ECDC and antimicrobial resistance: consequences for international travellers

Dominique L. Monnet, on behalf of ECDC Antimicrobial Resistance and Healthcare-Associated Infections (ARHAI) Programme

Stockholm, 3 May 2018

Antimicrobial resistance: what does it really mean?

Several, inter-related compartments of healthcare, (i.e. patients in primary care, hospitals, nursing homes and long-term care facilities), food animals, food, environment

Many types of human infections, i.e. respiratory tract, urinary tract, skin and soft tissue, bloodstream, surgical site, related to medical devices, etc.)

Many bacteria/microorganisms

Many antimicrobials and mechanisms of resistance

Patients with infections due to resistant bacteria!

Patient stories

Mohammed

Cancer chemotherapy had weakened Mohammed's immune system, allowing an infection with a highly resistant type of *E. coli* to take hold. His doctors were able to successfully treat him with last-line antibiotics.

Read his story >

Daphne

Daphne Deckers, a Dutch author, television host and actor, campaigns to raise awareness about antibiotic resistance following her personal experience with an *E.coli* superbug infection (*Courtesy of WHO/Europe*)

Watch a video by WHO/Europe >

Peggy

Christian Lillis, son of Peggy Lillis, shares his personal story of losing his mother to an *Clostridium difficile infection (C. difficile)* caused by antibiotic use. (*Courtesy of CDC*)

Watch a video by CDC >

Kelly

Antibiotics are being "overprescribed", leading to greater resistance, a former patient says. Kelly Strudwick was diagnosed with a urinary tract infection. (*Courtesy of BBC*)

Watch a video on the BBC website >

Paolo

Paolo fell ill with a serious urinary tract infection with an *E. coli* resistant to many antibiotics. It took two months and three courses of different antibiotics before his infection was successfully treated.

Read his story >

Lill-Karin

Lill-Karin caught a bacterium resistant to multiple antibiotics after a traffic accident followed by hospital stay while on holiday abroad. When transferred to a hospital back home, she had to be placed in a special room, isolated from other patients.

Read her story >

https://antibiotic.ecdc.europa.eu/en/patient-stories

Burden of antimicrobial resistance (AMR) for the EU/EEA

25 000 deaths

each year in the EU/EEA
attributable to
5 multidrug-resistant bacteria
4 main healthcare-associated infections (HAIs)

Update: **2018**

Source: ECDC, 2009.
In: http://ecdc.europa.eu/en/publications/Publications/0909_TER_The_Bacterial_Challenge_Time_to_React.pdf

Antimicrobial Resistance and Healthcare-Associated Infections (ARHAI) Networks

- **European Antimicrobial Resistance Surveillance Network (EARS-Net)**
  (formerly EARSS, integrated in January 2010)

- European Surveillance of Antimicrobial Consumption Network (ESAC-Net)
  (formerly ESAC, integrated in July 2011)

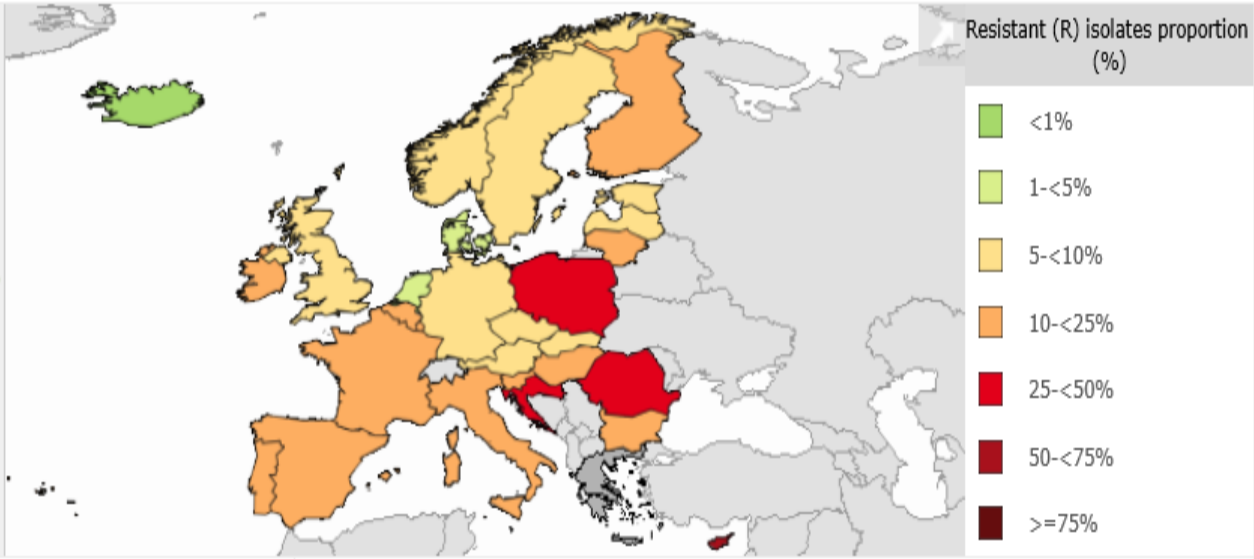
- Healthcare-Associated Infections surveillance Network (HAI-Net)
  (formerly HELICS / IPSE, integrated in July 2008)

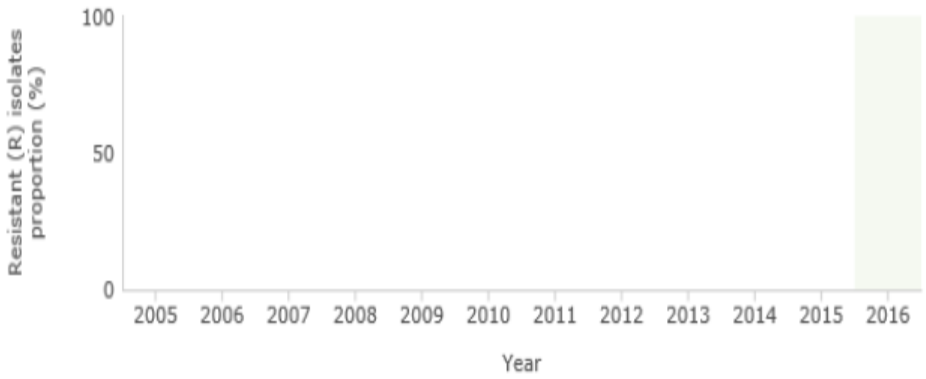
Surveillance Atlas of Infectious Diseases

Antimicrobial resistance | Streptococcus pneumoniae | Macrolides | Resistant (R) isolates proportion

2016

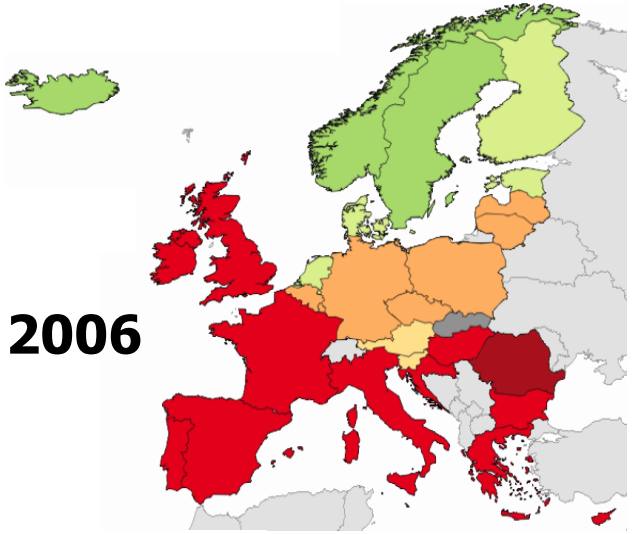
Region	Resistant (R) isolates proportion (%)
Austria	8.6
Belgium	15.7
Bulgaria	21.9
Croatia	33.8
Cyprus	60.0
Czech Republic	7.2
Denmark	4.8
Estonia	7.0
Finland	11.4

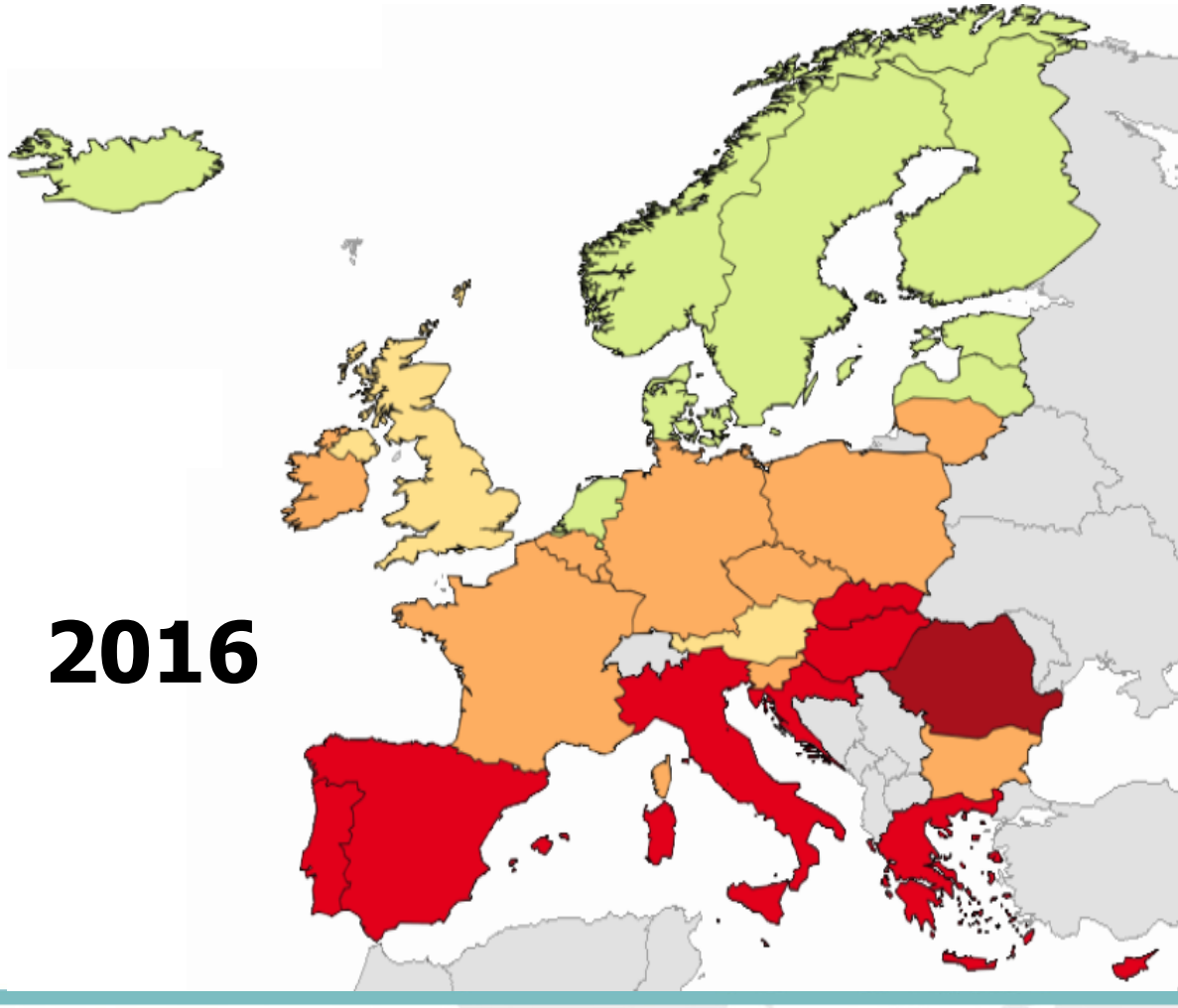




https://atlas.ecdc.europa.eu

Staphylococcus aureus: % of invasive isolates with resistance to meticillin (MRSA), EU/EEA, 2006 & 2016

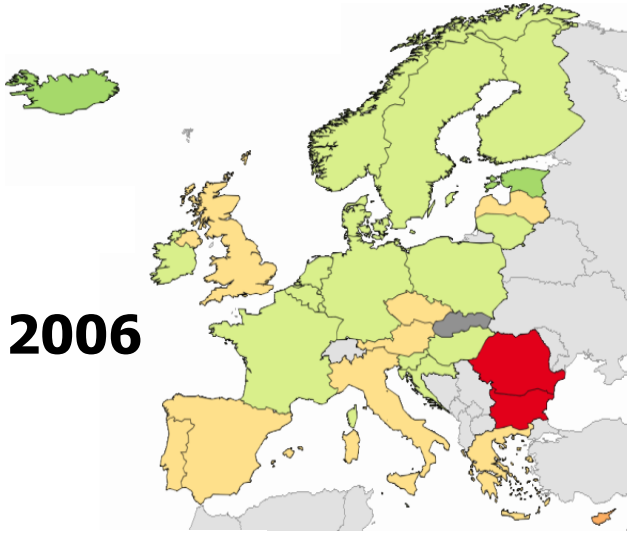


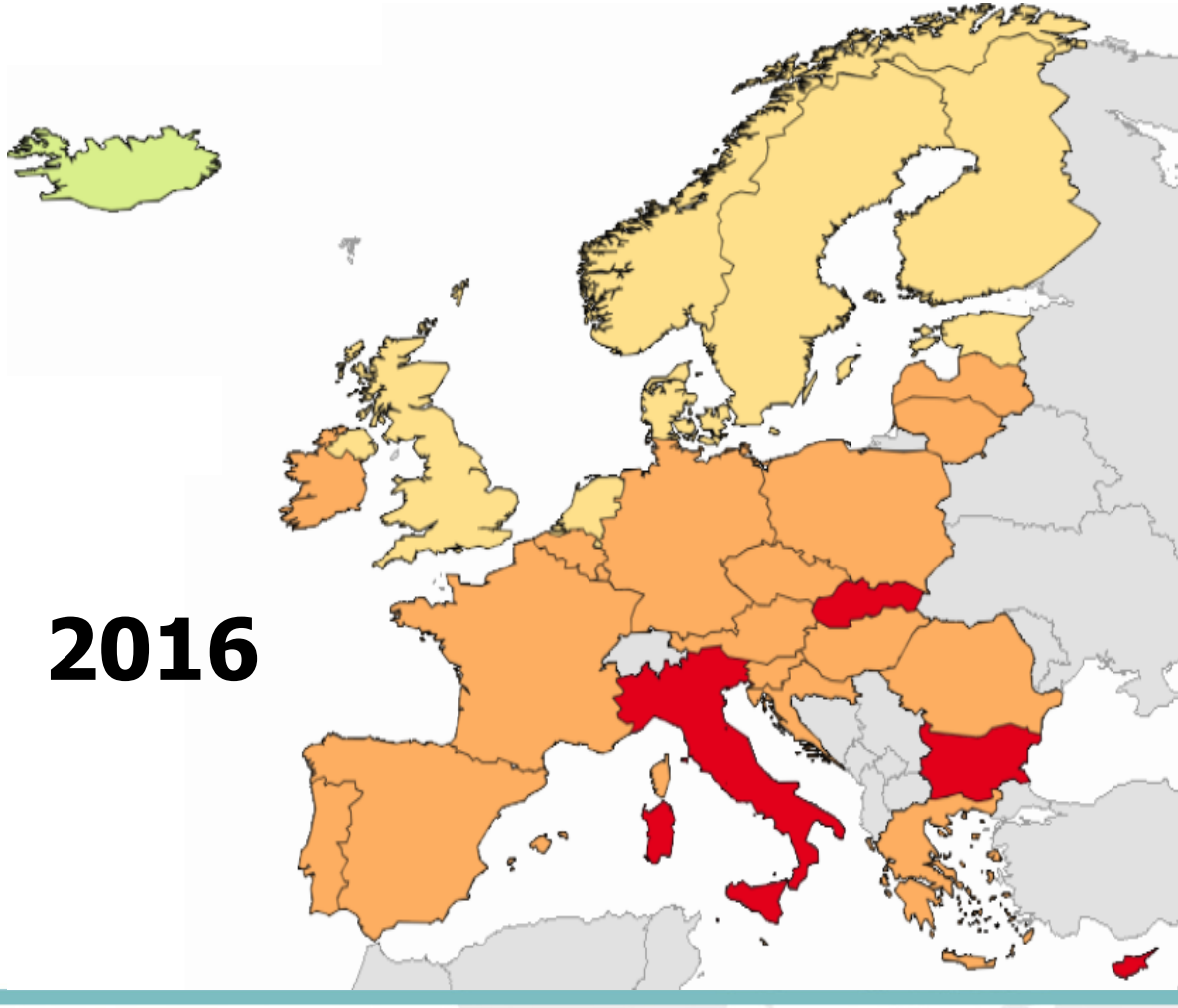


- <1%
- 1-<5%
- 5-<10%
- 10-<25%
- 25-<50%
- 50-<75%
- >=75%
- Not calculated

Source: EARS/EARS-Net, 2017 (https://atlas.ecdc.europa.eu).

Escherichia coli: percentage of invasive isolates resistant to third-generation cephalosporins, EU/EEA, 2006 & 2016

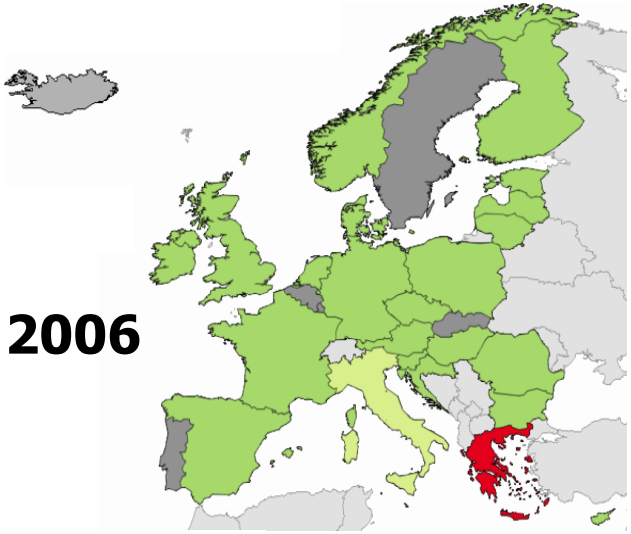


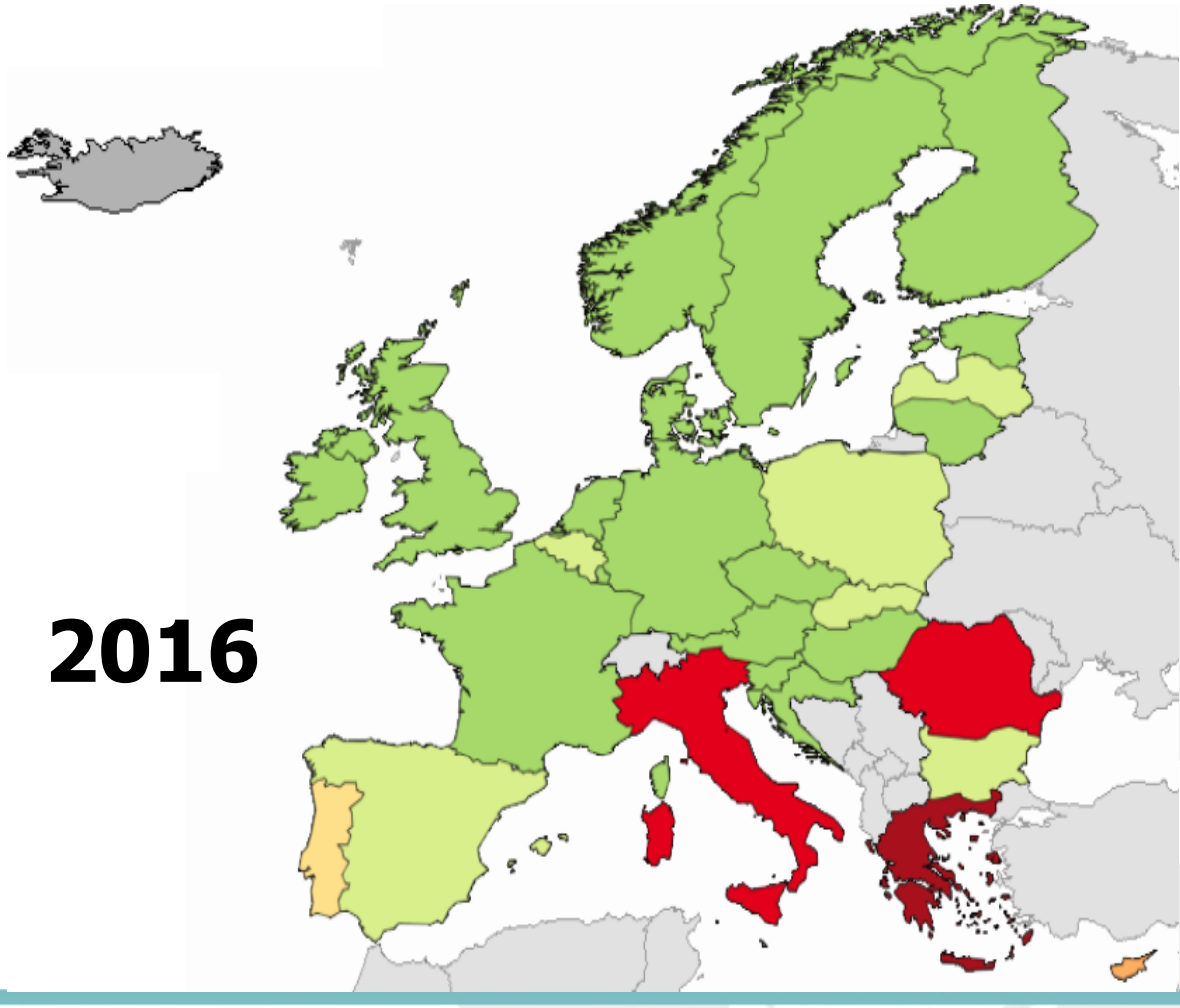


- <1%
- 1-<5%
- 5-<10%
- 10-<25%
- 25-<50%
- 50-<75%
- >=75%
- Not calculated

Source: EARS/EARS-Net, 2017 (https://atlas.ecdc.europa.eu).

Klebsiella pneumoniae: % of invasive isolates with resistance to carbapenems, EU/EEA, 2006 & 2016





- <1%
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- 10-<25%
- 25-<50%
- 50-<75%
- >=75%
- Not calculated

Source: EARS/EARS-Net, 2017 (https://atlas.ecdc.europa.eu).

Carbapenem-resistant *Enterobacteriaceae*: a challenge for appropriate patient therapy

1. Klebsiella pneumoniae ESBL-CARBA > E5 CFU/mL

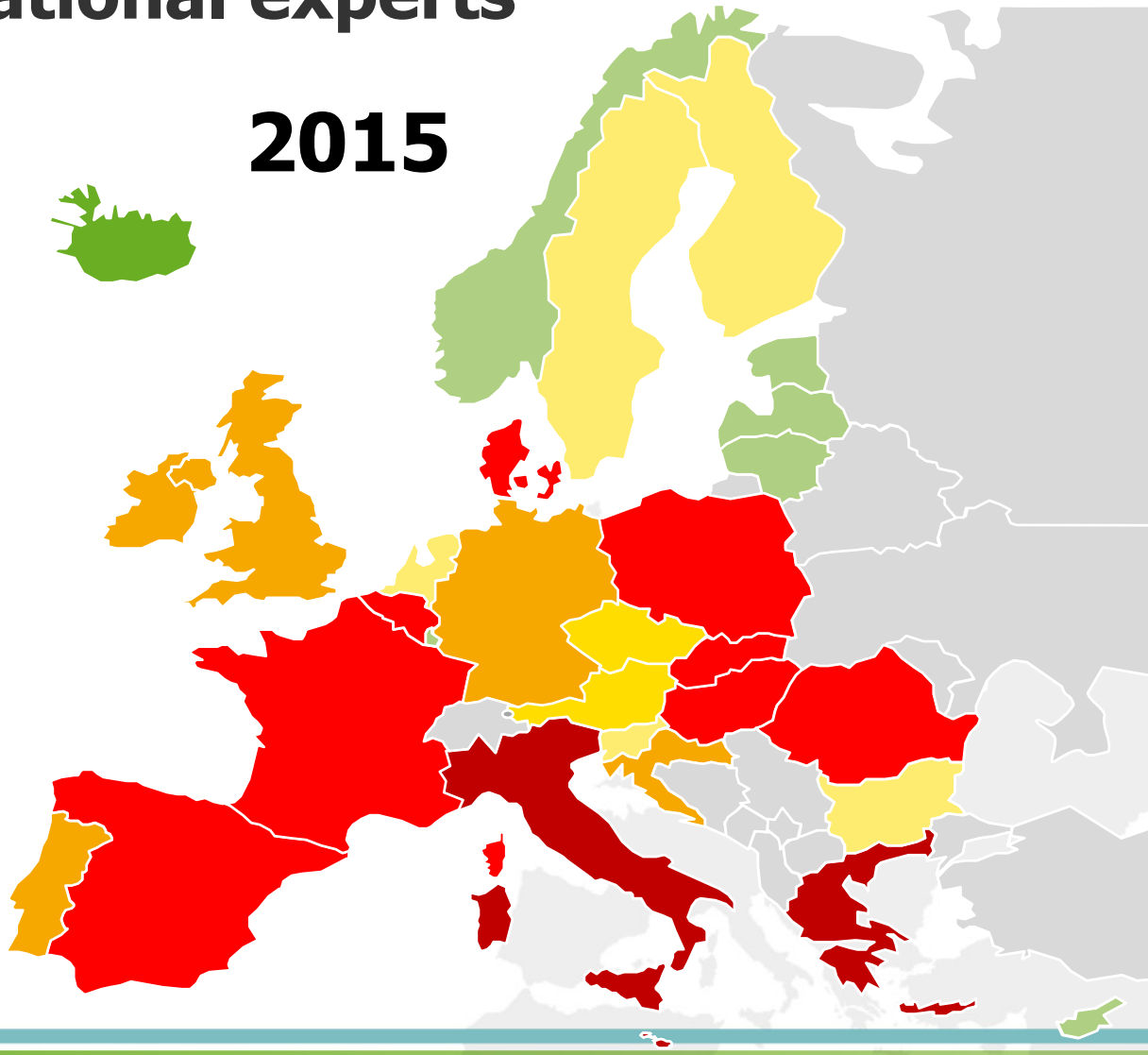
MIC: Aztreonam = 0.25 mg/L = S
MIC: Colistin = 0.12 mg/L = S
MIC: Kloramfenikol = 256 mg/L = R
MIC: Tobramycin = <256 mg/L = R
MIC: Amikacin = <256 mg/L = R
MIC: Netilmicin = <256 mg/L = R
MIC: Nitrofurantoin = 512 mg/L = R
MIC: Gentamicin = <256 mg/L = R
Obs! Stammen bildar ESBL-CARBA (ICD-10 kod U82.2). Klinisk anmälningsplikt och smittspårningsplikt enl smittskyddslagen. Kontakta alltid vårdhygien. För mer information: www.smittskyddstockholm.se

ANTIBIOTIKUM	
Ampicillin.....	R
Piperacillin/tazobaktam.	R
Cefadroxil.....	R
Imipenem.....	R
Meropenem.....	R
Ertapenem.....	R
Aztreonam.....	S
Colistin.....	S
Kloramfenikol.....	R
Tobramycin.....	R
Amikacin.....	R
Netilmicin.....	R
Trimetoprim.....	R
Trimetoprim-sulfa.....	R
Nitrofurantoin.....	R
Cefotaxim.....	R
Ceftazidim.....	R
Gentamicin.....	R
Ciprofloxacin.....	R

Svarskommentar:
Sammanfattning/Övrigt:
Obs! Mycket omfattande resistensprofil. Endast känslig för colistin.

Courtesy: C. Giske. Karolinska University Hospital, Stockholm, Sweden. Photo: www.microbiologie.info.

Spread of carbapenem- resistant *Enterobacteriaceae* (CRE) in the EU/EEA: assessment by national experts



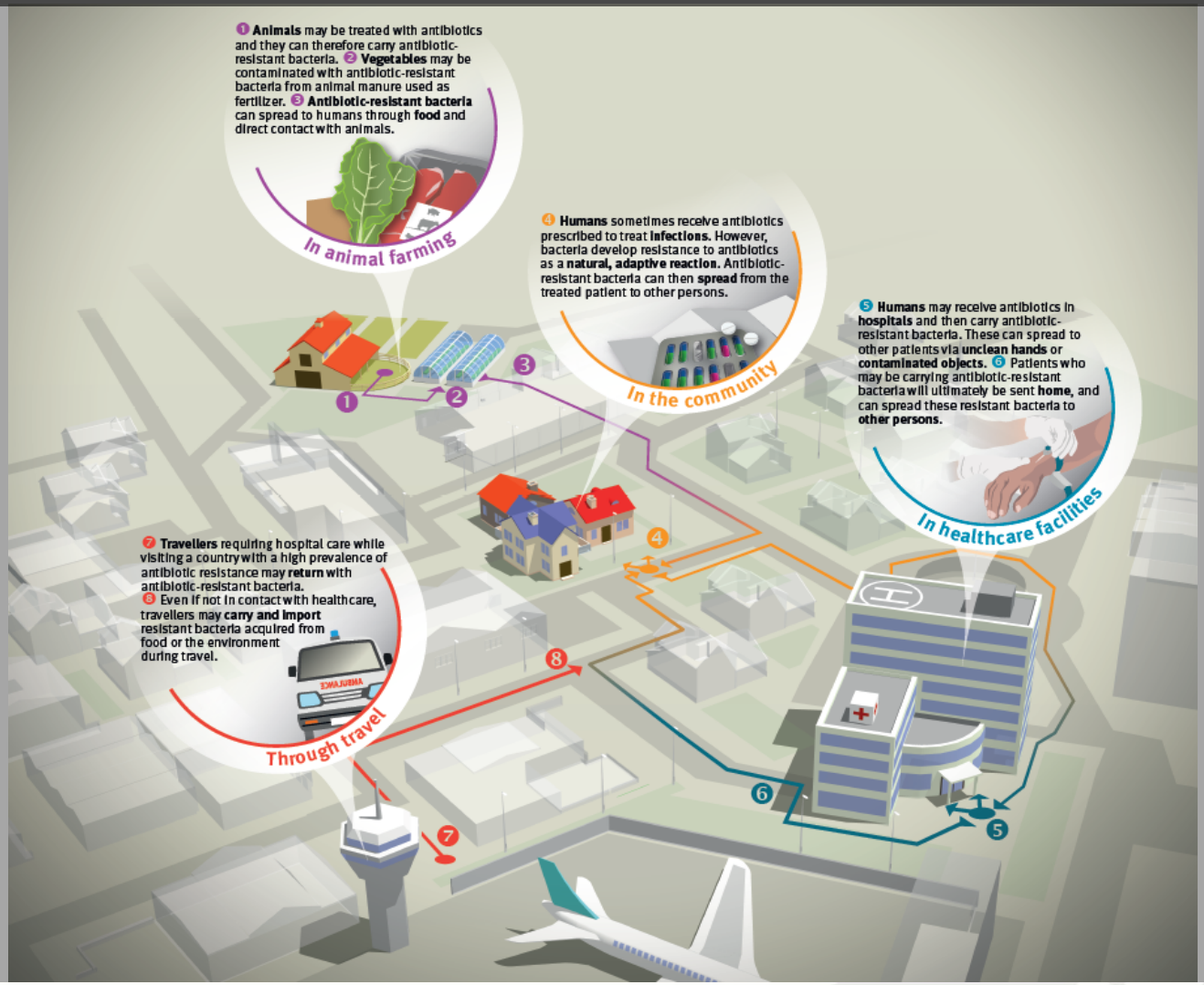
- No case reported
- Sporadic occurrence
- Single hospital outbreaks
- Sporadic hospital outbreaks
- Regional spread
- Interregional spread
- Endemic situation

Not participating or not reporting

Non-EU/EEA countries

Source: Albiger B, et al. Eurosurveillance 2015; 20(45) (12 November 2015).

How does antibiotic resistance spread?

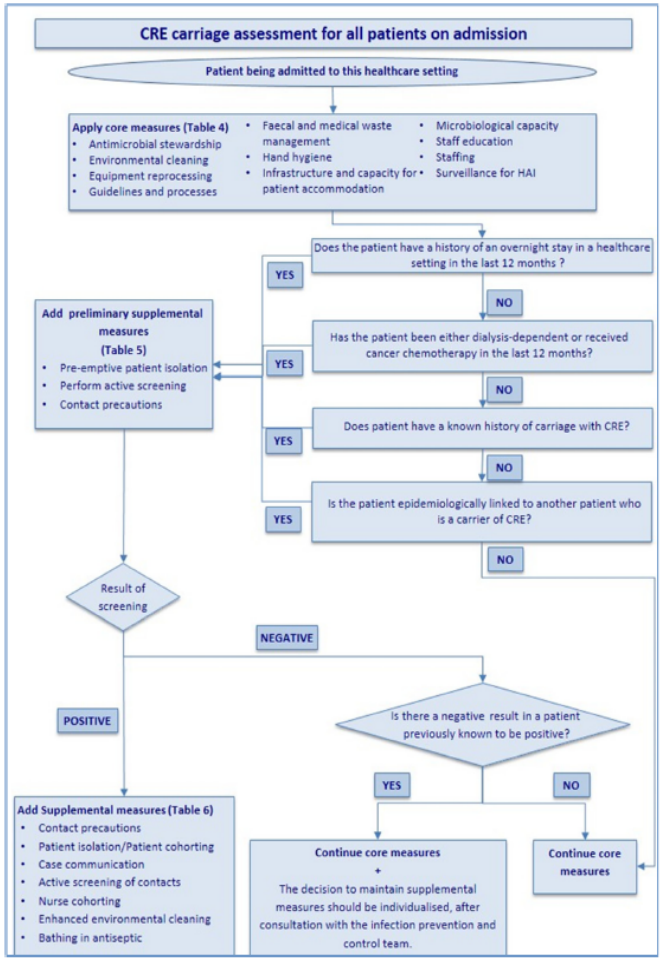


https://ecdc.europa.eu/en/publications-data/antibiotic-resistance-how-does-antibiotic-resistance-spread


Lill-Karin
(Norway)
https://antibiotic.ecdc.europa.eu/en/patient-stories

Infection prevention and control measures and tools to prevent entry of carbapenem-resistant *Enterobacteriaceae* (CRE) into healthcare settings: ECDC guidance

- **Core measures**
- Profile for **<u>"at risk" patients</u>** who require supplemental measures
- **Preliminary supplemental measures** (at admission, for "at risk" patients)
- **Supplemental measures** (for confirmed CRE-positive patients)

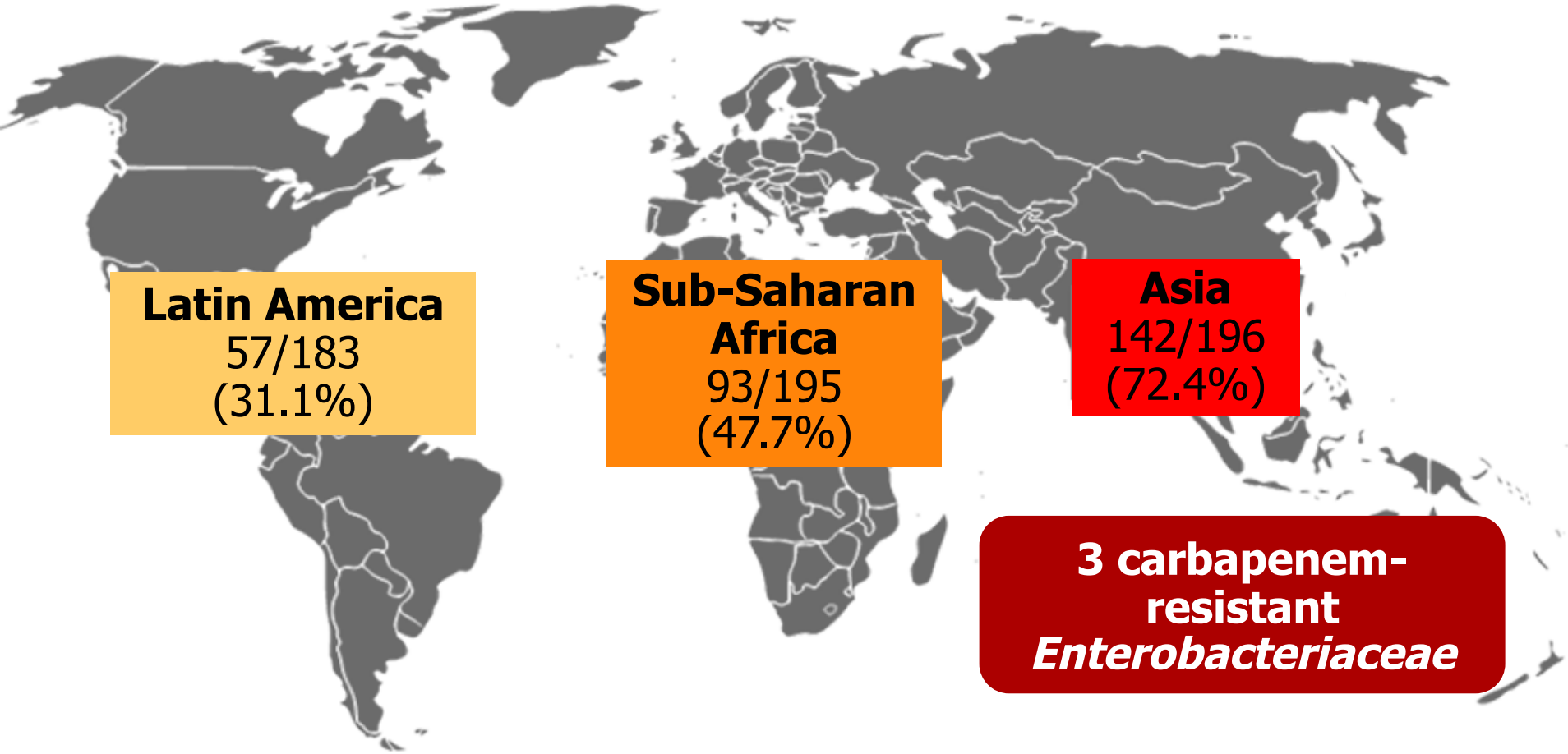


Source: Magiorakos *et al.* Antimicrob Resist Infect Control (15 November 2017).

International travel

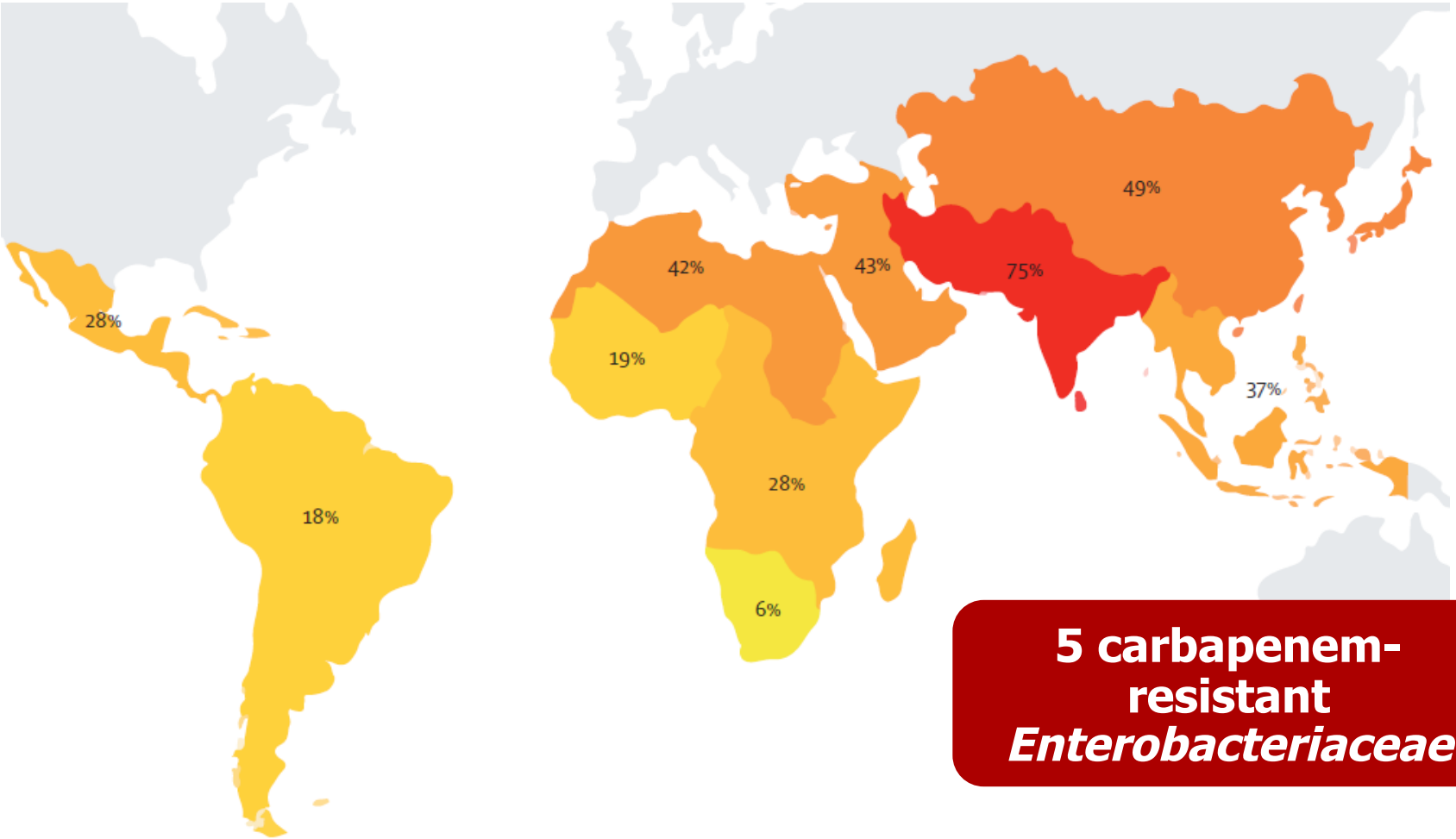
Date	Departure	Destination
Today	14:10	MULTIDRUG-RESISTANT MICROORGANISMS
Today	14:35	MULTIDRUG-RESISTANT MICROORGANISMS
Today	14:40	MULTIDRUG-RESISTANT MICROORGANISMS
Today	14:45	MULTIDRUG-RESISTANT MICROORGANISMS
Today	14:55	Baxjö
Today	15:00	Holmen
Today	15:00	MULTIDRUG-RESISTANT MICROORGANISMS
Today	15:00	MULTIDRUG-RESISTANT MICROORGANISMS
Today	15:05	MULTIDRUG-RESISTANT MICROORGANISMS
Today	15:05	MULTIDRUG-RESISTANT MICROORGANISMS
Today	15:10	Wasserdam
Today	15:15	MULTIDRUG-RESISTANT MICROORGANISMS
Today	15:15	Mørup

Frequency of fecal carriage of multidrug-resistant *Enterobacteriaceae* in international travellers, February 2012-April 2013



Source: Ruppé E, et al. Clin Infect Dis 2015 Aug 15;61(4):593-600.
Ruppé E, et al. Eurosurveillance 2014 Apr 10;19(14). pii: 20768.

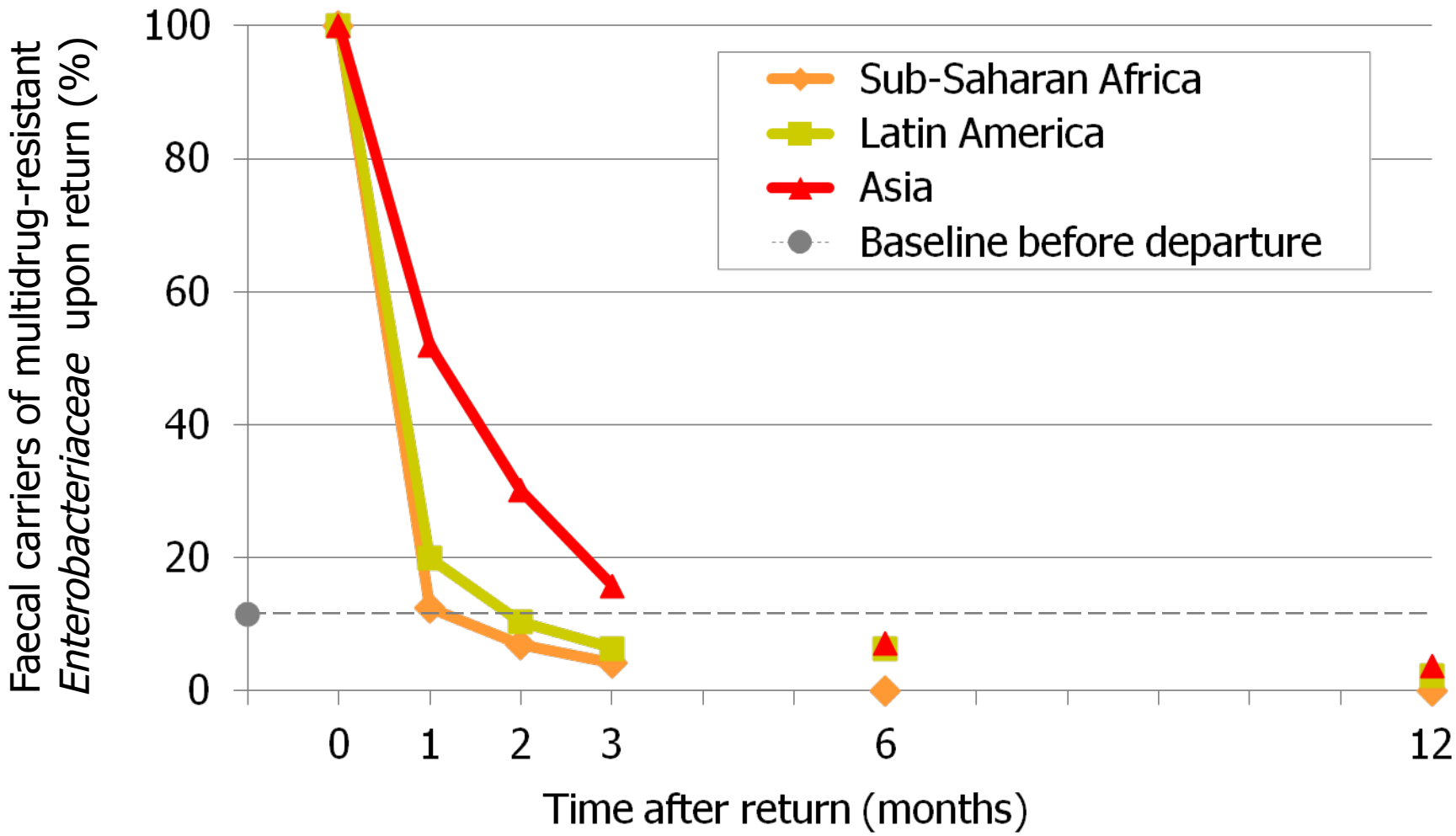
Percentage of international travellers that acquired β-lactamase-producing Enterobacteriaceae, 2012-2013



5 carbapenem-resistant *Enterobacteriaceae*

Source: Arcilla MS, et al. Lancet Infect Dis 2017;17(1):78-85.;
Van Hattem JM, et al. Future Microbiol 2016; 11(7): 857-64.

Duration of faecal carriage of multidrug-resistant *Enterobacteriaceae* in international travellers, February 2012-April 2013



Source: Ruppé E, et al. Clin Infect Dis 2015 Aug 15;61(4):593-600.

ECDC expert opinion "Risks from digestive colonisation by multidrug-resistant Enterobacteriaceae after international travel"

- Risk factors and duration of carriage
- Implications for infection control
- **Implications for patient management**
- **Advice to travellers**
- Methods for screning returning travellers for digestive carriage

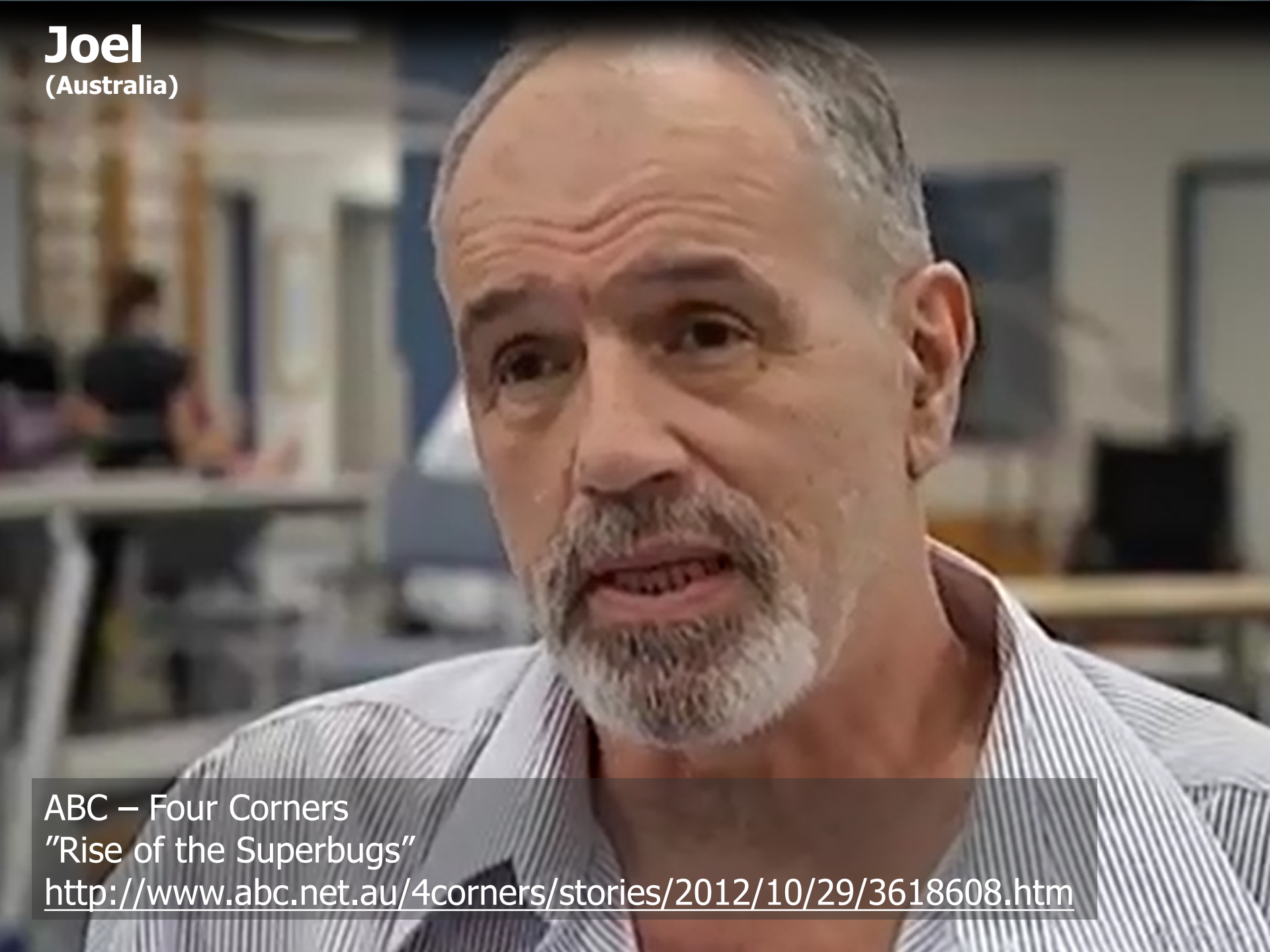
Source: ECDC, 2018 (in preparation).

Implications for patient management (1)

- ”All patients with symptomatic infections potentially caused by *Enterobacteriaceae* should be asked if they recently travelled in a high-risk region”
- If ‘yes’ (**past 3 months**):
  - Appropriate samples submitted for microbiologcial culture, even for uncomplicated infections
  - Appropriate infection control measures if hospital admission
  - Mild, non-severe infections: standard therapy, may be changed after checking microbiological results or in case of clinical failure.
  - Severe sepsis, or invasive infection suspected in an immunocompromised patient: therapy active against ESBL+ Enterobacteriaceae. Empirical treatment must be reviewed after antimicrobial susceptibility results are available.
  - Therapy covering carbapenem-R *Enterobacteriaceae* NOT recommended unless patient has been hospitalised in a high-risk region

Source: ECDC expert opinion ”Risks from digestive colonisation by multidrug-resistant *Enterobacteriaceae* after international travel”, 2018 (in preparation).


Mohammed
(United Kingdom)
https://antibiotic.ecdc.europa.eu/en/patient-stories


Joel
(Australia)
ABC – Four Corners
”Rise of the Superbugs”
http://www.abc.net.au/4corners/stories/2012/10/29/3618608.htm

Implications for patient management (2)

- ”Travellers are particularly at risk if undergoing scheduled invasive medical procedures upon return such as transrectal prostate biopsy or abdominal surgery with opening of the intestine.”
- Options:
  - Postpone elective invasive procedures whenever the risk associated with delaying the procedure is negligible
  - Preoperative screening for digestive colonisation
  - Short-term antibiotic prophylaxis active against ESBL+ *Enterobacteriaceae*
  - Trans-perineal approach (for prostate biopsy)

Source: ECDC expert opinion ”Risks from digestive colonisation by multidrug-resistant *Enterobacteriaceae* after international travel”, 2018 (in preparation).

Advice for travellers (1)

- So far, no evidence that an intervention regimen, e.g. probiotics, could *per se* protect against multidrug-resistant *Enterobacteriaceae*

- Avoid colonisation:
  - Prevention of travellers' diarrhoea (limited effect);
  - Abstain for unnecessary antimicrobial use for travellerss' diarrhoea;
  - Abstain for unnecessary antimicrobial use for upper respiratory tract infection;
  - Other (limited evidence):
    - Hygiene / hand hygiene
    - Street food

Source: ECDC expert opinion "Risks from digestive colonisation by multidrug-resistant *Enterobacteriaceae* after international travel", 2018 (in preparation).

Advice for travellers (2)

- Prevent spread to household contacts:
  hand hygiene (toilet, preparation of food)

- If hospitalised or healthcare contact after travel:
  inform of travel or hospitalisation during travel

Source: ECDC expert opinion "Risks from digestive colonisation by multidrug-resistant *Enterobacteriaceae* after international travel", 2018 (in preparation).

Public transportation (buses, metro)

- **Porto (Portugal)**
  - 36% of 199 buses with MRSA
  - 2 of 3 major clones are the same as in hospitals
  - Association between proportion of MRSA contamination and bus serving more than 3 hospitals
- **Midwestern U.S. (urban)**
  - 63% of 40 buses with MRSA
- **New York Subway**
  - *Acinetobacter baumannii* at 220/466 stations sampled

Source: Conceição T, et al. PLoS ONE 2014;8(11): e77812; Lutz JK, et al. Am J Infect Control 2014;42:1285-90; Afshinnekoo E, et al. Cell Systems 2015; 1: 1–15. http://dx.doi.org/10.1016/j.cels.2015.01.001.

Mobile communication devices

- **Review of literature**
  - 9-25% mobile communication devices with pathogenic bacteria
  - 0-10% with MRSA
- **UK**
  - 16% of 390 mobile phones in 12 cities contaminated with *E. coli* (London School of Hygiene and Tropical Medicine and Queen Mary, University of London)

Source: Brady RRW, et al. J Hosp Infect 2009;71:295-300. Batty D. The Guardian 13 Oct 2011.

Hand hygiene

Extensively drug-resistant (XDR) *Neisseria gonorrhoeae*

ECDC rapid risk assessment (in preparation, 4 May 2018 tbc).

A plausible worst-case scenario for Sweden, 2025-2030: increasing carriage of carbapenem-resistant *Escherichia coli*

- *Q1: Could 5% of the population in southern Sweden become carriers of carbapenem-resistant* E. coli*?* Possible or even likley in 10-15 years.
- *Q3: What would be the consequences of the scenario on society?* Increased demand on healthcare.
- *Q4: What measures should be taken to prevent or manage the scenario?*
  - Initiate long-term screning programmes (human health, animal health, feeds, food, water, environment, outflow of sewage treatment plants, hospitals, etc.);
  - Hygienic and cleaning routines must be improved and enforced (hospitals, nursing homes, daycare centers);
  - Strategies and plans to prevent and handle this threat.

Source: Roffey R. Et al. Health Security 2015;13(3):174-183.

Thank you!

EUROPEAN ANTIBIOTIC AWARENESS DAY

A EUROPEAN HEALTH INITIATIVE

18 November 2018

E-mail: EAAD@ecdc.europa.eu
Website: https://antibiotic.ecdc.europa.eu
Facebook: EAAD.EU
Twitter: @EAAD_EU (#EAAD)
Global Twitter: #AntibioticResistance

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WORLD ANTIBIOTIC AWARENESS WEEK

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ANTIBIOTICS HANDLE WITH CARE