Diagnostic Stewardship – Focus on Testing for CDI

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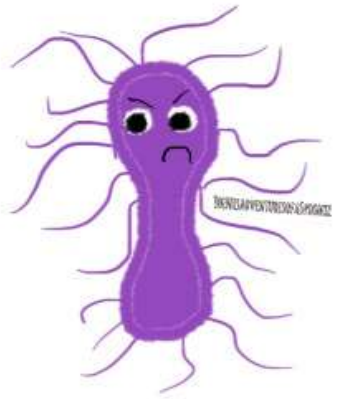
C. difficile Tests

- 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

IDSA Guidelines

- **Unexplained** and **new-onset** episode of diarrhea defined as >= 3 unformed stools in 24 hour period

Other clinically acceptable indication

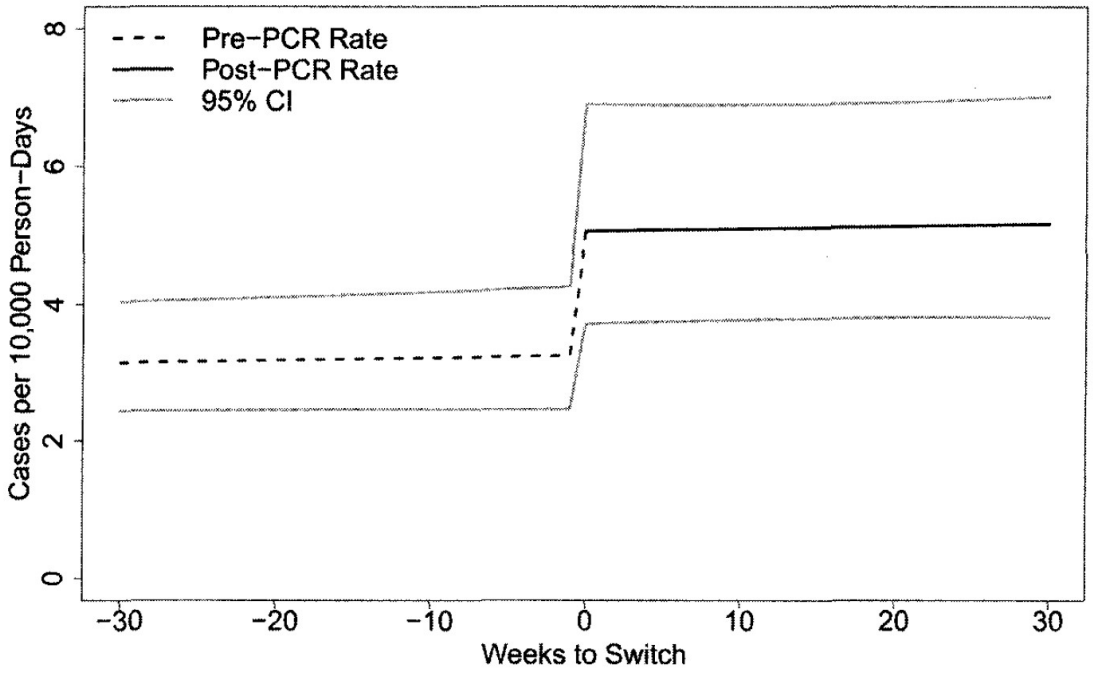
- When there is strong clinical suspicion for toxic megacolon based on clinical presentation, radiographic findings, and patient risk factors even in the absence of diarrhea

McDonald et al. Clin Infect Dis 2018; 66(7):e1-e48

Strategies for Diagnostic Stewardship

- 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)

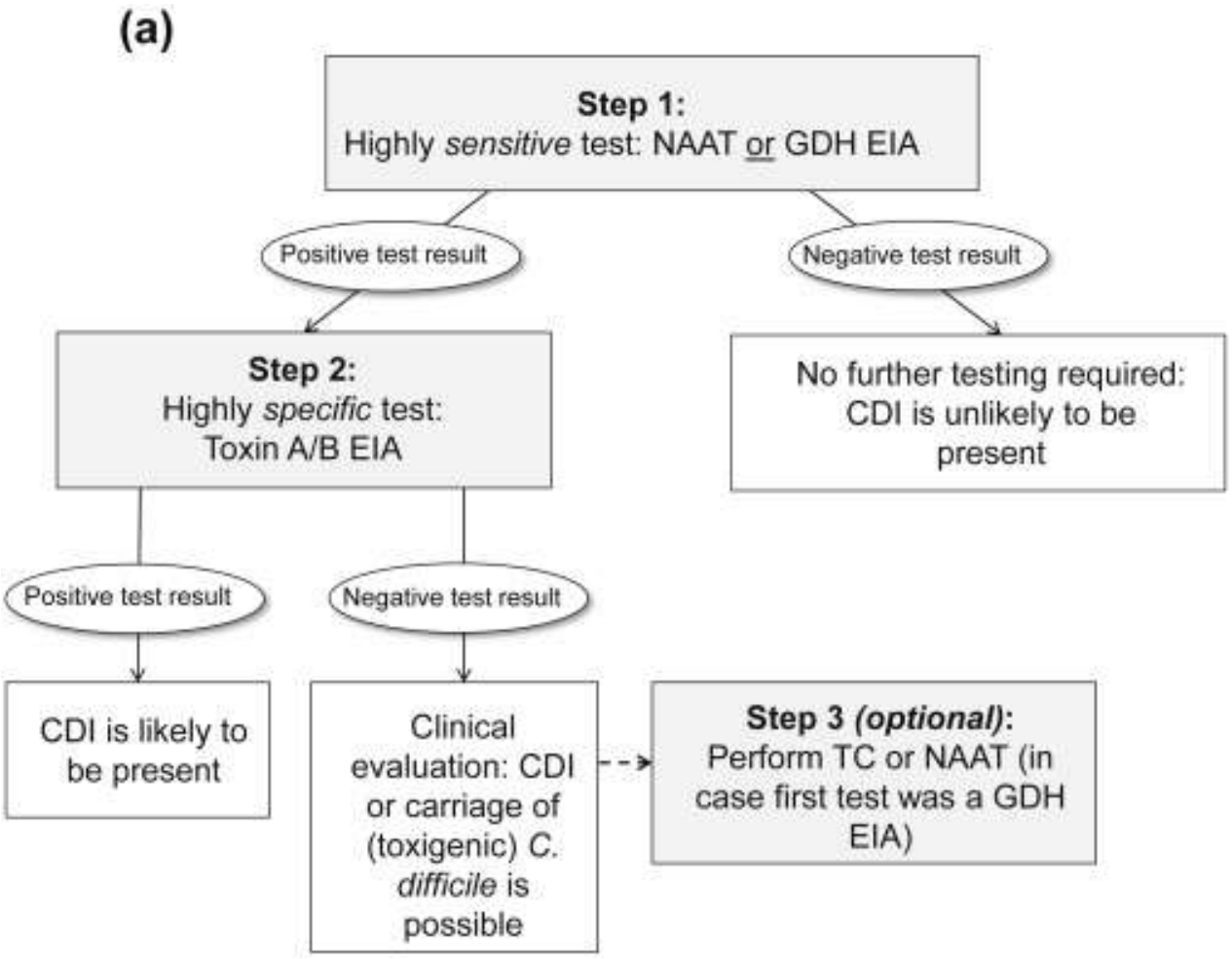
Moehring et al. Infect Control Hosp Epidemiol 2013;34(10):1055-1061

2-Step Algorithm

Most Common:

High Sensitivity NAAT first,

Toxin to confirm



Crobach et al CMI 2016

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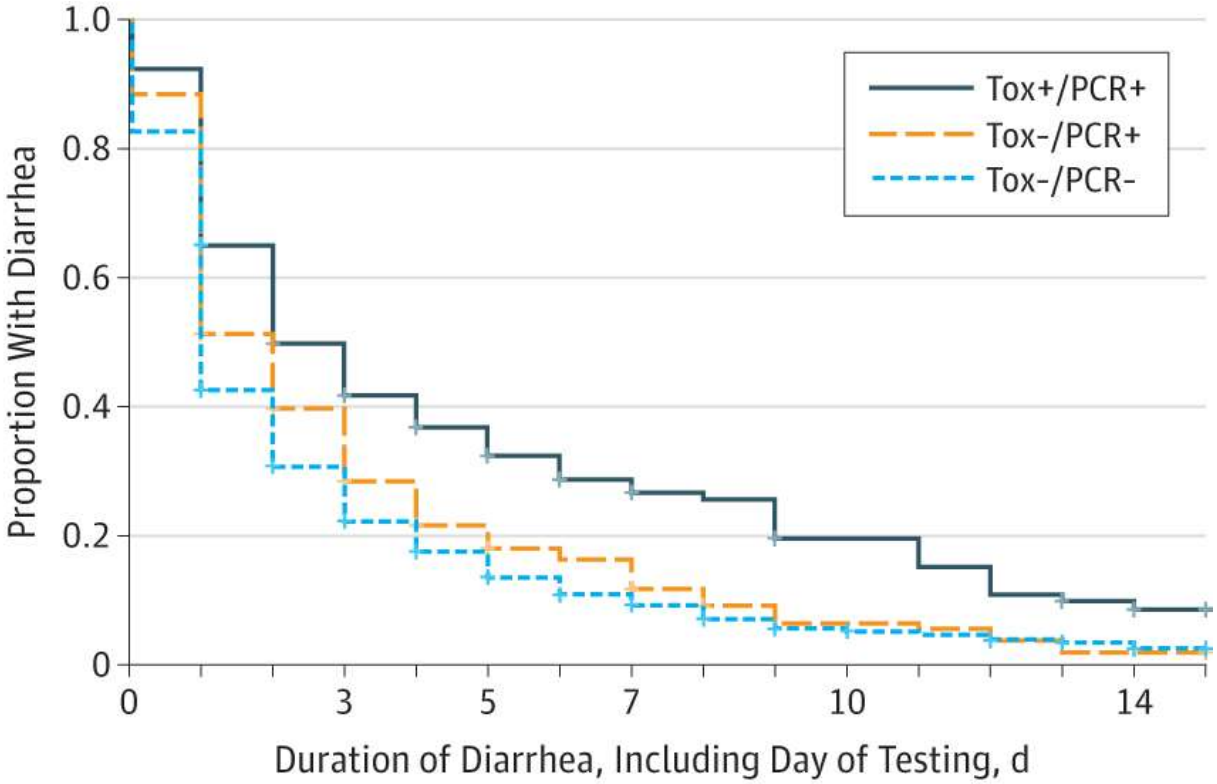
Why 2-step Testing?

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

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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

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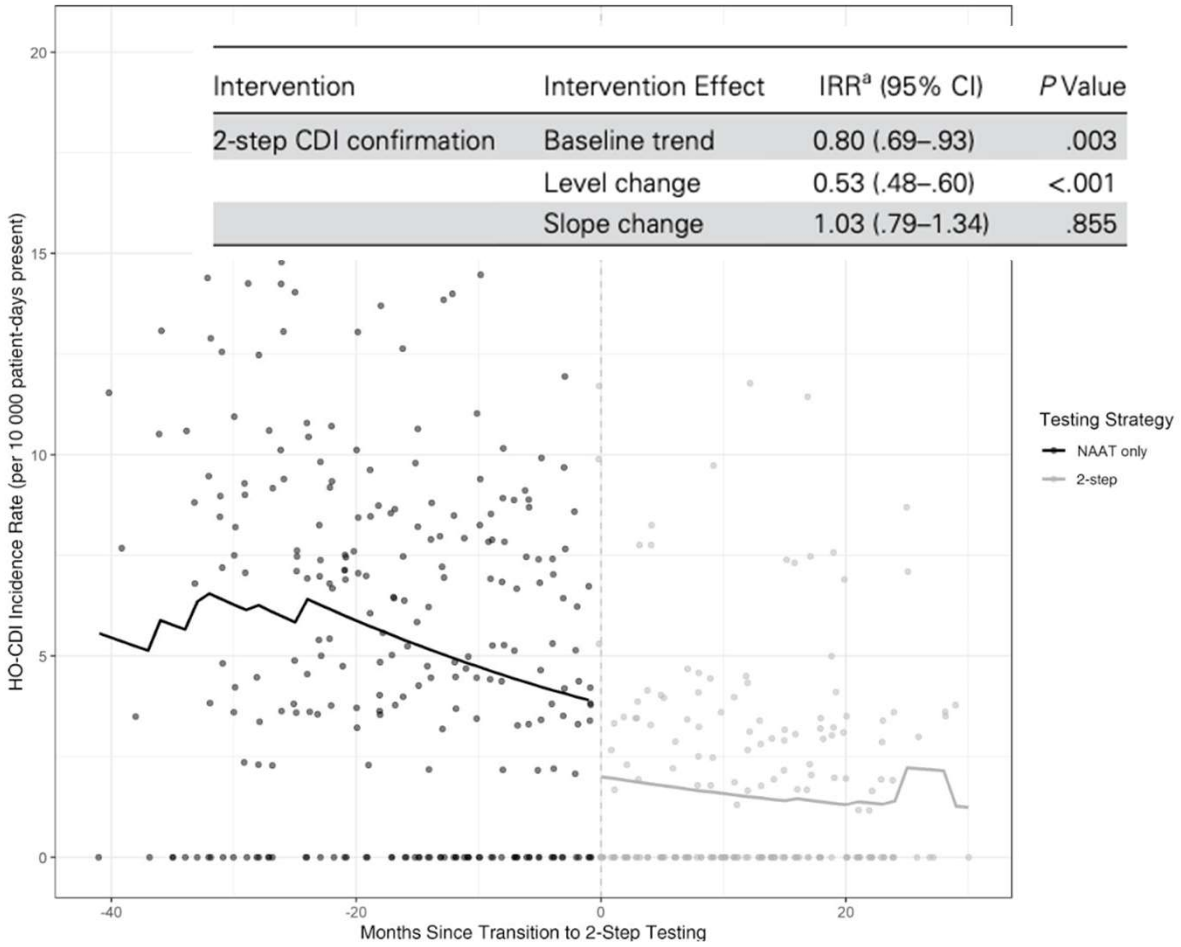
Intervention	Intervention Effect	IRR[a] (95% CI)	*P* Value
2-step CDI confirmation	Baseline trend	0.80 (.69–.93)	.003
	Level change	0.53 (.48–.60)	<.001
	Slope change	1.03 (.79–1.34)	.855

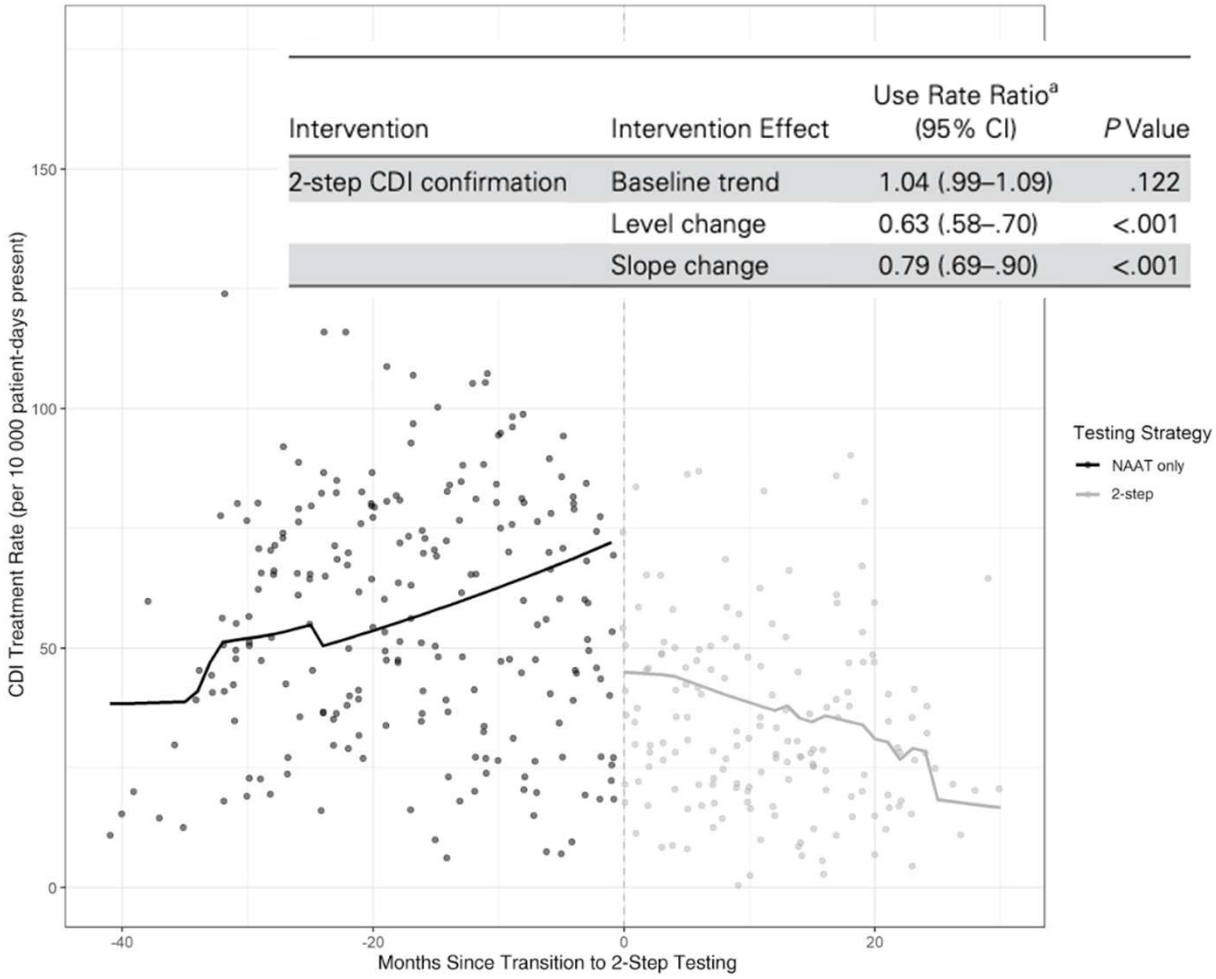


Turner et al CID 2023;77:1043.

Use of 2-step testing

Impact on treatment (PO Vanco + Fidax)

Intervention	Intervention Effect	Use Rate Ratio[a] (95% CI)	*P* Value
2-step CDI confirmation	Baseline trend	1.04 (.99–1.09)	.122
	Level change	0.63 (.58–.70)	<.001
	Slope change	0.79 (.69–.90)	<.001



Turner et al CID 2023;77:1043

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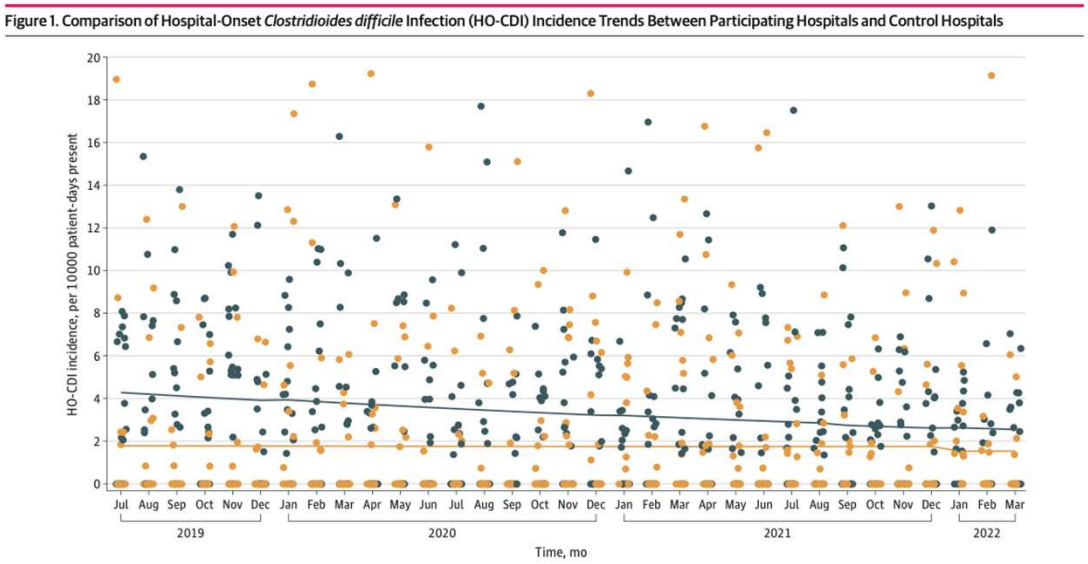
CDC Framework Implementation

- 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



Turner et al. JAMA Netw Open 2024;7(3):e243846

Evaluation of Individual Components

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

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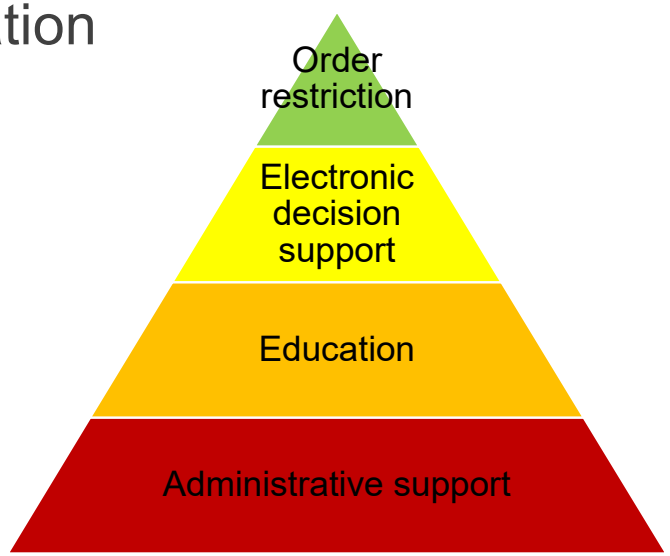
- Impact on HO-CDI

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)*

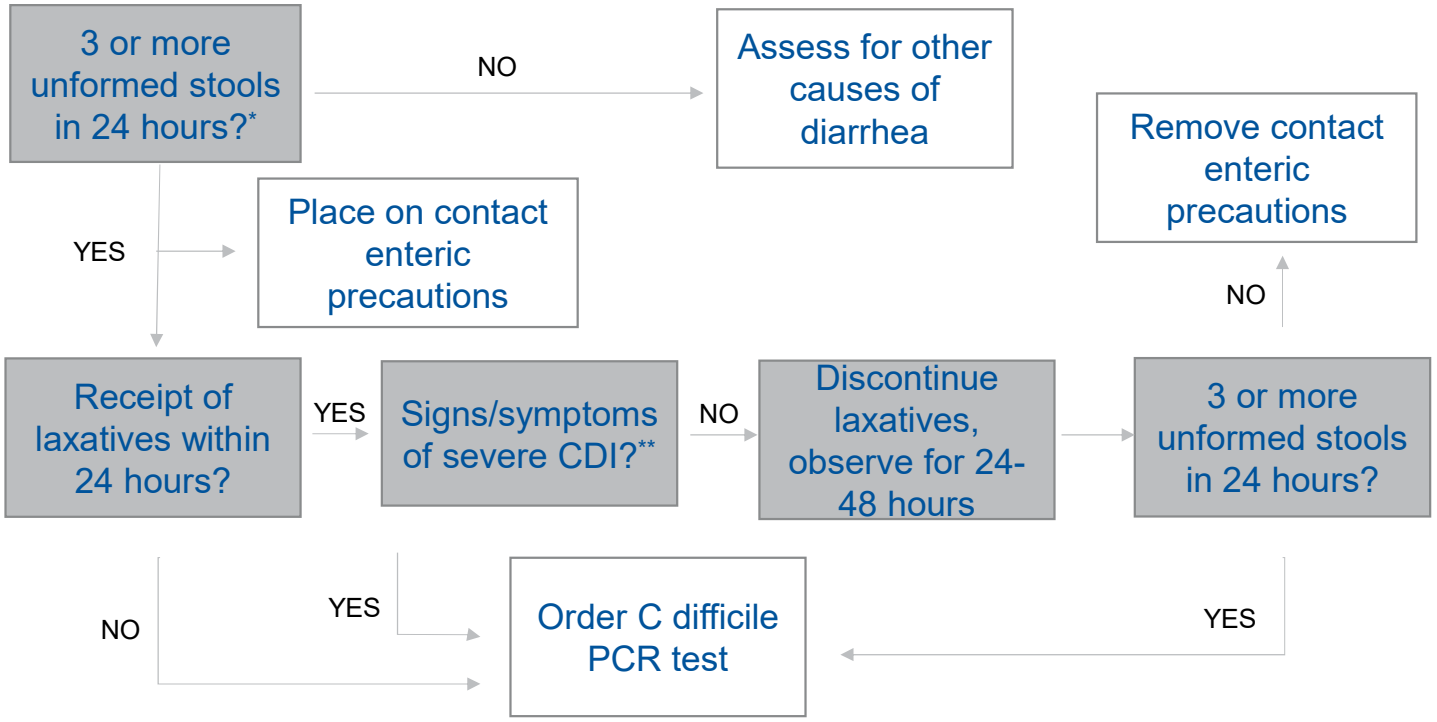
Turner et al. JAMA Netw Open 2024;7(3):e243846

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?

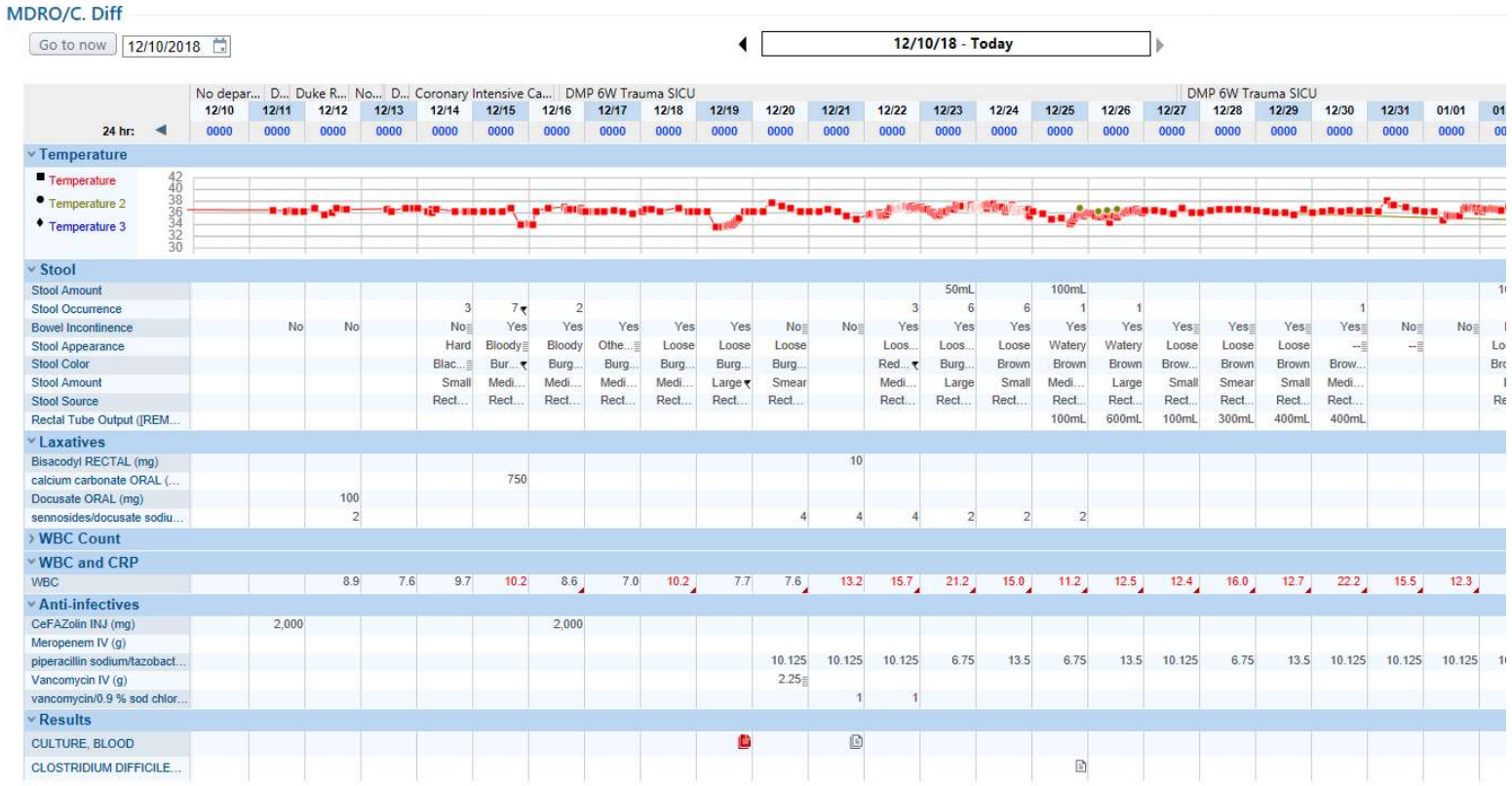


Example CDI Testing Algorithm



*if clinical concern for toxic megacolon, consider abdominal imaging/surgical consultation
**septic shock, WBC > 15, and/or abdominal tenderness

Tools for Clinicians



Temperature curve

Stool documentation

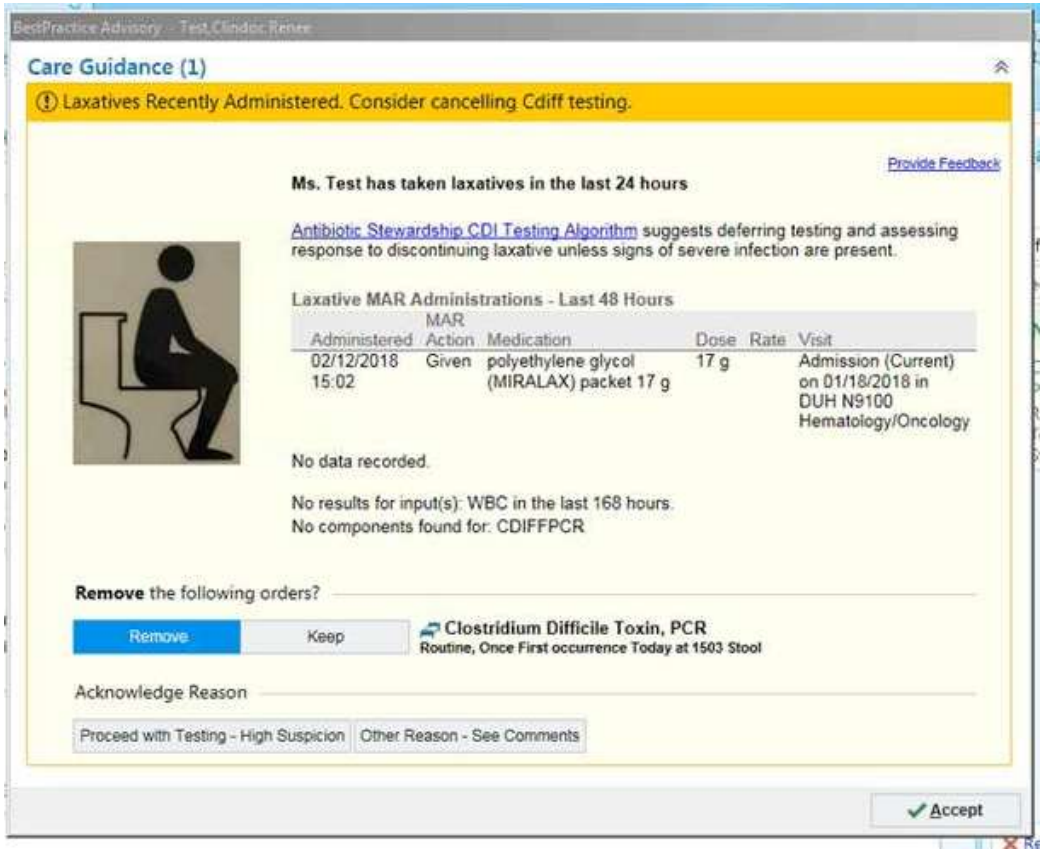
Laxative admin

WBC

Antibiotic admin

Culture data

Electronic decision support – Laxative Alert



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

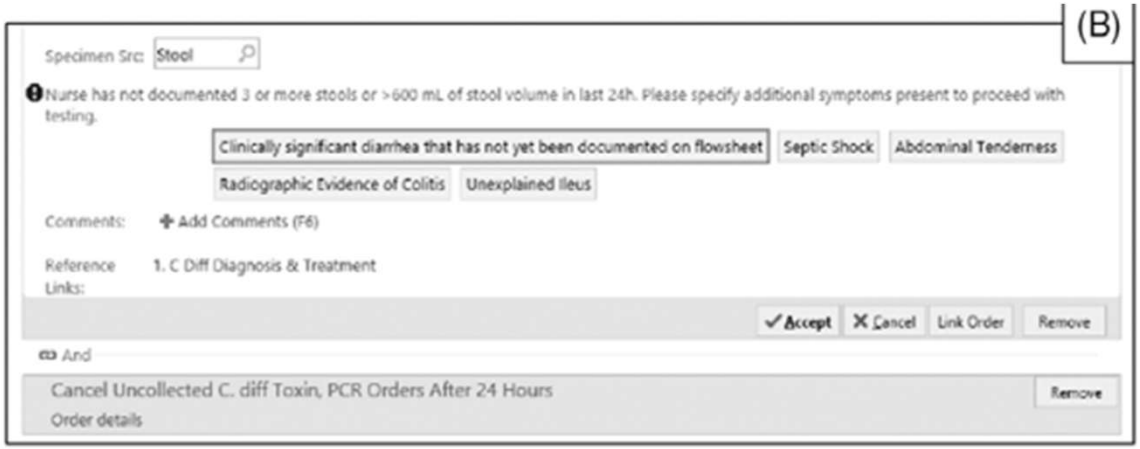
- Provider alert-fatigue
- Easily over-ridden

Karlovich et al. ICHE 2022;43:840-7.

Electronic decision support – Contextual Rules

Stool Documentation

WBC



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Karlovich et al. ICHE 2022;43:840-7.

Or Restrict?

3 hospitals initiative

EHR Interventions

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

Gatekeeper intervention

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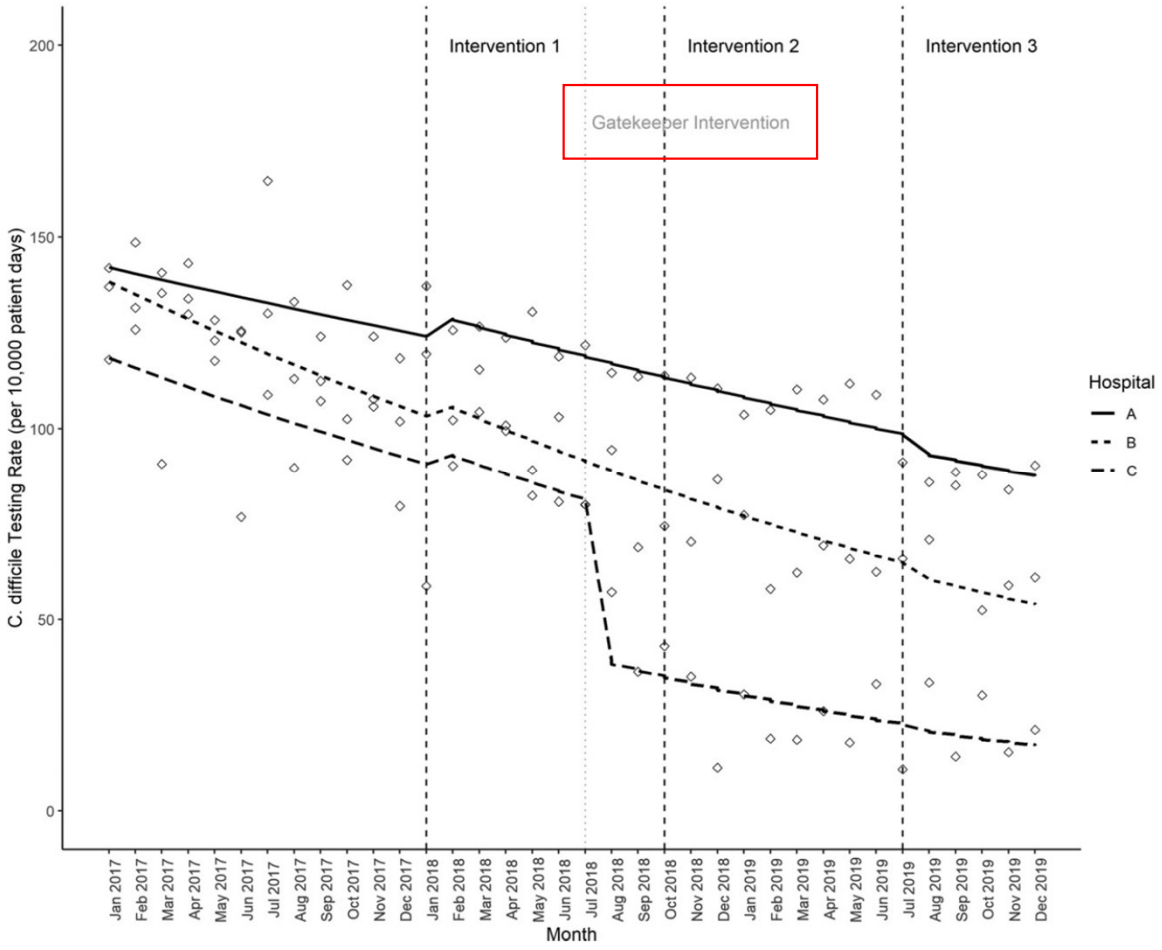

Gatekeeper – ID or CMO approval required if ordered >3 days after admission

Karlovich et al. ICHE 2022;43:840-7.

Take Home Points

- **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?

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