# Clostridium difficile Infections: Lessons from the Quebec Experience

**Prof. Yves Longtin, Laval University**

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## *Clostridium difficile* infections: lessons from the Québec experience

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Hosted by Paul Webber
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## Objectives

1. Review the evolving epidemiology of *C.difficile* infection in Québec
2. Review the advantages, disadvantages and potential limitations of mandatory surveillance of *C.difficile* infection
3. Identify future challenges in the prevention and control of *C.difficile* infection and surveillance



## Province of Québec

- Eastern part of Canada
- Population, 8 million
  - A quarter of Canadian population
- Universal Health coverage
- Single payer: Ministère de la Santé du Québec
- Healthcare Approx. 45% of provincial budget
- French-speaking

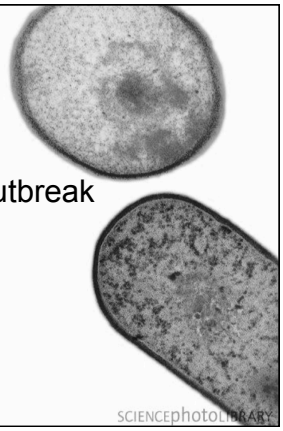


## Some figures will be in French





## 2003-2004 Detection of the outbreak







## Sherbrooke, Québec 1991 - 2003

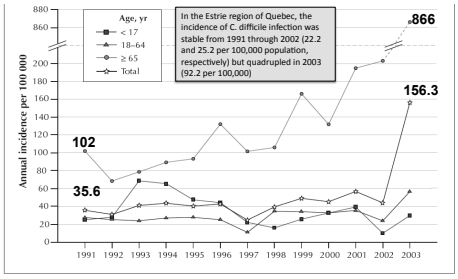



Fig. 1: Annual incidence (per 100 000 population) of *Clostridium difficile*-associated diarrhea (CDAD) in Sherbrooke, Que., 1991–2003.

Retrospective chart review



Pepin J *et al.* CMAJ 2004;171:466-72

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Predominantly Clonal Multi-Institutional Outbreak of *Clostridium difficile*–Associated Diarrhea with High Morbidity and Mortality

Vivian G. Loo, M.D., Louise Poirier, M.D., Mark A. Miller, M.D., Matthew Oughton, M.D., Michael D. Libman, M.D., Sophie Michaud, M.D., M.P.H., Anne-Marie Bourgault, M.D., Tuyen Nguyen, M.D., Charles Frenette, M.D., Mirabelle Kelly, M.D., Anne Vibien, M.D., Paul Brassard, M.D., Susan Fenn, M.L.T., Ken Dewar, Ph.D., Thomas J. Hudson, M.D., Ruth Horn, M.D., Pierre René, M.D., Yury Monczak, Ph.D., and André Dascal, M.D.

- Prospective study 12 hospitals in Québec
- Incidence rate: 22.5/1000 admissions
- 30-day attributable mortality: 6.9%

Loo V. et al. N Engl J Med 2005;353:2442-9

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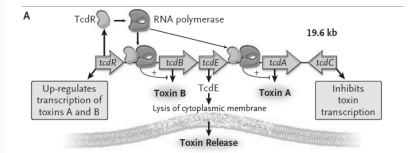
## New strain – NAP1/027

- C.difficile strain
  - Resistant to fluoroquinolones
    - Use of FQ also a risk factor (OR, 3.9)
  - Partial deletion of *tcdC* gene




Kelly CP. N Engl J Med 2008;359:1932-40.

Loo V. et al. N Engl J Med 2005;353:2442-9

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## Retrospective analysis of CDI rates in Québec

When did the outbreak start exactly?

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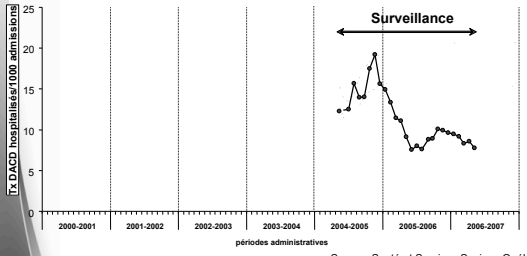
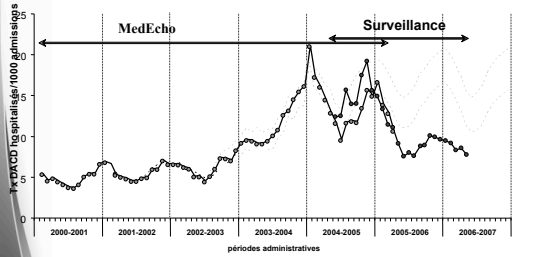
## Incidence des nouveaux cas de DACD/ 1000 admissions – MedÉcho et surveillance provinciale




Source: Santé et Services Sociaux Québec

Source: INSPQ, Système de surveillance provincial, Rodica Gilca adaptation par BSV MSSS nov 2006

## Incidence des nouveaux cas de DACD/ 1000 admissions – MedÉcho et surveillance provinciale

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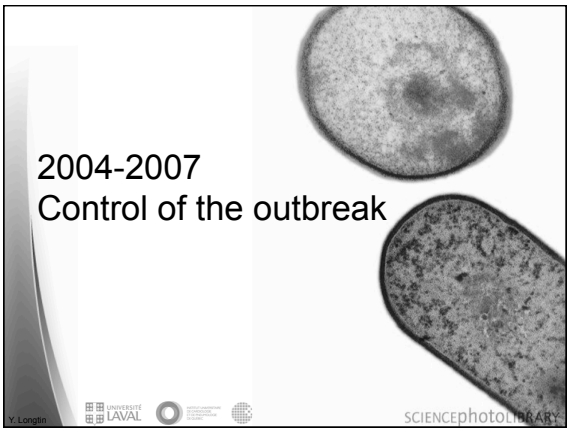


## Interventions to control outbreak

- Implementation of CDI surveillance
- Involvement of stakeholders at every level
  - Provincial, regional, local
  - Support from experts (INSPQ, TRPIN)
- Site visits by public health officials
- Guidelines
  - C.difficile
  - Antibiotic use
- Creation of 200 additional infection control nurses positions
- Evaluation of process indicators

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- Published guidelines
  - Control of CDI in acute care hospitals (2005)
  - Environmental control regarding CDI (2006)


www.msss.gouv.qc.ca/hygiene-salubrite

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## Prerequisites to good surveillance

- **Precision**
- **Validity**
- **Reproducibility**
- **Ease of gathering data**
- **Avoiding collection of "unnecessary" data**
- **Clear definition of indicators and data collection techniques**
- **Education / training**
- **Risk adjustment**
- **Timely analysis and feedback of results**
- **Valid interpretation of results**

(AJIC Am J Infect Control 1995;23:215–23)

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## Quebec surveillance of CDI

- Implemented in August 2004
  - Nap1/027 epidemics
- All 95 acute-care hospitals admitting >1000 patients per year must participate
  - excluding psychiatry, newborn units and NICU
- Smaller hospitals welcome to participate on a voluntary basis
  - Data more volatile

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## Surveillance, 2004-2011

- 95 participating hospitals
- 4'286'415 admissions
- 35'295'162 patient-days of data
- 28'384 cases of HA-CDI
- Global incidence rate: 8,04/10 000 patient-days

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## Quebec surveillances of HAI

- CDI is one of numerous surveillance programs in the Province:
  - CDI
  - Bloodstream infections
    - Hospital-wide
    - CLA-BSI
    - BSI in hemodialysis patients
    - *S.aureus* (MRSA and MSSA)
  - VRE acquisition
  - Laboratory surveillances
    - Carbapenem-producing enterobacteriaceae

Engrained culture of surveillance

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## CDI definition

Presence of diarrhea
≥ 3 loose stools in < 24 hours
and
Symptoms last ≥ 24 hours
and
No other obvious cause for symptom

PLUS

Presence of ToxA and/or ToxB by laboratory testing
or
Visualization of Pseudomembranes by colonoscopy
or
Histopathological diagnosis (with or without diarrhea)

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## Denominators

- Data aggregated
  - No individual patient data
- 4-week periods (13 per year)
- CDI cases per 10'000 patient-days
  - More robust
- CDI cases per 1'000 admission
  - Less robust
  - Easier to grasp for less knowledgeable individuals

**Incidence rates in HA-CDI, Québec, 2010-2011**

| No. cases (cat. 1) | No. patient-days | No. admissions |
|---|---|---|
| Denominator | 5 155 373 | 620 121 |
| Incidence | 7.23/10 000 patient-days | 6.34/1000 admissions |

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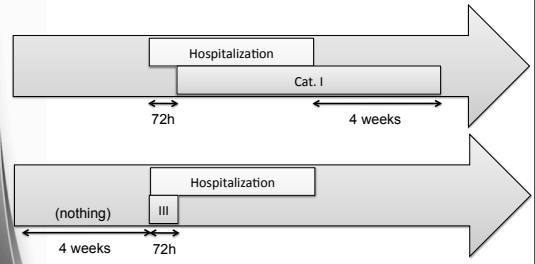
## Categories – time cutoffs

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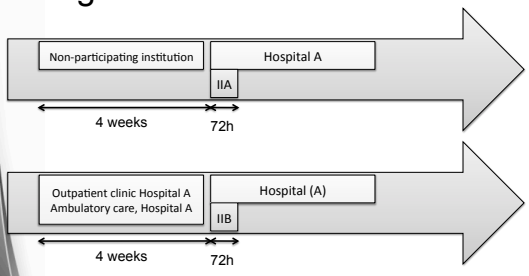


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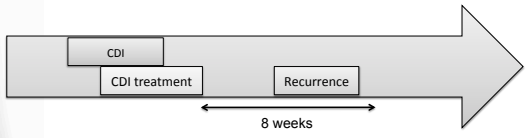
## Categories – time cutoffs

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## Categories of CDI, 2009-2010

| Category | Origin of acquisition | n | % |
|---|---|---|---|
| Cat. 1 | HA-CDI linked to the reporting Institution | 3167 | 69.3 |
| Cat. 2a | HA-CDI linked to another non-participating Institution | 324 | 7.1 |
| Cat 2b | HA-CDI linked to ambulatory care | 269 | 5.9 |
| Cat. 3 | CA-CDI | 558 | 12.2 |
| Cat. 4 | Unknown origin | 249 | 5.5 |
| | Total hospitalized | 4567 | 100 |

**Note. Only hospitalized cases are reported**

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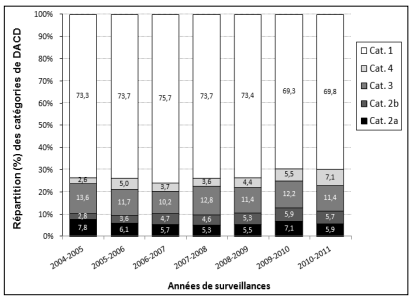
## Categories of CDI, 2009-2010

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## CDI surveillance

- Monitoring of complication rates also part of surveillance programs
  - Death (10-day and 30-day mortality)
    - No distinction between attributable and associated
    - Poor inter-observer correlation
  - Toxic megacolon and colectomy
  - Admission to ICU for CDI
  - Readmission for CDI

Mandatory

Voluntary

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## Complications

| | '04-'05 | | '05-'06 | | '06-'07 | | '07-'08 | | '08-'09 | | '09-'10 | | '10-'11 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | %[†] | N | %[†] | N | %[†] | N | %[†] | N | %[†] | N | %[†] | N | %[†] |
| **Total de cas de cat. 1** | 6350 | | 4055 | | 4544 | | 3254 | | 3322 | | 3167 | | 3934 | |
| Nombre de cas suivis[‡] | 5817 | **91,6** | 3535 | **87,2** | 3446 | **75,8** | 2350 | **72,2** | 2941 | **88,5** | 2893 | **91,3** | 3661 | **93,1** |
| **Décès dans les 30 jours[§]** | 1034 | **17,8** | 522 | **14,8[¶]** | 561 | **16,3[¶]** | 335 | **12,7[¶]** | 457 | **15,5[¶]** | 478 | **16,5** | 619 | **16,9** |
| Décès dans les 0-10 jours[§] | ND | | ND | | ND | | ND | | 236 | **8,0** | 263 | **9,1** | 358 | **9,8** |
| Décès dans les 11-30 jours[§] | ND | | ND | | ND | | ND | | 221 | **7,5** | 215 | **7,4** | 261 | **7,1** |
| **Autres complications** | | | | | | | | | | | | | | |
| Colectomie[§] | 56 | **1,0** | 33 | **0,9** | 36 | **1,0** | 23 | **1,0** | 49 | **1,7** | 48 | **1,7** | 63 | **1,7** |
| Réadmission[§] | 348 | **6,0** | 196 | **5,5** | 185 | **5,4** | 132 | **5,6** | 143 | **4,9** | 132 | **4,6** | 193 | **5,3** |
| Transfert aux soins intensifs[§] | 138 | **2,4** | 71 | **2,0** | 83 | **2,4** | 56 | **2,4** | 59 | **2,0** | 86 | **3,0** | 104 | **2,8** |

* Déclaration volontaire des décès.
† Déclaration obligatoire des décès.
‡ Nombre de cas suivis et proportion par rapport au total des cas de catégorie 1 (cat. 1).
§ Installations participantes ayant fourni des données sur les complications ou qui n'avaient aucun cas à suivre.
¶ En comparaison avec les installations n'ayant pas fourni des données sur les complications par rapport au total des installations participantes pour cette année.
En comparaison avec 2004-2005, $p < 0,05$.
Représentent les pourcentages du nombre de cas suivis par rapport au nombre total de cas de cat.1 ou le pourcentage des autres catégories par rapport au nombre de cas suivis.
En 2008-2009 un centre s'est fusionné avec un autre pour former une nouvelle installation.
ND : non disponible.

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## Data entry

- Data entered in secure web portal
  - Must be entered within 1 month of end of period
  - Complications must be entered within 2 months of end of period

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## Reporting of CDI rates

- Weekly reports
  - Automated surveillance
  - Non-validated data, confidential
- Quarterly reports
  - Validated data
  - Some analysis
- Yearly report
  - Validated data, public
  - Sub analysis (strain analysis)


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## Weekly report

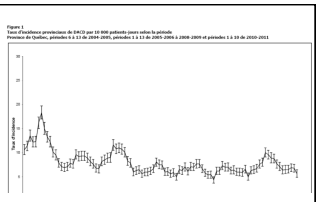

Tableau 2a.
Surveillance des infections à C. Difficile
Installations qui présentent des taux élevés (dépassant le 90e percentile) de C. Difficile sur plusieurs périodes*
Province de Québec

| Région | Installation No | Installation Nom | Caractéristiques Mise à Jour | Caractéristiques Proportion de personnes âgées de plus de 65 ans en % | Taux d'incidence de DACD d'origine nosocomiale par 10 000 pat./jrs. 2010-2011 9 | 10 | 11 | 12 | 13 | 2011-2012 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 10 | CSSS DE ROMOUSKI-NEIGETTE – HÔPITAL RÉGIONAL DE RIMOUSKI | 200-249 | 35-49 | 5 | 2 | 7 | 7 | 10 | 10 | 12 | **30** | **16** | 9 | **28** | **30** | 11 | **17** |
| | 61 | CSSS DE KAMOURASKA – HÔPITAL NOTRE-DAME-DE-FATIMA | <100 | >=50 | 0 | 0 | **25** | 14 | **46** | **32** | 0 | **26** | 0 | **53** | 0 | 0 | **14** | 0 |
| | 77 | CSSS DE LA MATAPÉDIA – HÔPITAL D'AMQUI | <100 | >=50 | 0 | 0 | 0 | **61** | **65** | **39** | 0 | 12 | **36** | 0 | 0 | **18** | **13** | 14 |
| 3 | 99 | CSSS DE CHAMPLAIN/CSSS – HÔPITAL DE LA MALBAIE | <100 | 35-49 | 10 | **32** | **19** | 10 | 17 | 0 | 11 | 0 | 0 | **18** | **35** | 0 | **48** | **27** |
| 6 | 3 | L'HÔPITAL GÉNÉRAL JUIF (DE MONTRÉAL) & DAWS | >=250 | 35-49 | 14 | **22** | 6 | **33** | **26** | **20** | **19** | **20** | 12 | **16** | 14 | **19** | 10 | 10 |
| | 103 | HÔPITAL CATHERINE BOOTH DE L'ARMÉE DU SALUT | <100 | >=50 | 10 | 4 | 4 | **36** | **53** | 10 | **18** | 0 | 9 | 0 | 14 | **17** | 0 | 0 |
| 8 | 70 | RSSS DES AURORES BORÉALES – CH LA SARRE | <100 | 35-49 | 0 | 13 | 0 | 0 | 0 | 15 | 0 | 0 | 0 | 0 | 12 | **23** | 0 | 0 |
| 9 | 71 | CSSS DE SEPT-ÎLES – HÔPITAL ET CH DE SEPT-ÎLES | <100 | >50 | 0 | 12 | 0 | 11 | 0 | 7 | 0 | 0 | 0 | 0 | 0 | 0 | **19** | **18** |
| 14 | 14 | CSSS DU NORD DE LANAUDIÈRE – CHR DE LANAUDIÈRE | >=250 | 35-49 | **15** | **21** | 12 | **26** | **20** | **20** | 15 | 11 | 12 | **16** | 9 | 5 | **16** | 10 |
| 15 | 101 | CSSS IDVIÈRE (OUEST) / NORD-DE-MEMBRE – HÔTEL-DIEU DE SAINT-JÉRÔME | >=250 | 35-49 | 10 | 4 | 13 | 15 | 13 | 11 | 9 | 9 | 10 | 4 | 10 | 11 | **24** | **15** |

Source : Surveillance des diarrhées associées au Clostridium difficile (DACD), INSPQ-LSPQ, 27 janvier 2012
Notes : Les installations sont tenues de déclarer les cas de DACD et le nombre de patients-jours jusqu'à un maximum de 20 jours après la fin de chaque période.
Les données périodiques affichées ne sont pas valables avant ce délai de 28 jours. Le nombre d'installations déclarantes à la dernière période 10 est de 84.

## Risk stratification

- CDI incidence rates are stratified according to 3 different non-modifiable variables
  - University status
  - Proportion of patients >65 years of age (cutoff = 35%)
  - Hospital size (cutoff= 100 beds)

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Taux d'incidence des DACD d'origine nosocomiale, rapports de taux bruts (analyses univariées) et rapports de taux ajustés (analyses multivariées) selon les caractéristiques des installations, 2010-2011

| Caractéristique | CH (N) | Indicateur de distribution Min | 25 % | 50 % | 75 % | 90 % | Max | Taux d'incidence [IC 95 %] | RT brut[a] [IC 95 %] | RT ajusté[a] [IC 95 %] |
|---|---|---|---|---|---|---|---|---|---|---|
| **Selon le nombre de lits (taille de l'installation)** | | | | | | | | | | |
| <100 lits | 35 | 0 | 2,5 | 4,8 | 8,4 | 13,3 | 22,0 | 5,8 [5,2 ; 6,4] | (Réf.) | |
| 100-249 lits | 34 | 1,3 | 3,5 | 5,7 | 8,1 | 13,2 | 14,1 | 6,3 [6,0 ; 6,7] | **1,2 [1,1 ; 1,4]** | **1,2 [1,1 ; 1,4]** |
| ≥ 250 lits | 26 | 1,0 | 5,1 | 7,2 | 12,9 | 15,4 | 16,9 | 8,8 [8,5 ; 9,2] | **1,6 [1,4 ; 1,8]** | **1,4 [1,2 ; 1,6]** |
| **Selon la proportion de personnes âgées de plus de 65 ans (clientèle)** [1] | | | | | | | | | | |
| < 35 % | 15 | 0,4 | 3,3 | 5,8 | 8,1 | 12,9 | 13,6 | 6,7 [6,2 ; 7,2] | (Réf.) | |
| ≥ 35% | 72 | 0 | 3,9 | 6,1 | 10,0 | 13,7 | 22,0 | 8,3 [8,0 ; 8,6] | **1,2 [1,1 ; 1,3]** | **1,3 [1,2 ; 1,4]** |
| **Selon le statut universitaire (mission)** | | | | | | | | | | |
| Centre hospitalier | 63 | 0 | 3,4 | 5,3 | 8,8 | 13,3 | 22,0 | 6,6 [6,3 ; 6,9] | (Réf.) | |
| Centre universitaire | 24 | 0,4 | 5,2 | 7,4 | 13,1 | 13,8 | 16,9 | 9,4 [9 ; 9,8] | **1,4 [1,3 ; 1,5]** | **1,3 [1,2 ; 1,4]** |
| Centre de réadaptation | 6 | 0 | 2,1 | 2,5 | 5,1 | 12,6 | 12,6 | 3,7 [3,0 ; 4,5] | **0,6 [0,5 ; 0,7]** | 1,0 [1,0 ; 1,0] |
| Centre pédiatrique | 2 | 2,0 | 2,0 | 4,0 | 5,9 | 5,9 | 5,9 | 3,2 [2,2 ; 4,3] | **0,5 [0,3 ; 0,7]** | 1,0 [1,0 ; 1,0] |

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## Public reporting

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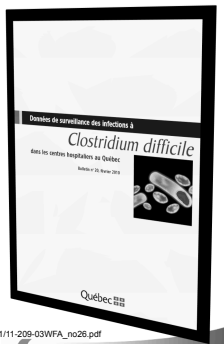
## Public reporting

- Public report published quarterly
- Available on msss website
- Validated data
- Basic terms and everyday language
- Raw data, no extensive analysis
- Scrutinized by journalists




http://publications.msss.gouv.qc.ca/acrobat/f/documentation/2011/11-209-03WFA_no26.pdf

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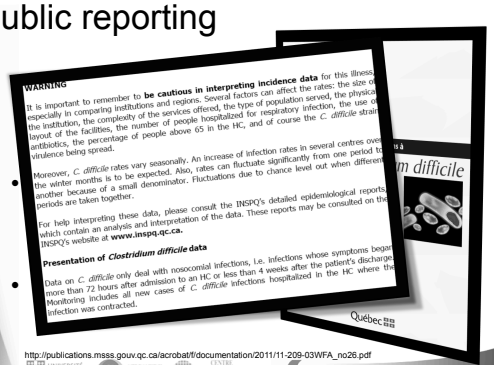
## Public reporting

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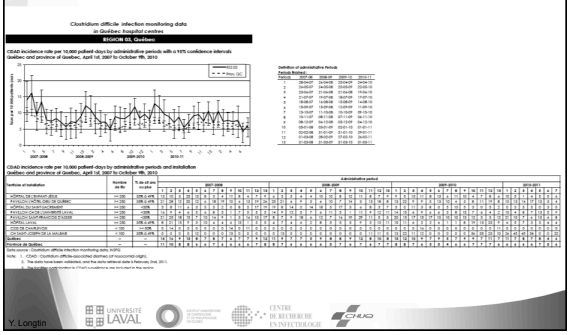

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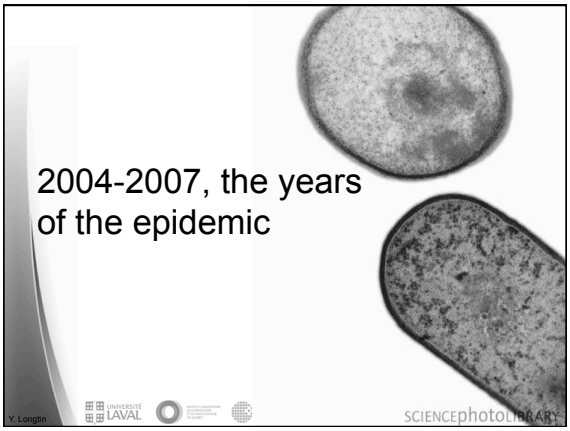
## 2004-2007, the years of the epidemic



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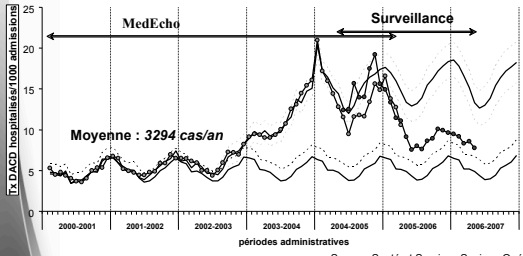
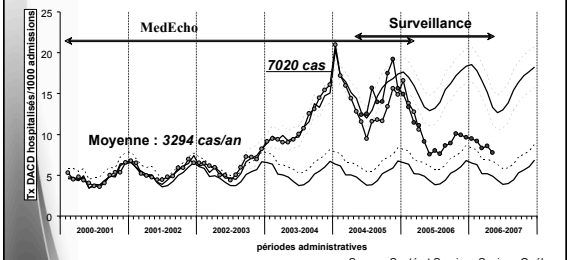
## Incidence des nouveaux cas de DACD/ 1000 admissions – MedÉcho et surveillance provinciale




Source: Santé et Services Sociaux Québec

Source: INSPQ, Système de surveillance provincial, Rodica Gilca adaptation par BSV MSSS nov 2006

## Incidence des nouveaux cas de DACD/ 1000 admissions – MedÉcho et surveillance provinciale




Source: Santé et Services Sociaux Québec

Source: INSPQ, Système de surveillance provincial, Rodica Gilca adaptation par BSV MSSS nov 2006

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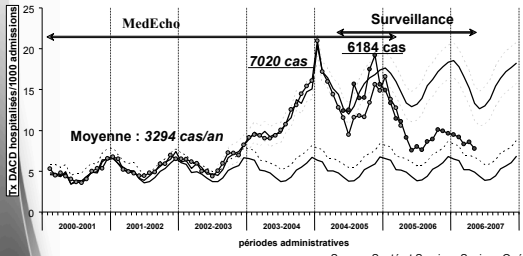


Source: Santé et Services Sociaux Québec

Source: INSPQ, Système de surveillance provincial, Rodica Gilca adaptation par BSV MSSS nov 2006

# Clostridium difficile Infections: Lessons from the Quebec Experience

**Prof. Yves Longtin, Laval University**

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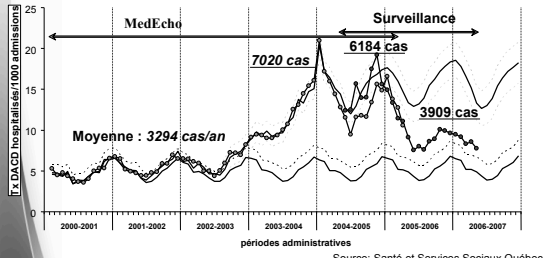


Source: Santé et Services Sociaux Québec

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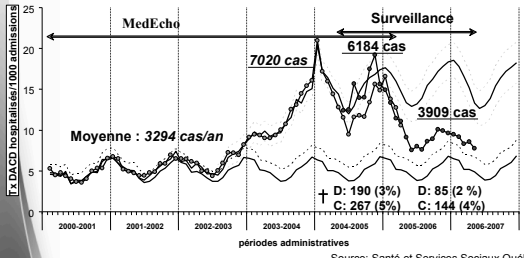
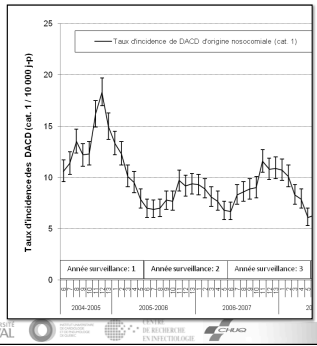



Source: Santé et Services Sociaux Québec

Source: INSPQ, Système de surveillance provincial du, Rodica Gilca adaptation par BSV MSSS nov 2006

## Trends in CDI, 2004-2007

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## Comparons le comparable (58 CH)

| Variable | An 1<br>22 août 2004 - 20 août 2005 | An 2<br>21 août 2005 - 19 août 2006 | Évolution |
|---|---|---|---|
| Cas DACD | 3660 | 2266 | - 38 % |
| Décès cause principale | 134 (4 %) | 56 (2 %) | - 58 % |
| Décès cause contributive | 177 (5 %) | 79 (3 %) | - 55 % |
| Colectomie | 33 (1 %) | 23 (1 %) | - 30 % |
| Réadmission | 243 (7 %) | 135 (6 %) | - 44 % |
| Adm. USI | 89 (2 %) | 47 (2 %) | - 47 % |

Source: Santé et Services Sociaux Québec

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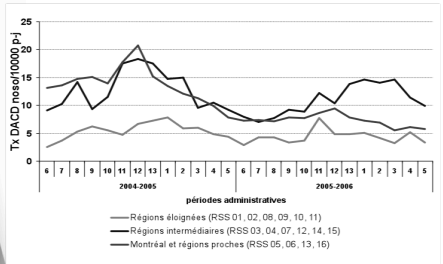
## Incidence des DACD d'origine nosocomiale par regroupement régions




Source: Santé et Services Sociaux Québec

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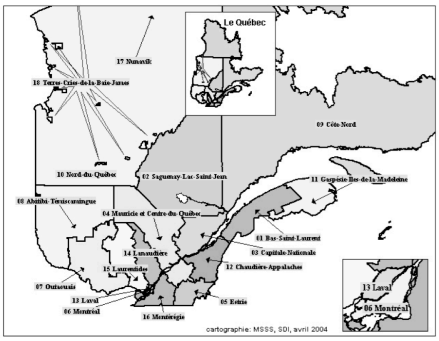


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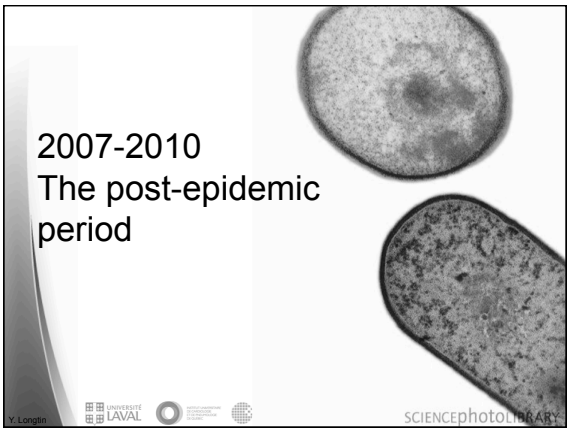


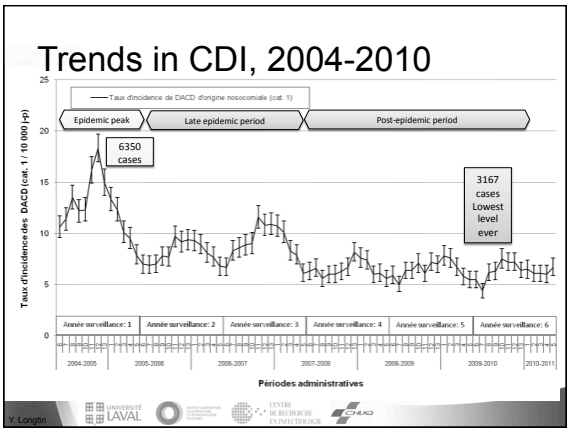


## Trends in CDI, 2004-2010

| Indicateurs | 2004-2007 | 2007-2008 | 2008-2009 | 2009-2010 |
|---|---|---|---|---|
| Nombre d'installations participantes | 88 - 94 | 94 | 96 | 95 |
| Admissions | 607 222 – 611 212 | 607 553 | 611 935 | 609 830 |
| Jours-présence | 4 978 695 – 5 042 166 | 5 023 663 | 5 121 788 | 5 097 192 |
| DACD hospitalisés | 5 505 – 8 663 | 4 417 | 4 523 | 4 567 |
| DACD d'origine nosocomiale (cat.1) | 4 055 – 6 350 | 3 254 | 3 322 | 3 167 |

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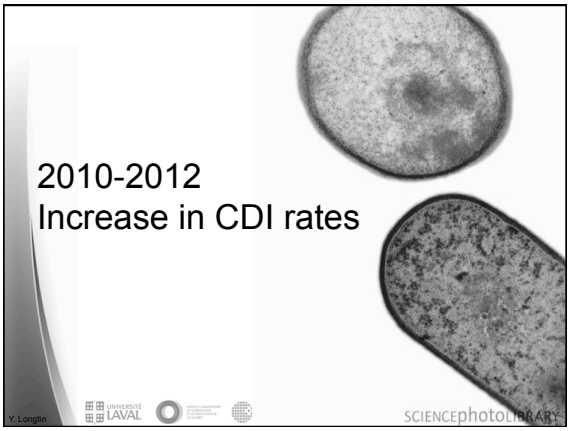


## Trends in CDI, 2004-2011

| Indicateurs | Pic épidémique 2004-2005 | Période épidémique tardive 2005-2007* | Période post-épidémique 2007-2010* | Période à l'étude 2010-201 |
|---|---|---|---|---|
| Nombre d'installations participantes | 88 | 91 - 94 | 94 - 95 | 95 |
| Admissions (adm.) | 607 222 | 609 165 - 611 212 | 607 553 - 609 392 | 620 121 |
| Jours-présence (j-p) | 5 042 166 | 4 978 695 - 4 997 123 | 5 023 663 - 5 096 484 | 5 155 37 |
| DACD déclarées | 8 663 | 5505 – 5 999 | 4 417 – 4 568 | 5 633 |
| DACD d'origine nosocomiale (cat. 1) | 6 350 | 4 055 – 4 544 | 3 167 – 3 254 | 3 934 |
| Taux d'incidence (cat. 1)/10 000 j-p | 12,59 | 8,14 - 9,09 | 6,21 - 6,48 | 7,63 |
| Taux d'incidence (cat. 1)/1000 adm. | 10,46 | 6,63 - 7,46 | 5,2 - 5,36 | 6,34 |

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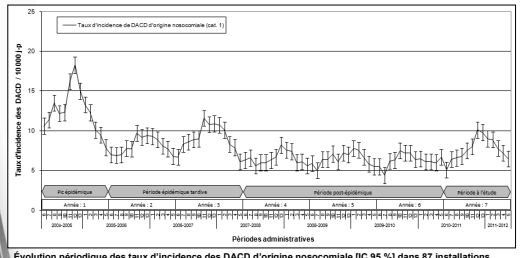
## Trends in CDI, 2004-2011




**Évolution périodique des taux d'incidence des DACD d'origine nosocomiale [IC 95 %] dans 87 installations ayant participé à toutes les années de surveillance**

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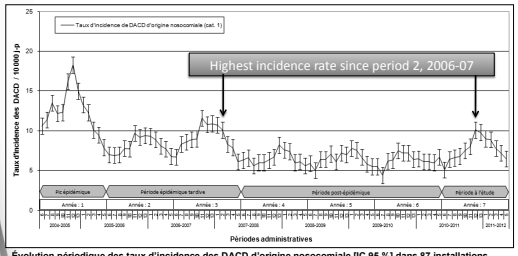
## Trends in CDI, 2004-2011

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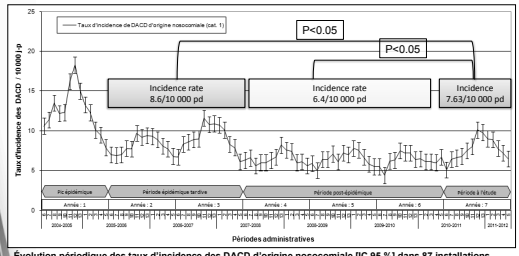


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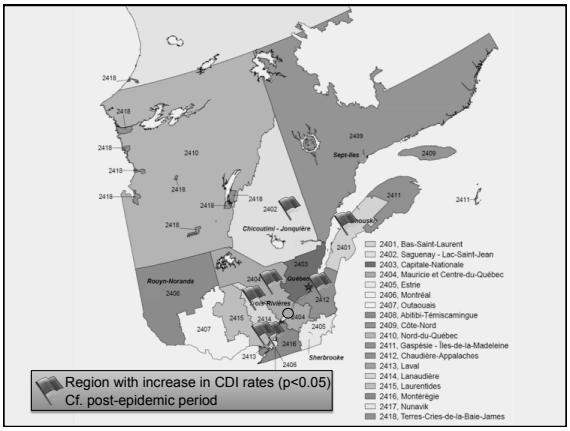
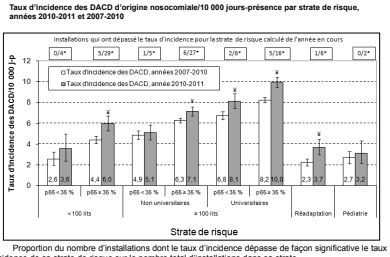



## Incidence rates per stratum




* Proportion du nombre d'installations dont le taux d'incidence dépasse de façon significative le taux d'incidence de sa strate de risque sur le nombre total d'installations dans sa strate.

¥ Différence significative par rapport au taux d'incidence de la période post-épidémique (2007-2010).

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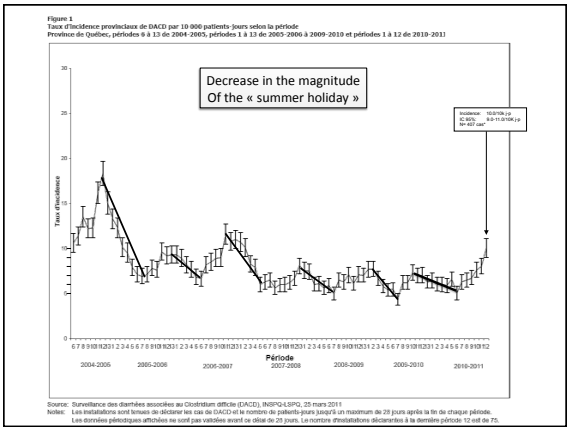


Notes: Les installations sont tenues de déclarer les cas de DACD et le nombre de patients-jours jusqu'à un maximum de 28 jours après la fin de chaque période.
Les données périodiques affichées ne sont pas validées avant ce délai de 28 jours. Le nombre d'installations déclarantes à la dernière période: 12 mill de 75.

## Complications

| | 2004-2005* | | 2005-2006* | | 2006-2007* | | 2007-2008* | | 2008-2009¥ | | 2009-2010¥ | | 2010-2011¥ | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | %† | N | %† | N | %† | N | %† | N | %† | N | %† | N | %† |
| Number of Cat. 1 cases | 6350 | | 4055 | | 4544 | | 3254 | | 3322 | | 3167 | | 3934 | |
| No. Cases with follow-up[1] | 5817 | 91,6 | 3535 | 87,2 | 3446 | 75,8 | 2350 | 72,2 | 2941 | 88,5 | 2893 | 91,3 | 3661 | 93,1 |
| **Mortality** | | | | | | | | | | | | | | |
| Mortality within 30 days | 1034 | 17,8 | 522 | 14,8[4] | 561 | 16,3[4] | 299 | 12,7[4] | 457 | 15,5[4] | 478 | 16,5 | 619 | 16,9 |
| Mortality between 0 and 10 days | ND | | ND | | ND | | ND | | 236 | 8,0 | 263 | 9,1 | 358 | 9,8 |
| Mortality between 11 and 30 days | ND | | ND | | ND | | ND | | 221 | 7,5 | 215 | 7,4 | 261 | 7,1 |
| **Other complications** | | | | | | | | | | | | | | |
| Colectomy | 56 | 1,0 | 33 | 0,9 | 36 | 1,0 | 23 | 1,0 | 49 | 1,7 | 48 | 1,7 | 63 | 1,7 |
| Readmission for CDI | 348 | 6,0 | 196 | 5,5 | 185 | 5,4 | 132 | 5,6 | 143 | 4,9 | 132 | 4,6 | 193 | 5,3 |
| Transfer to ICU for CDI | 138 | 2,4 | 71 | 2,0 | 83 | 2,4 | 56 | 2,4 | 59 | 2,0 | 86 | 3,0 | 104 | 2,8 |

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## Which factor(s) is (are) responsible for the increase in CDI rate?

- New strain?
- Impact of co-pathogens?
- Antibiotic use?
- Impact of new diagnostic test?
- Lowering of the guard? (i.e. Infection control burnout)?
- Random variation?

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- Lowering of the guard? (i.e. Infection control burnout)?
- Random variation?

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## Strain typing

- Conducted yearly since 2005
  - Laboratoire de Santé Publique du Québec
- PFGE
- 10 stool samples positive for CDI per hospital per year
  - 15 per hospital with high incidence rates since 2010

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## Strain analysis, 2005-2011

| Period | 2005<br>10 à 1<br>2004-05 | 2006<br>10 à 1<br>2005-06 | 2007<br>10 à 1<br>2006-07 | 2008<br>11 à 4<br>2007-08 | 2010<br>12 à 5<br>2009-10 | 2011<br>13 à 2<br>2010-11 |
|---|---|---|---|---|---|---|
| Strain | n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| Pulse type A | 274 (57,4) | 174 (52,4) | 248 (66,7) | 205 (53,1) | 210 (46,5) | 161 (49,7) |
| Pulse type A2-5 | - | - | - | - | 55 (12,2) | 22 (6,8) |
| Pulse type B | 49 (10,3) | 21 (6,3) | 7 (1,9) | 13 (3,4) | - | 1 (0,3) |
| Pulse type B1 | 37 (7,8) | 6 (1,8) | 17 (4,6) | 3 (0,8) | 2 (0,4) | 1 (0,3) |
| Other pulse types | 117 (24,5) | 131 (39,5) | 100 (26,9) | 165 (42,7) | 185 (40,9) | 139 (42,9) |
| Total | 477 | 332 | 372 | 386 | 452 | 324 |

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## Nap1/027 and CDI rates

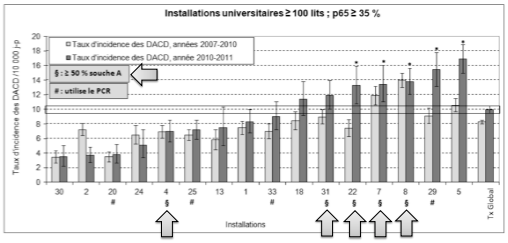


**Figure 11 Taux d'incidence de DACD/10 000 jours-présence dans les centres hospitaliers universitaires de plus de 100 lits ayant une proportion supérieure à 35 % de patients de 65 ans et plus, 2010-2011**

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## Nap1/027 and CDI rates

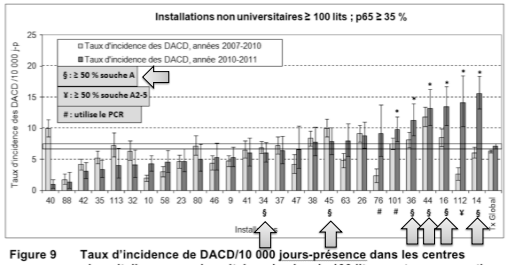


**Figure 9 Taux d'incidence de DACD/10 000 jours-présence dans les centres hospitaliers non universitaires de plus de 100 lits ayant une proportion supérieure à 35 % de patients de 65 ans et plus, 2010-2011**

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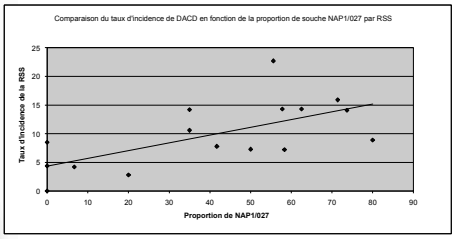
## Nap1/027 and CDI rates

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## Impact de la prédominance du pulsovar A sur l'incidence du DACD en période de haute saisonnalité 2009-2010

| | Année de surveillance | | | | | |
|---|---|---|---|---|---|---|
| | 2005 | 2006 | 2007 | 2008 | 2010 | 2010 |
| Pulsovars | A | A | A | A | A | A2-5 |
| Taux d'incidence dans les installations avec prédominance* de la souche NAP1 ou du pulsovar A2-5 | 22,5 | 13,2 | 14,9 | 10,2 | 8,9 | 9,5 |
| Taux d'incidence dans les installations sans prédominance de la souche NAP1 ou du pulsovar A2-5 | 13,9 | 9,3 | 10,7 | 7,7 | 6,0 | |
| Rapport de taux, installation avec prédominance *versus* installation sans prédominance, analyse univariée | 1,6 | 1,4 | 1,4 | 1,3 | 1,36 | 1,46 |
| Rapport de taux, installation avec prédominance *versus* installation sans prédominance, analyse multivariée ajustée pour la taille, la proportion de personnes de 65+ et la situation géographique | 1,8 | 1,8 | 1,9 | 1,4 | 1,55* | 1,85 * |

* La prédominance de la souche NAP1/027 et du pulsovar A2-5 est définie comme étant observée dans au moins 50 % des souches identifiées dans une installation.

## Which factor(s) is (are) responsible for the increase in CDI rate?

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- Antibiotic use?
- Impact of new diagnostic test?
- Lowering of the guard? (i.e. Infection control burnout)?
- Random variation?

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## CDI, Influenza and RSV

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Seasonal Variations in *Clostridium difficile* Infections Are Associated with Influenza and Respiratory Syncytial Virus Activity Independently of Antibiotic Prescriptions: a Time Series Analysis in Québec, Canada

**Rodica Gilca,[a] Élise Fortin,[a] Charles Frenette,[b] Yves Longtin,[c] and Marie Gourdeau[d]**

Institut National de Santé Publique du Québec, Québec, Québec, Canada[a]; McGill University Health Center, Montreal, Québec, Canada[b]; Centre Hospitalier Universitaire de Québec, Québec, Québec, Canada[c]; and CHA Hôpital de l'Enfant-Jésus, Québec, Québec, Canada[d]

Gilca R. et al. *Antimicrob. Agents Chemother. 2012, 56(2):638*

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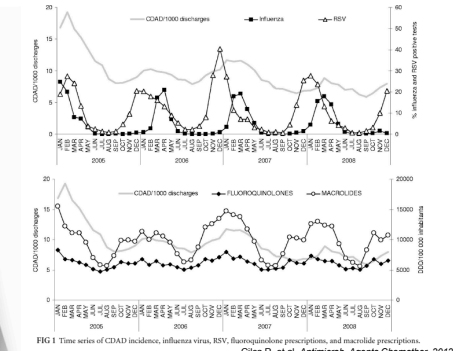


FIG 1 Time series of CDAD incidence, influenza virus, RSV, fluoroquinolone prescriptions, and macrolide prescriptions.

Gilca R. et al. *Antimicrob. Agents Chemother. 2012, 56(2):638*

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## CDI, Influenza and RSV

TABLE 3 Multivariable Box-Jenkins transfer function model used to estimate times series having impact on CDAD incidence[a]

| | CDAD incidence | | | | | |
|---|---|---|---|---|---|---|
| | January 2005-December 2008 | | | August 2005-December 2008 | | |
| Time series | Order[b] | Parameter value (SE) | *P* value | Order | Parameter value (SE) | *P* value |
| CDAD incidence | AR1[c] | 0.97774 (0.02868) | <0.0001 | AR1 | 0.90329 (0.06822) | <0.0001 |
| Influenza virus | 1 | 0.03975 (0.01964) | 0.043 | 1 | 0.03587 (0.01808) | 0.0472 |
| RSV | 1 | 0.05093 (0.0434) | 0.0040 | 1 | 0.03885 (0.01328) | 0.0034 |
| Fluoroquinolones | 2 | 0.00038 (0.0136) | 0.0136 | 2 | 0.00029 (0.00014) | 0.0433 |
| Macrolides | 1 | 0.00012 (0.00006) | 0.0542 | 1 | 0.00011 (0.00006) | 0.0484 |

[a] Reported parameters for influenza virus, RSV, and antibiotics describe the transfer functions.
[b] Delay in months before the effect is observed.
[c] AR1, autoregressive term of first order representing the past values of the CDAD incidence.

Gilca R. et al. *Antimicrob. Agents Chemother. 2012, 56(2):638*

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- Antibiotic use?
- Impact of new diagnostic test?
- Lowering of the guard? (i.e. Infection control burnout)?
- Random variation?

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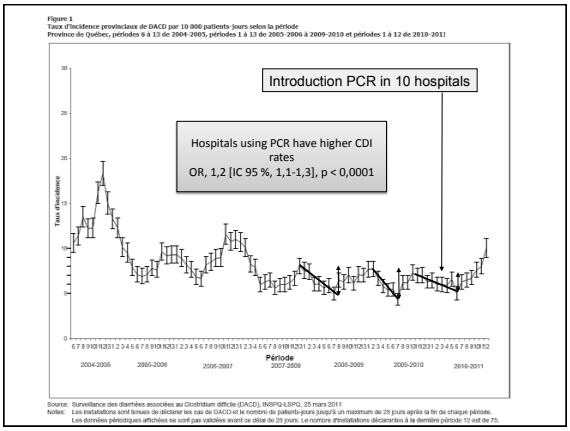
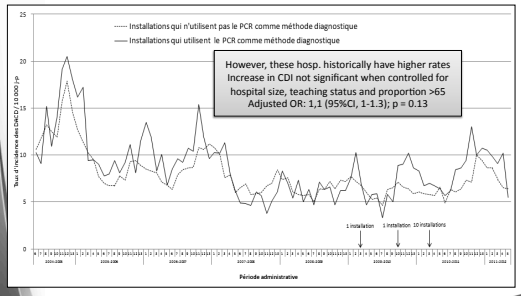



## Increase also present in non-PCR institutions

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## Which factor(s) is (are) responsible for the increase in CDI rate?

- New strain?
- Impact of co-pathogens?
- Antibiotic use? ← upcoming mandatory program
- Impact of new diagnostic test?
- Lowering of the guard? (i.e. Infection control burnout)? ← Ongoing survey
- Random variation? ← The future will tell

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## Lessons learned

- Need to intensify surveillance
  - Decrease lag time between end of period and analysis of data
    - To less than 1 month!
  - Take seasonality into account when analyzing data
    - An outbreak during summer months can go unnoticed!

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## Incidence rates estimation

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## Incidence rates estimation

- Incidence rates
  - Reported per 10'000 patient-days
    - The most precise method to report incidence
    - Requires to obtain denominators
      - Typically the most difficult data to obtain
        - » Not under the control of Infection Control Programs
  - Volatility of Incidence rates in Quebec
    - Need to follow rates very closely
      - Question: could we estimate incidence rates without using patient-days?

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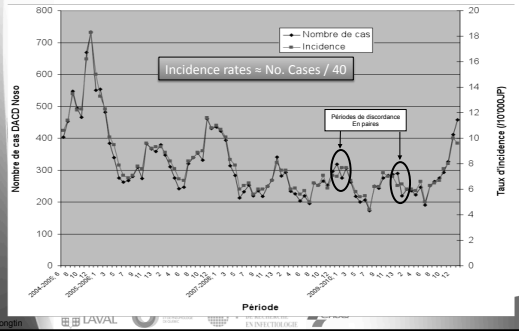
## Incidence rates vs. No. of cases

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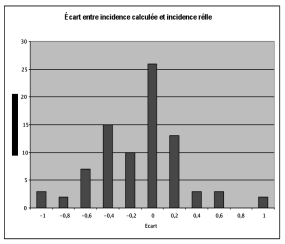
## Incidence rates vs. No. of cases




| Bin limit | Frequency count |
|---|---|
| > -1 | 3 |
| -0,8 | 2 |
| -0,6 | 7 |
| -0,4 | 15 |
| -0,2 | 10 |
| 0 | 26 |
| 0,2 | 13 |
| 0,4 | 3 |
| 0,6 | 3 |
| 0,8 | 0 |
| >1 | 2 |

91% of observations ± 0.6 actual incidence rate

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## Incidence rates vs. No. of cases

- Correction for the length of period
  - Typical period = 28 days
- Number days vary around April 1st
  - Shortest = 23 days
  - Longest = 35 days

Incidence rate = (No. cases/40) / (No. days/28)

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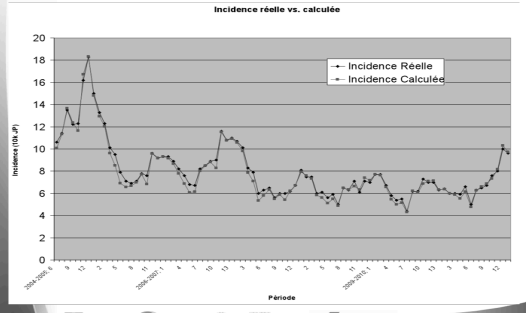
## Incidence rates vs. No. of cases

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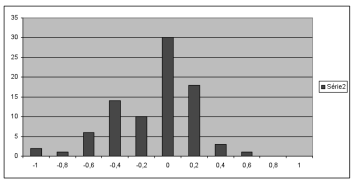
## Incidence rates vs. No. of cases

| Bin Limit | Frequency Count |
|---|---|
| -1 | 2 |
| -0,8 | 1 |
| -0,6 | 6 |
| -0,4 | 14 |
| -0,2 | 10 |
| 0 | 30 |
| 0,2 | 18 |
| 0,4 | 3 |
| 0,6 | 1 |
| 0,8 | 0 |
| 1 | 0 |




96% observations ± 0.6 actual incidence rate

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# Clostridium difficile Infections: Lessons from the Quebec Experience

**Prof. Yves Longtin, Laval University**

**Teleclass Sponsored by Vernacare www.vernacare.com**

## Incidence rates vs. No. of cases

- Why are denominators (almost) irrelevant?

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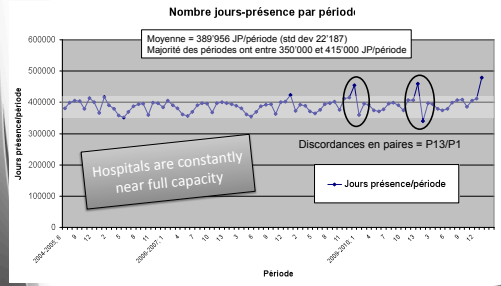
## Incidence rates vs. No. of cases




Std dev = 5.6% seulement!

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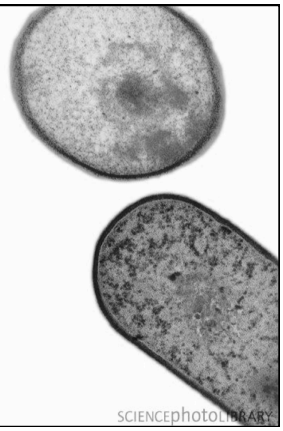
## Threshold levels



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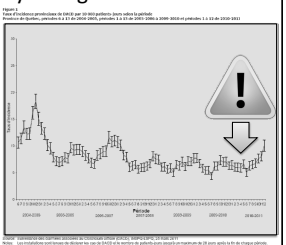
## Threshold levels

- Need to detect rapidly any change in incidence rates
  - Including during summer months
- Solution
  - Creation of threshold levels that take into account seasonality



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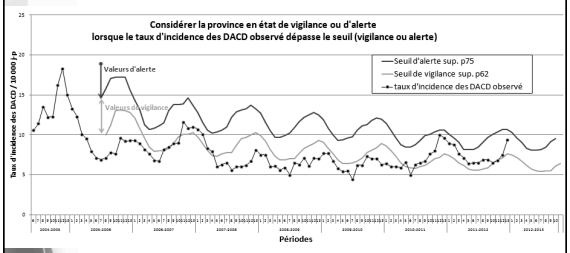
## Threshold levels

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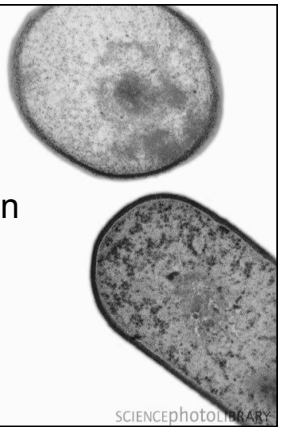
## Data presentation



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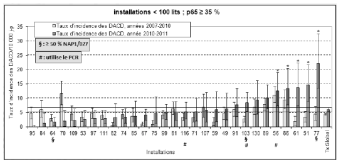
## Data presentation

- Ranking hospitals may lead to "misinterpretation" by non-initiated individuals





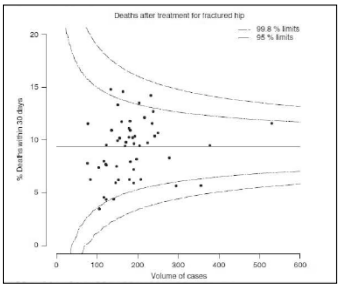

## Data presentation

- Funnel plot
  - Initially created to detect publication bias in metanalysis
  - Allows to represent more accurately random variation due to sample size

(Spiegelhalter, SJ, Statist. Med. 24: 1185-1202, 2005).
(van Dishoeck AM, BMJ Qual Saf, 20(8), 651-7, 2011).

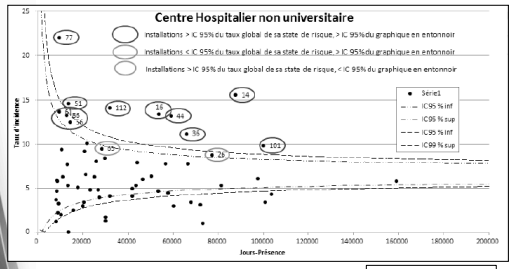


## Example of funnel plot






## Funnel plot of CDI incidence rates




Garenc C. INSPQ, 2012



## Impact of the type diagnostic assay on *Clostridium difficile* infection and complication rates in the context of a mandatory reporting program

**Y. Longtin MD**; S.Trottier MD MSc; G. Brochu PhD; B. Paquet-Bolduc, RN; C. Garenc, PhD; V. Loungnarath, MD; C. Beaulieu, MD; D. Goulet, RN, MSc; J. Longtin MD.

Institut Universitaire de Cardiologie et Pneumologie de Québec (IUCPQ), Laval University
Québec, Canada

Québec *C.Difficile* infection surveillance network

22nd ECCMID, London - Abstract No. 1146



## Background

- *Clostridium difficile* infections (CDI) are present worldwide and cause significant morbidity
- Surveillance has been implemented in numerous countries to improve control

## CDI surveillance

- Guidelines have been published regarding optimal surveillance methods[1,2]
  - Provide standardized case definitions
  - Suggest denominators and infection rates
  - Improves comparability between institutions

1. McDonald, L.C., et al., *Recommendations for surveillance of Clostridium difficile-associated disease.* Infect Control Hosp Epidemiol, 2007. **28**(2): p. 140-5.
2. Cohen, S.H., et al., *Clinical practice guidelines for Clostridium difficile infection in adults: 2010 update by SHEA and the IDSA.* Infect Control Hosp Epidemiol, 2010. **31**(5): p. 431-55.

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## CDI surveillance

- However, no guidance is provided regarding the type of laboratory test to diagnose CDI
  - Choice of test is left at the discretion of each participating institution
  - Incidence rates are not adjusted for the type of test

1. McDonald, L.C., et al., *Recommendations for surveillance of Clostridium difficile-associated disease.* Infect Control Hosp Epidemiol, 2007. **28**(2): p. 140-5.
2. Cohen, S.H., et al., *Clinical practice guidelines for Clostridium difficile infection in adults: 2010 update by SHEA and the IDSA.* Infect Control Hosp Epidemiol, 2010. **31**(5): p. 431-55.

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## Laboratory tests to diagnose CDI

- Wide range of options
- Toxigenic culture
  - Detection of *C.difficile* by anaerobic culture followed by detection of toxin by cell culture cytotoxicity assay
  - The gold standard
  - Rarely used in diagnostic labs
  - Long turnaround time, impractical

Cohen, S.H., et al., Infect Control Hosp Epidemiol, 2010. **31**(5): p. 431-55

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## Laboratory tests to diagnose CDI

- Enzyme immunoassay
  - Detect Tox A and Tox B directly from sample
  - Very practical, simple
  - Very short turnaround time
  - Not very sensitive
  - Often combined with GDH detection by EIA
    - More sensitive but less specific

Planche, T., et al., Lancet Infect Dis, 2008. **8**(12): p. 777-84.

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## Laboratory tests to diagnose CDI

- Cell culture cytotoxicity assay
  - Often considered the reference standard in non-research setting
  - Very sensitive
  - Slow turnaround time
  - Technically more complex than EIA

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## Laboratory tests to diagnose CDI

- PCR
  - Targeting toxin genes *tcdB* or *tcdA*
  - Rapid, sensitive and specific

Peterson, L.R., et al., Clin Infect Dis, 2007. **45**(9): p. 1152-60
Deshpande, A., et al., Clin Infect Dis, 2011. **53**(7): p. e81-90

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## Laboratory tests too diagnose CDI

- Multi-step algorithms
  - GDH detection followed by CCA, toxigenic culture or PCR
  - Sensitive
  - Cost-saving

Wilcox, M.H., et al., J Clin Microbiol, 2010. **48**(12): p. 4347-53

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## Study objective

- Determine whether incidence and complication rates can vary depending on the type of diagnostic test
  - Single insitution (Quebec Heart & Lung Institute)
  - Compare rates obtained by 2 different diagnostic tests:
    - EIA/CCA (used by approximately 70% of hospitals)
    - PCR (used by approximately 10% of Qc hospitals)

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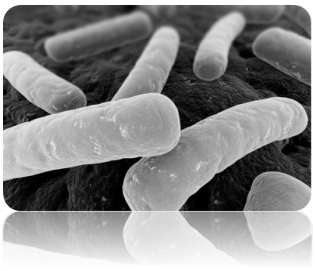
## Methods



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## Methods

- Case definition – CDI
  - Patient with diarrhea
    - ≥3 loose or liquid stools in <24 hours

    AND
  - Positive laboratory assay for *C.difficile* toxins A or B from a stool sample or positive PCR for *tcdB*

    OR
  - Clinical diagnosis
    - Histopathology or visualisation of pseudomembranes

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## Methods

- Complications
  - Death < 30 days (attributable or associated)
  - Colectomy
  - Admission to ICU
  - Readmission for CDI

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## Infection control considerations

- Patients placed into Contact Precautions according to PCR
  - Glove use
  - Gown
  - Hand hygiene with soap and water
  - Disinfection with chlorine-based product
  - Duration: up to 72h after resolution of symptoms
- HCWs blinded to the result of EIA/CCA

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# Clostridium difficile Infections: Lessons from the Quebec Experience

**Prof. Yves Longtin, Laval University**

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## Methods

- Prospective observational study
  - 12-month period ending July 31st, 2011
- All samples submitted to lab for *C.difficile* tested in parallel using 2 different diagnostic approaches

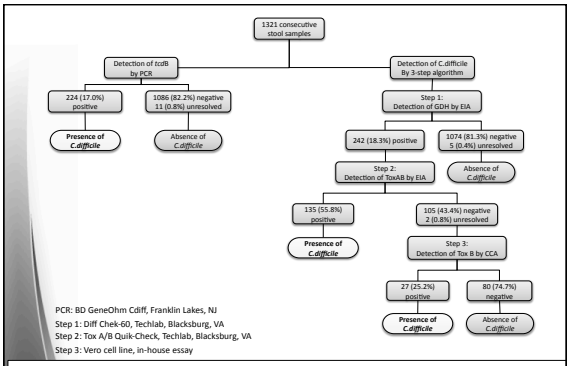
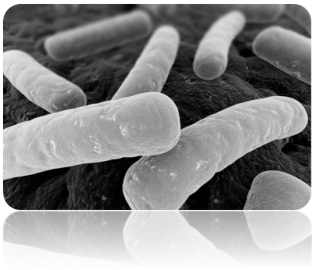



**Figure 1.** Flow chart of laboratory diagnosis *of C.difficile* in stool samples by PCR and by the 3-step algorithm. Abbreviations: *tcd*B: Toxin B gene; GDH: glutamate deshydrogenase; EIA: enzyme immunoflurescent assay; ToxAB: *C.difficile* toxins A or B; CCA: cell culture cytotoxicity assay

## Results



## Results

- From August 1st, 2010 – July 31st, 2011
  - 95 759 patient-days
  - 1321 stool samples submitted and analyzed in parallel
    - 888 patients

**Table 2. Summary of *C.difficile* infection and incidence rates as detected by PCR and by EIA/CCA algorithm, August 2010 to July 2011**

| Outcome | CDI detected by PCR | CDI detected by EIA/CCA | P-value |
|---|---|---|---|
| No. patient-days | 95 750 | 95 750 | - |
| No. of analysed stool samples | 1321 | 1321 | - |
| No. of positive samples (%) | 224 (17.0) | 162 (12.3) | 0.001[a] |
| No. nosocomial cases (%) | 85 (6.4) | 56 (4.2) | 0.01[a] |
| Incidence density, CDI per 10 000 patient-days (95% CI) | 8.9 (7.1-10.9) | 5.8 (4.4-7.4) | 0.014 |
| No. of periods above government-imposed target (%) | 7/13 (53) | 4/13 (31) | 0.42[b] |
| Incidence rate ratio[c] (95% CI) | 1.52 (1.08-2.13) | 1 [Reference] | 0.015 |

[a] By Chi-square test
[b] By Fisher's exact test
[c] Ratio based on Poisson regression analysis

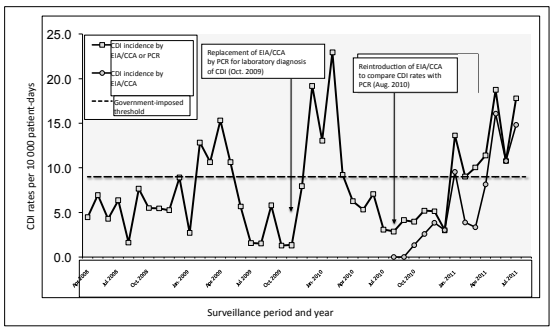



**Figure 2.** Incidence of hospital-onset *Clostridium difficile* infection (CDI), according to standardized surveillance definition, April 2008- July 2011. A switch from a three-step algorithm detecting glutarate deshydrogenase and Toxins A and B by EIA and cell culture cytotoxin assay (EIA/CCA) to a PCR-based diagnosis of CDI occurred in October 2009 at Quebec Heart and Lung Institute (IUCPQ). EIA/CCA was reintroduced and conducted in parallel with PCR on August 2010 for comparative purposes.

**Table 3. Summary of *C.difficile* infection complication rates as detected by PCR and by EIA/CCA algorithm, August 2010 to July 2011**

| Complications | CDI detected by PCR | CDI detected by EIA/CCA | P-value |
|---|---|---|---|
| 30-day mortality (%) | 11/85 (12) | 10/56 (16) | 0.46[a] |
| Colectomy (%) | 1/85 (1) | 1/56 (2) | 1.00[b] |
| Admission to intensive care unit | 1/85 (1) | 1/56 (2) | 1.00[b] |
| Readmission for CDI (%) | 11/85 (12) | 11/56 (18) | 0.31[a] |
| Any complication (%) | 23/85 (27) | 22/56 (39) | 0.16[a] |

[a] By Chi-square test
[b] By Fisher's exact test

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**Table 4. Frequency of complications associated with *Clostridium difficile* infection as detected by PCR only and by both PCR and EIA/CCA algorithm**

| Complications | CDI Cases detected by PCR but not by EIA/CCA (n=29) | CDI Cases detected by both PCR and EIA/CCA (n=56) | p-value[a] |
|---|---|---|---|
| 30-day mortality (%) | 1 (3) | 10 (18) | 0.09 |
| Colectomy (%) | 0 (0) | 1 (2) | 1.00 |
| Admission to intensive care unit (%) | 0 (0) | 1 (2) | 1.00 |
| Readmission for CDI (%) | 0 (0) | 11 (20) | 0.01 |
| Occurrence of ≥ 1 complication (%) | 1 (3) | 22 (39)[b] | <0.001 |

[a] By fisher's exact test
[b] One patient with colectomy was admitted to the intensive care unit

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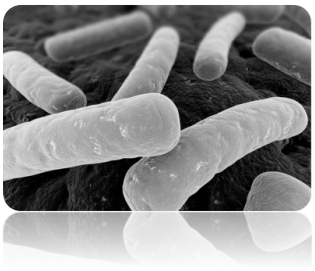
## Discussion



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## Conclusion

- CDI surveillance is increasingly popular
- To ensure inter-facility comparison, rates must be adjusted to take into account differences not attributable to the quality of infection control programs
  - Case-mix
  - Hospital size

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## Conclusion

- Incidence and complication rates can differ significantly depending on the type of diagnostic test
  - This variable should be taken into account to improve inter-hospital comparison
  - Methods remain to be determined
    - Stratification?
    - Standardization of diagnostic methods?

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## Conclusion

- How to take into account differences in laboratory testing?
  - Stratification?
  - Standardization of diagnostic methods?

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# Clostridium difficile Infections: Lessons from the Quebec Experience

**Prof. Yves Longtin, Laval University**

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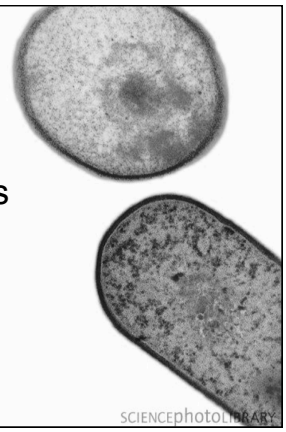
## Future directions





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## Future directions

- Survey of local practices (2012)
- Outbreak management guidelines
- Standardization diagnostic testing
- Validation of data entry
- Obtain patient-level data on a sample of cases
- Stratification according to % NAP1 strain
- Improve understanding the heterogeneity between institutions
  - Modifiable factors?
- Antimicrobial use

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## Members of SPIN-CD committee

| Member | Affiliation |
|---|---|
| **M. Daniel Bolduc** | Dir. de la santé publique et des soins de santé primaire, région Bas-Saint-Laurent |
| **Mme Caroline Duchesne** | CSSS Ahuntsic Montréal Nord |
| **Dr Charles Frenette** | Centre universitaire de santé McGill, président SPIN |
| **Dre Lise-Andrée Galarneau** | Centre hospitalier régional de Trois-Rivières, présidente du CINQ |
| **M. Christophe Garenc** | Institut national de santé publique du Québec |
| **M. Simon Lévesque** | Laboratoire de santé publique du Québec |
| **Dr Yves Longtin** | Institut universitaire de cardiologie et de pneumologie du Québec, président SPIN-CD |
| **Dre Vivian Loo** | Centre universitaire de santé McGill |
| **Mme Isabelle Rocher** | Institut national de santé publique du Québec |
| **Mme Mélissa Trudeau** | Institut national de santé publique du Québec |
| **Mme Josée Vachon** | CSSS de la région Thetford |
| **Dre Louise Valiquette** | Direction de la santé publique de Montréal |

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## Now recruiting!

- Hospitals outside Québec to participate in CDI surveillance
- To compare provincial and foreign rates
  - Chance to compare yourself with other institutions
  - Quarterly and Yearly reports
  - Strain analysis
  - Online data entry
- Contact: Yves.longtin@crchuq.ulaval.ca



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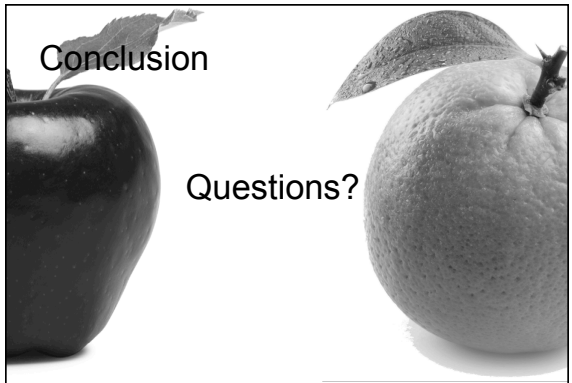
## Conclusion

Questions?



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## Coming Soon

03 May **Meet the Press – Tips and Techniques for Dealing With the Media**
Speaker: Jim Armour, Summa Strategies, Ottawa

07 May *(Free WHO Teleclass … Europe)* **Keeping the Hand Hygiene Agenda Alive: Acting on Data and the Influence of Global Surveys**
Speaker: Prof. Didier Pittet, World Health Organsation
Sponsored by WHO First Global Patient Safety Challenge – Clean Care is Safer Care

10 May **Best Practices for Eliminating CAUTIs**
Speaker: Robert Garcia, Stoney Brook Medical Center, New York
Sponsored by Sage Products Inc. (www.sageproducts.com)

17 May **Bug Basics – Essential Microbiology for Everyone**
Speaker: Jim Gauthier, Providence Continuing Care, Kingston

24 May **Healthcare Workplaces – Moving from Discord to Patient-Centered**

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