Controversies and Current Issues in Diagnosis, Surveillance, and Treatment of *Clostridium difficile* infection

L. Clifford McDonald, MD
Senior Advisor for Science and Integrity
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The findings and conclusions in this presentation are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
**Clostridium difficile** Infection (CDI)

- Anaerobic bacterium
- Not normal intestinal bacterium
- Fecal-oral spread
- Forms spores that persist
- Toxins produce colitis
  - Diarrhea
  - More severe disease, death
- 2-steps to infection
  - Antibiotics result in vulnerability
  - New acquisition via transmission

Figure courtesy of D. Gerding and S. Johnson
Controversies and Current Issues

- Are CDI rates beginning to decrease?
- How should CDI be diagnosed?
- What is the role of asymptomatic carriers in transmission?
- How long should patients with CDI be isolated?
- Is there transmission in outpatient healthcare settings?
Discharges (primary and secondary) Coded for *Clostridium difficile* infection (CDI), United States

## Hospital-Onset CDI LabID Events: The NHSN Baseline

<table>
<thead>
<tr>
<th></th>
<th>Baseline 2010-2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facilities reporting</td>
<td>846</td>
</tr>
<tr>
<td>States represented</td>
<td>40 (5 with mandates)</td>
</tr>
<tr>
<td>Facility quarters</td>
<td>5,086</td>
</tr>
<tr>
<td>Facility-wide patient days</td>
<td>62,262,776</td>
</tr>
<tr>
<td>Facility-wide admissions</td>
<td>13,102,078</td>
</tr>
<tr>
<td>HO-CDI LabID events</td>
<td>45,323</td>
</tr>
</tbody>
</table>
NHSN CDI Risk Adjusted SIR Accounts for More Sensitive Testing and Prevalence on Admission

Variables from Final Model to be included for Risk Adjustment in SIR Calculation

<table>
<thead>
<tr>
<th>Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td></td>
</tr>
<tr>
<td>Facility Bed Size</td>
<td>&gt; 245</td>
</tr>
<tr>
<td></td>
<td>101-245</td>
</tr>
<tr>
<td></td>
<td>≤ 100</td>
</tr>
<tr>
<td>Teaching Type</td>
<td>Major</td>
</tr>
<tr>
<td></td>
<td>Graduate</td>
</tr>
<tr>
<td></td>
<td>Limited &amp; Non</td>
</tr>
<tr>
<td>CDI Test Type</td>
<td>NAAT (PCR)</td>
</tr>
<tr>
<td></td>
<td>EIA</td>
</tr>
<tr>
<td></td>
<td>All Other</td>
</tr>
<tr>
<td>Prevalence</td>
<td>Continuous (no CO-HCFA)</td>
</tr>
</tbody>
</table>

Data Sources and Submission

- CDI test type, facility bed size, and teaching type are collected on the required Annual Facility Survey.
- The survey is completed after the end of each year for accuracy in describing a full year’s worth of data.
- Survey data for 2012 will be submitted by facilities January - March 2013.
- Due to reporting requirements from CMS, quarterly data are complete 4.5 months after the end of each quarter.
## HO-CDI LabID Events Predictive Model (2)

<table>
<thead>
<tr>
<th>Effect</th>
<th>Parameter Estimate</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-7.8983</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CDI Test Type (NAAT vs. non-NAAT/EIA others)</td>
<td>0.3850</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CDI Test Type (EIA vs. non-NAAT/EIA others)</td>
<td>0.1606</td>
<td>0.0013</td>
</tr>
<tr>
<td>Prevalence rate (continuous)*</td>
<td>0.3338</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Facility Bedsize (&gt;245 vs. ≤100)</td>
<td>0.2164</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Facility Bedsize (101-245 vs. ≤100)</td>
<td>0.0935</td>
<td>0.0022</td>
</tr>
<tr>
<td>Medical School Affiliation (Major teaching vs. Undergraduate/Non-Teaching)</td>
<td>0.1870</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Medical School Affiliation (Graduate vs. Undergraduate/Non-Teaching)</td>
<td>0.0918</td>
<td>0.0038</td>
</tr>
</tbody>
</table>

*Number of community-onset CDI LabID events X 100
Number of admissions to the facility
NATIONAL

Healthcare-associated infections (HAIs) are infections patients can get while receiving medical treatment in a healthcare facility. Working toward the elimination of HAIs is a CDC priority. The standardized infection ratio (SIR) is a summary statistic that can be used to track HAI prevention progress over time; lower SIRs are better. The infection data are collected through CDC’s National Healthcare Safety Network (NHSN). HAI data for nearly all U.S. hospitals are published on the Hospital Compare website.

CLABSIs

CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTIONS

When a tube is placed in a large vein and not put in correctly or kept clean, it can become a way for germs to enter the body and cause deadly infections in the blood.

- U.S. hospitals reported a significant decrease in CLABSIs between 2012 and 2013.
- 9% Among the 2,389 hospitals in U.S. with enough data to calculate an SIR, 9% had an SIR significantly worse than the national SIR of 0.34.

CAUTIs

CATHETER-ASSOCIATED URINARY TRACT INFECTIONS

When a urinary catheter is not put in correctly, not kept clean, or left in a patient for too long, germs can travel through the catheter and infect the bladder and kidneys.

- U.S. hospitals reported a significant increase in CAUTIs between 2012 and 2013.
- 12% Among the 2,751 U.S. hospitals with enough data to calculate an SIR, 12% had an SIR significantly worse than the national SIR of 1.06.

MRSA Bacteremia

LABORATORY IDENTIFIED HOSPITAL-ONSET BLOODSTREAM INFECTIONS

Methicillin-resistant Staphylococcus aureus (MRSA) is bacteria usually spread by contaminated hands. In a healthcare setting, such as a hospital, MRSA can cause serious bloodstream infections.

- U.S. hospitals reported a significant decrease in MRSA Bacteremia between 2012 and 2013.
- 7% Among the 2,002 U.S. hospitals with enough data to calculate an SIR, 7% had an SIR significantly worse than the national SIR of 0.92.

SSIs

SURGICAL SITE INFECTIONS

See page 3 for additional procedures

SSI: Abdominal Hysterectomy

14% LOWER COMPARED TO NAT’L BASELINE

- U.S. hospitals reported no significant change in SSIs related to abdominal hysterectomy surgery between 2012 and 2013.
- 6% Among the 765 U.S. hospitals with enough data to calculate an SIR, 6% had an SIR significantly worse than the national SIR of 0.86.

SSI: Colon Surgery

8% LOWER COMPARED TO NAT’L BASELINE

- U.S. hospitals reported a significant increase in SSIs related to colon surgery between 2012 and 2013.
- Several changes to the NHSN 2013 SSI protocol likely contributed to an increase in the national and some state-specific colon surgery SIRs compared to 2012.
- 7% Among the 2,030 U.S. hospitals with enough data to calculate an SIR, 7% had an SIR significantly worse than the national SIR of 0.92.

C. difficile Infections

LABORATORY IDENTIFIED HOSPITAL-ONSET C. DIFFICILE INFECTIONS

When a person takes antibiotics, good bacteria that protect against infection are destroyed for several months. During this time, patients can get sick from Clostridium difficile, bacteria that cause potentially deadly diarrhea, which can be spread in healthcare settings.

- U.S. hospitals reported a significant decrease in C. difficile infections between 2012 and 2013.
- 13% Among the 3,557 U.S. hospitals with enough data to calculate an SIR, 13% had an SIR significantly worse than the national SIR of 0.90.

*Statistically significant.

This report is based on 2013 data, published January 2015.
Relative Sensitivity of *C. difficile* Tests

Culture + Toxin Confirmation >
NAAT (RT-PCR, LAMP) >
GDH EIA >
Cell Cytotoxin >
Toxin A & B EIA >
Toxin A EIA >
GDH Latex Test >
Endoscopy
Understanding Predictive Value for Diagnosis of Disease

Is CDI Testing a Function of Clinical Probability of CDI?

• If labs have no clinical input and accept all unformed stools for testing, it may be most appropriate to use a test that better identifies likely CDI, such as highly sensitive test for toxin in stool, but we lack proof for this.

• If patients are screened carefully for clinical symptoms likely associated with CDI (at least 3 loose or unformed stools in 24h or less with history of antibiotic exposure?), then a sensitive test such as NAAT or toxigenic culture, or GDH+toxin detection may be best.
Asymptomatic Carriers Equal or Exceed CDI Cases and Increase with Healthcare Exposure


Figure 2. Times to Health Care–Associated Clostridium difficile Infection and Colonization during Hospitalization.
Analyses of the cumulative probability of C. difficile infection or colonization excluded the 184 patients with C. difficile colonization on admission. The dashed lines indicate 95% confidence intervals.
Point Prevalence Estimates of Asymptomatic *C. difficile* Colonization During Healthcare

- Loo VG et al.: 4.4% asymptomatic carriers, ~1.8% CDI
- Eyre DW et al.: 11% (~5% on admission?)
- Leekha S et al.: 9.7% on admission
- Alasmari F et al.: 15% on admission
- Riggs MM et al.: 51% cross-section nursing home
- Marciniak C et al.: 16% on admission to rehab
- Dumford DM et al.: 50% cross-section spinal cord ward

Eyre DW, et al. PlosONE 8(11): e78445
Increasing Recognition of Asymptomatic Carriers as a Source for *C. difficile* Transmission

- **Eyre et al.**
  - Enzyme immunoassay for CDI diagnosis
  - Only 38% of new cases linked to a symptomatic (CDI) source

- **Curry et al.**
  - Cell cytotoxin neutralization assay for diagnosis
  - At least 29% of new cases linked to an asymptomatic source

- **As better infection control contains transmission from symptomatic (CDI) source, asymptomatic (and mildly symptomatic) patients play a larger role in transmission**

- **The sensitivity of a diagnostic impacts infection control**

Infection Control Implications of Diagnostic and Therapeutic Approaches

- Asymptomatic carriage increases with healthcare and especially antibiotic exposures in later life
- Asymptomatic carriage contributes to transmission
  - Even mild diarrhea and incontinence may promote spread
- Infection control and treatment decisions currently linked based on diagnosis of CDI
  - Use of more sensitive diagnostics may reduce transmission but also lead to unnecessary treatment
- Treatments that reduce the duration and degree of asymptomatic shedding could have added benefit for reduced transmission
Patients Commonly Remain Colonized After Treatment of CDI

Degree of Intestinal Colonization is a Likely Determinant of Contagiousness

**Original Investigation**

**Epidemiology of Community-Associated *Clostridium difficile* Infection, 2009 Through 2011**

Amit S. Chitnis, MD. MPH; Stacy M. Holzbauer, DVM, MPH; Ruth M. Belflower, RN. MPH; Lisa G. Winston, MD; Wendy M. Bamberg, MD; Carol Lyons, MPH; Monica M. Farley, MD; Ghinwa K. Dumyati, MD; Lucy E. Wilson, MD. ScM; Zintars G. Beldavs, MS; John R. Dunn, DVM, PhD; L. Hannah Gould, PhD, MS; Duncan R. MacCannell, PhD; Dale N. Gerding, MD; L. Clifford McDonald, MD; Fernanda C. Lessa, MD, MPH

<table>
<thead>
<tr>
<th>Outpatient Health Care Exposure</th>
<th>No./Total No. (%) (n = 984)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No exposure</td>
<td>177 (18.0)</td>
</tr>
<tr>
<td>Low-level exposure*</td>
<td>400 (40.7)</td>
</tr>
<tr>
<td>Physician office visit</td>
<td>359/400 (89.8)</td>
</tr>
<tr>
<td>Dentist office visit</td>
<td>119/400 (29.8)</td>
</tr>
<tr>
<td>Other outpatient visit</td>
<td>11/400 (2.8)</td>
</tr>
<tr>
<td>High-level exposure*</td>
<td>407 (41.4)</td>
</tr>
<tr>
<td>Surgery or procedure</td>
<td>229/407 (56.3)</td>
</tr>
<tr>
<td>Inpatient care but not an overnight admission</td>
<td>116/407 (28.5)</td>
</tr>
<tr>
<td>Emergency department or urgent care visit</td>
<td>98/407 (24.1)</td>
</tr>
<tr>
<td>Job required direct contact with patients</td>
<td>69/407 (17.0)</td>
</tr>
<tr>
<td>Dialysis</td>
<td>12/407 (2.9)</td>
</tr>
</tbody>
</table>

*a Variables are not mutually exclusive.
Outpatient Healthcare Settings and Transmission of *Clostridium difficile*

Lucy A. Jury¹, Brett Sitzlar¹, Sirisha Kundrapu², Jennifer L. Cadnum², Kim M. Summers³, Christine P. Muganda⁴, Abhishek Deshpande², Ajay K. Sethi⁴, Curtis J. Donskey¹,²*

¹Geriatric Research Education and Clinical Center, Cleveland Veterans Affairs Medical Center, Cleveland, Ohio, United States of America, ²Division of Infectious Diseases, Department of Medicine, Case Western Reserve University, Cleveland, Ohio, United States of America, ³Research Service, Cleveland Veterans Affairs Medical Center, Cleveland, Ohio, United States of America, ⁴Department of Population Health Sciences, University of Wisconsin, Madison, Wisconsin, United States of America

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![Flowchart showing the proposed algorithm for management of patients with recent *Clostridium difficile* infection (CDI) presenting to outpatient clinics.](chart.png)

Enhanced Precautions includes wearing gloves when examining patients and cleaning high-touch surfaces with sporicidal disinfectants after visits.

## Medication Use in Community-associated CDI, 2009-2011

<table>
<thead>
<tr>
<th>Medication use within 12 wk before <em>C difficile</em> infection, No./total No. (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>631 (64.1)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antibiotics&lt;sup&gt;b&lt;/sup&gt;</strong></td>
<td></td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>149/631 (23.6)</td>
</tr>
<tr>
<td>β-Lactam or β-lactamase inhibitors</td>
<td>145/631 (23.0)</td>
</tr>
<tr>
<td>Penicillins</td>
<td>143/631 (22.7)</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>139/631 (22.0)</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>119/631 (18.9)</td>
</tr>
<tr>
<td>Macrolides</td>
<td>60/631 (9.5)</td>
</tr>
<tr>
<td>Folic acid inhibitors</td>
<td>38/631 (6.0)</td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>15/631 (2.4)</td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
<td>273 (27.7)</td>
</tr>
<tr>
<td>H&lt;sub&gt;2&lt;/sub&gt;-receptor antagonists</td>
<td>90 (9.1)</td>
</tr>
<tr>
<td>Immune-suppressing agents&lt;sup&gt;c&lt;/sup&gt;</td>
<td>91 (9.2)</td>
</tr>
</tbody>
</table>

Most common reasons for antibiotics: upper respiratory and dental procedures

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov  Web: www.cdc.gov

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