Entérobactéries résistantes en communauté : Où en est-on ?

Gabriel Birgand

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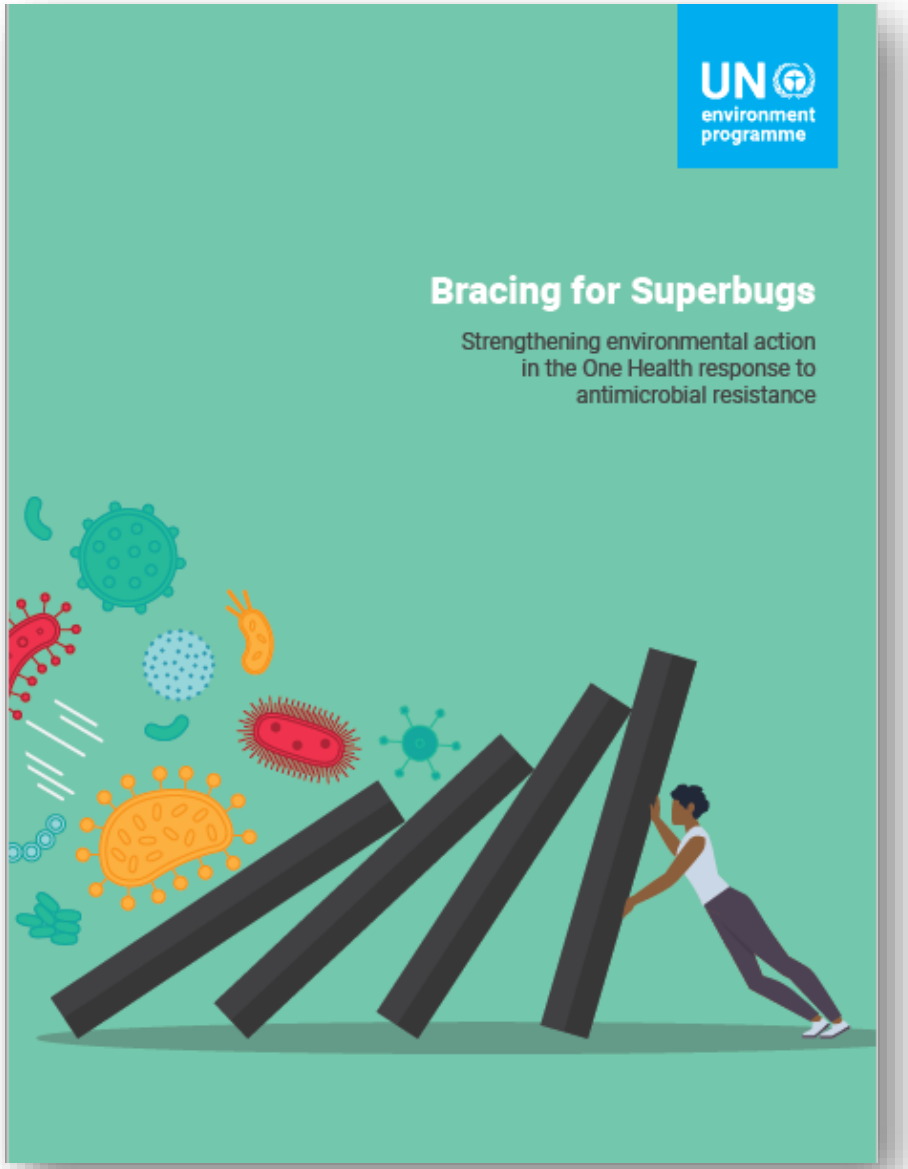
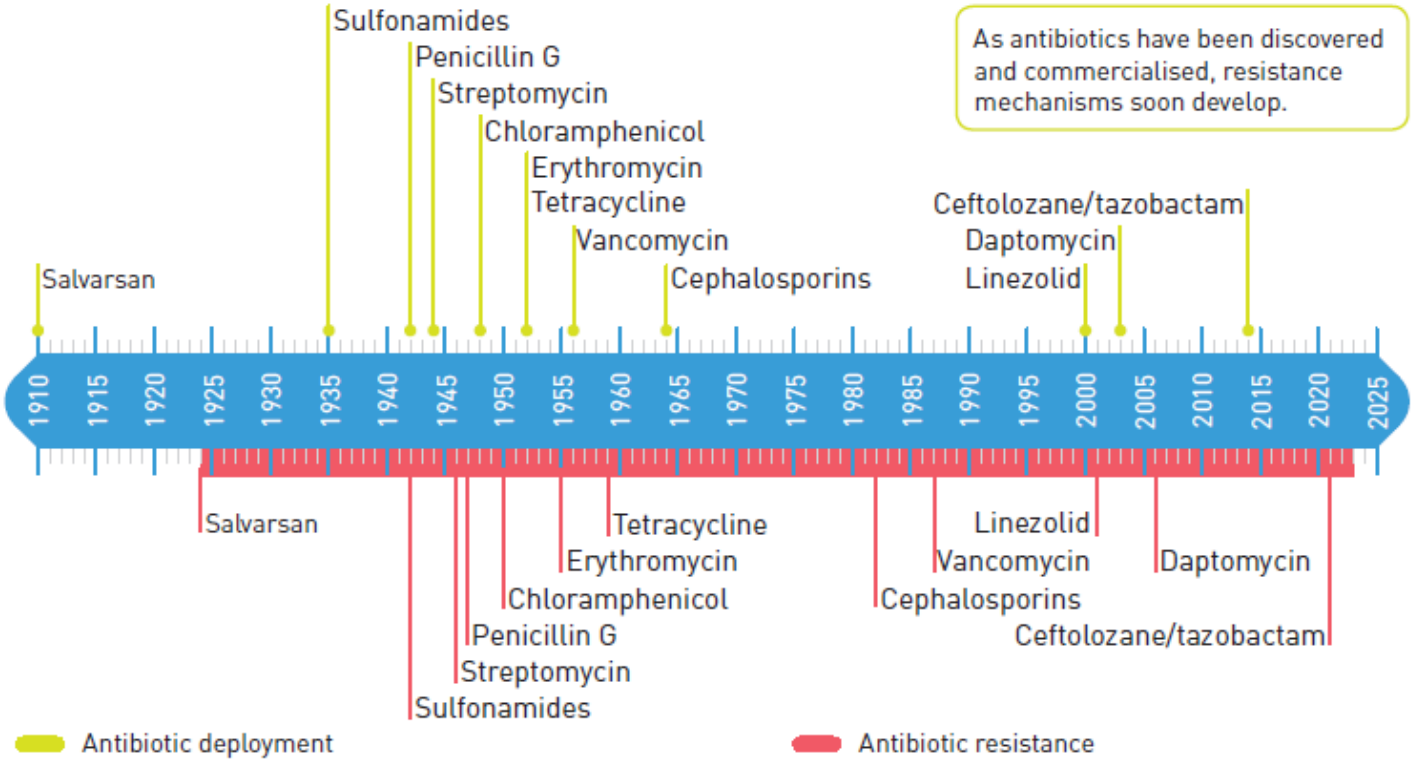
Webinaire ECPCI 2023

Imperial College London

CPias Pays de la Loire





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Predicted mortality from AMR

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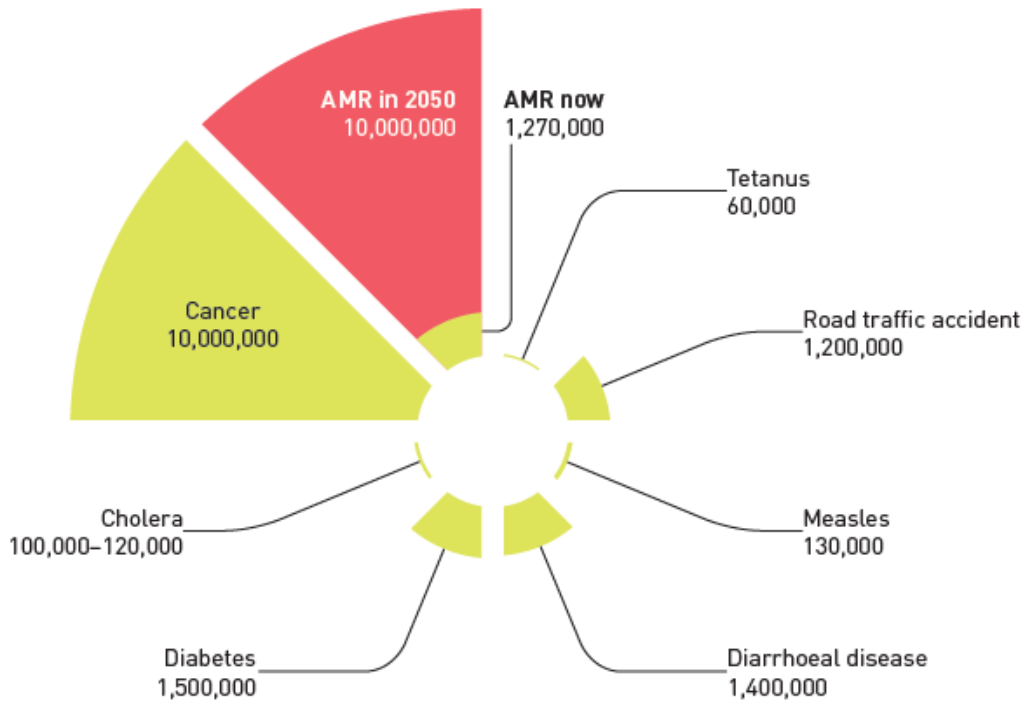

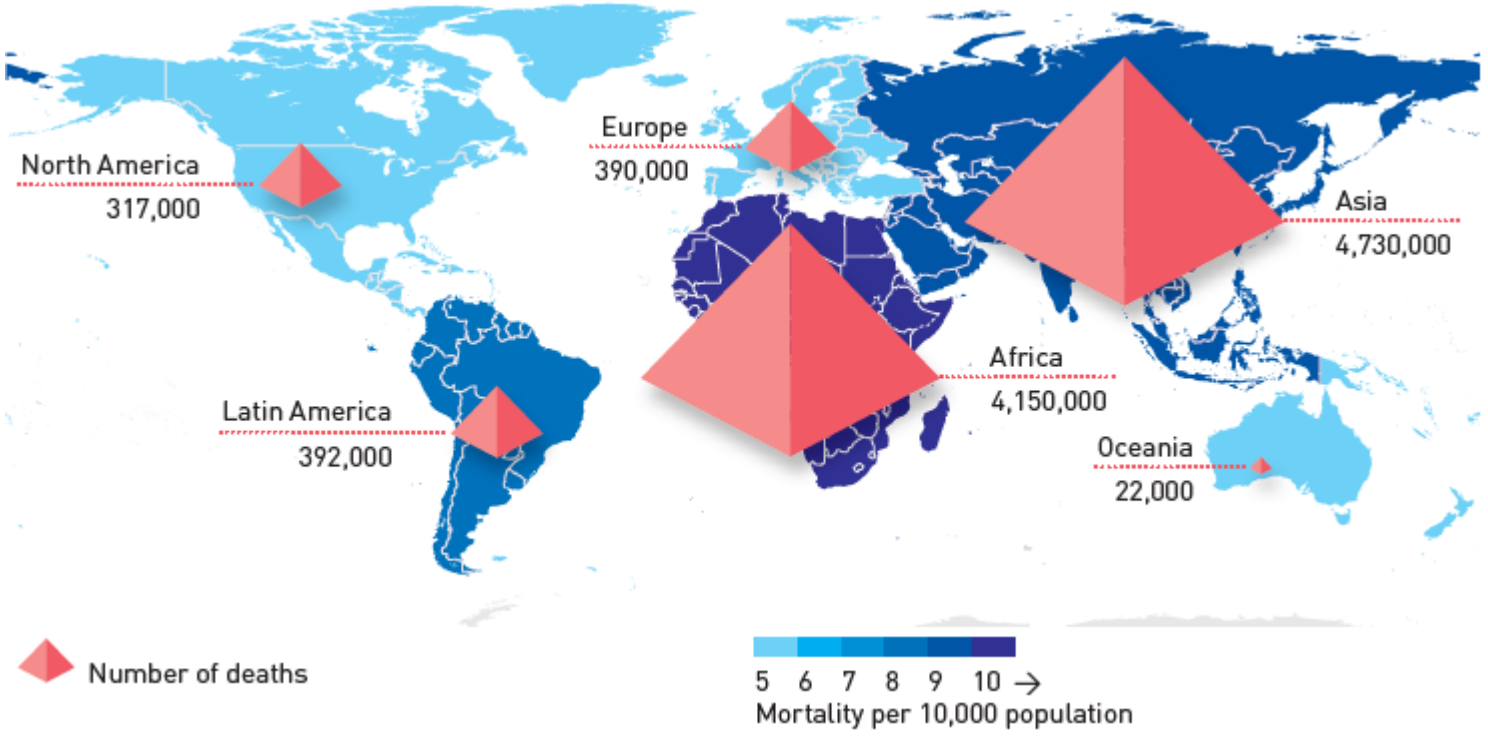

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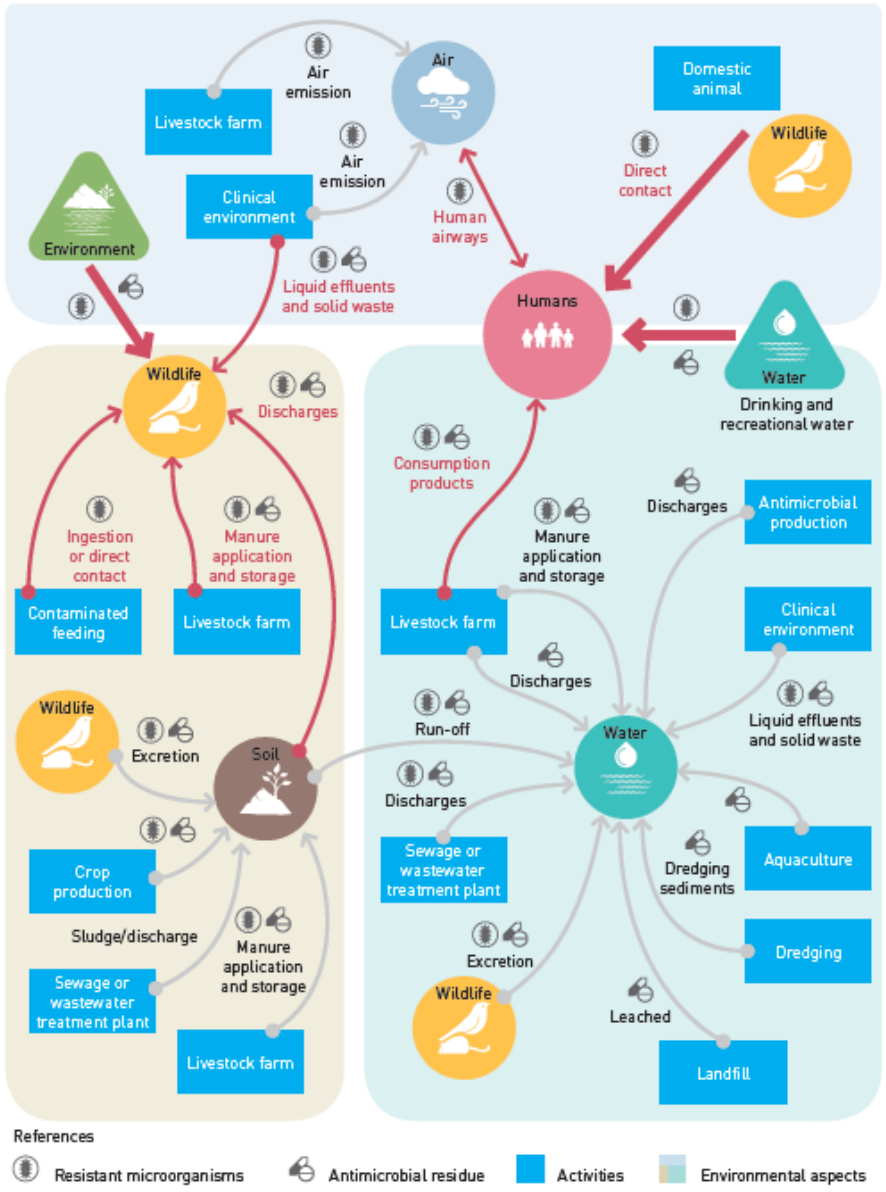
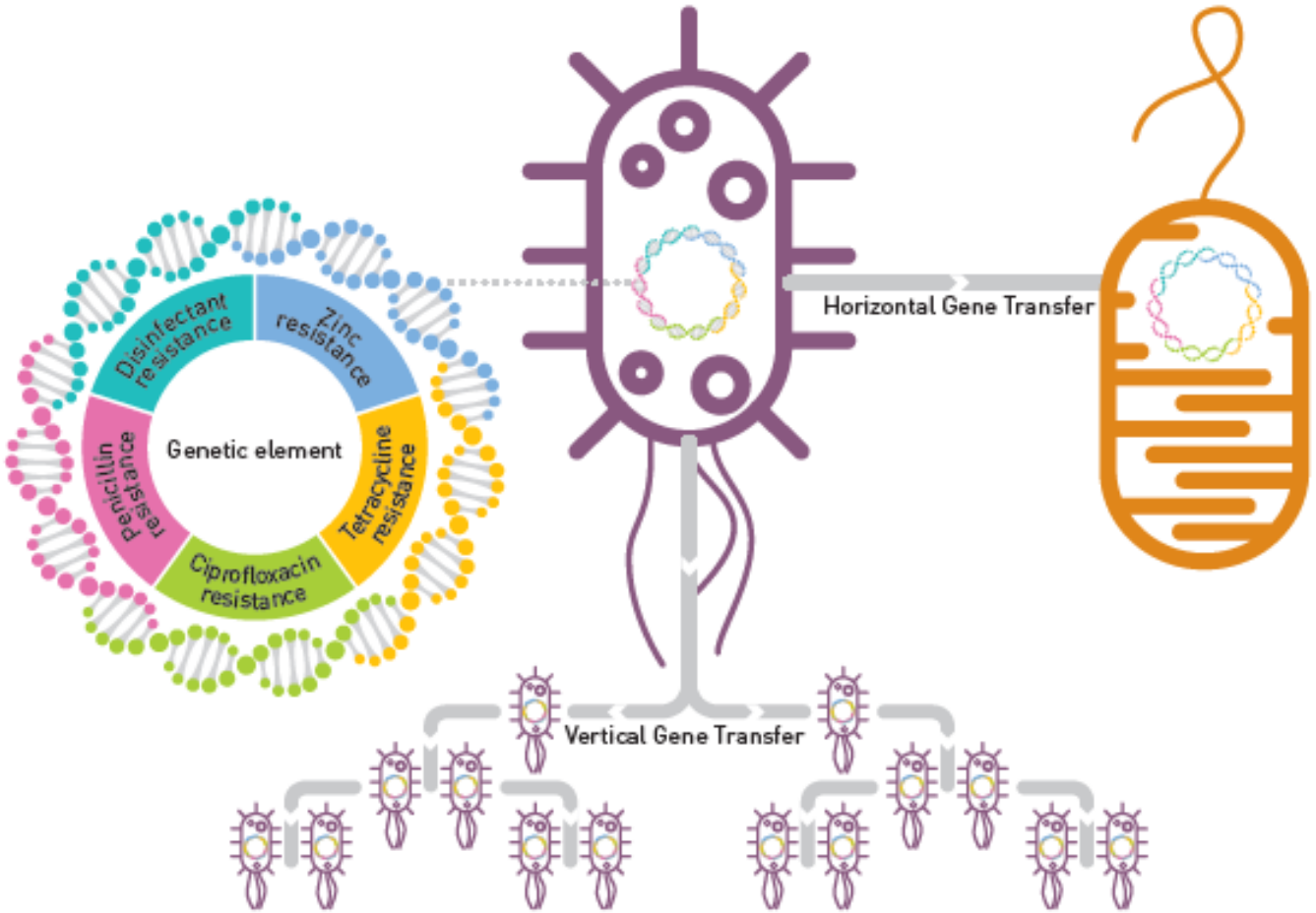
Complexities in spread of AMR

CPias Pays de la Loire



Horizontal and Vertical Gene Transfer



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Complexities in spread of AMR

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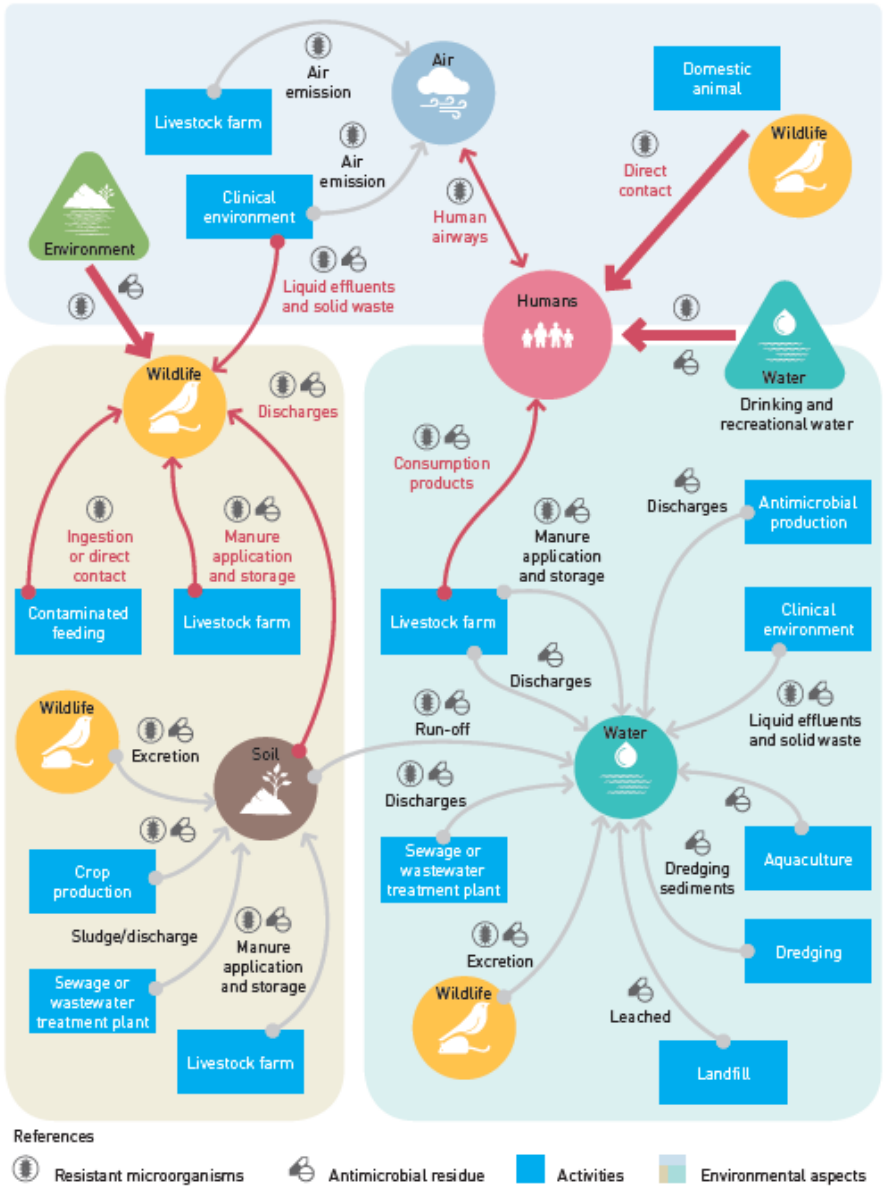
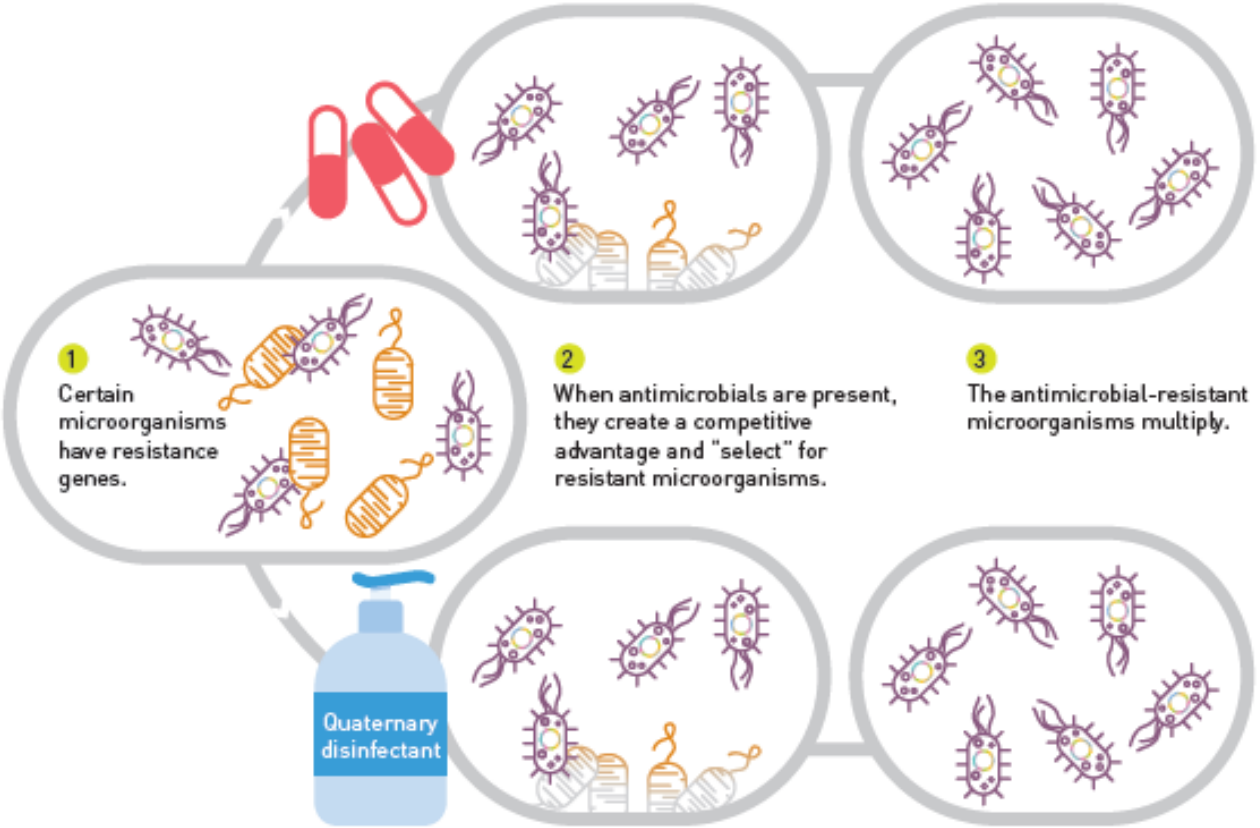


Selection pressure and antimicrobial resistance



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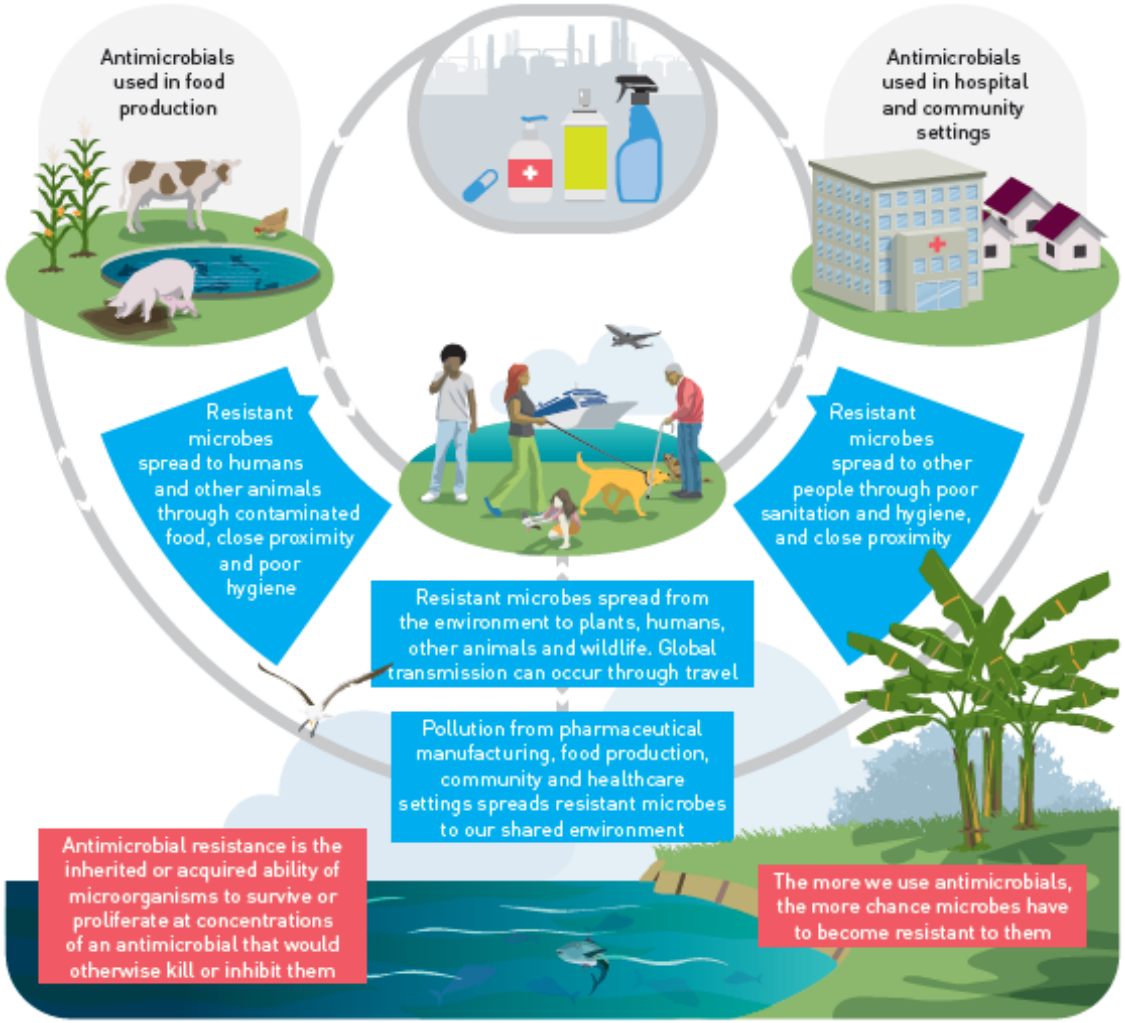
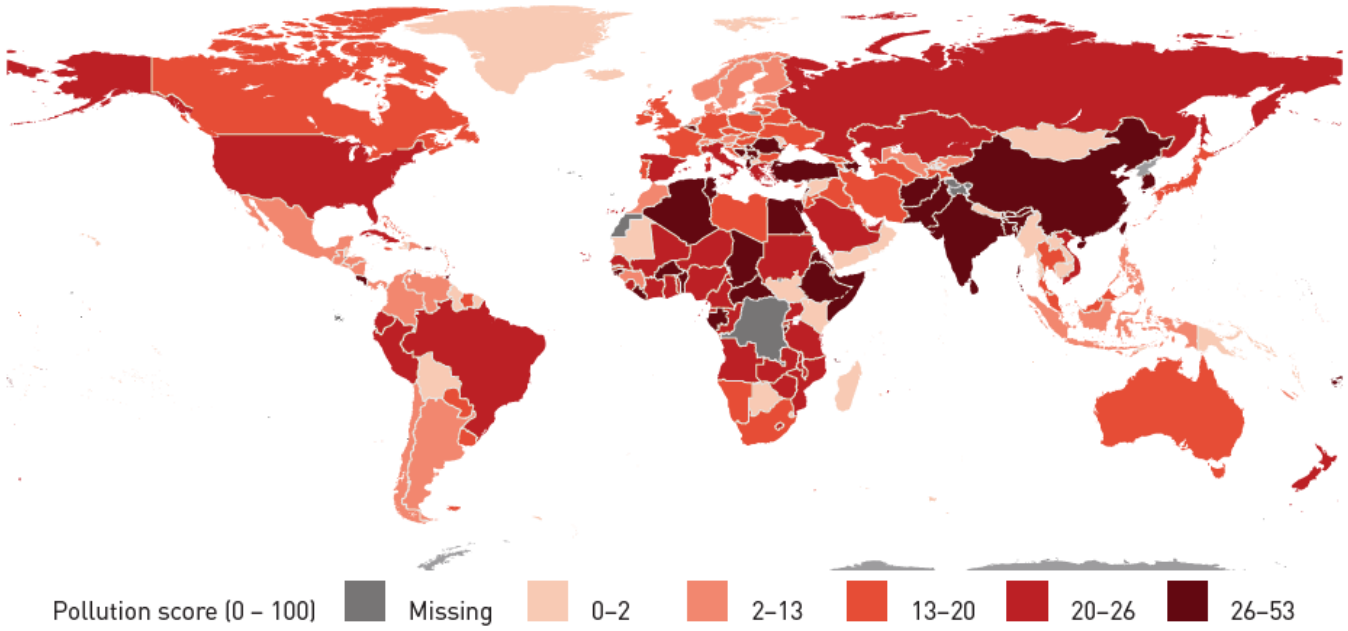
Complexities in spread of AMR

CPias Pays de la Loire



Estimated global environmental water contamination from antimicrobials



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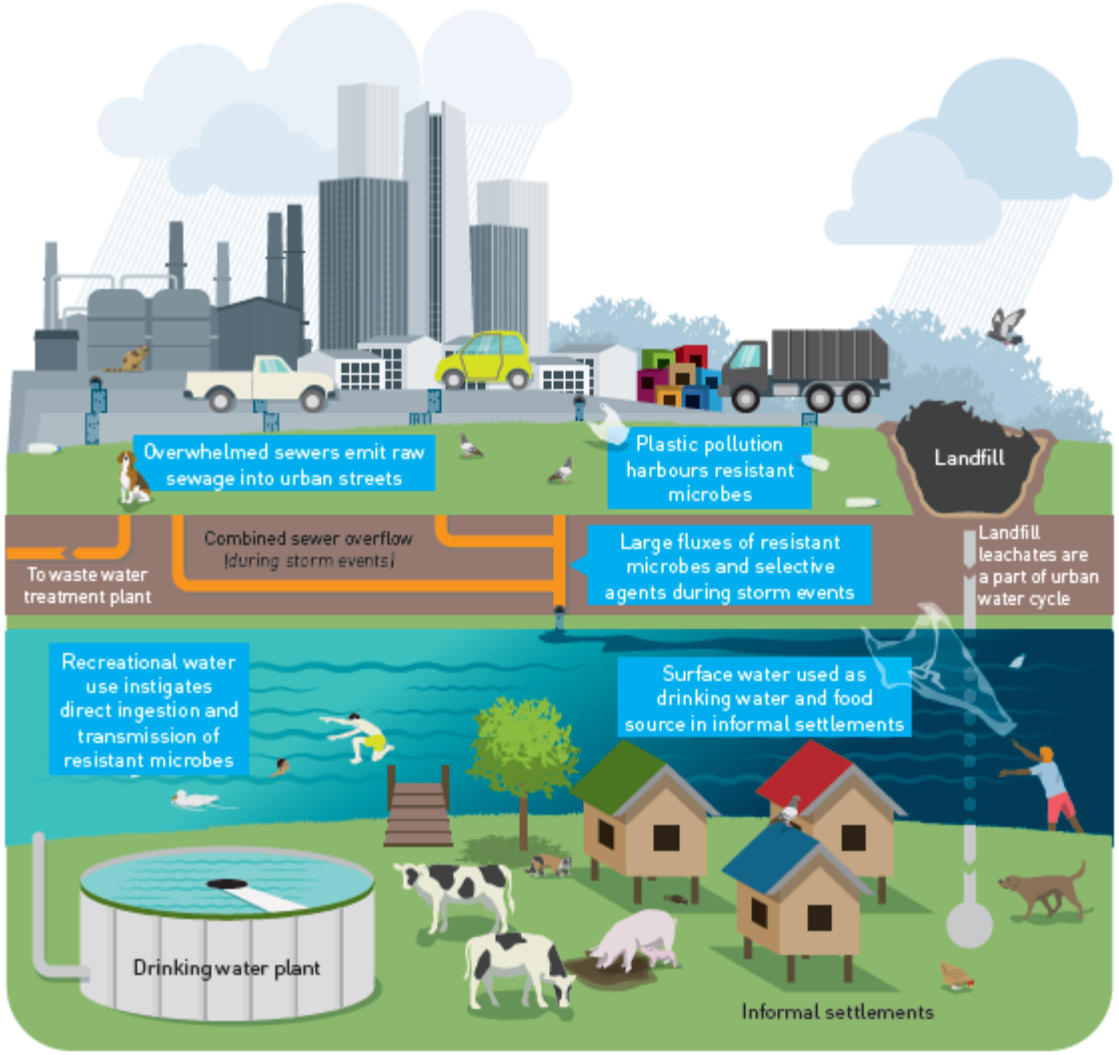
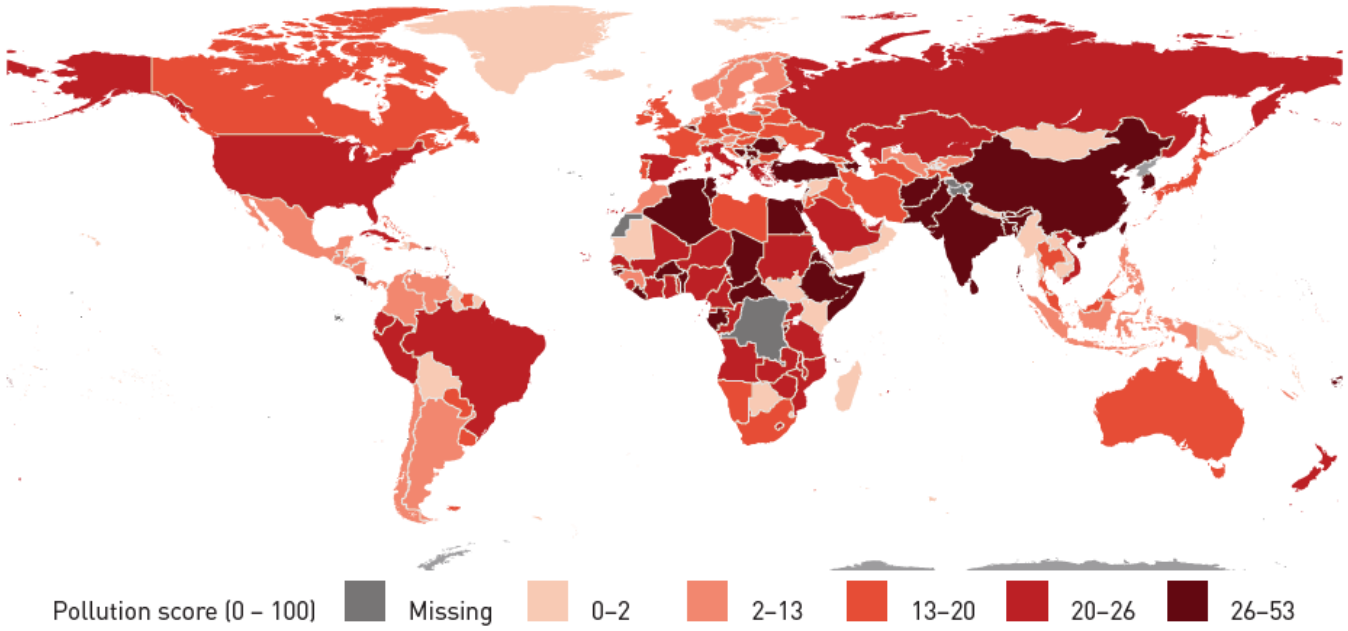
Complexities in spread of AMR

CPias Pays de la Loire



Estimated global environmental water contamination from antimicrobials



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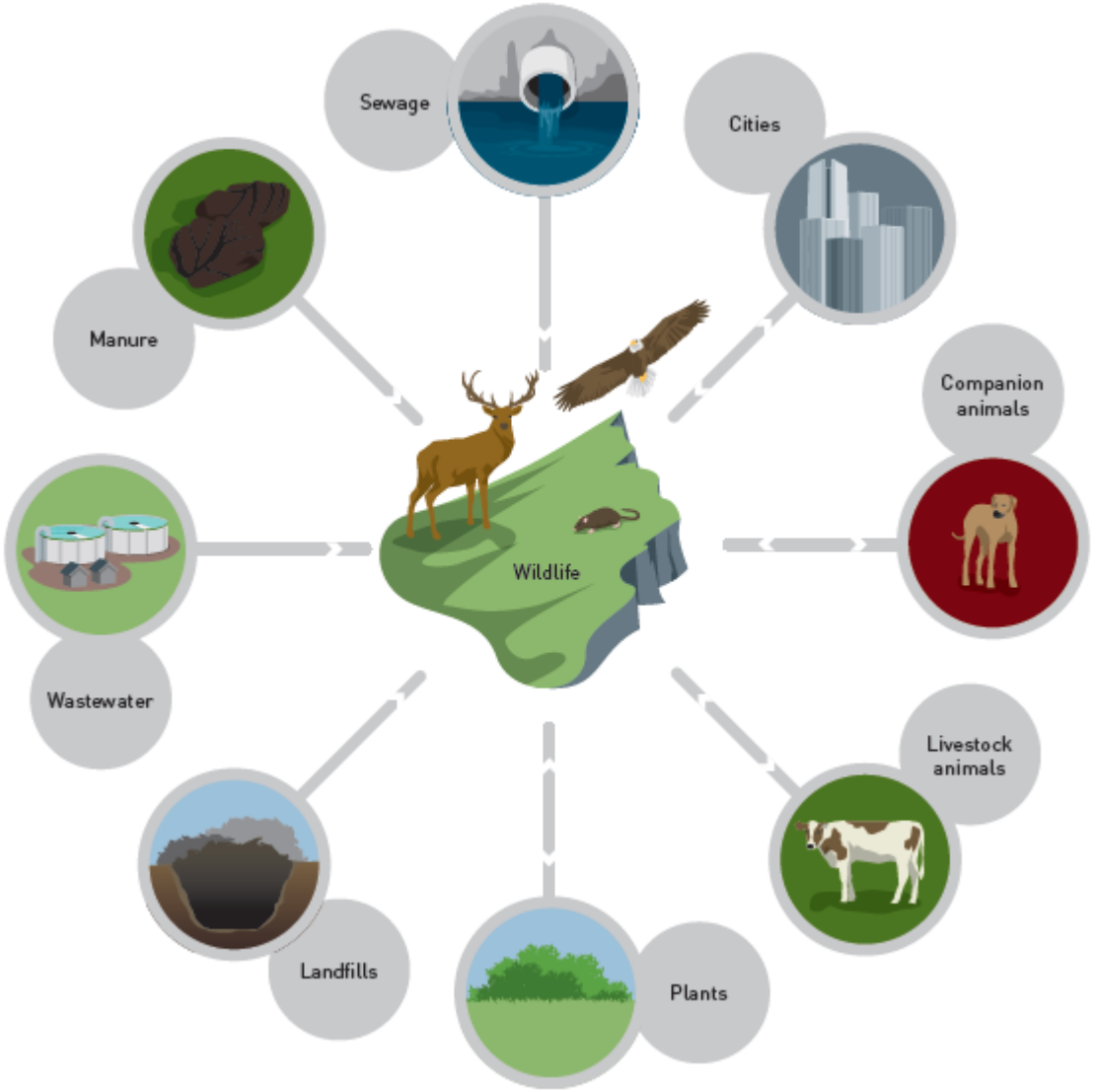
Complexities in spread of AMR

CPias Pays de la Loire



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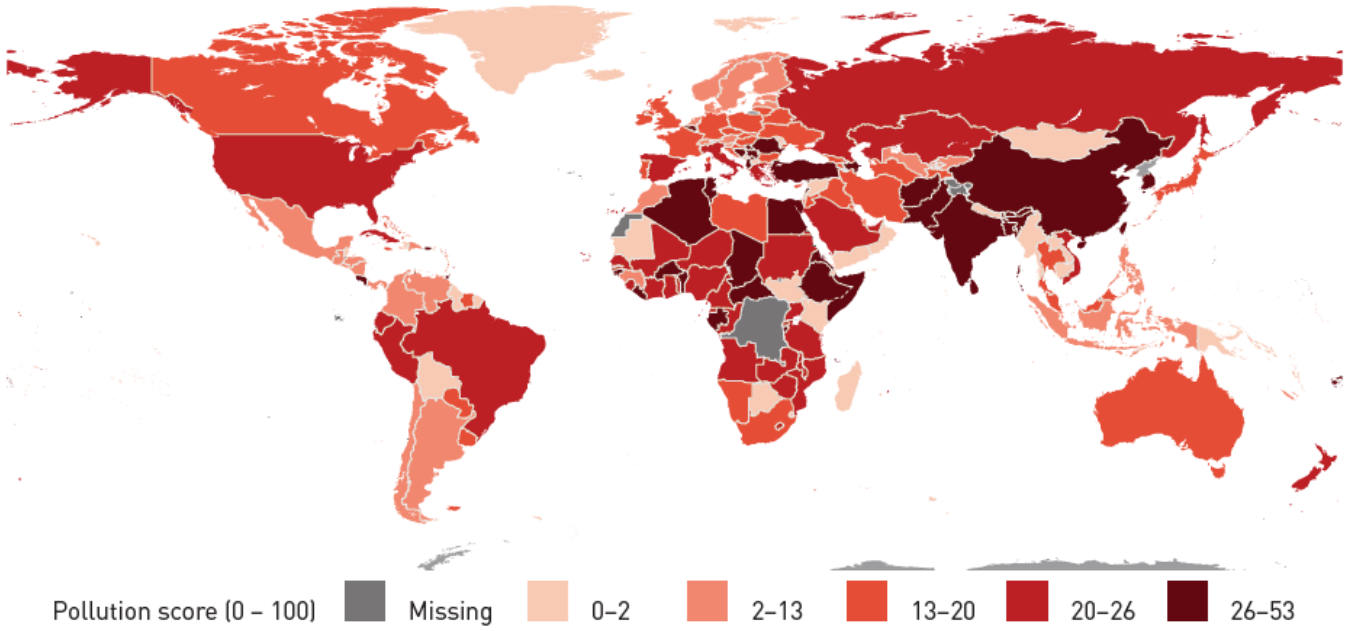

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Main challenge in preventing AMR

Patients infected

Patients colonised

Few infections

Invisible spread +++

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Which organism to prioritize?

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Saprophytic or Commensal?

- Commensal: MRSA, ESBLE and CPE, *E. faecium*
  - Prolonged carriage: cross transmission beyond high risk units (ICU, ..) = collective risk
  - Individual risk by raise of the morbi-mortality rates
- Saprophytic: *P. aeruginosa*, *A. baumannii*
  - Short carriage, excepted in high risk units
  - But increasing level of resistance, and raise in mortality

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Which organism to prioritize?

Resistance mechanisms

Selection of mutants R

(Chrom.)

Rapid selection on ATB +/- clonal spread

P. aeruginosa *(HyperCases)*

Eb Gpe III (Sm, *E. cloacae*)

Reversible resistance

Acquisition of Genetic material

(Plasmid.) Clonal diss.

(Chrom.) Clonal diss.

+/- slow selection on ATB

ESBL (CTX-M, TEM, SHV)

CPE (OXA, NDM, KPC)

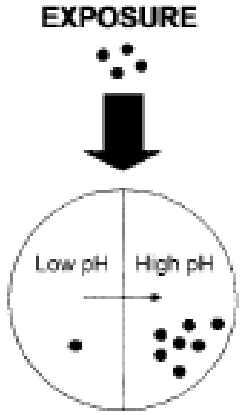
VRE (vanA, vanB)

MRSA (mecA)

Stable resistance and transmissible across species

ESBL-E:
Extended spectrum beta-lactamase Entérobacteriaceae

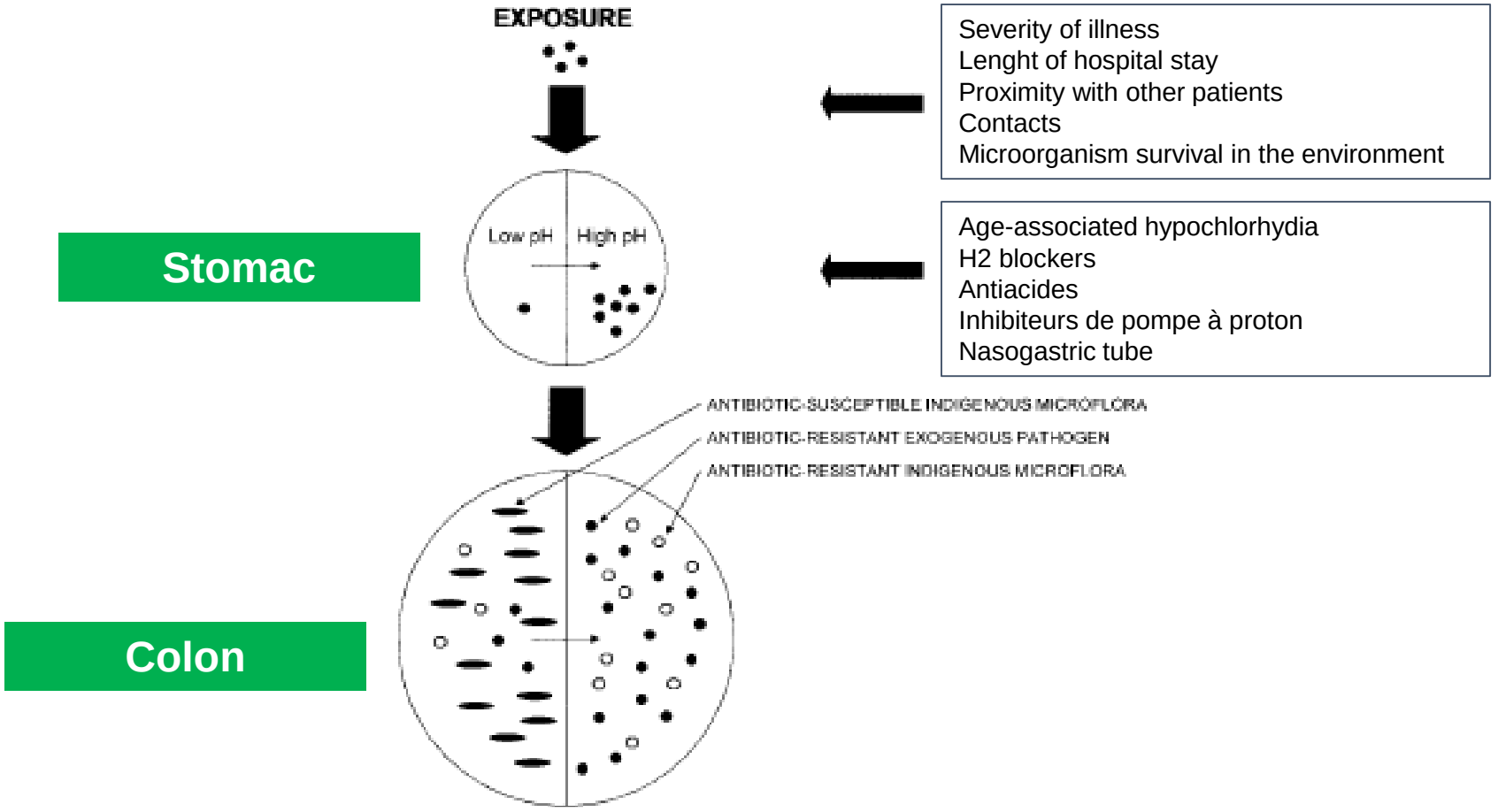
Stomac



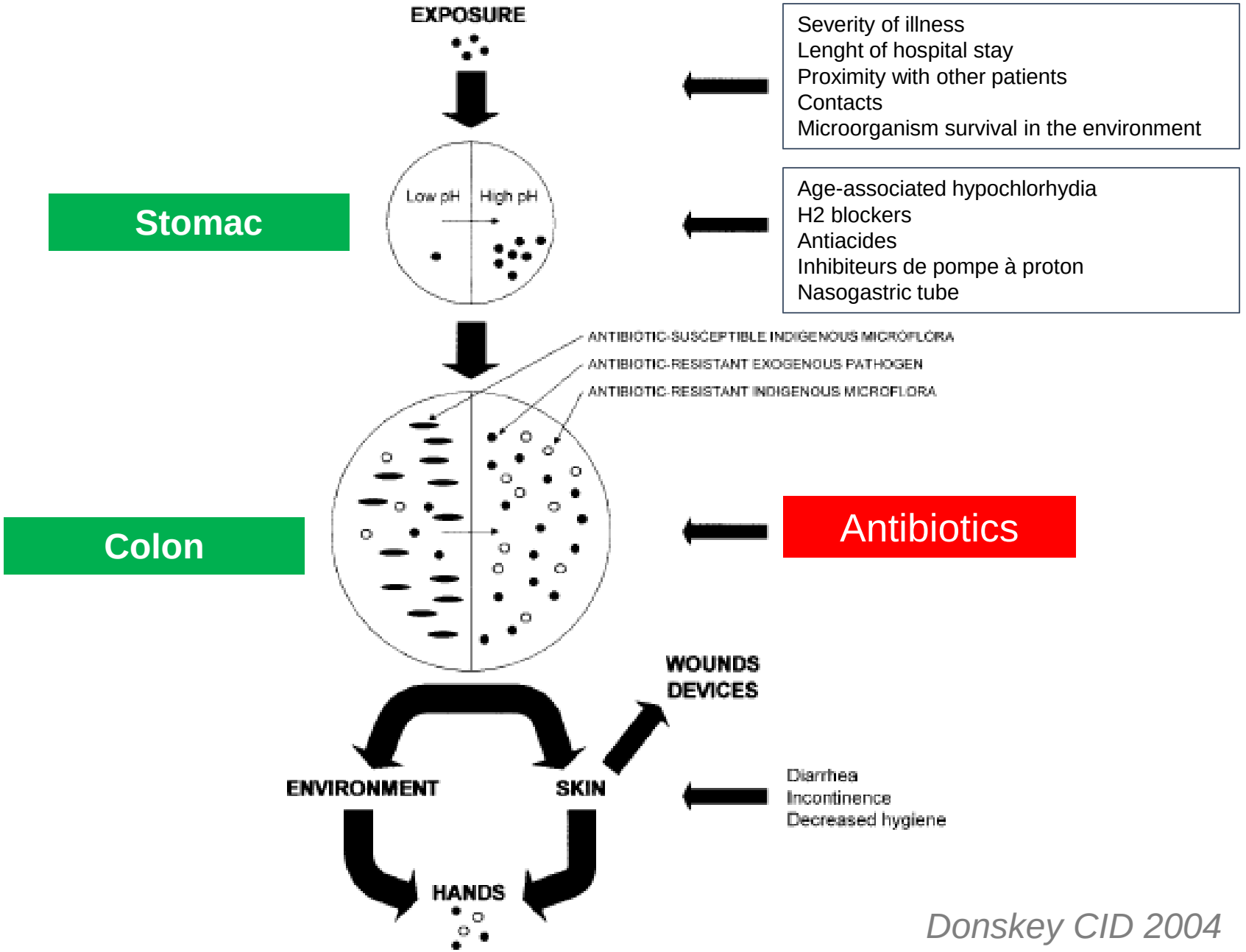
- Severity of illness
- Lenght of hospital stay
- Proximity with other patients
- Contacts
- Microorganism survival in the environment

- Age-associated hypochlorhydia
- H2 blockers
- Antiacides
- Inhibiteurs de pompe à proton
- Nasogastric tube

Donskey CID 2004

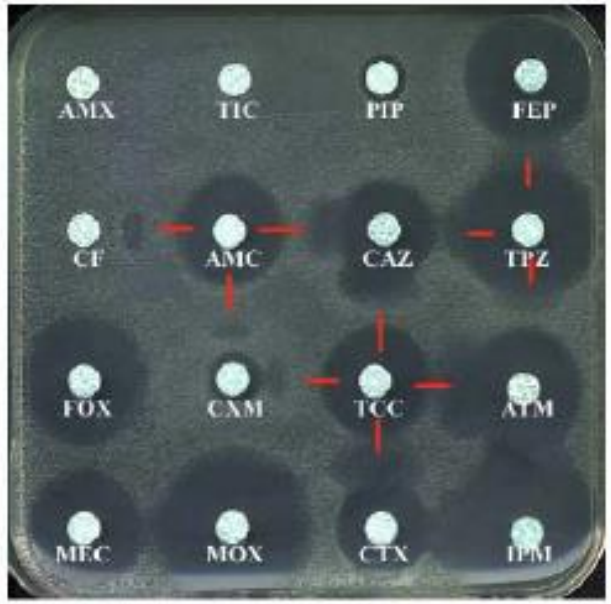


Donskey CID 2004



Donskey CID 2004

Changement de profil des β-lactamases



Années 90 → **Années 2000**

Klebsiella pneumoniae productrice de BLSE

Enterobacter hyperproducteur de cephalosporinase et de BLSE

Escherichia coli producteur de BLSE

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ESBL-E reservoir

Extretas (stools and urines) = major reservoir

- ~ 10^{10} ESBL-E produced in stools per day by carriers
- ~ 10^{9} BLSE-E in urine of patient colonized or infected
- ~ 10^{7} bacteria on the skin

Aim: To evaluate the use of equipment for the management of excreta and to review practices of healthcare workers in their disposal.

71% of the units the bedpan was rinsed before disinfection, mostly in the patient's bathroom (62%).

Only 9% of questioned healthcare workers said they followed an educational programme about excreta disposal.

Lepainteur, Journal of Hospital Infection, Volume 91, Issue 4, December 2015, Pages 346-350

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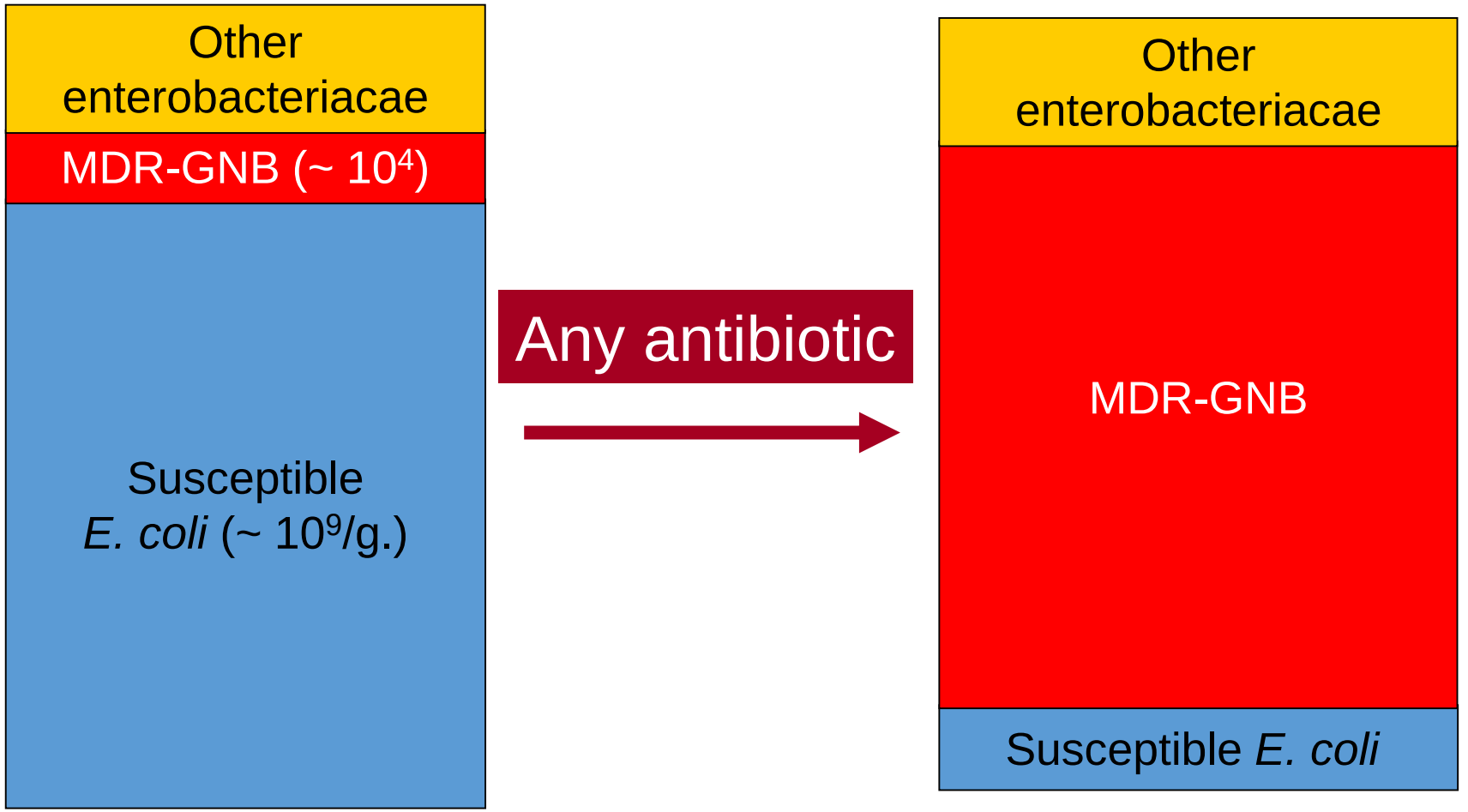
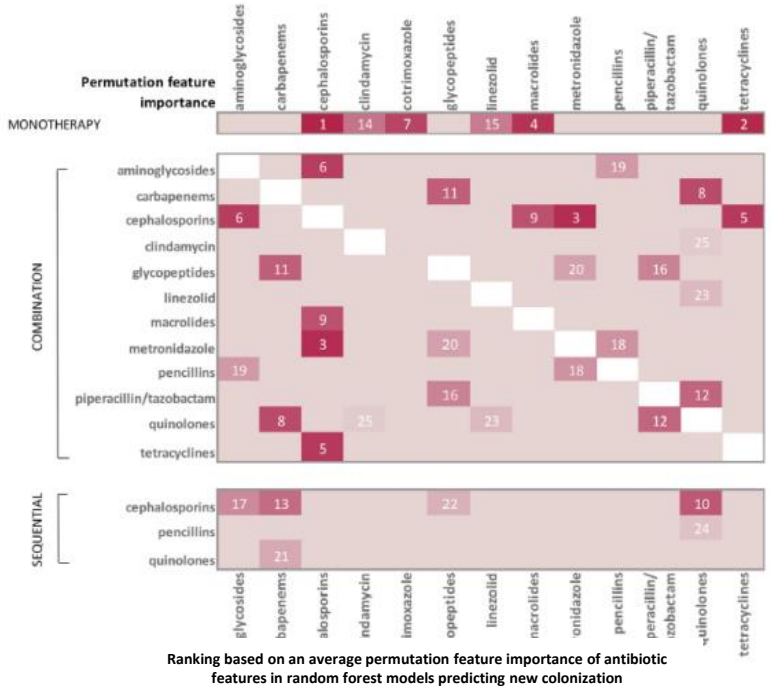
Antibiotics & ESBL-E



Antibiotics & ESBL-E

Estimating the association between antibiotic exposure and colonization with ESBL-GNB using machine learning methods: a multicentre, prospective cohort study

- To measure the impact of antibiotic exposure on the acquisition of colonization with ESBL-GNB accounting for individual- and group-level confounding using machine-learning methods
  - 2010-2013: 3-year multicentre, prospective, cohort study in 12 wards (six medical and six surgical) in 3 university hospitals in Italy, Serbia and Romania



Ranking based on an average permutation feature importance of antibiotic features in random forest models predicting new colonization

Table 3
Predicted hazard ratios reflecting the time-dependent effects of antibiotic therapy according to days of antibiotic exposure based on the parametric survival regression for the development of new colonization with ESBL-producing Gram-negative bacteria in 5781 hospitalized patients

Covariates: days of antibiotic exposure[c]	Number of patients	Number of patients colonized with ESBL-GNB (%)	Univariate analysis[a]		Multivariable analysis[a,b]	
			Unadjusted hazard ratio (95% CI)	p value	Adjusted hazard ratio (95% CI)	p value
No exposure	2313	185 (8)				
1 to 3 days	429	78 (18)	2.87 (1.97–5.39)	0.002	2.34 (1.31–4.45)	0.02
4 to 7 days	1117	310 (28)	4.15 (1.97–8.72)	0.008	3.03 (1.83–5.97)	<0.001
8 to 14 days	1034	323 (31)	4.29 (3.61–5.36)	<0.001	3.03 (2.06–4.45)	<0.001
15 to 21 days	421	107 (25)	2.87 (2.28–3.61)	<0.001	2.03 (1.31–3.14)	0.023
>21 days	467	158 (34)	2.29 (1.78–2.95)	<0.001	1.7 (1.15–2.62)	0.07

- Monotherapy ranked higher than combination therapy in promoting ESBL-GNB colonization.
- Monotherapy: cephalosporins > tetracycline >macrolide >cotrimoxazole
- Ranking of cephalosporins was lower when used in combination.
- Combinations not including cephalosporins, quinolones plus carbapenems ranked highest (eighth).
- Among sequential therapies, quinolones ranked highest (tenth) when prescribed within 30 days of therapy with cephalosporins.

→ **Evidence from our study suggests that antibiotic resistance is an unavoidable adverse event of antibiotic therapy.**

→ **New ESBL-GNB colonization is therefore a very common (>10% frequency) adverse effect of cephalosporins**

E. Tacconelli Clin Microbiol Infect 2019

Imperial College London

ESBL-E epidemiology

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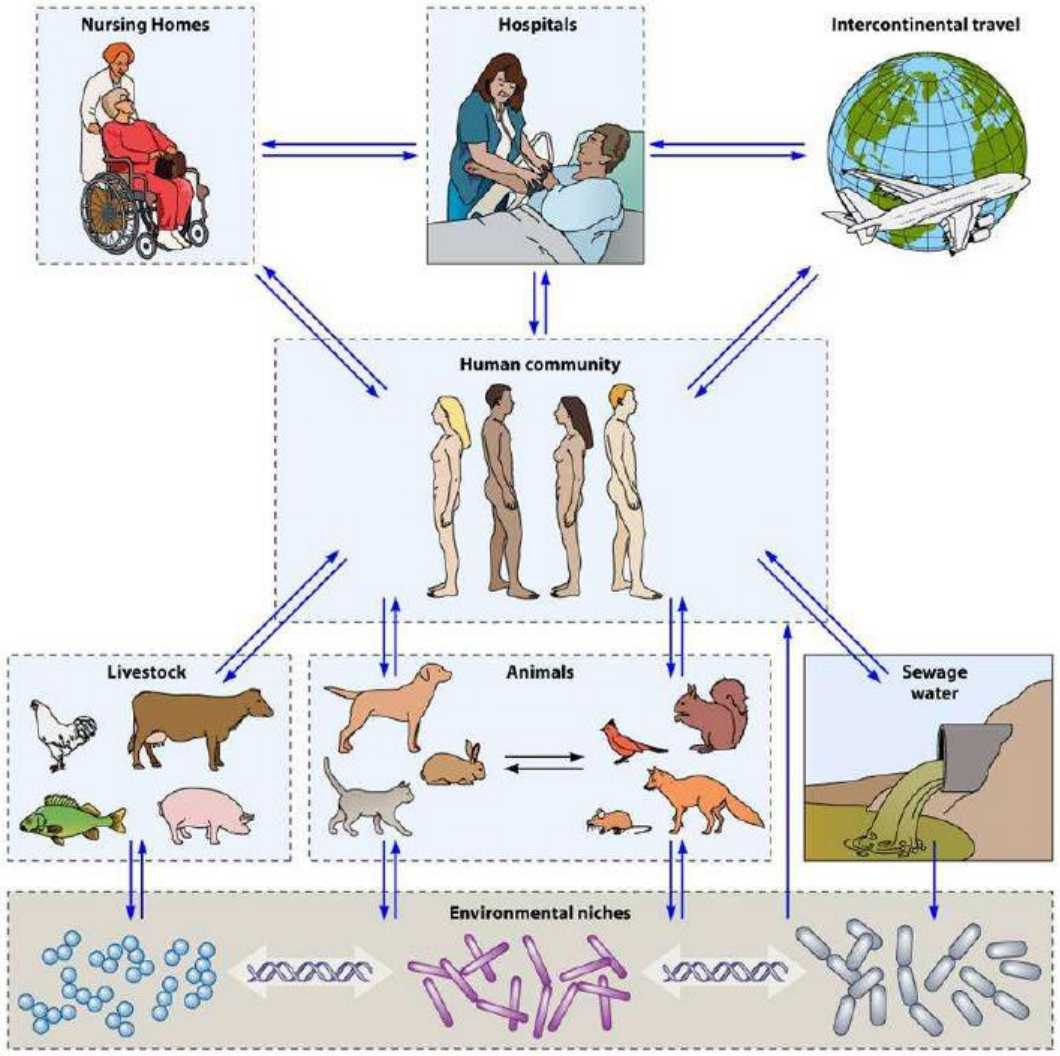
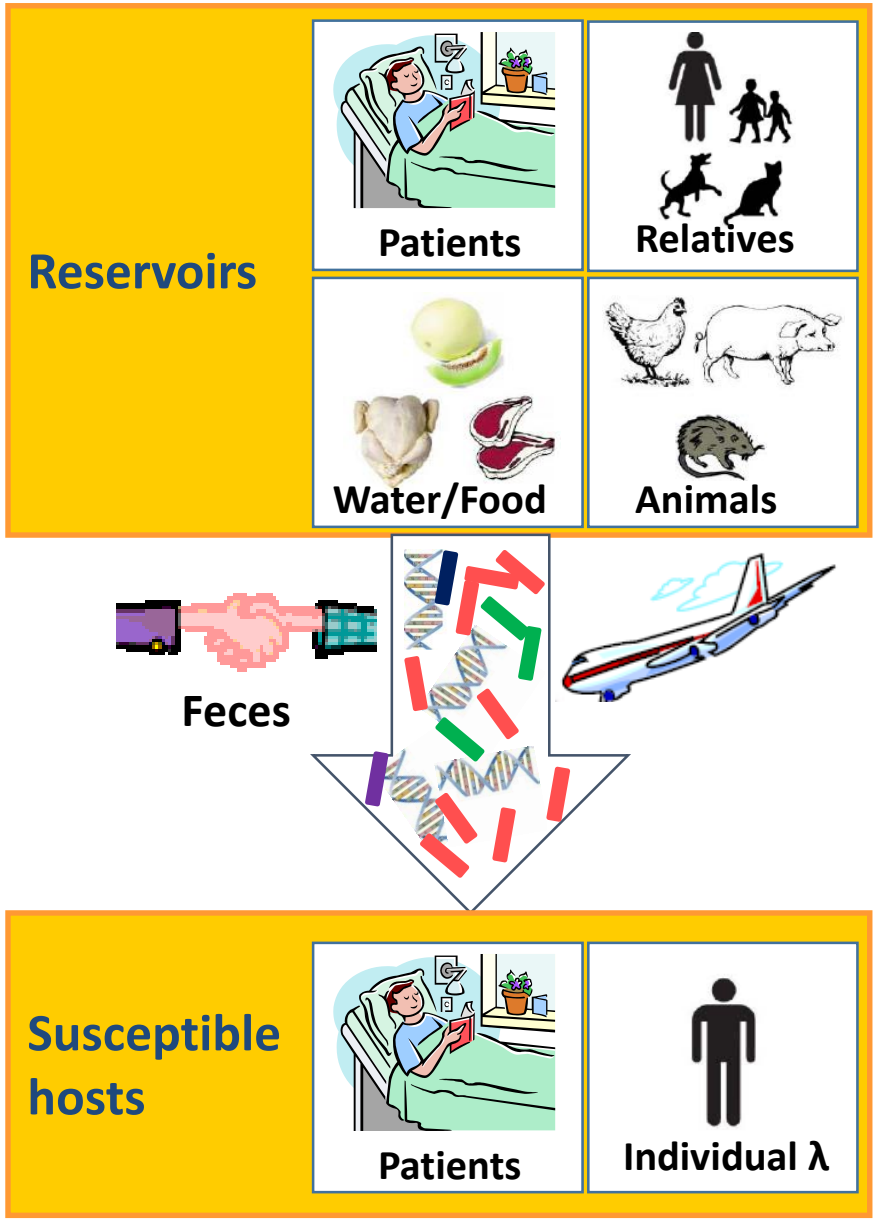


PL Woerther CMR 2013



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Evolution in UK

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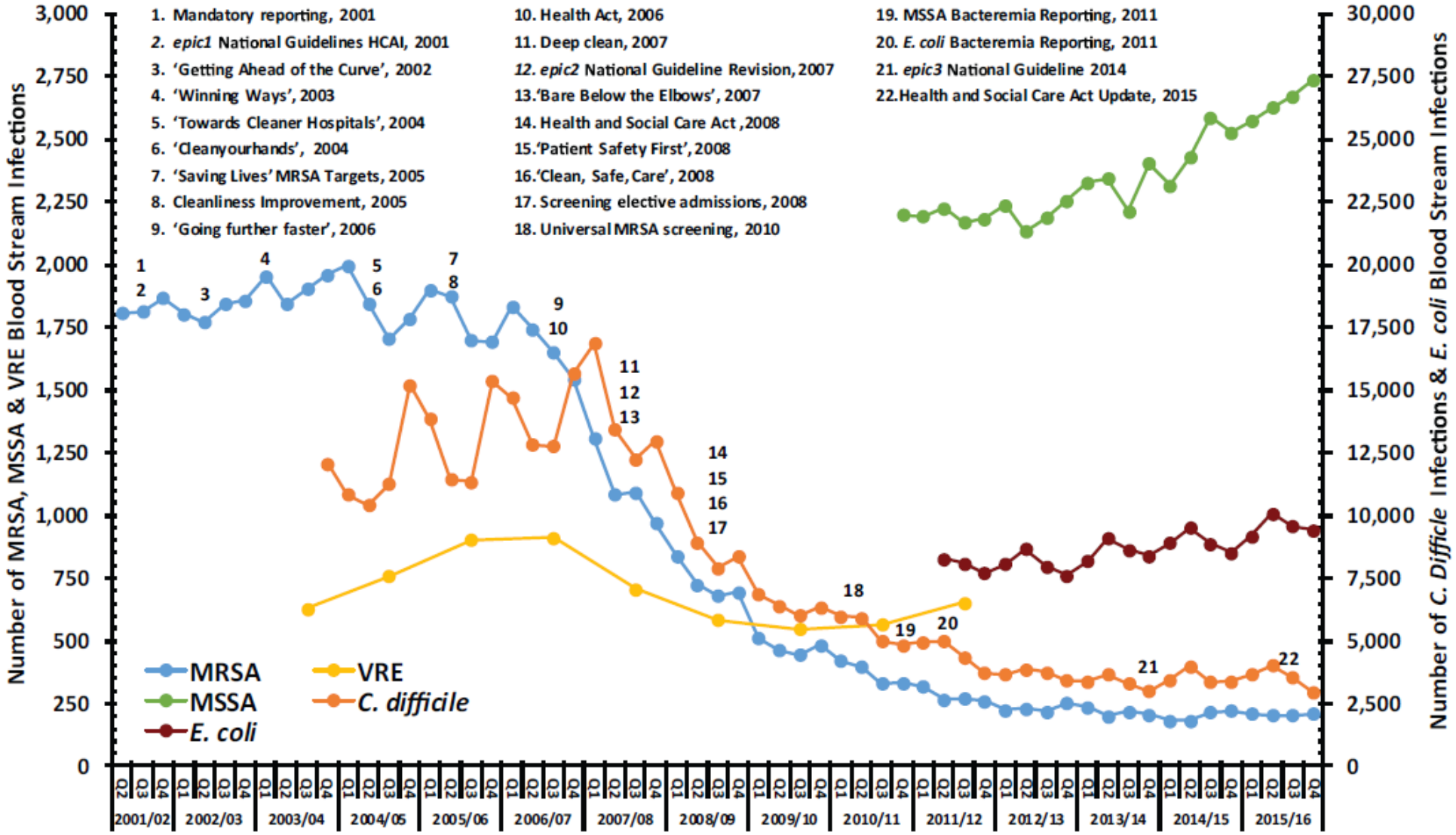


Jonathan D. Edgeworth CID 2020

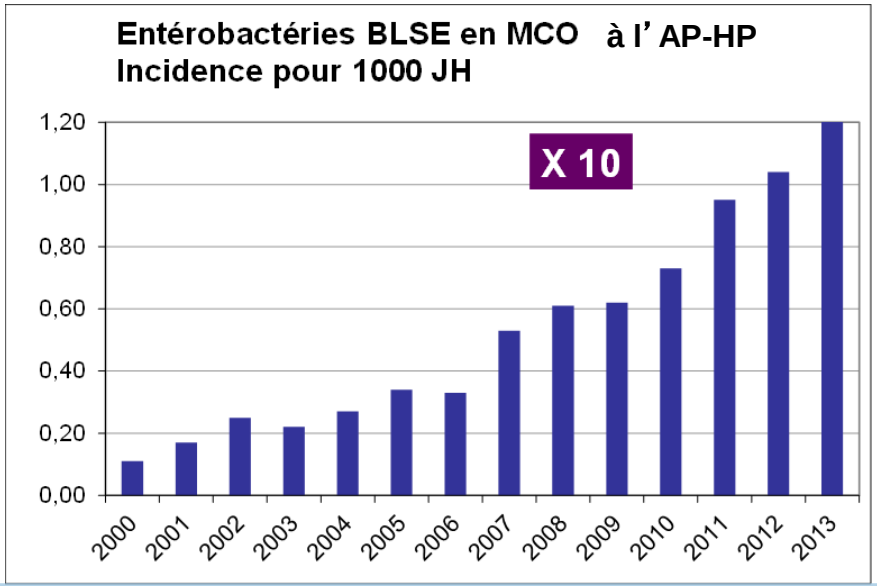
EPC:
Entérobactéries productrices de carbapénèmase

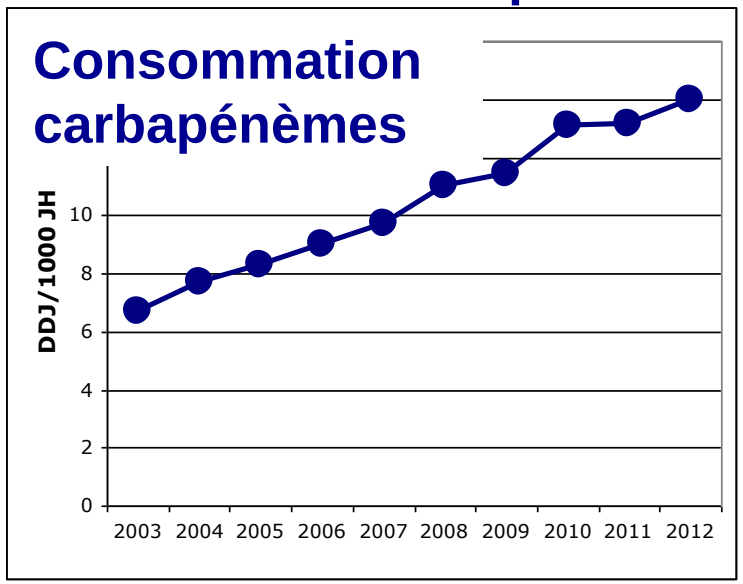
Entérobactéries multi résistantes

Antibiotiques C3G, FQ

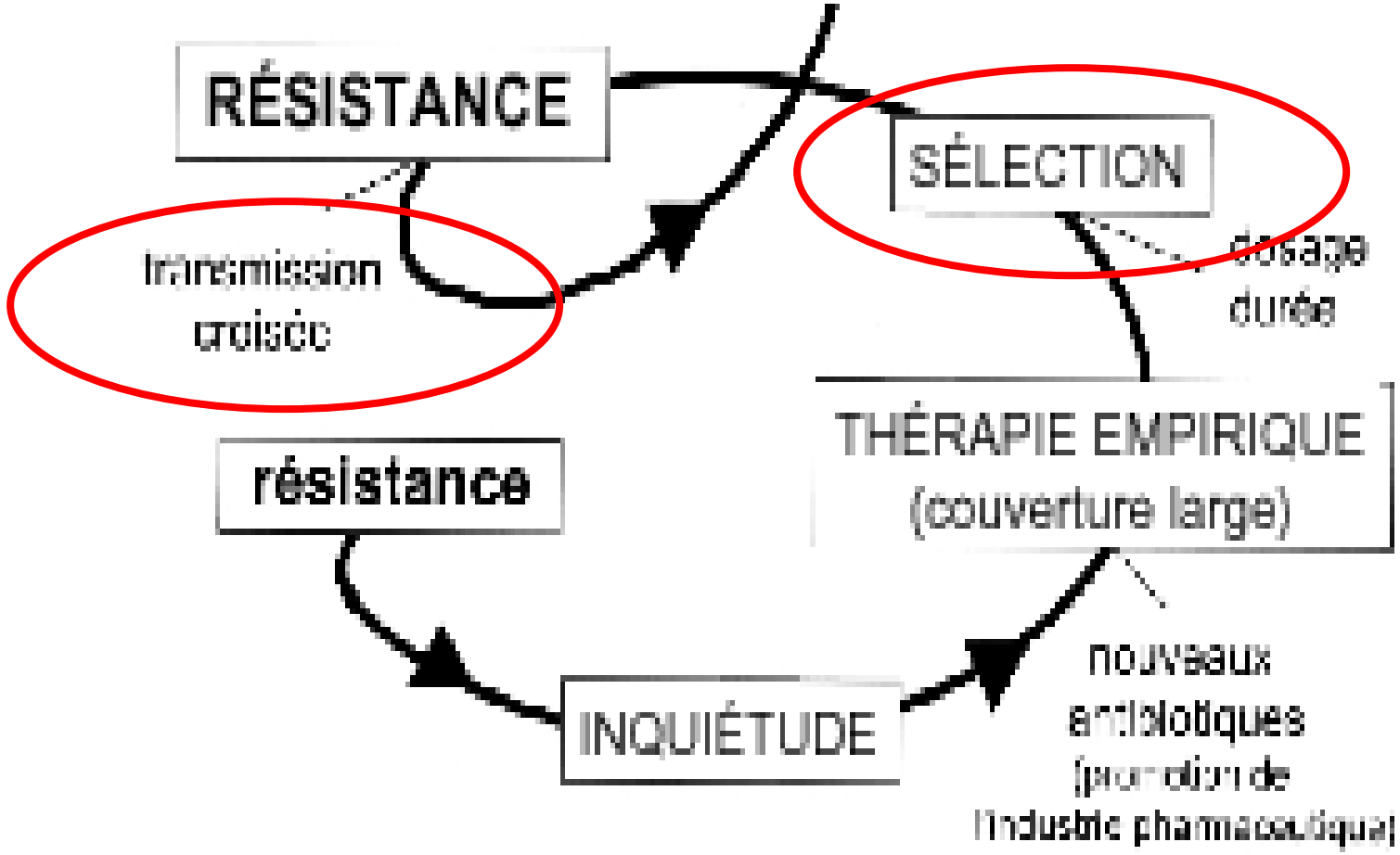
Carbapénèmes

Entérobactéries sensibles → **Entérobactéries multirésistantes = EBLSE** → **Entérobactéries résistantes aux carbapénèmes**
- **Imperméabilité**
- **Carbapénèmase**





Rôle de la pression de sélection des antibiotiques



Spirale de la résistance (J. CARLET)

Epidémiologie de la Résistances

Molecular class	Representative β-lactamase	Characteristic(s)	Inhibitor(s)	Enzyme currently found in areas of endemicity	Area(s) of endemicity
A	KPC, GES, SMC	Serine β-lactamase, plasmid encoded	Boronic acid derivatives	KPC	North America, Greece, Italy, Poland, Colombia, Argentina, Israel, China
				GES-5	Brazil
B	NDM, VIM, IMP, GIM-1, SPM	Metallo-β-lactamase, zinc requiring, plasmid encoded/chromosomal	EDTA, dipicolinic acid	NDM	Indian subcontinent, Kenya, China
				VIM	Indian subcontinent, Greece, Italy, southern France, Japan, Lebanon, Brazil, Portugal, Ireland, UK, Germany, Poland
				IMP	Indian subcontinent, Greece, Japan, China
C	CMY-10	Serine β-lactamase, cephalosporinases, mobile or chromosomal, uncommon	Cloxacillin, boronic acid derivatives	AmpC	Worldwide
D	OXA-48, OXA-181, OXA-204, OXA-162, OXA-23, OXA-24	Serine β-lactamases, weak activity of those that are carbapenemases, plasmid encoded	No specific inhibitors available	OXA-48	France, Belgium, Canada, South Africa, Middle East, Turkey, northern Africa, Switzerland, Germany, Lebanon, Israel, Morocco

Viau et al. Clinical Microbiology Reviews January 2016 Volume 29 Number 1

Epidémiologie des Entérobactéries résistantes en communauté

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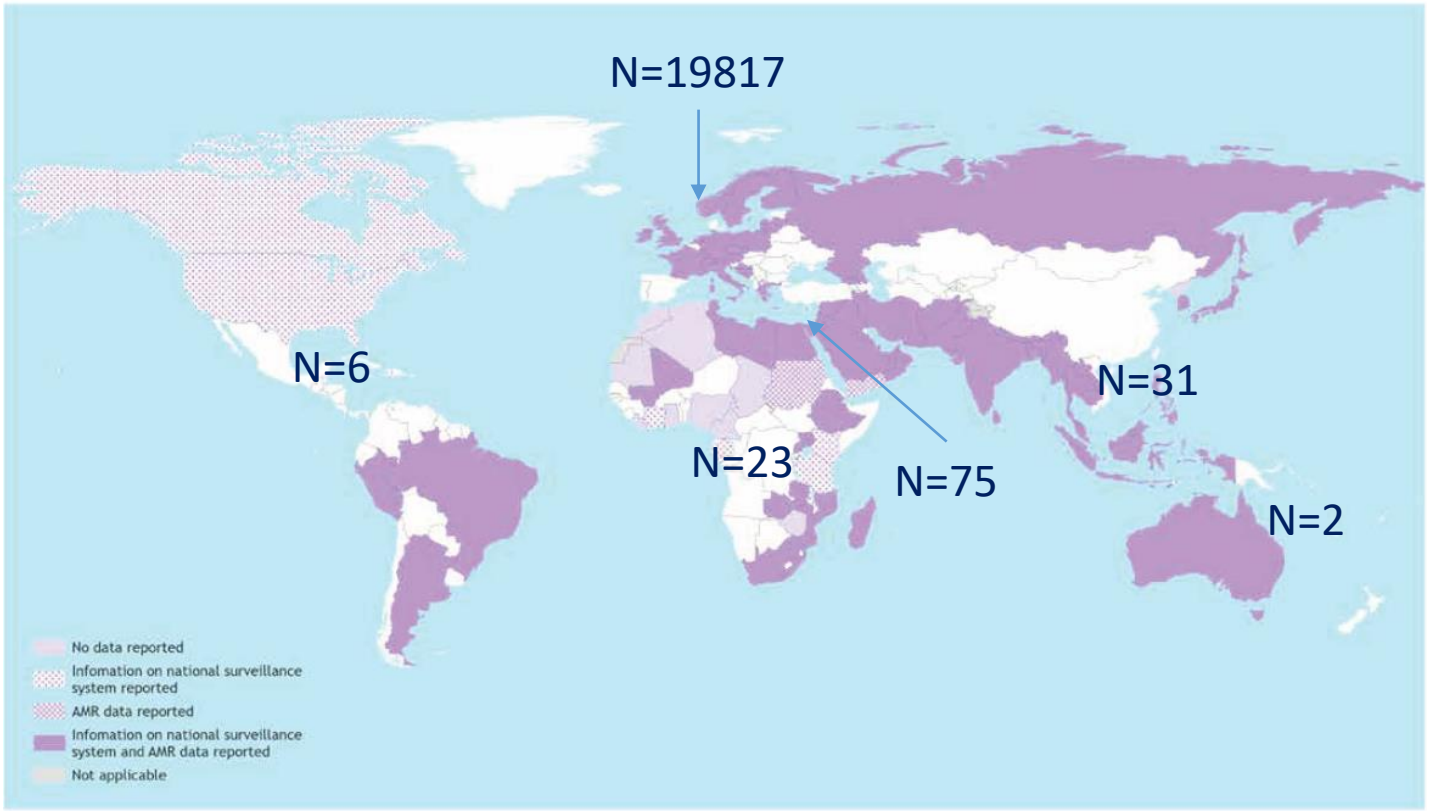
Epidémiologie de la Résistances

Données mondiales 2019/2022 - GLASS-AMR

Nombre de cliniques ambulatoires + laboratoires participants



Données 2019-2020:

- 68 pays avec hémocultures
- 47 pays avec prélèvements urinaires
- 19 721 cliniques ambulatoires, et 2860 hopitaux avec ambulatoire

	E. coli	*K. pneu*
Hémocultures	61 080	19 008
Prélèvt urinaire	459 221	77 198

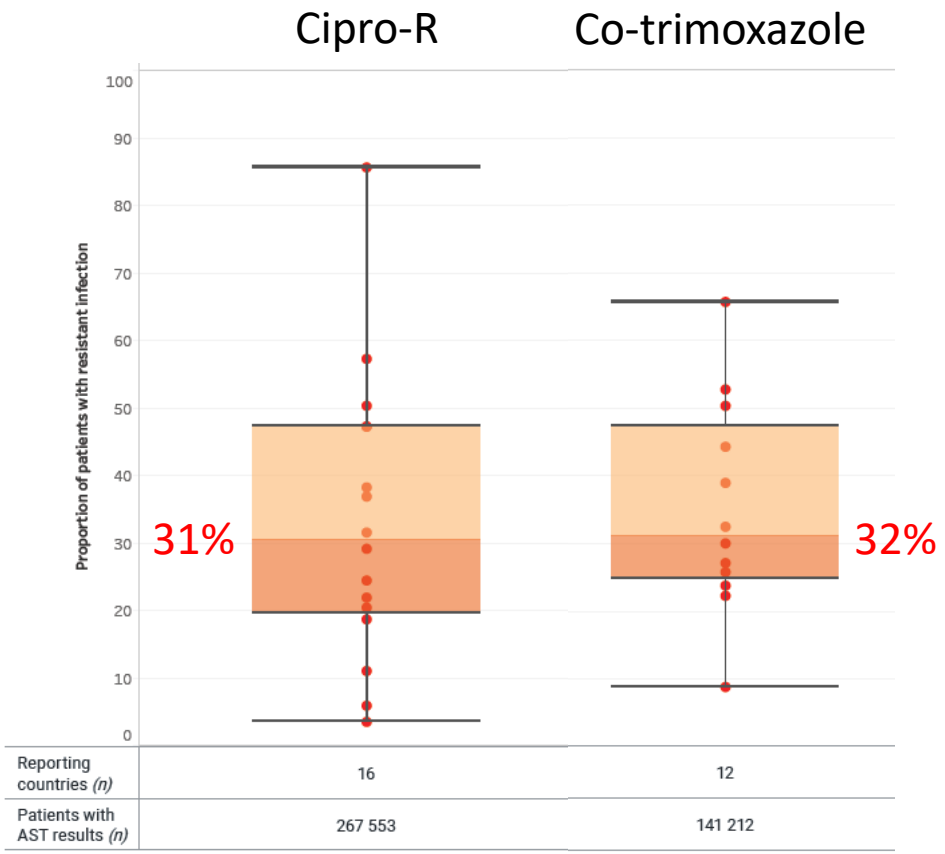
Majeure partie des données provenant d'Europe

GLASS report 2022

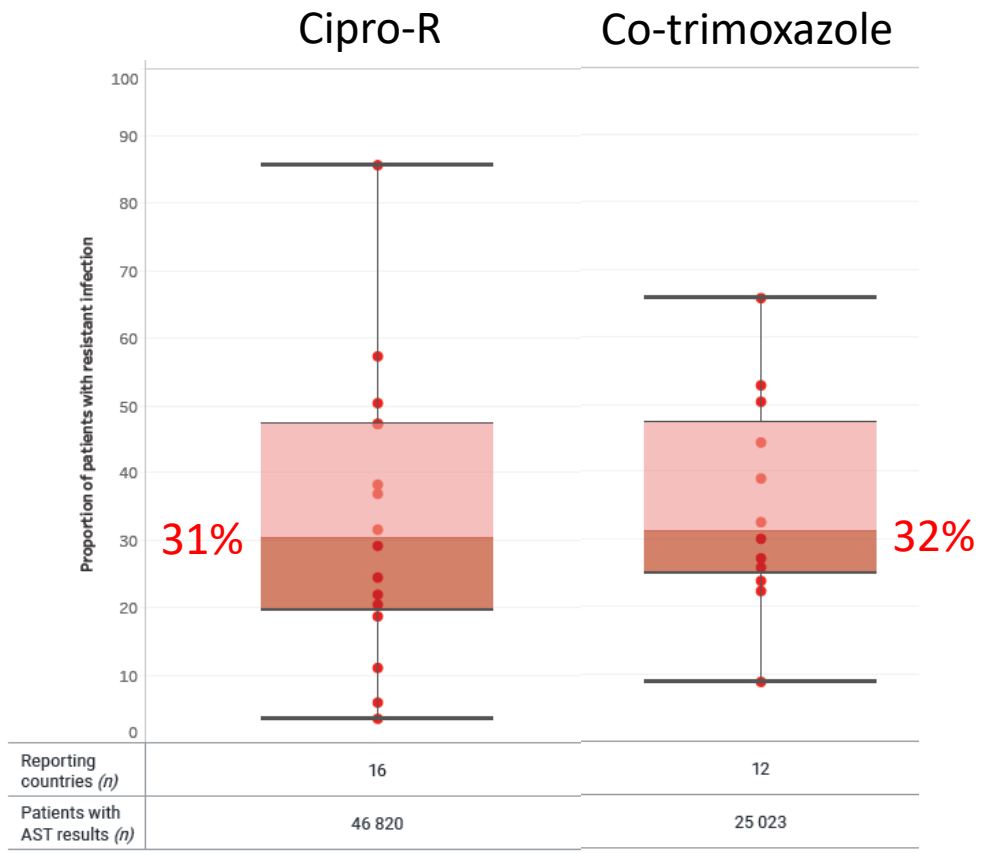
Epidémiologie de la Résistances

Données mondiales 2019/2022 - GLASS-AMR

E. coli IUs



K. pneumoniae IUs



Autres antibiotiques à visée urinaires ? Et Multi-résistance ?

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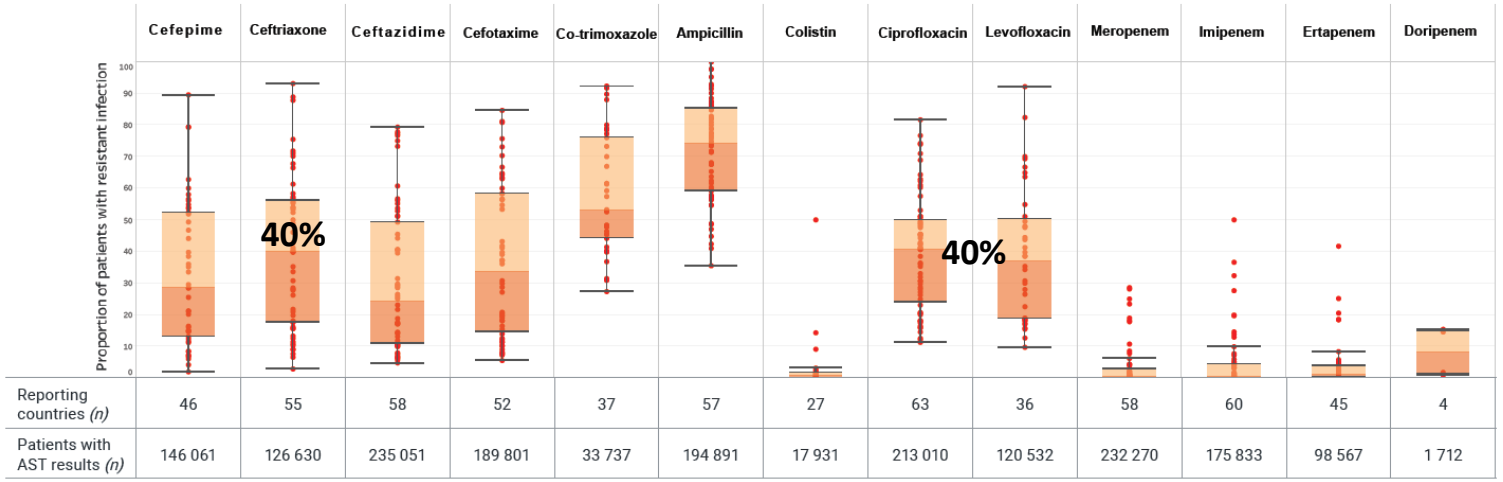
Epidémiologie de la Résistances

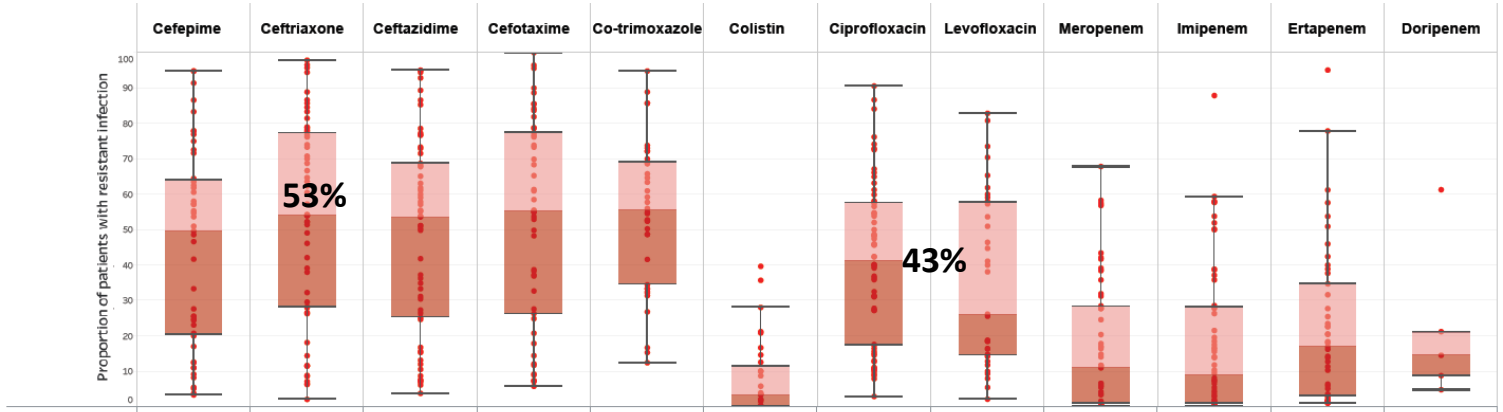
Données mondiales 2019/2022 - GLASS-AMR

E. coli IUs



	Cefepime	Ceftriaxone	Ceftazidime	Cefotaxime	Co-trimoxazole	Ampicillin	Colistin	Ciprofloxacin	Levofloxacin	Meropenem	Imipenem	Ertapenem	Doripenem
Reporting countries *(n)*	46	55	58	52	37	57	27	63	36	58	60	45	4
Patients with AST results *(n)*	146 061	126 630	235 051	189 801	33 737	194 891	17 931	213 010	120 532	232 270	175 833	98 567	1 712

K. pneumoniae IUs



	Cefepime	Ceftriaxone	Ceftazidime	Cefotaxime	Co-trimoxazole	Colistin	Ciprofloxacin	Levofloxacin	Meropenem	Imipenem	Ertapenem	Doripenem
Reporting countries *(n)*	47	56	57	50	38	31	62	35	59	58	45	5
Patients with AST results *(n)*	59 726	45 414	81 448	69 088	23 946	11 202	75 627	39 047	82 783	68 190	38 556	947

GLASS report 2022

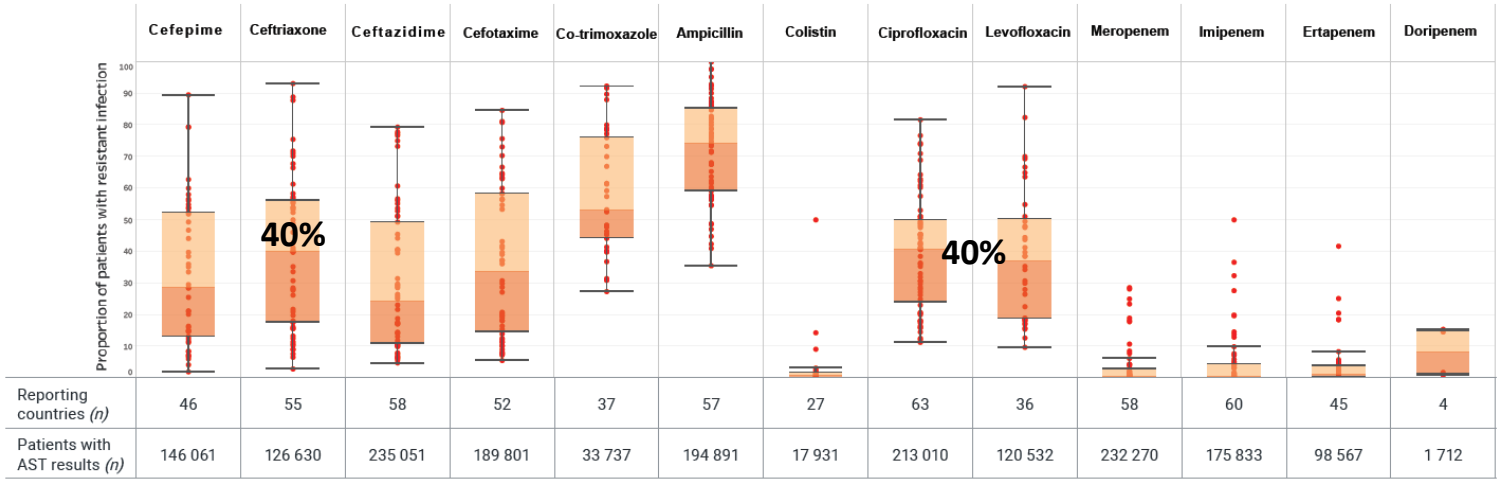
Epidémiologie de la Résistances

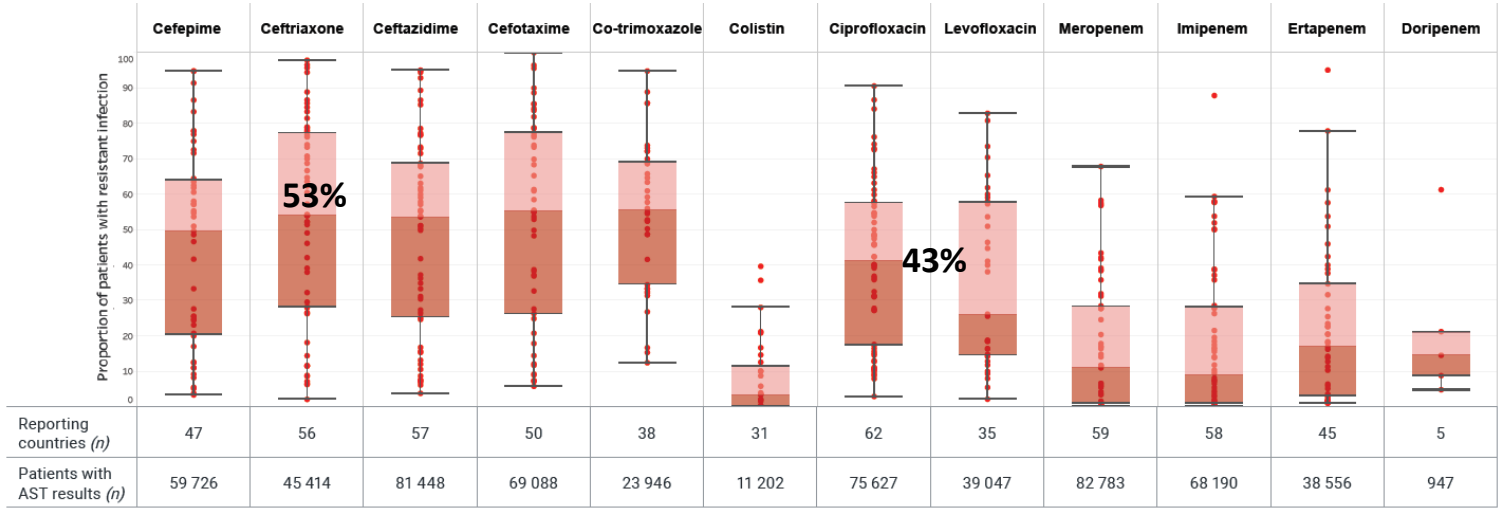
Données mondiales 2019/2022 - GLASS-AMR

E. coli IUs

Données communautaires?
Mélange :
- Ville / hôpital
- Pays faibles / haut revenus

K. pneumoniae IUs





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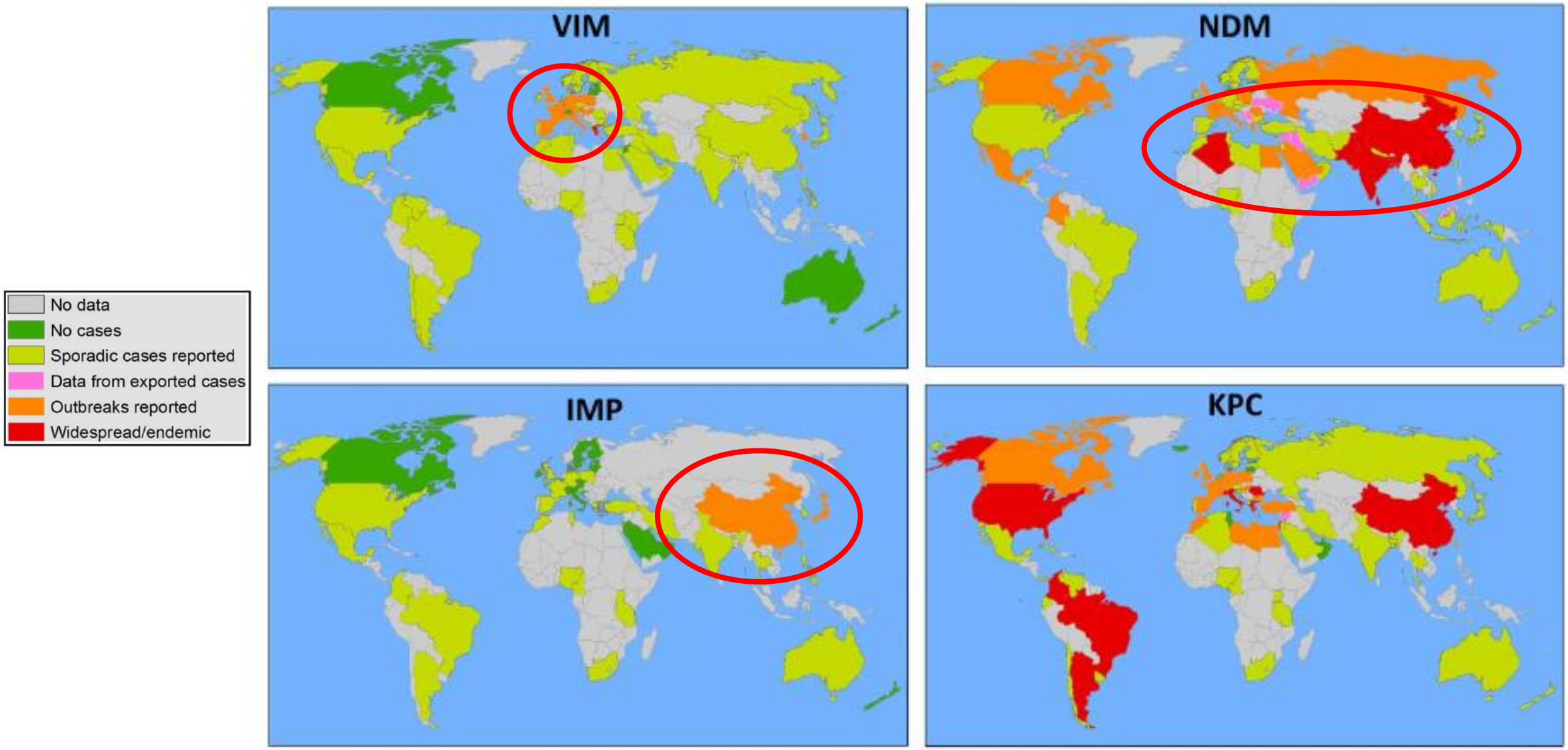
Epidémiologie de la Résistances



Friedman, infection control & hospital epidemiology may 2017, vol. 38, no. 5

Epidémiologie de la Résistances

Données mondiales – OXA-48-Type Carbapenemases

Causes of nosocomial outbreaks in European coutries:

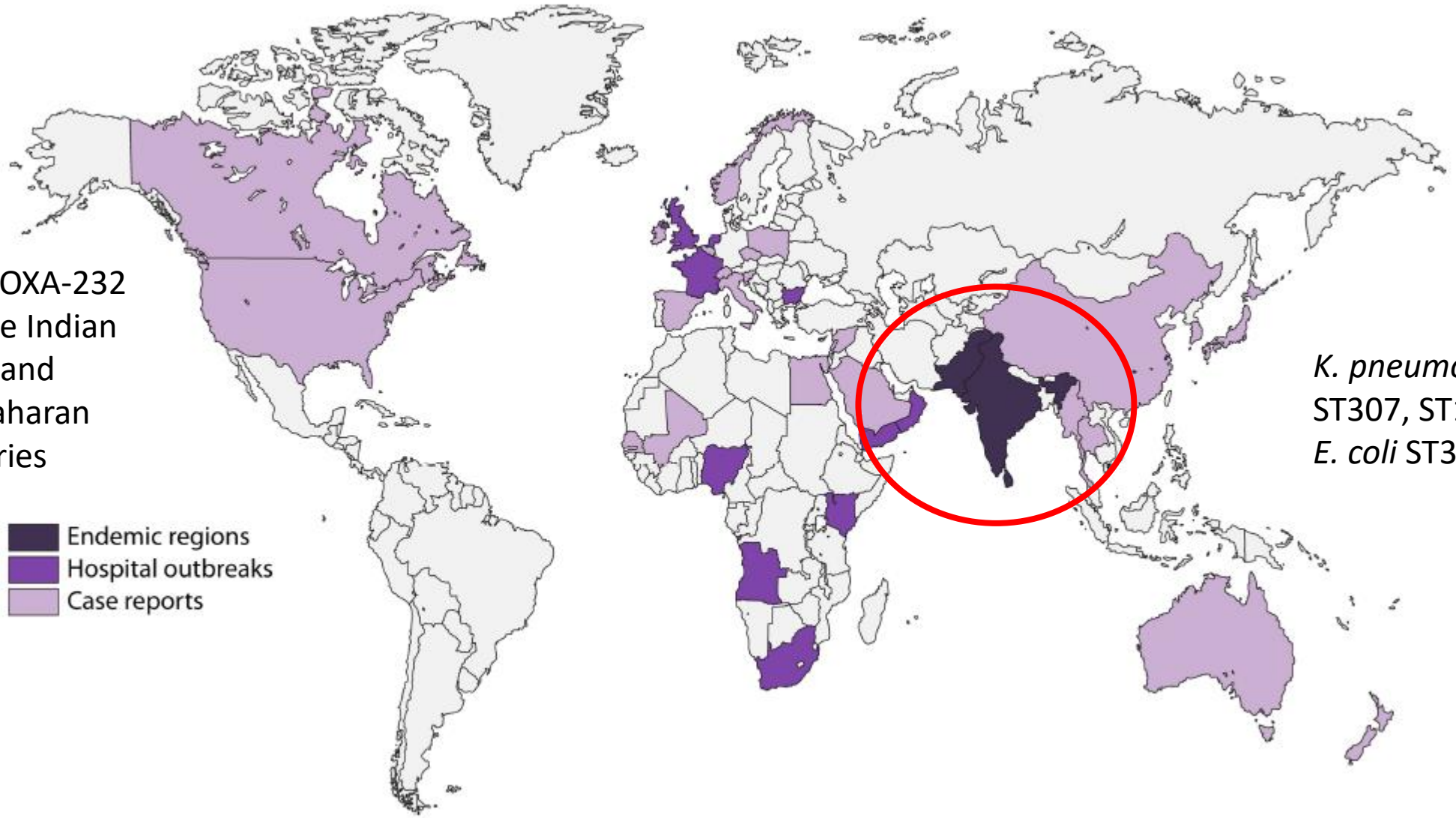
1. OXA-48,
2. OXA-181
3. OXA-232
4. OXA-204
5. OXA-162
6. OXA-244

Pitout Clinical Microbiology Reviews January 2020 Volume 33 Issue 1 e00102-19

Epidémiologie de la Résistances

Données mondiales – OXA-181 Carbapenemases

OXA-181 and OXA-232
Endemic in the Indian subcontinent and certain sub-Saharan African countries



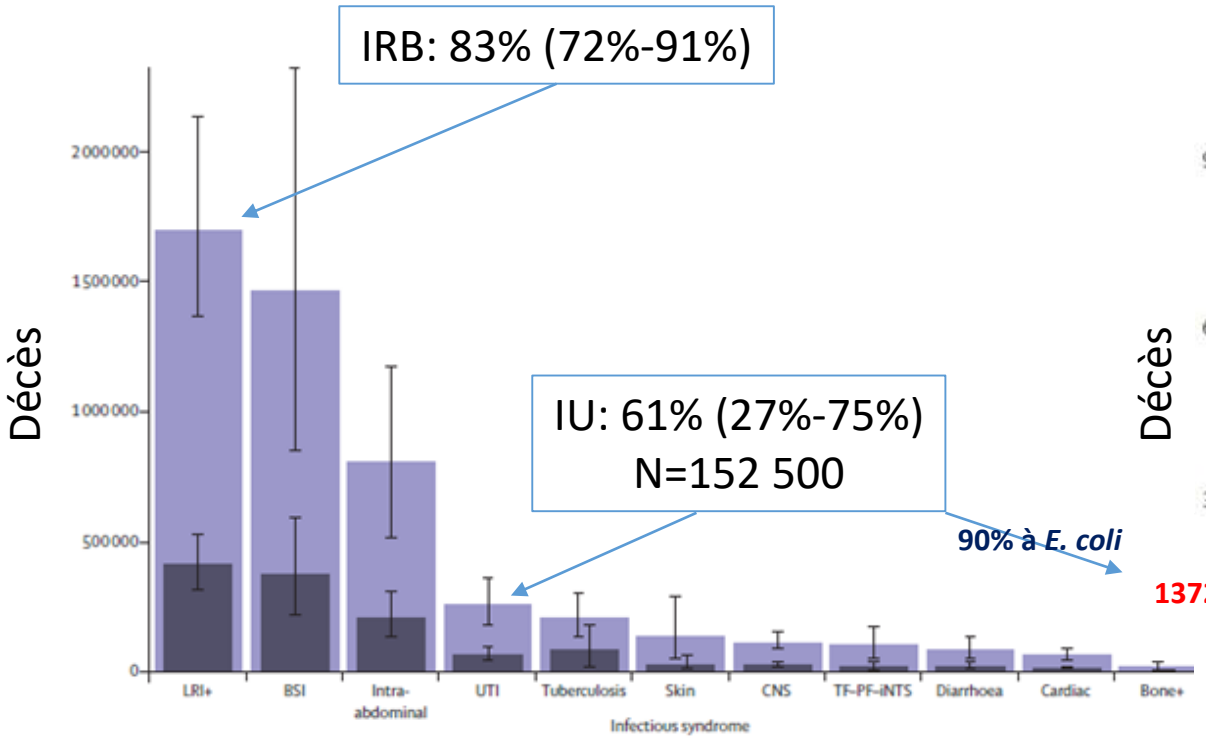
K. pneumoniae ST147, ST307, ST15, ST14
E. coli ST38, ST410

Pitout Clinical Microbiology Reviews January 2020 Volume 33 Issue 1 e00102-19

Epidémiologie de la Résistances

Données mondiales 2019 – Global burden

% estimé d'infections d'origine communautaire

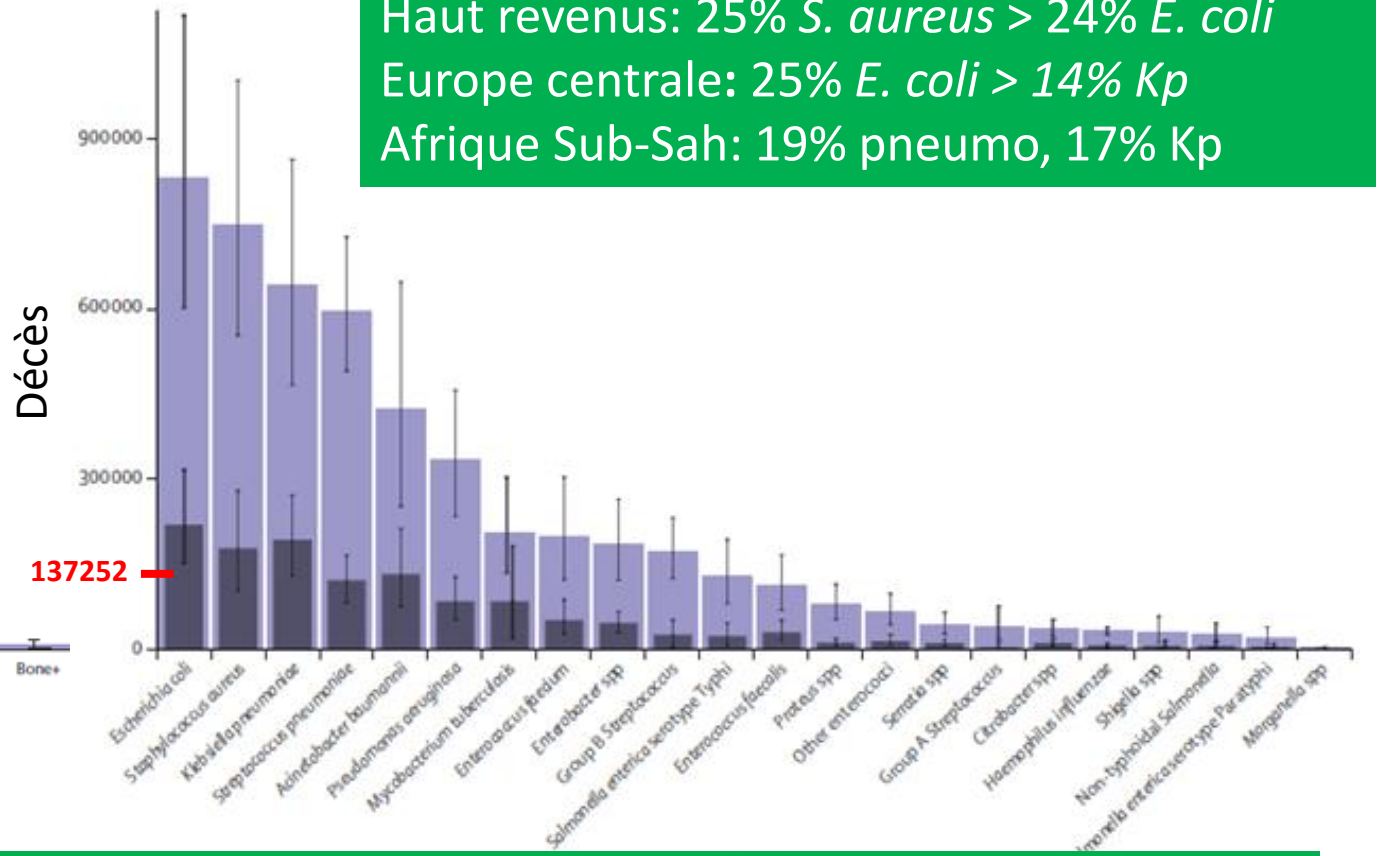


% des décès associés à RATB

Haut revenus: 25% *S. aureus* > 24% *E. coli*

Europe centrale**:** 25% *E. coli* > *14% Kp*

Afrique Sub-Sah: 19% pneumo, 17% Kp



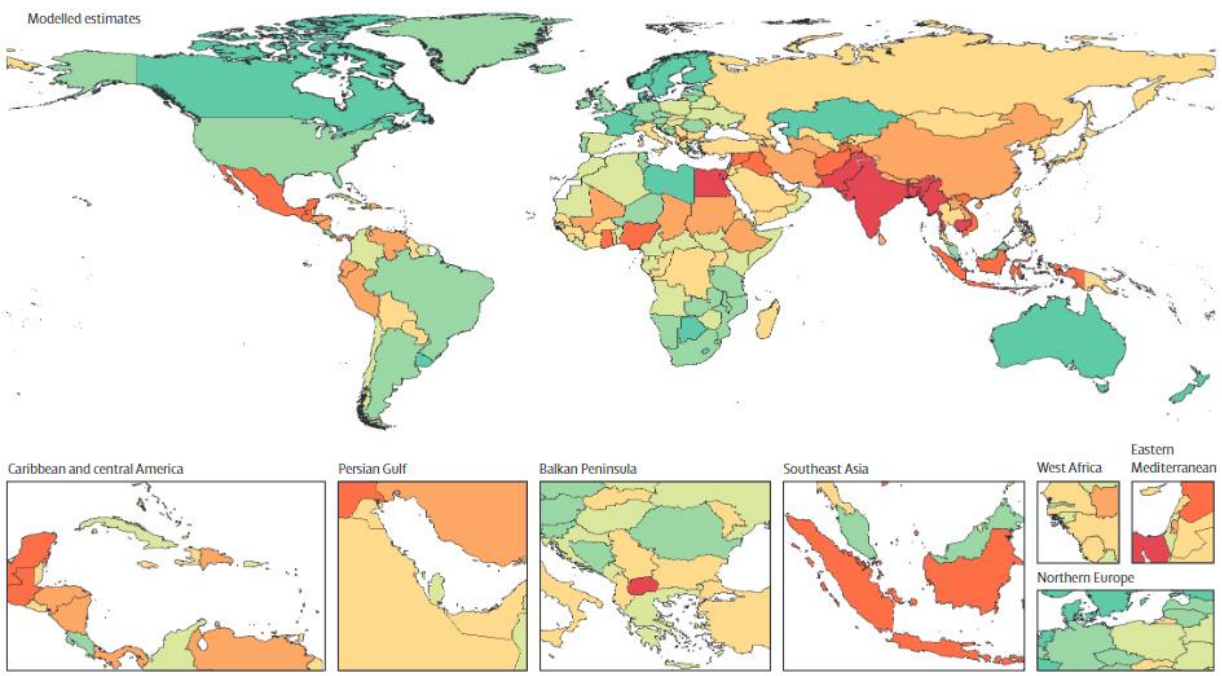
Antimicrobial Resistance Collaborators Lancet
https://doi.org/10.1016/S0140-6736(21)02724-0

Profil de résistance + Site infecté + Communautaire ?

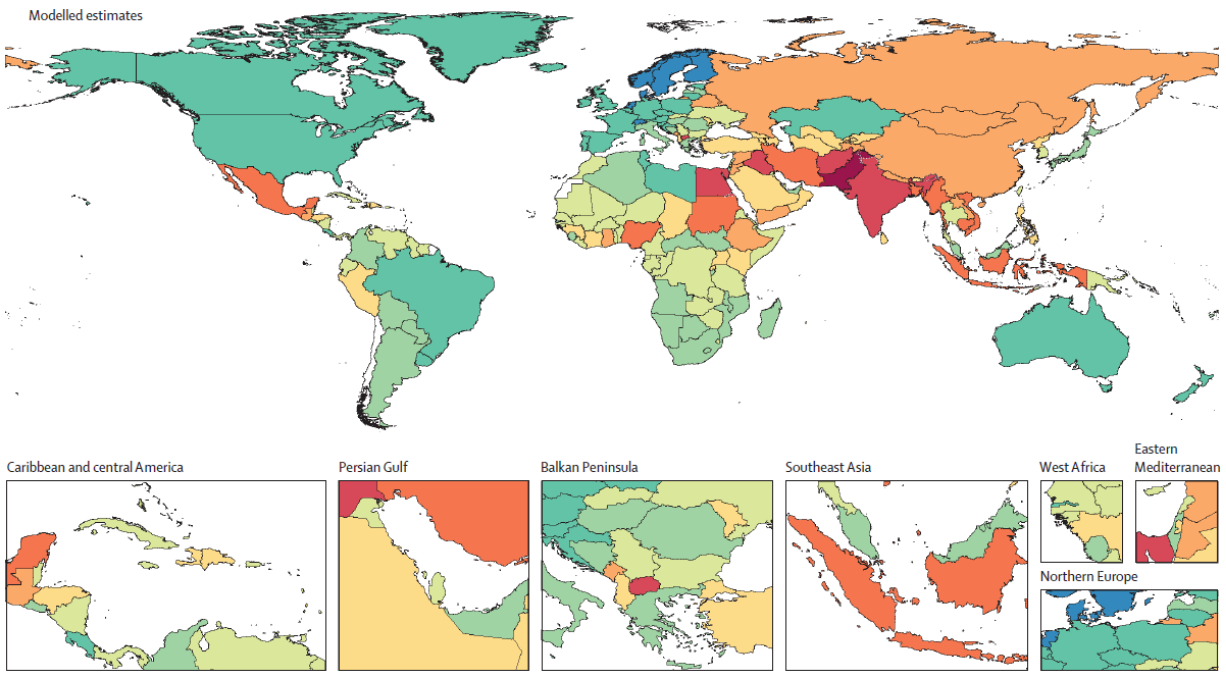
Epidémiologie de la Résistances

Données mondiales 2019 – Global burden

E. coli FQ-R



E. coli C3G-R



Percentage of isolates with resistance

<5%	40 to <50%
5 to <10%	50 to <60%
10 to <20%	60 to <70%
20 to <30%	70 to <80%
30 to <40%	≥80%

Antimicrobial Resistance Collaborators Lancet
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Epidémiologie de la Résistances

Données mondiales 2019 – Global burden

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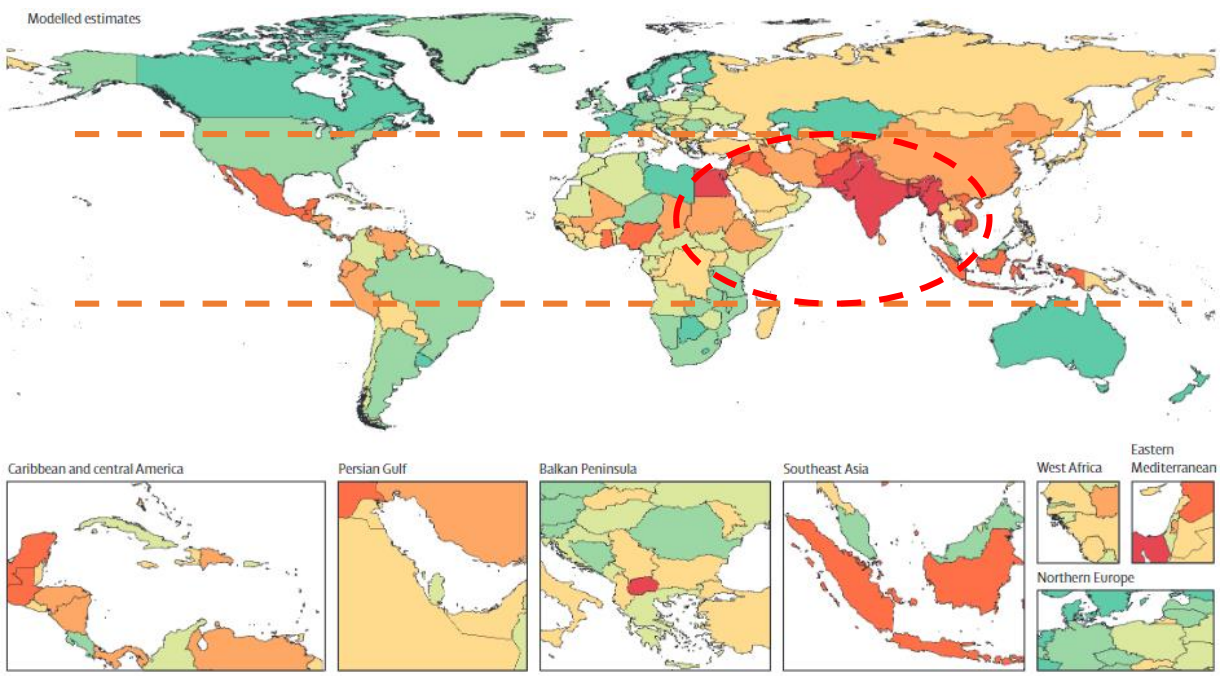
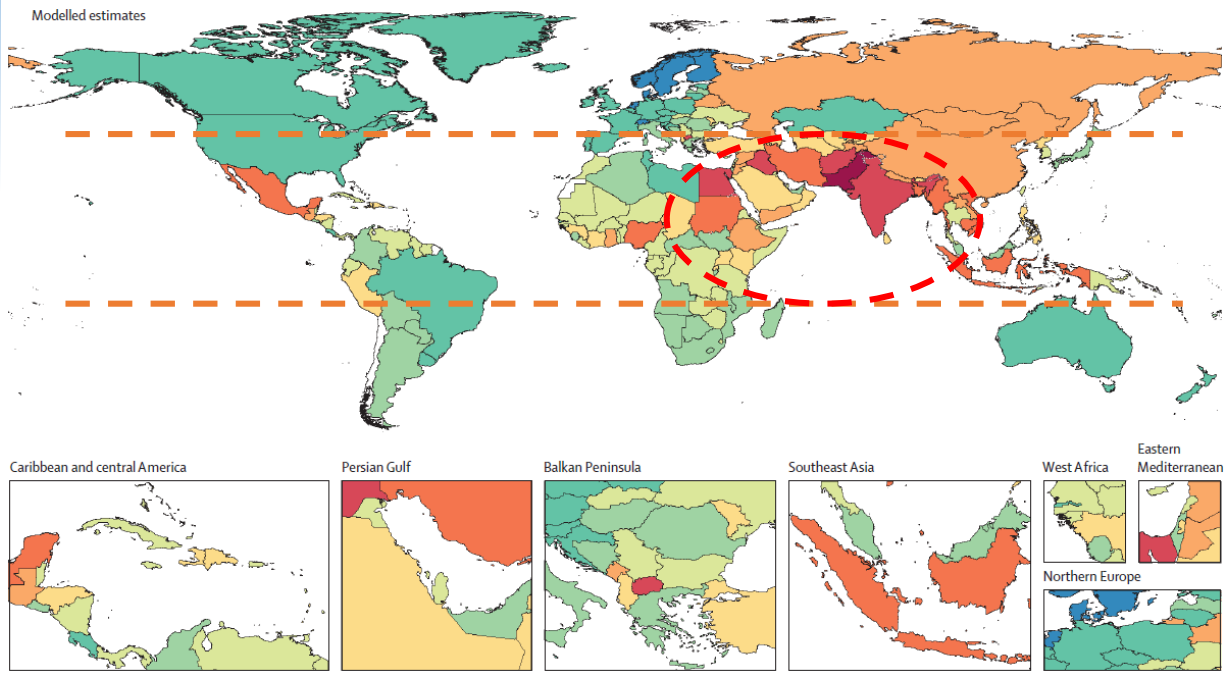


E. coli C3G-R



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Antimicrobial Resistance Collaborators Lancet
https://doi.org/10.1016/S0140-6736(21)02724-0

Epidémiologie de la Résistances

Systèmes de surveillance nationaux

Pays	Nom	Secteur	Cible	*E. coli* C3G-R
Suisse	ANRESIS	Hôp/Com	Toutes bactéries, urine vs autres	2021: 5.8% urine
UK	ESPAUR	Hôp/Com	BSI, CRE, incidence	2019: 15% BSI
England, West Midlands	AmSurv	Hôp/Com	Tous résultats	2013: 5.5% urine
Australie	AURA	Hôp/Com	Tous résultats	2019: 7.8% urine
Hong Kong	CHP	Com	*S.aureus*, *E.coli* urinaire	2020: 11.8% urine

Systèmes de surveillance influencés par:

- L'organisation nationale du système de soins
- Facilité de collecte de données
- Interprétation et signification clinique des résultats

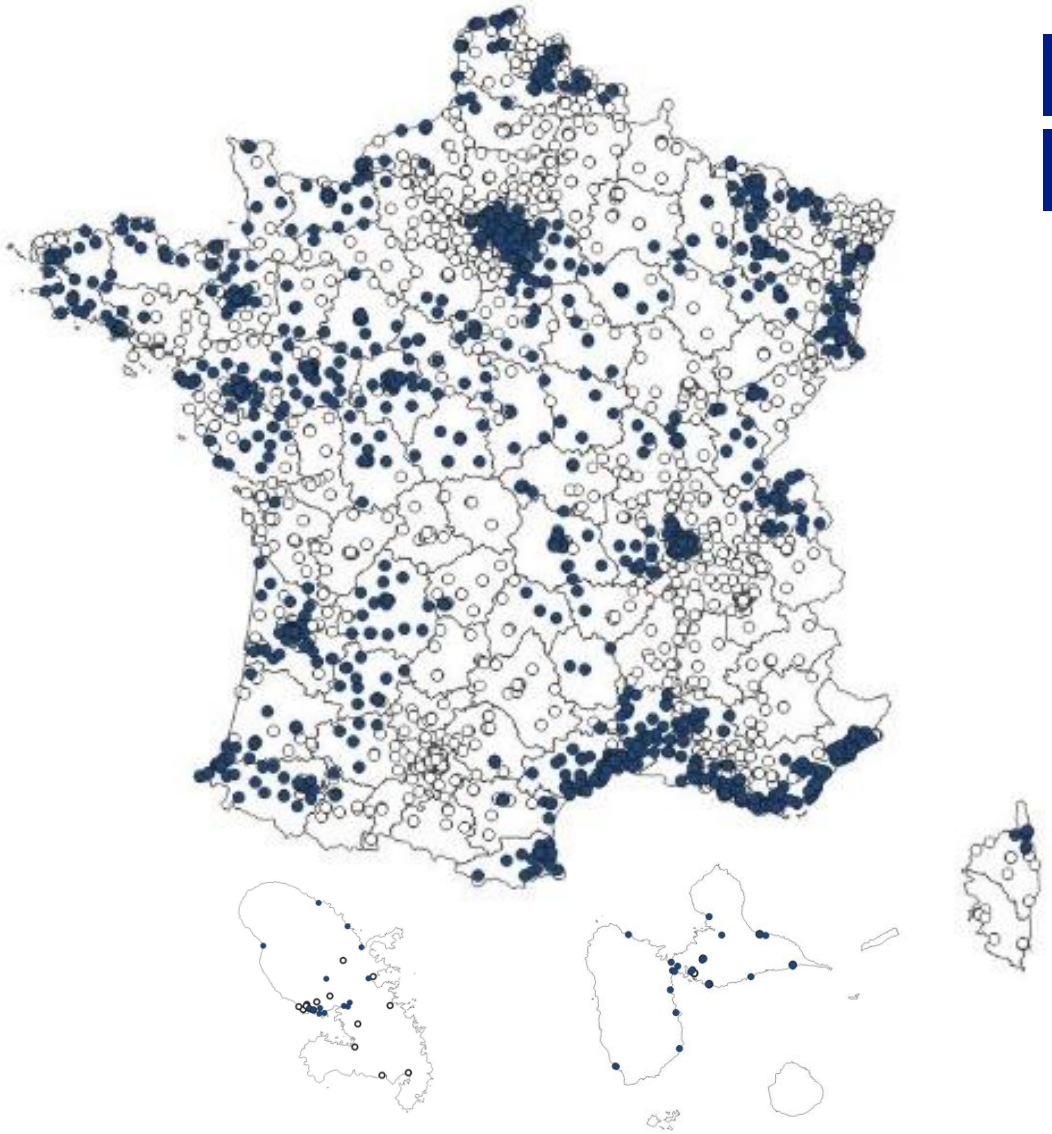
Critères requis pour la surveillance de la résistance aux antibiotiques

- Timely, coût-efficace et durable
- Capacité d'alerte
- Sites acculturé à la surveillance
- Définitions claires
- Collecte de données standardisées
- Différentiation entre types de prélèvements (sonde)
- Méthode microbio standard/commune
- Possibilité de retour vers la souche
- Evaluation du fardeau
- Retro-info régulière avec expertise, vers les bon acteurs
- Résultats orientés vers la clinique/adaptation recos
- Utilisation dans un but de recherché
- Audit et évaluation du système

Chin JAC 2016

Epidémiologie de la Résistances

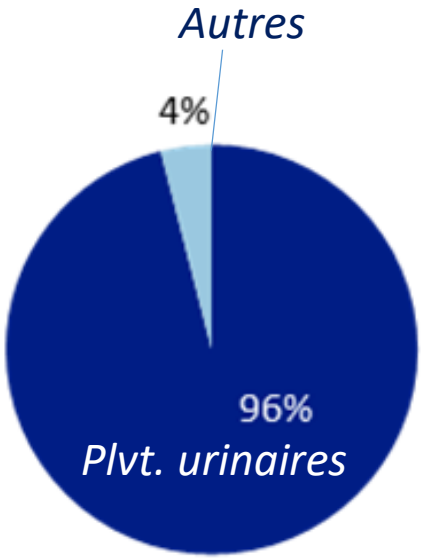
Données françaises –Réseau PRIMO 2021



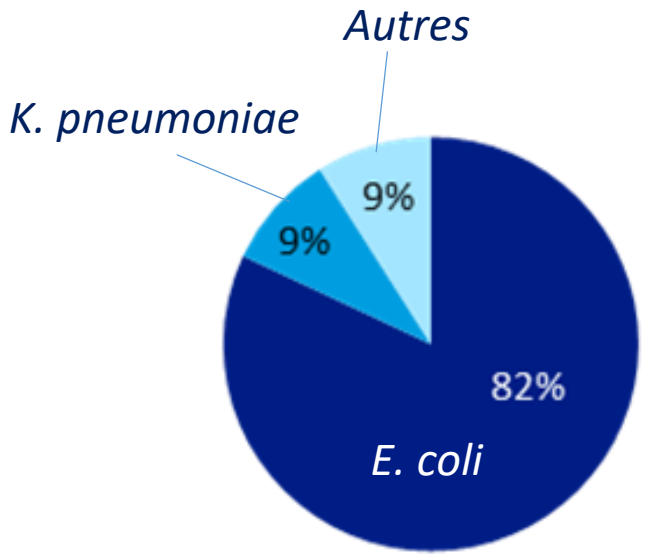
1 564 LABORATOIRES DE BIOLOGIE MÉDICALE

DANS 15 RÉGIONS

759 765 Antibiogrammes

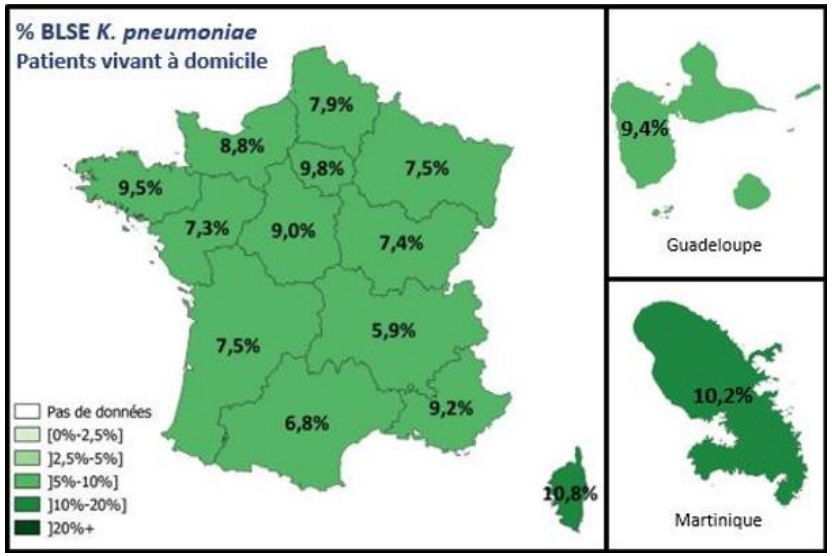


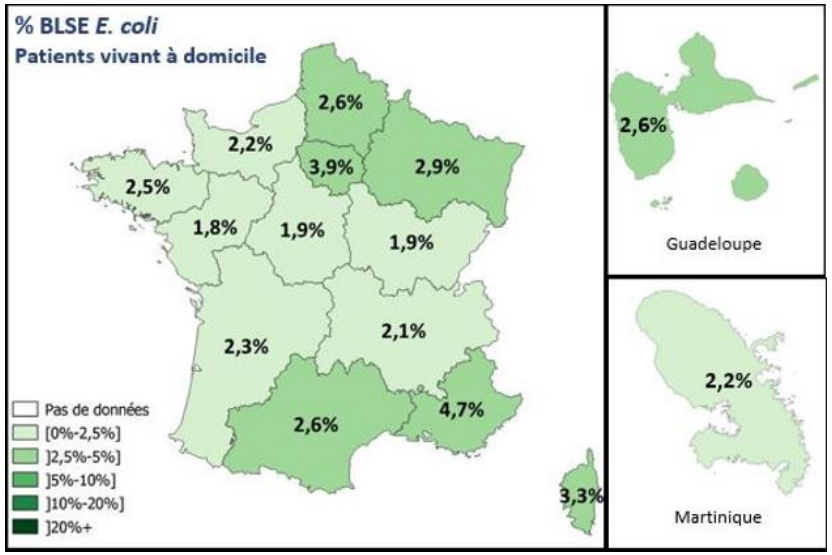
725 704 Atbg urinaires

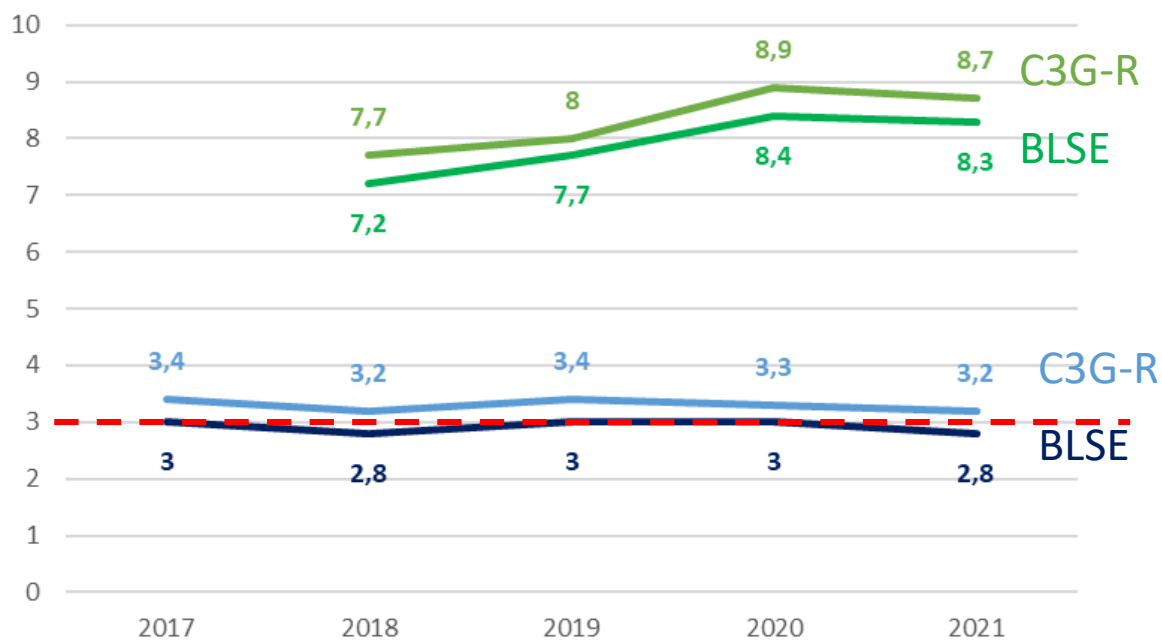


Epidémiologie de la Résistances

Données françaises –Réseau PRIMO 2021







= *K. pneu*

E. coli ↘

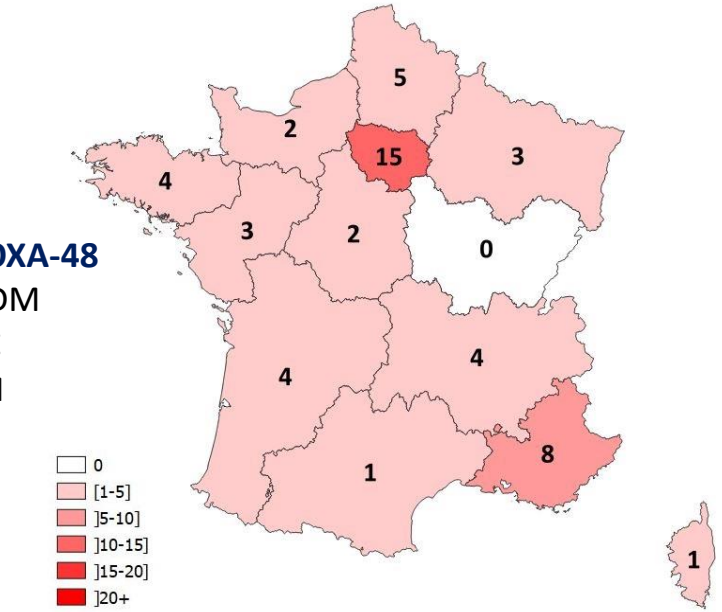
Epidémiologie de la Résistances

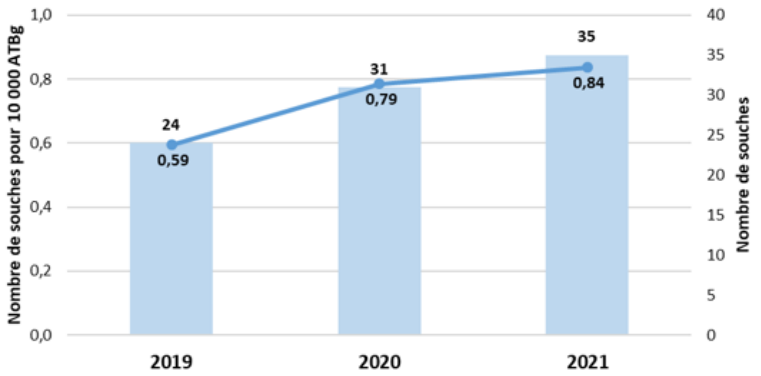
Données françaises –Réseau PRIMO 2021

16:15 - 16:30 Salle 351

E. coli IUs

79% (n=41) OXA-48
13% (n=7) NDM
4% (n=2) KPC
2% (n=1) VIM

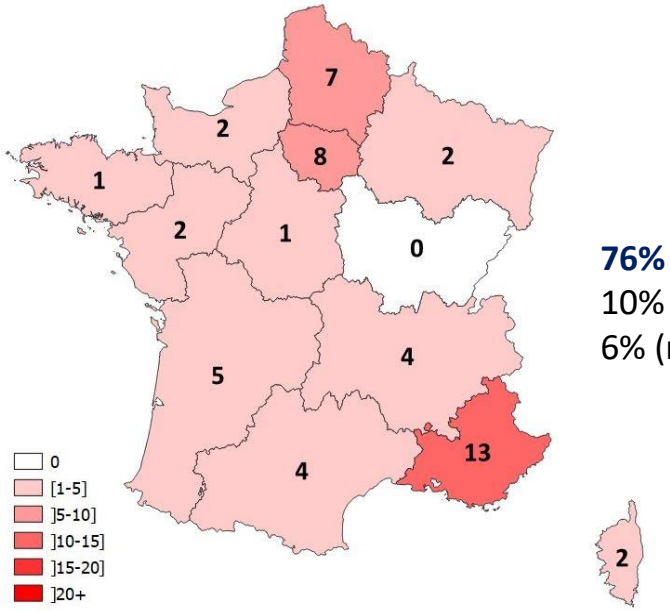


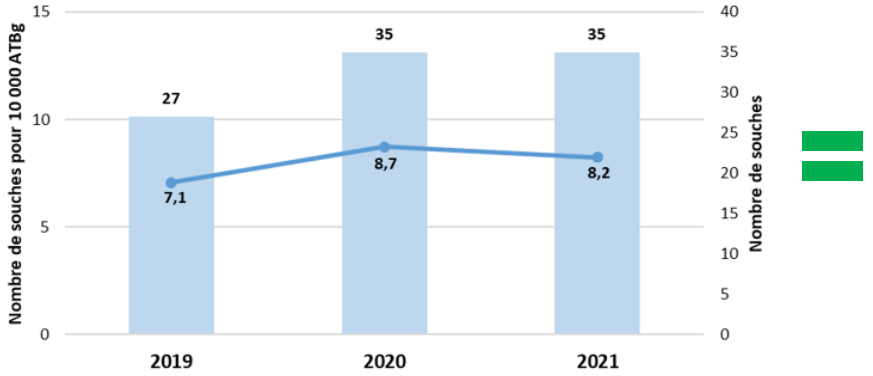


Production de Carbapénémases

K. pneumoniae IUs

76% (n=39) OXA-48
10% (n=5) KPC
6% (n=3) NDM





Epidémiologie de la Résistances

Systèmes de surveillance nationaux

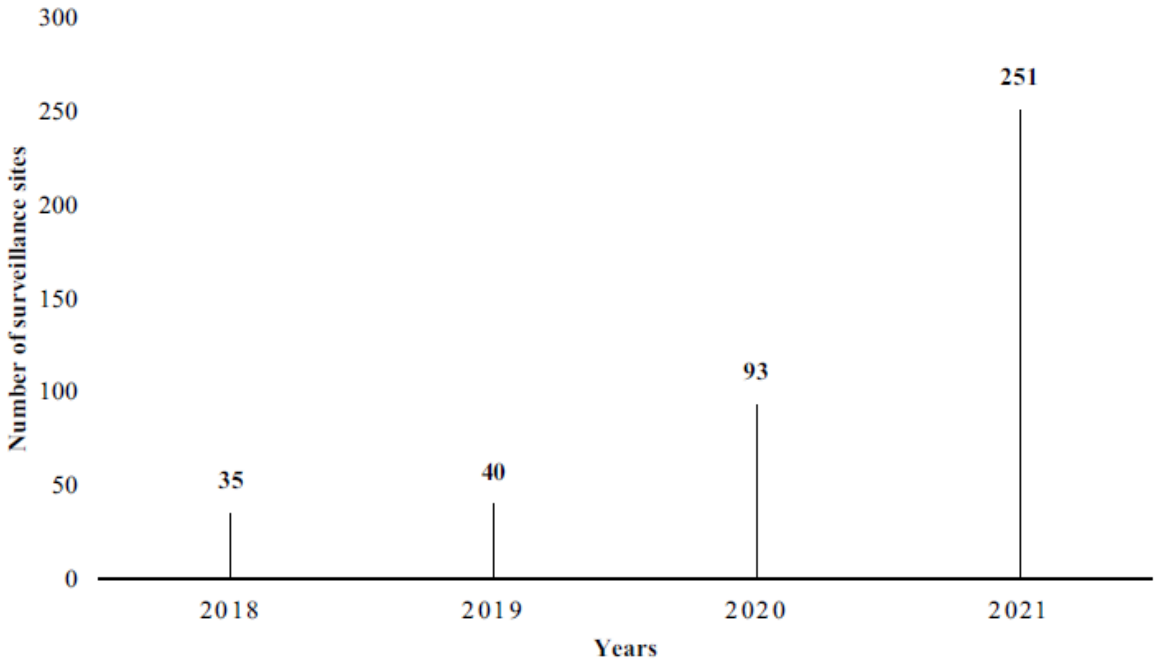
- Objective: To identify, classify and assess gaps in GLASS reporting and NAP implementation in Africa
  - AMR surveillance systems in 47 countries (WHO African region), providing prevalence or incidence, continuously or periodically, with a methodology and performance indicators
- **41 surveillance systems** identified 30 national and 11 transnational
  - **23 national surveillance systems** met the inclusion criteria

Pays	Secteur	*E.coli*	*K.pneu*	*Salmon.*	Autres
Algeria	Hosp/Outpts	X			X
Burundi	Hosp/Outpts	X		X	
Ethiopia	Hosp/Outpts	X	X		X
Gabon	Lab?	X			
Kenya	Hosp/Outpts	X		X	
Madagascar	Lab?	X	X	X	
Malawi	Hosp/Outpts	X		X	
Mali	Hosp/Outpts	X	*X*	X	
Nigeria	Hosp/Outpts	X	X	X	X
South Africa	Hosp/Outpts	X	X	X	X
Uganda	Hosp/Outpts	X	X	X	X
Zambia	Hosp/Outpts	X	X	X	X

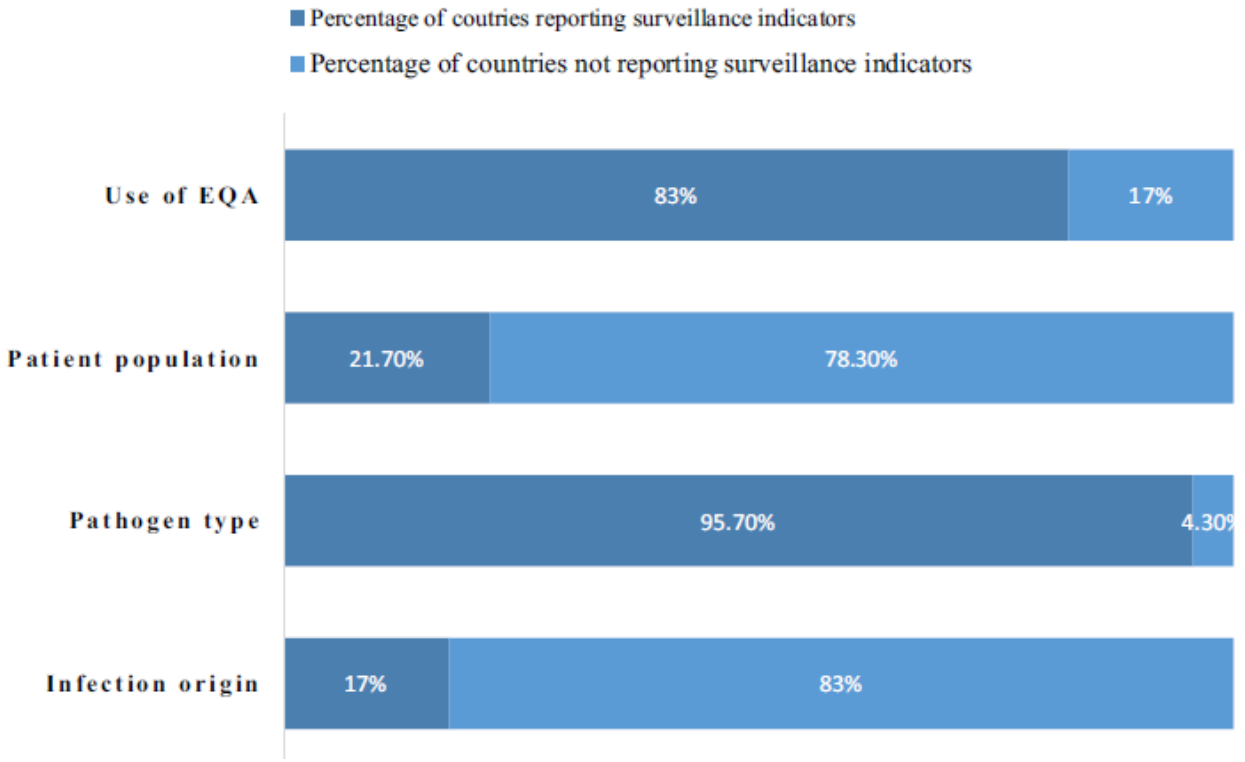
Epidémiologie de la Résistances

Systèmes de surveillance nationaux

Surveillance sites reporting data to GLASS



% of systems reporting important surveillance indicators

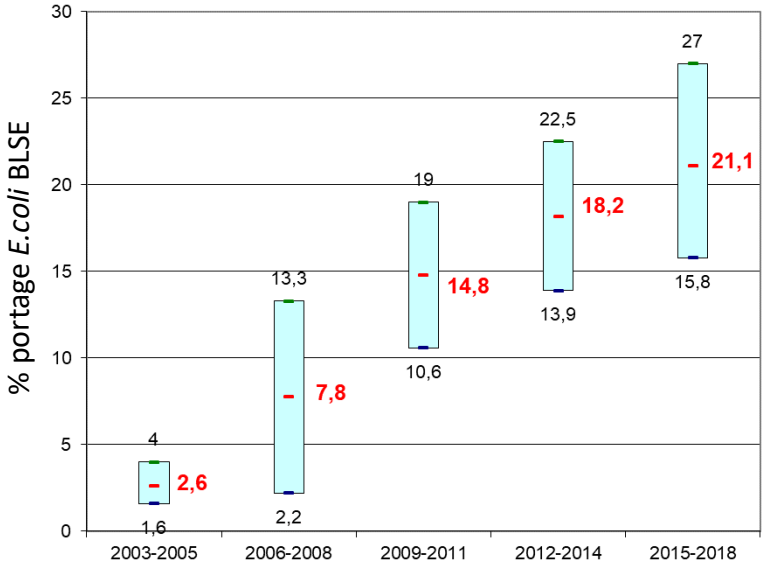


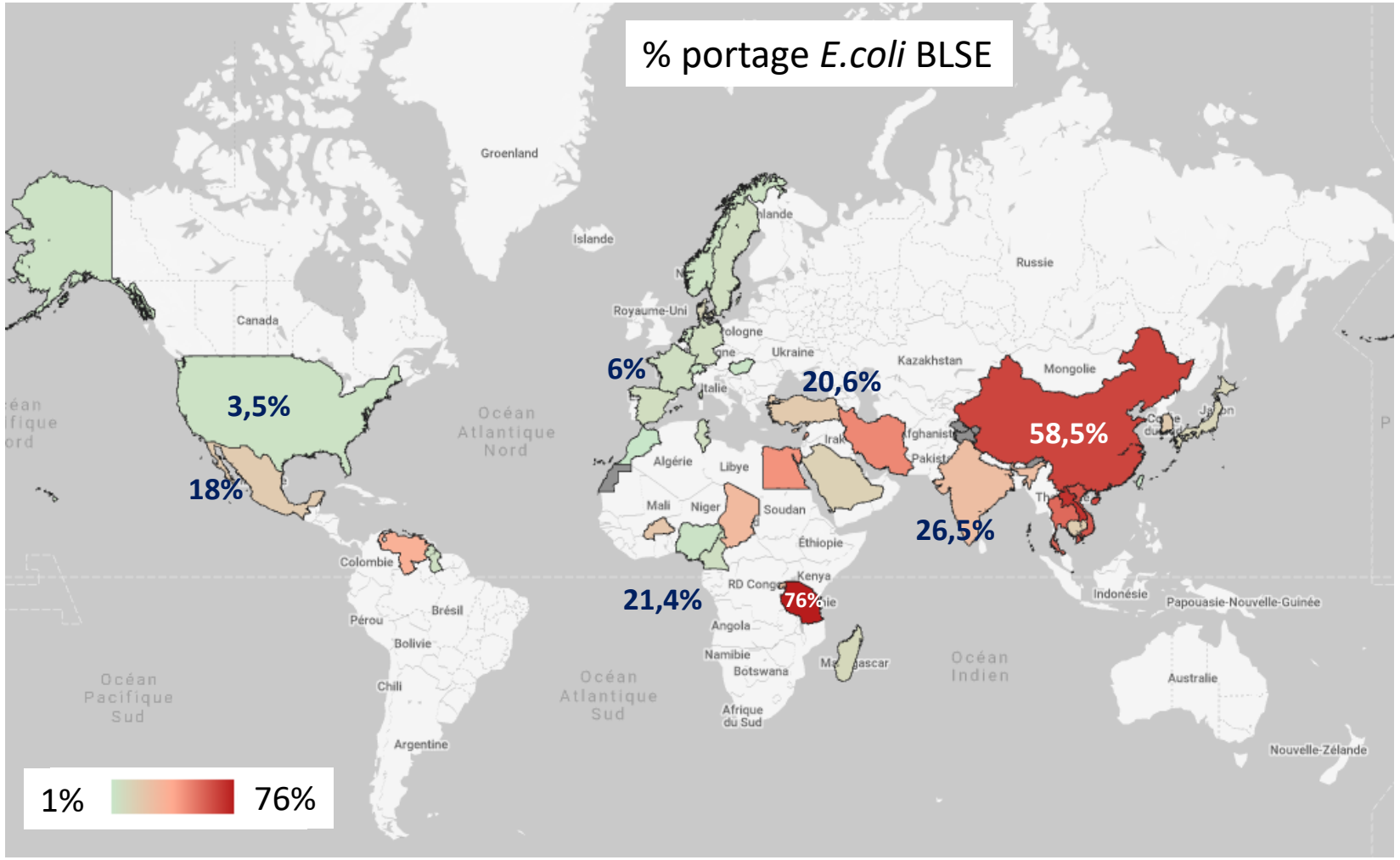
Jovita Okolie JAC AMR 2023

Epidémiologie de la Résistances

Portage digestif d'EBLSE

- % portage fécale *d'E. coli* BLSE chez l'homme dans la communauté
- Revue de 62 articles entre 2000 et 2020





Yihienew M. Bezabih J Antimicrob Chemother 2021

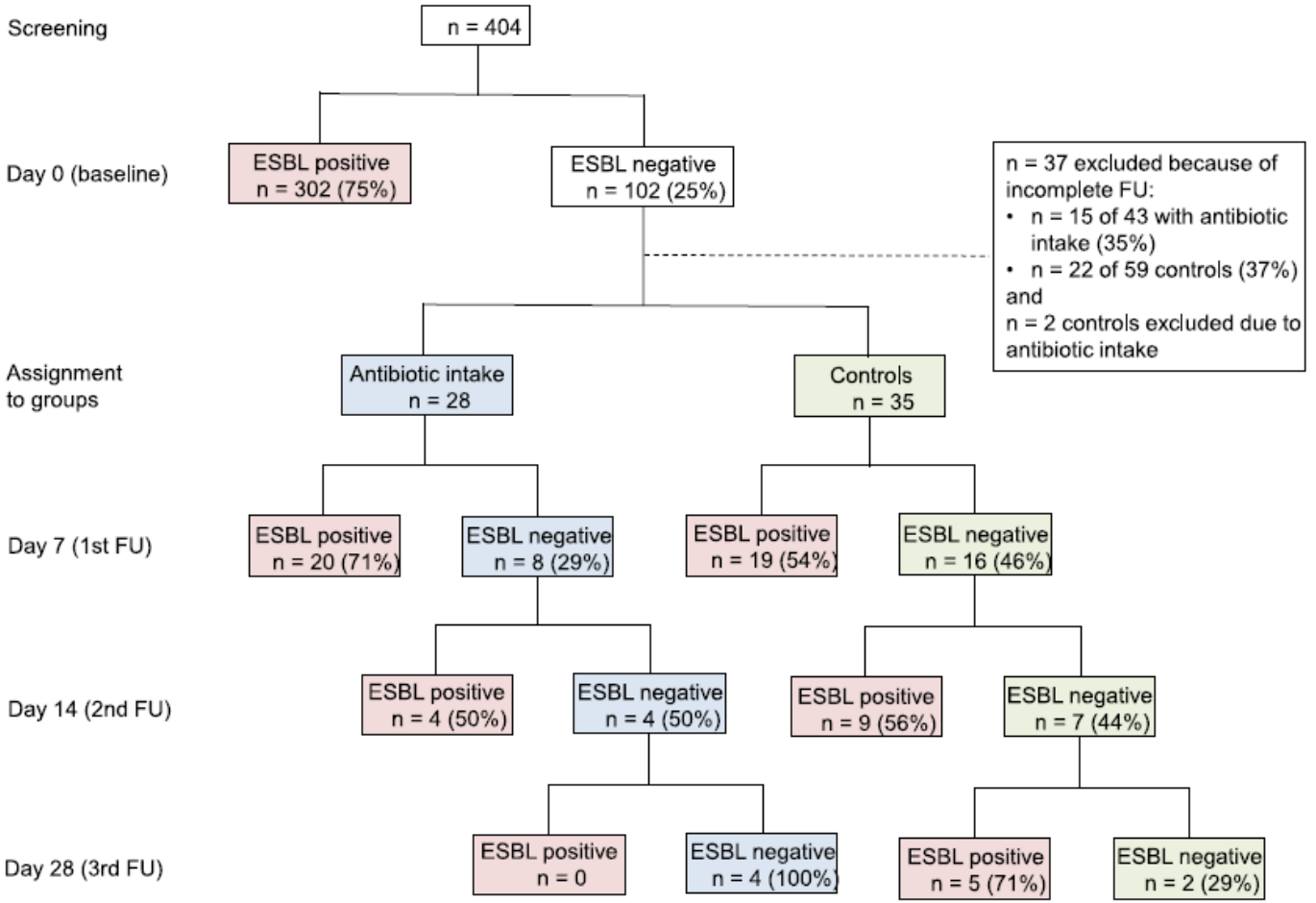
Relation conso/résistances

Impact of antibiotic intake on ESBL carriage in Ghana

Screening for ESBL-PE in 4 independent pharmacies in Kumasi, Ghana

- Case: Pharmacy customers purchasing antibiotics
- Control: customers buying non-antibiotic drugs
- Participants negative for ESBL-PE provided follow-up swabs for up to 28 days

Results suggest that the real incidence of intestinal ESBL-PE in individuals in Kumasi, Ghana, may reach approximately 90%

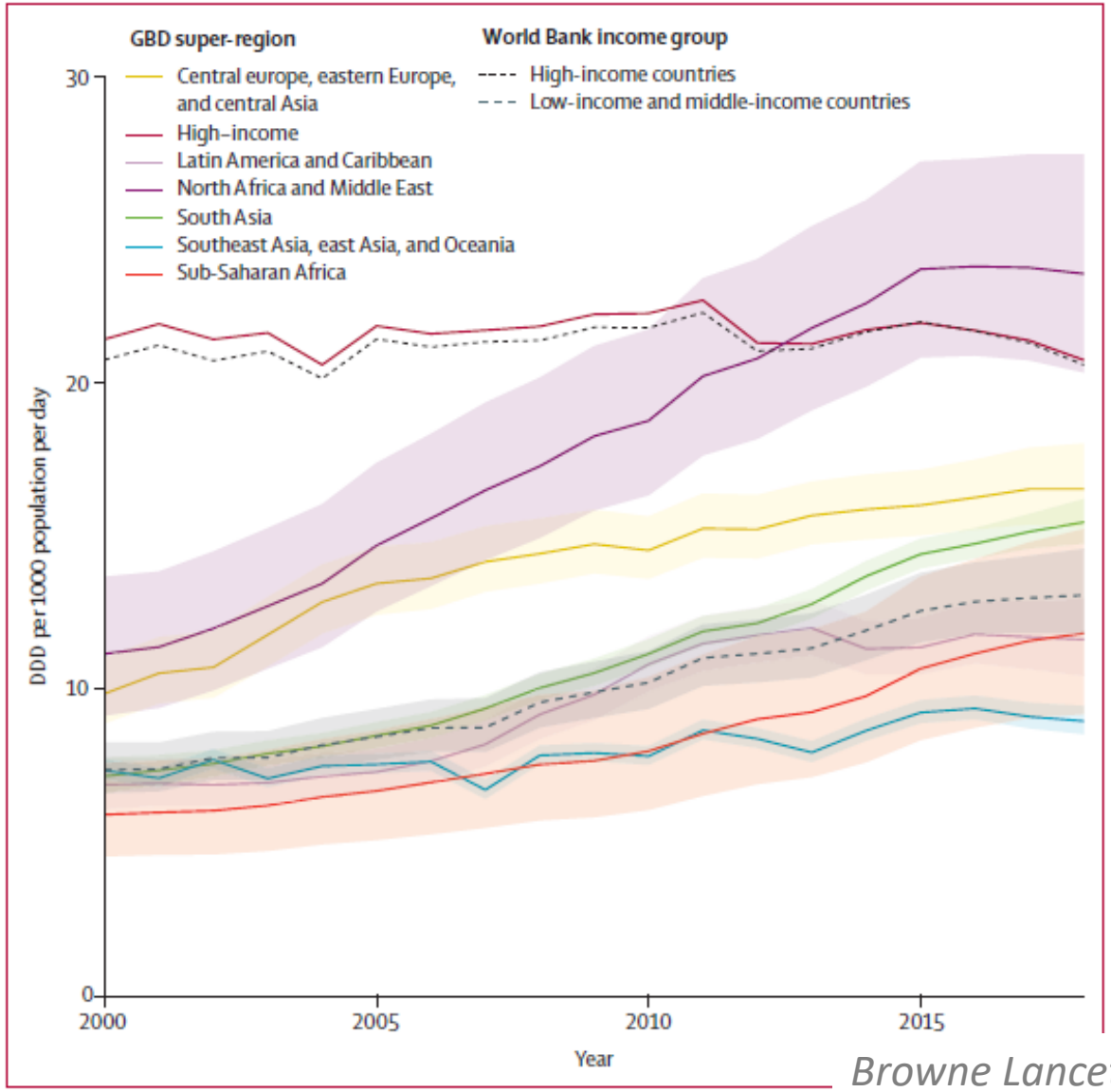


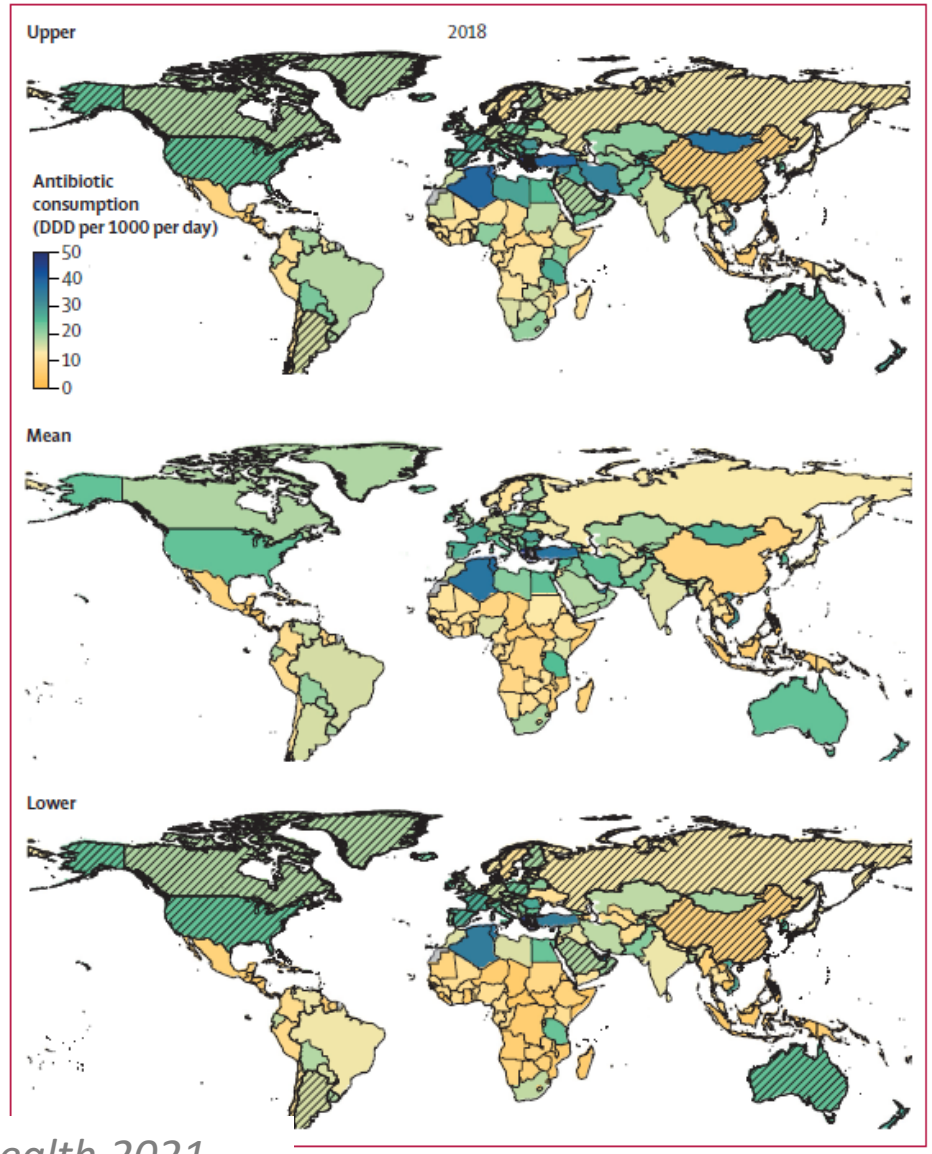
Heinemann CMI 2023

Quelles sont les facteurs associés à la résistance en communauté ?

Consommation des antibiotiques

Tendances mondiales





Browne Lancet Plan Health 2021

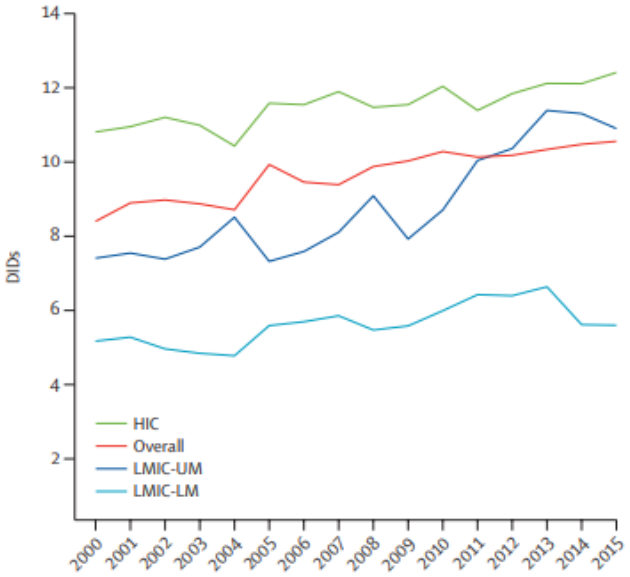
Consommation des antibiotiques

Tendances mondiales

Access

First-line antibiotics
Low resistance potential
e.g. Amoxicillin, Nitrofurantoin etc.

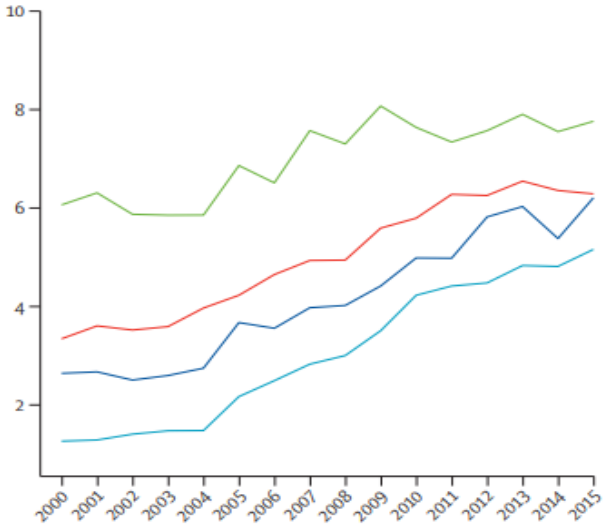
48

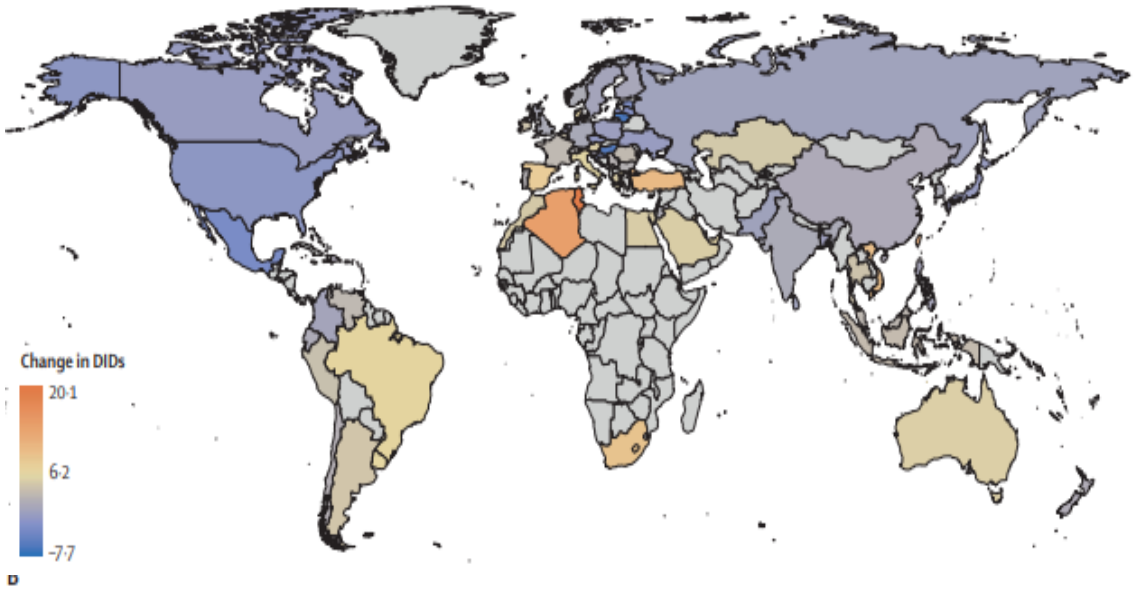


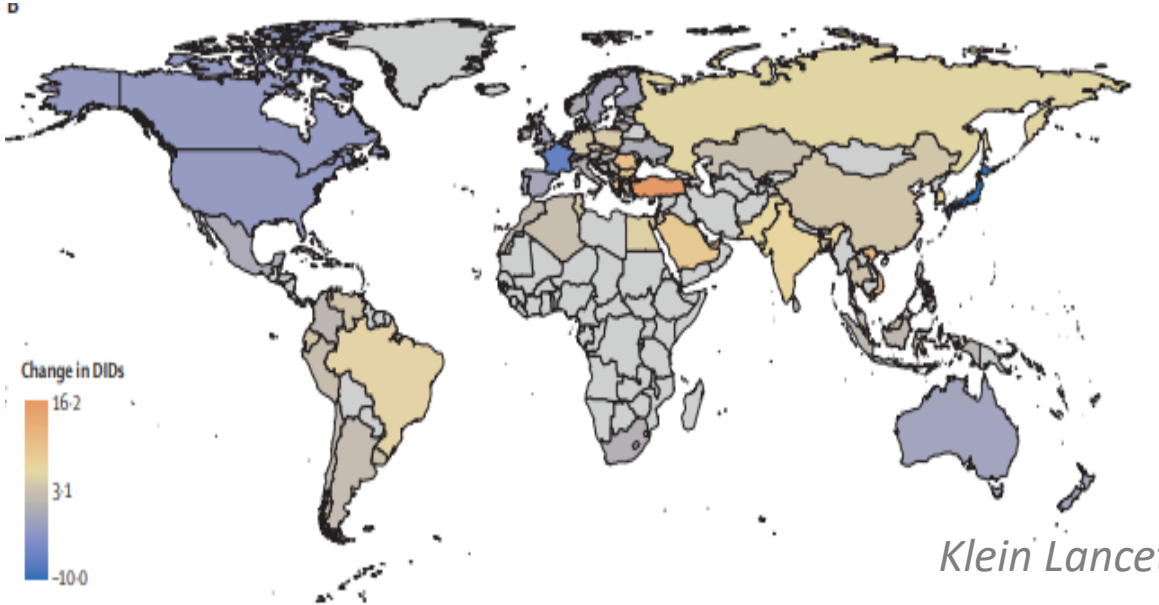
Watch

Critically important antibiotics
High resistance potential
e.g. Quinolones, Macrolides etc.

110



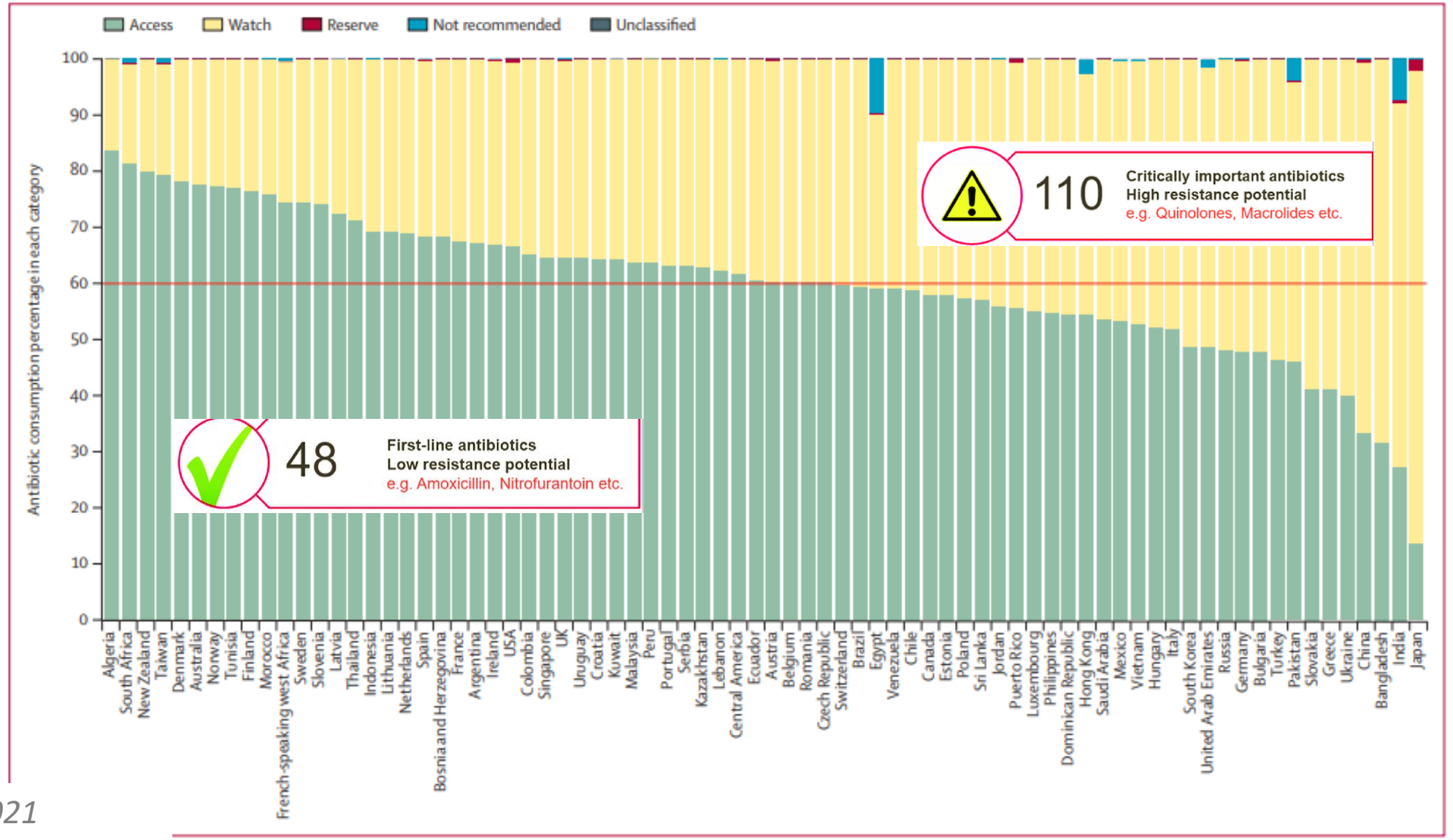




Klein Lancet ID 2021

Consommation des antibiotiques

Tendances mondiales

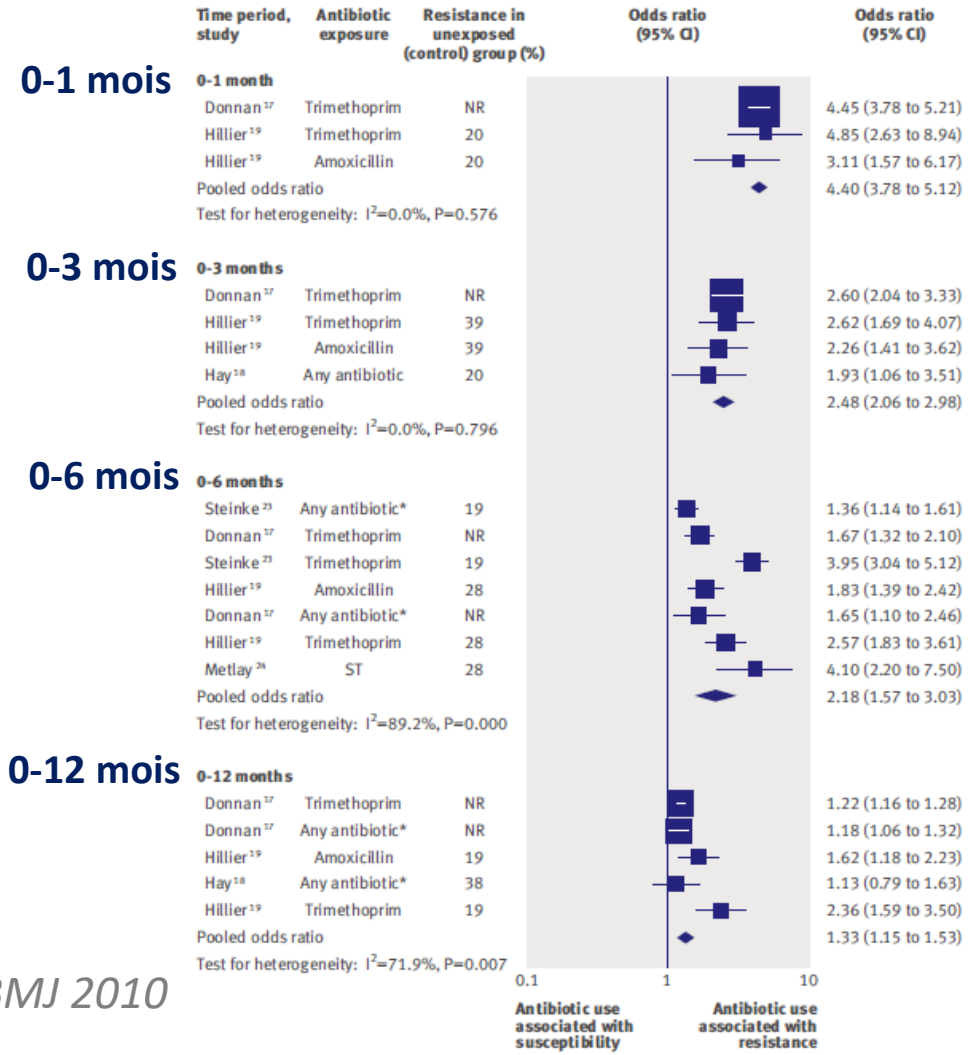


Klein LID 2021

Relation conso/résistances

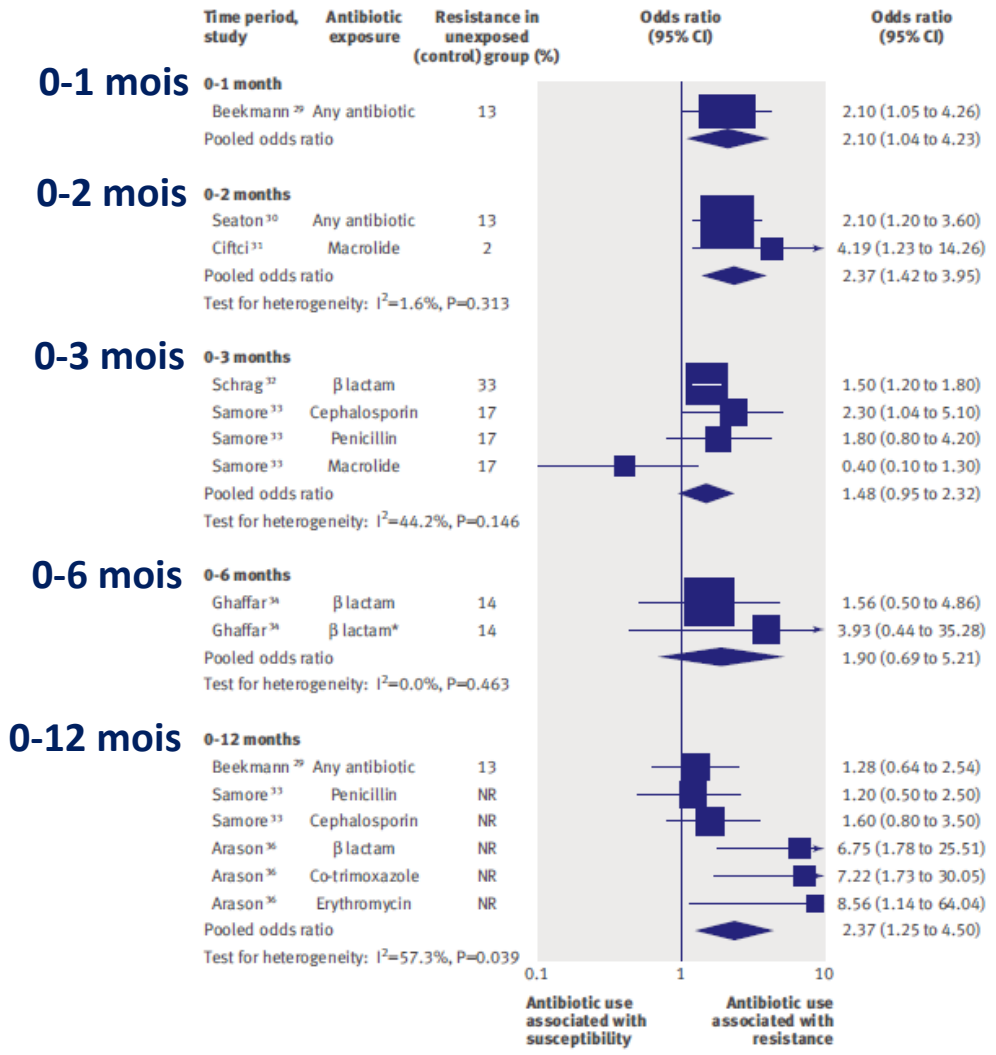
Méta-analyse 24 études individuelles en soins primaires

E. coli urinaires



Costelloe BMJ 2010

Prélèvements respiratoires



Relation conso/résistances

Voisinage et risque de résistance

Influence des consommations de fluoroquinolone du voisinage sur le risque individuel d'infection urinaire à *E.coli* résistant

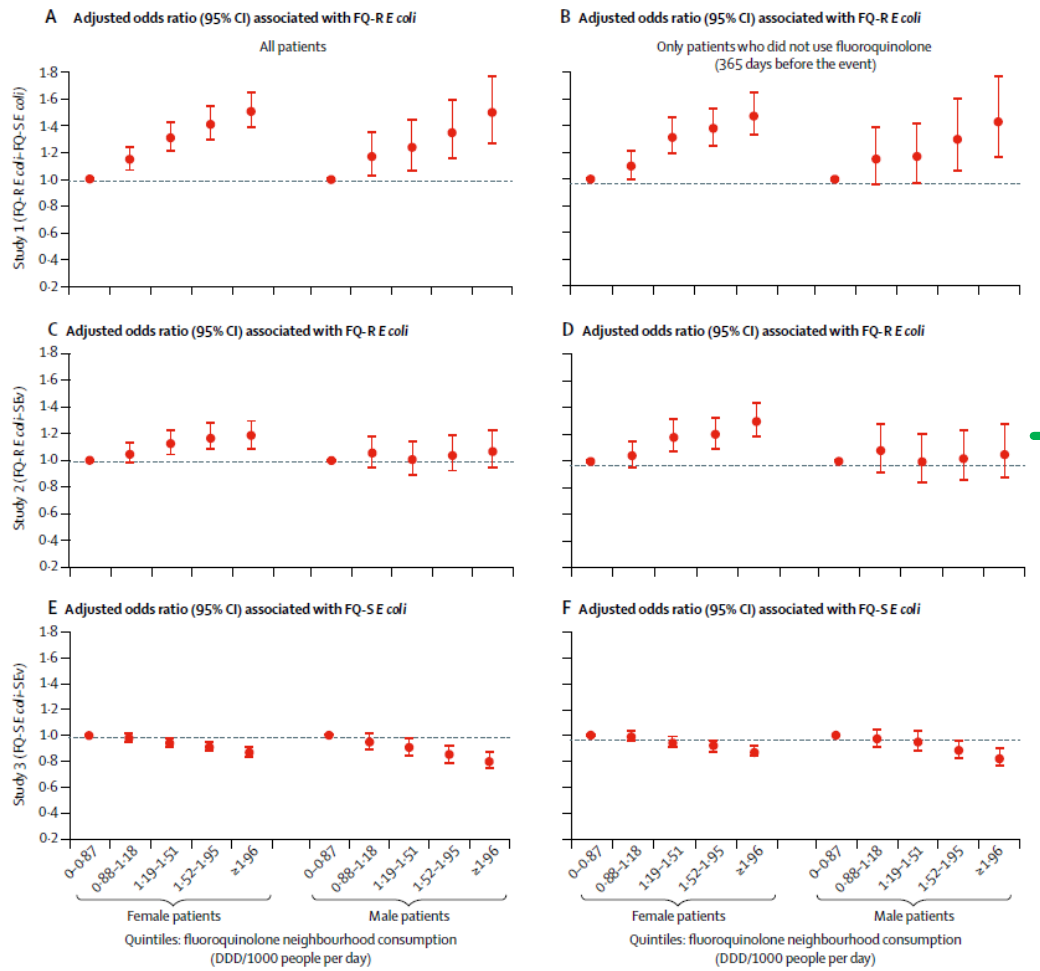
- **Données :** 2010-2014
  - Système de santé Clalit (CHS): 53% de la population Israélienne, 14 hôpitaux, >1400 cabinet de ville, 53% of the total population
- **Design :**
  - Etude 1: Patients ECBU+ à *E. coli* **R-FQ** vs patients ECBU *E. coli* **S-FQ**
  - Etude 2*:* Patients ECBU+ à *E. coli* **R-FQ** vs patients ECBU stérile
  - Etude 3: Patients ECBU+ à *E. coli* **S-FQ** vs patients ECBU stérile
  - Analyse univariée, multivariée et modèle hiérarchique
- **Définition d'IU à *E.coli* communautaire** :
  - ECBU+ à *E.coli* >30 jours après une hospitalisation ou ECBU

Marcelo Low Lancet Infect Dis 2019; 19: 419–28

Relation conso/résistances

Voisinage et risque de résistance

ORa de *E.coli*-R et S associé à la conso voisinage



- Consommation individuelle de FQ associée à un risque > d'*E.coli* R-FQ
  - R: 58% vs S: 20% vs stérile 16%
  - Effet dose - réponse
  - Femme en quartier dense
- Idem pour la consommation du voisinage
  - Indépendamment de l'utilisation personnelle passée et des FdR d'ATBR

Marcelo Low Lancet Infect Dis 2019; 19: 419–28

Relation conso/résistances

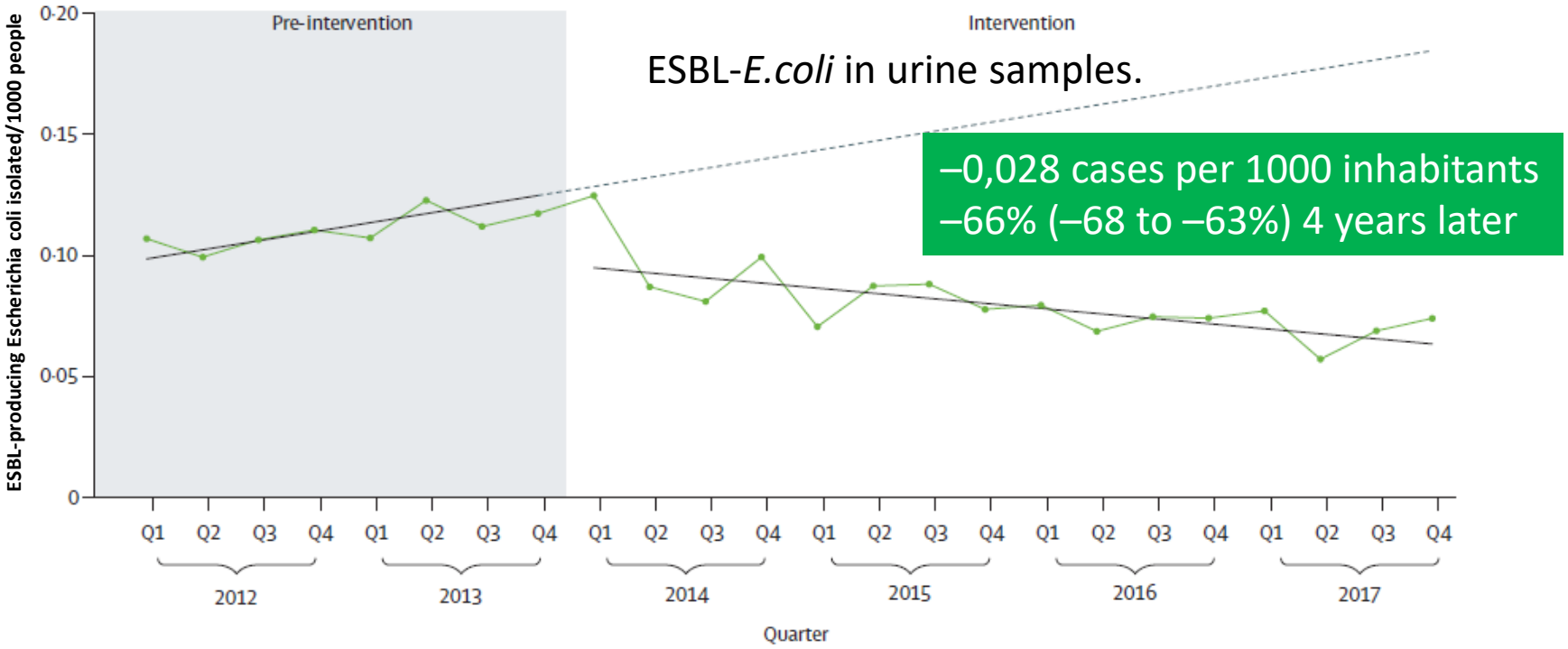
Initiative PIRASOA-FIS en Espagne

- 214 primary health centres of four primary health-care districts in Andalusia
- Local multidisciplinary, multimodal, education-based ASP

  → one-to-one educational interviews (n=5 per prescriber per study year)

Inappropriate ATB prescribing:
- 2014: 36,5%
- 2017: 26,9%

–15,9% ciprofloxacin
–22,6% cephalosporins
22,2%, amoxicillin
6,1% fosfomycin trometamol



Germán Peñalva Lancet Infect Dis 2020; 20: 199–207

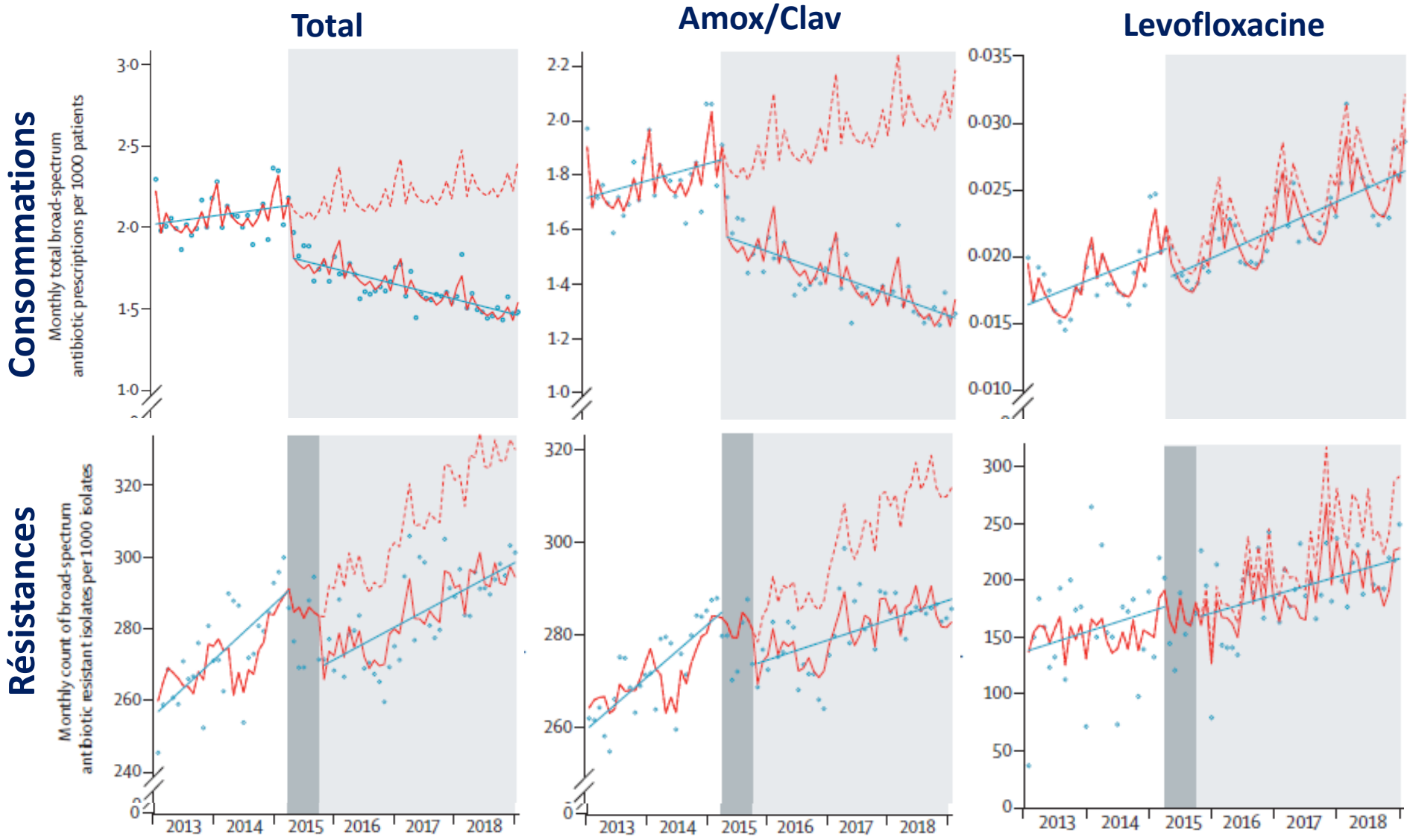
Relation conso/résistances

Impact Quality Premium 2013-2018

6882 (99.3%) GPs
7002756 prescriptions
138787 *E coli* bactériémies

Analyse écologique
Séries chrono et GEE
Effet immédiat NS
Effet à 39 mois: 0.047

Conclusion: Interventions de BUA insuffisantes pour maîtriser la RATB

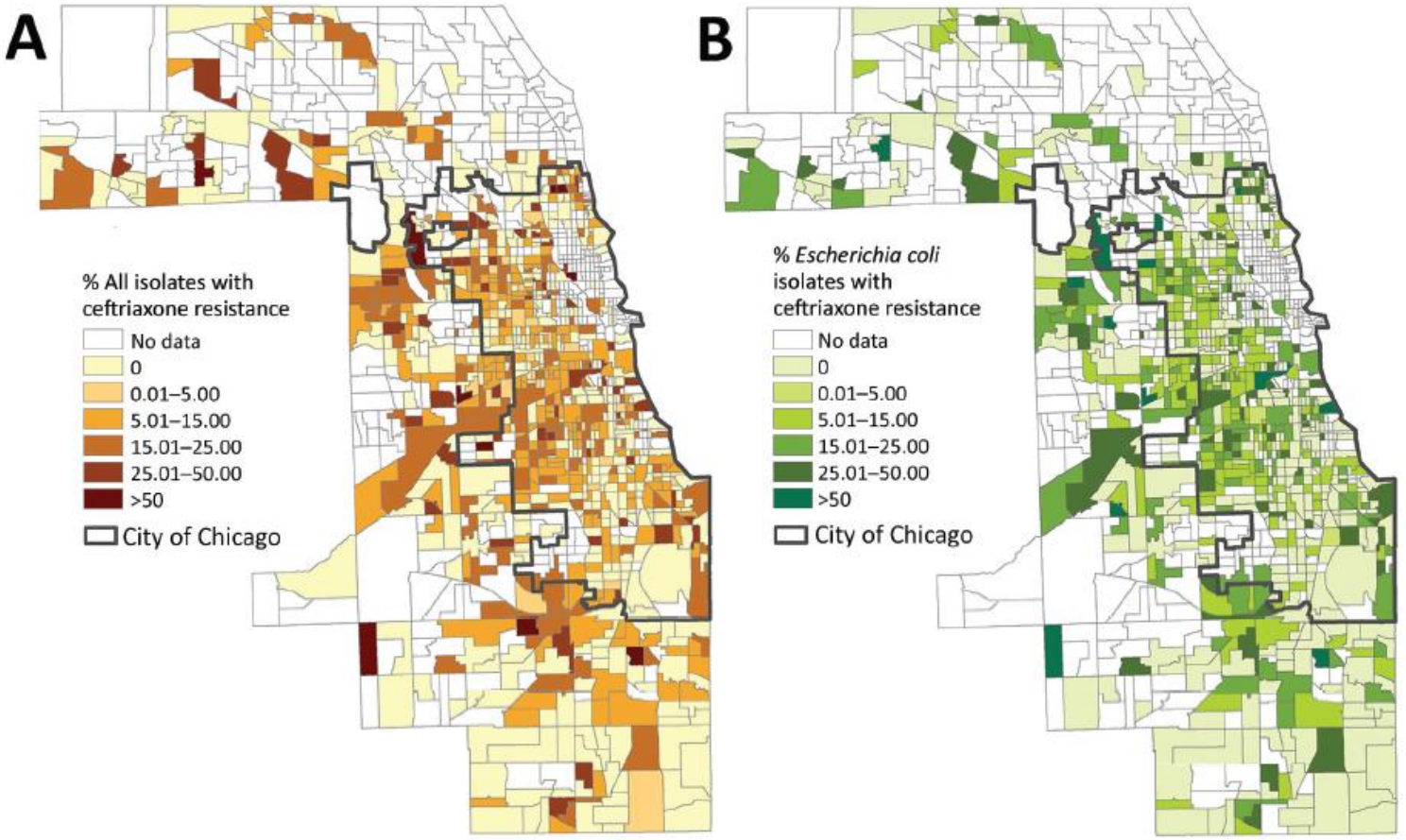


Aliabadi LID 2021

Facteurs associés infections E-C3GR

Analyse spatiale, écologique et épidémiologique

% de souches Ceftriaxone-R à Chicago



Sarda Emerg. ID 2021

Analyse bivariée des facteurs associés

	OR	p
Non-Hispanic White	0.99 (0.99–1.00)	0.44
Non-Hispanic Black	0.98 (0.98–0.99)	<0.01
Hispanic population	1.03 (1.02–1.03)	<0.01
Foreign-born	1.04 (1.03–1.05)	<0.01
Households below poverty	0.99 (0.98–1.00)	0.24
Overcrowding	1.25 (1.04–1.53)	0.02
Uninsured	1.08 (1.06–1.11)	<0.01

Sources attribuables d'*E. coli*-BLSE

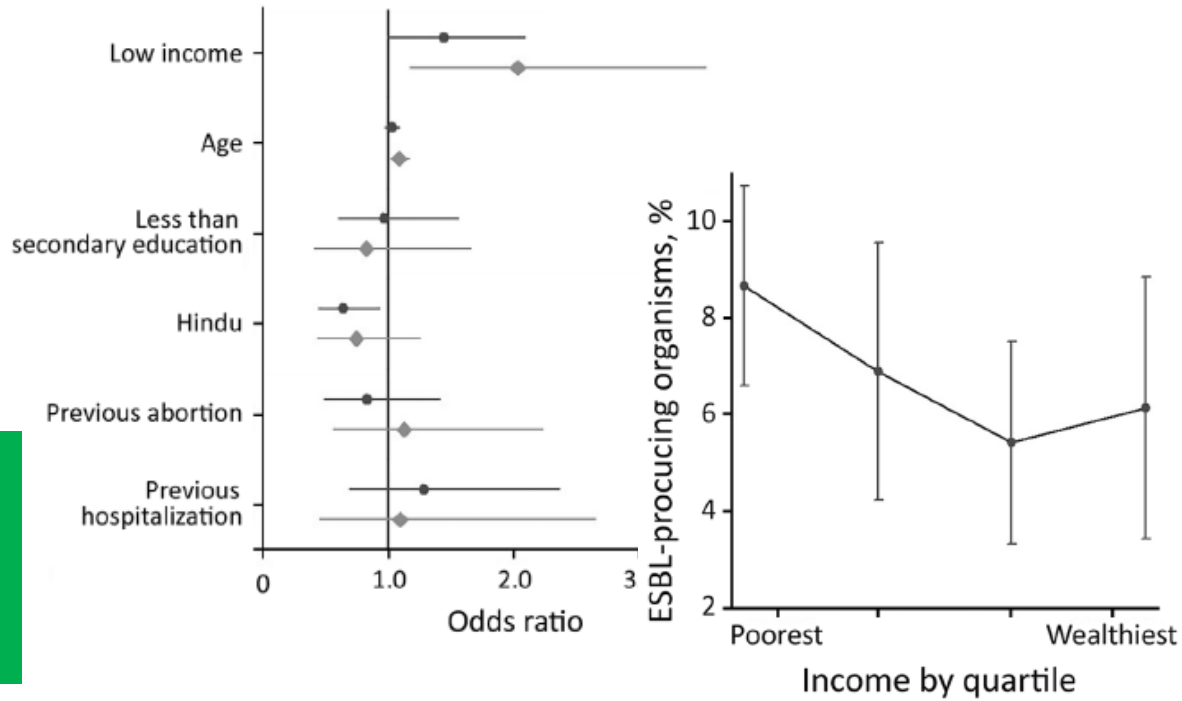
Cross-sectional observational study, pregnant women seeking antenatal care, in Hyderabad, **India**, from Oct 2015 to Sept 2016

- Urine culture + structured interview on residence, occupation, husband's occupation, household income, religion, caste, education level, dietary and hygiene practices, tablet consumption

	ESBL+, n=60	ESBL-, n=1776	p
Mean age	22.65	21.78	**0.06**
Low income*	40 (67)	892 (50)	**0.01**
No treat water	45 (75)	1,294 (73)	0.77
Sewage not piped	4 (6.7)	86 (4.9)	0.53
Strictly vegetarian	2 (3.3)	140 (7.9)	0.32
Handwashing <5 times/d	15 (25.0)	330 (18.6)	0.24

*Total household income in previous 30 d

Adjusted OR of bacteriuria and community-acquired ESBL-PE

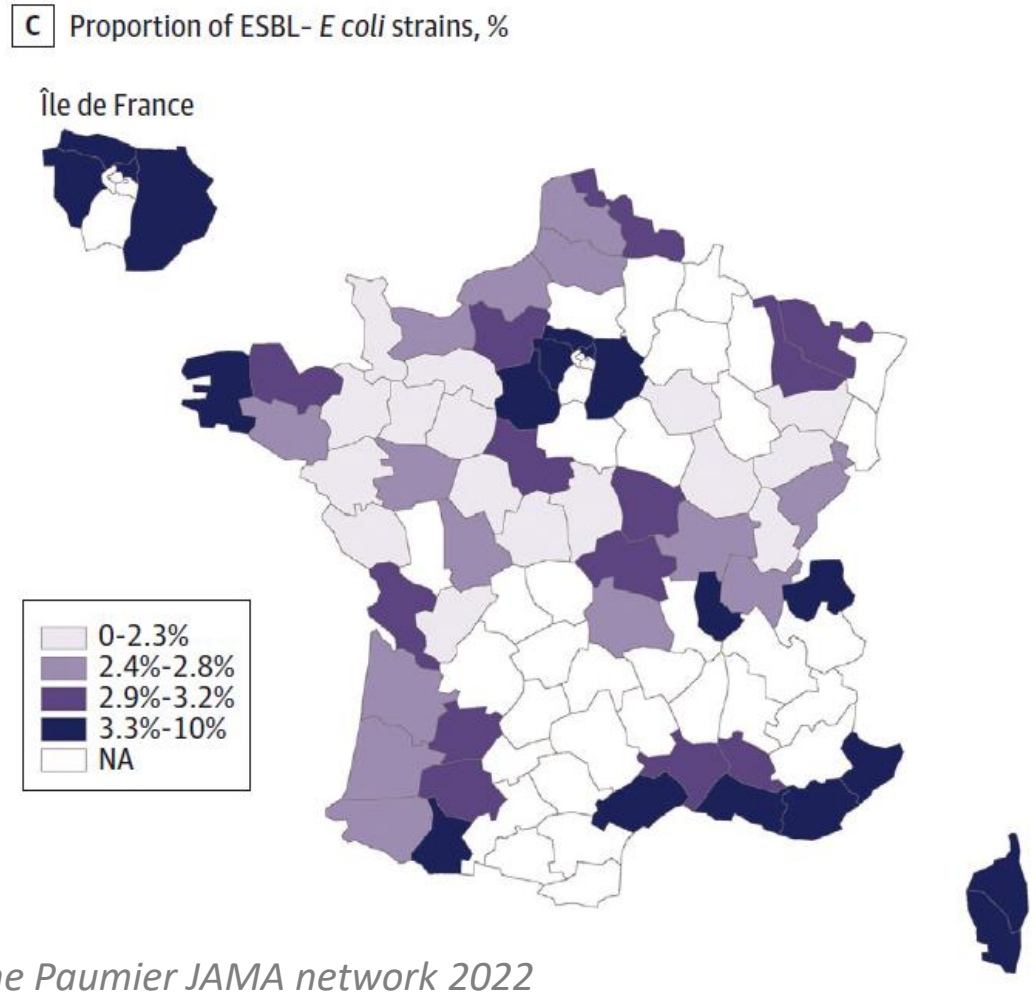


If factors correlated with poverty (environmental antimicrobial drug exposures) increase risk for AMR in these women, then a policy response should focus on identifying and mitigating such exposures.

Facteurs associés IU à *E. coli*-BLSE

Analyse spatiale, écologique et épidémiologique

- Factors associated with the heterogeneity of community acquired ESBL-*E.coli* UTI



Adeline Paumier JAMA network 2022

444,281 *E. coli* isolates, 3% ESBL from urine samples in 2019

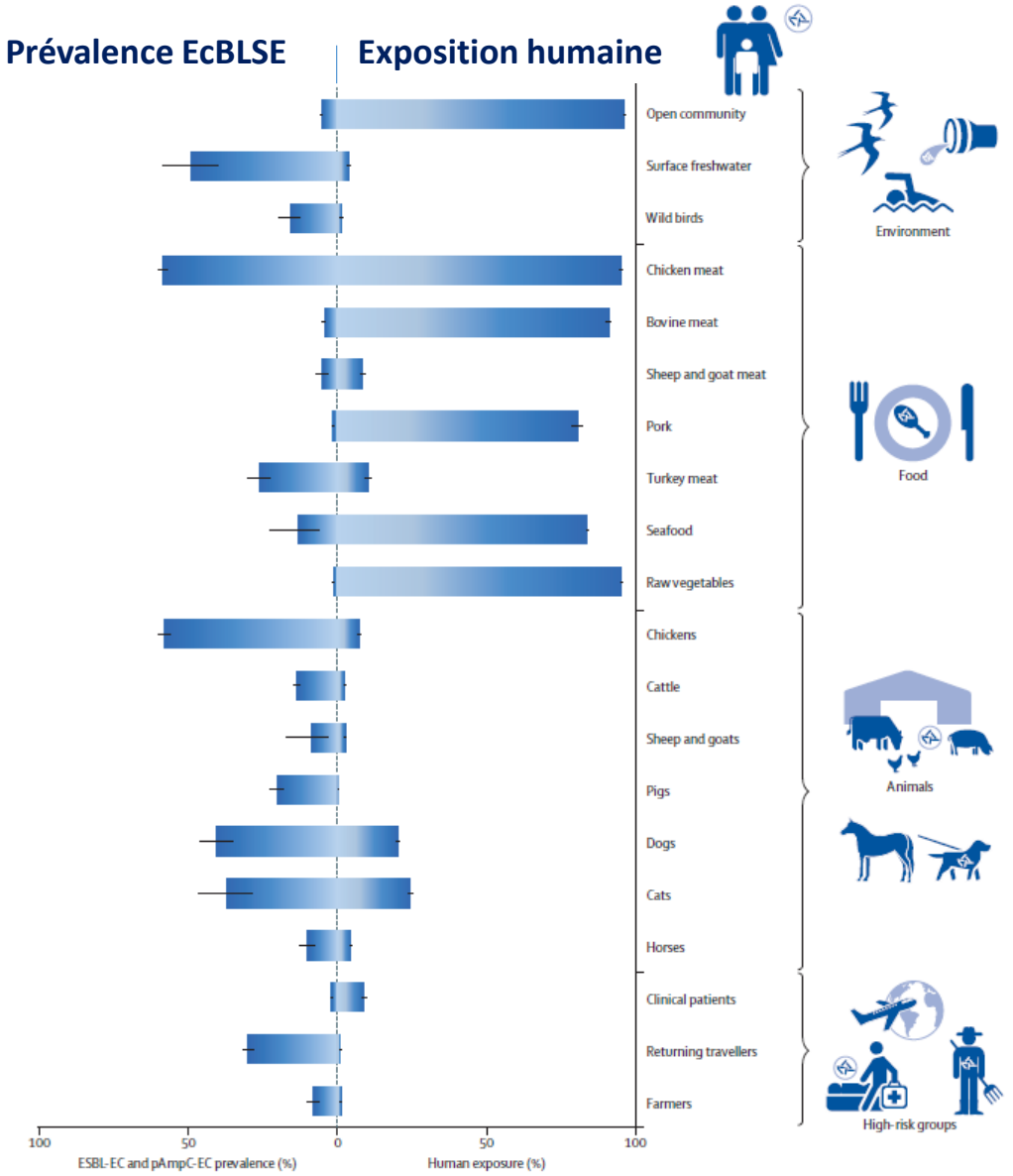
Table 3. Multivariate Regression Analysis of French Administrative Department Characteristics Associated With Community-Acquired Extended-Spectrum β-Lactamase–Producing *Escherichia coli* Urinary Tract Infections

Characteristic	Adjusted β_1 (95% CI)	*P* value
Health care-related		
Fluoroquinolones consumption	0.002 (0.001 to 0.002)	<.001
Tetracycline consumption	0.0002 (0.00004 to 0.00039)	.02
Sociodemographic		
Proportion of people aged <5 y	0.112 (0.040 to 0.185)	.004
Deprivation index	−0.115 (−0.165 to −0.064)	<.001
Living conditions		
Overcrowded households	0.049 (0.034 to 0.062)	<.001
Agriculture and environment		
Water surface area	−0.052 (−0.081 to −0.024)	.001
Poultry density	0.0001 (0.0001 to 0.0002)	<.001

Additional research is needed to explore the determinants of the transmission of ESBL among household members

Sources attribuables d'*E. coli*-BLSE

- Genes BLSE et pAmpC de *E coli*, Pays-Bas 2005–17
  - Sources humaine, animale, environmentale
  - Modèle d'attribution de source basée sur le typage des souches, modèle de hald
- Portage acquis en communauté
  - 60,1% transmission interhumaine au sein/entre maisonnée
  - 18,9% à partir de l'alimentation
  - 7,9% animaux de compagnie
  - 6,9% transmission interhum. secondaire / groupe à risque
  - 3,6% animaux d'élevage
  - 2,6% d'eau de baignade et oiseaux
- *R*0 transmission intracom. = 0.63 (IC, 0.42–0.77)



Lapo Mughini-Gras Lancet Planet Health 2019:3: 357–69

Sources attribuables d'*E. coli*-BLSE

Objectives: To identify risk factors of co-carriage within houseolds human–pet pairs

- 1 person per household → Questionnaire + faecal sample of them & Dog/cat at D-0, M-1 and M-6

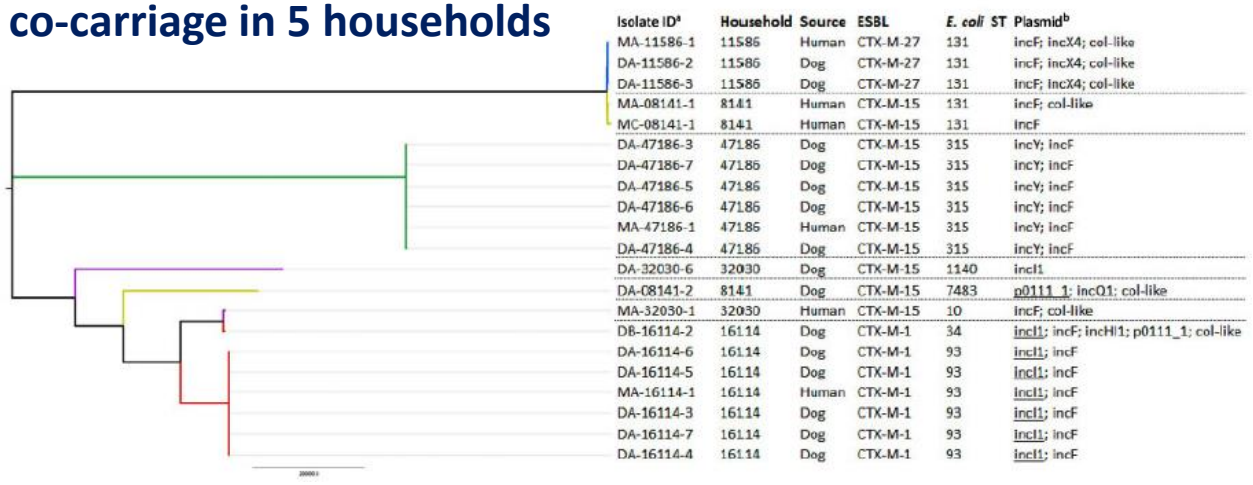
ESBL-E carriage:

- 3.8% for 550 human participants
- 10.7% for 555 dogs, 13.2% after 6months
- 1.4% for 285 cats

Human–cat co-carriage was not observed.

ESBL-E in dogs	ESBL-E neg n=496 (89.4%)	ESBL-E + n=59 (10.6%)	aOR
Walking the dog in forest	288 (59.9)	46 (78.0)	2.2 (1.1–4.6)
Fed with raw meat	44 (9.1)	31 (52.5)	8.8 (4.7–16.4)
Fed with dry feed	456 (94.6)	44 (74.6)	0.2 (0.1–0.5)

Human–dog co-carriage in 5 households



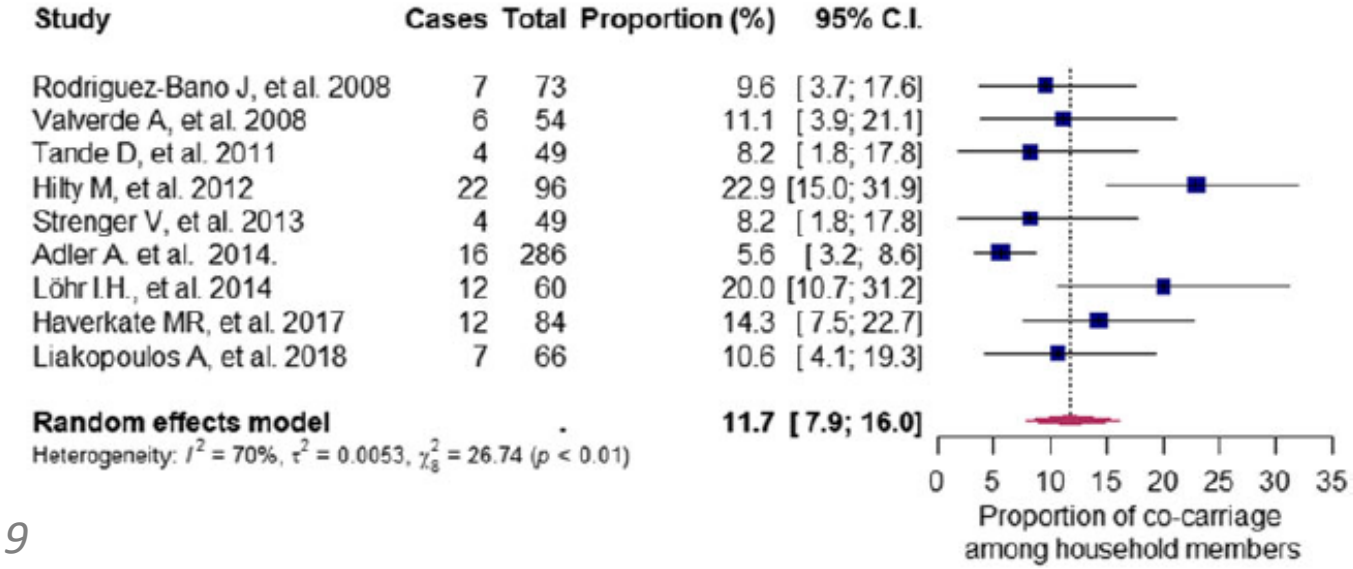
Isolate ID[a]	Household	Source	ESBL	*E. coli* ST	Plasmid[b]
MA-11586-1	11586	Human	CTX-M-27	131	incF; incX4; col-like
DA-11586-2	11586	Dog	CTX-M-27	131	incF; incX4; col-like
DA-11586-3	11586	Dog	CTX-M-27	131	incF; incX4; col-like
MA-08141-1	8141	Human	CTX-M-15	131	incF; col-like
MC-08141-1	8141	Human	CTX-M-15	131	incF
DA-47186-3	47186	Dog	CTX-M-15	315	incY; incF
DA-47186-7	47186	Dog	CTX-M-15	315	incY; incF
DA-47186-5	47186	Dog	CTX-M-15	315	incY; incF
DA-47186-6	47186	Dog	CTX-M-15	315	incY; incF
MA-47186-1	47186	Human	CTX-M-15	315	incY; incF
DA-47186-4	47186	Dog	CTX-M-15	315	incY; incF
DA-32030-6	32030	Dog	CTX-M-15	1140	incI1
DA-08141-2	8141	Dog	CTX-M-15	7483	p0111_1; incQ1; col-like
MA-32030-1	32030	Human	CTX-M-15	10	incF; col-like
DB-16114-2	16114	Dog	CTX-M-1	34	incI1; incF; incHI1; p0111_1; col-like
DA-16114-6	16114	Dog	CTX-M-1	93	incI1; incF
DA-16114-5	16114	Dog	CTX-M-1	93	incI1; incF
MA-16114-1	16114	Human	CTX-M-1	93	incI1; incF
DA-16114-3	16114	Dog	CTX-M-1	93	incI1; incF
DA-16114-7	16114	Dog	CTX-M-1	93	incI1; incF
DA-16114-4	16114	Dog	CTX-M-1	93	incI1; incF

- Co-carriage in dogs and humans within household occurred more often than expected based on chance only
- Clonal transmission, or exposure to the same source.

van den Bunt J Antimicrob Chemother 2020; 75: 342–350

Co-portage d'EBLSE dans le foyers

- Systematic literature review of **ESBL-PE cocarriage and acquisition in households**
- 13 studies:
  - 863 household members of ESBL-PE positive index cases
  - Prevalence of ESBL-PE cocarriage ranged from 8% to 37%
  - 12% (CI 8%–16%) of subjects had a clonally related strain.
    - higher for *Klebsiella pneumoniae* (20%–25%) than for *Escherichia coli* (10%–20%).
  - Acquisition rates of clonally related ESBL-PE among 180 initially ESBL-PE–free household members of a previously identified carrier ranged between 1.56 and 2.03 events per 1,000 person weeks of follow-up.



Romain Martischang ICHE 2019

Transmission d'EBLSE dans le foyers

- Cohorte de patients **colonisés à EBLSE (*Ec*, *Kp*)** et leurs contact au sein de maisonnée, 5 villes Européennes
  - Suivi 4 mois après hospitalization → Prlvt de selles + WGS
  - 71 patients index inclus (45 *Ec*-BLSE, 20 *Kp*-BLSE, 6 deux) + 102 contacts

19 transmissions (clones identiques)

- Facteurs associés
  - Cas index : Education, autonomie; cancer, incontinence fécale, historique d'infection abdo, sonde urinaire, IPP, ≥3 ATB, ≥ hospit., assistance de la famille (gestion des excreta)
  - Maisonnée : Conjoint, ATB, aide active au cas index

	Cas index → contact		
N	7 Ec	6 Kp	13
Incidence/100 participants-semaine	0,53	1	0,8

- Patient EBLSE en sortie d'hospitalisation sont des sources de transmission communautaire
- Risque dans les 2 mois, liés aux soins a domicile

Riccio CMI 2020
https://doi.org/10.1016/j.cmi.2020.12.024

Transmission d'EPC dans le foyers

Toronto, maisonnées avec **cas index EPC** inclus entre 2015-2018
Ecouvillon rectal des contacts à M 0, 3, 6, 9, et 12, culture puis PCR en 2017

- **M-0**
  - 95 cas index/177 contacts
  - 9 EPC+
- **M-3**
  - 75 cas index/142 contacts
  - 4 EPC+
- **M-6**
  - 70 cas index/131 contacts
  - 0 EPC+
- **M-9**
  - 64 cas index/119 contacts
  - 1 EPC+
- **M-12**
  - 54 cas index/97 contacts
  - 2 EPC+

- WGS, transmission dans la maisonnée
  - Confirmée : 3/177 (2%) → *E. coli* NDM
  - Probable : 2/177 (1%), Possible : 9/177 (5%)

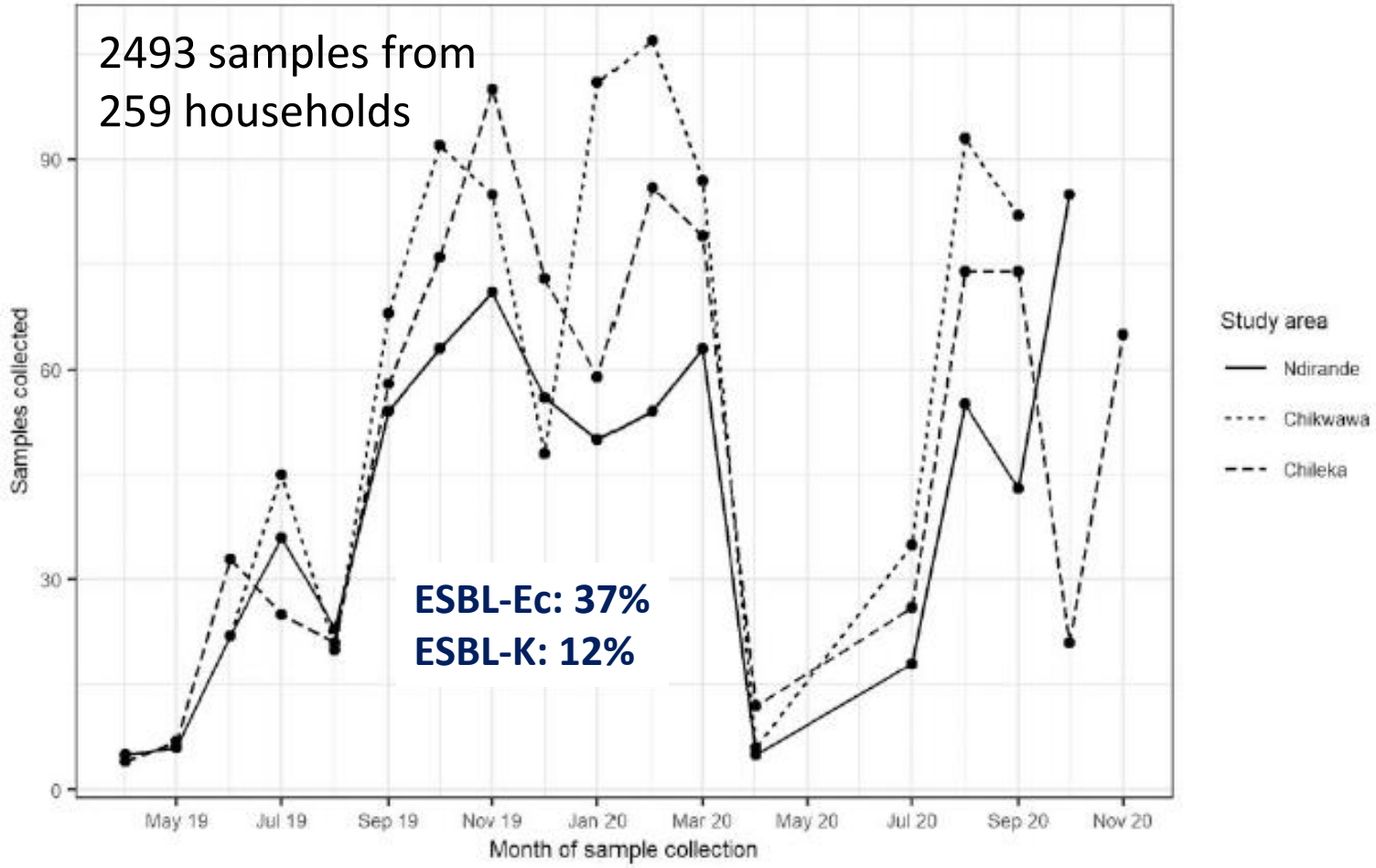
	Contact-	Contact+	p
Age, median	41	68	0,001
Charlson score ≥1	7%	25%	0,04
Conjoint	26%	88%	<0,001
Voyage en Inde	42%	75%	0,04
Tjs partager salle d'eau	47%	88%	0,002

Alainna J. Jamal CID 2021;73(11):e4607–15

BLSE-PE Colonization in Malawi

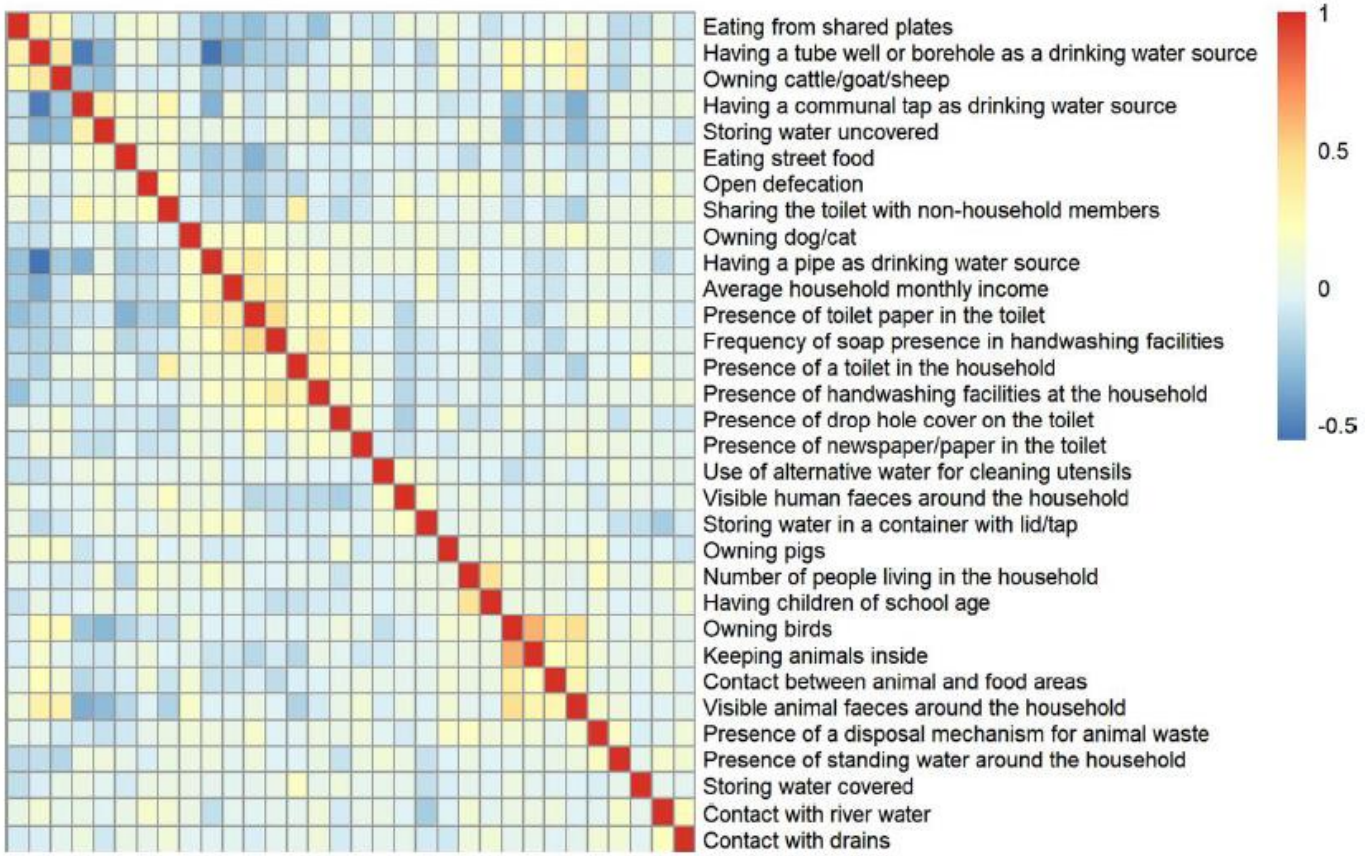
Analysis of an **18-month longitudinal cohort** study using microbiological, household, and **WASH surveys** (human and animal feces, hygiene, and food hygiene)

- Malawian areas: Ndirande (urban), Chileka (periurban), and Chikwawa (rural)
- Repeated-measures of individuals clustered into households
- **Sample at 4 timepoints over 6 months**: human stool, animal and environmental sampling



Sammarro Clin Inf Dis 2023

BLSE-PE Colonization in Malawi



- 75% (202/259) of households had between 3 and 6 members, with a median of 4 individuals
- Positive correlation:
  - Bird owners more likely to keep animals inside, more likely to come into contact with food preparation areas
  - Increasing income > household's water drinking from a pipe, rather than a tube well or borehole; > presence of hand washing facilities and soap in the household, and of cleaning materials near the toilet.
- Negative correlation:
  - Eating from shared plates with sanitation
  - Higher household income < shared plates

Sammarro Clin Inf Dis 2023

BLSE-PE Colonization in Malawi

Factors associated with ESBL-producing *E. coli* colonization

Risk factors

Univariable models:

- Drinking source = tube well or a borehole
- Allowing animal contact with food areas
- Older age
- Visible open defecation in the area
- Owning cattle, sheep, or goats
- Contact with river water

Hierarchical model:

- Tube well/borehole as drinking source: OR, 1.5; CrI, 1–2.4
- Contact with standing water: OR, 0.7; CrI, .6–.9

Protective factors

Univariable models:

- Drop hole cover on the toilet + clean paper
- Male sex; higher income
- Disposal mechanism for animal waste
- Piped water drinking source storing water in a container with lid and tap

Hierarchical model:

- Being Men: OR, 0.7; CrI, .7–.9

Samples from same household obtained >77 days apart uncorrelated,
Individual's ESBL status at 78 days is not influenced by the status at baseline

BLSE-PE Colonization in Malawi

- Higher prevalence during the wet season:
  - Accumulation of mud and floodwater → more contact with contaminated soil /water
  - Increased time spent indoors → higher within household transmission
- 37% of ESBL-E.coli carriage:
  - > 18% (95% CI, 11%–28%) for community members in sSA
- Women more likely to perform domestic duties
  - ie, laundry, housework, and childcare: higher risk of contact with the fecally contaminated environment
- Drop hole cover → role of flies in transporting and transmitting *E. coli*

WASH factors and environmental hygiene
are key drivers of AMR transmission in Malawi

Sammarro Clin Inf Dis 2023

Que retenir de tout ça ?

- Surveillance de la RATB en **communauté parcellaire voir inexistante**…
  - A l'international: peu de systèmes en place, pas de standardisation
  - Pas de surveillance du portage → Evaluation indirecte par eaux usées
- Collaboration internationale +++
- Nécessité de mieux comprendre les déterminants de la transmission communautaire d'EBLSE et EPC
  - Potentiels déterminants :
    - **Transmission intra-maisonnée +++** → étude de la dynamique, saisonnalité
    - Contexte très différents → Epidémiologie différente
    - Facteurs socio-économiques : populations défavorisés, conditions de vie, WASH
    - Actions de BUA ? Actions individualisées

LIENS UTILES

RéPIAS
Réseau de Prévention des Infections Associées aux Soins

www.antibioresistance.fr

Surveillance de la résistance aux antibiotiques

Prévention de la résistance aux antibiotiques

Prévention des infections associées aux soins

ANTIBIOCLIC
Antibiothérapie rationnelle en soins primaires

https://antibioclic.com/

ANTIBIOCLIC est un outil indépendant d'aide à la décision thérapeutique en antibiothérapie, pour un bon usage des antibiotiques. Ce site est à usage des professionnels de santé.

Santé publique France

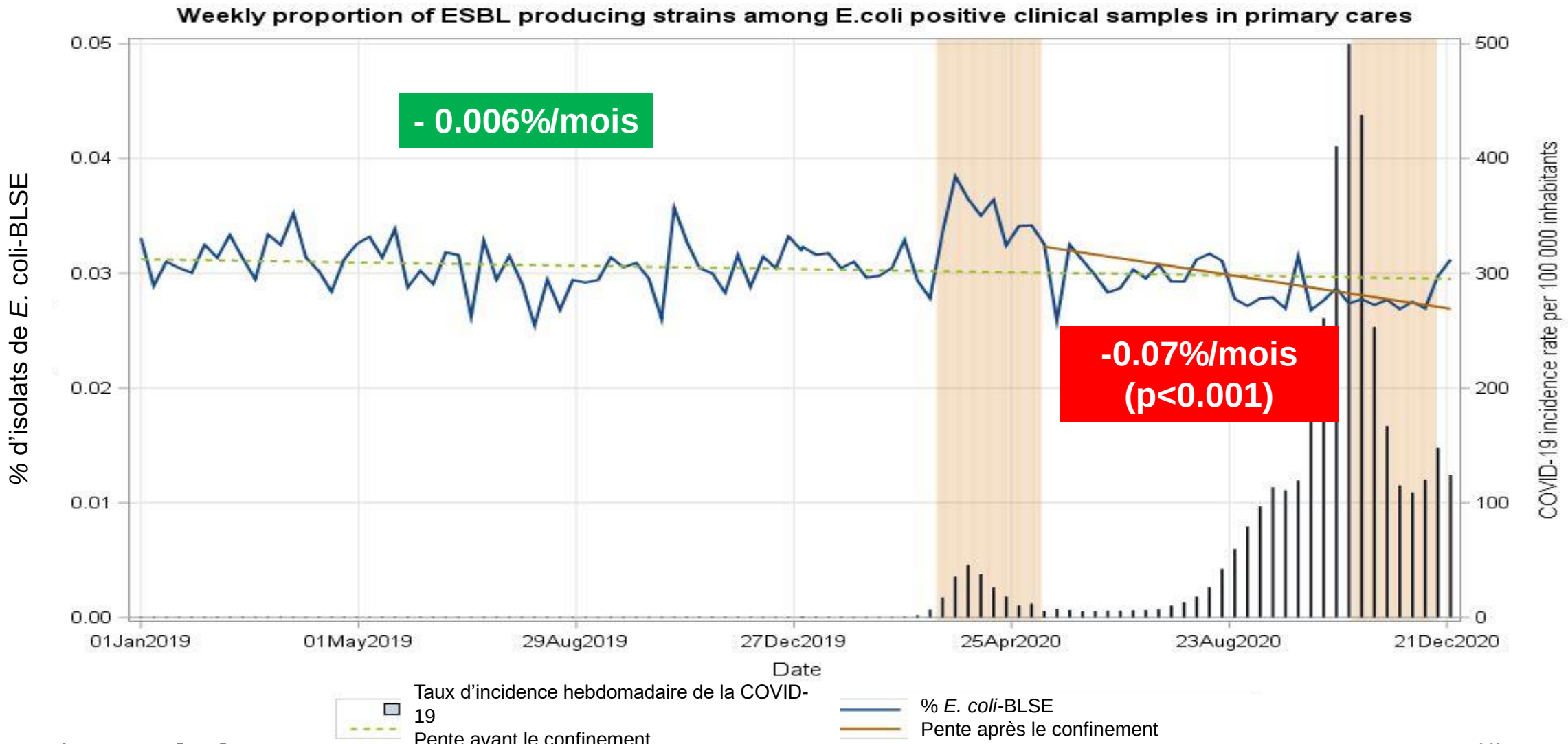
https://geodes.santepubliquefrance.fr/

Géodes est l'observatoire cartographique des indicateurs épidémiologiques produits par Santé publique France.

RéPIAS
Réseau de Prévention des Infections Associées aux Soins

Epidémiologie de la Résistances

Impact COVID-19 – Réseau PRIMO 2020



Lemenand Journ of Inf 2021

Imperial College London

MDRO during the COVID-19 pandemic

Opinion and Hypothesis in 2020

CPias Pays de la Loire

Affected area	Impact
Hand hygiene	↘ Transmission
Social distancing	↘ ATB prescr.
Less isolation in hospitals	↗ Transmission
Cancellation of procedures	↘ in MDRO carriage
Diversion of PPE	↗ Transmission
Increased empirical antimicrobial therapy	↗ Selection
Increased telemedicine	↗ or ↘ ATB prescr.
Redeployment AMS teams	↘ of AMS culture
Maintenance team dynamics	↘ of best practices
Overcrowding	↗ Transmission
Structural resources	↘ side-room capacity

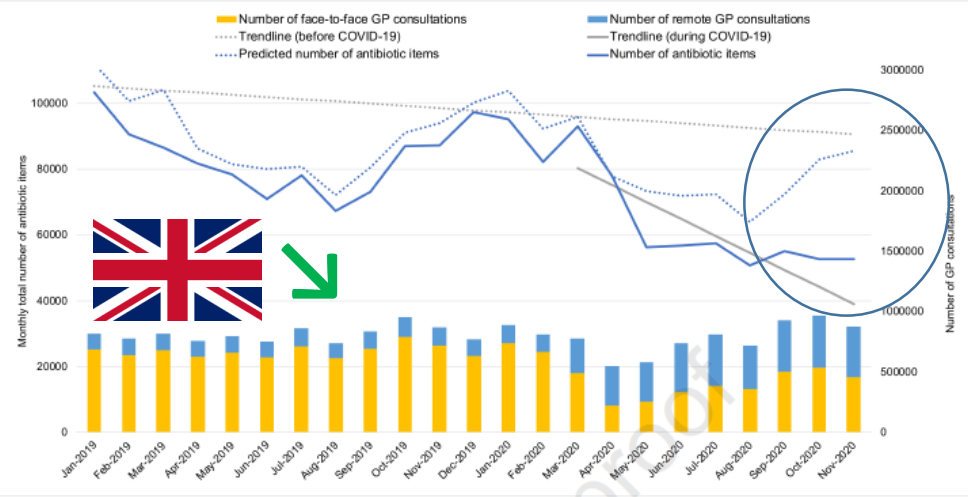
Potential solutions:

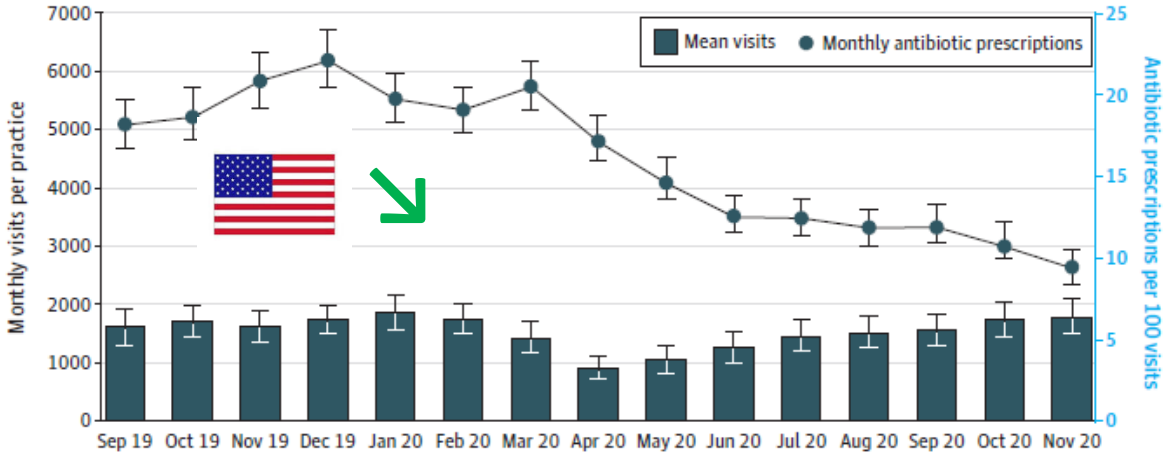
- Resources available
- AMR surveillance systems
- Staff/patient education and training
- Clustered cohorting
- Appropriate **PPE indications**
- Clear guidelines for ATB for COVID-19
- Re-establishment of AMS oversight
- Rapid diagnostics
- AMS for **telemedicine**
- Technology to support risk stratification
- **Agility to absorb new individuals**
- Routine MDRO **screening**
- Contingency plans for outbreaks

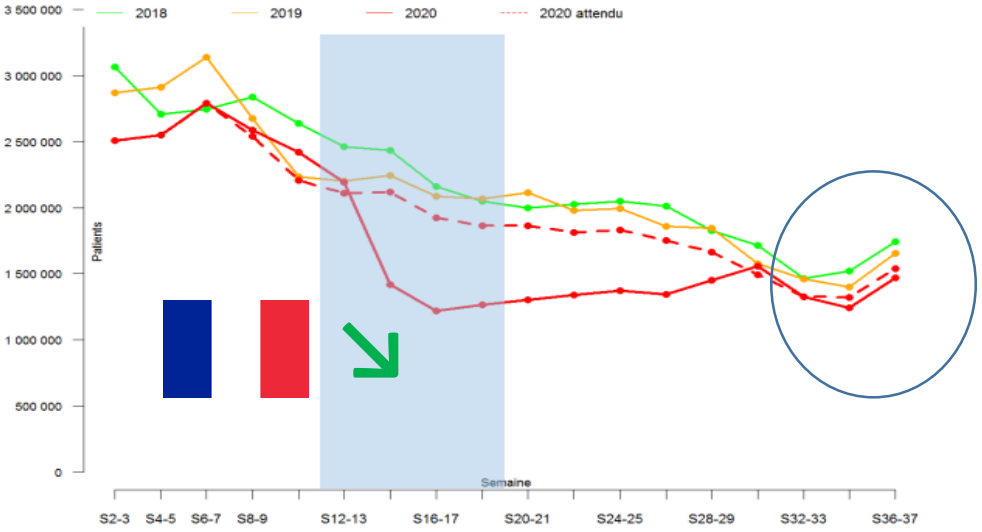
Timothy M. Rawson J Antimicrob Chemother
doi:10.1093/jac/dkaa194

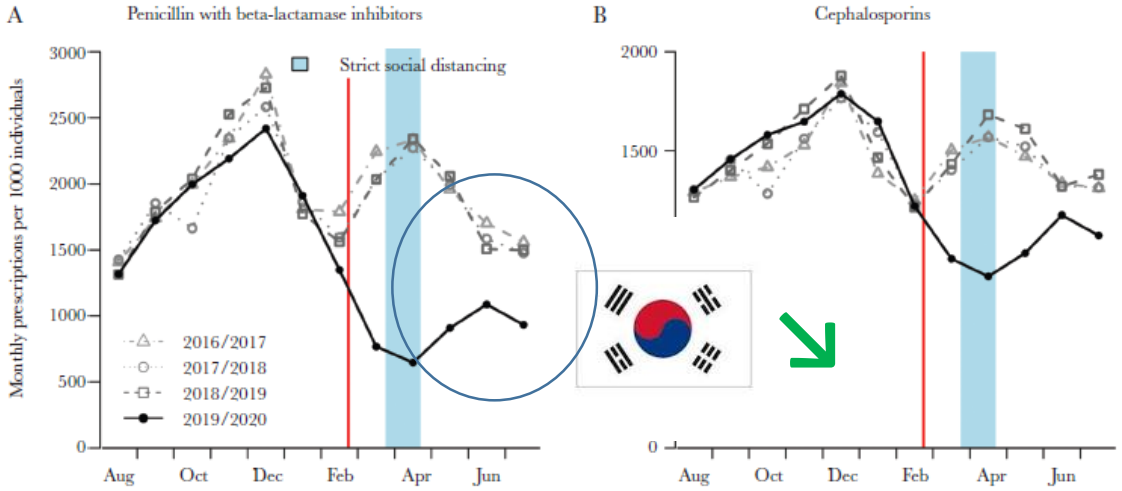
MDRO during the COVID-19 pandemic

Antibiotic usage in primary care





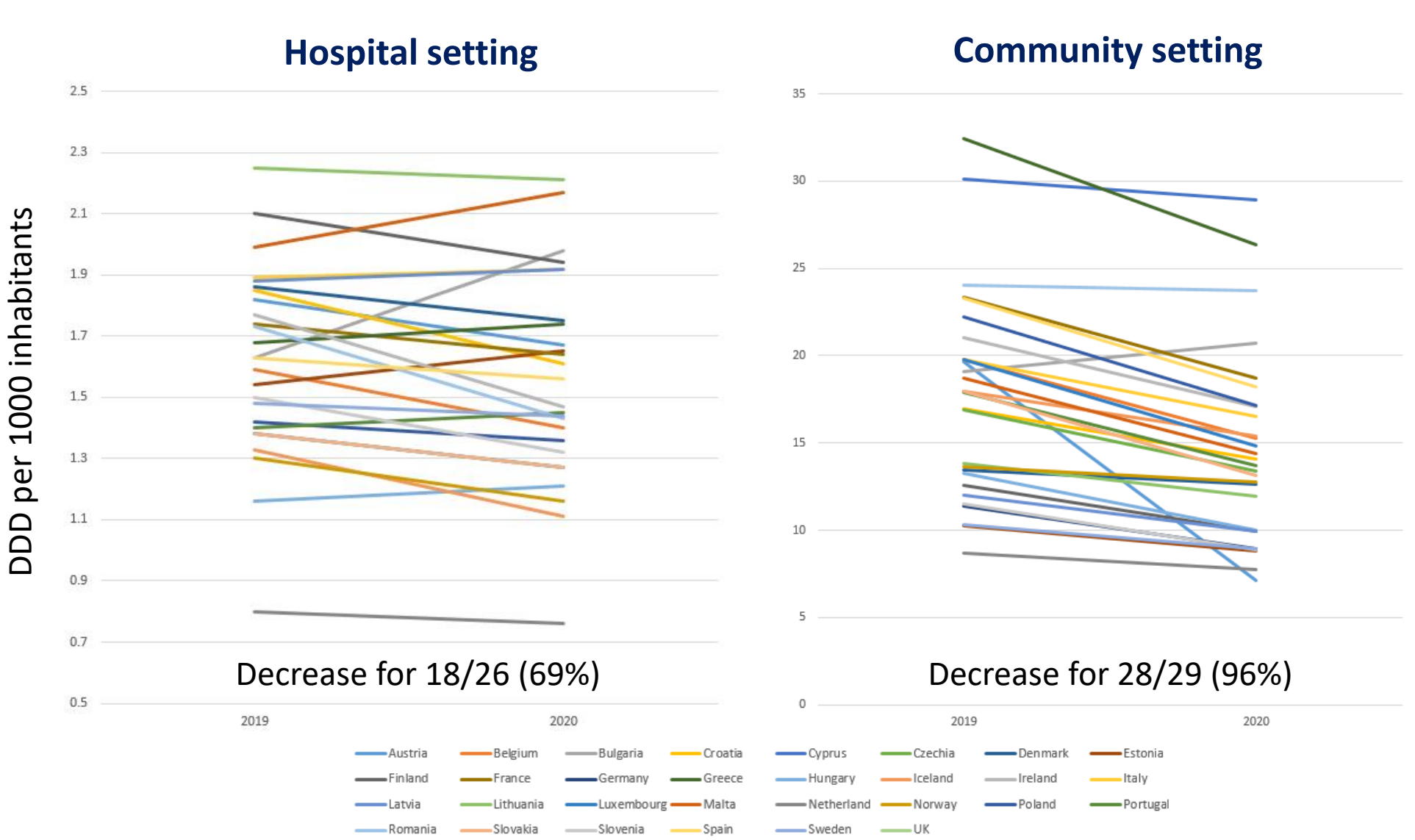




Laura M. King CID 2021; Sara C. Keller JAMAopen; Zhu CMI 2021; Epiphare

MDRO during the COVID-19 pandemic

Antibacterials for systemic use in hospitals

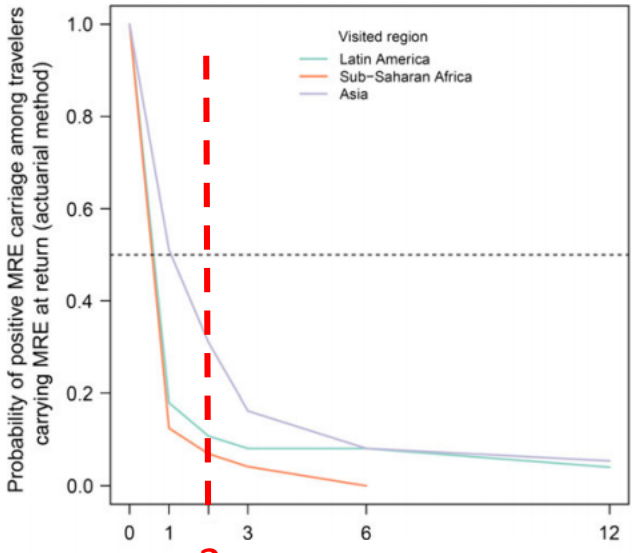


ECDC Atlas 2021

Epidémiologie de la Résistances

Portage digestif d'EBLSE

- 574 participants :
  - Consultation vaccination voyageur
  - Selles avant voyage et au retour
- 292 (51%) porteurs BMR au retour
  - Amérique latine : 32%
  - Afrique sub-saharienne : 48%
  - Asie du Sud-Est: 72% (Inde 91%)



Facteurs associés multivariée	OR (IC 95%)	p
ß-lactamine durant le voyage	4.08 (1.39–11.97)	0.011
Diarrhée durant le voyage	1.90 (1.31–2.75)	<.001
Type de voyage		0.033
Sac à dos	2.74 (1.07–7.06)	
Tour organisé	2.42 (.95–6.15)	
Familial	1.95 (.76–4.98)	
Région visitée		<.001
Afrique sub-saharienne	2.21 (1.40–3.48)	
Asie	5.72 (3.55–9.24)	

Ruppé, CID 2015

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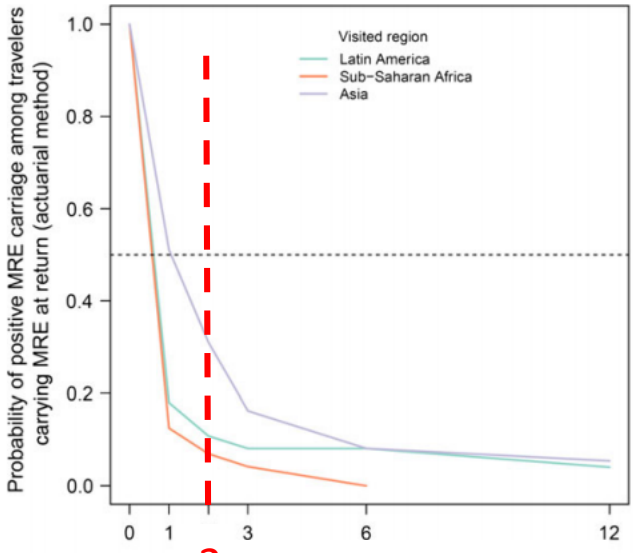

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RAPID COMMUNICATIONS

Acquisition of carbapenemase-producing *Enterobacteriaceae* by healthy travellers to India, France, February 2012 to March 2013

E Ruppé (etienne.ruppe@gmail.com)[1,2,3], L Armand-Lefèvre[1,2], C Estellat[4,5], A El-Mniai[1], Y Boussadia[4,5], P H Consigny[6], P M Girard[7], D Vittecoq[8], O Bouchaud[9], G Pialoux[10], M Esposito-Farèse[4,5], B Coignard[11], J C Lucet[2,3,12], A Andremont[1,2,3], S Matheron[3,13]

Ruppé, CID 2015

Epidémiologie de la Résistances

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Prévalence portage EBLSE, Paris 2016

- 17% (146/844) porteurs d'EBLSE
- 11,5% (97/844) non identifiés porteurs dans l'année précédente

S. Jolivet, CMI 2019
https://doi.org/10.1016/j.cmi.2018.03.008

Epidémiologie de la Résistances

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Dépistage admission, Londres 2015

- 9% (360/4006) porteurs d'EBLSE
  - Origine asiatique 22,8%
  - Voyage Asie (< 12 mois) 17,8 %
  - Origine africaine 11,2 %
  - Voyage Afrique (< 12 mois) 16,3 %
  - Voyage Europe (< 12 mois) 6,5 %
  - Hospitalisation à l'étranger 24,4 %
  - Maisonnée ≤2 pièces 10,8%

J. Otter, CMI 2019
https://doi.org/10.1016/j.cmi.2018.03.008