

# Diagnostic Stewardship – Focus on Testing for CDI

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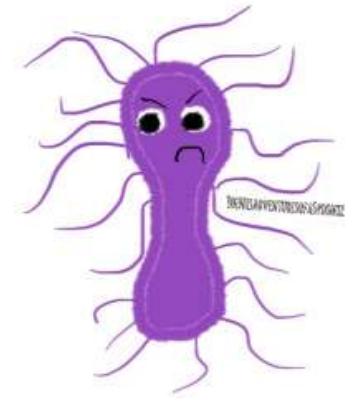
# *C. difficile* Tests

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- NAATs (including PCR) detect one or more genes specific to toxigenic strains
  - Specific for toxigenic strains
  - Do not test for active toxin protein production and are capable of detecting asymptomatic carriers of *C. difficile*
  - Overdiagnosis of CDI has emerged as a risk of NAATs
- Enzyme immunoassay (EIA) for *C. difficile* toxins A and B
  - Commercially available
  - Results are available within hours
  - Sensitivity of EIA for toxins A and B is on average about 75 percent, but the sensitivity varies depending on the specific assay used

# Potential Consequences of Over-Testing

- Unnecessary antibiotic treatment which can contribute to prolonged shedding and promotion of ongoing gut “dysbiosis”
- Increased vancomycin exposure → VRE?
- Misdiagnosis or delayed diagnosis of another cause of diarrhea



# Strategies for diagnostic stewardship

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## IDSA Guidelines

- **Unexplained** and **new-onset** episode of diarrhea defined as  $\geq 3$  unformed stools in 24 hour period

## Other clinically acceptable indication

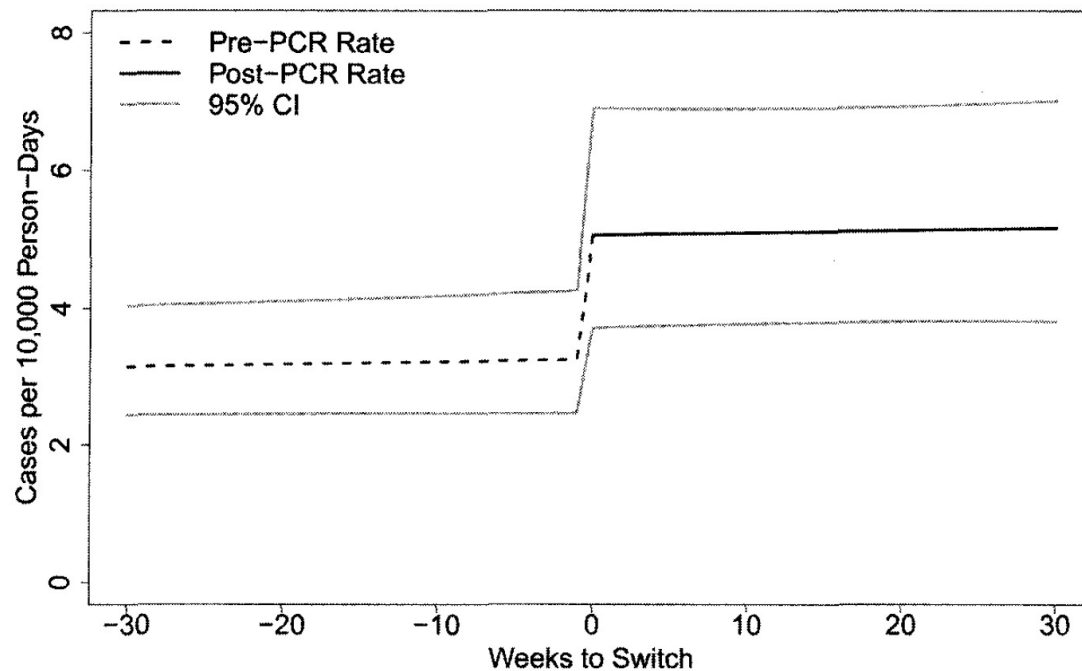
- When there is strong clinical suspicion for toxic megacolon based on clinical presentation, radiographic findings, and patient risk factors even in the absence of diarrhea

# Strategies for Diagnostic Stewardship

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- Improve diagnostic specificity
- Establish criteria for CDI test collection, processing, and test interpretation
  - Particularly with NAAT testing
- Establish clinical practice guideline for treatment
- Focus on appropriateness
  - Diarrhea that persists: 3 or more unformed stools per 24 hours

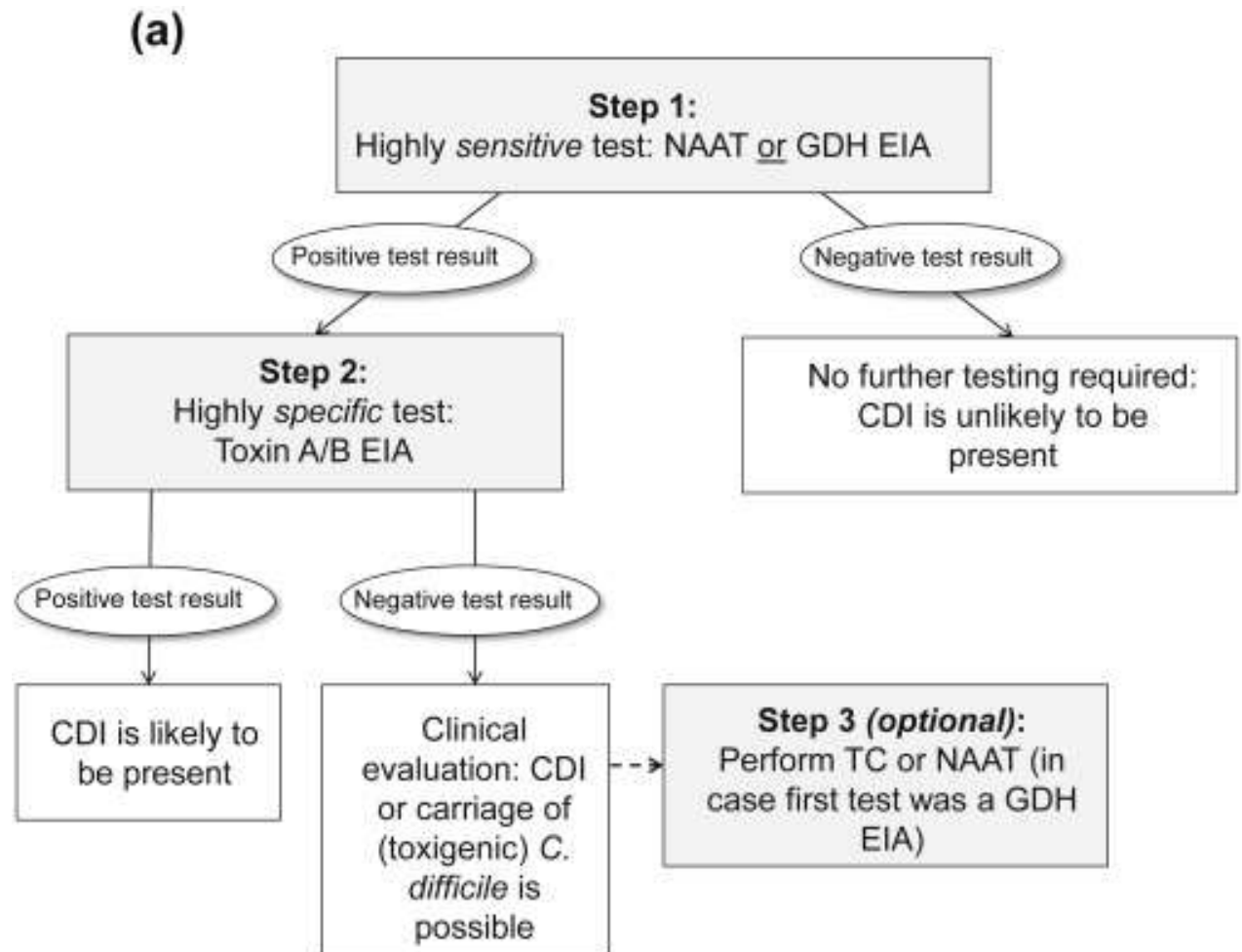
# Impact of molecular testing on CDI rates



aIRR 1.56 (95% CI 1.28-1.90)

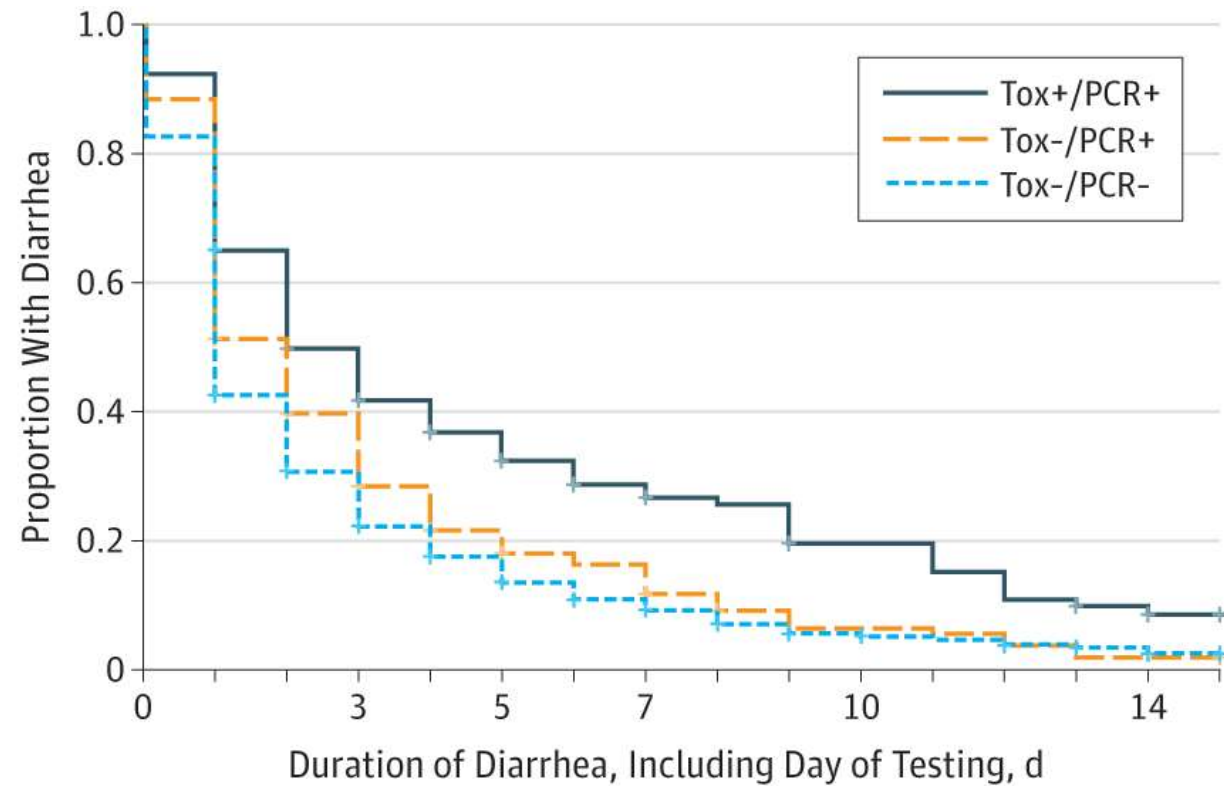
# 2-Step Algorithm

Most Common:  
High Sensitivity NAAT first,  
Toxin to confirm



# Why 2-step Testing?

Patients with PCR+/Tox- have same outcomes of PCR- patients



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



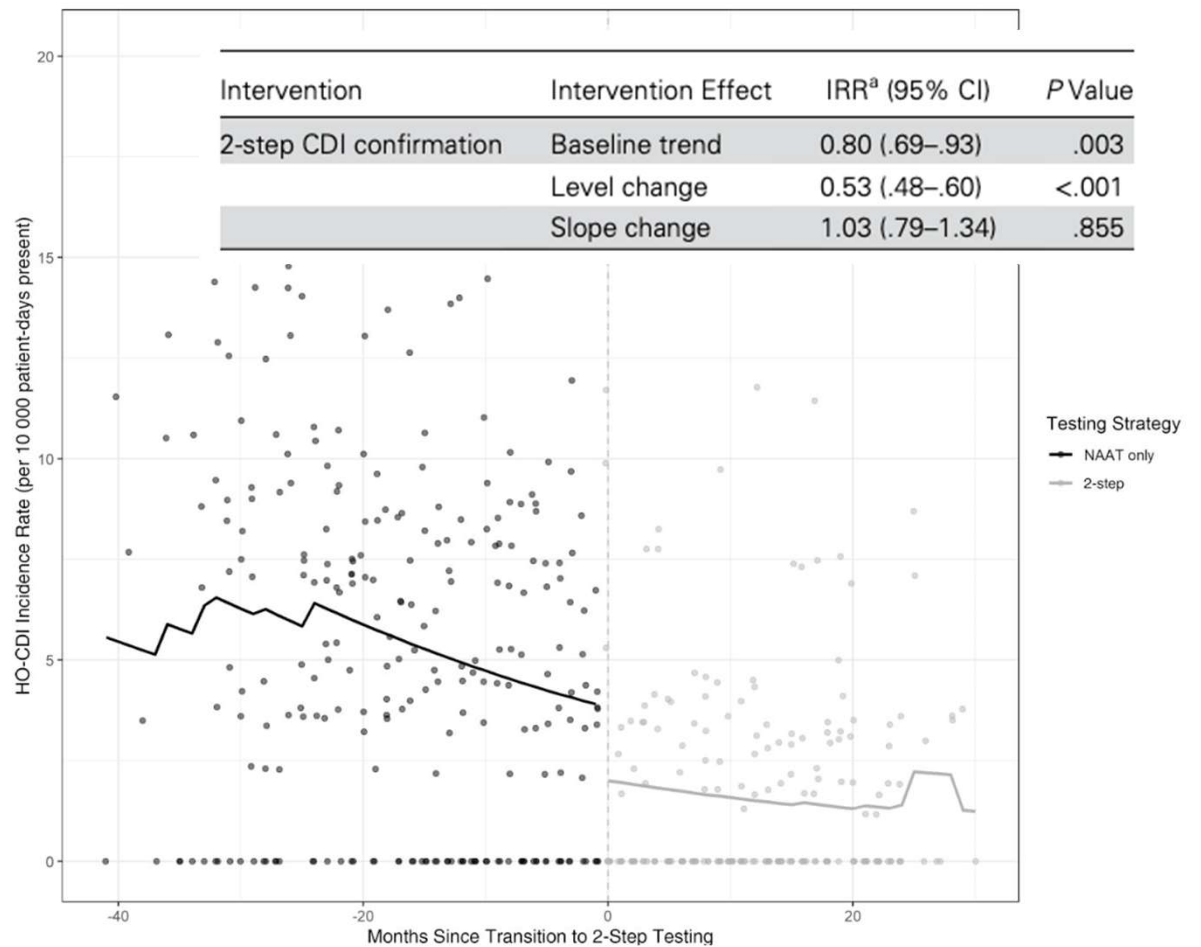
Duke Center for  
Antimicrobial Stewardship  
and Infection Prevention

Polage et al *JAMA Int Med* 2015

# Use of 2-step testing

8 hospitals changed to NAAT followed by Toxin

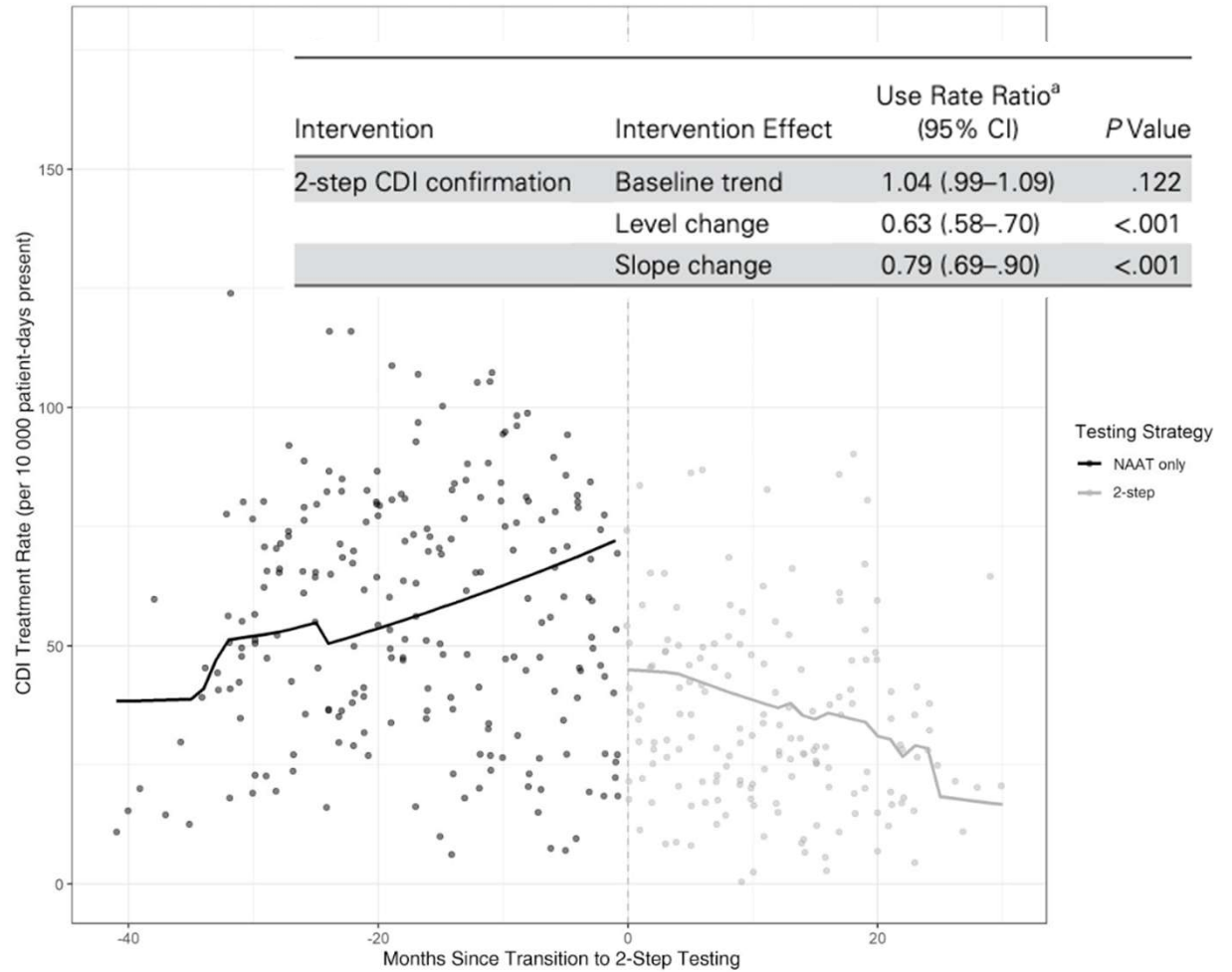
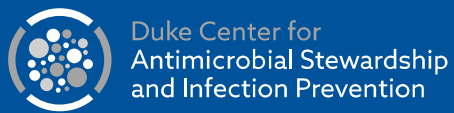
2.6 million patient days over 5-year period



Turner et al CID 2023;77:1043.

# Use of 2-step testing

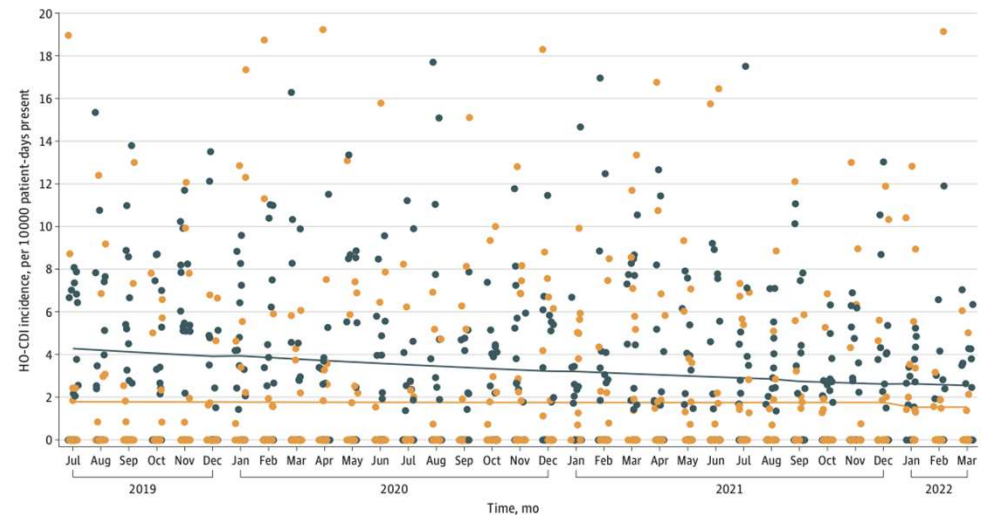
Impact on treatment (PO Vanco + Fidax)



# CDC Framework Implementation

- Framework
  - Isolation/contact precautions
  - CDI confirmation
  - EVS
  - Infrastructure
  - Stewardship
- Implementation study in 20 hospitals
  - Compare to 26 non-participating
- Outcome: HO-CDI
  - Overall, no difference
- Alas, study impacted by COVID

Figure 1. Comparison of Hospital-Onset *Clostridioides difficile* Infection (HO-CDI) Incidence Trends Between Participating Hospitals and Control Hospitals



# Evaluation of Individual Components

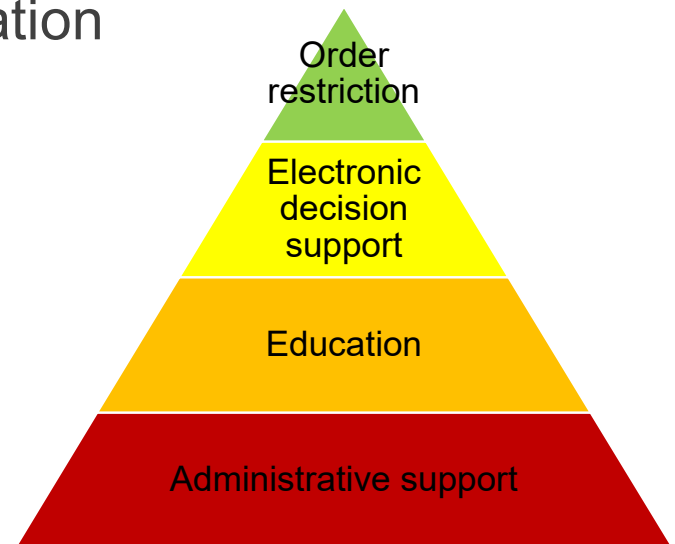
Used by at least 2 hospitals and in place for > 6 months

- Impact on HO-CDI

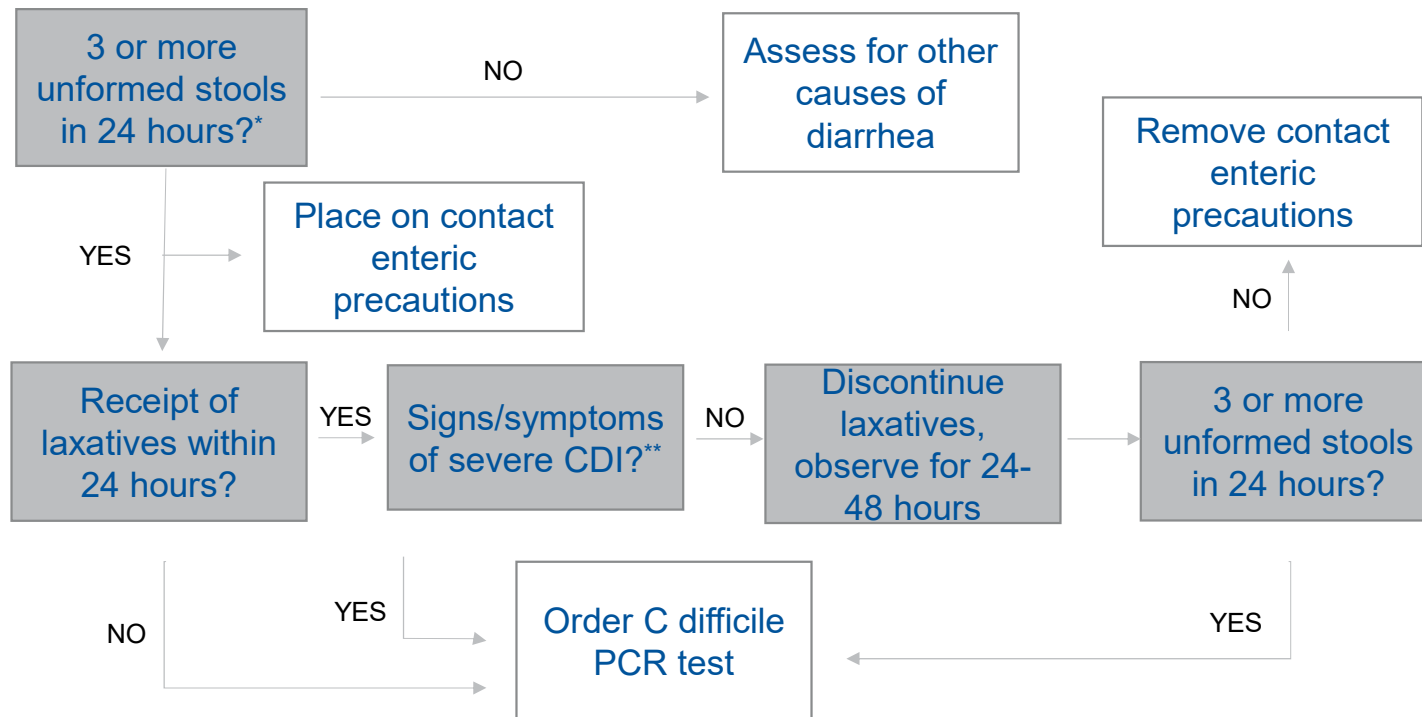
Baseline trend	0.90 (0.79-1.02)
Isolation auditing, slope	1.13 (0.94-1.34)
Case reviews, slope	0.81 (0.68-0.96)*
Two-step testing, level	0.50 (0.42-0.59)*
EVS audits	1.12 (0.95-1.32)
Stewardship, high yield	0.77 (0.60-0.99)*

# Implementing a CDI Testing Algorithm

- How easy/hard is it to determine if testing is appropriate?
  - E.g., is stool documentation accurate?
- Does the hospital infrastructure support education of clinicians regarding appropriate testing?
- Does the local culture support restriction of test orders?
- At what point will the restriction occur?
  - Lab?
  - At the time of order?
  - Post-order review?



# Example CDI Testing Algorithm



\*if clinical concern for toxic megacolon, consider abdominal imaging/surgical consultation

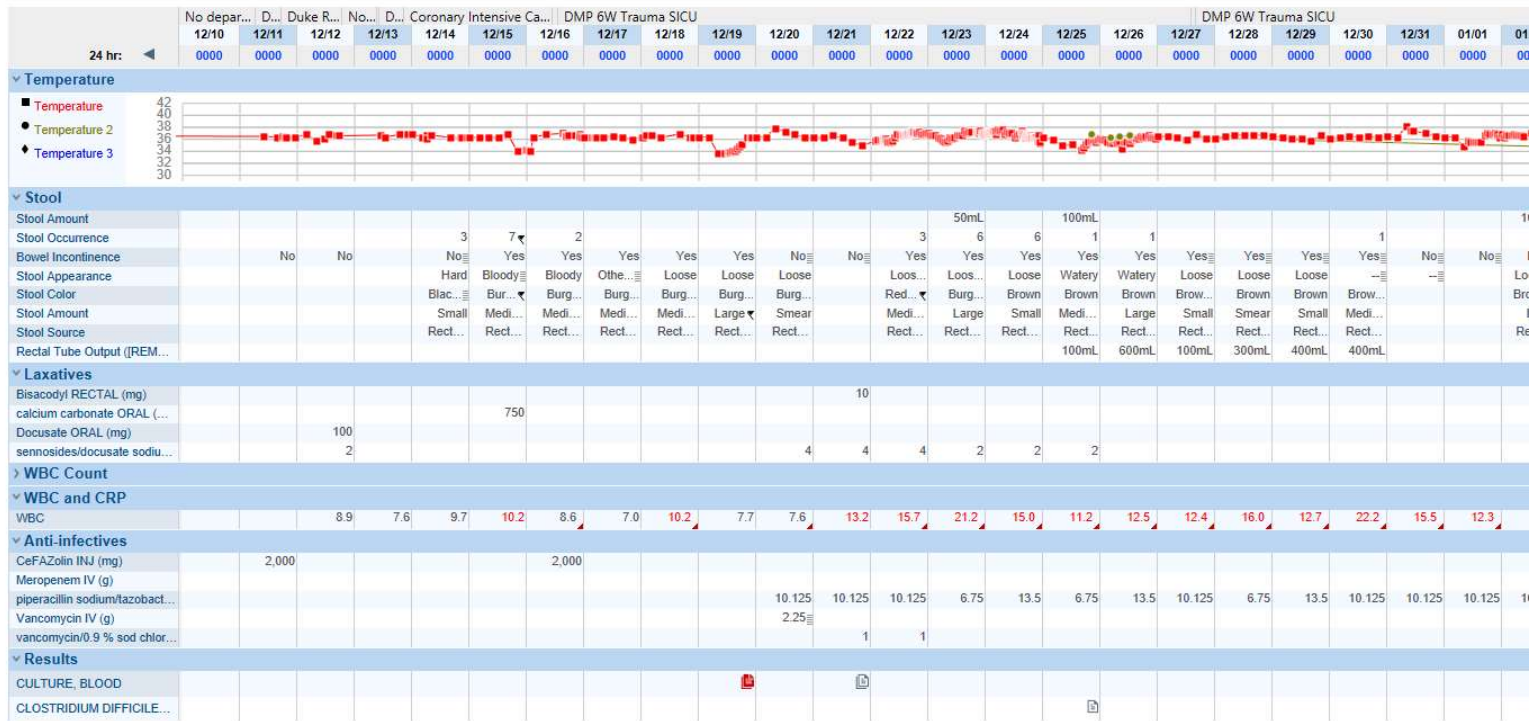
\*\*septic shock, WBC > 15, and/or abdominal tenderness

# Tools for Clinicians

MDRO/C. Diff

Go to now 12/10/2018

12/10/18 - Today



Temperature curve

Stool documentation

Laxative admin

WBC

Antibiotic admin

Culture data

# Electronic decision support – Laxative Alert

The screenshot shows a clinical decision support interface. At the top, a yellow banner reads: "Laxatives Recently Administered. Consider cancelling Cdiff testing." Below this, a message states: "Ms. Test has taken laxatives in the last 24 hours" with a "Provide Feedback" link. A link to the "Antibiotic Stewardship CDI Testing Algorithm" is provided, suggesting deferring testing. A table titled "Laxative MAR Administrations - Last 48 Hours" shows one entry: polyethylene glycol (MIRALAX) packet 17 g administered on 02/12/2018 at 15:02. Below the table, it notes "No data recorded" and "No results for input(s): WBC in the last 168 hours." At the bottom, there is a section to "Remove the following orders?" with a "Remove" button and a "Keep" button. The order listed is "Clostridium Difficile Toxin, PCR Routine, Once First occurrence Today at 1503 Stool". An "Acknowledge Reason" section has two options: "Proceed with Testing - High Suspicion" and "Other Reason - See Comments". An "Accept" button is at the bottom right.

Administered	MAR	Action	Medication	Dose	Rate	Visit
02/12/2018	15:02	Given	polyethylene glycol (MIRALAX) packet 17 g	17 g		Admission (Current) on 01/18/2018 in DUH N9100 Hematology/Oncology

## TIPs for Successful EDS:

- Displays for right provider at right time
- Link to existing facility guidelines
- Contains pertinent clinical information
  - Laxative administration
  - WBC, temperature curve

## Potential Pitfalls of EDS

- Provider alert-fatigue
- Easily over-ridden

# Electronic decision support – Contextual Rules

Stool Documentation

WBC

(B)

Specimen Src:

**i** Nurse has not documented 3 or more stools or >600 mL of stool volume in last 24h. Please specify additional symptoms present to proceed with testing.

Comments: [+ Add Comments \(F6\)](#)

Reference Links: 1. C Diff Diagnosis & Treatment

Accept  Cancel

**And**

Cancel Uncollected C. diff Toxin, PCR Orders After 24 Hours

Order details

(C)

Specimen Src:

**i** Laxatives have recently been administered and patient has WBC > 4 and < 11 in last 2 days. This test will be canceled by clinical lab. Please call lab to provide justification and request exception to policy. Recommendation: Stop laxatives and Reassess.

Comments: [+ Add Comments \(F6\)](#)

Last Resulted: Lab Test Results

Component	Time Elapsed	Value	Range	Status
<b>WBC (White Blood Cell Count)</b>	1 day (06/18/19 1204)	4.1	3.2 - 9.8 x10 <sup>9</sup> /L	Final result

Reference Links: 1. C Diff Diagnosis & Treatment

Accept  Cancel

**And**

Cancel Uncollected C. diff Toxin, PCR Orders After 24 Hours

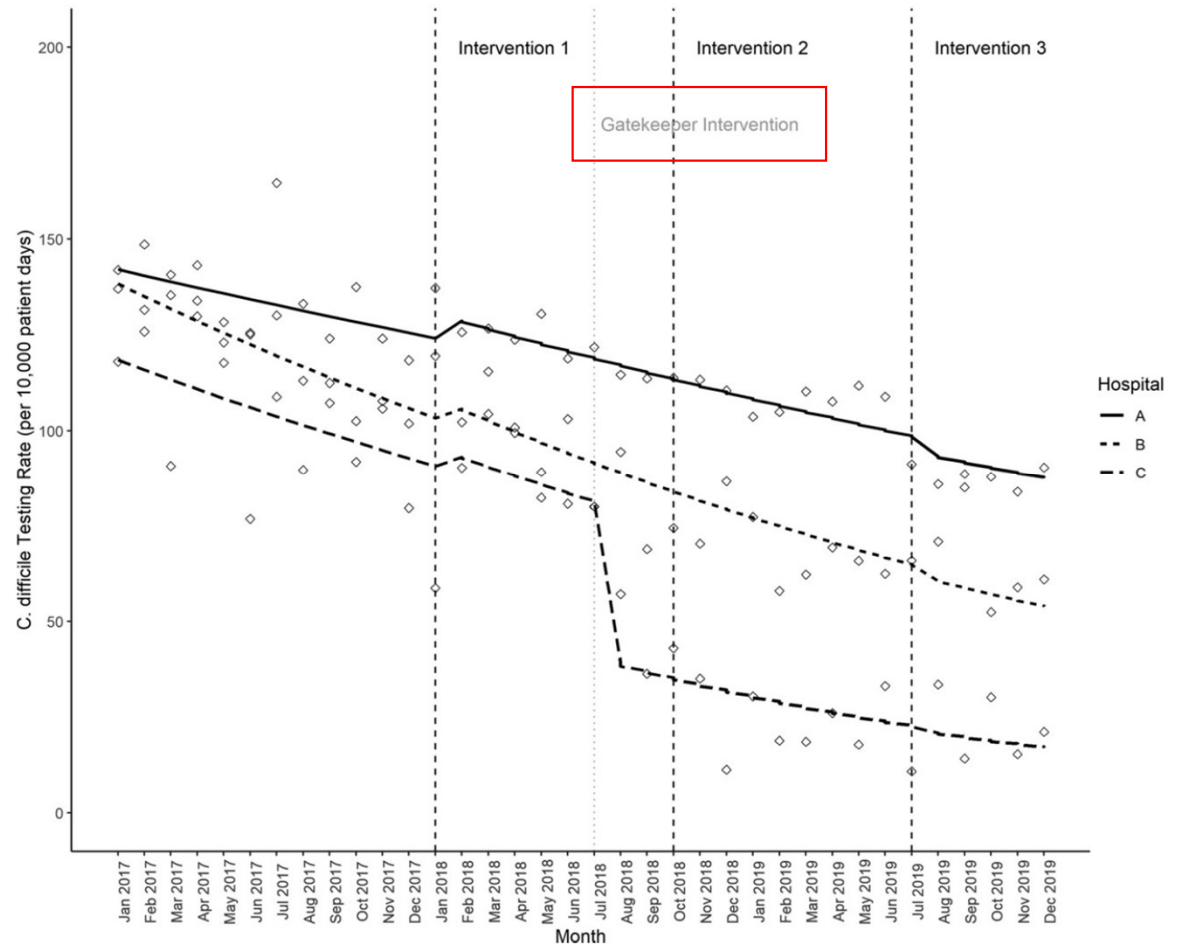
Order details

# Or Restrict?

3 hospitals initiative

EHR Interventions

- 1) Laxatives alert
  - 2) Cancel order if no sample 24 hours
  - 3) Contextual justification
- Gatekeeper intervention



Gatekeeper – ID or CMO approval required if ordered >3 days after admission

# Take Home Points

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- **Improving the appropriateness of diagnostic testing reduces**
  - Inaccurate diagnosis
  - Unnecessary antibiotic exposure for patients
  - HO infections and impact on CMS measures
- **Target the low-hanging fruit**
  - Two-step testing
  - Appropriate patients
  - Algorithms
- **More sophisticated strategies (electronic decision-support, order restriction)** may be helpful but require administrative support, education, and clinician buy-in

# Questions?