SURVEILLANCE REPORT

Clostridioides (Clostridium) difficile infections

Annual Epidemiological Report for 2016–2017

Key facts

- On 1 January 2016, ECDC started coordinating the surveillance of *Clostridioides (Clostridium) difficile* infection (CDI) in acute care hospitals in EU/EEA countries. ECDC's surveillance protocol provides a standardised tool for hospitals to measure and monitor CDI incidence rates, with three surveillance options, i.e. a 'minimal', a 'light' and an 'enhanced' option, the latter linking case-based epidemiological and microbiological data [1]. This report includes CDI surveillance data from 2016–2017.
- In 2016–2017, 24 EU/EEA countries/administrations (UK devolved administrations are counted separately) reported CDI data to ECDC, of which 23 countries had data suitable for analysis. These countries/administrations reported 1 559 hospital surveillance periods corresponding to >18.3 million patient admissions and >109 million patient-days.
- For 2017, CDI data were contributed by >21% acute care hospitals in the participating countries/administrations, and >10% of all acute care hospitals in the EU/EEA. Ten participating countries/administrations (Belgium, Hungary, Iceland, Ireland, Lithuania, the Netherlands, Malta, UK-England, UK-Scotland and UK-Wales) had 85%–100% national coverage in 2016 or 2017, in terms of the number of participating acute-care hospitals or acute care hospital beds. However, comparisons between the two years should only be made cautiously, as only 14 (61%) countries/administrations contributed data for both 2016 and 2017.
- Overall in 2016–2017, 72.0% of the CDI cases with case-based data were above 64 years old and the majority (56.4%) were female. More than half (n=3 446/5 863; 58.8%) of the CDI cases had had contact with healthcare in the three months before the current healthcare admission, of which the vast majority (n=2 804/3 446; 81.4%) had had contact with a hospital. Fewer were reported to have had contact with a long-term care facility (LTCF) (n=431; 12.5%).
- Information on the outcome of CDI was available for 11 568/26 825 (43.1%) cases, of which 2 029 (17.5%) cases died, from any cause. Death was reported as 'possibly' or 'definitely' related to CDI for 480 (4.1%) of 11 568 CDI cases with known outcome. Considering this rate, and that there were an estimated 189 526 healthcare-associated (HA) CDI cases (cumulative 95% confidence interval (95% CI): 105 154–340 978) in EU/EEA countries/administrations annually in 2016–2017 [2], this suggests that there were 7 864 fatal HA CDI cases (95% CI: 4 363–14 148) annually in the EU/EEA for whom CDI had contributed to their fatal outcome.

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- At the case-level ECDC CDI incidence surveillance data for 2016–2017, there were 1 792/12 097 (14.8%) cases that were reported to have a 'complicated course of infection', according to the ECDC and European Society of Clinical Microbiology and Infectious Diseases (ESCMID) definition, i.e. admission due to community-onset CDI; admission to an intensive care unit (ICU); surgery (colectomy) for toxic megacolon, perforation or refractory colitis; or death.
- In 2016–2017, the crude incidence density of CDI was 3.48 cases per 10 000 patient-days. This was higher in tertiary care hospitals (3.87 cases per 10 000 patient-days) than in secondary or primary care hospitals (3.46 and 2.28 cases per 10 000 patient-days, respectively). Tertiary hospitals were commonly large, university-affiliated, teaching hospitals while primary hospitals were commonly general hospitals with no teaching activity and few specialities and laboratory services. The crude incidence density was the lowest in the heterogeneous group of 'specialised' hospitals (2.24 cases per 10 000 patient-days).
- In 2016–2017, 23 052/37 857 (60.9%) cases were HA CDI. The vast majority of HA CDI cases had their origin in the current hospital (n=13 576/16 101; 84.3%), with far fewer cases being associated with another hospital (n=815; 5.1%), an LTCF (n=514; 3.2%) or 'other healthcare' (n=228; 1.4%). Tertiary care hospitals had the highest mean hospital-level HA CDI incidence (2.75 cases per 10 000 patient-days), followed by secondary care, specialised and primary care hospitals (2.21, 1.63 and 1.46 cases/10 000 patient-days, respectively).
- In 2016–2017, 2 439/37 857 (6.4%) CDI cases were reported to be recurrent. Amongst the recurrent CDI cases, death during the current hospitalisation was reported as 'possibly' or 'definitely' related to CDI for 50/160 (31.3%) fatal recurrent CDI cases, which was 67% more than for fatal non-recurrent CDI cases (224/1 273; 17.6%) (p=0.001). Additionally, recurrent cases were almost twice as likely to have a complicated course of infection (290/1 162; 25.0%) than non-recurrent cases (1 140/8 079; 14.1%) (p<0.0001).
- In 2016–2017, 12 366/37 857 (32.7%) CDI cases were community-associated (CA CDI), or CDI of unknown association (UA CDI). The proportion of CA CDI cases reported to have had prior contact with an LTCF was 13.6% (107/787), which was more than twice the proportion reported for all CDI cases (n=324/5 076; 6.4%).
- In 2016–2017, while the mean hospital rate of CDI testing was 96.1 stool tests per 10 000 patient-days, the median rate was 38.6 stool tests per 10 000 patient-days, as many hospitals tested relatively infrequently.
- ESCMID-recommended diagnostic algorithms were used during 902/1 175 (76.8%) hospital surveillance periods [3,4].
- 10 countries/administrations reported PCR ribotype (RT) data for their CDI cases, of which three countries/administrations (Belgium, the Netherlands and UK-Wales) reported 3 889/4 832 (80.5%) of these cases. Therefore, the RT data are not likely to be representative of the EU/EEA as a whole.
- 14 of the 20 most commonly reported RTs were Clade 1, including the most common RT, RT014/020 (814/4 865 reports; 16.8%). RT014/020 was the most frequent, or the second most frequently reported RT in seven countries/administrations. RT078 (Clade 5), which is commonly detected in one-health investigations, particularly involving pigs, was reported relatively frequently by Belgium, Czechia, Ireland and the Netherlands (7–11% cases).
- RT027, which is known for its hypervirulence [5,6], was the third most frequently reported RT in 2016–2017. It was notably prevalent in the cases reported by Hungary (67.6%), Poland (63.0%) and Slovenia (44.4%), compared to cases from all other countries/administrations (2.5%). Four countries (Czechia, Hungary, Poland and Slovakia) reported 78/86 (90.7%) of RT027-like RTs (*C. difficile* Clade 2, multi-locus sequence type (MLST) 1, e.g. RT176, RT036/198, RT016 and RT181). RT181 strains were also identified in cases reported by Greece.
- The reports of the detection of metronidazole resistance by E-test are of concern, as metronidazole was among the first-line treatment options recommended by ESCMID and the Infectious Diseases Society of America (IDSA) for certain subsets of CDI cases [7,8]. The 2021 update of the ESCMID guidelines no longer recommends metronidazole for treatment of CDI when fidaxomicin or vancomycin are available [9].
- In 2016–2017, all but one of the metronidazole-resistant isolates were RT027 (20/26; 76.9%) or the RT027-like strain, RT036/198 (5/26; 19.2%). EU/EEA countries should consider confirming metronidazole resistance and vancomycin resistance of *C. difficile* isolates by agar dilution methods, performed by a reference laboratory, and conducting additional investigations to elucidate the transmission mechanisms.
- ECDC recommends continual incidence surveillance of CDI for a period of 12 months. If not feasible, ECDC recommends a minimum surveillance period of three months. The update of the ECDC surveillance protocol for 2020 also contains structure and process indicators of infection prevention and control, including the optional collection of antimicrobial consumption data in participating hospitals.

Introduction

ECDC started coordinating the surveillance of *Clostridioides* (*Clostridium*) *difficile* infection (CDI) in acute care hospitals on 1 January 2016 [10]. The process uses a common surveillance protocol, to provide a tool for hospitals and countries to estimate the incidence of CDI; to assess the burden of adverse outcomes of CDI, including death; and to describe the epidemiology of *C. difficile* at the local, national and European level [1]. The protocol is based on a pilot protocol that was tested in 14 European countries in May–November 2013, during the ECDC ECDIS-Net project [11].

ECDC has coordinated two point prevalence surveys (PPSs) of healthcare-associated infections (HAIs) and antimicrobial use in European acute care hospitals. The first PPS was coordinated in 2011–2012, with 1 149 hospitals in 30 EU/EEA countries/administrations (UK devolved administrations counted separately); the second PPS was coordinated in 2016–2017, with 8 299 hospitals in 29 EU/EEA countries/administrations. Both PPSs included validation surveys performed by national validation teams composed of members of the national coordination teams, using the ECDC HAI case definitions as 'gold' standard. Validation surveys were performed by four countries in the first PPS and by 28 countries/administrations in the second PPS [12]. Therefore, the results may be considered as robust.

Between 2011–2012 and 2016–2017, the prevalence of CDI, as reported in these PPSs, increased from 3.6% to 4.8% of HAIs and the frequency of microbiological detection of *C. difficile* within all reported HAIs increased from the eighth to the sixth most frequent. Also, the proportion of reported healthcare-associated gastrointestinal infections that were reported to be CDI, increased between these two PPSs, from 48.0% to 54.6%, suggesting a reduction in under-diagnosis of CDI [2,13].

Methods

This report is based on data for 2016 and 2017 retrieved from The European Surveillance System (TESSy) on 5 February 2020. TESSy is a system, managed by ECDC, for the collection, analysis and dissemination of data on communicable diseases in the EU/EEA.

For a detailed description of methods used to produce this report, please refer to the 'Methods' chapter [14].

An overview of the national surveillance systems is available online and in Annex 1 [14] .

A subset of the data used for this report is available through ECDC's online tool, *Surveillance Atlas of Infectious Diseases* [15].

Surveillance protocols

This surveillance report is based on CDI surveillance data collected by the ECDC Healthcare-associated Infections Surveillance Network (HAI-Net). The protocol specifies three permitted levels of data collection: 'minimal' (aggregate numerators and denominators); 'light' (aggregate denominators and case-based numerators); or 'enhanced' (the 'light' option, plus directly linked, case-based microbiological data for at least the first five cases during a surveillance period).

The protocol recommends that hospitals use European Committee on Antimicrobial Susceptibility Testing (EUCAST) clinical breakpoints for interpretation of antimicrobial susceptibility test results, specifying variables to collect data for moxifloxacin, metronidazole and vancomycin [1,4].

ECDC started the collection of surveillance data that are compatible with the ECDC CDI surveillance protocol [1] on 1 January 2016. The surveillance data were collected through two different schemes:

- During the start-up phase, countries/administrations were invited to report data by 31 March 2016. Data were collected using the ECDC CDI surveillance protocol during at least one month in January–February 2016 and from at least one hospital.
- During biannual data collection, countries/administrations were invited to upload to TESSy CDI surveillance data compatible with the ECDC CDI surveillance protocol for hospital surveillance periods of at least three months per year. Biannual data collection enables the estimation of burden and trends; the surveillance system is not designed to detect outbreaks.

All hospitals used the ECDC CDI surveillance protocol, except for all hospitals reported by nine countries/administrations (Belgium, France, Finland, Hungary, Ireland, the Netherlands, UK-England, UK-Scotland, UK-Wales), which used national surveillance protocols, in 2016 and/or 2017, that are compatible with the ECDC protocol. Noteworthy differences between national and ECDC protocols are listed below.

Hungary:

- 2016 data: The Hungarian national surveillance coordinating centre invited Hungarian acute care hospitals to participate in the ECDC CDI surveillance on a voluntary basis. Participating hospitals participated in the surveillance for one month during the January–March 2016 'start-up phase' (45 facilities) and/or for three months in October–December 2016 (49 facilities), following the ECDC CDI surveillance protocol 'enhanced surveillance option'. Data reported to ECDC TESSy are fully compliant with the ECDC CDI surveillance protocol.
- 2017 data: Annual national data covering both acute and chronic care hospitals (92 facilities) were converted to meet the specifications of the ECDC CDI 'minimal surveillance option'. State-mandated reporting by hospitals was only required for new cases of healthcare-associated CDI (HA CDI) where the origin of the infection may have been the current hospital or another hospital. Cases identified in hospitals that had an origin in long-term care facilities (LTCFs) were reported voluntarily and under a separate category, i.e. 'LTCF CDI'. In contrast, the ECDC CDI surveillance protocol counts these cases as HA CDI. Cases of community-associated CDI (CA CDI), of unknown association (UA CDI) as well as recurrent cases of any origin were also reported voluntarily.

The Netherlands: The Dutch surveillance protocol contains differences to the ECDC protocol, as described in the annual reports of the Dutch *C. difficile* reference laboratory [16]. These include:

- All hospitals except one had surveillance periods for the 12-month period from 1 May until 30 April, rather than 1 January until 31 December.
- Patients younger than two years old are excluded.
- There is no discrimination between 'Screening with NAAT, confirmation with toxin A/B EIA' and 'Screening with GDH EIA, confirmation with toxin A/B EIA', as they are combined into one option.
- There is no discrimination between multiple episodes from one patient and multiple episodes from multiple patients.
- No data is collected on healthcare admissions in the previous three months. Therefore, the origin of CDI cases, as defined in the ECDC protocol, was estimated by the Netherlands using the variables in the Dutch protocol including 'location onset of symptoms', 'direct transfer from another healthcare facility', 'admission date', and 'date of onset of CDI symptoms' or 'sampling date'.
- 'Patient outcome' (e.g. death) is assessed within 30 days, whereas the ECDC protocol requests in-hospital outcome.
- 'Complicated course of infection' does not include the subcategory 'admission to a healthcare facility for treatment of community-onset CDI'.
- Antimicrobial susceptibility testing (AST) results are not representative of the Netherlands as AST is only performed on request.

The United Kingdom (UK): Three of the four UK devolved administrations participated, each providing data compatible with a different surveillance option (UK-England: 'light'; UK-Scotland: 'minimal'; UK-Wales: 'enhanced').

- UK-England: National reporting in UK-England follows the financial year (April–March) rather than calendar year (January–December). Public Health England (PHE) reported CDI data for April–December to TESSy for each year. Therefore, the annual totals reported by ECDC are not the annual totals reported by PHE. Additionally, the PHE protocol uses an episode length of 28 days rather than 14 days. UK-England did not report enhanced data as its Clostridium difficile ribotyping network (CDRN) data are not yet linked to the PHE surveillance data [17]. The PHE protocol does not include data on whether there was hospitalisation in the preceding three months, the McCabe score, the presence of CDI symptoms at admission, the patient and ward speciality, a complicated course of infection, or the infection outcome. In 2019, PHE updated the definition in its protocol for trust-apportioned and non-trust-apportioned cases to be compatible with the ECDC protocol.
- UK-Scotland: The Health Protection Scotland (HPS) CDI surveillance protocol [18] uses laboratory-based CDI surveillance which is mandatory for patients aged 15 years and above. It applies an episode length of 28 days rather than 14 days; and includes outpatient day cases. Each submitting Health Board validates each episode against the CDI case definition. HPS assigns CDI cases to the ECDC definition of HA, CA or UA CDI by linking validated cases to hospital discharge records, using the date of specimen collection rather than the date of symptom onset. Recurrent cases are identified from laboratory results using the definitions in the ECDC protocol. Unlike nationally reported CDI figures for National Health Service (NHS) Scotland, the data submitted to ECDC only include cases with specimens collected in acute care hospitals.

- UK-Wales: Public Health Wales was able to convert laboratory surveillance data to the 'enhanced' surveillance option of the ECDC protocol metadata sufficiently, as it has patient-days denominator for each participating hospital surveillance period. However, the Welsh protocol is unable to discriminate HA CDI from other CDI cases. As a result, HA CDI is reported as 'missing' and CA/UA CDI cases in UK-Wales includes HA CDI cases, as this category also includes cases with unknown origin. Additionally, the only case-level data from the 'light' surveillance option reported by UK-Wales were age, gender, whether the case was recurrent, and the date of the first positive laboratory sample.

Data analysis

The following data imputation and analysis methods were applied to the 2016–2017 ECDC CDI surveillance dataset:

- If a case did not have a symptom onset date reported, the 'first positive laboratory sample date' or otherwise the 'sampling date' were used as a proxy.
- There were 38 hospital surveillance periods lacking denominator data for the number of beds (n=25/1 806; 1.4%) and/or the number of patient-days (n=2/1 806; 0.1%) and/or the number of admissions or discharges (n=15/1 806; 0.8%). The missing data were imputed from the hospital surveillance periods with non-missing denominator data, using database medians. Two hospitals, including the effectively national-level hospital in Iceland, only had denominator data on the number of beds. For these two hospitals, the number of patient-days was estimated using the calculation [(number of beds) × (95% bed occupancy) × (the number of days in the surveillance period for that hospital)], rather than the database median.
- Unless otherwise stated, all totals exclude missing data.
- All analysis performed using STATA 14.0. All p-values refer to chi-squared tests for categorical variables.

Microbiological methods

To support EU/EEA countries in their acquisition of accurate and comparable surveillance data, ECDC outsourced specified activities for microbiological support to European CDI surveillance, in a project that adopted the name ECDIS-Net-2[1], provided by a consortium led by the Leiden University Medical Center (LUMC), the Netherlands. ECDIS-Net-2 developed standard operating procedures (SOPs) for diagnostics and typing, harmonised with ESCMID guidance, that were developed and agreed with all EU/EEA countries [19]. In May 2017, ECDIS-Net-2 held a train-the-trainer workshop in its use for nationally designated microbiologists. Additionally, in 2017 and 2019, ECDIS-Net-2 coordinated external quality assessment (EQA) exercises, in European national reference laboratories (NRLs), of PCR ribotyping (RT) of *C. difficile* strains that are common in Europe and/or difficult to type. ECDIS-Net-2 also accepted and investigated *C. difficile* isolates sent directly from individual hospitals. This resulted in the recognition of new emerging RTs (RT036, RT181 and RT198) that are very similar to RT027 and also caused outbreaks in Greece, Romania and one European Neighbourhood Policy (ENP) country in 2016–2019 [20].

ECDIS-Net-2 has worked collaboratively with NRLs for *C. difficile* to promote use of a common reference database of the 106 most common PCR ribotypes (RTs). In 2019, this included collaboration with Sciensano, Belgium, to identify the European (ECDC-Brazier-Leeds-Leiden) RT nomenclature for strains that had been reported to TESSy ≥10 times in 2016–2017 with a national RT nomenclature. Additionally, in 2019, collaboration with the Austrian Agency for Health and Food Safety (AGES) ensured that its NRL, which manages the online *C. difficile* RT nomenclature database WEBRIBO [21], has the appropriate reference strains. Several strains from a potential outbreak, that had capillary electrophoresis (CE) PCR data incorrectly categorised by WEBRIBO as AI-33, were re-categorised as the RT027-like RT181, following confirmation by ECDIS-Net-2 using whole genome multi-locus sequence typing (wgMLST).

As RT014 and RT020 are difficult to distinguish by CE PCR ribotyping, all reports of these RTs are amalgamated as 'RT014/020'. Indeed, several countries/administrations and hospitals already report these as RT014/020.

The ECDC surveillance protocol recommends that hospitals report antimicrobial susceptibility results according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) clinical breakpoints, or otherwise EUCAST epidemiological cut-off values (ECOFFs), Clinical and Laboratory Standards Institute (CLSI) breakpoints or national breakpoints, or the measured minimal inhibitory concentration (MIC) and testing method.

[1] The ECDC project, 'Microbiological support to European surveillance of *Clostridium difficile* infections' was initiated and funded by ECDC through a framework service contract (ECDC/2016/016), following an open call for Tender (OJ/05/11/2015-PROC/2015/029). It was awarded to a consortium led by Leiden University Medical Center (LUMC), Leiden, the Netherlands. The consortium members are Prof. Dr. E.J. Kuijper (LUMC); Dr. D.W. Notermans, Centre for Infectious Disease Control (CIb), RIVM, Bilthoven, the Netherlands; Prof. M.H. Wilcox, University of Leeds, Microbiology, Leeds, United Kingdom; Prof. Dr. F. Allerberger, Austrian Agency for Health and Food Safety (AGES), Vienna, Austria; and Prof. Dr. F. Barbut, UHLIN National Reference Laboratory for *Clostridium difficile*, Hôpitaux Universitaires Est Parisien (HUEP), Paris, France. The project adopted the name 'European *Clostridium difficile* Infection Surveillance Network 2' (ECDIS-Net-2).

Participation

In 2016–2017, 23 EU/EEA countries/administrations (UK devolved administrations counted separately) reported data for 1 559 hospital surveillance periods from 1 522 hospitals with over 18.3 million patient admissions, covering 109 million patient-days (Table 1). Additionally, Romania reported that at least 25 hospitals had used the ECDC surveillance protocol in 2016, although these data were unavailable for this report. Austria, Greece and Italy only participated during the 'start-up' phase of surveillance (n=5 hospitals). Comparisons between 2016 and 2017 data should be made with caution as only 14/23 (60.8%) countries/administrations participated in both years (Table 1).

Ten countries/administrations (Belgium, Hungary, Iceland, Ireland, Lithuania, the Netherlands, Malta, UK-England, UK-Scotland and UK-Wales) reported data with 85%–100% country/administration coverage in 2016 or 2017, in terms of the number of participating acute care hospitals or their hospital beds. Overall, the 2017 data includes >10.2% of acute care hospitals in all EU/EEA countries, and >21.6% in participating countries/administrations.

While 523/1 559 (33.5%) hospital surveillance periods were for the minimum three-month duration, 658 (42.2%) were from continuous surveillance. Croatia performed continual surveillance from June 2016 onwards. Although there were a similar number of hospitals participating in 2016 and 2017 (701 and 858 hospitals, respectively), there were more than double the number of patient admissions in 2017 (4 994 939 and 13 350 921, respectively), mostly due to the inclusion of complete national-level data from UK-England for April–December 2017 (Table 1).

France, which had converted its national database, reported the majority of hospital surveillance periods that had used the 'minimal' surveillance option in 2016–2017 (n=410/555; 73.9%). The majority of surveillance periods using the 'light' surveillance option (n=425) were reported by UK-England (n=147; 34.6%), Belgium (n=84; 19.8%) and Croatia (n=48; 11.3%). The most commonly used option was the 'enhanced' option, used by 13 countries/administrations during 579 hospital surveillance periods (Table 1).

The majority of hospital surveillance periods were from primary (n=493; 31.6%) or secondary (n=463; 29.7%) acute care hospitals (Table 1). Primary hospitals are commonly general hospitals, with no teaching activity and few specialities and laboratory services. Secondary hospitals commonly have five-to-ten clinical specialities, often receiving referrals from primary hospitals. Tertiary hospitals provide highly differentiated clinical specialties, commonly receiving referrals from primary and secondary hospitals; and are often associated with a university.

The majority of the hospital surveillance periods from specialised hospitals (n=81/140; 57.8%) were reported by Hungary (n=37/81; 45.7%) and UK-Wales (n=44/81; 54.3%). The specialisations of these hospitals were identified for 108/140 (77.1%) hospitals. Of these, the two most commonly reported specialisations were psychiatric hospitals (n=43/108; 39.8%), of which 40 were reported by UK-Wales; and hospitals that included rehabilitation as a specialisation (n=27/108; 25.0%), of which 22 were reported by Hungary (Table 1).

No information was available on 'hospital type' for 297 hospitals. In 2016, 129/131 (98.5%) hospitals with unknown 'hospital type' were in Belgium; and 147/166 (88.6%) in 2017 were in UK-England (Table 1). This was because Belgium started collecting data on 'hospital type' in 2017, and UK-England did not collect such data.

Primary hospitals (n=493) were as likely to have used the 'enhanced' surveillance option as the 'minimal' option (n=198; 35.7% and n=210; 36.3%, respectively). Indeed, primary hospitals were the most common type of hospital for the 'enhanced' option (n=210/579; 36.3%), more common than secondary (146; 25.2%), tertiary (n=72; 12.4%) or specialised hospitals (n=62; 10.7%) (Table 1).

Table 1. Participating hospitals by country* and type of hospital, EU/EEA, 2016–2017

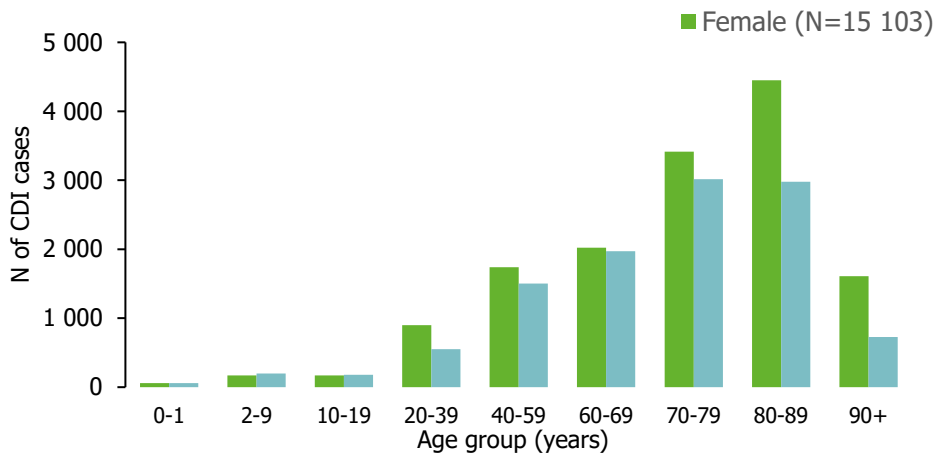
		2016					2017					Total
		N of hospitals		N of beds	N of discharges	N of patient-days	N of hospitals		N of beds	N of discharges	N of patient-days	N of hospital surveillance periods
		(M/L/E)	N				(M/L/E)	N				
Country/administration (N=23)*	Austria	0/1/0	**1**	1 990	8 067	42 630	ND	**ND**	ND	ND	ND	**1**
	Belgium	11/45/73	**129**	43 843	1 477 305	10 224 812	0/39/79	**118**	41 211	1 172 696	7 781 652	**247**
	Croatia	0/24/0	**24**	11 511	303 358	2 195 903	0/24/0	**24**	10 995	437 233	3 014 629	**48**
	Czechia	0/3/16	**19**	11 945	124 722	924 021	ND	**ND**	ND	ND	ND	**19**
	Estonia	1/3/0	**4**	3 107	7 455	49 010	0/2/0	**2**	909	6 981	66 295	**6**
	Finland	0/13/0	**13**	5 538	506 272	1 447 411	0/13/0	**13**	6 651	510 617	1 399 457	**26**
	France	203/0/0	**203**	44 401	592 376	3 056 445	207/0/0	**207**	41 526	579 377	2 894 286	**410**
	Greece	2/0/0	**2**	1 480	7 556	72 535	ND	**ND**	ND	ND	ND	**2**
	Hungary	0/37/57	**94****	82 281	550 311	3 714 597	91/1/0	**92**	66 005	1 972 926	17 045 170	**186**
	Iceland	ND	**ND**	ND	ND	ND	0/0/1	**1**	650	10 777	225 388	**1**
	Ireland	0/1/0	**1**	820	1 984	19 894	0/0/55	**55**	11 855	678 361	3 948 147	**56**
	Italy	0/0/2	**2**	1 800	5 106	43 724	ND	**ND**	ND	ND	ND	**2**
	Latvia	0/1/0	**1**	866	3 738	20 609	ND	**ND**	ND	ND	ND	**1**
	Lithuania	0/1/2	**3**	4 191	13 380	98 530	0/0/16	**16**	11 238	215 447	1 653 038	**19**
	Malta	0/1/0	**1**	1 029	57 799	298 878	0/1/0	**1**	1 016	61 567	314 960	**2**
	Netherlands	0/0/22	**22**	14 828	561 960	3 010 478	0/0/22	**22**	14 220	537 999	2 842 621	**44**
	Poland	0/32/14	**46**	21 581	102 154	485 479	ND	**ND**	ND	ND	ND	**46**
	Slovakia	0/21/16	**37****	18 529	172 559	1 116 805	0/0/30	**30**	14 401	550 535	3 495 840	**67**
	Slovenia	0/0/3	**3**	3 894	13 785	82 307	0/0/1	**1**	419	20 454	113 471	**4**
	Spain	0/4/0	**4**	3 248	11 202	78 018	ND	**ND**	ND	ND	ND	**4**
	UK-England	ND	**ND**	ND	ND	ND	0/147/0	**147**	310 563	5 319 998	25 878 135	**147**
	UK-Scotland	0/1/2	**3**	1 456	15 124	78 014	40/0/0	**40**	14 963	815 205	4 366 919	**43**
	UK-Wales	0/5/84	**89**	10 777	458 726	3 448 983	0/5/84	**89**	10 635	460 748	3 378 005	**178**
	EU/EEA	217/193/291	**701**	289 115	4 994 939	30 509 083	338/232/288	**858**	557 257	13 350 921	78 418 013	**1 559**
Type of hospital	Primary	82/52/71	**205**	40 790	436 564	3 084 316	116/33/139	**288**	58 807	1 537 863	10 756 614	**493**
	Secondary	100/42/73	**215**	98 700	1 676 494	8 877 972	141/34/73	**248**	86 293	3 119 788	18 693 349	**463**
	Tertiary	15/32/45	**92**	91 341	1 280 525	7 373 339	37/10/27	**74**	74 999	2 784 041	17 793 998	**166**
	Specialised	9/20/29	**58**	13 480	74 635	806 229	44/5/33	**82**	13 545	308 995	3 418 821	**140**
	Unknown	11/47/73	**131**	44 804	1 526 721	10 367 227	0/150/16	**166**	323 613	5 600 234	27 755 231	**297**
	EU/EEA	217/193/291	**701**	289 115	4 994 939	30 509 083	338/232/288	**858**	557 257	13 350 921	78 418 013	**1 559**

*Key: * UK devolved administrations are counted separately; ** refers to the number of hospital surveillance periods rather than number of hospitals, because, in 2016, 1/36 hospitals in Slovakia and 36/58 hospitals in Hungary participated in two surveillance periods; M: 'minimal' surveillance option; L: 'light' surveillance option; E: 'enhanced' surveillance option; ND: no data*

Epidemiology

In 2016–2017, participating hospitals reported 37 857 CDI cases, of which 1 004/1 559 hospitals reported case-based data for 26 825 cases (Table 2—Table 5). Overall, 72.0% cases with case-based data were above 64 years old, and the majority (15 103/26 794; 56.4%) were female (Figure 1).

Figure 1. CDI cases by age and gender, EU/EEA, 2016–2017



Total CDI cases

Although the crude annual incidence density of CDI was lower in 2017 than in 2016 (3.22 and 3.57 cases/10 000 patient-days, respectively; p<0.0001), this is largely explained by the participation of different countries/administrations and/or hospitals in those two years (see Table 1, Table 2, Table 3). For example, in Hungary, the 2016 data were collected using the ECDC protocol, with an over-representation of secondary and tertiary hospitals; while the 2017 data were collected using the national protocol and reported for all hospitals.

Overall for 2016–2017, the crude incidence density of CDI was 3.48 cases/10 000 patient-days (Table 4). In those two years, the highest national annual crude CDI incidence densities were all reported in 2016, by Lithuania (7.51 cases/10 000 patient-days), Poland (7.50 cases/10 000 patient-days) and Estonia (5.92 cases/10 000 patient-days) (Table 2; Figure 2 and Figure 3).

The crude incidence density in 2016–2017 was higher in tertiary hospitals (3.87 cases/10 000 patient-days) than in secondary or primary hospitals (3.46 and 2.45 cases/10 000 patient-days, respectively). Additionally, tertiary hospitals also had the highest mean hospital-level incidence rate (5.25 (95% confidence interval (CI): 4.05–6.44) cases/10 000 patient-days); which was higher than the rate in secondary hospitals (3.90 (95% CI: 3.41–4.40) cases/10 000 patient-days) and primary hospitals (2.28 (95% CI: 2.00–2.57) cases/10 000 patient-days) (Table 4; Figure 6).

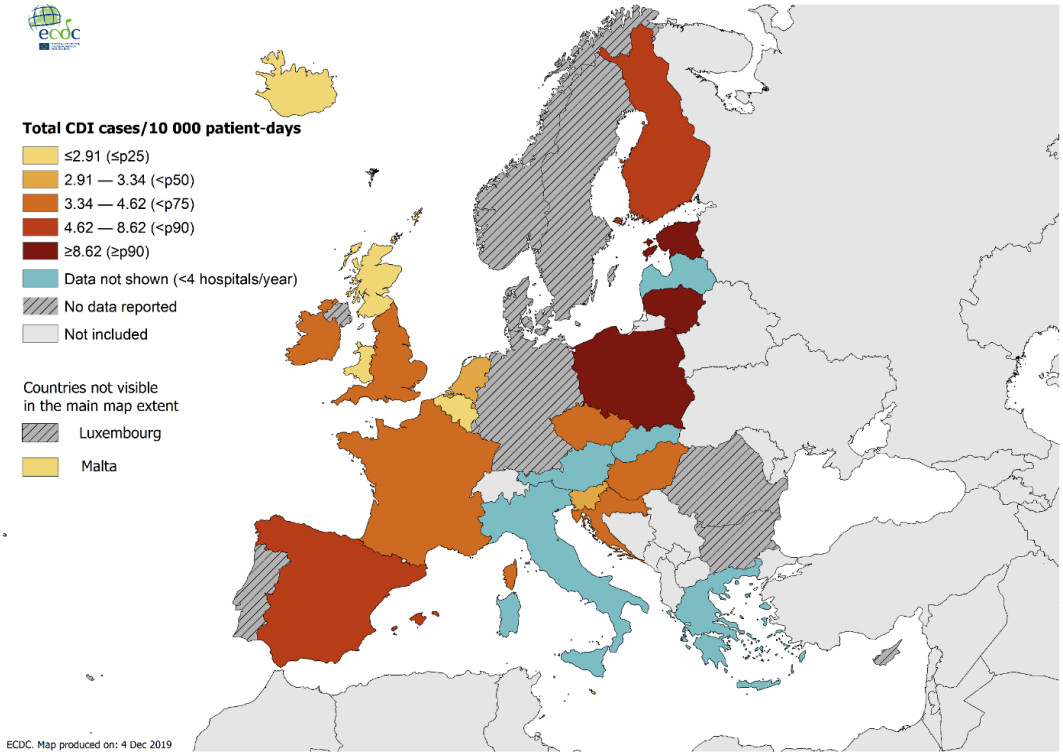
The heterogeneous group of 'specialised hospitals', which were the least commonly reported type of hospital had the lowest crude incidence of any type of hospital in 2016–2017 (2.18 cases/10 000 patient-days) (Table 4). There were 52/149 (34.9%) surveillance periods in these hospitals that reported zero cases, which largely explains their relatively low median incidence (0.67 cases/10 000 patient days). Conversely however, in 2016, specialised hospitals had the highest crude annual incidence of any type of hospital (3.71 cases/10 000 patient days) (Table 2). In part, this relates to the participation of 15 specialised hospitals in Poland in 2016, whereas no hospitals in Poland participated in 2017 (Table 2 and Table 3). The mean CDI incidence density in these 15 hospitals was 10.0 cases/10 000 patient-days, which was higher than the mean in all other specialised hospitals that participated in 2016–2017 (2.0 cases/10 000 patient-days) (Table 4).

In 2016–2017, more than half the CDI cases (n=3 446/5 863 cases with available data; 58.8%) had had contact with healthcare in the three months before the current acute care hospital admission (Table 5). Of these, the majority (n=2 804/3 446; 81.3%) had had contact with a hospital, with far fewer reported to have had contact with an LTCF (n=431; 12.5%). The majority of cases were admitted for clinical conditions that were scored by physicians as non-fatal (2 855/4 819; 59.2%; Table 5).

There were 1 792/12 097 (14.8%) cases that were reported to meet the ECDC and ESCMID definition of a 'complicated course of infection', i.e. admission due to community-onset CDI; admission to an intensive care unit (ICU); surgery (colectomy) for toxic megacolon, perforation or refractory colitis; or death [1,22].

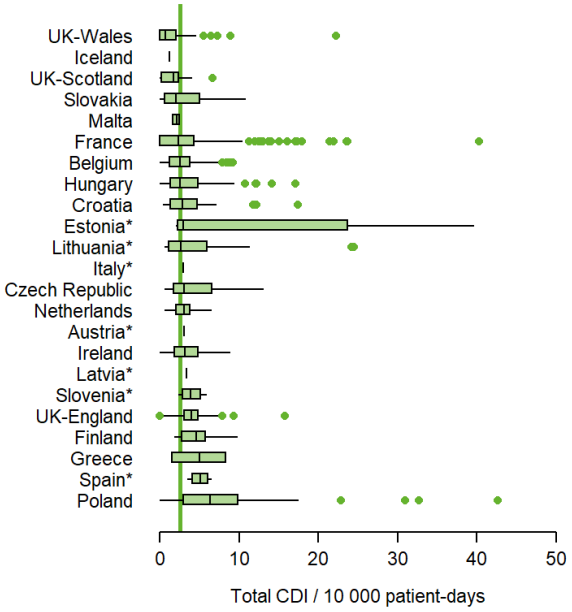
Information on CDI outcome was available for 11 568/26 825 (43.1%) cases, of which 2 029 (17.5%) cases died, from any cause. For the majority of the fatal cases (1 147/2 029; 56.5%), death was reported to have been unrelated to the CDI. This is not unexpected, considering that the McCabe scores provided by the attending physician indicated that 601/4 819 (12.5%) CDI cases had a 'rapidly fatal underlying disease', i.e. they were seriously ill patients. Indeed, 312 (51.9%) of these 601 patients died during the current hospitalisation. However, there were 480/11 568 (4.14%) cases with a known outcome who died, for whom CDI 'possibly' or 'definitely' contributed to their fatal outcome (Table 5). Amongst the CDI cases with information on underlying disease severity and outcome, the fatal cases that had CDI 'possibly'/'definitely' contributing to death were less likely to have had a 'rapidly fatal underlying illness' (78/242; 32.2%) than other fatal cases (234/562; 41.6%) (p=0.005).

Figure 2. Total CDI cases per 10 000 patient-days in participating hospitals by country/administration*, EU/EEA, 2016–2017



** UK devolved administrations are shown separately.*

Figure 3. Hospital-level incidence density of CDI cases, by country/administration, 2016–2017**



*Key: * <5 hospitals and <80% national beds; vertical green line: median incidence density of all hospital surveillance periods; ** UK devolved administrations are shown separately.*

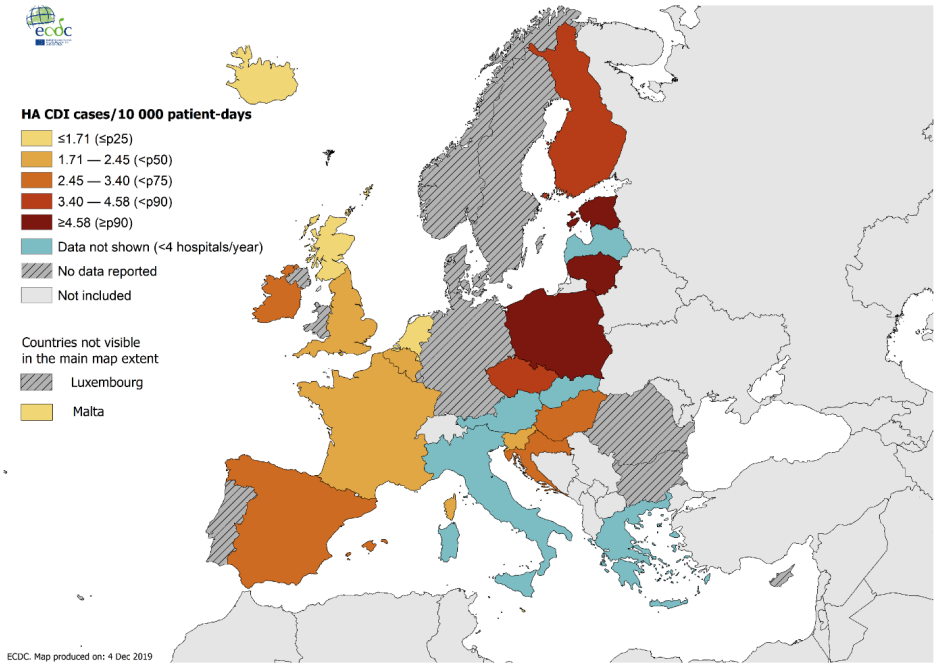
Healthcare-associated CDI cases

In 2016–2017, 23 052/37 857 (60.9%) cases were HA CDI and the crude incidence density of HA CDI was 2.12 cases/10 000 patient-days (Table 4). The vast majority of HA CDI cases had their origin in the current hospital (n=13 576/16 101; 84.3%), with far fewer having originated in another hospital (n=815; 5.1%), LTCF (n=514; 3.2%) or 'other healthcare' (n=228; 1.4%) (Table 5).

At country/administration level, the crude annual incidence density in 2016–2017 was the highest in Estonia, Lithuania and Poland (all in 2016; 4.69–5.99 cases/10 000 patient-days) and the lowest in Iceland, Malta, the Netherlands and UK-Scotland (all in 2017; 0.58–1.42 cases/10 000 patient-days; Table 2, Table 3, Figure 4 and Figure 5). The type of hospital with the highest mean hospital-level HA CDI incidence was tertiary hospitals, followed by secondary and specialised hospitals (Table 4 and Figure 6).

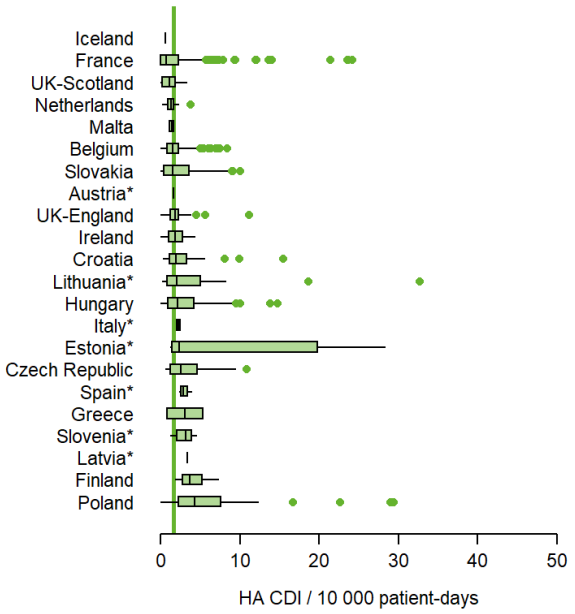
There were 1 674/8 400 (19.9%) HA CDI cases who died in hospitals during the surveillance period; and in 388/8 400 (4.61%) HA CDI cases, death was considered by the hospital to be 'possibly' or 'definitely' related to CDI. Considering that the ECDC PPS 2016–2017 estimated that there were 189 526 HA CDI cases in the EU/EEA annually (cumulative 95% CI: 105 154–340 978) [2], this suggests that there were 7 864 (95% CI: 4 363–14 148) deaths annually in the EU/EEA with HA CDI as a contributing cause.

Figure 4. Healthcare-associated CDI cases per 10 000 patient-days in participating hospitals by country/administration*, EU/EEA, 2016–2017



*Key: * UK devolved administrations are shown separately.*

Figure 5. Hospital-level incidence density of HA CDI cases, by country/administration, EU/EEA, 2016–2017**



*Key: * <5 hospitals and <80% national beds; vertical green line: median incidence density of all hospital surveillance periods; ** UK devolved administrations are shown separately.*

Community-associated CDI cases and CDI with unknown origin of cases

In 2016–2017, 12 366/37 857 (32.7%) cases were community-associated CDI or CDI with unknown origin of cases (CA/UA CDI) (Table 4). Case-level information was available for 5 351 CA CDI cases and 1 667 UA CDI cases. The vast majority of CA CDI cases had symptoms present on admission rather than appearing within the first two days of hospitalisation (n=2 821/3 076; 91.7%; no data available for n=2 275 CA CDI cases). The mean age of CA CDI cases (mean: 65.2 years; 95% CI: 64.6–65.8 years) was less than that of HA CDI cases (mean: 71.4 years; 95% CI: 71.1–71.7 years; p=0.001).

It was twice as common for CA CDI cases to report prior contact with an LTCF in the previous three months (n=107/787; 13.6%) than for all other types of CDI cases (n=324/5 076; 6.38%) (p<0.001). Also, there were 2 531/5 076 (49.9%) CA CDI cases that were reported to have had contact with an acute care hospital in the past three months. However, some of these may have been misclassified UA CDI cases, considering that the definition of a UA CDI includes admission (i.e. an overnight stay) to an acute care hospital in the previous 4–12 weeks. This would imply an under-estimation of the proportion of CA CDI cases that reported no contact with healthcare (2 071/5 076; 40.8%).

The CA CDI incidence density is presented in Tables 2–4, with patient-days and also patient admissions (or discharges) as a denominator. In 2016–2017, the crude incidence density of CA CDI was 0.41 cases/1 000 admissions (or discharges). Differences in country/administration-level CA CDI rates partially reflects differences in healthcare structure. In 2016–2017, the mean hospital-level annual incidence of CA CDI was the highest in primary hospitals, followed by secondary and tertiary hospitals (Table 4 and Figure 6).

Recurrent CDI cases

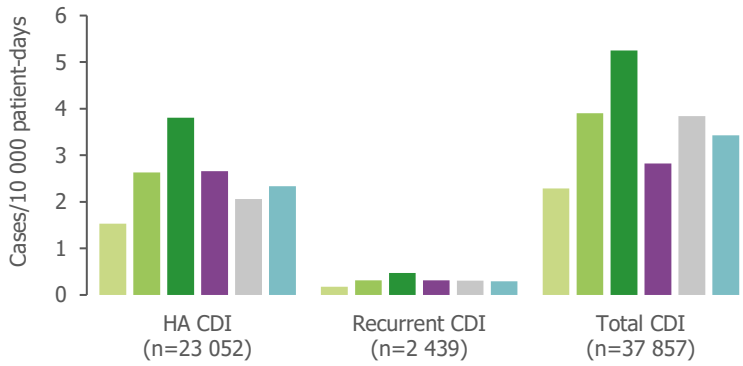
In 2016–2017, there were 2 439/37 857 (6.4%) cases classified as recurrent, with a crude incidence density of 0.22 recurrent CDI cases/10 000 patient-days. The mean hospital-level incidence density of recurrent CDI cases was the highest in tertiary hospitals, followed by secondary and primary hospitals (Table 4 and Figure 6).

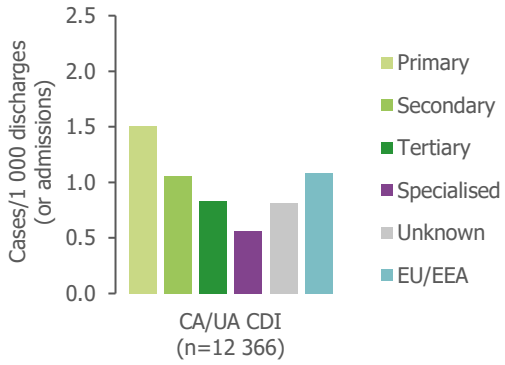
In the case-level data for 2016–2017, 1 988/23 358 (8.5%) CDI cases were reported to be recurrent cases (no data available for 3 467 cases). CDI symptoms were present on hospital admission for 853/1 350 (63.2%) recurrent cases (no data available for 638 recurrent cases). The McCabe score reported by the attending physician indicated that 200/460 (43.5%) recurrent cases were admitted for a disease deemed to be fatal within five years, including 53 cases expected to survive for less than a year. There were also 260/460 (56.5%) recurrent CDI cases with a non-fatal underlying disease, which presumably included cases admitted solely for recurrent CDI.

Recurrent CDI cases were twice as likely to have a complicated course of infection (290/1 162; 25.0%) than non-recurrent cases (1 140/8 079; 14.1%) (p<0.0001).

The outcome of CDI was reported for 1 176/1 988 (59.2%) recurrent cases, of which 160/1 176 (13.6%) died from any cause. Death was reported to be 'possibly' or 'definitely' related to CDI for 50/160 (31.3%) fatal recurrent CDI cases, which was higher than for fatal non-recurrent CDI cases (292/1 391; 21.0%) (p=0.003).

Figure 6. Mean incidence density in hospital surveillance periods in 2016–2017, by type of hospital and origin of CDI, EU/EEA





Key: HA CDI: healthcare-associated CDI; CA/UA CDI: community-associated CDI and CDI with unknown case origin; Total CDI: total cases, equal to HA CDI (n=23 052) + CA/UA CDI (n=12 366) + Recurrent CDI (n=2 439)

Table 2. Incidence of CDI cases by country/administration, type of hospital and origin of CDI, EU/EEA, 2016

2016		N of hospitals	HA CDI			CA/UA CDI					Recurrent CDI			Total CDI[a]		
				Inc. density (cases/10 000 pd)			Inc. density (cases/10 000 pd)		Incidence (cases/1 000 adm)			Inc. density (cases/10 000 pd)			Inc. density (cases/10 000 pd)	
			N	Crude	Mean	N	Crude	Mean	Crude	Mean	N	Crude	Mean	N	Crude	Mean
Country/administration[b] (N=23)	Austria	1	7	1.64	1.64	5	1.17	1.17	0.62	0.62	1	0.23	0.23	13	3.05	3.05
	Belgium	129	1 861	1.82	1.93	831	0.81	0.84	0.56	0.59	307	0.30	0.27	2 999	2.93	3.04
	Croatia	24	394	1.79	2.37	100	0.46	0.58	0.33	0.43	56	0.26	0.27	550	2.50	3.21
	Czechia	19	229	2.48	3.42	38	0.41	0.45	0.30	0.31	40	0.43	0.72	307	3.32	4.60
	Estonia	4	23	4.69	12.93	3	0.61	1.88	0.40	0.78	3	0.61	2.13	29	5.92	16.94
	Finland	13	518	3.58	3.85	71	0.49	0.78	0.14	0.21	ND	ND	ND	589	4.07	4.64
	France	203	588	1.92	2.52	507	1.66	1.60	0.86	1.28	ND	ND	ND	1 095	3.58	4.12
	Greece	2	15	2.07	3.09	6	0.83	1.03	0.79	0.83	4	0.55	0.84	25	3.45	4.96
	Hungary	94[c]	1 297	3.49	3.18	196	0.53	0.47	0.36	0.53	108	0.29	0.26	1 601	4.31	3.90
	Iceland	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	Ireland	1	6	3.02	3.02	2	1.01	1.01	1.01	1.01	1	0.50	0.50	9	4.52	4.52
	Italy	2	10	2.29	2.26	2	0.46	0.50	0.39	0.39	1	0.23	0.21	13	2.97	2.97
	Latvia	1	7	3.40	3.40	0	0.00	0.00	0.00	0.00	0	0.00	0.00	7	3.40	3.40
	Lithuania	3	59	5.99	7.88	6	0.61	0.78	0.45	0.50	9	0.91	1.37	74	7.51	10.03
	Malta	1	51	1.71	1.71	24	0.80	0.80	0.42	0.42	2	0.07	0.07	77	2.58	2.58
	Netherlands	22	446	1.48	1.36	376	1.25	1.24	0.67	0.64	138	0.46	0.44	960	3.19	3.04
	Poland	46	261	5.38	6.18	56	1.15	1.40	0.55	0.65	47	0.97	1.04	364	7.50	8.62
	Slovakia	37[c]	292	2.61	2.39	52	0.47	0.49	0.30	0.30	14	0.13	0.11	358	3.21	2.99
	Slovenia	3	17	2.07	2.49	6	0.73	0.79	0.44	0.45	1	0.12	0.08	24	2.92	3.37
	Spain	4	23	2.95	3.01	10	1.28	1.25	0.89	0.86	6	0.77	0.81	39	5.00	5.07
	UK-England	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	UK-Scotland	3	15	1.92	1.99	3	0.38	0.56	0.20	0.28	1	0.13	0.10	19	2.44	2.64
	UK-Wales	89	ND	ND	ND	629	1.82	1.24	1.37	3.00	42	0.12	0.18	671	1.95	1.41
	EU/EEA	701	6 119	2.01	2.87	2 923	0.96	1.08	0.10	1.06	781	0.26	0.36	9 823	3.22	3.83
Type of hospital																
	Primary	205	421	1.36	1.86	270	0.88	1.04	0.62	1.80	34	0.11	0.20	725	2.35	2.55
	Secondary	215	1 814	2.04	3.30	1 094	1.23	1.27	0.65	0.85	204	0.23	0.42	3 112	3.51	4.56
	Tertiary	92	1 775	2.41	4.43	640	0.87	1.16	0.50	0.89	203	0.28	0.55	2 618	3.55	5.95
	Specialised	58	196	2.43	4.17	71	0.88	0.92	0.95	0.53	32	0.40	0.60	299	3.71	4.01
	Unknown	131	1 913	1.85	1.96	848	0.82	0.84	0.56	0.58	308	0.30	0.27	3 069	2.96	3.07
	EU/EEA	701	6 119	2.01	2.87	2 923	0.96	1.08	0.10	1.06	781	0.26	0.36	9 823	3.22	3.83

Key: [a] Total cases are equal to (HA CDI + CA/UA CDI + Recurrent CDI); [b] UK devolved administrations are counted separately; [c] number of hospital surveillance periods rather than number of hospitals, because, in 2016, 1/36 hospitals in Slovakia and 36/58 hospitals in Hungary participated in two surveillance periods; Inc.: incidence; ND: no data; pd: patient-days; adm: patient discharges (or admissions); crude: N of cases divided by either 10 000 patient-days or 1 000 admissions (or discharges); mean: mean incidence density of participating hospitals.

Table 3. Incidence of CDI cases by country/administration, type of hospital and origin of CDI, EU/EEA, 2017

2017		N of hospitals	HA CDI			CA/UA CDI					Recurrent CDI			Total CDI[a]		
				Inc. density (cases/10 000 pd)			Inc. density (cases/10 000 pd)		Incidence (cases/1 000 adm)			Inc. density (cases/10 000 pd)			Inc. density (cases/10 000 pd)	
			N	Crude	Mean	N	Crude	Mean	Crude	Mean	N	Crude	Mean	N	Crude	Mean
Country/administration[b] (N=23)	Austria	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	Belgium	118	1 397	1.80	1.66	651	0.84	0.72	0.56	0.54	194	0.25	0.20	2 242	2.88	2.58
	Croatia	24	801	2.66	3.01	177	0.59	0.53	0.40	0.39	121	0.40	0.43	1 099	3.65	3.98
	Czechia	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	Estonia	2	14	2.11	1.93	5	0.75	0.86	0.72	3.86	1	0.15	0.12	20	3.02	2.91
	Finland	13	506	3.62	4.04	60	0.43	0.85	0.12	0.24	ND	ND	ND	566	4.04	4.88
	France	207	580	2.00	1.53	472	1.63	1.57	0.81	1.51	ND	ND	ND	1 052	3.63	3.10
	Greece	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	Hungary	92	5 403	3.17	2.49	537	0.32	0.28	0.27	0.33	322	0.19	0.17	6 262	3.67	2.93
	Iceland	1	13	0.58	0.58	1	0.04	0.04	0.09	0.09	13	0.58	0.58	27	1.20	1.20
	Ireland	55	993	2.52	1.89	732	1.85	1.39	1.08	0.81	181	0.46	0.28	1 906	4.83	3.56
	Italy	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	Latvia	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	Lithuania	16	348	2.11	4.36	114	0.69	2.36	0.53	1.52	92	0.56	2.10	554	3.35	8.82
	Malta	1	35	1.11	1.11	12	0.38	0.38	0.19	0.19	4	0.13	0.13	51	1.62	1.62
	Netherlands	22	374	1.32	1.22	375	1.32	1.27	0.70	0.68	129	0.45	0.40	878	3.09	2.90
	Poland	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	Slovakia	30	811	2.32	2.41	251	0.72	0.73	0.46	0.46	62	0.18	0.18	1 124	3.22	3.32
	Slovenia	1	52	4.58	4.58	4	0.35	0.35	0.20	0.20	11	0.97	0.97	67	5.90	5.90
	Spain	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	UK-England	147	4 987	1.93	1.89	5 127	1.98	1.97	0.96	0.95	407	0.16	0.15	10 521	4.07	4.00
	UK-Scotland	40	619	1.42	1.06	233	0.53	0.48	0.29	0.28	47	0.11	0.07	899	2.06	1.60
	UK-Wales	89	ND	ND	ND	692	2.05	1.12	1.50	3.06	74	0.22	0.12	766	2.27	1.24
	EU/EEA	**858**	**16 933**	**2.16**	**1.91**	**9 443**	**1.20**	**1.21**	**0.12**	**1.11**	**1 658**	**0.21**	**0.24**	**28 034**	**3.57**	**3.09**
Type of hospital																
	Primary	288	1 598	1.49	1.32	886	0.82	0.90	0.58	1.30	178	0.17	0.16	2 662	2.47	2.09
	Secondary	248	4 290	2.29	2.05	1 751	0.94	1.26	0.56	1.25	400	0.21	0.23	6 441	3.45	3.33
	Tertiary	74	5 138	2.89	3.03	1 470	0.83	1.15	0.53	0.75	510	0.29	0.36	7 118	4.00	4.38
	Specialised	82	492	1.44	1.75	88	0.26	0.60	0.28	0.58	69	0.20	0.12	649	1.90	1.99
	Unknown	166	5 415	1.95	2.14	5 248	1.89	1.98	0.94	0.99	501	0.18	0.34	11 164	4.02	4.46
	EU/EEA	**858**	**16 933**	**2.16**	**1.91**	**9 443**	**1.20**	**1.21**	**0.12**	**1.11**	**1 658**	**0.21**	**0.24**	**28 034**	**3.57**	**3.09**

Key: [a] Total cases are equal to (HA CDI + CA/UA CDI + Recurrent CDI); [b] UK devolved administrations are counted separately; Inc.: incidence; ND: no data; pd: patient-days; adm: patient discharges (or admissions); crude: N of cases divided by either 10 000 patient-days or 1 000 admissions (or discharges); mean: mean incidence density of participating hospitals.

Table 4. Incidence of CDI cases by country/administration, type of hospital and origin of CDI, EU/EEA, 2016–2017

2016–2017		N of hospital surveillance periods [c]	HA CDI			CA/UA CDI					Recurrent CDI			Total CDI[a]		
				Inc. density (cases/10 000 pd)			Inc. density (cases/10 000 pd)		Incidence (cases/1 000 adm)			Inc. density (cases/10 000 pd)			Inc. density (cases/10 000 pd)	
			N	Crude	Mean	N	Crude	Mean	Crude	Mean	N	Crude	Mean	N	Crude	Mean
Country/administration [b] (N=23)	Austria	1	7	1.64	1.64	5	1.17	1.17	0.62	0.62	1	0.23	0.23	13	3.05	3.05
	Belgium	247	3 258	1.81	1.81	1 482	0.82	0.78	0.56	0.56	501	0.28	0.24	5 241	2.91	2.83
	Croatia	48	1 195	2.29	2.69	277	0.53	0.56	0.37	0.41	177	0.34	0.35	1 649	3.16	3.60
	Czechia	19	229	2.48	3.42	38	0.41	0.45	0.30	0.31	40	0.43	0.72	307	3.32	4.60
	Estonia	6	37	3.21	9.26	8	0.69	1.54	0.55	1.80	4	0.35	1.46	49	4.25	12.26
	Finland	26	1 024	3.60	3.94	131	0.46	0.82	0.13	0.23	ND	ND	ND	1 155	4.06	4.76
	France	410	1 168	1.96	2.02	979	1.65	1.59	0.84	1.40	ND	ND	ND	2 147	3.61	3.60
	Greece	2	15	2.07	3.09	6	0.83	1.03	0.79	0.83	4	0.55	0.84	25	3.45	4.96
	Hungary	186 [c]	6 700	3.23	2.84	733	0.35	0.37	0.29	0.43	430	0.21	0.21	7 863	3.79	3.42
	Iceland	1	13	0.58	0.58	1	0.04	0.04	0.09	0.09	13	0.58	0.58	27	1.20	1.20
	Ireland	56	999	2.52	1.91	734	1.85	1.38	1.08	0.81	182	0.46	0.29	1 915	4.83	3.58
	Italy	2	10	2.29	2.26	2	0.46	0.50	0.39	0.39	1	0.23	0.21	13	2.97	2.97
	Latvia	1	7	3.40	3.40	0	0.00	0.00	0.00	0.00	0	0.00	0.00	7	3.40	3.40
	Lithuania	19	407	2.32	4.92	120	0.69	2.11	0.52	1.36	101	0.58	1.98	628	3.59	9.01
	Malta	2	86	1.40	1.41	36	0.59	0.59	0.30	0.31	6	0.10	0.10	128	2.09	2.10
	Netherlands	44	820	1.40	1.29	751	1.28	1.26	0.68	0.66	267	0.46	0.42	1 838	3.14	2.97
	Poland	46	261	5.38	6.18	56	1.15	1.40	0.55	0.65	47	0.97	1.04	364	7.50	8.62
	Slovakia	67 [c]	1 103	2.39	2.40	303	0.66	0.60	0.42	0.37	76	0.16	0.14	1 482	3.21	3.14
	Slovenia	4	69	3.52	3.02	10	0.51	0.68	0.29	0.39	12	0.61	0.30	91	4.65	4.00
	Spain	4	23	2.95	3.01	10	1.28	1.25	0.89	0.86	6	0.77	0.81	39	5.00	5.07
	UK-England	147	4 987	1.93	1.89	5 127	1.98	1.97	0.96	0.95	407	0.16	0.15	10 521	4.07	4.00
	UK-Scotland	43	634	1.43	1.12	236	0.53	0.48	0.28	0.28	48	0.11	0.07	918	2.07	1.68
	UK-Wales	178	ND	ND	ND	1 321	1.93	1.18	1.44	3.03	116	0.17	0.15	1 437	2.10	1.33
	EU/EEA	**1 559**	**23 052**	**2.12**	**2.34**	**12 366**	**1.14**	**1.15**	**0.41**	**1.08**	**2 439**	**0.22**	**0.29**	**37 857**	**3.48**	**3.43**
Type of hospital																
	Primary	493	2 019	1.46	1.53	1 156	0.84	0.95	0.59	1.51	212	0.15	0.18	3 387	2.45	2.28
	Secondary	463	6 104	2.21	2.63	2 845	1.03	1.27	0.59	1.06	604	0.22	0.31	9 553	3.46	3.90
	Tertiary	166	6 913	2.75	3.81	2 110	0.84	1.15	0.52	0.83	713	0.28	0.47	9 736	3.87	5.25
	Specialised	140	688	1.63	2.66	159	0.38	0.73	0.41	0.56	101	0.24	0.31	948	2.24	2.83
	Unknown	297	7 328	1.92	2.06	6 096	1.60	1.48	0.86	0.81	809	0.21	0.31	14 233	3.73	3.84
	EU/EEA	**1 559**	**23 052**	**2.12**	**2.34**	**12 366**	**1.14**	**1.15**	**0.41**	**1.08**	**2 439**	**0.22**	**0.29**	**37 857**	**3.48**	**3.43**

Key: [a] Total cases are equal to (HA CDI + CA/UA CDI + Recurrent CDI); [b] UK devolved administrations are counted separately; [c] number of hospital surveillance periods rather than number of hospitals, because, in 2016, 1/36 hospitals in Slovakia and 36/58 hospitals in Hungary participated in two surveillance periods; Inc.: incidence; ND: no data; pd: patient-days; adm: patient discharges (or admissions); crude: N of cases divided by either 10 000 patient-days or 1 000 admissions (or discharges); mean: mean incidence density of participating hospitals

Table 5. Descriptors of CDI cases and outcome of CDI, EU/EEA, 2016–2017

			2016	2017	2016–2017
			N (%*)	N (%*)	N (%*)
Previous healthcare admission**	Yes		1 876 (62.4)	1 570 (55.0)	3 446 (58.8)
		Hospital	1 627 (54.1)	1 213 (42.5)	2 840 (48.4)
		LTCF	121 (4.0)	310 (10.9)	431 (7.4)
		Both hospitals and LTCFs	3 (0.1)	17 (0.6)	20 (0.3)
		Other or unknown	125 (4.2)	30 (1.1)	155 (2.6)
	No		1 132 (37.6)	1 285 (45.0)	2 417 (41.2)
	Unknown		4 693	16 269	20 962
	Total*		**3 008 (100.0)**	**2 855 (100.0)**	**5 863 (100.0)**
McCabe score		Non-fatal (≥5 years)	1 453 (57.1)	1 402 (61.6)	2 855 (59.2)
		Ultimately fatal (1–4 years)	753 (29.6)	610 (26.8)	1 363 (28.3)
		Rapidly fatal (<1 year)	338 (13.3)	263 (11.6)	601 (12.5)
		Unknown	5 157	16 849	22 006
	Total*		**2 544 (100.0)**	**2 275 (100.0)**	**4 819 (100.0)**
CDI present at admission	Yes		2 420 (38.5)	2 867 (42.5)	5 287 (40.6)
	No		3 867 (61.5)	3 874 (57.5)	7 741 (59.4)
	Unknown		1 414	12 383	13 797
	Total*		6 287 (100.0)	6 741 (100.0)	13 028 (100.0)
Recurrent case	Yes		721 (12.4)	1 267 (7.2)	1 988 (8.5)
	No		5 086 (87.6)	16 284 (92.8)	21 370 (91.5)
	Unknown		1 894	1 573	3 467
	Total*		**5 807 (100.0)**	**17 551 (100.0)**	**23 358 (100.0)**
CDI case origin	HA CDI		5 385 (77.3)	10 716 (66.3)	16 101 (69.6)
		Current hospital	4 596 (66.0)	8 980 (55.6)	13 576 (58.7)
		Other hospital	369 (5.3)	446 (2.8)	815 (3.5)
		LTCF	146 (2.1)	368 (2.3)	514 (2.2)
		Other healthcare	165 (2.4)	63 (0.4)	228 (1.0)
		Unknown	109 (1.6)	859 (5.3)	968 (4.2)
	CA CDI		1 364 (19.6)	3 987 (24.7)	5 351 (23.1)
	UA CDI		219 (3.1)	1 448 (9.0)	1 667 (7.2)
	Unknown		733	2 973	3 706
	Total*		**6 968 (100.0)**	**16 151 (100.0)**	**23 119 (100.0)**
Complicated course	Yes		950 (15.1)	842 (14.5)	1 792 (14.8)
	No		5 333 (84.9)	4 972 (85.5)	10 305 (85.2)
	Unknown		1 418	13 310	14 728
	Total*		**6 283 (100.0)**	**5 814 (100.0)**	**12 097 (100.0)**
Patient outcome	Discharged alive		4 885 (80.5)	4 871 (80.7)	4 668 (84.4)
	Died		1 163 (19.3)	866 (15.6)	2 029 (17.5)
		Definitely or possibly related to CDI	225 (3.7)	255 (4.6)	480 (4.1)
		Not related to CDI	677 (11.2)	470 (8.5)	1 147 (9.9)
		Relationship to CDI unknown	261 (4.3)	141 (2.5)	402 (3.5)
	Unknown		1 667	13 590	15 257
	Total*		**6 034 (100.0)**	**5 534 (100.0)**	**11 568 (100.0)**

*Key: * for each indicator, the calculation of totals and percentages excludes all cases with an unknown status for that indicator; ** in the previous four weeks; LTCF: long-term care facility; HA: healthcare-associated; CA: community-associated; UA: CDI with unknown origin of cases.*

Microbiology

CDI testing

In 2016–2017, ESCMID-recommended diagnostic algorithms [3,4] were used during 902/1 175 (76.8%) hospital surveillance periods, whereas less optimal algorithms were used during 273/1 175 (23.2%) surveillance periods. No information was reported on the diagnostic algorithms used by 384 hospitals.

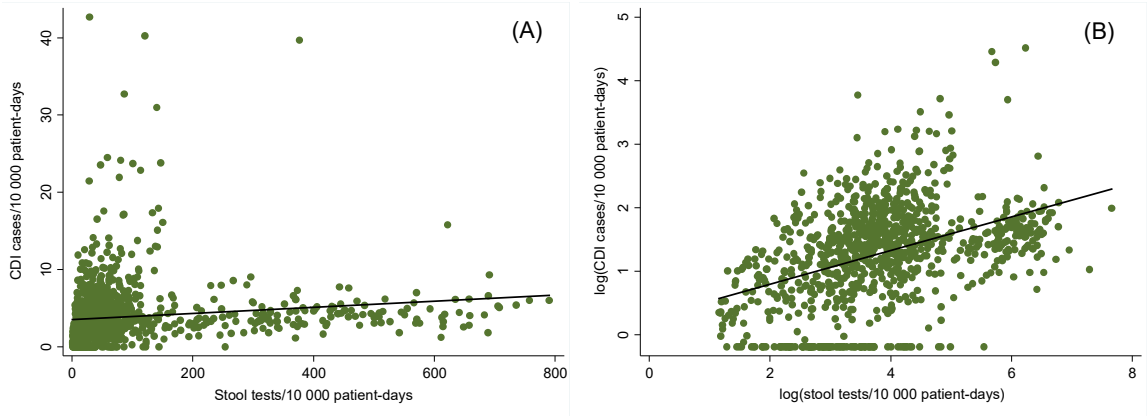
There were 1 355 668 reported stool tests for CDI, 32 788 of which (2.4%) were positive. There were 70 hospitals in six countries in which >50% stool samples were positive, which strongly suggests an insufficient testing rate in those hospitals. Their median size was 302 beds, and 45/70 (64.3%) were primary or secondary hospitals.

While the mean hospital rate of CDI testing in 2016–2017 was 96.1 stool tests/10 000 patient-days, the median rate was 38.6 stool tests/patient-days, partly because many hospitals tested infrequently, but also because UK-England reported over seven times the testing rate reported by other countries/administrations (418 and 58.0 tests/10 000 patient-days, respectively).

The median testing rate was higher in tertiary hospitals (47.1 tests/10 000 patient-days) than in secondary or primary hospitals (39.3 and 20.7 tests/10 000 patient-days, respectively).

In 2016–2017, the incidence density of CDI cases was correlated[2] with the incidence density of stool tests for CDI in the participating hospitals (Spearman's rho=0.45; Figure 7), i.e. hospitals that performed more stool tests for CDI in 2016–2017 found more CDI and vice versa. When the regression model was adjusted for country/administration, the percentage of data explained by the model increased from 17% to 37%, suggesting that a sizeable portion of the differences in CDI incidence are explained by country/administration-level differences other than simply CDI testing rates alone.

Figure 7. Incidence density* of CDI case and CDI testing in participating hospitals in (A) linear scale; and (B) log scale, EU/EEA, 2016–2017



*Key: *cases or tests/10 000 patient-days; one dot represents one hospital surveillance period, solid line represents linear trend. (A) incidence density of total CDI and incidence density of total stool testing (Spearman's rho=0.45); and (B) log-transformed incidence density of total CDI and log-transformed incidence density of total stool testing (Spearman's rho=0.45).*

Tests of toxin production

In 2016–2017, data on the detection of toxins A/B and binary toxin was reported by 12/13 and 8/13 countries/administrations that used the enhanced surveillance option, respectively. Toxins A/B was detected in isolates from 4 617/4 865 (94.9%) CDI cases with data available. Binary toxin genes were detected in 461/754 (61.1%) CDI cases with data available.

In 2016–2017, there were 752 cases with data available on both production of toxins A/B and the presence of binary toxin genes. Of these, 446 (59.3%) cases tested positive for both, 281 (37.3%) tested positive for toxins A/B but negative for binary toxin genes, and 13 (1.7%) only tested positive for binary toxin genes.

[2] Linear regression of log-transformed incidence density of CDI tests per 10 000 patient-days and total CDI cases per 10 000 patient-days, by hospital in 2016–2017 has r^2: 0.17.

Table 6. CDI testing frequency by country/administration and type of hospital, EU/EEA, 2016–2017

		2016				2017			
		N of hospitals [a,b]	Crude positivity rate t/T (%)	Testing rate (tests/10 000 pd)		N of hospitals [a]	Crude positivity rate t/T (%)	Testing rate (tests/10 000 pd)	
				Crude	Median			Crude	Median
Country/administration (N=23) [c]	Austria	1	12/418 (2.9)	98.1	98.1	0	ND/ND (NA)	ND	ND
	Belgium	0	ND/ND (NA)	ND	ND	76	ND/41 708 (NA)	75.7	62.7
	Croatia	24	636/4 937 (12.9)	22.5	19.8	24	1 220/11 046 (11.0)	36.6	27.8
	Czechia	19	360/2 929 (12.3)	31.7	36.1	0	ND/ND (NA)	ND	ND
	Estonia	4	31/285 (10.9)	58.2	87.6	2	24/374 (6.4)	56.4	63.0
	Finland	13	ND/16 406 (NA)	113.3	108.5	10	ND/14 379 (NA)	126.9	128.5
	France	203	1 434/14 474 (9.9)	47.4	39.0	207	1 337/13 099 (10.2)	45.3	35.3
	Greece	2	21/284 (7.4)	39.2	45.9	0	ND/ND (NA)	ND	ND
	Hungary	94 [b]	1 966/10 740 (18.3)	28.9	19.7	85	8 723/37 527 (23.2)	24.1	12.4
	Iceland	0	ND/ND (NA)	ND	ND	0	ND/ND (NA)	ND	ND
	Ireland	1	19/332 (5.7)	166.9	166.9	0	1 904/ND (NA)	ND	ND
	Italy	1	17/111 (15.3)	55.3	55.3	0	ND/ND (NA)	ND	ND
	Latvia	1	9/58 (15.5)	28.1	28.1	0	ND/ND (NA)	ND	ND
	Lithuania	3	66/247 (26.7)	25.1	21.9	16	478/2 953 (16.2)	17.9	13.1
	Malta	1	80/2 197 (3.6)	73.5	73.5	1	57/2 362 (2.4)	75.0	75.0
	Netherlands	21	2 165/31 749 (6.8)	108.5	98.6	21	2 240/32 014 (7.0)	115.9	98.2
	Poland	46	343/1 617 (21.2)	33.3	29.0	0	ND/ND (NA)	ND	ND
	Slovakia	37 [b]	507/4 463 (11.4)	40.0	31.0	30	2 766/13 328 (20.8)	38.1	26.7
	Slovenia	3	24/265 (9.1)	32.2	36.1	1	87/530 (16.4)	46.7	46.7
	Spain	4	33/469 (7.0)	60.1	63.4	0	ND/ND (NA)	ND	ND
	UK-England	0	ND/ND (NA)	ND	ND	138	3 407/1 032 914 (0.3)	417.7	401.5
	UK-Scotland	3	16/529 (3.0)	67.8	64.8	11	1 485/60 924 (2.4)	257.8	260.7
	UK-Wales	0	ND/ND (NA)	ND	ND	0	ND/ND (NA)	ND	ND
	EU/EEA	**481**	**8 368/92 510 (9.0)**	**48.5**	**31.5**	**622**	**24 420/1 263 158 (1.9)**	**177.1**	**49.2**
Type of hospital									
	Primary	154	943/9 294 (10.1)	40.1	17.4	182	1 449/40 308 (3.6)	52.3	24.7
	Secondary	200	4 127/43 160 (9.6)	62.9	40.0	188	8 875/100 300 (8.8)	74.4	39.0
	Tertiary	89	2 924/37 079 (7.9)	54.3	41.3	55	9 427/83 373 (11.3)	62.6	58.6
	Specialised	36	364/1 823 (20.0)	31.1	29.2	41	745/2 941 (25.3)	11.3	7.4
	Unknown	2	10/1 154 (0.9)	81.0	75.5	156	3 924/1 036 236 (0.4)	391.1	370.2
	EU/EEA	**481**	**8 368/92 510 (9.0)**	**55.3**	**31.5**	**622**	**24 420/1 263 158 (1.9)**	**198.6**	**49.2**

Key: [a] hospital surveillance periods that included data sufficient to count the crude positivity rate; [b] refers to the number of hospital surveillance periods rather than number of hospitals, because, in 2016, 1/36 hospitals in Slovakia and 36/58 hospitals in Hungary participated in two surveillance periods; [c] UK devolved administrations are counted separately; t: number of stool tests that were positive for CDI; T: number of stool tests for CDI; ND: no data; pd: patient-days; adm: patient admissions (or discharges); NA: not applicable; ND: no data

PCR ribotyping

Nine countries/administrations reported PCR RT data for their CDI cases, of which three countries/administrations (Belgium, the Netherlands and UK-Wales) reported 3 889/4 865 (80.1%) of these PCR RT data (Table 7). Therefore, although the PCR RT data were representative of strains in Belgium, Ireland and the Netherlands, they are not likely to be representative of the EU/EEA as a whole.

Fourteen of the 20 most frequently reported RTs in 2016–2017 were *C. difficile* Clade 1, i.e. RT001, RT002, RT003, RT005, RT011, RT012, RT013, RT014/020, RT015, RT029, RT050, RT070, RT081 and RT106 [23]. Together, these comprised 2 466/4 865 (50.7%) strains for CDI cases with RT data (Table 7). At country/administration-level, the most common or the second most commonly reported RT was RT014/020 (7/9 countries/administrations), RT001 (3/9 countries/administrations) or RT002 (3/9 countries/administrations) (Table 7 and Figure 8).

RT027, which is known for its hypervirulence [4,6], was the third most frequently reported RT overall in 2016–2017, with majority of the RT027 cases reported by Hungary (238/394; 60.4%). Indeed, RT027 was notably prevalent in the cases reported by Hungary (67.6%), Poland (63.0%) and Slovenia (44.4%). By comparison, RT027 was much less common in the other six countries/administrations that reported RT data (n=111/4 390; 2.5%) (Table 7 and Figure 8).

RT027 is within *C. difficile* Clade 2, multi-locus sequence type (MLST) 1. The other ST1 RTs that were reported to ECDC were, RT176 (n=61), RT036/198 (n=16), RT016 (n=3) and RT181 (n=3). Four countries (Czechia, Hungary, Poland and Slovakia) reported 78/86 (90.7%) of these RT027-like RTs. For example, Hungary reported 13/16 cases that were RT036 (Table 7).

ECDC CDI surveillance does not provide an early warning system for emerging RTs, but may provide some indication of emerging strains becoming established. For example, only three CDI cases of the RT027-like RT181 were reported in both 2016 and 2017, whilst ECDIS-Net-2 received requests to type strains from multi-hospital outbreaks in 2019 that were predominantly RT181.

The fourth most frequent RT, RT078 (Clade 5, ST11), is commonly detected in one-health investigations, notably in pigs [24]. RT078 represented 7%–11% of the RTs reported by four countries (Belgium, Czechia, Ireland and the Netherlands) (Table 7 and Figure 8).

Antimicrobial susceptibility

In 2016–2017, six countries/administrations (Czechia, Hungary, the Netherlands, Poland, Slovakia and UK-Scotland) reported data on the susceptibility of *C. difficile* isolates from CDI cases to metronidazole, of which five countries/administrations also reported data on susceptibility to moxifloxacin and vancomycin.

Moxifloxacin resistance was reported for 365/536 (68.1%) cases with data on moxifloxacin susceptibility.

Metronidazole resistance was reported for 27/571 (4.7%) cases with data on metronidazole susceptibility. All 27 cases had the minimal inhibitory concentration (MIC) for metronidazole measured using an E-test [25]. The reported MICs exceeded the EUCAST clinical breakpoint for resistance (>2mg/L), which is based on ECOFFs, and none exceeded the CLSI breakpoint for resistance (≥32mg/L). Slovakia reported 13/79 (16.5%) cases with metronidazole-resistant isolates, also tested using an E-test. However, these isolates were found to be metronidazole-susceptible when retested by a central reference laboratory using agar dilution [26], which is considered the 'gold' standard.

All but one of the metronidazole-resistant isolates were RT027 (20/26; 76.9%) or the RT027-like strain RT036/198 (5/26; 19.2%). All metronidazole-resistant RT027 and RT036/198 isolates were reported to be resistant to moxifloxacin. This co-resistance is not unexpected, as moxifloxacin resistance was commonly reported for isolates from Clade 2, for example RT027 (218/243 isolates; 89.7%), RT176 (47/50 isolates; 94.0%) and RT036/198 (11/12 isolates; 91.7%). These three Clade 2 RTs comprised 276/394 (70.1%) of all moxifloxacin-resistant isolates. RT001, which is an RT from Clade 1, was the third most frequently reported moxifloxacin-resistant RT (55/394; 14.0%).

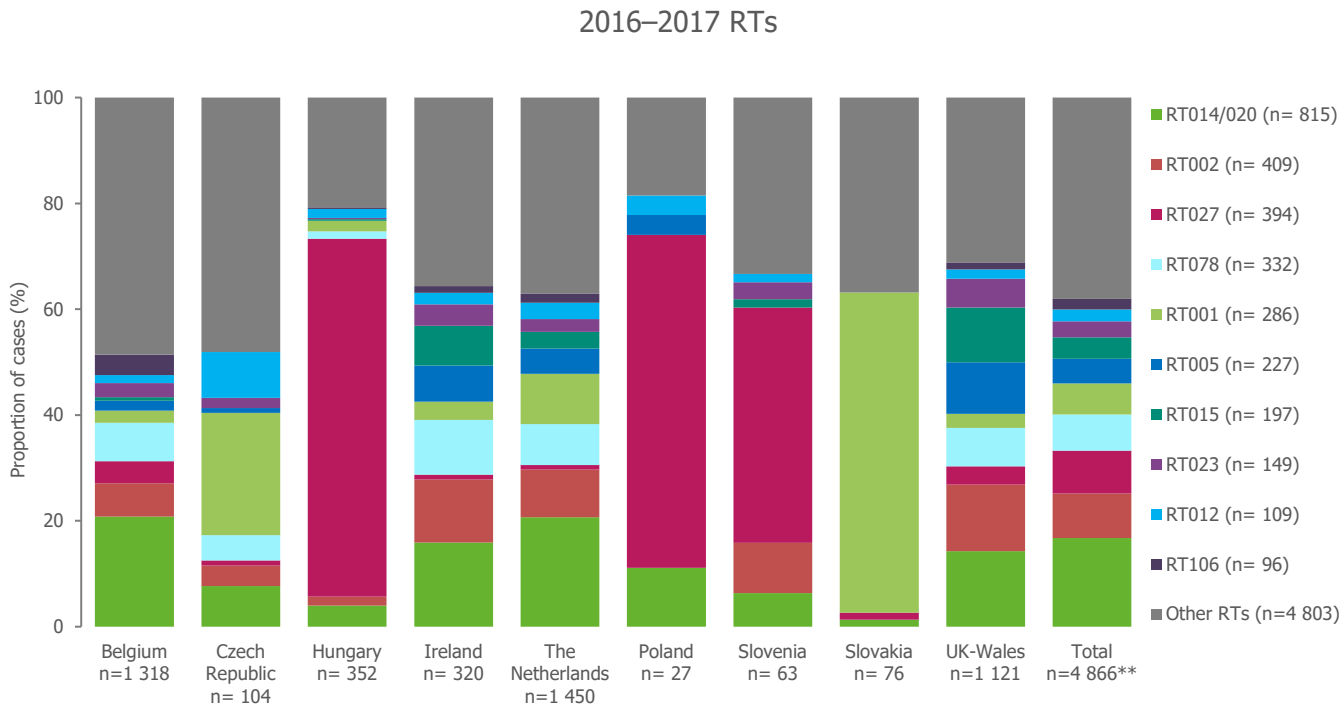
One case was reported to have an isolate that was resistant to vancomycin with an MIC of 6 mg/L, as tested by an E-Test at the NRL in Czechia, although testing of this isolate by the ECDIS-Net-2 reference laboratory (LUMC, the Netherlands) found it to be susceptible to vancomycin.

Table 7. PCR ribotypes of strains from CDI cases, nine EU/EEA countries or administrations, 2016–2017 (N=4 865 isolates; N=10/33 countries or administrations[a,b])

PCR ribotype	Country/administration									
	BE	CZ	HU	IE	NL	PL	SI	SK	UK-WLS	Total (%)
RT014/020	274	8	14	51	300	3	4	1	160	815 (16.8)
RT002	83	4	6	38	131	0	6	0	141	409 (8.4)
RT027	55	1	238	3	12	17	28	1	39	394 (8.1)
RT078	96	5	5	33	112	0	0	0	81	332 (6.8)
RT001	30	24	7	11	138	0	0	46	30	286 (5.9)
RT005	25	1	0	22	69	1	0	0	109	227 (4.7)
RT015	9	0	1	24	46	0	1	0	116	197 (4.0)
RT023	35	2	1	13	35	0	2	0	61	149 (3.1)
RT012	20	9	6	7	45	1	1	0	20	109 (2.2)
RT106	51	0	1	4	25	0	0	0	15	96 (2.0)
RT126	9	1	1	0	51	0	0	0	13	76[b] (1.6)
RT176[b]	0	22	15	0	0	1	0	23	0	61 (1.3)
RT017	14	0	0	8	22	2	0	3	8	57 (1.2)
RT003	12	1	0	5	16	0	0	0	22	56 (1.2)
RT029	14	3	1	9	17	1	0	0	7	52 (1.1)
RT011	2	0	1	7	18	0	0	0	22	50 (1.0)
RT081	14	3	3	2	18	0	0	0	8	48 (1.0)
RT070	17	2	0	3	13	0	0	1	7	43 (0.9)
RT013	0	2	0	3	11	0	0	0	24	40 (0.8)
RT050	2	0	0	2	13	0	0	0	21	38 (0.8)
RT026	3	0	0	5	11	0	0	0	17	36 (0.7)
RT054	3	0	0	3	10	0	0	0	19	35 (0.7)
RT087	16	1	0	0	9	0	0	0	9	35 (0.7)
Belgium-005	34	0	0	0	0	0	0	0	0	34 (0.7)
RT018	0	0	1	6	4	1	0	0	22	34 (0.7)
Belgium-015	32	0	0	0	0	0	0	0	0	32 (0.7)
RT056	6	1	1	4	1	0	0	0	19	32 (0.7)
RT076	8	0	0	3	11	0	0	0	7	29 (0.6)
RT046	2	0	1	3	9	0	0	0	13	28 (0.6)
RT072	19	0	0	0	2	0	0	0	4	25 (0.5)
Belgium-076	24	0	0	0	0	0	0	0	0	24 (0.5)
RT265	0	0	0	0	24	0	0	0	0	24 (0.5)
Total (RTs with ≥24 reports in 2016–2017)	**909**	**90**	**303**	**269**	**1 173**	**27**	**42**	**75**	**1 014**	**3 903**
N=3–23 reports in 2016–2017 (n=83; RT024, RT216, RT036, RT137, RT258, RT010, RT021, RT039, RT220, Belgium-010, Belgium-126, Belgium-207, Belgium-258, RT328, Belgium-296, RT001/072, Belgium-002, Belgium-026, Belgium-052, Belgium-2, Belgium-054, Belgium-154, Belgium-216, Belgium-328, Belgium-430, RT009, RT042, Belgium-011, RT035, RT045, RT052, RT057, RT059, RT156, Belgium-006, Belgium-081, Belgium-093, Belgium-103, 'Belgium-220*', RT034, Belgium 12a, RT077, RT103, RT181[c], Belgium-014, 'Belgium-014*', Belgium-050, Belgium-127, RT031, RT053, RT062, RT083, RT163, RT351, Belgium-001, Belgium-039, Belgium-107, Belgium-159, RT006, RT154, RT449, Belgium-013, Belgium-015*, Belgium-046, Belgium-057, Belgium-193, Belgium-220, Belgium-265, 'Belgium-284*', Belgium-473, Belgium-555, RT002/014, RT007, RT016, RT022, RT037, RT043, RT049, RT066, RT097, RT127, RT150, RT175, RT454)									548 (11.9)
N=1 or N=2 reports in 2016–2017 (n=194)										381 (7.8)
Total (All isolates)	**1 318**	**104**	**352**	**320**	**1 450**	**27**	**63**	**76**	**1 121**	**4 865 (100.0)**

Key: RT — PCR ribotype; [a] UK devolved administrations shown separately; [b] UK-Scotland (not shown in the table) reported the RT of one CDI case, which was RT126, that is included in the total rows; [c] AI33 and RT181 are near-identical by CE PCR ribotyping. BE: Belgium, CZ: Czechia, HU: Hungary, IE: Ireland, NL: the Netherlands, PL: Poland, SI: Slovenia, SK: Slovakia, UK-WLS: UK-Wales.

Figure 8. PCR ribotypes of CDI cases by country/administration*, nine EU/EEA countries or administrations, 2016–2017



*Key: * UK devolved administrations are shown separately; **N=1 RT126 not shown for UK-Scotland*

Discussion

Use of a common CDI surveillance protocol enabled the acquisition of comparable data for analysis [1]. Data from the 'minimal' surveillance option, which was used almost as frequently as the 'enhanced' option, yielded useful epidemiological information from its 12 collected variables, such as incidence, testing frequency and the testing methodology.

Although the reported annual CDI incidence density declined between 2016 and 2017, this was largely due to the conversion of compatible national surveillance data from countries/administrations with long-established comprehensive national CDI surveillance and lower CDI incidence [27]. The ECDC point prevalence surveys (PPSs) in acute care hospitals identified an increasing prevalence of CDI in EU/EEA countries between 2011–2012 and 2016–2017 (3.6% and 4.8%, respectively) [2]. The ECDC CDI incidence data for 2016–2017 indicate that in 1 in 24 HA CDI cases who died, CDI was a potential factor contributing to death. By combining the analysis from these two datasets, ECDC estimates that there were about 8 700 deaths annually in the EU/EEA with HA CDI as a contributing cause.

Even though the case fatality for CDI is notable, other serious outcomes of CDI were relatively common, with 14.8% cases having a 'complicated course of infection', which includes the requirement for admission to an intensive care unit, or surgery (colectomy) for toxic megacolon, perforation or refractory colitis.

Recurrent cases have a higher morbidity and longer hospital stays than non-recurrent cases [28,29]. Due to the ECDC definition, the reported recurrent cases include both patients who incompletely recovered from a CDI episode as well as patients who were infected with a different strain, following a full recovery from a previous episode of CDI. In the ECDC incidence data for 2016–2017, recurrent CDI cases were twice as likely to have a 'complicated course of infection' compared to non-recurrent cases, and 1.5-times more likely to have a fatal outcome with CDI as a possible contributing cause. Guidelines from ESCMID, the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) recognise the strong evidence for the effectiveness of faeces microbiota transplantation (FMT) for the treatment of multiple recurrent CDI episodes [7,8].

A common perception is that patients from LTCFs are a significant reservoir of CDI cases in hospitals. In the 2016–2017 surveillance data, LTCF contact was only reported for 12.5% CDI cases who reported any healthcare contact in the three months prior to the current hospitalisation. Moreover, only 1 in 20 HA CDI cases had the origin associated with an LTCF, whereas the overwhelming majority (almost 7 in 8) originated from the current hospital. Additionally, at least 40% CA CDI cases had not had contact with healthcare, which is likely to be an under-estimate, due to the likelihood of some misclassification of UA CDI cases as CA CDI cases.

ECDC's ECDIS-Net surveys estimated that the proportion of European laboratories using the recommended diagnostic algorithm for CDI increased from 29% in 2011 to 61% in 2014 [30]. From ECDC incidence surveillance, it appeared that this increase continued in 2016–2017, with over three quarters of participating hospitals using ESCMID-recommended diagnostic algorithms [3,4]. The increase in the rates of stool testing for CDI between the two ECDC PPSs was a positive development. However, the differences in testing rates in the ECDC CDI incidence surveillance, between or even within countries for CDI suggest that the optimal testing practices are not being applied by all hospitals.

The 10 European countries/administrations that reported RT data in 2016–2017 are all in the west, centre and east of Europe, with none in the north or south. Still, there was a striking pattern in the reported data. The Visegrád Group of countries (Czechia, Hungary, Poland and Slovakia) reported a high proportion of cases that had RT027 and/or RT027-like strains. Conversely, this proportion was lower in the countries in the west of Europe that reported ribotype data in 2016–2017, even though they had reported high proportions of RT027 in the 2000s [5]. Strategies to reduce the incidence of RT027 *C. difficile* strains have included implementation of comprehensive national CDI surveillance, including subtyping of isolates; and antimicrobial stewardship, including for fluoroquinolones [6,31].

Although the RT-specific moxifloxacin resistance observed in this 2016–2017 incidence data is well documented, the apparent emergence of metronidazole resistance and a report of vancomycin resistance is of concern as they are among the first-line treatment options for CDI in certain cases [7,8,27]. Therefore, EU/EEA countries should consider confirming metronidazole and vancomycin resistance of *C. difficile* isolates by agar dilution methods with additional investigations to elucidate the transmission mechanisms [32]. Additionally, plasmid-mediated metronidazole resistance has recently been reported for *C. difficile*, with some evidence of horizontal plasmid transfer [33].

Public health implications

The participation in the coordinated surveillance of CDI, by >1 in 10 acute care hospitals from over two-thirds of all the EU/EEA countries during the first two years of ECDC-coordinated CDI surveillance, underscores the importance of CDI prevention and control in Europe. ECDC recommends that all countries implement CDI surveillance. This is also recommended by the 2019 ESCMID guidance for the prevention and control of CDI in acute care hospitals, which was generated through a systematic review [34]. In this guidance, the strongest quality of evidence is for antimicrobial stewardship, particularly restricting the use of certain antimicrobial classes/agents. This strength of the evidence for antimicrobial stewardship to reduce CDI incidence is confirmed by independent meta-analyses [35,36].

In November 2018, following a review of the side effects of quinolones (J01M) and fluoroquinolones (J01MA), the European Medicines Agency (EMA) concluded that the marketing authorisation of four quinolones should be suspended and recommended that national authorities implement restrictions on the prescription of all other fluoroquinolones/quinolones. The restrictions meant that other fluoroquinolones/quinolones should not be used a) to treat infections that may improve without treatment or are not severe (such as throat infections); b) for non-bacterial infections; c) as prophylaxis for travellers' diarrhoea or recurring lower urinary tract infections; or d) for mild or moderate bacterial infections, unless other antibacterial medicines commonly recommended for these infections cannot be used [37]. On 11 March 2019, the European Commission issued a legally binding decision based on this advice [38]. Although it was not a consideration for the EMA conclusion, restriction of the use of fluoroquinolones/quinolones in acute care hospitals in the EU/EEA has the potential to reduce the incidence of infections with fluoroquinolone-resistant *C. difficile* subtypes [6,31,34-36].

In 2019, ECDC worked with nationally designated representatives from EU/EEA countries (National Focal Points for healthcare-associated infections, and Operational Contact Points for epidemiology and microbiology for CDI) to incorporate the structure and process indicators of CDI prevention and control that were recommended in the 2018 ESCMID guidance, into an update of the ECDC CDI surveillance protocol [34,39]. These include voluntary hospital-level surveillance of antimicrobial consumption, most preferably for fluoroquinolones (Anatomical Therapeutic Chemical classification system (ATC) group J01MA), and also, if possible, for the total 'antibacterials for systemic use' (J01), cephalosporins (J01DB–J01DE), amoxicillin-clavulanic acid (J01CR02) and clindamycin (J01FF01).

The activities of ECDIS-Net-2 helped to ensure that optimal CDI diagnostic and typing practices were used in hospitals in the EU/EEA, particularly promotion of the ECDC standard operating procedure (SOP) for diagnostics as well as typing and support to harmonisation of RT nomenclature. The ECDC surveillance protocol recommends that hospitals that are not typing *C. difficile* strains do consider storing samples if feasible, in case of a future opportunity to retrospectively confirm the distribution of notable strains.

The apparent emergence of metronidazole resistance is of concern as it was commonly used in the first-line treatment of CDI [7]. The 2021 update of the ESCMID guidelines no longer recommends metronidazole for treatment of CDI when fidaxomicin or vancomycin are available [9]. Indeed, the 2021 updates of both the ESCMID and IDSA-SHEA guidelines recommend fidaxomicin, or otherwise vancomycin, as the preferred treatment for an initial CDI episode [9,40]. EU/EEA countries should consider confirming metronidazole resistance and vancomycin resistance of *C. difficile* isolates by agar dilution methods with additional investigations to elucidate the transmission mechanisms.

Annex 1. Surveillance systems overview, 2016–2017

Country / administration*	Data Source	Hospital surveillance periods**		Sentinel	Comprehensive	Surveillance option	Case definition
		2016	2017				
Belgium	BE-HAICDI	129	118	N	Y	L, M	EU
Croatia	HR-HAI	26	0	UNK	UNK	L	EU
Czechia	CZ-HAI	19	0	Y	N	E	EU
Estonia	EE-HAIICU	4	2	UNK	UNK	M, L	EU
Finland	FI-SIRO	13	13	Y	N	L	EU
France	FR-RAISIN	203	207	N	Y	M	EU
Hungary	HU-CDI	94	92	UNK	UNK	M, L, E	EU
Iceland	IS-HAI	0	1	UNK	UNK	E	EU
Ireland	IE-HAI-CDI	0	55	N	Y	L, E	EU
Latvia	LV-HAICDI	1	0	UNK	UNK	L	EU
Lithuania	LT-Institute of Hygiene	0	16	UNK	UNK	L, E	EU
Malta	MT-MDH-ICU	1	1	N	Y	L	EU
Netherlands	NL-HAICDI	22	22	Y	N	E	EU
Poland	PL-HAICDI	46	0	UNK	UNK	M, L, E	EU
Slovakia	SK-HAI	36	30	UNK	UNK	M, E	EU
Slovenia	SI-HAICDI	3	1	UNK	UNK	E	EU
Spain	ES-HAICDI	4	0	UNK	UNK	L	EU
UK-England	UK-EN-CDI	0	147	UNK	UNK	M, E	EU
UK-Scotland	UK-SC-CDI	3	40	N	Y	M, E	EU
UK-Wales	UK-WLS-CDI	89	89	UNK	UNK	M, L	EU

*Key: * UK devolved administrations are shown separately; ** hospitals had one or more surveillance periods per year, each ranging from a minimum duration of three months to a maximum of 12 months. In 2016, 1/36 hospitals in Slovakia and 36/58 hospitals in Hungary participated in two surveillance periods; Y: yes; N: no; UNK: unknown; M: minimal; L: light; E: enhanced; EU: case definition specified in ECDC protocol v2.2—v2.3 and EU/2018/945.*

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