ECDC EVIDENCE BRIEF

November 2015

Update on the spread of carbapenemase-producing *Enterobacteriaceae* in Europe

Summary of the May 2015 expert assessment

The EuSCAPE project

This ECDC Evidence Brief identifies urgent priorities for action to combat the occurrence and spread of carbapenemase-producing *Enterobacteriaceae* (CPE) in Europe. It draws on country data reported by 38 European countries to ECDC following the completion of the 'European Survey on Carbapenemase-Producing *Enterobacteriaceae*' (EuSCAPE) project. The EuSCAPE project aimed to improve understanding of the occurrence and spread of CPE and build laboratory capacity for their diagnosis and surveillance.
In 2013, ECDC published the results of a pre-EuSCAPE self-assessment by national experts on the spread of CPE and the national capacity for containment of CPE in terms of surveillance, laboratory capacity, reference services and infection control measures [1,2]. Following this self-assessment, EuSCAPE supported a laboratory capacity building workshop, an external quality assessment and the collection and characterisation of CPE isolates in European hospitals. In 2015, a post-EuSCAPE self-assessment [3] was conducted to re-assess the spread of CPE in European countries, as well as improvements in the capacity for containment of CPE in these countries since 2013.

Why focus on carbapenemase-producing *Enterobacteriaceae?*

The global rise of carbapenemase-producing *Enterobacteriaceae* (CPE) is alarming and represents an increasing threat to healthcare delivery and patient safety. It also results in higher healthcare costs, prolonged hospital stays, treatment failures and sometimes death.

Carbapenems are a major last-line class of antibiotics to treat infections with multidrug-resistant gram-negative bacteria, including *Enterobacteriaceae* such as *Klebsiella pneumoniae*. But CPE are resistant to carbapenems due to the production of an enzyme – a carbapenemase.

There are only few remaining treatment options for patients infected with CPE. These are limited to combination therapy and to older antibiotics such as polymyxins (e.g. colistin). Countries with already high percentages of carbapenem resistance due to the spread of CPE also report increasing numbers of isolates with polymyxin resistance [4], indicating a further loss of effective antibiotic treatment for these infections.

Specific infection control measures, combined with prudent use of antibiotics, are key to controlling the spread of CPE in European hospitals. Failing this, Europe may rapidly face hospital outbreaks of extensively drug-resistant (XDR), or even pandrug-resistant (PDR), *Enterobacteriaceae*.

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What is the situation in Europe?

In 2015, four countries reported an endemic situation for CPE, and nine countries reported interregional spread of CPE.

The occurrence and spread of CPE in Europe has continued to worsen over the last two years. Thirteen (34%) countries reported interregional spread[i] of or an endemic situation[ii] for CPE in 2015, compared to six (15%) countries in 2013 (Figures 1 and 2).

Figure 1. Occurrence of CPE using an epidemiological scale of nationwide spread in 38 European countries, 2013 (top) and 2015 (bottom)

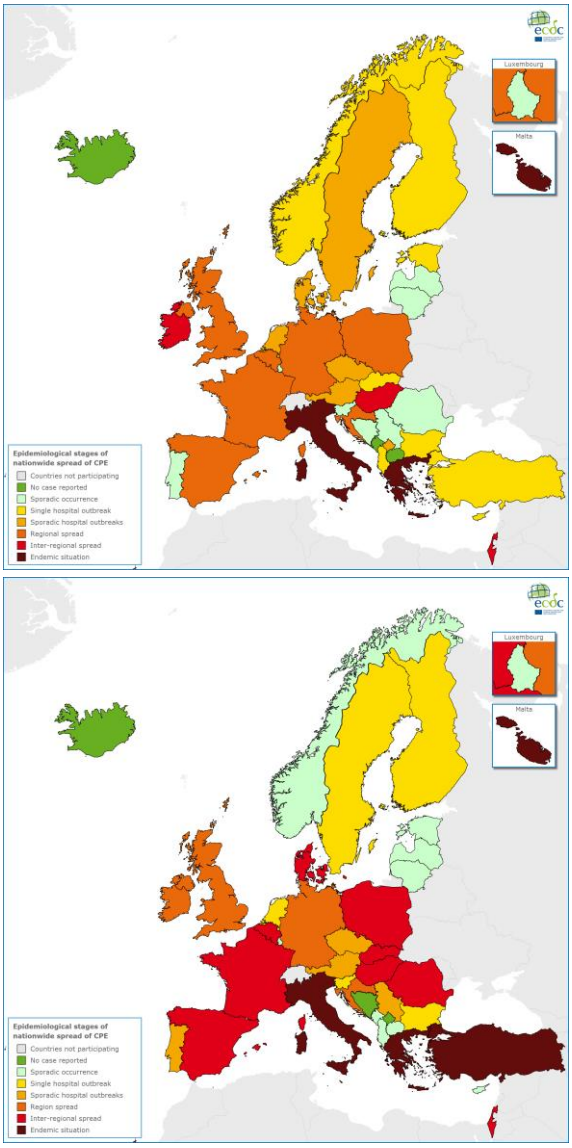
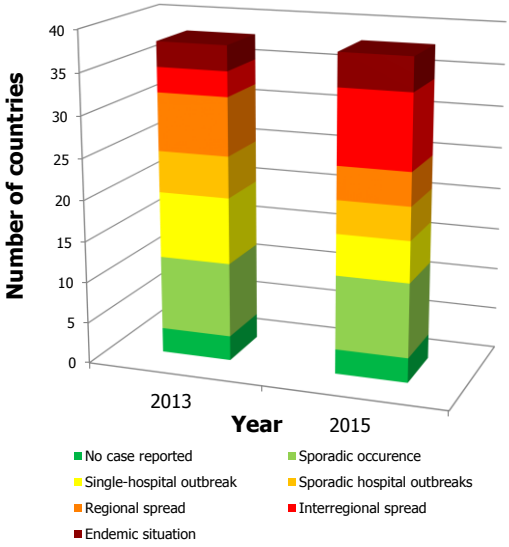


Figure 2. Change in epidemiological level for CPE between 2013 and 2015



[i] Interregional spread whereby multiple epidemiologically-related hospital outbreaks are reported from different regions or health districts, suggesting interregional autochthonous interinstitutional transmission

[ii] Endemic situation whereby most hospitals in a country are repeatedly seeing cases admitted from autochthonous sources

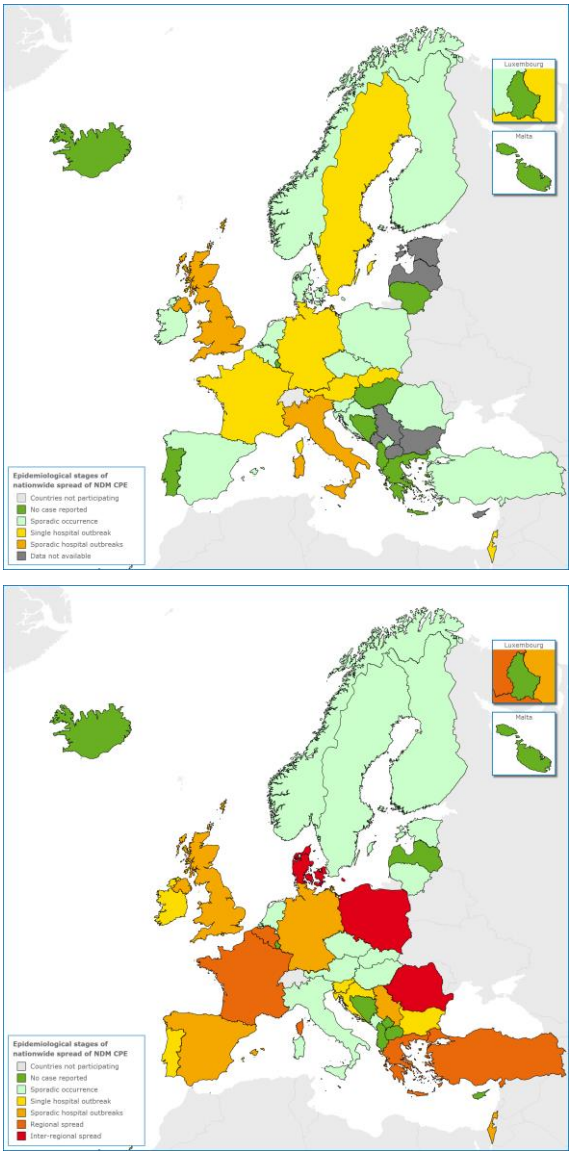
In 2013, only two countries reported sporadic hospital outbreaks of NDM CPE[iii].

In 2015, five countries reported sporadic hospital outbreaks of NDM CPE, and seven countries reported regional and interregional spread of NDM CPE.

NDM CPE is rapidly spreading in European hospitals. Since the first case was published in 2009, the number of NDM CPE cases reported by most European countries has remained relatively low compared with other CPEs. In 2013, only Italy and the United Kingdom reported sporadic hospital outbreaks[iv].

The situation dramatically changed in 2015, with five countries reporting sporadic hospital outbreaks and seven countries reporting regional[v] and interregional spread.

Figure 3. Comparison of nationwide spread of NDM CPE, 2013 (top) and 2015 (bottom)



[iii] NDM CPE: New Delhi metallo-beta-lactamase-producing CPE

[iv] Sporadic hospital outbreaks with more than one hospital outbreak reported, but all outbreaks are epidemiologically unrelated or caused by different clones (no autochthonous interinstitutional transmission)

[v] Regional spread with more than one epidemiologically-related hospital outbreak reported, but confined to hospitals of the same region or health district, suggesting regional autochthonous interinstitutional transmission

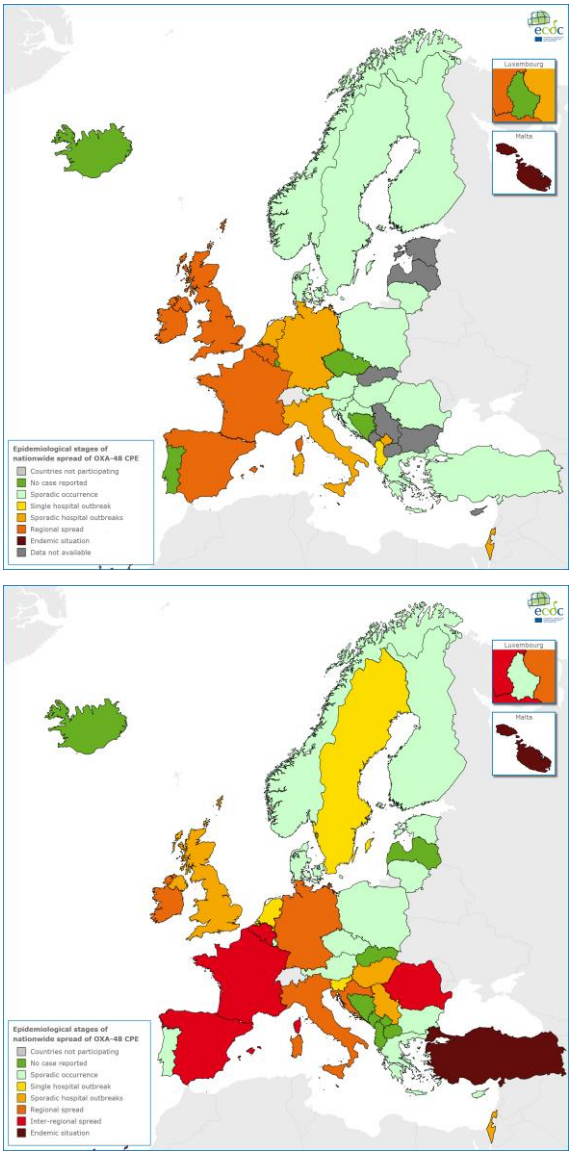
In 2013, only one country reported an endemic situation, and no country reported interregional spread of OXA-48 CPE[vi].

In 2015, two countries reported an endemic situation, and four countries reported interregional spread of OXA-48 CPE.

OXA-48 CPE also continue to spread rapidly in European hospitals. Since the first reported case in Turkey in 2003, OXA-48 CPE have spread worldwide and are now commonly found in Europe.

In 2013, only one European country had reported an endemic situation of OXA-48 CPE, while in 2015, two countries reported an endemic situation and four countries reported interregional spread.

Figure 4. Comparison of nationwide spread of OXA-48 CPE, 2013 (top) and 2015 (bottom)



[vi] OXA-48 CPE: Carbapenem-hydrolysing oxacillinase-48-producing CPE

What are the main challenges?

Four countries do not have a national reference/expert laboratory for CPE.

Seven countries do not have a national surveillance system dedicated to CPE.

Ten countries replied that there is no system for notification of CPE cases to health authorities.

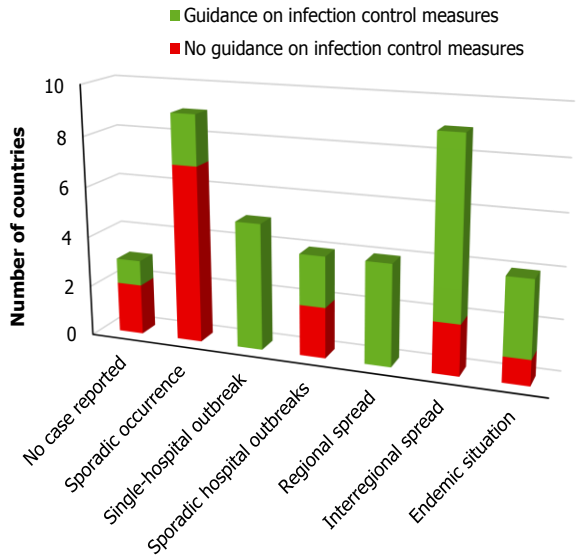
Fourteen countries do not have national guidelines for prevention and control of CPE.

Twenty-seven countries do not have a national plan for containment of CPE.

The cornerstones for effective prevention and control of CPE are the establishment of a dedicated national surveillance system, based on the notification of cases to health authorities, supported by reference laboratory confirmation and identification as well as infection control measures.

Over the last two years, many European countries have developed a dedicated national surveillance system, designated a reference laboratory, and implemented mandatory laboratory participation in surveillance or mandatory reporting of all CPE cases in an attempt to control the increasing spread of CPE. However, not all European countries have put these measures in place. In particular, many countries still do not have guidance on infection control measures to prevent the spread of CPE.

Figure 5. Presence or absence of national recommendations or guidelines on infection control measures to prevent the spread of CPE, May 2015



What can be done?

Options for policymakers to support the prevention and control of the spread of carbapenemase-producing *Enterobacteriaceae,* based on the EuSCAPE Project

- Establish a national plan for containment of (or preparedness to contain) CPE.
- Establish a dedicated surveillance system for CPE.
- Support the establishment of a reference laboratory for antimicrobial resistance, including CPE.
- Implement mandatory reporting of CPE by clinical microbiology laboratories to the reference laboratory.
- Implement notification of CPE cases to health authorities.
- Implement national guidelines for prevention and control of CPE.

Measures to prevent and control outbreaks of carbapenemase-producing *Enterobacteriaceae* in hospitals and other healthcare settings

The following measures were identified in an ECDC systematic review and an ECDC risk assessment [5,6]. There is only evidence that these measures are effective when they are applied together as a bundle of measures.

Active surveillance

- Identify patients at high risk for CPE, including those transferred across borders.
- Rectal screening for CPE on admission for high-risk patients
- Consider pre-emptive isolation of patients at high risk for CPE (see below).
- Additional active surveillance by rectal screening for CPE during outbreaks
- Fast diagnostic turnaround time and timely communication of the results of rectal screening by the laboratory to the ward and the infection control team
- Case notification/flagging and contact tracing.

Isolation and contact precautions

- Patient isolation and contact precautions (gloves and gowns) for all CPE-positive patients
- Cohort nursing by separate dedicated staff and equipment for all CPE-positive patients
- Consider geographic cohorting of all CPE-positive patients.
- Monitoring of compliance with the above measures.

Hygiene precautions

- Enforced hand hygiene
- Environmental cleaning.

Education of staff

- Education about the above measures

Prudent use of antibiotics

- Prudent use of antibiotics, including restriction of certain antibiotics/antibiotic groups such as carbapenems.

More information, including on national guidelines, can be found online [7].

References

1 Glasner C, Albiger B, Buist G, Tambic Andrasevic A, Canton R, Carmeli Y, et al. Carbapenemase-producing Enterobacteriaceae in Europe: a survey among national experts from 39 countries, February 2013. Euro Surveill. 2013;18(28). pii: 20525.

2 European Centre for Disease Prevention and Control. Carbapenemase-producing bacteria in Europe: interim results from the European Survey on carbapenemase-producing Enterobacteriaceae (EuSCAPE) project. Stockholm: ECDC; 2013.

3 Albiger B, et al. 2015. In press.

4 European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2014. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm: ECDC; 2015. In press.

5 European Centre for Disease Prevention and Control. Systematic review of the effectiveness of infection control measures to prevent the transmission of carbapenemase-producing Enterobacteriaceae through cross-border transfer of patients. Stockholm: ECDC; 2014

6 European Centre for Disease Prevention and Control. Risk assessment on the spread of carbapenemase-producing Enterobacteriaceae (CPE) through patient transfer between healthcare facilities, with special emphasis on cross-border transfer. Stockholm: ECDC; 2011

7 ECDC directory of guidance on prevention and control of carbapenem-resistant *Enterobacteriaceae,* available from:
http://ecdc.europa.eu/en/healthtopics/Healthcare-associated_infections/guidance-infection-prevention-control/Pages/guidance-prevention-control-infections-CRE.aspx