P0753

Second report from the EUropean, multi-centre, prospective bi-annual point prevalence study of CLostridium difficile Infection in hospitalised patients with Diarrhoea (EUCLID)

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INTRODUCTION

Clostridium difficile is still the major cause of infective, nosocomial diarrhoea in the developed world. Rapid and accurate diagnosis is paramount for patient care and infection prevention[1]. There has been an increase in the measured incidence of C. *difficile* infection (CDI) in countries with active surveillance programmes, and a marked shift in epidemiology over the last decade[2]. Sub-optimal case ascertainment, either due to inadequate laboratory diagnosis or lack of clinical suspicion, means that the true burden of CDI remains unclear[3-6].

The first report from the EUCLID study demonstrated that CDI rates in 2011-2012 had increased compared with those reported in a previous European epidemiological survey carried out in 2008 (European CDI surveillance: ECDIS); 6.6 and 4.1 CDI cases/10,000 patient bed days, respectively[7,8]. This was against a background of increased testing rates; 67.1 and 52.1 tests/10,000 patient bed days for EUCLID and ECDIS studies, respectively[7,8].

Additionally, across the 20 European countries a quarter of CDI cases on one day (in winter; Dec 2012/Jan 2013) were missed due to lack of clinical suspicion (i.e. 82 patients never received a test). A further 166 patients received a misdiagnosis (either false-positive or false-negative)due to inadequate laboratory diagnostics.

This study aimed to measure the extent of under-testing and under-detection of CDI across 20 countries in Europe during summer, and to compare the results with the previous winter sampling period.

METHODS

Study questionnaire

Data were collected from PHs on local policy for CDI testing and reporting, laboratory methods used for CDI diagnosis, local rates of testing and the local reported CDI rate for the period Sept 2012 - August 2013 .

Samples at PHs

All in-patient diarrhoeal samples submitted to the PHs laboratory on a single day were sent to the EUCLID national coordinating laboratory (NCL), regardless of original test requested. Sample forms were completed for each sample by the PH recording patient's age, gender and clinical specialty of the patient location, whether the sample was tested for CDI and if so what was the result.

Samples at NCLs

Samples were tested using an optimised 2-stage algorithm for CDI diagnosis: membrane enzyme immunoassay (EIA) for glutamate dehydrogenase (GDH)/membrane EIA for toxins A & B (*C.DIFF QUIK CHEK COMPLETE®*, Techlab, USA). The results for each sample at the PH and NCL were compared. Confirmation assays (either culture/PCR for toxin genes or cytotoxigenic culture) were performed if EIA results were GDH positive/toxin positive or GDH positive/toxin negative.

Data analysis

All data were uploaded to the EUCLID web-based data management system. The database was locked once data querying and cleaning were completed. Data analyses were carried out by the EUCLID European coordinator. Local testing rates and CDI positive reporting rates were compared for each country and across Europe. Rates during the 2012-2013 collection period were compared with those reported via a previous questionnaire for the period 2011-2012.

Results were compared for each submitted sample and the original PH result were designated to be correct, false positive, false negative or not tested. Rates of under-diagnosis and misdiagnosis were compared for the summer and previous winter sampling periods.

RESULTS

There were **482 PHs from 20 European countries** participating in the study. The PHs submitted 3389 faecal samples to NCLs (mean 7.0, range 3.5-17.2 per hospital), compared with a mean of 8.2 (country range 5.3-13.5) in the previous winter collection period. The mean CDI positivity rate at the NCL was 9.2% (country range 0-20.4%) compared with 8.8% (country range 0-19.7%) in winter. There was therefore no clear evidence of seasonality of CDI cases.

Questionnaire results:

Fig 1. Reported testing rates/10,000pbds

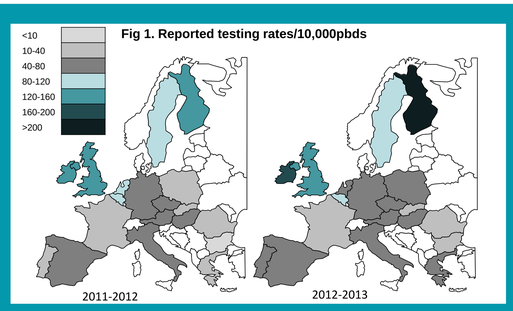


Fig 2. Reported CDI case rates/10,000pbds

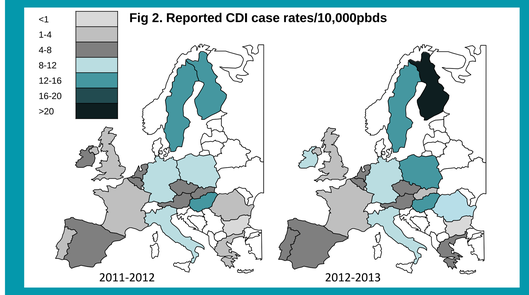
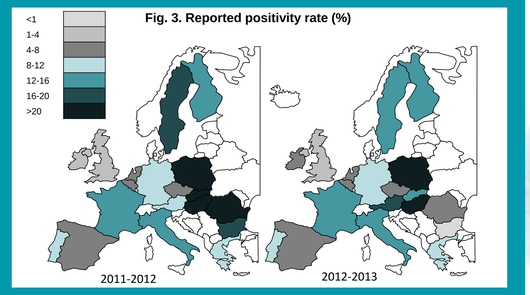


Fig. 3. Reported positivity rate (%)



Testing policy:

Fig. 4. Testing policy 2011-2012

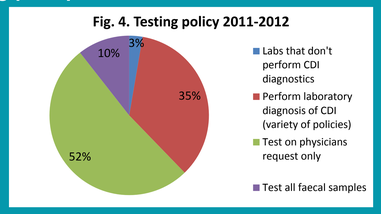
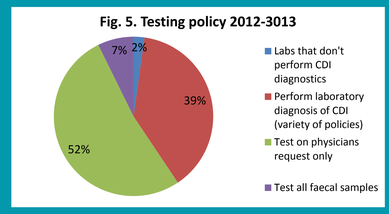


Fig. 5. Testing policy 2012-3013



Testing methodology:

Fig. 6. Testing methodology 2011-2012

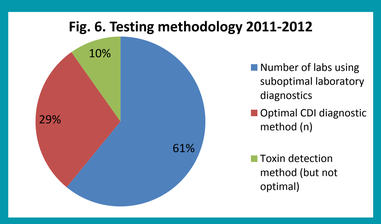
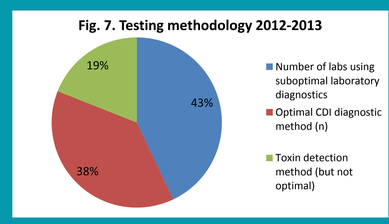


Fig. 7. Testing methodology 2012-2013



Sample results:

	Winter			Summer		
Country	No. of undiagnosed cases N (% of all positives)	No. of false positives at PH N (% of total samples)	No. of false negatives at PH N (% of total samples)	No. of undiagnosed cases N (% of all positives)	No. of false positives at PH N (% of total samples)	No. of false negatives at PH N (% of total samples)
Austria	1 (50.0)	0 (0.0)	2 (0.0)	0 (0.0)	4 (12.1)	0 (0.0)
Belgium	0 (0.0)	2 (3.6)	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.8)
Bulgaria	6 (100.0)	N/A	N/A	1 (50.0)	0 (0.0)	1 (6.3)
Czech Republic	1 (10.0)	14 (19.4)	2 (4.0)	0 (0.0)	3 (4.9)	0 (0.0)
Finland	2 (50.0)	1 (3.6)	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)
France	6 (35.3)	8 (3.6)	2 (1.0)	2 (22.2)	6 (3.2)	0 (0.0)
Germany	36 (25.2)	40 (5.8)	22 (4.1)	25 (23.1)	41 (6.4)	10 (1.6)
Greece	1 (50.0)	3 (10.7)	0 (0.0)	2 (66.7)	0 (0.0)	0 (0.0)
Hungary	4 (33.3)	1 (1.3)	0 (0.0)	2 (7.1)	2 (2.3)	0 (0.0)
Ireland	0 (0.0)	4 (7.5)	2 (4.2)	1 (100)	2 (2.8)	1 (1.4)
Italy	5 (15.6)	10 (4.1)	2 (1.0)	10 (23.3)	11 (5.1)	1 (0.5)
Netherlands	0 (0.0)	2 (4.1)	1 (0.0)	0 (0.0)	2 (5.7)	0 (0.0)
Poland	6 (22.2)	13 (13.1)	4 (5.8)	4 (16.0)	12 (13.3)	1 (1.1)
Portugal	2 (14.3)	1 (2.2)	2 (5.9)	0 (0.0)	2 (4.8)	0 (0.0)
Romania	8 (57.1)	4 (25.0)	0 (0.0)	14 (73.7)	3 (16.7)	2 (11.1)
Slovakia	0 (0.0)	1 (3.7	0 (0.0)	2 (28.6)	2 (7.4)	1 (3.7)
Slovenia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Spain	2 (14.3)	5 (3.6)	4 (3.2)	0 (0.0)	10 (6.8)	1 (0.7)
Sweden	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	1 (2.2)	0 (0.0)
UK	2 (10.5)	7 (1.6)	6 (1.4)	3 (18.8)	11 (2.9)	3 (0.8)
Europe	**82 (24.7)**	**118 (5.0)**	**46 (2.3)**	**67 (21.8)**	**114 (5.1)**	**22 (1.0)**

Table 1. Results of samples tested or not tested for CDI in winter and summer

DISCUSSION

- The **reported CDI testing frequency has increased** from that recorded in 2011-2012 (67.1) to 77.4 tests/10,000 patient bed days in 2012-2013[8].
- There has also been an **increase in measured CDI incidence from 6.8 to 7.9 CDI cases/10,000 patent bed days** from 2011-2012 to 2012-2013, respectively[8].
- Over half (52.1%) of PHs still only test for CDI on physician request (51.6% the previous year)[8]. However, 65.5% of samples received at the NCLs had a previous test at the PH, possibly indicating accurate clinical suspicion in some PHs.
- The use of optimised laboratory diagnostics has increased from 29% of PHs to 38%. False-positive rates decreased in those countries where diagnostics had improved e.g. Czech Republic (table 1.).
- Testing policy and methodology is in a state of flux with large numbers of PHs changing both between the 2011/2012 and 2012/2013 survey periods.
- The false-positive rate at the PHs across Europe was similar in both sampling periods; 5.0% (country range 0-25%) and 5.1% (country range 0.0-13.3%) in winter and summer, respectively. The false-negative rate decreased slightly from 2.3% (country range 0-6.7%) to 1.0 (country range 0.0-11.1) from winter to summer, respectively. Although these rates appear low, they equate to **an average of 152 patients with a CDI misdiagnosis on one day**.
- The **rate of under-diagnosis (samples tested positive at NCL but no original test performed at PH) was 21.8%**. This is similar to the 24.6% of inpatients under-diagnosed in the winter[8].
- Across Europe **on a single day an average of 75 CDI patients were missed due to lack of clinical suspicion**.

CONCLUSIONS

There have been marked recent shifts in CDI testing policy and methodology across Europe, resulting in improved testing policies and selection of laboratory methods.

However, in the PHs studied, an average of 96 in-patients with CDI are not diagnosed due to lack of clinical suspicion or inadequate laboratory diagnostics every day in Europe, equating to >39,000 missed cases per annum.

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