Reversing antimicrobial resistance in Europe: the way forward

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Declaration of interest

No conflict of interest

Personal expert point of view, not ECDC or EU position

Antibiotic resistance – an increasing threat to human health

33000 deaths

Each year, 33000 people die from an infection due to bacteria resistant to antibiotics. This is comparable to the total number of passengers of more than 100 medium-sized airplanes.

75 %
healthcare-associated infections

75% of the burden of bacteria resistant to antibiotics in Europe is due to healthcare-associated infections. This could be minimised through adequate infection prevention and control measures, as well as antibiotic stewardship in healthcare settings.

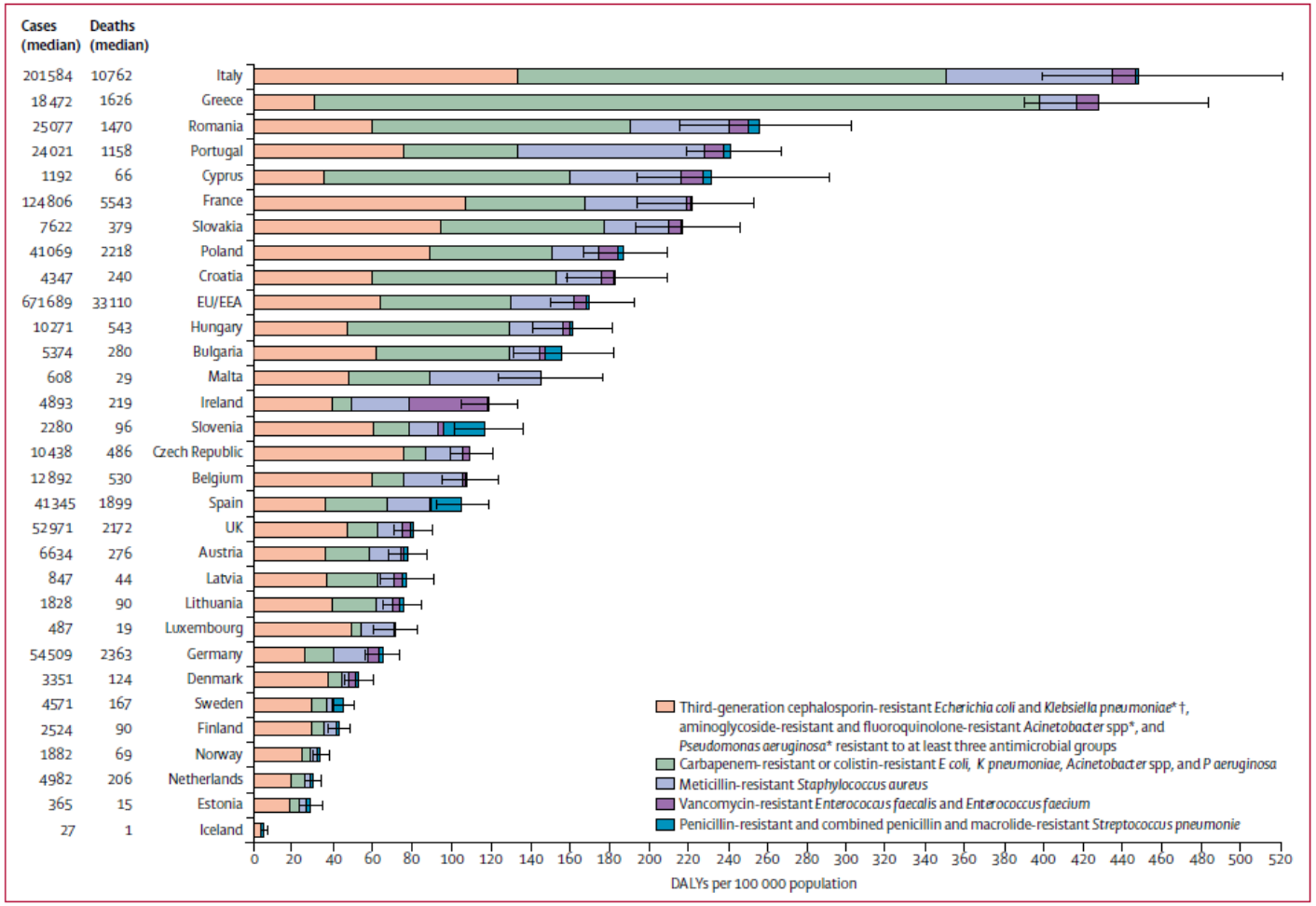


Figure 3: Burden of infections with antibiotic-resistant bacteria in DALYs, EU and European Economic Area, 2015

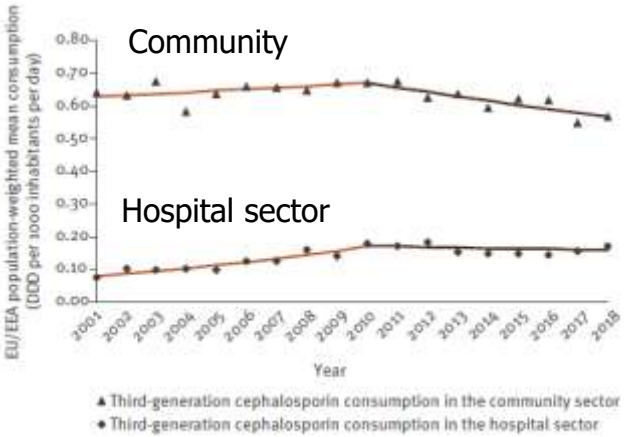
Source: Cassini *et al*. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the EEA in 2015. *Lancet Infect Dis* 2019; 19: 56–66

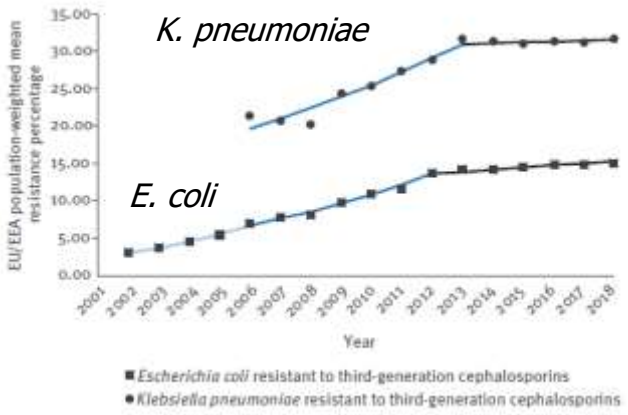
Trends in antimicrobial consumption and resistance, population-weighted means, EU/EEA, 2001-2018

Consumption (DDD per 1,000 inh. per day)

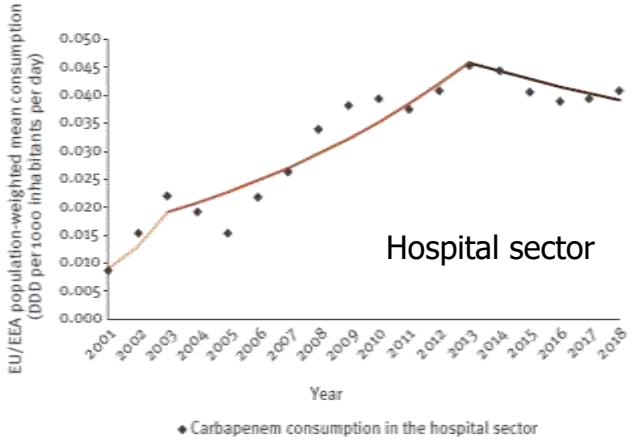
Resistance (% isolates)

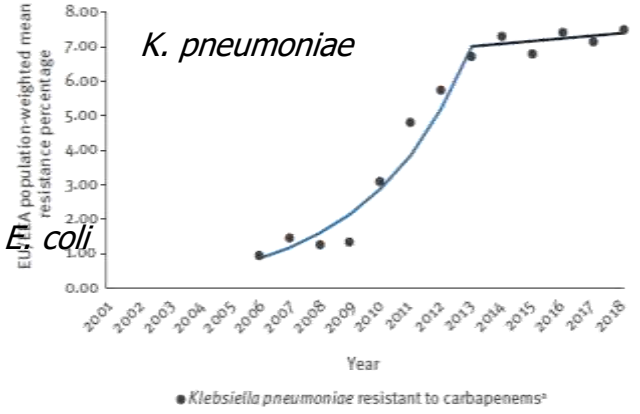
Third-generation cephalosporins





Carbapenems

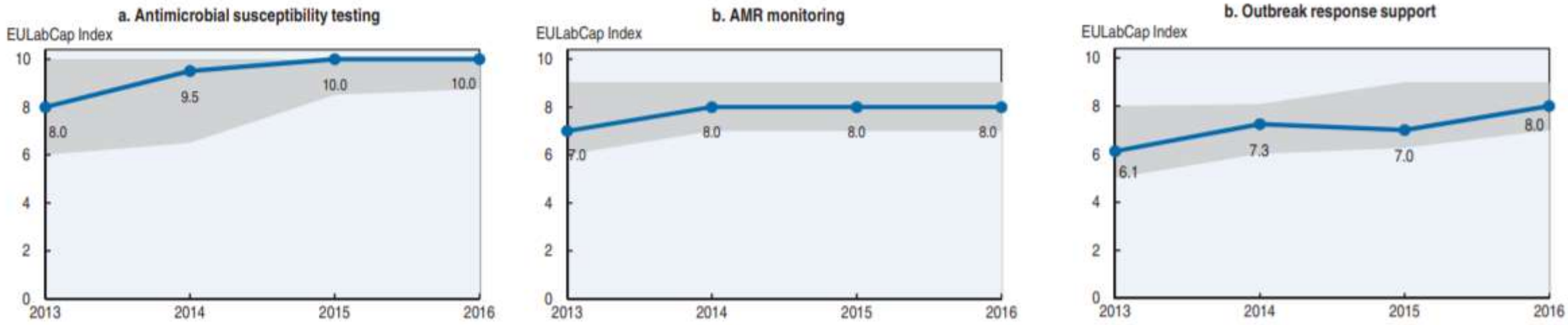




Source: Peñalva G, et al.; EARS-Net; ESAC-Net. Eurosurveillance November 2019.

Improving capabilities of EU microbiology services for AMR detection, monitoring and control

8.6. Antimicrobial susceptibility testing and resistance monitoring, average across EU countries, 2013 to 2016



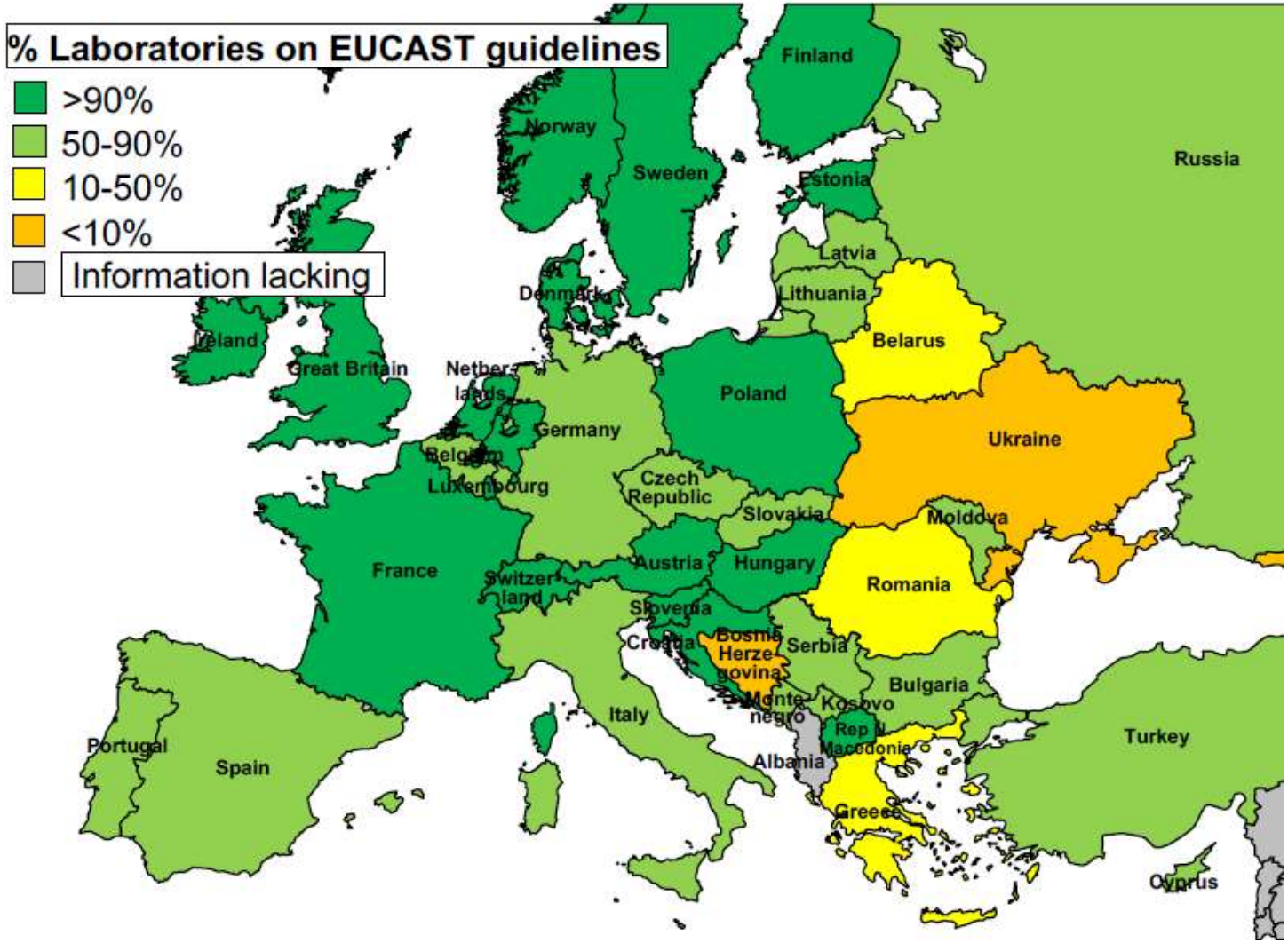
Note: The shaded area shows the minimum and maximum values.
Source: ECDC (2018).

StatLink http://dx.doi.org/10.1787/888933836827

Source: OECD *Health at a Glance Europe* 2018 report

Health at a Glance: Europe 2018
STATE OF HEALTH IN THE EU CYCLE

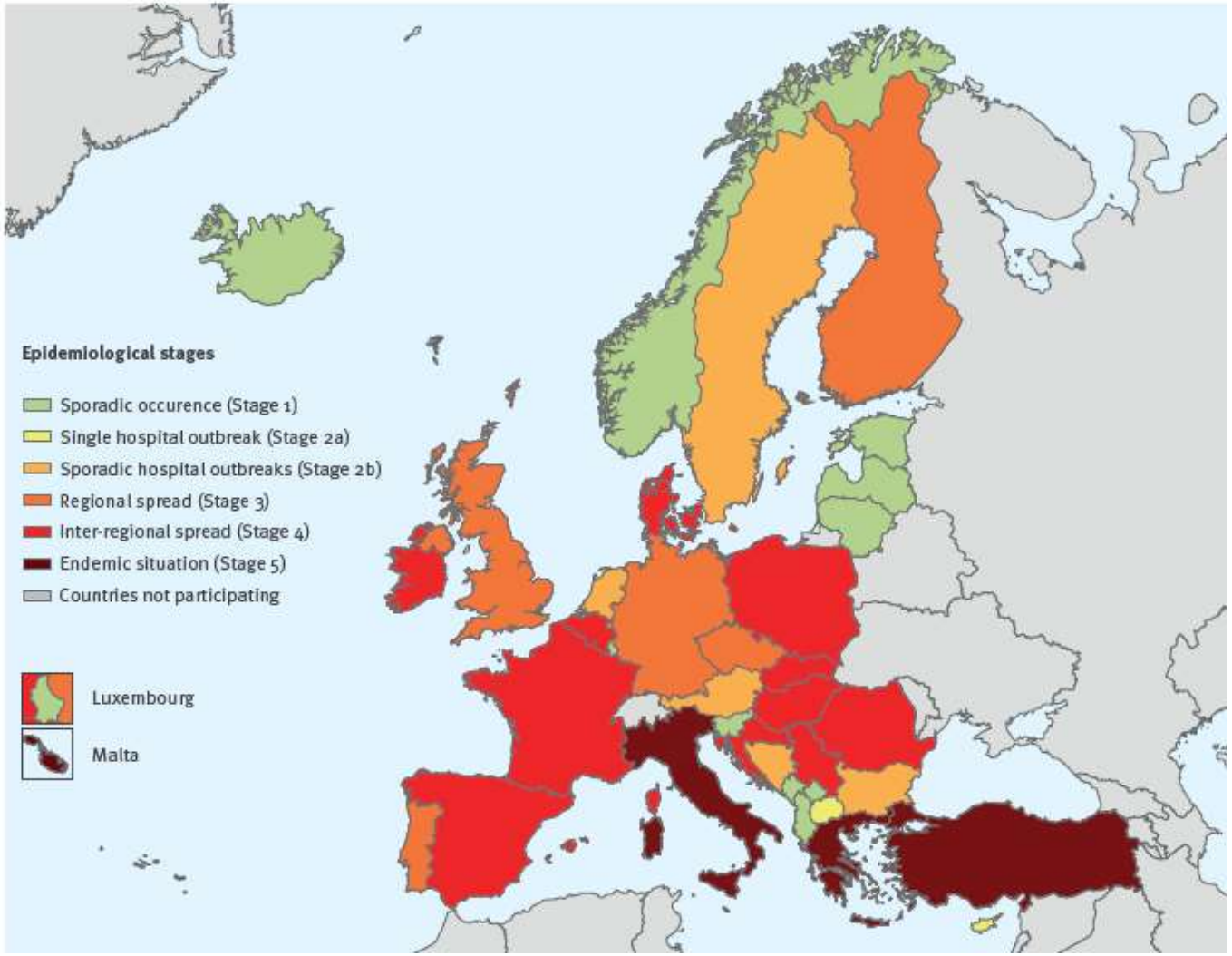
Implementation of EUCAST clinical breakpoints (EU case definition for AMR surveillance) by clinical laboratories, 2019



Source: EUCAST, 2019

Carbapenem resistance dissemination in Europe, 2018

Epidemiological situation of carbapenemase-producing Enterobacteriaceae, assessment by national experts in European countries, July 2018 (n = 37)



Brolund A et al. *Euro Surveill.* 2019;24(9):pii=1900123

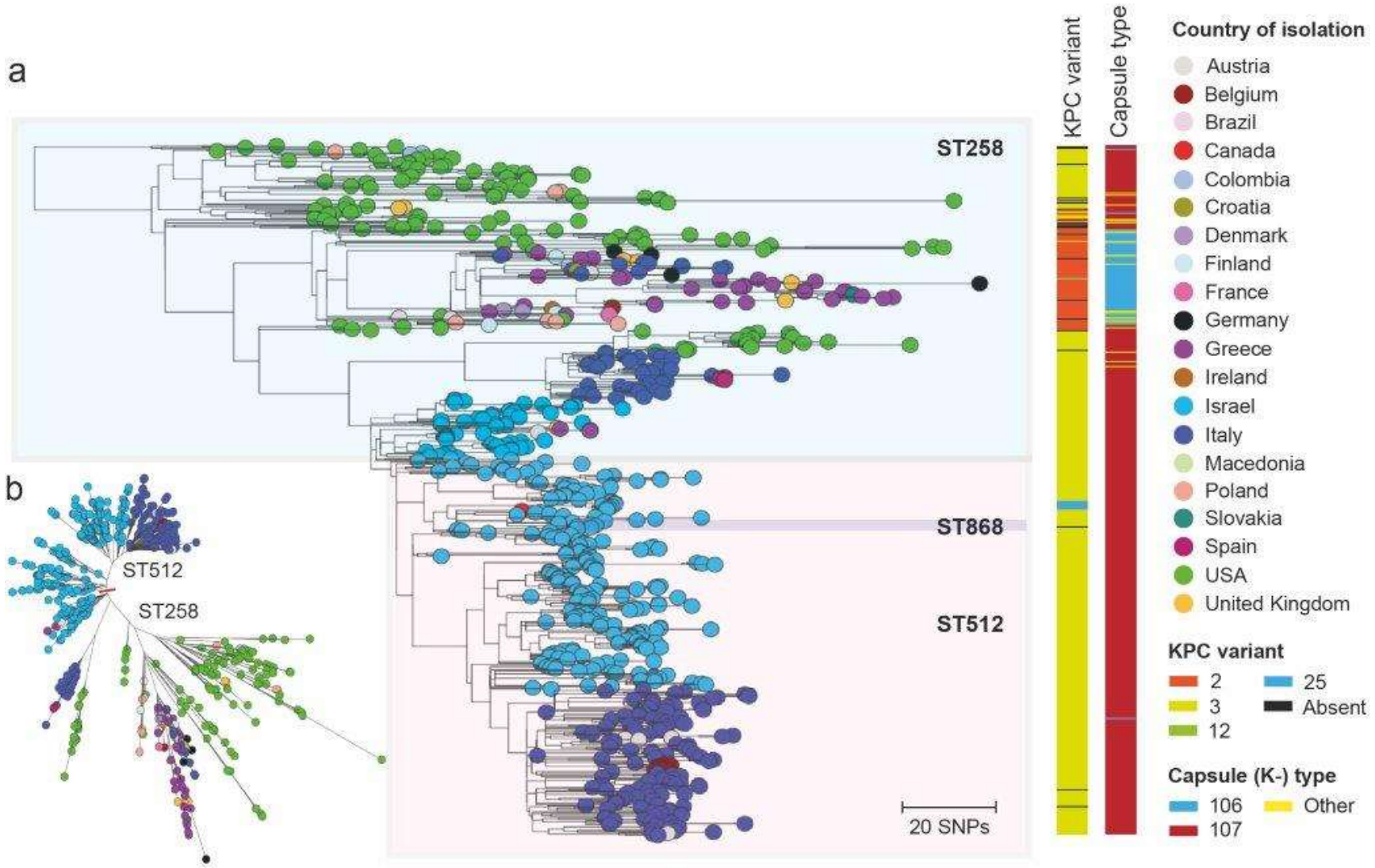
European AMR genomic surveillance network, 2019

European Antimicrobial Resistance Genes Surveillance Network (EURGen-Net)

The European Antimicrobial Resistance Genes Surveillance Network (EURGen-Net) is a surveillance network for genomic-based surveillance of multidrug-resistant bacteria of public health importance, coordinated by the European Centre for Disease Prevention and Control (ECDC).

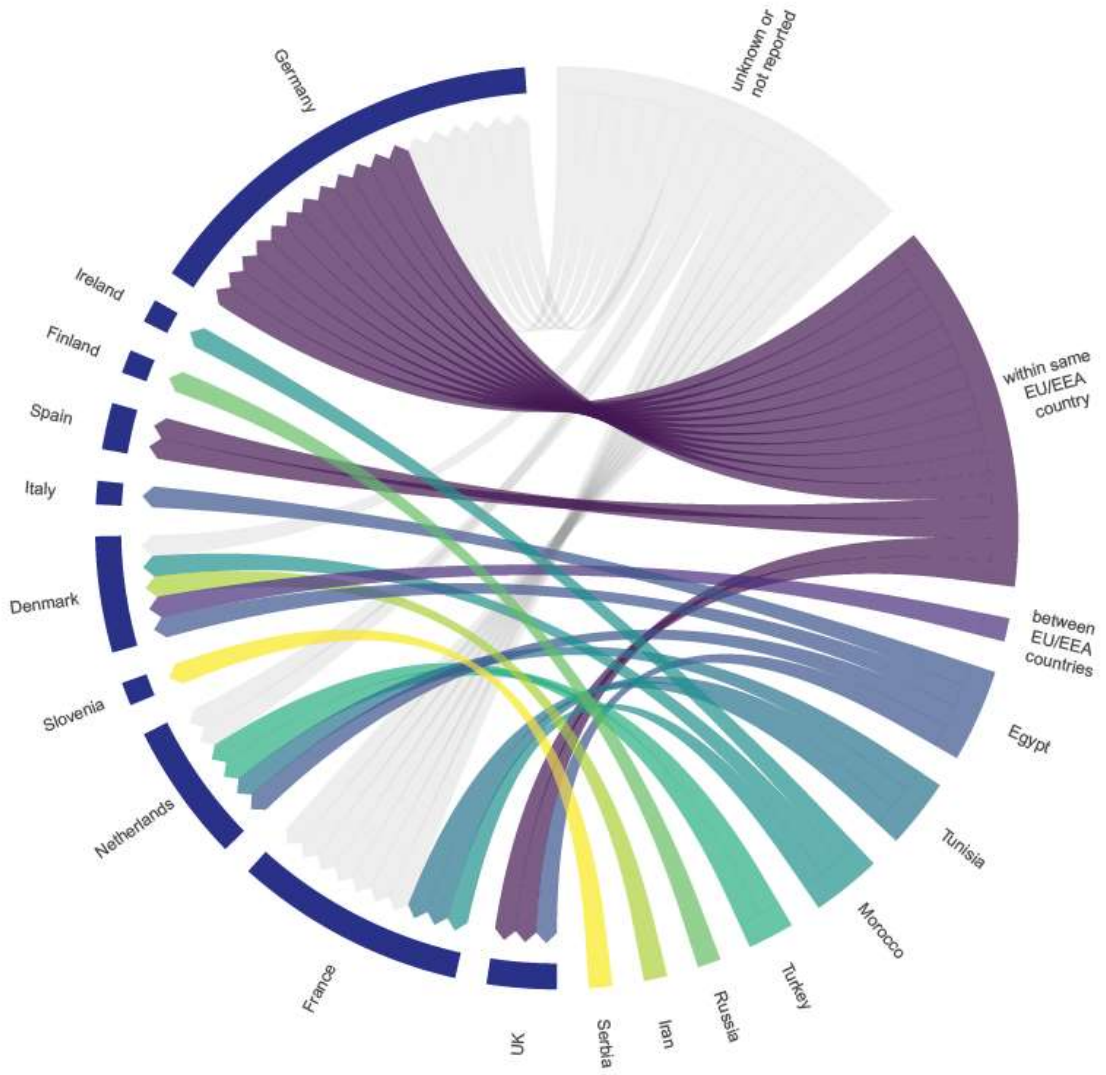
Antimicrobial resistance

International spread of KPC-producing *K. pneumoniae* ST258/512: phylogeographic analysis, 1999-2014



Source: David S *Nature Microbiol* 2019: 29 July 2019

Cross-border spread of *bla*$_{NDM-1}$- and *bla*$_{OXA-48}$-positive *Klebsiella pneumoniae* clades in Europe and beyond



Epi link: travel or hospitalization past 6 months

Source: Ludden C et al. *Euro Surveill*. 2020;25(20):pii=2000627 (European collaborative analysis of whole genome sequencing and epidemiological data, 2014 to 2019; n= 15 clusters of which 10 linked to travel outside EU)

Spread of "stealth carbapenemase"-producing *E.coli*

Figure 1. Neighbour joining tree of *E. coli* ST38 non-outlier sequences collected from EU/EEA countries and the UK and from the open-access databases (n=458)

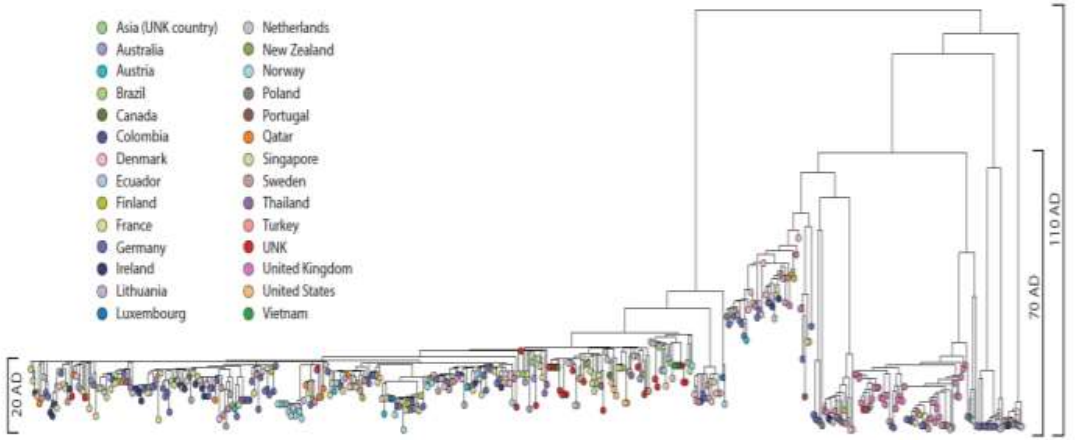


Figure 2. Number of OXA-244-producing *E. coli* ST38 isolates per year, EU/EEA and the UK, 2013–2020 (n=348)*

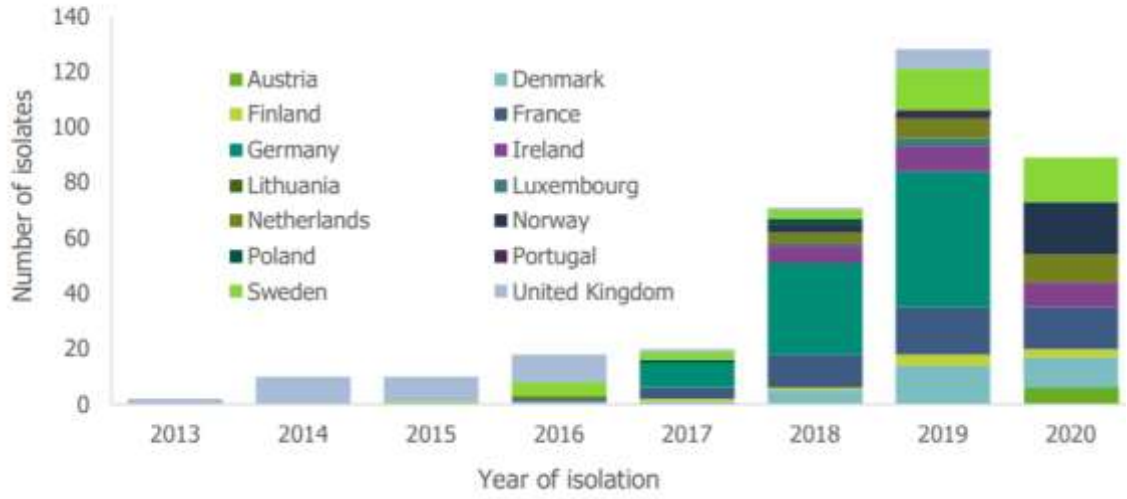
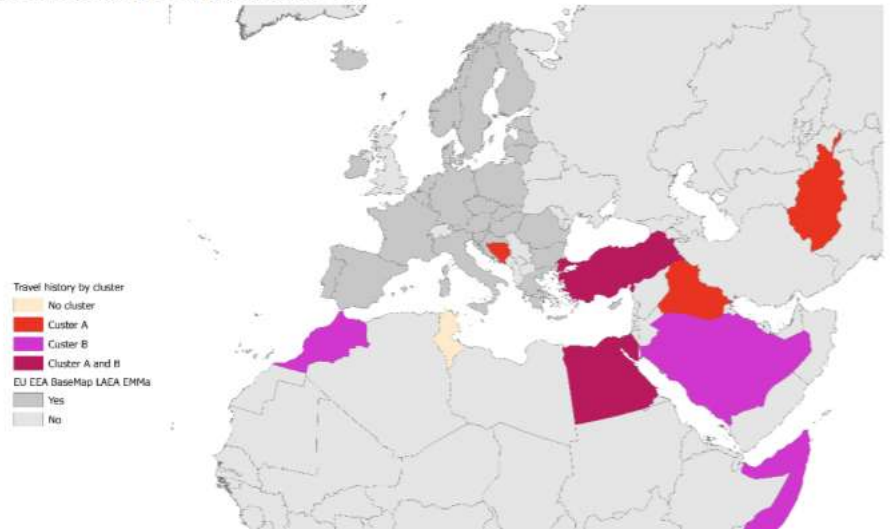


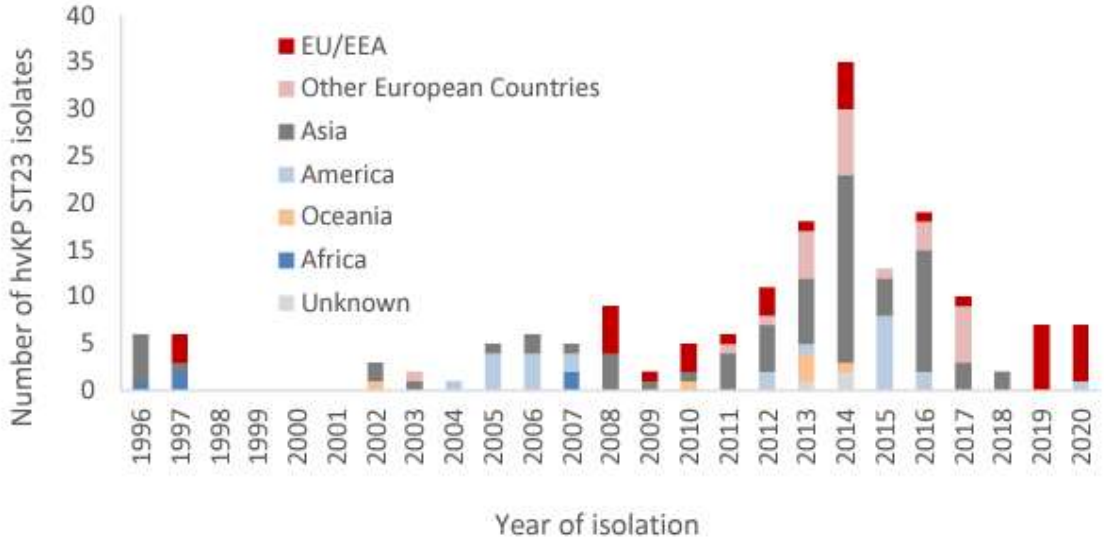
Figure 4. Countries of travel outside of the EU/EEA for cases of OXA-244-producing *E. coli* ST38, in the 12 months prior to detection (n =28)

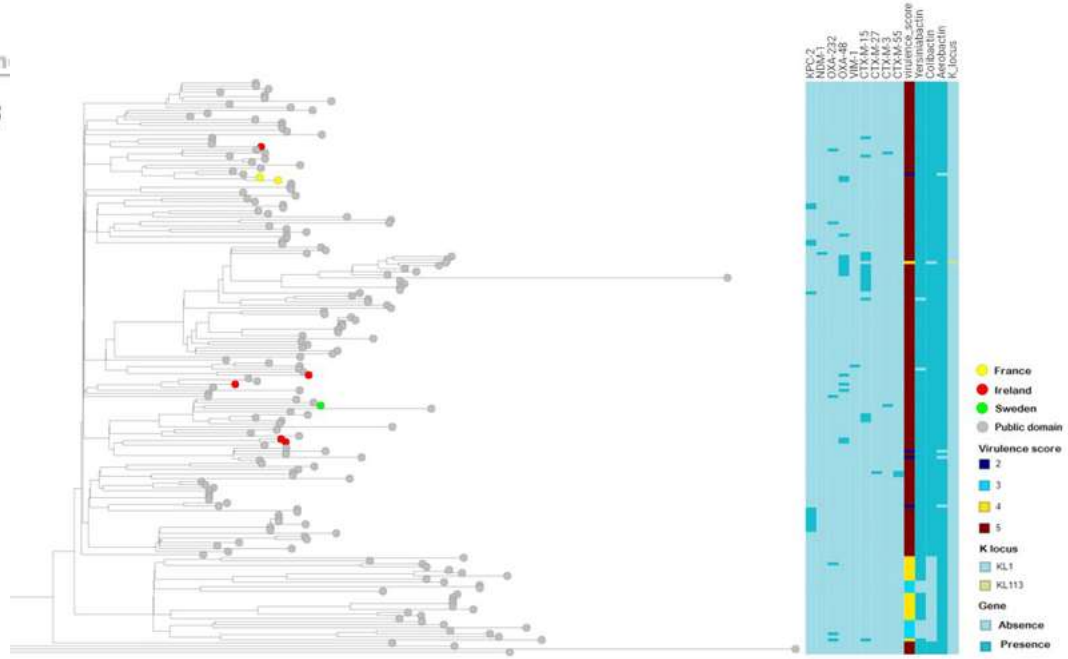


Emergence of hypervirulent CR *K.pneumoniae*

Figure 2. Main K1 ST23 clade with neighbouring relationships of hypervirulent *Klebsiella pneumoniae* (hvKp) ST23 isolates submitted for this study (coloured by country) and from open-access databases (grey) (n=188)

Figure 1. Time distribution of hypervirulent *Klebsiella pneumoniae* (hvKp) ST23 isolates this analysis, by continent and year (n=178)*†





Key components of effective infection-prevention programmes in hospitals

- Organisation of infection control at the hospital level
- Bed occupancy, staffing, workload
- Access to materials and equipment and ergonomics
- Appropriate use of guidelines
- Education and training
- Auditing, surveillance and feedback
- Multimodal and multidisciplinary prevention programmes that include behavioural change & engagement of champions
- Positive organisational culture.

Source: Zingg W et al. *Lancet Infect Dis* 2015;15:212 (SR of 92 studies from 1996 to 2012; expert consensus)

CRE control measures

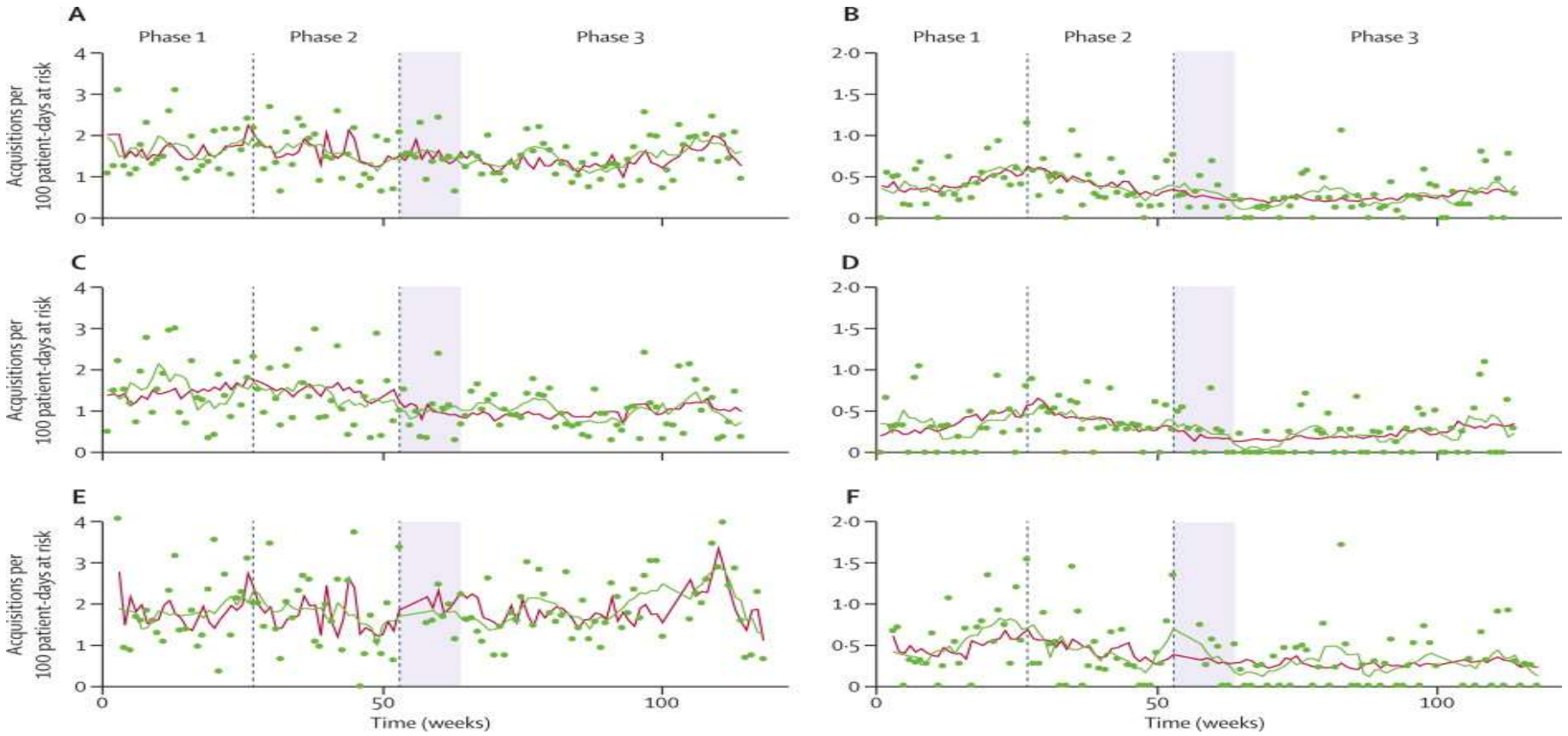
- Antibiotic restriction and stewardship
- Hand hygiene compliance
- Rectal screening on admission to ICU and facility transfers
- Pre-emptive patient isolation on admission
- Colonised patient isolation
- Contact precautions, patient cohorting, dedicated nursing
- Case notification and contact tracing
- Environmental cleaning and decontamination
- Staff education, auditing and feedback

Source: ECDC SR 2014; ECDC RA 2019, ESCMID Guidelines; WHO Guidelines 2017; US CDC Guidance 2015.

MOSAR multicentre study: active screening in Intensive Care Unit patient population

All MDRO

MRSA



Active screening had **no effect** in MDRO acquisition in settings with high level horizontal measures (hand hygiene and chlorhexidine wash)

Derde LP. *Lancet Infect Dis.* 2014;14(1):31-9

CRE-CRAB-CRPsA control measures: systematic review and re-analysis of quasi-experimental studies

- Multimodal interventions (≥3 components) highly effective
- Multimodal IPC strategies with specific components to consider in the context of local epidemiology and resources (tailored implementation)

Source: Tomczyk et al. *CID* 2019;68:873 (ITS analysis of 17 EPOC compatible studies)

A multimodal IPC intervention in medical ICU on carbapenem-resistant *Klebsiella pneumoniae*

IPC measures	Baseline	Intervention
De-escalation interventions		
Active surveillance cultures		X
Contact precautions and hand hygiene	X	X
Disinfection and sterilization	X	X
Department staff education	X	X
Pre-emptive interventions		
Contact precautions of shared equipment		X
Patient isolation: single room isolation if possible		X
And de-escalation interventions		X
AMR interventions		
Patient isolation: single room isolation or cohorting		X
Cohorting of medical care		X
Enhanced external medical staff education		X
Enhanced terminal room disinfection		X
And pre-emptive interventions		X
Targeted catheter-related infection prevention bundles		
Intravascular catheter-related infection		X
Ventilation associated pneumonia		X
Catheter-associated urinary tract infection		X

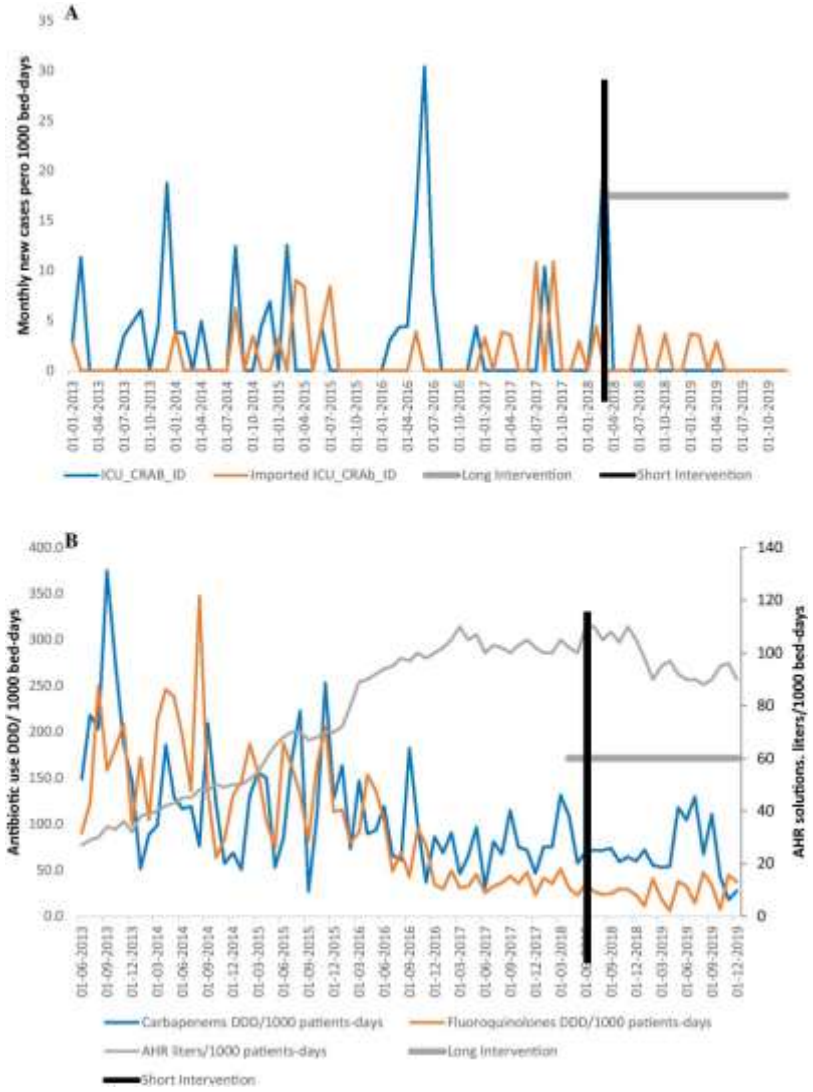
AMR, antimicrobial resistance.

Period	Incidence of ICU-acquired CRKP Cases per 1,000 patient-days		
	Mean	Median	p^c
Baseline	9.88 ± 6.44	10.08 (4.43–16.43)	–
2017	0.96 ± 1.54	0.00 (0.00–2.27)	0.005
2018	1.27 ± 1.53	0.98 (0.00–2.11)	0.009
2019	1.26 ± 1.46	1.00 (0.00–2.17)	0.009

Source: Dai et al. *Front Med* Jul 2021 8:692813 (Ruijin Hospital, Shanghai, 2017-19)

A five-component infection control bundle to permanently eliminate a carbapenem-resistant *Acinetobacter baumannii* spreading in an ICU

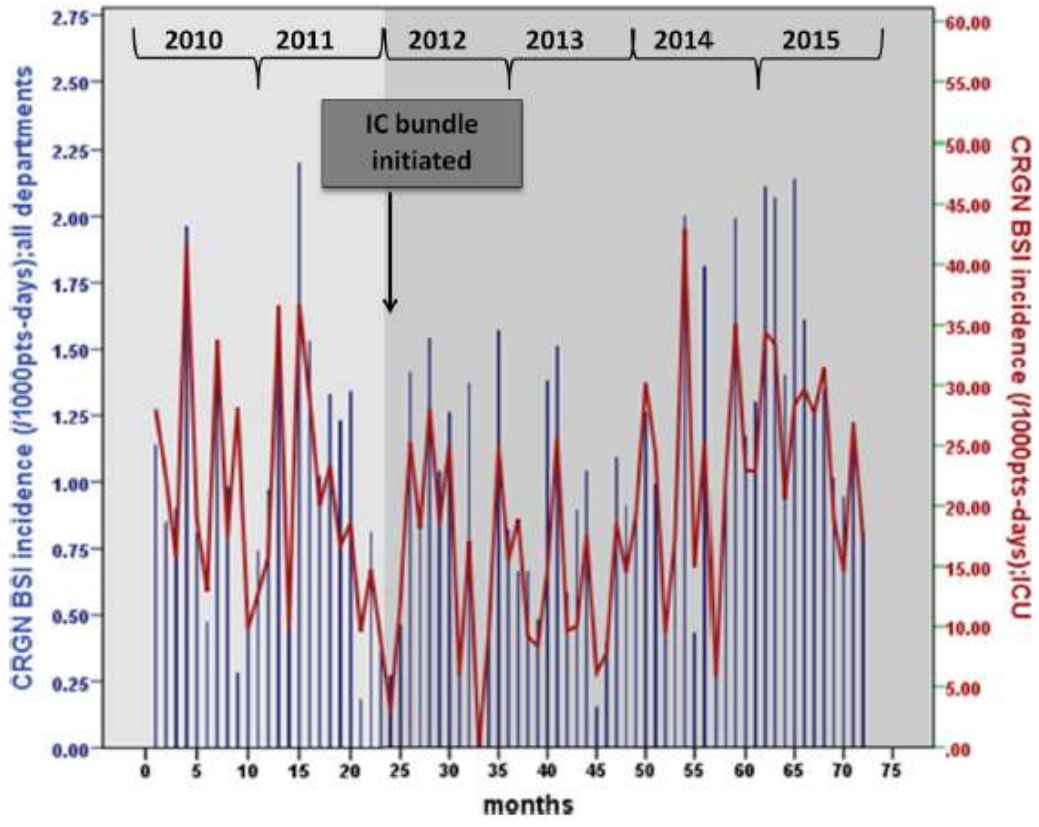
- hand hygiene improvement
- universal contact precautions
- extended screening including the patients and *environment*
- radical environmental *cleaning*



Source: Meschiari et al. *ARIC* 2021 Aug 19;10(1):123

IPC interventions affected by resource shortages: impact on BSI by carbapenem-resistant pathogens

Eur J Clin Microbiol Infect Dis (2018) 37:43–50



Factors	Pearson *r* coefficient	*p*-Value
Educational sessions* (*n*)	−0.658	**<0.0001**
Personnel attending educational sessions (%)	−0.657	**<0.0001**
Written reports for supplies shortages (*n*)	0.527	**<0.0001**
Nurse/bed ratio	−0.544	**<0.0001**
Rectal ASC (*n*)	−0.091	0.540
HH compliance (%)	−0.884	**<0.0001**
Admissions (*n*)	0.023	0.877
LOS	0.071	0.633
Blood culture sets (*n*)	0.896	**<0.0001**
McCabe non-fatal index	−0.029	0.845
McCabe ultimate fatal index	−0.138	0.348
McCabe rapid fatal index	0.215	0.142

ASC, active surveillance cultures; HH, hand hygiene; LOS, length of stay

Source: Kousouli et al *EJCMID* 2018;37:43

AMR healthcare management and prevention : the way forward

- Hospital and national level
  - Improving antibiotic use, IPC and laboratory practices and public health integration
  - WGS- based MDRO characterisation and tracing: global, complex gene eco-epidemiology
  - One-Health imported resistance (resistant organisms/genes from the community, other country/healthcare facilities, hospital environment, food and water supply)
  - Fiscal policy affects healthcare resources and patient safety
- European level
  - Need for multi-centre integrated intervention studies in endemic settings: REVERSE Action!
  - EURGen-Net platform for multi-country MDRO outbreak alert and response
  - Post-pandemic public health capacity building and integration (EU4Health)