

SURVEILLANCE REPORT

Clostridioides difficile infections

Annual Epidemiological Report for 2018–2020

Key facts

- This report presents surveillance data on *Clostridioides* (*Clostridium*) *difficile* infection (CDI) in acute care hospitals in European Union/European Economic Area (EU/EEA) countries, the UK, and Serbia. It includes previously unpublished data from 2018–2020 with a focus on data from 2020, and comparisons with previous years. Since the European Centre for Disease Prevention and Control (ECDC) began coordinating this surveillance on 1 January 2016, 26 countries/administrations have reported CDI data to the Centre, corresponding to 331 million patient-days.
- In 2020, and 2021, ECDC did not issue a formal data call for CDI surveillance data, recognising the priority for national and EU responses to COVID-19 in the EU/EEA. As a result, fewer countries reported CDI data, especially case-based CDI data, for 2020 than for previous years. For 2018, 15 countries reported CDI data, for 2019, 13 countries reported and for 2020 eight countries reported. Therefore, year-on-year comparisons at EU/EEA level should be made with caution, and the reported surveillance data for 2020 have insufficient coverage to draw definitive conclusions on how the COVID-19 pandemic affected CDI in the EU/EEA.
- Overall, data for a total of 1 798 hospital surveillance periods were reported by 17 countries for 2018–2020. For 2020, 736 hospital surveillance periods were reported by eight countries (Austria, Estonia, Germany, Hungary, Ireland, Lithuania, Portugal, and Slovenia), two of which (Germany and Portugal) submitted data for the first time. Germany provided the largest dataset (554 hospital surveillance periods, 75% of the total for 2020) after converting its national CDI surveillance data to the ECDC data specification.
- For healthcare-associated (HA) CDI, the reported mean hospital incidence density was 2.58 (95% CI: 2.42–2.75, median: 2.05) cases per 10 000 patient-days in 2020, compared to 2.02 (95% CI: 1.82–2.24, median: 1.50) in 2019 and 2.79 (95% CI: 1.83–4.04, median: 1.70) in 2018. For community-associated or unknown association (CA/UA) CDI, the reported mean hospital incidence was 1.35 (95% CI: 1.23–1.48, median: 1.03) cases per 1 000 patient discharges or admissions in 2020, compared to 0.69 (95% CI: 0.56–0.84, median: 0.47) in 2019 and 0.69 (95% CI: 0.59–0.79, median: 0.41) in 2018. The 2020 datum for CA/UA CDI is strongly influenced by Germany's sample, which is both the largest in the 2020 dataset and is also characterised by a comparatively higher incidence of CA/UA CDI than the other countries/administrations. For recurrent CDI, the reported mean hospital incidence was 0.25 (95% CI: 0.21–0.30; median: 0.06) cases per 1 000 patient discharges or admissions in 2020, 0.27 (95% CI: 0.15–0.43, median: 0.06) in 2019, and 0.24 (95% CI: 0.16–0.36; median: 0.06) in 2018.
- Only six countries (Austria, Estonia, Ireland, Lithuania, Portugal and Slovenia) reported case-based data for 2020, covering 2 568 CDI cases, compared to 11 countries in 2019 (17 592 cases), and 13 countries (20 990 cases) in 2018. Most case-based data were reported by Ireland (66% of cases) for 2020 and by the UK (England) for 2019 and 2018 (67.7% and 60.2%, respectively). The patterns of CDI case characteristics and outcomes were similar in 2020 and in 2018–2019, with moderately higher reported rates of recurrent CDI, CDI with a complicated course and CDI-associated mortality in 2020 than in previous years. The differences were possibly also due to a variation in the relative country representativeness between years.

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- In 2018–2020, for most hospital surveillance periods (81.6% of those with data), suspected cases of CDI were tested using European Society of Clinical Microbiology and Infectious Diseases (ESCMID)-recommended diagnostic algorithms. In 2018–2020, there were 93 hospital surveillance periods with likely insufficient CDI testing rates: over half of the tests for CDI in these hospitals were positive, and the median CDI testing rate was only 7.46 stool tests per 10 000 patient-days. By comparison, the interquartile range for the CDI testing rate in the other hospitals in 2020 was 15.6–95.0 stool tests per 10 000 patient-days.
- Seven countries reported PCR ribotype (RT) data for CDI cases in 2018–2020, with the majority being reported by Belgium, Ireland, and the Netherlands. The most frequent RTs were RT014/020, RT002, and RT078. These results were expected, given the countries that reported.
- Countries are urged to report compatible CDI surveillance data to ECDC to enable the analysis of CDI epidemiology during the COVID-19 pandemic, which altered healthcare-seeking behaviour, patient pathways and infection prevention and control (IPC) practices. It is recommended that countries use the current ECDC surveillance protocol, which specifies the optional collection of selected structure and process indicators of IPC aligned with ESCMID guidance, and to aggregate hospital-level antimicrobial consumption data aligned with the European Surveillance of Antimicrobial Consumption Network (ESAC-Net), preferably for fluoroquinolones.

Background

Clostridioides difficile infection (CDI) has a high impact on the EU/EEA population. In 2009–2013, healthcare-associated (HA) CDI had the fourth highest health burden, in terms of disability-adjusted life years (DALYs) of any single infectious disease under surveillance in the EU/EEA [1]. In 2016–2017, there were an estimated 189 526 (95% confidence interval (CI): 105 154 – 340 978) cases of healthcare-associated (HA) CDI in acute care hospitals annually, with an estimated 7 419 (95% CI: 4 111–13 331) deaths annually for which CDI was reported as a possible contributing factor [2,3].

In 2016–2017, 21 EU/EEA countries participated in ECDC-coordinated surveillance of CDI in acute care hospitals in the EU/EEA. Among the reported CDI cases with information on infection outcome, 20.7% died from any cause during the current hospitalisation. These include 3.5% of fatal cases for which death was reported as 'possibly' or 'definitely' related to CDI [4].

On 17 December 2019, ECDC published the current version of its surveillance protocol for European surveillance of CDI [5]. For the first time, this update included the optional collection of data on selected structure and process indicators of IPC, aligned with ESCMID guidance [6]; aggregate hospital-level consumption data, preferably for fluoroquinolones, aligned with ESAC-Net [7]; and variables to document the geographical location of the acquisition or analysis of positive *C. difficile* samples from CDI cases.

Methods

In 2020 and 2021, ECDC did not issue a formal TESSy data call to EU/EEA countries, to request CDI data for the previous calendar year, recognising the priority for national and EU responses to COVID-19 in the EU/EEA. Therefore, the data for 2019 and 2020 are less complete than the preceding years.

This report includes surveillance data for 2018–2020 not previously published, focussing on data reported for 2020. It also includes selected comparisons with data from all years of surveillance – i.e. since 2016. The data were retrieved from The European Surveillance System (TESSy) on 18 April 2022. TESSy is a system for the collection, analysis, and dissemination of data on communicable diseases. A subset of the data used for this report is available through ECDC's online 'Surveillance Atlas of Infectious Diseases' [8].

This surveillance report is based on CDI surveillance data collected by the ECDC Healthcare-Associated Infections Surveillance Network (HAI-Net). The surveillance protocol specifies three options for data collection: 'minimal' (aggregate numerators and denominators), 'light' (case-based numerators and aggregate denominators) 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 EUCAST¹ clinical breakpoints to interpret antimicrobial susceptibility testing (AST) results, specifying variables to collect data for metronidazole, moxifloxacin and vancomycin [5,7,9].

For a detailed description of the methods used to produce this report, please refer to the surveillance protocol [5] as well as Annexes 1–3. An overview of the national surveillance systems is available online [8] and in Annex 1. Selected aspects of the national systems for CDI surveillance in the countries reporting data for this report are

¹ European Committee on Antimicrobial Susceptibility Testing

presented in Annex 2. European-level activities to harmonise and analyse the data received, including data imputation, are presented in Annex 3.

ECDC started collecting surveillance data compatible with the ECDC CDI surveillance protocol [10] on 1 January 2016. The surveillance data were collected through two different schemes:

- 1) During the start-up phase, countries/administrations were invited to report data by 31 March 2016. Data were collected using the ECDC surveillance protocol for at least one month during January–February 2016 and from at least one hospital.
- 2) During the following periodic data collections (biannual for 2016–2017, annual since 2018), countries/administrations were invited to upload to TESSy CDI surveillance data compatible with the ECDC surveillance protocol for a period of at least three months per year for each hospital [5]. This enables the estimation of the health burden and trends. The surveillance system is not designed to detect outbreaks.

Furthermore, in the framework of the technical collaboration project on preparatory measures for the participation of national public health authorities from EU candidate countries and potential candidates (namely, Western Balkans and Türkiye) in ECDC activities, during 2018–2019 the countries were invited to participate in ECDC-coordinated surveillance of CDI alongside the EU/EEA countries. Only Serbia established the necessary surveillance and reported CDI data pertaining to 2018. The CDI data collected from the participating Serbian hospitals are presented in this report.

This report uses the terms 'hospital surveillance periods' to identify data collected in a given year, country and hospital combination, which is useful when describing data covering multiple years. When describing data related to a single year, this report uses either 'hospital surveillance periods' or 'hospital', which are equivalent in this setting. There was only one year (2016) in which two countries had multiple hospital surveillance periods for a subset of hospitals in the same year (see Table A5 in Annex 4).

As outlined in Annex 2, hospital surveillance data from the Netherlands span from May of a given year to the end of April of the following year. The starting year is used as the label for this data collection period. For instance, data from the Netherlands labelled '2018' in this report represents cases from May 2018 through to April 2019. This labelling criterion applies to all data from the Netherlands in this report, with the exception of the 2019 data, which cover the period May 2019 to December 2020. The UK did not report data to ECDC for 2020 due to its withdrawal from the EU on 1 February 2020.

Participation

Since January 2016, 26 countries/administrations have reported CDI data for 3 374 hospital surveillance periods, with 331 million patient bed-days. These include 22 EU/EEA countries, three UK devolved administrations (England, Scotland, and Wales), and one EU candidate country (Serbia).

Eight EU/EEA countries (Austria, Estonia, Germany, Hungary, Ireland, Lithuania, Portugal, and Slovenia) reported data for 2020 for a total of 736 hospitals covering 275 193 beds and 67 859 342 patient-days. Most hospital surveillance periods (544/736, 73.9%) were reported by Germany (Figure 1, Table 5). None of the countries that collected data for 2020 reported any of the new optional variables described in the December 2019 update of the ECDC surveillance protocol [5].

In 2018 and 2019, a larger number of countries submitted data (13 for 2019 and 15 for 2018) than in 2020; however, the overall number of hospital surveillance periods was smaller (410 for 2019 and 652 for 2018) than in 2020. This difference is due to the large number of hospital surveillance periods reported by Germany for 2020.

Some countries reported data consistently between years, and, in most cases, from the same hospitals (Table 5). Therefore, some aggregation of EU/EEA data across these years can be appropriate, but caution should be exercised when extrapolating results to the entire EU/EEA or when making advanced analyses in order to take participation into account. Figure 1a describes the relative country participation for all years since 2016.

Overall, 648/736 (88.0%) of hospital surveillance periods in 2020 had data compatible with the 'minimal' (i.e. hospital-level aggregated data) surveillance option. All other surveillance periods (88/736, 12.0%) followed one of the two options that included case-based data. By contrast, in 2018–2019, 74.0% (786/1 062) of hospital surveillance periods included case-based data. This difference was mainly due to Germany and Hungary, two of the major data contributors for 2020, having only reported data compatible with the 'minimal' surveillance option.

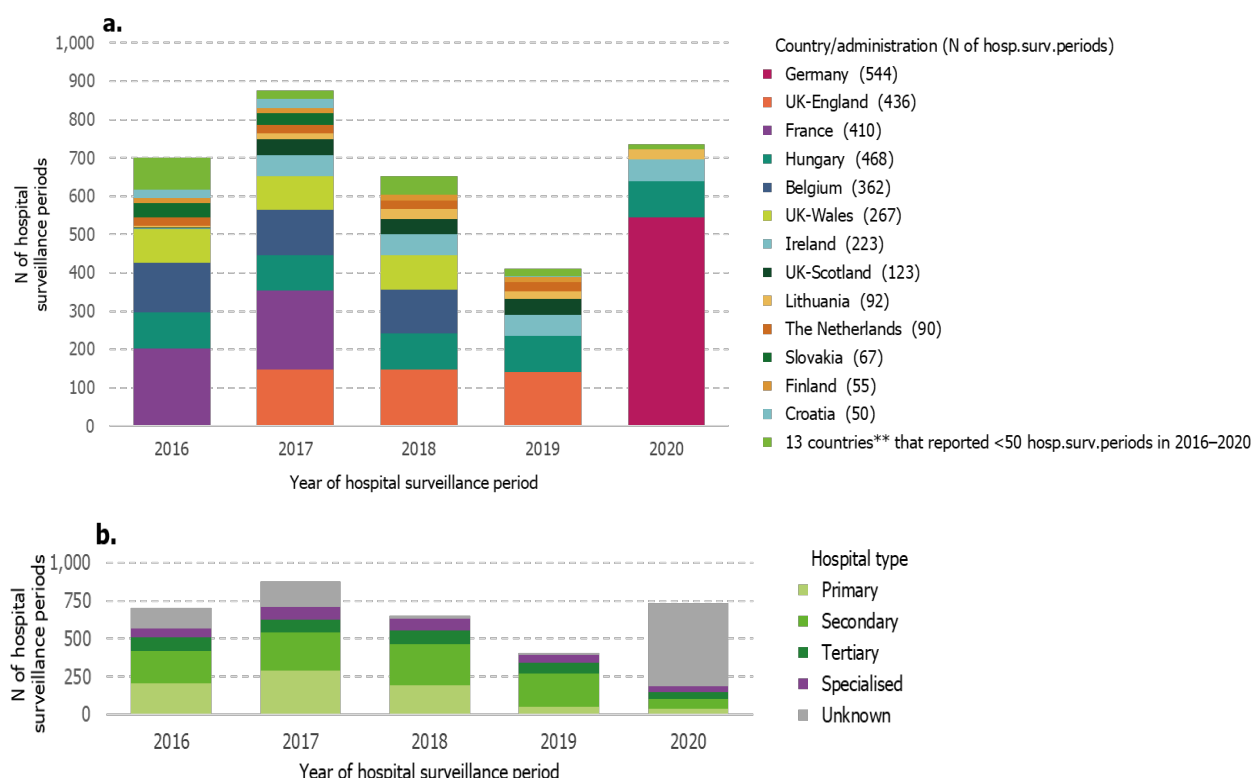
All countries reported the data on the type of hospital for all their participating hospitals, except Germany for 2020 and Finland for 2018 and 2019.

In 2020, among 192 hospitals reporting data on the type of hospital, 37 (19.3%) were primary care hospitals (often general hospitals with few specialties), 71 (37.0%) were secondary care hospitals (often peripheral hospitals that receive referrals from primary hospitals), 41 (21.4%) were tertiary care hospitals (large, usually regional hospitals, commonly associated with a university), and 43 (22.4%) were 'specialised hospitals'. In 2018, these figures were primary care hospitals: 30.0%, secondary care hospitals: 43.4%, tertiary care hospitals: 14.7%,

'specialised hospitals': 12.0%, and in 2019, primary care hospitals: 13.4%, secondary care hospitals: 55.8%, tertiary care hospitals: 18.4%, 'specialised hospitals': 12.4%. Figure 1b presents the distribution of reported CDIs by type of hospital for all years since 2016.

Annex 4 presents additional denominator data for 2016–2020. Table A5 presents the denominator data reported by participating countries/administrations in 2016–2020. Figure A5 presents the national coverage of the participating acute care hospitals in 2018–2020. Figures 6 and 7 present the number of included surveillance days per participating country and type of hospital, respectively, for 2016–2020.

Figure 1. Number of hospital surveillance periods with *Clostridioides difficile* infection (CDI) surveillance data reported to ECDC, by year and (a) European country/UK administration*; (b) type of hospital, 2016–2020



* 22 EU/EEA countries, the UK (England, Scotland and Wales) and Serbia; UK 2020 data not included due to the withdrawal of the UK from the EU (see Methods section)

** Poland (n=46), Serbia (n=39), Czechia (n=35), Estonia (n=18), Slovenia (n=14), Portugal (n=12), Austria (n=9), Malta (n=4), Spain (n=4), Greece (n=2), Italy (n=2), Iceland (n=1) and Latvia (n=1).

Epidemiology

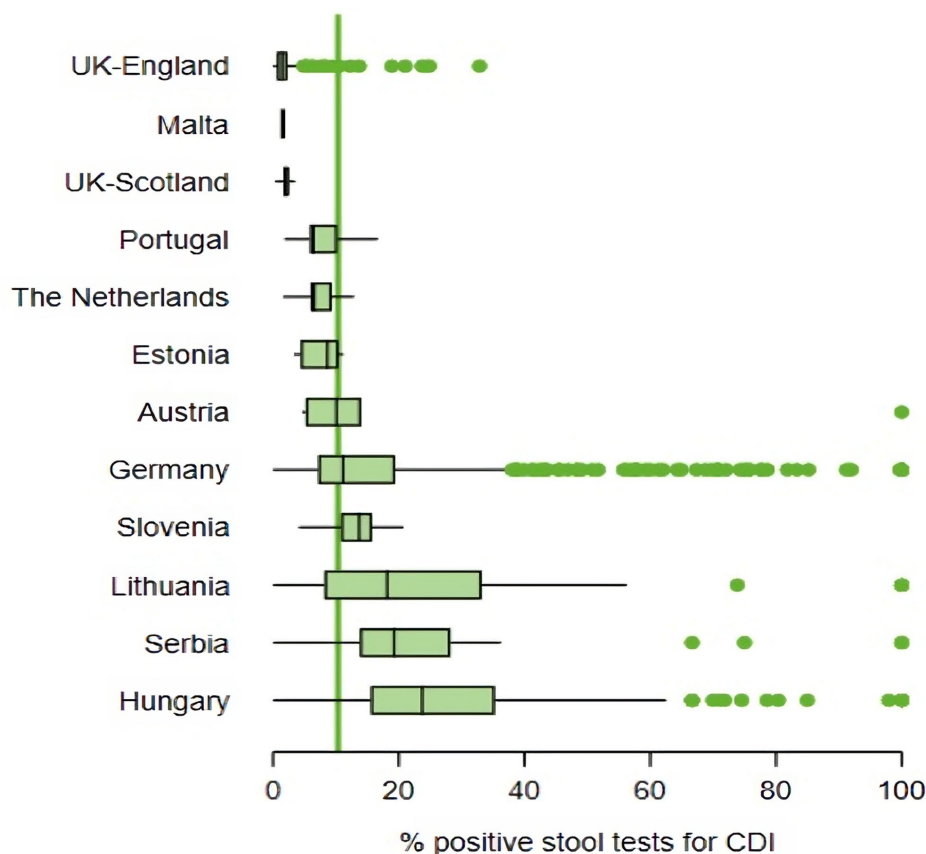
Testing for CDI

Fourteen countries/administrations reported the diagnostic algorithm used by participating hospitals to identify CDI cases in 2018–2020, providing data for 860 hospital surveillance periods. The choice of the diagnostic algorithm was not reported for 938 hospital surveillance periods from eight countries. ESCMID-recommended diagnostic algorithms [5,9,11] were used during 702/860 (81.6%) hospital surveillance periods, whereas other, less optimal, algorithms were used during 158 (18.4%) hospital surveillance periods. The most frequently reported diagnostic algorithm (407/860; 47.3%) included initial screening for glutamate dehydrogenase (GDH) using an enzyme immunoassay (EIA), with confirmation by an EIA for toxin A/B, and optional secondary confirmation with a nucleic acid amplification test (NAAT) or toxigenic culture. The second most frequent algorithm (197; 22.9%) was almost identical, except that it combined the GDH EIA and toxin A/B EIA into the initial step. Both algorithms are consistent with the ESCMID recommendation.

In 2018–2020, 13 countries reported that the participating hospitals had performed 1 639 806 stool tests for CDI, 98 333 of which were positive (crude percentage: 6%). The median percentage of positive tests was 10.3% among the hospital surveillance periods with data available on the number of tests and positive tests. The lowest median percentages at the national level were reported in UK (Scotland), Malta, and UK (England) and the highest in Lithuania, Serbia, and Hungary (Figure 2).

There were 93 hospital surveillance periods in 2018–2020, with >50% positivity of the reported stool tests for CDI, suggesting an insufficient testing rate in these hospitals. The median testing rate in these hospitals was 7.5 tests per 10 000 patient-days. During this period, the interquartile range (IQR) for the testing rate among all hospital surveillance periods was 15.6–95.0 stool tests per 10 000 patient-days, with the highest median testing rate observed for secondary and tertiary care hospitals (90.6 and 37.1 stool tests per 10 000 patient-days, respectively) and the lowest in specialised hospitals (7.91 stool tests per 10 000 patient-days).

Figure 2. Distribution of positive laboratory stool tests rates for *Clostridioides difficile* infection (CDI) per hospital surveillance period by European country/UK administration*, 2018–2020



The vertical line represents the overall hospital median.

* No data available for Belgium, Croatia, Finland, Ireland, or UK (Wales), as there was no numerator and/or denominator. UK 2020 data not included due to the withdrawal of the UK from the EU (see Methods section).

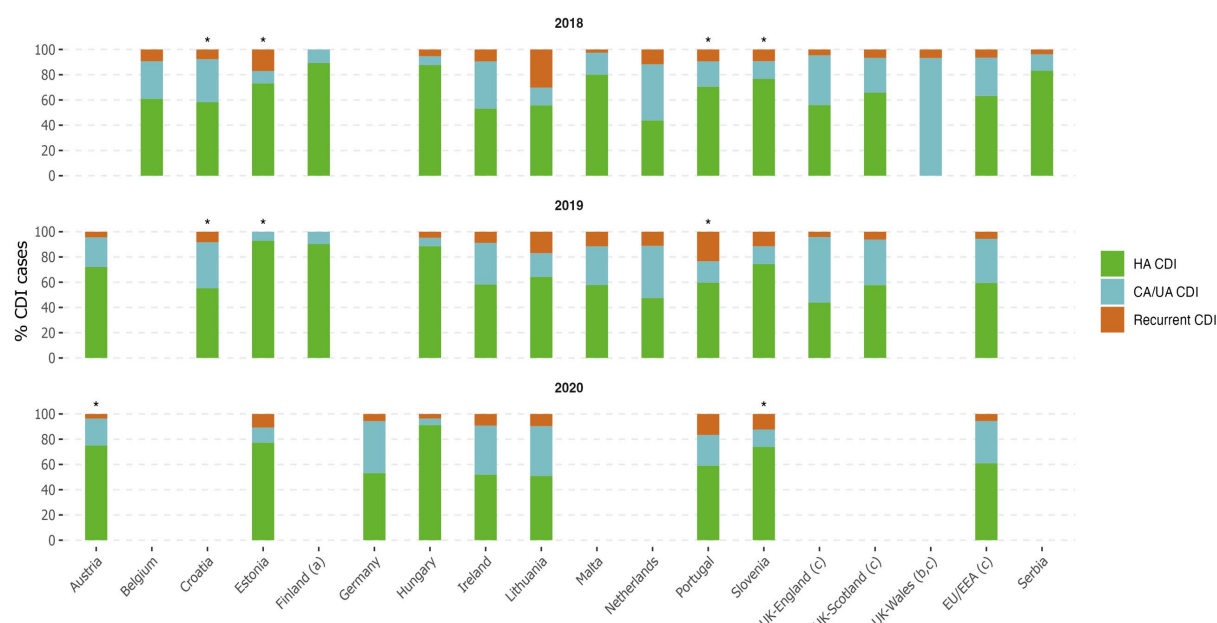
Reported CDI cases

CDI case origin and incidence

A total of 31 731 CDI cases were reported for 2020 (the majority reported by Germany, 22 826 cases), 25 145 cases for 2019 and 29 158 cases for 2018.

In the hospital-level dataset, the distribution of CDI cases by origin was similar between 2018 and 2020. The proportion of CDI cases that were healthcare-associated (HA CDI), community-associated or with unknown association (CA/UA CDI), or recurrent was 60.9%, 33.5% and 5.6%, respectively in 2020; 59.4%, 35.0%, and 5.6% in 2019, and 63.1%, 30.4%, and 6.4% in 2018. Figure 3 presents the distribution of CDI cases by origin and country during the period 2018–2020.

Figure 3. Case origin distribution of *Clostridioides difficile* infection (CDI) cases reported to ECDC, by year and European country/UK administration^c, 2018–2020

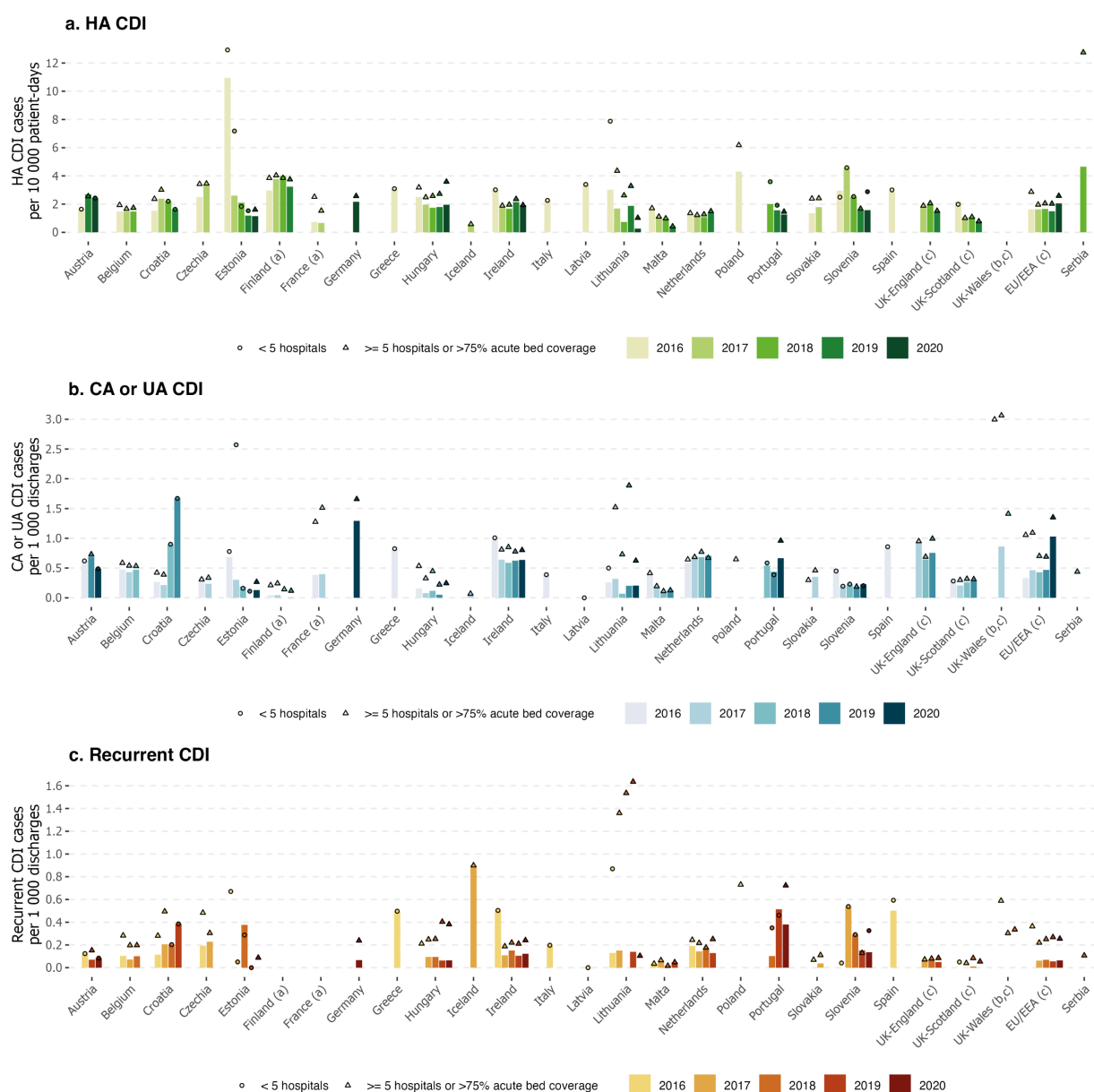


Key: HA – healthcare-associated CDI; CA/UA CDI – community-associated CDI and CDI with unknown association.

* Data from less than five acute care hospitals in a given year, unless the hospitals included have >75% national acute care hospital beds (e.g. Malta).^a Finland's national surveillance system does not report recurrent CDI cases.^b UK (Wales) national surveillance is unable to discriminate HA CDI from UA CDI.^c UK 2020 data not included due to the withdrawal of the UK from the EU (see Methods section).

Figure 4 presents the mean and median hospital incidence density of HA CDI (per 10 000 patient-days), and mean and median hospital incidence of CA/UA and recurrent CDI (per 1 000 discharges) by year in 2016–2020. The estimates are presented both by country/administration and for the whole of the EU/EEA. Confidence intervals (CIs) were computed according to a quasi-Poisson model that takes into account the compound country variability. Estimates are only reported for countries with more than five surveyed hospitals. Incidence trends across the years should be interpreted with caution since different hospitals in a particular country may have participated each year.

Figure 4. a) Hospital incidence density of healthcare-associated *Clostridioides difficile* infection (CDI), b) hospital incidence of community-associated CDI, or CDI with unknown association, c) hospital incidence of recurrent CDI, by year and European country/UK administration^c, 2016–2020



The bars represent the medians of the hospital incidence (recurrent and CA/UA CDI) and incidence density (HA); the shapes represent the means, which show the influence of high-incidence outliers, with the triangle shape identifying years where data is collected from at least five hospitals, unless the included hospitals cover >75% of the national acute-care hospital beds (e.g. Iceland and Malta), and the circle indicating a lower representativity.

Key: HA – healthcare-associated CDI; CA/UA CDI – community-associated CDI and CDI with unknown association.

^a Finland and France: the national surveillance systems do not report recurrent CDI cases.

^b UK (Wales): the national surveillance system was unable to discriminate between HA CDI and UA CDI. UK 2020 data not included due to the withdrawal of the UK from the EU (see Methods section).

For HA CDI, the reported mean hospital incidence density for the whole EU/EEA was 2.58 (95% CI: 2.42–2.75; median: 2.05) cases per 10 000 patient-days in 2020, with Lithuania reporting the lowest incidence density (hospital mean: 1.03, 95% CI: 0.58–1.66; median: 0.27), and Hungary the highest incidence density (hospital mean: 3.58, 95% CI: 3.09–4.13; median: 1.96). In comparison, the overall reported mean incidence density was 2.02 (95% CI: 1.82–2.24; median: 1.50) in 2019, and 2.79 (95% CI: 1.83–4.04; median: 1.70) in 2018. No general EU/EEA trend was detected, with most countries (e.g. Estonia, Lithuania, Malta, Slovenia, UK) showing a decrease in incidence and only a few (e.g. Hungary, the Netherlands) showing an apparent increase (Figure 4a). It is interesting to note that Hungary and Lithuania both showed a marked increase and decrease, respectively, in incidence in 2020 compared to previous years.

For CA/UA CDI, the reported mean hospital incidence for the whole EU/EEA was 1.35 (95% CI: 1.22–1.48; median: 1.03) cases per 1 000 patient discharges or admissions in 2020, with Hungary reporting the lowest incidence (hospital mean: 0.25, 95% CI: 0.13–0.42; median: 0.00), and Germany the highest incidence (hospital mean: 1.66, 95% CI: 1.51–1.81; median: 1.29).

The reported mean incidence of CA/UA CDI was notably lower in 2018 and 2019 than in 2020: 0.69 cases per 1 000 patient discharges or admissions (95% CI: 0.56–0.84; median: 0.47) in 2019, and 0.70 cases per 1 000 patient discharges or admissions (95% CI: 0.61–0.81; median: 0.43) in 2018. The higher incidence in 2020 was due to the participation of Germany, which reported a significantly higher CA/UA CDI incidence than other countries and represented >70% of the surveyed hospitals in the 2020 dataset. Among countries with a more representative number of participating hospitals (Figure 4b), Finland, Hungary and Malta showed a consistent decreasing trend in incidence over multiple years, while Croatia reported an increased incidence, albeit for a varying subset of hospitals.

For recurrent CDI, the reported mean hospital incidence of recurrent CDI for the whole EU/EEA was 0.25 cases per 1 000 patient discharges or admissions (95% CI: 0.21–0.30; median: 0.06) in 2020. The lowest incidence was reported by Lithuania (hospital mean: 0.10, 95% CI: 0.02–0.32; median: 0) and the highest by Hungary (hospital mean: 0.38, 95% CI: 0.26–0.54; median: 0.06). A similar incidence was reported in 2019 (0.27 cases per 1 000 discharges, 95% CI: 0.15–0.43; median: 0.06) and 2018 (0.24 cases per 1 000 discharges, 95% CI: 0.16–0.36; median: 0.06). Among countries with a more representative number of participating hospitals (Figure 4c), the Netherlands showed the most consistent decrease in incidence of recurrent CDI over the years. For other countries, the low number of reporting hospitals or years of reporting hinder a robust assessment of trends.

Table 1 presents the mean hospital incidence for each category of case origin and by type of hospital for 2020. Tertiary hospitals had the highest incidence (or incidence density) of both HA CDI and CA/UA CDI, while specialised hospitals reported the highest incidence of recurrent CDI, but the lowest incidence of both HA CDI and CA/UA CDI. These results are strongly influenced by three countries which reported most of the data on 'hospital type' (Hungary (49.5%), Ireland (29.2%) and Lithuania (14.1%)). As noted above, all 544 hospitals with 'unknown hospital type' in 2020 were reported by Germany. For CDI incidence by type of hospital for 2018 and 2019, see Tables A7 and A8 in Annex 5. The higher risk of HA CDI in tertiary care hospitals than in other hospitals has been consistent over the years, but was particularly evident in 2018. On the other hand, CA/UA CDI was much more common in primary (2018) and secondary (2019) care hospitals than in tertiary care hospitals, as in 2020. Finally, the higher risk of recurrent CDI cases in specialised hospitals was confirmed by 2018 and 2019 data.

Table 1. Incidence density or incidence of *Clostridioides difficile* infection (CDI) cases in hospitals, by origin of cases and hospital category, EU/EEA*, 2020

Origin of CDI cases	Type of hospital	No. of hospitals ^a	Hospital mean	95% confidence interval ^b	Hospital median
HA CDI					
			Incidence density (cases per 10 000 patient-days)		
	Primary	37	1.75	1.17 – 2.48	1.20
	Secondary	71	3.28	2.50 – 4.21	1.92
	Tertiary	41	3.49	2.76 – 4.34	2.92
	Specialised	43	1.44	0.95 – 2.08	0.71
	Unknown	544	2.57	2.40 – 2.74	2.16
	All hospitals	736	2.58	2.42 – 2.75	2.05
CA/UA CDI					
			Incidence (cases per 1 000 discharges or admissions)		
	Primary	37	0.57	0.33 – 0.90	0.27
	Secondary	71	0.51	0.37 – 0.68	0.29
	Tertiary	41	0.65	0.43 – 0.94	0.32
	Specialised	43	0.19	0.08 – 0.38	0.00
	Unknown	544	1.66	1.50 – 1.82	1.29
	All hospitals	736	1.35	1.23 – 1.48	1.03
Recurrent CDI cases					
			Incidence (cases per 1 000 discharges or admissions)		
	Primary	37	0.23	0.12 – 0.40	0.00
	Secondary	71	0.14	0.10 – 0.20	0.06
	Tertiary	41	0.29	0.19 – 0.42	0.13
	Specialised	43	0.63	0.31 – 1.12	0.00
	Unknown	544	0.24	0.20 – 0.29	0.07
	All hospitals	736	0.25	0.21 – 0.30	0.06
All CDI cases					
			Incidence (cases per 1 000 discharges or admissions)		
	Primary	37	2.48	1.80 – 3.31	1.90
	Secondary	71	3.10	2.41 – 3.92	1.96
	Tertiary	41	3.54	2.88 – 4.30	3.35
	Specialised	43	4.00	2.44 – 6.11	1.56
	Unknown	544	4.08	3.66 – 4.53	2.94
	All hospitals	736	3.87	3.53 – 4.23	2.75

Key: HA – healthcare-associated CDI; CA/UA CDI – community-associated CDI and CDI with unknown association.

* Eight EU/EEA countries, UK 2020 data not included due to the withdrawal of the UK from the EU (see Methods section).

^a Number of hospitals with data to compute the incidence (density)

^b 95% confidence intervals based on a quasi-Poisson model to account for overdispersion.

Description of CDI cases and outcomes

Case-based CDI data for 2020 were provided by six countries (Austria, Estonia, Ireland, Lithuania, Portugal and Slovenia) that reported a total of 2 568 cases. In contrast, 11 countries provided data for 17 592 cases for 2019, while for 2018, thirteen countries provided data for 20 990 cases. For 2020, most case-based data were provided by Ireland (66.5%), while in the previous years, most data were reported by UK (England).

In 2020, the median age of cases was 75 years (IQR: 59–82) and 57% were female; these figures were similar to the figures for 2018 and 2019.

Table 2 presents the clinical characteristics of cases collected between 2018 and 2020; percentages in the table and in the following paragraphs are relative to the total number of cases with data for each characteristic.

Table 2. Characteristics of *Clostridioides difficile* infection (CDI) cases and outcome of CDI, in European countries/UK administrations* reporting case-based data to ECDC, 2018–2020

	Categories	Sub-categories	2018 13 countries	2019 11 countries	2020 6 countries
Cases with data by country/ administration	Austria		0 (0.0%)	277 (1.6%)	131 (5.1%)
	Belgium		2 506 (11.9%)	0 (0.0%)	0 (0.0%)
	Croatia		193 (0.9%)	179 (1.0%)	0 (0.0%)
	Estonia		68 (0.3%)	124 (0.7%)	202 (7.9%)
	Finland		666 (3.2%)	585 (3.3%)	0 (0.0%)
	Ireland		2 030 (9.7%)	2 185 (12.4%)	1 707 (66.5%)
	Lithuania		561 (2.7%)	624 (3.5%)	382 (14.9%)
	Malta		40 (0.2%)	26 (0.1%)	0 (0.0%)
	Netherlands		867 (4.1%)	1 414 (8.0%)	0 (0.0%)
	Portugal		99 (0.5%)	47 (0.3%)	78 (3.0%)
	Serbia		677 (3.2%)	0 (0.0%)	0 (0.0%)
	Slovenia		129 (0.6%)	226 (1.3%)	68 (2.6%)
	UK-England		12 642 (60.2%)	11 905 (67.7%)	0 (0.0%)
	UK-Wales		512 (2.4%)	0 (0.0%)	0 (0.0%)
	Total ^b		20 990	17 592	2 568
Previous healthcare admission ^a	No		679 (40.9%)	739 (37.4%)	329 (42.5%)
	Yes		983 (59.1%)	1 239 (62.6%)	445 (57.5%)
		Both hospitals and LTCFs	5 (0.3%)	13 (0.7%)	4 (0.5%)
		Hospital	875 (52.6%)	1 103 (55.8%)	425 (54.9%)
		LTCF	64 (3.9%)	88 (4.4%)	13 (1.7%)
		Other or not specified	39 (2.3%)	35 (1.8%)	3 (0.4%)
	Total ^b		1 662	1 978	774
	Unknown ^c		19 328 (92.1%)	15 614 (88.8%)	1 794 (69.9%)
McCabe score	Non-fatal (5+yrs)		825 (72.1%)	840 (60.6%)	135 (52.7%)
	Ultimately fatal (1-4yrs)		240 (21.0%)	393 (28.4%)	85 (33.2%)
	Rapidly fatal (<1yr)		80 (7.0%)	153 (11.0%)	36 (14.1%)
	Total ^b		1 145	1 386	256
	Unknown ^c		19 845 (94.5%)	16 206 (92.1%)	2 312 (90.0%)
CDI present at admission	No		3 569 (57.7%)	2 252 (59.7%)	881 (62.2%)
	Yes		2 615 (42.3%)	1 522 (40.3%)	536 (37.8%)
	Total ^b		6 184	3 774	1 417
	Unknown ^c		14 806 (70.5%)	13 818 (78.5%)	1 151 (44.8%)
Recurrent CDI	No		18 132 (92.7%)	15 257 (93.5%)	2 096 (90.0%)
	Yes		1 427 (7.3%)	1 054 (6.5%)	233 (10.0%)
	Total ^b		19 559	16 311	2 329
	Unknown ^c		1 431 (6.8%)	1 281 (7.3%)	239 (9.3%)
CDI case origin	CA CDI		5 479 (27.6%)	4 043 (24.2%)	579 (24.1%)
	HA CDI		12 655 (63.8%)	9 325 (55.9%)	1 571 (65.4%)
		Current hospital	9 308 (46.9%)	7 738 (46.4%)	1 174 (48.9%)
		LTCF	319 (1.6%)	220 (1.3%)	95 (4.0%)

	Categories	Sub-categories	2018 13 countries	2019 11 countries	2020 6 countries
		Not specified	2 426 (12.2%)	1 164 (7.0%)	209 (8.7%)
		Other hospital	525 (2.6%)	153 (0.9%)	76 (3.2%)
		Other healthcare	77 (0.4%)	50 (0.3%)	17 (0.7%)
	UA CDI		1 696 (8.6%)	3 307 (19.8%)	252 (10.5%)
	Total^b		19 830	16 675	2 402
	Unknown ^c		1 160 (5.5%)	917 (5.2%)	166 (6.5%)
Complicated course	No		4 887 (91.5%)	2 948 (90.0%)	559 (83.1%)
	Yes		454 (8.5%)	327 (10.0%)	112 (16.6%)
	Total^b		5 341	3 275	673
	Unknown ^c		15 649 (74.6%)	14 317 (81.4%)	1 895 (73.8%)
Patient outcome	Discharged alive		4 195 (85.4%)	2 396 (85.6%)	674 (83.8%)
	Deceased (all causes)		717 (14.6%)	404 (14.4%)	128 (15.9%)
		Definitely or possibly related to CDI	139 (2.8%)	115 (4.1%)	40 (5.0%)
		Not related to CDI	469 (9.5%)	231 (8.2%)	75 (9.3%)
		Relationship to CDI unknown	109 (2.2%)	58 (2.1%)	13 (1.6%)
	Total^b		4 912	2 800	804
	Unknown ^c		16 078 (76.6%)	14 792 (84.1%)	1 764 (68.7%)

Key: HA – healthcare-associated; CA – community-associated; UA – CDI with unknown association; LTCF – long-term care facility.

* UK 2020 data not included due to the withdrawal of the UK from the EU (see Methods section).

^a In the previous four weeks.

^b The totals represent the cases with data for each characteristic, the category/subcategory percentages are related to these totals.

^c Cases with no data for a given characteristic, with percentages over the total number of cases for a given year, reported in the country/administration year totals.

In 2020, among 256 CDI cases with data available for the McCabe score², 121 (47.3%) were reported with an estimated survival time of under five years, compared to 39% in 2019 and 28% in 2018, denoting a sample for which the prognosis had deteriorated.

Most CDI cases with available admission data had an admission to a healthcare setting within the previous four weeks (57.5% in 2020, 62.6% in 2019, and 59.1% in 2018). Almost all of these were acute-care admissions to a hospital, with very few cases that had previous admission to a long-term care facility (only 1.7% in 2020 and 4.0% in 2018–2019).

More than half (between 57.7% in 2018 and 62% in 2020) of the CDI cases did not have symptoms of CDI at the time of admission to the reporting hospital. Recurrent CDI, which are usually associated with longer hospital stays and higher case fatality than non-recurrent episodes [12], represented 10.0% of cases in 2020, a larger proportion than in 2018 (7.3%) and 2019 (6.5%).

A 'complicated course of infection' [5] was reported for 16.7% of cases with available data in 2020, a higher rate than that observed in 2019 (10%) and 2018 (8.5%). This was mirrored by a larger proportion of deaths possibly or definitely related to CDI in 2020 (40 cases, 5%) than in 2019 (115 cases, 4.1%) or 2018 (139 cases, 2.8%). Nevertheless, the overall mortality rate was relatively low and comparable between years (14.4% to 15.9%).

The rate of data 'missingness' for several variables was considerable, especially for the McCabe score (more than 90% missing data in all three years); the presence of a previous healthcare admission (from 69.9% in 2020 to 92.1% missing data in 2018); complicated course of disease (from 73.8% in 2020 to 81.4% missing data in 2019); patient outcome (68.7%, 76.6%, and 84.1% missing data in 2020, 2018, and 2019, respectively), and presence of CDI at admission (from 44.8% in 2020 to 70.5% in 2018 and 78.5% missing data in 2019). In comparison, the percentage of missing data was low for the CDI origin (5.2% to 6.5% missing data) and for whether CDI was recurrent (6.8% to 9.3% missing data). The rate of missing data tended to be lower in 2020 than in the years before.

² The McCabe score is a subjective assessment of the likely survival time of a patient based on their reason for admission, irrespective of their CDI case status. It is usually applied by an attending physician.

Due to the year-to-year variation in the set of reporting countries/administrations, the uneven distribution of reported data among these countries/administrations, and the notable percentages of missing data, it was impossible to determine whether changes in patient outcomes in 2020 were due to a disruption of healthcare services resulting from the COVID-19 pandemic, or intrinsic differences in the sampled population. Additional 2020 data in the subsequent data calls will possibly enable advanced analyses to better evaluate the impact of the COVID-19 pandemic on CDI and related outcomes in the EU/EEA.

Results from microbiological testing

Toxin production

For 2020, data on toxin A/B detection were reported for 80.4% (2 067/2 568) of all cases with case-based data, but by only three countries: Ireland (1 707 cases, 100% of Irish case-based data), Lithuania (288 cases, 75.4%), and Portugal (70 cases, 89.7%). In comparison, data on toxin A/B detection were reported for 3 071 cases for 2019 (17.5% of all case-based data for that year) by four countries: Ireland (2 185 cases, 100% of the Irish case-based data), Lithuania (622 cases, 99.7%), Slovenia (226 cases, 100.0%) and Portugal (38 cases, 80.9%); and for 3 370 cases for 2018 (16.1% of all case-based data for that year) by six countries: Ireland (2 030 cases, 100.0%), Belgium (570, 22.7%), Lithuania (558 cases, 99.5%), Slovenia (129 cases, 100.0%), Portugal (76 cases, 76.8%) and Estonia (seven cases, 10.3%).

The toxin A/B detection test was positive for 98.6%, 97.9%, and 98.7% of cases with available results for 2020, 2019 and 2018, respectively. The toxin detection method (Immuno Enzymatic Assay of TcdA and TcdB toxin or PCR detection of toxin genes) was not reported by any of the participating hospitals.

For 2020, binary toxin gene detection was only reported for 132 (5.1%) cases and by only two countries: Portugal (87.2% of case-based data) and Lithuania (16.8%). In comparison, binary toxin gene detection was reported for 402 cases (2.3%) by three countries (Lithuania: 55.6% of cases, Portugal: 76.6% and Slovenia: 8.4%) for 2019 and for 336 (1.6%) by the same three countries (Lithuania: 31.6% of cases, Portugal: 60.6% and Slovenia: 76.7%) for 2018.

Binary toxin gene detection was positive for 54 (40.9%) cases in 2020, 253 (62.9%) in 2019 and 174 (51.8%) in 2018.

Double positivity – i.e. both toxin A/B detection and binary gene detection – was found in 48 cases in 2020 (36.6% of cases with results for both tests), 230 cases (57.4%) in 2019, and 171 cases (51.0%) in 2018.

For 2020, 553 CDI cases were detected in hospitals based on 'NAAT alone' as the standard case detection algorithm. Of these cases, 412 (75%) were toxin A/B positive (three of which were also binary toxin gene positive). However, since the A/B testing modality was never reported, it is not known whether toxin A/B production was assessed in addition to presence of the gene(s). For two (0.4%) cases, both toxin A/B and binary toxin gene detection were negative. In 139 (25%) cases, there was no data reported for toxin A/B or binary toxin gene detection. Therefore, for these 551 (412 + 139) reported cases in 2020 (21.5% of all cases with case-based data), there was no confirmation of active toxin production, in addition to colonisation with *C. difficile*.

Antimicrobial susceptibility

To date, AST results for *C. difficile* cases for 2018–2020 were only reported for 281 cases from the Netherlands (43 hospital surveillance periods, 109 tested cases), Portugal (12 hospital surveillance periods, 165 tested cases) and Estonia (one hospital surveillance period, seven tested cases); and only Portugal reported AST data for 2020.

Metronidazole and vancomycin susceptibility data were available for 281 cases. All of these were vancomycin-susceptible, and only two cases were metronidazole-resistant (MIC by agar dilution: 4mg/L and 8mg/L, respectively). Moxifloxacin susceptibility data were available for 237 cases, of which 48 (20.3%) were non-susceptible.

Reported PCR ribotypes

For 2018–2020, seven countries reported 397 unique RTs for 4 438 cases, including 153 RTs reported to be 'new' or 'rare'. Less RT data were reported each year, with seven countries reporting RT data on 2 272 cases for 2018, four countries reporting RT data on 1 718 cases for 2019, and two countries (Ireland and Portugal) reporting RT data on 448 cases for 2020.

Table 3 below lists the RTs reported more than five times in 2018–2020, during the year with the most available RT data. For example, the table presents 2019 data for the Netherlands (1 082 isolates), which also reported RT data on 693 isolates in 2018 and no data in 2020.

RT014/020, RT002 and RT078 were among the most frequently reported RTs, as expected from the participating countries, given the historical predominance of these RTs in the countries/administrations [13,14]. For example, RT078 is commonly associated with *C. difficile* in livestock, such as pigs, and the Netherlands has a relatively high population density of pigs [13]. Outbreak-prone RT027 only was the eleventh most frequently reported RT, following its predominance and subsequent control during the previous decade in most of the participating countries. There were relatively few other RTs reported that are similar to RT027 (e.g. RT176, RT036, RT181, RT198 with the same ST1/Clade 2), and these were predominantly reported by Czechia, Slovakia and Poland, as documented elsewhere [15–17].

Table 3. PCR ribotypes of *Clostridioides difficile* cases reported to ECDC, by EU/EEA country/UK administration*, 2018–2020

PCR ribotype	Belgium (2018)	Estonia (2018)	Ireland (2019)	The Netherlands (2019)	Portugal (2018)	Slovenia (2018)	UK-Wales (2018)	Total (N)	Total (%)
RT014/020	126	1	69	196	7	20	83	502	17.7
RT002	45	-	193	106	-	7	61	412	14.5
RT078	49	-	58	75	5	1	30	218	7.7
RT005	21	-	23	71	1	-	29	145	5.1
RT015	15	-	29	44	-	2	52	142	5.0
RT001	6	4	14	78	1	-	7	110	3.9
RT023	11	-	12	40	1	1	42	107	3.8
RT106	31	-	11	17	6	1	3	69	2.4
RT012	11	-	6	23	3	3	7	53	1.9
RT017	8	-	6	17	14	-	3	48	1.7
RT027	11	-	2	3	3	22	4	45	1.6
RT081	6	-	7	23	-	1	7	44	1.6
RT126	13	-	1	19	5	-	3	41	1.4
RT056	3	-	25	11	-	-	1	40	1.4
RT011	7	-	9	13	-	-	4	33	1.2
RT013	6	1	5	9	-	1	7	29	1.0
RT076	8	-	7	9	-	-	5	29	1.0
RT029	7	-	4	9	-	2	4	26	0.9
RT018	-	-	4	6	-	-	14	24	0.8
RT070	8	-	4	7	-	2	3	24	0.8
RT050	7	-	2	6	-	-	7	22	0.8
RT054	2	-	2	12	-	-	6	22	0.8
RT258	6	-	-	16	-	-	-	22	0.8
RT003	3	-	1	12	-	-	4	20	0.7
RT087	1	-	1	10	-	4	2	18	0.6
RT046	2	-	3	11	-	-	-	16	0.6
RT072	16	-	-	-	-	-	-	16	0.6
RT154	12	-	2	2	-	-	-	16	0.6
RT021	-	-	4	8	-	-	3	15	0.5
RT026	1	-	2	5	-	-	6	14	0.5
RT052	13	-	-	-	-	-	-	13	0.5
RT216	2	-	3	5	-	-	3	13	0.5
RT010	3	1	2	4	-	-	2	12	0.4
RT045	-	-	5	4	-	-	1	10	0.4
RT328	3	-	-	7	-	-	-	10	0.4
RT111	-	-	2	1	-	-	6	9	0.3
RT150	-	-	-	2	-	3	4	9	0.3
RT097	2	-	-	5	-	1	-	8	0.3
RT103	-	-	-	6	-	2	-	8	0.3
RT207	2	-	2	2	-	-	2	8	0.3
RT220	2	-	3	3	-	-	-	8	0.3
RT430	6	-	-	2	-	-	-	8	0.3
RT043	1	-	1	3	-	-	2	7	0.2
RT057	1	-	1	4	-	-	1	7	0.2
RT159	2	-	-	5	-	-	-	7	0.2
RT213	-	-	7	-	-	-	-	7	0.2
RT011/049	-	-	-	-	-	6	-	6	0.2
RT077	-	-	2	4	-	-	-	6	0.2
RT198	-	-	1	5	-	-	-	6	0.2
RT265	1	-	-	5	-	-	-	6	0.2
RT296	5	-	-	1	-	-	-	6	0.2
Total (reported n>5)	485	7	535	926	46	79	418	2 496	87.9
Total	570	7	581	1 082	60	90	448	2 838	100.0

As of 4 April 2022, PCR RT data available for Ireland for 2018, 2019 and 2020, for the Netherlands, Portugal and Slovenia for 2018 and 2019, and for Belgium, Estonia, and UK (Wales) for 2018.

Key: PCR RT – PCR ribotype.

* UK 2020 data not included due to the withdrawal of the UK from the EU (see Methods section).

Discussion

The use of a common surveillance protocol allows for the acquisition of comparable data on CDI within and between countries.

In 2020, only eight countries reported data, and most surveillance periods were provided by Germany, which in 2020 converted its national CDI surveillance protocol to the ECDC specification, similar to other countries (e.g. France, Finland, the Netherlands, UK (England), UK (Wales)) in previous years. In contrast, 2018 saw 15 countries/administrations participating and in 2019 there were 13. The COVID-19 pandemic probably had an impact on country participation, due to the reprioritisation of resources. The pandemic affected hospital surveillance in general. A large worldwide survey by WHO reported that in 2020, 67% of participating countries had limited capability to conduct antimicrobial resistance surveillance programmes, due to a lack of personnel and resources [18]. As of 2020, the UK stopped reporting due to its withdrawal from the EU, further decreasing the size of the sample.

For 2020, 31 731 CDI cases were reported. Most cases were healthcare-associated, highlighting the critical role of healthcare settings in the transmission of CDI. The report also shows a high incidence of CDI in tertiary care hospitals, which are often large regional hospitals associated with universities. This could be due to the high patient turnover and the patient case-mix in these hospitals.

The trends in the incidence of CDI in the EU/EEA and the UK displayed a dynamic pattern, mostly due to changes in the number of participating countries every year and in the subset of reporting hospitals.

The reported mean hospital incidence density of HA CDI in 2018, 2019 and 2020 period was 2.79, 2.02, and 2.58 cases per 10 000 patient-days, respectively, which was lower than in 2016 (2.87 cases per 10 000 patient-days) but higher than in 2017 (1.91 cases per 10 000 patient-days). A difference in the incidence of CA/UA CDI showed even more pronounced variations. The reported mean hospital incidence density of CA/UA CDI was 1.06 and 1.11 cases per 1 000 discharges or admissions, respectively, in 2016 and 2017. This then decreased in 2018 and 2019 (0.69 and 0.70 cases per 1 000 discharges or admissions), before increasing in 2020 (1.35 cases per 1 000 discharges or admissions). In 2020, the largest impact on CA/UA CDI incidence was due to the inclusion of the German data, which represented 74% of the reporting hospitals for that year and was characterised by a higher CA/UA incidence (1.66 cases per 1 000 discharges or admissions) than in the other participating countries. It is interesting to note that some countries displayed apparent trends in their incidence estimates. For example, most countries showed a decrease in HA CDI and CA/UA CDI incidence over the years, while Hungary, the Netherlands (for HA CDI) and Croatia (for CA/UA CDI) showed an increasing trend. More consistent data over the years and more advanced analyses would be needed to properly evaluate temporal trends.

The COVID-19 pandemic probably affected CDI epidemiology in the EU/EEA as it modified healthcare-seeking behaviour, hospital patient pathways, IPC practices and antimicrobial consumption in healthcare and the community and CDI-specific services, such as faecal microbiota stool banks [19]. For 2020–2021, peer-reviewed literature reported a decrease in hospital CDI incidence in countries as diverse as Ireland, Mexico, Spain, and the USA [20,21]. However, informal reports from EU/EEA countries describe an increased incidence in 2020–2021, potentially associated with changes to hospital-sector antimicrobial consumption and IPC practices. The geographical coverage of the 2020 surveillance data in this report is insufficient to definitively comment on such changes in the whole EU/EEA. However, few countries reported a marked positive or negative change in both HA and CA/UA CDI incidence in 2020, as previously mentioned.

Case-based data for 2020 suggested poorer CDI outcomes (e.g. toxic megacolon, surgery or ICU admission). This finding is in agreement with results from studies on CDI outcomes during the first year of the COVID-19 pandemic, pointing to delayed diagnosis of CDI as a cause of more severe disease progression [22]. However, only a subset of countries participated in all years and with varying hospital participation, which hinders comparisons. Case-based data were only provided for a minority of cases and with a limited number of countries providing most data at the case level. In 2020, case-based data were provided for only 2 568 cases by six countries, with 66% of such cases being reported by Ireland.

In 2020, the vast majority of hospitals reported using ESCMID-recommended diagnostic algorithms to confirm CDI cases [11], but other diagnostic practices, not based on active detection of toxin production, were still relatively common. In addition, the countries and hospitals that had the highest CDI testing rates tended to also report the lowest CDI incidence [4]. Several hospitals still have a high percentage of tests that were positive, implying insufficient testing rates to control CDI. Antimicrobial susceptibility testing results were reported sporadically (only 281 cases from three countries) and resistance to vancomycin or to metronidazole was only rarely detected.

Public health implications

Before 2020, the burden of CDI in hospitals in the EU/EEA was high, compared to other diseases under surveillance at the European level [1,2]. The impact of the COVID-19 pandemic on CDI in the EU/EEA is still unclear and may be better assessed once more CDI surveillance data have been reported by EU/EEA countries. In spite of this, IPC and antimicrobial stewardship remain of paramount importance for the prevention and control of CDI in the EU/EEA [6,23]. The current ECDC CDI surveillance protocol specifies new optional variables to record aggregate hospital-level antimicrobial consumption (e.g. fluoroquinolone consumption), as well as structure and process indicators of IPC, in order to enable locally-tuned interventions to reduce the hospital, and in turn, national CDI incidence [5,24].

All previous versions of this protocol recorded CDI testing rates and the underlying diagnostic practices. Therefore, given the reported CDI testing rates, the ongoing increase in the use of ESCMID-recommended diagnostic practices is promising, as it enables the identification of *C. difficile*, an outbreak-prone pathogen with a relatively high case-fatality rate.

Various *C. difficile* strains are associated with different risks of outbreak and poor infection outcomes [13,14], as well as variations in the effectiveness of antimicrobial stewardship interventions [24]. Therefore, in 2021–2022, ECDC coordinated surveys of recent *C. difficile* strains from CDI cases in EU/EEA countries, to support subsequent risk assessment, by enabling the potential extrapolation of strain-specific findings from sub-national, national, or multi-country activities to the EU/EEA.

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Annex 1. Surveillance systems overview

Table A4. Overview of the characteristics of surveillance systems in countries which participated in European *Clostridioides difficile* infection (CDI) surveillance, 2020

Country	Surveillance options
Austria	L
Estonia	L
Germany	M
Hungary	M*
Ireland	E
Lithuania	M, L, E
Portugal	E
Slovenia	L

Key: Y – yes; N – no; UNK – unknown; M – minimal; L – light; E – enhanced; EU – case definition specified in ECDC protocol v2.2–v2.4 and EU/2018/945.

* Data collected according to the light surveillance option, but only data compatible with the minimal surveillance option was reported to ECDC due to current protocol differences in Hungary's case-based dataset.

Annex 2. National data sources and harmonisation

National data sources

All hospitals used the ECDC CDI surveillance protocol [5], 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 that are compatible with the ECDC protocol. Noteworthy differences between national and ECDC protocols are listed below.

Hungary

- For the 2016 data: the Hungarian national surveillance coordinating centre invited Hungarian acute-care hospitals to participate in the ECDC CDI surveillance on a voluntary basis. Selected hospitals participated for one month during a January–March 2016 ‘start-up phase’ (45 hospitals) and/or for three months in October–December 2016 (49 hospitals), following the ECDC CDI surveillance protocol ‘enhanced surveillance option’. Data reported to ECDC TESSy are fully compliant with the ECDC CDI surveillance protocol.
- For the 2017 data and subsequent years: annual national surveillance data covering both acute and chronic care hospitals (92 hospitals) were converted to meet the specifications of the ECDC CDI ‘minimal surveillance option’. State-mandated case-based reporting by hospitals is 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) are 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) and recurrent cases of any origin are also reported voluntarily. Information on hospital type, number of stool samples tested for toxin-producing *C. difficile*, and number of positive stool samples come from other national data sources.

The Netherlands

The Dutch surveillance protocol contains differences from the ECDC protocol, as described in the annual reports of the Dutch *C. difficile* reference laboratory [25]. These include:

- Data were collected from 1 May until 30 April of the following year, rather than 1 January until 31 December as per protocol. The last data collection was longer, from 1 May 2019 to 31 December 2020; therefore, Dutch data labelled as 2019 also cover all the data from 2020.
- Patients younger than two years were not included.
- 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 previous healthcare admissions. Therefore, the origin of CDI cases, as defined in the ECDC protocol, was estimated by the Netherlands using the variables ‘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 between 2016 and 2019 (not all years, see below), each providing data compatible with a different surveillance option (UK (England): light; UK (Scotland): minimal; UK (Wales): enhanced). The UK had to interrupt its participation in the ECDC CDI surveillance starting as of 2020 following its withdrawal from the European Union.

- UK-England (from 2017 to 2019): national reporting in UK (England) follows the financial year (April–March) rather than the 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. In addition, the PHE protocol uses an episode length of 28 days rather than 14 days. UK (England) did not report enhanced data as its *Clostridioides difficile* Ribotyping Network (CDRN) data are not yet linked to the PHE surveillance data [26]. In 2019, PHE updated the definition in its protocol for trust-apportioned and non-trust-apportioned cases to be compatible with the definition in the ECDC protocol [26].

- UK (Scotland) (from 2016 to 2019): the Health Protection Scotland (HPS) CDI surveillance protocol [27] 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 NHS Scotland, the data submitted to ECDC only include cases with specimens collected in acute-care hospitals.
- UK (Wales) (from 2017 to 2018): 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-day denominators 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 Wales include HA CDI cases, as this category also includes cases with unknown association. In addition, the only case-level data from the 'light' surveillance option reported by UK (Wales) were age and gender, whether the case was recurrent, and the date of the first positive laboratory sample [28].

Annex 3. European-level data harmonisation and analyses

Harmonisation of ribotype nomenclature

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 named ECDIS-Net-2³, provided by a consortium led by Leiden University Medical Centre (LUMC), the Netherlands. ECDIS-Net-2 developed standard operating procedures (SOP) for diagnostics and typing, harmonised with ESCMID guidance, that were developed and agreed with all EU/EEA countries [29]. In May 2017, ECDIS-Net-2 held a train-the-trainer workshop in its use for nationally designated microbiologists. In October 2018, ECDC published this SOP as the 'Laboratory procedures for diagnosis and typing of human *Clostridium difficile* infection' [29]. In addition, in 2017 and 2019, ECDIS-Net-2 coordinated external quality assessment (EQA) exercises in European national reference laboratories (NRLs), for the capillary electrophoresis (CE) PCR ribotyping (RT) of *C. difficile* strains that are common in European and/or difficult to type. ECDIS-Net-2 also worked collaboratively with national reference laboratories to promote use of a common reference database of the 96 most common PCR ribotypes (RTs). In 2019, LUMC worked with national teams (e.g. NRL for *C. difficile* and Sciensano, Belgium) to identify the European RT nomenclature for strains that had been reported to TESSy >10 times in 2016–2017 with a national RT nomenclature.

Data imputation

- If a case did not have a symptom-onset date reported, the 'first positive laboratory sample date' or the 'sampling date' was used as a proxy.
- Missing denominator data were imputed using the database means. If the total number of beds was available for a hospital, missing values for patient-days were replaced by the 'occupied bed-days', computed as (number of beds) × (bed occupancy) × (the number of days in the surveillance period for that hospital), with bed occupancy assumed to be 95%.
- During some years, countries reported hospital surveillance periods with case-based data (i.e. the 'light' or 'enhanced' surveillance option) and also some periods with no cases, which therefore have no case-based data. In this scenario, the surveillance option is assumed to be the most detailed surveillance option reported by that country that year. For example, they were recoded to have followed the 'enhanced' option if countries reported any 'enhanced' data that year.

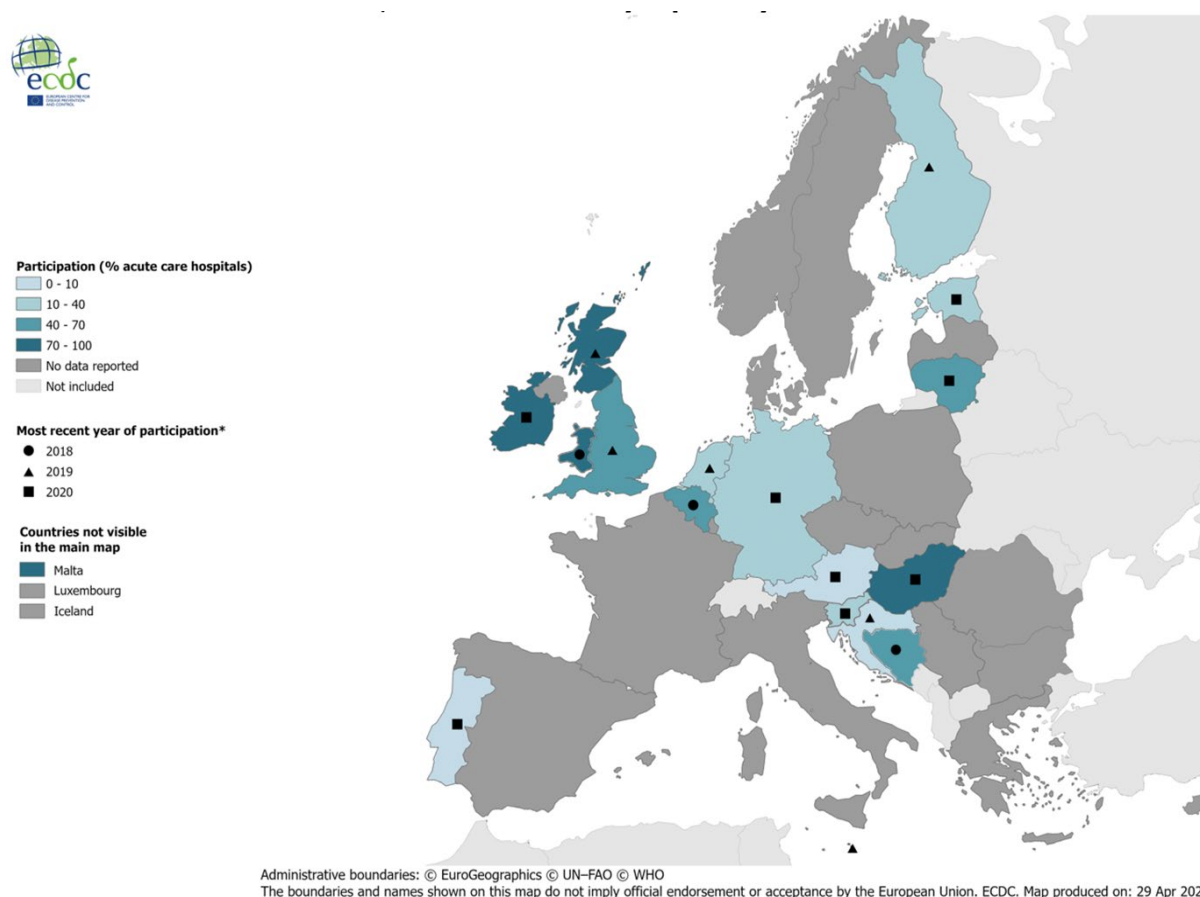
Data analysis

All analyses were performed using STATA 14.0 and R 4.2.0.

³ 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 Centre (LUMC), Leiden, the Netherlands. The consortium members are: Prof. Dr. E.J. Kuijper (LUMC); Dr. D.W. Notermans, Center for Infectious Diseases Control (Cib), RIVM, Bilthoven, the Netherlands; Prof. M.H. Wilcox, University of Leeds, Microbiology, Leeds, United Kingdom; Univ. Prof. Dr. F. Allerberger, Österreichische Agentur für Gesundheit und Ernährungssicherheit (AGES), Wien, Austria; and Prof. Dr. F. Barbut, UHLIN National Reference Laboratory for *Clostridium difficile*, Groupe Hospitalier de l'Est Parisien (HUEP), Paris, France. The project adopted the name 'European *C. difficile* Infection Surveillance Network 2' (ECDIS-Net-2).

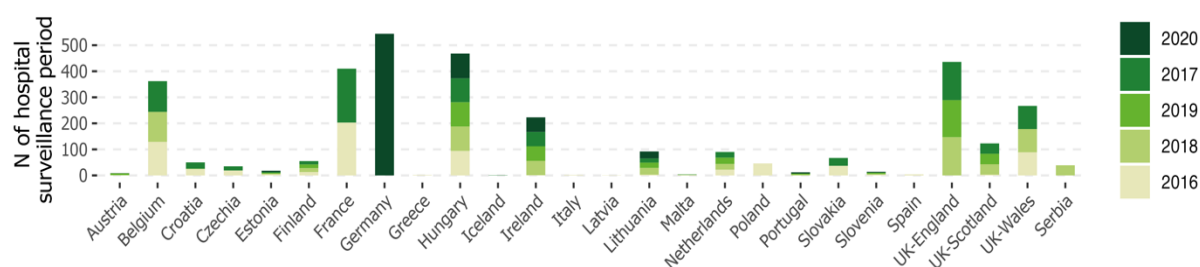
Annex 4. National denominators

Figure A5. National coverage of acute-care hospitals participating in ECDC-coordinated surveillance of *Clostridioides difficile* infection (CDI), for the most recently-reported year during 2018–2020



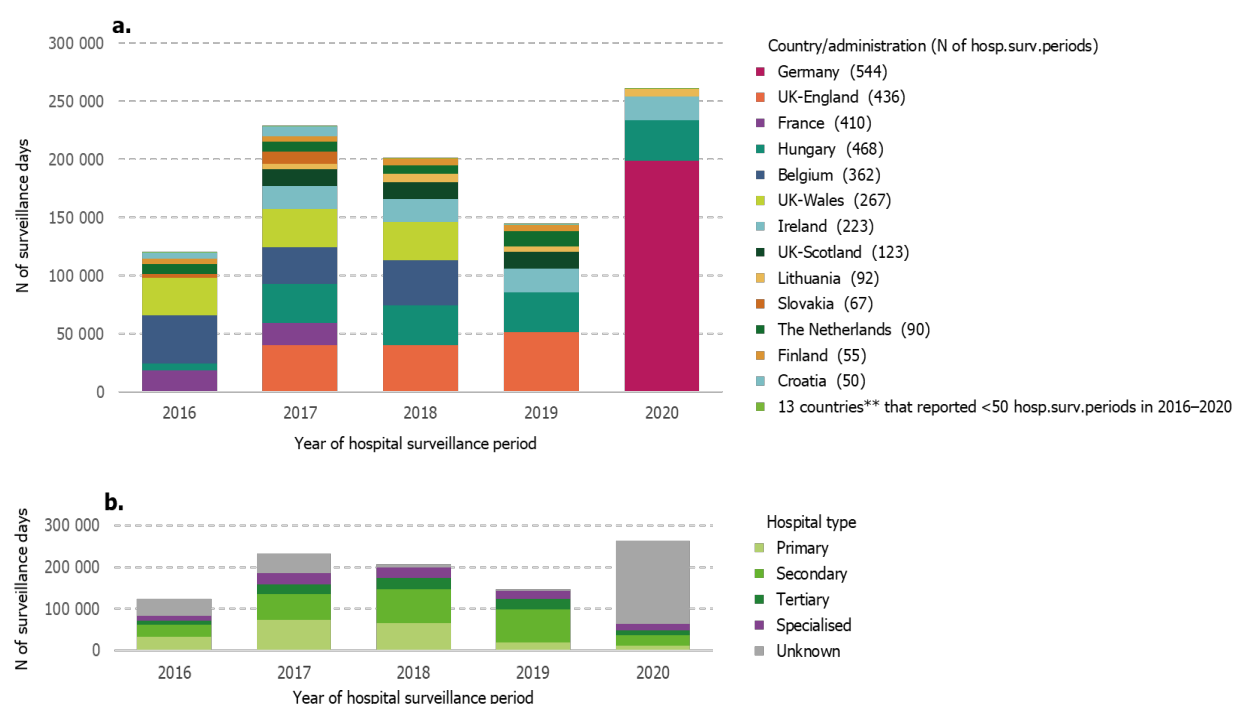
Malta is displayed as 70–100% national coverage, even though only one hospital participated, as that hospital has >75% of all acute-care hospital beds.

Figure A6. Number of hospital surveillance periods with *Clostridioides difficile* infection (CDI) surveillance data reported to ECDC, by European country/UK administration* and year, 2016–2020



* UK 2020 data not included due to its withdrawal from the EU (see Methods section).

Figure A7. Number of surveillance days included in the surveillance data reported to ECDC, by year and (a) European country/UK administration*, or (b) type of acute-care hospital, 2016–2020



* 22 EU/EEA countries, the UK (England, Scotland and Wales) and Serbia. UK 2020 data not included due its withdrawal of the UK from the EU (see Methods section).

** Poland (number of hospitals: 46), Serbia (39), Czechia (35), Estonia (18), Slovenia (14), Portugal (12), Austria (9), Malta (4), Spain (4), Greece (2), Italy (2), Iceland (1) and Latvia (1).

Table A1. National denominators reported to ECDC by participating European country/UK administration*, 2016–2020

Country/ administration*	Hospital surv. periods	2016			2017			2018			2019			2020		
		Patient-days	Discharges	Hospital surv. periods	Patient-days	Discharges	Hospital surv. periods	Patient-days	Discharges	Hospital surv. periods	Patient-days	Discharges	Hospital surv. periods	Patient-days	Discharges	
Austria	1	42 630	8 067	-	-	-	-	-	-	7	760 130	122 872	1	419 509	59 360	
Belgium	129	10 224 812	1 477 305	118	7 781 652	1 172 696	115	9 613 161	1 457 899	-	-	-	-	-	-	
Croatia	24	2 195 903	309 145	24	3 014 629	437 233	1	480 918	68 892	1	606 813	38 904	-	-	-	
Czechia	19	924 021	124 722	16	1 029 839	150 643	-	-	-	-	-	-	-	-	-	
Estonia	4	49 010	7 455	3	84 390	9 994	3	198 293	40 973	3	387 710	49 896	5	506 796	71 091	
Finland	13	1 447 411	506 272	13	1 399 457	510 617	15	1 726 818	594 723	14	1 608 548	517 765	-	-	-	
France	203	3 056 445	592 376	207	2 894 286	579 377	-	-	-	-	-	-	-	-	-	
Germany	-	-	-	-	-	-	-	-	-	-	-	-	544	48 086 369	7 463 173	
Greece	2	72 535	7 556	-	-	-	-	-	-	-	-	-	-	-	-	
Hungary**	94	3 714 597	550 311	92	17 045 170	1 972 926	94	16 935 562	1 977 696	93	16 754 240	1 964 229	95	12 686 176	1 498 992	
Iceland	-	-	-	1	225 388	14 450	-	-	-	-	-	-	-	-	-	
Ireland	1	19 894	1 984	55	3 948 147	677 733	55	4 048 789	683 315	56	4 115 812	686 927	56	3 527 262	602 629	
Italy	2	43 724	5 106	-	-	-	-	-	-	-	-	-	-	-	-	
Latvia	1	20 609	3 738	-	-	-	-	-	-	-	-	-	-	-	-	
Lithuania	3	98 530	13 380	16	1 653 038	215 447	26	2 270 371	288 691	20	1 856 921	241 255	27	1 961 323	262 076	
Malta	1	298 878	57 799	1	314 960	61 567	1	325 208	62 598	1	357 861	63 391	-	-	-	
The Netherlands	22	3 010 478	561 830	22	2 842 621	537 873	22	2 671 490	511 550	24	3 911 874	779 835	-	-	-	
Poland	46	485 479	102 154	-	-	-	-	-	-	-	-	-	-	-	-	
Portugal	-	-	-	-	-	-	3	216 332	28 331	4	161 657	21 515	5	396 794	48 281	
Slovakia**	37	1 116 805	172 559	30	3 495 840	550 535	-	-	-	-	-	-	-	-	-	
Slovenia	3	82 307	13 785	1	113 471	20 454	2	465 454	73 295	5	1 108 022	189 672	3	275 113	45 907	
Spain	4	78 018	11 202	-	-	-	-	-	-	-	-	-	-	-	-	
UK-England	-	-	-	147	25 878 135	5 319 998	147	34 521 855	7 762 044	142	34 922 329	7 831 275	-	-	-	
UK-Scotland	3	78 014	15 124	40	4 366 919	815 588	40	4 336 691	803 733	40	4 349 626	820 642	-	-	-	
UK-Wales	89	3 448 983	458 726	89	3 378 005	460 748	89	3 030 927	466 703	-	-	-	-	-	-	
EU/EEA*	701	30 509 083	5 000 596	875	79 465 947	13 507 879	613	80 841 869	14 820 443	410	70 901 543	13 328 228	736	67 859 342	10 051 509	
Serbia	-	-	-	-	-	-	39	1 352 338	203 093	-	-	-	-	-	-	
Total	701	30 509 083	5 000 596	875	79 465 947	13 507 879	652	82 194 207	15 023 536	410	70 901 543	13 328 228	736	67 859 342	10 051 509	

In total, 26 countries/administrations: 22 EU/EEA countries, with the three participating UK devolved administrations (England, Scotland, and Wales), shown separately and one EU candidate country (Serbia).

* UK 2020 data not included due to its withdrawal from the EU (see Methods section).

** In 2016, 1/36 hospitals in Slovakia and 36/58 hospitals in Hungary participated in two surveillance periods.

Annex 5. National CDI incidence estimates

Table A6. CDI crude incidence and incidence density estimates by participating country/UK administration*, 2016–2020

Country/ Administration*	2016					2017					2018					2019					2020				
	HA Inc. Dens. ^a	CA/UA Inc. ^b	Recurrent Inc. ^b	Total Inc. ^b	Surv. Periods	HA Inc. Dens. ^a	CA/UA Inc. ^b	Recurrent Inc. ^b	Total Inc. ^b	Surv. Periods	HA Inc. Dens. ^a	CA/UA Inc. ^b	Recurrent Inc. ^b	Total Inc. ^b	Surv. Periods	HA Inc. Dens. ^a	CA/UA Inc. ^b	Recurrent Inc. ^a	Total Inc. ^b	Surv. Periods	HA Inc. Dens. ^a	CA/UA Inc. ^b	Recurrent Inc. ^b	Total Inc. ^b	Surv. Periods
Austria	1.64	0.62	0.12	1.61	1	-	-	-	-	-	-	-	-	-	-	2.75	0.55	0.11	2.36	7	2.43	0.49	0.08	2.29	1
Belgium	1.82	0.56	0.21	2.03	129	1.8	0.56	0.17	1.91	118	1.77	0.57	0.18	1.91	115	-	-	-	-	-	-	-	-	-	-
Croatia	1.79	0.32	0.18	1.78	24	2.66	0.4	0.28	2.51	24	2.2	0.9	0.2	2.64	1	1.63	1.67	0.39	4.6	1	-	-	-	-	-
Czechia	2.48	0.3	0.32	2.46	19	3.2	0.35	0.34	2.87	16	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Estonia	4.69	0.4	0.4	3.89	4	5.45	0.5	0.1	5.2	3	1.51	0.1	0.17	1	3	0.34	0.02	0	0.28	3	2.41	0.27	0.24	2.22	5
Finland	3.58	0.14	-	1.16	13	3.62	0.12	-	1.11	13	3.45	0.12	-	1.12	15	3.28	0.11	-	1.13	14	-	-	-	-	-
France	1.92	0.86	-	1.85	203	2	0.81	-	1.82	207	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Germany	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2.52	1.26	0.17	3.06	544
Greece	2.07	0.79	0.53	3.31	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hungary	3.49	0.36	0.2	2.91	94	3.17	0.27	0.16	3.17	92	3.28	0.23	0.17	3.2	94	3.38	0.21	0.16	3.25	93	4.57	0.22	0.15	4.24	95
Iceland	-	-	-	-	-	0.58	0.07	0.9	1.87	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ireland	3.02	1.01	0.5	4.54	1	2.52	1.08	0.27	2.81	55	2.66	1.11	0.28	2.97	55	3.09	1.05	0.28	3.18	56	2.51	1.1	0.26	2.83	56
Italy	2.29	0.39	0.2	2.55	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Latvia	3.4	0	0	1.87	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lithuania	5.99	0.45	0.67	5.53	3	2.11	0.53	0.43	2.57	16	1.55	0.31	0.66	2.19	26	2.16	0.48	0.44	2.59	20	1.02	0.6	0.14	1.51	27
Malta	1.71	0.42	0.03	1.33	1	1.11	0.19	0.06	0.83	1	0.98	0.11	0.02	0.64	1	0.42	0.13	0.05	0.41	1	-	-	-	-	-
Netherlands	1.48	0.67	0.25	1.71	22	1.32	0.7	0.24	1.63	22	1.37	0.73	0.19	1.64	22	1.72	0.75	0.2	1.82	24	-	-	-	-	-
Poland	5.38	0.55	0.46	3.56	46	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Portugal	-	-	-	-	-	-	-	-	-	-	2.77	0.6	0.28	3	3	1.73	0.37	0.51	2.18	4	1.16	0.39	0.27	1.62	-
Slovakia	2.61	0.3	0.08	2.07	37	2.32	0.46	0.11	2.04	30	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Slovenia	2.07	0.44	0.07	1.74	3	4.58	0.2	0.54	3.28	1	2.13	0.25	0.16	1.76	2	1.52	0.17	0.14	1.19	5	1.96	0.22	0.2	1.59	-
Spain	2.95	0.89	0.54	3.48	4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
UK-England	-	-	-	-	-	1.93	0.96	0.08	1.98	147	2.15	0.67	0.08	1.71	147	1.56	0.82	0.07	1.59	142	-	-	-	-	-
UK-Scotland	1.92	0.2	0.07	1.26	3	1.36	0.31	0.06	1.1	40	1.33	0.3	0.07	1.09	40	0.98	0.33	0.06	0.9	40	-	-	-	-	-
UK-Wales	-	1.37	0.09	1.46	89	-	1.5	0.16	1.66	89	-	1.09	0.08	1.17	89	-	-	-	-	-	-	-	-	-	-
EU/EEA*	2.01	0.58	0.16	1.96	701	2.17	0.7	0.13	2.11	875	2.22	0.58	0.12	1.92	613	2.11	0.66	0.11	1.89	410	2.85	1.06	0.18	3.16	736
Serbia	-	-	-	-	-	-	-	-	-	0	4.34	0.45	0.13	3.48	39	-	-	-	-	-	-	-	-	-	-
Total	2.01	0.58	0.16	1.96	701	2.17	0.7	0.13	2.11	875	2.26	0.58	0.12	1.94	652	2.11	0.66	0.11	1.89	410	2.85	1.06	0.18	3.16	736

In total, 26 countries/administrations: 22 EU/EEA countries, with the three participating UK devolved administrations (England, Scotland, and Wales), shown separately and one EU candidate country (Serbia).

* UK 2020 data not included due to the withdrawal of the UK from the EU (see Methods section)

^a Incidence density is calculated over 10 000 patients-days.

^b Incidence is calculated per 1 000 discharges or admissions.

Table A7. Incidence density or incidence of *Clostridioides difficile* infection (CDI) cases in acute care hospitals, by origin of cases and hospital category, EU/EEA* and Serbia, 2018

Origin of CDI cases	Type of hospital	No. of hospitals ^a	Hospital mean	95% confidence interval ^b	Hospital median
HA CDI					
			Incidence density (cases per 10 000 patient-days)		
	Primary	139	1.72	1.36 - 2.15	1.30
	Secondary	261	2.46	2.20 - 2.74	1.93
	Tertiary	91	6.17	1.64 - 15.51	2.12
	Specialised	54	1.1	0.75 - 1.54	0.46
	Unknown	18	3.81	3.17 - 4.53	3.70
	All hospitals	563	2.79	1.83 - 4.04	1.70
CA/UA CDI					
			Incidence (cases per 1 000 discharges or admissions)		
	Primary	189	0.93	0.70 - 1.20	0.37
	Secondary	275	0.67	0.58 - 0.76	0.57
	Tertiary	93	0.53	0.40 - 0.69	0.32
	Specialised	75	0.46	0.16 - 0.99	0.00
	Unknown	18	0.22	0.10 - 0.40	0.00
	All hospitals	650	0.69	0.59 - 0.79	0.41
Recurrent CDI					
			Incidence (cases per 1 000 discharges or admissions)		
	Primary	189	0.26	0.15 - 0.40	0.00
	Secondary	275	0.12	0.10 - 0.14	0.08
	Tertiary	93	0.26	0.14 - 0.44	0.08
	Specialised	75	0.64	0.15 - 1.72	0.00
	Unknown	3	0.41	0.11 - 1.03	0.44
	All hospitals	635	0.24	0.16 - 0.36	0.06
All CDI cases					
			Incidence (cases per 1 000 discharges or admissions)		
	Primary	189	2.27	1.85 - 2.75	1.28
	Secondary	275	2.16	1.96 - 2.38	1.73
	Tertiary	93	2.72	2.22 - 3.29	2.14
	Specialised	75	2.98	1.63 - 4.94	0.32
	Unknown	18	1.60	1.13 - 2.18	1.39
	All hospitals	650	2.35	2.10 - 2.62	1.62

Key: HA – healthcare-associated CDI; CA/UA CDI – community-associated CDI and CDI with unknown association.

* 11 EU/EEA countries, three UK administrations and Serbia. UK-Wales national surveillance is unable to discriminate HA CDI from UA CDI.

^a Number of hospitals with data to compute the incidence density or incidence.

^b 95% confidence intervals based on a quasi-Poisson model to account for overdispersion.

Table A8. Incidence density or incidence of *Clostridioides difficile* infection (CDI) cases in acute care hospitals, by origin of cases and hospital category, EU/EEA*, 2019

Origin of CDI cases	Type of hospital	No. of hospitals ^a	Hospital mean	95% confidence interval ^b	Hospital median
HA CDI					
			Incidence density (cases per 10 000 patient-days)		
	Primary	52	1.41	1.07 - 1.80	1.03
	Secondary	218	1.98	1.78 - 2.20	1.61
	Tertiary	73	2.48	2.02 - 3.01	1.81
	Specialised	49	1.69	0.79 - 3.11	0.49
	Unknown	14	3.75	2.99 - 4.63	3.24
	All hospitals	406	2.02	1.82 - 2.24	1.50
CA/UA CDI					
			Incidence (cases per 1 000 discharges or admissions)		
	Primary	52	0.60	0.24 - 1.21	0.33
	Secondary	218	0.73	0.66 - 0.81	0.68
	Tertiary	73	0.59	0.40 - 0.83	0.22
	Specialised	49	0.90	0.26 - 2.20	0.00
	Unknown	14	0.12	0.04 - 0.25	0.00
	All hospitals	406	0.69	0.56 - 0.84	0.47
Recurrent CDI					
			Incidence (cases per 1 000 discharges or admissions)		
	Primary	52	0.22	0.11 - 0.39	0.00
	Secondary	218	0.11	0.09 - 0.13	0.06
	Tertiary	73	0.20	0.14 - 0.29	0.08
	Specialised	49	1.12	0.35 - 2.58	0.00
	Unknown	0			
	All hospitals	392	0.27	0.15 - 0.43	0.06
All CDI cases					
			Incidence (cases per 1 000 discharges or admissions)		
	Primary	52	2.00	1.25 - 2.99	1.41
	Secondary	218	2.00	1.80 - 2.20	1.56
	Tertiary	73	2.59	2.06 - 3.21	1.99
	Specialised	49	5.64	2.72 - 10.14	0.94
	Unknown	14	1.24	0.97 - 1.56	1.01
	All hospitals	406	2.52	2.06 - 3.04	1.52

Key: HA – healthcare-associated CDI; CA/UA CDI – community-associated CDI and CDI with unknown association.

* 11 EU/EEA countries and two UK administrations.

^a Number of hospitals with data to compute the incidence (density).

^b 95% confidence intervals based on a quasi-Poisson model to account for overdispersion.