Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

hpsc

Clostridium difficile Infection

Summary

- In 2014, 1,802 cases of *Clostridium difficile* infection (CDI) were notified. Of those, 1,613 (89.5%) were classified as new cases, 155 (8.5%) as recurrent, with 34 (2%) of unknown case type. This represents a national crude incidence rate of 38.5 cases per 100,000 population, which represents a small decrease compared to the rate reported in 2013 (41.3)
- Of the 1,802 CDI cases, 1,202 (67%) were reported from patients aged 65 years or older
- The voluntary enhanced CDI surveillance scheme received information on 1,780 CDI cases from 53 hospitals, covering 94% of all cases notified to Public Health Departments. Of those, 928 were healthcare-associated, representing a national CDI incidence rate of 2.3 cases per 10,000 bed days used for 2014, a decrease from 2.4 in 2013
- 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 (7% of all CDI) and in the community (34% of all CDI)
- Of 290 *C. difficile* isolates with available ribotyping data (16% of all cases) reported from 20 hospitals, the most frequent ribotypes reported in 2014 were: 078 and 014 (both n=31; 11%), 015 (n=27, 9%) and 005 (n=18, 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 2014, 1,802 cases of CDI were notified to Public Health Departments via the Computerised Infectious Diseases Reporting (CIDR) system. Of those, 1,613 (89.5%) were classified as new, 155 (8.5%) as recurrent, with 34 (2%) of unknown case type. All cases were laboratory-confirmed.

The national crude incidence rate (CIR) of new CDI cases in 2014 was 35.1 per 100,000 population, a decrease of 3.3% from 37.5 per 100,000 population in 2013. Taking both new and recurrent cases into account, the overall CIR for 2014 was 38.5 per 100,000 population, which is lower than the reported rate in 2013 (41.3).

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 2014 (n=155) compared to 2013 (n=146). Identification of seasonal patterns from CIDR notification data is hindered by delayed and batched laboratory notifications.

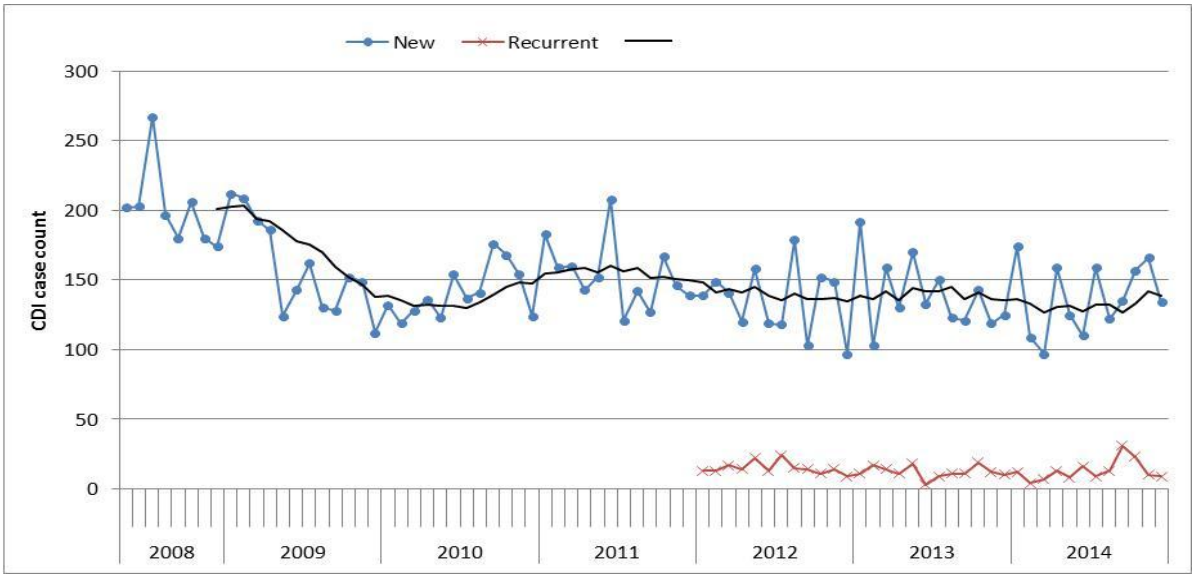
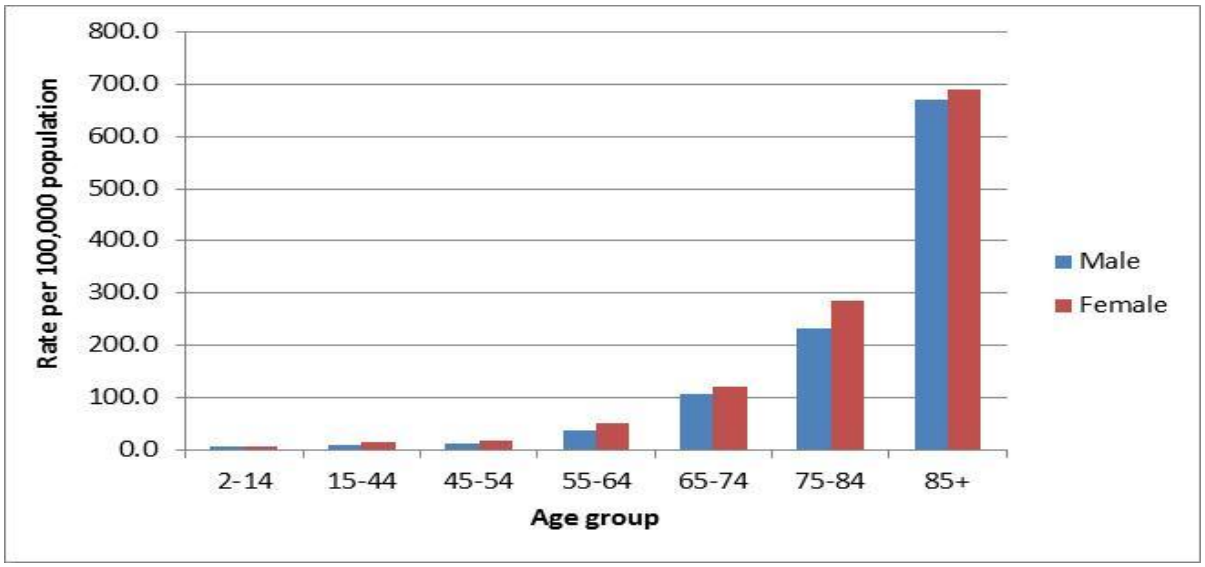


Figure 1. Numbers of CDI notifications by month and case type (2008 – 2014)

Figure 2 displays the gender and age breakdown of patients with CDI. The majority were female (61%). The mean age was 67 years (range: 2 – 100 years), with 1,202 cases (67%) reported in patients aged 65 years and older.



* Rates calculated using 2011 census data

Figure 2: Age and gender distribution of CDI in Ireland, 2014 (Source: CIDR)

Regarding patient location at the time of CDI diagnosis, most were classified as 'hospitalised' (72%), with 13% from general practice, 6% from the emergency department, 4% from outpatients or day patients and 4% from either 'other', or 'unknown' patient location. This is similar to that reported in 2013. However, this 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 2014, 22 deaths were reported in patients with CDI, which is lower than that reported in 2013. One death was attributed to CDI, 12 were not attributed to CDI and for the remaining 9 deaths, the contribution of CDI to death was unknown.

Notifiable C. difficile infection: Outbreaks

In 2014, 10 CDI outbreaks, nine of which were healthcare-associated and involving 43 patients, were notified to Public Health Departments as displayed in **Table 1**. Four were linked to hospitals, three to nursing homes, two to residential institutions, and one specified as "other".

Table 1. CDI outbreaks reported in Ireland in 2014 by public health region (Source: CIDR)

Public Health Region	Outbreak location	Total number ill
East	Hospital	4
East	Hospital	6
East	Hospital	7
East	Other	3
East	Nursing Home	3
East	Nursing Home	11
South	Residential	2
South	Nursing Home	2
Midwest	Residential	2
West	Hospital	3

Enhanced surveillance of C. difficile infection

Although notifiable CDI data provides important preliminary information on the burden of CDI in Ireland, it represents an underestimate of the true burden of CDI, as it does not capture information on the origin, onset or severity of CDI. National collation of *C. difficile* enhanced surveillance information 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 2014, 53 acute hospitals participated in the voluntary enhanced surveillance CDI scheme, comprising 45 (94%) public hospitals [27 general (100%), nine tertiary (100%) and nine specialist hospitals (75%)] and eight private hospitals (67%).

In 2014, 1,780 CDI cases were reported to the enhanced surveillance scheme (94% of all the CDI cases notified via CIDR). Of those, 1,522 (86%) were classified as new, 149 (8%) as recurrent and 109 (6%) of unknown CDI case type.

Of the reported cases, 52% (n=928) originated within the reporting healthcare facility. The overall national CDI incidence rate of new and recurrent cases combined, acquired within the reporting healthcare facility was 2.3 cases per 10,000 bed days used (BDU), a decrease from 2.4 in 2013. The incidence rate of new CDI was 2.1 cases per 10,000 BDU, a decrease from 2.2 in 2013. The incidence of recurrent cases remained at 0.2 cases, unchanged from 2013. 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 hospital activity data from the HSE Business Intelligence Unit, Corporate Planning and Corporate Performance (CPCP), with private hospital activity data provided directly by participating hospitals.

Since enhanced surveillance began in 2009, the national CDI rate has declined from 3.1 cases per 10,000 BDU (2009) to 2.8 (2010), with an increase to 3.0 (2011). Since 2011, the rate steadily decreased from 2.7 (2012) to 2.3 (2014) (**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. Throughout 2013 and 2014, 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 2013 (range, 0 – 6.5 cases per 10,000 BDU; median = 1.8 cases). In 2013, tertiary hospitals (n = 9) had a median CDI rate of 2.3 cases per 10,000 BDUs (range: 2.1 – 4.5), which was higher when compared to that of general hospitals (n = 27), with a median rate of 1.8 (range: 0 – 6.5). Since 2011, the median CDI rate in both tertiary (3.0 to 2.3 cases per 10,000 BDU) and general hospitals (2.4 to 1.8 cases per 10,000 BDU) declined.

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 and surveillance resources. No obvious seasonal trend for CDI is distinguishable from enhanced surveillance data in 2014.

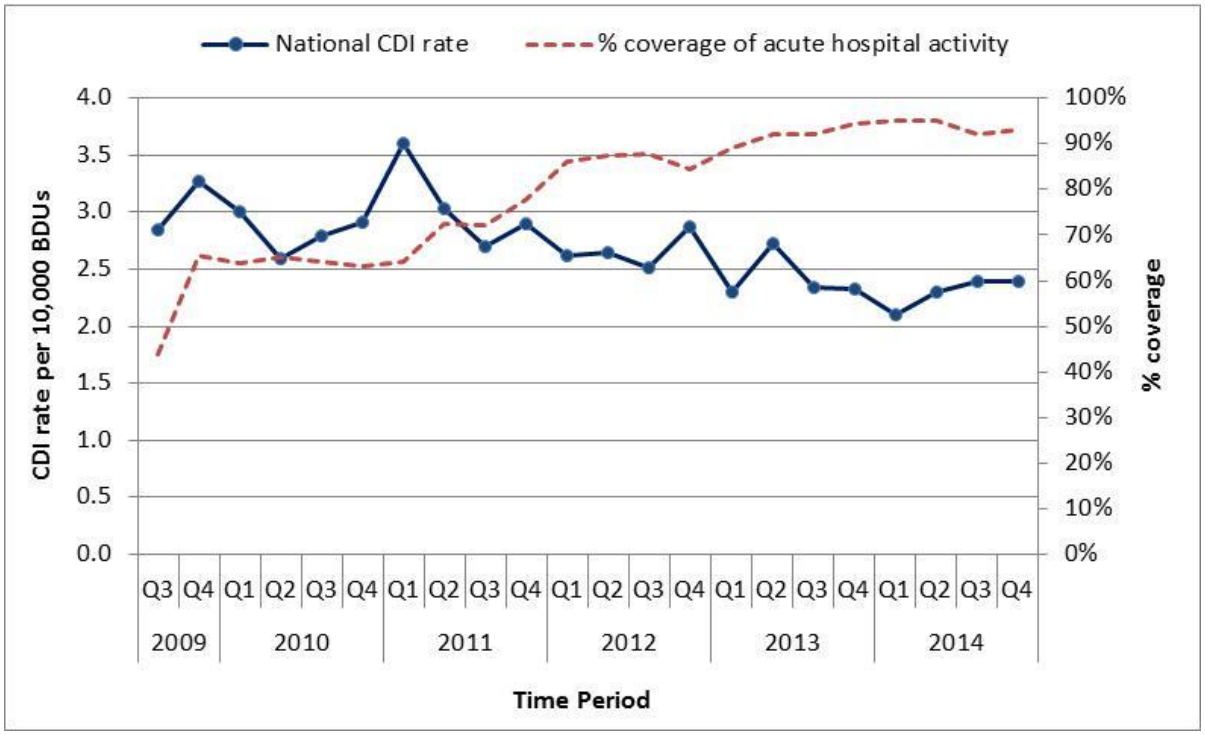


Figure 3. Quarterly national rate of healthcare-associated CDI (new and recurrent): 2009 – 2014

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 2014, 26 (1.4%) severe CDI cases were reported, similar to 2013 (1.7%).Eight patients required both surgery and ICU admission, six required surgery only and 12 required ICU admission without surgery.

Onset & Origin of CDI

Onset: Patient location when symptoms of CDI commenced

Fifty nine percent (n=1,049) of patients had CDI symptom onset in a healthcare facility (healthcare-onset), 34% (n=608) had symptom onset in the community and for 7% (n=123), location at CDI onset was unknown (**Table 2**).

Of the 1,049 patients with healthcare onset CDI, 75% (n=783) had onset in the reporting hospital, 4% (n=42) in another hospital, 18% (n=192) in a long term care facility (LTCF) and for the remaining 4% (n=46) onset location was unknown.

Between 2012 and 2014, there was a decrease in the proportion of patients with CDI symptom onset in a healthcare facility (64 to 59%), with the exception of LTCFs, where a slight increase was noted (16 to 18%). Community onset decreased from 30% to 29% between 2012 and 2013, but increased to 34% in 2014 (**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=1,131; 63.5%). Community-associated cases accounted for 21.5% (n = 383) and in 6% (n = 111) the origin 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 9% (n = 155) of cases, the origin was unknown (**Table 2**).

Of the 1,131 healthcare-associated CDI cases, 76% (n=860) originated in the reporting hospital, 4.5% (n=52) originated in a hospital other than the reporting hospital, 16.5% (n=189) originated in a LTCF and 3% (n=33) originated in another unspecified healthcare facility or were of unknown origin.

Between 2012 and 2014, there was a decrease in the proportion of cases associated with a healthcare facility (68 to 64%), although the reporting hospital and other hospital categories remained stable. The proportion of cases associated with the community increased from 17% to 21%, but there was little change in cases classified as indeterminate. Cases classified as 'unknown' increased from 10% to 14% between 2012 and 2013 but decreased to 9% in 2014 (**Table 2**).

Table 2. Origin and onset of CDI, 2012 – 2014

	Year		
	2012	**2013**	**2014**
	%	%	%
ONSET: Location of where patient symptoms occurred			
Healthcare-onset	64	60	59
Breakdown of healthcare-onset cases:			
Within reporting hospital	77	76	75
Other hospital	4	2	4
Nursing home/LTCF	16	18	18
Unknown	3	4	3
Community-onset	30	29	34
Unknown	6	11	7
ORIGIN: Location of where infection was acquired			
Healthcare-associated	68	64	64
Breakdown of healthcare-associated cases:			
Within reporting hospital	76	76	76
Other hospital	6	5	5
Nursing home/LTCF	15	17	16
Unknown	3	2	3
Community-associated	17	18	21
Indeterminate	5	5	6
Unknown	10	14	9

Of the 1,131 cases of healthcare-associated CDI:

- 87% (n=982) experienced onset of CDI symptoms at least 48 hours following admission to a healthcare facility (healthcare-onset, healthcare-associated)
- 13% (n=147) experienced symptom onset in the community, within four weeks of discharge from a healthcare facility (community-onset, healthcare-associated)
- 0.1% (n = 2) had no information recorded on symptom onset

Of the 383 cases of community-associated CDI:

- 91.5% (n=350) experienced CDI symptom onset while outside a healthcare facility and without a history of discharge from a healthcare facility within the previous 12 weeks
- 8% (n=31) 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
- 0.5% (n = 2) had no information recorded on symptom onset

Information was also captured on the location where the patient's faeces specimen was taken. The reporting hospital accounted for the majority (77%) of specimens (n=1,366), with 10% (n=183) taken in the GP surgery, 9% (n=160) in LTCF and 2.5% (n=44) in a hospital other than the reporting hospital. For the remaining 1.5% (n=27), 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 2014, while the enhanced surveillance system shows a decrease in the CDI rate during this time period, including a decrease in the number of new CDI cases acquired in an acute hospital. The reasons for this decrease are unknown, but may be attributed to improved hand hygiene compliance and other infection control practices, changes in antimicrobial prescribing or changes in laboratory testing practices.

In 2014, recurrent CDI accounted for 8% of notifications through the enhanced surveillance scheme, a slight decrease from 8.5% in 2013. 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 2014, 11% of cases had onset in LTCF, with 34% having onset in the community. Of the 383 community-associated cases reported in 2014, 91% 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 and to send specimens in a timely fashion for laboratory diagnosis.

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 2014, ribotyping data was provided for 290 *C. difficile* isolates (16% of all samples) from 20 hospitals (**Table 3**). The most common ribotypes reported in 2014 were: 078 and 014 (both n=31; 11%), 015 (n=27, 9%) and 005 (n=18, 6%) (**Figure 4**).

Table 3. National Reporting of *C. difficile* ribotyping data: 2011 - 2014

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

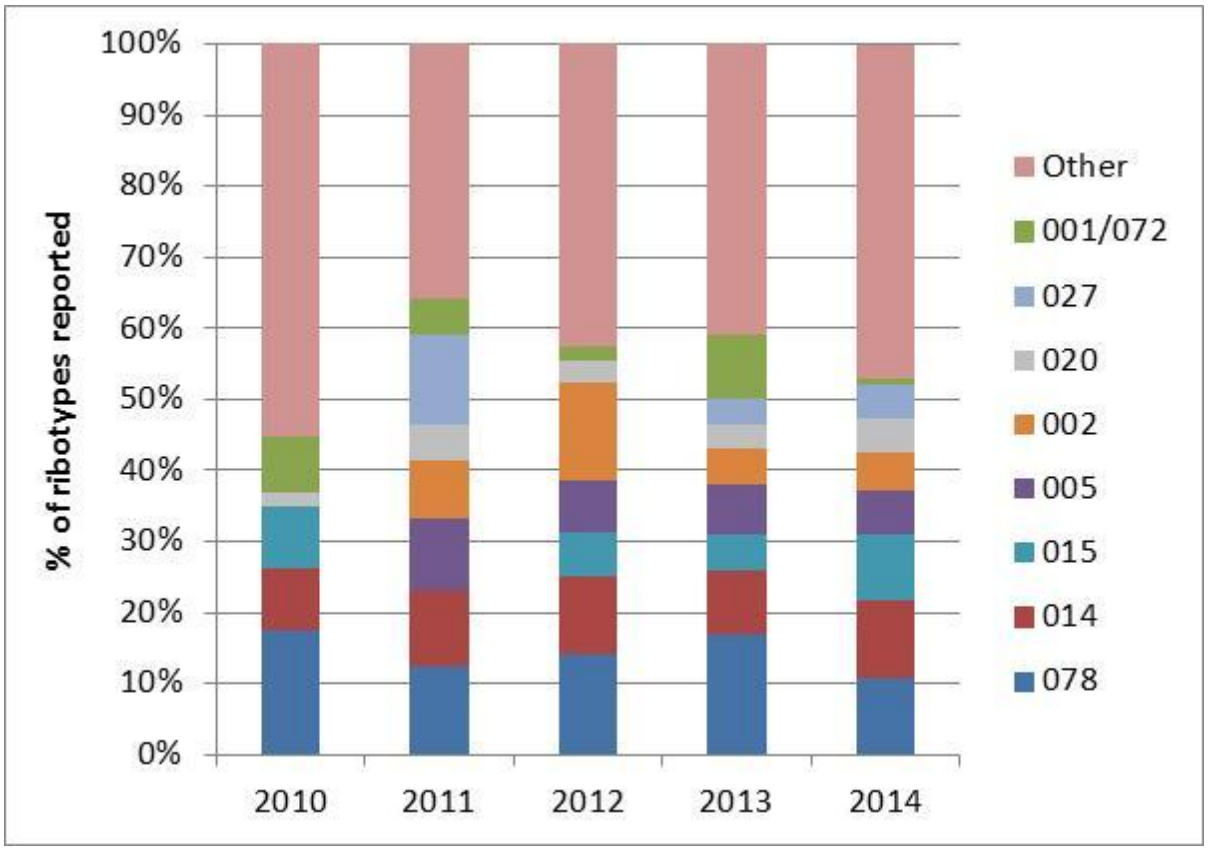


Figure 4. Most frequently reported *C. difficile* ribotypes in Ireland: 2010 – 2014

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 the first quarter of 2010, the majority of hospitals participating in the enhanced surveillance project were using a one step Toxin EIA (60%). In the last quarter of 2014, this had reduced to 0%. All hospitals participating in the enhanced surveillance system are now using a method which complies with what is recommended 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 considerable 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.

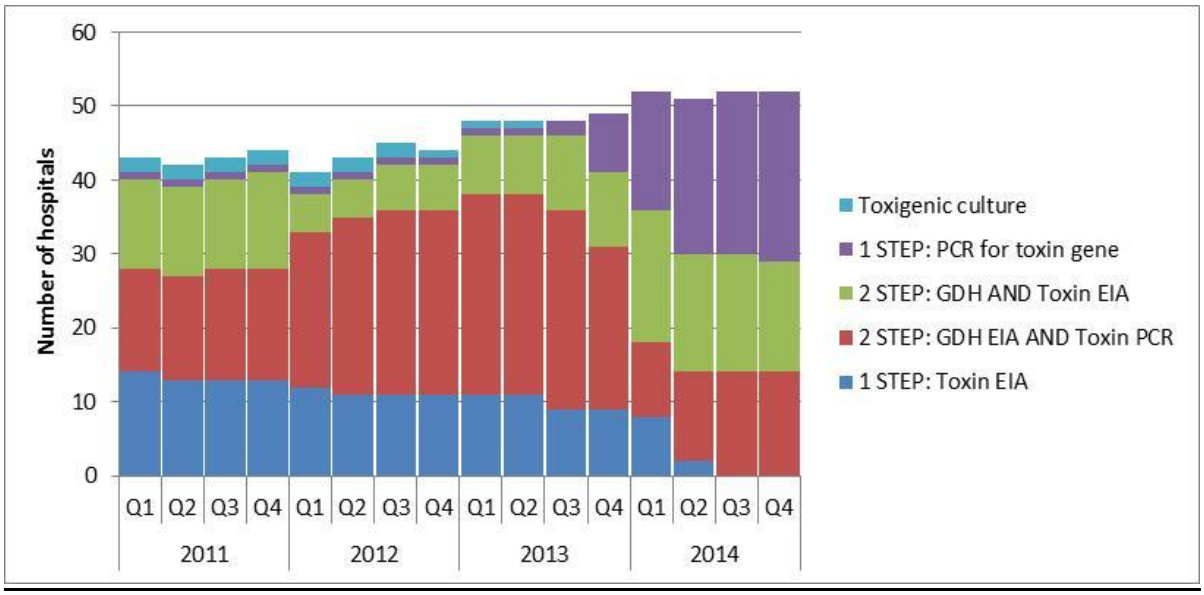


Figure 5. Changes in *C. difficile* laboratory testing protocols: 2011 - 2014

Toxigenic culture: a culture method for the detection of toxin-producing *C. difficile*; **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 a PCR for the detection of TcdA and/or TcdB genes; **1 STEP: Toxin EIA:** EIA for the detection of *C. difficile* TcdA and/or TcdB.

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 updated 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/.