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

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September 16, 2015

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No Financial Disclosures

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

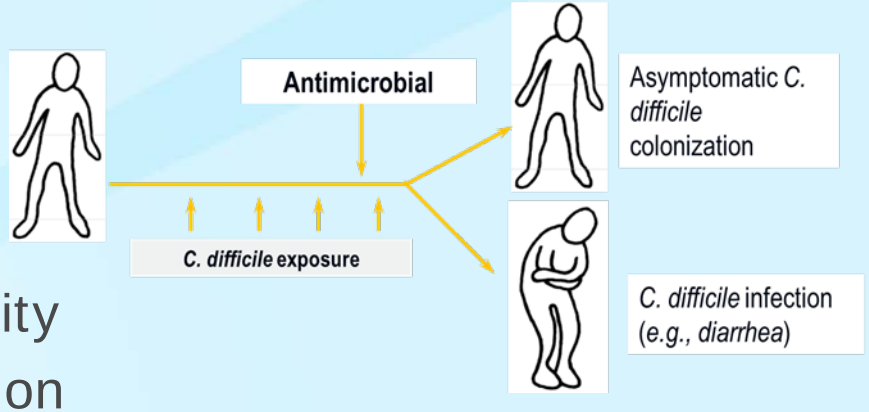


Figure courtesy of D. Gerding and S. Johnson

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

HCUPnet, Healthcare Cost and Utilization Project. Agency for Healthcare Research and Quality, Rockville, MD. http://hcupnet.ahrq.gov/

Hospital-Onset CDI LabID Events: The NHSN Baseline

	Baseline 2010-2011
Facilities reporting	846
States represented	40 (5 with mandates)
Facility quarters	5,086
Facility-wide patient days	62,262,776
Facility-wide admissions	13,102,078
HO-CDI LabID events	45,323

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

Factor	Description
Intercept	
Facility Bed Size	> 245
	101-245
	≤ 100
Teaching Type	Major
	Graduate
	Limited & Non
CDI Test Type	NAAT (PCR)
	EIA
	All Other
Prevalence	Continuous (no CO-HCFA)

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)

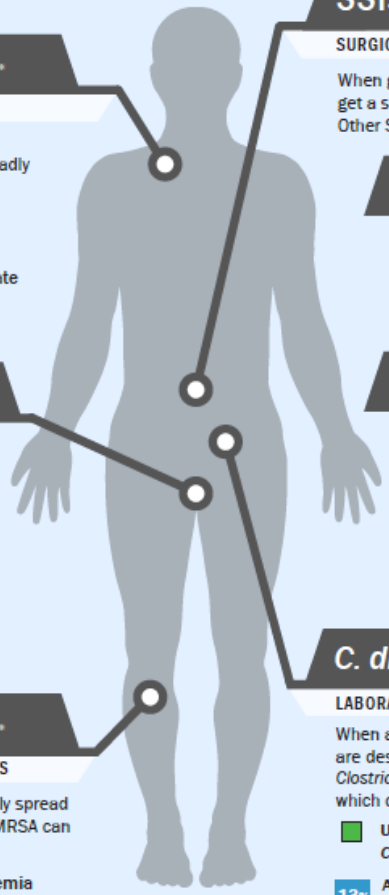
Effect	Parameter Estimate	p-value
Intercept	-7.8983	<0.0001
CDI Test Type (NAAT vs. non-NAAT/EIA others)	0.3850	<0.0001
CDI Test Type (EIA vs. non-NAAT/EIA others)	0.1606	0.0013
Prevalence rate (continuous)*	0.3338	<0.0001
Facility Bedsize (>245 vs. ≤100)	0.2164	<0.0001
Facility Bedsize (101-245 vs.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

*$\frac{\text{Number of community-onset CDI LabID events}}{\text{Number of admissions to the facility}} \times 100$

NATIONAL

HEALTHCARE ASSOCIATED INFECTIONS PROGRESS

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

↓ 46% LOWER COMPARED TO NAT'L BASELINE*

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 0.54.

CAUTIs

↑ 6% HIGHER COMPARED TO NAT'L BASELINE*

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 2,781 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

↓ 8% LOWER COMPARED TO NAT'L BASELINE*

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*

When germs get into an area where surgery is or was performed, patients can get a surgical site infection. Sometimes these infections involve only the skin. Other SSIs can involve tissues under the skin, organs, or implanted material.

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

↓ 10% LOWER COMPARED TO NAT'L BASELINE*

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* (*C. 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

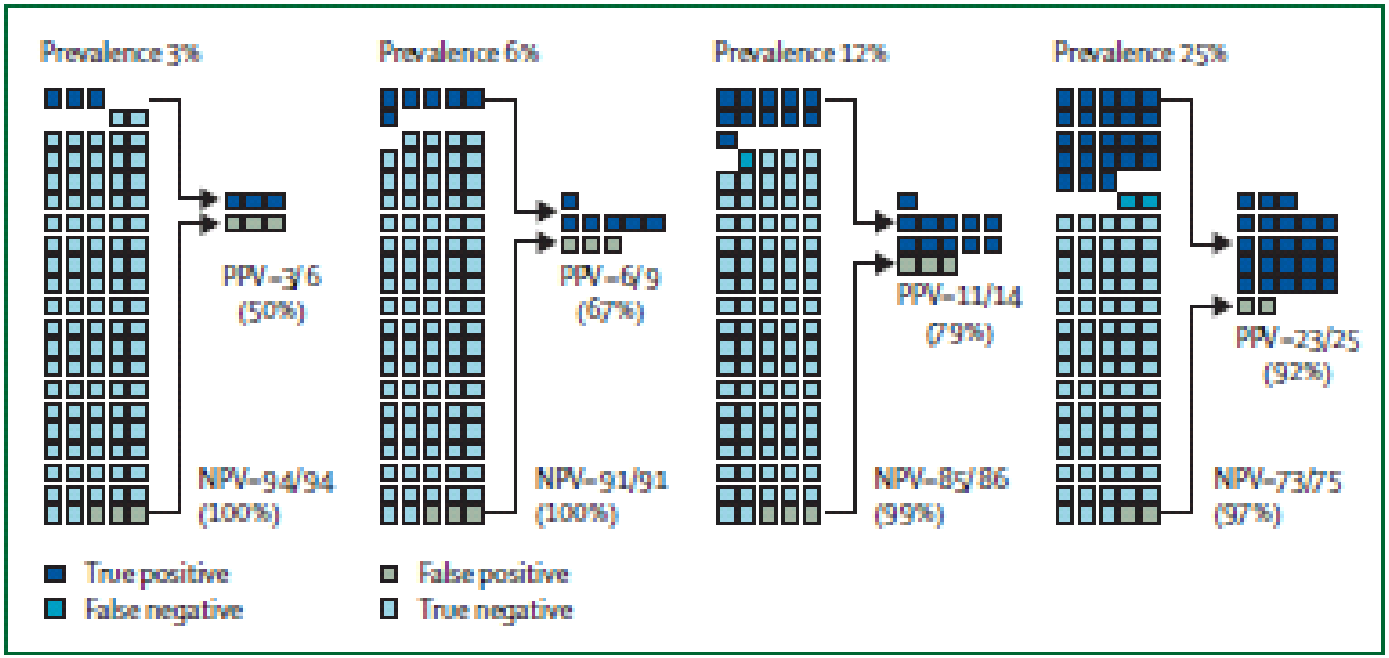


Figure 1: Effect of varying prevalence on the PPV and NPV of a theoretical *Clostridium difficile* toxin assay with a sensitivity of 92% and a specificity of 97%

NPV=negative predictive value. PPV=positive predictive value.

- T Planche et al. *Lancet Infect Dis* 8: 777–84, 2008

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

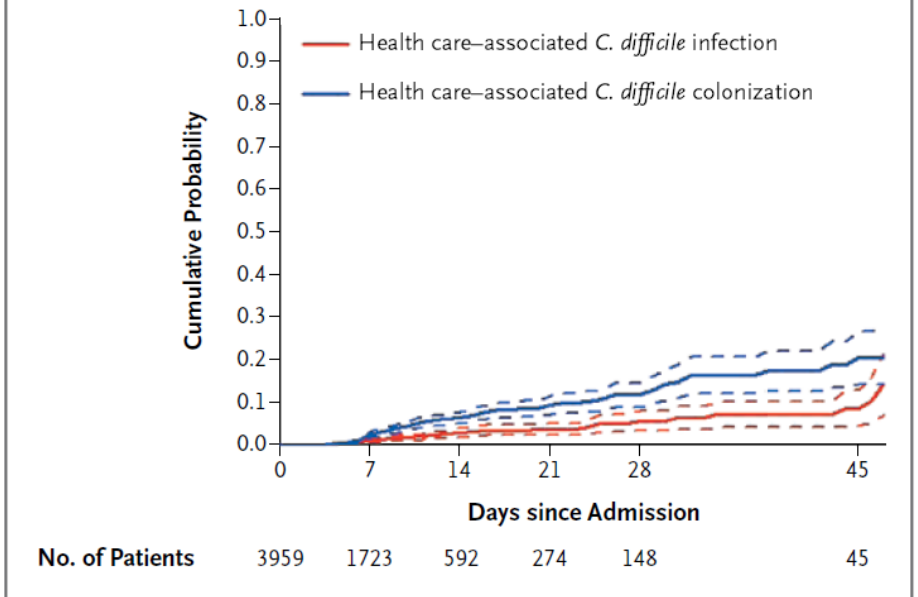


Figure 2. Times to Health Care–Associated *Clostridium difficile* Infection and Colonization during Hospitalization.

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.

Loo VG et al. N Engl J Med 2011;365:1693-703.

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

Loo VG, et al. N Engl J Med 2011;365:1693-703.
Eyre DW, et al. Plos ONE 8(11): e78445
Leekha S et al. A J of Infect Contrl 41 (2013) 390-3
Alasmari F et al. Clin Infect Dis 2014;59(2):216–22
Riggs MM et al. Clin Infect Dis 2007;45:992-8
Marciniak et al. Arch Phys Med Rehabil 2006; 87: 2086-9
Dumford DM et al. J Spinal Cord Med 2011; 34(1): 22-7

Increasing Recognition of Asymptomatic Carriers as a Source for *C. difficile* Transmission

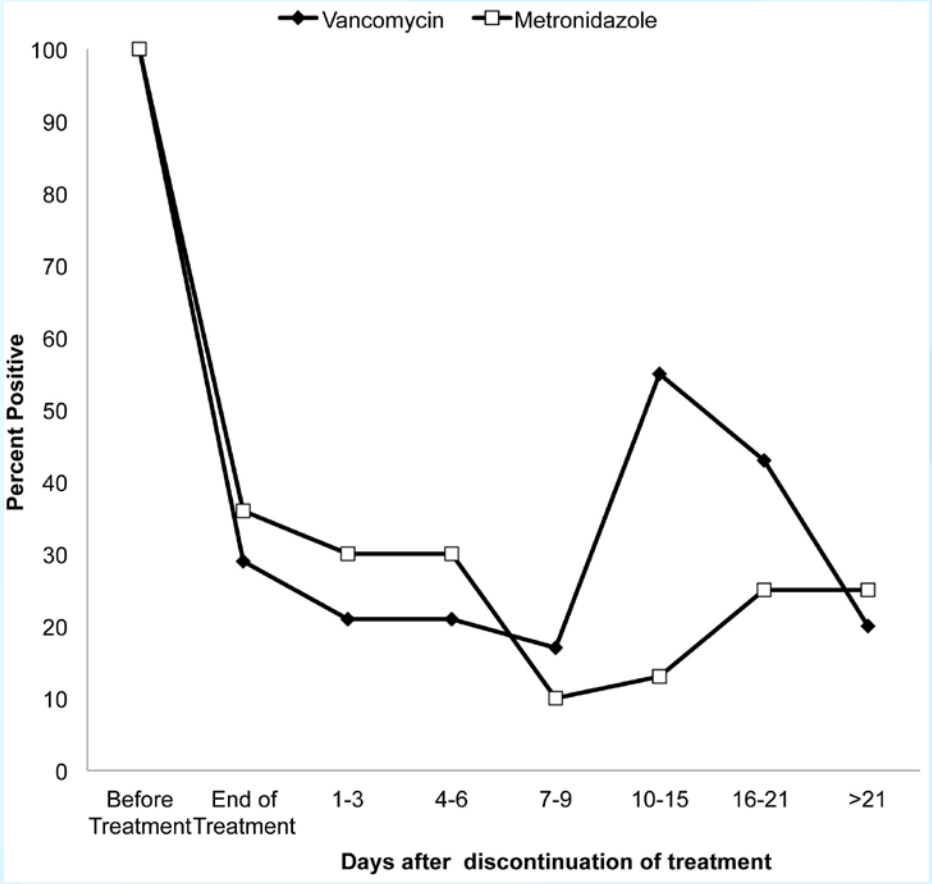
- Eyre et al.
  - Enzyme immunoassay for CDI diagnosis
  - Only 38% of new cases linked to a symptomatic (CDI) source
- Curry et al.
  - Cell cytotoxin neutralization assay for diagnosis
  - At least 29% of new cases linked to an asymptomatic source
- As better infection control contains transmission from symptomatic (CDI) source, asymptomatic (and mildly symptomatic) patients play a larger role in transmission
- The sensitivity of a diagnostic impacts infection control

Curry SR et al. Clin Infect Dis 2013; 57:1094–102.
Eyre DW et al. N Engl J Med 2013;369:1195-205.

Infection Control Implications of Diagnostic and Therapeutic Approaches

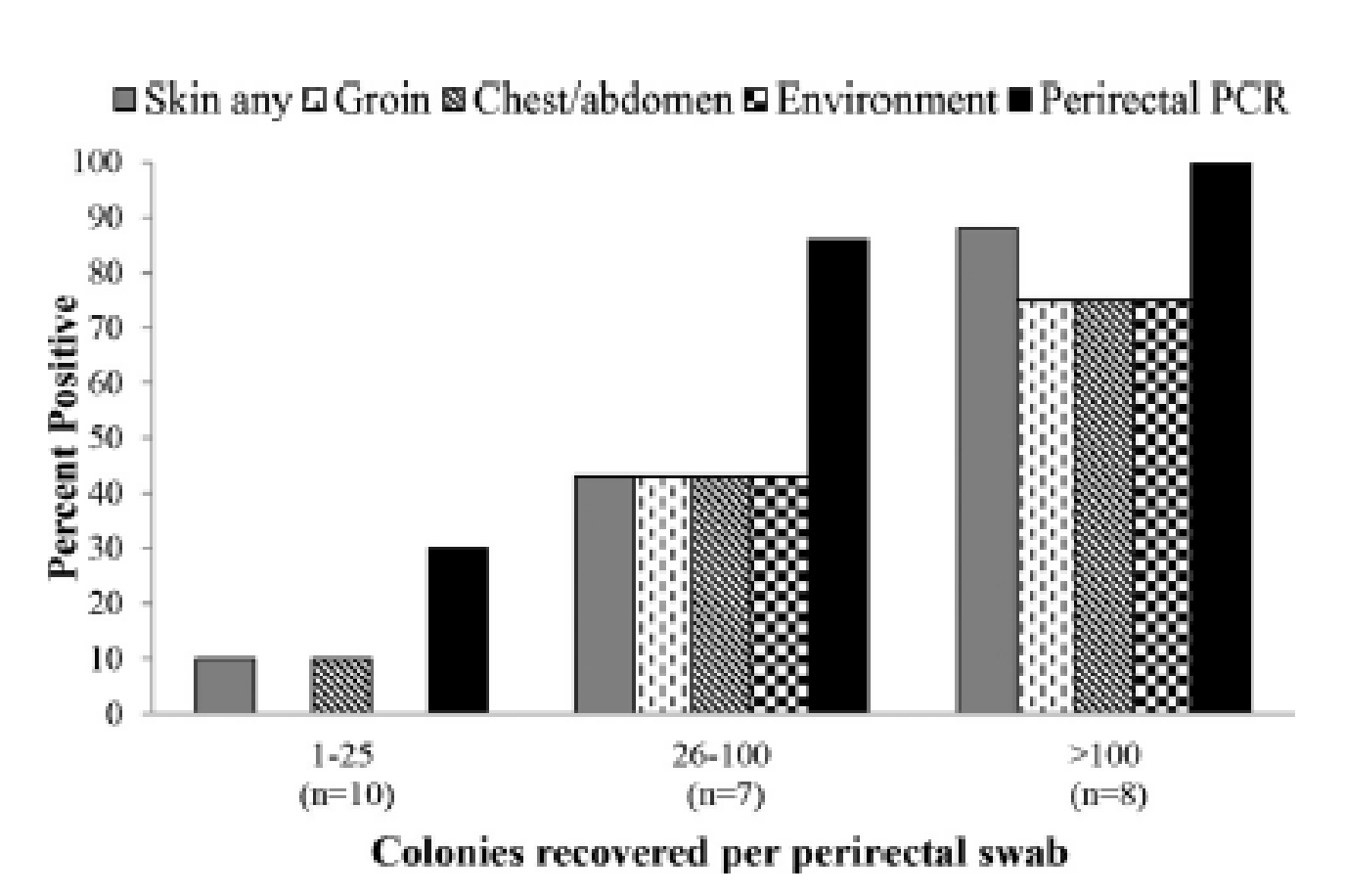
- Asymptomatic carriage increases with healthcare and especially antibiotic exposures in later life
- Asymptomatic carriage contributes to transmission
  - Even mild diarrhea and incontinence may promote spread
- Infection control and treatment decisions currently linked based on diagnosis of CDI
  - 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



Abujamel T et al. PLoS One. 2013 Oct 2;8(10):e76269

Degree of Intestinal Colonization is a Likely Determinant of Contagiousness



Donskey CJ et al. J Clin Microbiol 52(1):315; 2013

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 2. Frequency and Type of Outpatient Health Care Exposure in the 12 Weeks Before Community-Associated *Clostridium difficile* Infection, 2009 Through 2011

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

[a] Variables are not mutually exclusive.

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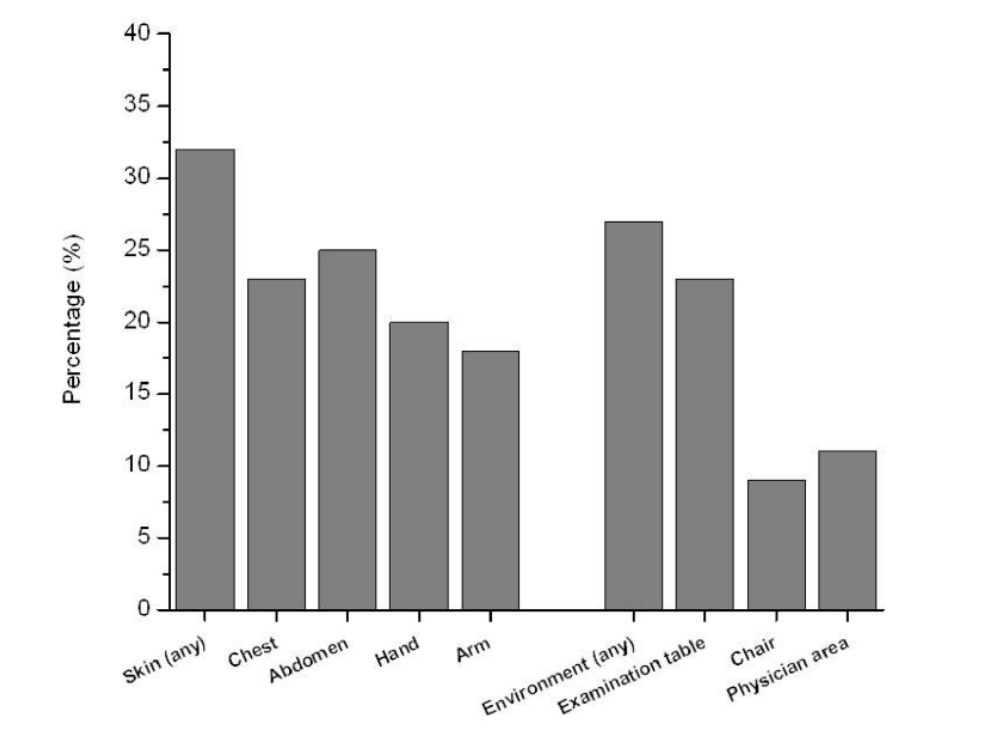
PLOS ONE

Outpatient Healthcare Settings and Transmission of *Clostridium difficile*

Lucy A. Jury[1], Brett Sitzlar[1], Sirisha Kundrapu[2], Jennifer L. Cadnum[2], Kim M. Summers[3], Christine P. Muganda[4], Abhishek Deshpande[2], Ajay K. Sethi[4], Curtis J. Donskey[1,2]*

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



Jury LA et al. PLoS ONE 8(7): e70175.

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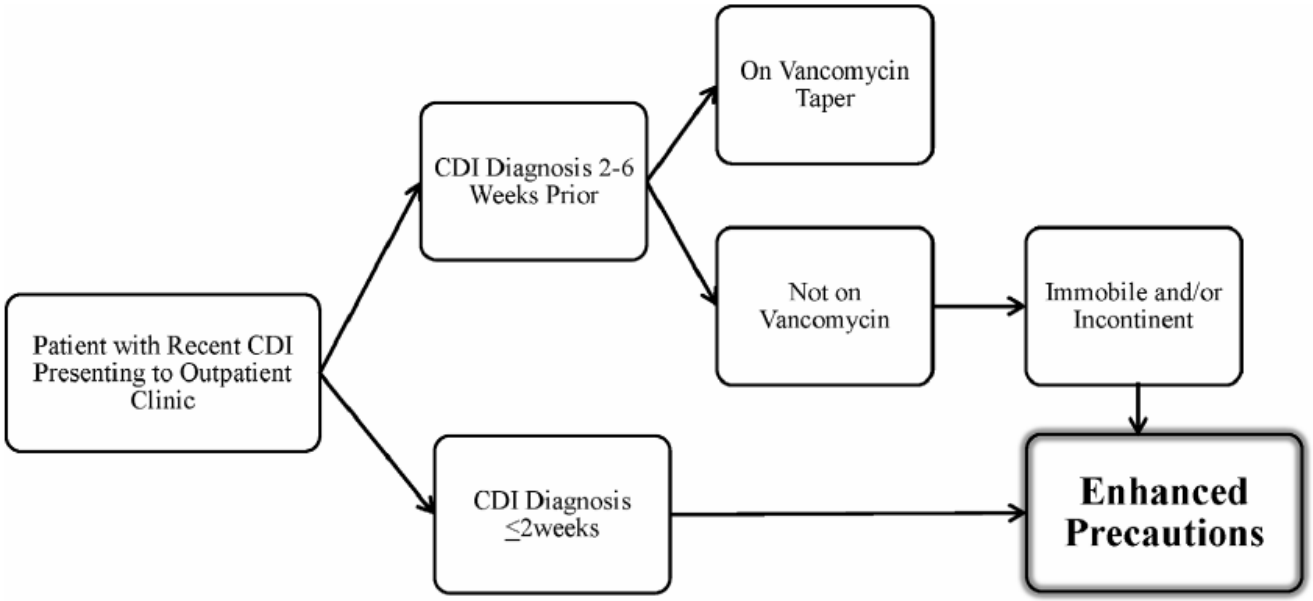

Figure 2. Proposed algorithm for management of patients with recent *Clostridium difficile* infection (CDI) presenting to outpatient clinics. Enhanced precautions includes wearing gloves when examining patients and cleaning high-touch surfaces with sporicidal disinfectants after visits.

Jury LA et al. PLoS ONE 8(7): e70175.

Medication Use in Community-associated CDI, 2009-2011

Medication use within 12 wk before *C difficile* infection, No./total No. (%)[a]	
Antibiotics[b]	631 (64.1)
Cephalosporins	149/631 (23.6)
β-Lactam or β-lactamase inhibitors	145/631 (23.0)
Penicillins	143/631 (22.7)
Fluoroquinolones	139/631 (22.0)
Clindamycin	119/631 (18.9)
Macrolides	60/631 (9.5)
Folic acid inhibitors	38/631 (6.0)
Tetracyclines	15/631 (2.4)
Proton pump inhibitors	273 (27.7)
H_2-receptor antagonists	90 (9.1)
Immune-suppressing agents[c]	91 (9.2)

Most common reasons for antibiotics: upper respiratory and dental procedures

Chitnis et al. JAMA Intern Med. 2013;173(14):1359-1367

For More Information

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