Scientific advice: A European perspective on CPE: the necessity to turn the tide

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European Centre for Disease Prevention and Control

Joint Annual Meeting of the ARHAI Networks

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The importance of "getting it right"

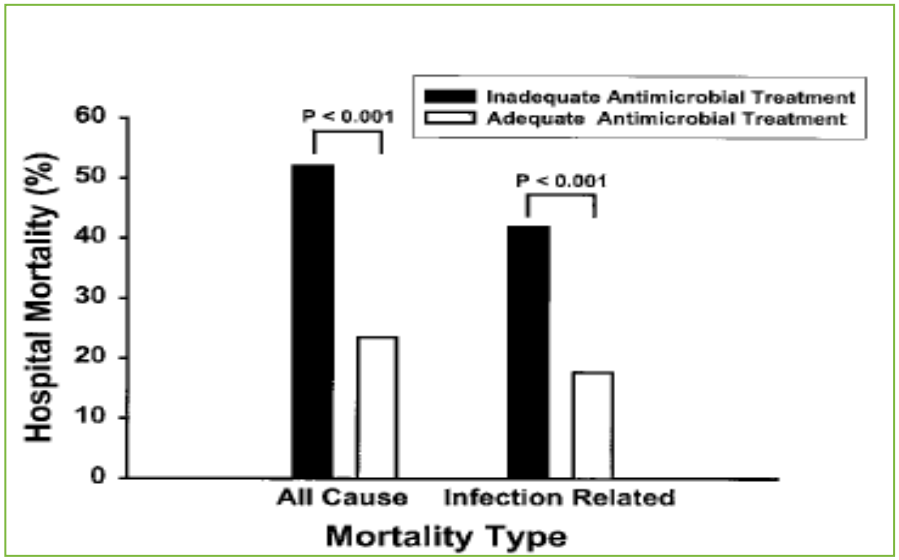
CHEST

Original Research

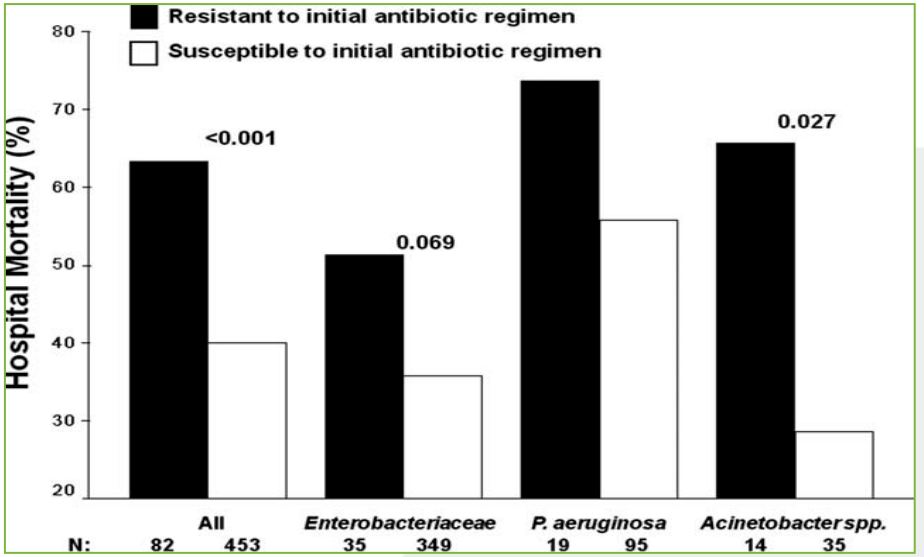
CRITICAL CARE MEDICINE

Initiation of Inappropriate Antimicrobial Therapy Results in a Fivefold Reduction of Survival in Human Septic Shock

*Anand Kumar, MD; Paul Ellis, MD; Yaseen Arabi, MD, FCCP; Dan Roberts, MD; Bruce Light, MD; Joseph E. Parrillo, MD, FCCP; Peter Dodek, MD; Gordon Wood, MD; Aseem Kumar, PhD; David Simon, MD; Cheryl Peters, RN; Muhammad Ahsan, MD; Dan Chateau, PhD; and the Cooperative Antimicrobial Therapy of Septic Shock Database Research Group**



Adapted from: Kollef *et al*.1999



Adapted from: Micek *et al*.2011

Kumar et al. Chest. 2009 Nov;136(5):1237-48
Kollef et al. Chest. 1999 Feb;115(2):462-74

Micek *et al*. J Hosp Med. 2011 Sep;6(7):405-10

Behind the statistics there are patients

EUROPEAN ANTIBIOTIC AWARENESS DAY

A European Health Initiative

European Antibiotic Awareness Day P
Lill-Karin (Norway)

My name is Lill-Karin; I am a
teacher, with three grown-
grandchildren. I have lived
and I spend my time readi
poems and travelling.

I have been to India seve
Kerala, so in 2010 I plan
with a local family.

Things went wrong very quickly. My host picked m
could see the city, his car collided with a lorry. I h
rushed to hospital lying on the floor of an ambul

After arriving at the hospital, I spent two days o
surrounded by sick people. I was given a bowl
broken leg meant I couldn't move to wash my
there in the heat.

Eventually, I was moved to a private room ar
India, your family is expected to look after y
doctors or nurses. It was a very lonely few
eventually I was allowed to come home.

Back in Norway, I had to go straight back
room and anyone who came to see me h

The doctors found that I had an antibiot
a urinary catheter that I had had fitted
symptoms of the infection, but it was a
so were scared to visit me, in case the
baptisms. Being alone

EUROPEAN ANTIBIOTIC AWARENESS DAY

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Paolo (Italy)

Paolo is a 55 year
Rome, Italy. In Au
motor-boating al
off the coast of I
felt that he had
infection, but d
at the time, be
could have be
summer heat

After a whil
with shakin
urinary tra
consulted
medical
in Ponza

take ciprofloxacin, a fluoroquinolone antibioti
used antibiotics for urinary tract infections. C
is easy to take and is usually effective in trea
condition did not improve over the next thr
Despite this, he continued the course of ci
hope of being well enough to motor-boat
examination and laboratory tests.

Paolo was on the island of Ponza where
of his urine to better understand which
was aware that it would be important
order for a doctor to prescribe the co

EUROPEAN ANTIBIOTIC AWARENESS DAY

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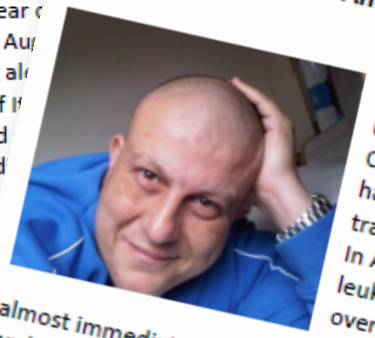
European Antibiotic Awareness Day Patient Stories
Mohammed (UK)



My name is Mohammed and I'm 37 years o
up in the UK but have spent the last 10 years
Cairo, running a software development comp
have a lot of family in Egypt so living out there
travelling back and forth to the UK has been gr
In April 2011, I was diagnosed with acute myelo
leukaemia, a type of cancer where your body
overproduces white blood cells and your immun
system stops working properly. I started treatme
almost immediately. Leukaemia itself isn't that painful – you mostly just feel un
and rundown – but the fact that your immune system isn't functioning properly
means that you are more likely to pick up infections. These can be both
uncomfortable and extremely dangerous.

While I was in hospital having my second cycle of chemotherapy, I developed a high
fever which the doctors struggled to control with regular antibiotics. For three days
my temperature spiked uncontrollably, reaching dangerous levels as high as 40°C.
Having realised there was something unusual about my infection, the doctors
eventually managed to bring the fever under control using a specific combination of
high-dose antibiotics. At that point the unknown nature of the infection was really
scary; we were dealing with the leukaemia but no-one knew what had caused the
fevers.

Further investigations showed that I had an infection with a bacterium called
Escherichia coli (E. coli), which normally lives in the intestine. For reasons unkn
to my doctors, I was carrying a very resistant type of *E. coli*. No
where I got this very resistant type of bug from, or h
in my intestine. The doctors thought
similar resistance types
chemother

Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance

A.-P. Magiorakos[1], A. Srinivasan[2], R. B. Carey[2], Y. Carmeli[3], M. E. Falagas[4,5], C. G. Giske[6], S. Harbarth[7], J. F. Hindler[8], G. Kahlmeter[9], B. Olsson-Liljequist[10], D. L. Paterson[11], L. B. Rice[12], J. Stelling[13], M. J. Struelens[1], A. Vatopoulos[14], J. T. Weber[2] and D. L. Monnet[1]

Bacterium	MDR	XDR	PDR
Staphylococcus aureus	The isolate is non-susceptible to at least 1 agent in ≥ 3 antimicrobial categories listed in Table 1a*	The isolate is non-susceptible to at least 1 agent in all but 2 or fewer antimicrobial categories in Table 1a.	Non-susceptibility to all agents in all antimicrobial categories for each bacterium in Tables 1a-1e
***Enterococcus* spp.**	The isolate is non-susceptible to at least 1 agent in ≥ 3 antimicrobial categories listed in Table 1b	The isolate is non-susceptible to at least 1 agent in all but 2 or fewer antimicrobial categories in Table 1b.	
Enterobacteriaceae	The isolate is non-susceptible to at least 1 agent in ≥ 3 antimicrobial categories listed in Table 1c	The isolate is non-susceptible to at least 1 agent in all but 2 or fewer antimicrobial categories in Table 1c.	
Pseudomonas aeruginosa	The isolate is non-susceptible to at least 1 agent in ≥ 3 antimicrobial categories listed in Table 1d	The isolate is non-susceptible to at least 1 agent in all but 2 or fewer antimicrobial categories in Table 1d.	
***Acinetobacter* spp.**	The isolate is non-susceptible to at least 1 agent in ≥ 3 antimicrobial categories listed in Table 1e	The isolate is non-susceptible to at least 1 agent in all but 2 or fewer antimicrobial categories in Table 1e.	

Carbapenemases: main types of enzymes

Acronym	Name or type	First isolated
KPC	*Klebsiella pneumoniae* carbapenemase	1996
VIM	Verona integron-encoded metallo-beta-lactamase	1997
OXA-48	OXA-type carbapenemase	2001
NDM-1	New Delhi metallo-beta-lactamase	2008

- Mobile genetic elements- propensity to spread

Limited treatment options

- Resistant to all beta-lactams, carbapenems
- Aminoglycosides, fluoroquinolones
- Tigecycline, colistin
- Fosfomycin

Mortality rates of infections with carbapenem resistant *Enterobacteriaceae*

Patel et al. 2008 **Outcomes of patients with carbapenem-resistant *K. pneumoniae* BSI**	**Risk factor for mortality in invasive infections with *K. pneumoniae*** **OR=4.69 (95% CI 1.9-11.58), P=0.001**
Marchaim et al. 2008 **Infection with imipenem-resistant *Enterobacter* spp.**	**↑ in-hospital mortality** **OR=8.3 (95% CI, 1.07-64), P=0.043**
Gasink *et al.* 2009 **KPC-producing *K. pneumoniae* infections**	**↑ in-hospital mortality** **AOR, 3.60 (95% CI, 1.87–6.91)**
Borer *et al.* 2009 **Outcomes of patients with *K. pneumoniae* BSI vs non BSI**	**Mortality risk ratio 3.3 (95% CI, 2.9–28.5)**
Ben-David *et al.* 2011 **Outcomes of patients with BSI with carbapenem resistant *K. pneumoniae* BSI vs ESBL vs sensitive**	**• ↑infection- related mortality CRKP** **• Differences in appropriate empirical antimicrobial therapy (79%, 39%, 12%; P <0.001)**

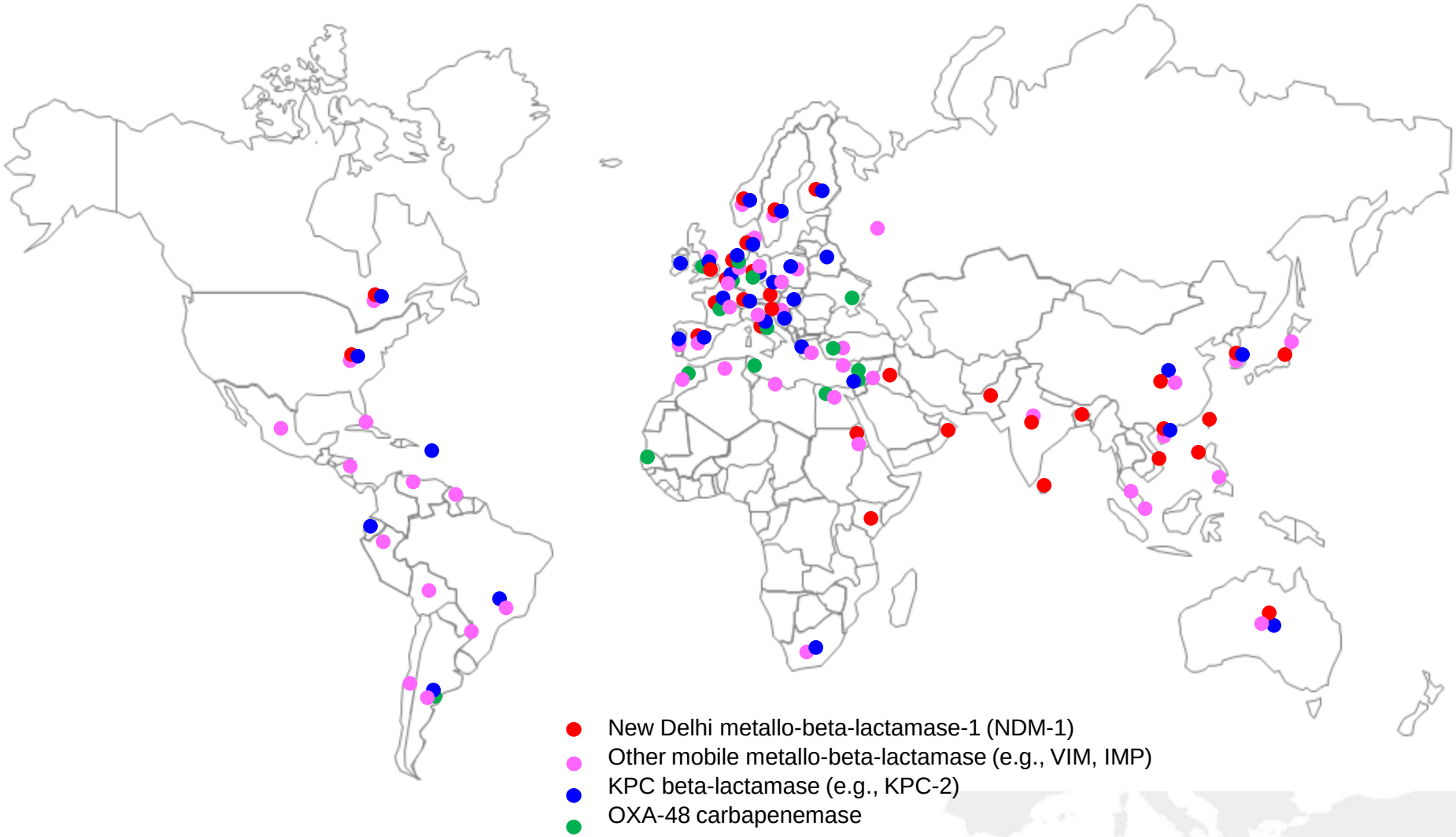
Patel et al. Infect Control Hosp Epidemiol. 2008 Dec;29(12):1099-106
Borer et al. Infect Control Hosp Epidemiol. 2009 Oct;30(10):972-6
Ben-David *et al.* Clin Microbiol Infect. 2011 Feb 1
Marchaim et al. AAC.2008 Apr;52(4):1413-8.
Gasink et al. ICHE. 2009; 30(12): 1180–1185.
Schwaber et al. AAC. 2008 April; 52(4): 1413–1418

Worldwide geographic distribution of *Klebsiella pneumoniae carbapenemase (KPC) producers.*

France (Naas et al. 2005)	KPC-2
Colombia (Villegas et al. 2006)	KPC-2
Israel (Leavitt et al. 2007)	KPC-2, KPC-3
Greece (Tsakris *et al.* 2008)	KPC-2
United Kingdom (Woodford *et al.* 2008)	KPC-3
Ireland (Roche *et al.* 2009)	KPC-2

Adapted from: Nordmann *et al.* Emerg Infect Dis. 2011 Oct;17(10):1791-8

Worldwide emergence and spread of carbapenemases (as of March 2011)



Adapted and updated from: Walsh T. Int J Antimicrob Agents 2010;36(Suppl 3): S8-S14.

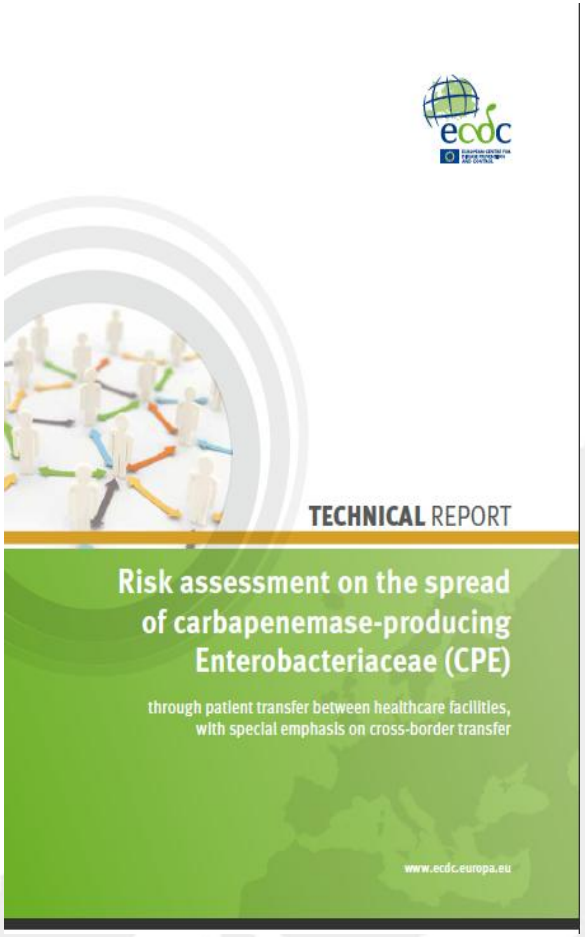
ECDC Risk Assessment on Carbapenemases

Focus:

- *Enterobacteriaceae*
- All carbapenemases
- Healthcare settings, including patient inter-facility and cross-border transfer

Two systematic reviews of the literature

1. Which are the **risk factors** for patient colonization or infection with carbapenemase-producing *Enterobacteriaceae*?
2. What is the effectiveness of using screening and/or targeted or other infection control interventions in decreasing the incidence of healthcare-facility - acquired colonization or infection with carbapenemase-producing *Enterobacteriaceae*?



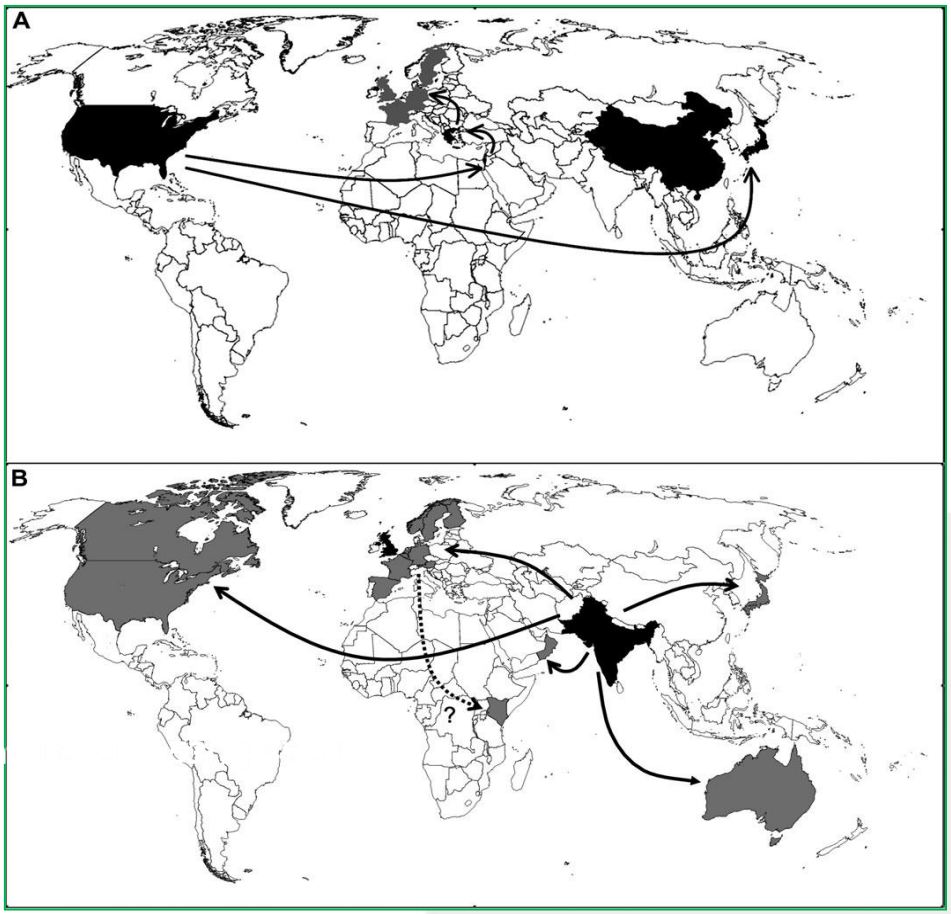
ECDC Technical Report, September 13 2011;
http://ecdc.europa.eu/en/publications/Publications/110913_Risk_assessment_resistant_CPE.pdf

ECDC Risk Assessment on CPE
Patient mobility and transfer

Cross-border transfer of patients

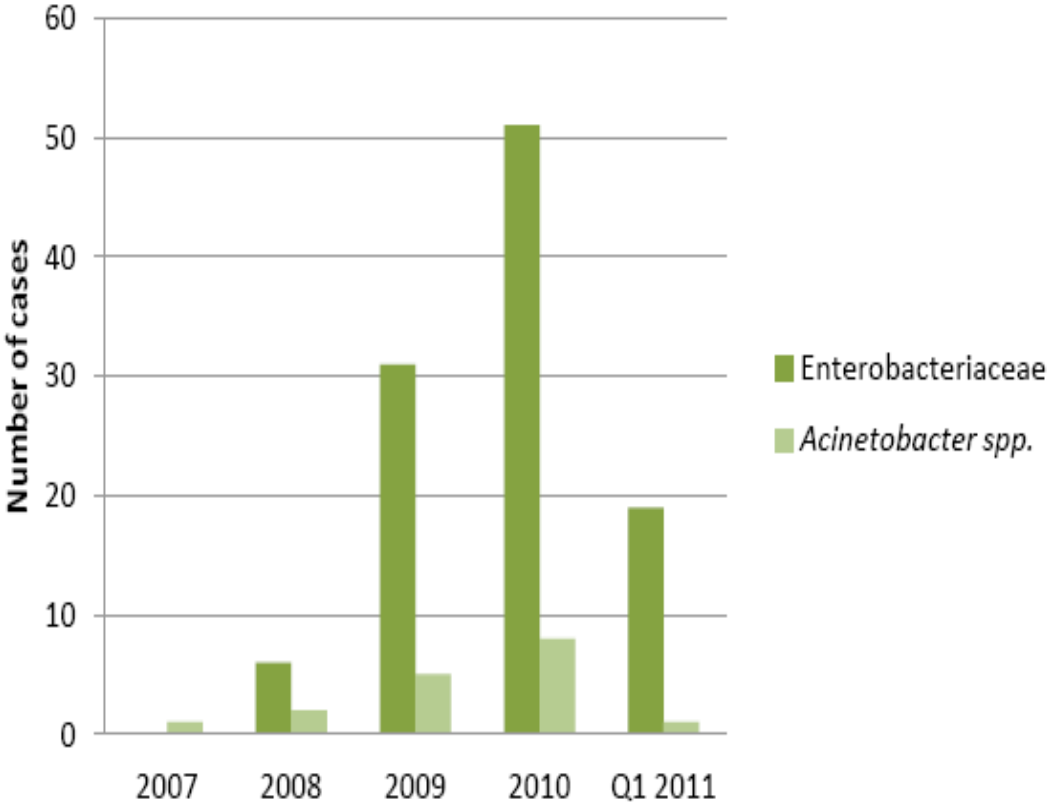
Strong evidence that it is associated with risk for transmission when:

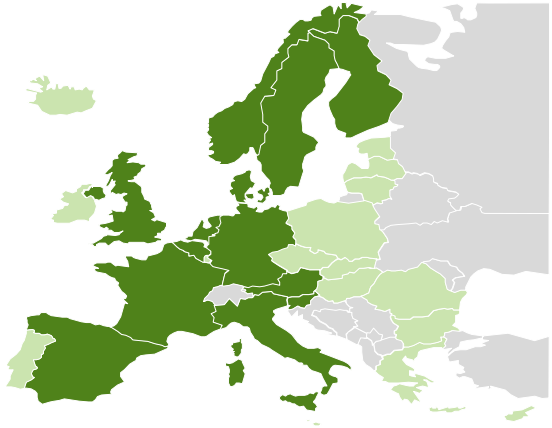
- Patients are transferred from countries with high rates of CPE to healthcare facilities in other countries
- Patients had received medical care abroad in areas with high rates of CPE



Adapted from Rogers *et al*. 2011

Trends in the number of cases annually of New Delhi metallo-β-lactamase (NDM)-producing *Enterobacteriaceae* and *Acinetobacter* spp. in EU/EEA countries, 2007-Q1 2011



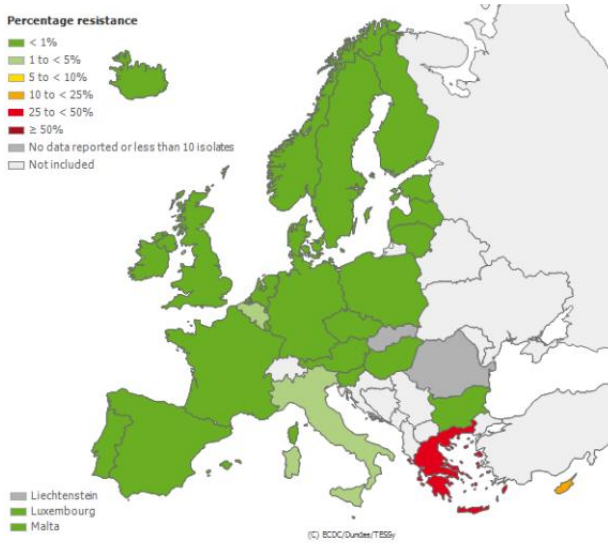


Only Germany and UK reported data on NDM-producing *Acinetobacter* spp.

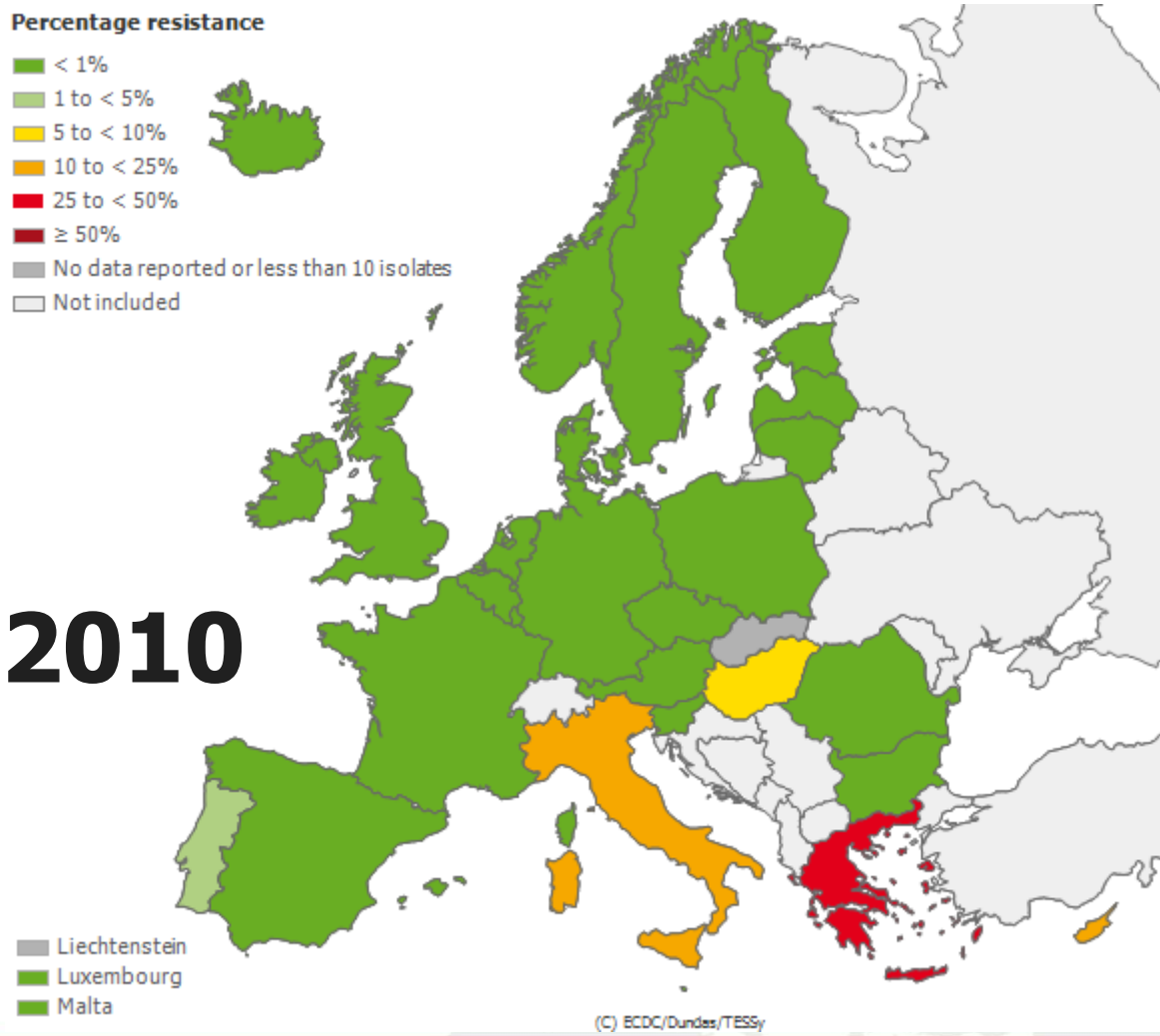
- **106 cases in 13 countries**
- **Among 55 travel history available**
- **31 cases received healthcare or travelled to India or Pakistan**
- **5 cases had received healthcare in the Balkans**
- **13 cases of presumed secondary transmission in Europe**

Source: European Centre for Disease Prevention and Control. Updated risk assessment on the spread of NDM and its variants within Europe. Stockholm: ECDC; 2011

Klebsiella pneumoniae: proportion of invasive isolates resistant to carbapenems; EU/EEA, 2009–2010



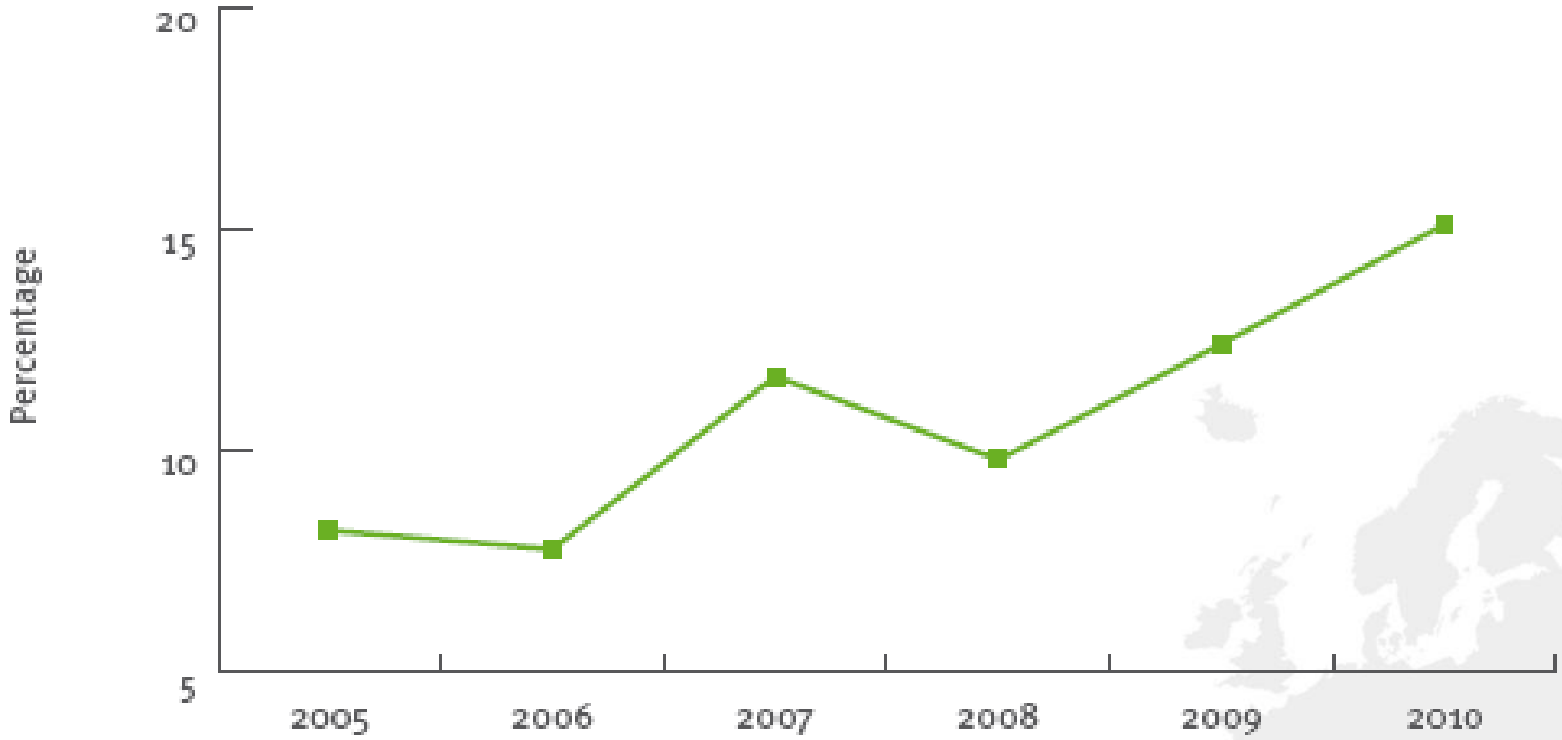
2009



2010

Source: ECDC, Antimicrobial resistance surveillance in Europe 2010. Annual Report. EARS-Net. ECDC, 2011

Klebsiella pneumoniae: percentage carbapenem-resistant invasive isolates reported to EARSS/EARS-Net by year, 2005–2010



Only laboratories that continuously reported susceptibility results for carbapenems during the period 2005–2010 are included in the analysis.

Source: ECDC, Antimicrobial resistance surveillance in Europe 2010. Annual Report. EARS-Net. ECDC, 2011

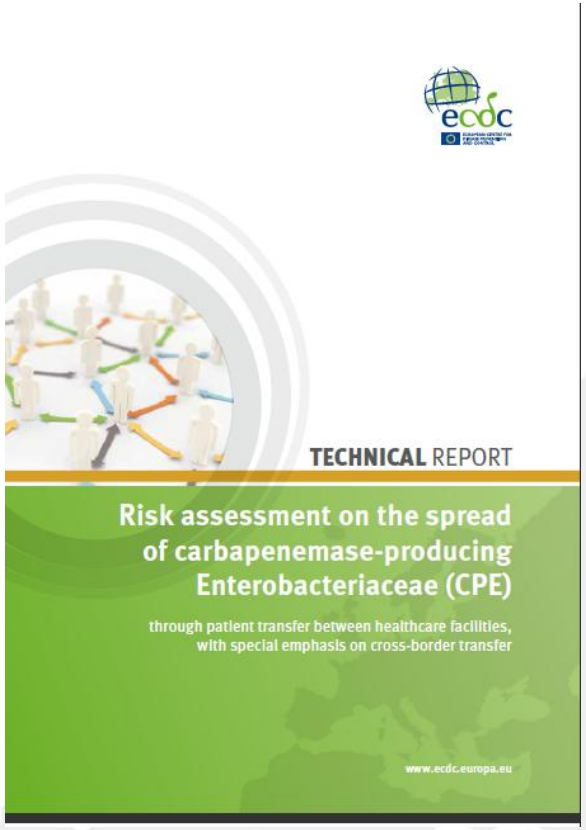
Risk assessment on the spread of carbapenemase-producing *Enterobacteriaceae*

Infection control during outbreaks

- Active surveillance by rectal screening
- Cohort nursing for carrier patients
- Additional contact precautions for carrier patients

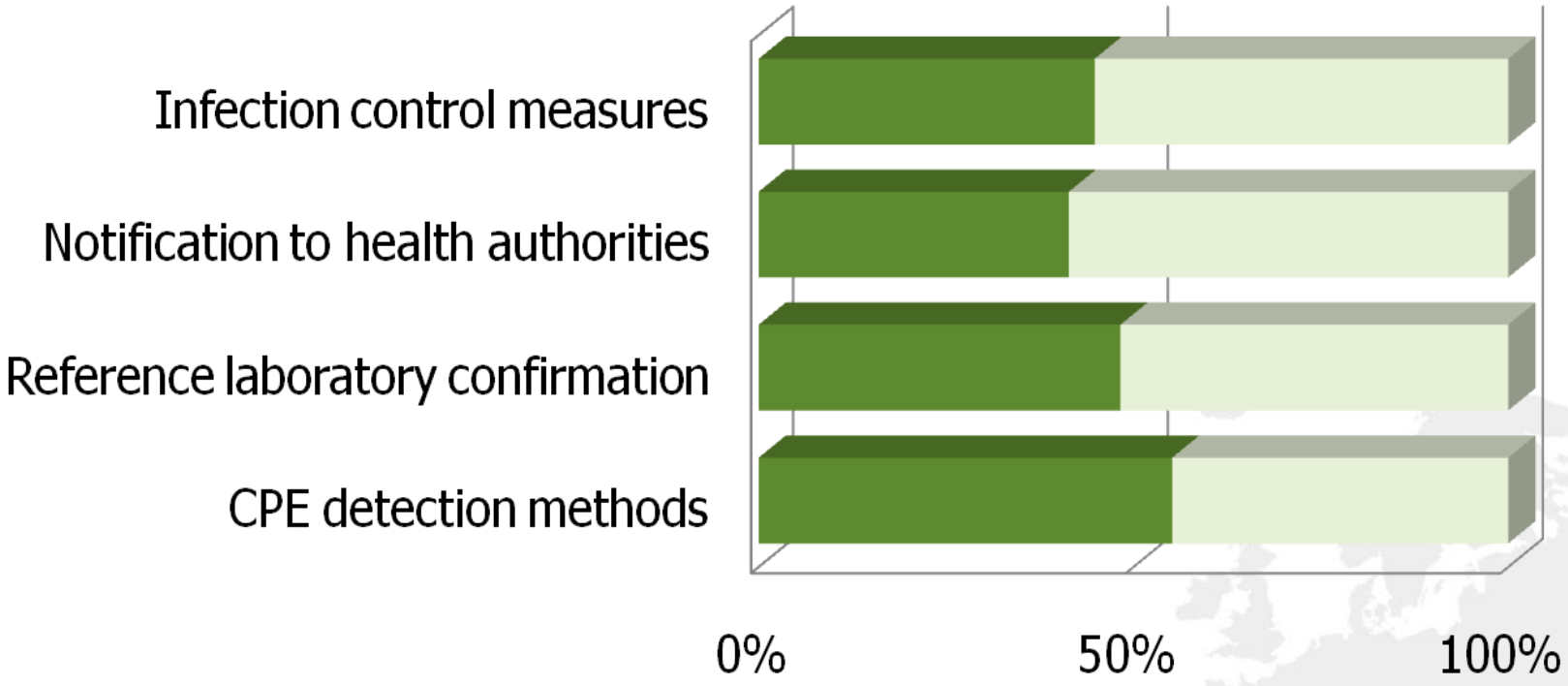
Additionally

- Prudent use of antibiotics
- Control of ESBL
- Notification of public health authorities
- Surveillance



Source: ECDC, Risk assessment on the spread of carbapenemase-producing *Enterobacteriaceae* (CPE) Technical Report. 13 September 2011

National guidance for detection and control of carbapenemase-producing *Enterobacteriaceae* in Europe (as of June 2011)



% countries with national guidance on

Source:European Centre for Disease Prevention and Control. Updated risk assessment on the spread of NDM and its variants within Europe. Stockholm: ECDC; 2011. Update from Struelens M, et al. Eurosurveillance 2010;15(46). pii: 19716.

How to contain inter-facility spread of CPE

Enhanced detection, surveillance & preparedness at national and EU level

Epidemic intelligence at European level

- Sharing of information between public health authorities, European Commission and ECDC:
  - Early warning and response system (EWRS): authorities
  - Information exchange systems (EPIS): experts
  - Epidemiological bulletins (*Eurosurveillance*): public

Why and how to turn the tide?

- National guidance documents
- Need for vigilance and active screening high risk patients
- Culture data communicated to healthcare facilities when transferring patients
- Rapid notification of clinicians and public health authorities
- Strict hand hygiene and infection control measures
- Antibiotic stewardship-prudent use of antimicrobials
- Standardisation of antimicrobial resistance breakpoints and MDR/XDR/PDR definitions
- Need for further research on molecular epidemiology and reservoirs of CPE

Thank you