

October 11, 2022

Agenda

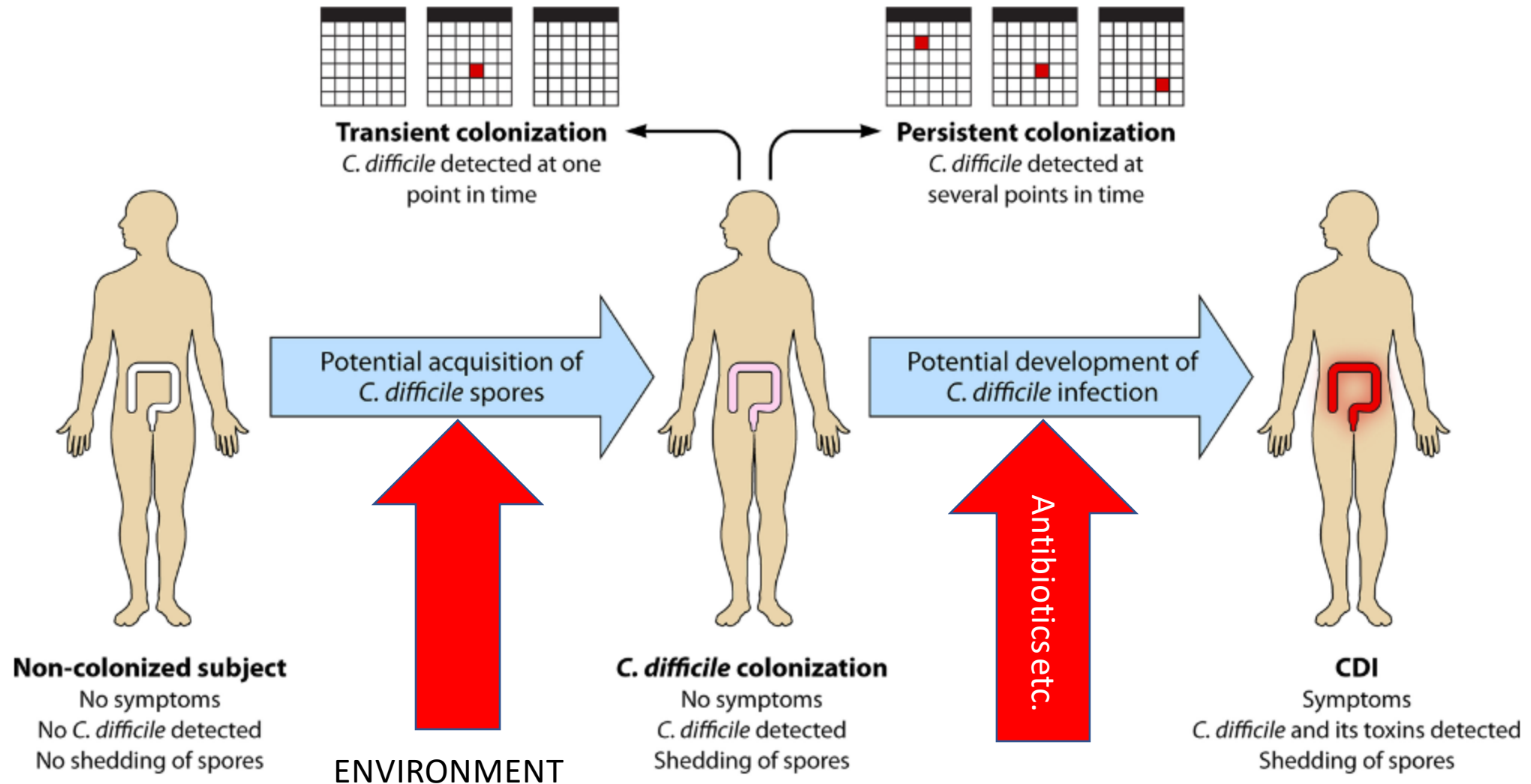
- Will Simmons: *C difficile* Diagnostics
- Case Discussions
- Open Discussion

Outline

1. C difficile is everywhere
2. Tests for C difficile are bad at their jobs
 1. They find a lot of colonization
3. Best approach: testing stewardship



Colonized patients can test positive



Colonization vs. Infection

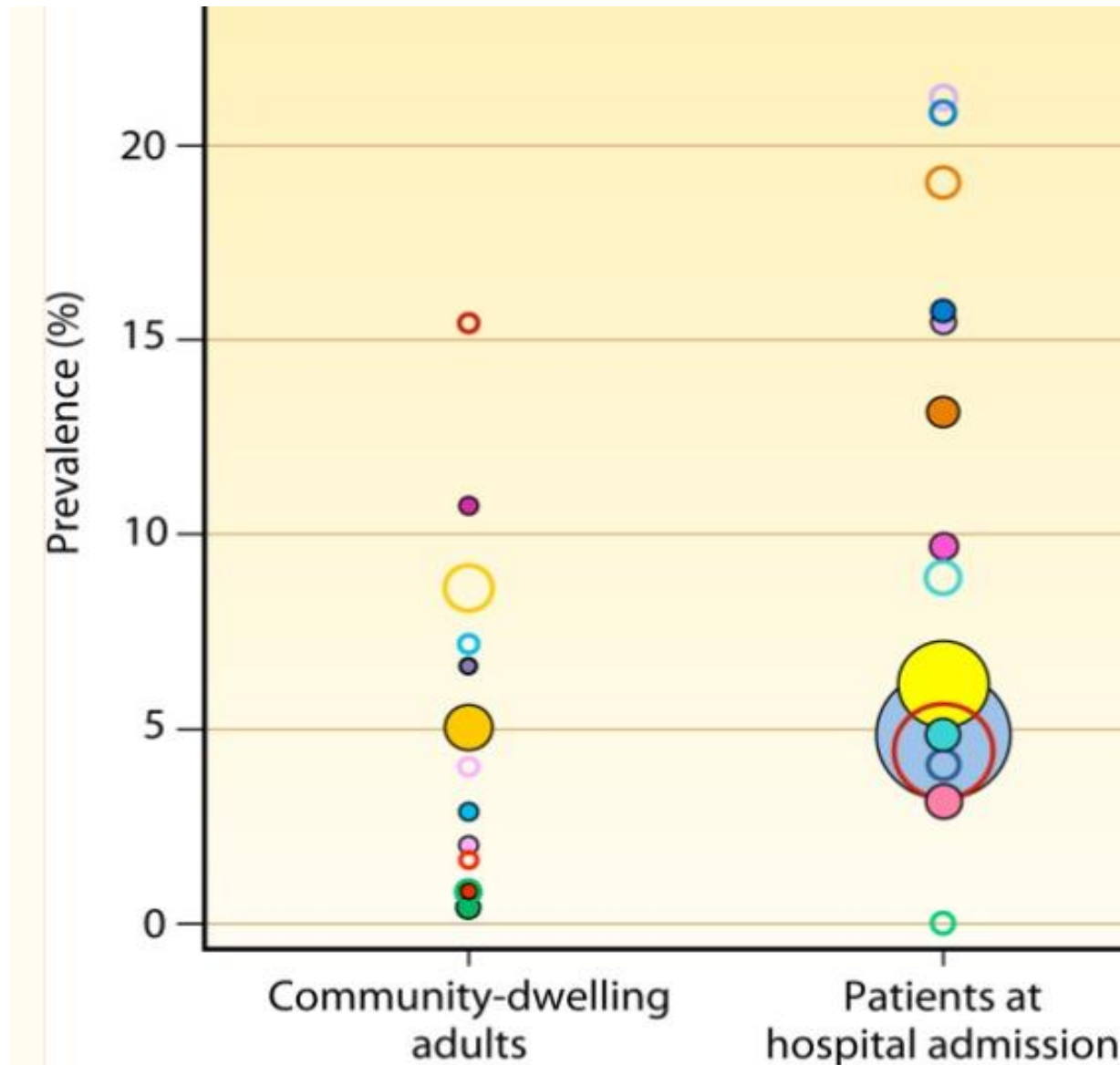
- Colonization: C difficile present, no diarrhea, no symptoms
 - Or has diarrhea from another cause, C difficile innocent bystander

VS.

- Infection: C difficile present and causing diarrhea



Rates of C diff colonization

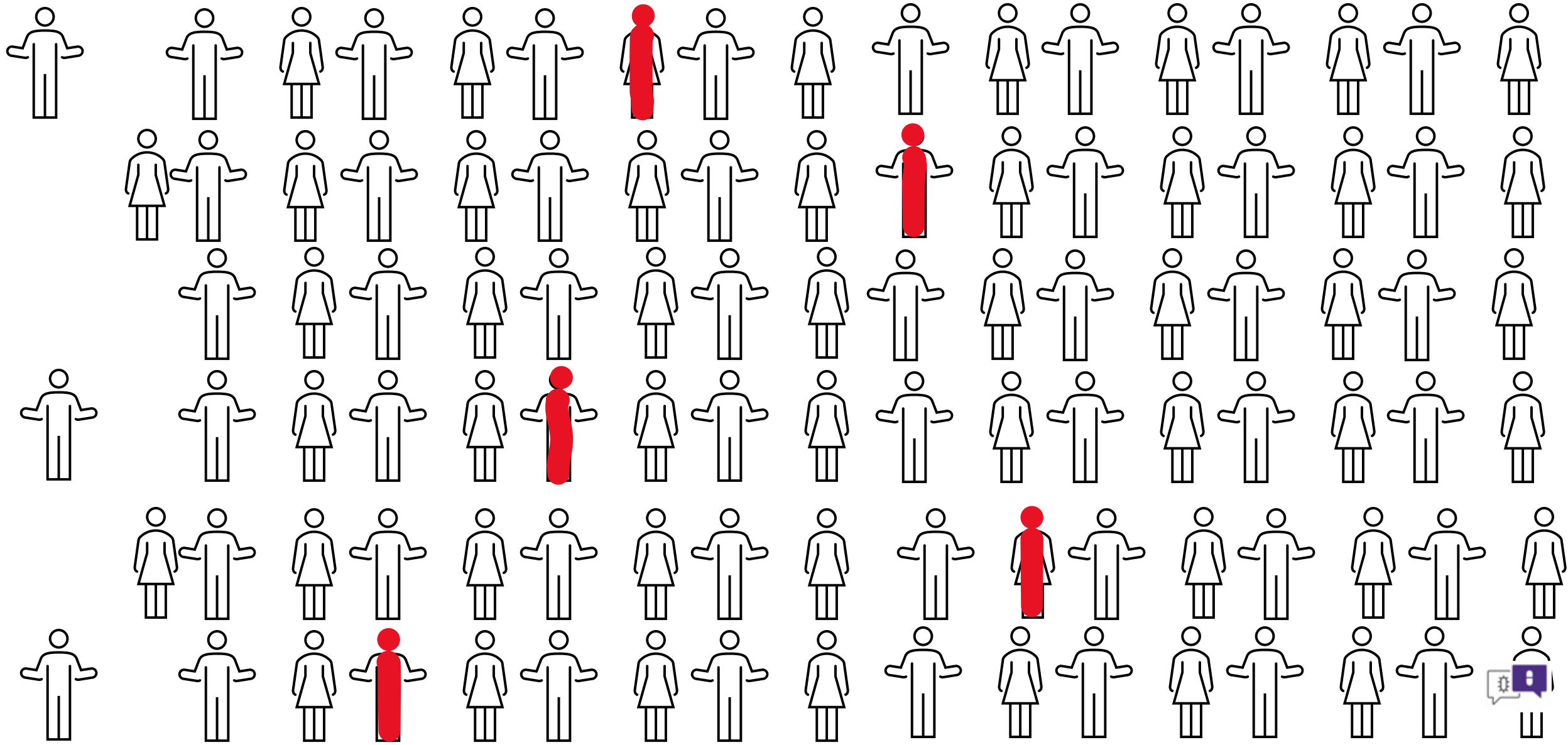


The tests for C difficile are bad

- Tests don't distinguish infection and colonization
- Over-testing will find a lot of colonization
- Let's make up a hospital



Diarrhea hospital: 100 patients, 5% w/ C diff



GDH Enzyme Immunoassay (EIA)

- Tests for an enzyme made by ALL *C difficile*
- Very sensitive, cheap (and if negative, you're done)
- Needs a second test (alone will catch tons of colonization)
 - Only 1 in every 3 positive tests actually *C difficile* infection



Toxin A/B Enzyme Immunoassay

- Directly detects toxins produced by C difficile
- Needs to be a lot of toxin to turn positive
- Some infected patients will test negative
- Could miss about 25% of C difficile infection



PCR/NAAT for Toxigenic *C difficile*

- Detects gene for C difficile toxin
- Very sensitive – detects lots of colonization
- Expensive (and can take time if not run in-house)
- 1 in 2 positive tests may not actually have infection



The answer? Algorithms?

- GDH test: only 1 in 3 positives actually has infection
- Toxin EIA: misses up to 20% of infections potentially
- Their powers combined: super sensitive test (GDH) doesn't miss folks, and then more specific tests weeds out some of the colonized patients???



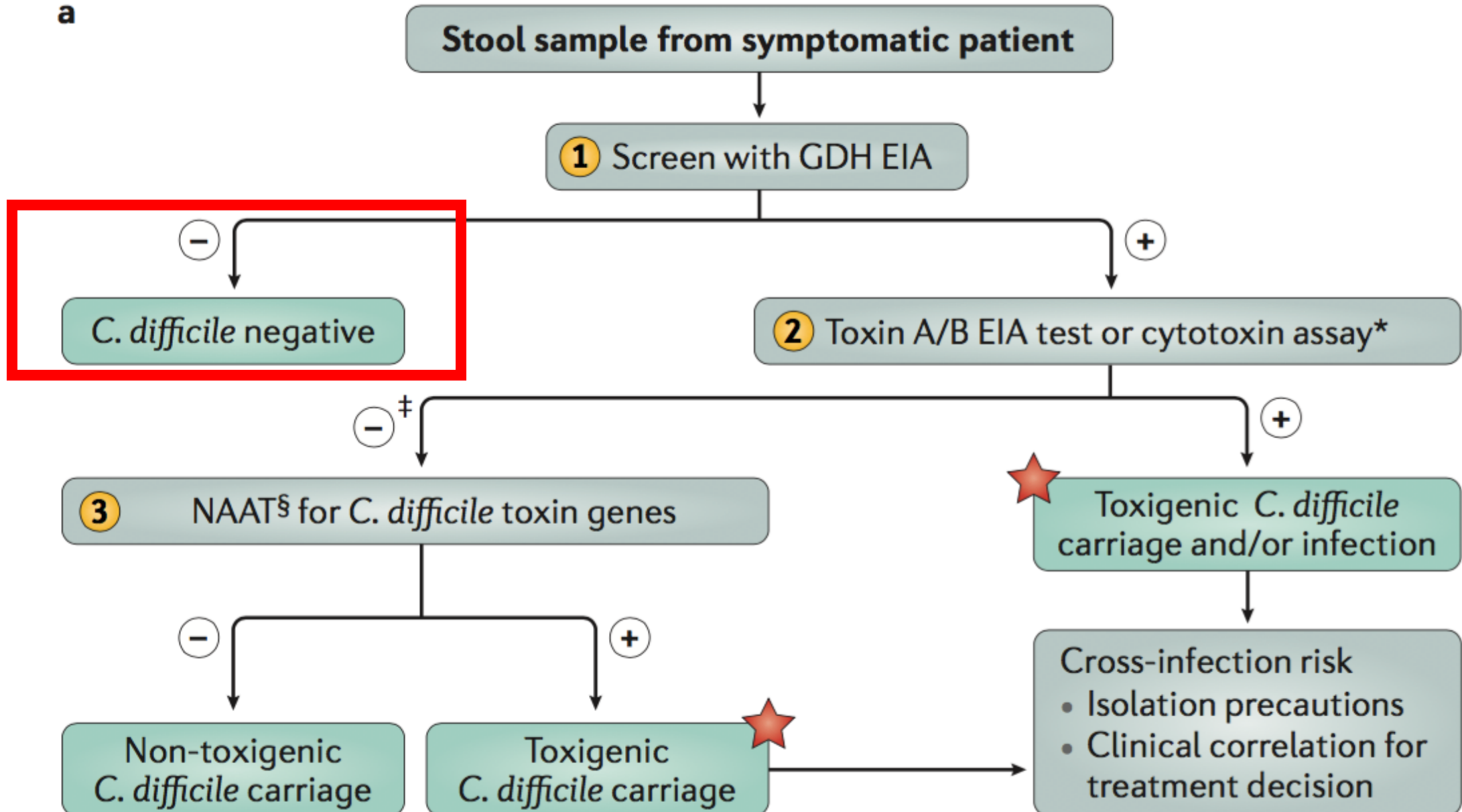
How does your institution test for C difficile?

- One step PCR/NAAT
- Two step with GDH+Toxin, no tiebreaker
- Two step test with GDH+Toxin test w/ PCR/NAAT tiebreaker
- Two step with NAAT/PCR + Toxin
- Other
- Not sure



Clostridioides difficile Algorithm 1

a



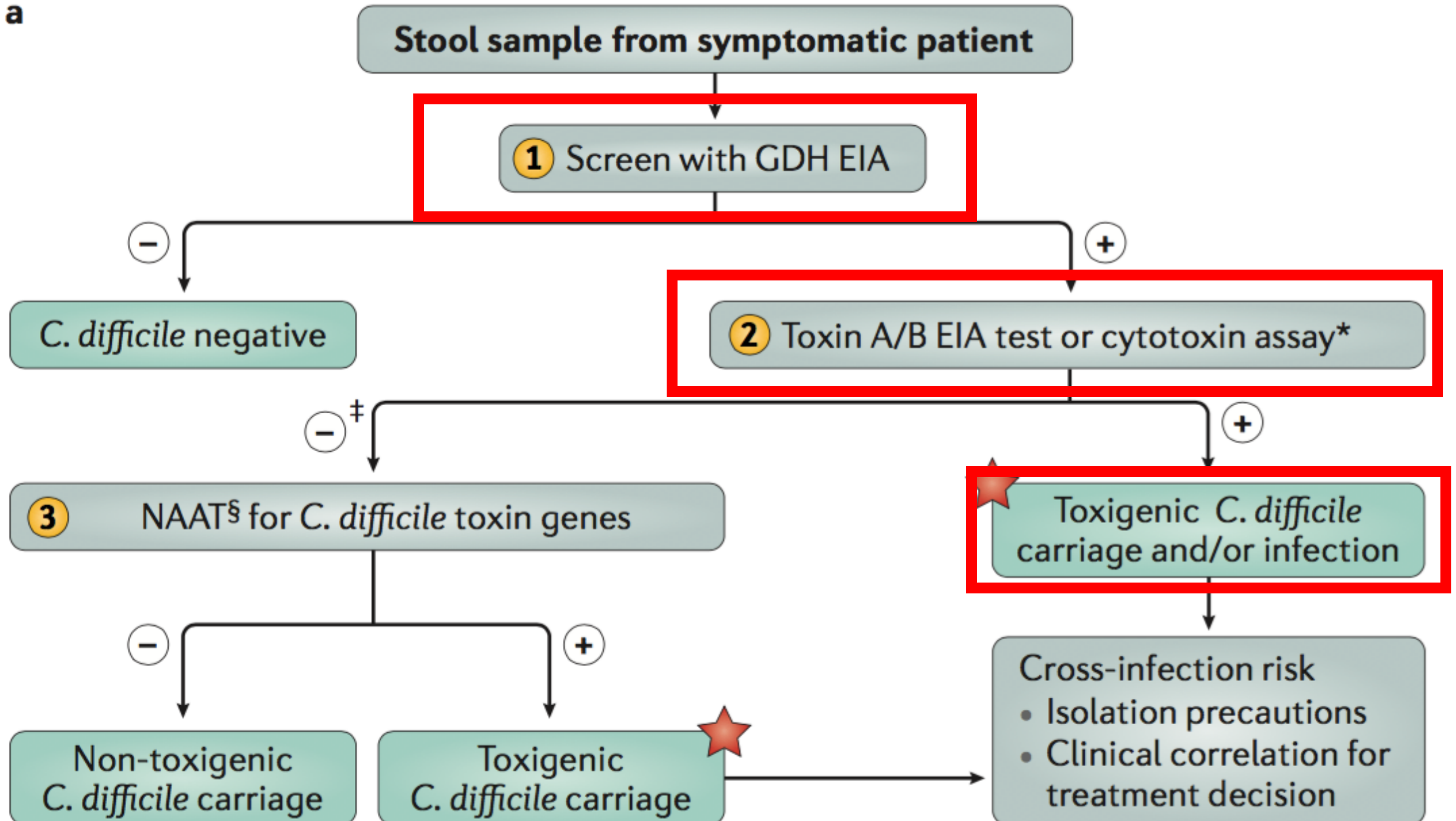
Possible testing results

GDH	Toxin	Interpretation	Problem
Negative	Not done	Not C difficile	NONE!



Clostridioides difficile Algorithm 1

a



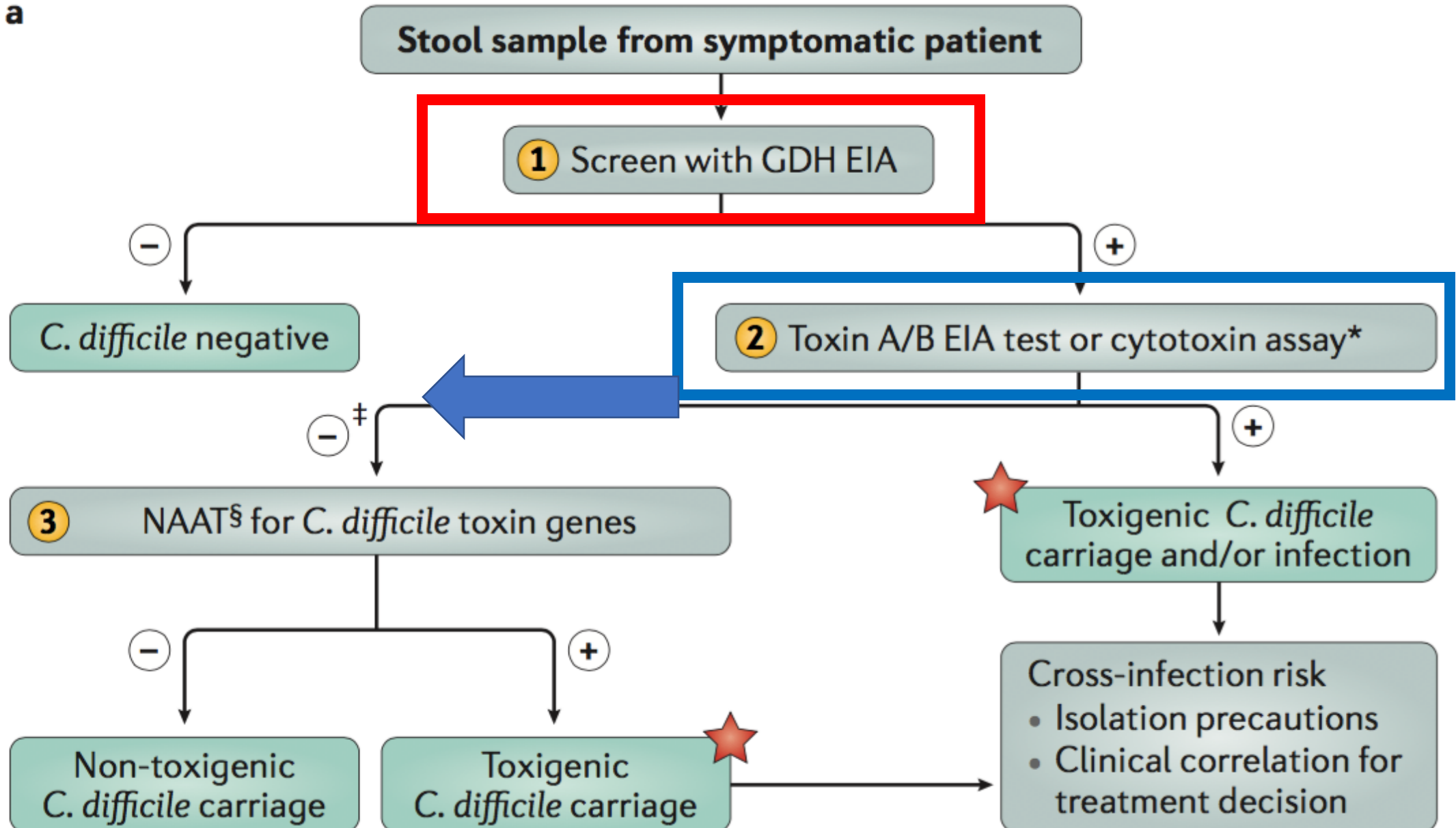
Possible testing results

GDH	Toxin	Interpretation	Problem
Negative	Not done	Not C difficile	
Positive	Positive	C difficile infection	A few false positives



Clostridioides difficile Algorithm 1

a



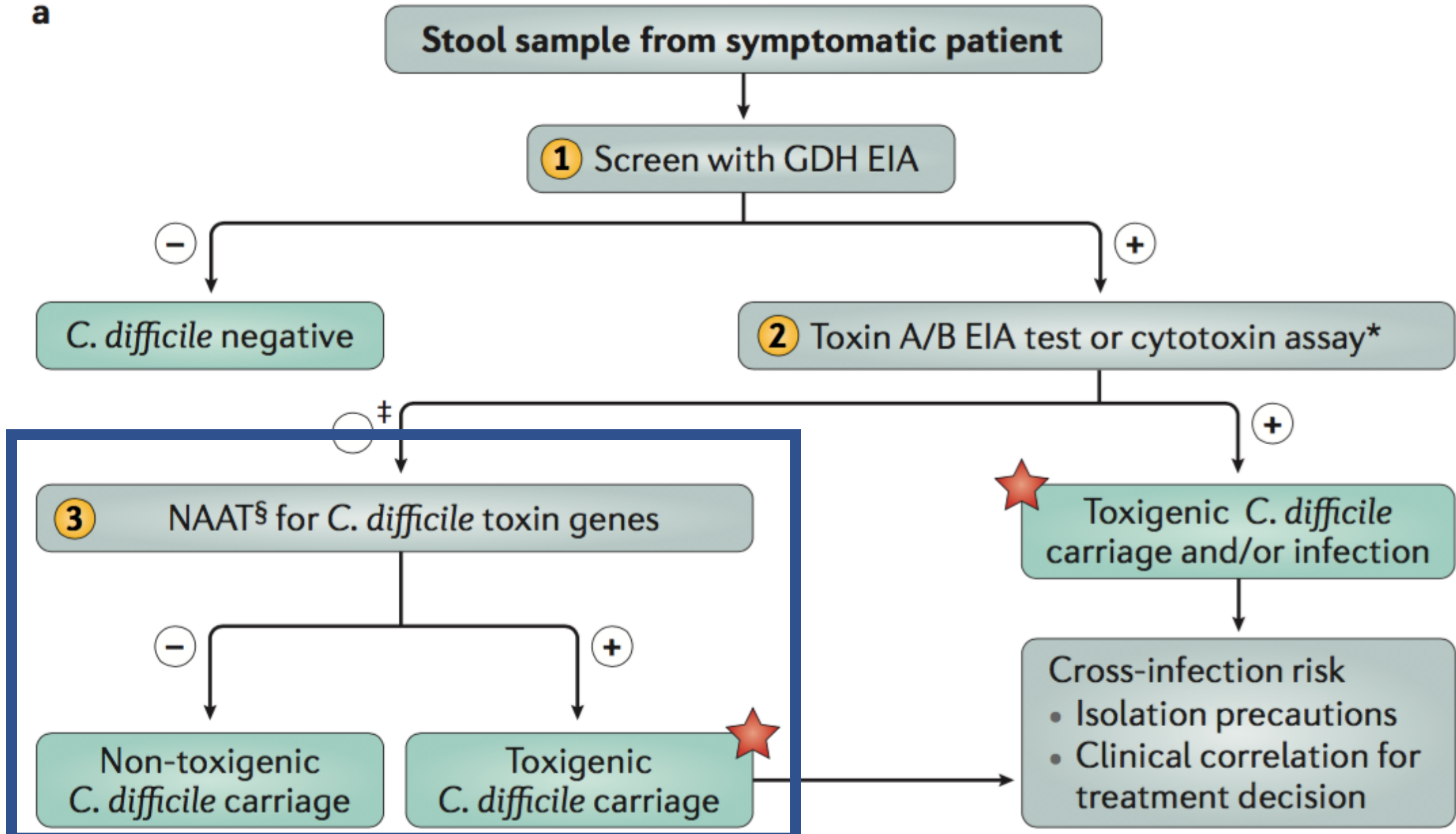
Possible testing results

GDH	Toxin	Interpretation	Problem
Negative	Not done	Not C difficile	
Positive	Positive	C difficile	A few false positives
Positive	Negative	“Indeterminate”	Now what?



Clostridioides difficile Algorithm 1

a



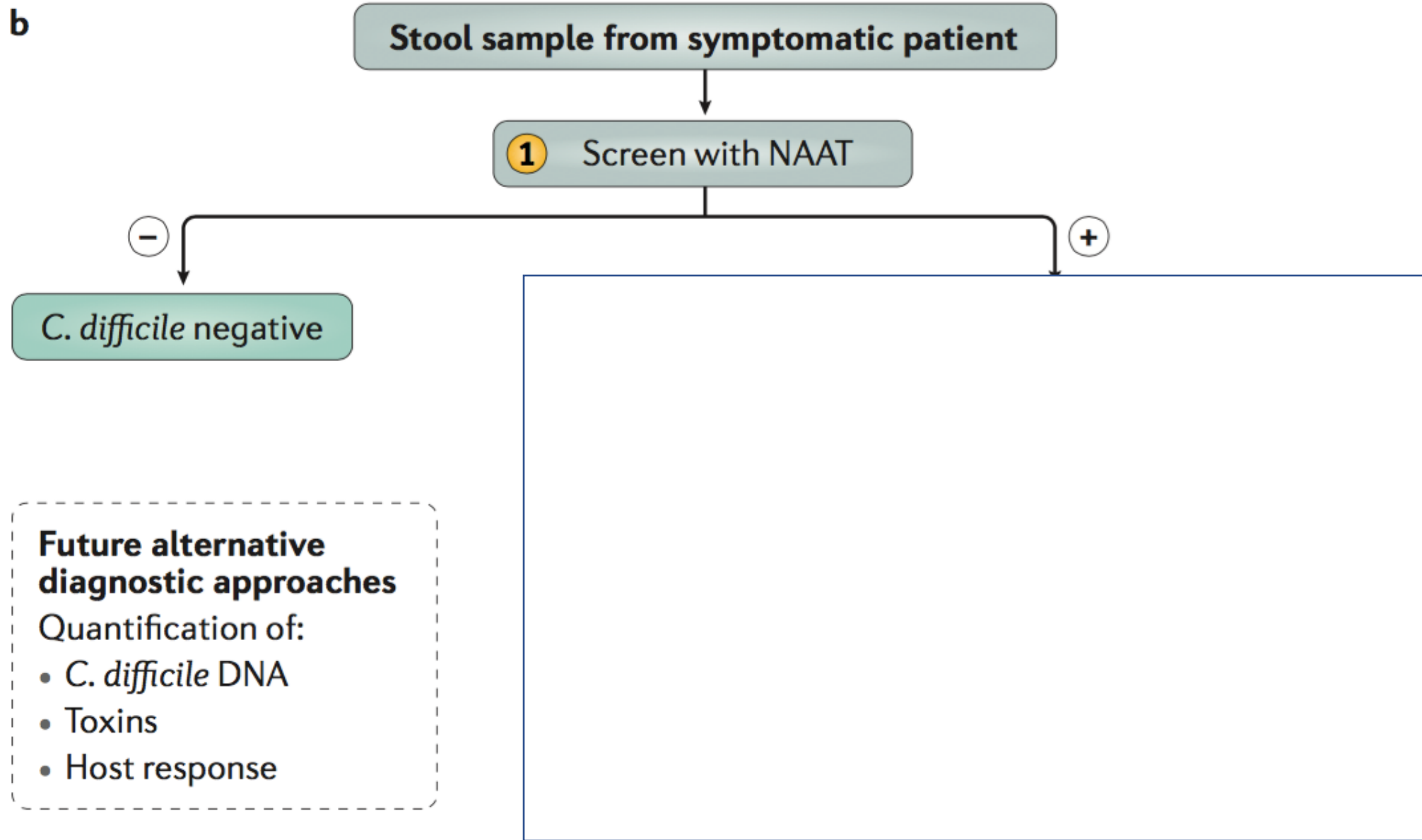
What a mess

- PCR as a tiebreaker: best of 3?
- If GDH and PCR positive, toxin negative → positive?? But definitely could be colonization
- If GDH positive and PCR negative, toxin negative → negative
- How do you explain/display for providers?

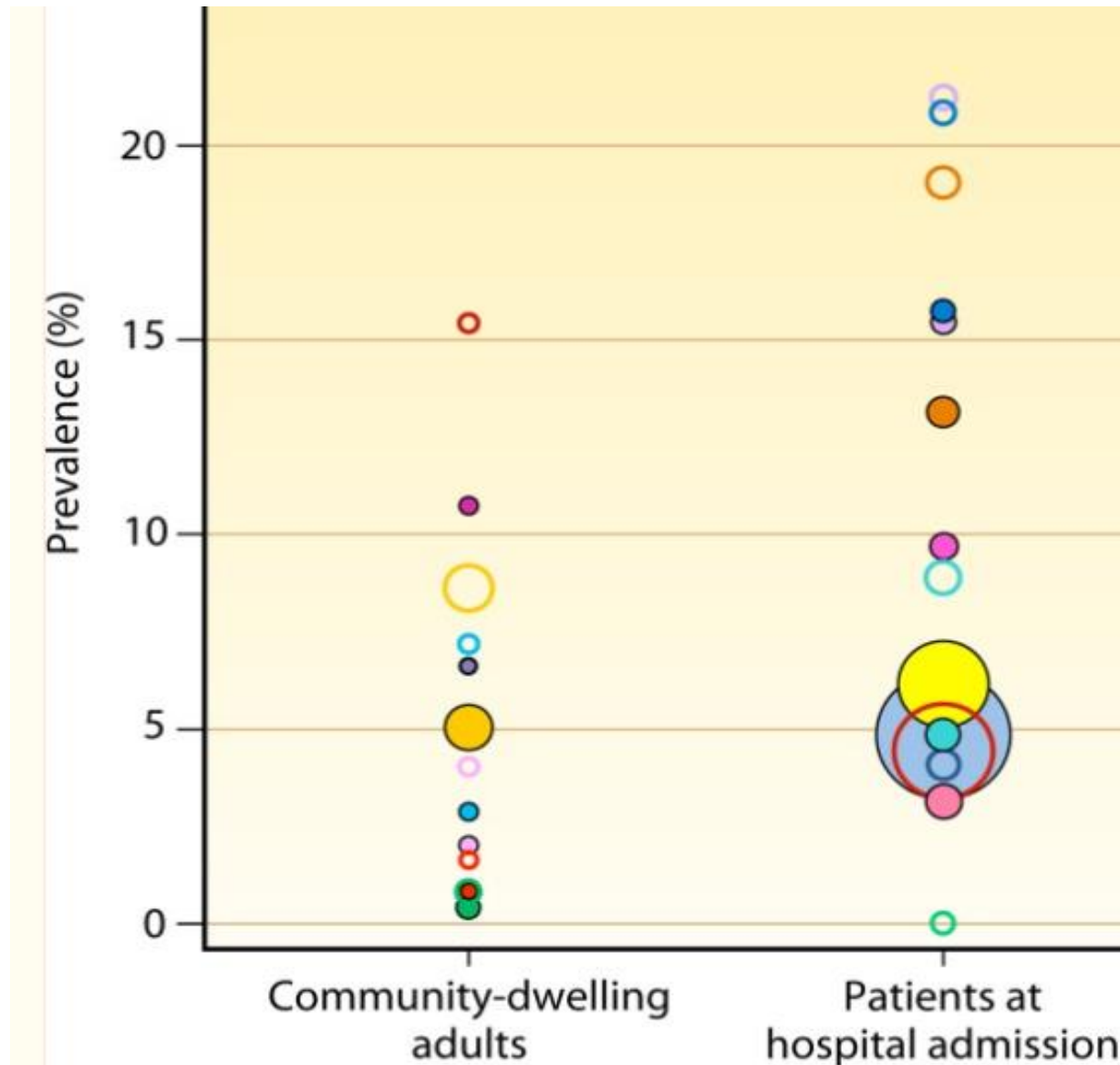


PCR/NAAT Up Front testing

b



Rates of C diff colonization



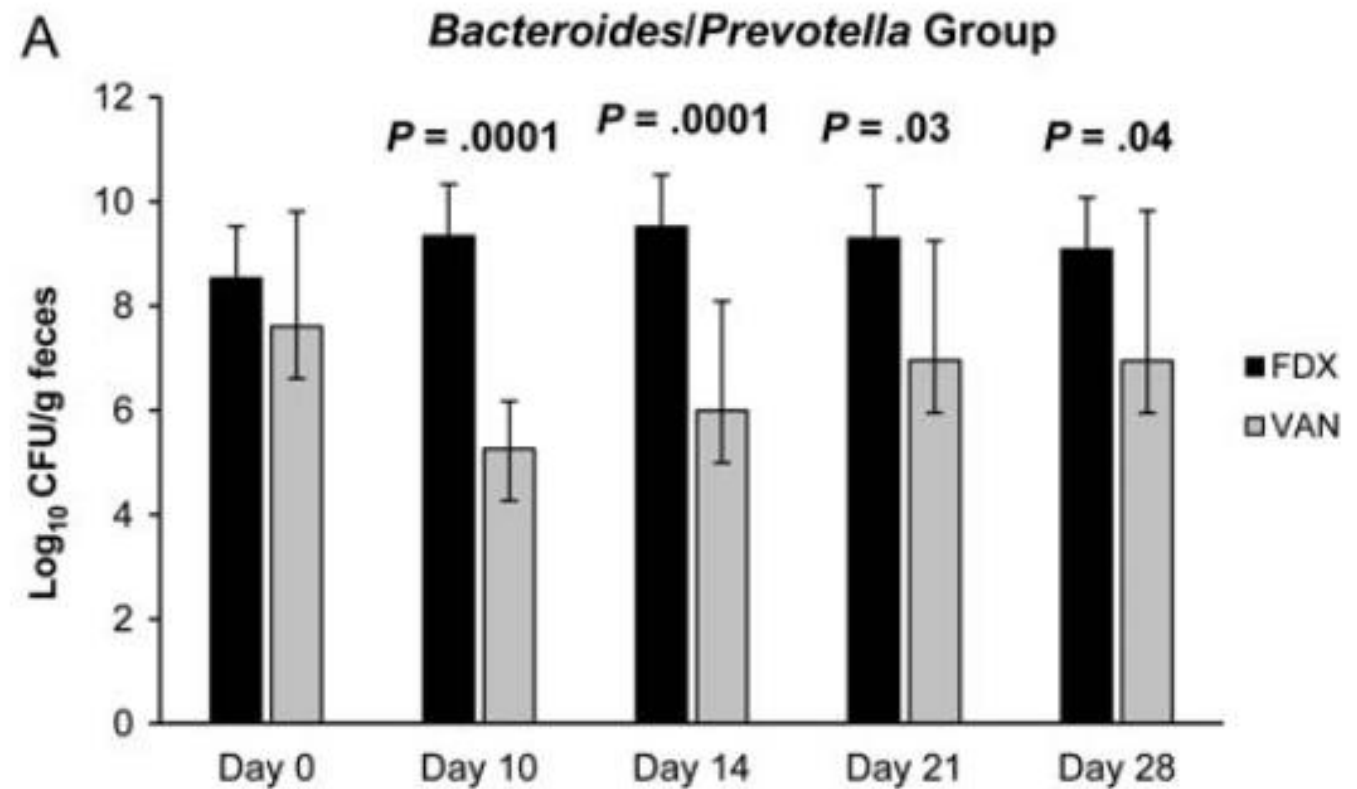
How do we get around this

- The problem: Positive PCR/NAAT tests as well as “indeterminate” GDH+/Toxin- tests will detect a lot of colonization
- If we treat them all, we’re going to overuse PO vancomycin



PO Vancomycin kills “good” gut bacteria

- Vancomycin kills good bacteria (and it can take months to come back)
- Is drug resistance going to be a problem someday?



Who to test

- New diarrhea (>3 unformed (liquid) stools in 24 hours)
- No alternate explanation (trial hold of laxatives if on them)
- Clinical signs: fevers, abdominal pain, cramping, sepsis, shock, toxic megacolon



Ideas about limiting testing?



Takeaways

1. C difficile colonization is common
2. Not everyone with diarrhea and a positive test has C diff infection
3. Tests are inaccurate: over-testing leads to LOTS of overtreatment
4. Limit testing to people likely to have C difficile

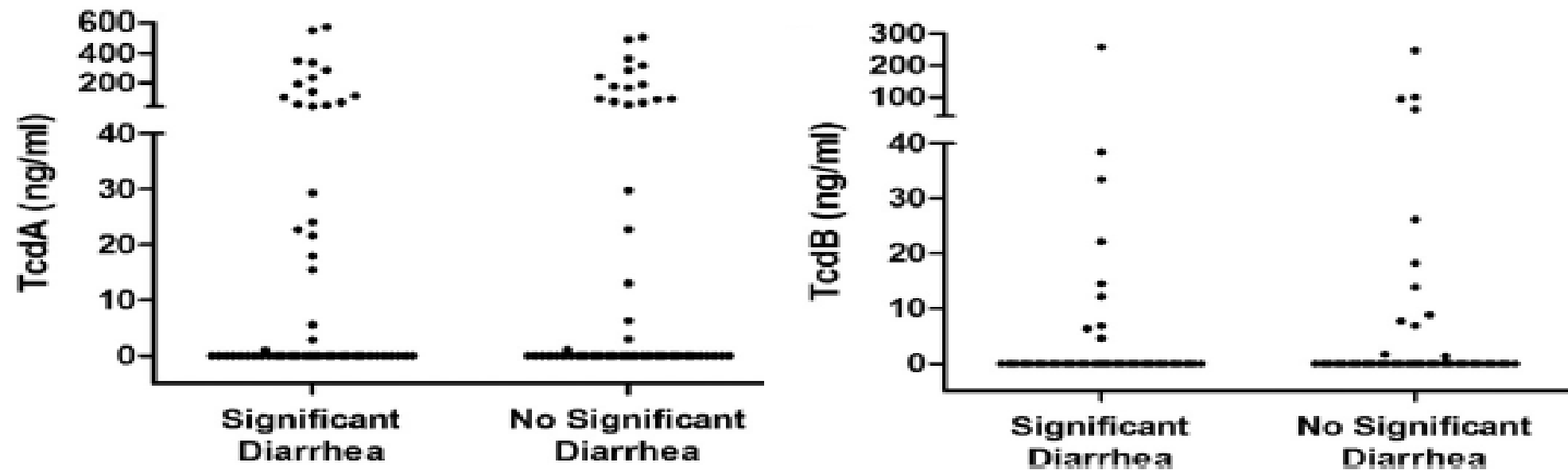


Thank You

- John Lynch
- Chloe Bryson-Cahn
- Whitney Hartlage
- Jeannie Chan
- Rupali Jain
- Ferric Fang



Toxin Assays Cannot Distinguish Asymptomatic Carriage from CDI



REF: Anikst et al., Diagn Microbiol Infect Dis, 2015.



Three tests available for C difficile

TEST	GDH Enzyme Immunoassay	Toxin Enzyme Immunoassay	NAAT/PCR
How it works	Tests for an enzyme produced by ALL Clostridium	Test for Stool Toxin	Test for C diff gene that produces toxin
PRO	Cheap Very sensitive	Also cheap Possibly better at true disease vs. colonization	Very sensitive Can be quick if in-house
CON	Detects all c difficile, Will detect colonization Needs second test	Misses not infrequently	Catches colonization More expensive per test

