Flexibility in testing for *Clostridioides difficile* and its disease

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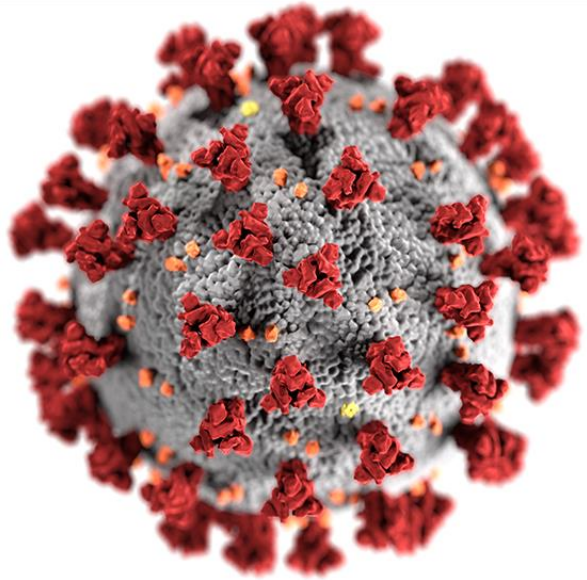
COVID-19 and *C. difficile* testing

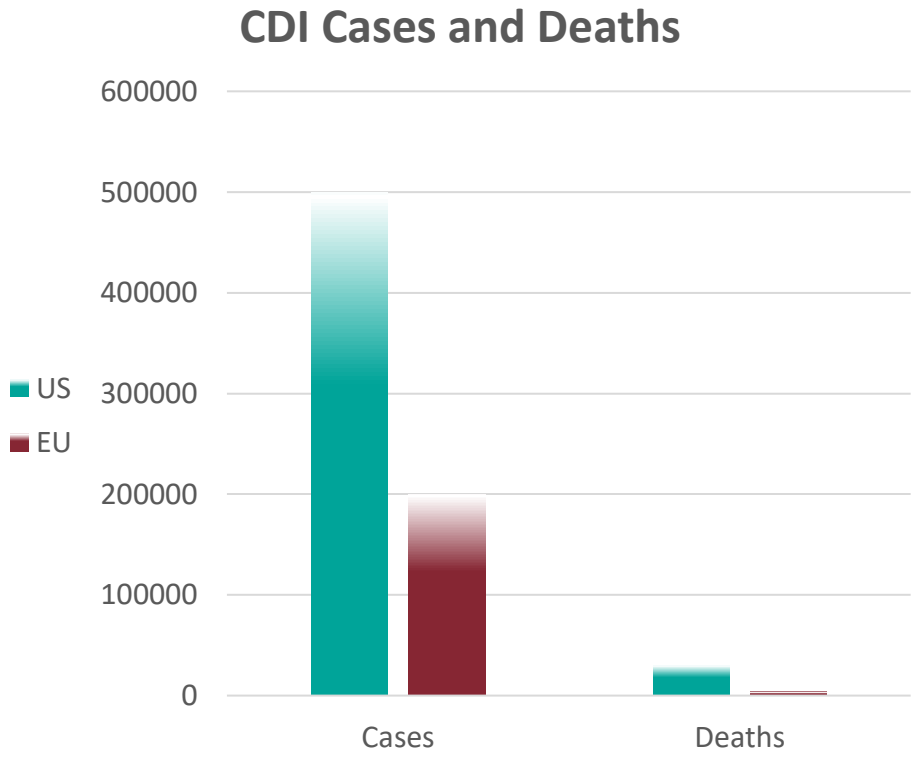
- Limited availability of lab instruments, supplies and personnel make lab testing more difficult
- Laboratories are looking for flexible workflows



Are there ways of testing for *C. difficile* Infection (CDI) that can provide flexibility for the lab?

Image from: https://www.fmi.org/food-safety/coronavirus

Impact of CDI on Healthcare Systems



Significant challenge:

25% Recurrence Rate

Increasing cases of COVID-19 make lab testing more difficult due to limited availability on lab instruments, supplies, and personnel

Lessa F et al. 2015. N Engl J Med 372:2368-2370. 2019 AR Threats Report
European Centre for Disease Prevention and Control. Point prevalence survey of healthcare- associated infections and antimicrobial use in European acute care hospitals. Stockholm: ECDC; 2013.

C. difficile Infection

CDI: The most common hospital-acquired infection

- *C. difficile* spores are shed by patients and easily spread throughout healthcare facilities
- Challenge to diagnose
  - The presence of *C. difficile* does not always equal disease
  - A greater percentage of hospitalized patients are carriers
  - Can present as a co-infection and in patients with Inflammatory Bowel Disease (IBD)
  - Most commonly recognized cause of diarrhea in healthcare facilities (unless a norovirus outbreak is underway)
- Associated healthcare costs are estimated at $4.8 billion
- Enhanced protective measures are effective but supplies are limited

C. difficile Diagnostic Tests

Immunoassays for toxins A and B

- Lower sensitivity
- Provides higher positive predictive values than GDH or NAAT testing

Immunoassays for Glutamate Dehydrogenase (GDH)

- Does not differentiate between toxigenic and nontoxigenic strains
- Provides high negative predictive values

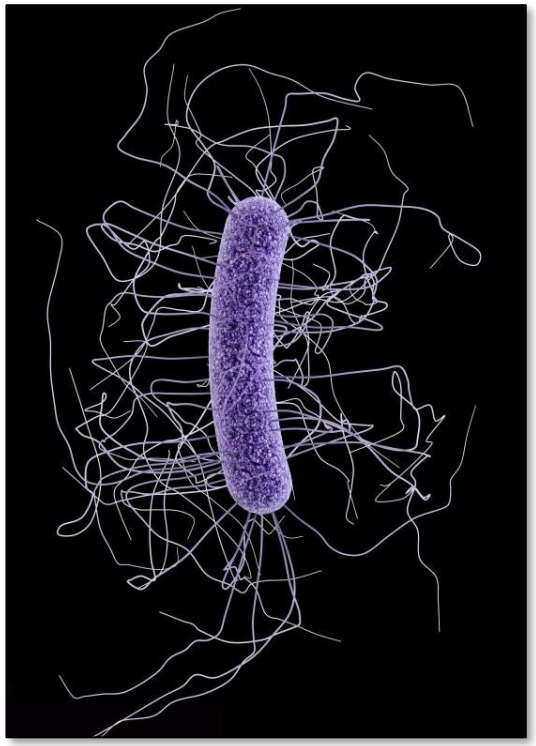
Nucleic acid amplification tests (NAAT)

- Detect the toxin genes, but do not confirm the presence of toxin
- High sensitivity may lead to overdiagnosis

NAAT assays require instrumentation that may be needed for SARS-CoV-2 testing.

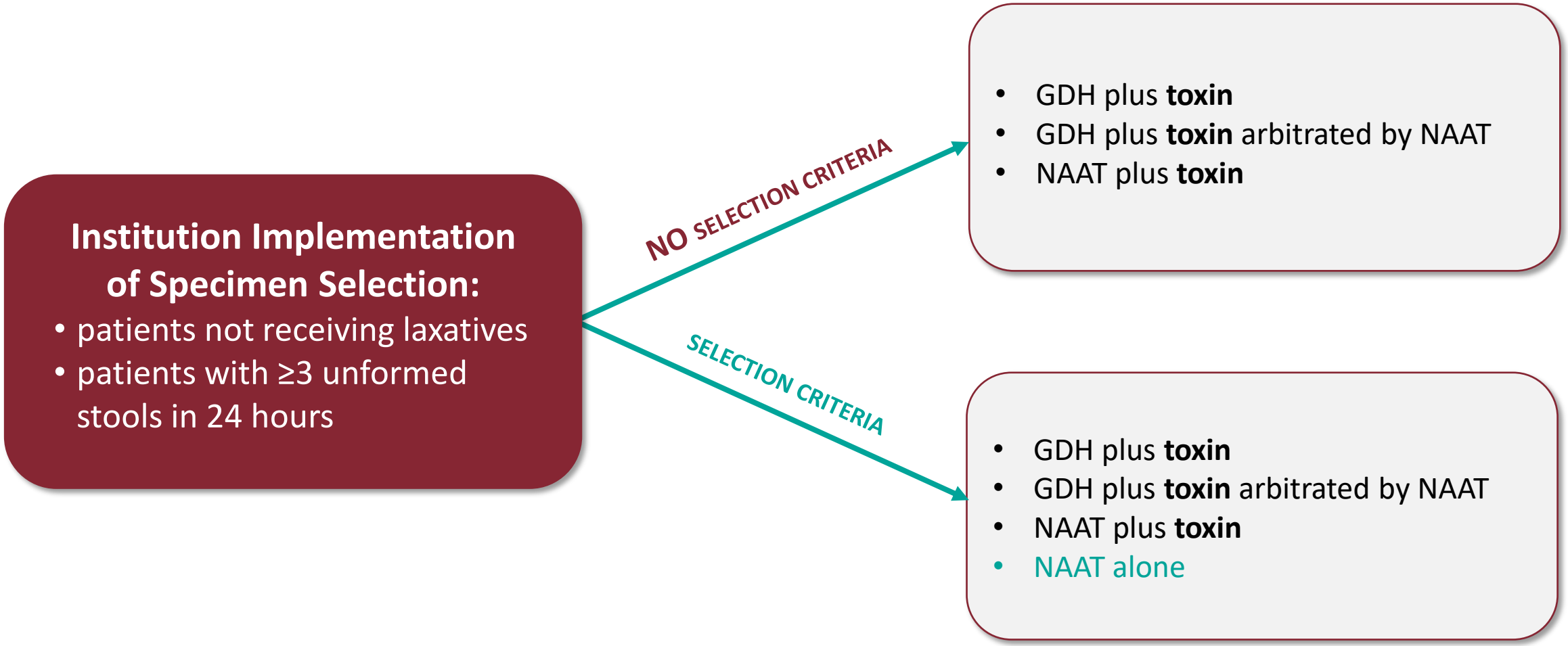
CDI Testing Recommendations

- European Society of Clinical Microbiology and Infectious Diseases (ESCMID) – 2016
- Infectious Diseases Society of America and Society for Healthcare Epidemiology of America (IDSA/SHEA) – 2017
- American Society for Microbiology (ASM) – 2019



Crobach M et al. 2016. Clin Microbiol Infect 22: S63-S81.
McDonald L et al. 2017. Clin Infect Dis Vol 66:1–48.
Kraft C et al. Clin Microbiol Rev 32:e00032-18

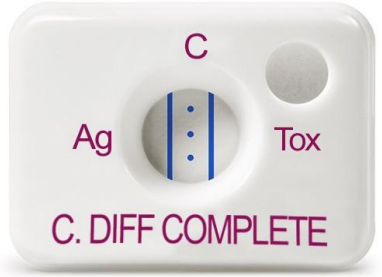
IDSA/SHEA Guidelines



McDonald L et al. 2017. Clin Infect Dis Vol 66:1–48.

The *C. DIFF QUIK CHEK COMPLETE®* Test

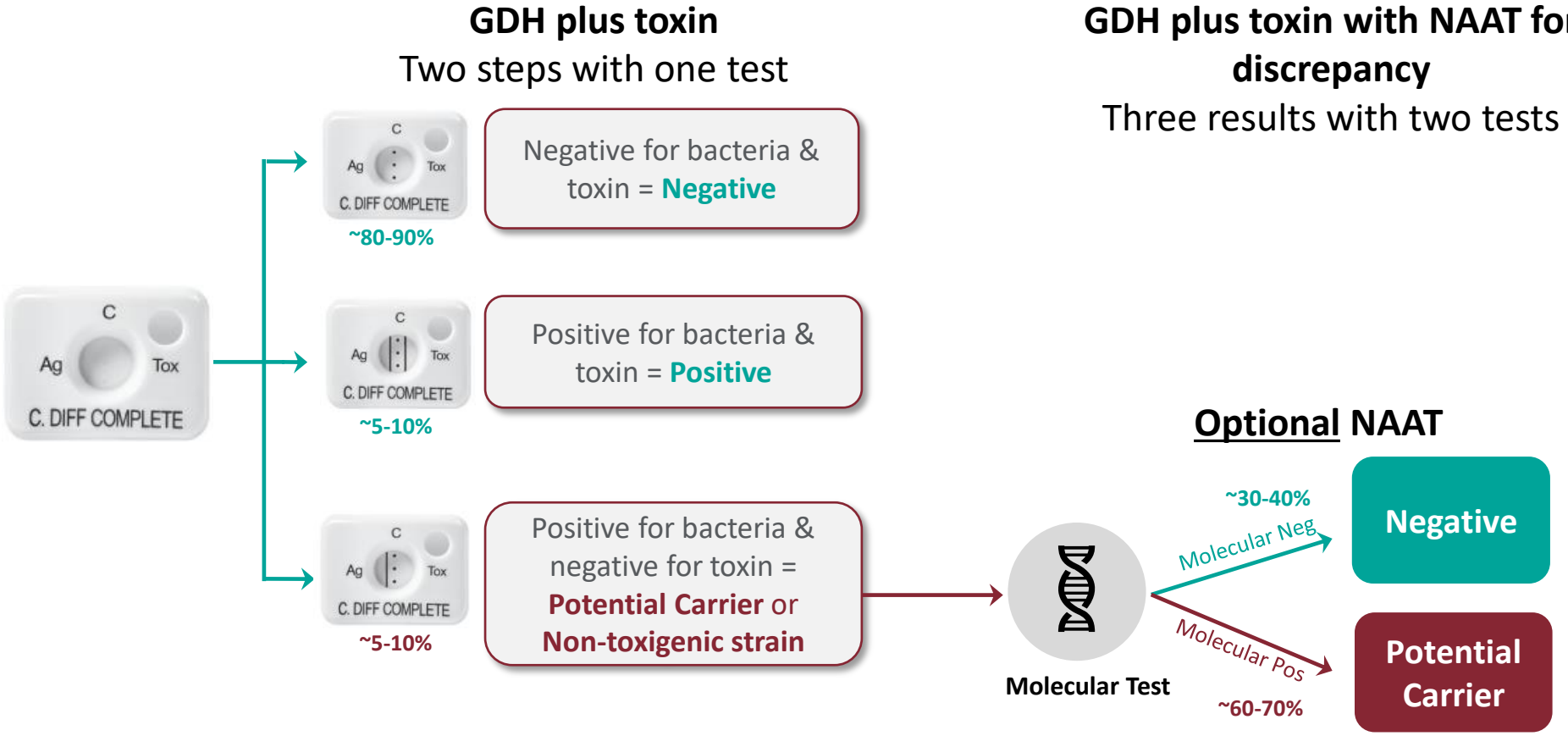
One cassette + one sample provides a multistep algorithm



- **Glutamate dehydrogenase (GDH) detection** indicates presence of the organism
  - Metabolic enzyme produced when the organism is actively growing
  - Provides high negative predictive value comparable to that of NAAT assays
  - Absence of GDH accurately rules out CDI

- **Toxin detection** is emphasized in the guidelines
  - Accurate biomarkers of CDI
  - Provides higher predictive positive values than NAAT assays
  - Patients who are positive for toxin have worse clinical outcomes, more severe symptoms, and longer hospital stays

C. difficile Testing Algorithm



ASM Sept 21 2010. Practical guidance document for laboratory detection of toxigenic *Clostridium difficile*
McDonald et al. *Clin Infect Dis* 2018; cix1085, https://doi.org/10.1093/cid/cix1085

Algorithm Approach

Proven performance that provides lab flexibility and testing workflow

GDH plus toxin algorithms are recommended by IDSA/SHEA

- Important to select immunoassays that have proven performance

The algorithm approach:

- Minimizes overdiagnosis while accurately identifying CDI
- Helps to meet the challenge of antibiotic stewardship

The *C. DIFF QUIK CHEK COMPLETE*® test provides algorithm testing in a single cassette

- Provides a flexible option for CDI testing in the midst of the Coronavirus pandemic

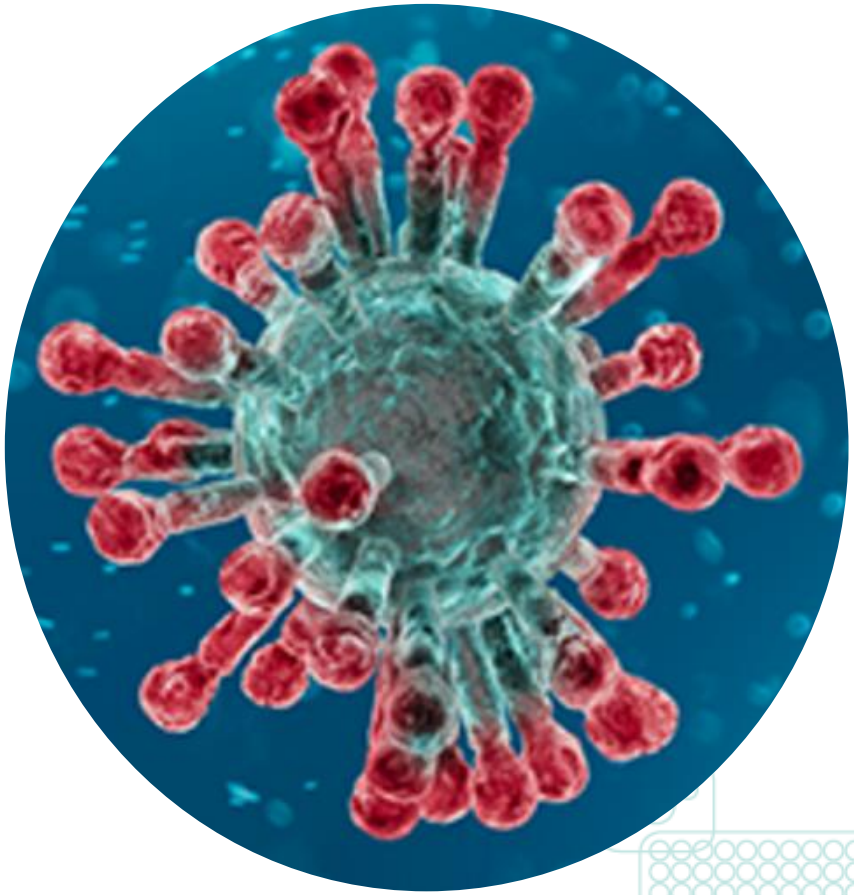
CDI: The Challenge will Continue

- Elderly hospitalized patients treated with antibiotics will continue to be the most susceptible population
- Community-acquired cases are increasing
- Implementation of antibiotic stewardship must be a primary goal for optimal patient care
- Inaccurate CDI diagnosis increases inappropriate treatment, putting the patient at risk for CDI
- Need to understand the important role of inflammation in CDI

What lies ahead?

What happens with CDI during flu season?

- The epidemiologic characteristics follow a pattern that is seasonal and associated with influenza
- The incidence is significantly higher during flu season compared to levels reported during the summer
- Hospital pneumonia and influenza prevalence are followed by increased cases of CDI downstream, especially in older patients.



COVID-19 and C. difficile testing

- Can we expect CDI to increase during this pandemic as it does for flu season?
- How will treatments for COVID-19 affect the normal intestinal microbiome?

What lies ahead?

The Coronavirus pandemic will lead to:

- Increased testing demand on laboratories
- Increased uptake of antibiotics because of secondary bacterial pneumonia
- Increased hospital crowding
- Interhospital transfers

The incidence of CDI will likely increase, which may further **strain lab resources**.

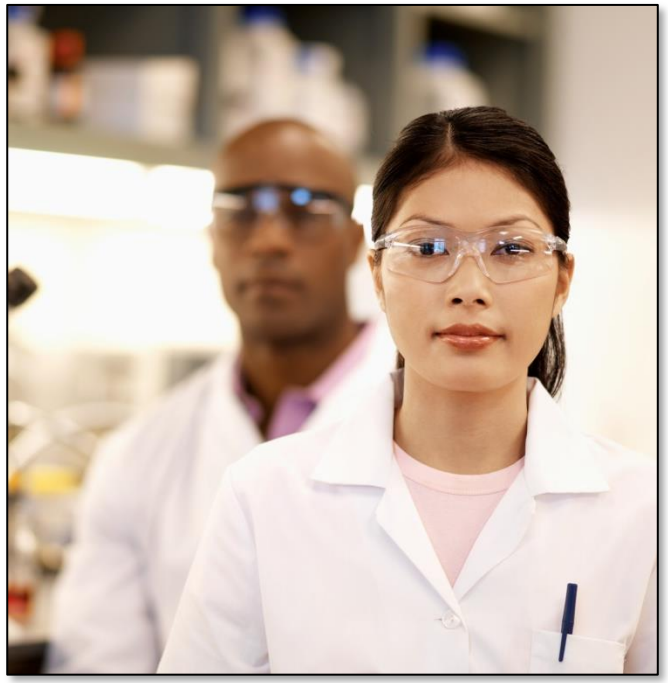
Brown et al. 2013. Amer J Epidemiol 178:118-125. https://doi.org/10.1093/aje/kws463

Summary

As resources are stretched, laboratories can consider GDH-toxin algorithm testing for CDI requiring no instrumentation for increased flexibility and improved workflow.

The multi-step algorithm meets IDSA/SHEA guideline recommendations and can help labs during this crisis by freeing up essential instrumentation and personnel that may be required for Coronavirus testing.

During the COVID-19 pandemic, there is higher probability for increased antibiotic usage due to secondary bacterial pneumonias → possible increased rates of CDI



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