9.1 *Clostridium difficile* Infection

Key Points

- In 2016, 1,871 cases of *Clostridium difficile* infection (CDI) were notified to Public Health Departments via the Computerised Infectious Disease Reporting (CIDR) System, representing a national crude incidence rate (CIR) of 40.4 cases per 100,000 population, a 1% reduction on 2015 (41.4). The majority of CDI occurred in patients aged ≥65 years (1,237; 66%). When further divided by case type, there were 1,483 new cases (79%), 174 recurrent (9%) and for 214 cases (11%) it was not known whether the patient had new or recurrent CDI
- There were 1,877 CDI cases reported to the CDI enhanced surveillance scheme from 54 hospitals. Healthcare-associated (HCA) CDI accounted for 60% of cases (n=1,116), representing a national combined incidence rate for new and recurrent HCA CDI of 2.2 per 10,000 bed days used in 2016, a reduction from 2.5 in 2015
- Enhanced surveillance collects data on patient location at symptom onset and shows that CDI is not confined to hospitals. In 2016, CDI was commonly encountered in long-term care facilities (LTCF) (10% of all CDI) and in the community (39% of all CDI)
- Of 300 *C. difficile* isolates with available ribotyping data (16% of all cases) reported from 16 hospitals, the most frequent ribotypes reported in 2016 were: 078 (n=51, 17%), 014 (n=33, 11%) and 002 (n=29, 10%)

Background

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 been a notifiable infection in its own category, with both new and recurrent CDI cases notifiable to Public Health Departments via the Computerised Infectious Disease Reporting (CIDR) system.

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 CDI enhanced surveillance commenced on a voluntary basis on 1st August 2009. Information on case type, origin, onset and infection severity is collected using European CDI case definitions.

Notifiable *C. difficile* infection

In total, 1,871 cases of *Clostridium difficile* infection (CDI) were notified to Public Health Departments via the Computerised Infectious Disease Reporting (CIDR) System, representing an overall national crude incidence rate (CIR) of 40.4 cases per 100,000 population, a 1% reduction on 2015 (41.4). The national CIR of new CDI cases alone was 32 (2016), a 3.9% reduction on 2015 (35.9). The majority of CDI occurred in patients aged ≥65 years (1,237; 66%). When further divided by case type, there were 1,483 new cases (79%), 174 recurrent (9%) and for 214 cases (11%) it was not known whether the patient had new or recurrent CDI. All cases were laboratory-confirmed.

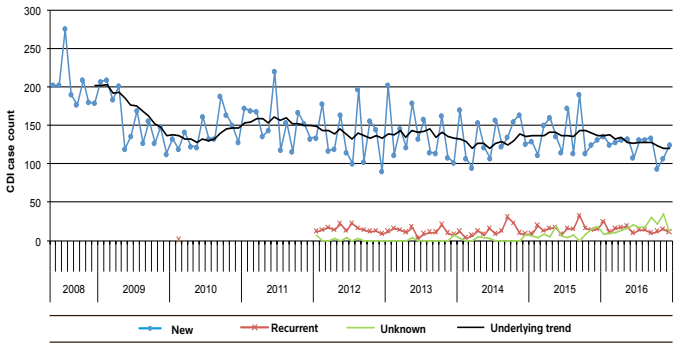

Figure 1. Numbers of CDI notifications by month and case type (2008 – 2016).

Since surveillance began in 2008, there has been an overall decrease in the incidence of CDI in Ireland, with the rate remaining relatively stable since 2012 (**Figure 1**). There was a slight decrease in the number of recurrent cases notified in 2016 than in 2015 (n=174 versus n=192) and an increase in the number of cases of unknown type for the same period (n=214 versus n=104). Identification of seasonal patterns from CIDR notification data is hindered by delayed and batched laboratory notifications.

Figure 2 displays the gender and age breakdown of patients with CDI. The majority were female (60%). The mean age was 66.9 years (range: 2 – 103), with the majority of cases (n=1,237; 66%) reported in patients ≥65 years.

Notifiable *C. difficile* infection: Outbreaks

In 2016, seven CDI outbreaks, all of which were healthcare-associated and involving 24 patients were notified to Public Health Departments, as displayed in **Table 1**. Four were linked to nursing homes, two to hospitals and one to a residential institution.

Enhanced surveillance of *C. difficile* infection

To the end of 2016, 54 acute hospitals participated in enhanced CDI surveillance, comprising 45 public hospitals (96% of all public hospitals). Public hospitals were further categorised into: general (n=27; 100%), tertiary (n=9; 100%) and specialist (n=9; 75%), with nine private hospitals (75%) also participating.

In 2016, 1,877 CDI cases were reported to the enhanced surveillance scheme. Of those, 1,566 (83%) were classified as new, 191 (10%) as recurrent and 120 (7%) of unknown CDI case type.

Of the reported cases, 44% (n=830) originated within the reporting hospital. The overall HCA CDI rate is based on the total number of CDI cases that originated in the participating hospital (i.e., new, recurrent and unknown combined). The bed days used data for acute public hospitals was sourced from the HSE Business Information Unit, with private hospital activity data provided directly by participating hospitals. In 2016, the overall HCA CDI rate was 2.2 cases per 10,000 bed days used (BDU), a decrease from 2.5 in 2015 and the lowest recorded annual rate since surveillance began in 2009 (3.1), as shown in **Figure 3**. The 2016 incidence rate of new HCA CDI was 1.9, a reduction from 2.3 in 2015. The incidence rate of recurrent HCA CDI remained stable at 0.3, as found in 2015.

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

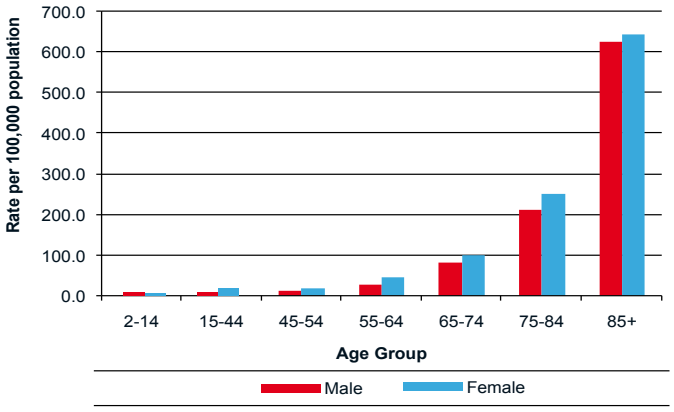

Figure 2: Age and gender distribution of CDI in Ireland, 2016 (Source: CIDR).

* Rates calculated using 2016 census of the population data

Table 1. CDI outbreaks reported in Ireland in 2016 by public health region (Source: CIDR)

Public Health Region	Outbreak location	Total number ill
MWHB	Nursing home	2
MWHB	Nursing home	8
NEHB	Nursing home	3
NEHB	Nursing home	3
NEHB	Hospital	5
WHB	Residential institution	4
WHB	Hospital	3

Table 2. Origin and onset of CDI, 2014 – 2016

	2014 %	2015 %	2016 %
ORIGIN: Location of where infection was acquired			
Healthcare-associated	64	62	60
Hospital	48	47	44
NH/LTCF	11	9	10
Other	5	6	5
Community-associated	18	22	25
Indeterminate	5	6	7
Unknown	13	10	9
ONSET: Location of where patient symptoms occurred			
Healthcare-onset	59	59	56
Hospital	44	45	41
NH/LTCF	11	9	10
Other	4	5	4
Community-onset	34	34	39
Unknown	7	7	5

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 2014 to 2016, most hospitals have participated in the scheme and a similar profile of testing is evident over time with more hospitals incorporating molecular methods (Please also refer to the section on laboratory testing for *C. difficile)*

In 2016, a wide range in the CDI incidence rate in participating hospitals was observed (range = 0 – 5.0; median = 1.3). The median rate was higher in nine tertiary hospitals (2.9; range = 1.3 – 3.9) than in 27 general hospitals (1.6; range = 0 – 5.0). Since 2012, the overall trend for general hospitals has declined slightly (median CDI rate from 1.9 to 1.6). However, in the same period, the overall trend for tertiary hospitals increased, although the median CDI rate of 2.9 in 2016 was slightly lower than that of 3.2 (2015).

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 2016.

The percentage coverage of acute hospital activity was calculated using bed days data from participating hospitals as a percentage of total acute hospital bed day 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. In 2016, 30 (1.6%) severe CDI cases were reported, similar to 2015 (1.5%). Five patients required both surgery and ICU admission, eight required surgery only and 17 required ICU admission without surgery.

Onset & Origin of CDI

Onset: Patient location when symptoms of CDI commenced

CDI symptom onset occurred in a healthcare facility for 56% of patients (n=1,047; healthcare-onset), while 39% had symptom onset in the community (n=735; community-onset) and for 5% (n=95), location at CDI onset was unknown (**Table 2**).

Of the 1,047 patients with healthcare onset CDI, 74% (n=772) had onset in the reporting hospital, 5% (n=50) in another hospital, 18% (n=192) in a long term care facility (LTCF) and for the remaining 3% (n=33) onset location was unknown. Between 2014 and 2016, there was a slight reduction in the proportion of patients with CDI symptom onset in a healthcare facility (59 to 56%). Over the same period, community-onset CDI increased from 34% to 39% (**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; HCA) (n=1,116; 60%). Community-associated; CA accounted for 25% (n=459) and in 7% (n = 133) the origin was indeterminate and could not be assigned as either HCA or CA, as the patient had been discharged from a healthcare facility between four and 12 weeks prior to the CDI onset date. For the remaining 9% (n = 169) of cases, the origin was unknown (**Table 2**).

Of the 1,116 healthcare-associated CDI cases, 74% (n=830) originated in the reporting hospital, 7% (n=74) originated in a hospital other than the reporting hospital, 17% (n=186) originated in a LTCF and 2% (n=24) originated in another unspecified healthcare facility or were of unknown origin.

Between 2014 and 2016, there was a decrease in the proportion of cases associated with a healthcare facility (64 to 60%), which was demonstrated primarily in the reporting hospital. The proportion of cases associated with the community increased from 18% to 25%, and there was a slight increase in cases classified as indeterminate (from 5% to 7%). Cases classified as 'unknown' decreased from 13% to 9% between 2014 and 2016 (**Table 2**).

Of the 1,116 cases of healthcare-associated CDI:

- Healthcare-onset, healthcare-associated: 86.7% (n=968) experienced onset of CDI symptoms at least 48 hours following admission to a healthcare facility
- Community-onset, healthcare-associated: 12.5% (n=139) experienced symptom onset in the community, within four weeks of discharge from a healthcare facility
- No information on symptom onset provided for 0.8% (n = 9)

Table 3. National reporting of C. difficile ribotyping data: 2012 - 2016

Year	Total number of CDI cases reported	Number (%) of cases with ribotype data	Number of hospitals providing ribotype data
2012	1735	263 (15%)	14
2013	1801	258 (14%)	19
2014	1780	290 (16%)	20
2015	1955	219 (11%)	22
2016	1877	300 (16%)	16

Of the 459 cases of community-associated CDI:

- Community-onset, community-associated: 91.7% (n=421) experienced CDI symptom onset while outside a healthcare facility and without a history of discharge from a healthcare facility within the previous 12 weeks
- Healthcare-onset, community-associated: 7.4% (n=34) experienced symptom onset within the first 48 hours of admission to a healthcare facility, without a history of admission to or residence in a healthcare facility within the previous 12 weeks
- No information on symptom onset provided for 0.9% (n=4)

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=1,434), with 13% (n=241) taken in the GP surgery, 7% (n=137) in a LTCF and 3% (n=47) in a hospital other than the reporting hospital. For the remaining 1% (n=18), 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 decreasing trend since 2009. The notifiable surveillance system, which reflects total burden of disease, shows that the CDI rate remained stable between 2012 and 2016, while the enhanced surveillance system shows a decrease in the CDI rate between 2012 and 2016. For the second consecutive year, cases reported to enhanced CDI surveillance in 2016 exceeded those notified to public health departments.

In 2016, recurrent CDI accounted for 10% of notifications through the enhanced surveillance scheme, which is a slight decrease from 11% in 2015. Recurrent CDI 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 2016, 10% of cases had onset in a LTCF, with 39% having onset in the community; a 5% increase since 2015 (34%). Of the 459 community-associated cases reported in 2016, 92% 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.

C. difficile PCR ribotyping

As part of the voluntary *C. difficile* enhanced surveillance scheme, participating hospitals are asked 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 2016, ribotyping data was provided for 300 *C. difficile* isolates (16% of all samples) from 16 hospitals (**Table 3)**. The most frequent ribotypes reported in 2016 were: 078 (n=50, 17%), 014 (n=33, 11%) and 002 (n=29, 10%) (**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 2016, this had reduced to 0%, with all hospitals participating in the enhanced surveillance system using a method compliant with recommendations in the latest update of the 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=31) (**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.

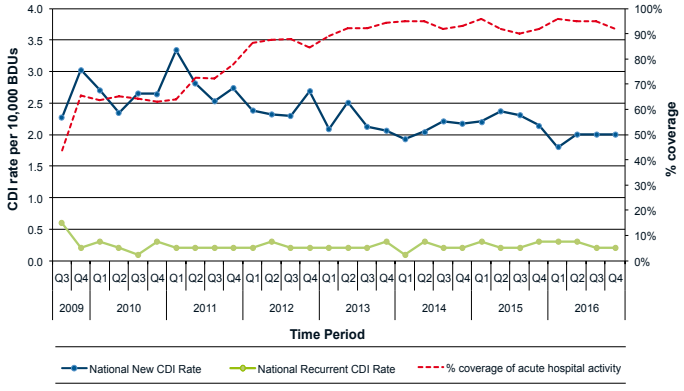

Figure 3. Quarterly national rate of healthcare-associated HCA CDI (new and recurrent): 2009 – 2016

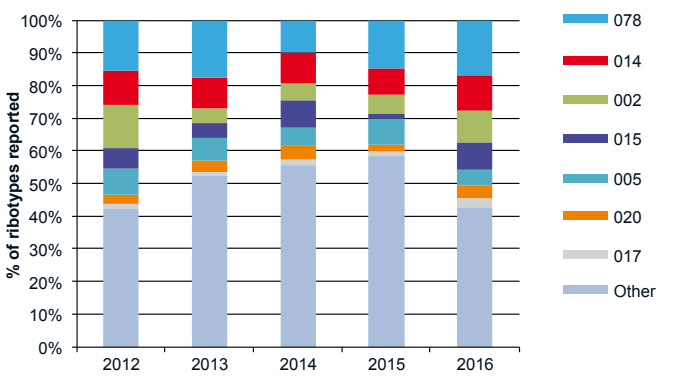

Figure 4. Most frequently reported C. difficile ribotypes in Ireland: 2012 – 2016

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/

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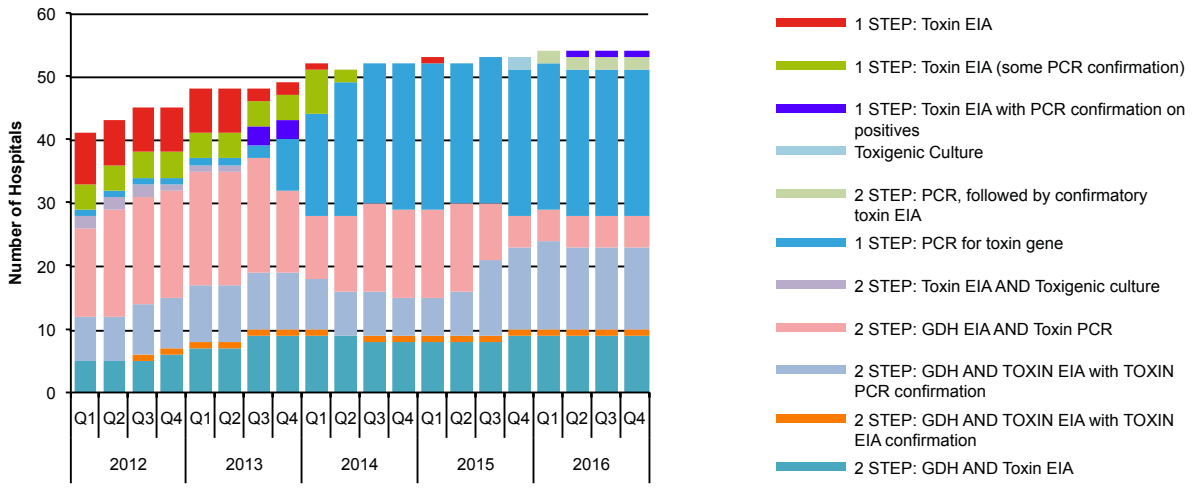

Figure 5. Changes in C. difficile laboratory testing protocols: 2012 - 2016

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;