

Round Table on emerging problems

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smart weapons
against smart microorganisms

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The Roadmap

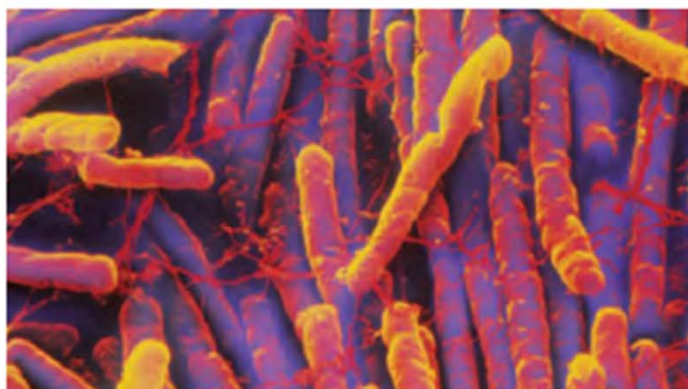
- **Why C diff in a session on AMR**
- **Epidemiological relevance in Europe and Italy**
- **Underdiagnosis: where are we?**
- **CA CDI**
- **What can we do? The UK experience**
- **Some highlights on prevention and control**



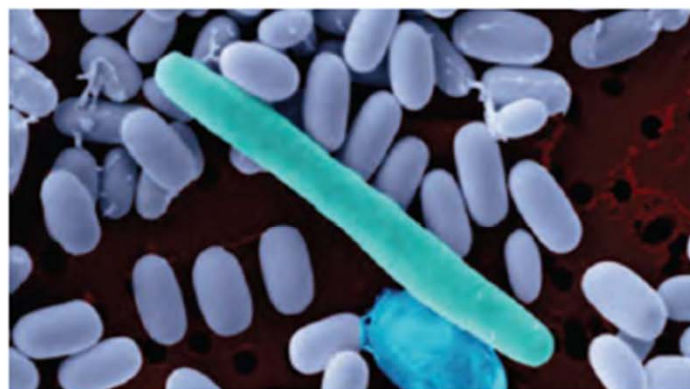
Introduction to *C. difficile*

- *C. difficile* is a Gram-positive, spore-forming, anaerobic bacillus that was first identified in 1935¹
- *C. difficile* is the leading cause of infective nosocomial diarrhoea in industrialised countries²
- *C. difficile* passes through a life cycle where it exists in two forms; as vegetative cells and as spores³

Vegetative form



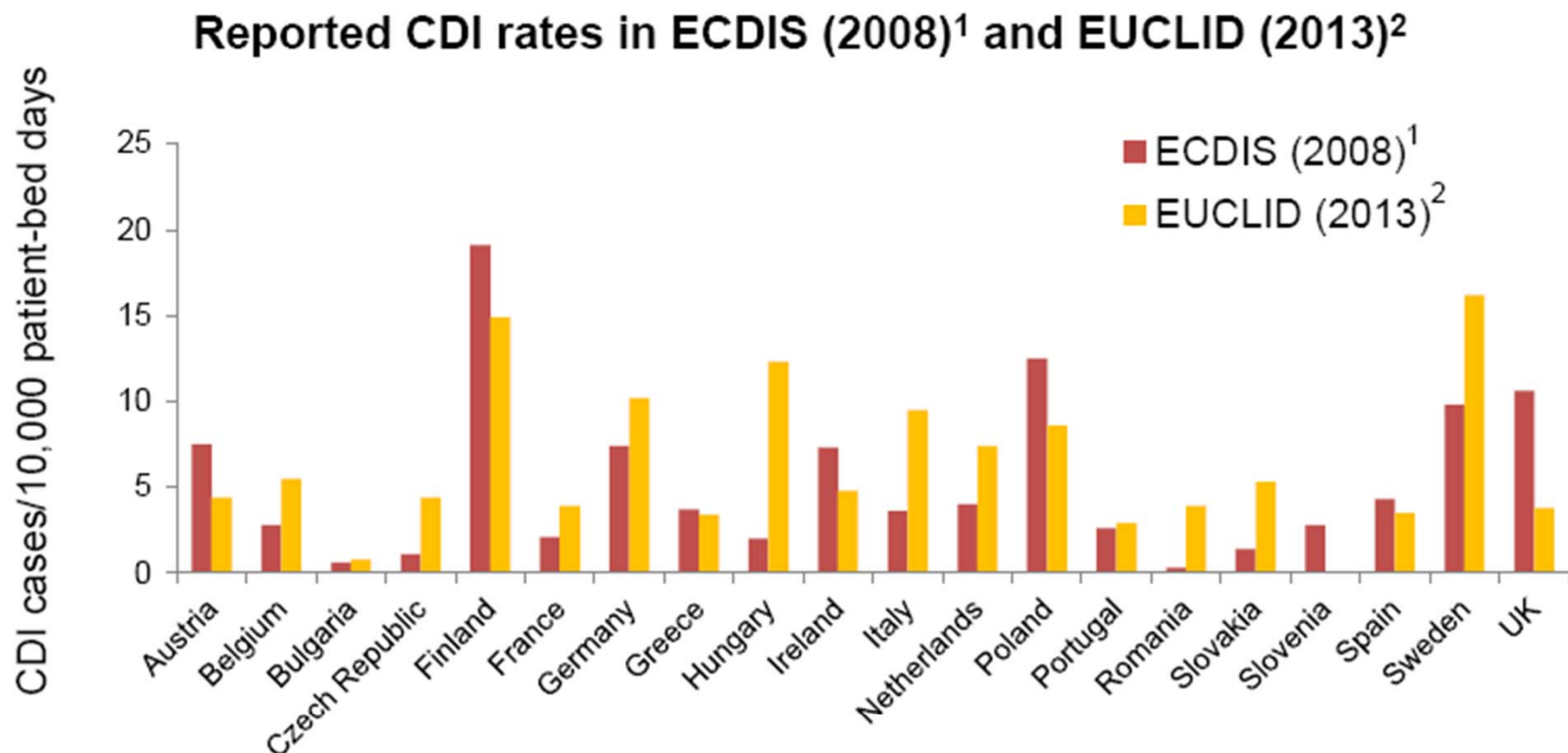
Spores surrounding a vegetative cell



1. Hall IC, O'Toole E. Am J Dis Child 1935;49:390–402;
2. Crobach MJT, et al. Clin Microbiol Infect 2009;15:1053–66;
3. Poutanen S, Simor AE. CMAJ 2004;171:51–8.

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Comparison of reported CDI rates between two large European studies



- Mean of 6.6 cases/10,000 patient-bed days in EUCLID (482 hospitals)² compared with mean of 4.1 cases/10,000 patient-bed days reported by ECDIS (87 hospitals)¹

ECDIS, European *C. difficile* infection surveillance network; EUCLID, European, multi-centre, prospective, bi-annual point-prevalence study of *C. difficile* infection in hospitalised patients with diarrhoea

1. Bauer MP, et al. Lancet 2011;377:63–73;

2. Davies KA, et al. Poster presented at ECCMID 2013; LB2968.

Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals 2011–2012



- **In 2011–2012, 29 EU/EEA Member States and Croatia participated in the first EU-wide, ECDC-coordinated point prevalence survey (PPS) of healthcare-associated infections (HAIs) and antimicrobial use in acute care hospitals.**
- **231 459 patients from 947 hospitals were included in the final European sample for analysis.**

- The prevalence of patients with at least one HAI in acute care hospitals in the PPS sample was 6.0% (country range 2.3%–10.8%).

- Of a total of 15 000 reported HAIs, the most frequently reported HAI types were
 - respiratory tract infections (pneumonia 19.4% and lower respiratory tract 4.1%),
 - surgical site infections (19.6%),
 - urinary tract infections (19.0%),
 - bloodstream infections (10.7%) and
 - gastro-intestinal infections (7.7%), with Clostridium difficile infections accounting for 48% of the latter.**

Figure 3. *Clostridium difficile* infections and other gastro-intestinal infections (excluding hepatitis) as a percentage of all HAIs, by country, ECDC PPS 2011–2012

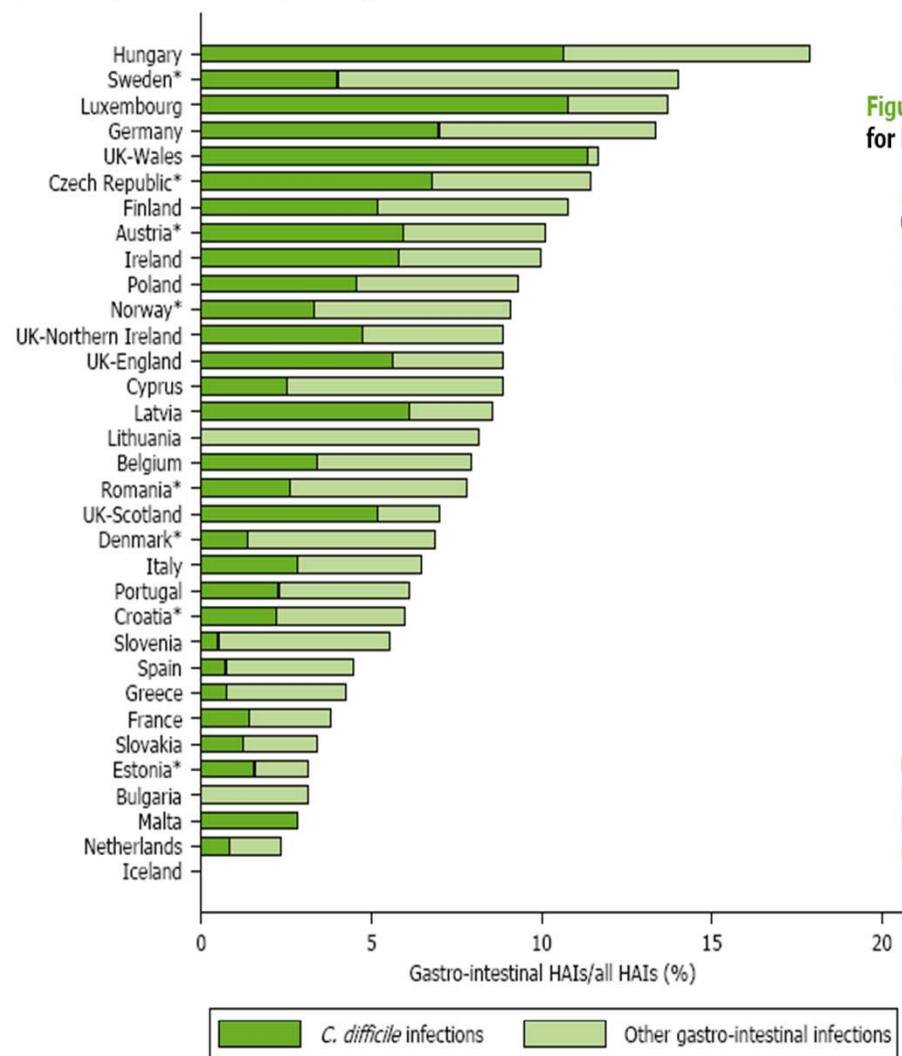
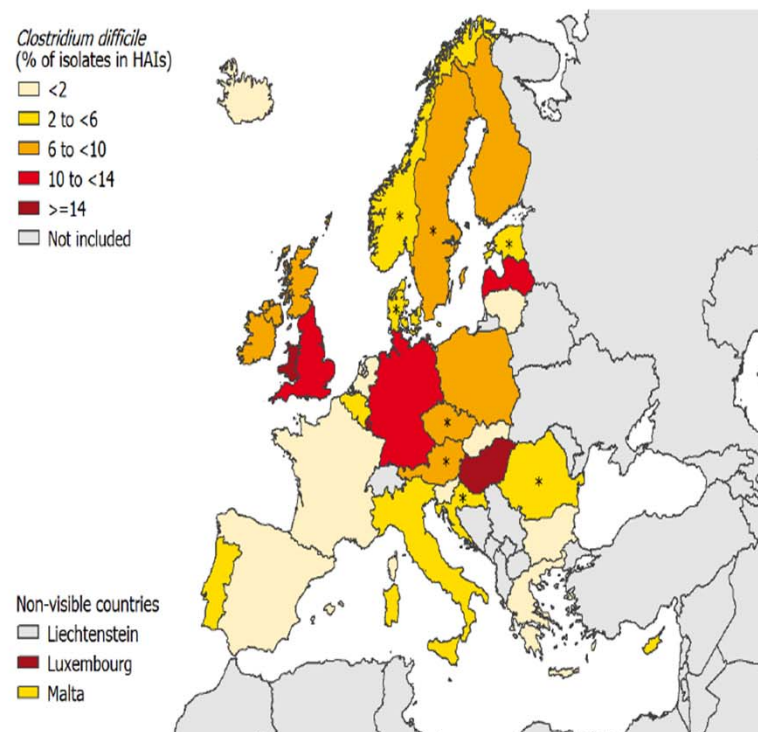


Figure 42. Relative frequency of *Clostridium difficile* as a percentage of all microorganisms reported for HAIs, by country (n=548 isolates), ECDC PPS 2011–2012



Effect of antibiotics on normal colonic microflora

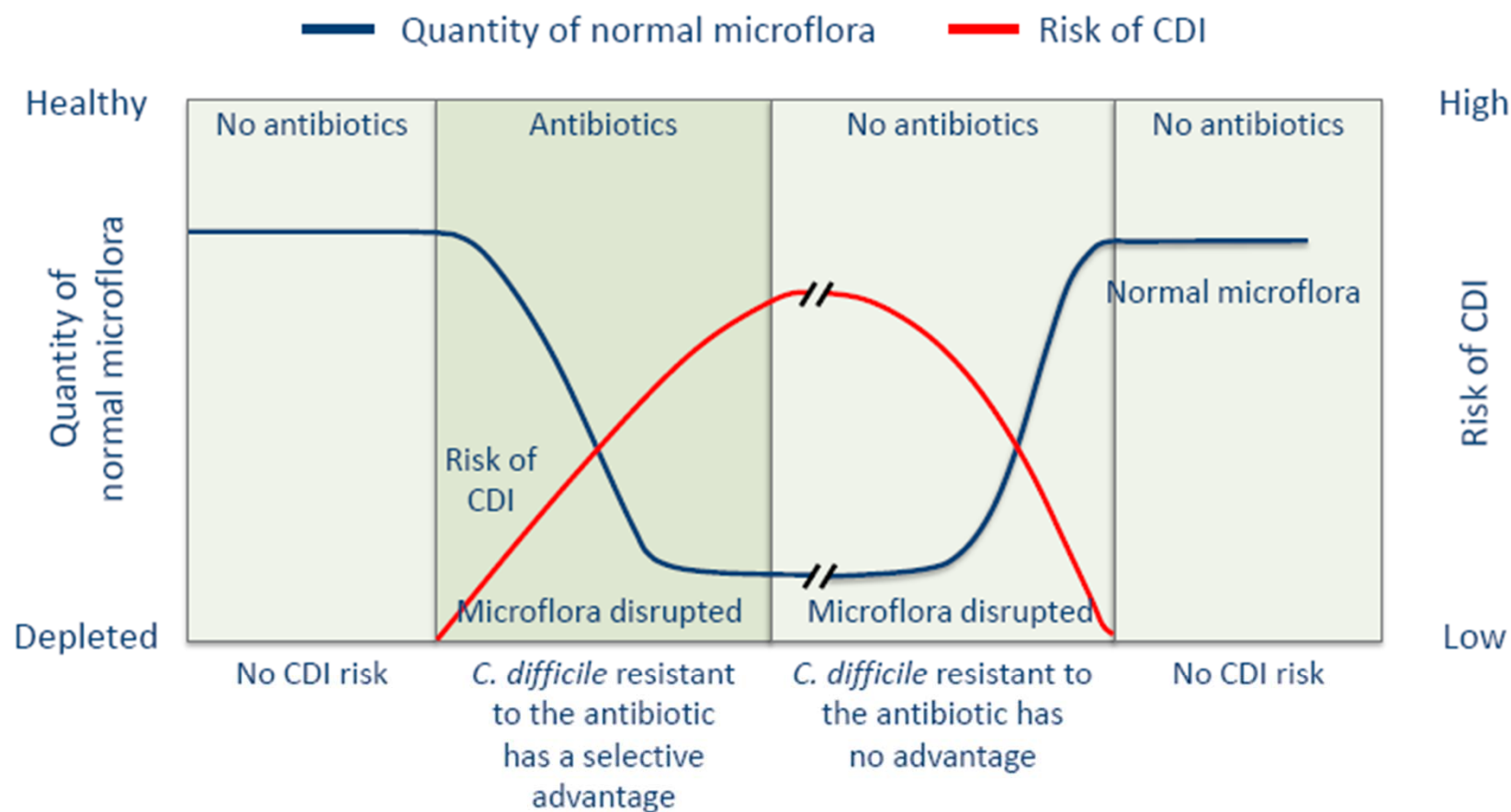


Figure 55. Indications for antimicrobial use in European acute care hospitals, ECDC PPS 2011-2012

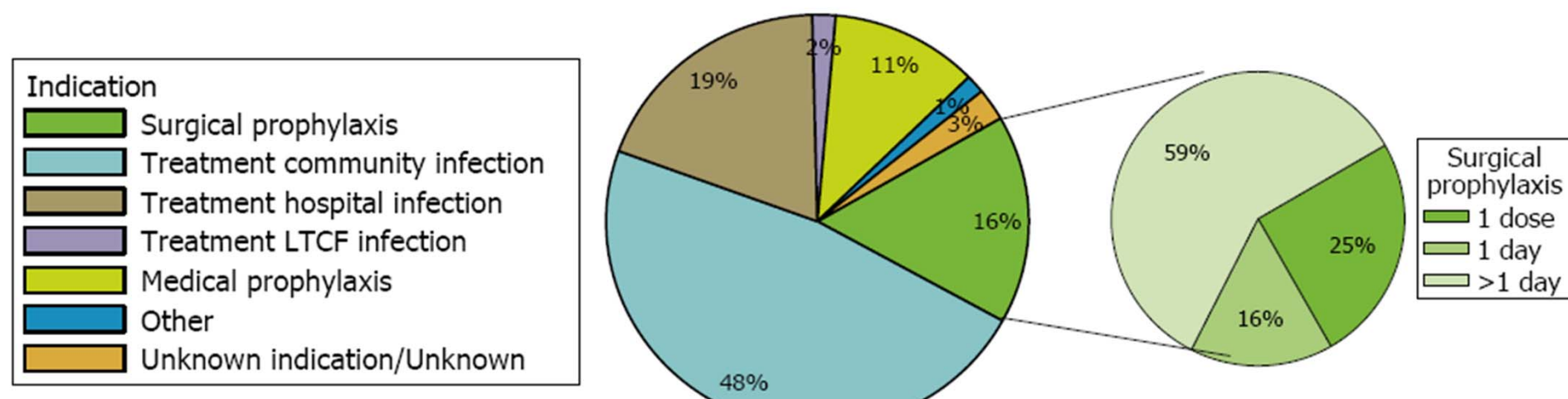


Table 19. Indication for antimicrobial use, route of administration and documentation of the reason for antimicrobial use in the patient notes, ECDC PPS 2011-2012

	Number of patients	Prevalence %	N of antimicrobials	Relative frequency %
Total	80951	35.0	110151	100.0
Indication for antimicrobial use				
Treatment	54630	23.6	75332	68.4
Community infection	38977	16.8	52391	47.6
Hospital infection	14733	6.4	21001	19.1
Other healthcare-associated infection	1490	0.6	1953	1.8
Surgical prophylaxis	15056	6.5	17992	16.3
Single dose	3998	1.7	4512	4.1
One day	2619	1.1	2846	2.6
>1 day	8762	3.8	10653	9.7
Medical prophylaxis	9956	4.3	12480	11.3
Other indication	1261	0.5	1606	1.5
Unknown indication, verified	1147	0.5	1383	1.3
Unknown/missing	1133	0.5	1393	1.3
Route of administration				
Parenteral	58359	25.2	77738	70.6
Oral	27131	11.7	31763	28.8
Other/unknown	559	0.2	650	0.6
Reason in notes				
Yes	64397	27.8	87471	79.4
No	15310	6.6	19113	17.4
Unknown	2711	1.2	3567	3.2

Underdiagnosis of *Clostridium difficile* across Europe:
the European, multicentre, prospective, biannual,
point-prevalence study of *Clostridium difficile* infection
in hospitalised patients with diarrhoea (EUCLID)

- **482 participating hospitals across 20 European countries.**
- **During the study period, participating hospitals reported a mean of 65.8 tests (country range 4.6–223.3) for C difficile infection per 10 000 patient-bed days and a mean of 7.0 cases (country range 0.7–28.7) of C difficile infection per 10,000 patient-bed days.**
- **Only two-fifths of hospitals reported using optimum methods for testing of C difficile infection.**

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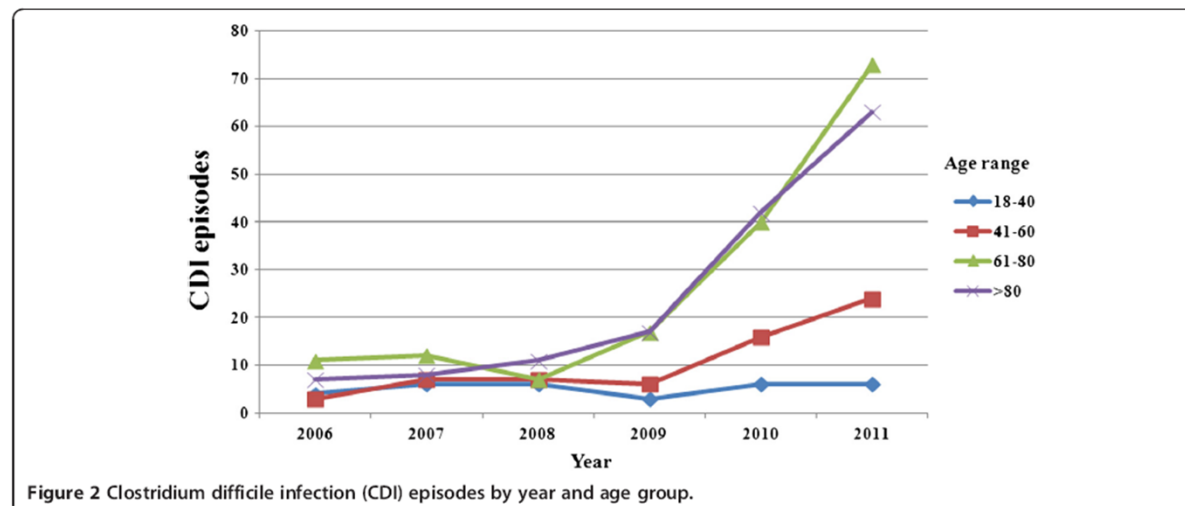
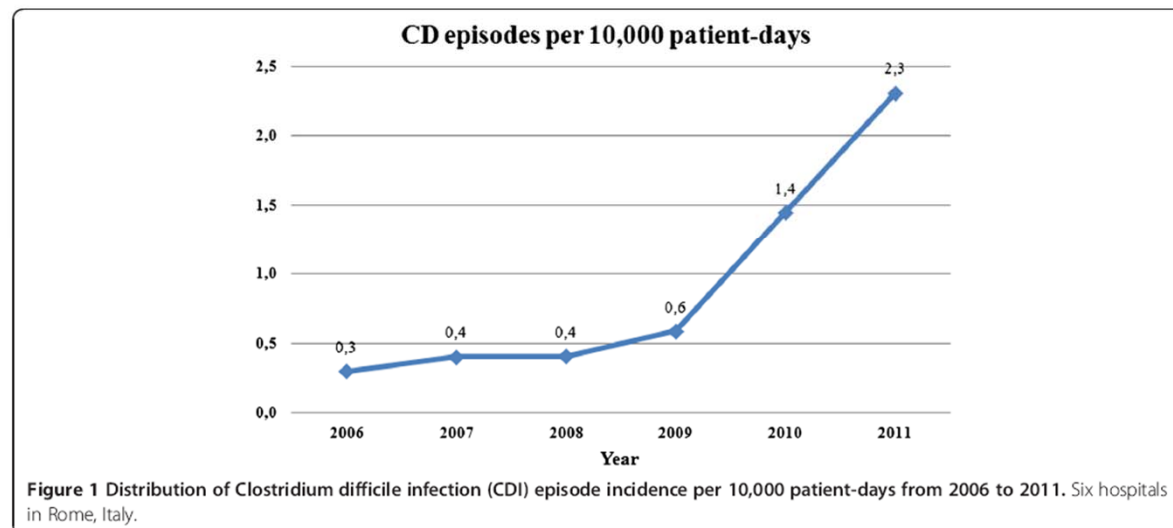
- Across all 482 European hospitals on the two sampling days, 148 (23%) of 641 samples positive for *C. difficile* infection (as determined by the national laboratory) were not diagnosed by participating hospitals because of an absence of clinical suspicion, equating to about

74 missed diagnoses per day

Clostridium difficile infection in Italian urban hospitals: data from 2006 through 2011

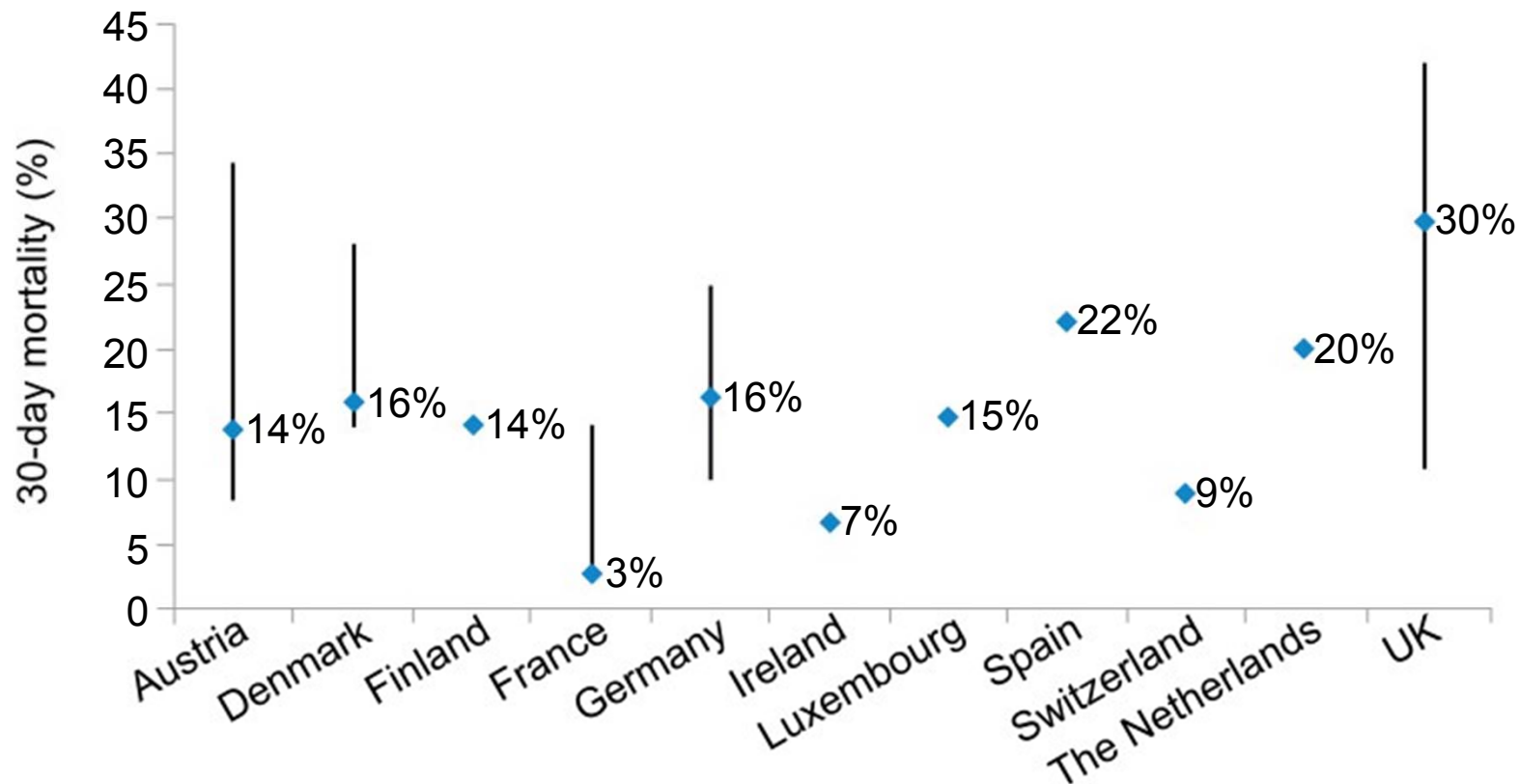
Stefano Di Bella¹, Maria Musso¹, Maria A Cataldo¹, Marcello Meledandri², Eugenio Bordi¹, Daniela Capozzi³, Maria C Cava⁴, Patrizia Chiaradonna⁵, Grazia Prignano⁶ and Nicola Petrosillo^{1*}

BMC Infectious Diseases 2013, **13**:146



Mortality rates associated with CDI across Europe

Weighted average 30-day mortality in patients with healthcare facility-acquired CDI by country



- Data from a systematic review found the weighted average 30-day mortality from CDI ranged from 3-30%

The Epidemiology of Community-acquired *Clostridium difficile* infection: A population-based study

Comparison of community-acquired and hospital-acquired *Clostridium difficile* infection

Characteristic	Community-acquired (n=157)	Hospital-acquired (n=192)	p-value
Age, median (range)	50 (0.1–102)	72 (0.1–99)	<0.001
< 18, n (%)	21 (13)	8 (4)	
18–65, n (%)	87 (55)	63 (33)	
>65, n (%)	49 (31)	121 (63)	
Female gender, n (%)	119 (76)	115 (60)	0.002
Antibiotic exposure, n (%)	123 (78)	181 (94)	<0.001
Acid suppression use, n (%)	35 (22)	90 (47)	<0.001
Mean Charlson co-morbidity index	1.3	3.3	<0.0001
Inflammatory bowel disease, n (%)	8 (5)	5 (3)	0.22
Malignancy diagnosis, n (%)	26 (17)	61 (32)	<0.0001
Severe CDI [‡] , n/N (%)	32/106 (30)	60/162 (37)	0.25
Severe CDI [•] , n/N (%)	32/157 (20)	60/192 (31)	<0.01
Severe complicated CDI, n (%)	7 (5)	14 (7)	0.27
Recurrent CDI, n (%)	44 (28)	58 (30)	0.66

The zoonotic aspect of *C. difficile* is not completely clarified.

- ***C. diff* has been found in :**

- **Livestock**

- **Pigs**

- **Calves**

- **Poultry**

- **Meat (retail mince meal)**

- **Pets....**

- **The same ribotypes may occur both in humans and animals, with ribotype 078 having emerged at the same time in humans and livestock.**

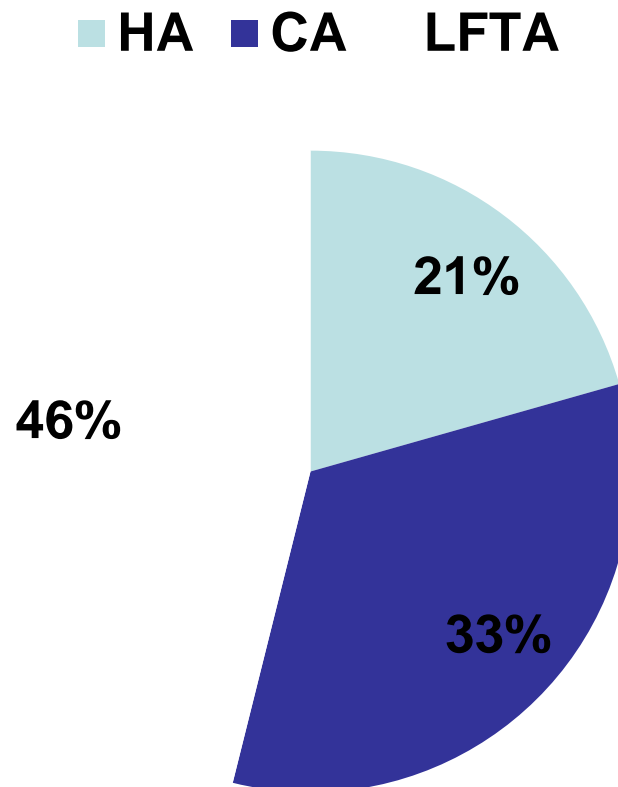
- **Furthermore, the identical *C. difficile* strains were already found in diseased pigs and humans.**

Epidemiology of *Clostridium difficile*-associated disease: a shift from hospital-acquired infection to long-term care facility-based infection

Garg S et al, Dig Dis Sci. 2013;58:3407-12

❖ A retrospective study included 400 randomly selected patients with a diagnosis of CDI.

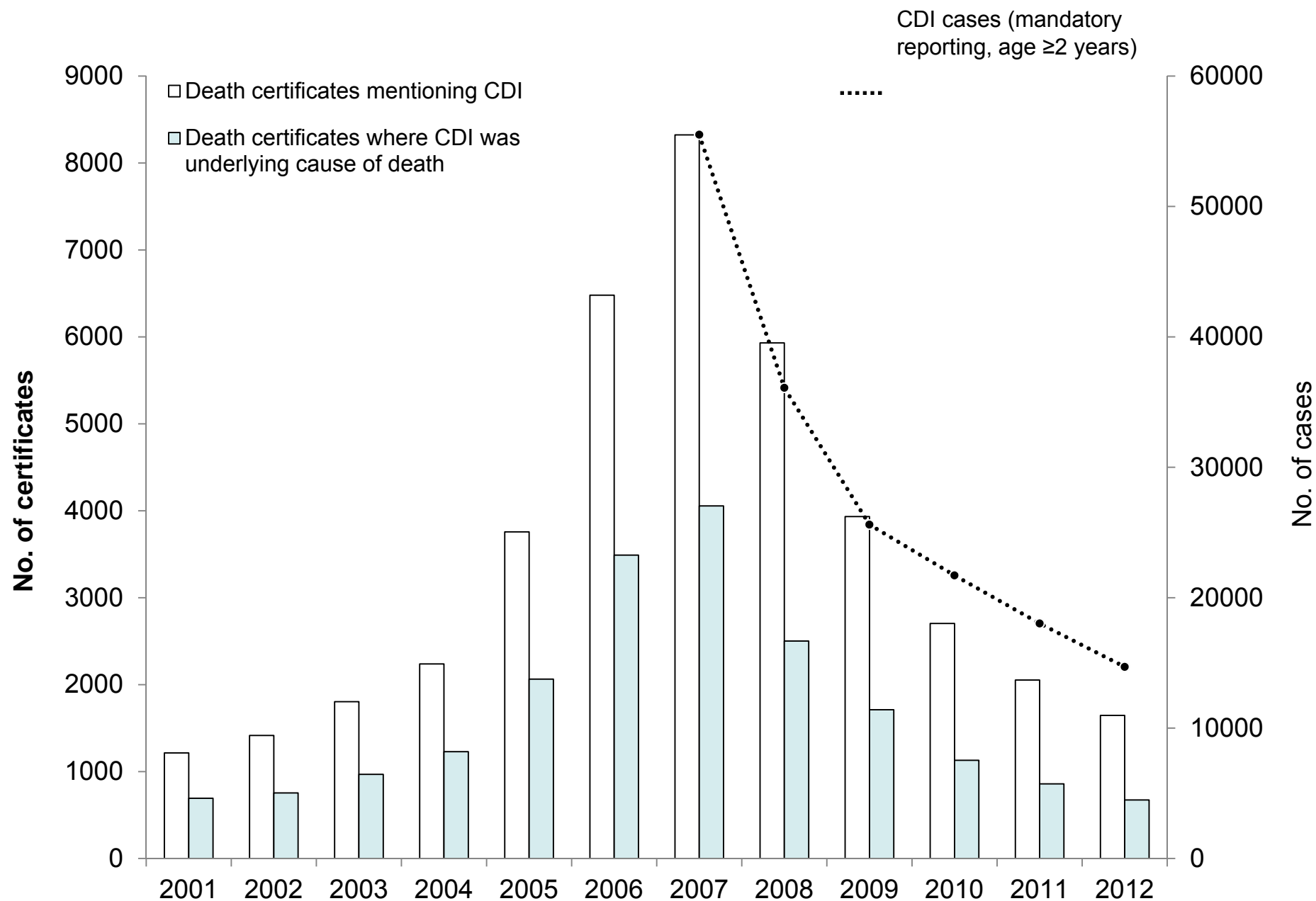
❖ Most LTCF patients (84.8%) had non-diarrheal symptoms as their presenting complaint.



- In the UK, a ‘high impact intervention’ bundle has been implemented to prevent CDI and to control outbreaks caused by the type 027 strain [Dept of Health 2010].

- The annual number of CDI cases in England has decreased by approximately 80% since mandatory reporting was introduced in 2007/8, with a corresponding fall in the number of deaths.

Fig. 2. Annual number of death certificates mentioning CDI, and where CDI was the underlying cause of death, and of toxin-positive CDI cases (based on mandatory surveillance from 2007) in hospitals in England and Wales, 2001-2012 [ONS; PHE].



CDI Europe recommendations: infection control and prevention

- *Improvements in CDI diagnosis and treatment are vital to infection control and prevention, as well as to optimise the standard of care for individual patients*
- *Policymakers need to support and communicate the need for CDI-specific interventions and guidance to be integrated within policies and initiatives on patient safety and HAI prevention and control*
- *Infection control should be a priority in all relevant aspects of healthcare management, including facility design and planning*
- *Improving compliance with infection control measures for all HAI, among all healthcare staff, is crucial.*
 - *Routine infection control should be encouraged through high-profile education and communications directed to all staff throughout institutions*
 - *Compliance should be audited regularly*

CDI Europe recommendations: infection control and prevention

- *CDI-specific performance indicators should be assessed and used to help drive up patient safety and quality of care*
 - Infection control data should ideally be publicly available
 - Sharing best practice internationally may help improve standards
- *Specific protocols for cleaning and disinfection against *C. difficile* should be developed and implemented*
- *New, user-friendly disinfectants active against *C. difficile* are required*
 - Policymakers at European and national levels should support the introduction of standardised tests and laboratory services
- *Infection control procedures in nursing homes need to be assessed and improved where necessary*
- *Further research is required to address outstanding questions*
 - Sources of *C. difficile* contamination, modes of transmission, the optimal, cost-effective means of infection prevention and control