National Public Health Service for Wales
Gwasanaeth Iechyd Cyhoeddus Cenedlaethol Cymru

Infection and Communicable Disease Service
Gwasanaeth Heintiau a Chlefydau Trosglwyddadwy

Welsh Healthcare Associated Infections Programme (WHAIP)
Rhaglen Heintiau sy'n Gysylltiedig a Gofal Iechyd Cymru (RHGGIC)

Clostridium difficile
PCR Ribotype Surveillance in Wales

2008

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Summary

- 92 *C. difficile* samples from Trusts around Wales were PCR ribotyped and tested for susceptibility to 6 antibiotics. A surveillance questionnaire was completed for 91% of these.

- A total of 19 PCR ribotypes were identified. PCR ribotype 027 was the most commonly isolated strain, accounting for 38% of the sample.

- Results were not uniform across Wales. 027 predominated in the Trusts in South East Wales; 106 was the most common strain in the Trusts in North Wales and there was no predominant PCR ribotype in the South West Wales Trusts.

- There has been a large increase in the frequency of PCR ribotype 027 and a large decrease in the frequency of PCR ribotype 001 in Wales since the previous PCR ribotyping survey in 2005.

- No MIC levels were detected that might equate to clinical resistance to metronidazole; however, the 3 most common PCR ribotypes (027, 106, 001) did have higher MICs to metronidazole, erythromycin and moxifloxacin than the less common strains.

- In the majority of patients, the stool sample was taken within 1 day of the onset of diarrhoea.

- *C. difficile* infection was most commonly associated with mild diarrhoea i.e. 3 episodes or less of diarrhoea per day with no other symptoms. The 027 strain was not associated with more severe diarrhoea than the other strains.

- Approximately one third of patients were known to have died by the end of the 30 day surveillance period. *C. difficile* was indicated to have been the cause of death in 12% of the patients (3/26). A further 38% were noted to have *C. difficile* as a contributory factor in their death; however "contributing to death" was not defined in the questionnaire and this must be considered to be a crude assessment of death due to *C. difficile* which warrants further investigation. A regular review should be conducted of deaths within 30 days of diagnosis of *C. difficile* infection to ensure a common standard of assessment of cause of death or contribution to death is being applied.

- The proportion of deaths attributable to *C. difficile* was the same for patients with 027 as for the patients with the other strains.

- For patients known to be alive at the end of the 30 day surveillance period, nearly 70% had recovered from the *C. difficile* associated diarrhoea. Patients who still had ongoing or relapsed *C. difficile* diarrhoea were significantly more likely to have the 027 strain than the other strains.

- Some changes to the methodology and improvements in communication between and within the different staff groups involved will be required to run this survey on an annual basis, as recommended by the WHAISG *C. difficile* Task Group.

1. Introduction

Because of increasing concerns regarding the incidence and severity of cases of *Clostridium difficile* across the UK, a *C. difficile* Task Group was set up in Wales by the Welsh Healthcare Associated Infection Sub-Group (WHAISG) of the Welsh Assembly Government. The task group made recommendations regarding changes to the surveillance of *C. difficile* in Wales, which were agreed by the WHAISG in May 2008. One of the changes was to develop a regular survey of the *C. difficile* PCR ribotypes that are causing disease in Wales, coupled with enhanced surveillance of the severity and outcome of disease. This would allow some understanding to be gained on the contribution different PCR ribotypes of *C. difficile* are currently making to the epidemiology of *C. difficile* in Wales.

The WHAIP team in conjunction with the Anaerobe Reference Laboratory co-ordinated a pilot study in 2008 for the ongoing enhanced surveillance of *C. difficile* PCR ribotypes in Wales. This report provides the results of the pilot study.

2. Methods

Between 1st July and 7th September 2008, NHS Trusts in Wales submitted a pre-determined number of stool samples positive for *C. difficile* toxins for culture and PCR ribotyping. The number of samples requested from each Trust was based on the numbers of cases reported in the mandatory *C. difficile* surveillance scheme in 2007, with the overall aim of processing 100 samples from Wales.

Stool samples positive for *C. difficile* toxins were sent for culture at 3 different regional laboratories. The specimens from Trusts in South East Wales (Cardiff & Vale, Gwent and Cwm Taf) were cultured in NPHS Microbiology Cardiff; the ones from Trusts in South West Wales (Abertawe Bro Morgannwg University and Hywel Dda) were cultured in NPHS Microbiology Swansea and the specimens from Trusts in North Wales (North Wales and North West Wales) were cultured in Wrexham Maelor Hospital microbiology laboratory. Isolates of putative *C. difficile* were then sent to the Anaerobe Reference Laboratory (ARL) in Cardiff for PCR ribotyping and susceptibility testing. Isolates were susceptibility tested against 6 antibiotics (metronidazole, vancomycin, erythromycin, moxifloxacin, co-amoxyclavulanate and piperacillin/tazobactam) using the E test method (AB Biodisk, Solna, Sweden). The following breakpoints were used: metronidazole =>16µg/ml; vancomycin =>4µg/ml; erythromycin=>4µg/ml; moxifloxacin=>32µg/ml; co-amoxyclavulanate =>16µg/ml; piperacillin-tazobactam =>128 µg/ml.

Trusts were also asked to complete a short questionnaire (see Appendix) on the patients whose stool samples were sent for *C. difficile* culture. The questionnaire examined the severity of the *C. difficile*-associated disease and the outcome for the patient at 30 days. The definitions used for disease severity were taken from the draft Department of Health (England) / HPA document "*Clostridium difficile*: How to deal with the problem" which was out for consultation at the time and has subsequently been published, available at: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1232006607827.

PCR ribotyping results were returned to the culture centres and the originating laboratories by the 19th October 2008. These results were then forwarded to the Trusts, where the PCR ribotyping results were added to the questionnaires. No patient identifiable information was provided on the questionnaires. The ARL issued a unique record identifier for each sample, which were used as unique identifiers on the questionnaires. Questionnaires were then sent to WHAIP and the results entered into a database and analysed.

3. Results

3.1 PCR Ribotyping & Antibiotic Susceptibility Results

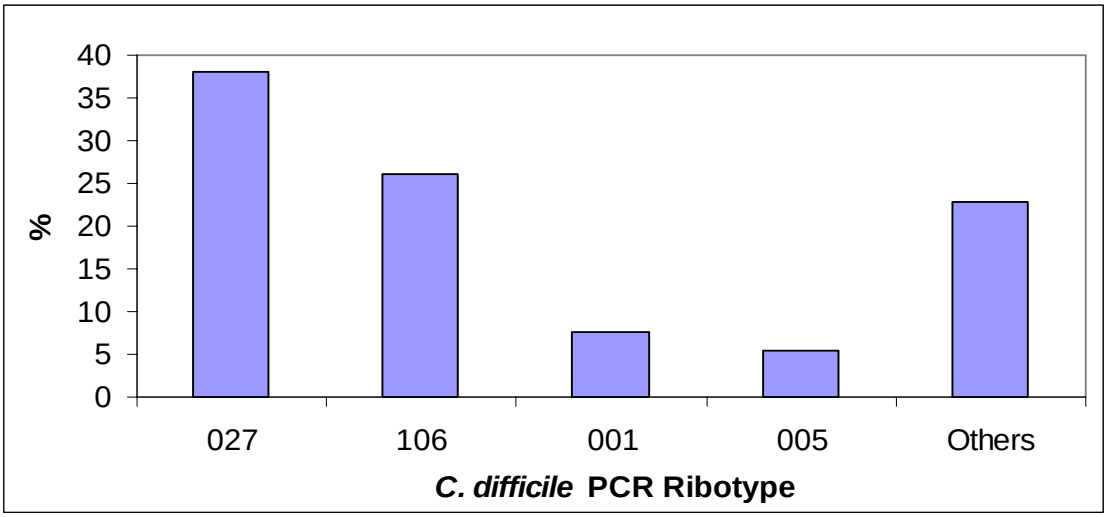
- 92 *C. difficile* samples from Trusts around Wales (Table 1) were PCR ribotyped and tested for susceptibility to 6 antibiotics.

Table 1. Number of *C. difficile* samples PCR ribotyped by site for the enhanced PCR ribotyping survey in Wales, 2008

Region (Culture Centre)	Trust	No of Samples
South East Wales (NPHS Microbiology Cardiff)	Cardiff & Vale	16
	Gwent Healthcare	20
	Cwm Taf (North)	3
	Cwm Taf (South)	5
South West Wales (NPHS Microbiology Swansea)	ABMU (East)	4
	ABMU (West)	9
	Hywel Dda (Bronglais)	4
	Hywel Dda (Carmarthen)	4
	Hywel Dda (Withybush)	4
North Wales (Wrexham microbiology laboratory)	North Wales (Central)	5
	North Wales (East)	10
	North West Wales	8

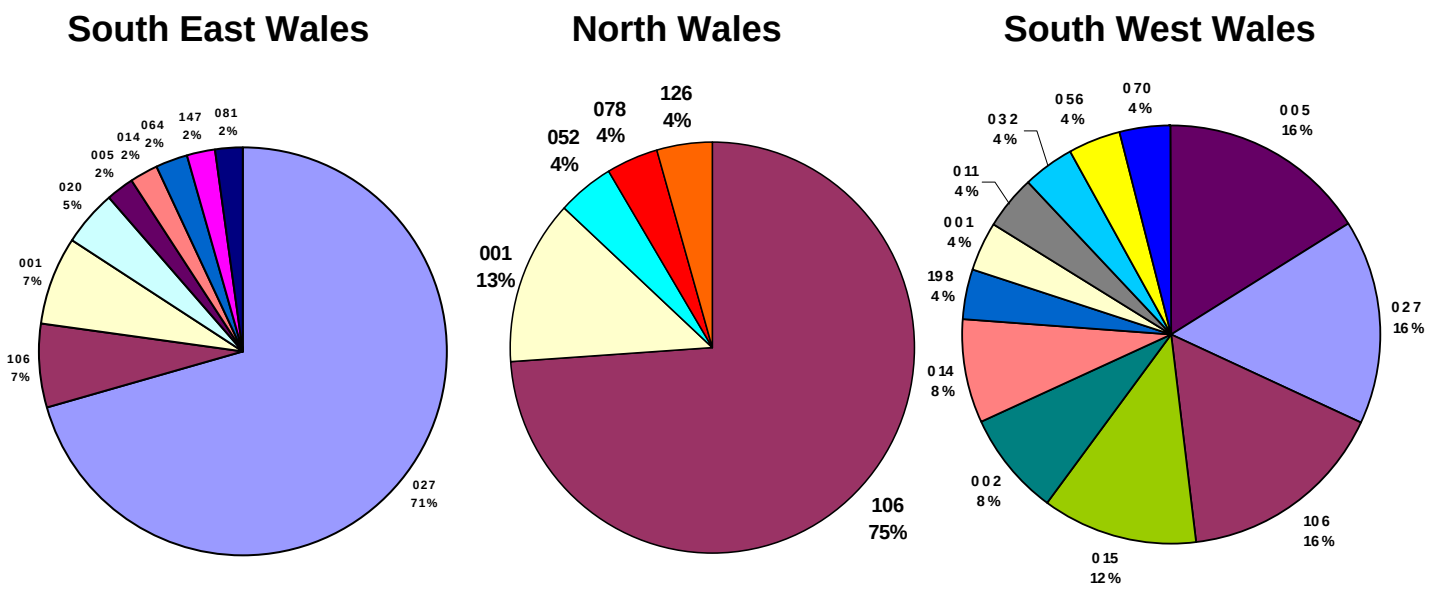
- A total of 19 PCR ribotypes were identified. PCR ribotype 027 was the most commonly isolated strain, accounting for 38% of the sample (Figure 1).

Figure 1. Percentage distribution of PCR ribotypes of *C. difficile* in the enhanced PCR ribotyping survey in Wales, 2008



- Results were not uniform across Wales (Figure 2). 027 predominated in the Trusts in South East Wales; 106 was the most common strain in the Trusts in North Wales and there was no predominant PCR ribotype in the South West Wales Trusts.

Figure 2. *C. difficile* PCR ribotypes by Trust region in the enhanced PCR ribotyping survey in Wales, 2008



- There has been a large increase in the frequency of PCR ribotype 027 and a large decrease in the frequency of PCR ribotype 001 in Wales since the previous PCR ribotyping survey in 2005.

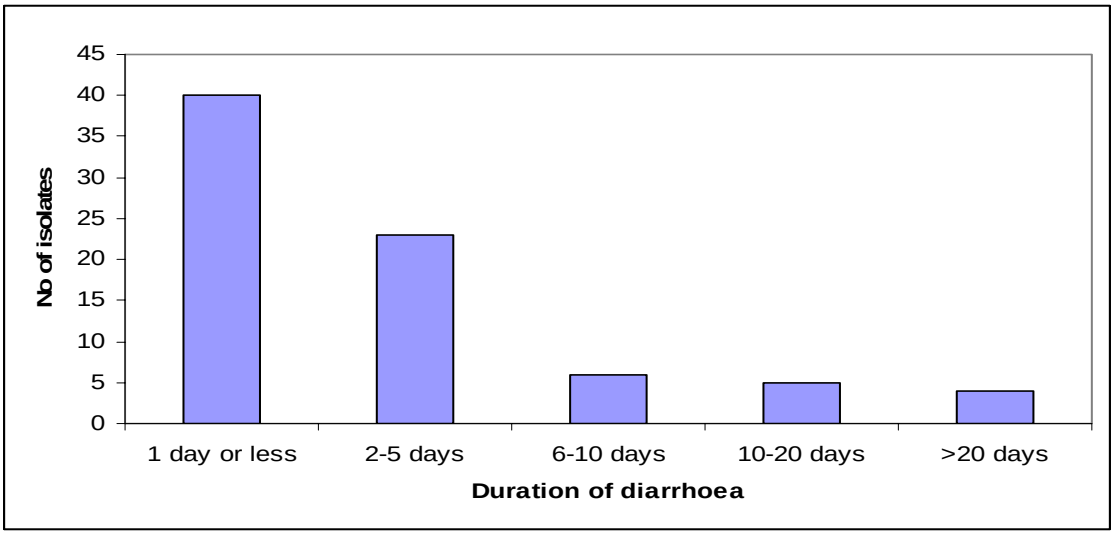
- No MIC levels were detected that might equate to clinical resistance to metronidazole; however, the 3 most common PCR ribotypes (027, 106, 001) did have higher MICs to metronidazole, erythromycin and moxifloxacin than the less common strains.

3.2 Survey Results

- A surveillance questionnaire was completed for 91% of the *C. difficile* samples.

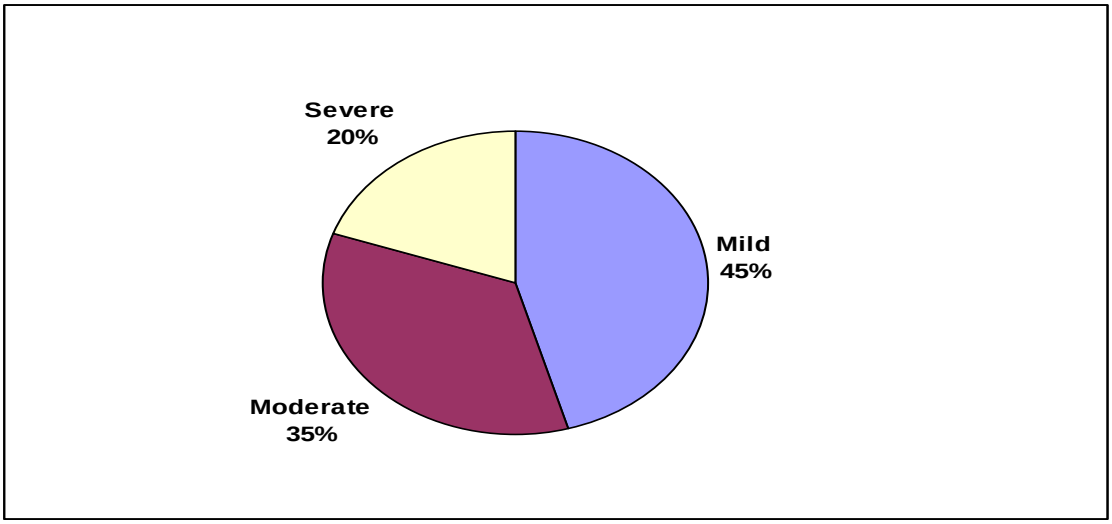
- In the majority of patients, the stool sample was taken within 1 day of the onset of diarrhoea (Figure 3).

Figure 3. Duration of diarrhoea pre-positive *C. difficile* test in the enhanced PCR ribotyping survey in Wales, 2008



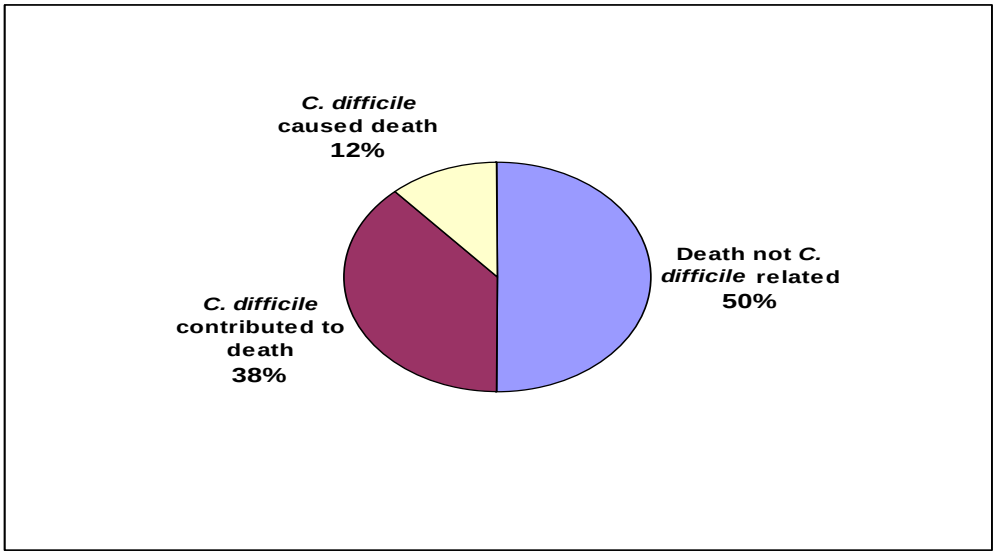
- *C. difficile* infection was most commonly associated with mild diarrhoea i.e. 3 episodes or less of diarrhoea per day with no other symptoms (Figure 4). The 027 strain was not associated with more severe diarrhoea than the other strains.

Figure 4. The severity of diarrhoea associated with *C. difficile* infection in the enhanced PCR ribotyping survey in Wales, 2008



- Approximately one third of patients were known to have died by the end of the 30 day surveillance period. *C. difficile* was indicated to have been the cause of death in 12% of the patients (3/26) (Figure 5). A further 38% were noted to have *C. difficile* as a contributory factor in their death; however "contributing to death" was not defined in the questionnaire and this must be considered to be a crude assessment of death due to *C. difficile* which warrants further investigation. A regular review should be conducted of deaths within 30 days of diagnosis of *C. difficile* infection to ensure a common standard of assessment of cause of death or contribution to death is being applied.

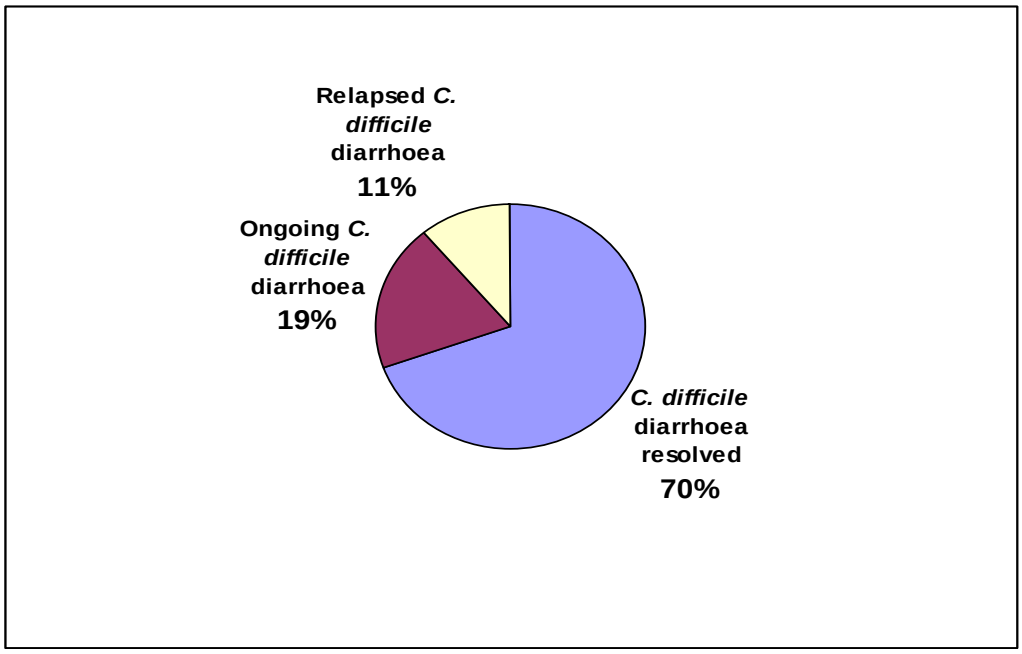
Figure 5. Causes of death for patients known to be deceased at 30 days following a positive *C. difficile* sample in the enhanced PCR ribotyping survey in Wales, 2008



- The proportion of deaths attributable to *C. difficile* was the same for patients with 027 as for the patients with the other strains.

- For patients known to be alive at the end of the 30 day surveillance period, nearly 70% had recovered from the *C. difficile* associated diarrhoea (Figure 6). Patients who still had ongoing or relapsed *C. difficile* diarrhoea were significantly more likely to have the 027 strain than the other strains.

Figure 6. *C. difficile* status of patients known to be alive 30 days following a positive *C. difficile* sample in the enhanced PCR ribotyping survey in Wales, 2008



- Some changes to the methodology and improvements in communication between and within the different staff groups involved will be required to run this survey on an annual basis, as recommended by the WHAISG *C. difficile* Task Group.

4. Appendix

C. difficile PCR Ribotyping Surveillance Questionnaire

Clostridium difficile Ribotype Enhanced Surveillance Form

The WHAIP Team **CANNOT** accept any patient identifiable data. Please enter a **UNIQUE** serial code which will allow you to identify from which patient the specimen came from (**DO NOT** use a Hospital/NHS number). The serial code can be any length from 1-10 digits and can consist of numbers, letters or both.

Date of first positive *Clostridium difficile* test: ☐☐ / ☐☐ / ☐☐

Ribotype: ☐☐☐

Duration of diarrhoea* pre positive test: ☐☐☐ Days

***Diarrhoea = stool consistency type 5-7 on Bristol Stool Chart**

Severity of disease: Cross **ONE** box only

- ☐ **Mild:** 3 or less type 5-7 stools on Bristol Stool Chart per day and normal white cell count (WCC).
- ☐ **Moderate:** 4 or more type 5-7 stools on Bristol Stool Chart per day and a raised WCC <15,000.
- ☐ **Severe:** A WCC >15,000 *or* a temperature of >38.5°C or acute rising serum creatinine (e.g. >50% increase above baseline) *or* evidence of severe colitis (abdominal or radiological signs). The number of stools may be a less reliable indicator of severity.
- ☐ **Complicated:** Hypotension or partial ileus *or* CT evidence of severe disease.
- ☐ **Life threatening:** Complete ileus or toxic megacolon.

Outcome at 30 days: Cross **ONE** box only

- ☐ Recovered (diarrhoea stopped >48hrs)
- ☐ Discharged/Transferred/Outcome unknown
- ☐ Ongoing diarrhoea
- ☐ Relapse/Recurrent disease
  Definition = Resolved case (>48hrs diarrhoea free) followed by further *Clostridium difficile* toxin positive diarrhoea
- ☐ Colectomy
- ☐ Death caused by *Clostridium difficile*
- ☐ Death where *Clostridium difficile* contributed
- ☐ Death by other cause

5. Acknowledgements

We would like to acknowledge the staff of the ARL, WHAIP, the culture laboratories and the infection control teams in the NHS trusts in Wales, for their contributions to this report.