



Update on the global situation of antimicrobial resistance. Impact of COVID-19

Jordi Vila
Department of Clinical Microbiology
Hospital Clinic
Barcelona



WHO PRIORITY PATHOGENS FOR R&D OF NEW ANTIBIOTICS

March 2017



Priority 1: CRITICAL[#]

Acinetobacter baumannii, carbapenem-resistant

Pseudomonas aeruginosa, carbapenem-resistant

*Enterobacteriaceae**, carbapenem-resistant, 3rd generation
cephalosporin-resistant

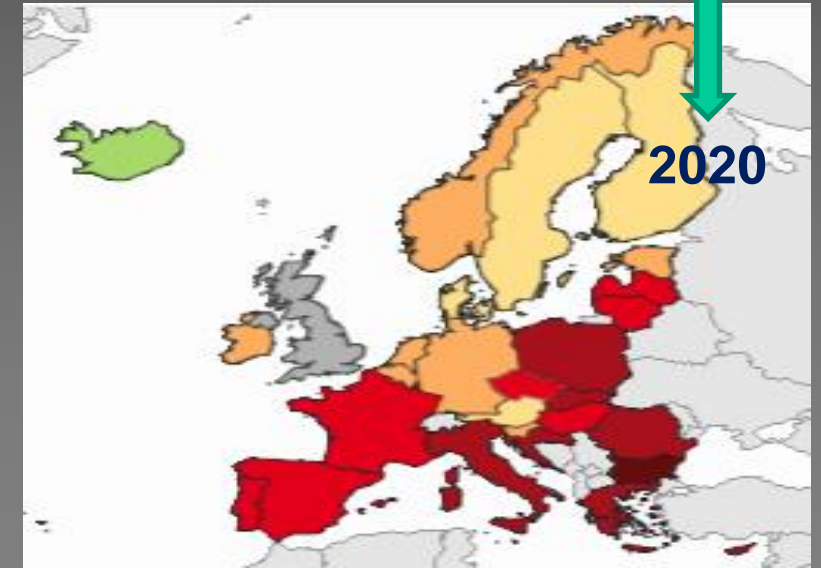
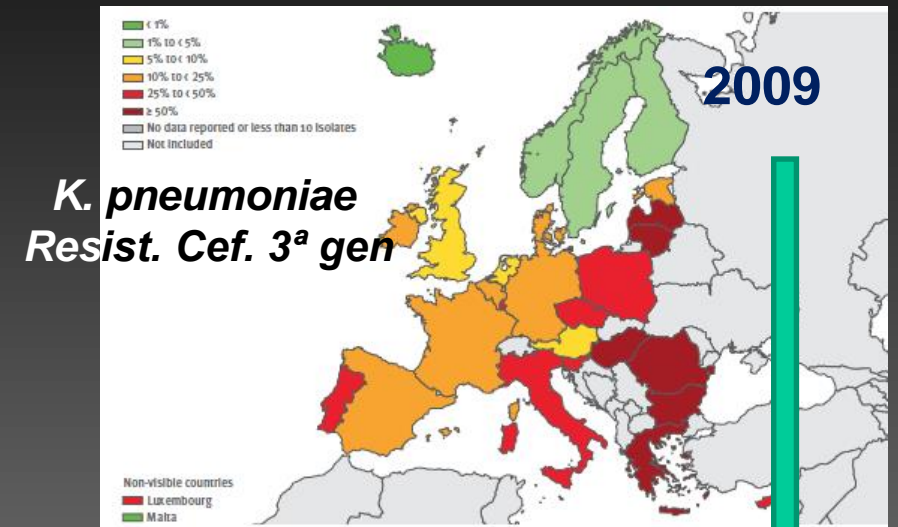
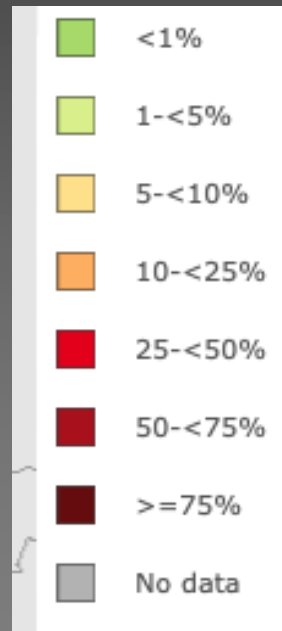
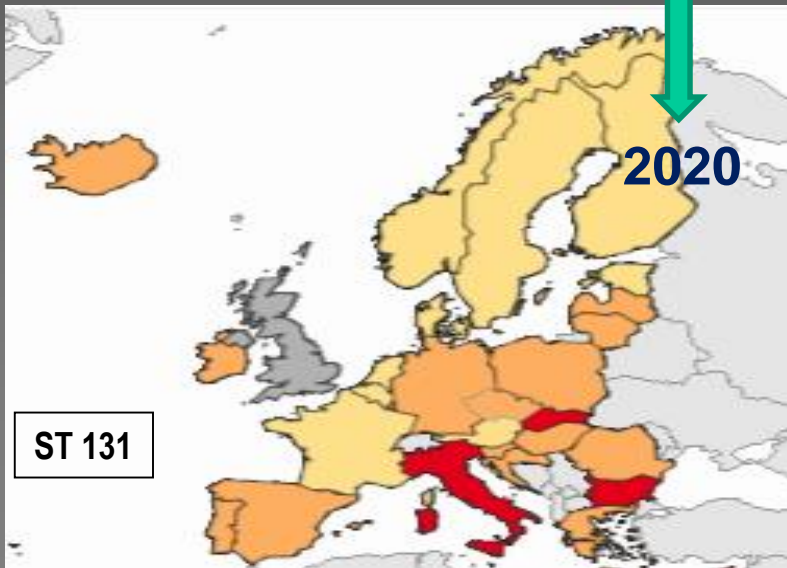
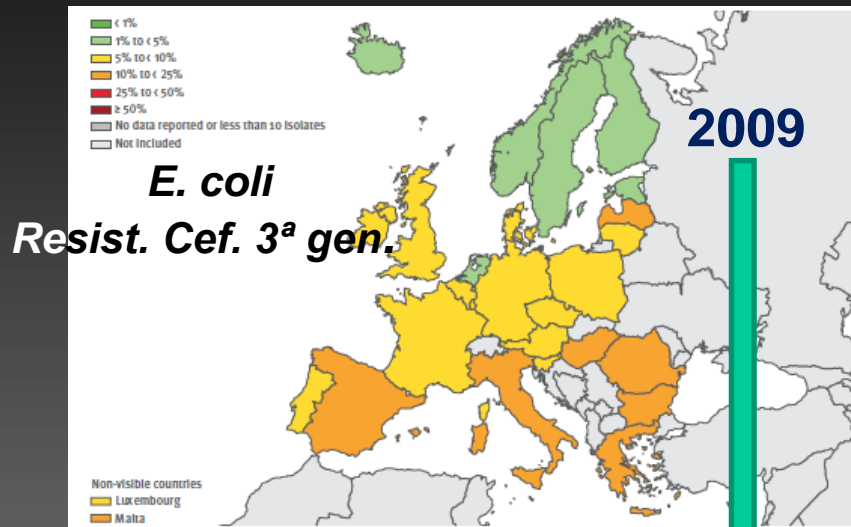
MAIN RESISTANT MICROORGANISMS

- Extended-spectrum β -lactamase (ESBL)-producing *Enterobacterales*
- Carbapenem-resistance *Enterobacterales*
- *Pseudomonas aeruginosa* and *Acinetobacter baumannii* multi, extensively and pandrug resistant

MAIN RESISTANT MICROORGANISMS

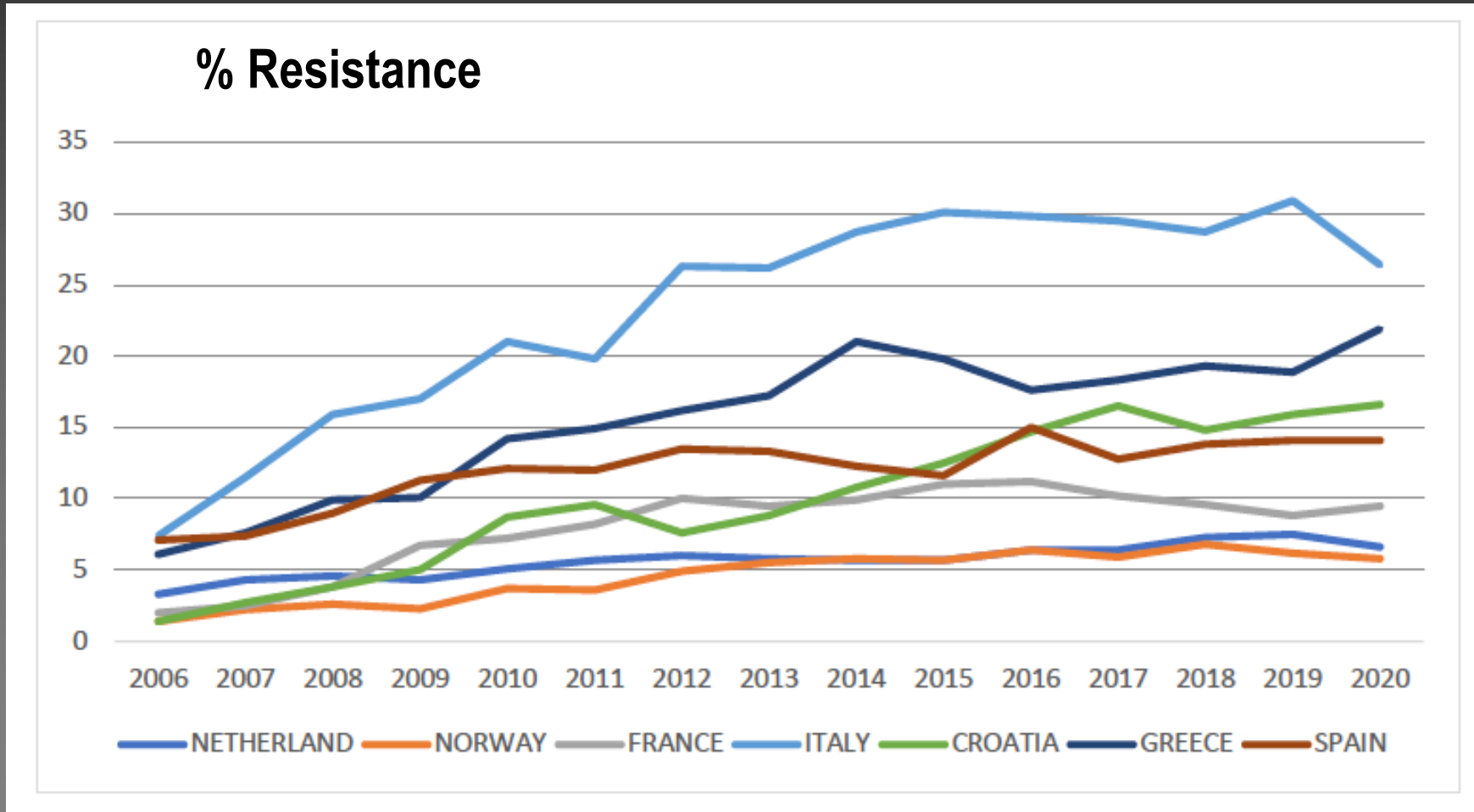
- Extended-spectrum β -lactamase (ESBL)-producing *Enterobacterales*
- Carbapenem-resistance *Enterobacterales*
- *Pseudomonas aeruginosa* and *Acinetobacter baumannii* multi, extensively and pandrug resistant

Enterobacteriales: ESBL



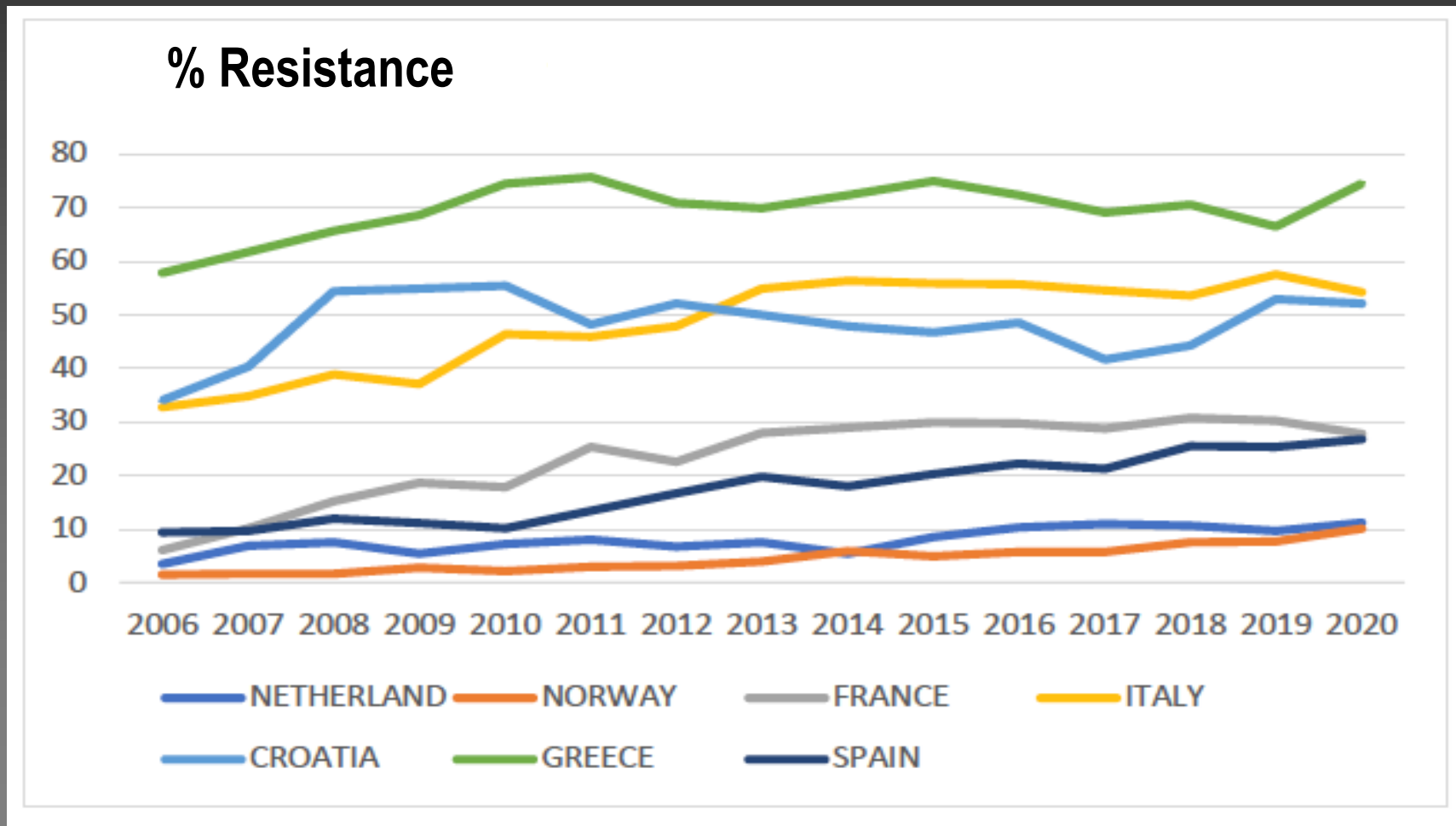
Evolution of AR in different countries in Europe

ESBL producing E. coli



Evolution of AR in different countries in Europe

ESBL producing K. pneumoniae



MAIN RESISTANT MICROORGANISMS

- Extended-spectrum β -lactamase (ESBL)-producing *Enterobacterales*
- Carbapenem-resistance *Enterobacterales*
- *Pseudomonas aeruginosa* and *Acinetobacter baumannii* multi, extensively and pandrug resistant

Carbapenemases

Class	Type	Clavulanic ac. inh.	EDTA	Susceptibility to ATM	Genetic location
A	GES	+	-	S	P
	IMI	+	-	R	C
	SME	+	-	R	C
	KPC	+	-	R	P
B	NDM	-	+	S	C/P
	VIM	-	+	S	C/P
	IMP	-	+	S	C/P
D	OXA	+/-	-	S	C/P

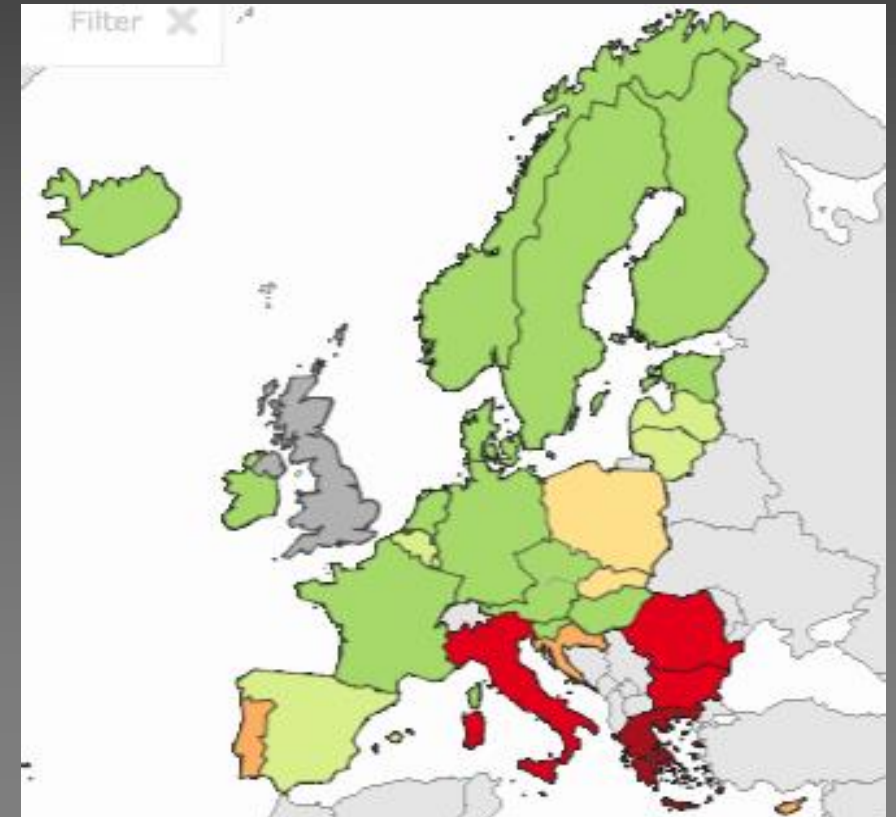
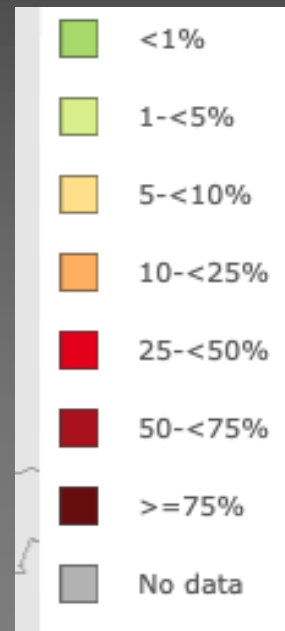
Enterobacteriales: carbapenemases

Resistance to carbapenems

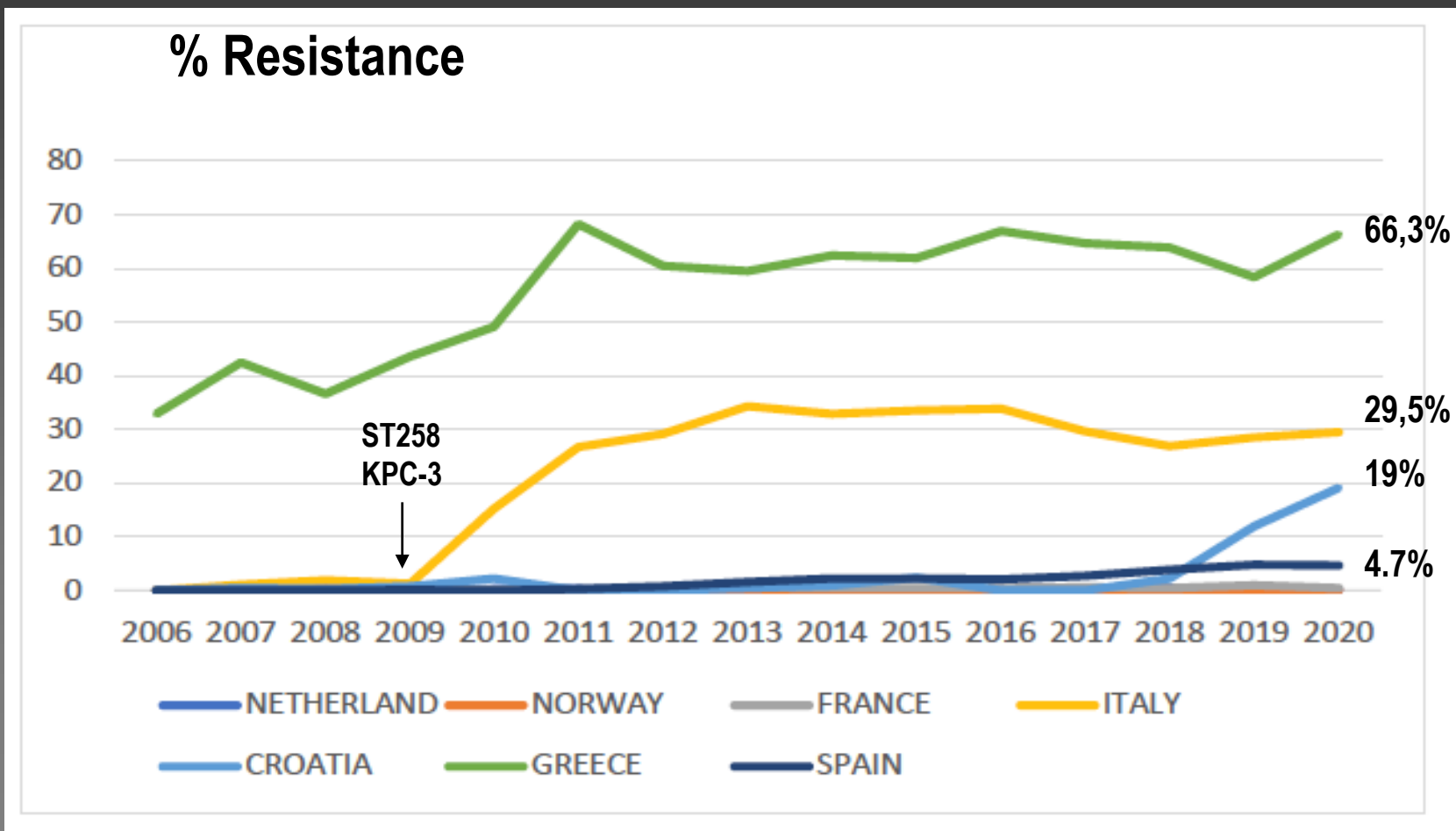
E. coli

2020

K. pneumoniae



Carbapenemase producing *K. pneumoniae*

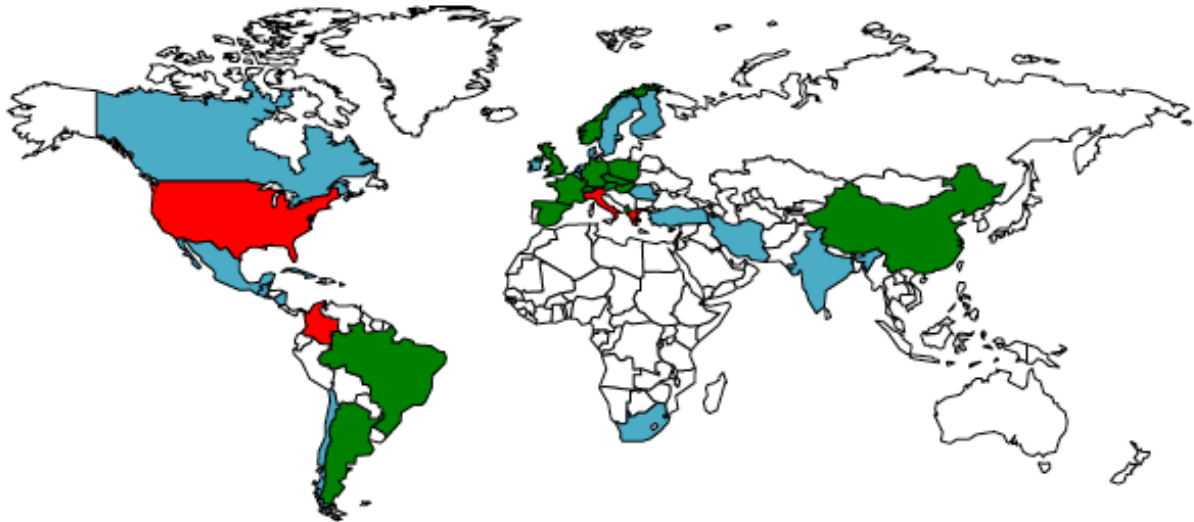


Global dissemination of carbapenemases

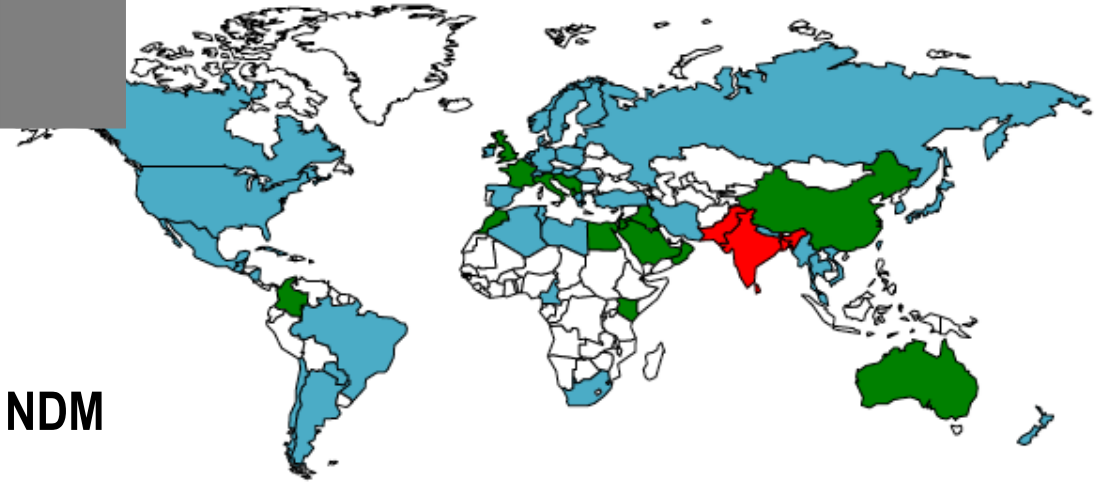
KPC

- Unknown distribution of KPC producers
- Sporadic spread of KPC producers
- Outbreaks caused by KPC producers
- Endemicity of KPC producers

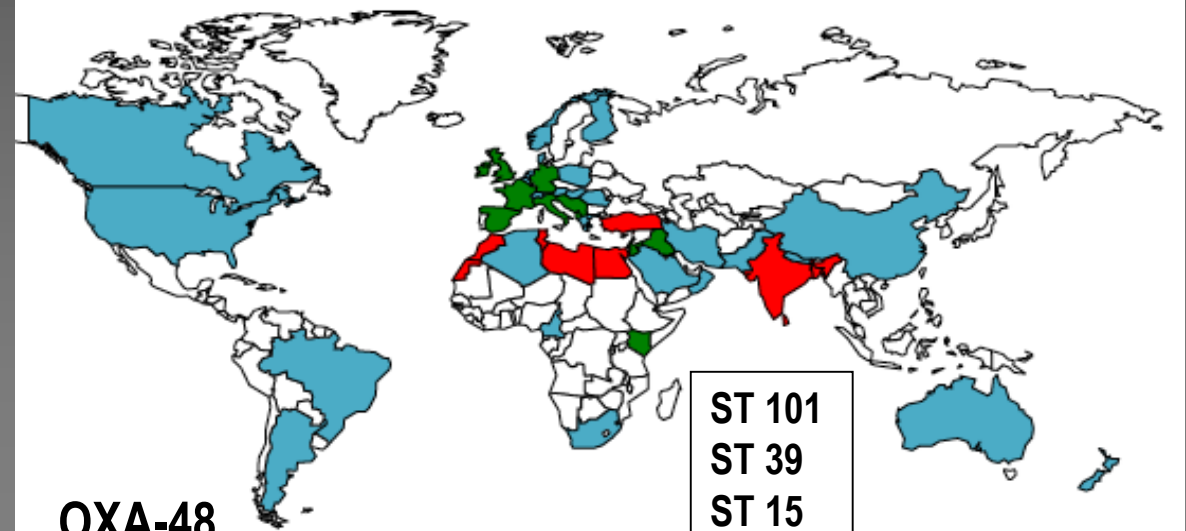
CC258



NDM



OXA-48

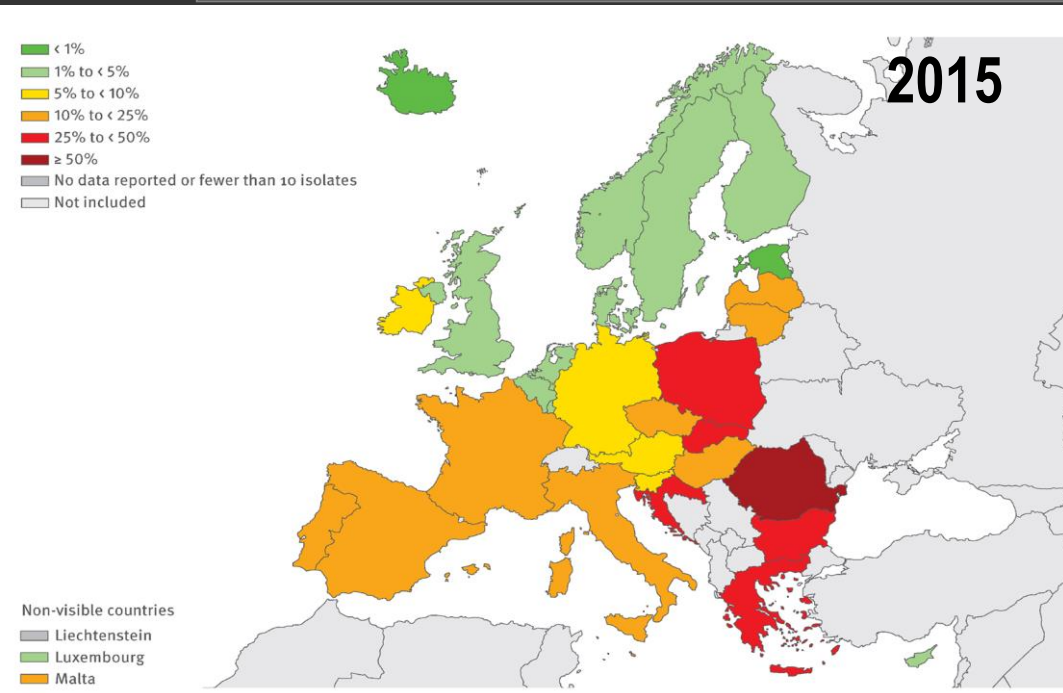


MAIN RESISTANT MICROORGANISMS

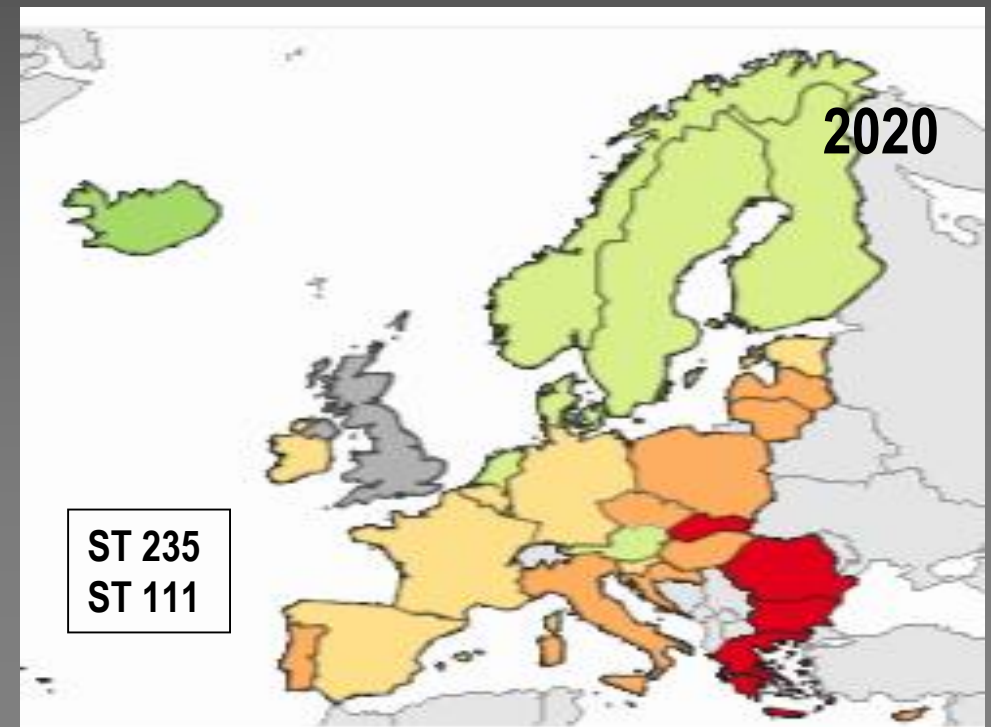
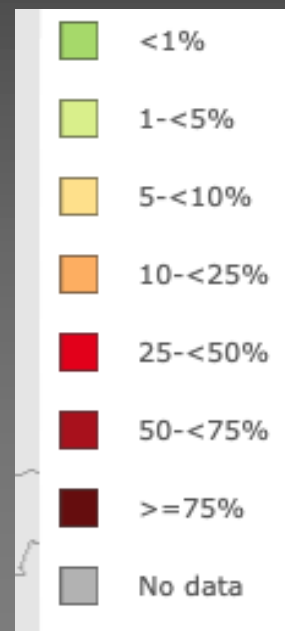
- Extended-spectrum β -lactamase (ESBL)-producing *Enterobacterales*
- Carbapenem-resistance *Enterobacterales*
- *Pseudomonas aeruginosa* and *Acinetobacter baumannii* multi, extensively and pandrug resistant

Multidrug resistant *P. aeruginosa*

EARSS-Net report



3,3 % in Denmark
55,4% in Romania
21,8% in Spain
Overall mean in Europe 16,5%



MAIN RESISTANT MICROORGANISMS

- Extended-spectrum β -lactamase (ESBL)-producing *Enterobacterales*
- Carbapenem-resistance *Enterobacterales*
- *Pseudomonas aeruginosa* and *Acinetobacter baumannii* multi, extensively and pandrug resistant

Evolución de la resistencia en *Acinetobacter baumannii*

Antibiotic	GEIH-Ab 2000 (n=221) %	GEIH-Ab 2010 (n=446) %	Difference	p value
Piperacillin	93	94	1	0.74
Ceftazidime	83	99	16	0.000
Sulbactam	53	65	12	0.0042
Imipenem	48	82	34	0.000
Meropenem	43	83	40	0.000
Doripenem	NT	86	ND	ND
Gentamicin	96	70	-27	0.000
Tobramycin	79	60	-19	0.0001
Amikacin	65	49	-17	0.0001
Tetracycline	91	83	-8	0.0096
Doxycycline	68	70	2	0.53
Minocycline	34	30	-4	0.30
Tigecycline	NT	23.9	ND	ND
Ciprofloxacin	98	94	-5	0.0074
Rifampicin	51	30	-21	0.000
Colistin	0	3	3	0.000

NT: no probado, ND: no determinado



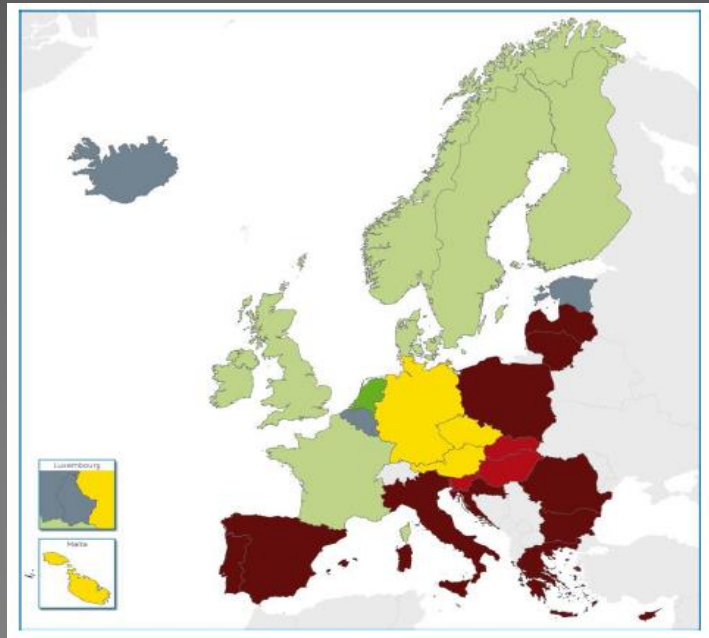
MDR: 98%
XDR: 86 %
PDR: 2 %

Multidrug resistance in *A. baumannii*

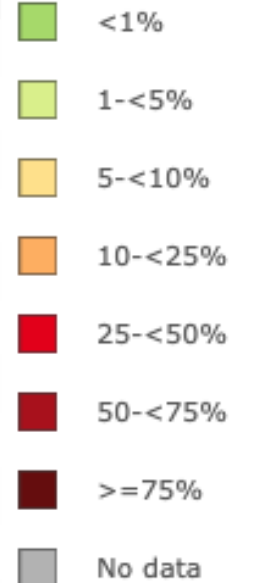
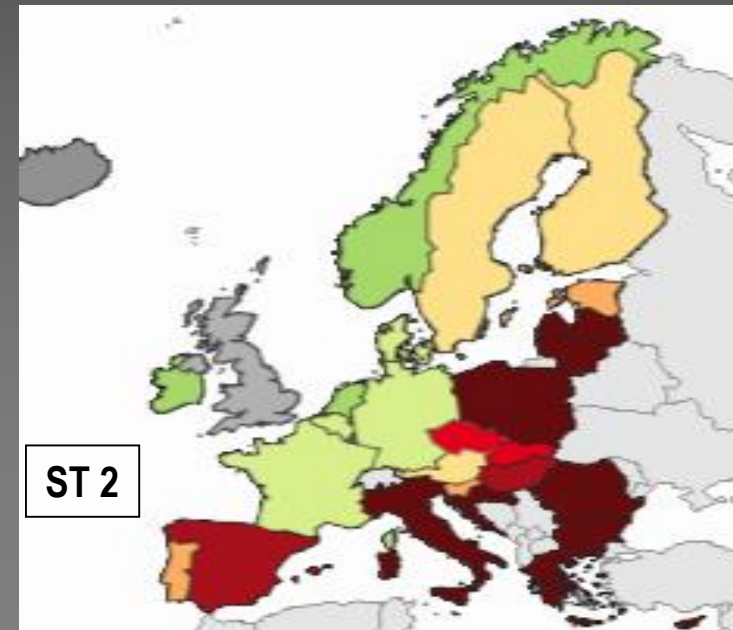
EARSS-Net report

Acinetobacter spp. resistant to carbapenems

2014



2019

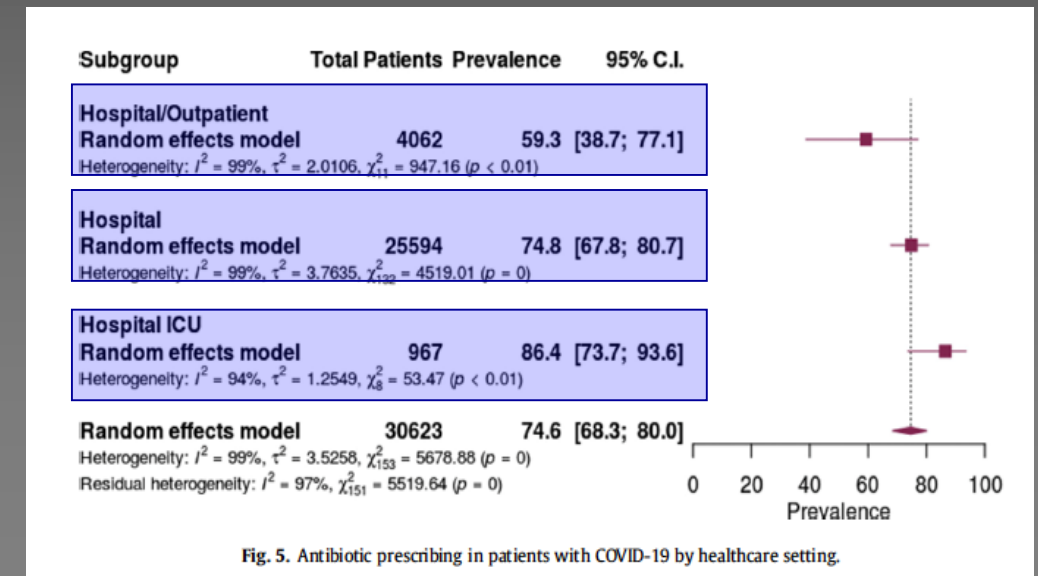
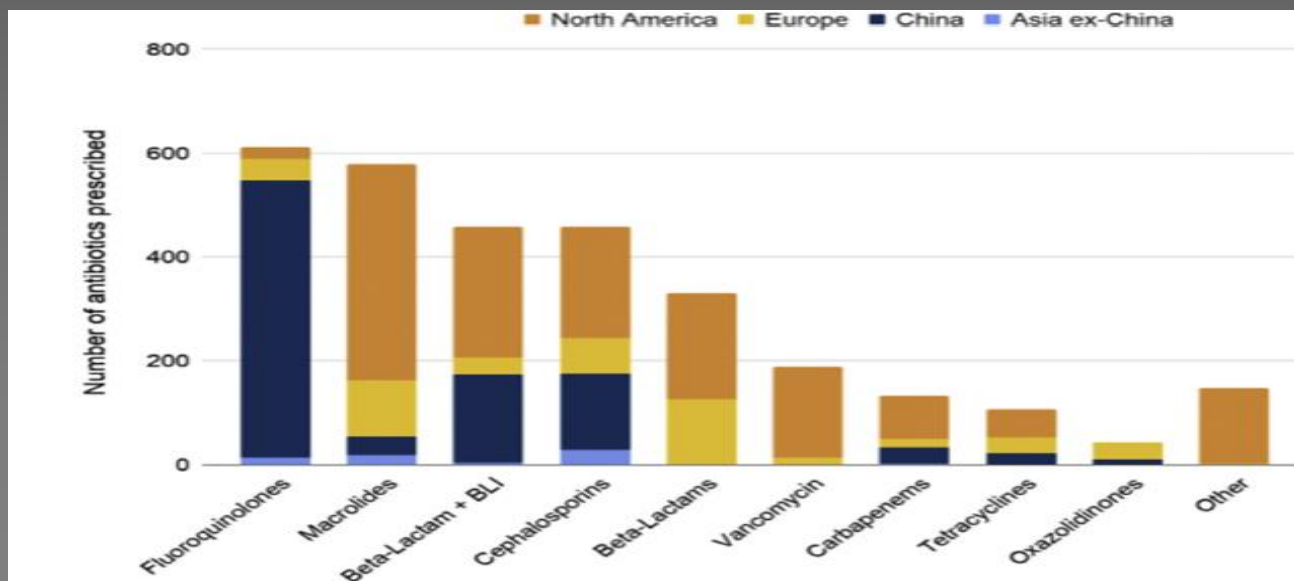


COVID-19 – ANTIBIOTIC RESISTANCE

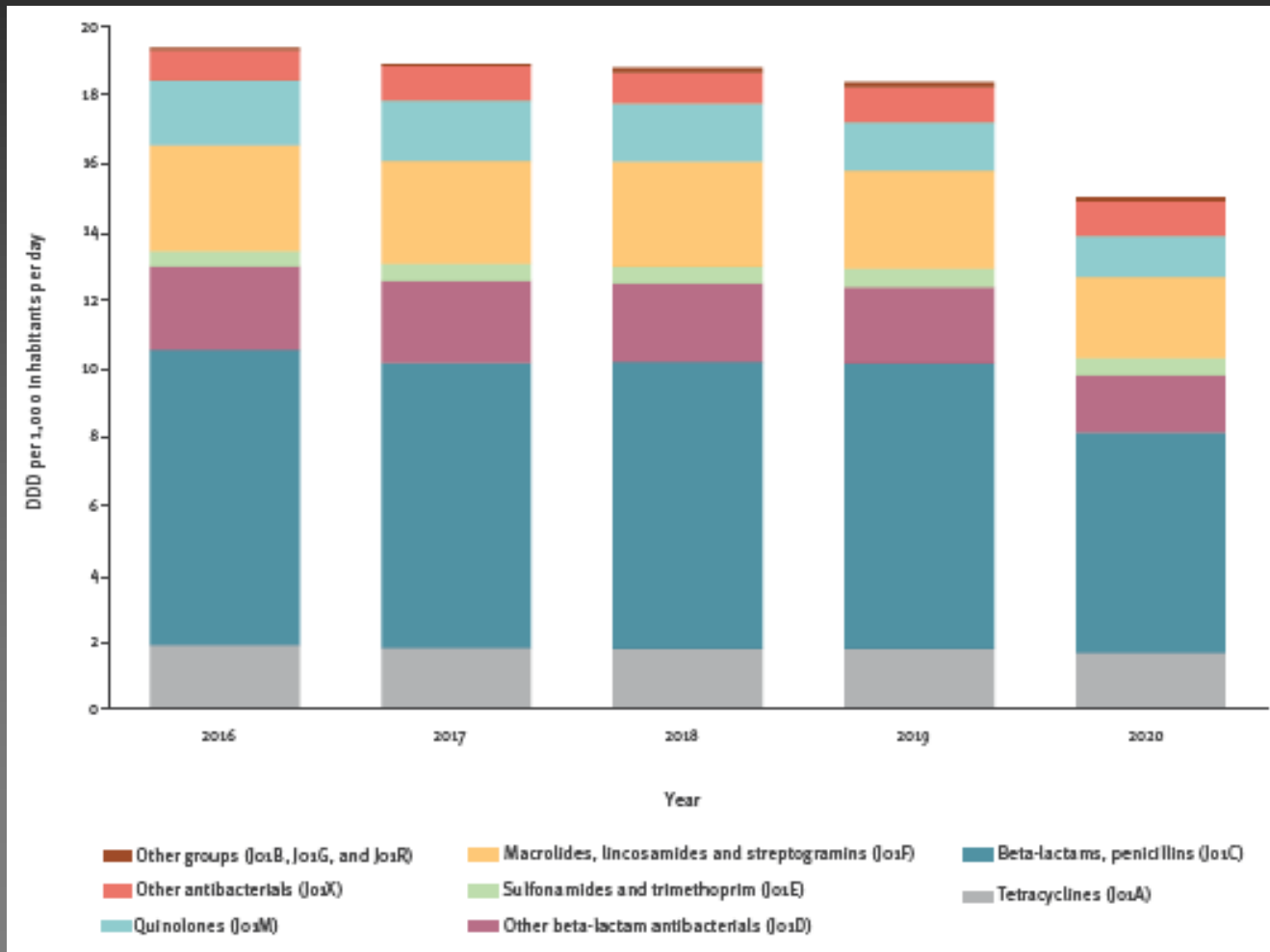
Langford, B et al: Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis

Clinical Microbiology and Infections 2021; 27: 520

- Antibiotic use data were available for **30,623** patients.
- The prevalence of antibiotic prescription was **74.6%** (95% CI 68.3 and 80.0%).
- In the univariate meta-regression, the prescription of antibiotics was lower in children (odds ratio for prescribing prevalence (OR) 0.10, 95% CI 0.03e0.33) compared to adults.
- The prescription of antibiotics was **higher with increasing age of the patient** (OR 1.45 per 10-year increase, 95% CI 1.18 to 1.77) and **higher with an increasing proportion of patients requiring mechanical ventilation** (OR 1.33 per 10% increase, 95% CI 1.15 e1.54).



Diaz Högberg, L et al: Decrease in community antibiotic consumption during the COVID-19 pandemic, EU/EEA, 2020
Euro Surveillance 2021; 26: pii=2101020.



It is still unclear whether this reduced community antibiotic consumption was sustained throughout 2021 and what implications it may have on antibiotic resistance

Knight, BD et al: The impact of COVID-19 on community antibiotic use in Canada: an ecological study
Clinical Microbiology and Infection 2021; in press

Table 1

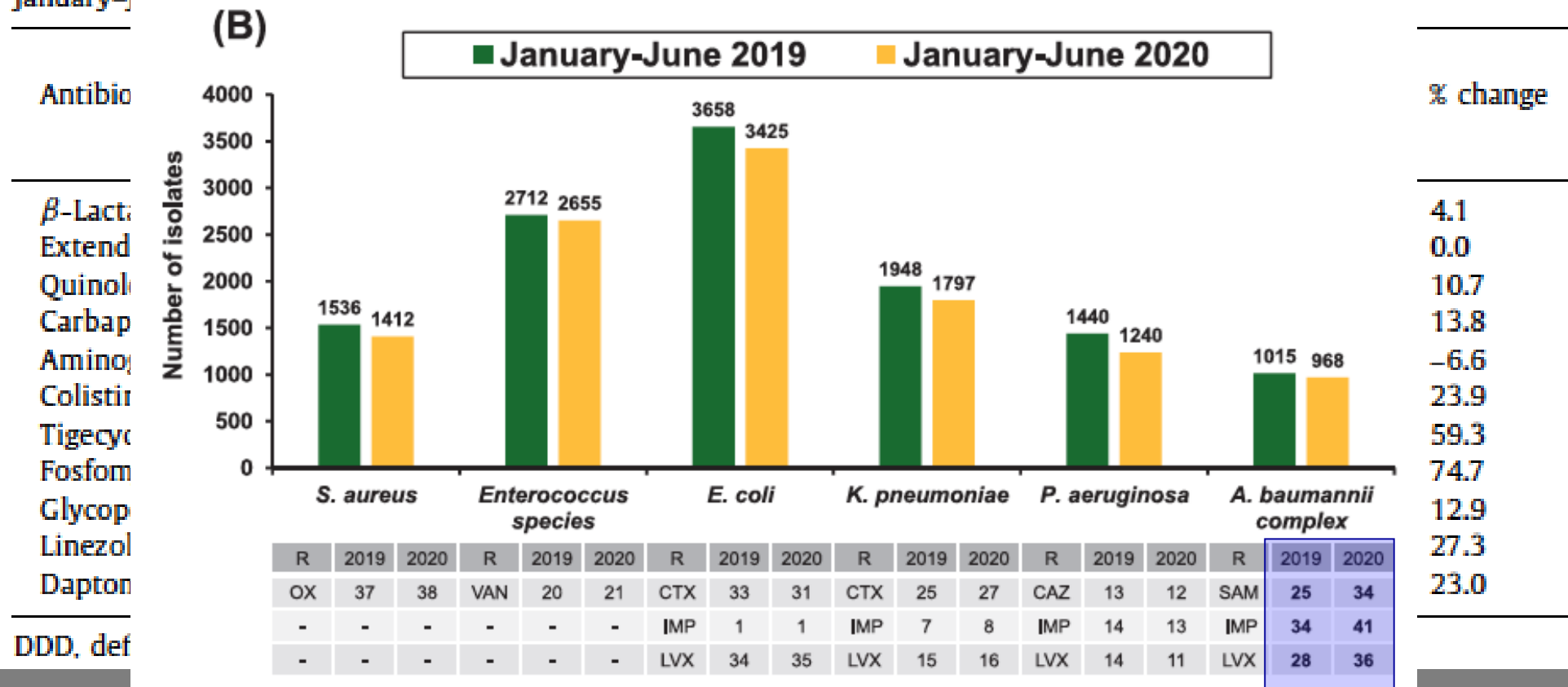
Rate of community-dispensed antibiotic prescriptions, 2019–2020, Canada

Month	Antibiotic prescriptions dispensed per 1000 inhabitants		
	2019	2020	Percent change (2019–2020)
January	60.03	61.33	2.17
February	49.68	50.62	1.89
March	54.71	48.38	–11.57
April	53.96	33.42	–38.07
May	52.73	31.87	–39.56
June	46.72	35.18	–24.70
July	47.49	36.88	–22.34
August	45.23	35.58	–21.34
September	47.94	36.83	–23.18
October	54.21	38.06	–29.79
Average (March to October)	50.37	37.03	–26.50

Lai L et al. Increased antimicrobial resistance during the COVID-19 pandemic International Journal of Antimicrobial Agents (2021) 57:106324

Table 1

Consumptions of broad-spectrum antimicrobial agents at National Taiwan University Hospital during two time periods: January–

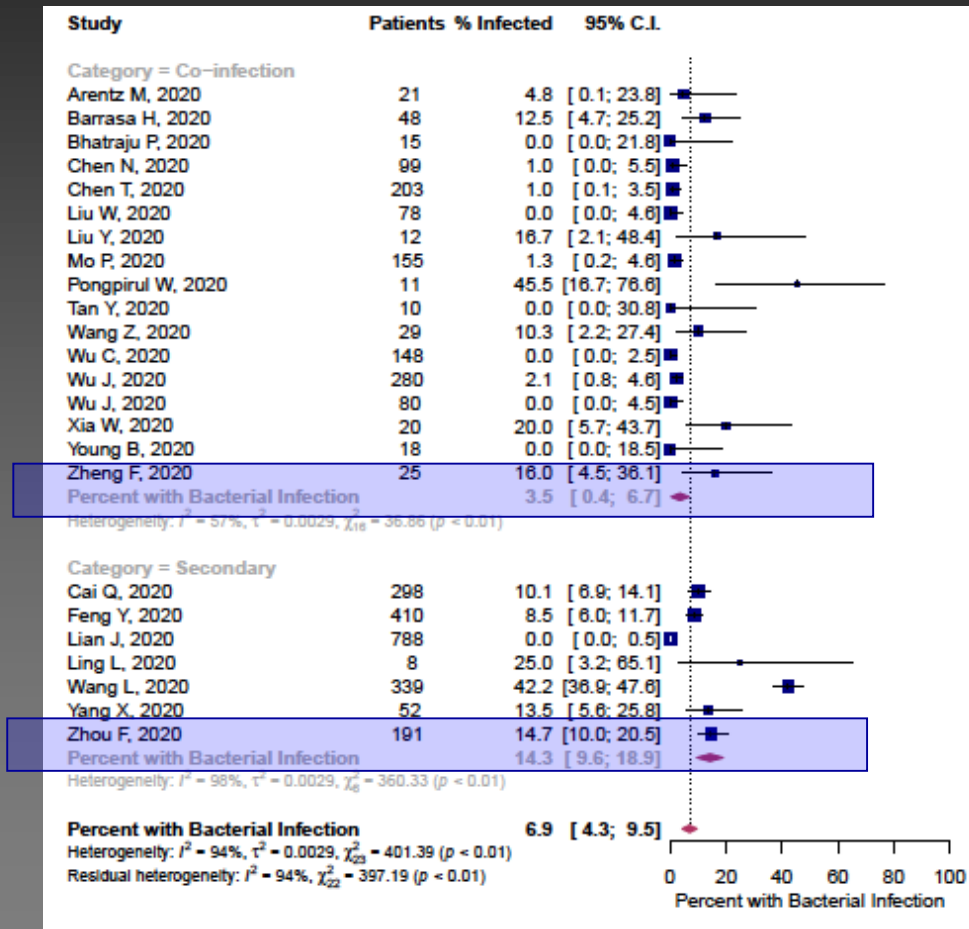


CO-INFECTIONS IN PATIENTS WITH COVID-19

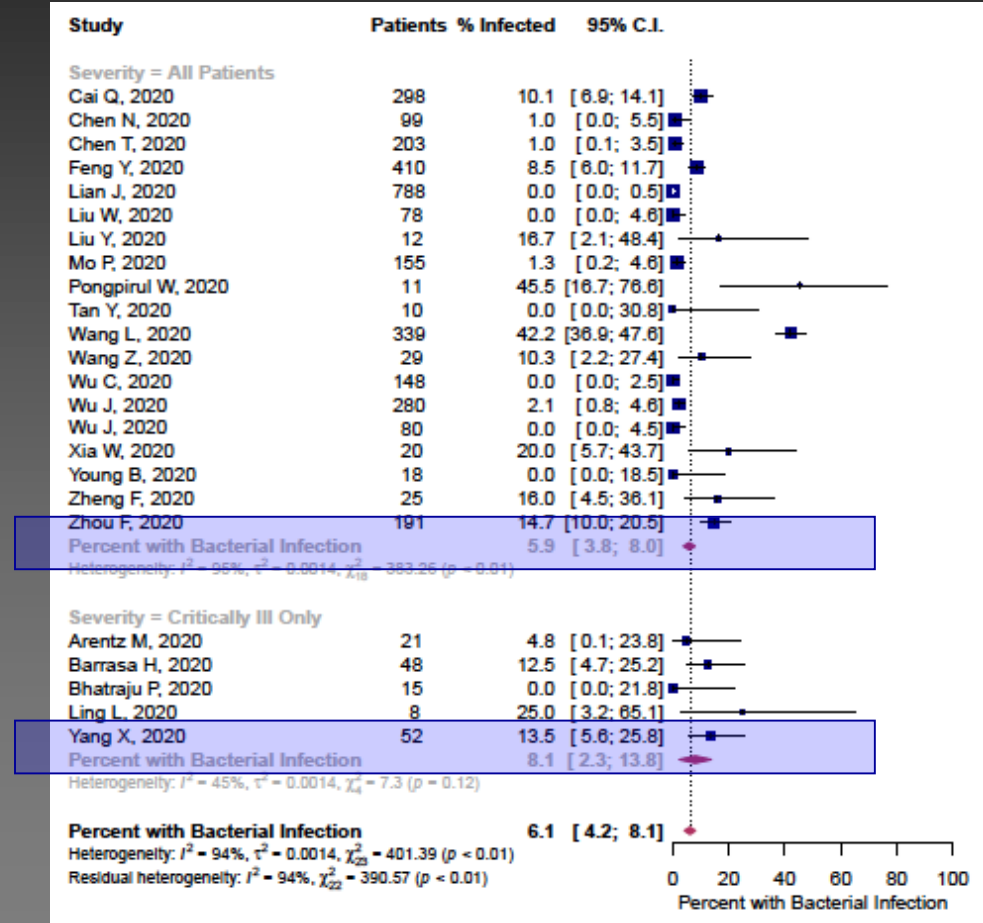
Population	Country	Nº co-infections	Treatment	Ref.
99	China	2/99 (2%)	70/99 (70%)	Lancet (20) 395:507
29 / 69	China	5/29 (17%)	66/69 (95%)	CID (20) ciaa272
41	China	4/41 (9.7%)	41/41(100%)	Lancet (20) 395:497
191	China	28/191 (14.6%)	181/191 (94.7%)	Lancet (20) 395:1054
92	France	26/92 (28%)	SARM 31%	Ann Inten Care (20) 10:119
836	UK	26/836 (3.2%)	---	CMI (20) 26:1395
338	USA	19/338 (5.6%)	---	NEJM (20) 382:8732
21	USA	1/21 (4.7%)	pacientes de UCI	JAMA (20) 323:1612
1396	UK	37/1396 (2.7%)	97.8%	JAC (21) 76:796

Langford, B et al: Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis

Clinical Microbiology and Infections 2021; 26: 1622



At diagnosis vs in hospital



All patients vs critical patients

Garcia-Vidal, C et al: Incidence of co-infections and superinfections in hospitalized patients with COVID-19: a retrospective cohort study

Clinical Microbiology and Infections 2021; 27: 83

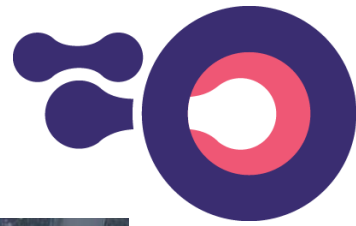
Table 3
Detailed epidemiology of microbiologic documented bacterial infections in 74 patients hospitalized with COVID-19

Bacterial co-infection	n/N (%)
Infection at COVID-19 diagnosis	30/74 (40.5)
Community-acquired pneumonia co-infection	21/30 (70)
<i>Streptococcus pneumoniae</i>	12/21 (57.1)
<i>Staphylococcus aureus</i>	6/21 (28.6)
<i>Haemophilus influenzae</i>	2/21 (9.5)
<i>Moraxella catarrhalis</i>	1/21 (4.8)
Lower respiratory co-infection in patients with bronchiectasis	2/30 (6.6)
<i>Pseudomonas aeruginosa</i>	2/2 (100)
Concurrent urinary tract infection	7/30 (23.3)
<i>Escherichia coli</i>	1/7 (14.2)
<i>Klebsiella pneumoniae</i>	1/7 (14.2)
<i>Enterococcus faecium</i>	1/7 (14.2)
<i>Proteus mirabilis</i>	1/7 (14.2)
<i>Citrobacter koseri</i>	1/7 (14.2)
<i>S. aureus</i>	1/7 (14.2)
Hospital-acquired superinfections complicating patients admitted for COVID-19	44/74 (59.5)
Ventilator-associated pneumonia	11/44 (25)
<i>S. aureus</i>	4/11 (36.4)
<i>P. aeruginosa</i>	3/11 (27.3)
<i>Stenotrophomonas maltophilia</i>	2/11 (18.2)
<i>K. pneumoniae</i>	1/11 (9)
<i>Serratia marcescens</i>	1/11 (9)
Hospital-acquired pneumonia	4/44 (9)
<i>S. aureus</i>	1/4 (25)
<i>P. aeruginosa</i>	1/4 (25)
<i>S. maltophilia</i>	1/4 (25)
<i>K. pneumoniae</i>	1/4 (25)
Bacteraemia	16/44 (36.3)
Coagulase-negative staphylococci	7/16 (43.7)
<i>P. aeruginosa</i>	3/16 (18.7)
<i>E. faecium</i>	3/16 (18.7)
<i>E. coli</i>	2/16 (12.5)
<i>Streptococcus anginosus</i>	1/16 (6.2)
Urinary tract infection	12/44 (27.3)
<i>E. coli</i>	4/12 (33.5)
<i>K. pneumoniae</i>	3/12 (25)
<i>Enterococcus faecalis</i>	2/12 (16.7)
<i>E. faecium</i>	1/12 (8.3)
<i>P. aeruginosa</i>	1/12 (8.3)
<i>S. marcescens</i>	1/12 (8.3)
Polymicrobial intra-abdominal infection (<i>E. coli</i> , <i>E. faecium</i> , <i>E. faecalis</i>)	1/44 (2.3)

- **989** adults admitted with COVID-19 (Spain) for more than 48 hours, **7.4%** co-infection (*S. pneumoniae* (16.2%); *S. aureus* (16.2%), *P. aeruginosa* (13.5%), *E. coli* (9.5%), *K. pneumoniae* (8.1%), *E. faecium* (5.4%) and *H. influenza* (2.7%))
- *S. pneumoniae* and *H. influenza* were associated with community acquired pneumonia while *S. aureus* was associated with CAP and HAP.

Impact of COVID on AMR

- **Emergence of multi-resistant bacteria**
 - Overprescribing antibiotics
 - Limited resources
- **Spread of multi-resistant bacteria**
 - Strict lockdown
 - Social distancing
 - Extensive implementation of hand hygiene and masks at both the health center and community levels
 - Limitation of international travel and migration



AMRDETECTOOL

Detection in 30 min



Thanks

Gracies

Gracias

Detection in 30 min



AMRDETECTOOL



EIT Health is supported by the EIT,
a body of the European Union