

9.1 *Clostridium difficile* Infection

Key Points

- In 2015, 1,943 cases of *Clostridium difficile* infection (CDI) were notified. Of those, 1,647 (85%) were classified as new cases, 192 (10%) as recurrent, with 104 (5%) of unknown case type. This represents a national crude incidence rate (CIR) for new and recurrent CDI combined of 42.3 cases per 100,000 population, an increase of 3.8% compared to the rate reported in 2014 (38.5)
- Of the 1,943 CDI cases, 1,323 (68%) were reported from patients aged 65 years or older
- For the first time since it was established in 2009, there were slightly more CDI cases reported to the voluntary enhanced CDI surveillance scheme than were notified to Public Health Departments. Enhanced data was received on 1,955 CDI cases from 54 hospitals. Of those, 1,221 (62%) were healthcare-associated, representing a national CDI incidence rate for new and recurrent healthcare-associated CDI combined of 2.5 cases per 10,000 bed days used for 2015, an increase from 2.3 in 2014
- Data collected on patient location at symptom onset highlights that CDI is not confined to acute healthcare facilities. It is commonly encountered in long term care facilities (9% of all CDI) and in the community (34% of all CDI)
- Of 219 *C. difficile* isolates with available ribotyping data (11% of all cases) reported from 20 hospitals, the most frequent ribotypes reported in 2015 were: 078 (n=33, 15%), 005 and 014 (both n=18, 8%), and 002 (n=14, 6%)

Notifiable *C. difficile* infection

In May 2008, new cases of CDI in persons two years or older became notifiable in Ireland under the disease category “acute infectious gastroenteritis” (AIG). Since January 2012, CDI has become a notifiable infection in its own category, with both new and recurrent CDI cases now notifiable. In 2015, 1,943 cases of CDI were notified to Public Health Departments via the Computerised Infectious Diseases Reporting (CIDR) system. Of those, 1,647 (85%) were classified as new, 192 (10%) as recurrent, with 104 (5%) of unknown case type. All cases were laboratory-confirmed. Taking both new and recurrent cases into account, the overall CIR for 2015 was 42.3 per 100,000 population, which is higher than the reported rate in 2014 (38.5). At 35.9 per 100,000 population, the national CIR of new CDI cases in 2015 was a slight increase of 0.8% from 35.1 per 100,000 population in 2014.

Since surveillance began in 2008, there has been a decrease in the incidence of CDI in Ireland (**Figure 1**). Since 2012, the CDI incidence rate has remained stable. There was a slight increase in the number of recurrent cases notified in 2015 (n=192) compared to 2014 (n=155). Identification of seasonal patterns from CIDR notification data is hindered by delayed and batched laboratory notifications.

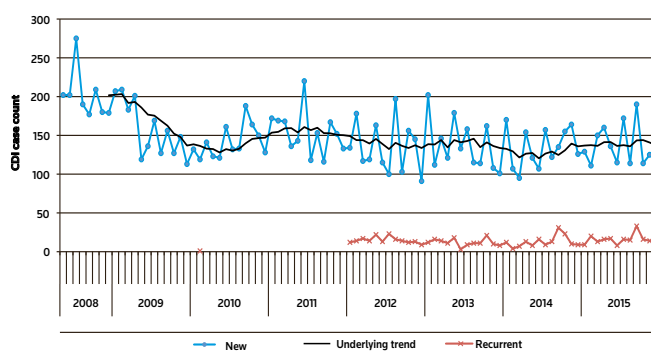


Figure 1. Numbers of CDI notifications by month and case type (2008 – 2015)

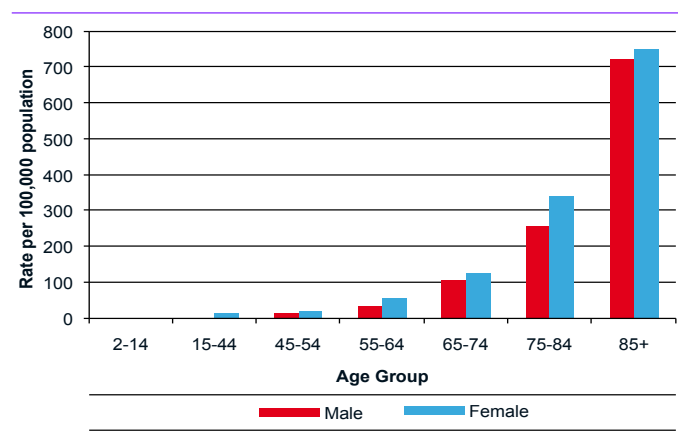
Figure 2 displays the gender and age breakdown of patients with CDI. The majority were female (62%). The mean age was 67 years (range: 2 – 102), with 1,323 cases (68%) reported in patients aged 65 years and older.

Regarding patient location at the time of CDI diagnosis, most were classified as 'hospitalised' (69%), with 14% from general practice, 6% from the emergency department, 4% from outpatients or day patients and 7% from either 'other', or 'unknown' patient location. This is similar to that reported in 2014. However, notifiable CDI data does not provide information on the origin or onset of CDI, as that information is collected as part of the enhanced CDI surveillance scheme.

In 2015, 35 deaths were reported in patients with CDI, which is higher than that reported in 2014 (n=22). Of those, 28 deaths were deemed not attributed to CDI, for six cases the contribution of CDI to death was unknown and one death was attributed to CDI.

Notifiable *C. difficile* infection: Outbreaks

In 2015, 12 CDI outbreaks, 11 of which were healthcare-associated and involving 42 patients, were notified to Public Health Departments, as displayed in **Table 1**. Nine were



* Rates calculated using 2011 census data
 Figure 2. Age and gender distribution of CDI in Ireland, 2015
 (Source: CIDR)

Table 1. CDI outbreaks reported in Ireland in 2015 by public health region (Source: CIDR)

Public Health Region	Outbreak location	Total number ill
East	Hospital	2
East	Hospital	2
East	Hospital	-
East	Nursing home	6
East	Other	3
MWHB	Hospital	4
NEHB	Comm. Hosp/Long-stay unit	3
NEHB	Hospital	5
WHB	Hospital	3
WHB	Hospital	3
WHB	Hospital	3
WHB	Hospital	8

linked to hospitals, two to nursing homes, and one specified as "other".

Enhanced surveillance of *C. difficile* infection

Although notifiable CDI data provides important preliminary information on the burden of CDI in Ireland, it does not capture information on the origin, onset or severity of CDI. National *C. difficile* enhanced surveillance commenced on a voluntary basis on 1st August 2009. Information on case type, origin, onset and infection severity is collected using the European Society for Clinical Microbiology and Infectious Diseases Study Group on *C. difficile* (ESCMID-ESGCD) interim case definitions. To the end of 2015, 54 acute hospitals participated in enhanced CDI surveillance, comprising 45 public hospitals [94% of all public hospitals: 27 general (100%), nine tertiary (100%) and nine specialist (75%)] and nine private hospitals (75%).

In 2015, 1,955 CDI cases were reported to the enhanced surveillance scheme. Of those, 1,667 (85%) were classified as new, 208 (11%) as recurrent and 80 (4%) of unknown CDI case type.

Of the reported cases, 62% (n=1,221) originated within the reporting healthcare facility. The CDI rate is based on the number of new and recurrent CDI cases that originated in the participating healthcare facility (both public and private hospitals). The rate is calculated using acute public

Table 2. Origin and onset of CDI, 2013 – 2015

	Year		
	2013 %	2014 %	2015 %
ORIGIN: Location of where infection was acquired			
Healthcare-associated	64	64	62
Hospital	49	48	47
NH/LTCF	11	11	9
Other	4	5	6
Community-associated	18	18	22
Indeterminate	5	5	6
Unknown	13	13	10
ONSET: Location of where patient symptoms occurred			
Healthcare-onset	61	59	59
Hospital	45	44	45
NH/LTCF	11	11	9
Other	4	4	5
Community-onset	29	34	34
Unknown	11	7	7

hospital activity data from the HSE Business Intelligence Unit, with private hospital activity data provided directly by participating hospitals. The overall national CDI incidence rate of new and recurrent healthcare-associated CDI cases combined was 2.5 cases per 10,000 bed days used (BDU), an increase from 2.3 in 2014. The incidence rate of new CDI was 2.3 cases per 10,000 BDU, an increase from 2.1 in 2014. The incidence of recurrent cases also increased to 0.3 cases per 10,000 BDU from 0.2 in 2014.

Since enhanced surveillance began, the national annual combined new and recurrent CDI rate declined from 3.1 cases per 10,000 BDU (2009) to the lowest recorded rate of 2.3 (2014), followed by an increase to 2.5 in 2015 (**Figure 3**).

Caution should be taken when interpreting national CDI trends, particularly prior to 2012 due to:

- (i) Changes in the numbers of participating hospitals, as displayed in **Figure 3**. Throughout 2012, the total number of hospitals participating in enhanced CDI surveillance stabilised. Since 2012, there has been a complete participation in CDI enhanced surveillance by all tertiary and general hospitals
- (ii) Changes in *C. difficile* laboratory testing protocols: From 2013 to 2015, there were fewer changes in laboratory testing protocols. Please also refer to the section on laboratory testing of *C. difficile* in Ireland

There was a wide range in the incidence of CDI among participating hospitals in 2015 (range, 0 – 4.9 cases per 10,000 BDU; median = 1.8). In 2015, tertiary hospitals (n = 9) had a median CDI rate of 3.2 cases per 10,000 BDUs (range: 1.9 – 4.1), which was higher when compared to that of general hospitals (n = 27), with a median rate of 1.0 (range: 0 – 4.5). Since 2011, the median CDI rate in general hospitals declined from 2.4 to 1.0. However, for tertiary hospitals, 2015 marked the first increase in median CDI rate since 2010.

The differences in CDI median incidence rates may reflect inter-hospital variation with regard to patient case mix, *C. difficile* ribotypes, laboratory testing protocols, antimicrobial prescribing policies, antimicrobial stewardship interventions, infrastructure and access to *en suite* isolation rooms and surveillance resources. No obvious seasonal trend for CDI is distinguishable from enhanced surveillance data in 2015.

The percentage coverage of acute hospital activity was calculated using bed days used data from participating hospitals as a percentage of total acute hospital bed days used activity in Ireland

Severe CDI

A severe case of CDI is defined as (i) a patient requiring admission to an intensive care unit (ICU) for treatment of CDI or its complications, (ii) a patient requiring colectomy or (iii) death within 30 days after diagnosis, if CDI is either the primary or contributory cause of death. The enhanced CDI surveillance scheme does not collect information on patient outcome. Therefore, surgery and ICU admission for CDI are the two markers of severity captured via enhanced surveillance. In 2015, 30 (1.5%) severe CDI cases were reported, similar to 2014 (1.4%). One patient required both surgery and ICU admission, five required surgery only and 24 required ICU admission without surgery.

Onset & Origin of CDI

Onset: Patient location when symptoms of CDI commenced

Fifty-nine percent (n=1,159) of patients had CDI symptom onset in a healthcare facility (healthcare-onset), 34% (n=669) had symptom onset in the community and for 7% (n=127), location at CDI onset was unknown (**Table 2**).

Of the 1,159 patients with healthcare onset CDI, 76% (n=876) had onset in the reporting hospital, 4% (n=52) in another hospital, 16% (n=183) in a long term care facility (LTCF) and for the remaining 4% (n=48) onset location was unknown. Between 2013 and 2015, there was a decrease in the proportion of patients with CDI symptom onset in a healthcare facility (61 to 59%). Community onset increased from 29% to 34% between 2013 and 2014, where it remained unchanged in 2015 (**Table 2**).

Origin: Location where the patient acquired the CDI

For the majority of CDI cases, the infection was acquired in a healthcare setting (healthcare-associated) (n=1,221; 62%). Community-associated cases accounted for 22% (n=420) and in 6% (n=123) the origin was indeterminate and could not be assigned as either healthcare or community-associated, as the patient had been discharged from a healthcare facility between four and 12 weeks prior to the CDI onset date. For the remaining 10% (n=191) of cases, the origin was unknown (**Table 2**).

Table 3. National reporting of *C. difficile* ribotyping data: 2011 - 2015

Year	Total number of CDI cases reported	Number (%) of cases with ribotype data	Number of hospitals providing ribotype data
2011	1511	211 (14%)	10
2012	1735	263 (15%)	14
2013	1801	258 (14%)	19
2014	1780	290 (16%)	20
2015	1955	219(11%)	22

Of the 1,221 healthcare-associated CDI cases, 76% (n=928) originated in the reporting hospital, 7% (n=83) originated in a hospital other than the reporting hospital, 14% (n=173) originated in a LTCF and 3% (n=37) originated in another unspecified healthcare facility or were of unknown origin.

Between 2013 and 2015, there was a small decrease in the proportion of cases associated with a healthcare facility (64 to 62%), which was demonstrated in the reporting hospital, as well as LTCF. The proportion of cases associated with the community increased from 18% to 22%, and there was slight increase in cases classified as indeterminate (from 5% to 6%). Cases classified as 'unknown' decreased from 13% to 10% between 2014 and 2015 (Table 2).

Of the 1,221 cases of healthcare-associated CDI:

- 87.5% (n=1,068) experienced onset of CDI symptoms at least 48 hours following admission to a healthcare facility (healthcare-onset, healthcare-associated)
- 12% (n=147) experienced symptom onset in the community, within four weeks of discharge from a healthcare facility (community-onset, healthcare-associated)
- 0.5% (n=6) had no information recorded on symptom onset

Of the 420 cases of community-associated CDI:

- 93% (n=389) experienced CDI symptom onset while outside a healthcare facility and without a history of discharge from a healthcare facility within the previous 12 weeks (community-onset, community-associated)
- admission to or residence in a healthcare facility within the previous 12 weeks (healthcare-onset, community-associated)

Information was also captured on the location where the patient's faeces specimen was taken. The reporting hospital accounted for the majority (76%) of specimens (n=1,490),

with 12% (n=225) taken in the GP surgery, 8% (n=156) in LTCF and 3% (n=65) in a hospital other than the reporting hospital. For the remaining 1% (n=19), no information was provided.

Discussion

The collation of national data on *C. difficile* through CIDR notifications and the enhanced CDI surveillance system has provided a valuable insight into the burden of CDI in Ireland. Both surveillance systems present a similar decreasing trend since 2009. The notifiable surveillance system, which reflects total burden of disease, shows that the CDI rate stabilised between 2012 and 2015, while the enhanced surveillance system shows a decrease in the CDI rate between 2012 and 2014, but a slight increase in 2015. For the first time in 2015, cases reported to enhanced CDI surveillance exceeded those notified to public health departments.

In 2015, recurrent CDI accounted for 11% of notifications through the enhanced surveillance scheme, which is an increase from 8% in 2014. Recurrent CDI may result in severe infection, which places a further burden on limited hospital isolation resources and results in significant patient morbidity.

CDI is not confined to acute healthcare settings and is increasingly common in LTCF and the community. In 2015, 9% of cases had onset in LTCF, with 34% having onset in the community. Of the 420 community-associated cases reported in 2015, 93% experienced CDI symptom onset in the community, without a history of discharge from a healthcare facility within the previous 12 weeks. It is important to consider CDI in the differential diagnosis of all patients presenting with diarrhoea of potentially infectious origin, regardless of patient location and to send a faeces specimen in a timely fashion for laboratory diagnosis, which should routinely include testing for *C. difficile* in patients aged over two years, in keeping with national CDI guidelines.

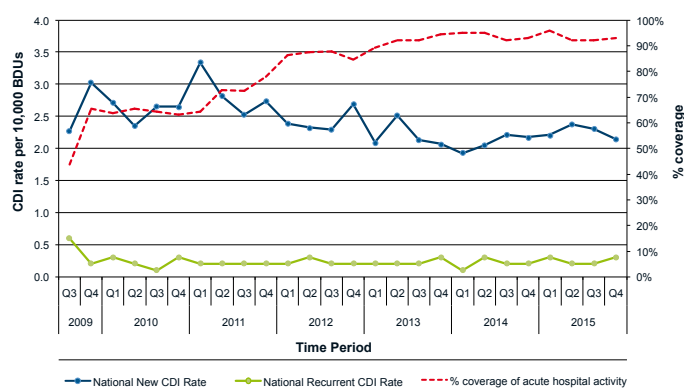


Figure 3. Quarterly national rate of healthcare-associated CDI (new and recurrent): 2009 – 2015

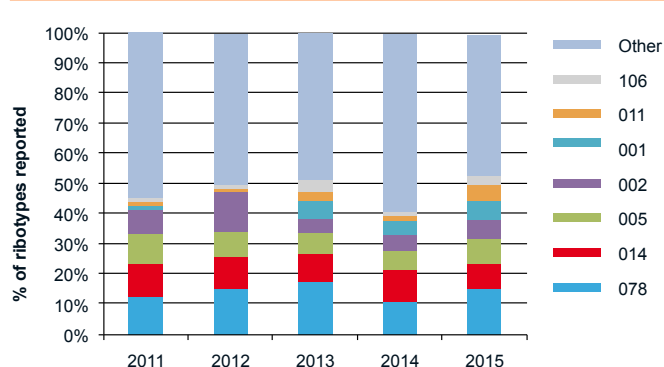


Figure 4. Most frequently reported *C. difficile* ribotypes in Ireland: 2010 – 2015

C. difficile PCR ribotyping

As part of the voluntary *C. difficile* enhanced surveillance scheme, participating hospitals are requested to provide *C. difficile* PCR ribotyping information, where available. Ireland does not yet have a national *C. difficile* reference laboratory or ribotyping service. Therefore, laboratories submit specimens abroad for ribotyping. In 2015, ribotyping data was provided for 219 *C. difficile* isolates (11% of all samples) from 20 hospitals (**Table 3**). The most frequent ribotypes reported in 2015 were: 078 (n=33, 15%), 005 and 014 (both n=18, 8%), and 002 (n=14, 6%) (**Figure 4**).

Laboratory Testing of *C. difficile* in Ireland

Since 2010, information on *C. difficile* testing has been collected quarterly as part of the enhanced surveillance system. In Q1 2010, the majority of hospitals participating in the enhanced surveillance project were using a one-step Toxin EIA (60%). By Q4 2015, this had reduced to 0%. All hospitals participating in the enhanced surveillance system are now using a method which complies with recommendations in the 2014 update of the 2008 Irish *C. difficile* guidelines. This includes either a PCR test for detection of toxin genes (43%, n=23) or a two-step testing method (57%, n=30) (**Figure 5**). Owing to variations in current Irish laboratory *C. difficile* testing methodologies, inter-hospital comparison of CDI rates is not recommended

where testing methods differ, as the data in the national quarterly enhanced surveillance reports are not adjusted for differences in the sensitivities of the different diagnostic methodologies.

Conclusion

The continued excellent participation in the voluntary CDI enhanced surveillance scheme ensures that a significant amount of information is collected regarding the burden of CDI in Ireland. The National Clinical Guidelines on the Surveillance, Diagnosis and Management of CDI in Ireland were updated in 2013 and endorsed by the National Clinical Effectiveness Committee in 2014. The updated guidelines may be accessed on the HPSC website at: <http://www.hpsc.ie/A-Z/Gastroenteric/Clostridiumdifficile/Guidelines/>.

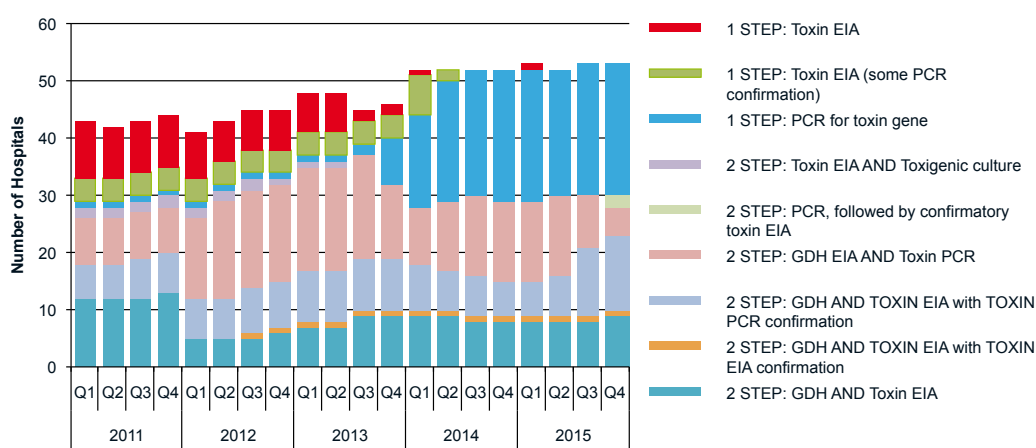


Figure 5. Changes in *C. difficile* laboratory testing protocols: 2011 - 2015

1 STEP: Toxin EIA: EIA for the detection of *C. difficile* TcdA and/or TcdB. **1 STEP: PCR for toxin gene:** Polymerase chain reaction (PCR) for the detection of TcdA and/or TcdB genes; **2 STEP: GDH AND TOXIN EIA:** Enzyme immunoassay (EIA) for the detection of glutamate dehydrogenase (GDH) of *C. difficile* as well as or followed by an EIA for the detection of *C. difficile* TcdA and/or TcdB.; **2 STEP: GDH EIA AND Toxin PCR:** EIA for the detection of GDH of *C. difficile* as a first screening test, followed by PCR for the detection of TcdA and/or TcdB genes;