

# *Clostridium difficile* Infections & Diagnostic Stewardship

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*Clostridium*

***Clostridioides*** *difficile* Infections &  
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# Outline

## 1. *Clostridioides difficile* Infections (CDI): What's New in 2018?

- Epidemiology
- Prevention
- Treatment
- Diagnosis

## 2. The Need for Diagnostic Stewardship

- Definition
- Potential Benefits and Harms

## 3. CDI and the Impact of Diagnostic Stewardship

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# CDI: Epidemiology

- CDI is the most common cause of healthcare-associated infection (HAI) in the USA
- Every year in the United States:
  - ~500,000 incident CDI
  - ~30,000 deaths
- Mid-2000s: Emergence of ribotype 027 epidemic strain (aka NAP1) → Changing epidemiology of CDI in hospitals

# CDI: Impact of Changing Epidemiology

- Increased morbidity
  - ↑ Recurrence
  - ↑ Readmissions
  - ↑ Requirement for ICU care
  - ↑ Colectomies
  - ↑ Discharge to Long Term Care Facilities (LTCFs)
- Increased mortality:
  - Prior to 2000: <2% cases
  - Since 2000: 4.5 – 5.7%
  - During epidemic periods: 6.9 – 16.7%
- Increased costs
  - Attributable cost for hospitals: \$5,000 - \$10,000 per episode
  - Total US costs attributable to CDI: \$1.2 – 5.9 billion



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# CDI: Prevention

- Preemptive contact precautions (gowns and gloves) pending test results for suspected CDI
- Contact precautions until discharge if high CDI rates
- In CDI outbreaks/sustained high rates, soap and water hand hygiene preferred instead of alcohol
- Consider terminal room cleaning with a sporicidal agent
- Measure cleaning adequacy
- Implement antibiotic stewardship and consider restricting fluoroquinolones, clindamycin and cephalosporins

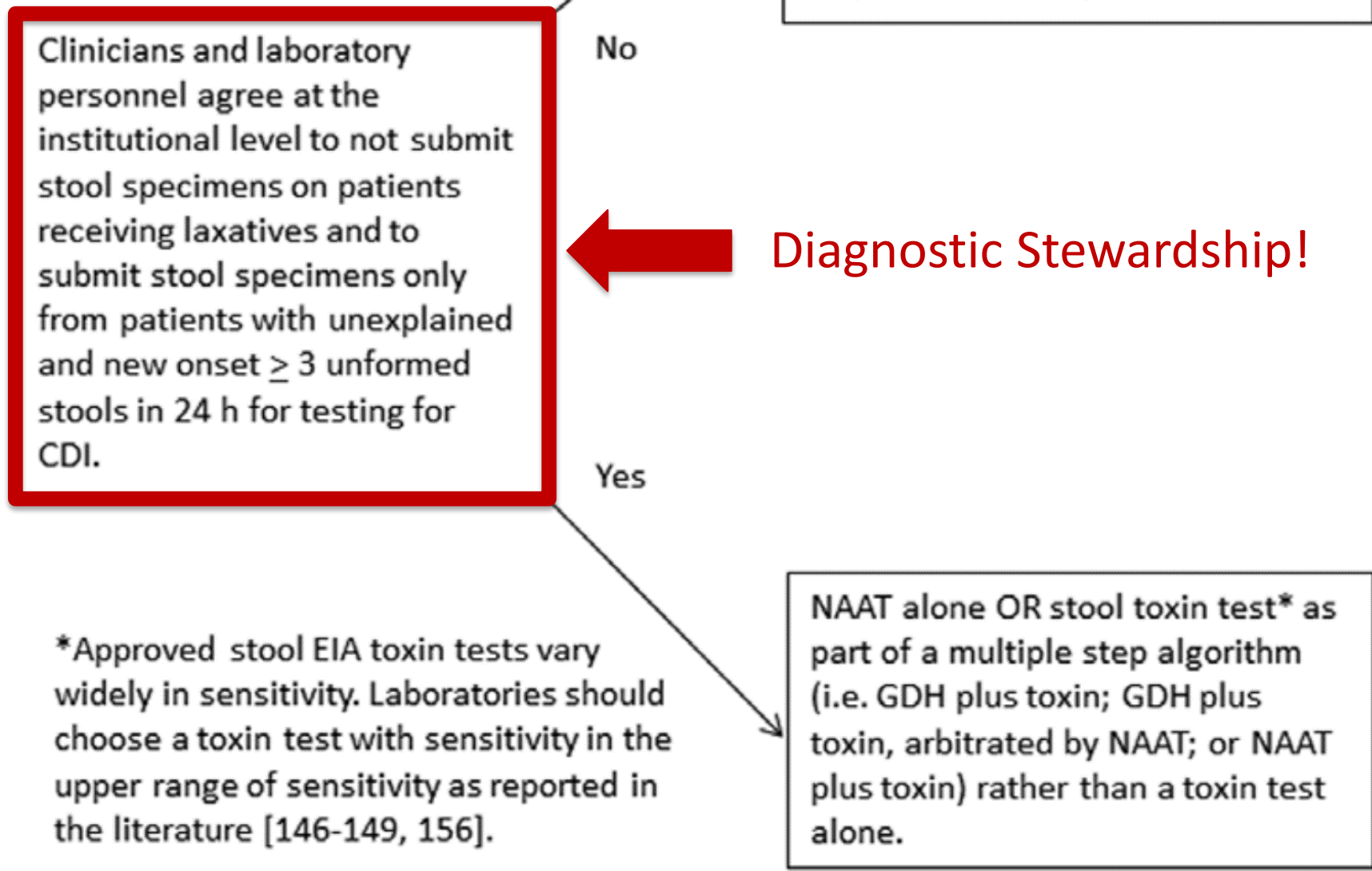
# CDI: Treatment Update

Clinical Definition	Supportive Clinical Data	Recommended Treatment <sup>a</sup>	Strength of Recommendation/ Quality of Evidence
Initial episode, non-severe	Leukocytosis with a white blood cell count of $\leq 15,000$ cells/mL and a serum creatinine level $< 1.5$ mg/dL	<ul style="list-style-type: none"> <li>VAN 125 mg given 4 times daily for 10 days, OR</li> <li>FDX 200 mg given twice daily for 10 days</li> <li>Alternate if above agents are unavailable: metronidazole, 500 mg 3 times per day by mouth for 10 days</li> </ul>	Strong/High Strong/High Weak/High
Initial episode, severe <sup>b</sup>	Leukocytosis with a white blood cell count of $\geq 15,000$ cells/mL or a serum creatinine level $> 1.5$ mg/dL	<ul style="list-style-type: none"> <li>VAN, 125 mg 4 times per day by mouth for 10 days, OR</li> <li>FDX 200 mg given twice daily for 10 days</li> </ul>	Strong/High Strong/High
Initial episode, fulminant	Hypotension or shock, ileus, megacolon	<ul style="list-style-type: none"> <li>VAN, 500 mg 4 times per day by mouth or by nasogastric tube. If ileus, consider adding rectal instillation of VAN. Intravenously administered metronidazole (500 mg every 8 hours) should be administered together with oral or rectal VAN, particularly if ileus is present.</li> </ul>	Strong/Moderate (oral VAN); Weak/Low (rectal VAN); Strong/Moderate (intravenous metronidazole)
First recurrence	...	<ul style="list-style-type: none"> <li>VAN 125 mg given 4 times daily for 10 days if metronidazole was used for the initial episode, OR</li> <li>Use a prolonged tapered and pulsed VAN regimen if a standard regimen was used for the initial episode (eg, 125 mg 4 times per day for 10–14 days, 2 times per day for a week, once per day for a week, and then every 2 or 3 days for 2–8 weeks), OR</li> <li>FDX 200 mg given twice daily for 10 days if VAN was used for the initial episode</li> </ul>	Weak/Low Weak/Low Weak/Moderate
Second or subsequent recurrence	...	<ul style="list-style-type: none"> <li>VAN in a tapered and pulsed regimen, OR</li> <li>VAN, 125 mg 4 times per day by mouth for 10 days followed by rifaximin 400 mg 3 times daily for 20 days, OR</li> <li>FDX 200 mg given twice daily for 10 days, OR</li> <li>Fecal microbiota transplantation<sup>c</sup></li> </ul>	Weak/Low Weak/Low Weak/Low Strong/Moderate



# CDI: Diagnosis

- What is the best method? It depends on whether a system of diagnostic stewardship is in place!



\*Approved stool EIA toxin tests vary widely in sensitivity. Laboratories should choose a toxin test with sensitivity in the upper range of sensitivity as reported in the literature [146-149, 156].

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# Diagnostic Stewardship: Defined

- “The appropriate use of laboratory testing to guide patient management”
- “The right test, for the right patient, at the right time”
- **Goal: Optimize Patient Outcomes!**
- ***Note: Although diagnostic stewardship may promote the cost effective use of laboratory tests, **minimizing costs is NOT the primary goal of diagnostic stewardship!*****
- Diagnostic Stewardship Produces Value (Quality/Cost)



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# Diagnostic Stewardship: 3 Stages

## 1. PREanalytic:

- ORDERING
- test-related decision making (e.g. “Is this patient having diarrhea?”)
- specimen collection

## 2. Analytic:

- PERFORMING
- Laboratory practices
- Includes protocolized or reflex test algorithms (e.g. No urine culture performed if no pyuria on u/a)

## 3. POSTanalytic:

- REPORTING
- e.g., selective reporting of antimicrobial susceptibility data to encourage use of narrow spectrum agents



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# The Need for Diagnostic Stewardship

- Clinicians order tests for patients ***without symptoms specific for the disease process!***
  - Low pre-test likelihood of infection
  - Example 1: Urine culture for patient without UTI symptoms
  - Example 2: CDI testing in patients without diarrhea
- Positive test results in this setting are often:
  - False-positives
  - Colonization rather than true infection
  - BUT, often result in ↓ quality of care:
    - unnecessary antibiotic therapy
    - increased risk of antimicrobial resistance
    - avoidable adverse drug effects



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# The Need for Diagnostic Stewardship

- Laboratory tests
  - currently account for only 4% of healthcare costs, BUT
  - most rapidly growing segment of the healthcare budget***
  - Impact of new molecular assays
  - Need to address *value* (Quality/Cost)
- At least 20% of available tests are overused AND underused
  - delayed/incorrect diagnoses
  - delayed/inappropriate treatment
  - adverse patient outcomes
  - increase costs



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# Diagnostic Stewardship: Potential Benefits

Improve the *accuracy* of a diagnosis

- ↑ True-positive results and ↓ False-positive results
  - ↑ **Appropriate** (and timely) antibiotic use
  - ↓ Adverse drug effects
  - ↓ Length of stay



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# Diagnostic Stewardship: Potential Harms

Will improving the positive predictive value of testing result in **missed diagnoses?**

***Prior to implementing a diagnostic stewardship intervention, need to identify outcomes that can be tracked to monitor for unintended patient harm***



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# Diagnostic Stewardship: Potential Benefits

## Example 1: “The Puzzle of Mr. P”

cc: “altered mental status”

Hx: 75 yo M w/ HTN, BPH with a chronic indwelling urinary catheter, and “frequent UTIs” presents with altered mental status x 3 days. Recently started on beta-blocker.

PE: elderly white male, non-toxic appearing, oriented only to self. GU: Catheter draining clear-appearing urine

Labs:

-u/a: 3 WBC per HPF

-urine culture: **NOT PERFORMED (per lab urine reflex protocol)**

Clinical Dx: Drug-Induced Delirium (secondary to beta-blocker)?

Course:

1. Beta-blocker held and supportive care ->
2. Complete resolution of symptoms

# Diagnostic Stewardship: Potential Benefits

## Example 2: “The Puzzle of Mr. P”

### Labs:

-u/a: 3 WBC per HPF

-urine culture: >100,000 *E. coli* CFU/ml

Dx: Delirium secondary to recurrent UTI?

### Course:

1. Started on ciprofloxacin → Worsening Delirium
2. Diarrhea → Stool positive for CDI by PCR
3. Fever, Tachycardia, Hypotension, Increasing WBC to 50,000  
→ Transfer to MICU for sepsis
4. Aggressive volume resuscitation → Acute Resp Failure
5. Prolonged ICU stay → D/C'd to SNF

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# CDI and the Impact of Diagnostic Stewardship

- 1/2014: National Healthcare Safety Network (NHSN) requires all participating health care facilities to report all positive C diff tests, ***regardless of clinical circumstances***
- Any positive C diff test on sample collected on or after day 4 of hospitalization is counted as a hospital onset C diff infection (HO-CDI), ***regardless if symptoms were present on admission***
- Health care facilities with C diff rates above national benchmarks will see a decrease in reimbursement

# CDI and the Impact of Diagnostic Stewardship

## The Johns Hopkins Experience

- 01/2015-06/2016: Infection Prevention prospective chart review for each HO-CDI LabID event
- “True HO-CDI”
  - clinically significant diarrhea ( $\geq 3$  episodes in 24 hours)
  - not present on admission
  - no laxatives in preceding 48 hours
- Results stratified by service line to target for future diagnostic stewardship interventions



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# CDI and the Impact of Diagnostic Stewardship

## The Johns Hopkins Experience

- 490 HO-CDI LabID events
  - 284 (58%) were “True HO-CDI”
  - 206 (42%) were “Nontrue HO-CDI”
    - 49.5% with no significant diarrhea
    - 41% with laxative use in previous 48 hours
    - 9.5% with delayed testing
- ***92% patients who were inappropriately tested received treated for CDI!!!***

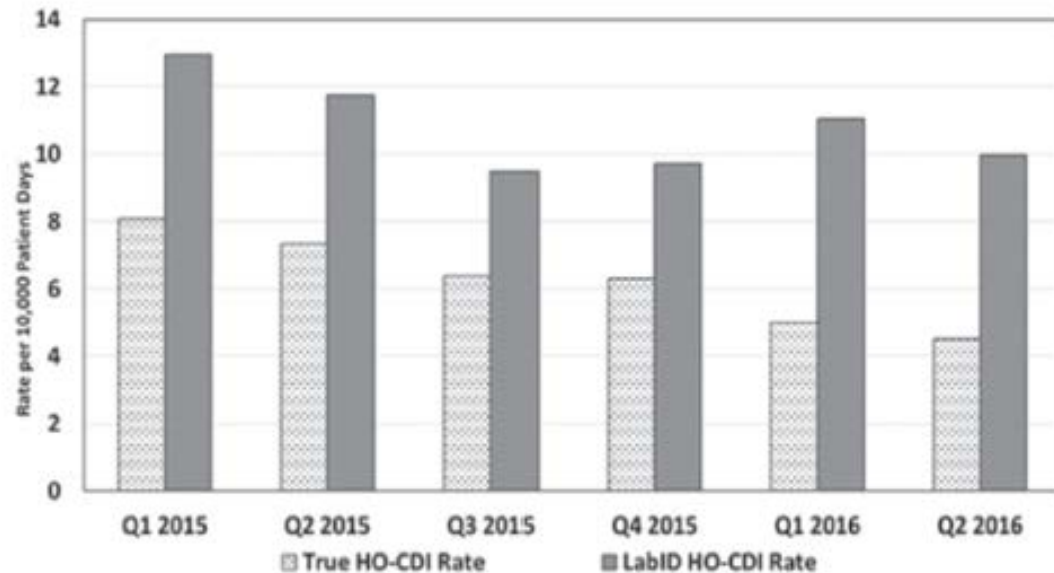


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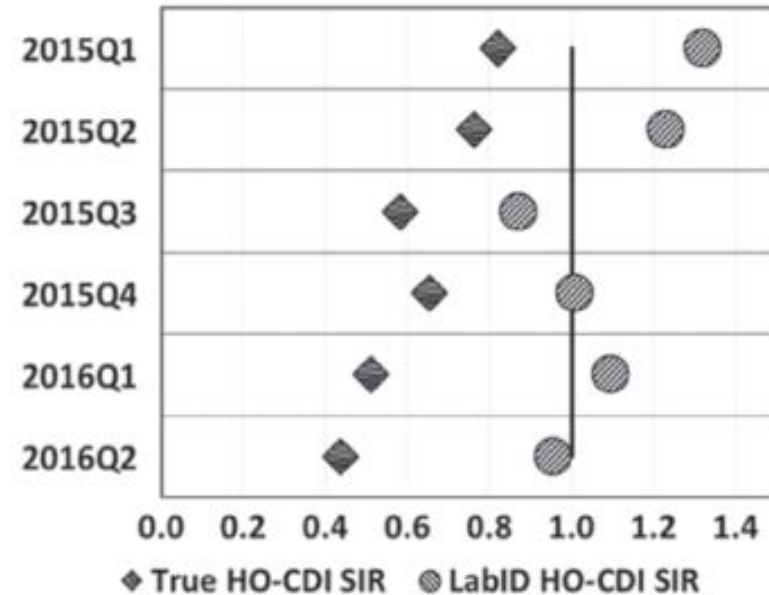
# CDI and the Impact of Diagnostic Stewardship

## The Johns Hopkins Experience

a: True HO-CDI Rate vs NHSN LabID HO-CDI Rate



b: True HO-CDI SIR vs NHSN LabID HO-CDI Event SIR



*Conclusion: Education and best practice alerts to help clinicians avoid ordering a test when a patient doesn't have diarrhea or received a recent laxative may increase the pretest probability of true CDI*



# CDI and the Impact of Diagnostic Stewardship

## The Stanford Experience

- 06/2015-06/2016: Real-time electronic patient data tracking used by the laboratory to enforce testing criteria
  - clinically significant diarrhea ( $\geq 3$  episodes in 24 hours)
  - no laxatives in preceding 48 hours
  - rejection of repeat orders within a 7-day interval
- When criteria for testing were not met, order was cancelled and the provider was notified.



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# CDI and the Impact of Diagnostic Stewardship

## The Stanford Experience

- 2,321 orders for *C. difficile* testing
  - 211 (9.1%) cancelled because of receipt of laxatives
  - 164 (7.1%) cancelled due to absence of diarrhea
- *C. difficile* test utilization decreased from 208.8 tests to 143 tests per 10,000 patient-days ( $P = 0.001$ )
- HO-CDI incidence rate decreased from 13 cases to 9.7 cases per 10,000 patient-days ( $P = 0.008$ )
- Oral vancomycin days of therapy decreased from 13.8 days to 9.4 days per 1,000 patient-days ( $P = 0.009$ )



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# CDI and the Impact of Diagnostic Stewardship

## The USC Experience

- 05/2016 – 12/2017: Retrospective review of medical records of patients whose providers ordered C. difficile testing
- “True HO-CDI”
  - clinically significant diarrhea ( $\geq 3$  episodes in 24 hours)
  - no laxatives in preceding 48 hours
  - at least 1 of the following symptoms:**
    1. temperature  $\geq 38^{\circ}\text{C}$
    2. abdominal pain
    3. abdominal tenderness documented on exam
    3. WBC  $> 12,000/\mu\text{L}$



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# CDI and the Impact of Diagnostic Stewardship

## The USC Experience

- 01/2017:
  - Hospital-wide educational campaign on *C. difficile* testing
    - campus-wide memo to providers
    - hospital-wide screensaver listing clinical criteria for a true (+) CDI test
    - presentations at surgical and medicine grand rounds
  - 2 diagnostic stewardship measures
    1. Order cancelled if stool sample not received within 24 hours of order placement
    2. Lab rejected formed specimens if failed “stick test”



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# CDI and the Impact of Diagnostic Stewardship

## The USC Experience

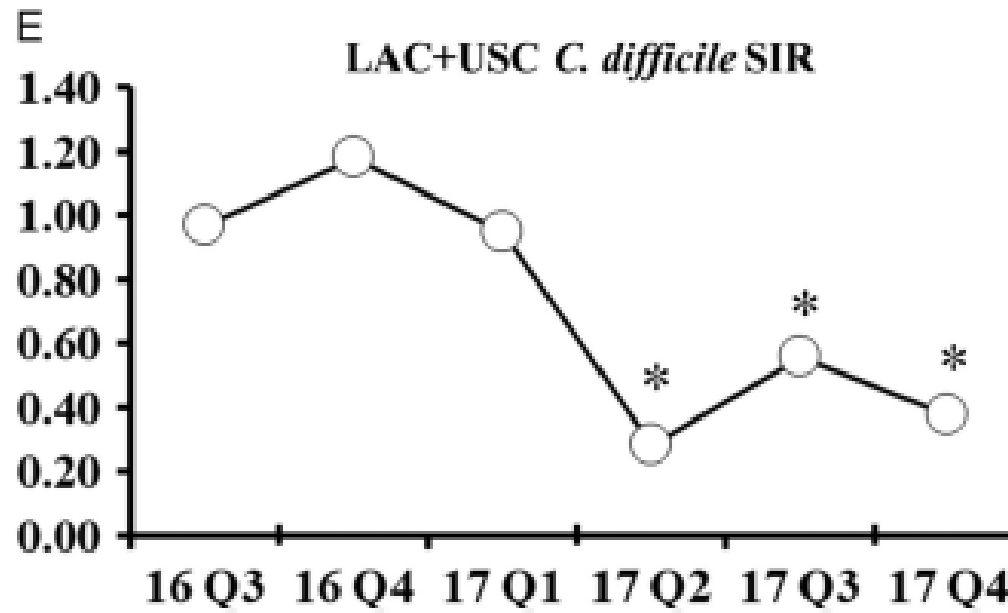
- 05/2016 – 12/2016: Baseline period
  - 70% false-positive rate
- 01/2017: After education and lab protocol
  - 43% decrease in tests ordered
  - 36% decrease in positive tests
- No increase in complications from delayed diagnosis and treatment (e.g. colectomies, ICU admissions post-intervention)



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# CDI and the Impact of Diagnostic Stewardship

## The USC Experience



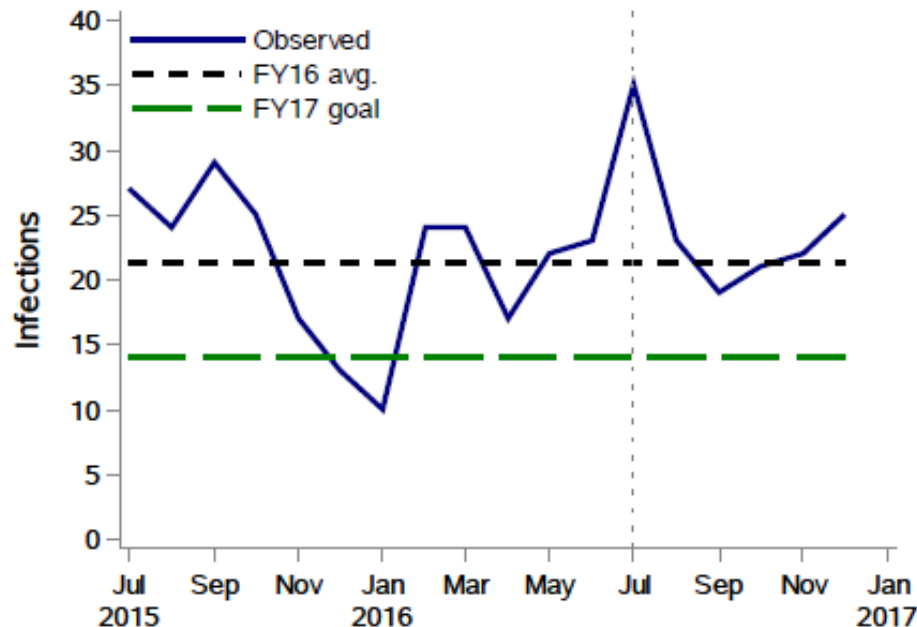
- Statistically significant ↓ Standardized Infection Ratio (SIR)
- Decreased lab costs: \$2,017.80 per month
- Decreased drug costs: ~\$5,000 per month

# CDI and the Impact of Diagnostic Stewardship

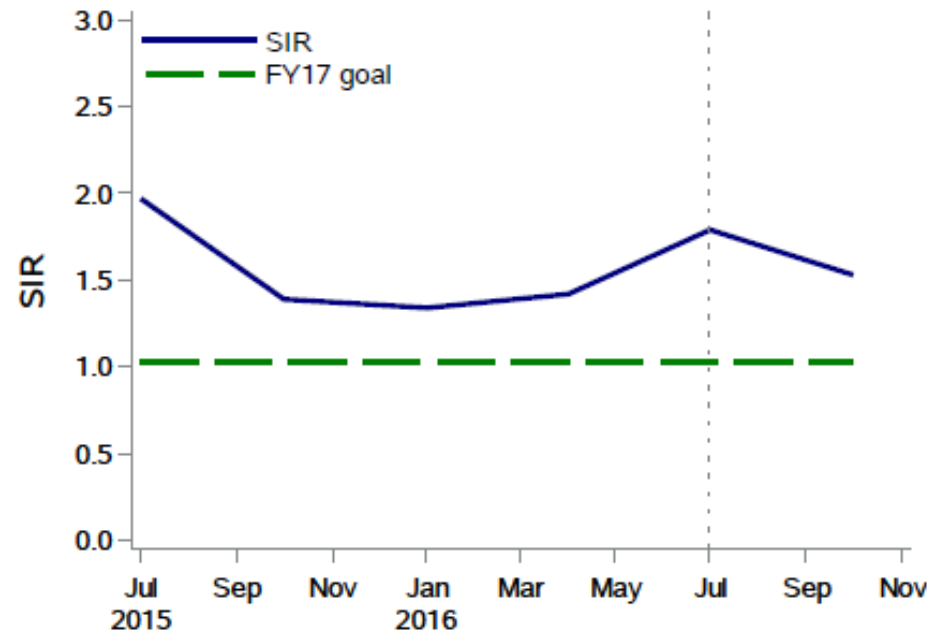
## Emory University Hospital Experience

- 12/31/2016:
  - 172 HO-CDI FY2017 to achieve SIR 1.0
  - On track for **292 HO-CDI (SIR: 1.66)**
  - **>40% above target!** ☹️

EUH C diff infections per month, #



EUH C diff SIR, quarterly



# CDI and the Impact of Diagnostic Stewardship

## Emory University Hospital Experience

- 02/2017: Implementation of 3 diagnostic stewardship interventions
  1. Order cancelled if stool sample not received within 48 hours of order placement
  2. EMR pop-up alert if C difficile testing ordered in patient receiving laxative
  3. Hospital protocol defining appropriateness criteria for C. difficile testing
    - based on diarrhea decision tree utilized at Emory St. Josephs Hospital and Emory Johns Creek Hospital associated with significant ↓ (>50%) in HO-CDI
    - modified after multiple meetings with key stake holders
      - hospital medicine
      - intensive care units
      - solid organ transplant units
      - bone marrow transplant units
      - infectious diseases

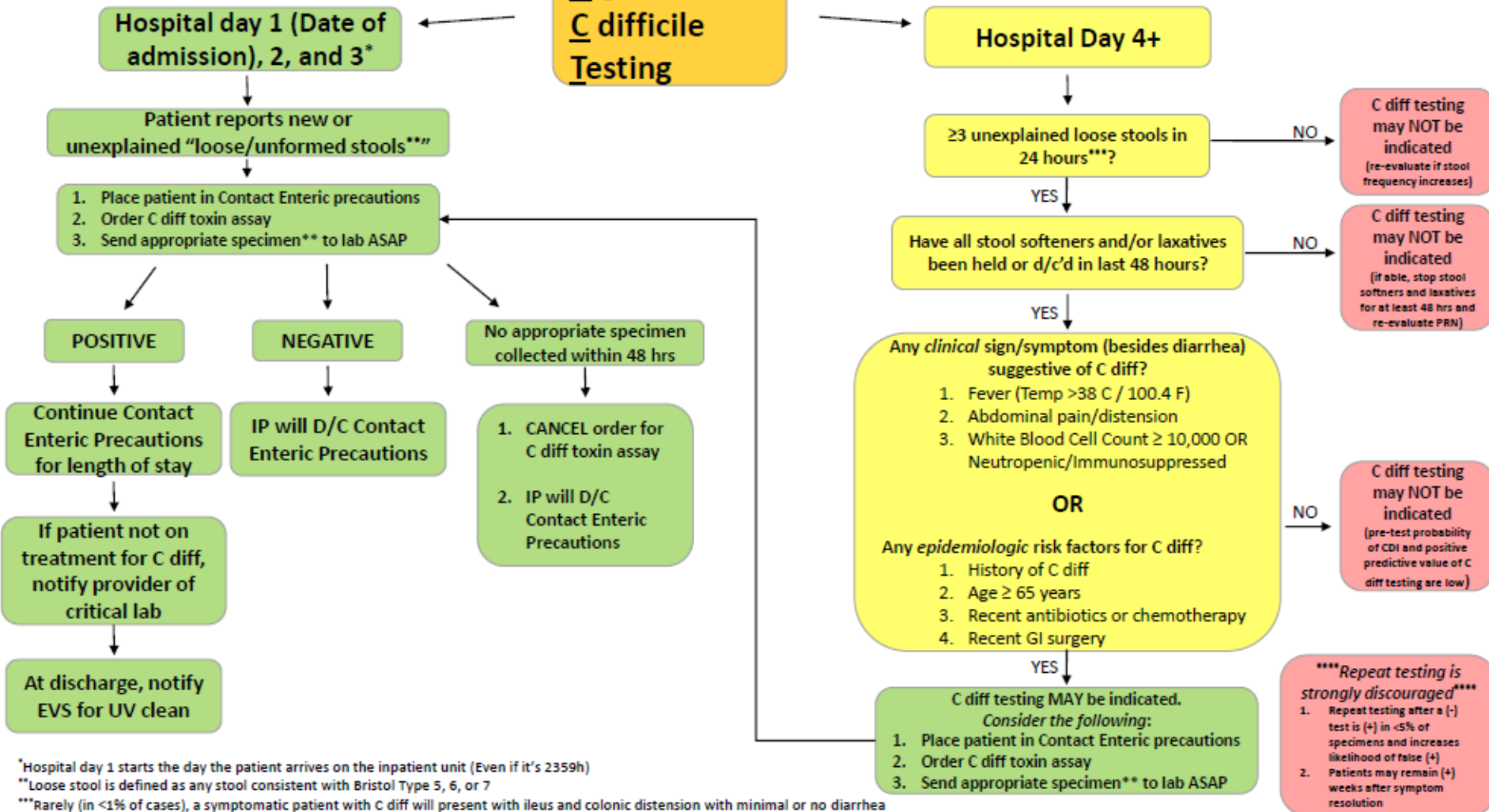


# CDI and the Impact of Diagnostic Stewardship

## Emory University Hospital Experience

Version 3.0: Draft 11/15/2017

### Algorithm for C difficile Testing



\*Hospital day 1 starts the day the patient arrives on the inpatient unit (Even if it's 2359h)

\*\*Loose stool is defined as any stool consistent with Bristol Type 5, 6, or 7

\*\*\*Rarely (in <1% of cases), a symptomatic patient with C diff will present with ileus and colonic distension with minimal or no diarrhea

# CDI and the Impact of Diagnostic Stewardship

## Emory University Hospital Experience

Hospital day 1 (Date of admission), 2, and 3\*

Patient reports new or unexplained "loose/unformed stools\*\*"

1. Place patient in Contact Enteric precautions
2. Order C diff toxin assay
3. Send appropriate specimen\*\* to lab ASAP

POSITIVE

NEGATIVE

No appropriate specimen collected within 48 hrs

Continue Contact Enteric Precautions for length of stay

IP will D/C Contact Enteric Precautions

1. CANCEL order for C diff toxin assay
2. IP will D/C Contact Enteric Precautions

If patient not on treatment for C diff, notify provider of critical lab

At discharge, notify EVS for UV clean

### ACT Goals: Day 1, 2, and 3

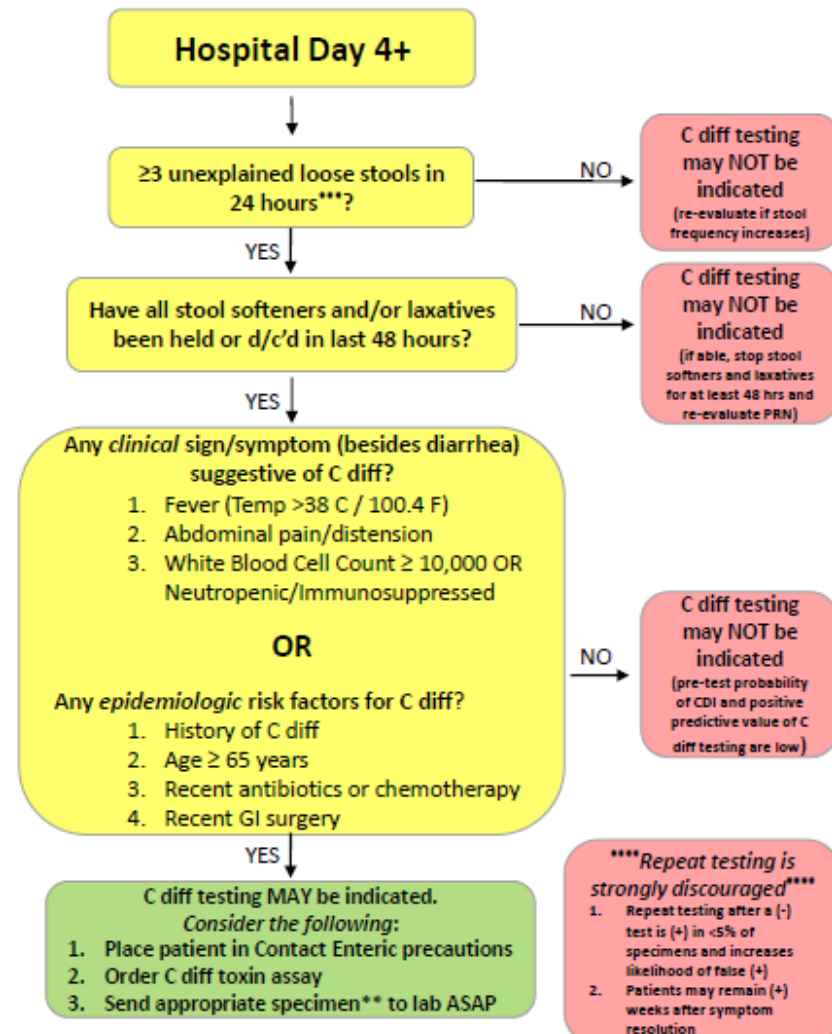
1. Increase **sensitivity** to diagnose **community-onset** *C. difficile* infections
2. Minimize time to implementation of appropriate **infection control precautions** (i.e. gowns and gloves) to **limit horizontal transmission** of *C. difficile* to other hospitalized patients
3. Minimize time to starting effective **treatment** for *C. difficile*
4. Minimize time of patients in contact enteric precautions who test negative for *C. difficile*
5. Limit *C. difficile* testing to patient who are having diarrhea ( $\geq 3$  unformed stools in  $\leq 24$  consecutive hours)

# CDI and the Impact of Diagnostic Stewardship

## Emory University Hospital Experience

### ACT Goals: Day 4+

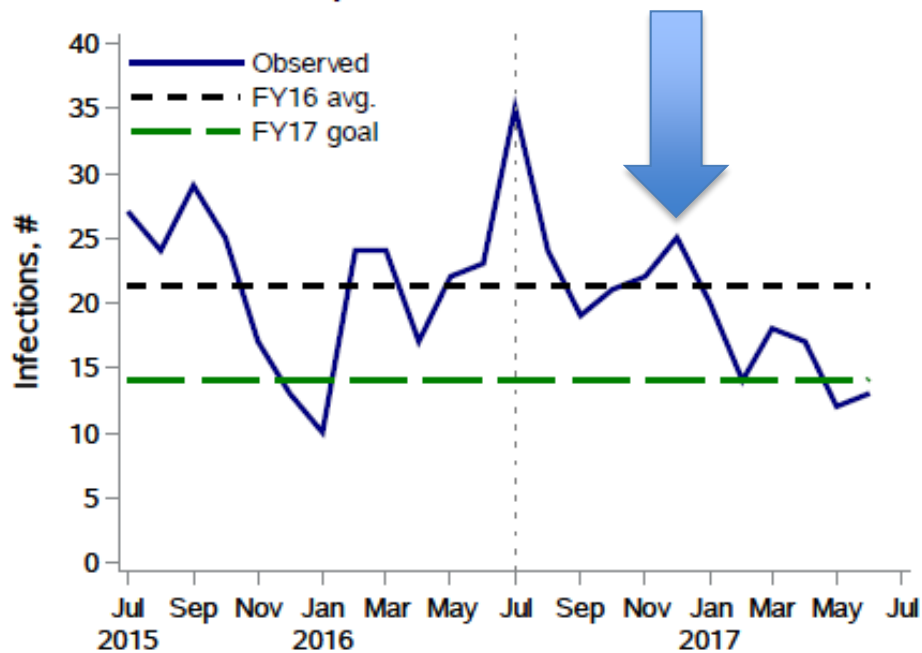
1. Increase **specificity** to diagnose **hospital-onset** *C. difficile* infections
2. Minimize detection of **asymptomatic** colonization with *C. difficile*
3. Identify reversible causes of **non-infectious** diarrhea (e.g. laxatives)
4. Minimize unnecessary contact enteric precautions for patients with low pre-test probability for CDI
5. **Limit inappropriate testing and strongly discourage repeat testing**
  - most patients with a negative *C. difficile* PCR do **not** require re-testing
  - patients with a positive PCR should **not** have a “test of cure” performed



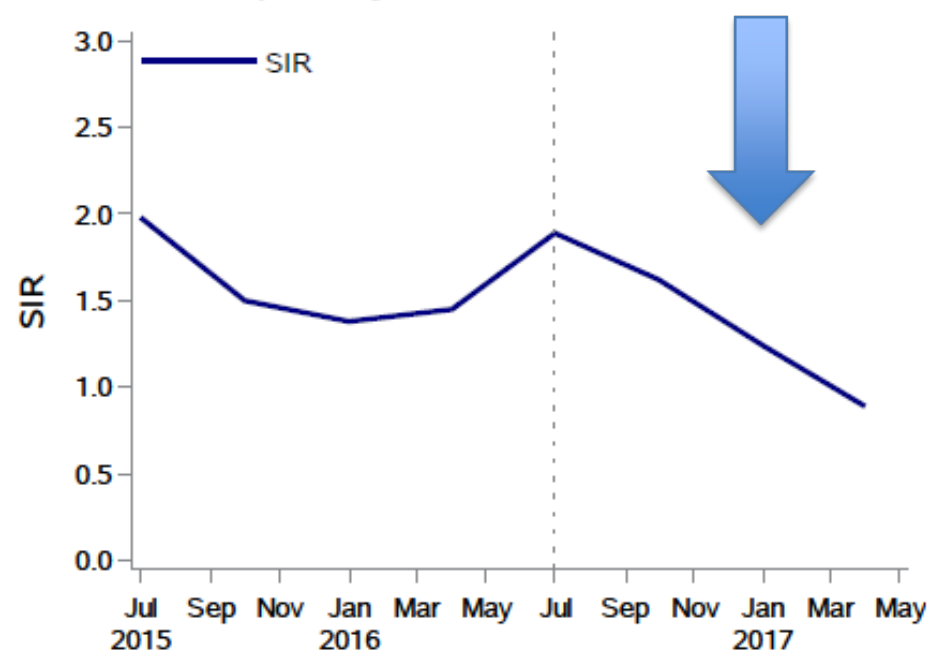
# CDI and the Impact of Diagnostic Stewardship

## Emory University Hospital Experience

EUH C diff infections per month



EUH C diff SIR, quarterly

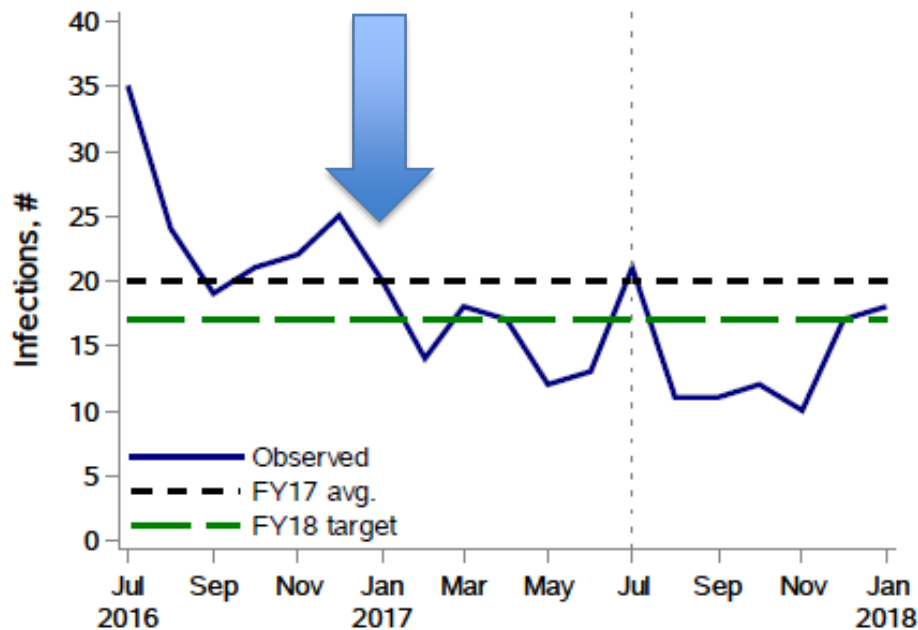


>30% reduction in HO-CDI sustained over time  
No increase in colectomies/death secondary to CDI

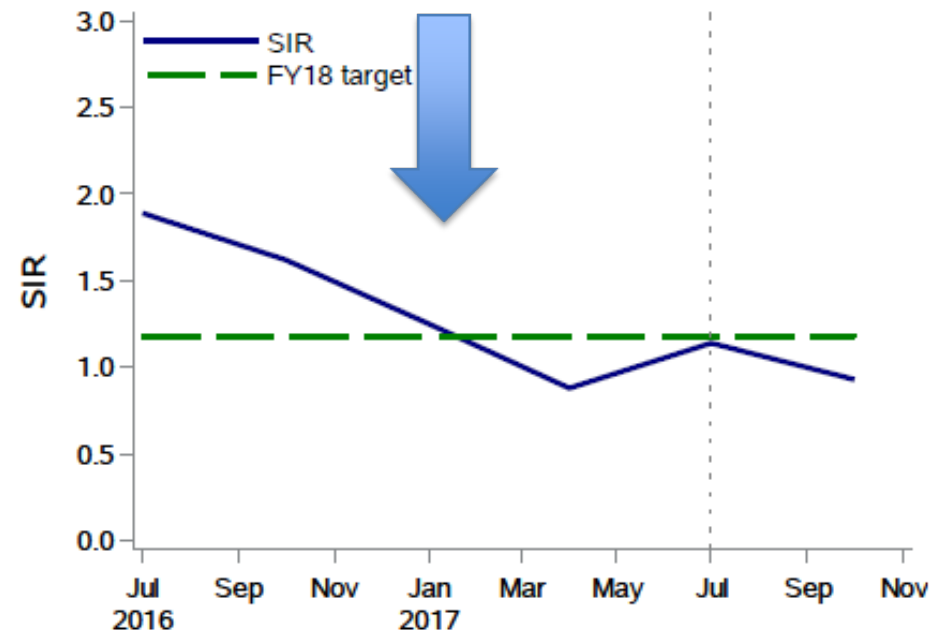
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EUH C diff infections per month



EUH C diff SIR, quarterly



>30% reduction in HO-CDI sustained over time  
No increase in colectomies/death secondary to CDI

# CDI and the Impact of Diagnostic Stewardship

## Potential Barriers and Ways to Overcome

1. No one-size-fits-all approach
  - not a limitation for antibiotic stewardship programs!
2. Lack of **specific** consensus guidelines from professional societies
  - requires high quality evidence from clinical studies
3. Provider pushback from reduced autonomy
  - hospital administration support
  - transparency when changing testing processes
  - must be flexible—**not absolute**



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# Concluding Thoughts

1. CDI remains the #1 HAI in the United States with significant morbidity and mortality
2. Diagnostic Stewardship improves the quality of care we provide, reduces costs, and thus, provides value to patients, health care systems and public health.
3. When applied to CDI, diagnostic stewardship can improve the accuracy of CDI diagnosis, reduce HAI rates by reducing false positive tests, and improve the appropriateness of treatment

THANK YOU!