**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, Québec, 1991-2003.

[Graph showing incidence trends over time]

**Retrospective chart review**
**Clostridium difficile Infections: Lessons from the Quebec Experience**

Prof. Yves Longtin, Laval University

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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

**Retrospective analysis of CDI rates in Québec**

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

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

Source: Santé et Services Sociaux Québec

---

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Control of the outbreak

2004-2007

Interventions to control outbreak

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

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

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

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
**Quebec surveillances of HAI**

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

**CDI definition**

- Presence of diarrhea
  - ≥ 3 loose stools in < 24 hours
  - Symptoms last ≥ 24 hours
  - 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)

**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

**Categories – time cutoffs**

- Hospitalization
  - Cat. I
  - 72h
  - 4 weeks

- (nothing)
  - 72h
  - 4 weeks

- CDI
  - CDI treatment
  - Recurrence
  - 8 weeks

---

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Categories of CDI, 2009-2010

<table>
<thead>
<tr>
<th>Category</th>
<th>Origin of acquisition</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat. 1</td>
<td>HA-CDI linked to the reporting institution</td>
<td>3167</td>
<td>69.3</td>
</tr>
<tr>
<td>Cat. 2a</td>
<td>HA-CDI linked to another non-participating institution</td>
<td>324</td>
<td>7.1</td>
</tr>
<tr>
<td>Cat. 2b</td>
<td>HA-CDI linked to ambulatory care</td>
<td>269</td>
<td>5.9</td>
</tr>
<tr>
<td>Cat. 3</td>
<td>CA-CDI</td>
<td>558</td>
<td>12.2</td>
</tr>
<tr>
<td>Cat. 4</td>
<td>Unknown origin</td>
<td>249</td>
<td>5.5</td>
</tr>
<tr>
<td>Total</td>
<td>Hospitalized</td>
<td>4567</td>
<td>100</td>
</tr>
</tbody>
</table>

Note. Only hospitalized cases are reported.

CDI surveillance

- Monitoring of complication rates also part of surveillance programs
  - Death (10-day and 30-day mortality)
  - Poor inter-observer correlation
- Toxic megacolon and colectomy
- Admission to ICU for CDI
- Readmission for CDI

Complications

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

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)
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)

---

Weekly report

---

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

---

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Public reporting

2004-2007, the years of the epidemic

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

Source: Santé et Services Sociaux Québec

Moyenne : 3294 cas/an

7020 cas

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

Moyenne : 3294 cas/an

6184 cas

Source: Santé et Services Sociaux Québec

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

Source: Santé et Services Sociaux Québec
Incidence des nouveaux cas de DACD/1000 admissions – MedÉcho et surveillance provinciale

Source: Santé et Services Sociaux Québec

Comparons le comparable (58 CH)

<table>
<thead>
<tr>
<th>Variable</th>
<th>An 1</th>
<th>An 2</th>
<th>Évolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cas DACD</td>
<td>3660</td>
<td>2266</td>
<td>-38 %</td>
</tr>
<tr>
<td>Décès cause principale</td>
<td>134 (4 %)</td>
<td>56 (2 %)</td>
<td>-58 %</td>
</tr>
<tr>
<td>Décès cause contributive</td>
<td>177 (5 %)</td>
<td>79 (3 %)</td>
<td>-55 %</td>
</tr>
<tr>
<td>Colectomie</td>
<td>33 (1 %)</td>
<td>23 (1 %)</td>
<td>-30 %</td>
</tr>
<tr>
<td>Réadmission</td>
<td>243 (7 %)</td>
<td>135 (6 %)</td>
<td>-44 %</td>
</tr>
<tr>
<td>Adm. USI</td>
<td>89 (2 %)</td>
<td>47 (2 %)</td>
<td>-47 %</td>
</tr>
</tbody>
</table>

Source: Santé et Services Sociaux Québec

Incidence des DACD d’origine nosocomiale par regroupement régions

Source: Santé et Services Sociaux Québec


Source: Santé et Services Sociaux Québec

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### Trends in CDI, 2004-2010

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Nombre d'installations participantes</td>
<td>88 - 94</td>
<td>94</td>
<td>96</td>
<td>95</td>
<td></td>
</tr>
<tr>
<td>Admissions</td>
<td>687 222 - 611 712</td>
<td>607 533</td>
<td>611 935</td>
<td>609 830</td>
<td></td>
</tr>
<tr>
<td>Jours-présence</td>
<td>4 976 065 - 5 042 166</td>
<td>5 023 163</td>
<td>5 121 708</td>
<td>5 097 192</td>
<td></td>
</tr>
<tr>
<td>DADC hospitalisée</td>
<td>5 355 - 6 661</td>
<td>4 417</td>
<td>4 523</td>
<td>4 567</td>
<td></td>
</tr>
<tr>
<td>DADC d'origine nosocomiale (cat. 1)</td>
<td>4 015 - 6 360</td>
<td>3 254</td>
<td>3 302</td>
<td>3 167</td>
<td></td>
</tr>
</tbody>
</table>

---

### Trends in CDI, 2010-2012

Increase in CDI rates

---

**Trends in CDI, 2004-2011**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
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<td>3 254</td>
<td>3 302</td>
<td>3 167</td>
</tr>
</tbody>
</table>

---

**Trends in CDI, 2004-2011**

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Trends in CDI, 2004-2011

Incidence rates per stratum

Complications
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?

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

Strain analysis, 2005-2011

<table>
<thead>
<tr>
<th>Period</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strain</td>
<td>% (n)</td>
<td>% (n)</td>
<td>% (n)</td>
<td>% (n)</td>
<td>% (n)</td>
<td>% (n)</td>
<td>% (n)</td>
</tr>
<tr>
<td>Pulse type A</td>
<td>27% (274)</td>
<td>17% (174)</td>
<td>25% (248)</td>
<td>20% (205)</td>
<td>22% (210)</td>
<td>16% (161)</td>
<td></td>
</tr>
<tr>
<td>Pulse type A2-5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>12% (55)</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Pulse type B</td>
<td>10% (49)</td>
<td>6% (21)</td>
<td>2% (7)</td>
<td>3% (13)</td>
<td>-</td>
<td>0.3% (1)</td>
<td></td>
</tr>
<tr>
<td>Pulse type B1</td>
<td>7% (37)</td>
<td>1.8% (6)</td>
<td>4.6% (17)</td>
<td>0.8% (3)</td>
<td>0.4% (2)</td>
<td>0.3% (1)</td>
<td></td>
</tr>
<tr>
<td>Other pulse types</td>
<td>24.5% (117)</td>
<td>39.5% (131)</td>
<td>26% (100)</td>
<td>42.7% (165)</td>
<td>40.9% (185)</td>
<td>42.9% (139)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>47%</td>
<td>33%</td>
<td>37%</td>
<td>38%</td>
<td>45%</td>
<td>32%</td>
<td></td>
</tr>
</tbody>
</table>

Nap1/027 and CDI rates

![Graph showing Nap1/027 and CDI rates](image1.png)

Figure 11: Taux d’incidence de DACOVIS 098 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

![Graph showing Nap1/027 and CDI rates](image2.png)

Figure 9: Taux d’incidence de DACOVIS 098 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

Impact of the predominance of pulsovar A on the incidence of DACD in the Quebec region from 2009-2010

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?

CDI, Influenza and RSV

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

CDI, Influenza and RSV

TABLE 3: Multivariable time series transfer function model used to estimate time series having impact on CDI incidence*
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?

Introduction PCR in 10 hospitals

Hospitals using PCR have higher CDI rates

OR, 1.2 [95% CI, 1.1-1.3], p < 0.0001

Increase also present in non-PCR institutions

However, these hospitals historically have higher rates. Increase in CDI not significant when controlled for hospital size, teaching status and proportion of >65.

Adjusted OR: 1.1 (95% CI, 1.0-1.3); p = 0.13

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!

Incidence rates estimation
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?

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)

91% of observations ± 0.6 actual incidence rate
Incidence rates vs. No. of cases

- Why are denominators (almost) irrelevant?

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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--

**Data presentation**

- Ranking hospitals may lead to “misinterpretation” by non-initiated individuals

---

**Funnel plot**

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

---

**Example of funnel plot**

---

**Funnel plot of CDI incidence rates**

---

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

Y. Longtin MD; D.Trotier MD MSc; G. Brochu PhD; B. Paquet-Bédard, RN; C. Garanc, PhD; V. Javouhey MD; C. Beaulieu MD; D. Goulet RN, MSc; Y. Longtin MD

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

---

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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


---

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


- Enzyme immunoassay
  - Detect ToxA and ToxB 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


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

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

Laboratory tests to diagnose CDI

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


Study objective

- Determine whether incidence and complication rates can vary depending on the type of diagnostic test
  - Single institution (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)

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 visualization of pseudomembranes

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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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

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

<table>
<thead>
<tr>
<th>Outcome</th>
<th>CDI detected by PCR</th>
<th>CDI detected by EIA/CCA</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. patient-days</td>
<td>85 759</td>
<td>85 759</td>
<td>-</td>
</tr>
<tr>
<td>No. of analyzed stool sample</td>
<td>1221</td>
<td>1221</td>
<td>-</td>
</tr>
<tr>
<td>No. of positive samples (%)</td>
<td>224 (17.3%)</td>
<td>182 (14.9%)</td>
<td>0.005*</td>
</tr>
<tr>
<td>No. non-smoothed cases (%)</td>
<td>85 (6.6%)</td>
<td>55 (4.2%)</td>
<td>0.017*</td>
</tr>
<tr>
<td>Incidence density, CDI per 10,000 patient-days (95% CI)</td>
<td>8.9 (4.7-10.9)</td>
<td>5.8 (4.4-7.4)</td>
<td>0.014</td>
</tr>
<tr>
<td>No. of periods above government-imposed target (%)</td>
<td>7/13 (53%)</td>
<td>4/13 (31%)</td>
<td>0.42</td>
</tr>
<tr>
<td>Incidence rate ratio (95% CI)</td>
<td>1.52 (1.08-2.13)</td>
<td>1.0 (Reference)</td>
<td>0.015</td>
</tr>
</tbody>
</table>

* By Chi-square test
  * By Fisher's exact test
  ** Rate based on Poisson regression analysis

---

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

<table>
<thead>
<tr>
<th>Complication</th>
<th>PCR detected by PCR</th>
<th>EIA/CCA detected by EIA/CCA</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-day mortality (%)</td>
<td>11/85 (12)</td>
<td>10/56 (16)</td>
<td>0.48*</td>
</tr>
<tr>
<td>Colectomy (%)</td>
<td>1/85 (1)</td>
<td>1/56 (2)</td>
<td>1.00*</td>
</tr>
<tr>
<td>Admission to intensive care unit</td>
<td>1/85 (1)</td>
<td>1/56 (2)</td>
<td>1.00*</td>
</tr>
<tr>
<td>Readmission for CDI (%)</td>
<td>11/85 (12)</td>
<td>11/56 (16)</td>
<td>0.31+</td>
</tr>
<tr>
<td>Any complication (%)</td>
<td>23/85 (27)</td>
<td>22/56 (39)</td>
<td>0.18*</td>
</tr>
</tbody>
</table>

*By Chi-square test
* By Fisher’s exact test

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

<table>
<thead>
<tr>
<th>Complication</th>
<th>PCR only detected by PCR (n=29)</th>
<th>Both detected by PCR and EIA/CCA (n=56)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-day mortality (%)</td>
<td>1 (3)</td>
<td>10 (18)</td>
<td>0.09</td>
</tr>
<tr>
<td>Colectomy (%)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>1.00</td>
</tr>
<tr>
<td>Admission to intensive care unit</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>1.00</td>
</tr>
<tr>
<td>Readmission for CDI (%)</td>
<td>0 (0)</td>
<td>11 (20)</td>
<td>0.01</td>
</tr>
<tr>
<td>Occurrence of ≥ 1 complication (%)</td>
<td>1 (3)</td>
<td>22 (39)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*By Fisher’s exact test
a One patient with colectomy was admitted to the intensive care unit

Discussion

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?

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

Conclusion

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

Members of SPIN-CD committee

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</tr>
</tbody>
</table>

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

Conclusion

Questions?

Coming Soon

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

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

10 May Best Practices for Eliminating CAUTIs
Speaker: Robert Garcia, Stony 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

Hosted by Paul Webber paul@webbertraining.com
A Webber Training Teleclass
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