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Health Quality Innovation Network

Thank you

Virginia HAI Advisory Group;

Antimicrobial Stewardship Workgroup

HQI
HEALTH QUALITY INNOVATORS

VDH VIRGINIA DEPARTMENT OF HEALTH

VHHA
CENTER FOR HEALTHCARE EXCELLENCE
Improving the Quality & Safety of Healthcare

[HAI Advisory Group - HAIAR (virginia.gov)]

Health Quality Innovation Network

Today's Presenter

Heather L. Cox, PharmD, BCIDP

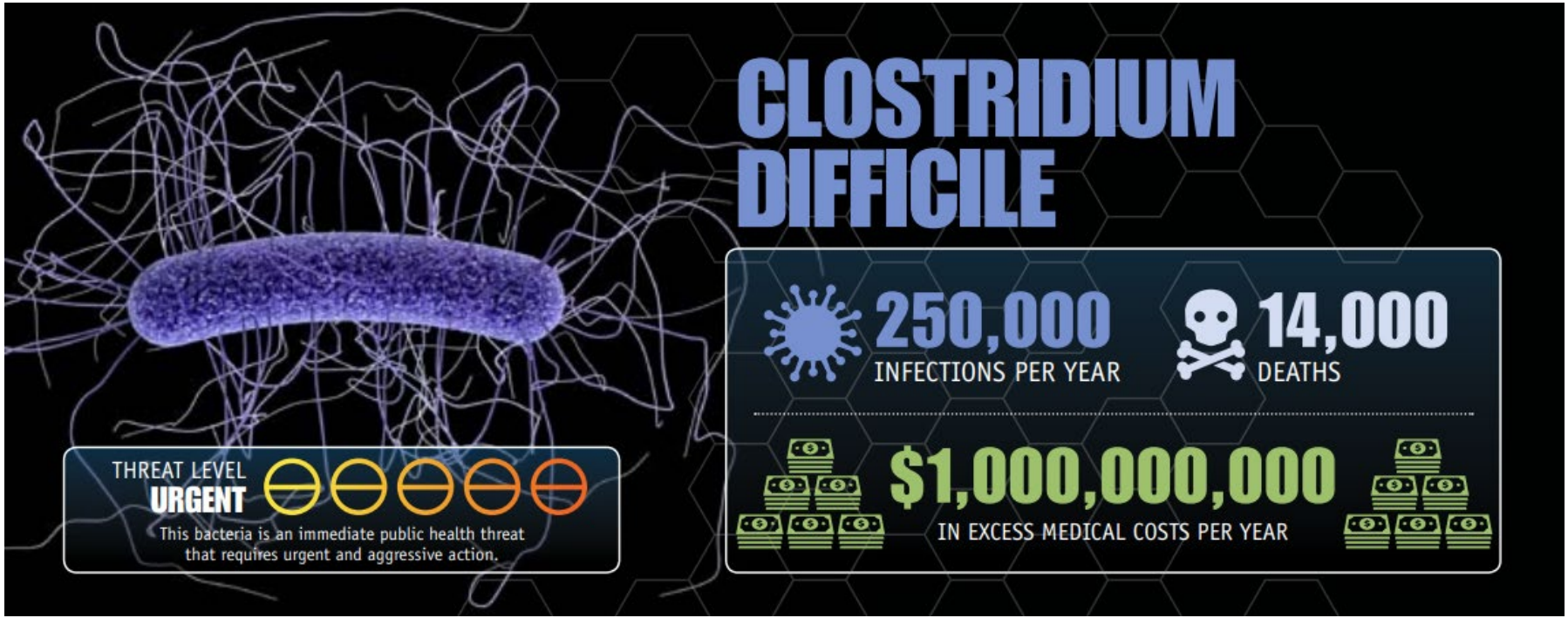
Lead Pharmacist, Infectious Diseases
Associate Director, Antimicrobial Stewardship
Clinical Assistant Professor, Division of Infectious Diseases and International Health
University of Virginia Health

Health Quality Innovation Network

Reducing Hospital-Onset *C. difficile* infection (HO-CDI) Through Diagnostic Stewardship: The University of Virginia Experience

August 31, 2022

CDC. Antibiotic resistance threats in the United States, 2019. Atlanta, GA: US DHHS, CDC; 2019.



CDC. Antibiotic resistance threats in the United States, 2013. Atlanta, GA: US DHHS, CDC; 2013.

U.S. DHHS 2013 Action Plan for HAI Prevention:
30% ↓ in HO-CDI by 2020

Created value-based incentive programs linking financial penalties to hospital performance:
HO-CDI rates reported to NHSN beginning October 2016

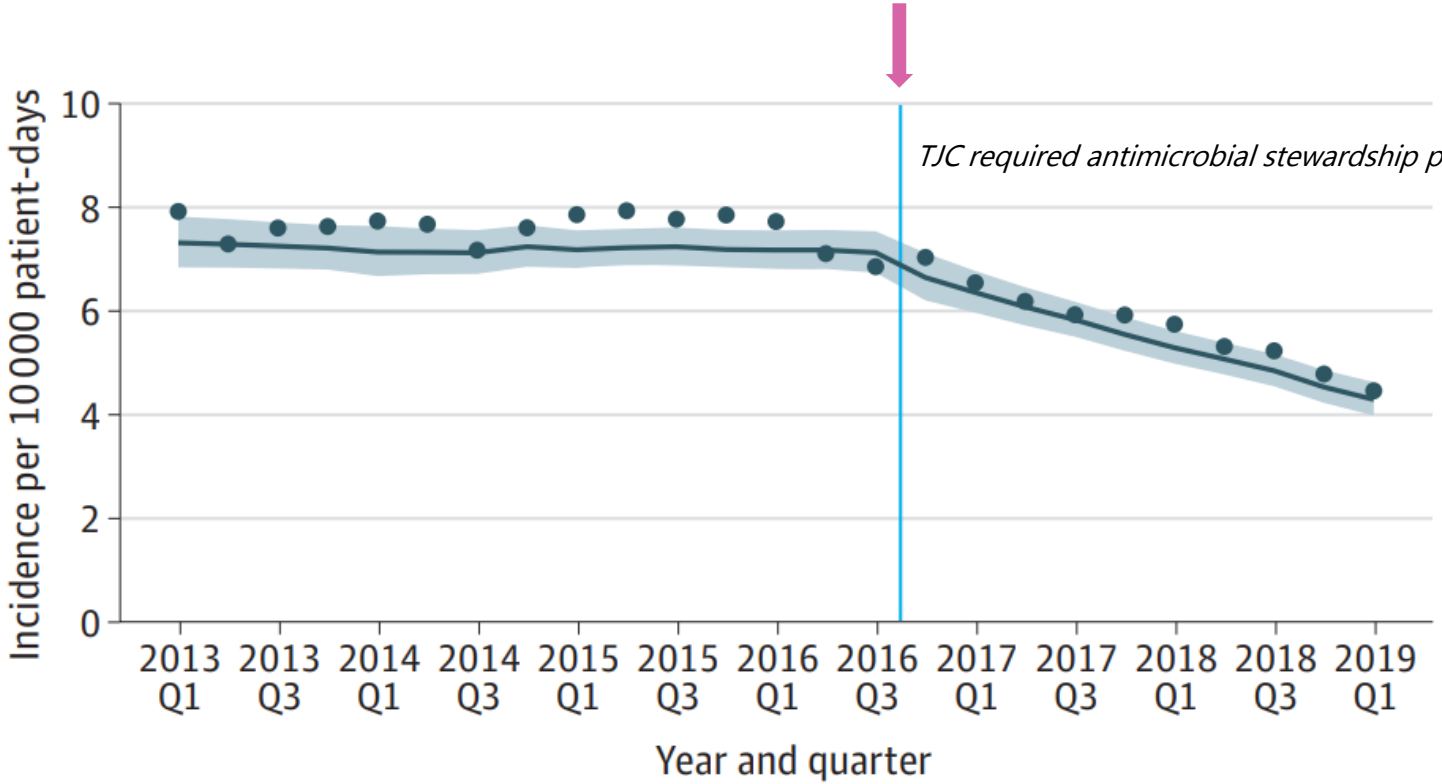
JAMA Network | Open™

Original Investigation | Infectious Diseases

Assessment of Federal Value-Based Incentive Programs and In-Hospital *Clostridioides difficile* Infection Rates

Mohammad Alrawashdeh, PhD, MSN; Chanu Rhee, MD, MPH; Heather Hsu, MD, MPH; Rui Wang, PhD; Kelly Horan, MPH; Grace M. Lee, MD, MPH

Value-based incentive program began including HO-CDI: 6% decline in 1st quarter, 4% per quarter thereafter



 Alrawashdeh M, et al. JAMA Network Open 2021;4:e2132114.

UVA Health

My goals today:

Explore diagnostic stewardship opportunities to reduce HO-CDI through the lens of the UVA Health experience.

Share our tools, outcomes and lessons learned.

UVA Health

Let's rewind to Sept 2016…

"*C. difficile* Coalition" established

UVA Health

Quality & Performance Improvement

- Chief as executive sponsor
- Coach

Antimicrobial Stewardship

- Medical Director (co-chair)
- Associate Director

Infection Prevention & Control

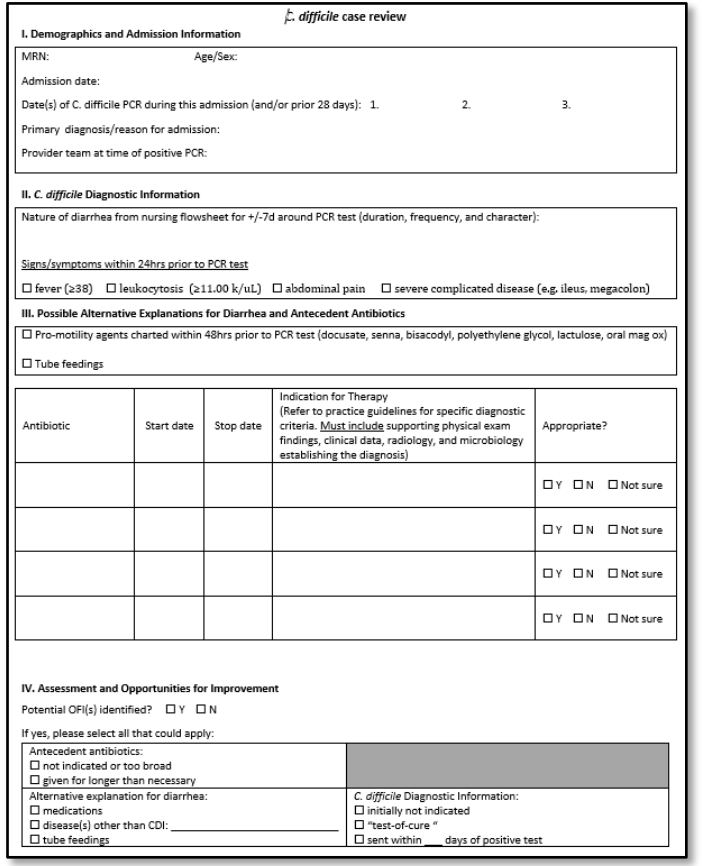
- Hospital Epidemiologist (co-chair)
- Infection Preventionists

Informatics

- Associate Chief Medical Information Officer
- Data analysts

Coalition Expectations:

- Review HO-CDI cases within 1 business day
- Connect with unit-based nurse and physician leaders following their independent review (using new case review tool)
- Identify opportunities for improvement (OFIs)
- Support unit leadership in presenting OFIs at "daily huddle" (M→F)
- Present data and action plans quarterly



C. difficile case review

I. Demographics and Admission Information

MRN: Age/Sex:

Admission date:

Date(s) of C. difficile PCR during this admission (and/or prior 28 days): 1. 2. 3.

Primary diagnosis/reason for admission:

Provider team at time of positive PCR:

II. *C. difficile* Diagnostic Information

Nature of diarrhea from nursing flowsheet for +/-7d around PCR test (duration, frequency, and character):

Signs/symptoms within 24hrs prior to PCR test

☐ fever (≥38) ☐ leukocytosis (≥11.00 k/uL) ☐ abdominal pain ☐ severe complicated disease (e.g, ileus, megacolon)

III. Possible Alternative Explanations for Diarrhea and Antecedent Antibiotics

☐ Pro-motility agents charted within 48hrs prior to PCR test (docusate, senna, bisacodyl, polyethylene glycol, lactulose, oral mag ox)

☐ Tube feedings

Antibiotic	Start date	Stop date	Indication for Therapy (Refer to practice guidelines for specific diagnostic criteria. Must include supporting physical exam findings, clinical data, radiology, and microbiology establishing the diagnosis)	Appropriate?
				☐ Y ☐ N ☐ Not sure
				☐ Y ☐ N ☐ Not sure
				☐ Y ☐ N ☐ Not sure
				☐ Y ☐ N ☐ Not sure

IV. Assessment and Opportunities for Improvement

Potential OFI(s) identified? ☐ Y ☐ N

If yes, please select all that could apply:

Antecedent antibiotics: ☐ not indicated or too broad ☐ given for longer than necessary	
Alternative explanation for diarrhea: ☐ medications ☐ disease(s) other than CDI: _____ ☐ tube feedings	*C. difficile* Diagnostic Information: ☐ initially not indicated ☐ "test-of-cure " ☐ sent within ___ days of positive test

Daily Huddle

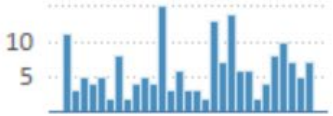
View all metrics »

Mortalities

7

30-day Readmissions
All Cause

0



Pressure Injuries
Stage I and Above

0

Patient Handling
Team Member Injuries

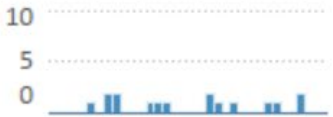
0

Inpatient Falls with Injury

0

Potential CLABSI Notifications

0



CAUTI Notifications

0

Potential C. *diff* Infections

1

OFIs assigned to 3 “buckets” with leaders for each

UVA Health

Infection control measures to limit the spread of *Clostridium difficile*

R.-P. Vonberg[1], E. J. Kuijper[2], M. H. Wilcox[3], F. Barbut[4], P. Tüll[5], P. Gastmeier[1], on behalf of the European C. difficile-Infection Control Group and the European Centre for Disease Prevention and Control (ECDC), P. J. van den Broek[2], A. Coltville[6], B. Coignard[7], T. Daha[8], S. Dehast[9], B. I. Duerden[10], S. van den Hof[11], T. van der Kooi[11], H. J. H. Maarleveld[2], E. Nagy[12], D. W. Notermans[11], J. O'Driscoll[13], B. Patel[14], S. Stone[15] and C. Wiuff[16]

[1]Institute for Medical Microbiology and Hospital Epidemiology, Medical School Hannover, Hannover, Germany, [2]Leiden University Medical Centre, Leiden, The Netherlands, [3]Department of Microbiology, Leeds Teaching Hospitals and University of Leeds, Leeds, UK, [4]Unité d'Hygiène et de Lutte contre les Infections Nosocomiales, Hôpital Saint-Antoine, Paris, France, [5]European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden, [6]Royal Devon and Exeter Hospital NHS Foundation Trust, Exeter, UK, [7]Institut de Veille Sanitaire, Saint-Maurice, France, [8]The Dutch Working Party Infection Control, Leiden, [9]Meander Medical Centre, Amersfoort, The Netherlands, [10]Department of Health, London, UK, [11]Centre for Infectious Disease Control Netherlands, National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands, [12]Institute of Clinical Microbiology, Faculty of Medicine, University of Szeged, Szeged, Hungary, [13]Stoke Mandeville Hospital, Stoke Mandeville, Buckinghamshire, UK, [14]Health Protection Agency, London, UK, [15]Academic Department of Geriatric Medicine, Hampstead Campus, Royal Free and University College Medical School, London, UK and [16]Health Protection Scotland, Glasgow, UK

ABSTRACT

Clostridium difficile-associated diarrhoea (CDAD) presents mainly as a nosocomial infection, usually after antimicrobial therapy. Many outbreaks have been attributed to *C. difficile*, some due to a new hypervirulent strain that may cause more severe disease and a worse patient outcome. As a result of CDAD, large numbers of *C. difficile* spores may be excreted by affected patients. Spores then survive for months in the environment; they cannot be destroyed by standard alcohol-based hand disinfection, and persist despite usual environmental cleaning agents. All these factors increase the risk of *C. difficile* transmission. Once CDAD is diagnosed in a patient, immediate implementation of appropriate infection control measures is mandatory in order to prevent further spread within the hospital. The quality and quantity of antibiotic prescribing should be reviewed to minimise the selective pressure for CDAD. This article provides a review of the literature that can be used for evidence-based guidelines to limit the spread of *C. difficile*. These include early diagnosis of CDAD, surveillance of CDAD cases, education of staff, appropriate use of isolation precautions, hand hygiene, protective clothing, environmental cleaning and cleaning of medical equipment, good antibiotic stewardship, and specific measures during outbreaks. Existing local protocols and practices for the control of *C. difficile* should be carefully reviewed and modified if necessary.

Keywords *Clostridium difficile*, evidence-based guidelines, infection control measures

Clin Microbiol Infect 2008; **14** (Suppl. 5): 2–20

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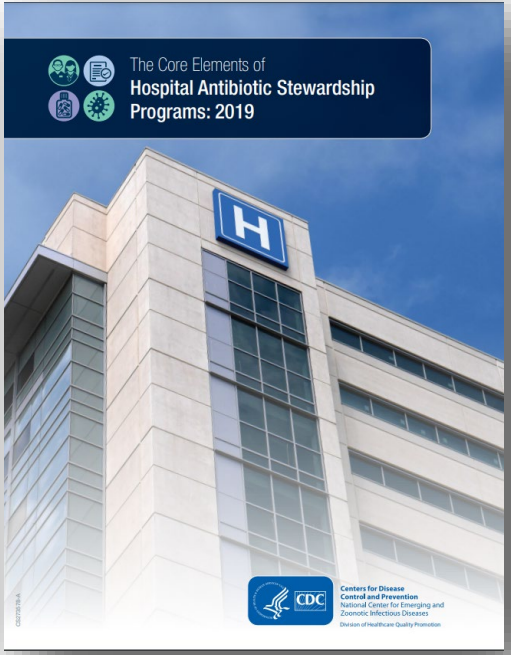
The authors declare that they have no financial conflicts of interest.

Journal Compilation European Society of Clinical Microbiology and Infectious Diseases, *CMI*, **14** (Suppl. 5), 2–20

Environmental Stewardship



Antimicrobial Stewardship

ORIGINAL ARTICLE

Inappropriate *Clostridium difficile* Testing and Consequent Overtreatment and Inaccurate Publicly Reported Metrics

Sean G. Kelly, MD;[1] Michael Yarrington, MD;[2] Teresa R. Zembower, MD;[1,3] Sarah H. Sutton, MD;[1,3] Christina Silkaitis, MT;[4] Michael Postelnick, RPh;[4] Anessa Mikolajczak, BSN;[4] Maureen R. Bolon, MD[1,3]

BACKGROUND. The nationally reported metric for *Clostridium difficile* infection (CDI) relies solely on laboratory testing, which can result in overreporting due to asymptomatic *C. difficile* colonization.

OBJECTIVE. To review the clinical scenarios of cases of healthcare facility-onset CDI (HO-CDI) and to determine the appropriateness of *C. difficile* testing on the basis of presence of symptomatic diarrhea in order to identify areas for improvement.

DESIGN. Retrospective cohort study.

SETTING. Northwestern Memorial Hospital, a large, tertiary academic hospital in Chicago, Illinois.

PATIENTS. The cohort included all patients with a positive *C. difficile* test result who were reported to the National Healthcare Safety Network as HO-CDI during a 1-year study period.

METHODS. We reviewed the clinical scenario of each HO-CDI case. On the basis of documentation and predefined criteria, appropriateness of *C. difficile* testing was determined; cases were deemed appropriate, inappropriate, or indeterminate. Statistical analysis was performed to compare demographic and clinical parameters among the categories of testing appropriateness.

RESULTS. Our facility reported 168 HO-CDI cases to NHSN during the study period. Of 168 cases, 33 (19.6%) were judged to be appropriate tests, 25 (14.8%) were considered inappropriate, and 110 (65.5%) were indeterminate. Elimination of inappropriate testing would have improved our facility's standardized infection ratio from 0.962 to 0.819.

CONCLUSION. Approximately 15% of HO-CDI cases were judged to be tested inappropriately. Testing only patients with clinically significant diarrhea would more accurately estimate CDI incidence, reduce unnecessary antibiotic use, and improve facilities' performance of reportable CDI metrics. Improved documentation could facilitate targeted interventions.

Infect Control Hosp Epidemiol 2016;37:1395–1400

Clostridium difficile infection (CDI) has become the most common healthcare-associated infection in the United States, surpassing even methicillin-resistant *Staphylococcus aureus*.[1] CDI is substantially burdensome; inpatient CDI has been estimated to cost up to $15,000 per episode, with a national annual hospital cost of up to $4.8 billion.[2] Further, CDI increases length of stay, increases likelihood of discharge to a long-term care facility, and imparts a mortality of up to 10%.[3] Molecular diagnostics may contribute to the nationally increasing incidence of CDI owing to the high sensitivity of polymerase chain reaction (PCR) in detecting the presence of *C. difficile*.[3] This testing modality may lead to overdiagnosis of CDI in patients who have asymptomatic colonization with *C. difficile*. Polage et al[4] demonstrated that only 44.7% of patients with positive results for *C. difficile* by PCR had detectable *C. difficile* toxin by a concurrent toxin assay, suggesting that more than 50% of positive PCR tests represent asymptomatic colonization, thus overestimating the true incidence of infection.

Currently, the National Healthcare Safety Network (NHSN) requires that acute care hospitals report laboratory-identified CDI as the sole means of surveillance. NHSN classifies CDI types into 3 categories: healthcare facility-onset CDI (HO-CDI: laboratory identification of *C. difficile* in a stool specimen collected ≥4 days after admission to the facility), community-associated CDI (laboratory identification of *C. difficile* in a stool specimen collected in an outpatient location or an inpatient location <4 days after admission to the facility), and community-onset healthcare facility-associated (laboratory identification of *C. difficile* in a stool specimen collected from a

Affiliations: 1. Vanderbilt University School of Medicine, Division of Infectious Diseases, Nashville, Tennessee; 2. Northwestern Feinberg School of Medicine, Department of Medicine, Chicago, Illinois; 3. Northwestern Memorial Hospital, Department of Healthcare Epidemiology and Infection Prevention, Chicago, Illinois; 4. Northwestern Memorial Hospital, Department of Pharmacy, Chicago, Illinois; 5. Northwestern Memorial Healthcare, Department of Healthcare Epidemiology and Infection Prevention, Winfield, Illinois.

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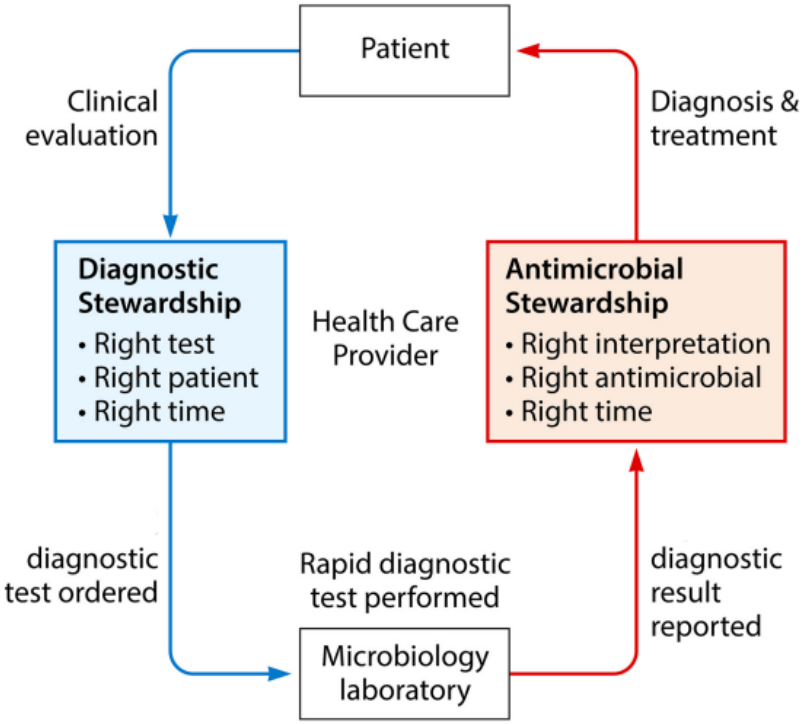
 0899-823X/2016/3712-0005. DOI: 10.1017/ice.2016.230

Diagnostic Stewardship

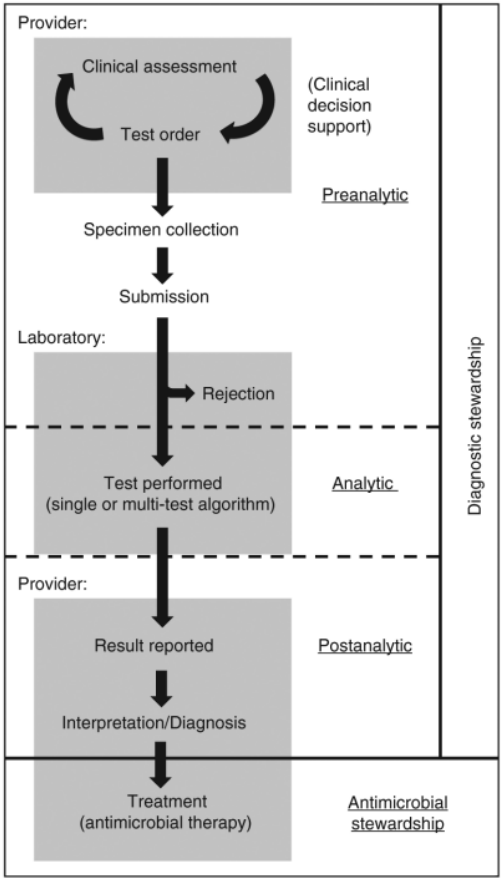
Slide adapted courtesy of Costi Sifri, MD

Diagnostic stewardship goals

Selecting the right test  **for the right patient**  **at the right time**  **to optimize clinical outcomes and antimicrobial use.** 



 Messacar K, et al. J Clin Microbiol 2017;55:715-23.



Diagnostic stewardship in 3 stages:

Pre-analytic: Test decision-making and specimen collection

Analytic: Which test(s) to offer?

Post-analytic: Results interpretation and reporting

Madden GR, Poulter MD, Sifri CD. Diagnosis 2018;5:119-25.

The challenge of CDI diagnostics

- **12-32%** of hospitalized patients develop diarrhea BUT **<20%** is attributable to CDI
- Asymptomatic carriage occurs in **3.4-8.1%** upon admission and up to **~50%** in patients with cystic fibrosis or those in rehab or long-term care facilities
- No testing strategy can definitively confirm CDI
- No prospectively validated diagnostic criteria for CDI exist → based on combination of clinical and laboratory findings

Infect Control Hosp Epidemiol 2010;31:431-55; BMC Infect Dis 2015; 15 :516; Clin Infect Dis 2018;66:e1-e48; Infect Dis Ther 2021;10:687-97.

Poll: What is the primary testing method for *C. difficile* used most often by your facility's laboratory or the laboratory where your facility's testing is performed?

A. Single-step: Enzyme immunoassay (EIA) for toxin
B. Single-step: Nucleic acid amplification test (NAAT) e.g. PCR
C. Multistep: NAAT + EIA
D. Multistep: glutamate dehydrogenase (GDH) + EIA
E. Multistep: GDH + EIA arbitrated by NAAT
F. Other
G. Not sure

Table 1 Summary of available tests for *Clostridium difficile* infection [5, 6, 12]

Test	Sensitivity	Specificity	Substance detected
Toxigenic culture (TC, reference test)	> 95%	80–90%	*C. difficile* bacteria or spores
Nucleic acid amplification test (NAAT)	92–97%	83–100%	*C. difficile* nucleic acid (toxin genes)
Glutamate dehydrogenase (GDH)	86–99%	88–100%	*C. difficile* common enzyme
Toxin A and B enzyme immunoassays (EIA)	51–63%	91–100%	Presence of active toxin production
Glutamate dehydrogenase + toxin A/B immunoassay (GDH + Toxin EIA)	83–100%	91–100%	Suggestive of CDI if compatible signs and symptoms present
Nucleic acid amplification + Toxin immunoassay (NAAT + Toxin EIA)	77–100%	91–100%	Suggestive of CDI if compatible signs and symptoms present

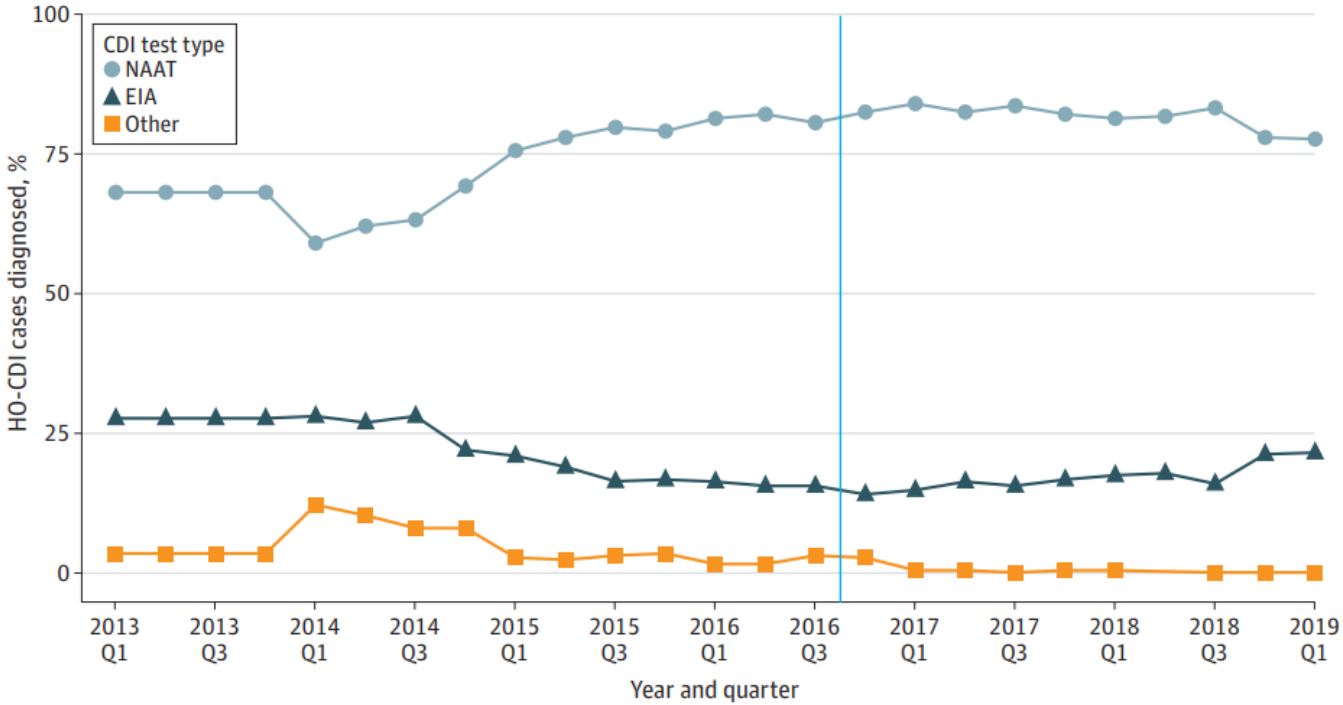
JAMA Network Open™

Original Investigation | Infectious Diseases

Assessment of Federal Value-Based Incentive Programs and In-Hospital *Clostridioides difficile* Infection Rates

Mohammad Alrawashdeh, PhD, MSN; Chanu Rhee, MD, MPH; Heather Hsu, MD, MPH; Rui Wang, PhD; Kelly Horan, MPH; Grace M. Lee, MD, MPH

Figure 1. Percentage of Cases of Health Care Facility–Onset *Clostridioides difficile* Infection (HO-CDI) Diagnosed by Different Testing Methods at 265 US Hospitals, 2013 to 2019



Most hospitals used NAAT as the predominant testing method

BUT

since it cannot distinguish between infection and colonization…

 Alrawashdeh M, et al. JAMA Network Open 2021;4:e2132114.

Research

Original Investigation

Overdiagnosis of *Clostridium difficile* Infection in the Molecular Test Era

Christopher R. Polage, MD, MAS; Clare E. Gyorke, BS; Michael A. Ke
David L. Chin, PhD; Susan Wang, BS; Hien H. Nguyen, MD, MAS; Bin
Lenora W. Lee, MD; Kyoungmi Kim, PhD; Sandra Taylor, PhD; Patricl
Edward A. Panacek, MD, MPH; Parker B. Goodell, BS, MPH; Jay V. S

ORIGINAL ARTICLE

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REVIEW

Clostridium difficile: Diagnosis and the Consequence of Over Diagnosis

Helen S. Lee · Kamryn Plechot · Shruti Gohil · Jennifer Le

 Polage CR, et al. JAMA Intern Med 2015;175:1792-1801. Kelly SG, et al. ICHE 2016; 37:1395-1400; Lee HS, et al. Infect Dis Ther 2021;10:687-97.

Pre-analytic phase

How were we deciding to test?
Were our specimens appropriate?

UVA Health

Case Reviews:

Example Quarterly Summary of Diagnostic Opportunities for Improvement

UVA Health

Case	Service	OFI type	Detail
1	Digestive Health	Low probability Lack of signs/symptoms	High ileostomy output after total colectomy No fever, WBC, abdominal pain
2	Medical subspecialties	Alternative explanation	Laxative use Suspected opioid withdrawal
3	Medical subspecialties	Lack of signs/symptoms	Aspiration pneumonia, loose stools resolved without treatment
4	Oncology	Alternative explanation	Chemotherapy-associated diarrhea No fever, WBC, abdominal pain
5	Heart & Vascular	Alternative explanation Lack of signs/symptoms Delayed collection	Laxative use No fever, WBC, abdominal pain Ordered on admission, sent hospital day 4

Other feedback: smell is not predictive, lack of documentation, testing not appropriate for patient placement, formed stool sent to lab

Should I send this stool for Clostridium Difficile (CD) testing?

When to suspect CD: ≥ 3 Loose or Watery Stools in 24 hours[1] while not on agents that induce diarrhea (i.e. laxatives, antacids, tube feeds, etc.) and presence of clinical signs/symptoms consistent with CD (fever | increased WBC | abdominal pain/distension)

Please send only 1 specimen per patient as increased testing does not increase sensitivity.

Patient with a recent positive test (last 28 days) with clinical signs of symptoms of C. diff do not need additional testing[2] but may require retreatment.

NO YES

Fast Fact: *1 in 5 patients in the hospital are colonized with C. diff[3] and 1 in 2 in long term care facilities[4], so think before you test: "Does my patient have colitis?"*

For more information:

1) ICHE May 2010, vol. 31, no. 5

2) Clin Infect Dis. 2011 Nov;53(10):1003-6. Epub 2011 Oct 5.

3) N Engl J Med. 2000;342(6):390

4) Clin Infect Dis. 2007;45(8):992

Initial education focused on best practice assessment to send tests when there was a high pre-test probability of disease

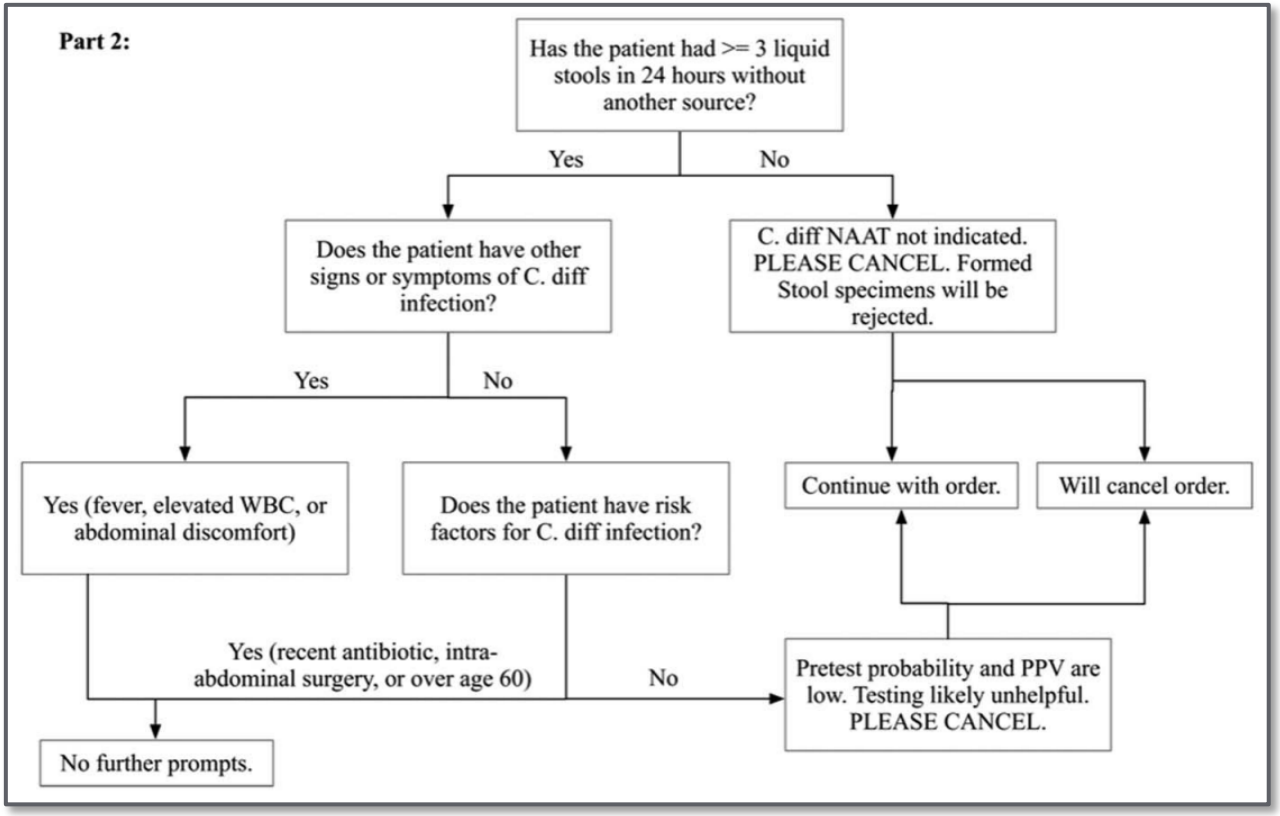
Video create by coalition and housewide distribution ensured by executive leadership

Flyers posted in workrooms and part of screensaver used on all workstations

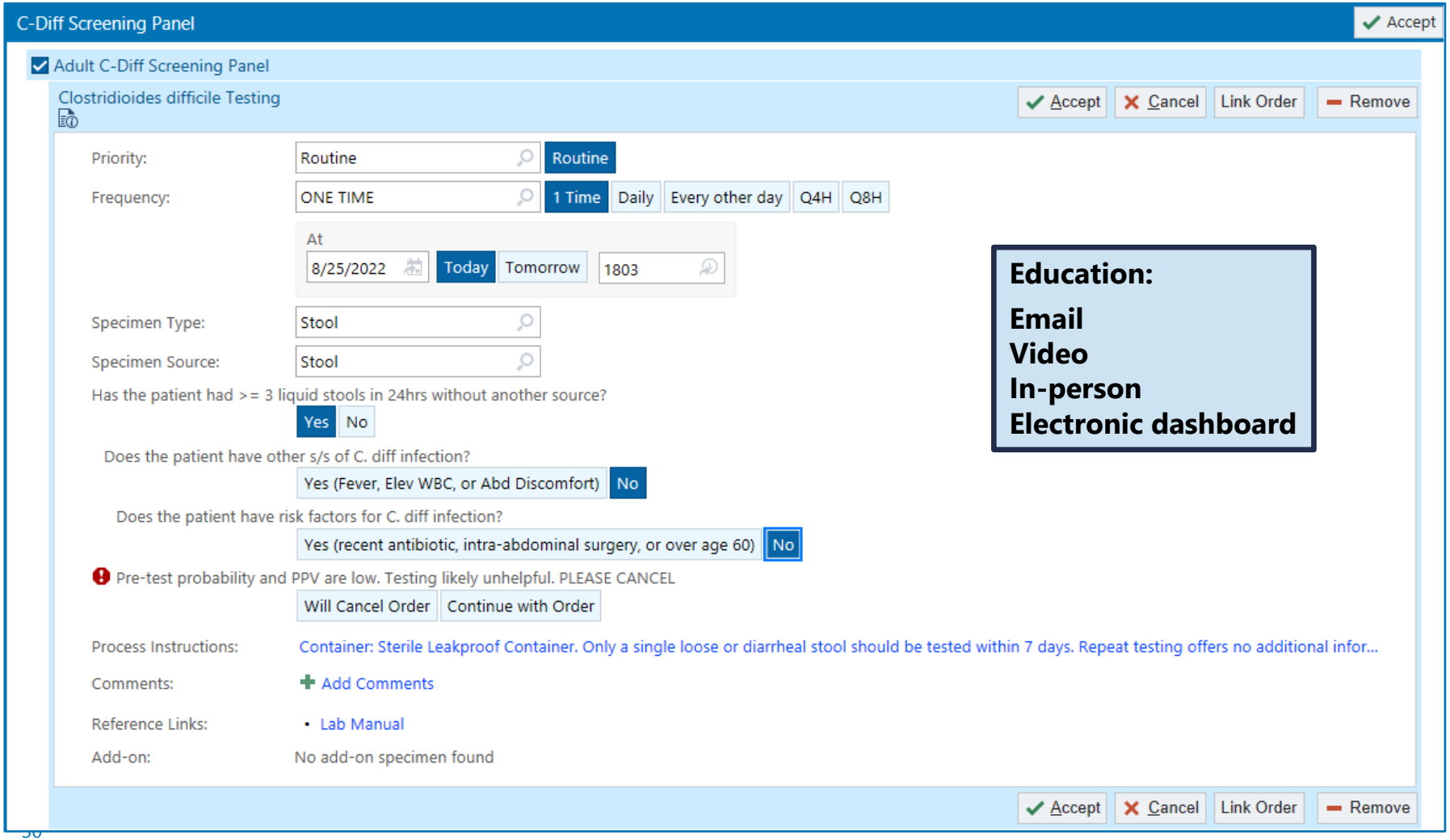
Interventions

Problem	Intervention
Delayed testing	48 hour lockout on testing following the initial order
Formed stool sent for testing	Tracked inappropriate specimens rejected for testing on QPI dashboard with real-time feedback to medical leaders and frontline staff
Low pre-test probability of disease	Computerized clinical decision support tool

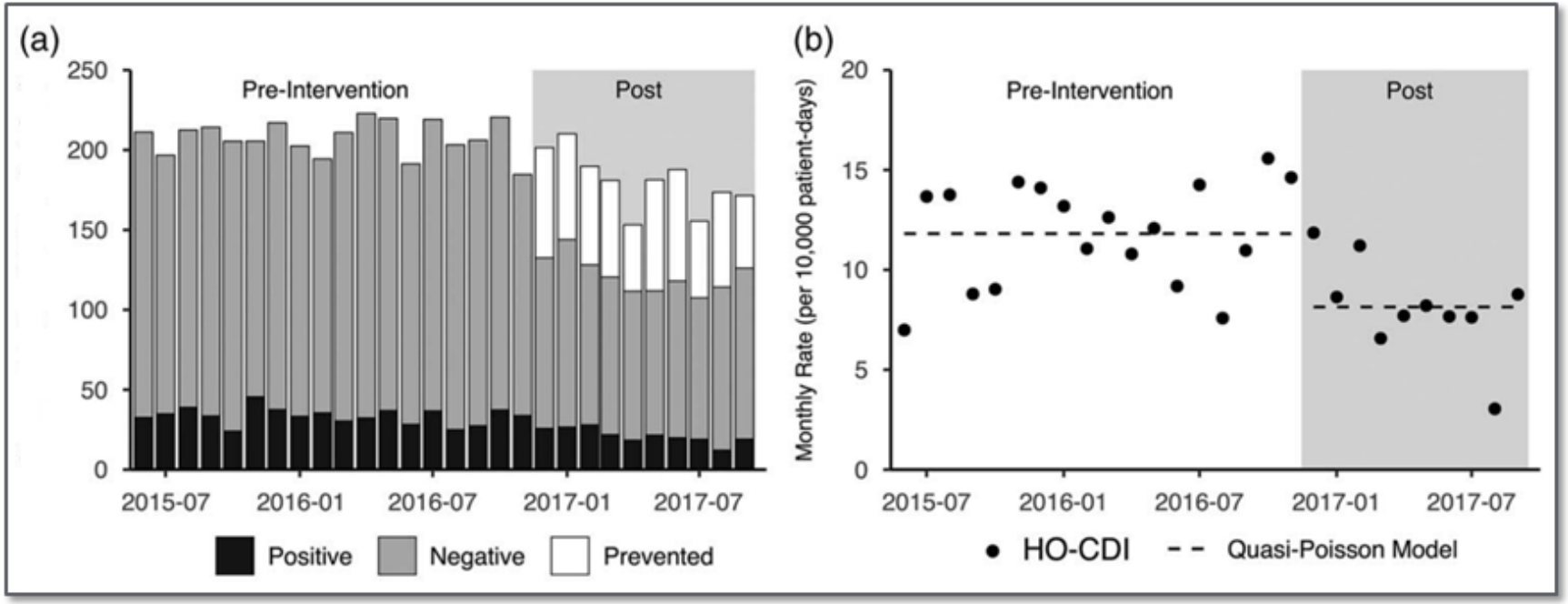
Computerized clinical decision support (CCDS) tool



Madden GR, Mesner IG, Cox HL, et al. Infect Control Hosp Epidemiol 2018;39:737-40.


C-Diff Screening Panel
Accept
Adult C-Diff Screening Panel
Clostridioides difficile Testing
Accept
Cancel
Link Order
Remove
Priority:
Routine
Routine
Frequency:
ONE TIME
1 Time
Daily
Every other day
Q4H
Q8H
At
8/25/2022
Today
Tomorrow
1803
Specimen Type:
Stool
Specimen Source:
Stool
Has the patient had >= 3 liquid stools in 24hrs without another source?
Yes
No
Does the patient have other s/s of C. diff infection?
Yes (Fever, Elev WBC, or Abd Discomfort)
No
Does the patient have risk factors for C. diff infection?
Yes (recent antibiotic, intra-abdominal surgery, or over age 60)
No
Pre-test probability and PPV are low. Testing likely unhelpful. PLEASE CANCEL
Will Cancel Order
Continue with Order
Process Instructions:
Container: Sterile Leakproof Container. Only a single loose or diarrheal stool should be tested within 7 days. Repeat testing offers no additional infor...
Comments:
Add Comments
Reference Links:
Lab Manual
Add-on:
No add-on specimen found
Accept
Cancel
Link Order
Remove
Education:
Email
Video
In-person
Electronic dashboard

CCDS tool:
41% fewer tests and 31% fewer LabID HO-CDI events



Madden GR, Mesner IG, Cox HL, et al. Infect Control Hosp Epidemiol 2018;39:737-40.

Institution	Test methodology	Provider or lab-based [primary intervention(s)]	Provider education	Hard stop[a]	Reduction in:		Patient safety systematically examined?
					Testing	CDI events	
University of Virginia [10]	NAAT	Provider (CCDS focusing on duplicate tests and indications for testing) [3]	Yes (email, video, in-person education, electronic dashboard)	No	41%	31% ↓ HO-CDI	No
University of California, Irvine [11]	NAAT	Provider (CCDS requiring indications and notified if laxative within 24 h)	None described	Yes (ID/GI specialist approval)	56%	54% ↓ HO-CDI	No
University of Pennsylvania [12]	EIA for GDH and toxin A/B then NAAT for discordant toxin results	Provider (integrated order set triggered for patients who had received laxatives within 36 h)	Yes (email, screensaver)	No	Not statistically significant (proportion inappropriate tests significantly reduced)	Not reported	Yes (no significant increase in CDI-related complications among patients with HO-CDI)
Cambridge Health Alliance [13]	NAAT (switched to GDH and toxin A/B EIA for > hospital day 3 during study)	Provider (CCDS, testing protocol triggered on hospital days 1-3 by diarrhea documentation to facilitate early testing)	Yes	No	Not reported	Statistically significant reduction in standardized infection ratio for *C. difficile*	No
Royal Victoria Hospital, UK [14]	EIA for toxin A/B	Provider (permanent decision-making algorithm visual aid checklist disseminated to staff)	Yes (memorandum)	No	4.3% (proportion inappropriate tests significantly reduced)	50% ↓ All positive tests	No
Christiana Hospital [15]	NAAT	Provider (CCDS, laxative alert)	None described	Yes (telephone laboratory approval)	30%	45% ↓ HO-CDI (not statistically significant)	No
Children's Mercy Hospital [16]	EIA for GDH and toxin A/B then NAAT for discordant toxin results	Provider (CCDS-based ordering algorithm) and lab (stolid stool specimen refusal)	Yes (lecture, newsletter article)	No	No sustained changes ordering practices observed	Not reported	No
University of Southern California [17]	NAAT	Lab (specimen refusal based on time to collection or solid stool)	Yes (memo, grand rounds, screensaver)	N/A	43%	60% ↓HO-CDI	Yes (no increase in CDI-related complications)
Stanford University [18]	NAAT	Lab (specimen refusal based on absence of clinical criteria)	None described	N/A	31%	25% ↓HO-CDI	Yes (no significant increase in leukocytosis, ICU admission, or 30 day mortality)

Madden GR, Poulter MD, Sifri CD. Diagnosis 2018;5:119-25.

Prevented tests were not associated with worse outcomes

Table 3. Univariate Analyses of Associations Between Baseline Characteristics and Combined ICU Transfer or Inpatient Mortality

Baseline Characteristics	OR (95% CI)	*P*
Age	0.996 (0.986–1.008)	.528
Male gender	1.176 (0.787–1.760)	.428
Charlson comorbidity index	0.940 (0.870–1.008)	.097
White race (reference = nonwhite)	1.737 (1.044–3.027)	.041
WBC, 10^9/L	1.063 (1.038–1.090)	<.001
Serum creatinine, mg/dL	1.050 (0.910–1.195)	.475
Vasopressors	6.11 (3.184–11.822)	<.001
ICU	4.301 (2.833–6.561)	<.001
Prevented test (reference = negative test result)	0.781 (0.466–1.267)	.332

Abbreviations: CI, confidence interval; ICU, intensive care unit location at time of trigger; OR, odds ratio; WBC, white blood cell count.

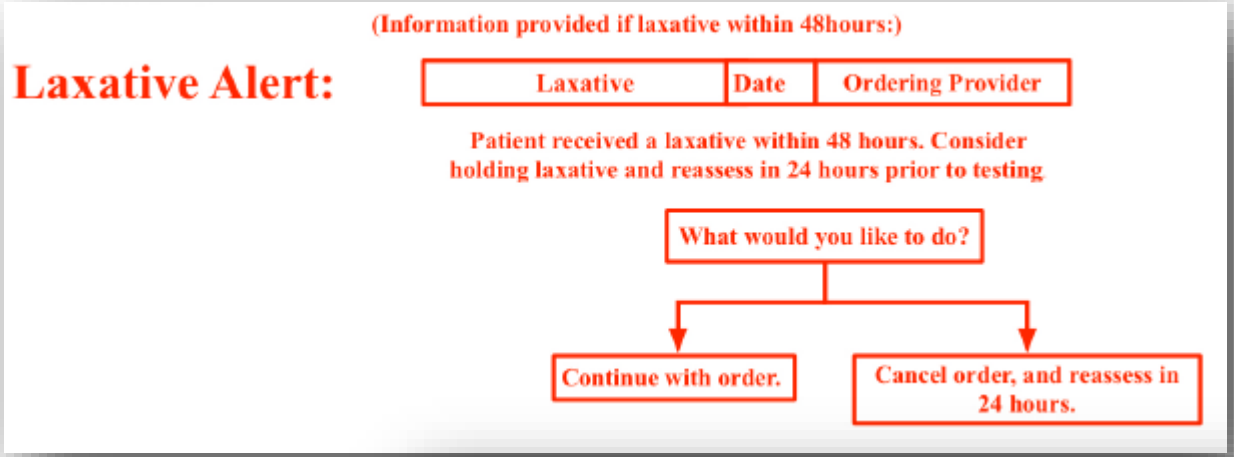
Table 4. Multivariate Analysis of Factors Associated With ICU Transfer or Inpatient Mortality

Baseline Characteristics	AOR (95% CI)	*P*
Age	0.992 (0.979–1.005)	.208
Charlson comorbidity index	0.954 (0.875–1.032)	.255
White race (vs nonwhite)	1.706 (0.971–3.140)	.073
WBC, 10^9/L	1.046 (1.021–1.074)	<.001
Vasopressors	3.467 (1.718–7.016)	<.001
ICU	2.792 (1.752–4.446)	<.001
Prevented test	0.912 (0.513–1.571)	.747

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; ICU, intensive care unit location at time of trigger; WBC, white blood cell count.

 Madden GR, Enfield KB, Sifri CD. Open Forum Infect Dis 2020 Mar18;7(4).

Laxative use feature later added to CCDS tool

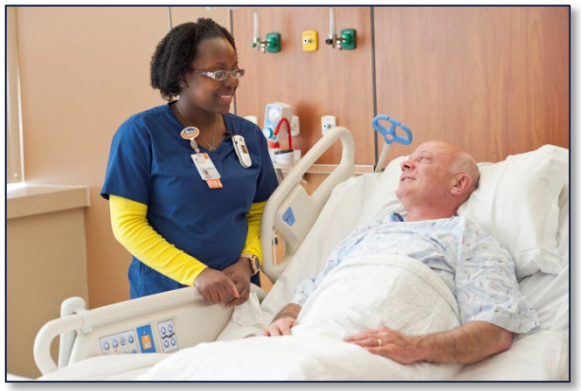


	Mean (SD)		Mean difference (95% CI)	*P*
	Original CCDS (n=25 months)	CCDS-LA (n=10 months)		
Monthly completed tests per 10,000 patient days	117.5 (12.8)	95.8 (8.8)	21.7 (12.7, 30.7)	p<0.0001
Monthly HO-CDI rate per 10,000 patient days	7.8 (2.2)	5.8 (2.0)	2.0 (0.37, 3.7)	p=0.0222

 Lau CE, Morse RG, Sifri CD, Madden GR. SHEA 2020.

Engaging our nurse colleagues in diagnostic stewardship efforts

- Bedside nurses responsible for laxative administration (often PRN orders) and stool documentation → overwhelmingly first to alert team to changes
- Case reviews revealed that nurses frequently recommended testing
- We needed to engage them in the conversation
- Created standard work for testing assessment
- Nursing leadership highly engaged and led education



UVA Health

Should I send stool for *C. difficile* testing?

General recommendations for testing in adult inpatients

The nose knows not!
Testing based on specimen odor is poorly predictive of *C. difficile* infection.

1. Frequency, Symptomatology, and Risk Factors

At least **3** watery stools within the last **24** hours **AND** clinical signs/symptoms or risk factors?

e.g. fever, ↑ WBC, abdominal pain/distension, recent antibiotics, intra-abdominal surgery, age > 60

NO → **Do NOT test**

YES ↓

2. Consistency

Stools take the **shape** of the container

NO → **Do NOT test**

YES ↓

3. Prior Testing *(including those from outside facilities)*

Is there a *C. difficile* test in the last **7** days for the **same** episode of diarrhea?

Is there a **POSITIVE** test in the last **28** days?

YES → **Do NOT test**

NO ↓

4. Alternative Explanations *for diarrhea*

Is the diarrhea explained by another cause such as new **medications?**

e.g. laxatives, chemotherapy, antibiotics, tube feedings

YES → **Do NOT test**

NO ↓

Testing is likely appropriate: discuss with LIP

UVA CDI Guidelines for CDI Diagnosis/Management & Requirements for Patient Isolation

Nursing decision support tool_v2 11/2/20

UVA Health

Should I send stool for *C. difficile* testing?

Symptomatology & Risk Factors

Clostridioides difficile ("C. diff") infection (CDI) is commonly characterized by symptoms such as watery diarrhea, fever, loss of appetite, nausea, and abdominal pain/tenderness. Leukocytosis is a frequent laboratory finding. The most important modifiable risk factor is antibiotic exposure (especially fluoroquinolones, third/fourth generation cephalosporins, clindamycin, carbapenems), while other risk factors include: gastrointestinal surgery, age > 60, prolonged hospital length of stay, and immunocompromising conditions.

Stool Characteristics

C. difficile testing may be appropriate for patients with unexplained and new-onset diarrhea characterized by at least **3** unformed stools in 24 hours. Given that asymptomatic *C. difficile* colonization may be present in up to a quarter of adult inpatients, specimens appropriate for testing should take the shape of the container (Bristol Stool Chart type 6 or 7). Formed or semi-formed stool will be rejected by Clinical Microbiology and should not be sent. Finally, specimen odor is poorly predictive of CDI and should not inform the decision to test.

Type 1	Separate hard lumps	SEVERE CONSTIPATION
Type 2	Lumpy and sausage like	MILD CONSTIPATION
Type 3	A sausage shape with cracks in the surface	NORMAL
Type 4	Like a smooth, soft sausage or snake	NORMAL
Type 5	Soft blobs with clear-cut edges	LACKING FIBRE
Type 6	Mushy consistency with ragged edges	MILD DIARRHEA
Type 7	Liquid consistency with no solid pieces	SEVERE DIARRHEA

Prior Testing

Testing should not be repeated within 7 days for the same episode of diarrhea. If the initial test was negative, a repeat test result is unlikely to change. If the initial test was positive, there is no value to establishing a "test of cure" since >60% of patients may test positive for days to weeks, even after successful treatment. Similarly, repeat testing within 28 days of a prior positive test is unlikely to be helpful. The care team should ensure that test results from referring facilities are considered in decisions to test.

Alternative Explanations

Since laboratory testing alone cannot distinguish between *C. difficile* colonization and infection, it is important to test patients who have diarrhea that is more likely to be attributable to CDI. Complicating this is that the onset of new diarrhea in hospitalized patients is common. About 12-32% of patients admitted to the hospital develop diarrhea but fewer than 20% of cases are attributable to CDI. Alternative causes accounting for most nosocomial diarrhea include medications (e.g. laxatives, antibiotics, chemotherapy), enteral feeding, and underlying illness.

References: 1) Bagdasarian N, Rao K, Malani PN. Diagnosis and treatment of *Clostridium difficile* in adults. A systematic review. JAMA 2015;313:398-408. 2) McDonald LC, Gerding DN, Johnson S, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults and children: 2017 update by the Infectious Diseases Society of American (IDSA) and Society for Healthcare Epidemiology of America (SHEA). Clin Infect Dis 2018;66:e1-48. 3) Polage CR, Solnick JV, Cohen SH. Nosocomial diarrhea: evaluation and treatment of causes other than *Clostridium difficile*. Clin Infect Dis 2012; 55:982-9. 4) Rao K, Berland D, Young C et al. The nose knows not: poor predictive value of stool sample odor for detection of *Clostridium difficile*. Clin Infect Dis 2013;56:615-6. 5) www.cdc.gov/cdiff

Analytic phase

Are we using the most appropriate testing methodology?

Post-analytic phase

How are we displaying results to the end user?

UVA Health

Research

Original Investigation

Overdiagnosis of *Clostridium difficile* Infection in the Molecular Test Era

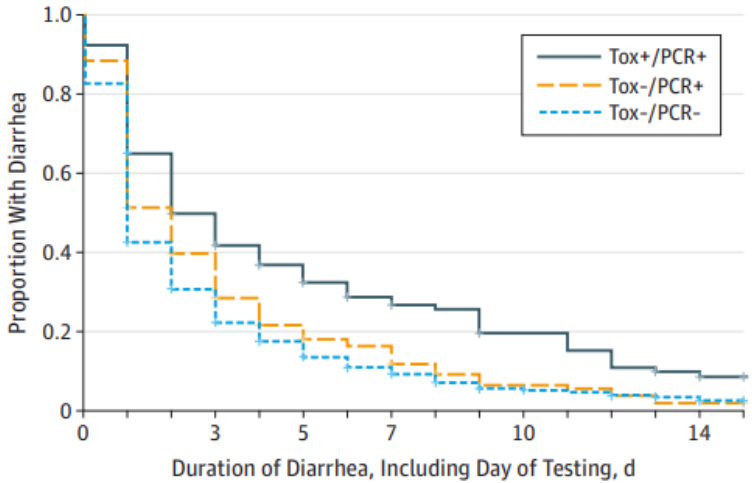
Christopher R. Polage, MD, MAS; Clare E. Gyorke, BS; Michael A. Kennedy, BS; Jhansi L. Leslie, BS; David L. Chin, PhD; Susan Wang, BS; Hien H. Nguyen, MD, MAS; Bin Huang, MD, PhD; Yi-Wei Tang, MD, PhD; Lenora W. Lee, MD; Kyoungmi Kim, PhD; Sandra Taylor, PhD; Patrick S. Romano, MD, MPH; Edward A. Panacek, MD, MPH; Parker B. Goodell, BS, MPH; Jay V. Solnick, MD, PhD; Stuart H. Cohen, MD

What if NAAT/PCR were paired with toxin testing?

 Polage CR, et al. JAMA Intern Med 2015;175:1792-1801.

What is the natural history and need for treatment of patients who are NAAT/PCR+ and toxin- for CDI?

Figure 2. Kaplan-Meier Curves of Time to Resolution of Diarrhea by *Clostridium difficile* Test Group



No. at risk

Tox+/PCR+	131	62	41	29	25	8
Tox-/PCR+	162	60	29	21	10	2
Tox-/PCR-	1123	328	172	99	42	23

- Of 293 PCR+, 55% were TOX-
- PCR+/TOX- specimens associated with milder symptoms and shorter duration of diarrhea

Polage CR, et al. JAMA Intern Med 2015;175:1792-1801.

Outcomes for PCR+/TOX- patients similar to PCR-/TOX- patients

Table 3. Nondiarrheal Outcomes and Treatment by *Clostridium difficile* Test Group

Outcome	*C difficile* Positive		*C difficile* Negative	
	Tox+/PCR+ (n = 131)	Tox−/PCR+ (n = 162)	Tox−/PCR− (n = 1123)	*P* Value[a]
***C difficile*-Related Complication or Death Within 30 d, No. (%)**				
Complication[b]	10 (7.6)	0	3 (0.3)	<.001
Death[c]	11 (8.4)	1 (0.6)	0	<.001
Complication or death	18 (13.7)	1 (0.6)	3 (0.3)	<.001

 Polage CR, et al. JAMA Intern Med 2015;175:1792-1801.

CONCLUSIONS AND RELEVANCE Among hospitalized adults with suspected CDI, virtually all CDI-related complications and deaths occurred in patients with positive toxin immunoassay test results. Patients with a positive molecular test result and a negative toxin immunoassay test result had outcomes that were comparable to patients without *C difficile* by either method. Exclusive reliance on molecular tests for CDI diagnosis without tests for toxins or host response is likely to result in overdiagnosis, overtreatment, and increased health care costs.

 Polage CR, et al. JAMA Intern Med 2015;175:1792-1801.

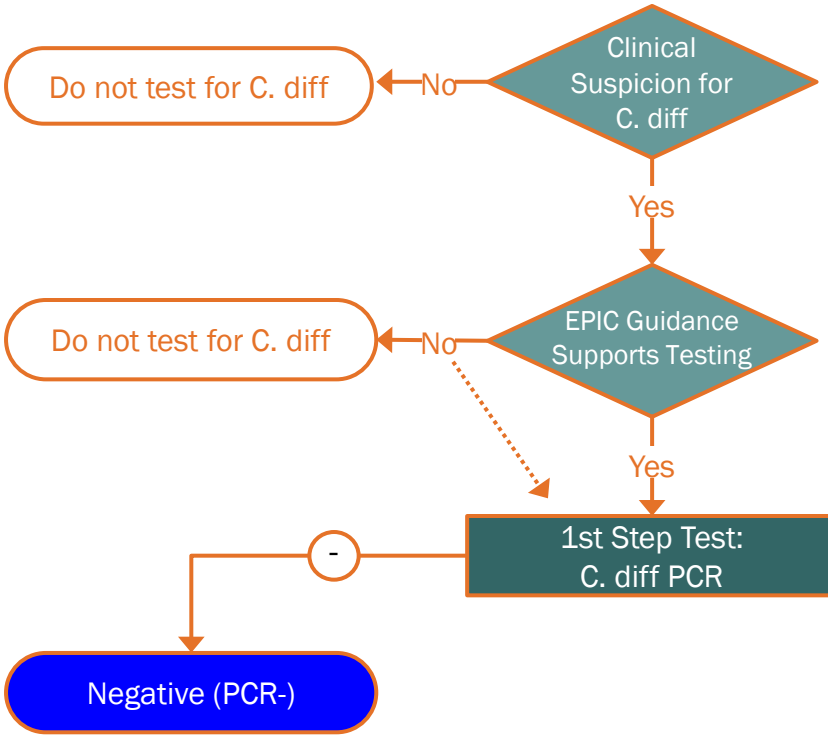
Meanwhile, the IDSA CDI Guidelines had been updated

1. Use a stool toxin test as part of a multistep algorithm rather than NAAT alone for all specimens when there are **NO** preagreed institutional criteria for patient stool submission **OR**

2. Use NAAT alone or a multistep algorithm for testing when there **ARE** preagreed institutional criteria for patient stool submission

Infectious Diseases Society of America (IDSA). Clin Infect Dis 2018;66:e1-e48.

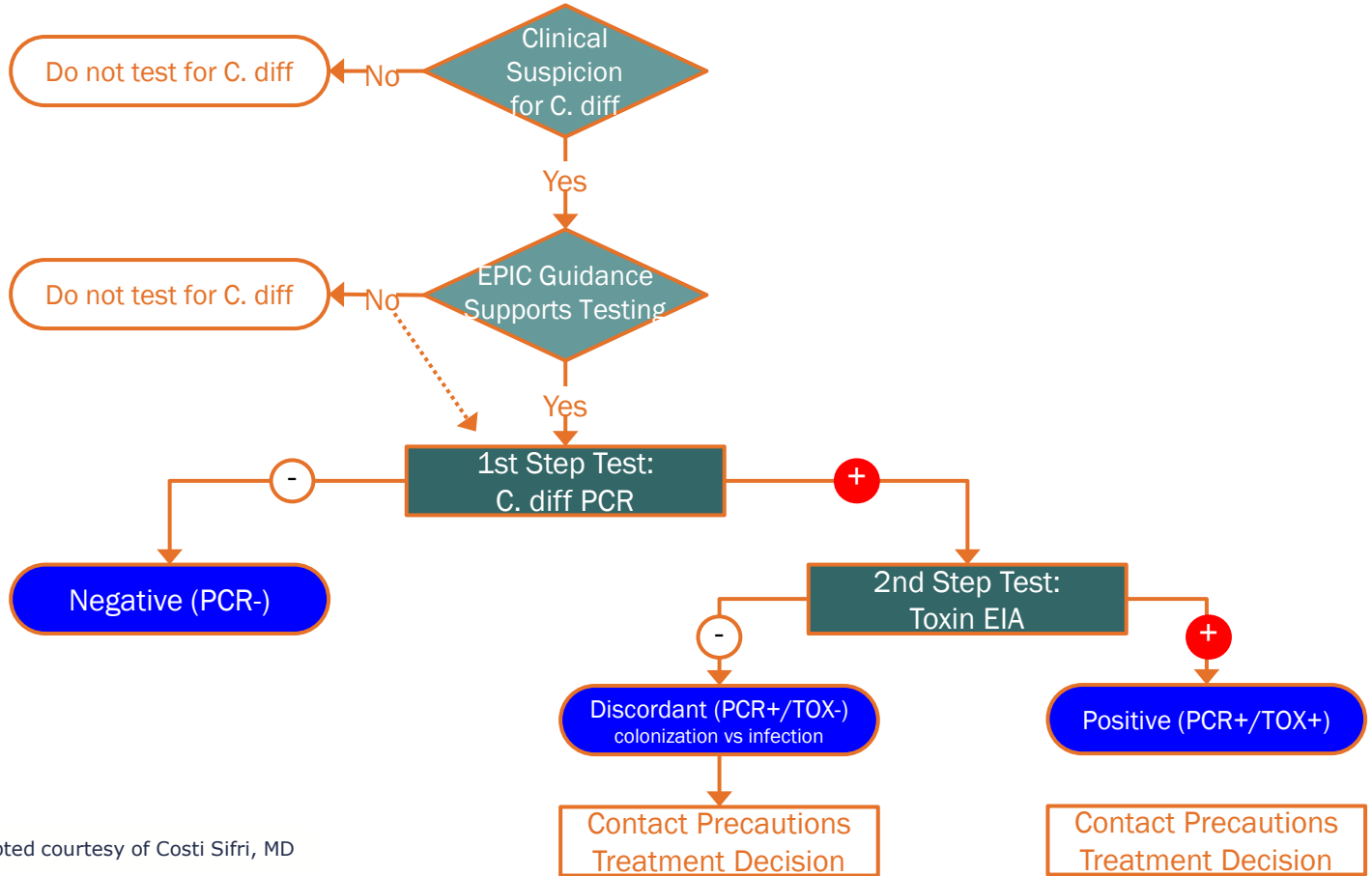
Current single step testing



Did everyone "preagree" on institutional criteria for patient sample submission?

Slide adapted courtesy of Costi Sifri, MD

New 2-step testing



Slide adapted courtesy of Costi Sifri, MD

PCR+

TOX+

Clostridioides difficile Testing

Status: **Final result**

Specimen Information: Stool

0 Result Notes

Component	Ref Range & Units	
PCR	Negative	**Positive !**
Comment: C. difficile isolation precautions required.		
Toxin Antigen	Negative	**Positive !**
Comment: Positive for toxin-producing C. difficile by PCR and Toxin Antigen, suggestive of active C. difficile infection.		
Resulting Agency		UVA MED LABS

PCR+

TOX-

Clostridioides difficile Testing

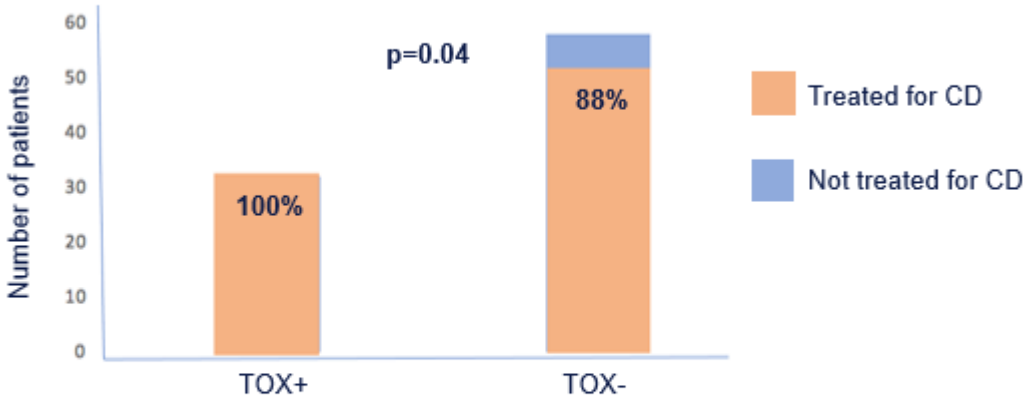
Status: **Final result**

Specimen Information: Stool

0 Result Notes

Component	Ref Range & Units	
PCR	Negative	**Positive !**
Comment: C. difficile isolation precautions required.		
Toxin Antigen	Negative	Negative
Comment: Discordant result (PCR positive, Toxin negative) may represent colonization or true infection. Clinical correlation required to determine significance. Consider an Infectious Disease consult.		
Resulting Agency		UVA MED LABS

Figure 2. Number of TOX+ versus TOX- patients receiving at least 1 dose of CD therapy



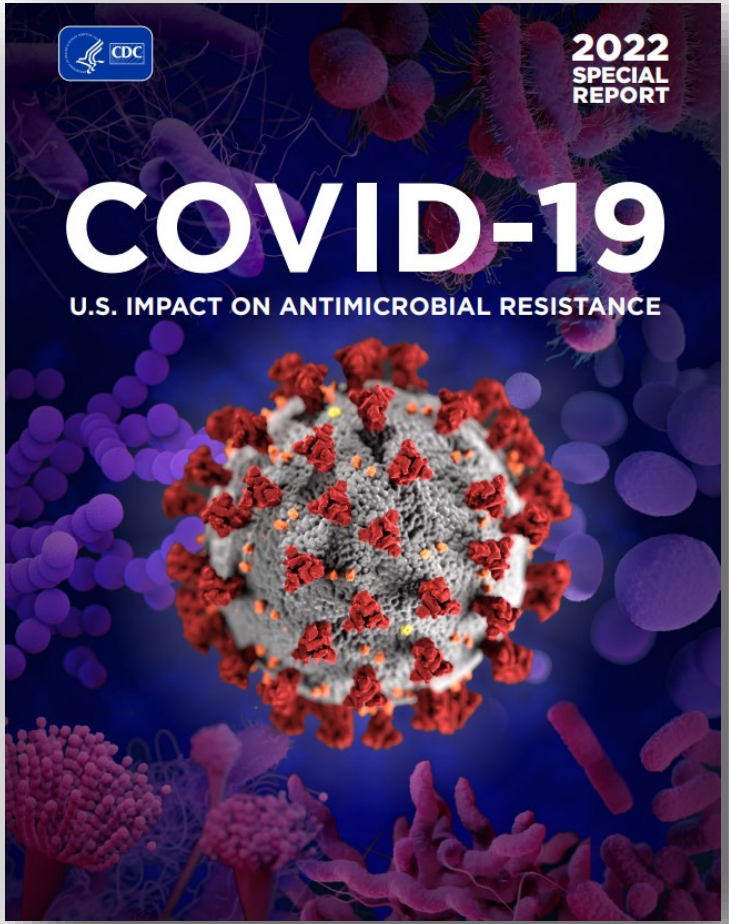
32 (100%) TOX+ (median days of therapy [IQR] = 14 [11-17])
versus
51 (88%) TOX- patients (median days of therapy [IQR] = 11 [7-14]) received CD therapy (p=0.04)

Toxin testing provided some with confidence to conclude colonization rather than infection, but not most.

ID consults often obtained but advice to stop CDI treatment often not followed.

5 in-hospital deaths with CDI as a contributing factor occurred in the TOX+ group vs none in the TOX- group.

 Dolan M, Cox H, Warren C, et al. IDWeek, 2021.



During the COVID-19 pandemic, hospitals treated sicker patients who required more frequent and longer use of catheters and ventilators. Hospitals also experienced supply challenges, reduced staff, and longer visits during the pandemic.

Unprecedented challenges could have contributed to reduced comprehensive prevention practices, which are key to stopping antimicrobial-resistant infections and their spread.

CDC. COVID-19: U.S. Impact on Antimicrobial Resistance, Special Report 2022. Atlanta, GA: US DHHS, CDC; 2022.

Clostridioides difficile (*C. diff*)

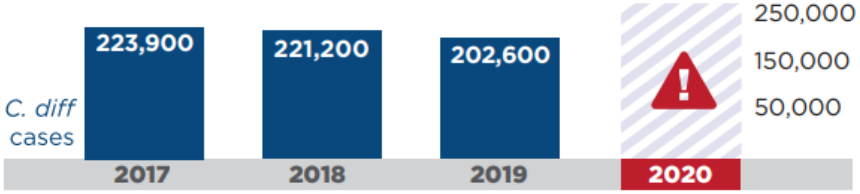
One of the most common healthcare-associated infections, affecting thousands of people every year

Other CDC data suggest a continued decrease for hospitalized *C. diff* infections in 2020 during the COVID-19 pandemic, likely driven in part by changes in healthcare-seeking behavior.

Factors that might have contributed to declines in hospitalized *C. diff* infections through 2019 include:

- Increased emphasis on diagnostic stewardship to reduce inappropriate testing
- Continued adherence to recommended infection prevention and control measures
- Continued implementation of inpatient antibiotic stewardship programs

The number of patients hospitalized with *C. diff* infections continues to decrease, building on nationwide declines since 2017. However, 2020 data were delayed by the pandemic.



The number of *C. diff* infections and deaths continued to decrease from 2017 through 2019. These estimates are not available for 2020 because data submission slowed when resources were diverted to the COVID-19 response.

What's Next

- *C. diff* is rarely resistant to the antibiotics commonly used to treat it. However, *C. diff* usually occurs in people who have taken antibiotics.
- Improving antibiotic use is an important strategy to reduce *C. diff* infections.
- CDC will continue monitoring how changes in antibiotic use may impact *C. diff* infections, including in 2020.

CDC. COVID-19: U.S. Impact on Antimicrobial Resistance, Special Report 2022. Atlanta, GA: US DHHS, CDC; 2022.

Available data show an alarming increase in resistant infections starting during hospitalization, growing at least 15% from 2019 to 2020.

- Carbapenem-resistant *Acinetobacter* (↑78%)
- Antifungal-resistant *Candida auris* (↑60%)*
- Carbapenem-resistant Enterobacterales (↑35%)
- Antifungal-resistant *Candida* (↑26%)
- ESBL-producing Enterobacterales (↑32%)
- Vancomycin-resistant Enterococcus (↑14%)
- Multidrug-resistant *P. aeruginosa* (↑32%)
- Methicillin-resistant *Staphylococcus aureus* (↑13%)

CDC. COVID-19: U.S. Impact on Antimicrobial Resistance, Special Report 2022. Atlanta, GA: US DHHS, CDC; 2022.

A new measure on the horizon?

Previously, the Hospital IQR Program included a CDI measure which only required CDI facility-wide Lab-ID event reporting (we refer readers to the FY 2012 IPPS/LTCH PPS final rule, 76 FR 51630 through 51631).[1065] The newly developed version of the measure would improve on the original version of the measure by requiring both microbiologic evidence of CDI in stool and evidence of antimicrobial treatment, whereas the original measure only required CDI facility-wide Lab-ID event reporting. The addition of anti-microbial treatment evidence may provide further validity in the reporting of CDIs, as it serves as a surrogate for test results that were clinically interpreted as true infections.

2022-16472.pdf (federalregister.gov)

Lessons learned

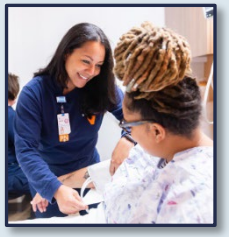
1

Culture set by institutional leadership important to generate & sustain engagement

2

Case review in partnership with frontline staff essential to understand current state and plan next steps

3



Nurses are integral to testing decisions. We should have engaged earlier!

4

IT support to build dashboard, track data, & develop custom EMR changes critical

Lessons learned

5

Aim for low hanging fruit and then optimize.

Diagnosing HO-CDI remains challenging. Ensure interventions don't discourage appropriate testing.

6

Work is time intensive but rewarding.

It takes a village!

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