One month National Surveillance, Typing and Antimicrobial Susceptibility of *Clostridium difficile* infection in Ireland

National Report

Executive Summary

Clostridium difficile infection (CDI) or *C. difficile*-associated disease (CDAD) has been a notifiable disease in Ireland since May 2008. All new cases of CDI are notified to the local public health department and from there to the Health Protection Surveillance Centre (HPSC) for national collation of data. Weekly reports are published by the HPSC (available at http://www.hpsc.ie/hpsc/NotifiableDiseases/WeeklyIDReports/). Although this has given important preliminary information on the burden of new cases of CDI in Ireland, it represents an underestimate of the true burden of infection (capturing new cases only) and does not capture information on the origin or onset of cases. Much of this enhanced surveillance data is being collected locally, however there is no national collation. In addition, as there is no *C. difficile* reference laboratory in Ireland, no systematic typing has been carried out here. During outbreaks, some hospitals have referred strains to the UK for typing, however these results are not available nationally, and even if they were, would not give an overview of the types circulating in this country. With this in mind HPSC, St. Vincent's University Hospital and University College Dublin undertook a one-month national enhanced surveillance, typing and antimicrobial susceptibility study of all cases of CDI in March 2009. This report summarises the main findings of the study. We are very grateful to Dr. Darina O'Flanagan and the HPSC for providing funding for this project.

Overall summary of national findings:

- Enhanced surveillance data and faecal specimens from 211 CDI cases from 33 health-care facilities were submitted in March 2009.
- Of the total CDI cases - 79% were new cases and 18% recurrent.
- The mean age of cases was 75 years (range 16-96 years) with a female preponderance. The majority of patients (77%) were on antibiotic therapy in the previous 8 weeks.
- 10% cases were community-associated and 83% healthcare-associated (81% from the reporting hospital, 13% from nursing homes and 5% from other hospitals).
- 17% cases were community onset and 78% healthcare onset (78% in the reporting hospital and 15% in nursing homes).
- The most common ribotypes were 027 (19%), 106 (13%), 078 (9%), 044 (9%), 014 (8%) and 001 (7%).
- Of the new CDI cases, ribotypes 027 (16%), 106 (14%) and 078 (9.5%) predominated. In contrast ribotypes 027 (30%), 078 (10%), 044 (16.7%) and 014 (10%) were the most common types in recurrent CDI cases.

- Most cases were health-care associated, (83.4%), the predominant ribotypes being 027, 106, 044, 078 and 014. Ribotypes 078, 027, 106, 050 and 014 were found amongst the community-associated cases.
- Of the total CDI cases – 1.4% (ribotypes 001 and 027) had ICU admission and 1.4% (ribotype 014) required surgery.
- 76% of all cases had documented exposure to antibiotics, most commonly penicillins, quinolones or macrolides.
- All strains were found to be susceptible to metronidazole and vancomycin, but fluoroquinolone resistance was common amongst all ribotypes.

Dr. Lynda Fenelon,

Dr. Lorraine Kyne,

Dr. Fidelma Fitzpatrick

1. Introduction

The national *Clostridium difficile* typing and enhanced surveillance project took place in March 2009. All Health Care Facilities (HCF's) were asked to participate in February 2009. Faecal samples from all patients in participating HCFs who had a diagnosis of CDI and a positive toxin A/B assay for *C. difficile* between the 01st and 31st March 2009 were included. For each specimen, corresponding clinical information (enhanced surveillance) on the patient was also collected. All participants were asked to capture enhanced surveillance information using a standardised form (appendix 1) and agreed case definitions (appendix 2). Information on case type, onset, origin, antibiotic exposure prior to onset and case severity was requested. Laboratory testing conducted included ribotype analysis and antimicrobial susceptibility analysis. HCF's sent enhanced surveillance information to the Health Protection Surveillance Centre (HPSC) and all *C. difficile* toxin positive stool samples to St. Vincents University Hospital in Dublin. Participating HCFs have been previously issued with their results and a summary of the national picture. This report presents a summary of enhanced surveillance, ribotype and antibiotic susceptibility results of CDI at a national level for the first time

2. Results

2.1 Participants

Participation in the project was in a voluntary capacity. Table 1 summarises the number of participating HCF's by region and speciality. Fifty HCF's agreed to participate. Of these, 33 facilities submitted *C. difficile* toxin positive faecal stools for inclusion in the project.

Table 1: Participating HCF by region and speciality

Region	General	Regional/Tertiary	Specialist	Other
Dublin	6	5	5	2
MidWest	3	1	2	0
NorthEast	5	0	0	0
South	5	1	3	2
SouthEast	3	1	0	0
West	4	1	0	0
NorthWest	1	0	0	0

2.2 Sample Information

The number of toxin positive faecal samples received in St. Vincents University Hospital is presented in table 2.

Table 2: Number of positive faecal samples by week

Sample Date[1]	Weekly no. of toxin positive samples - Nationally
01st March - 07th March	61
08th March - 14th March	48
15th March - 21st March	42
22nd March - 28th March	41
29th March to 31s March	19

Average number of toxin positive samples per participating HCF during study period	4.22

[1] Date sample was taken in HCF

As not all toxin positive faecal samples submitted for testing were successfully cultured (i.e. *C. difficile* was not isolated from the faecal sample) information on *C. difficile* testing practices within facilities was requested. These results are presented in table 3.

Table 3: Toxin Assay Kits Used by HCF's and Corresponding Non-Cultureable Data

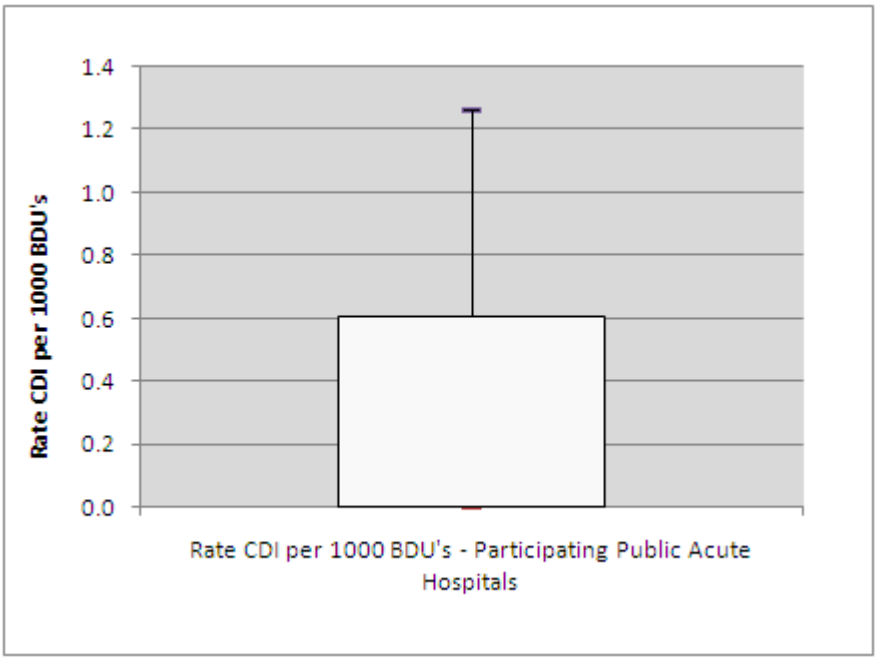
Toxin Assay Kit	Number of laboratories using kit	Number of toxin positive samples identified by kit	Number of toxin positive samples not isolated by culture	% of toxin positive samples not isolated by culture
Meridian Immunocard A&B	12	15	3	20%
Premier A&B	27	137	42	31%
Techlab Toxin A&B II	9	59	27	46%
Unknown	2	N/A	N/A	N/A

*N/A = Not available

2.3 CDI Rate per 1000 bed-days used

Figure 1 presents a box plot of national public acute hospitals CDI rates for the month of March 2009. The box plot shows the distribution of the data with minimum (min) and maximum (max) values, and the interquartile range (IQR). The IQR is the middle fifty percent of the data (i.e. where the middle 50% of the hospitals lie) and lies between quartile 1 (q1) and quartile 3 (q3) marked by the box.

Fig 1.0. Distribution of National CDI rate, March 2009



2.4 Epidemiological and Laboratory Data

Tables 4 and 5 summarise epidemiological data. 79% of CDI cases were new cases and 18% recurrent CDI (Table 4).The mean age of patients was 74 years (range 16-96 years) with a female preponderance. 10% of CDI cases were community-associated and 83% healthcare-associated (81% from the reporting hospital, 13% from nursing homes and 5% from other hospitals). The majority of patients (77%) were on antibiotic therapy in the previous 8 weeks, most commonly penicillins, quinolones or macrolides.

Table 4: Breakdown of CDI cases by case type

Case Type	National	
New Cases	*n = 166*	78.7%
Recurrent Cases	*n = 38*	17.5%
Unknown	*n = 7*	3.3%

Table 5: Enhanced Surveillance Information by Case Type.

		All Cases		New Cases		Recurrent Cases	
Patient Demographics		M: F		M: F		M: F	
Sex ratio (M|F)		1.0 : 1.5		1: 1.4		1.0 : 1.7	
Mean Age		75		74		73	
Age Range		16 to 96		26 to 96		45 to 96	
Origin of disease							
Community associated disease		*n = 21*	10.0%	*n = 20*	12.0%	*n = 1*	2.6%
Unknown		*n = 14*	6.6%	*n = 7*	4.2%	*n = 0*	0.0%
Healthcare associated disease		*n = 176*	83.4%	*n = 139*	83.7%	*n = 37*	97.4%
	Origin of health care associated C. difficile						
	Within reporting hospital	*n = 143*	81.3%	*n = 111*	79.9%	*n = 32*	86.5%
	Other Hospital	*n = 9*	5.1%	*n = 6*	4.3%	*n = 3*	8.1%
	Nursing Home	*n = 23*	13.1%	*n = 22*	15.8%	*n = 1*	2.7%
	Unknown	*n = 1*	0.6%	*n = 0*	0.0%	*n = 1*	2.7%
Onset location							
Community onset		*n = 37*	17.5%	*n = 31*	18.7%	*n = 6*	15.8%
Unknown		*n = 8*	3.8%	*n = 2*	1.2%	*n = 0*	0.0%
Healthcare facility onset		*n = 166*	78.7%	*n = 133*	80.1%	*n =32*	84.2%
	Location of health care associated patients						
	Within reporting hospital	*n = 130*	78.3%	*n = 104*	78.2%	*n = 25*	78.1%
	Other Hospital	*n = 9*	5.4%	*n = 6*	4.5%	*n = 3*	9.4%
	Nursing Home	*n = 26*	15.7%	*n = 22*	16.5%	*n = 4*	12.5%
	Unknown	*n = 1*	0.6%	*n = 1*	0.8%	*n = 0*	0.0%
Severity of Illness							
ICU Admission		*n = 3*	1.4%	*n= 2*	1.2%	*n = 1*	2.6%
Surgery		*n = 3*	1.4%	*n = 3*	1.8%	*n= 0*	0.0%
Antibiotic Exposure							
Yes		*n = 160*	75.8%	*n = 125*	75.3%	*n = 35*	92.1%
No		*n = 25*	11.8%	*n = 23*	13.9%	*n = 2*	5.3%
Unknown		*n = 26*	12.3%	*n = 18*	10.8%	*n = 1*	2.6%
	Of patients with antibiotic histories, number of antibiotics						
	One type of antibiotic	*n = 81*	38.4%	*n = 65*	52.0%	*n = 16*	45.7%
	Two types of antibiotics	*n = 42*	19.9%	*n= 32*	25.6%	*n = 10*	28.6%
	Three types of antibiotic	*n = 22*	10.4%	*n = 17*	13.6%	*n = 5*	14.3%
	Greater than three types	*n = 18*	8.5%	*n = 14*	11.2%	*n = 4*	11.4%

Tables 6-9 and Fig 2.0 present laboratory and correlated enhanced information. The most common ribotypes were 027 (19%), 106 (13%), 078 (9%), 044 (9%), 014 (8%) and 001 (7%) (Table 6 and Fig 2.0). Of the total CDI cases – 1.4% (ribotypes 001 and 027) had ICU admission and 1.4% (ribotype 014) required surgery. Of the new CDI cases, ribotypes 027 (16%), 106 (14%) and 078 (9.5%) predominated. In contrast ribotypes 027 (30%), 078 (10%), 044 (16.7%) and 014 (10%) were the most common types in recurrent CDI cases (Table 6). Most cases were health-care associated, (83.4%), the predominant ribotypes being 027, 106, 044, 078 and 014. Ribotypes 078, 027, 106, 050 and 014 were found amongst the community-associated cases. Table 8 outlines antibiotic exposure of CDI cases in relation to ribotype. All strains were found to be susceptible to metronidazole and vancomycin, but fluoroquinolone resistance was common amongst all ribotypes (Fig 3.0)

Table 6: Summary of *C. difficile* ribotypes by Case Type

	All cases		New Cases		Recurrent Cases	
Ribotype	**National**		**National**		**National**	
001	*n = 10*	7.2%	*n = 9*	8.6%	*n = 1*	3.3%
002	*n = 1*	0.7%	*n = 1*	1.0%	*n = 0*	0.0%
003	*n = 2*	1.4%	*n = 2*	1.9%	*n = 0*	0.0%
011	*n = 1*	0.7%	*n = 0*	0.0%	*n = 1*	3.3%
012	*n = 1*	0.7%	*n = 1*	1.0%	*n = 0*	0.0%
014	*n = 11*	7.9%	*n = 8*	7.6%	*n = 3*	10.0%
015	*n = 3*	2.2%	*n = 2*	1.9%	*n = 0*	0.0%
027	*n = 26*	18.7%	*n = 17*	16.2%	*n = 9*	30.0%
044	*n = 13*	9.4%	*n = 8*	7.6%	*n = 5*	16.7%
050	*n = 1*	0.7%	*n = 1*	1.0%	*n = 0*	0.0%
078	*n = 13*	9.4%	*n = 10*	9.5%	*n = 3*	10.0%
081	*n = 2*	1.4%	*n = 2*	1.9%	*n = 0*	0.0%
087	*n = 1*	0.7%	*n = 1*	1.0%	*n = 0*	0.0%
106	*n = 18*	12.9%	*n = 15*	14.3%	*n = 2*	6.7%
120	*n = 2*	1.4%	*n = 2*	1.9%	*n = 0*	0.0%
174	*n = 1*	0.7%	*n = 1*	1.0%	*n = 0*	0.0%
*Untypeable	*n = 4*	2.9%	*n = 0*	0.0%	*n = 0*	0.0%
**Not *C. difficile*	*n = 2*	1.4%	*n = 0*	0.0%	*n = 0*	0.0%
***Unknown	*n = 27*	19.4%	*n = 0*	0.0%	*n = 0*	0.0%

*Untypeable: Insufficient DNA obtained for ribotyping analysis
**Not *C. difficile*: Organism isolated was not found to have Clostridium difficile specific genes
***Unknown: Ribotype fingerprint not found in reference library

Table 7: *C. difficile* ribotypes and origin of CDI

Ribotype	Community	Healthcare	Unknown
001	0	10	0
002	0	1	0
003	0	2	0
011	0	1	0
012	0	1	0
014	1	9	1
015	0	2	1
027	1	25	0
044	0	13	0
050	1	0	0
078	2	11	0
081	0	2	0
087	0	1	0
106	1	13	4
120	0	2	0
174	0	1	0

Table 8: Ribotype Results and Known Antibiotic Exposure in Eight Weeks Prior to Onset

Ribotype	Penicillin	Quinolone	Cephalosporin	Clindamycin	Carbapenem	Macrolide	Metronidazole*	Other antibiotics
001	70.0%	50.0%	10.0%	0.0%	20.0%	20.0%	0.0%	30.0%
002	0.0%	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%	100.0%
003	50.0%	0.0%	50.0%	0.0%	0.0%	0.0%	50.0%	0.0%
011	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
012	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
014	81.8%	9.1%	18.2%	0.0%	9.1%	9.1%	0.0%	18.2%
015	66.7%	33.3%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
027	69.2%	23.1%	19.2%	0.0%	3.8%	3.8%	11.5%	19.2%
044	69.2%	46.2%	0.0%	0.0%	0.0%	15.4%	7.7%	23.1%
050	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
078	53.8%	0.0%	7.7%	0.0%	7.7%	0.0%	15.4%	23.1%
081	50.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	100.0%
087	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
106	66.7%	5.6%	11.1%	0.0%	5.6%	5.6%	16.7%	27.8%
120	50.0%	0.0%	0.0%	0.0%	50.0%	0.0%	0.0%	100.0%
174	0.0%	100.0%	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Unknown	51.9%	11.1%	11.1%	0.0%	0.0%	7.4%	7.4%	14.8%
Untypeable	75.0%	50.0%	25.0%	0.0%	0.0%	25.0%	25.0%	50.0%
Total	**62.6%**	**19.4%**	**12.2%**	**0.0%**	**5.0%**	**7.2%**	**9.4%**	**24.5%**

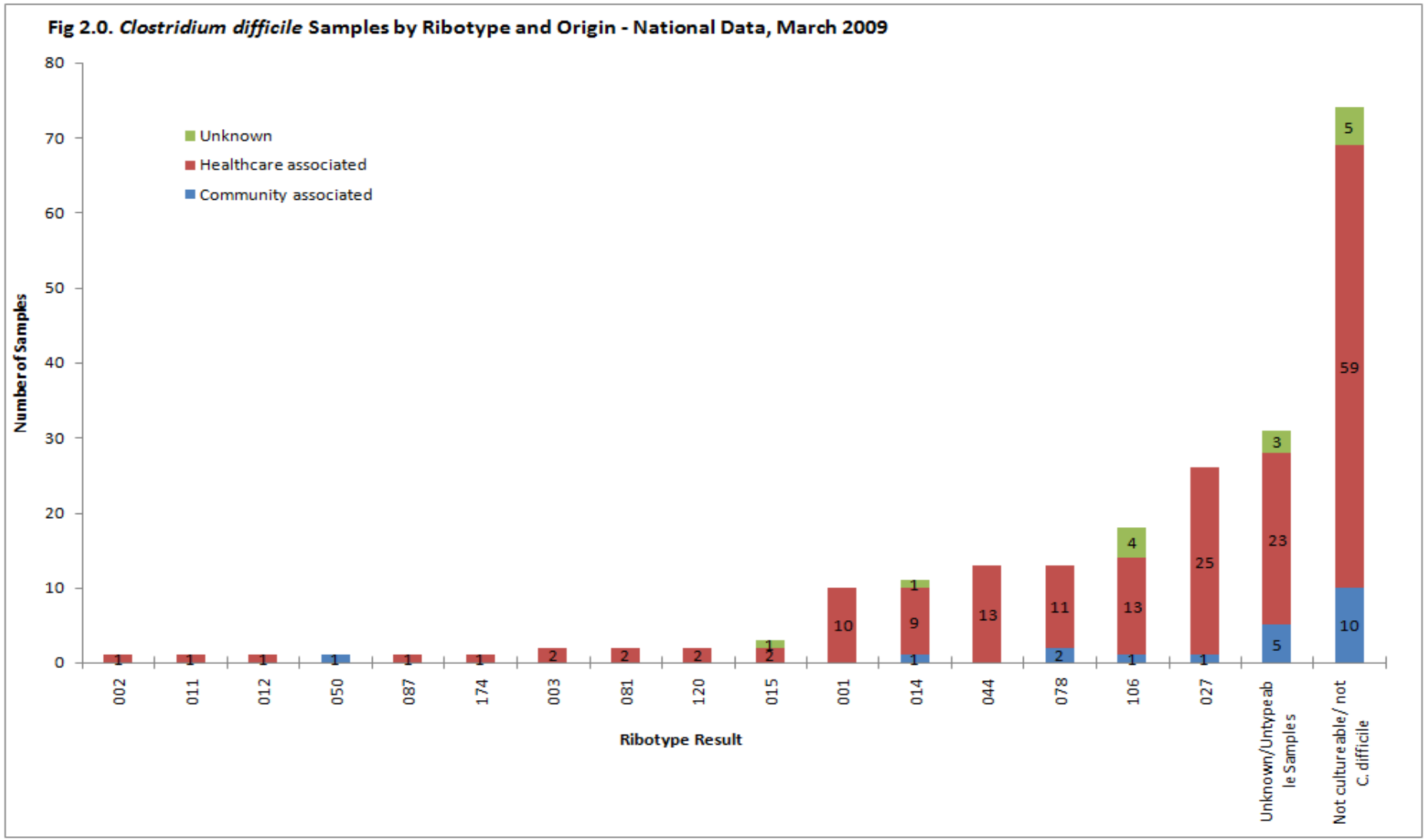


Fig 2.0. *Clostridium difficile* Samples by Ribotype and Origin - National Data, March 2009
Unknown
Healthcare associated
Community associated
Number of Samples
Ribotype Result
002
011
012
050
087
174
003
081
120
015
001
014
044
078
106
027
Unknown/Untypeable Samples
Not culturable/ not C. difficile

Figure 3 presents antibiotic susceptibility data of samples cultured where MIC breakpoints are available. All isolates typed were resistant to both ciprofloxacin and levofloxacin. Conversely all isolates typed were sensitivity to vancomycin, metronidazole, piperacillin-tazobactam and co-amoxiclav. Appendix 3 outlines the breakpoints used to calculate MIC's.

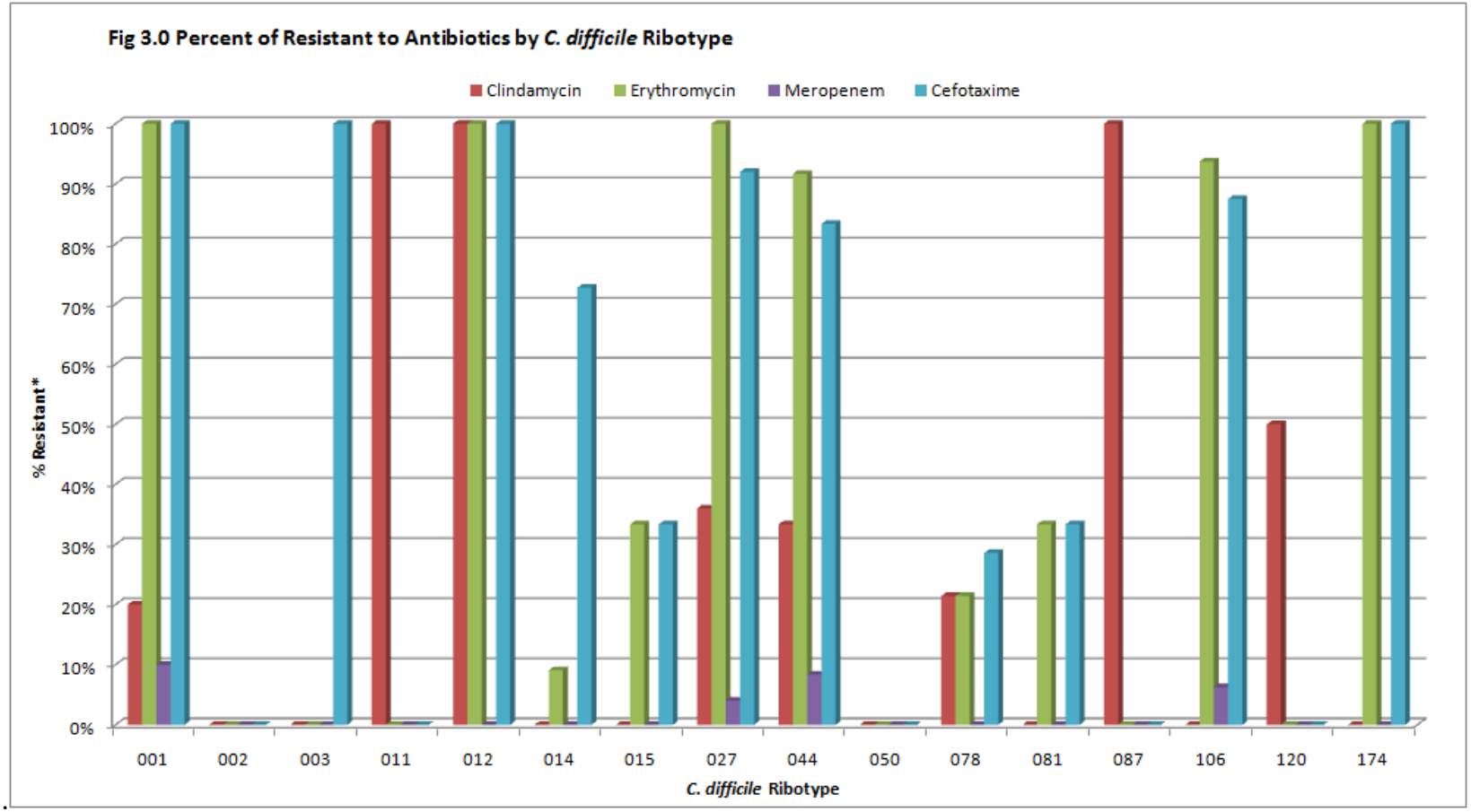


Table 9: Summary of Typing and Corresponding Epidemiological Information provided by HCF's.

		Case type			Onset location			Origin			Severity		
Type	Number of Samples	New	Recurrent	Mean Age	Community onset	Healthcare onset	Unknown	Community associated	Healthcare associated	Unknown	ICU Admission	Surgery	Antibiotics
001	10	90.0%	10.0%	78	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%	**10.0%**	0.0%	90.0%
002	1	100.0%	0.0%	78	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	100.0%
003	2	100.0%	0.0%	57	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	50.0%
011	1	0.0%	100.0%	48	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	100.0%
012	1	100.0%	0.0%	78	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	100.0%
014	11	72.7%	27.3%	76	9.1%	81.8%	9.1%	9.1%	81.8%	9.1%	0.0%	**9.1%**	81.8%
015	3	66.7%	0.0%	76	0.0%	66.7%	33.3%	0.0%	66.7%	33.3%	0.0%	0.0%	66.7%
027	26	65.4%	34.6%	80	15.4%	84.6%	0.0%	3.8%	96.2%	0.0%	**3.8%**	0.0%	96.2%
044	13	61.5%	38.5%	70	23.1%	76.9%	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	92.3%
050	1	100.0%	0.0%	78	100.0%	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%
078	13	76.9%	23.1%	74	23.1%	76.9%	0.0%	15.4%	84.6%	0.0%	0.0%	0.0%	84.6%
081	2	100.0%	0.0%	56	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	100.0%
087	1	100.0%	0.0%	52	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	0.0%
106	18	83.3%	11.1%	74	22.2%	72.2%	5.6%	5.6%	72.2%	22.2%	0.0%	0.0%	77.8%
120	2	100.0%	0.0%	70	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	100.0%
174	1	100.0%	0.0%	88	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	100.0%
Not *C. difficile*	2	50.0%	50.0%	66	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	100.0%
Unknown	27	77.8%	14.8%	77	18.5%	70.4%	11.1%	14.8%	74.1%	11.1%	0.0%	0.0%	55.6%
Untypeable	4	75.0%	25.0%	56	25.0%	75.0%	0.0%	25.0%	75.0%	0.0%	0.0%	0.0%	100.0%

Conclusions and Recommendations

This is the first time we have had national information on the origin and onset of CDI associated with *C. difficile* ribotypes. While information on new CDI cases does provide important epidemiological information on the burden of CDI in Ireland, it does not provide enough detail in terms of origin and onset of CDI to direct appropriate preventative and control programmes at a national level. Furthermore as there is no national *C. difficile* reference laboratory in Ireland, we do not have the ability to track strain differences over time or analyse emerging trends in terms of *C. difficile* types or antimicrobial resistance of isolates. This one month project has provided a valuable insight into the burden of CDI in Ireland, including the incidence of recurrent CDI and the burden of CDI outside acute hospitals. It is essential that similar information is collected prospectively in the future at a national level to enable us to monitor the effectiveness of preventative programmes and to ensure that prevention of CDI is a key patient safety issue.

Recommendations

1. **Ongoing national enhanced surveillance of CDI cases**
2. **CDI should be a notifiable disease in its own right**
3. **Funding for a national *C. difficile* reference laboratory should be prioritised**

Acknowledgements

- Participating healthcare facilities, infection prevention and control teams and laboratories.
- Dr. Darina O'Flanagan, HPSC
- Dr. Lorraine Kyne and Dr. Katie Solomon are supported by a Health Research Board Clinical Scientist Award

Appendix 1: Clinical Data Form

6531

National *Clostridium difficile* Surveillance Project
March 2009
Clinical Details

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

1. Patient Details:

Hospital Code: H
Patient ID:
Age:
Sex: M F Unk

Date of birth: / /
Was the patient admitted to hospital? Yes No Unknown
If admitted please give date of admission: / / 20

2. Case Type:

New Recurrent **Please refer to page two for new and recurrent case definitions.**

3. Isolate Details:

Specimen ID:
Specimen date: / / 2009

4. Onset of *C difficile* Infection (CDAD):

Healthcare onset: Symptoms start during a stay in a healthcare facility.
Community onset: Symptoms start in a community setting, outside healthcare facilities.
Date of onset: / / 2009
If patients onset of CDAD was within a health care facility, please specify in which facility this occurred: This hospital Other hospital Nursing home Other

5. Origin of *C difficile* Infection (CDAD):

Health-care associated case: This is a CDAD case with either
*Onset of symptoms at least 48 hours following admission to a healthcare facility (healthcare - onset, healthcare-associated
or
*Onset of symptoms in the community within 4 weeks following discharge from a healthcare facility (community onset, healthcare-associated)

Community-associated case: This is a CDAD case with either
*Onset of symptoms while outside a healthcare facility, and without discharge from a healthcare facility within the previous 12 weeks (community-onset, community-associated).
or
*Onset of symptoms within 48 hours following admission to a healthcare facility without residence in a healthcare facility within the previous 12 weeks (healthcare-onset,community-associated)

Unknown case: This is a CDAD case who was discharged from a healthcare facility 4-12 weeks before the onset of symptoms

If patients origin of CDAD was within a health care facility, please specify in which facility this occurred: This hospital Other hospital Nursing home Other

6. Severity: *(If applicable)*

ICU Admission for CDAD treatment or its complications: Yes No Unknown
Surgery (colectomy) for toxic megacolon, perforation or refractory colitis. Yes No Unknown

7. Antibiotic Exposure:

Exposure to antibiotics in eight weeks prior to onset? Yes No Unknown

If yes, please select type(s) of antibiotic:

Penicillin
Carbapenem (e.g. Meropenem)
Quinolone
Macrolide (e.g. Clarithromycin, Erythromycin)
Cephalosporin
Other 1
Clindamycin
Other 2

Page 1 of 2

6531

Definitions of Clostridium difficile Infection - CDAD Type

Clostridium difficile Infection - associated disease (CDAD) case:

This a patient to whom one or more of the following criteria applies:

- Diarrhoeal* stools or toxic megacolon, with either a positive laboratory assay for *C. difficile* toxin A (TcdA) and/or toxin B (TcdB) in stools or a toxin-producing *C. difficile* organism detected in stool via culture or other means.
- Pseudomembranous colitis (PMC) revealed by lower gastrointestinal edoscopy.
- Colonic histopathology characteristic of *C. difficile* infection (with or without diarrhoea) on a specimen obtained during endoscopy, colectomy or autopsy.

C. difficile Infection - recurrent CDAD case:

This is a patient with an episode of CDAD that occurs within 8 weeks following the onset of a previous episode provided that CDAD symptoms from the earlier episode resolved with or without therapy

***Diarrhoea is defined as three or more loose/watery bowel movements (which are unusual or different for the patient) in a 24 hour period**

Appendix 2: Case definitions

New Case of CDI: This is a patient to whom one or more of the following applies;

- Diarrhoeal stools or toxic megacolon, with either a positive laboratory assay for *C. difficile* toxin A (TcdA) and / or toxin B (TcdB) in stools or a toxin-producing *C. difficile* organism detected in stool via culture or other means.
- Pseudomembranous colitis (PMC) revealed by lower gastrointestinal endoscopy.
- Colonic histopathology characteristic of *C. difficile* infection (with or without diarrhoea) on a specimen obtained during endoscopy, colectomy or autopsy.

Recurrent CDI Case:

- This is a patient with an episode of CDI that occurs within 8 weeks following the onset of a previous episode provided that CDI symptoms from the earlier episode resolved with or without therapy

Onset of CDI symptoms:

- Healthcare onset » Symptoms start during a stay in a healthcare facility.
- Community onset » Symptoms start in a community setting, outside healthcare facilities.

Origin of CDI:

- Healthcare-associated case » This is a CDI case with either:
    - Onset of symptoms at least 48 hours following admission to a healthcare facility (healthcare-onset, healthcare-associated.
      or
    - With onset of symptoms in the community within 4 weeks following discharge from a healthcare facility (community-onset, healthcare-associated).
- Community-associated case » This is a CDI case patient with either:
    - Onset of symptoms while outside a healthcare facility, and without discharge from a healthcare facility within the previous 12 weeks (community-onset, community-associated).
      or
    - With onset of symptoms within 48 hours following admission to a healthcare facility without residence in a healthcare facility within the previous 12 weeks (healthcare-onset, community-associated).
    - Unknown case » This is a CDI case patient who was discharged from a healthcare facility 4-12 weeks before the onset of symptoms.

Severity:

- ICU admission – admission to an intensive care unit for treatment of CDI or its complications (e.g. for shock requiring vasopresser therapy).
- Surgery (colectomy) for toxic megacolon, perforation or refractory colitis.

Appendix 3: MIC Breakpoints Used

	MIC			
Antibiotic	**S**	**I**	**R**	***Source***
Vancomycin	<4		>=8	J. Brazier et al., 2004[2]
Metronidazole	<=8	8=<x>=32	>=32	CLSI[1]
Moxifloxacin	<=2	2=<x>=8	>=8	CLSI[1]
Clindamycin	<=2	2=<x>=8	>=8	CLSI[1]
Erythromycin	<4		>=8	J. Brazier et al., 2004[2]
PipTaz	<128		>=129	CLSI[1]
Augmentin	<=2	2=<x>=8	>=8	CLSI[1]
Meropenem	<=4	4=<x>=16	>=16	CLSI[1]
Cefotaxime	<=16	16=<x>=64	>=64	CLSI[1]
Ciprofloxacin	<=0.5		>=1	EUCAST[3]
Levofloxacin	<=1		>=2	EUCAST[3]

1. CLSI Manual M11/A7
2. 2. John R, Brazier JS. Antimicrobial susceptibility of polymerase chain reaction ribotypes of *Clostridium difficile* commonly isolated from symptomatic hospital patients in the UK. J Hosp Infect. 2005;61:11–4
3. EUCAST v2.6 2009 (breakpoints for non-related species)

Appendix 4: CDI project members

- Dr. Karen Burns - Specialist Registrar (Microbiology), Beaumont Hospital.
- Dr. Lynda Fenlon - Consultant Microbiologist, St. Vincents University Hospital.
- Dr. Fidelma Fitzpatrick - Consultant Microbiologist, HPSC and Beaumont Hospital.
- Dr. Lorraine Kyne - Consultant Physician in Medicine for the Older Person, Mater Misericordiae University Hospital and Senior Lecturer, University College Dublin.
- Dr. Sinead McDermott - Specialist Registrar (Microbiology), St. Vincents University Hospital.
- Ms. Louise Scott - Medical Scientist, (Microbiology), St. Vincents University Hospital.
- Ms. Mairead Skally - Surveillance Scientist, HPSC.
- Dr. Katie Solomon – Postdoctoral Researcher, *C. difficile,* Research Centre for Food Safety, University College Dublin.