

A Review of the Epidemiology and Current Issues of *Clostridium difficile* Infection (CDI) in Ontario

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PHO Rounds: November 1, 2011.



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Clostridium difficile

- Spore-forming bacteria
- Normal intestinal flora in 3-5% of healthy adults.
- Only toxigenic *C. difficile* strains are pathogenic.
- 3 types of toxins: Toxin A, Toxin B, Binary Toxin
- Clinical presentations range from mild episodes of diarrhea to severe outcomes such as colitis, toxic megacolon, and death.

Risk Factors for Hospital-Acquired CDI

- Advanced age
- Prolonged duration of hospitalization
- Exposure to antimicrobial agents
- Chemotherapy
- Immunosuppressive therapy
- Gastrointestinal surgery or manipulation of the GI tract (i.e. tube feeding)
- Acid-suppressing medications (histamine-2 blockers and proton pump inhibitors)

Epidemiological Situation in Canada

- Incidence rates in Canadian hospitals estimated to be:
 - 0.4 – 1.3 cases per 1,000 patient days Miller et al. ICHE. 2002; 23: 137-140
 - 2 – 12.8 cases per 1,000 admissions Gravel et al. CID 2009; 48: 568-576
 - 0.81 cases per 1,000 patient days, 5.9 cases per 1,000 admissions in Ontario
- CNISP conducted a prospective surveillance study of HA-CDI between November 2004 and April 2005. Miller et al. CID 2010;50:194-201
 - 34 hospitals across 9 Canadian provinces; 1008 patients
 - 31% infected with NAP1 strain
 - 22% of NAP1 isolates from Ontario
 - 13% of NAP1 cases had severe outcomes, when compared to 6% of non-NAP1 cases having severe outcomes (P<0.001).

Public Reporting of CDI in Ontario

- Since September 1, 2008, all public hospitals in Ontario are required to report:
 1. Monthly aggregate counts of CDI cases associated with the reporting facility, other health care facilities, unknown source / non-healthcare facility and patient days
(exclude children <1 year of age from numerator and denominator)
 2. CDI outbreaks in hospitals
 - CDI outbreaks and associated cases are to be reported to the local public health units who then report to the MOHLTC via iPHIS.

1. Patient Safety Indicator Reporting

(1) New nosocomial case of CDI associated with reporting facility

- CDI was not present on admission (Sx onset >72 hrs after admission)

OR

- Infection was present at time of admission but was related to a previous admission to the same facility within the last 4 wks AND the case has not had CDI in the past 8 wks.

(2) New nosocomial case of CDI associated with other healthcare facilities

- CDI was present on admission **or** Sx onset <72 hrs after admission

AND

- Case was exposed to any other healthcare facility (including LTC) other than the reporting facility within the last 4 wks AND the case has not had CDI in the past 8 wks.

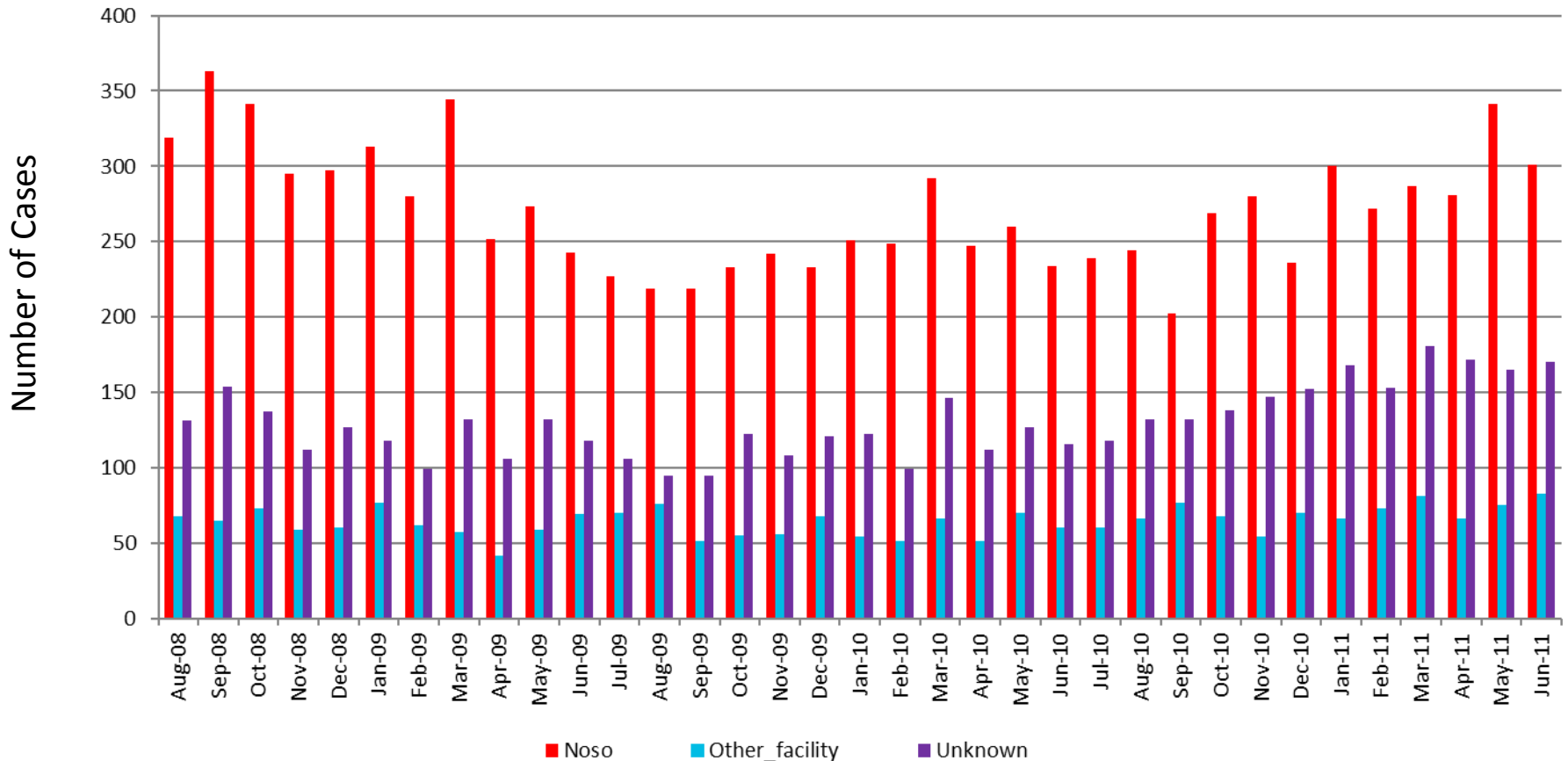
(3) New case of CDI associated with source other than a health care facility or indeterminate source

- CDI was present on admission **or** Sx onset <72 hrs after admission

AND

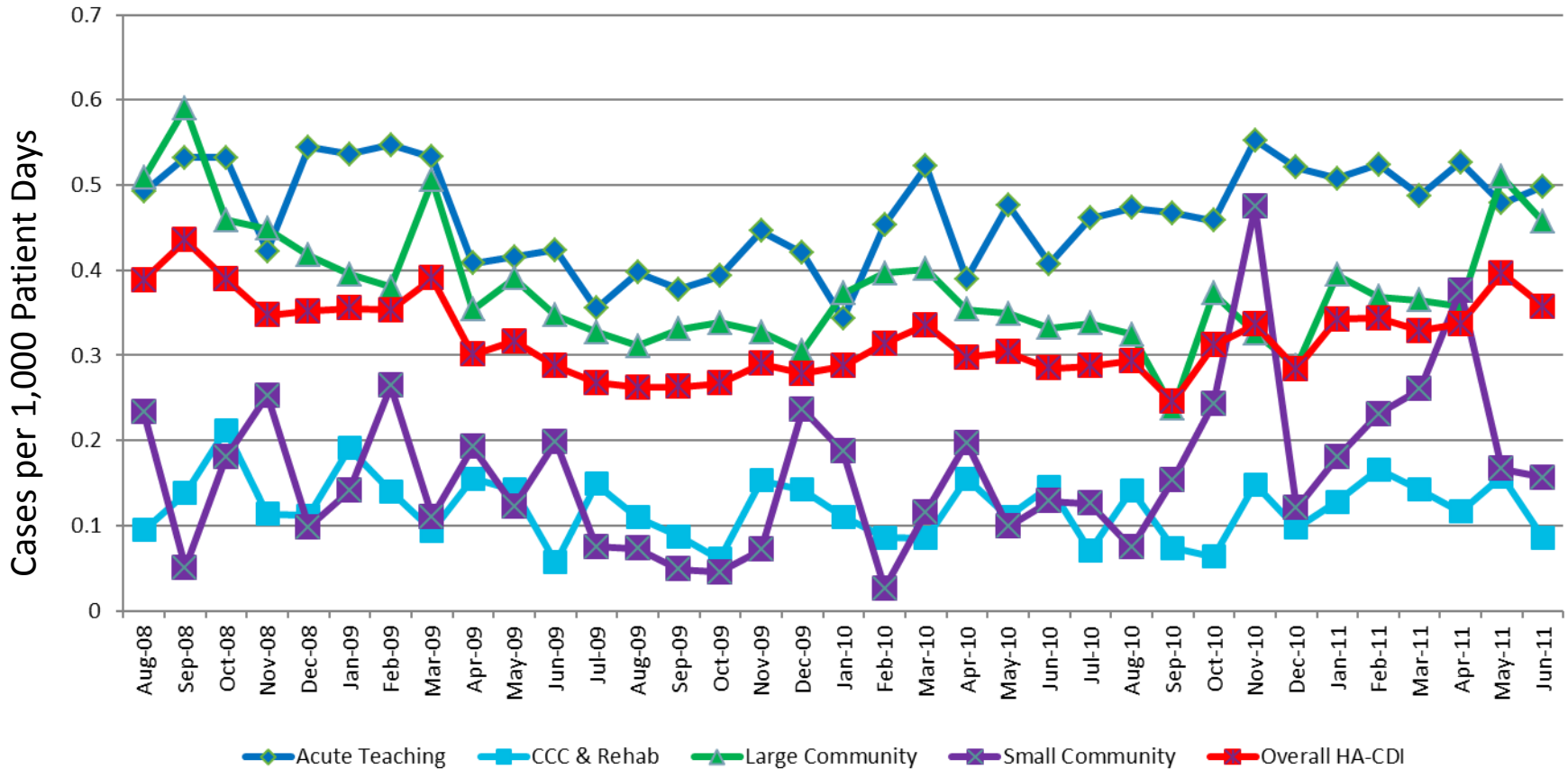
- No exposure to any healthcare facility within the last 4 wks or the source of infection cannot be determined AND the case has not had CDI in the past 8 wks.

Number of CDI Cases by Source of Acquisition (August 2008 – June 2011)



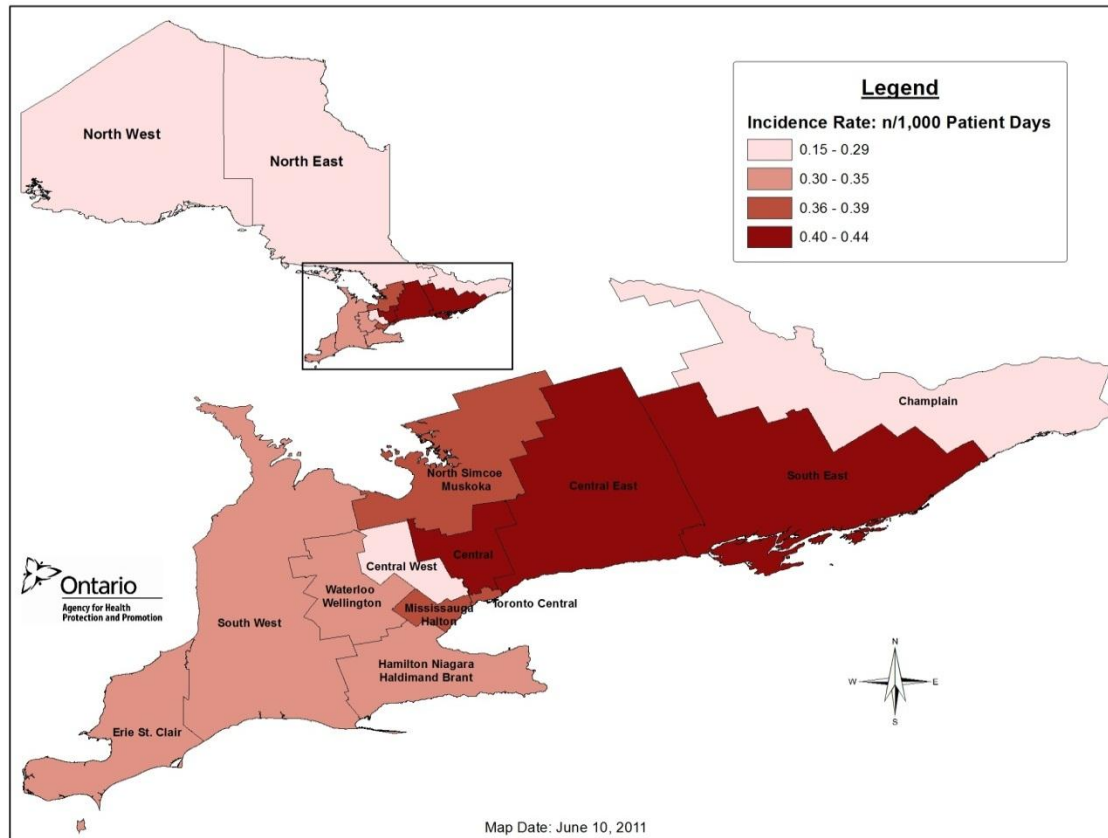
Data Source: Hospital self-reported data (Web-Enabled Reporting System), MOHLTC, July 2011.

Nosocomial CDI Rates by Hospital Type (August 2008 – June 2011)



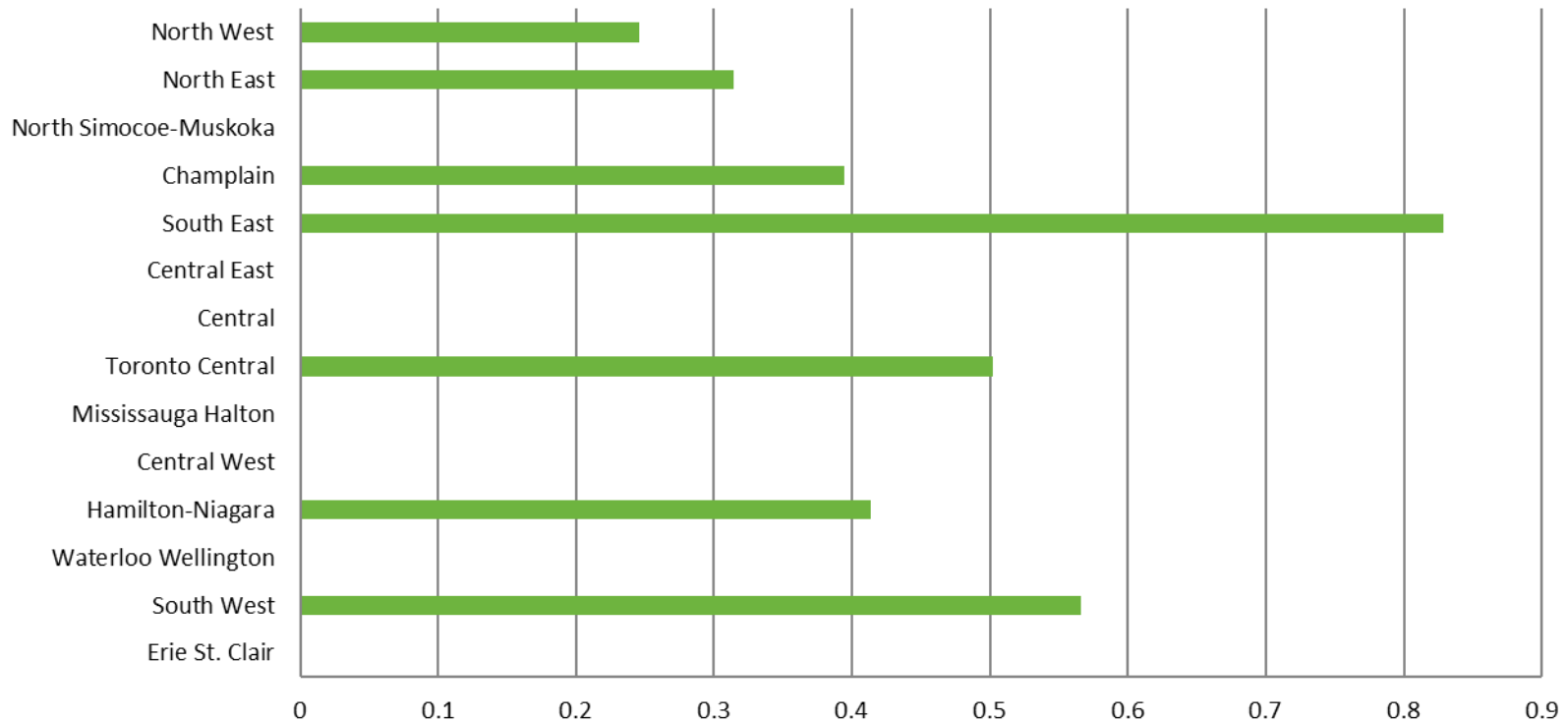
Data Source: Hospital self-reported data (Web-Enabled Reporting System), MOHLTC, July 2011.

Geographic Distribution of Nosocomical CDI Rates by LHIN (August 2008 – June 2011)



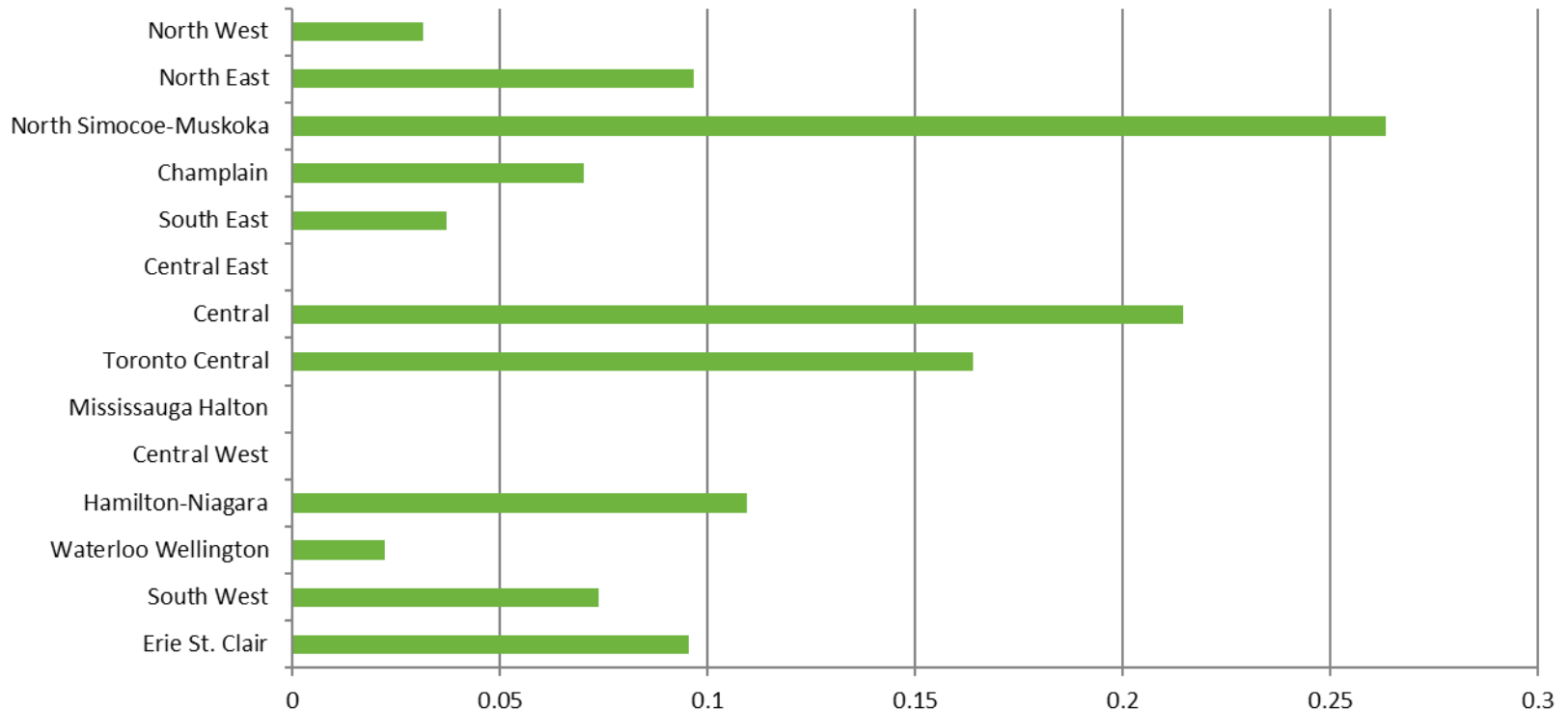
Data Source: Hospital self-reported data (Web-Enabled Reporting System), MOHLTC, July 2011.

Nosocomial Rates in Acute Teaching Facilities by LHIN (August 2008 – June 2011)



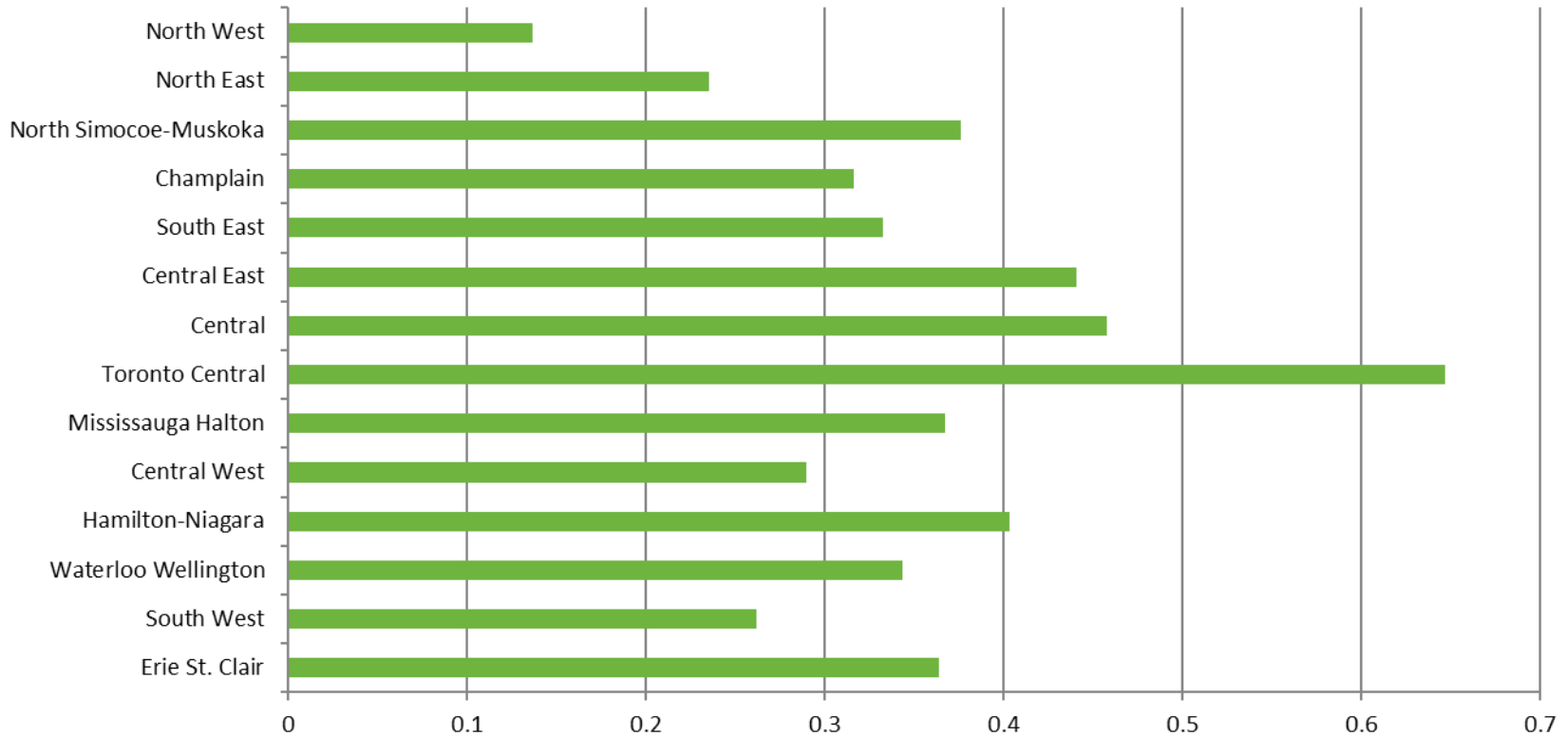
Data Source: Hospital self-reported data (Web-Enabled Reporting System), MOHLTC, July 2011.

Nosocomial Rates in CCC & Rehab Facilities by LHIN (August 2008 – June 2011)



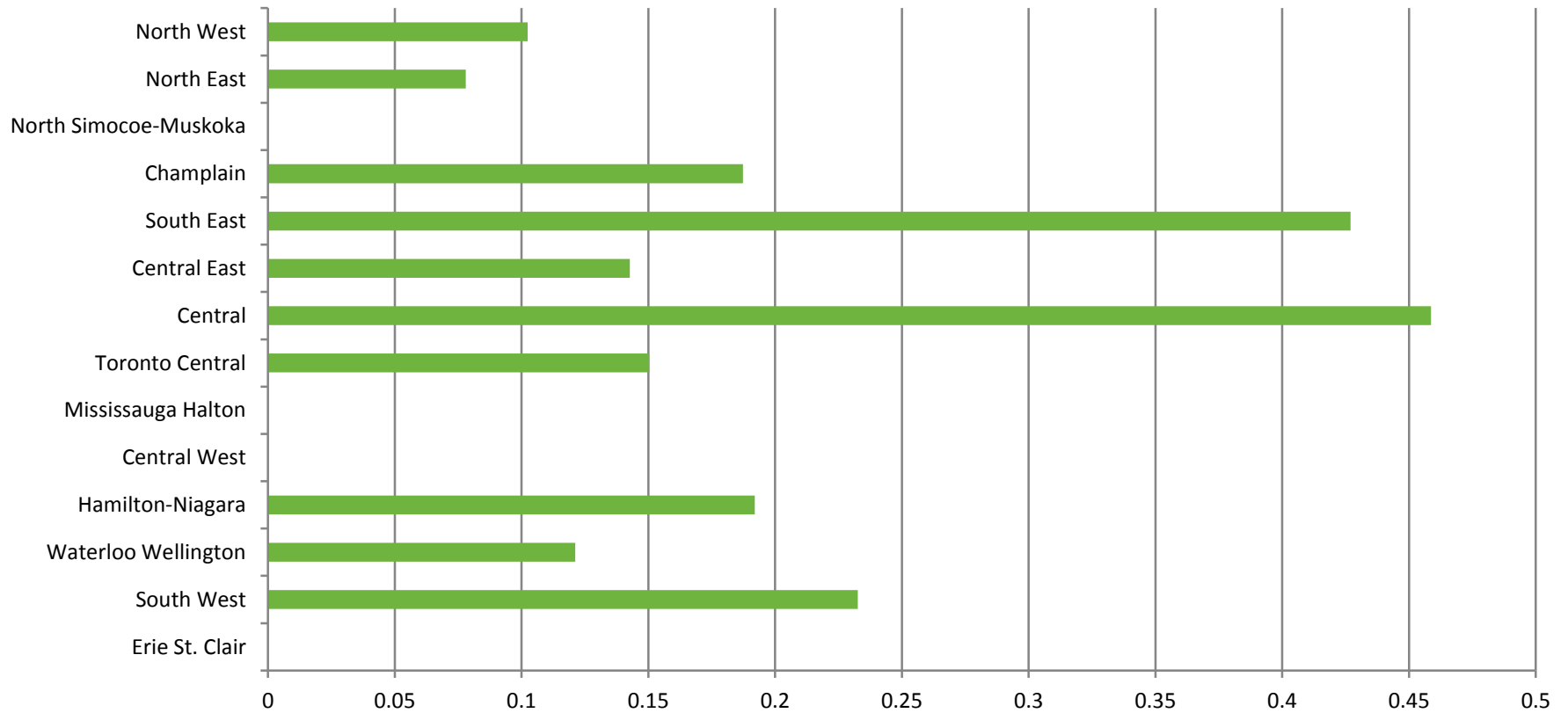
Data Source: Hospital self-reported data (Web-Enabled Reporting System), MOHLTC, July 2011.

Nosocomial Rates in Large Community Facilities by LHIN (August 2008 – June 2011)



Data Source: Hospital self-reported data (Web-Enabled Reporting System), MOHLTC, July 2011.

Nosocomial CDI Rates in Small Community Facilities by LHIN (August 2008 – June 2011)



Data Source: Hospital self-reported data (Web-Enabled Reporting System), MOHLTC, July 2011.

2. Reporting of CDI Outbreaks in Hospitals

- Public hospitals are required to report all CDI outbreaks and outbreak-associated cases to local public health units who then report to the Ontario Ministry of Health and Long-Term Care.
- Outbreak level data and outbreak-associated cases are entered into iPHIS.
- Public Health Ontario Laboratories offer specialized testing in support of CDI cluster and outbreak investigations.
- Specialized tests include:
 - Culture and typing of CDI strain by pulse-field gel electrophoresis (eg. NAP1 strain)
 - Antibiotic susceptibility testing
 - Specialized toxin typing by polymerase chain reaction (includes binary toxin elaborated by the “hyper-virulent” NAP1 strain)

Outbreak Threshold Definition

- For wards/units with ≥ 20 beds, 3 cases of nosocomial CDI identified on one ward/unit within a 7 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 7 day period or 4 cases within a 4 week period;

OR

- Hospitals that have a baseline CDI rate for 2 months that is at or above the 80th percentile for comparator hospitals;

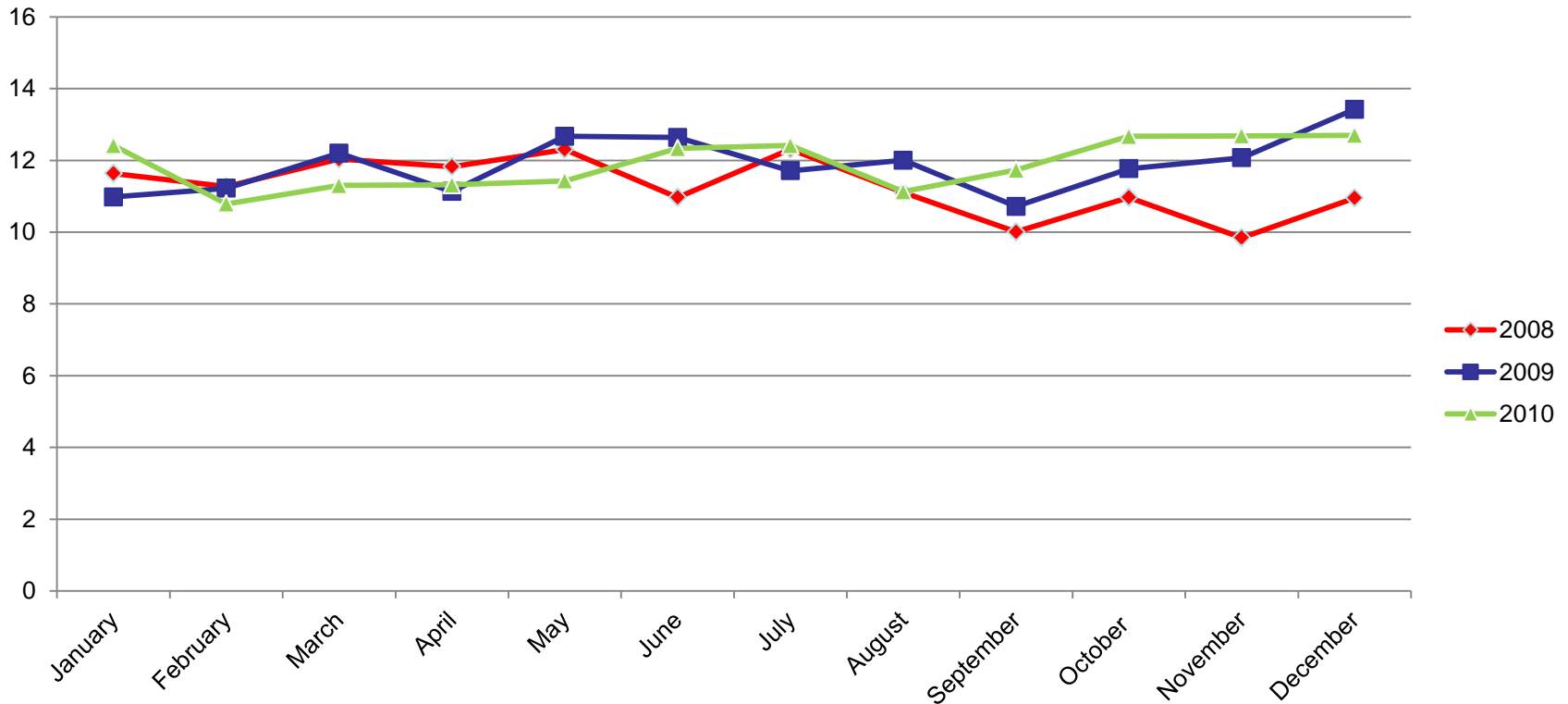
OR

- Hospitals that have a facility rate that is greater than or equal to 2 standard deviations above their baseline.

PHOL CDI Testing Statistics

- Toronto PHOL and 10 Regional Labs perform CDI testing.
(Hamilton, London, Peterborough, Orillia, Sudbury, Sault Ste. Marie, Timmins, Thunder Bay, Ottawa, Kingston).
- An average of 45,000 CDI tests are done on an annual basis across the laboratories.
- Toronto performs ~21150 CDI tests (47% of all tests in the province).
- Average percent positivity between 2008 and 2010 is 11.22%.

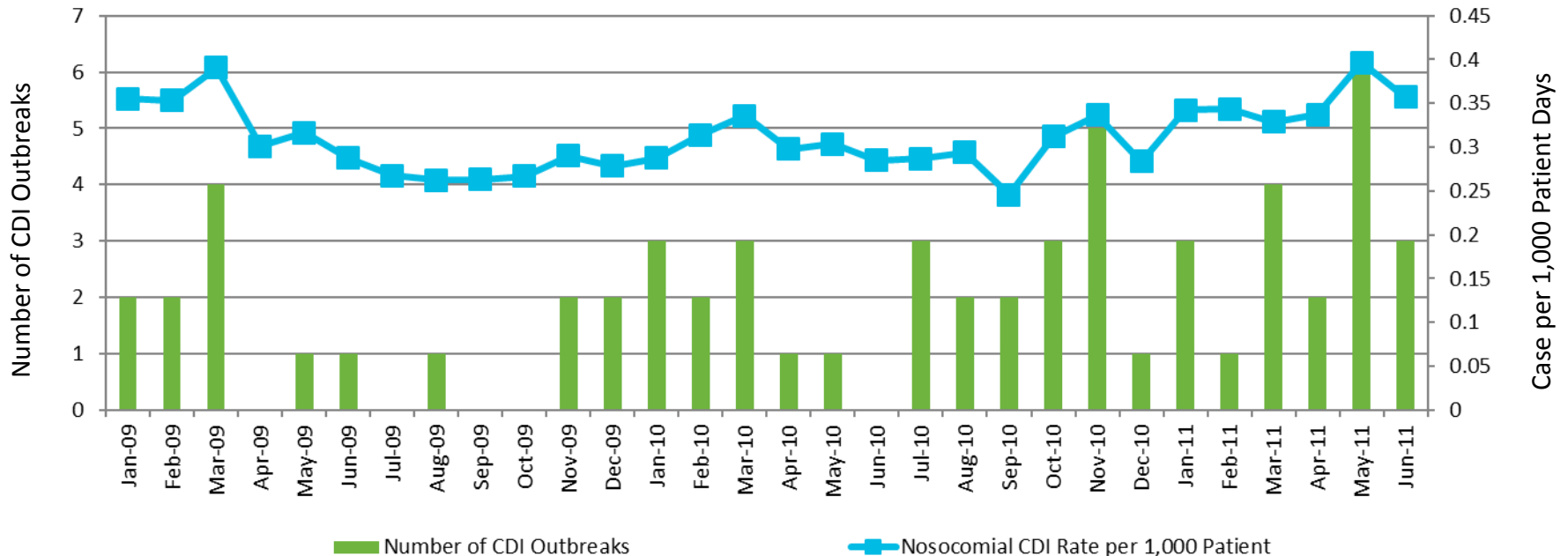
Average Percent Positivity by Month and Year



- There was no significant seasonal variation in CDI percent positivity across the PHOLs.

PHOL: Outbreak Surveillance

- 60 CDI outbreaks were reported by hospitals across Ontario between January 2009 – June 30, 2011.
 - 15 outbreaks reported in 2009
 - 26 outbreaks reported in 2010
 - 19 outbreaks reported up to June 30, 2011



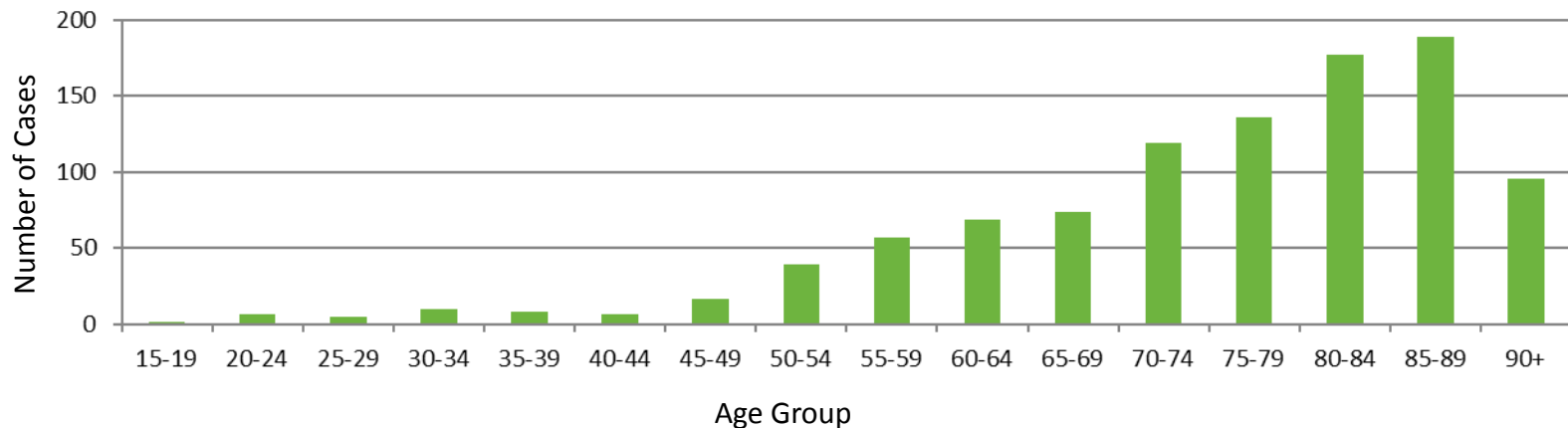
Characteristics of CDI Outbreaks

- The duration of CDI outbreaks ranged from 10 to 344 days.
 - Median duration: 59 days
 - Mean duration: 84 days
- 92% of CDI outbreaks occurred in acute teaching and large community hospitals.
 - 24/60 (40%) in acute teaching hospitals
 - 31/60 (52%) in large community hospitals
 - 3/60 (5%) in small community hospitals
 - 2/60 (3%) in complex continuing care & rehabilitation hospitals
- Attack rates ranged from 1.91% to 73.91%.
- Case-fatality rates ranged from 0% to 56%.

CDI Outbreak-Associated Cases

- 1029 laboratory-confirmed CDI cases associated with outbreaks
- 52% of cases were female
- Cases ranged from age 15 to 101 years
 - Median Age: 78.6 years
 - Mean Age: 75.2 years

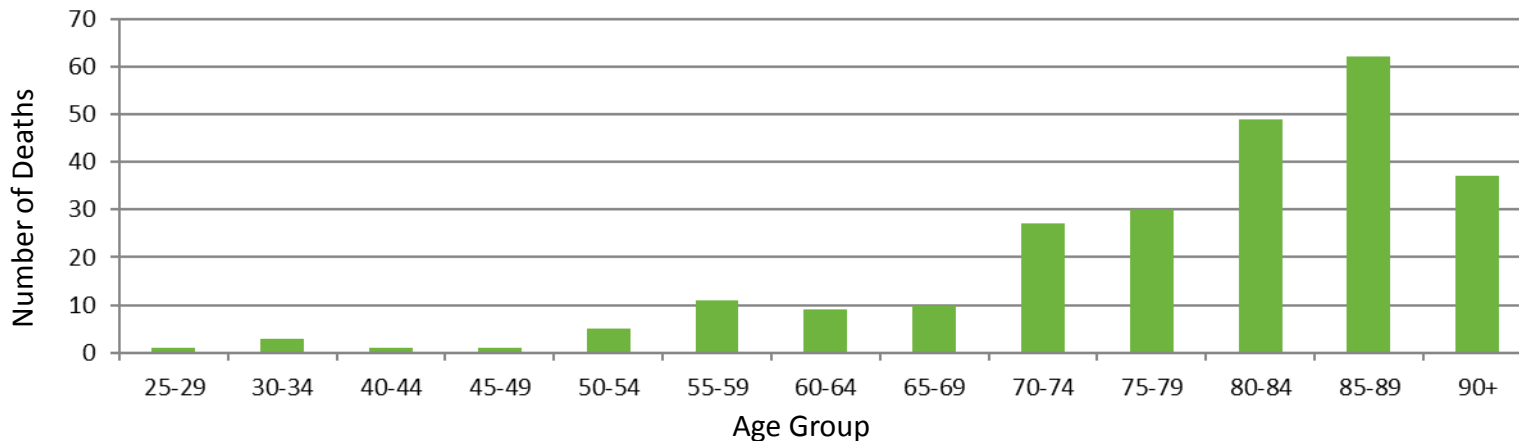
Number of CDI Cases by Age Group



Mortality

- Case fatality rate: 24.3% (250 all-cause deaths)
- Median time from episode onset to death: 11 days
- Age ranged from 25 to 100 years
 - Median age: 83.4 years; Mean age: 79.8 years

Number of Deaths by Age Group



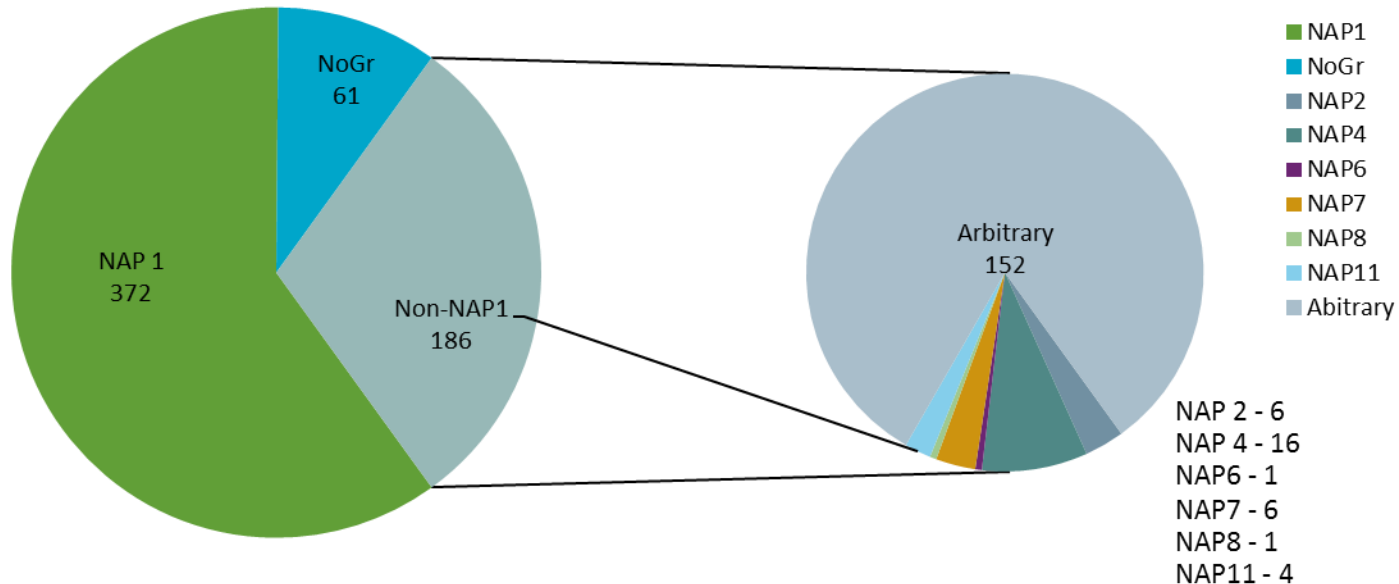
Mortality (cont'd)

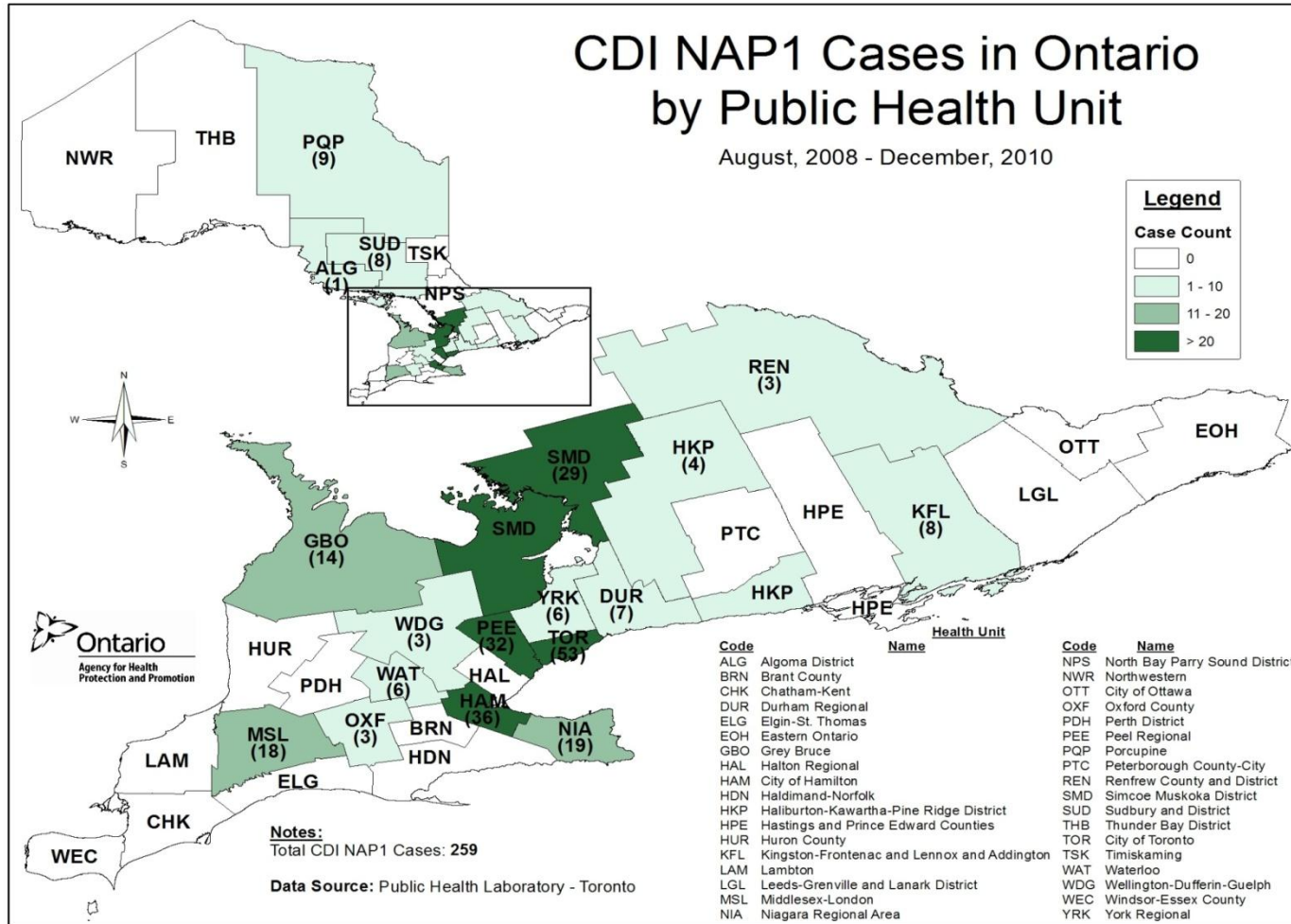
- All-cause mortality was significantly associated with older age.
 - 79.8 years vs. 73.7 years (P<0.0001)
- Patients \geq 65 years were more likely to die than those < 65 years of age.
 - (OR 3.69 [95%CI 1.55-9.18] P=0.001)
- Patients \geq 80 years were more likely to die than those between 65 and 79 years of age.
 - (OR 3.57 [95%CI 1.82-7.09] P=0.0005)

Laboratory Surveillance of CDI Outbreak Isolates

- PHOL provided specialized testing for 33/60 (55%) confirmed outbreaks, processing 619 isolates.
- NAP1 strain accounted for 60% (372/619) of all isolates.

Pulse-Field Gel Electrophoresis (PFGE) Typing of *Clostridium difficile* Isolates





* outbreaks only; not population-based

- All NAP1 isolates elaborated toxin A, toxin B, and binary toxins.
- 407 strains were tested for antimicrobial susceptibility.
- NAP1 isolates were more likely to be resistant to ampicillin and moxifloxacin than non-NAP1 isolates.

Antimicrobial	NAP1 Resistance N (%)	Non-NAP1 Resistance N (%)	P Value
Ampicillin	243 (62)	100 (25.4)	<0.0001
Clindamycin	257 (63.1)	135 (33.2)	0.2
Metronidazole	0 (0)	0 (0)	1
Moxifloxacin	262 (64.4)	22 (5.4)	<0.0001

NAP1 Strain in Ontario

- All but 2 outbreaks were polyclonal in nature.
- Proportion of NAP1 strain ranged from 11 to 100% in outbreaks.
- 27 outbreaks had $\geq 50\%$ of their submitted isolates positive for NAP1.
- Attack and case-fatality rates were not correlated with the proportion of NAP1 isolates in outbreaks.
- NAP1 strain was associated with increased age.
 - 78.3 vs. 71.5 years (P=0.0007)
- NAP1 strain was not associated with excess all-cause mortality.

Limitations

- **Public Health Reporting Data**
 - Accuracy of data entry
 - Completeness of data with respect to patient risk factors and outcomes
 - Case level data only available for outbreak-related cases
 - Some outbreak cases may not have been reported
 - Outbreak specimens may not have been tested at PHOL
- **Laboratory Data**
 - No outcome information unless linked with public health reporting data
 - May include some cases not associated with the outbreak such as:
 - Samples from cluster investigations
 - Samples sent post-outbreak
 - Samples from non-nosocomially acquired cases sent as part of the outbreak

Conclusions & Future Directions

- Mandatory reporting of CDI outbreaks to local public health units allows for monitoring and timely response and control of emergent outbreaks.
- Laboratory surveillance confirms that the NAP1 strain is primarily responsible for driving institutional CDI outbreaks in Ontario.
- Future re-evaluation of public health reporting data elements
 - Assess risk factors associated with CDI cases
 - Better link between iPHIS and laboratory surveillance data

Acknowledgements

- Ontario's Reporting Facilities
- Health Analytics Branch, Ministry of Health & Long-Term Care
- The PHOL staff conducting CDI testing and outbreak typing
- Key contributors:
 - Dr. Dylan Pillai, Medical Microbiologist
 - Dr. George Broukhanski, Molecular Scientist
 - Marina Lombos, Head Technologist
 - Michael Whelan, Senior Epidemiologist
 - Steven Johnson, GIS Analyst
 - Shilpa Raju, Epidemiologist (MOHLTC)

Practical and Evolving Issues of *Clostridium difficile* Infection (CDI) in Ontario

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Outline

- ICRTs and CDI outbreaks, what we've learned
- Fecal waste management options
- Issues in CDI mortality attribution
- Lab testing developments
- Outbreak declaration and termination issues
- *Excellent Care for All Act* and Hospital Quality Improvement Plans
- Antibiotic Stewardship
- Survey of hospital IP&C/CDI measures
- Evolving issues, especially community-associated CDI

What is an ICRT?

- Created in 2008 to provide assistance to hospitals with outbreaks of *C. difficile*
- Intended to support public health units in working with hospitals
- Group of ‘experts’ who would provide recommendations to the hospital to manage the outbreak
- ‘rapid response’
- Has evolved to provide assistance for CDI outbreaks and non-reportable outbreaks

How are ICRTs requested

- ICRT may be requested in a number of ways:
 - Request to PHO from the CMOH – usually initiated by the local MOH
 - Request to PHO directly from the hospital
 - Request to PHO jointly by hospital and local public health unit
- Hospital may make request under Quality of Care Information Protection Act (QCIPA)
 - In this case, report is sent only to the hospital and cannot be shared by PHO

Roles and Responsibilities of Contract ICRTs

- Respond within 7 business days of request from PHO
- Minimum team = 1 physician, 2 ICPs
 - May change if size of facility does not warrant this
- RICN Coordinator will participate on the team
- ICRT must provide a debrief to PHO within 24 hours of visit
- Final report provided to PHO within 2 weeks of visit

Team Expectations

- Review materials provided by facility prior to the visit
- Participate in a pre-visit briefing to discuss flow of visit and any issues
- Maintain professional manner throughout visit
- Base recommendations on scientific evidence wherever possible – identify what is expert opinion
- Remain objective – do not recommend specific products or services

Overview of the ICRTs

- ICRT visits to date

Year	CDI*	ARO
2008	4	-
2009	3	2
2010	8	1
2011	5	

- *Several CDI outbreaks also had outbreaks with AROs

Common ICRT Findings

- Support from/direct reporting to Senior Mgmt
- Human waste management
- Hand hygiene - infrastructure, auditing, shared responsibility
- Environmental cleaning – training, practice, audits, high-risk areas (EDs)
- Stockpiling, clean vs. dirty infrastructure
- Prompt institution of additional precautions
- Communication – internal , senior mgmt, external
- Antibiotic utilization/stewardship
- Outbreak declarations and termination
- Lab diagnostic advances, e.g. MMLVA

Evaluation of ICRTs

- Principle role of CFEP epi
- Synthesis of learnings
- Status of implementation of recommendations
- CDI trends pre-post ICRT + ICRT vs. other hospitals

Human Waste Management

- Huge array of existing challenges:
- Aging infrastructure – bathrooms, utility rooms, paucity of single rooms
- Outmoded/dangerous practices, especially spray wands
- Capital challenges – making the business case
- Engineering/retro-fitting challenges
- Training/practice challenges

Three principle options:

- Bedpan washers
- Macerators – disposable pulp bedpans
- Disposable hygienic bags

Human Waste Management Options – Pros and Cons

Bedpan washers:

- Capital and operating costs, especially water/electricity
- Retrofitting existing infrastructure
- Pace of operation
- Training/practice needs
- May not eliminate *C.difficile* spores

Macerators:

- Higher operating costs than washers
- Retrofitting to handle the increased volume of waste
- Training/practice needs

Hygienic bags:

- Highest operating costs
- Solid waste volumes

CDI Mortality Attribution

Substantial family/public/media interest

Public reportability/medico-legal ?

Multiple mechanisms/options:

- Death certificate
- 15/30-day mortality for CDI cases
- Clinical reviews/algorithms

Death certificates have very poor sensitivity/under-estimation

30-day all-cause mortality for CDI cases 80% sensitivity, need for replication

CDI Mortality Attribution (cont'd)

Detailed/labour-intensive chart reviews, e.g. Joseph Brant CDI outbreak, Burlington

UHN/Gardam criteria:

- Directly-caused → toxic megacolon, perforation, septic shock, radiology findings
- Strongly contributed → CDI Dx, CDI deterioration + other clinical factors, uncertainty
- Somewhat contributed → CDI Dx, other serious co-morbidities, didn't help/didn't cause
- Not related → CDI, treated/recovered, other terminal events

“Death Attribution Rules for Pts. Infected with CDI”, DARPIC, Dr. Mark Miller

Lab Testing

Array of testing modalities:

- Toxin assays, e.g. EIA's
- Cytotoxin tissue assays
- Cell culture
- GDH + follow-up confirmation
- PCR
- MMLVA

Lab Testing (cont'd)

Array of classification systems:

- Pulsotypes, e.g. NAP1, NAP7
- Ribotypes, e.g. 027, 078
- Toxinogenic types, e.g. II, III, V
- MMLVA

Multiple ways of seeing/classifying, at times with exquisite molecular clarity

What does it all mean?

Linkage of lab data with clinical and epi data to determine P&C utility

Outbreak Declaration/Termination

Case definition of nosocomial cases:

- 72 hours or more post-admission
- Acute symptoms and admission to same facility within previous 4 weeks

Vagaries of case definition:

- Symptom onset vs. lab submission vs. lab reporting at 72 hours
- Admission colonization vs. nosocomial acquisition

Baseline rate calculations → what goes into the calculations/time period?

Time/space clustering of nosocomial cases → epi assessment

Outbreak Declaration/Termination (cont'd)

Notification thresholds, especially 80% warning → discussion vs. declaration

Assessment of IP&C measures → comprehensive, compliance, auditing

Outbreak termination → certainty of return to baseline

- Disbenefits of outbreak measures/isolation
- Costs/morale/public relations

Excellent Care for All Act (ECFAA)/Hospital Quality Improvement Plans (QIP)

CDI one of the 6 safety indicators defined by *ECFAA*

All hospitals have posted QIPs as of April, 2011

Initial review/ assessment of QIPs by PHO/HQO:

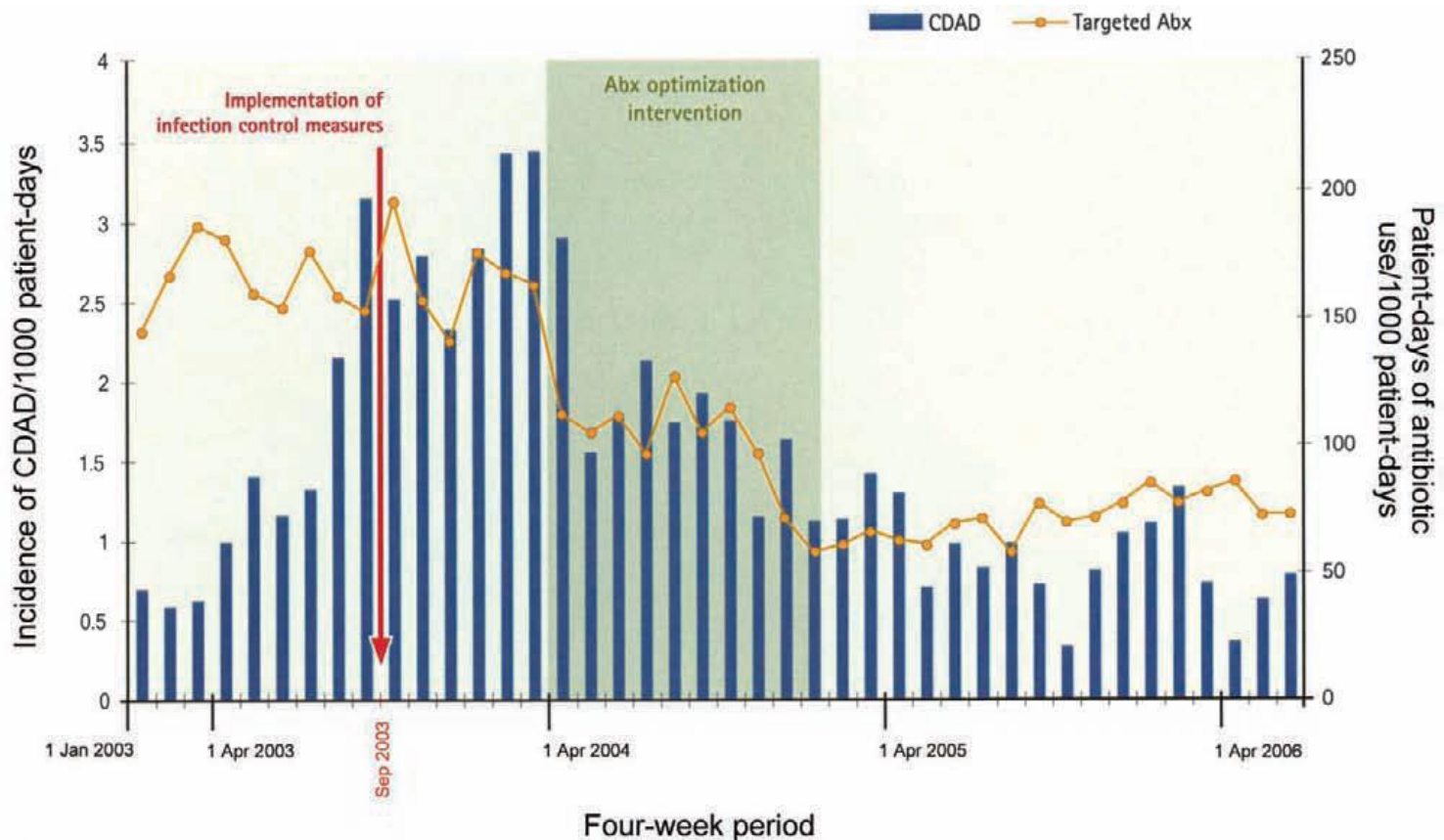
- CDI indicator chosen by <50%
- Choice doesn't appear related to rates/outbreak experience
- Targets vs. current monthly rates/1,000 patient days
- Variable range of strategies chosen (? new vs. existing)
- Low frequency of antibiotic stewardship programs

Antibiotic Stewardship Program (ASP) Development

PHO funding for development of a province-wide ASP as of July, 2011

Evolving evidence of ASP and CDI prevention/control

Prospective Audit & Feedback: Effect on a *C.difficile* Outbreak



Antibiotic Stewardship Program (ASP) Survey

AS Project launched by PHO/OHA August 2011

On-line hospital survey of ASP status/plans (122 responses across 150+ hospital corporations)

Have an existing ASP	39/122	32%
Considering/developing business case	60/83	60%

Variation across hospital types:

• Acute teaching	20/27	74%
• Large community	27/58	47%
• Small community	15/72	21%

Antibiotic Stewardship Program (ASP) Components

ASP components:

- Antibigram 85%
- Clinical pathways/guidelines 72%
- Utilization tracking system 64%
- Education 62%
- Standard order sets 62%

Survey of *C. difficile* IP&C Practices

Health Analytics Branch + support, e.g. PHO, OHA

Comprehensive survey:

- Structures,
- Resources
- Practices
- Education
- Detection/response

Data collected Feb-March, 2011

100% survey response

CDI Evolving Issues

Multiplicity of exposures:

- Environment
- Food ?food-borne pathogen
- Pets/therapeutic animals

The ecology of *C. diff* in human/animal populations:

- Community-acquired CDI
- More questions than answers
- Higher rate of carriage than previously estimated

CDI Evolving Issues

Prevention/treatment developments:

- Fidaxomicin → non-inferior to vanco, ↓ recurrences ?
- Fecal transplants → case series, vs. RCTs
- Probiotics
- Antibiotic stewardship