

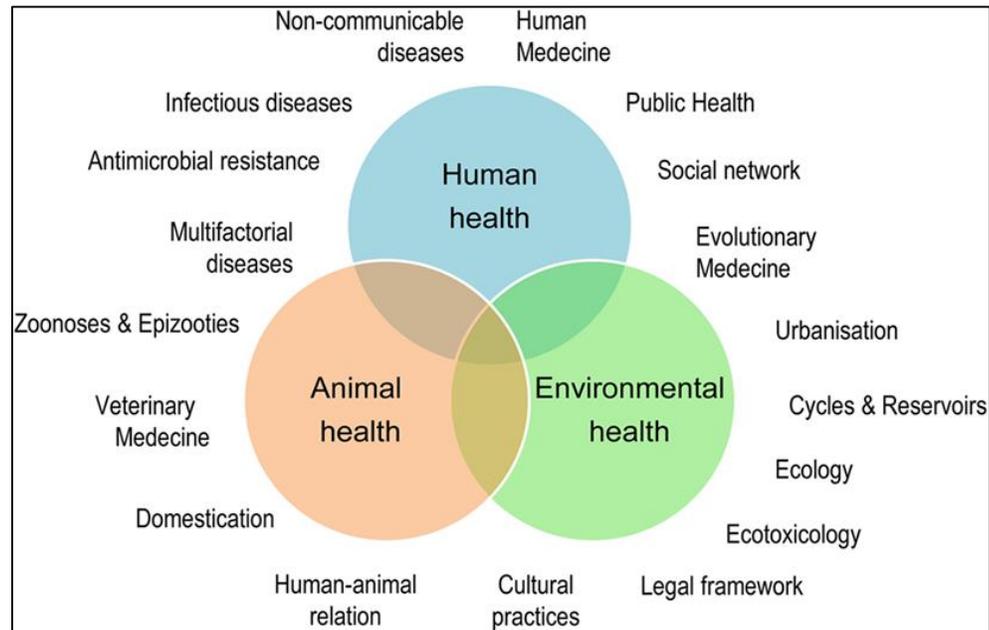
BHRe : épidémiologie, enjeux dans le contexte One health

Pr X. Bertrand



Le concept *One Health*

APPROCHE INTER-COMPARTMENTALE



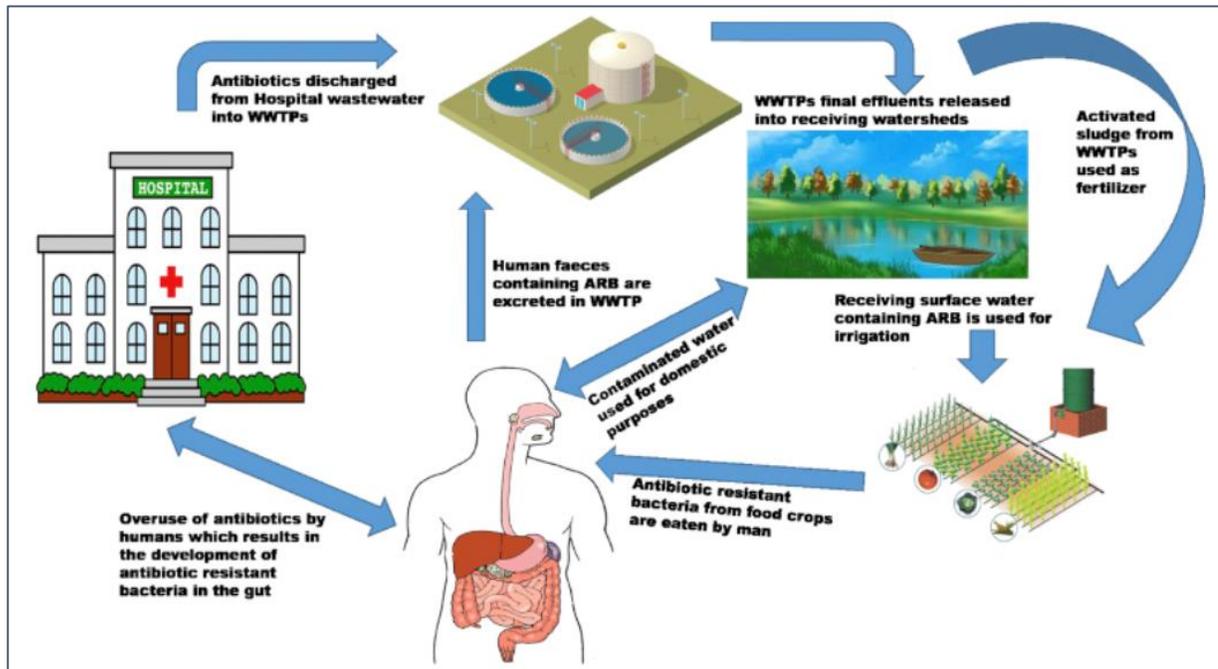
Destoumieux-Garzón *et al*, Front Vet Sci, 2018

- Émerge dans les années 2000
- Postulat selon lequel la santé de l'Homme
 - n'est pas *stricto sensu* liée à lui-même (vision anthropocentrique)
 - Mais également à son environnement (vision globale dite holistique)
- Approche pluridisciplinaire et globale des enjeux sanitaires
- Promu par l'OMS et les différentes sociétés savantes pour l'étude de l'Antibiorésistance (*European Joint Program, PPR AMR, ...*)

Le concept *One Health* appliqué à l'antibiorésistance

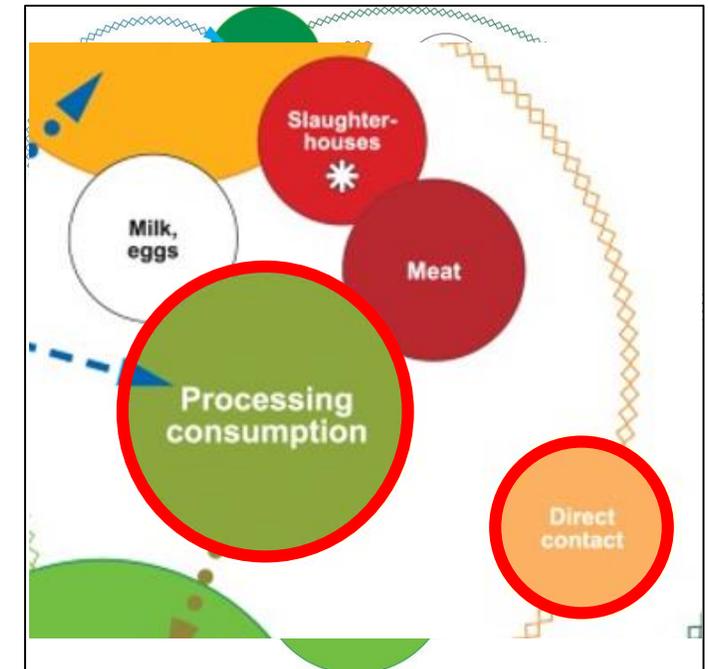
DES ÉCHANGES COMPLEXES ENTRE LES DIFFÉRENTES NICHES ÉCOLOGIQUES

- Lien Homme-Environnement



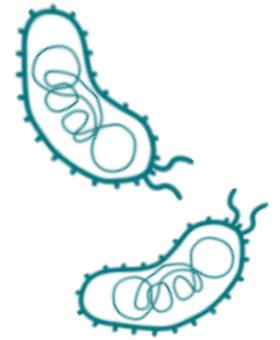
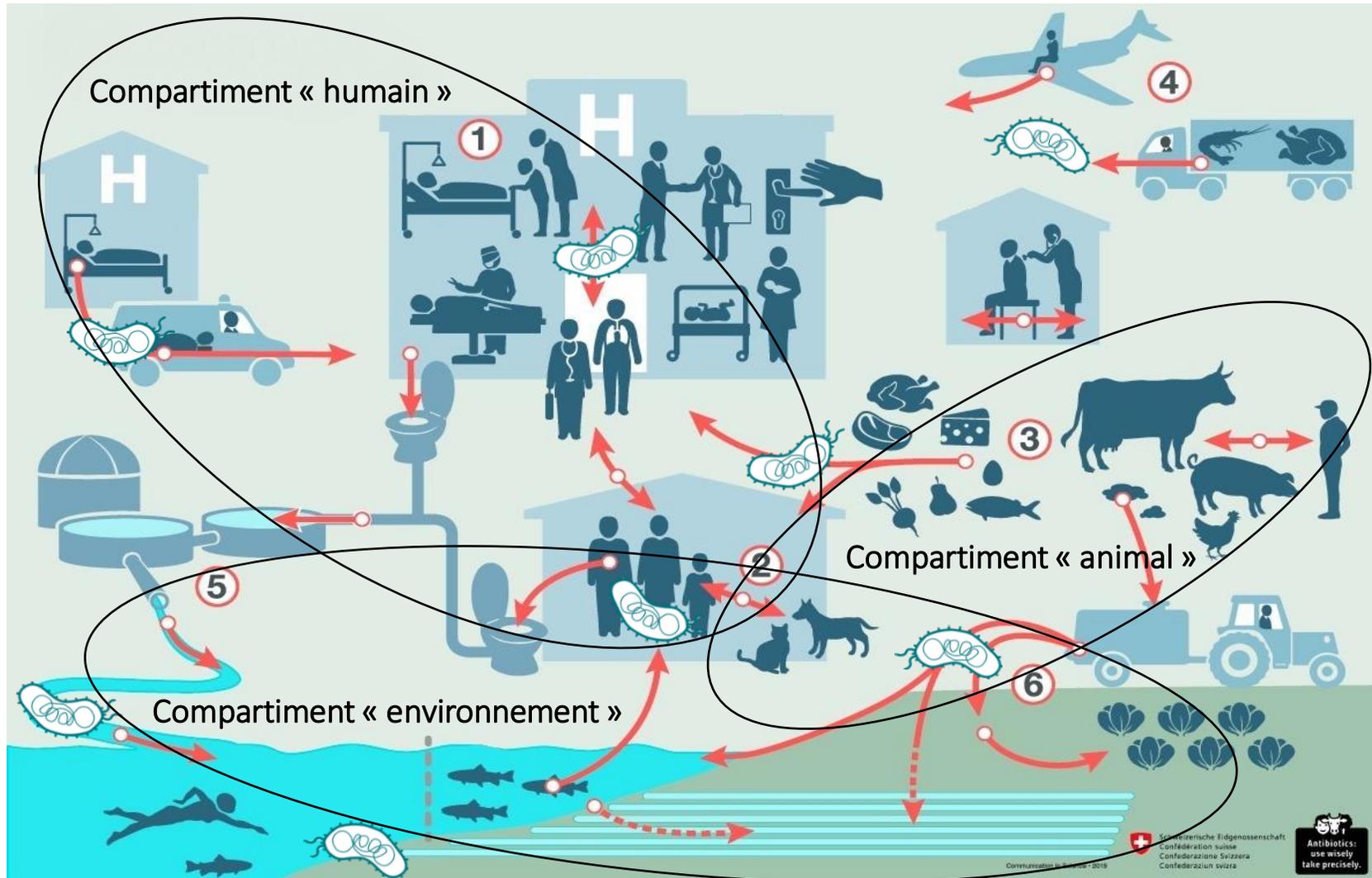
Ebomah *et al*, Heliyon, 2020

- Lien Homme-Animal



Thanner *et al*, mBio, 2016

Contexte



Les carbapénèmases

CLASSE A: Pases (TEM,SHV...) et BLSE (KPC, CTX-M...)

CLASSE B: MBL=Metallo- β -lactamases (IMP, VIM, NDM,...)

CLASSE C : Cases (AmpC)

CLASSE D : Oxacillinases (OXA-48...)

D'où proviennent ces enzymes : Bactéries environnementales

Classe A : KPC

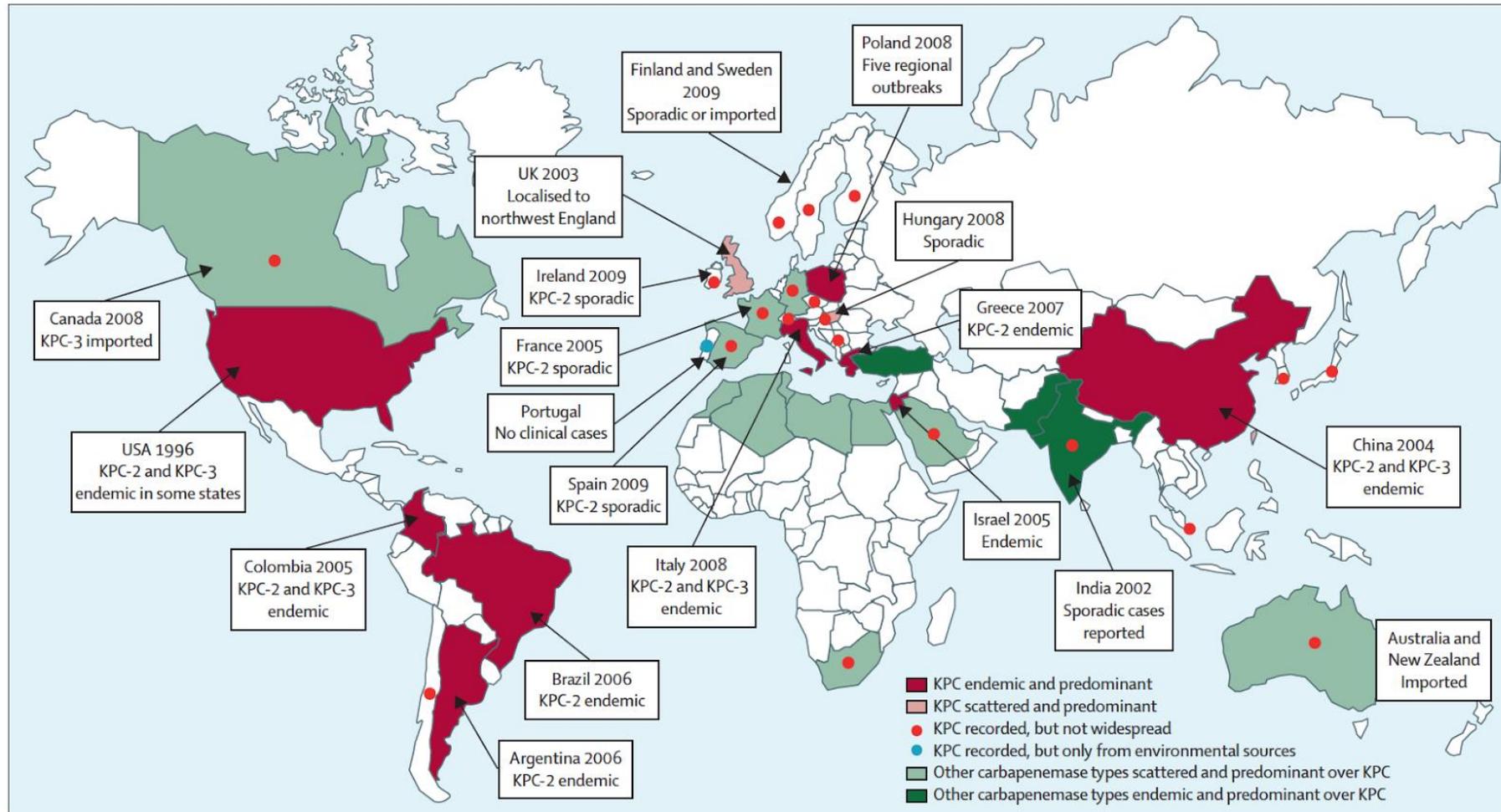
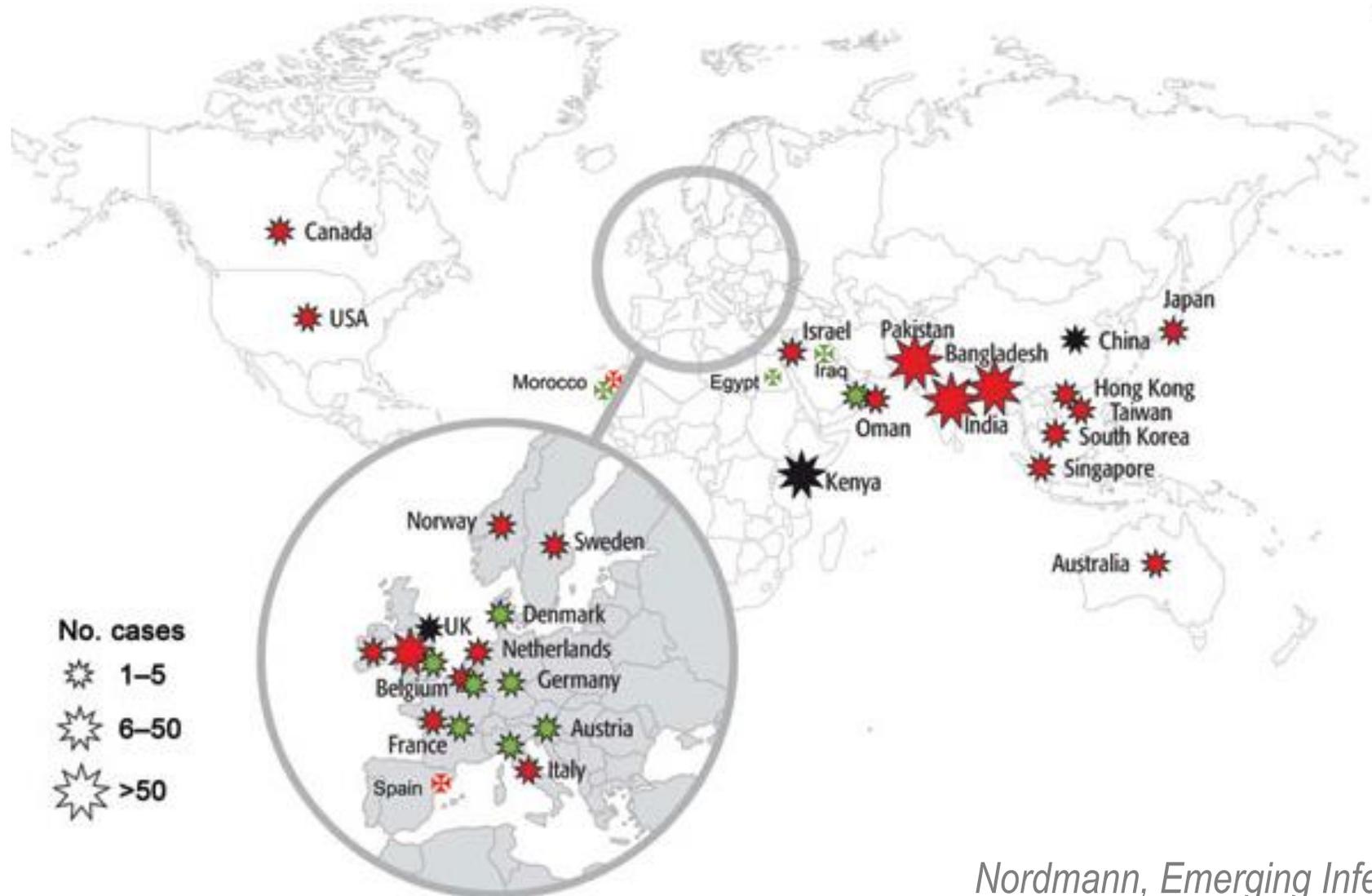
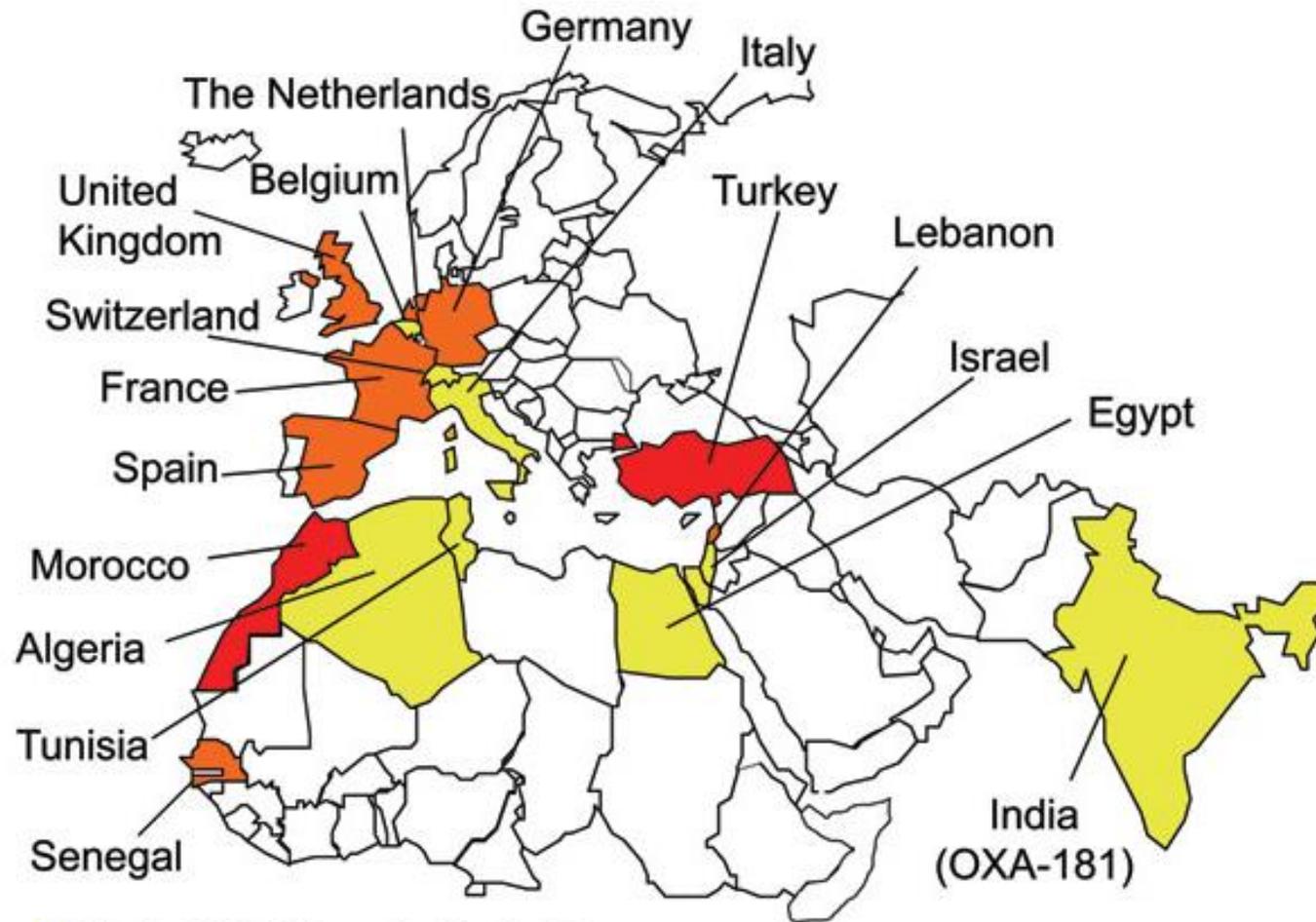


Figure: Epidemiological features of producers of *Klebsiella pneumoniae* carbapenemases by country of origin
Other carbapenemase types include VIM, OXA-48, or NDM. KPC=*Klebsiella pneumoniae* carbapenemase.

Classe B : NDM

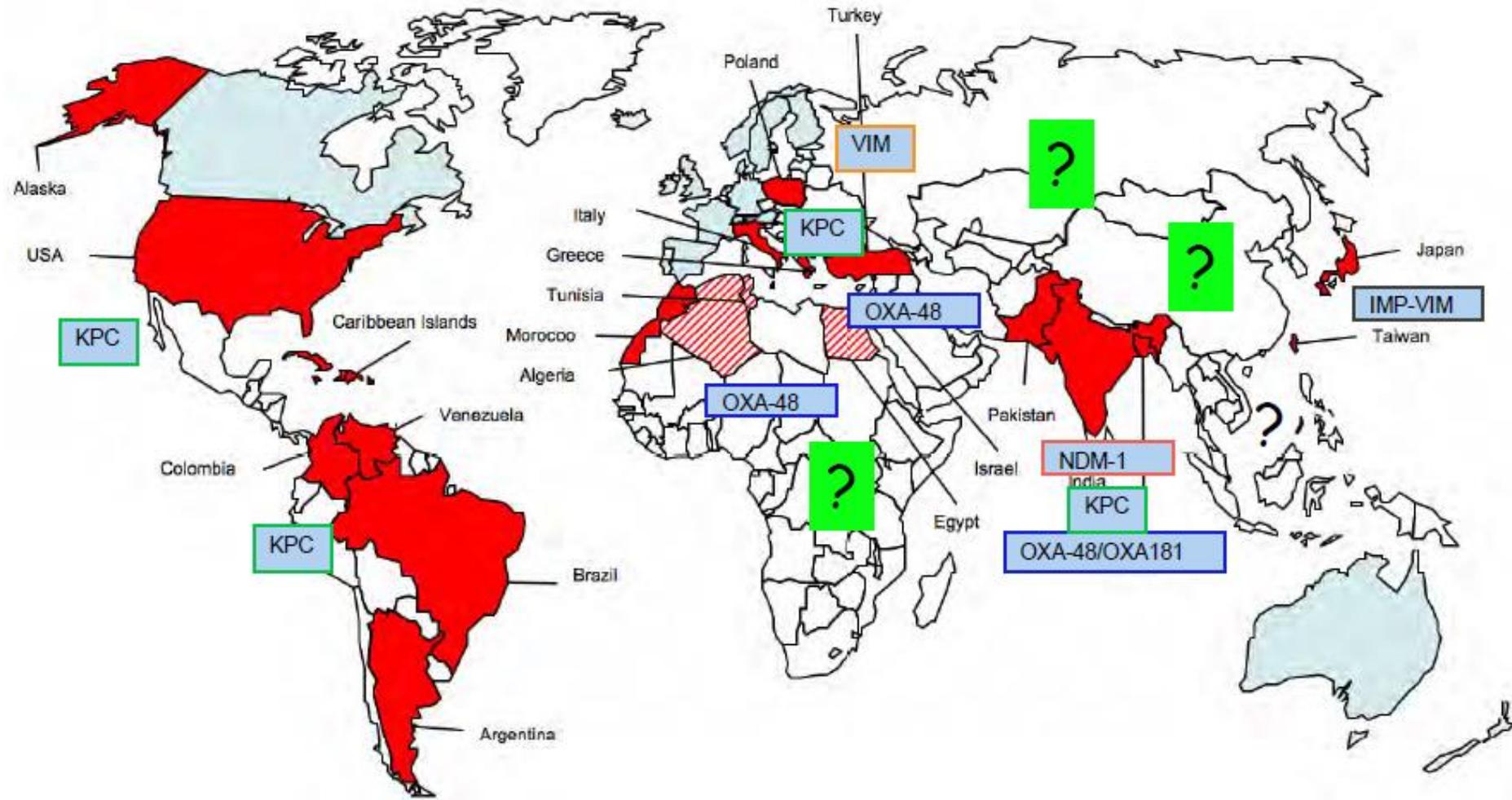


Classe D : OXA-48



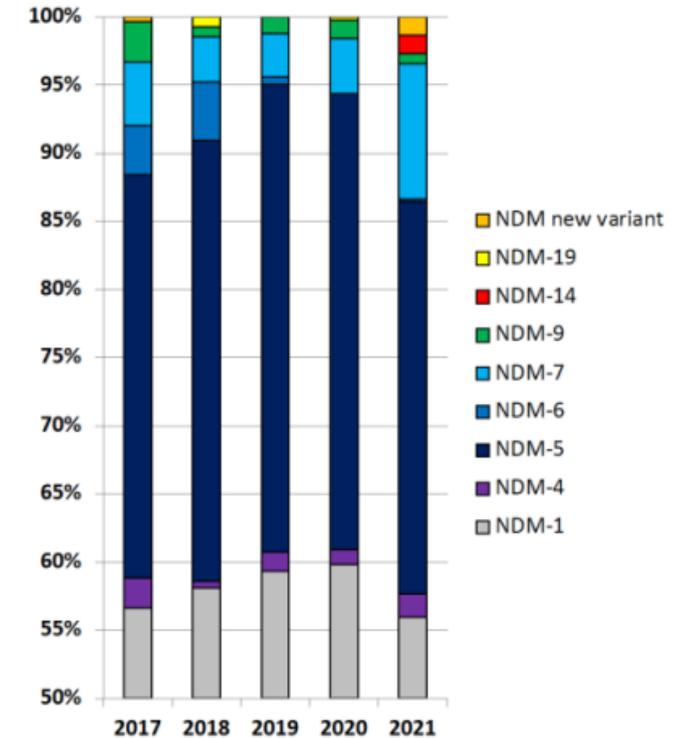
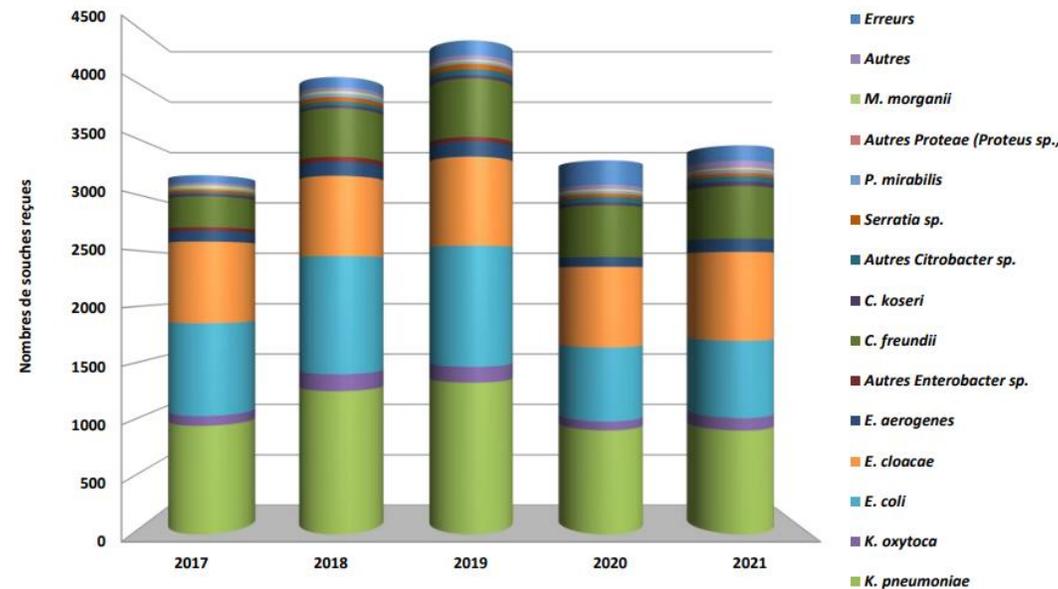
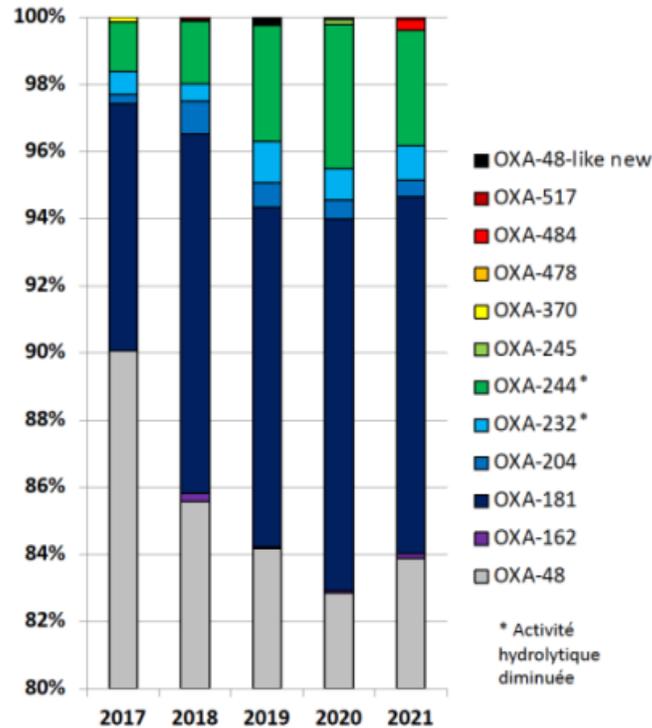
- Single OXA-48-producing isolates
- Outbreaks of OXA-48-producing isolates
- Nationwide distribution of OXA-48-producing isolates

Réservoirs EPC



EPC en France, 2021

Type de carbapenemase	Effectif	Pourcentage (%)
OXA-48-like	1599	64,6
KPC	62	2,5
NDM	520	21,0
VIM	195	7,9
IMI	15	0,6
OXA-48-like + NDM	65	2,6
OXA-48-like + VIM	7	0,3
KPC + NDM	1	0,04
NDM + VIM	4	0,2
OXA-23	7	0,3
Total	2475	100



EPC en France, 2021

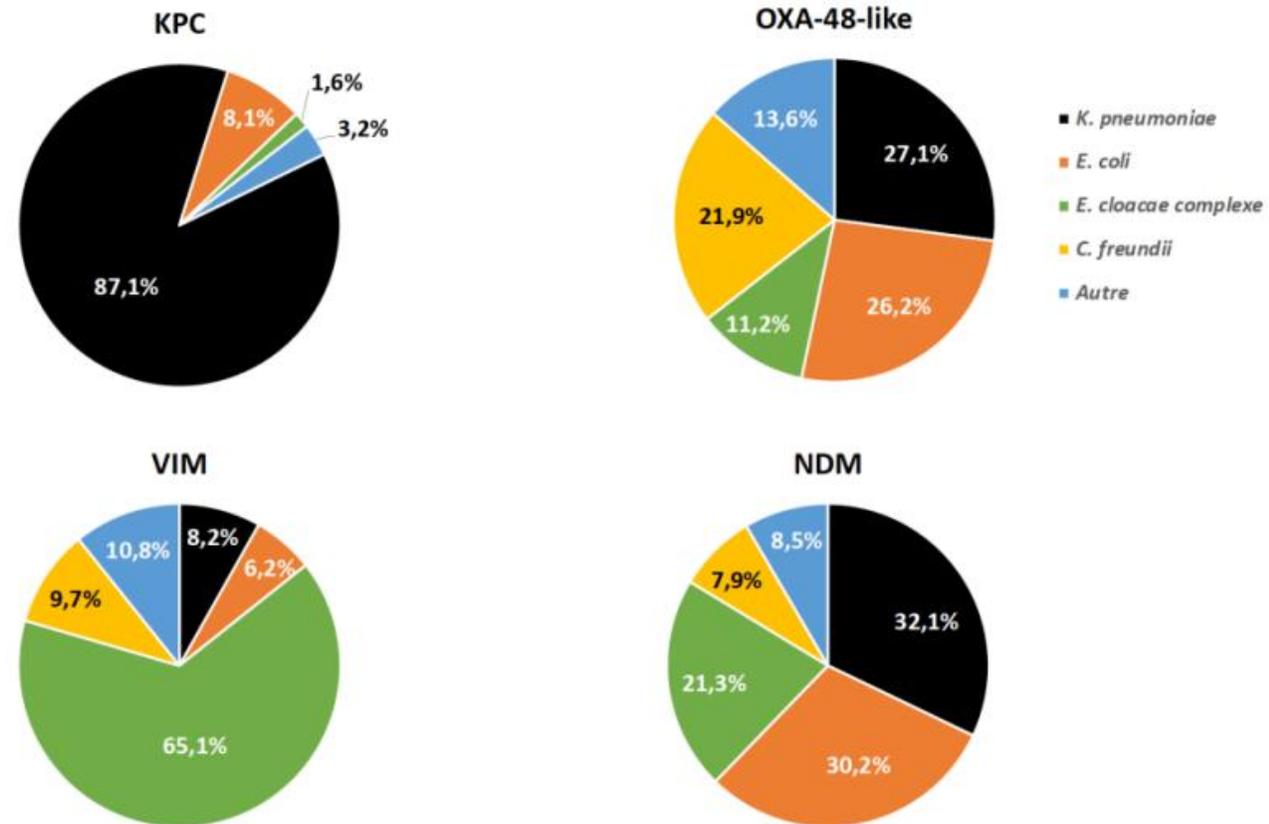


Figure 42: Distribution des différentes espèces d'entérobactéries selon le type de carbapénèmase identifiée en 2021.

EPC en France, 2021

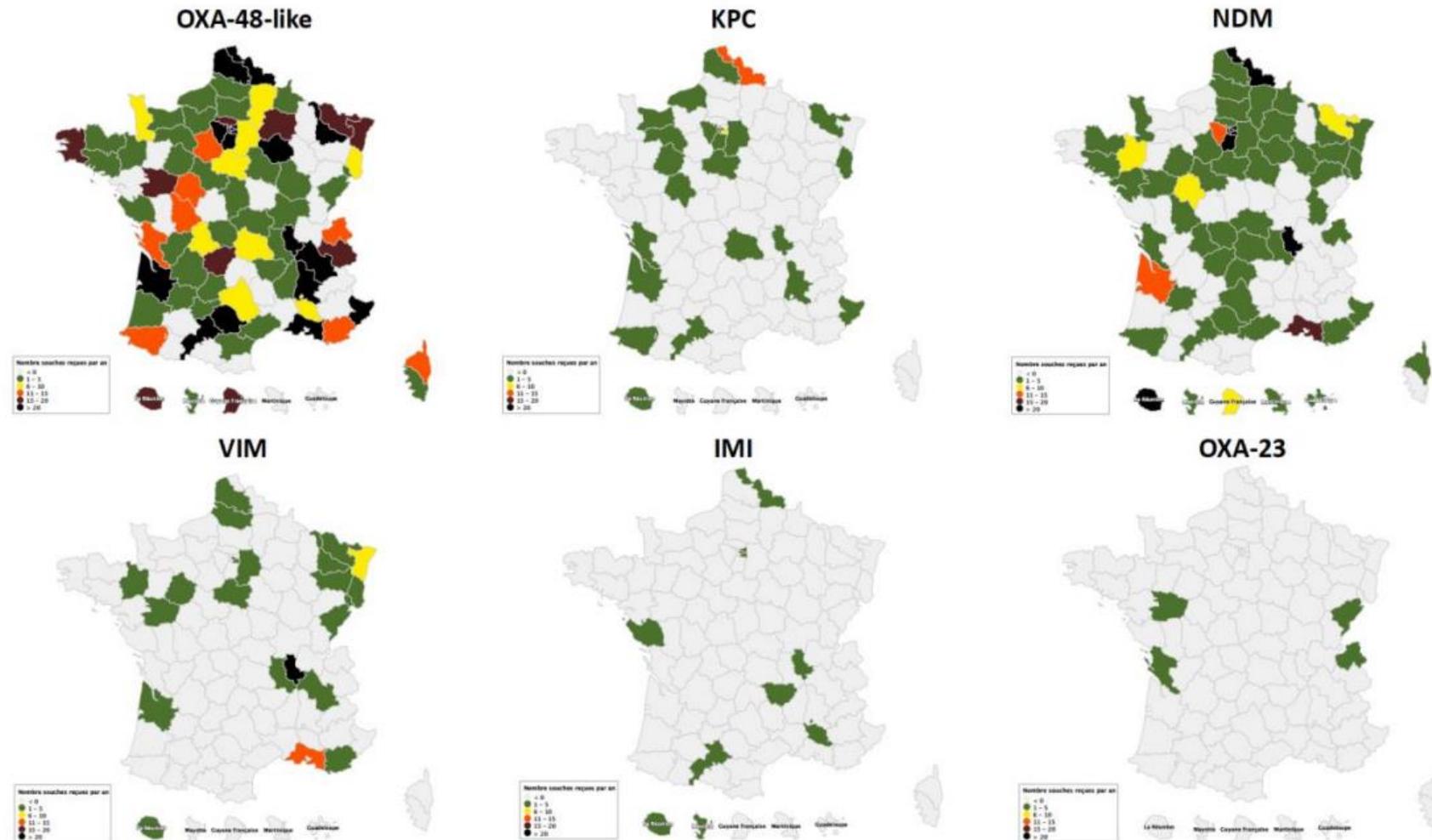
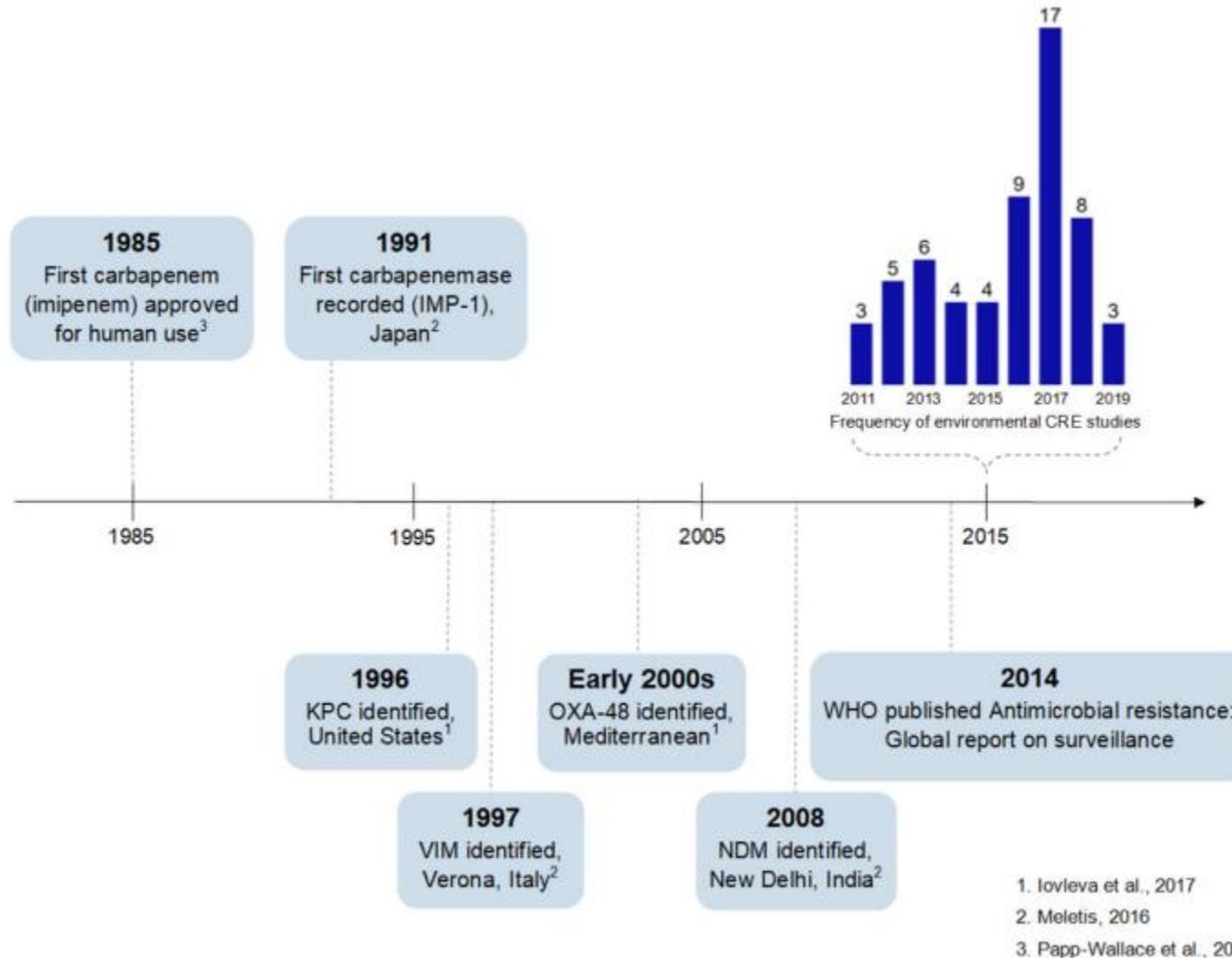
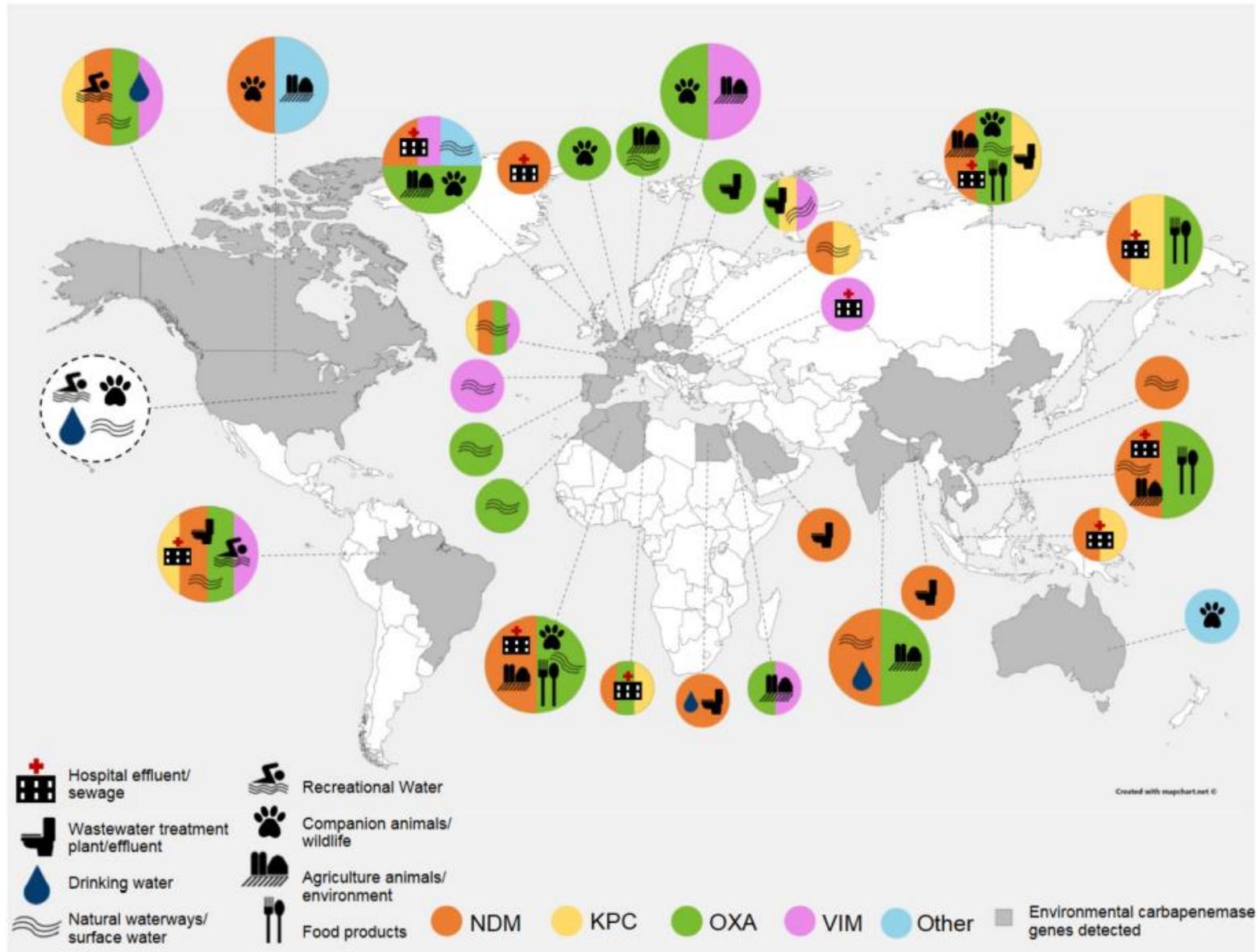


Figure 41: Répartition géographique par type d'EPC en 2021.

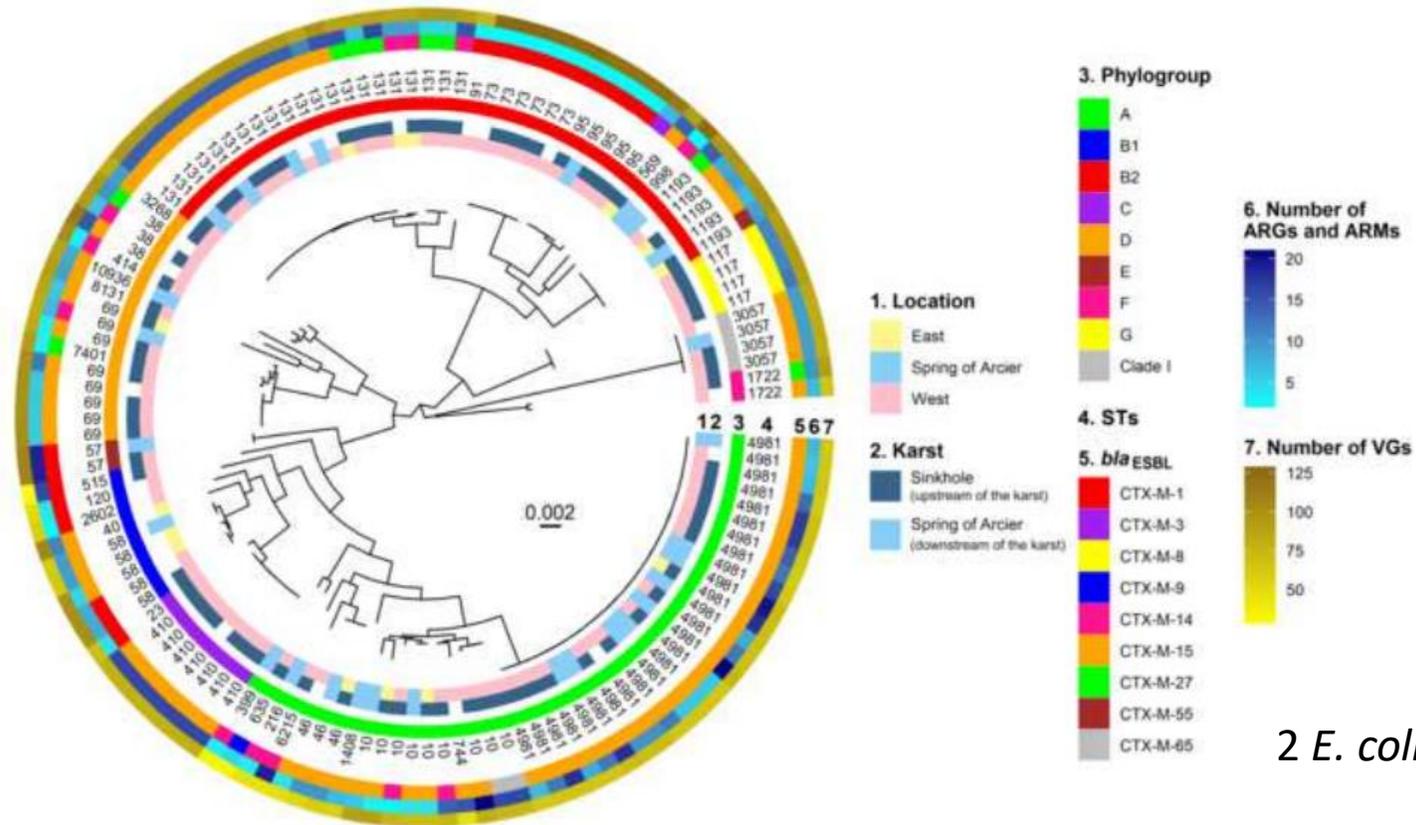
EPC, One health



EPC, One health



Contamination de l'eau de consommation, source d'Arcier



2 *E. coli* OXA-244 (ST10)



Review

What happens in hospitals does not stay in hospitals: antibiotic-resistant bacteria in hospital wastewater systems

D. Hocquet^{a, b, *}, A. Muller^{a, b}, X. Bertrand^{a, b}

Table I
Concentrations of enterobacteria and *Escherichia coli* (ESBL-producing or non-ESBL-producing) in wastewaters

Study	Setting (city, country)	Sampling period	<i>E. coli</i> count (cfu/mL)			No. of ESBL ^b rejected from WWTP per day	Main ESBL ^c
			Community effluents	Hospital effluents	WWTP ^a discharge		
Galvin <i>et al.</i> ¹¹	Galway (Ireland)	Aug 2006 to Jun 2008	ND ^d	5.4×10^6 <i>E. coli</i> 3.8% of ESBL ^b	4.8×10^4 <i>E. coli</i> 0.5% of ESBL ^b	—	CTX-M group 1
Chagas <i>et al.</i> ¹²	Rio de Janeiro (Brazil)	Jul to Dec 2008	ND	7.4×10^3 coliforms 39% of ESBL ^e	$0.3\text{--}2 \times 10^3$ coliforms 46–56% of ESBL ^e	—	CTX-M
Bréchet <i>et al.</i> ¹³	Besançon (France)	Jan to Apr 2011	7.5×10^5 <i>E. coli</i> 0.1% of ESBL ^b	3.5×10^5 <i>E. coli</i> 7.5% of ESBL ^b	3.7×10^3 <i>E. coli</i> 0.6% of ESBL ^b	6×10^{11}	CTX-M-1 (50%) CTX-M-15 (25%)
Ojer-Usoz <i>et al.</i> ¹⁴	Navarra (Spain)	Mar 2011 to Oct 2012	ND	ND	5.6×10^2 coliforms 0.4% of ESBL ^b	—	CTX-M-14 (32%) CTX-M-1 (16%)
Blaak <i>et al.</i> ¹⁵	Four sites in The Netherlands	Summers 2011 and 2012	ND	ND	1–10 ESBL ^b	$10^{10}\text{--}10^{11}$	CTX-M-15 (42%) CTX-M-1 (24%)
Kwak <i>et al.</i> ¹⁶	Stockholm (Sweden)	Jan 2013 to Feb 2014	7.4×10^4 <i>E. coli</i> 2.3% of ESBL ^b	3.7×10^4 <i>E. coli</i> 13.6% of ESBL ^b	$0.4\text{--}1.2 \times 10^2$ <i>E. coli</i> 2.3% of ESBL ^b	1.1×10^{12}	CTX-M group 1
Korzeniewska <i>et al.</i> ¹⁷	Olsztyn (Poland)	Unknown (13-month period)	$1\text{--}2.9 \times 10^6$ coliforms 19% of ESBL ^e	ND	$0.6\text{--}3.5 \times 10^4$ coliforms 9.8% of ESBL ^e	—	CTX-M group 1 (61%)
Oberlé <i>et al.</i> ⁵	Rouen (France)	Dec 2009	3.9×10^6 <i>E. coli</i>	8.3×10^4 <i>E. coli</i>	2.6×10^3 <i>E. coli</i>	—	—

^a WWTP, wastewater treatment plant.

^b ESBL^b, extended-spectrum β -lactamase-producing *E. coli*.

^c ESBL, extended-spectrum β -lactamase.

^d ND, not determined.

^e ESBL^e, extended-spectrum β -lactamase-producing enterobacteria.

E. coli, *E. coli* BLSE, eaux usées et STEP

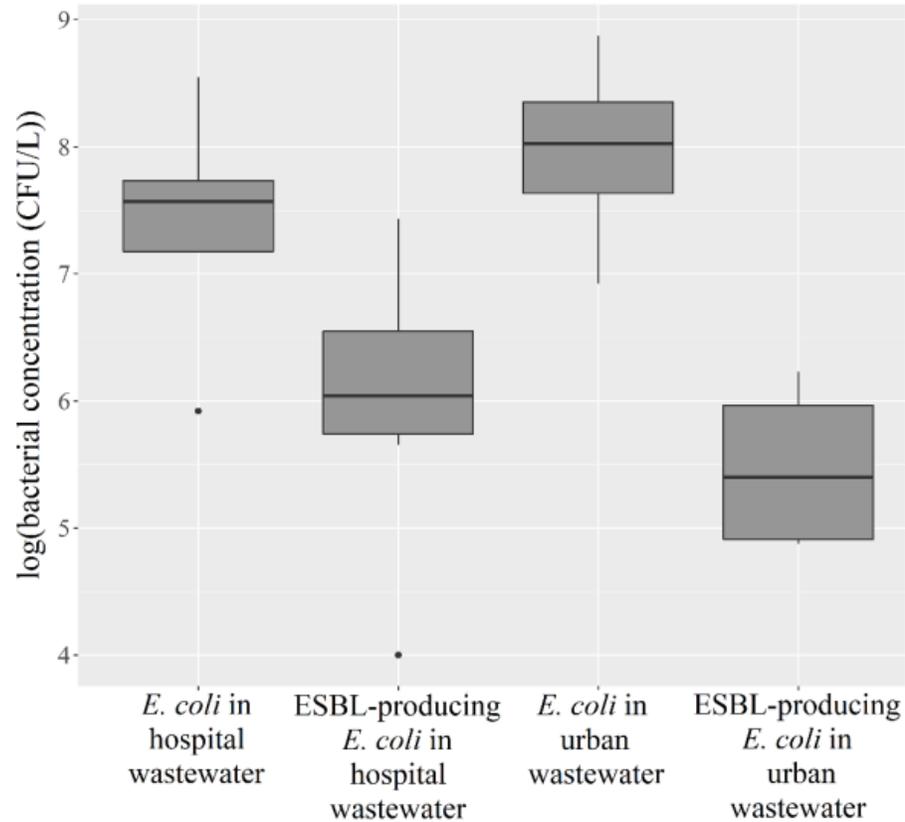


Figure 3. Comparison of *E. coli* and ESBL-producing *E. coli* in hospital and urban wastewater. Data collected from Servais et al. 2009; Galvin et al. 2010; Oberlé et al. 2012; Bréchet et al. 2014; Kwak et al. 2015; and Drieux et al. 2016 (CFU: colony forming units; ESBL: extended-spectrum β -lactamase).

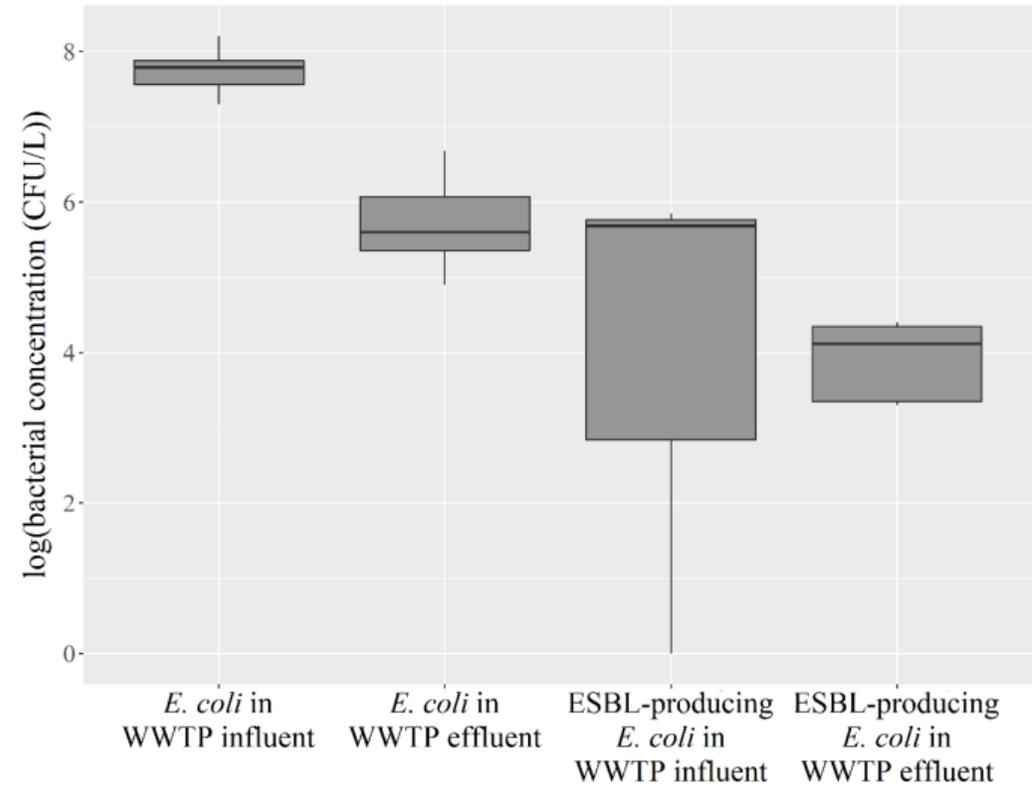


Figure 5. Comparison of *E. coli* and ESBL-producing *E. coli* in WWTP influent and effluent. Data collected from Reinthaler et al. 2003; Servais et al. 2009; Galvin et al. 2010; Oberlé et al. 2012; Blaak et al. 2014a; Bréchet et al. 2014; Ojer-Usoz et al. 2014; and Kwak et al. 2015 (ESBL: extended-spectrum β -lactamase; WWTP: wastewater treatment plant).



Review

What happens in hospitals does not stay in hospitals: antibiotic-resistant bacteria in hospital wastewater systems

D. Hocquet^{a,b,*}, A. Muller^{a,b}, X. Bertrand^{a,b}

Table IV

Clearance of antimicrobial-resistant bacteria by the wastewater treatment plants

Antibiotic-resistant bacteria	Presence in hospital wastewater ^a	Presence in urban wastewater ^b	Effect of the WWTP process	Environmental pollution
ESBL-producing <i>E. coli</i>	+++	++	Enhancing of the proportion of ESBL-producing <i>E. coli</i> among total <i>E. coli</i>	+++
Multidrug-resistant <i>P. aeruginosa</i>	+++	+/-	Decreasing of the proportion of multidrug-resistant <i>P. aeruginosa</i>	+
VRE	+++	+ ^c	Neutral	++

WWTP, wastewater treatment plant; ESBL, extended-spectrum β -lactamase; VRE, vancomycin-resistant enterococci.^a Depends on the prevalence of antibiotic-resistant bacteria in the studied setting or region or country.^b Surrounding the hospital wastewater.^c Depends on the prevalence of VRE in the community.

HEALTH AND MEDICINE

Antibiotic resistance in European wastewater treatment plants mirrors the pattern of clinical antibiotic resistance prevalence

Katariina M. M. Pärnänen^{1*}, Carlos Narciso-da-Rocha^{2*}, David Kneis^{3*}, Thomas U. Berendonk³, Damiano Cacace³, Thi Thuy Do⁴, Christian Elpers⁵, Despo Fatta-Kassinos⁶, Isabel Henriques⁷,

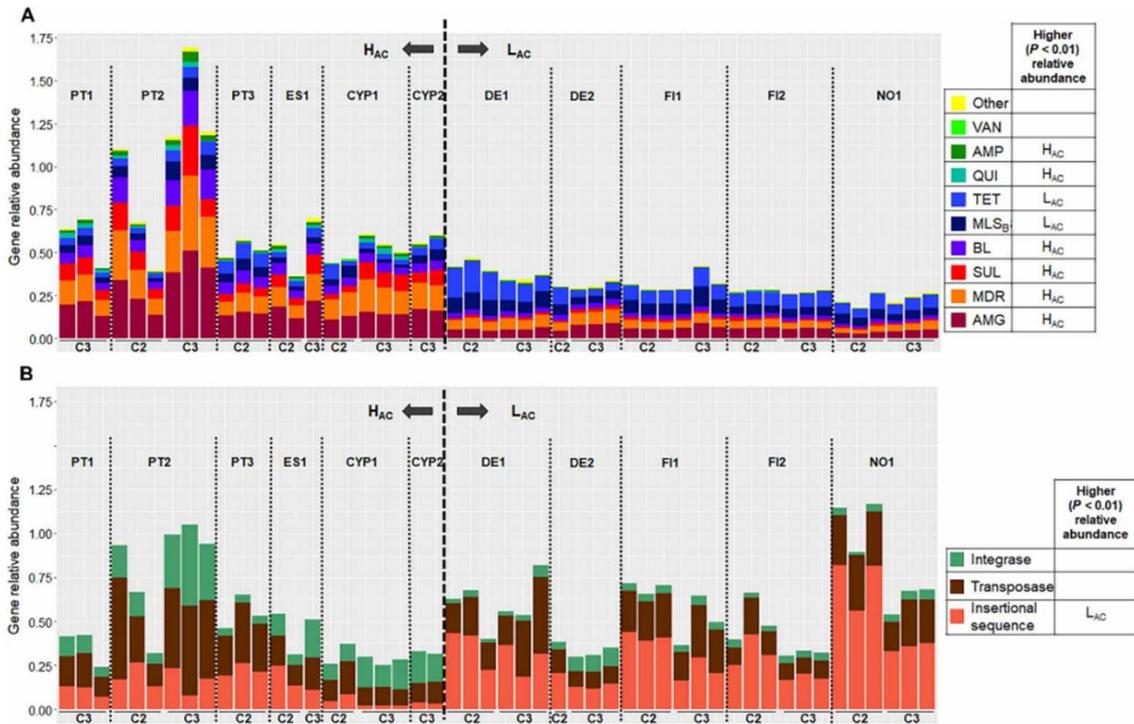


Fig. 2. Relative gene abundance observed in influent samples from H_{AC} and L_{AC} countries. Relative abundance of (A) resistance genes and (B) mobile genetic elements. The data refer to the sum of relative abundance of amplification (ratio ARG or MGE copy number: 16S rRNA gene copy) for a given pair of primers, organized in classes of “resistance” or “transfer and recombination.” In the legend, for each gene class, the country group, H_{AC} or L_{AC}, with significantly higher relative abundance ($P < 0.01$, Mann-Whitney U test) is indicated. Samples are organized according to the sampling campaign (C2, spring 2016; C3, autumn 2016), divided by H_{AC} and L_{AC}. Resistance categories: AMG (aminoglycosides), MDR (multidrug resistance), SUL (sulfonamides), BL (β -lactams), MLS_B, TET (tetracycline), QUI (quinolones), AMP (amphenicols), VAN (vancomycin), and others. Note: Ireland data are missing because of restrictions on influent wastewater sample collection.

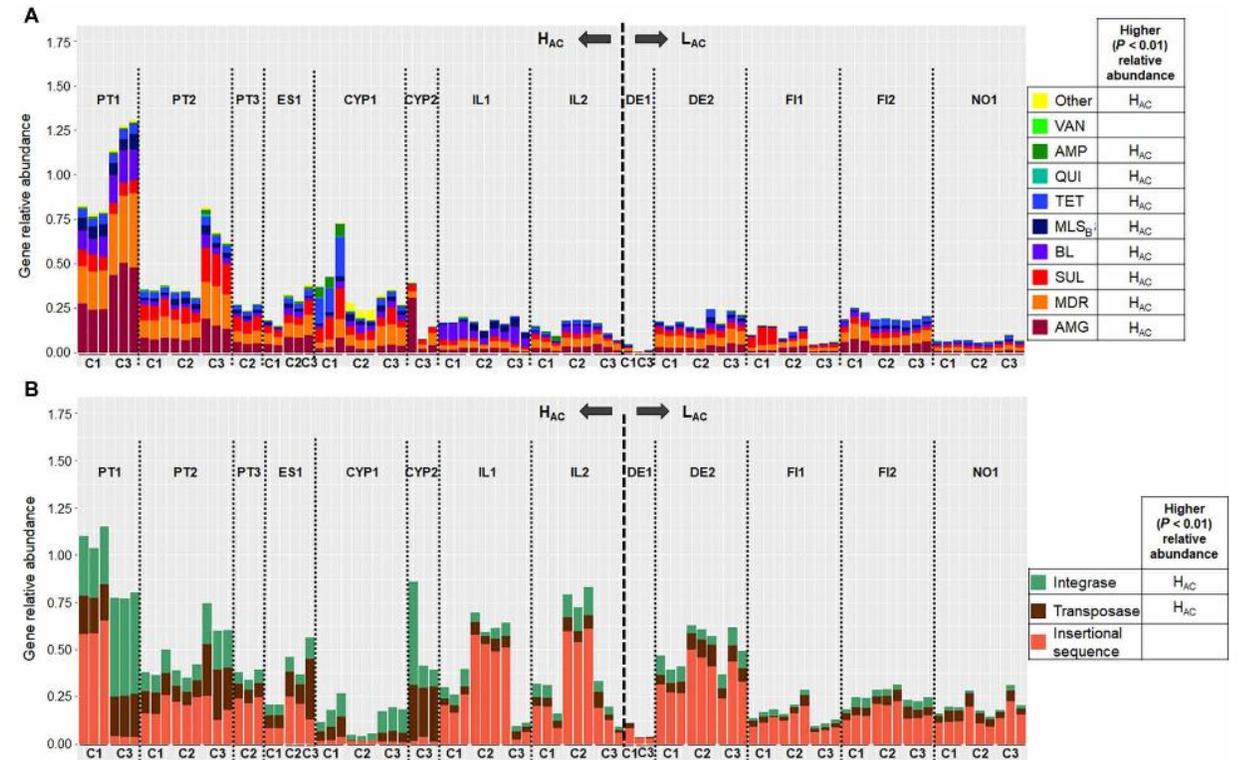
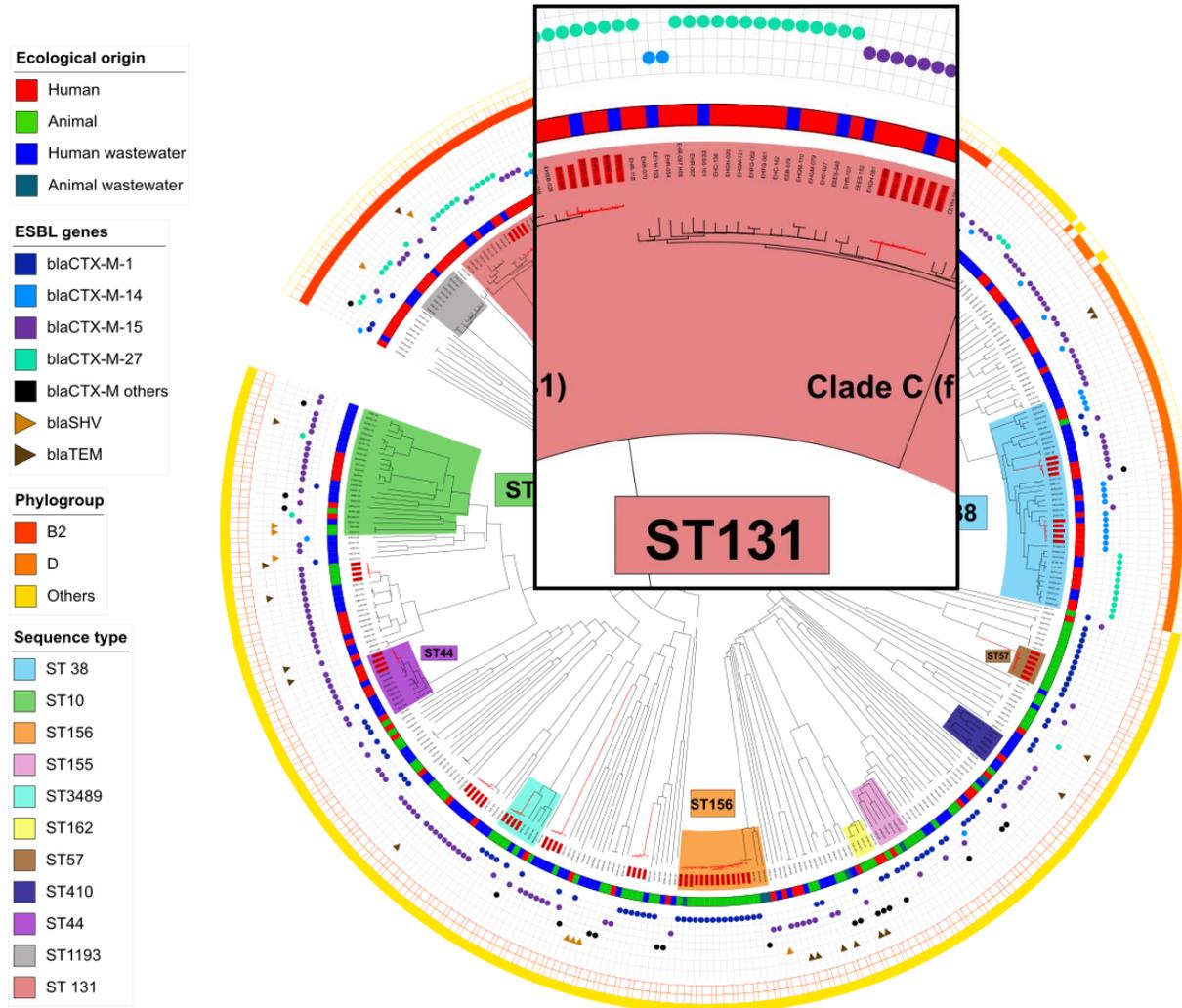
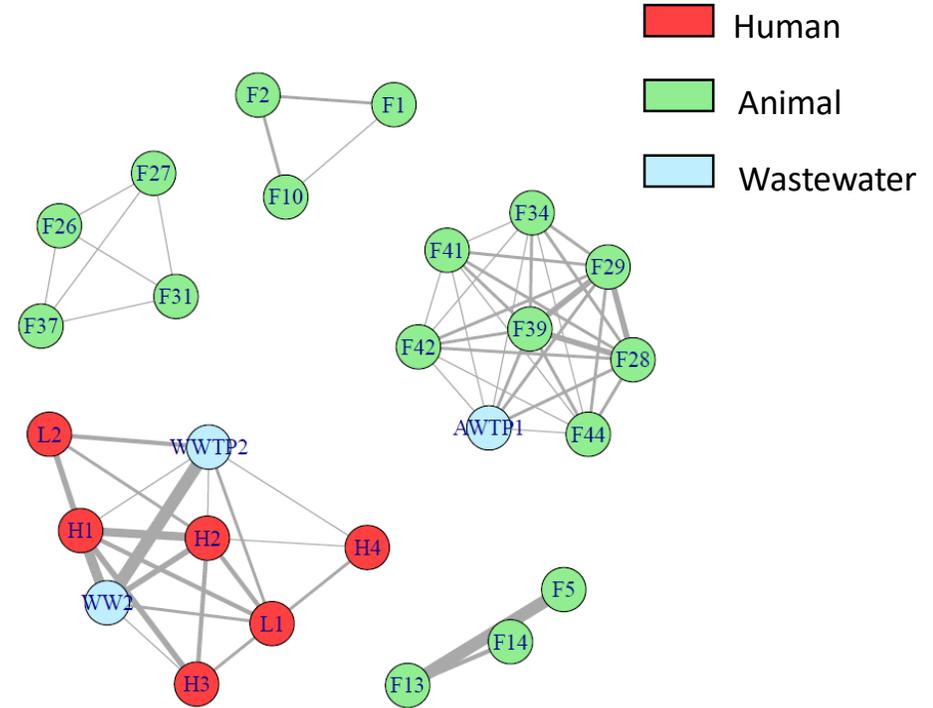


Fig. 3. Relative gene abundance observed in effluent samples from H_{AC} and L_{AC} countries. Relative abundance of (A) resistance genes and (B) mobile genetic elements. The data refer to the sum of relative abundance of amplification (ratio ARG or MGE copy number: 16S rRNA gene copy) for a given pair of primers organized in classes of resistance or transfer and recombination. In the legend, for each gene class, the country group, H_{AC} or L_{AC}, with significantly higher relative abundance ($P < 0.01$, Mann-Whitney U test) is indicated. Samples are organized according to the sampling campaign (C1, autumn 2015; C2, spring 2016; C3, autumn 2016), divided by H_{AC} and L_{AC}. Resistance categories: AMG (aminoglycosides), MDR (multidrug resistance), SUL (sulfonamides), BL (β -lactams), MLS_B, TET (tetracycline), QUI (quinolones), AMP (amphenicols), VAN (vancomycin), and others.

E. coli BLSE, analyse génotypique globale, apport du NGS



Réseau de clonalité



J Antimicrob Chemother 2022; 77: 1254-1262
<https://doi.org/10.1093/jac/dkac054> Advance Access publication 23 February 2022

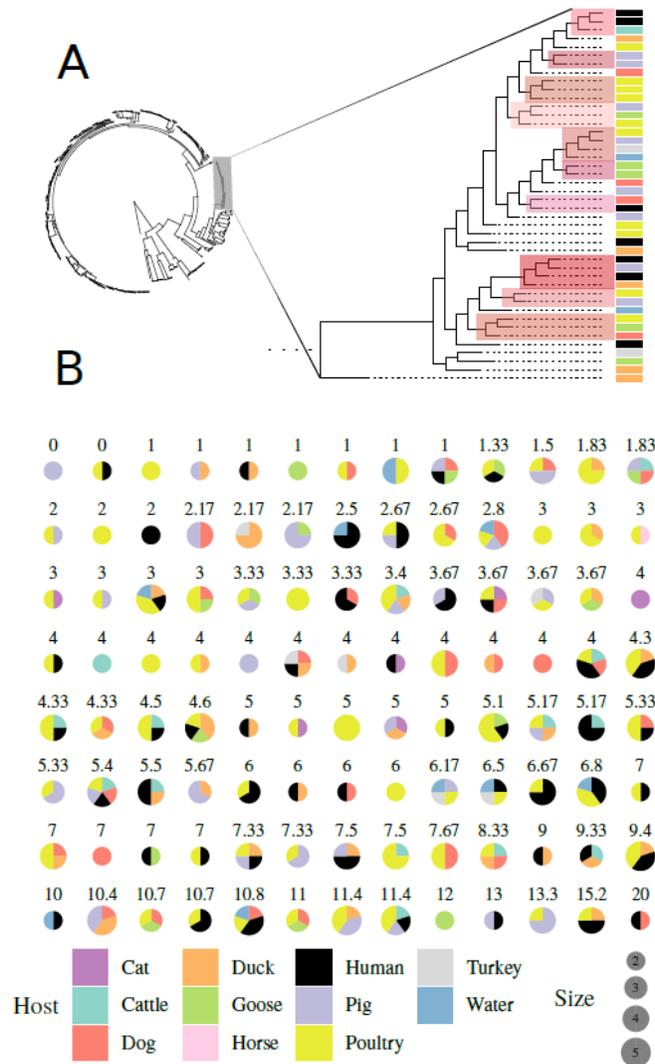
Journal of Antimicrobial Chemotherapy

One Health compartmental analysis of ESBL-producing *Escherichia coli* on Reunion Island reveals partitioning between humans and livestock

Guillaume Miltgen^{1,2*}, Daniel Martak^{3,4}, Benoit Valot⁴, Laure Kamus¹, Thomas Garrigou¹, Guillaume Verchere², Houssein Gbaguidi-Haore^{3,4}, Céline Ben Cimon⁵, Mahery Ramiandrisoa⁶, Sandrine Picot⁷, Anne Lignereux⁸, Geoffrey Masson⁹, Marie-Christine Jaffar-Bandjee¹, Olivier Belmonte¹, Eric Cardinale^{10,11}, Didier Hocquet^{3,4}, Patrick Mavingui² and Xavier Bertrand^{3,4}

Étude *One Health* à Madagascar

 RNB/hab. 520\$



- Étude menée en 2018 dans un district rural autour de Antananarivo (CIRAD-IPM)
- 510 *E. coli* BLSE issus de 1368 prélèvements Homme-animal-eau (de consommation)
 - Prévalence Animal (46%) > Homme (33%) > Water (18%)
- 181 génomes de *E. coli* BLSE séquencés
 - Diversité : 80 STs différents
 - 104 clusters (<20 SNPs) de faible effectifs dont 47% Homme-animal
 - Pas de spécificité d'hôtes retrouvée

→ Modèle *One Health* Homme-animal-environnement en PED

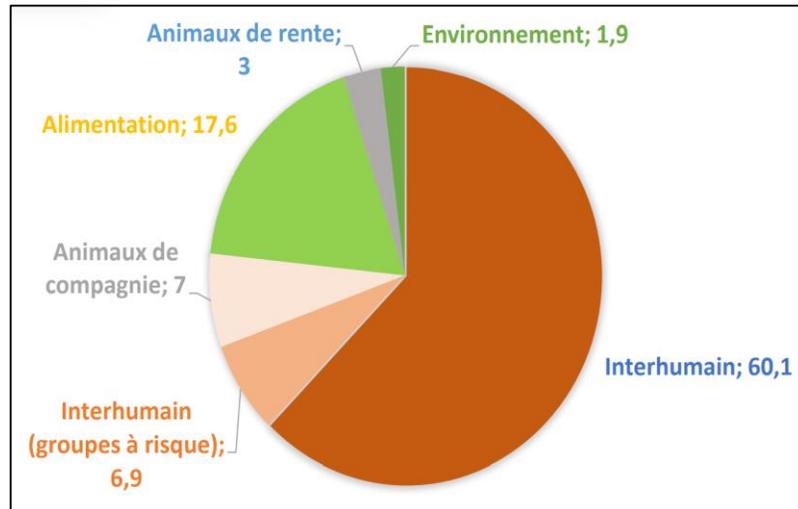
- Les bactéries multi-résistantes d'origine humaine (dont les BHRe) contaminent donc massivement notre environnement, notamment l'environnement aqueux
- Le niveau de contamination est proportionnel à la prévalence de la résistance dans la population humaine (quelle est la prévalence de portage des BHRe?)
- Quelles sont les conséquences en terme de santé publique?
- Dans quelle mesure cette contamination environnementale participe à l'épidémiologie de la multi-résistance bactérienne aux antibiotiques?

Modélisation des réservoirs de transmissions des EBLSE

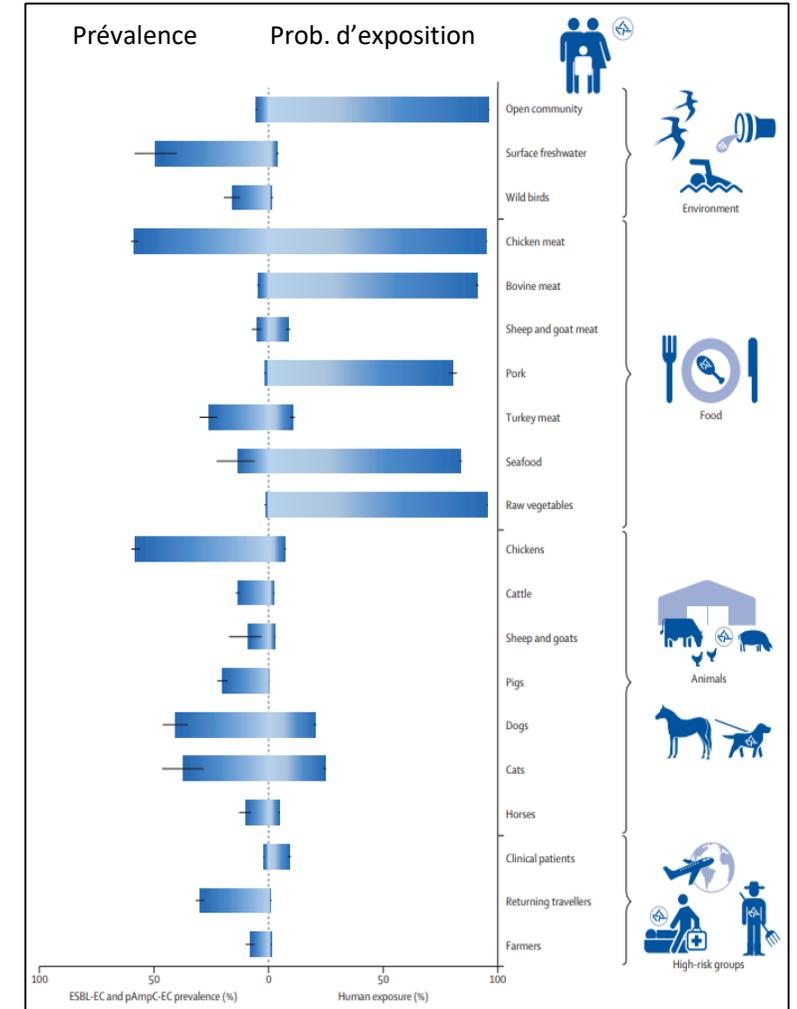
- Méta-analyse de 35 études aux Pays-Bas (2005-2017)
 - 1220 « occurrences » de gène bla_{BLSE} ou bla_{AmpC}
- Corrélation entre occurrence, prévalence dans chaque compartiment et probabilité d'exposition pour l'Homme
- Déduction d'une probabilité d'acquisition à partir de chaque réservoir y compris l'Homme

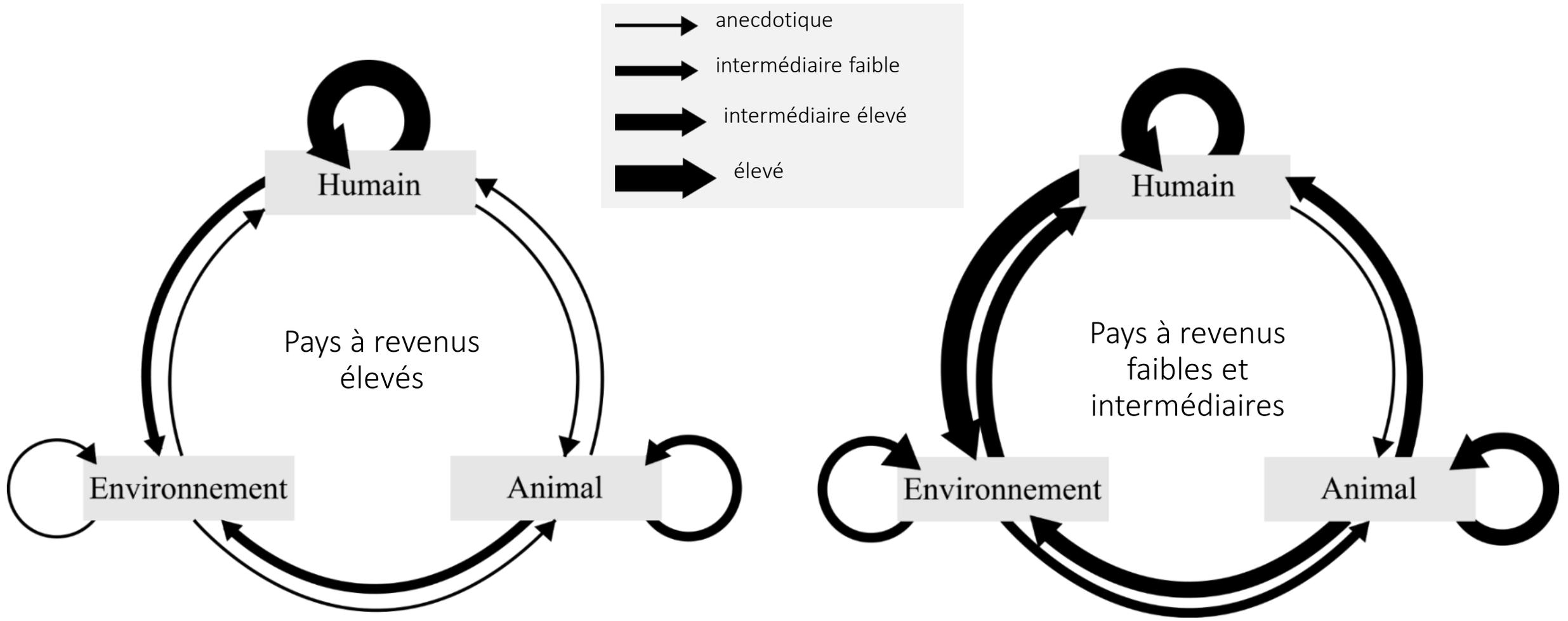
Alimentation
= 18%

Animal = 10%



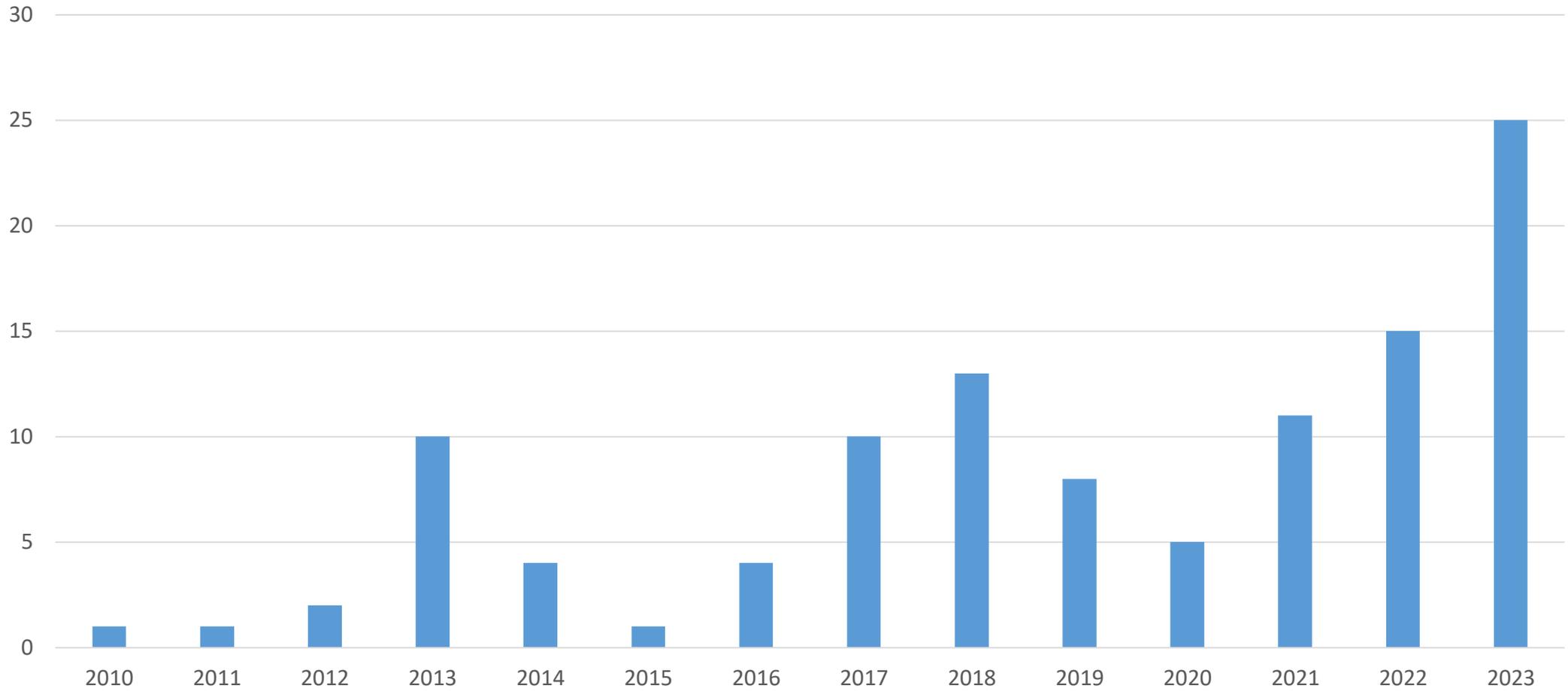
Homme =
67% = 2/3

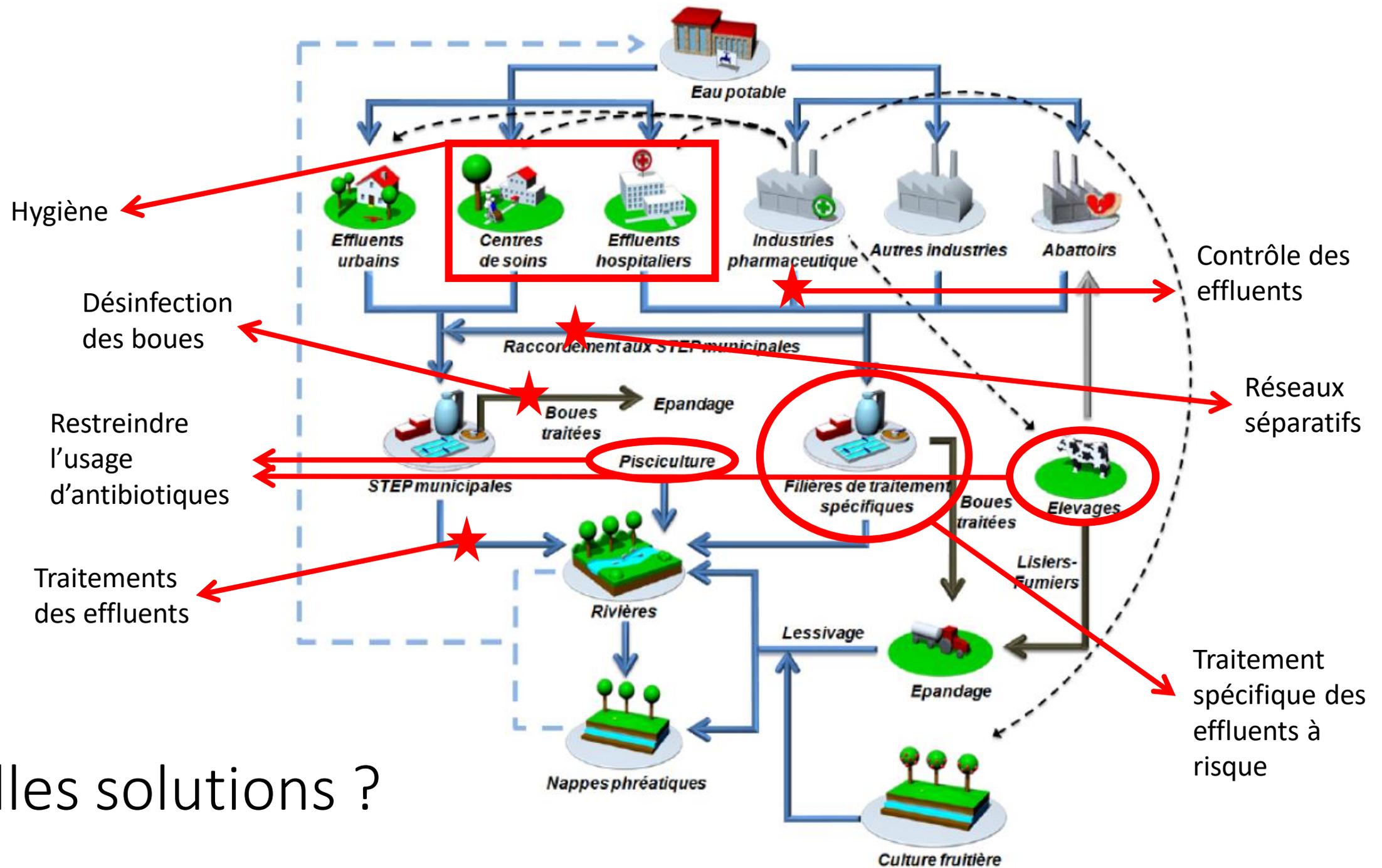




- 2 modèles d'interaction Homme-animal-environnement en fonction du développement du pays
 - *One Health in low-income countries* (PED) → Animal – Environnement = Réservoirs de BHRe
 - « *Two Health* » in high income-countries (PID) → Homme = Réservoir de BHRe pour l'Homme
- Implications dans la lutte contre l'antibiorésistance
 - Dans les PED, infrastructures sanitaires → lutte contre le péril oro-fécal → prévention de l'AR
 - Dans les PID :
 - Les politiques de diminution de la consommation chez l'animal → impact limité
 - C'est dans le compartiment humain qu'il faut agir pour avoir le plus d'impact (Hygiène et BUA)
- Modèles qui demandent à être confirmés sur BHRe par d'autres études (nationales) dans les PID, et par un accès au WGS dans les PED

EPC, CHU Besançon





Quelles solutions ?