

# Laboratory testing and laboratory surveillance data for CDI

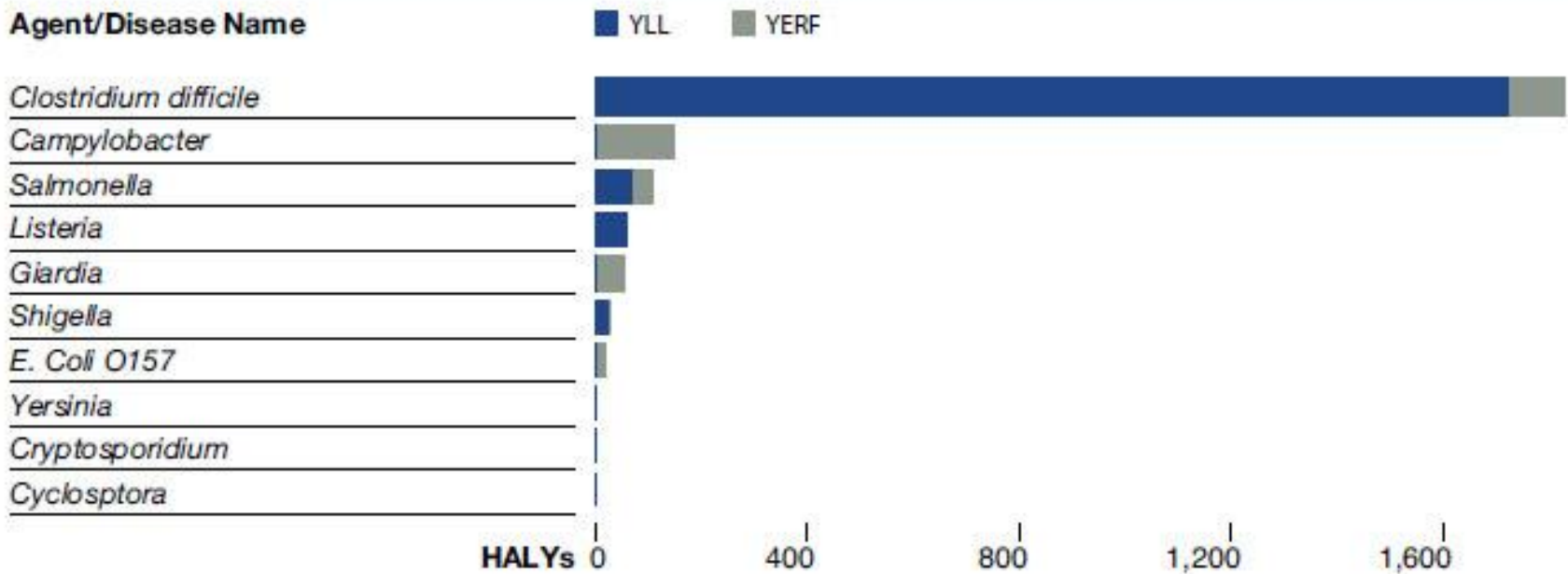


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Public Health Ontario Laboratories – Toronto

Outbreak Management Workshop  
September 28, 2011



## Years of life lost due to premature mortality (YLL), year-equivalents of reduced functioning (YERF) and health-adjusted life years (HALYs) for intestinal infections



Kwong JC, Crowcroft NS, Campitelli MA, Ratnasingham S, Daneman N, Deeks SL, Manuel DG. Ontario Burden of Infectious Disease Study Advisory Group; Ontario Burden of Infectious Disease Study: An OAHPP/ICES Report



## Number of presentations on some infections:

**HIV – 64**

***C. difficile* – 64**

**Influenza – 30**

***E. coli* - 19**

***Listeria* – 1**

## Keyword Index

HIV ..... A1-1726, A1-1728, D-1304, D-1305,  
..... D-1306, H1-1148, H1-1152, H1-1391,  
..... H1-1392, H1-1394, H1-1395, H1-1396,  
..... H1-1397, H1-1399, H1-1400, H1-1401,  
..... H1-1403, H1-1406, H1-1408, H1-1409,  
..... H2-782, H2-783, H2-784, H3-807,  
..... H3-808, H3-815, L1-268, M-1517

HIV drug resistance ..... H1-1150, H2-796

HIV epidemiology ..... H1-1149

HIV infection ..... G1-766, H1-1393,  
..... H1-371, H2-790, L2-892

HIV integrase inhibitor ..... F1-1370

HIV integrase ..... H1-374, H2-801

HIV prevention ..... H1-1151

HIV RNA ..... H1-373

HIV screening ..... H2-792

HIV testing ..... H1-1404, H1-1405

HIV therapy ..... F1-1371, H2-803

HIV transmission ..... H1-1151

HIV-1 ..... H1-1407, H2-795

HIV-1 inhibitors ..... F1-1369

HIV-1 resistance ..... H1-374, H2-800

HIV-1 RNA level ..... H1-1407

HIV-1 subtypes ..... F1-1371

HIV-1 tropism ..... H2-799

HIV-2 ..... H2-1410, H2-1411

HIV-exposed children ..... G3-1703

HIV-HCV coinfection .. H3-811, H3-812, H3-814

HIV-therapy ..... H1-375

HIV/AIDS ..... P-924

HIV/TB ..... A1-1723

*Clostridium difficile* ... A2-034, B-1190, B-1191,  
... B-1192, B-1193, B-1195, C1-631, C1-632,  
.. C1-633, C1-634, C1-635, C2-1807, D-1272,  
.. D-1273, D-1274, D-1275, D-1276, D-1277,  
..... D-1278, E-110, G1-767, K-193, K-195,  
.. K-196, K-197, K-198, K-200, K-201, K-202,  
..... K-203, K-204, K-205, K-211, K-1717,  
... K-1128, K-1130, K-1474, K-1710, K-1711,  
... K-1713, K-1714, K-1715, K-1716, K-1718

*Clostridium difficile* infection .. B-1189, B-1194,  
..... K-191, K-194, K-199, K-1712

*Clostridium difficile* toxin ..... B-1187, B-1188,  
..... B-1189, C1-635

fidaxomicin ..... A2-042, A2-043, A2-044,  
..... A2-045, B-1190, C1-631, C1-632,  
..... C1-634, C1-635, K-1476

influenza .. A1-1729, D-1309, D-1310, F1-1366,  
..... F2-1867, G1-755, G3-182, G3-184,  
..... H1-1399, K-1445, V-403, V-404, V-405,  
... V-1543, V-1544, V-1545, V-1547, V-1556

influenza A (H1N1) ..... D-1312, D-1313,  
..... G1-756, V-1551, V-1552

influenza infection ..... A1-1730, D-1308

influenza vaccination ..... K-1445

Influenza vaccine ..... G1-757

influenza virus ..... D-1311, F1-1367

influenza-like illness ..... V-1545

ESBL producing *Escherichia coli* ..... B-594,  
C1-476, C2-1232, C2-1233, C2-1243, F1-  
1858

*Escherichia coli* ..... C1-472, C1-473, C1-1219,  
..... C2-1230, C2-1231, E-137, E-1816,  
..... E-1823, K-839, K-1906, K-1915,

*Escherichia coli* O26 ..... L1-389

*Escherichia coli* ST131 ..... C1-469

antilisterial ..... F1-1356



difficile outbreak ontario

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C. **difficile outbreak** over in 3 **Ontario** hospitals - Toronto - CBC News

[www.cbc.ca/news/canada/toronto/story/2011/07/10/cdifficile-ontario.html](http://www.cbc.ca/news/canada/toronto/story/2011/07/10/cdifficile-ontario.html)

10 Jul 2011 – The number of **Ontario** hospitals fighting **outbreaks** of the persistent **s difficile** is down to seven from 10 earlier in the week, Health ...

C. **Difficile Outbreak: Ontario** Calls In Federal Expert

[www.huffingtonpost.ca/.../c-difficile-outbreak-ontario-federal-expert...](http://www.huffingtonpost.ca/.../c-difficile-outbreak-ontario-federal-expert...) - Cached

7 Jul 2011 – THE CANADIAN PRESS – OTTAWA - The federal government has sent detective" to help **Ontario** deal with a dangerous **outbreak** of ...

Anger over C. **difficile outbreak** in **Ontario** hospitals - CTV News

[www.ctv.ca/CTVNews/.../c-difficile-outbreak-southern-ontario-110706/](http://www.ctv.ca/CTVNews/.../c-difficile-outbreak-southern-ontario-110706/)

6 Jul 2011 – A deadly **outbreak** of C. **difficile** in southern **Ontario** is raising the ire of locals who say that the province's health system isn't doing ...

C. **difficile outbreak** ends at three **Ontario** hospitals | News | National

[news.nationalpost.com/.../c-difficile-outbreak-ends-at-three-ontario-...](http://news.nationalpost.com/.../c-difficile-outbreak-ends-at-three-ontario-...) - Cached

10 Jul 2011 – The death toll linked to a C. **difficile outbreak** across **Ontario** has increased, but the number of hospitals battling the superbug is down to seven ...

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Home : Canada : Anger over C. difficile outbreak in Ontario hospitals

### Anger over C. difficile outbreak in Ontario hospitals



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### Clostridium difficile outbreak in multiple Ontario hospital

By Glory Song



Photo credit: [cafemama](#)

A recent rise in C. dif hospitals in Ontario, outbreak declarati increasingly commo Kingston General Hc the past month, a 5 incidence of 8 cases Ontario, hospitals u Health Systems hav past 3 months. The [31 deaths](#) in the 1 after announcement government, Queen Ottawa also annour with [5 cases of its o](#)

### C. difficile outbreak ends at three Ontario hospitals



older hospital patients and typically occurs after use of antibiotic medication. [It can ca](#) ing the bug under cont :argeted doses of antib id rooms, the [public mu](#) of hand-cleaning static

## SHEA-IDSA Guideline (2010)

Clinical Practice Guidelines for Clostridium difficile Infection in Adults: 2010 Update by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA)

7. **Stool culture is the most sensitive test** and is essential for epidemiological studies (A-II)

9. Enzyme immunoassay (EIA) testing for C. difficile toxin A and B **is rapid but is less sensitive** than the cell cytotoxin assay, and it is thus a suboptimal alternative approach for diagnosis (B-II)

10. Toxin testing is most important clinically, but is hampered by its lack of sensitivity. **One potential strategy to overcome this problem is a 2-step method that uses EIA detection of glutamate dehydrogenase (GDH)** as initial screening and then uses the cell cytotoxicity assay or toxigenic culture as the confirmatory test for GDH-positive stool specimens only. Results appear to differ based on the GDH kit used; therefore, until more data are available on the sensitivity of GDH testing, this approach remains an interim recommendation (B-II)

11. **Polymerase chain reaction (PCR) testing appears to be rapid, sensitive, and specific** and may ultimately address testing concerns. More data on utility are necessary before this methodology can be recommended for routine testing (B-II)

- **Public Health Ontario Laboratories offer specialized testing in support of CDI cluster and outbreak investigations for any public hospitals**
- **The Medical Microbiologist will consult and determine appropriate testing for the institution**
- **Unpreserved faeces no more than 72 hours old or fresh-frozen faeces can be forwarded to Public Health Ontario Laboratories**
- **Specialized tests include:**
  - **Culture and typing of CDI strain by pulse-field gel electrophoresis (eg. NAP1 strain) and MMLVA**
  - **Antibiotic susceptibility testing, including metronidazole and vancomycin**
  - **Specialized toxin typing by polymerase chain reaction (includes binary toxin elaborated by the “hyper-virulent” NAP1 strain)**

## Public Health Ontario Labs CDI Testing Statistics

- PHOL-Toronto and 8 Regional Labs perform CDI testing (Hamilton, London, Peterborough, Orillia, Sudbury, Sault Ste. Marie, Timmins, Thunder Bay)
- An average of **45,000 CDI tests** are done on an annual basis across the laboratories
- PHOL – Toronto performs **~21,150 CDI tests**
- Average percent positivity at PHOL between 2008 – 2010 was **11.22 %**

## Antimicrobial Susceptibility Profiles

- 366 strains were tested for antimicrobial susceptibility
- NAP1 strains were more likely to be resistant to ampicillin and moxifloxacin than non-NAP1 strains
- All isolates were sensitive to metronidazole
- 76% of NAP1 strains had MIC values = 0.5 µg/ml to vancomycin

Antimicrobial	NAP1 Resistance N (%)	Non-NAP1 Resistance N (%)
Ampicillin	202 (55.2)	85 (23.2)
Clindamycin	210 (57.3)	115 (31.4)
Metronidazole	0 (0)	0 (0)
Moxifloxacin	229 (62.6)	34 (9.3)

## In Ontario, defining a *C. difficile* outbreak involves the concept of notification thresholds, which are more sensitive than outbreak definitions

- For wards/units with  $\geq 20$  beds, **3 cases of nosocomial *C. difficile* infection (CDI)** identified on one ward/unit within a seven day period or **5 cases within a 4 week period**; OR
- For wards/units with  $< 20$  beds, **2 cases of nosocomial CDI** identified on one ward/unit within a seven day period or **4 cases within a 4 week period**; OR
- Hospitals that have a baseline CDI rate for two months that is at or above the 80th percentile for comparator hospitals; OR
- Hospitals that have a facility rate that is greater than or equal to 2 standard deviations above their baseline

<http://www.health.gov.on.ca/en/ccom/cdi/outbreak.aspx>

## **PHOL: outbreak surveillance**

**A total of 47 outbreaks were reported to MOHLTC between August 2008 - December 2010**

**22/47 (47%) of CDI outbreak investigations were supported by Public Health Ontario Laboratories with specialized CDI testing**

**2008: 1/6 (17%)**

**2009: 5/15 (33%)**

**2010: 16/26 (62%)**

**PHOL supported 11 CDI cluster investigations**

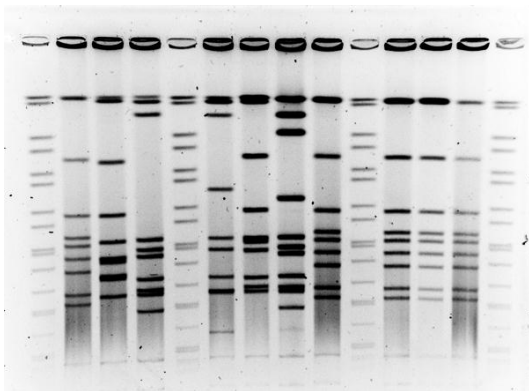
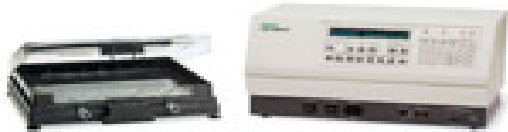
**2008: 2**

**2009: 7**

**2010: 2**

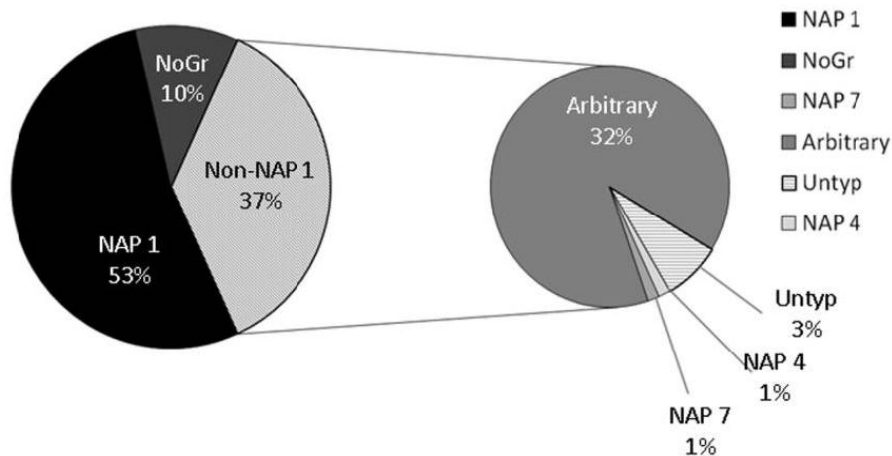
- **Currently outbreak investigation of CD in Canada is performed using PFGE typing**
- **PFGE lacks resolution in geographical regions where NAP1 strain (epidemic) is predominant (Quebec, Ontario etc)**
- **New genotyping method (MMLVA) was developed and implemented**
- **Interpretation of typing results has to be done in close collaboration with infection control**

## Pulsed Field Gel Electrophoresis (PFGE)

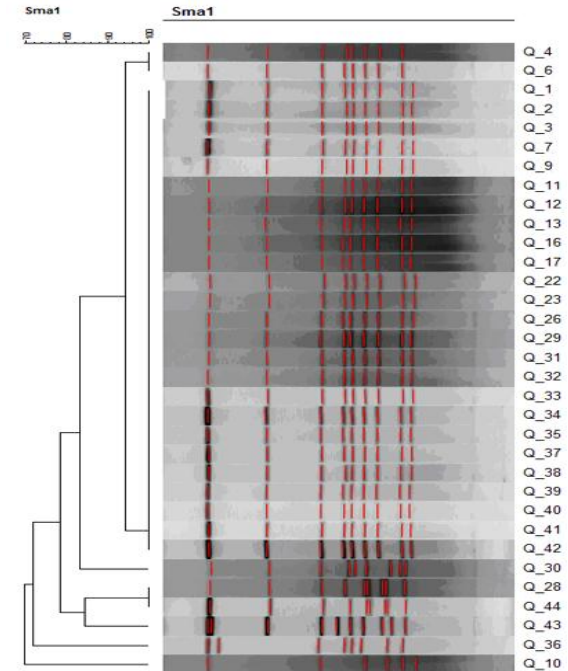


- Labour intensive – takes up to 10 days to get results
- Requires special equipment, casting gels, processing plugs, taking pictures, interpretation etc.
- **Lacks discriminatory power in outbreaks caused by NAP1 strains**

The predominant outbreak isolate in Ontario over 2008-9 was NAP1 strain, with a prevalence of 53%\*



\*Pillai DR et al. CID 2010;50:1685-6



Example of PFGE analysis of *C. difficile* strains isolated in a hospital

With NAP1 prevalence of 53% PFGE can not distinguish outbreak cluster from sporadic cases

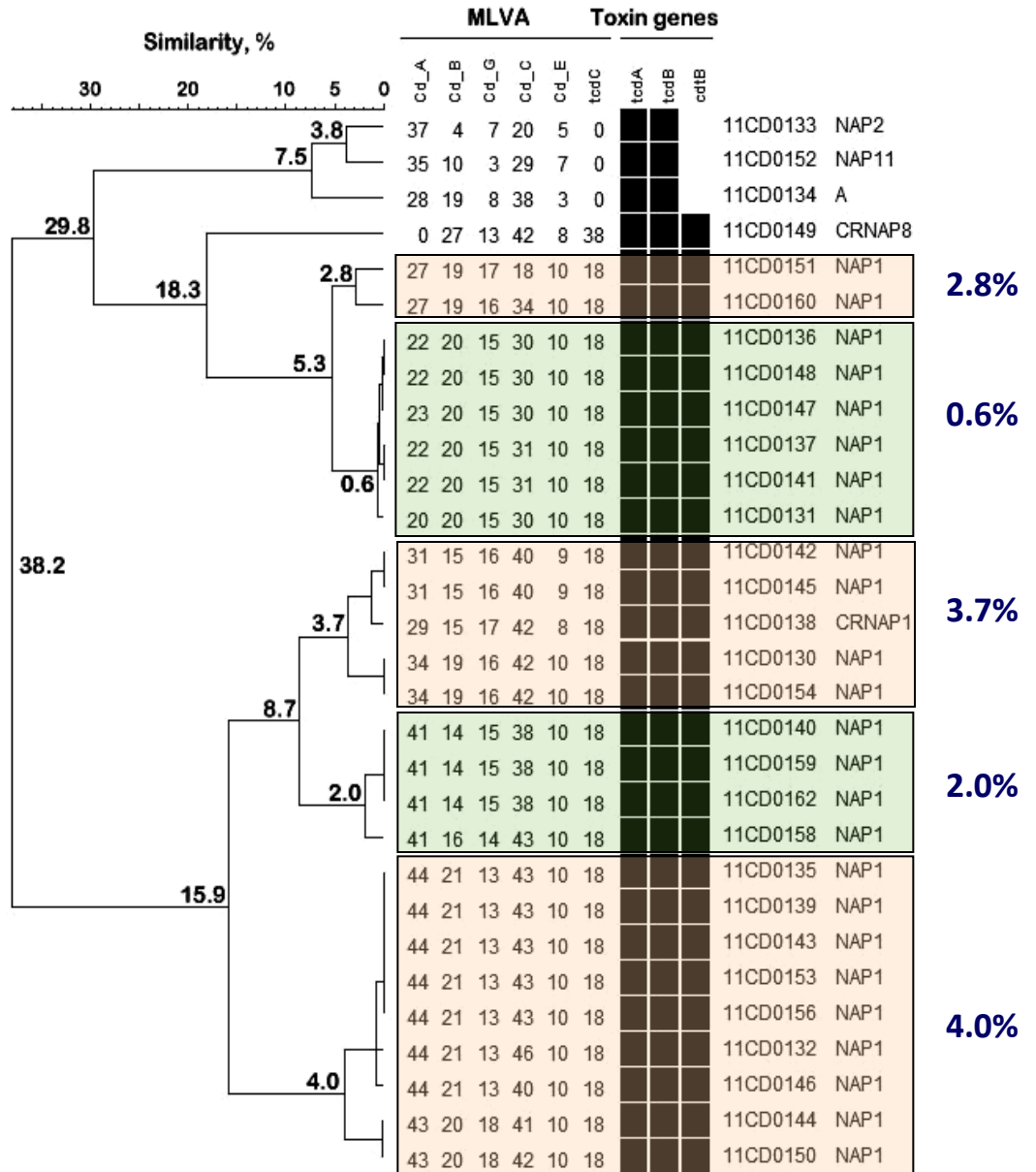




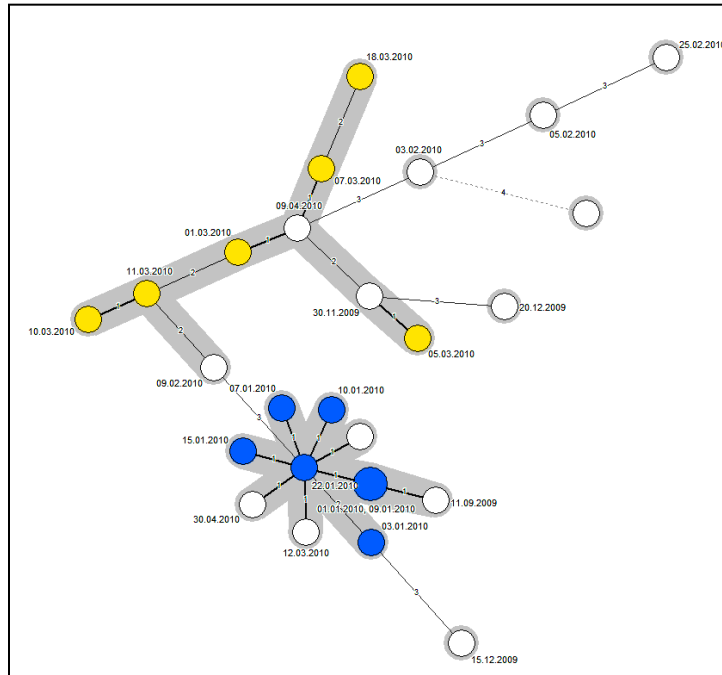
## Criteria for clustering of CD isolates

- **MLVA is a discriminatory typing method capable of defining clusters of NAP1 isolates**
- **The challenge is to determine cut-off values for clusters**
- **Population analysis suggests that a cut-off value of <1% is overly discriminatory, but a cut-off of 3-5% should capture true clusters**

# Outbreak analysis using MMLVA data



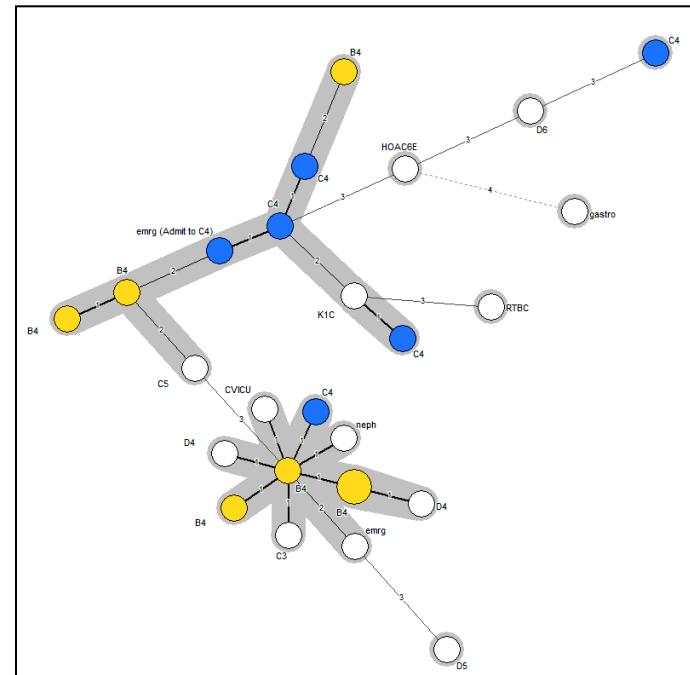
# Minimum spanning tree of NAP 1 isolates coupled to temporospatial data



**Date of admission**

**Blue nodes – January**

**Yellow nodes – March**



**Location**

**Blue nodes – C4**

**Yellow nodes – B4**

## Acknowledgments

- The PHOL staff conducting CDI testing and outbreaks typing
- The PHO S&E staff for analyzing the data

### Key contributors

Dylan Pillai: Medical Microbiologist

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