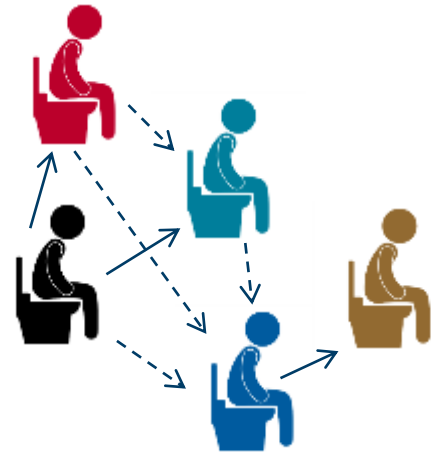


A cluster of *Clostridium difficile* infections caused by a binary toxin producing new PCR ribotype 826

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No conflicts of interest, nothing to disclose

Background

National sentinel CDI surveillance:

- Monitors CDI incidence rates, outbreaks and circulating ribotypes
- 23 participating hospitals, university-affiliated and general
- All CDI cases in hospitalised patients >2yrs old are registered
- National Reference Laboratory for typing and characterization (Leiden)

Stable CDI incidence of 3 per 10,000 patient-days
Only occasional outbreaks (RT027)



Background

Erasmus University Medical Centre

- 1320-bed tertiary care hospital, university-affiliated
- Participating in national sentinel CDI surveillance program since 2009
- Stable CDI incidence (1.5 per 10,000 patient-days, July 2009-November 2015), no outbreaks
- CDI diagnosis using stand-alone Xpert *C. difficile* (Cepheid AB, Solna, Sweden)

Gastro-intestinal surgical ward

- Stable CDI incidence (3.3 per 10,000 patient-days July 2009-November 2015)
- Period July 2009-November 2015: 19 CDI cases including 2 clusters (3x RT027, 2x RT017)

Description of the cluster

1 December 2015

- CDI case (A) reported on gastro-intestinal surgical ward, binary toxin+
- 83-year old male
- pancreaticoduodenectomy because of a carcinoma of the ductus choledochus 1 month earlier
- readmission because of infected ascites
- Mild hospital-acquired CDI, treated with metronidazole



Description of the cluster

8 December 2015

- Additional infection prevention measures implemented: daily cleaning and disinfection of the automatic bedpan washer, utility room and sanitation using 1000ppm chlorine, cleaning and disinfection of toilet chairs after each use using 1000ppm chlorine and use of only cardboard single use bedpans in toilet chairs



Local guidelines:

- Single room if CDI suspected or confirmed
- Protective disposable gown and gloves on entering the room
- Daily cleaning and disinfection with 1000ppm chlorine of toilets, all medical and nursing instruments that had been in contact with the patient and patient's room
- Cleaning and disinfection of patient's room after discontinuation of isolation precautions or patient's discharge



Description of the cluster

29 January 2016

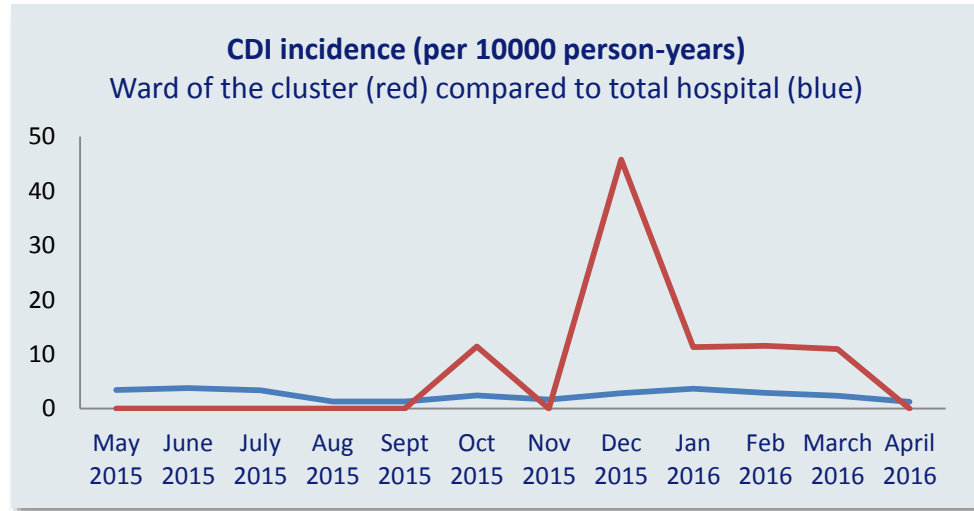
- Fourth CDI case (D) on same ward, binary-toxin positive
- Severe hospital-acquired CDI (severe colitis, leukocytosis, fever, rise in creatinin) treated with oral vancomycin



Description of the cluster

21 February 2016

- Case A readmitted because of CDI recurrence
- Severe CDI (mental status changes, leukocytes >15 , serum lactate >2.2), treated with oral vancomycin



Patient characteristics and characteristics of CDI episodes

Male (%)	2/5 (40)
Age, median (range)	68.1 (41-83)
Charlson comorbidity index, median (range)	2 (0-8)
<i>Initial CDI episode</i>	
<u><i>Previous healthcare contact</i></u>	
Previously admitted to the hospital <1y (%)	4/5 (80)
Transferred from other hospital (%)	1/5 (20)
ICU admission before CDI (during current admission) (%)	1/5 (20)
Surgery before CDI (during current admission) (%)	3/5 (60)
<u><i>Medication use in preceding 3 months</i></u>	
Proton pump inhibitors (%)	4/5 (80)
Systemic immunosuppressive agents or chemotherapy (%)	0/5 (0)
Antibiotics (%)	5/5 (100)
Total DDDs used, median (range)	26.9 (20.6-62.6)
Hospital onset (%)	5/5 (100)
Days admitted until CDI, median (range)	25 (3-50)
Severe disease (%)	1/5 (20)
<i>First recurrence</i>	
Hospital onset (%)	1/2 (50)
Severe disease (%)	2/2 (100)
<i>Second recurrence</i>	
Hospital onset (%)	1/5 (20)
Severe disease (%)	0/1 (0)
Severe disease (%)	1/1 (100)

Microbiological analyses



- tcdB+
- binary toxin+
- no TcdC Δ 117 deletion

Culture: *C. difficile*+



In-house PCRs on cultured isolates:

- TcdA+
- TcdB+
- Binary toxin+
- 39-bp deletion in TcdC
- PCR on a clade 5 specific marker+

Ribotyping by capillary gel-based electrophoresis:

- Same unique PCR ribotyping profile in 5 patients
- Profile not recognized in Dutch Reference Library
- Profile not recognized in any international database (including the Leeds collection, WEBRIBO system, CDC database and databases from Sweden, Portugal, Belgium and Canada)

Multilocus variable number of tandem repeats analysis (MLVA):

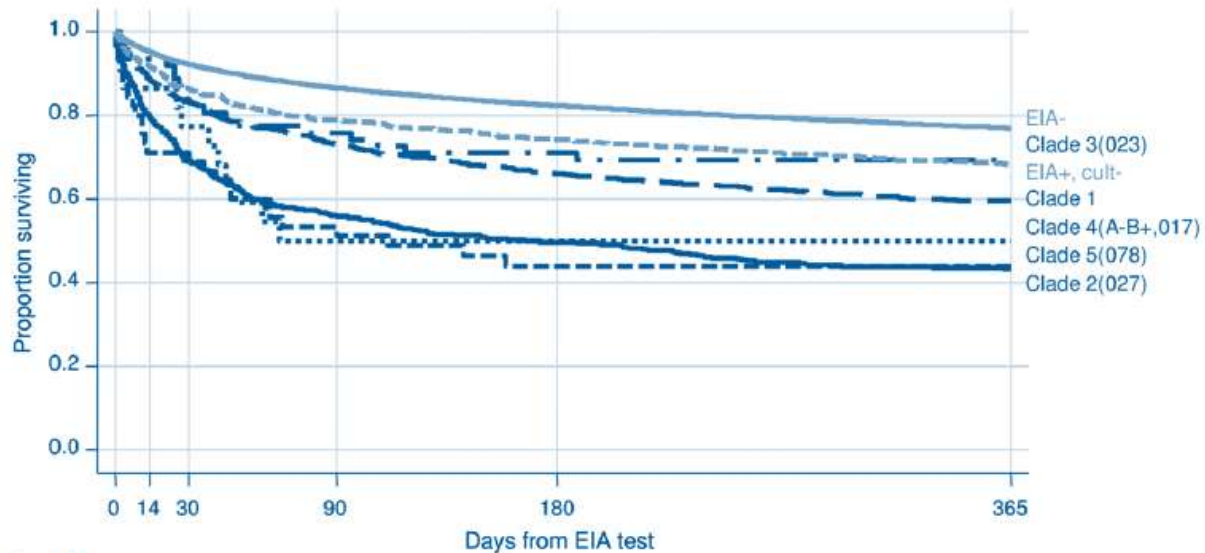
- Isolates 100% identical with 0 summed tandem-repeat differences (STRD)

Antimicrobial susceptibility testing by E-test:

- Susceptible for erythromycin (MIC 0.38-0.75), clindamycin (MIC 0.38-1.5), metronidazol (MIC 0.023-0.125) and vancomycin (MIC 0.38)
- Resistant to ciprofloxacin (MIC>32) and moxifloxacin (MIC>32)

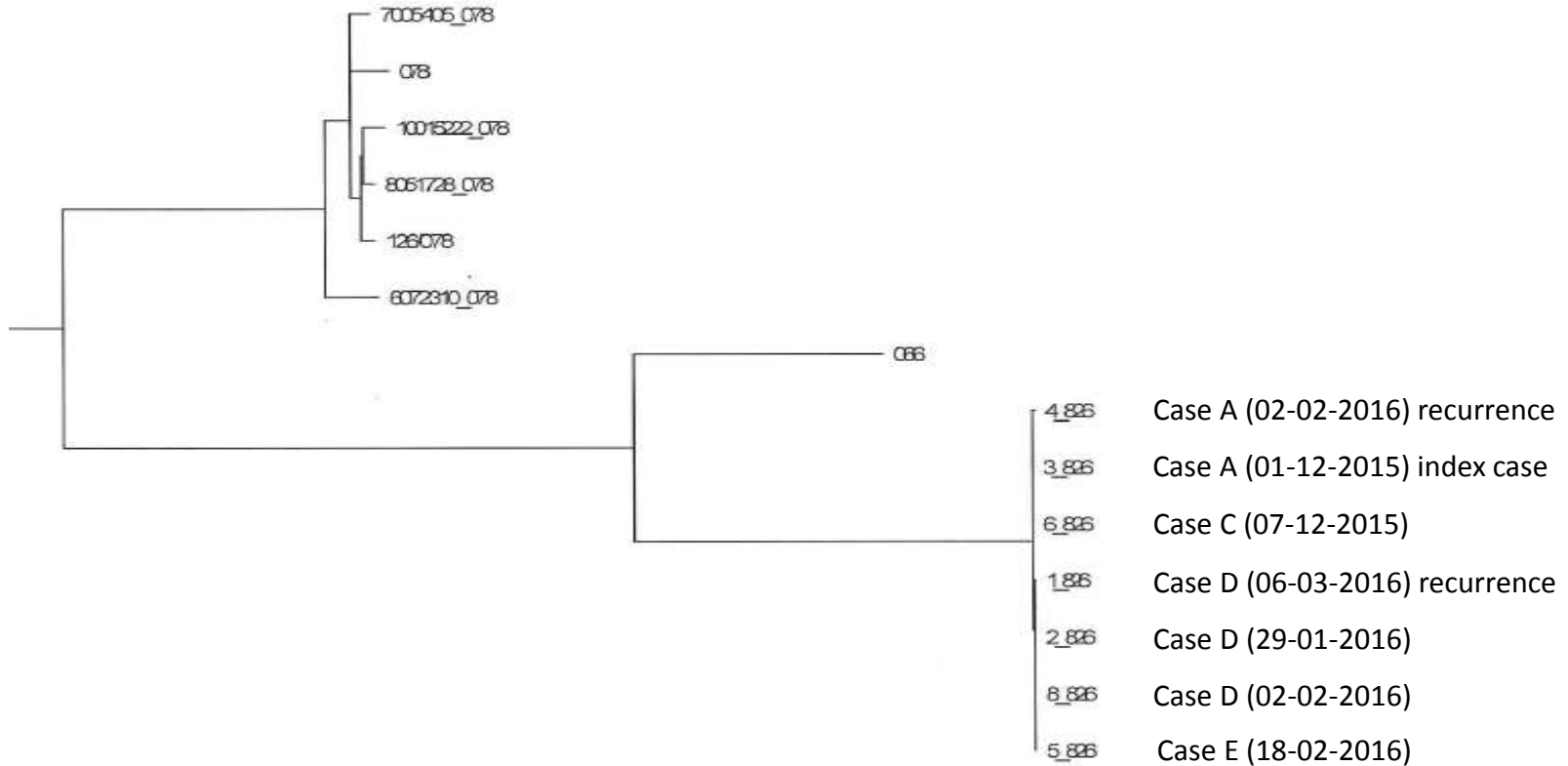
Microbiological analyses

- Ribotyping profile resembles 078, 126 and 066 most, all belonging to clade 5



- Ribotyping profile was assigned as **ribotype 826** by the Leeds Ribotyping reference network

Microbiological analyses - WGS



Additional analyses



C. difficile detected on 2/56 environmental swabs:

- Sack of laundry in shared bathroom after cleaning and disinfection RT826
- Shared bathroom non-toxigenic RT010

>> no detection of new cases



Source of *C. difficile* in the index patient unclear

- No remarkable profession or travel history
- Introduction by asymptomatic carrier?

Conclusions

Remarkable cluster of CDI cases:

- Occurred in a setting with only rare *C. difficile* transmission
- Associated with a high rate of recurrent and/or severe disease
- Due to a newly identified ribotype 826

RT826 resembles RT078 and we therefore assume that it has increased virulence, explaining the cluster

Recognition of this cluster indicates that new *C. difficile* ribotypes still emerge at unexpected locations and without a clear source

Ongoing CDI surveillance remains essential, and other institutions should now be aware of RT826

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