



# Antimicrobial resistance trends in Europe

Dominique L. Monnet, for the Antimicrobial Resistance & Healthcare-Associated Infections (ARHAI) Disease Programme

Rome, 22 December 2014

# What is the role of ECDC in its Founding Regulation?



... to identify, assess and communicate current and emerging health threats to human health from communicable diseases.

— ECDC Founding Regulation (851/2004), Article 3

- EU-level disease surveillance and epidemic intelligence
- Scientific opinions and studies
- Early Warning System and response
- Technical assistance and training
- Communication to scientific community
- Communication to the public



# Antimicrobial Resistance and Healthcare-Associated Infections (ARHAI) Networks



- **European Antimicrobial Resistance Surveillance Network (EARS-Net)**

(formerly EARSS, integrated in January 2010)

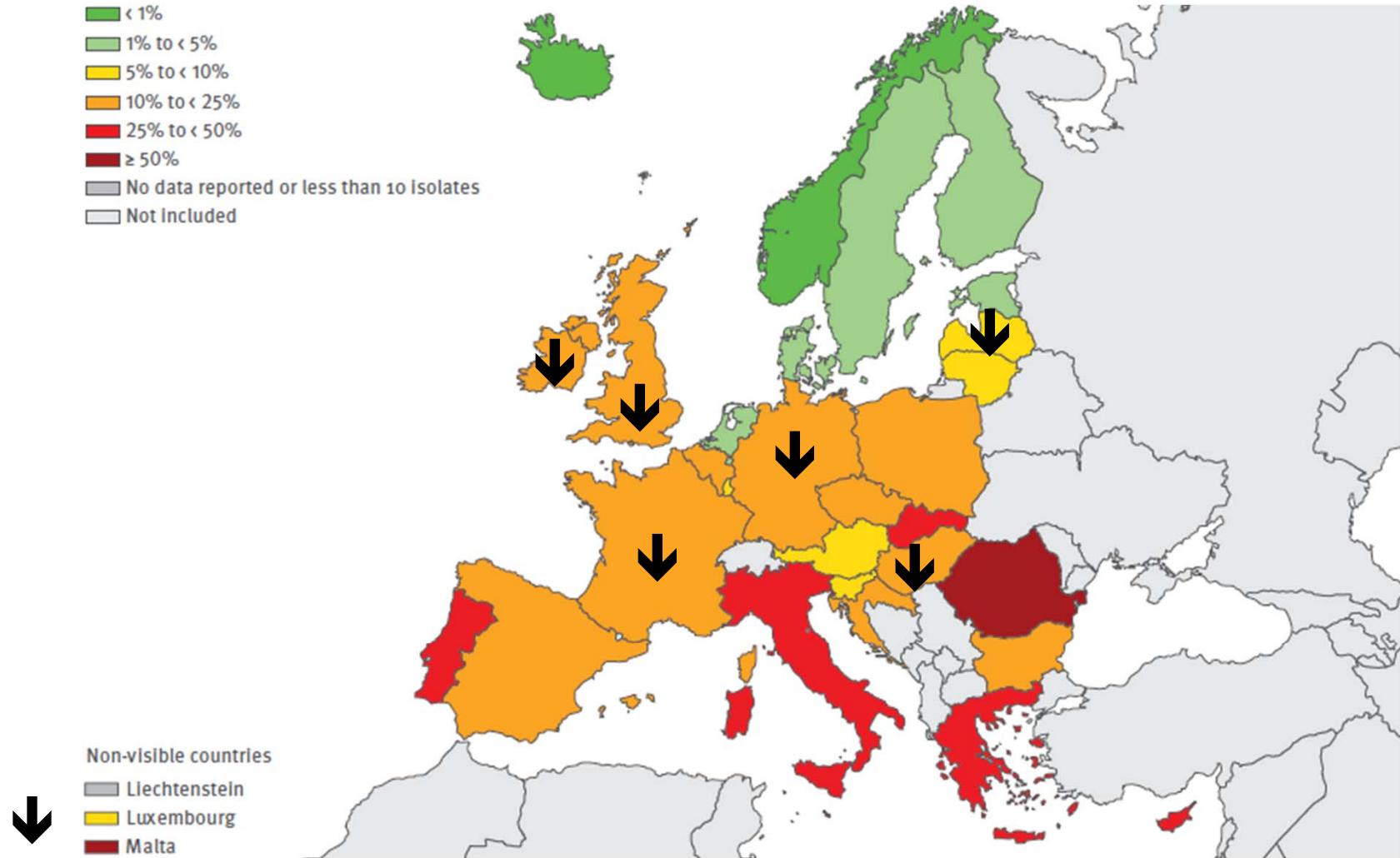
- **European Surveillance of Antimicrobial Consumption Network (ESAC-Net)**

(formerly ESAC, integrated in July 2011)

- **Healthcare-Associated Infections surveillance Network (HAI-Net)**

(formerly HELICS / IPSE, integrated in July 2008)

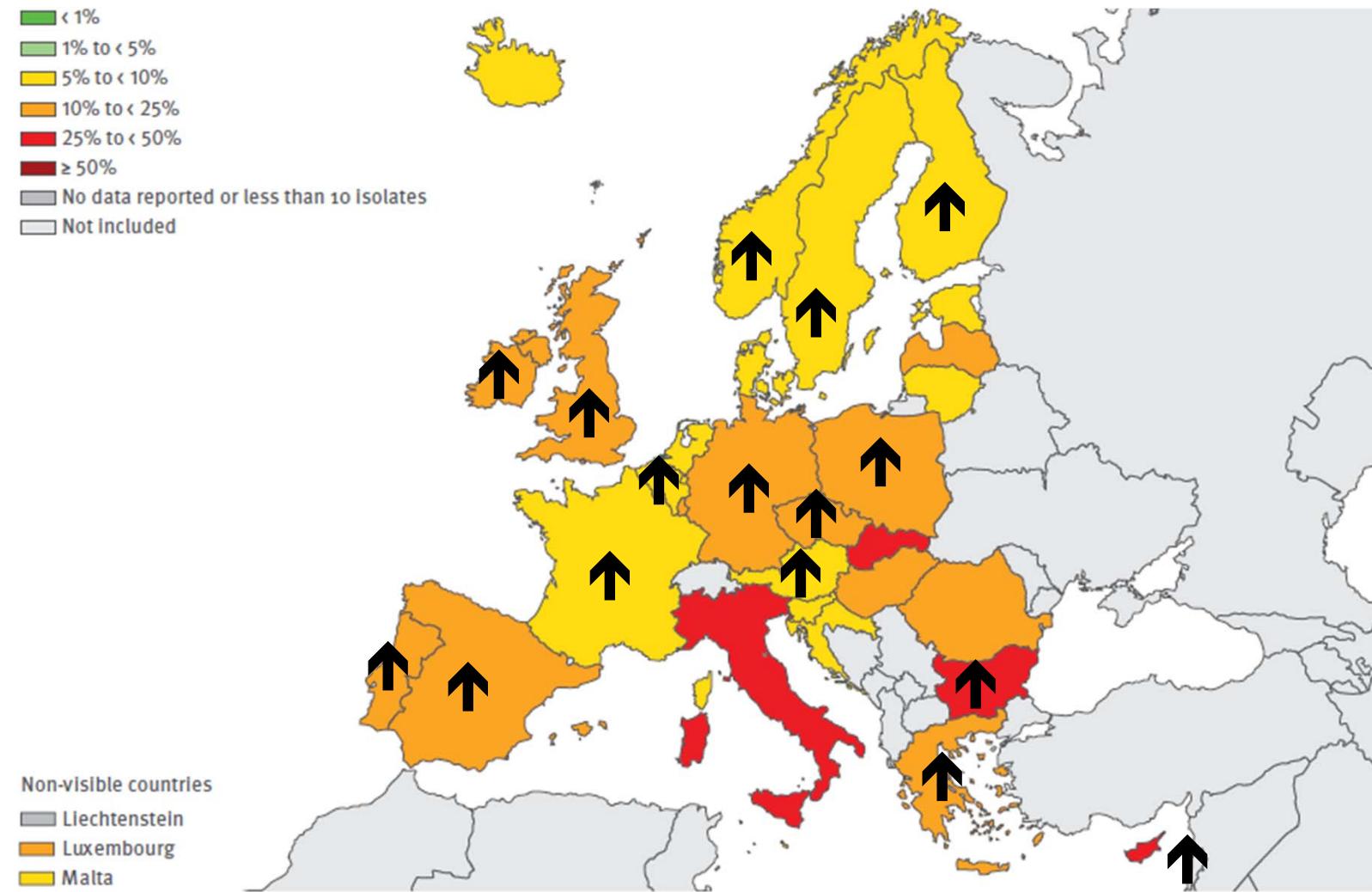
# *Staphylococcus aureus:* percentage of invasive isolates resistant to meticillin (MRSA); EU/EEA, 2013



Source: EARS-Net, 2014

The symbols ↑ and ↓ indicate a significant increasing or decreasing trend for the period 2010-2013, respectively. These trends were calculated on laboratories that consistently reported during this period.

# *Escherichia coli*: percentage of invasive isolates resistant to third-generation cephalosporins; EU/EEA, 2013



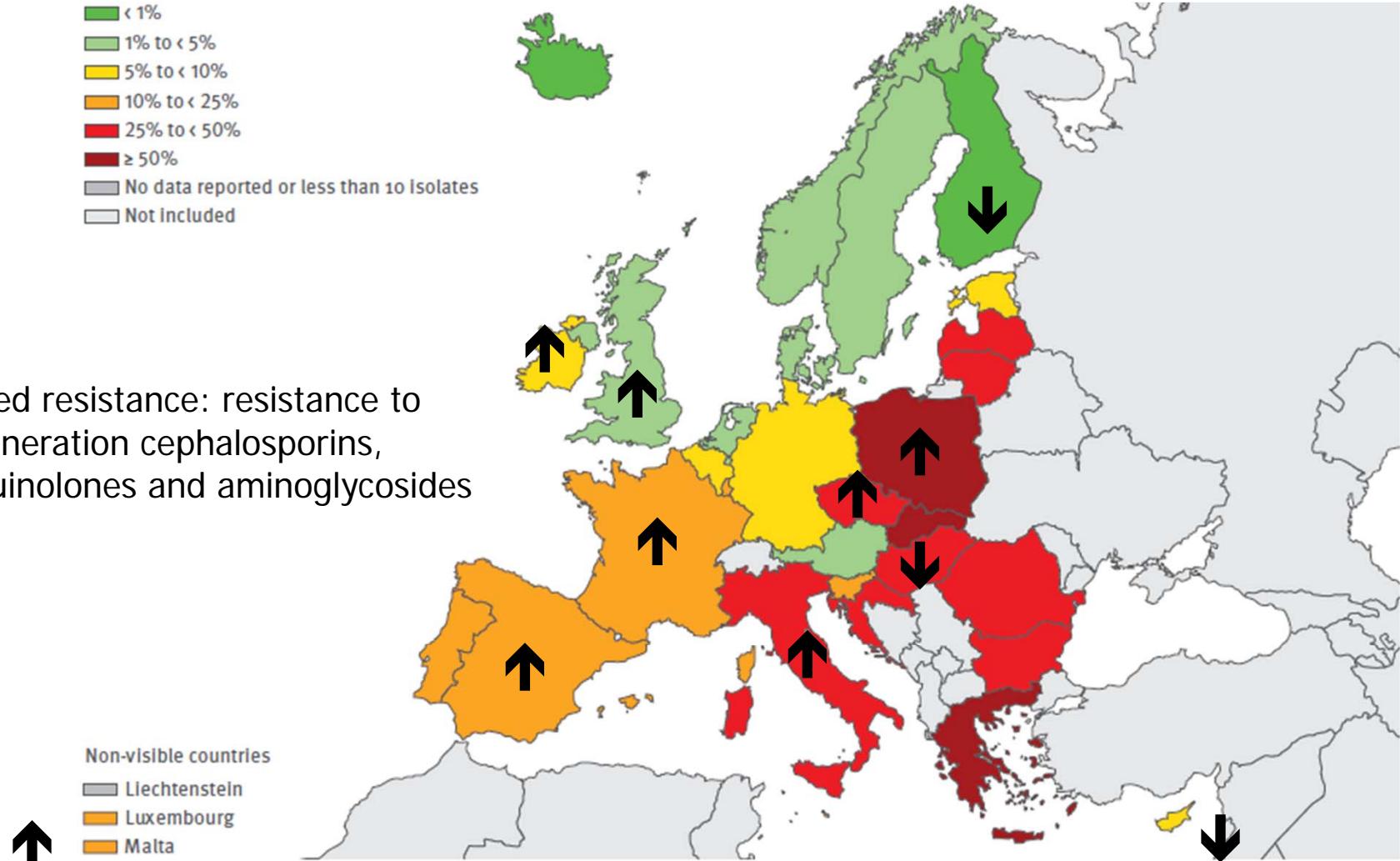
Source: EARS-Net, 2014

The symbols  $\uparrow$  and  $\downarrow$  indicate a significant increasing or decreasing trend for the period 2010-2013, respectively. These trends were calculated on laboratories that consistently reported during this period.

# *Klebsiella pneumoniae:* percentage of invasive isolates with combined resistance\*; EU/EEA, 2013

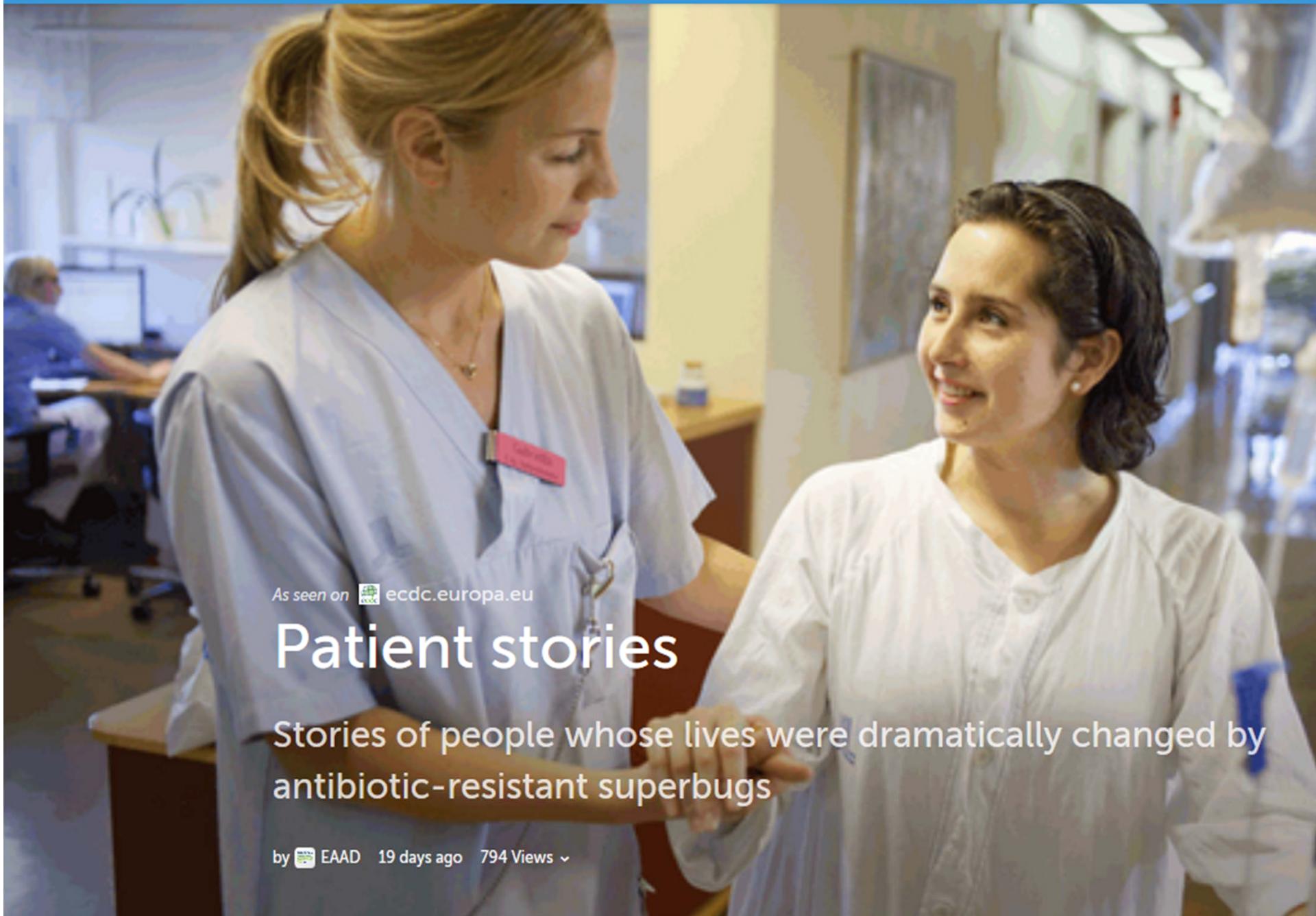


\*Combined resistance: resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides



Source: EARS-Net, 2014

The symbols ↑ and ↓ indicate a significant increasing or decreasing trend for the period 2010-2013, respectively. These trends were calculated on laboratories that consistently reported during this period.



**Mohammed**  
(United Kingdom)



[https://storify.com/EAAD\\_EU/patient-stories](https://storify.com/EAAD_EU/patient-stories)

# Carbapenem-resistant infections: 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 smittspärningsplikt enl  
smittskyddslagen. Kontakta alltid vårdhygien. För mer  
information: [www.smittskyddstockholm.se](http://www.smittskyddstockholm.se)

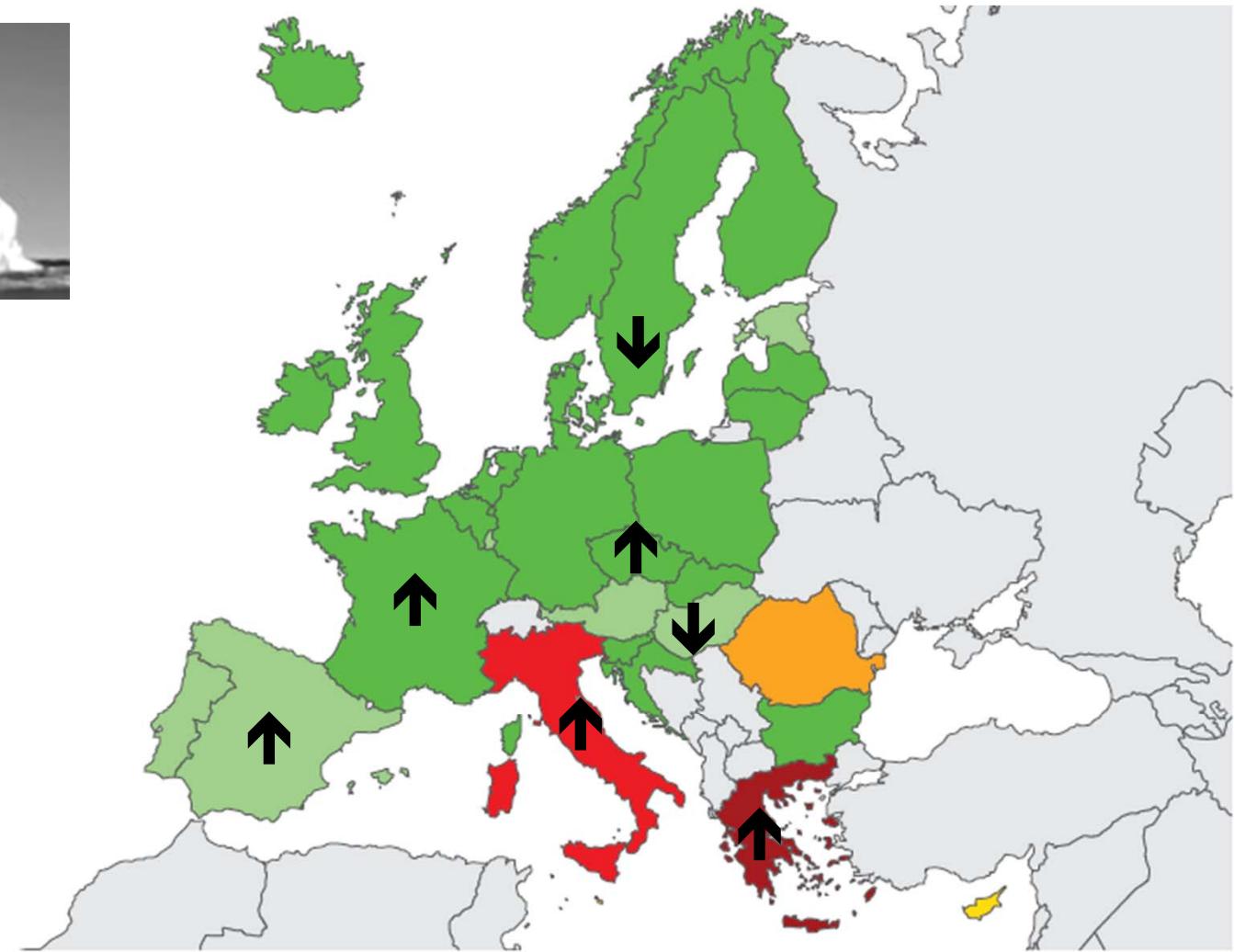
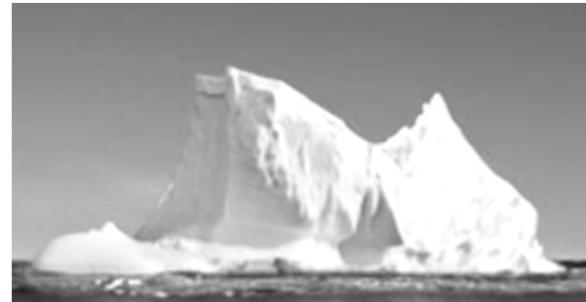
## ANTIBIOTIKUM

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

## Sammanfattning/Ovrigt:

Obs! Mycket omfattande resistensprofil. Endast känslig för colistin.

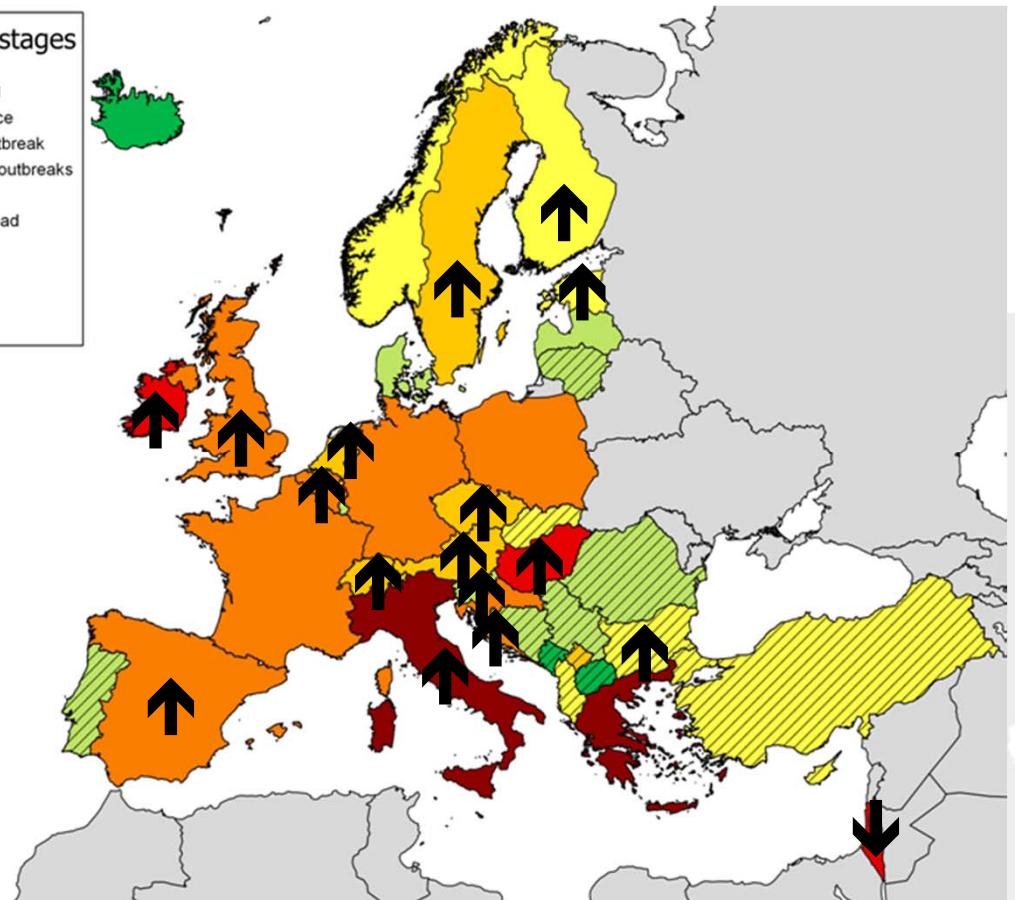
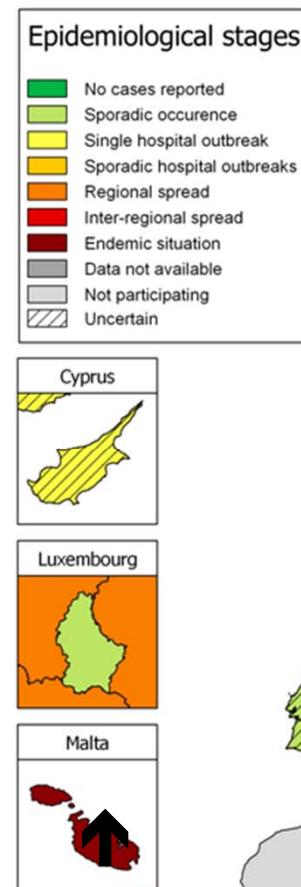
# *Klebsiella pneumoniae:* percentage of invasive isolates resistant to carbapenems; EU/EEA, 2013



Source: EARS-Net, 2014

The symbols ↑ and ↓ indicate a significant increasing or decreasing trend for the period 2010-2013, respectively. These trends were calculated on laboratories that consistently reported during this period.

# Country self-assessment of stages for spread of carbapenemase-producing *Enterobacteriaceae* (all isolates), 2010 and 2013



Source: Grundmann et al. Eurosurveill 2010, and EuSCAPE project, Glasner et al., Eurosurveill 2013.

The symbols ↑ and ↓ indicate a positive or negative change in stage between 2010 and 2013. This change could only be indicated for countries that reported for both years.

# ECDC risk assessment on the spread of carbapenemase-producing *Enterobacteriaceae*: risk factors for patient infection or colonisation

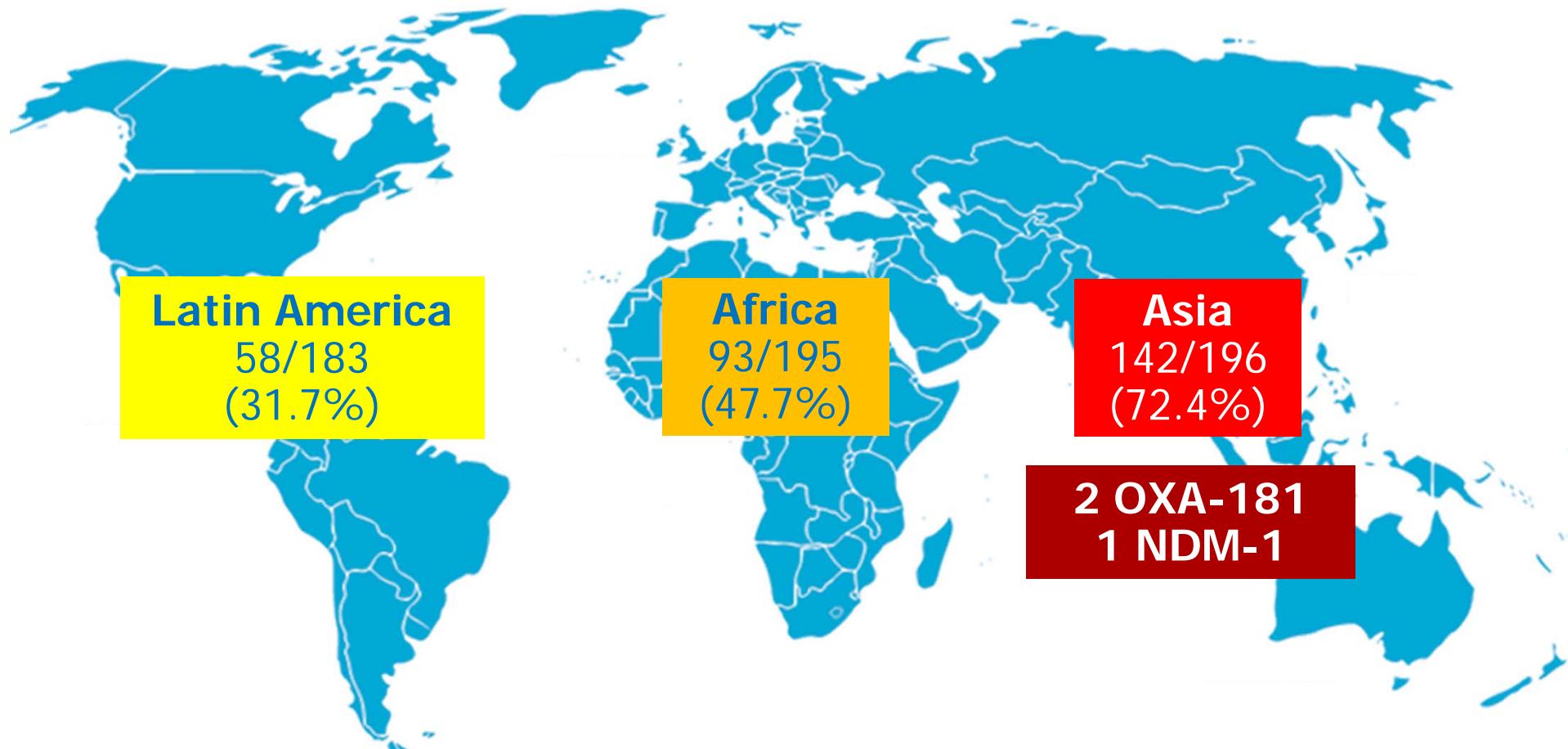


- **Prior use of antimicrobials**
  - Any antimicrobial
  - **Carbapenems** (associated with a high risk estimate)
  - Other antimicrobials (fluoroquinolones, cephalosporins, anti-pseudomonal penicillins, metronidazole)
- **Cross-border transfer of patients**

Strong evidence that it is associated with risk for transmission when:

  - Patients are transferred from countries with high rates of CPE to healthcare facilities in other countries
  - Patients had received medical care abroad in areas with high rates of CPE
- **Transfer of patients within units of same hospital**
- Immunosuppression, severity of illness, invasive procedures

# Carriage of multidrug-resistant *Enterobacteriaceae* in returning travellers, 2012-2013



Source: VOYAG-R Study. Ruppé E, et al. 33<sup>rd</sup> RICAI, Paris, 27-28 November 2013 [abstr. 195].;  
Ruppé E, et al. Eurosurveillance 2014 Apr 10;19(14). pii: 20768.

# Carbapenemase-producing *Enterobacteriaceae* (CPE): other issues



- **International travel**

VOYAG-R Study. Ruppé E, et al. 33<sup>rd</sup> RICAI, Paris, 27-28 November 2013 [abstr. 195].; Ruppé E, et al. Eurosurveillance 2014 Apr 10;19(14). pii: 20768.  
COMBAT Study. Penders J, et al. 3<sup>rd</sup> Euregional Maastricht Symposium on Immune Compromised Traveller, Maastricht, 24 March 2014.

- **Travelling healthcare workers**

suspected by Munier E, et al. Am J Infect Control 2014;42:85-6.

- **Refugees and war casualties (Libya)**

Pirš M, et al. Euro Surveill. 2011 Dec 15;16(50):20042.  
Hammerum AM, et al. Int J Antimicrob Agents. 2012 Aug;40(2):191-2.  
Kocsis E, et al. Clin Microbiol Infect. 2013 Sep;19(9):E409-11.

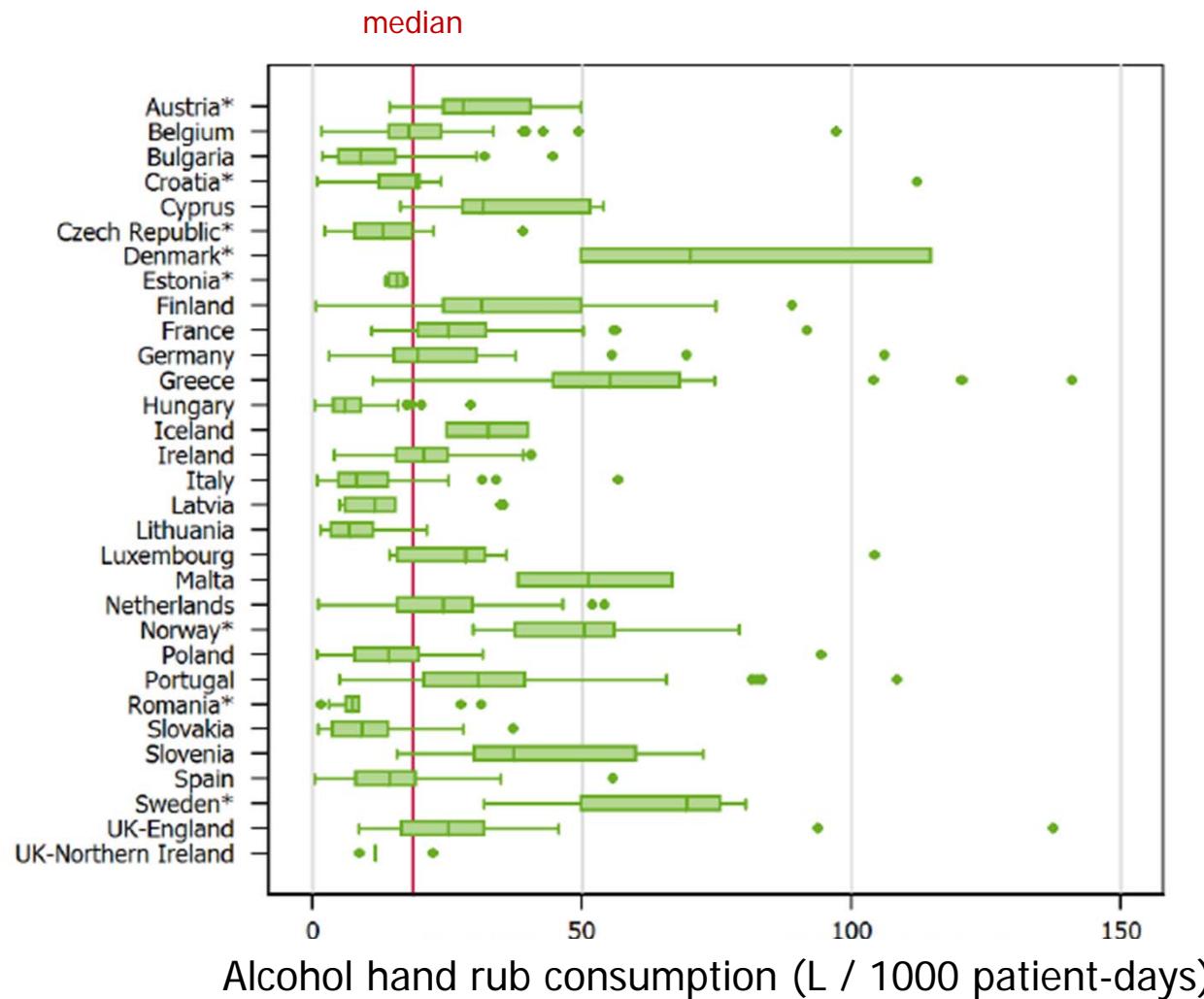
- **Environment (outside of hospitals)**

carbapenemase-producing *Serratia fonticola* from drinking water. Henriques I, et al. Genome Announc. 2013;1(6). pii: e00970-13.

- **Foodborne pathogens**

carbapenemase-producing *Salmonella* Kentucky  
Le Hello et al. Lancet Infect Dis. 2013 Aug;13(8):672-9.  
Seiffert SN, et al. Antimicrob Agents Chemother. 2014 Jan 27.

# ECDC PPS in European acute care hospitals, 2011-2012: example of indicator



\*PPS data representativeness was poor in Austria, Croatia, Czech Republic, Estonia, Norway and Romania and very poor in Denmark and Sweden. Red vertical line=median (18.7 litres/1000 patient-days).

Source: HAI-Net, ECDC, 2013.

<http://www.ecdc.europa.eu/en/publications/Publications/healthcare-associated-infections-antimicrobial-use-PPS.pdf>

# Trends in consumption of antibacterials for systemic use in the hospital sector (expressed in DDD per 1000 inhabitants and per day), EU/EEA, 2009-2013



	2009	2010	2011	2012	2013	Trends in antimicrobial consumption, 2009–2013	Average annual change 2009–2013	Statistical significance
<b>Total (J01)</b>	<b>2.1</b>	<b>2.0</b>	<b>2.0</b>	<b>2.0</b>	<b>2.0</b>		<b>-0.02</b>	<b>n. s.</b>
<b>Carbapenems (J01DH)</b>	<b>0.043</b>	<b>0.050</b>	<b>0.049</b>	<b>0.054</b>	<b>0.056</b>		<b>0.003</b>	<b>significant</b>
<b>Polymyxins (J01XB)</b>	<b>0.008</b>	<b>0.008</b>	<b>0.011</b>	<b>0.014</b>	<b>0.014</b>		<b>0.002</b>	<b>significant</b>

Source: ESAC-Net, 2014. <http://ecdc.europa.eu/en/eaad/Pages/antibiotics-data-reports.aspx>

# Extensively drug-resistant infections: an hypothetical challenge for Europe?

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

ANTIBIOTIKUM

Ampicillin.....	R
Piperacillin/tazobaktam.....	R
Cefadroxil.....	R
Imipenem.....	R
Meropenem.....	R
Ertapenem.....	R
Aztreonam.....	R
Colistin.....	R
Kloramfenikol.....	R
Tobramycin.....	R
Amikacin.....	R
Netilmicin.....	R
Trimetoprim.....	R
Trimetoprim-sulfa.....	R
Nitrofurantoin.....	R
Cefotaxim.....	R
Ceftazidim.....	R
Gentamicin.....	R
Tigecycline.....	?
Fosfomycin.....	?

?

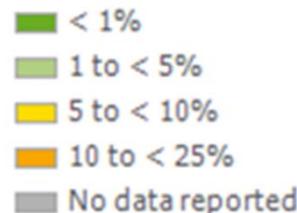
Sammanfattnings/Ovrigt:

Obs! Mycket omfattande resistensprofil.

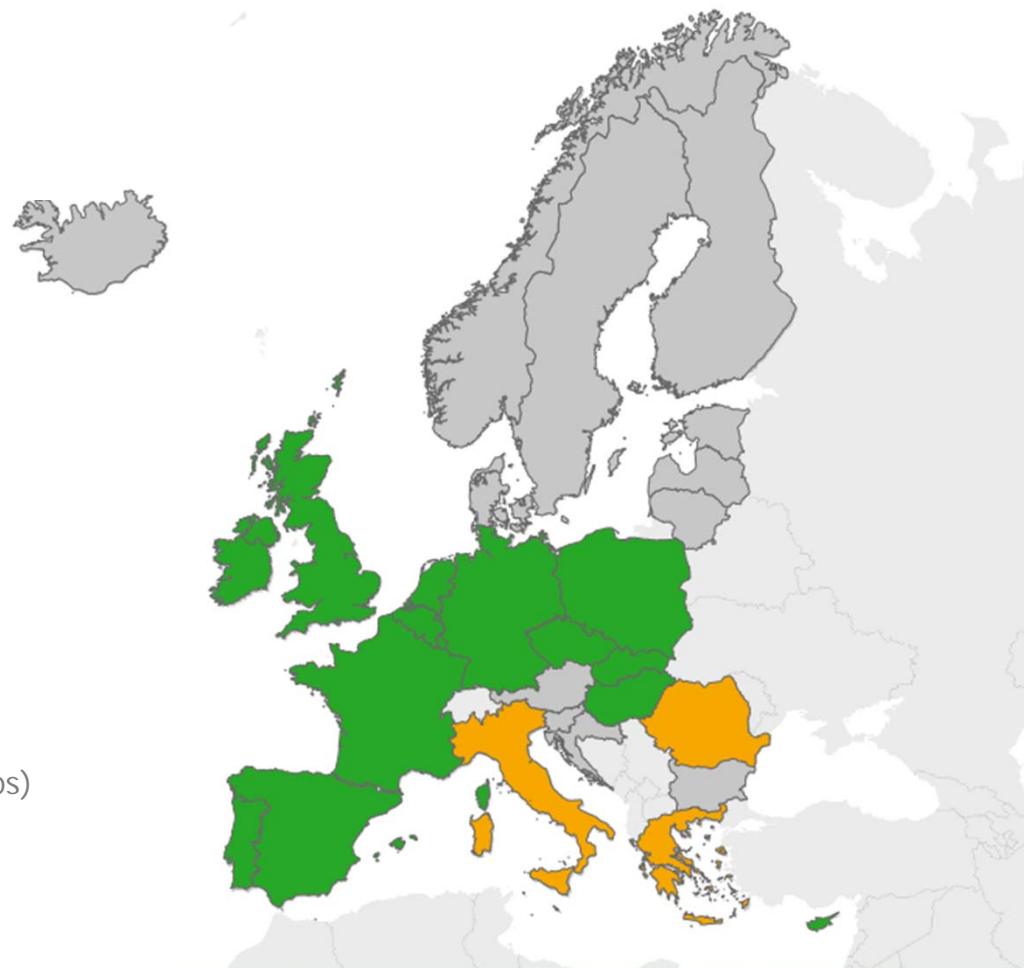
# *Klebsiella pneumoniae*: % of invasive isolates with resistance to all antibiotic groups under surveillance\*, EU/EEA, 2013

\*Third-generation cephalosporins,  
fluoroquinolones, aminoglycosides,  
carbapenems and colistin).

Only among isolates that were tested  
for susceptibility to all these antibiotic  
groups were included.



(i.e., less than 10 reported isolates were  
tested for susceptibility to all these antibiotic groups)



# Modern medicine: not possible without effective antibiotics



Hip / knee replacement

Organ transplant

Cancer chemotherapy

Intensive care

Care of preterm babies

# Main actions to prevent and control antimicrobial resistance (AMR)



**New antimicrobial agents**  
(with a novel mechanism of action,  
research, development)



**Infection prevention and control**  
(hand hygiene, screening, isolation)



**Prudent use of antimicrobial agents**  
(only when needed, correct dose,  
correct dose intervals, correct duration)

You are here: [Portal Home](#) > [English](#) > [Activities](#) > [Disease Programmes](#) > Antimicrobial Resistance and Healthcare-associated Infections

## Antimicrobial Resistance and Healthcare-associated Infections

- [About the programme](#)
- [Surveillance networks](#)
- [Interactive database](#)
- [News](#)
- [Publications](#)
- [Eurosurveillance articles](#)
- [ARHAI network meetings](#)
- [Relevant documents](#)
- [External sites](#)
- [Contact](#)

## Emerging and Vector-borne Diseases

## Food- and Waterborne Diseases and Zoonoses

## Influenza

## HIV, Sexually Transmitted Infections and viral Hepatitis

## Tuberculosis

## Vaccine-preventable Diseases

## Antimicrobial Resistance and Healthcare-associated Infections Programme

The programme on Antimicrobial Resistance and Healthcare-Associated Infections (ARHAI) covers two major public health issues:

- **Antimicrobial Resistance (AMR)**, i.e. the ability of microorganisms to become resistant to one or several antimicrobial agents used for therapy or prophylaxis;
- **Healthcare-Associated Infections (HAI)**, i.e. all infections associated with patient care, in particular hospitals and long-term care facilities.



The ARHAI programme focuses on 4 areas of public health: surveillance, response and scientific advice, training and communication to address the threat of antimicrobial resistance and healthcare-associated infections.

[Read more about the programme](#)

### IN FOCUS

#### Directory of online resources for prevention and control of antimicrobial resistance and healthcare-associated infections now includes CRE, MRSA and CDI

ECDC gathered guidance documents on prevention and control of infection with carbapenem-resistant Enterobacteriaceae (CRE), meticillin-resistant *Staphylococcus aureus* (MRSA) and *Clostridium difficile* infections (CDI) that are available online and are published by EU/EEA Member States, ECDC, other agencies and professional societies. This online directory gives an overview of available documents with measures to prevent and control antimicrobial resistance and healthcare-associated infections.

[Directory of online resources for prevention and control of antimicrobial resistance and healthcare-associated infections](#)

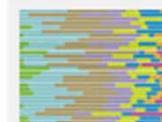
### INTERACTIVE DATABASES



Antimicrobial  
resistance interactive  
database (EARS-  
Net)



Antimicrobial  
consumption  
interactive  
database (ESAC-Net)



Point prevalence  
survey interactive  
database (HAI-Net  
PPS)

### GUIDANCE



Directory of  
online resources:  
Prevention and  
control of  
antimicrobial  
resistance and  
healthcare-  
associated  
infections

**Health Topics****Publications****Data & Tools****Activities****About****News & Media**You are here: [Portal Home](#) > [English](#) > [Health Topics](#) > [Healthcare-associated infections](#) > [Directory: Guidance on prevention and control](#) > [CRE: Guidance on infection prevention and control](#)**Healthcare-associated infections**[News](#)[Publications](#)[Events](#)[Eurosurveillance articles](#)**HAI-Net Annual Reports****Point prevalence survey****PPS interactive database****Directory: Guidance on prevention and control**[MRSA: Guidance on infection prevention and control](#)[CDI: Guidance on infection prevention and control](#)[CRE: Guidance on infection prevention and control](#)**CRE: Guidance on infection prevention and control**

Directory of guidance on prevention and control of Carbapenem-resistant *Enterobacteriaceae*, published by ECDC, EU/EEA Member States, international and national agencies and professional societies

B N S

**AGENCIES****EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL (ECDC)**

- Systematic review of the effectiveness of infection control measures to prevent the transmission of carbapenemase-producing *Enterobacteriaceae* through cross-border transfer of patients (2014)
- Risk assessment on the spread of carbapenemase-producing *Enterobacteriaceae* (CPE) through patient transfer between healthcare facilities, with special emphasis on cross-border transfer (2011)

**US CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)**

- CDC 2012 CRE Toolkit - Guidance for Control of Carbapenem-resistant *Enterobacteriaceae* (CRE)

**US AGENCY FOR HEALTHCARE RESEARCH AND QUALITY (AHRQ)**

- Carbapenem-resistant *Enterobacteriaceae* (CRE) Control and Prevention Toolkit

**PROFESSIONAL SOCIETIES****EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES (ESCMID)**

Suggestions for infection and control of carbapenemase-producing *Enterobacteriaceae* are part of the guidelines on multidrug-resistant Gram-negative bacteria (ESCMID, 2013)

- ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients

**MEMBER STATES****AUSTRIA**

Control of carbapenemase-producing *Enterobacteriaceae* in Austria (Ministry of Health, 2011)

- CRE – Carbapenemase produzierende Enterobakterien in Österreich - Carbapenemasen Kontrollieren

**CZECH REPUBLIC**

Control of imported cases of colonization and/or infection by carbapenemase-producing *Enterobacteriaceae* (Ministry of Health, 2012)

- Kontrola výskytu importovaných případů kolonizace a/nebo infekce enterobakteriemi produkujícími karbapenemázu (CPE – Carbapenemase Producing *Enterobacteriaceae*)

**FINLAND**

Guidance for the handling of infections by multiresistant bacteria. This document includes guidance for infection prevention and control of carbapenem-resistant *Enterobacteriaceae* (Terveyden ja hyvinvointi laitos – THL, 2014)

- Ohje moniresistenteen mikrobiinien tartunnantorjunnasta.

**FRANCE**

Prevention of cross-transmission of emerging highly resistant bacteria. This document includes guidance targeting carbapenemase-producing *Enterobacteriaceae* (Haut Conseil de la Santé Publique, 2013)

- Prévention de la transmission croisée des 'Bactéries Hautement Résistantes aux antibiotiques émergentes' (BRE)

**GERMANY**

Infection control measures for infections or colonisation by multidrug-resistant Gram-negative bacteria. This document applies to carbapenem-resistant *Enterobacteriaceae* (Robert Koch Institute, Commission for Hospital Hygiene and Infection Prevention, 2012)

- Hygienemaßnahmen bei Infektionen oder Besiedlung mit multiresistenten gramnegativen Stäbchen

**GREECE**

Action plan for the management of infections by multidrug-resistant Gram-negative pathogens in healthcare settings 'Prokrustis' Guidance on infection prevention and control of carbapenem-resistant *Enterobacteriaceae* is a part of the national action plan. (Hellenic Centre for Disease Control and Prevention, 2010)

- Σχέδιο θρόπος για την αντιμετώπιση λοιμώξεων από πολυυανθεκτικά Gram-αρνητικά παθογόνα σε χώρους παροχής υπηρεσιών υγίειας 'Προκρύστης'

**HUNGARY**

Guidance of National Center for Epidemiology on identification and prevention of spread of carbapenemase-producing *Enterobacteriaceae* in healthcare facilities (National Center for Epidemiology, 2011)

- Az Országos Epidemiológiai Központ ajánlása a carbapenemáz-termelő enterobacteriaceae törvisek azonosítására és terjedésére megelőzésére az egészségügyi intézményekben

**IRELAND**

Guidance for detection and infection prevention and control of carbapenem-resistant *Enterobacteriaceae* is part of the guidelines on multidrug-resistant organisms (Royal College of Physicians / HSE Quality and Safety, 2012)

- Guidelines for the Prevention and Control of Multi-drug resistant organisms (MDRO) excluding MRSA in the healthcare setting

**ITALY**

Surveillance and control of infections caused by carbapenemase producing bacteria (CRE) (Ministry of Health, 2013)

- Sorveglianza e controllo delle infezioni da batteri produttori di carbapenemasi (CPE)

**NETHERLANDS**

Guideline for multidrug-resistant microorganisms (MDRO). This document includes guidance for infection prevention and control of carbapenem-resistant *Enterobacteriaceae*. (Working Party on Infection Prevention, National Institute for Public Health and the Environment, 2011; updated 2013)

- WIP-richtlijn BRMO (Bijzonder Resistente Micro-Organismen)

**NORWAY**

Prevention and control of transmission of multidrug-resistant Gram-negative and ESBL-producing bacteria in healthcare facilities. This document applies to carbapenemase-producing *Enterobacteriaceae*. (Norwegian Institute of Public Health, 2009)

- Forebyggning og kontroll av spredning av multiresistente gramnegative stafabakterier og ESBL-holdige bakterier i helseinstitusjoner

**POLAND**

Recommendations for the control of sporadic cases and outbreaks caused by Gram negative bacteria of the family *Enterobacteriaceae*. This document focuses on carbapenemase-producing *Enterobacteriaceae*. (Ministry of Health, 2012)

- Zalecenia dotyczące postępowania w przypadku zachorowań sporadycznych i ognisk epidemicznych wywołanych przez Gram ujemne palezek z rodziny *Enterobacteriaceae*

**SLOVAK REPUBLIC**

Guidance for the diagnosis, prevention and control of infections by bacteria with clinically and epidemiologically important resistance mechanisms. This document includes guidance targeting MRSA (Ministry of Health, 2014)

- OU MZ SR pre diagnostiku a protiepidemické opatřenia pri výskytu bakteriálnych pôvodcov infekčných ochorenií s klinicky a epidemiologicky významnými mechanizmami rezistencie

**SLOVENIA**

Recommendations for the control of ESBL-positive bacteria and carbapenemase-positive bacteria (Ministry of Health - National Commission for the prevention and control of healthcare associated infections, 2010)

- Pripomočila za preprečevanje širjenja ESBL pozitivnih bakterij in karbapenemaza pozitivnih bakterij

**SPAIN**

Prevention and control against infection with carbapenemase-producing *Enterobacteriaceae* (Autonomous Community of Madrid, 2013)

- Plan de Prevención y control frente a la infección por enterobacterias productoras de carbapenemases (EPC) en la Comunidad de Madrid

**SWEDEN**

ESBL-producing enterobacteria - Knowledge base with draft notices to limit the spread of *Enterobacteriaceae* with ESBL. This document applies to carbapenemase-producing *Enterobacteriaceae* (Public Health Agency of Sweden, 2013)

- ESBL-producerande tarmbakterier – Kunskapsunderlag med förslag till handläggning för att begränsa spridningen av *Enterobacteriaceae* med ESBL

**UNITED KINGDOM**

Expert advice on the management of colonization or infection due to carbapenemase-producing *Enterobacteriaceae* in England, to prevent or reduce their spread into (and within) health and residential care settings (Public Health England, 2013)

- Acute trust toolkit for the early detection, management and control of carbapenemase-producing *Enterobacteriaceae*  
Set of recommendations based on scientific evidence (where available) and consensus of expert opinion to prevent cross-transmission of carbapenemase-producing *Enterobacteriaceae* within acute healthcare settings in Scotland. Supporting materials include, e.g. a prevention and management toolkit for inpatient areas (Health Protection Scotland, 2013)

- Interim guidance: Non-prescribing control measures to prevent cross transmission of Carbapenemase-Producing *Enterobacteriaceae* in acute settings

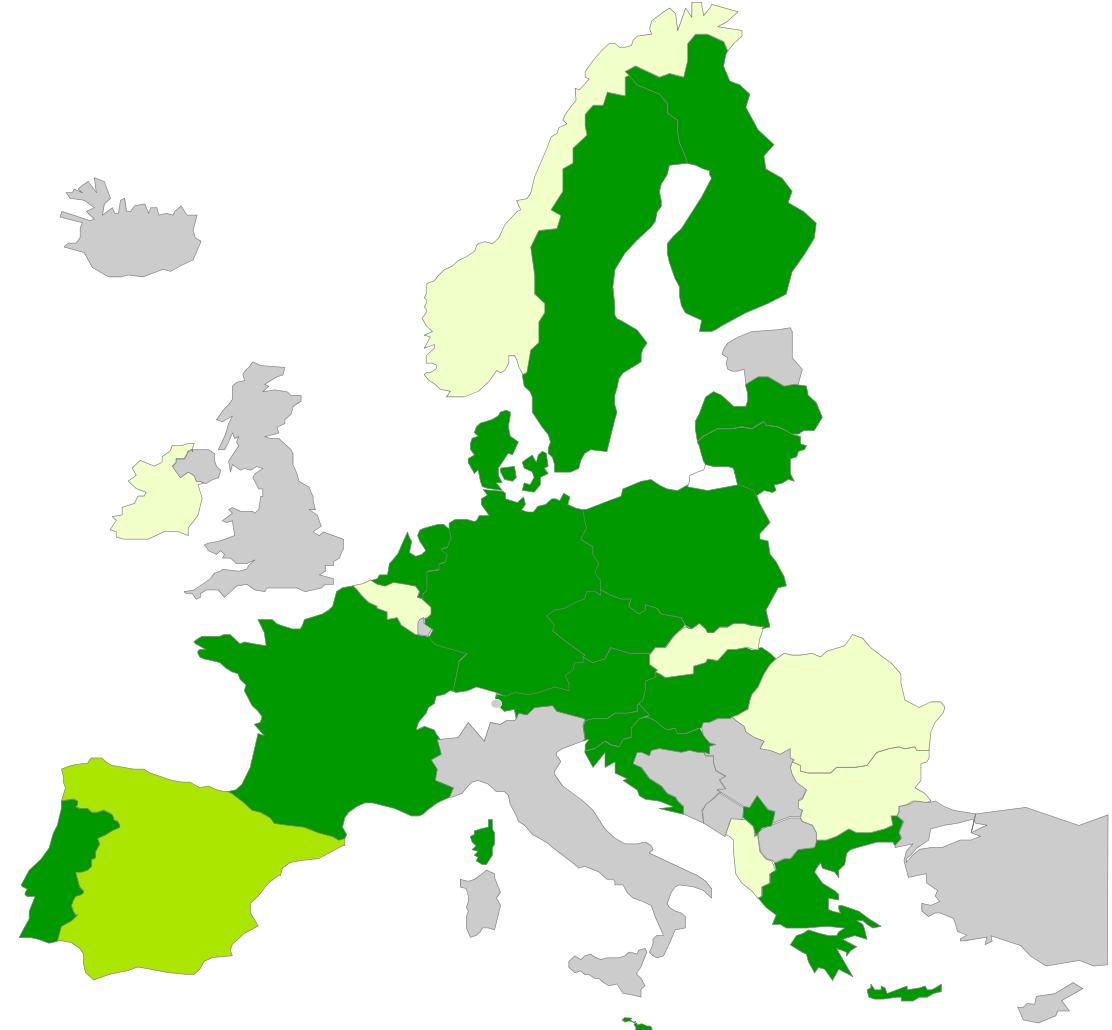
# Country visits to discuss antimicrobial resistance (AMR) issues, 2006-2014



- █ Done
- █ Planned
- █ Discussed

Country visits  
to discuss AMR issues  
(as of December 2014)

- Based on Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine (2002/77/EC)
- Reports (observations, conclusions, suggestions, examples of best practice)
- 18 initial visits (see map)
- 5 follow-up visits (Czech Rep., Greece x 2 and Hungary x 2)
- **2 additional visits budgeted for 2015**



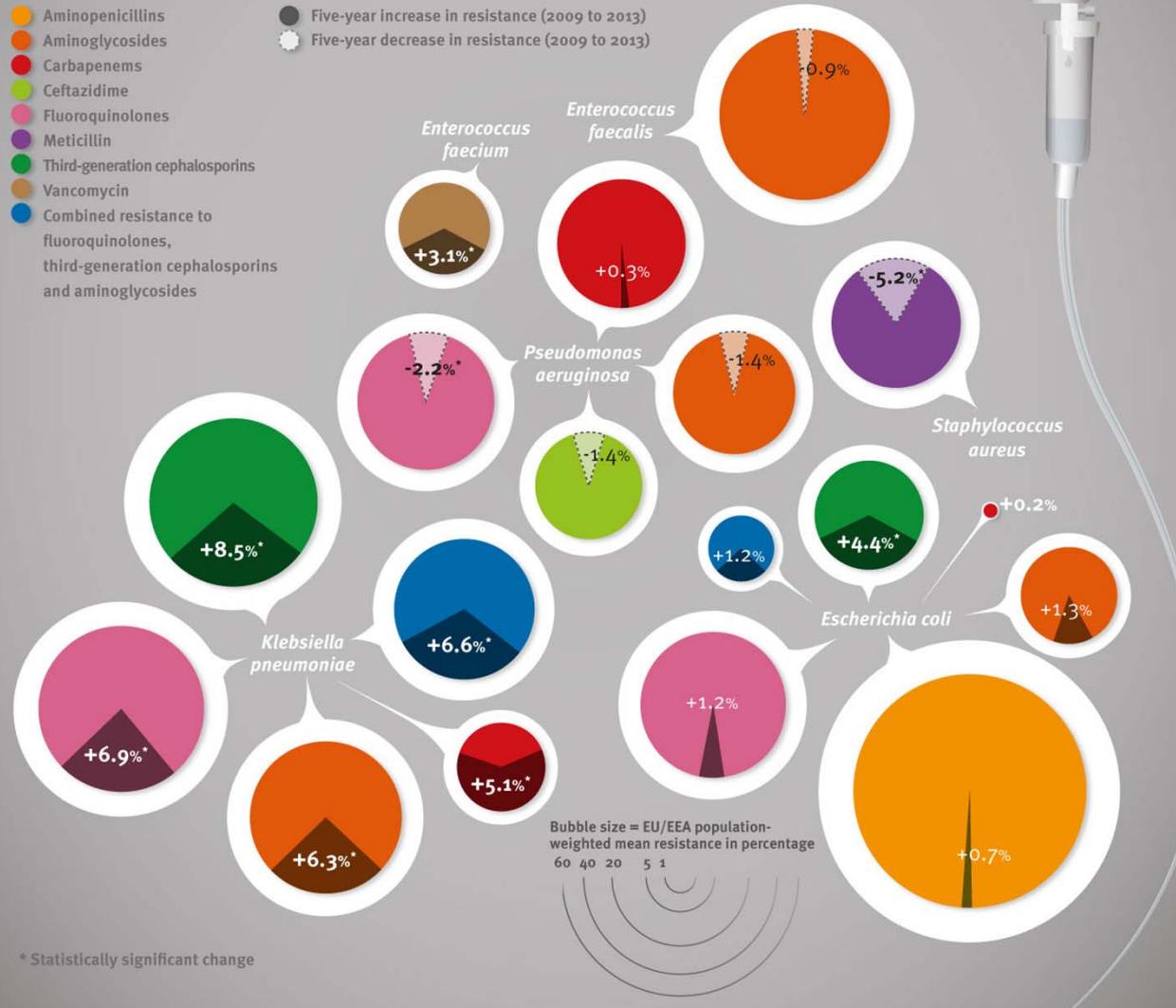
# Antimicrobial resistance in Europe

Each year, 30 EU/EEA countries report data on antimicrobial resistance to the European Antimicrobial Resistance Surveillance Network (EARS-Net), hosted at ECDC.



- Aminopenicillins
- Aminoglycosides
- Carbapenems
- Ceftazidime
- Fluoroquinolones
- Meticillin
- Third-generation cephalosporins
- Vancomycin
- Combined resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides

- Five-year increase in resistance (2009 to 2013)
- Five-year decrease in resistance (2009 to 2013)



Source: EARS-Net, 2014. Infographic: A. Haeger, ECDC.

Thank  
you!