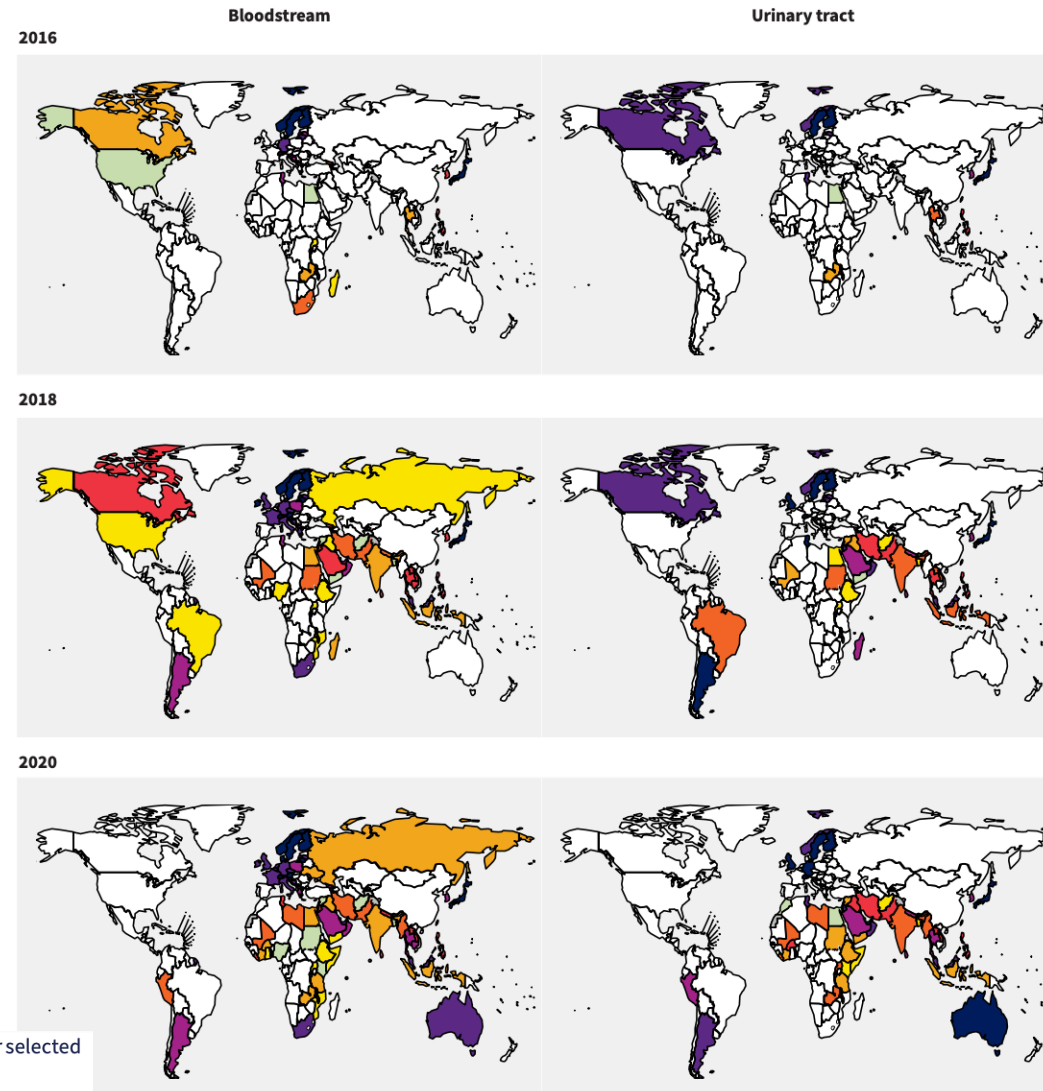
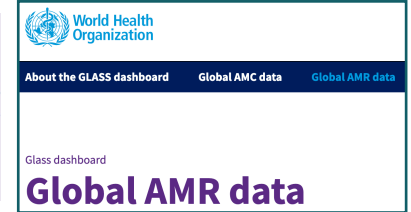
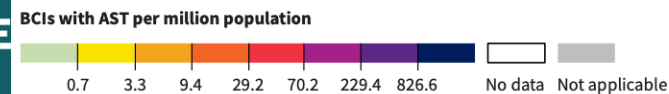
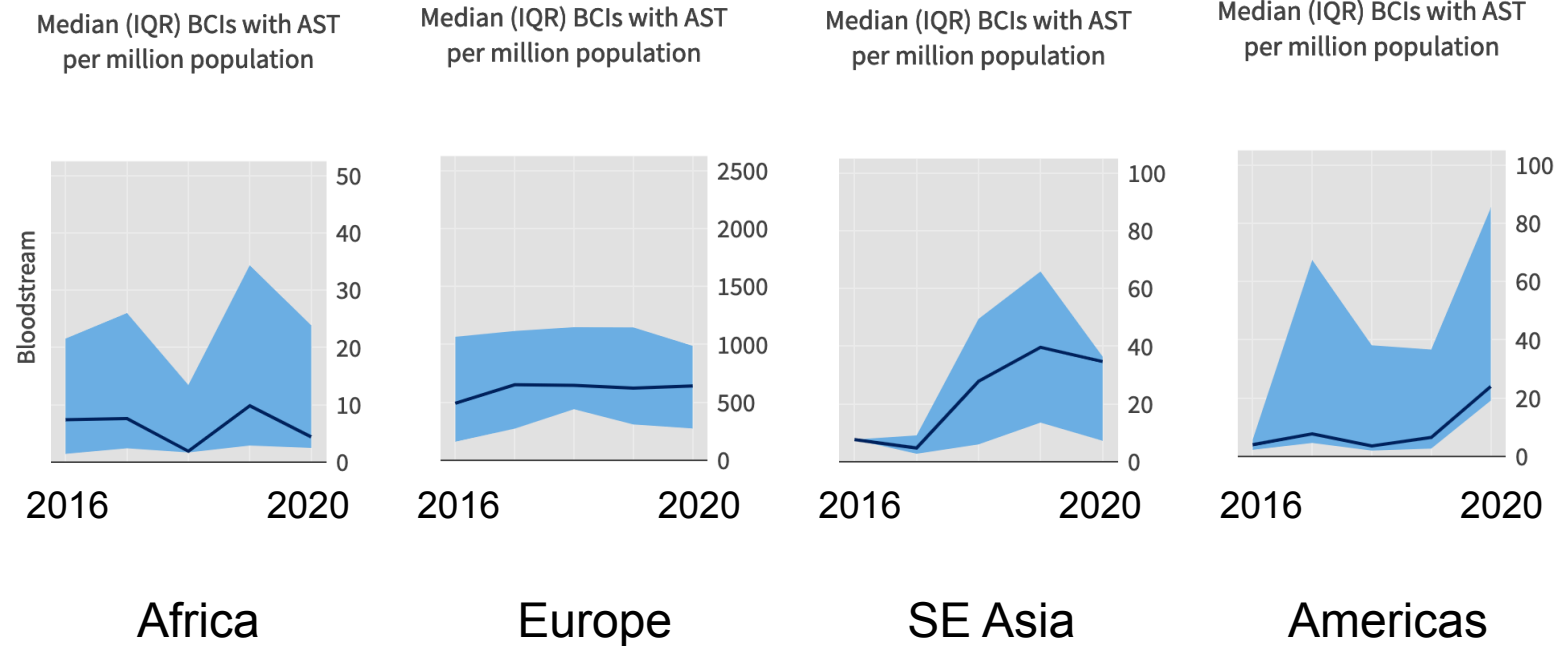
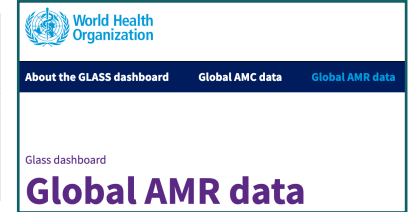


Fig. 3.4. BCIs with AST results reported to GLASS-AMR per one million population for selected infectious syndromes under surveillance (2016, 2018, 2020)



Résistance dans les LMIC

Données globales



Résistance dans les LMIC

Données globales

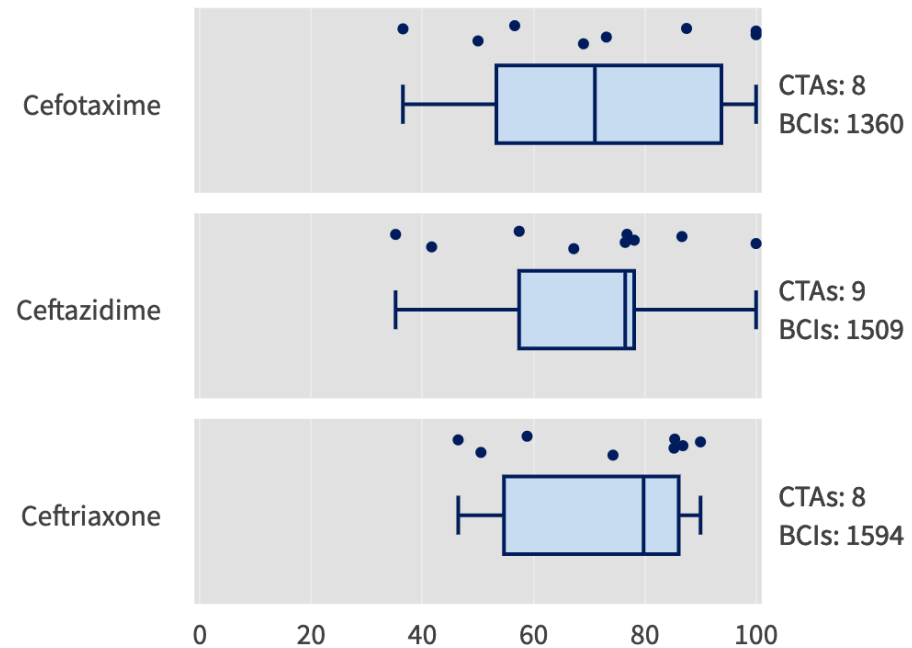


Region: African Region

Infectious syndrome: Urinary tract

Bacterial pathogen: Klebsiella pneumoniae

Third-generation cephalosporin resistance

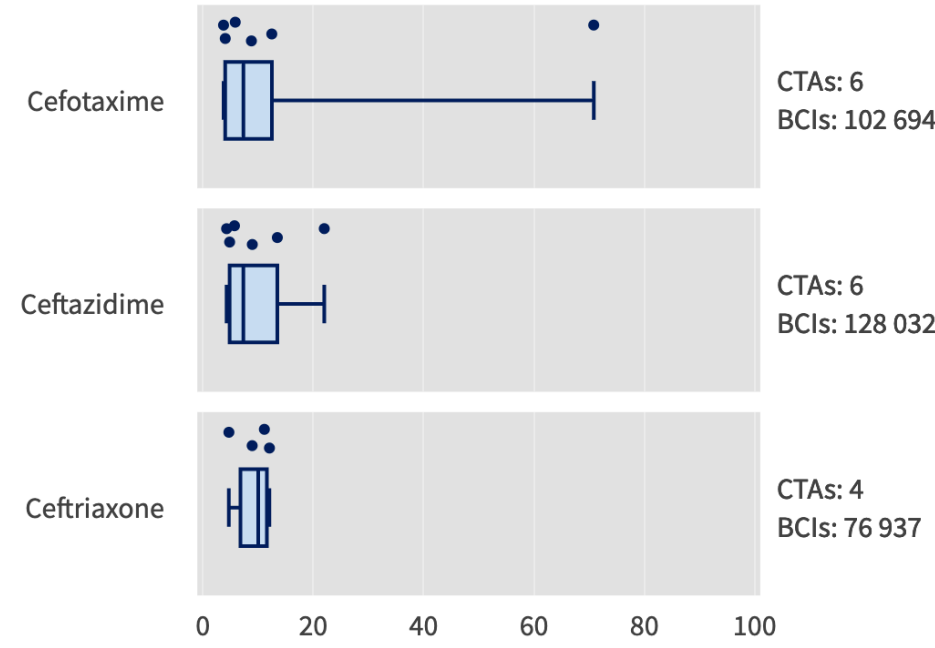


Region: European Region

Infectious syndrome: Urinary tract

Bacterial pathogen: Klebsiella pneumoniae

Third-generation cephalosporin resistance



Résistance dans les LMIC

Données globales



World Health Organization

[About the GLASS dashboard](#)[Global AMC data](#)[Global AMR data](#)

Glass dashboard

Global AMR data

Region

South-East Asia Region

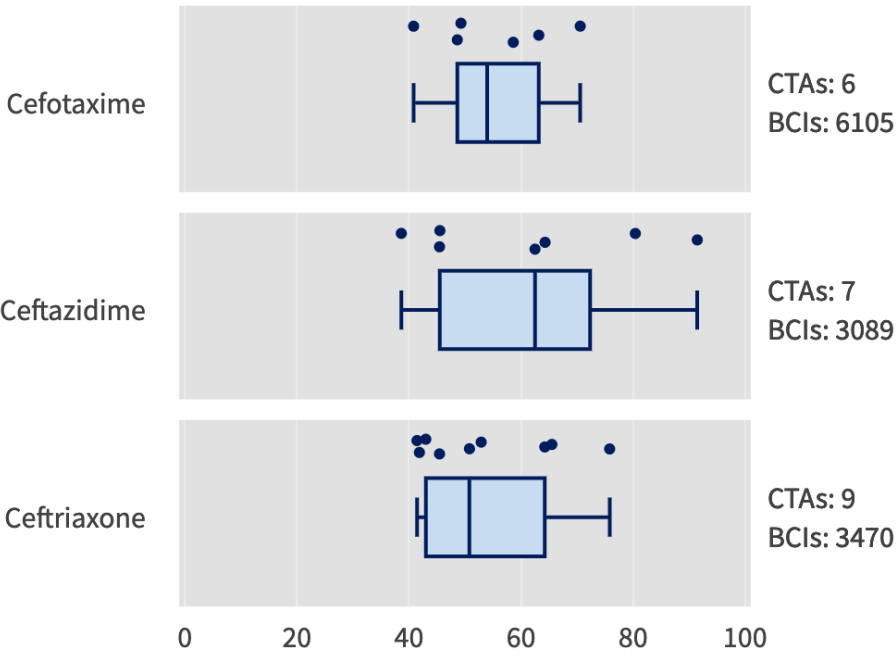
Infectious syndrome

Urinary tract

Bacterial pathogen

Klebsiella pneumoniae

Third-generation cephalosporin resistance



Region

Region of the Americas

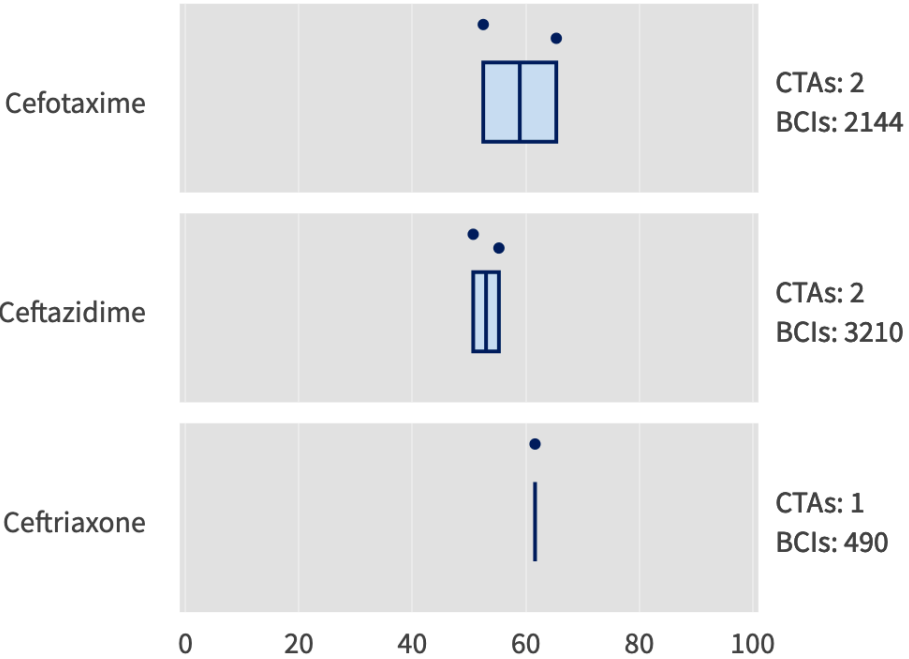
Infectious syndrome

Urinary tract

Bacterial pathogen

Klebsiella pneumoniae

Third-generation cephalosporin resistance



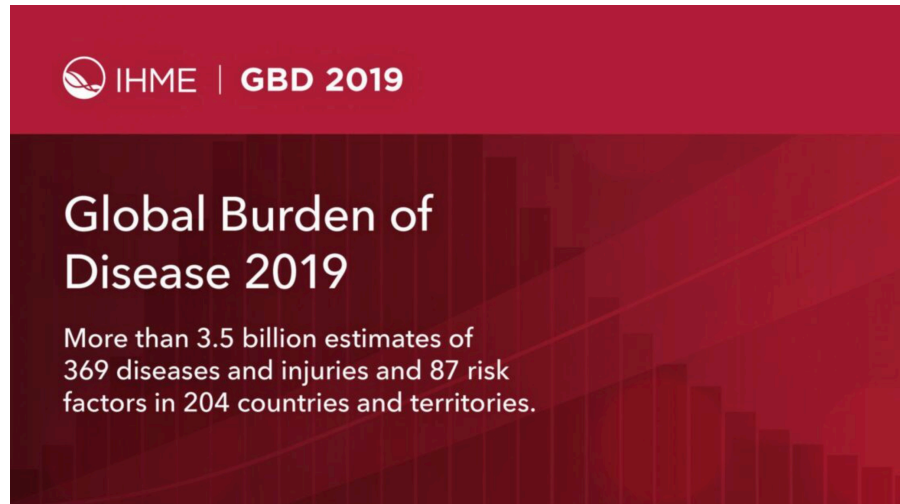
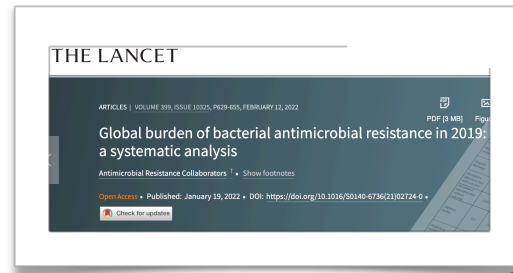
Résistance dans les LMIC

Données globales

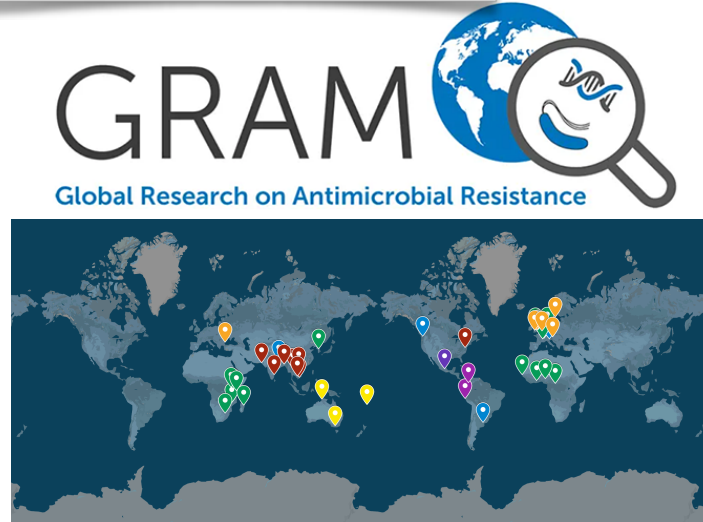


Résistance dans les LMIC

Données globales



+



+

Hôpitaux,
Essais cliniques
Compagnies pharma
Labo diagnostiques
Instituts de recherche
Réseaux de surveillance

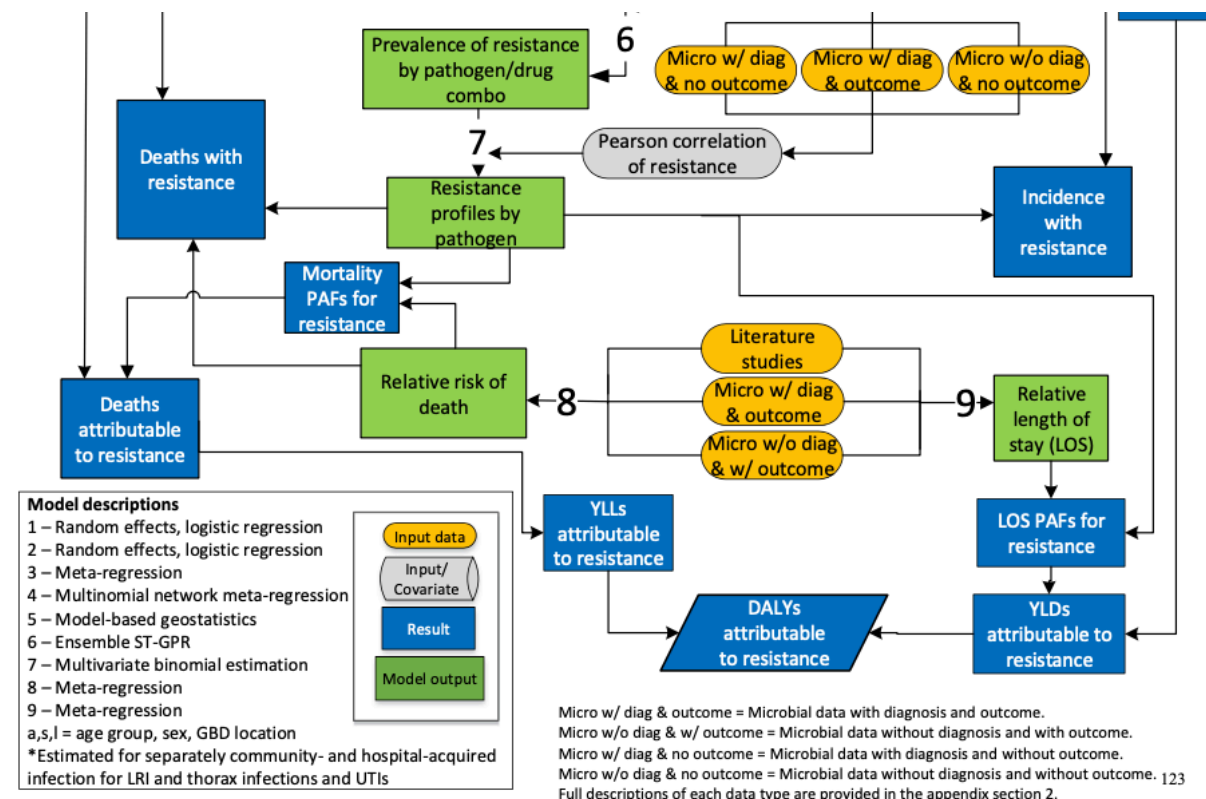
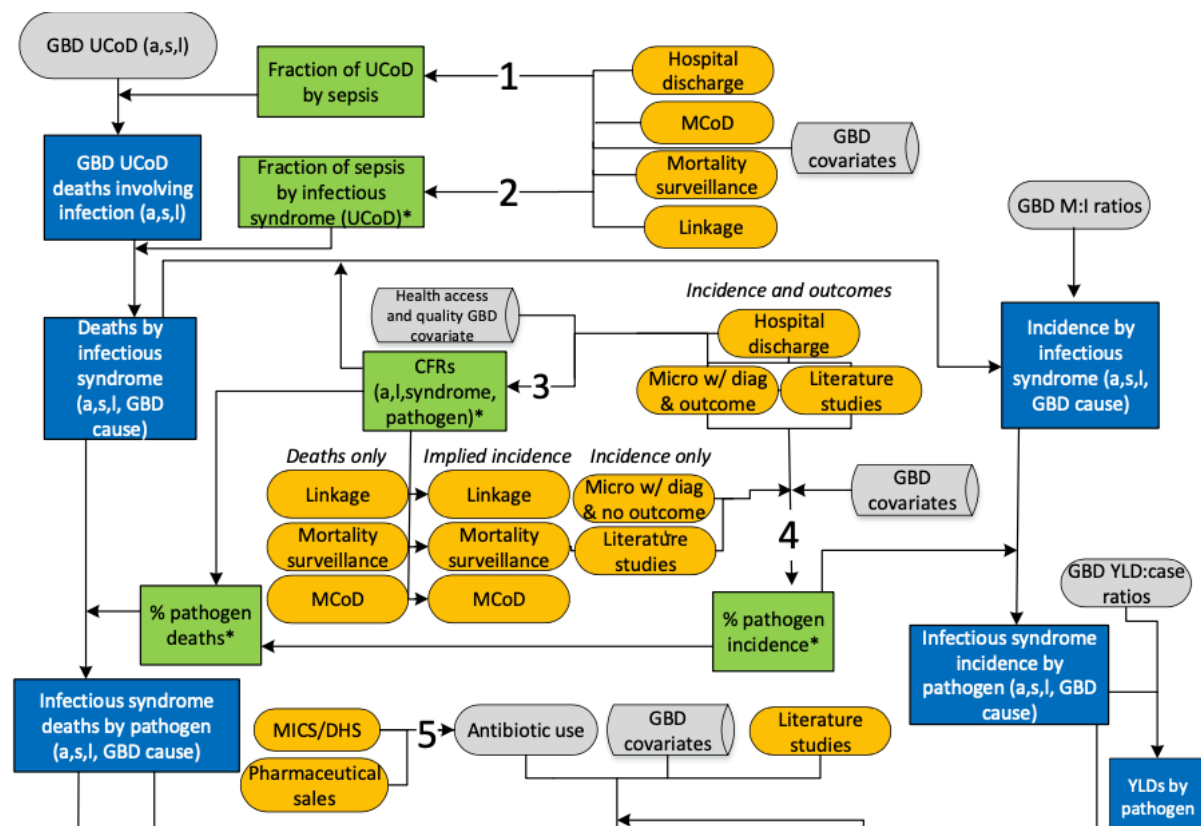
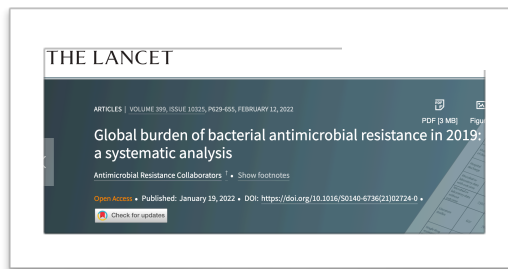
- 2 scenarios
 - Toutes les infections avec germes R remplacées par infections à germes S
—> « **Attribuables** »
 - Toutes les infections avec germes R remplacées par absence d'infection
—> « **Associées** »

- 12 Syndromes infectieux majeurs
- 23 bactéries
- 18 molécules
- 88 combinaisons bactérie/molécule
- 204 pays

Résistance dans les LMIC

Données globales

Modélisation

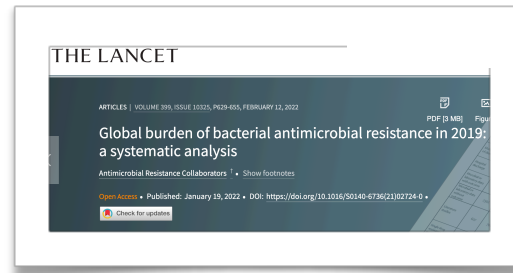


+ 10: + 10: Modéliser l'impact associé/attribuable à R à la molécule



Résistance dans les LMIC

Données globales



Pas de donnée partout

471M enregistrements

7585 lieux d'étude

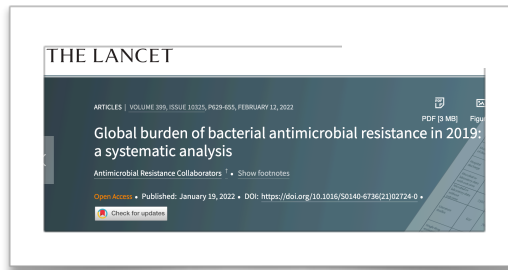
Input=
Données empiriques
uniquement

	Component 1: sepsis and infectious syndrome models*	Fraction of countries represented in component 1	Component 2: case-fatality ratio	Fraction of countries represented in component 2	Component 3: pathogen distribution	Fraction of countries represented in component 3	Component 4: fraction of resistance†	Fraction of countries represented in component 4	Component 5: relative risk	Fraction of countries represented in component 5
Andean Latin America	0	0/3	1784	2/3	12 010	2/3	538 644	3/3	4338	2/3
Australasia	320 909	1/2	94 818	1/2	6 294 677	2/2	4 653 832	2/2	5211	2/2
Caribbean	0	0/19	2858	5/19	6225	5/19	68 078	10/19	529	1/19
Central Asia	0	0/9	43 852	2/9	2785	1/9	304 341	9/9	6065	1/9
Central Europe	0	0/13	371 112	10/13	627 844	11/13	3 148 864	13/13	397 885	10/13
Central Latin America	8 130 066	2/9	3 932 601	9/9	11 641 626	8/9	829 686	9/9	20 210	5/9
Central sub-Saharan Africa	0	0/6	0	0/6	770	2/6	40 243	6/6	0	0/6
East Asia	1 189 309	1/3	385 443	2/3	257 522	2/3	2 501 536	3/3	185 980	2/3
Eastern Europe	0	0/7	118 754	4/7	64 212	5/7	968 565	7/7	102 904	4/7
Eastern sub-Saharan Africa	292	3/15	6388	4/15	68 791	9/15	474 280	14/15	3436	2/15
High-income Asia Pacific	0	0/4	135 907	3/4	99 042	3/4	18 909 332	4/4	7577	3/4
High-income North America	84 520 574	2/3	7 184 424	3/3	7 255 147	2/3	32 205 001	3/3	14 071 025	2/3
North Africa and Middle East	0	0/21	209 479	13/21	53 833	16/21	531 120	21/21	90 079	10/21
Oceania	0	0/18	0	0/18	20	1/18	4297	12/18	0	0/18
South Asia	54	1/5	77 811	4/5	51 810	4/5	1 413 840	5/5	97 131	4/5
Southeast Asia	0	0/13	195 087	9/13	91 259	8/13	3 128 014	12/13	172 947	8/13
Southern Latin America	0	0/3	200 665	3/3	73 512	2/3	740 385	3/3	5000	1/3
Southern sub-Saharan Africa	4 696 789	1/6	80 717	2/6	4 699 304	2/6	910 509	6/6	1051	1/6
Tropical Latin America	17 224 511	1/2	3 988 611	1/2	20 956 932	2/2	286 450	2/2	6443	1/2
Western Europe	10 599 906	2/24	94 506 554	20/24	105 183 184	21/24	18 909 732	21/24	932 016	21/24
Western sub-Saharan Africa	83	2/19	26 985	9/19	21 896	10/19	369 482	18/19	14 880	2/19



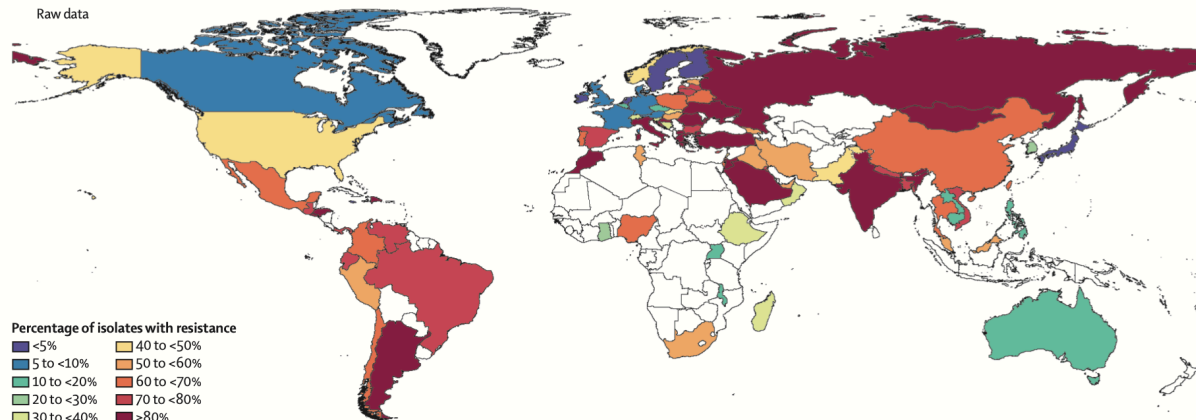
Résistance dans les LMIC

Données globales

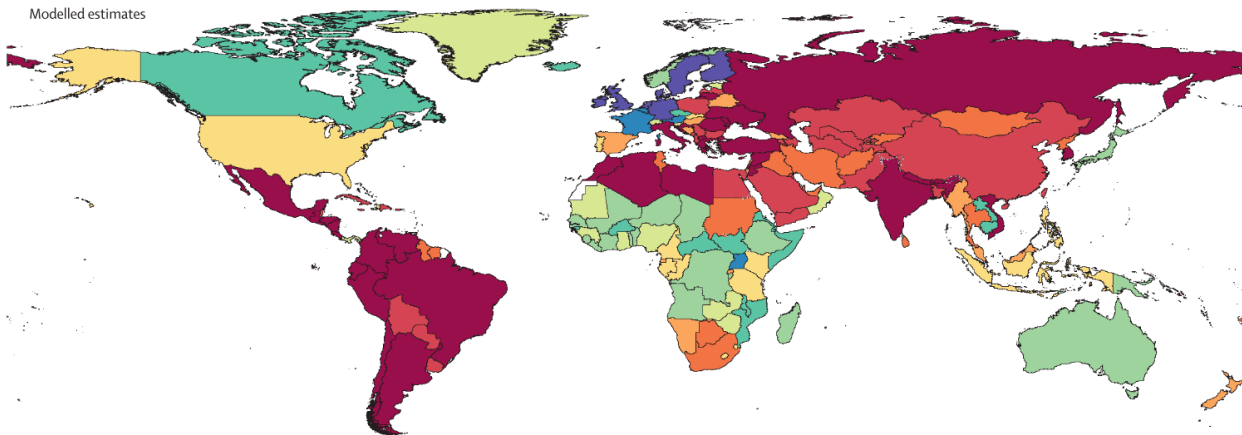


CRAb

D Carbapenem-resistant *Acinetobacter baumannii*
Raw data

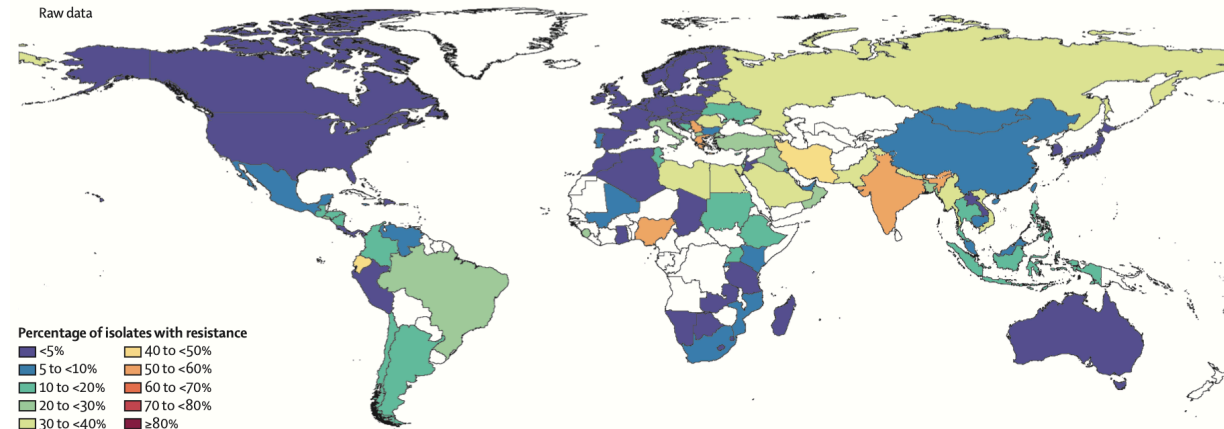


Modelled estimates

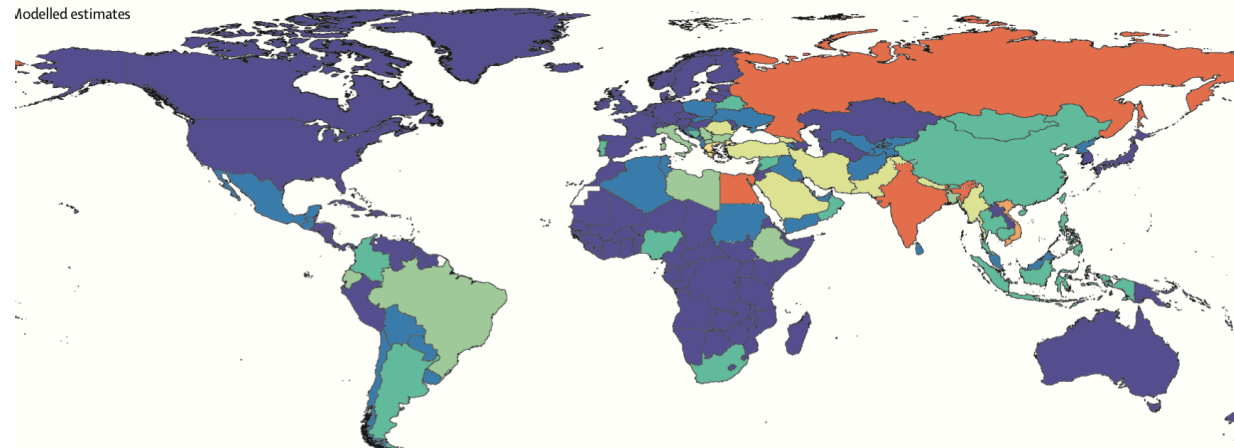


CRKp

F Carbapenem-resistant *Klebsiella pneumoniae*
Raw data

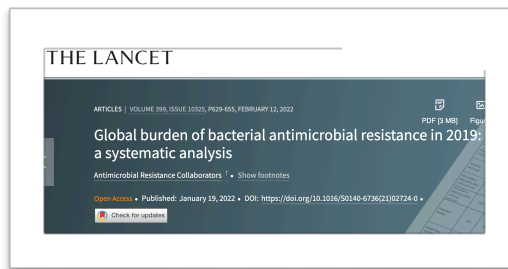


Modelled estimates



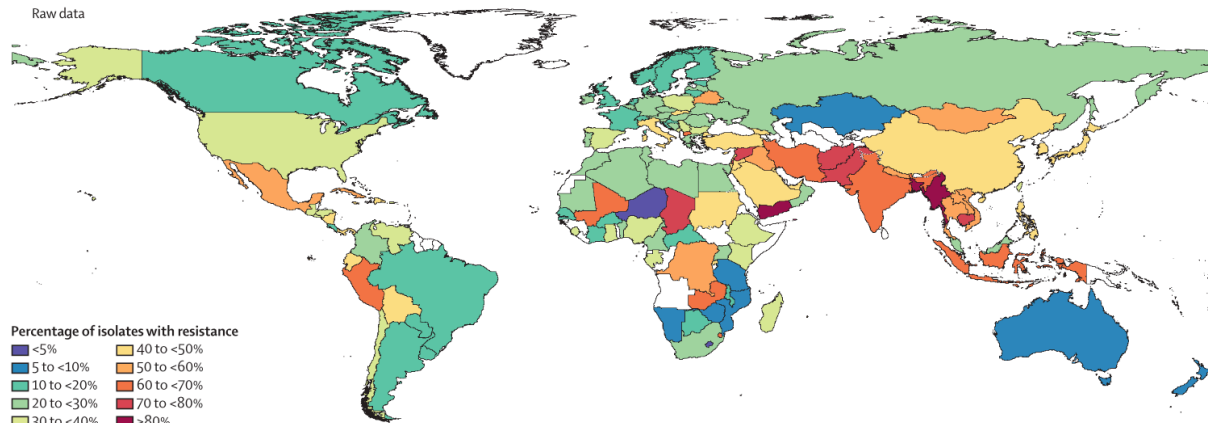
Résistance dans les LMIC

Données globales

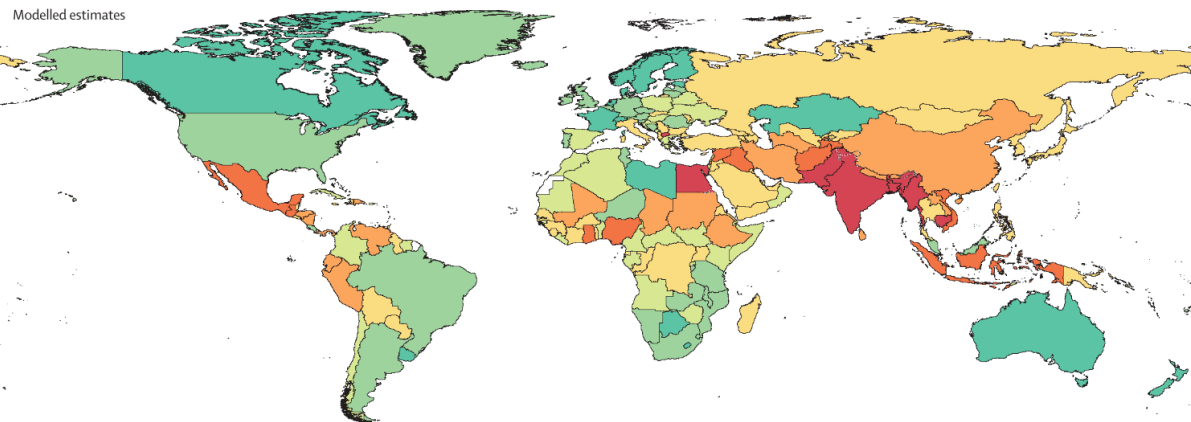


Ec R to FQ

E Fluoroquinolone-resistant *Escherichia coli*
Raw data

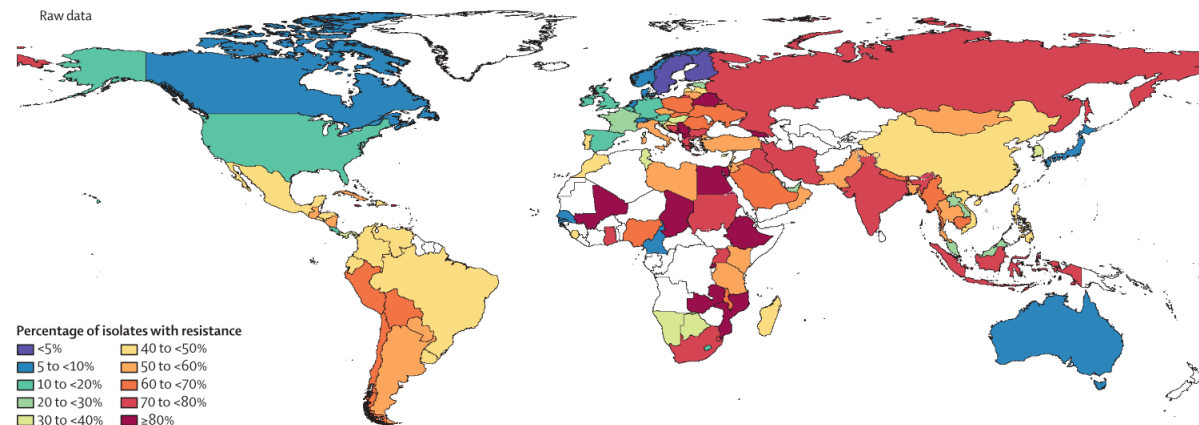


Modelled estimates

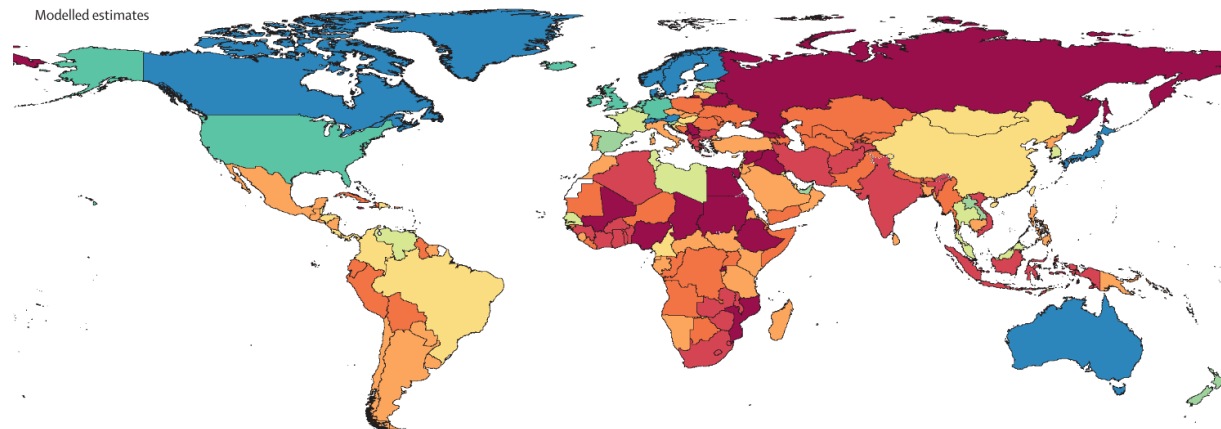


Kp R to 3G Ceph

Raw data

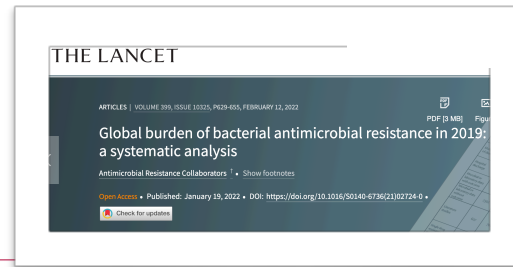


Modelled estimates



Résistance dans les LMIC

Données globales



1.27M morts
attribuables à la R en
2019

4.95M morts
associées à la R en
2019

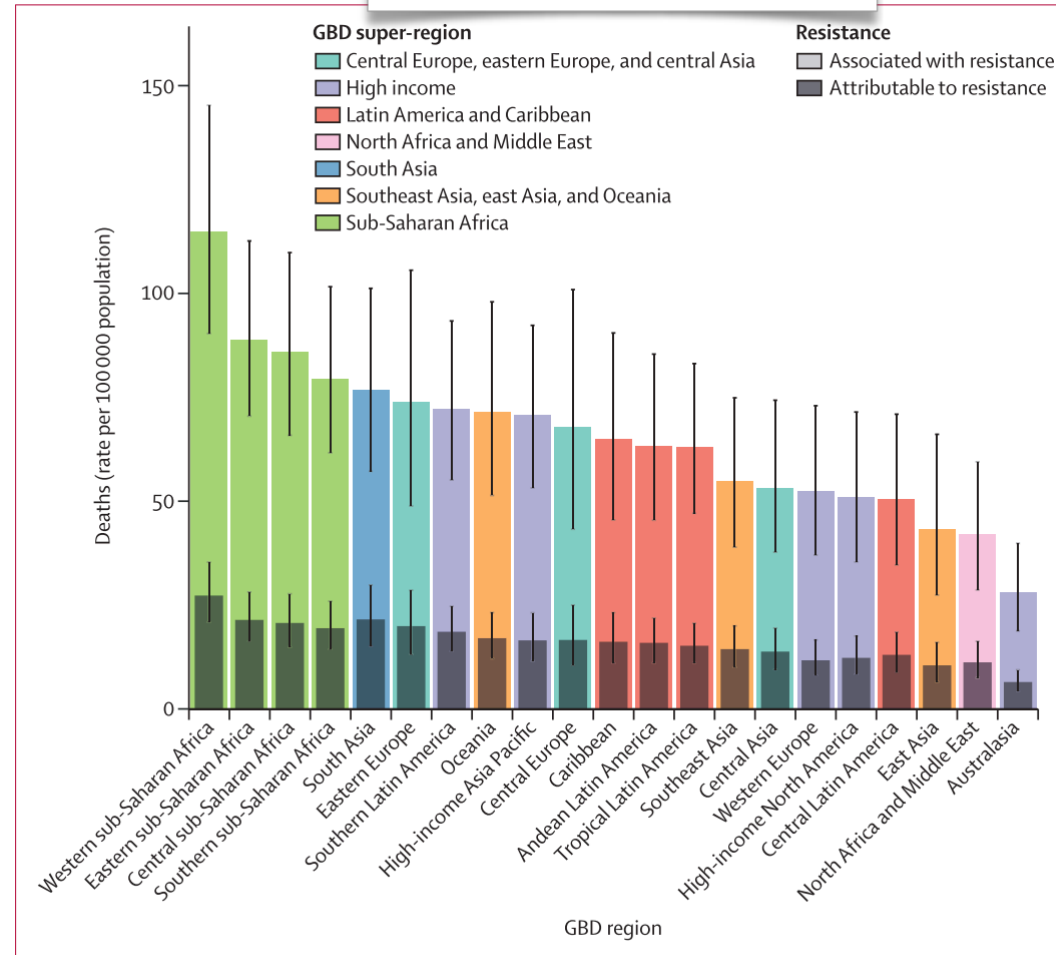


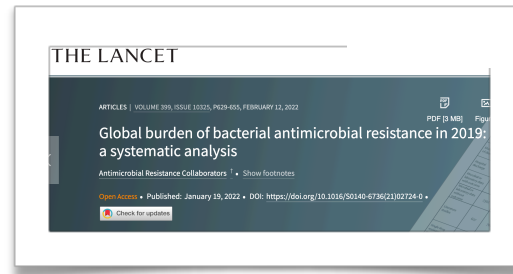
Figure 2: All-age rate of deaths attributable to and associated with bacterial antimicrobial resistance by GBD region, 2019



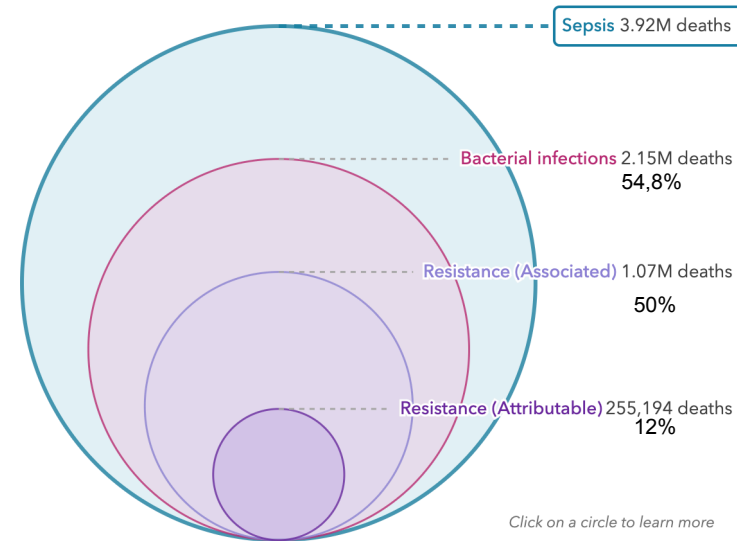
Résistance dans les LMIC

Données globales

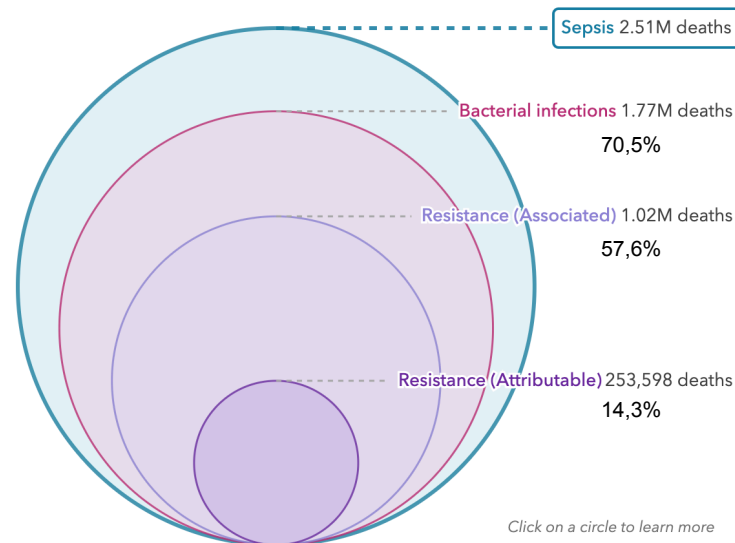
Mais...



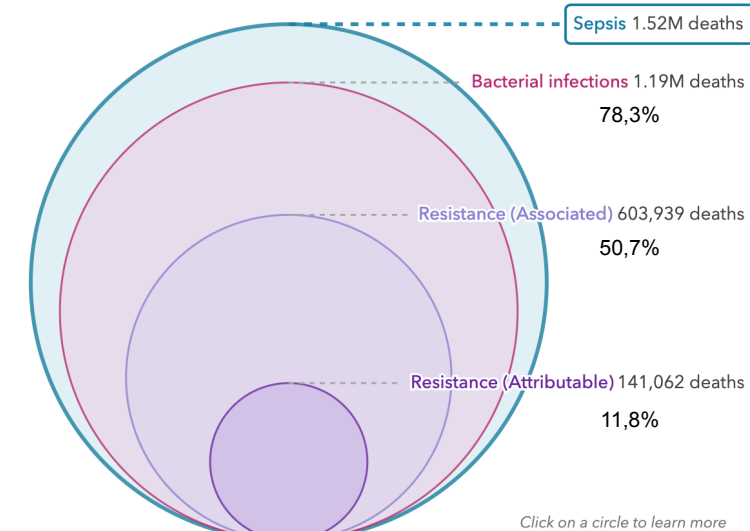
Composition of infection-related deaths in Sub-Saharan Africa



Composition of infection-related deaths in Southeast Asia, East Asia, and Oceania



Composition of infection-related deaths in High-income



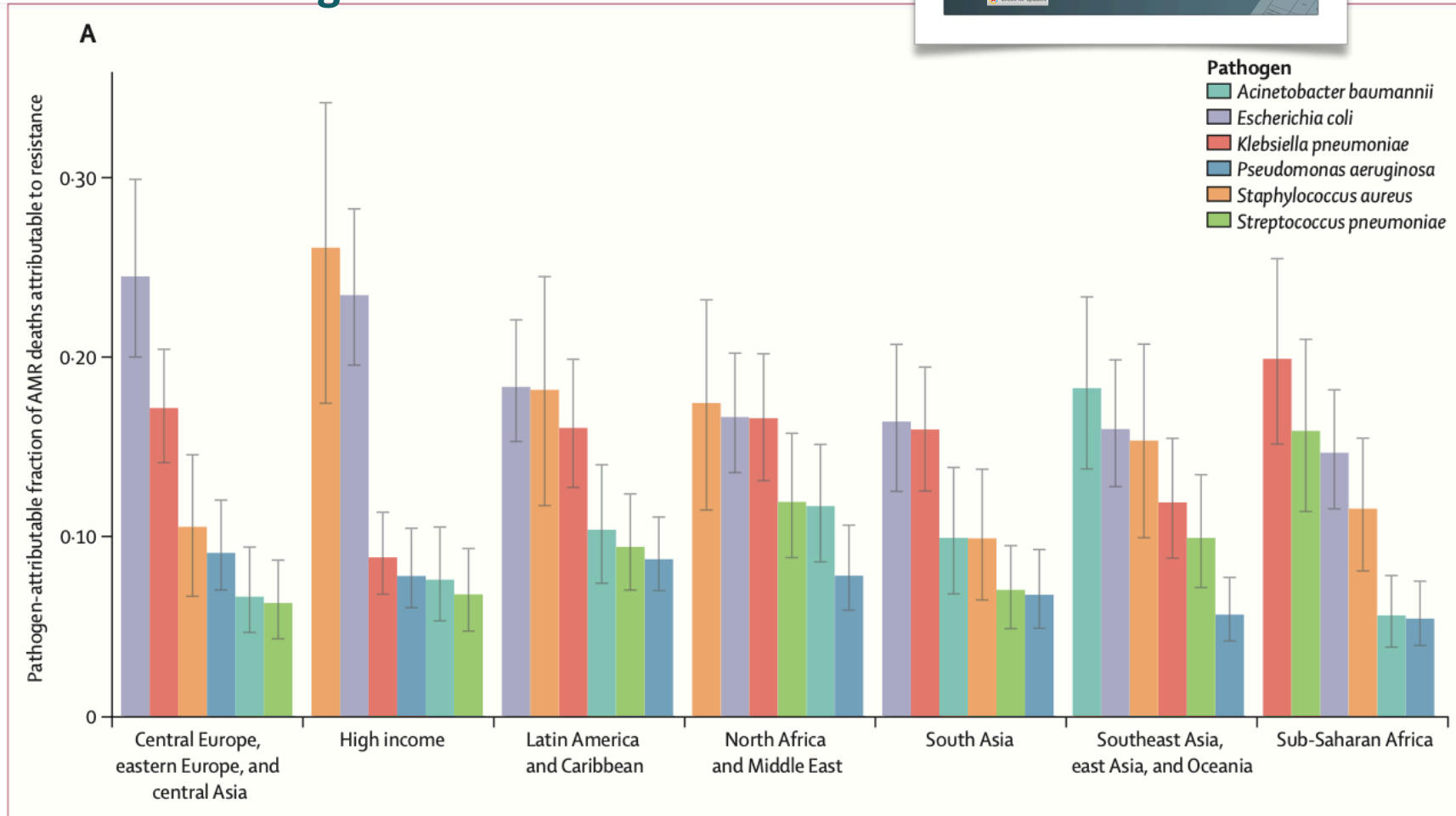
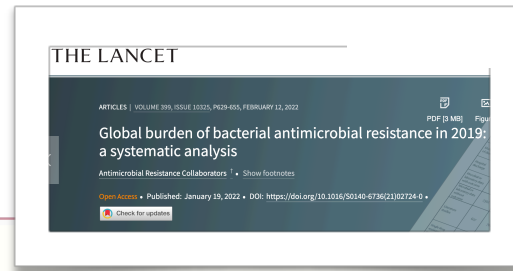
—> La raison pour laquelle les taux de décès attribuables/associés pour 100 000 habitants sont plus élevés en ASS est qu'il y a plus d'infections bactériennes (et de décès liés) par population.

Pas qu'il y a proportionnellement plus de décès associés à des infections par des bactéries résistantes ou que ces infections sont plus mortelles.



Résistance dans les LMIC

Données globales



	<u>PHR</u> : MRSA/E.coli
	<u>ASS</u> : Kp/Sp /E. coli/MRSA
	<u>ASE</u> : Ab /E.coli/MRSA

Figure 5: Pathogen-attributable fraction of deaths attributable to (A) and associated with (B) bacterial AMR for the six leading pathogens by GBD super-region, 2019

Error bars show 95% uncertainty intervals. AMR=antimicrobial resistance. GBD=Global Burden of Diseases, Injuries, and Risk Factors Study.



Résistance dans les LMIC

Exemple du Benin

Hauts taux de contamination !!
Pathogènes classiques

Ombelet et al. BMC Infectious Diseases (2022) 22:119
https://doi.org/10.1186/s12879-022-07077-z

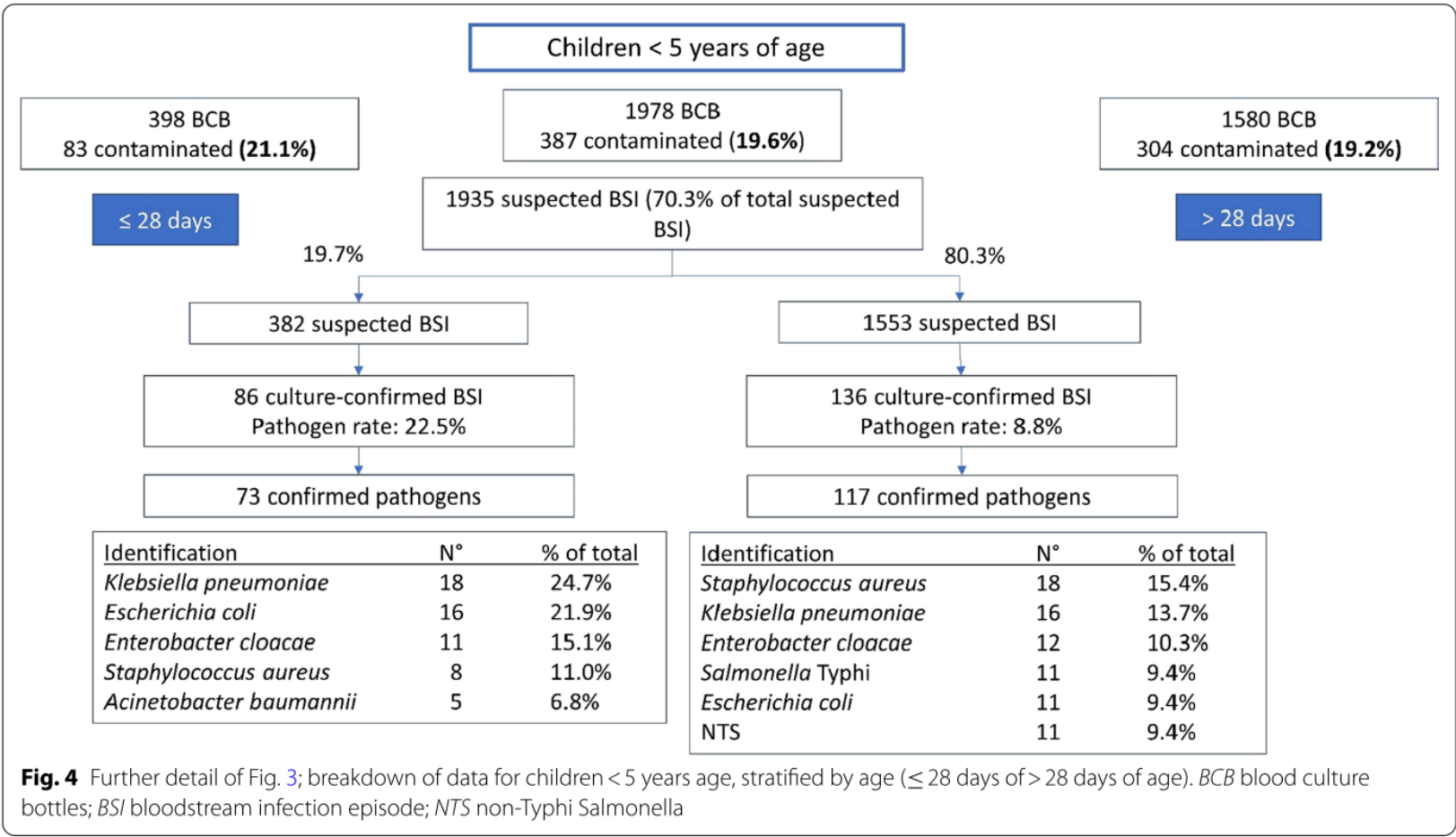
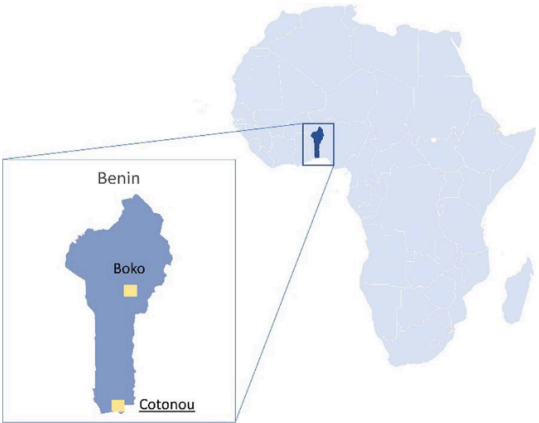
BMC Infectious Diseases

RESEARCH

Open Access

Blood culture surveillance in a secondary care hospital in Benin: epidemiology of bloodstream infection pathogens and antimicrobial resistance

Sien Ombelet^{1,2*}, Gutemberg Kpossou³, Carine Kotchare³, Ezenam Agbobil^{4,5}, Frédéric Sogbo^{4,5}, Faridath Massou^{4,5}, Katrien Lagrou^{2,6}, Barbara Barbé¹, Dissou Affolabi^{4,5} and Jan Jacobs^{1,2}



Résistance dans les LMIC

Exemple du Benin

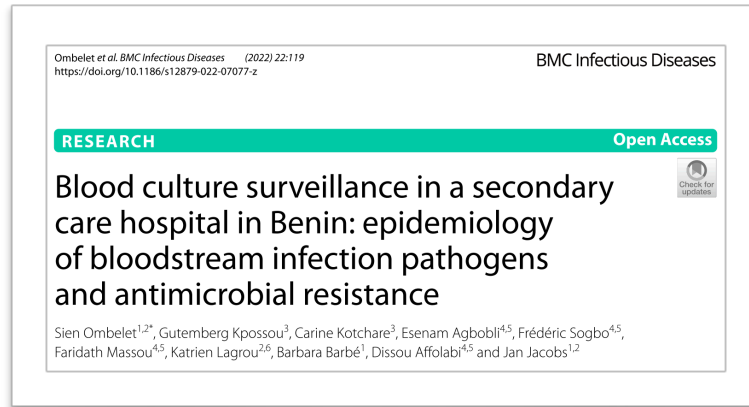


Table 3 Antibiotic resistance rates (% of isolates intermediate or resistant to the antibiotic listed) of Gram-negative bacterial isolates (only species for which n > 30) and proportion of isolates showing specific antibiotic resistance patterns and mechanisms

Antibiotic	<i>Enterobacter cloacae</i> n = 44	<i>Escherichia coli</i> n = 49*	<i>Klebsiella pneumoniae</i> n = 58*	<i>Salmonella Typhi</i> n = 53*
Antibiotic susceptibility rates (% susceptible)				
Ampicillin	–	73.5%	–	30.2%
Amoxicillin-clavulanic acid	–	41.7%	81.0%	–
Piperacillin-tazobactam	16.3%	18.7%	25.9%	–
Cefuroxime	72.7%	40.8%	79.3%	–
Ceftriaxone	70.5%	12.8%	77.6%	0%
Temocillin	7.0%	11.0%	0%	–
Meropenem	4.5%	4.1%	0%	0%
Ciprofloxacin	75.0%	35.4%	70.7%	24.5%
Trimethoprim-sulfamethoxazole	76.7%	36.7%	15.5%	39.6%
Gentamicin	68.2%	24.5%	74.1%	0%
Amikacin	2.3%	0%	3.4%	–
Chloramphenicol	65.9%	24.5%	37.9%	39.6%
Azithromycin	–	–	–	0%
Antibiotic resistance mechanisms and patterns				
ESBL	68.2%	28.6%	79.3%	0%
Carbapenemase	4.5%	4.1%	0%	0%
Combined resistance carbapenems–fluoroquinolones	2.3%	2.0%	0%	0%
MDR**	79.5%	69.4%	87.9%	39.6%
XDR**	22.7%	8.2%	32.8%	0%
PDR**	2.3%	2.0%	0%	0%
DCS**	–	–	–	24.5%



Résistance dans les LMIC

Exemple de l'Inde



icmr
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Annual Report

January 2021 to December 2021

Antimicrobial Resistance Research and Surveillance Network

India's Antimicrobial Resistance Surveillance & Research Initiative

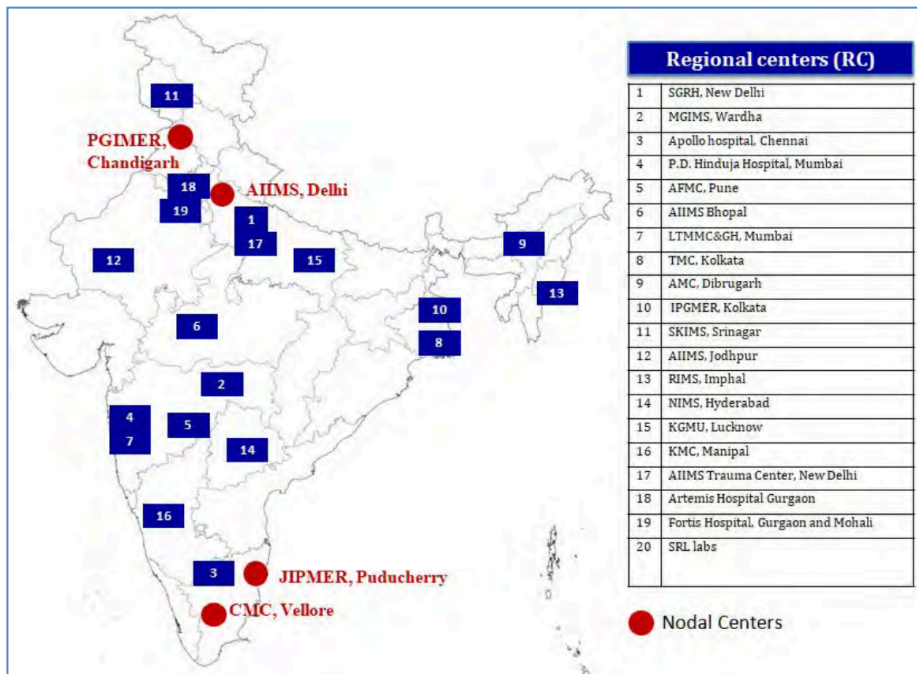


Figure (i): Antimicrobial Resistance Research & Surveillance Network (AMRSN): Nodal and Regional Centers

Table 1.2: Isolation distribution of top 10 isolates from different specimens

Organism	Total	Blood	LRT	Superficial Infection	Deep Infection	SS	Faeces	Urine
<i>Escherichia coli</i>	23629/95728 (24.7)	3096/18988 (16.3)	1338/16746 (8)	3980/19587 (20.3)	1911/8125 (23.5)	874/2787 (31.4)	0/651 (0)	10096/19319 (52.3)
<i>Klebsiella pneumoniae</i>	17216/95728 (18)	3270/18988 (17.2)	4238/16746 (25.3)	2952/19587 (15.1)	1158/8125 (14.3)	520/2787 (18.7)	0/651 (0)	3583/19319 (18.5)
<i>Acinetobacter baumannii</i>	12393/95728 (12.9)	2508/18988 (13.2)	5088/16746 (30.4)	1845/19587 (9.4)	752/8125 (9.3)	312/2787 (11.2)	0/651 (0)	415/19319 (2.1)
<i>Pseudomonas aeruginosa</i>	11622/95728 (12.1)	1336/18988 (7)	3291/16746 (19.7)	3066/19587 (15.6)	1085/8125 (13.4)	244/2787 (8.8)	0/651 (0)	1398/19319 (7.2)
<i>Staphylococcus aureus</i>	8827/95728 (9.2)	1663/18988 (8.8)	701/16746 (4.2)	3719/19587 (19)	1563/8125 (19.2)	109/2787 (3.9)	0/651 (0)	230/19319 (1.2)
<i>Enterococcus faecium</i>	2422/95728 (2.5)	700/18988 (3.7)	20/16746 (0.1)	402/19587 (2.1)	109/8125 (1.3)	124/2787 (4.4)	0/651 (0)	810/19319 (4.2)
<i>Enterococcus faecalis</i>	2373/95728 (2.5)	472/18988 (2.5)	14/16746 (0.1)	546/19587 (2.8)	129/8125 (1.6)	66/2787 (2.4)	0/651 (0)	871/19319 (4.5)
<i>Enterobacter cloacae</i>	1644/95728 (1.7)	356/18988 (1.9)	182/16746 (1.1)	462/19587 (2.4)	217/8125 (2.7)	40/2787 (1.4)	0/651 (0)	206/19319 (1.1)
<i>Proteus mirabilis</i>	1611/95728 (1.7)	71/18988 (0.4)	91/16746 (0.5)	607/19587 (3.1)	350/8125 (4.3)	35/2787 (1.3)	0/651 (0)	286/19319 (1.5)
<i>Enterococcus spp.</i>	852/95728 (0.9)	160/18988 (0.8)	31/16746 (0.2)	124/19587 (0.6)	71/8125 (0.9)	67/2787 (2.4)	0/651 (0)	257/19319 (1.3)

Résistance dans les LMIC

Exemple de l'Inde



Annual Report

January 2021 to December 2021

Antimicrobial Resistance Research and Surveillance Network

India's Antimicrobial Resistance Surveillance & Research Initiative

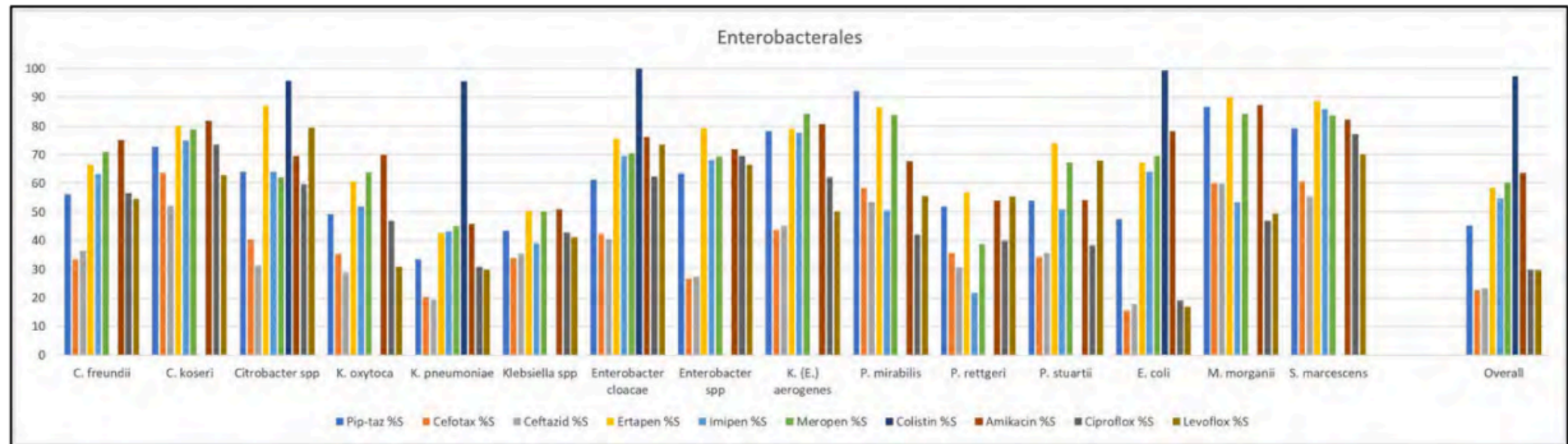


Figure 2.1. Species wise susceptibility of Enterobacterales isolated from of all specimens except urine and faeces



Résistance dans les LMIC

Exemple de l'Inde



India's Antimicrobial Resistance Surveillance & Research Initiative

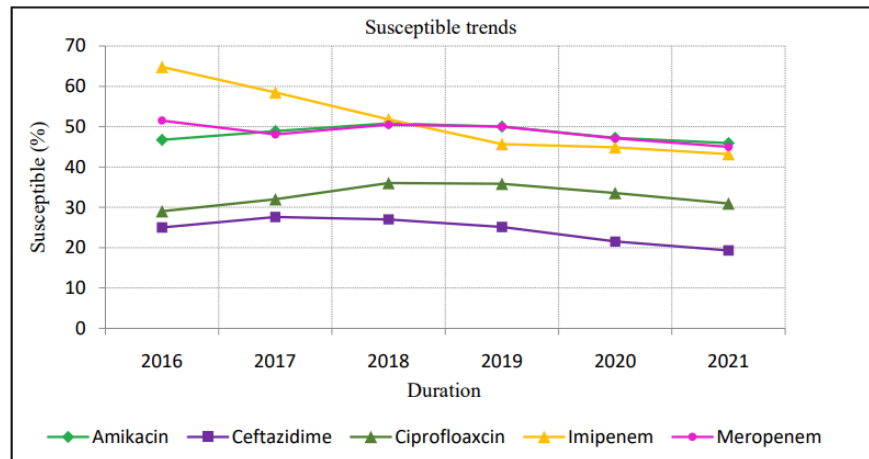


Figure 2.8. Yearly susceptibility trend of *Klebsiella pneumoniae* isolated from all samples (except faeces and urine)

Annual Report

January 2021 to December 2021

Antimicrobial Resistance Research and Surveillance Network

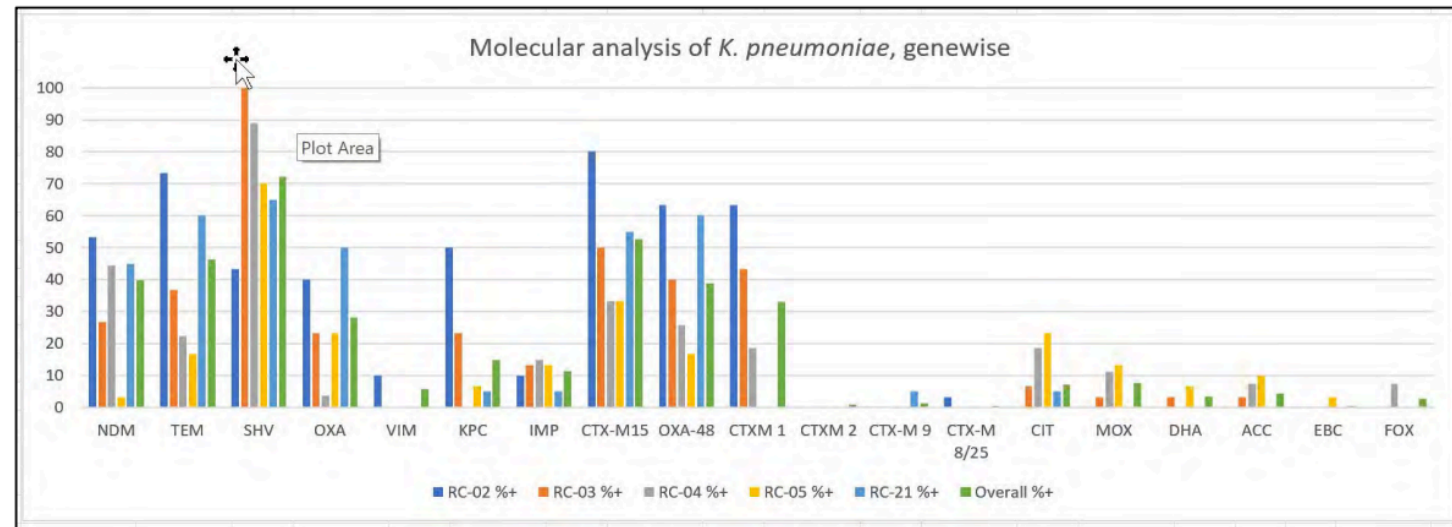
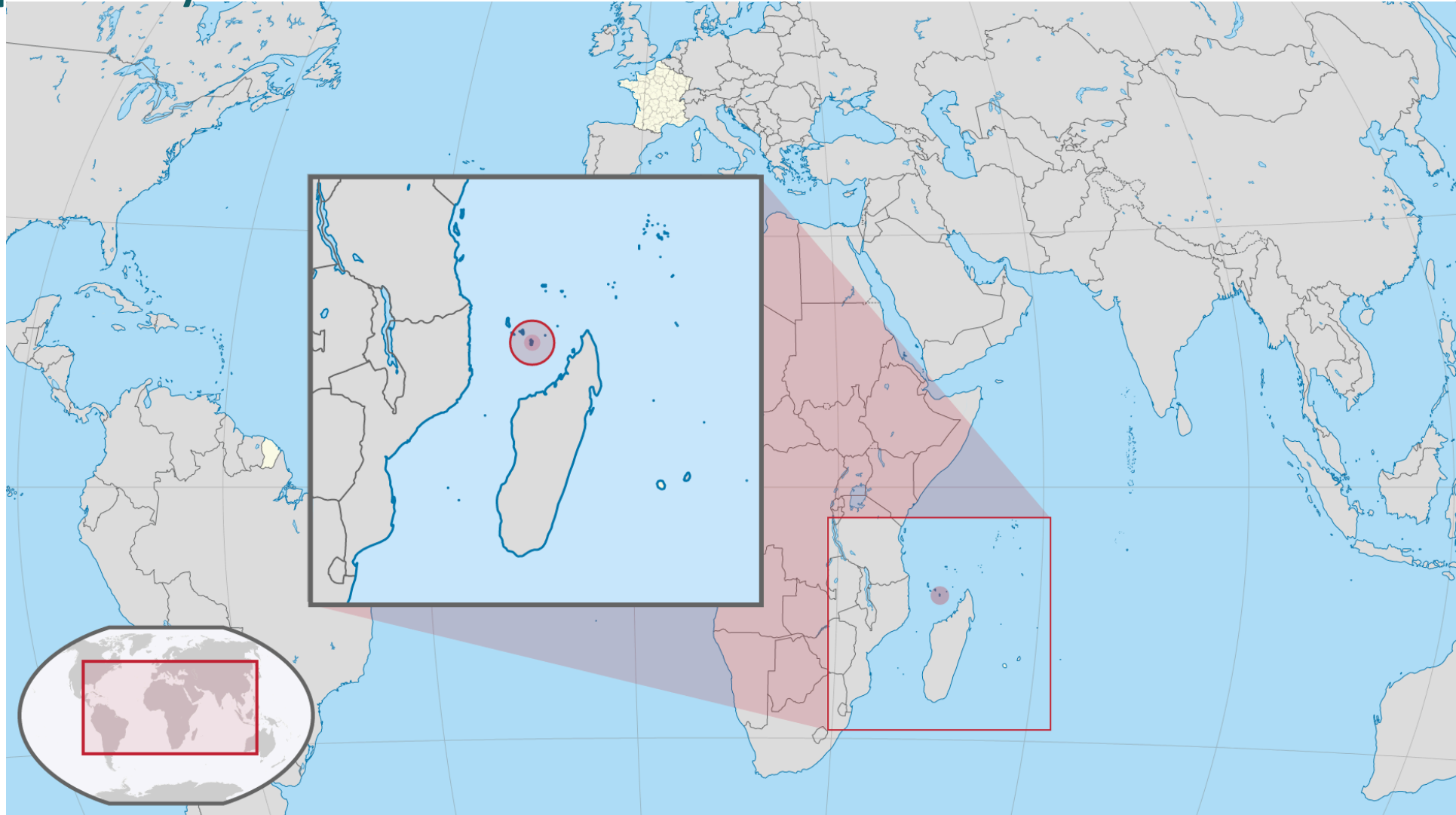


Figure 2.18. Showing positivity of various genes in *K. pneumoniae* isolates from various centers, gene wise and overall

Résistance dans les LMIC

Exemple de Mayotte



Résistance dans les LMIC

Exemple de Mayotte



Résistance dans les LMIC

Exemple de Mayotte



Résistance dans les LMIC

Exemple de Mayotte



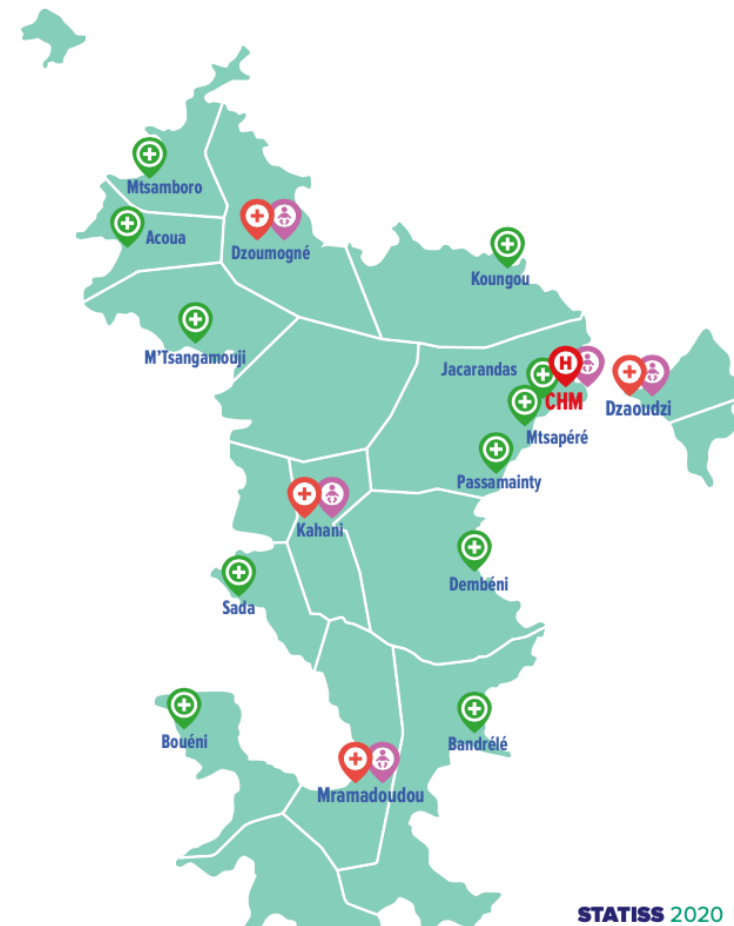
Données	Mayotte	Métropole
Superficie en km ²	374	543 941
Estimation de population au 1 ^{er} janvier 2020*	278 926	65 123 843
Densité en hab. / Km ² - 2017	686	119

Les établissements sanitaires à Mayotte

Au 1^{er} janvier 2020

-  Centre Hospitalier
-  Centre de référence
-  Dispensaire
(médecins correspondants du SMUR/accueil 24h/24)
-  Maternité

Source : ARS Mayotte
Réalisation : ARS Mayotte, service Etudes et Statistiques



STATISS 2020 | 11

Résistance dans les LMIC

Exemple de Mayotte

235 lits
11000 admissions/an
4 infectiologues
1 microbiologiste
1 hygiéniste

Disciplines court séjour		Mayotte
Hospitalisation complète (lits)		
Médecine	175	
Chirurgie	60	
Gynéco-Obstétrique	129	
Entrées totales en hospitalisation complète		
Médecine*	7 639	
Chirurgie	3 712	
Gynéco-Obstétrique	12 180	

Professions	EFFECTIF TOTAL		DONT LIBÉRAUX (Y compris mixte)		DENSITÉ** (Effectif total)	
	Mayotte	Métropole*	Mayotte	Métropole*	Mayotte	Métropole*
Médecins généralistes	119	82 815	31	57 073	43	127
Médecins spécialistes	103	116 426	8	56 751	37	179
Ensemble des médecins	222	199 241	39	113 824	80	306

Spécialités exercées	EFFECTIF TOTAL		DENSITÉ**	
	Mayotte	Métropole*	Mayotte	Métropole*
Spécialités médicales	62	65 709	13	101
dont Anesthésie-réanimation	12	10 157	4	16
Cardiologie et maladies vasculaires	2	6 789	1	10
Dermatologie et vénéréologie	0	3 522	0	5
Gastro-entérologie et hépatologie	2	3 656	1	6
Gynécologie médicale	3	2 246	4	8
Pédiatrie	24	7 570	20	66
Radio-diagnostic	4	7 699	1	12
Rhumatologie	1	2 403	0	4
Spécialités chirurgicales	26	26 027	9	40
dont Chirurgie générale	6	3 205	2	5
Gynécologie-obstétrique	11	4 849	13	17
Ophtalmologie	1	5 419	0	8
Oto-rhino-laryngologie et chirurgie cervico faciale	4	2 860	1	4
Stomatologie et chirurgie maxilo-faciale	0	1 037	0	2
Psychiatrie	8	14 700	3	23
Biologie médicale	2	2 798	1	4
Médecine du travail, santé publique	3	4 867	1	7
ENSEMBLE SPÉCIALITÉS ⁽¹⁾	101	114 101	36	175



Résistance dans les LMIC

Exemple de Mayotte

CRAB epidemic in March 2019

Isolate	Age	Sex	Origine	Ward	Hospital grounds	Isolation site	Diagnosis ^a	Treatment	Carbapenemases	Outcome
1	62	M	Comores	ICU	Chronic renal failure	Catheter	Infection	NON	NDM-1/OXA-23	Décès/L
2	41	M	Comores	Surgery	Polytraumatism	Urinary	Infection	NON	OXA-58	
3	76	M	Comores	ICU	Diabetes	Rectal swab	C	NON	NDM-1/OXA-23	
4	45	M	Comores	Surgery	Arthritis	Pneumonia	Infection	NON	NDM-1/OXA-23	Décès/L
5	38	M	Comores	ICU	Burn	Cutaneous	Infection	NON	NDM-1/OXA-23	
6	49	M	Comores	ICU	Pneumonia	BAF ^b	Infection	OUI	NDM-1/OXA-23	
7	66	M	Mahorais	ICU	Cerebral vascular	Catheter	Infection	NON	NDM-1/OXA-23	
8	57	M	Mahorais	ICU	Pneumonia	Catheter	C	NON	NDM-1/OXA-23	Décès/NL
9	65	M	Mahorais	ICU	Beri Beri	Rectal swab	C	NON	OXA-58	
10	3	M	Mahorais	Surgery	Genital infection	Urinary	C	NON	OXA-23	
11	61	M	Mahorais	ICU	Pneumonia	BAF ^b	Infection	OUI	NDM-1/OXA-23	Décès/L
12	55	M	Mahorais	medicine	Skin infection	Blood	Infection	OUI	NDM-1/OXA-23	
13	55	F	Comores	Surgery	Skin infection	Pus	Infection	NON	NDM-1	
14	75	M	Mahorais	medicine	Sepsis Urinary tract	Rectal swab	C	NON	OXA-58	Décès/NL
15	59	M	Comores	ICU	Pneumonia	Rectal swab	C	NON	NDM-1/OXA-23	
16	26	F	Comores	medicine	Pneumonia	Rectal swab	C	NON	OXA-58	
17	47	F	Malgache	Surgery	Skin infection	Pus	Infection	NON	NDM-1/OXA-23	
18	64	F	Comores	Surgery	Skin infection	Pus	Infection	NON	OXA-58	
19	62	M	Français	medicine	HIV	Blood	Infection	OUI	NDM-1/OXA-23	Décès/L
20	47	F	Malgache	medicine	Skin infection	Pus	C	NON	OXA-23	
21	56	M	Comores	ICU	Skin infection	Pus	C	NON	NDM-1/OXA-23	
22	65	M	Comores	emergency	Sepsis Urinary tract	Urinary	C	NON	OXA-23	
23	33	M	Mahorais	emergency	AVP	Blood	Infection	NON	OXA-23	
24	13	F	Comores	emergency	Skin infection	Pus	C	NON	NDM-1/OXA-23	
25	26	M	Comores	Surgery	Sepsis Urinary tract	Urinary	Infection	NON	NDM-1/OXA-23	
26	47	M	Mahorais	Surgery	Skin infection	Pus	C	NON	NDM-1/OXA-23	
27	48	M	Comores	ICU	cardiomyopathy	Rectal swab	C	NON	NDM-1/OXA-23	Décès/NL
28	3	F	Comores	ICU	Burn	Blood	Infection	OUI	OXA-23	
29	15	F	Comores	ICU	Burn	Cutaneous	Infection	OUI	NDM-1/OXA-23	
30	55	M	Comores	Surgery	Skin infection	Blood	Infection	OUI		
31	61	M	Comores	Surgery	Infection MOS ^c	Pus	Infection	NON		
32	49	F	Comores	Surgery	Skin infection	Pus	C	NON		

Refugiés: 22/32
(70%)

Infection: 18/32
(57%)

Mort: 7/18
(38,9%)



Résistance dans les LMIC

Exemple de Mayotte

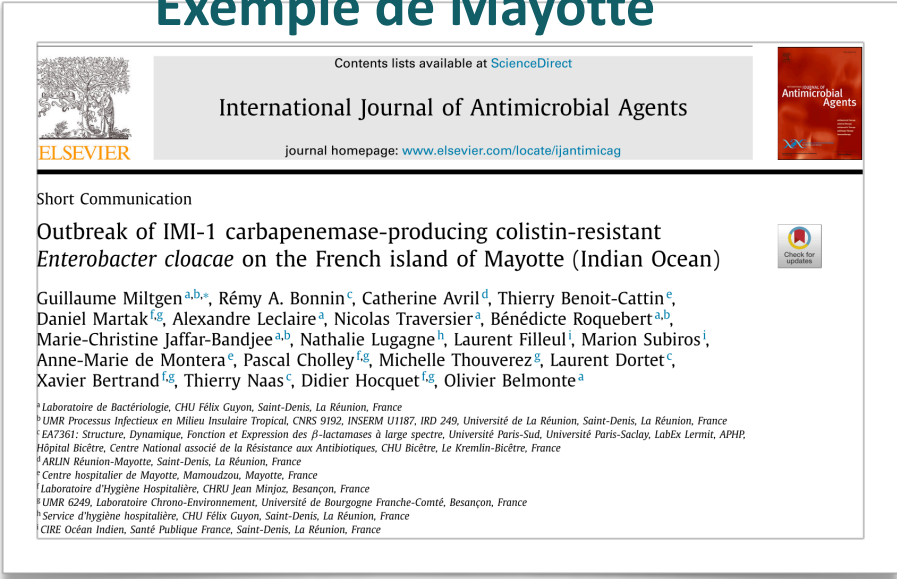


Table 1
Demographics and biological data of 17 patients colonised with IMI-1 carbapenemase-producing *Enterobacter cloacae* retrieved from rectal swabs in Mayotte between October 2015 and January 2017.

Isolate ID	Date of isolation (MM/YYYY)	Hospital	Hospital unit	Sex/age (years)	Time between admission and detection (days)	Co-colonisation with ESBL-E	Type of ESBL-E
E1	10/2015	MMC	ICU	F/65	1	Yes	<i>Escherichia coli</i>
E2	11/2015	FGUH	Cardiology	M/57	1	Yes	<i>E. coli</i>
E3	11/2015	MMC	ICU	M/5	1	Yes	<i>E. coli</i>
E4	11/2015	FGUH	ICU	M/49	6	No	
E5	01/2016	MMC	ICU	F/51	1	Yes	<i>E. coli</i>
E6	02/2016	MMC	ICU	F/29	7	No	
E7	02/2016	MMC	ICU	F/17	1	No	
E8	03/2016	MMC	ICU	M/51	4	Yes	<i>E. coli</i>
E9	04/2016	FGUH	Visceral paediatric surgical	F/1	1	Yes	<i>Klebsiella pneumoniae</i>
E10	05/2016	FGUH	Gynaecology and obstetrics	F/29	4	Yes	<i>E. coli</i>
E11	05/2016	FGUH	Cardiothoracic surgery	F/17	1	Yes	<i>E. coli</i>
E12a	06/2016	MMC	Neonatal	M/4	1	Yes	<i>E. coli</i>
E12b			ICU	months			
E13	09/2016	MMC	ICU	F/32	1	Yes	<i>K. pneumoniae</i>
E14	10/2016	MMC	Dialysis centre	M/72	0	Yes	<i>E. coli</i>
E15	11/2016	MMC	ICU	F/64	1	Yes	<i>E. coli</i>
E16	01/2017	MMC	Dialysis centre	F/18	0	No	
E17	01/2017	FGUH	Visceral paediatric surgical	M/2	1	No	

ESBL-E, extended-spectrum β -lactamase-producing Enterobacteriaceae; MMC, Mayotte Medical Center; FGUH, Félix Guyon University Hospital; ICU, intensive care unit.

17 patients. 2015 - 2017

IMI-1 & Colistine R (cluster XI)

Colonisation uniquement

Surtout détecté à l'admission (76,5%)

Aucun patient hospitalisé dans les 6 mois précédents —> **Environnemental**

Pas d'utilisation de CP aux Comores

Résistance dans les LMIC

Exemple de Mayotte

	2017	2022
Nombre absolu de BMR retrouvés	582	860
%age des admissions	5,1%	7,6%
%age de patients des Comores/Afrique	37,1 %	42,2 %
% BLSE de tous les germes MDR	77 %	71 %
%BLSE de toutes les souches isolés	29,2%	36,4%
%CPE de tous les germes MDR	2,5%	6,3%
%MRSA de tous les germes MDR	9,8%	5,24%



Résistance dans les LMIC

Causes?



REVIEW
published: 23 September 2019
doi: 10.3389/fmed.2019.00205



Diagnostic Bacteriology in District Hospitals in Sub-Saharan Africa: At the Forefront of the Containment of Antimicrobial Resistance

Jan Jacobs^{1,2*}, Liselotte Hardy¹, Makeda Semret³, Octavie Lunguya^{4,5}, Thong Phe⁶, Dissou Affolabi⁷, Cedric Yansouni³ and Olivier Vandenberg^{8,9,10}

TABLE 1 | Why low-and middle-income countries are hit hardest by antimicrobial resistance: attitudes, practices, and interactions between prescriber, dispenser, patients, diagnostics and health systems, related to human medicine⁴ (4, 24–36).

Prescriber considerations:

- Absence of local surveillance data obscures awareness and knowledge about AMR in the own practice ("No data, no problem")
- Poorly educated and trained in antibiotic use (see below)
- In the absence of diagnostic tools, he/she prefers to "cover" the patient for bacterial infections, preferably with broad-spectrum antibiotics
- Overuse but also suboptimal use: incorrect diagnosis, incorrect dose, timing, route, frequency and duration, no de-escalation (i.e., using an antibiotic of narrow spectrum based on microbiology reports)
- Extended use of antibiotics e.g., in the case of surgical prophylaxis (to "compensate" for inadequate infection control)
- The "Knowledge gap": knowing that antibiotics are not indicated but nevertheless prescribing them ("cough and cold," watery diarrhea)
- Fear of non-respecting and losing the patient when not prescribing antibiotics (taking his/her complaints not serious)
- Reliance on (own) clinical diagnosis

Patient's attitudes, beliefs and socio-cultural factors:

- Poor health literacy
- Out-of-pocket expenditure of healthcare costs
- Reluctance to blood sampling
- Patient or caretakers' pressure toward antibiotics (real or perceived by the prescriber)
- Auto-medication, non-prescription use of antibiotics (frequently associated with too low dose and too short duration)
- ABs are associated with power (strong, almost magical) and valued higher than the doctor's visit
- Poor awareness and knowledge about AMR: "the patient becomes resistant, not the bacteria,"
- "antibiotics protect against unsanitary conditions in the environment"
- Lay advice about antibiotics (friends, relatives)
- Storage of antibiotics left-overs at home—self/family medication
- Incorrect use—mixed with practices of traditional medicine

Dispenser and supply

- Poor access to antibiotics, inadequate supply leading to incorrect dose, timing, duration.
- Few professional pharmacists (pharmacy attendants, drug sellers)
- Economic incentives—e.g., selling particular brands
- Wants to fulfill the patients' demand: non-prescription sales of antibiotics, selling incomplete treatments, fear patient would go elsewhere
- Substandard (low content, expired, degraded) and falsified ABs

Diagnostics

at the first line:

- Moderate to low clinical competence among frontline health workers
- POC testing for malaria in the absence of diagnostic algorithms for other febrile diseases has increased antibiotic prescription
- POC testing is not always accepted as part of a patients' consultation (financial reason or uncertainty of interpretation)

at the second and third line:

- Few CBL, low volumes, low quality, not embedded in patient care

Health systems:

- Distrust in the quality of public (government-run) services
- Private market notably insensitive to regulation
- National Action Plans on AMR not yet developed or implemented
- Regulation (medicines, diagnostics) fragmented and poorly implemented
- No health insurance, "out of pocket" payment leads to underdiagnosis and under- or overtreatment

Healthcare facilities:

- Few or no programs of antibiotic stewardship available
- Poor infection prevention and control, fueling transmission of MDR organisms in hospitals, in turn increasing the use of antibiotics
- Payment per act in hospitals (consequences of AMR less visible)

Education of providers and prescribers:

- Professional education not adapted to needs)
- No registration, re-certification or continuing medical education
- Gaps in teaching of clinical microbiology and antibiotic prescription
- Poor awareness of local/national prescribing guidelines
- High influence of pharmaceutical drug promotion/representatives
- Hierarchic role model: respect of senior medical staff, reluctance to question prescribing decisions
- Autonomy of decision making (particularly in private hospitals)

General:

- Diagnostics market in low-and middle-income countries is uncertain
- Diagnostics for bacteriological cultures are considered as "low risk" products, hence low regulatory stringency
- No (supra)national "vertical" control programmes
- Fragmented donor landscape with competing interests

AMR, antimicrobial resistance; CBL, clinical bacteriology laboratory; MDR, multidrug resistant; POC, point-of-care testing.



Résistance dans les LMIC

Causes?

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- Poor access to antibiotics, inadequate supply leading to incorrect dose, timing, duration.
- Few professional pharmacists (pharmacy attendants, drug sellers)
- Economic incentives—e.g., selling particular brands
- Wants to fulfill the patients’ demand: non-prescription sales of antibiotics, selling incomplete treatments, fear patient would go elsewhere
- Substandard (low content, expired, degraded) and falsified ABs

Health systems:

- Distrust in the quality of public (government-run) services
- Private market notably insensitive to regulation
- National Action Plans on AMR not yet developed or implemented
- Regulation (medicines, diagnostics) fragmented and poorly implemented
- No health insurance, “out of pocket” payment leads to underdiagnosis and under- or overtreatment

Education of providers and prescribers:

- Professional education not adapted to needs)
- No registration, re-certification or continuing medical education
- Gaps in teaching of clinical microbiology and antibiotic prescription
- Poor awareness of local/national prescribing guidelines
- High influence of pharmaceutical drug promotion/representatives
- Hierarchic role model: respect of senior medical staff, reluctance to question prescribing decisions
- Autonomy of decision making (particularly in private hospitals)

Patient’s attitudes, beliefs and socio-cultural factors:

- Poor health literacy
- Out-of-pocket expenditure of healthcare costs
- Reluctance to blood sampling
- Patient or caretakers’ pressure toward antibiotics (real or perceived by the prescriber)
- Auto-medication, non-prescription use of antibiotics (frequently associated with too low dose and too short duration)
- ABs are associated with power (strong, almost magical) and valued higher than the doctor’s visit
- Poor awareness and knowledge about AMR: “the patient becomes resistant, not the bacteria,”
- “antibiotics protect against unsanitary conditions in the environment”
- Lay advice about antibiotics (friends, relatives)
- Storage of antibiotics left-overs at home—self/family medication
- Incorrect use—mixed with practices of traditional medicine

Diagnostics

at the first line:

- Moderate to low clinical competence among frontline health workers
- POC testing for malaria in the absence of diagnostic algorithms for other febrile diseases has increased antibiotic prescription
- POC testing is not always accepted as part of a patients’ consultation (financial reason or uncertainty of interpretation)

at the second and third line:

- Few CBL, low volumes, low quality, not embedded in patient care

Healthcare facilities:

- Few or no programs of antibiotic stewardship available
- Poor infection prevention and control, fueling transmission of MDR organisms in hospitals, in turn increasing the use of antibiotics
- Payment per act in hospitals (consequences of AMR less visible)

General:

- Diagnostics market in low-and middle-income countries is uncertain
- Diagnostics for bacteriological cultures are considered as “low risk” products, hence low regulatory stringency
- No (supra)national “vertical” control programmes
- Fragmented donor landscape with competing interests

AMR, antimicrobial resistance; CBL, clinical bacteriology laboratory; MDR, multidrug resistant; POC, point-of-care testing.

Causes principales:

Consommation d’antibiotiques/
Stewardship
< Mauvaise prescription
< Disponibilité/Distribution

Diagnostic/surveillance
insuffisants

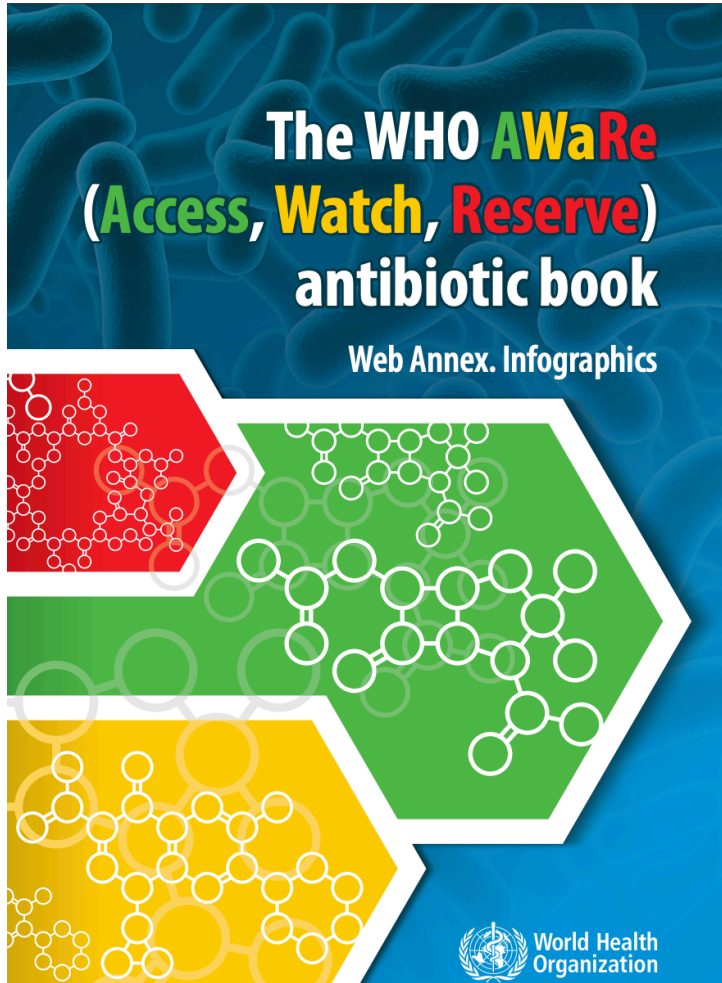
Hygiène - Infection control

Vaccination insuffisante



Résistance dans les LMIC

Exemple Ceftriaxone



Access	
• Amikacin	• Cloxacillin
• Amoxicillin	• Doxycycline
• Ampicillin	• Gentamicin
• Amoxicillin–clavulanic acid	• Metronidazole
• Benzathine benzylpenicillin	• Nitrofurantoin
• Benzylpenicillin	• Phenoxymethyl penicillin
• Cefazolin	• Procaine penicillin
• Chloramphenicol	• Spectinomycin
• Clindamycin	• Sulfamethoxazole–trimethoprim
Watch	
• Azithromycin	• Vancomycin (intravenous* and oral)
• Cefixime	• Ciprofloxacin
• Ceftriaxone	• Clarithromycin
• Cefotaxime	• Meropenem*
• Ceftazidime*	• Piperacillin–tazobactam
• Cefuroxime	
Reserve*	
• Fosfomycin (intravenous)	• Ceftazidime–avibactam
• Linezolid	• Meropenem–vaborbactam
• Colistin	• Plazomicin
• Polymyxin B	

= AB de choix pour les 25 infections les + fréquentes

= AB d'importance critique. Recommandés uniquement pour indications spécifiques & limitées

= Derniers recours

Figure: Antibiotics included in 2019 WHO Essential Medicines List by AWaRe group

*Antibiotics listed in the complementary list of the 2019 WHO Essential Medicines List, indicating the need for specialist supervision.



Résistance dans les LMIC

Exemple Ceftriaxone

Table 4.3. Antibacterial substances that made up 75% (DU75) of parenteral consumption in 26 CTAs in 2020

	Benin	Burkina Faso	Côte d'Ivoire	Ethiopia	Gabon	Mali	Uganda	United Republic of Tanzania	Colombia	Peru	Egypt	Iran (Islamic Republic of)	Jordan	Tunisia	Belgium	Cyprus	Denmark	Germany	Sweden	United Kingdom of Great Britain and Northern Ireland	Bhutan	Maldives	Nepal	Brunei Darussalam	Lao People's Democratic Republic	Mongolia	Median relative consumption (% (range))	Percentage of CTAs (%)
Ceftriaxone	2	1	1	2		2	1	1	4	1	1	1	2		5	3		1		7	1	1		1	1		23 (2-69)	77
Procaine benzylpenicillin							2			2		3															14 (0-20)	12
Combinations of beta-lactamase-sensitive penicillins								2																			12 (12-12)	4
Metronidazole				1	1				3	5			1	5		2	4			6	3			3			5 (1-68)	42
Gentamicin										3	5	4		2		9		3		3	5				2	2	5 (0-25)	38
Vancomycin										8					7	6		4									3 (0-10)	15
Amoxicillin			3																	8							2 (0-10)	8
Cefazolin									5			2		6	2			6			2					1	2 (0-71)	27
Ciprofloxacin	1					1										7							1				1 (0-77)	15
Ampicillin	3	2																			4				4		1 (0-16)	15
Benzathine benzylpenicillin		3	2															5									1 (0-17)	12
Clindamycin									1	6		6															1 (0-21)	12
Cefalotin									7																		1 (0-4)	4



Résistance dans les LMIC

Exemple Ceftriaxone

Infection and Drug Resistance

Dovepress

open access to scientific and medical research

Open Access Full Text Article

REVIEW

Appropriate Use of Ceftriaxone in Sub-Saharan Africa: A Systematic Review

15 études

8 en Ethiopie

3 en Tanzanie

1 au Ghana

1 au Soudan

1 en Ouganda

1 en Eritrée

4706 patients

S.n	Author Yr (Ref)	Study Country	Study Setting (Private or Public)	Sample Size (n)	Appropriate Prescribing Practice (%)	Common Indications						
						Pneumonia/ RTI (%)	Sepsis (%)	Meningitis (%)	UTI (%)	Prophylaxis (%)	No Indication (%)	Others ^a (%)
1	Abebe FA et al. 2012 ²⁴	Ethiopia	Public	296	35.8	21.4	19.4	4.9	14.5	33	NR	6.8
2	Afriyie DK et al. 2017 ²²	Ghana	Public	251	93	5.6	9.6	19.9	11.6	2.4	4.4 *	46.5
3	Ayele AA et al. 2018 ¹⁶	Ethiopia	Public	390	19.8	29.3	1.5	24.1	8.5	16.4	3.1	17.1
4	Ayinalem GA et al. 2013 ²⁵	Ethiopia	Public	316	54	36.4	4.7	30.4	20.9	0	0	7.6
5	Bantie et al. 2014 ²⁶	Ethiopia	Public	264	61	27.7	5.7	12.1	3.8	25	8.71	7.9
6	Berhe YH et al. 2019 ¹⁵	Eritrea	Public	109	27.5	36.7	21.8	2.8	5.5	0	2.3	30.9
7	Eulambius M et al. 2019 ²⁷	Tanzania	Public and Private	600	33.9	13.4	9.2	2.5	7.2	55	NR	12.5
8	Manirakiza L et al. 2019 ²⁸	Uganda	Public	100	53	19	19	22	9	2	1	28
9	Sasi P et al. 2019 ²⁹	Tanzania	Public	360	30	29.4	0	7.5	1.7	0	0	60
10	Hussien LA. 2019 ²³	Sudan	Public	90	6.7	3.3	31	2.2	31	0	NR	32.4
11	Negese S et al. 2017 ³⁰	Ethiopia	Public	127	29.9	22	12.6	7.1	3.9	15	NR	39.4
12	Shimels T et al. 2015 ³¹	Ethiopia	Public and Private	477	61.7	32.7	13.1	14.7	6.1	7.7	NR	25.8
13	Sonda TB et al. 2019 ¹⁴	Tanzania	Public	322	48.9	11.2	8.7	1.6	0	13.6	6.9	58
14	Geresu G et al. 2018 ³²	Ethiopia	Public	403	39.2	46.2	2.2	21.8	15.9	0	NR	13.8
15	Muhammed OS et al. 2020 ³³	Ethiopia	Public	601	60.6	24.8	2.7	3.2	5	39.8	NR	24.5

Notes: *Indication for suspecting of malaria with bacterial infection *Others include; typhoid

Abbreviations: NR, not reported; ref, reference; LRTI, Lower respiratory tract infection; U

cellulitis, sexually transmitted diseases, acute gastroenteritis, tuberculosis, PUD, cough, osteomyelitis and others.

43,67%

Résistance dans les LMIC

Conclusions

- « Pays du Sud » = Vaste
- Quelles données nous manquent? La majorité.
- Données brutes très incomplètes, mais inquiétantes. Projections pas beaucoup mieux
- ASS: BLSE >> CPE. ASE: CPE en augmentation inquiétante.
- Causes principales:**
 - Consommation d'antibiotiques/Stewardship
 - Manque de surveillance
 - Hygiène - Infection control

Mais...

- Nombres très faibles - Biais (Première ligne!)
- Projet **GLASS** (OMS) < Réseaux de surveillance nationaux prometteur
- Pas proportionnellement + de morts par infections à germes multiR



Merci pour votre attention !

