C. difficile Infection:
Interventions to Correctly Identify and Prevent

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Learner Objectives

- Identify risks associated with C. difficile infection (CDI)
- Review the challenges in the diagnosis and reporting of CDI
- Discuss the practices in C. difficile diagnosis and the most recent guidelines on CDI diagnosis, management and prevention

Why is there interest in CDI?

- CDI places a high burden on healthcare:
  - 250,000 hospitalizations
  - 14,000 deaths per year
  - 3.2 billion dollars in excess costs annually in the US (2000-2002)
- CDI was categorized by CDC as an urgent threat to patient safety
- California requires hospitals to report hospital onset (HO) CDI to NHSN through LAB-ID event module
- CDI is one of the Hospital Acquired Conditions (HAC) included in the HAC Reduction Program

What is CDI?

- *Clostridium difficile* infection (CDI) is the most common cause of healthcare associated diarrhea
- Toxins A and B produced by the *C. difficile* cause CDI
- Manifestations of CDI vary from colonization without symptoms, mild diarrhea, colitis, to pseudomembranous colitis
- Risk factors:
  - Advanced age
  - Prolonged admission
  - Antibiotics
  - GI surgery
  - GI procedure
  - Tube feeding
  - Chemotherapy
  - Immunosuppression
  - Gastric acid suppressants
- Definition of CDI:
  - Presence of diarrhea (≥3 unformed stools in ≤ 24 hours AND
  - A stool test result positive presence of toxigenic C. difficile or its toxins or colonoscopic or histopathologic findings of pseudomembranous colitis

CDI by Disease Severity

Table 2. Characteristics of patients with mild and severe CDI

Characteristic	Disease		Odds Ratio	P[a]
	Mild (n=83), %	Severe (n=60), %		
Male	39 (46.9)	32 (51.6)		
Number of patients with CA-CDI	38 (45.7)	18 (30)	1.51	0.05
Number of patients with documented recurrent disease	14 (16.8)	10 (16.6)	0.98	1.0
Average number of stools per day ± SD	3 ± 3.4	3 ± 2.6	-	0.43
Average duration of Symptoms (days ± SD)	8 ± 3.1	6 ± 3.8	-	0.16
Number of patients treated with immunosuppressive agent	25 (30.1)	10 (16.6)	0.67	0.09
Number of patients treated with stool softener	34 (40.9)	22 (36.6)	0.99	1.0
Number of patients with a GI Comorbidity	26 (31.3)	17 (28.3)	1.01	0.9
Mean Hospital Days ± Standard Deviation	17 ± 20	29 ± 29	-	0.002
Number of patients with all-cause 1 month mortality	0	10	2.66	0.0001

Humphries et al JCM 2013; 51: 869-873

Hospital Onset *C. difficile* Infections

- The state of California has disproportionately high numbers of HO CDI with Orange County the highest in the nation

CDI Table 1. Hospital-Onset *Clostridium difficile* Diarrheal Infections (CDI) Reported by California Hospitals,* January - December 2014

Hospitals highlighted in red did not participate in 2014 data validation; completeness of reported infections has not been evaluated

County	Hospital Name	2014					
		Hospital Onset Cases	Predicted Cases	Patient Days	SIR[a]	SIR 95% CI[b]	Comparison[c]
	STATE OF CALIFORNIA POOLED DATA	10588	9749.49	13723438	1.09**		
San Diego	Alvarado Hospital Medical Center	15	18.27	32780	0.82	(0.48,1.32)	N
San Diego	Grossmont Hospital	88	83.47	122032	1.05	(0.85,1.29)	N
San Diego	Kaiser Foundation Hospital, San Diego	104	77.78	85156	1.34	(1.10,1.61)	H
San Diego	Palomar Health Downtown Campus	1	9.92	22107	0.10	(0.01,0.50)	L
San Diego	Palomar Medical Center	74	53.00	82560	1.40	(1.10,1.74)	H
San Diego	Paradise Valley Hospital	10	41.04	58531	0.24	(0.12,0.43)	L
San Diego	Pomerado Hospital	24	14.62	26078	1.64	(1.08,2.41)	H
San Diego	Rady Children's Hospital - San Diego	23	42.33	62841	0.54	(0.35,0.80)	L
San Diego	Scripps Green Hospital	28	28.26	37246	0.99	(0.67,1.41)	N
San Diego	Scripps Memorial Hospital - Encinitas	35	30.17	41158	1.16	(0.82,1.60)	N
San Diego	Scripps Memorial Hospital - La Jolla	47	49.41	67422	0.95	(0.71,1.25)	N
San Diego	Scripps Mercy Hospital	83	84.86	92592	0.98	(0.78,1.21)	N
San Diego	Scripps Mercy Hospital Chula Vista	24	26.17	39097	0.92	(0.60,1.34)	N
San Diego	Sharp Chula Vista Medical Center	48	32.38	64107	1.48	(1.11,1.95)	H
San Diego	Sharp Coronado Hospital and Healthcare Center	2	3.22	6136	0.62	(0.10,2.05)	N
San Diego	Sharp Mary Birch Hospital For Women And Newborns	1	18.42	34066	0.05	(0.00,0.27)	L
San Diego	Sharp Memorial Hospital	117	83.19	98229	1.41	(1.17,1.68)	H
San Diego	Tri-City Medical Center	39	52.59	68400	0.74	(0.54,1.00)	N
San Diego	University of California, San Diego Medical Center	171	138.99	158846	1.23	(1.06,1.43)	H

- SIR model does not adjust for BMT or solid transplant populations, two groups known to be at very high risk
- The SIR model is not changing in the foreseeable future

Table 1. Numbers of Healthcare-Associated Infections (HAI) Reported by California Hospitals and Comparisons of Statewide HAI Incidence to National Baselines, 2014

	No. of HAI Reported by California Hospitals in 2014	2014 California HAI Data Compared with National Baselines*
CDI	10,588	↑ 9% since 2011
CLABSI	2809	↓ 49% since 2008
MRSA BSI	705	↓ 24% since 2011
VRE BSI	782	*No national baseline*
SSI – All Surgeries	4,316	↓ 40% since 2008
SSI – Colon Surgery	911	No difference from 2008
SSI – Hysterectomy	168	↓ 20% since 2008

**National baselines are based on surveillance data reported by U.S. hospitals to the Centers for Disease Control and Prevention's National Healthcare Safety Network.*

Table 4. Data for Action Strategy Targeting California Hospitals with High Healthcare-Associated Infection (HAI) Incidence, 2014

HAI	Criteria Used to Target Hospitals for Data for Action Outreach	# of Hospitals Targeted, 2014
CDI	Hospitals with significantly high CDI SIR in 2014 compared with 2011 national baseline.	**67**

CDPH Action Steps:

1. Target hospitals with high CDI rates and work with hospital medical providers (e.g., hospitalists) to implement strategies to prevent transmission of *C. difficile* and reduce inappropriate use of antimicrobials through enhanced antimicrobial stewardship efforts.
2. For those hospitals with high CDI incidence, recommend and offer assistance to assess adherence to core CDI prevention practices, including thoroughness of environmental cleaning, antimicrobial stewardship, and judicious use of contact precautions, hand hygiene, and establishing clear communication between facilities sharing potentially transmissible CDI patients.

Laboratory diagnosis of CDI

Table 2. Diagnostic testing for *C. difficile*

Test	Sensitivity	Specificity	Availability	Expensea	Utilization
C. difficile culture	Low	Moderate	Limited	$5–10	No diagnostic use; only toxigenic organisms cause disease
Toxigenic culture	High	High	Limited	$10–30	Reference method Epidemiologic tool Limited diagnostic use
CCNA	High	High	Limited	$15–25	Reference method Limited diagnostic use
GDH	High	Low	Widely	$5–15	Diagnostically as a screening test; must be confirmed
Toxin EIA tests	Low	High	Widely	$5–15	Must detect toxins A+B; inferior sensitivity
NAATs	High	High	Widely	$20–50	Use only in acute disease; false positives of concern

CCNA, *C. difficile* cytotoxin neutralization assay; GDH, glutamate dehydrogenase; EIA, enzyme immunoassay; NAAT, nucleic acid amplification tests.
[a]Cost of goods; does not reflect laboratory changes.

Surawicz et al. Am J Gastro 2013;108:478-498

Sensitivity and specificity of the tests

Table 8
Pooled sensitivities and specificities of categories of tests

Type	Test	Compared to CCNA			Compared to TC			Compared to culture		
		No. of studies	Sensitivity (95% CI)	Specificity (95% CI)	No. of studies	Sensitivity (95% CI)	Specificity (95% CI)	No. of studies	Sensitivity (95% CI)	Specificity (95% CI)
EIA GDH	Total	12	0.94 (0.89–0.97)	0.90 (0.88–0.92)	8	0.96 (0.86–0.99)	0.96 (0.91–0.98)	11	0.94 (0.86–0.97)	0.96 (0.92–0.98)
	Well type	5	0.94 (0.91–0.97)	0.92 (0.92–0.93)	1	0.94 (0.93–0.96)	0.94 (0.94–0.95)	4	0.89 (0.86–0.91)	0.91 (0.90–0.92)
	Membrane type	7	0.98 (0.78–1.00)	0.90 (0.87–0.93)	7	0.97 (0.84–1.00)	0.96 (0.90–0.99)	7	0.93 (0.84–0.97)	0.98 (0.95–0.99)
EIA toxins A/B	Total	27	0.83 (0.76–0.88)	0.99 (0.98–0.99)	29	0.57 (0.51–0.63)	0.99 (0.98–0.99)			
	Well type	18	0.85 (0.77–0.91)	0.98 (0.96–0.99)	16	0.60 (0.52–0.68)	0.98 (0.97–0.99)			
	Membrane type	9	0.79 (0.66–0.88)	0.99 (0.98–0.99)	13	0.53 (0.45–0.61)	0.99 (0.97–1.00)			
NAAT		14	0.96 (0.93–0.98)	0.94 (0.93–0.95)	32	0.95 (0.92–0.97)	0.98 (0.97–0.99)			

CI, confidence interval; CCNA, cell cytotoxicity neutralization assay; EIA, enzyme immunoassay; GDH, glutamate dehydrogenase; NAAT, nucleic acid amplification test; TC, toxigenic culture.

Crobach et al. Clin Micro and Infect 22 (2016) S63**e**S81

Positive predictive value (PPV) and negative predictive value (NPV) by CDI prevalence

Table 9

PPV and NPV for different categories of index tests at hypothetical CDI prevalences of 5, 10, 20 and 50%

Test type	CDI prevalence 5%		CDI prevalence 10%		CDI prevalence 20%		CDI prevalence 50%	
	PPV	NPV	PPV	NPV	PPV	NPV	PPV	NPV
Well-type EIA GDH	38	100	54	99	72	98	91	94
Membrane-type EIA GDH	34	100	52	100	71	99	91	98
Well-type EIA toxins A/B	69	99	83	98	91	96	98	87
Membrane-type EIA toxins A/B	81	99	90	98	95	95	99	83
NAAT	46	100	64	100	80	99	94	96

Pooled estimates of sensitivity and specificity compared to cell cytotoxicity neutralization assay were used to calculate the predictive values.

CDI, *Clostridium difficile* infection; EIA, enzyme immunoassay; GDH, glutamate dehydrogenase; NAAT, nucleic acid amplification test; NPV, negative predictive value; PPV, positive predictive value.

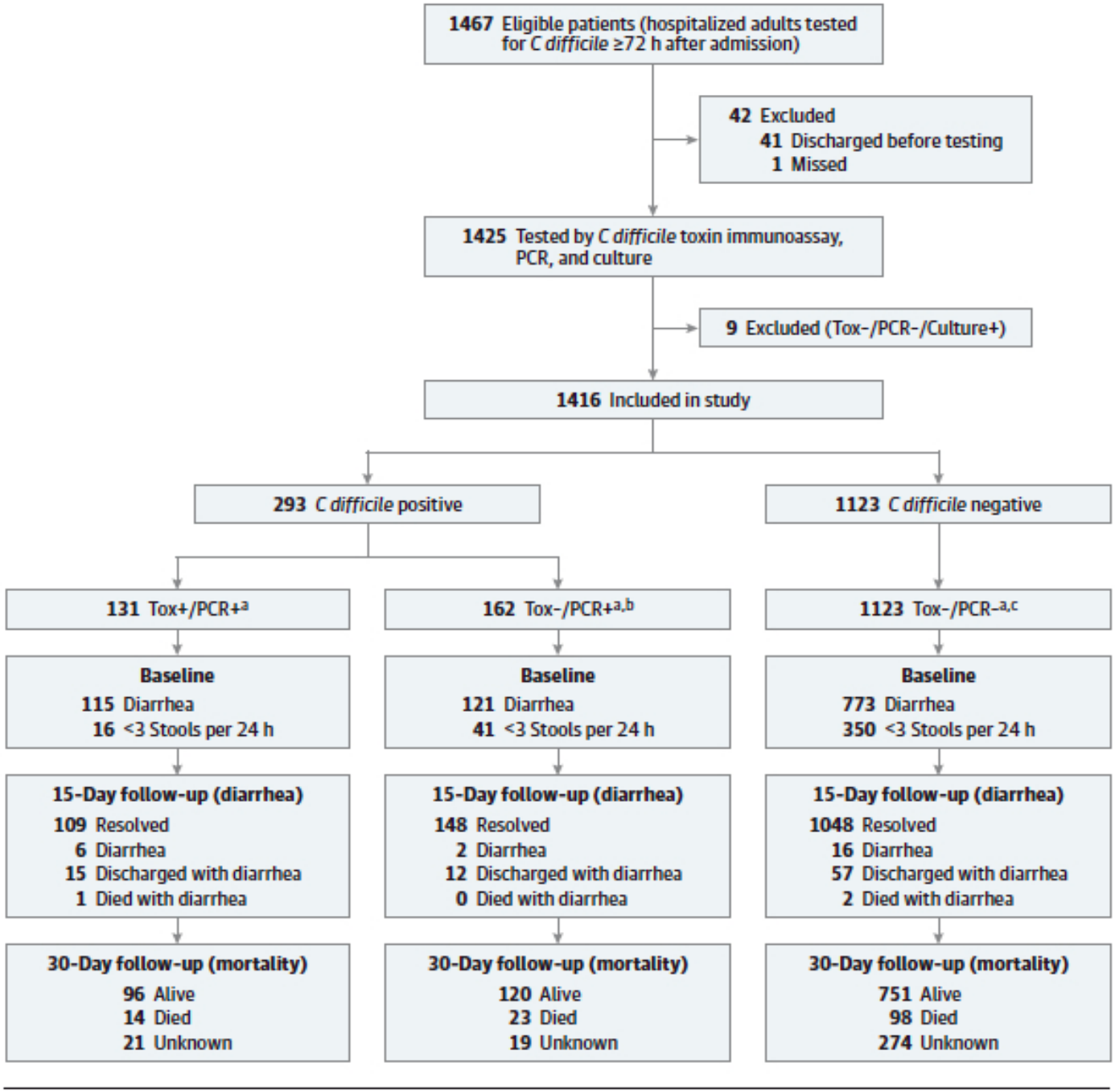
Crobach et al. Clin Micro and Infect 22 (2016) S63**e**S81

PCR alone likely overdiagnoses CDI

- Polage et al from UC Davis, found that 55.3% (162/293) of patients positive for PCR were negative for C. difficile toxin.
- PCR positive/C. diff toxin negative patients had similar outcomes to those who were PCR negative.

  Caveat: Switching to toxin alone will result in a significant decrease in the expected cases, thus reduction in the SIR would be far less than a 55% improvement
- These data suggest that a large proportion of CDI diagnosed by PCR represents colonization rather than actual infection

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



Tox+/PCR+ indicates *Clostridium difficile* toxin immunoassay positive and polymerase chain reaction positive; Tox−/PCR+, *C difficile* toxin immunoassay negative and polymerase chain reaction positive; and Tox−/PCR−, *C difficile* toxin immunoassay negative and polymerase chain reaction negative.

[a] *Clostridium difficile* test group based on US Food and Drug Administration–approved toxin immunoassay and polymerase chain reaction results.

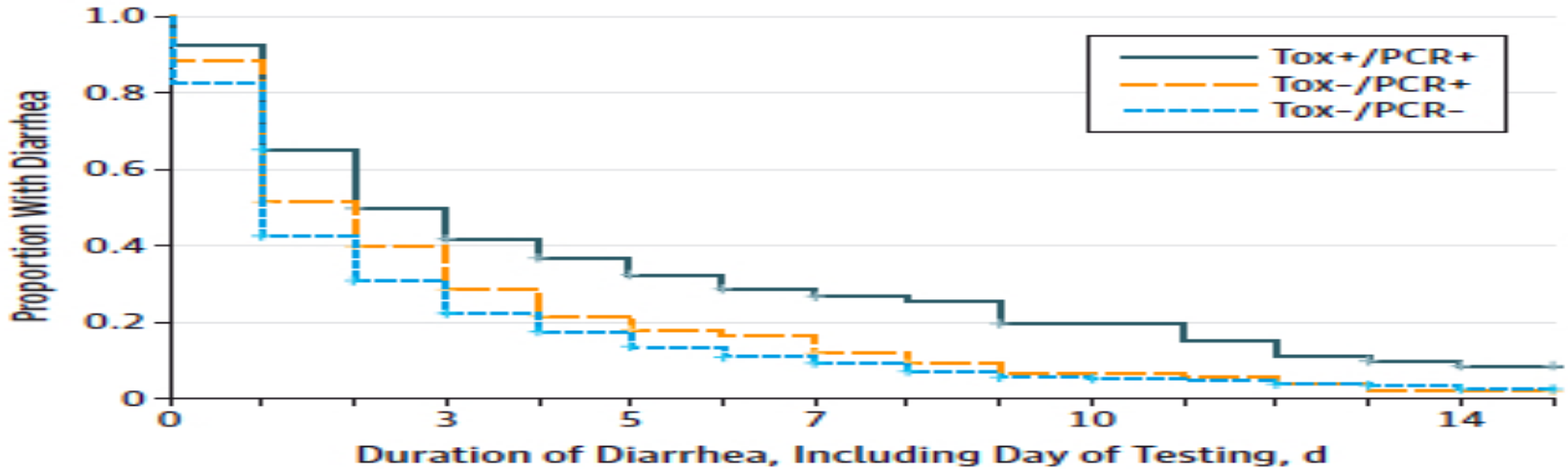
[b] Includes one patient with false-positive immunoassay.

[c] Includes 20 patients with false-positive immunoassay.

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

Kaplan-Meier Curves of Time to Resolution of Diarrhea by C. difficile Test Group

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

The median duration of diarrhea for patients with at least 1 day was 3 days (interquartile range, 1-6 days) for Tox+/PCR+ (121 of 131), 2 days (interquartile range, 1-4 days) for Tox−/PCR+, and 2 days (interquartile range, 1-3 days) for Tox−/PCR− (927 of 1123) ($P < .001$). Log-rank P values are $P < .001$ for all groups, $P = .003$ for Tox+/PCR+ vs Tox−/PCR+, (143 of 162) $P < .001$ for Tox+/PCR+ vs Tox−/PCR−, and $P < .001$ for Tox−/PCR+ vs Tox−/PCR−. Tox+/PCR+ indicates *C difficile* toxin immunoassay positive and polymerase chain reaction positive; Tox−/PCR+, *C difficile* toxin immunoassay negative and polymerase chain reaction positive; Tox−/PCR−, *C difficile* toxin immunoassay negative and polymerase chain reaction negative.

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

Polage et al. - Limitations

- Study was based on testing not on diarrhea
- 30% did not have diarrhea, ie ≥3 stools per day
- Median stools/day were 5 in the tox+/PCR+ vs. 3 tox-/PCR+ vs. 3 tox-/PCR-
- 2.3% in tox+/PCR+ vs. 19.8% in tox-/PCR+ vs. 16.4% in tox-/PCR- were on metronidazole or vanco within 48h before day 1
- 100% vs. 40.7% vs. 33.3% on metronidazole or vanco within 14 days
- 57.3% vs. 21.6% vs. 12.2% on metronidazole or vanco between 15 and 30 days

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

Performance of C. diff toxin enzyme immunoassay and PCR Stratified by Disease Severity

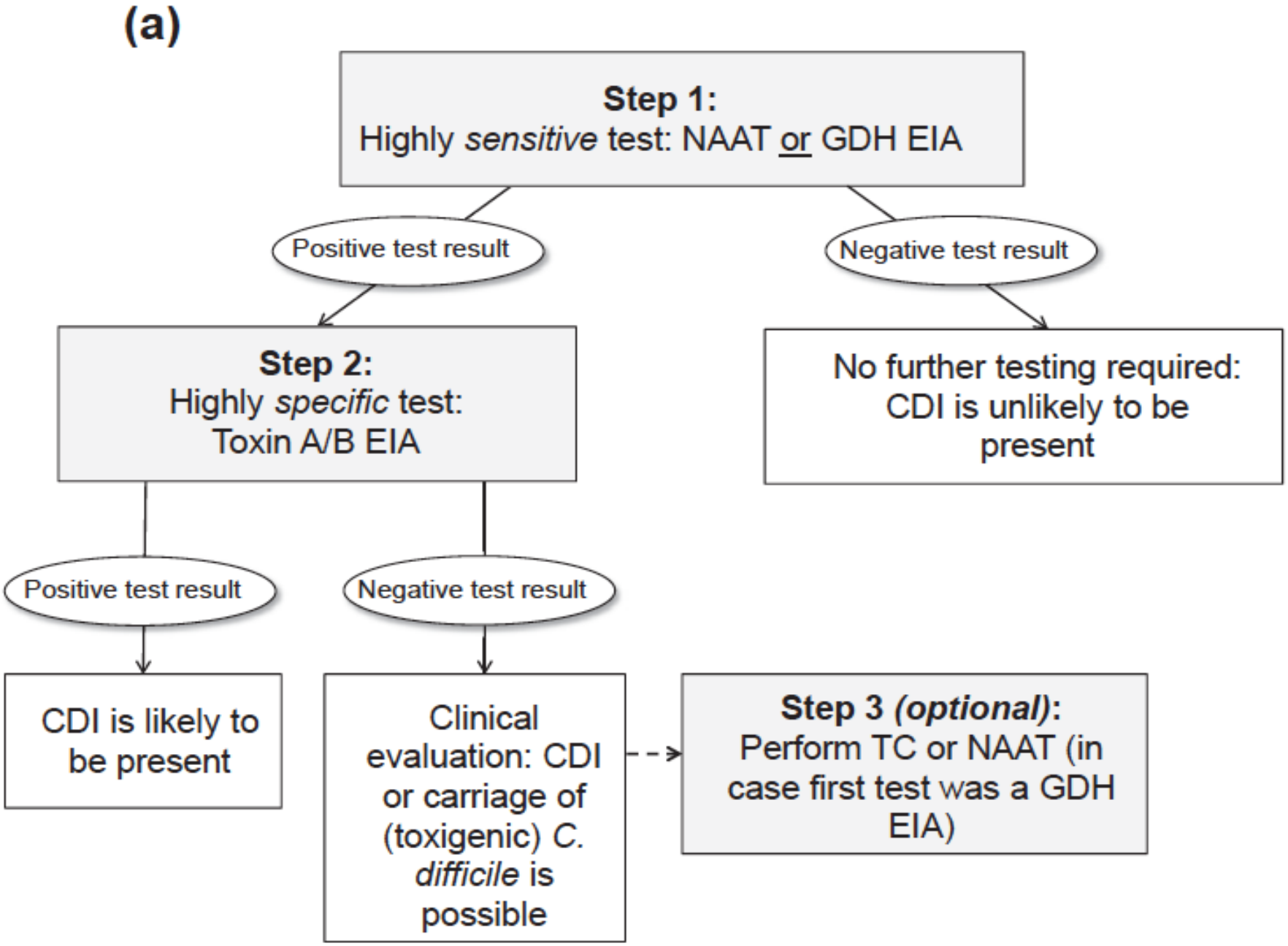
Case definition	Laboratory Test Results				Interpretation	Number of patients (N with severe disease)
	NAAT[1]	EIA	Toxigenic culture	Cepheid Xpert		
CDI	-	-	+	-	NAAT & EIA FN	3 (1)
CDI	+	-	+	NP	EIA FN	51 (19)
CDI	-	+	+	NP	NAAT FN	0 (0)
CDI	+	+	+	NP	TP	70 (32)
CDI	+	-	-	+	EIA FN	13 (5)
CDI	+	+	-	+	Culture FN	6 (3)
No CDI	+	+	-	-	NAAT & EIA FP	0 (n/a)
No CDI	+	-	-	-	NAAT FP	6 (n/a)
No CDI	-	+	-	NP	EIA FP	9 (n/a)
No CDI	-	-	-	NP	TN	138 (n/a)

CDI, *C. difficile* infection, NAAT, nucleic acid amplification, EIA, toxin A&B enzyme immunoassay, FN, false negative, TP, true positive, FP, false positive, TN, true negatives, NP, not performed

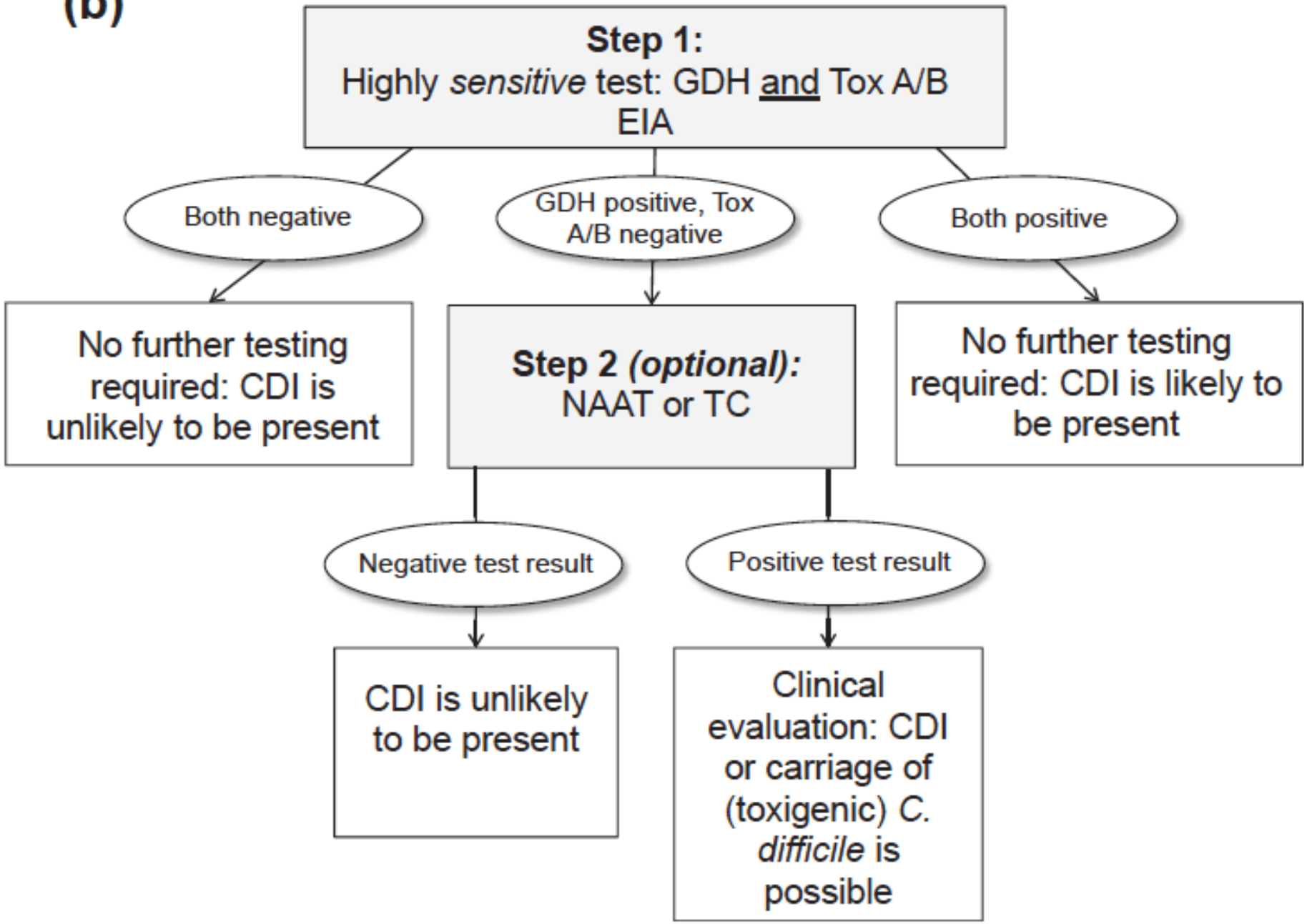
Humphries et al JCM 2013; 51: 869-873

Guidelines for CDI diagnosis in adults ESCMID, GI society, IDSA/SHEA

	ESCMID 2016	GI Society 2013	IDSA/SHEA 2010
MD order only	No	N/A	N/A
Testing algorithm	Yes, 2 step starting with NAAT or GDH, then EIA if positive	NAAT preferred or 2 or 3 step algorithm with subsequent toxin	NAAT preferred or 2 or 3 step algorithm with subsequent toxin
Unformed stool only	yes	yes	yes
Test of cure	No	No	No
Repeat test within same episode	No	No	No


(a)
Step 1:
Highly sensitive test: NAAT or GDH EIA
Positive test result
Negative test result
Step 2:
Highly specific test:
Toxin A/B EIA
No further testing required:
CDI is unlikely to be present
Positive test result
Negative test result
CDI is likely to be present
Clinical evaluation: CDI or carriage of (toxigenic) C. difficile is possible
Step 3 (optional):
Perform TC or NAAT (in case first test was a GDH EIA)

(b)


Step 1:
Highly sensitive test: GDH and Tox A/B EIA
Both negative
GDH positive, Tox A/B negative
Both positive
No further testing required: CDI is unlikely to be present
Step 2 (optional):
NAAT or TC
No further testing required: CDI is likely to be present
Negative test result
Positive test result
CDI is unlikely to be present
Clinical evaluation: CDI or carriage of (toxigenic) C. difficile is possible

The four legged stool of Hospital Onset *C. difficile*

- Over sensitivity of PCR test compared to two step resulting in inclusion of patients colonized with *Clostridium difficile* vs. true C. difficile colitis
- Failure to test patients with diarrhea in a timely fashion (ED vs. inpatient)
- Testing for diarrheal illness in patients on laxatives
- Information systems currently limit our ability in identifying high risk antibiotics upfront

No diarrhea = No testing

- About a third of patients tested do not have diarrhea
  - ≥ 3 unformed stools/day

Proposed action:

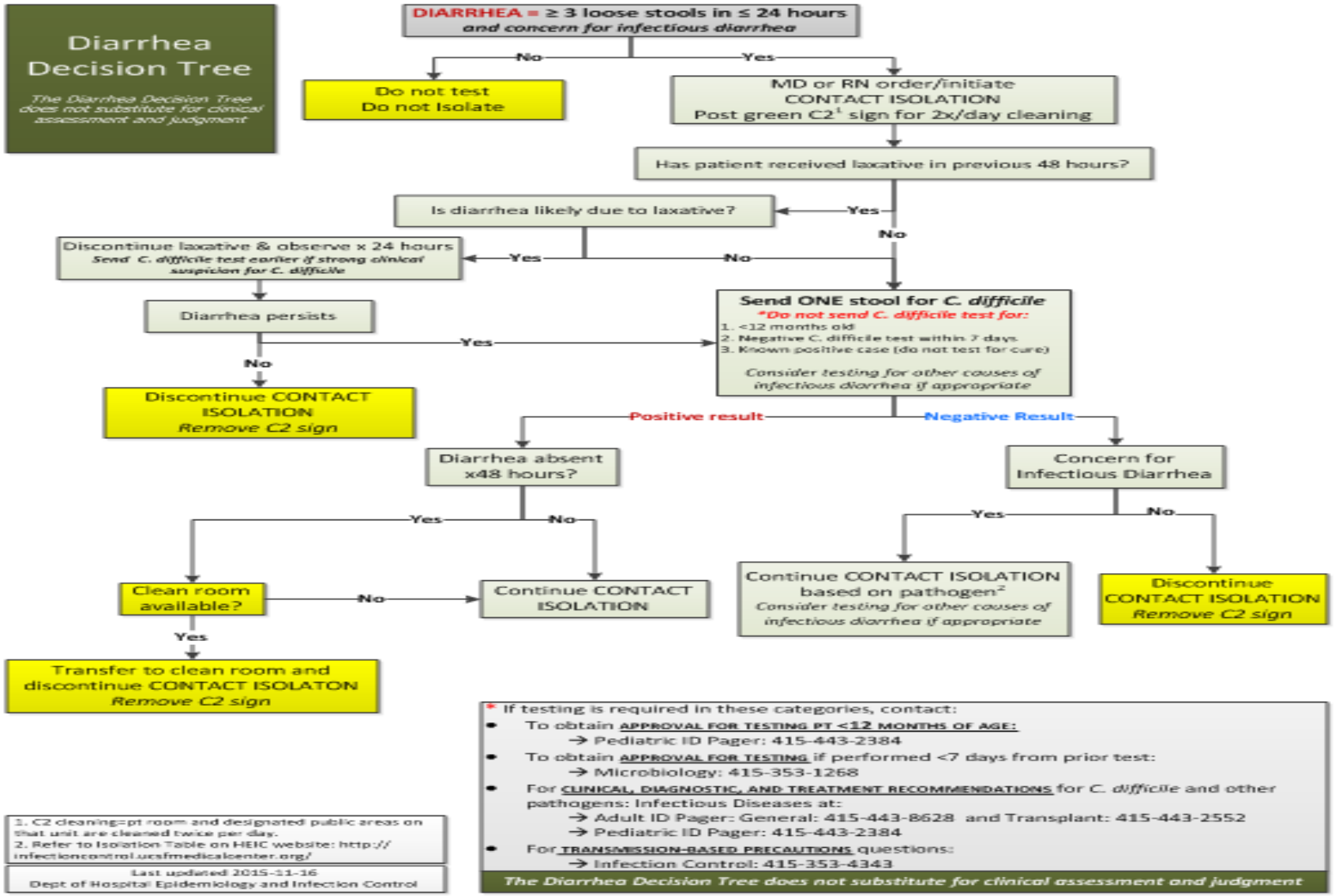
- Introduce the Bristol Stool Chart
- Empower nurses to alert MD that CDI testing order should be discontinued
- Use diarrhea decision tree

Bristol Stool Chart - Developed at University of Bristol

Type.1		Separate hard lumps, like nuts (hard to pass)
Type.2		Sausage-shaped but lumpy
Type.3		Like a sausage with cracks on its surface
Type.4		Like a sausage, smooth and soft
Type.5		Soft blobs, clear cut edges (passed easily)
Type.6		Fluffy pieces, ragged edges, mushy stool
Type.7		Watery, no solid pieces. Entirely liquid

Lewis SJ, Heaton KW (1997). "Stool form scale as a useful guide to intestinal transit time". *Scand. J. Gastroenterol.* **32** (9): 920–4

UC San Francisco's Diarrhea Decision Tree



Diagnosis of CDI in the ED: Not always a priority in patients awaiting admission

- Hospital Onset is defined as cases of *C. difficile* on ***calendar day 3*** or beyond (regardless of described symptoms)
- About a third of HO-CDI were diagnosed on D3 and D4

Proposed action:

- Increase testing in the ED
- Use GI NAT in ED

Use of laxatives

- Survey of 30 hospital onset randomly selected CDI cases

% on laxatives 2 days before + PCR	% on laxatives the day before + PCR	% on laxatives the day of + PCR	% restarted on laxatives <7 days after + PCR
56.7%	53.3%	53.3%	43.3%

  - Confidence interval (+ 16.4%)
  - Some patients continued to receive laxatives the entire duration of the 10 days surveyed

Proposed action:

- Use diarrhea decision tree

Additional action items to decrease HO CDI

- Collaborative work group (ED, Hosp Medicine, ID):
  - Achieve timely testing of CDI in ED ✓
  - Integrate the Bristol Stool Scale ✓
  - Implement assessment of laxative use before ordering CDI test ✓
  - Adapt UCSF diarrhea decision tree and integrate within EPIC ✓
  - Opportunity to use two step testing in difficult clinical scenarios (for example IBD and GVHD patients)

C. difficile order set in EPIC

Order Sets

IP GEN Clostridium Difficile Workup

Patient Care

Isolation — **1 of 1 selected**

☑ C. difficile Precautions

P Hospital Performed, Routine, ONGOING

Medications

Antibiotics

**Discontinue the following class of medications if clinically appropriate:

- Antibiotics
- Acid suppressants (PPI, H2RA)
- Antidiarrheal (loperamide, diphenoxylate/atropine)
- Prokinetic motility agents (metoclopramide, lactulose, other laxatives)

It is recommended to choose antibiotic treatment based on disease severity and number of CDI episodes.

Choose Mild-Moderate CDI Antibiotics for suspected initial or 1st recurrent *C. Difficile* infection in a patient that does not meet criteria for severe or severe, complicated infection (see below).

Choose Severe CDI Antibiotics for suspected initial or 1st recurrent *C. Difficile* infection in a patient that has any of the following:

- WBC > or = 15,000 cells/mL
- SCr > or = 1.5x baseline Scr
- Requires ICU Level of Care
- Severe immunosuppression (i.e., BMT, SOT, recent chemotherapy, CD4 <100)

Choose Severe, Complicated CDI Antibiotics for suspected initial or 1st recurrent *C. Difficile* infection in a patient that has:

- Any of the above criteria listed for Severe CDI AND any of the following:

- Hypotension or shock
- Ileus
- Toxic megacolon
- Pseudomembranous colitis

Choose Recurrent CDI Antibiotics for suspected *C. Difficile* infection beyond 1st recurrence in a patient with a previous CDI episode > or = 2 months prior to current episode.

○ Mild-Moderate CDI Antibiotics
○ Severe CDI Antibiotics
○ Severe, Complicated CDI Antibiotics
○ Recurrent CDI Antibiotics

Hospital Onset (HO) *C. difficile* Infections reporting to NHSN

- If the SIR for *C. difficile* is 1.4, meaning that the hospital has 40% more hospital onset *C. difficile* than CMS expects or, in patient terms, 60 more cases a year.
  - SIR model incorporates testing method (PCR vs. toxin testing)
  - SIR model does not adjust for BMT or solid transplant populations, two groups known to be at very high risk
  - The SIR model is not changing in the foreseeable future
- If the community onset (CO) rate is high, the expected number of hospital onset (HO) is going to be higher
  - Voluntary reporting of CO-CDI into NHSN should be encouraged!

Table 3. CDI severity scoring system and summary of recommended treatments

Severity	Criteria	Treatment	Comment
Mild-to-moderate disease	Diarrhea plus any additional signs or symptoms not meeting severe or complicated criteria	Metronidazole 500 mg orally three times a day for 10 days. If unable to take metronidazole, vancomycin 125 mg orally four times a day for 10 days	If no improvement in 5–7 days, consider change to vancomycin at standard dose (vancomycin 125 mg four times a day for 10 days)
Severe disease	Serum albumin <3 g/dl plus ONE of the following: WBC ≥15,000 cells/mm^3, Abdominal tenderness	Vancomycin 125 mg orally four times a day for 10 days	
Severe and complicated disease	Any of the following attributable to CDI: Admission to intensive care unit for CDI Hypotension with or without required use of vasopressors Fever ≥38.5 °C Ileus or significant abdominal distention Mental status changes WBC ≥35,000 cells/mm^3 or <2,000 cells/mm^3 Serum lactate levels >2.2 mmol/l End organ failure (mechanical ventilation, renal failure, etc.)	Vancomycin 500 mg orally four times a day and metronidazole 500 mg IV every 8 h, and vancomycin per rectum (vancomycin 500 mg in 500 ml saline as enema) four times a day	Surgical consultation suggested
Recurrent CDI	Recurrent CDI within 8 weeks of completion of therapy	Repeat metronidazole or vancomycin pulse regimen	Consider FMT after 3 recurrences

CDI, *Clostridium difficile* infection; FMT, fecal microbiota transplant; IV, intravenous; WBC, white blood cell.

Surawicz et al. Am J Gastro 2013;108:478-498

Infection Prevention Precautions

Infection Control and Prevention

30. A hospital-based infection control programs can help to decrease the incidence of CDI. (Conditional recommendation, moderate-quality evidence)
31. Routine screening for *C. difficile* in hospitalized patients without diarrhea is not recommended and asymptomatic carriers should not be treated. (Strong recommendation, low-quality evidence)
32. Antibiotic stewardship is recommended to reduce the risk of CDI. (Strong recommendation, high-quality evidence)
33. Contact precautions for a patient with CDI should be maintained at a minimum until the resolution of diarrhea. (Strong recommendation, high-quality evidence)
34. Patients with known or suspected CDI should be placed in a private room or in a room with another patient with documented CDI. (Strong recommendation, high-quality evidence)
35. Hand hygiene and barrier precautions, including gloves and gowns, should be used by all health-care workers and visitors entering the room of any patient with known or suspected CDI. (Strong recommendation, moderate-quality evidence)
36. Single-use disposable equipment should be used for prevention of CDI transmission. Non-disposable medical equipment should be dedicated to the patient's room and other equipment should be thoroughly cleaned after use in a patient with CDI. (Strong recommendation, moderate-quality evidence)
37. Disinfection of environmental surfaces is recommended using an Environmental Protective Agency (EPA)-registered disinfectant with *C. difficile*-sporicidal label claim or 5000 p.p.m. chlorine-containing cleaning agents in areas of potential contamination by *C. difficile*. (Strong recommendation, high-quality evidence)
38. Although there is moderate evidence that two probiotics (*Lactobacillus rhamnosus* GG and *Saccharomyces boulardii*) decrease the incidence of antibiotic associated diarrhea, there is insufficient evidence that probiotics prevent *C. difficile* infection. (Strong recommendation, low-quality evidence)

CDI, Clostridium difficile infection; CT, computerized tomography; EIA, enzyme immunoassay; IBD, inflammatory bowel disease.

Surawicz et al. Am J Gastro 2013;108:478-498

Thank you! Questions?