The Ins and Outs of *Closteroides difficile*

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Epidemiology

- *C difficile* is listed as a urgent threat per the CDC's most recent report on antimicrobial resistance. In 2017, estimated:
  - >200,000 hospitalized cases
  - 12,800 deaths
  - $1 billion healthcare costs

Johnson S et al CID 2021;XX(XX):0-0
CDC. Antibiotic Resistance Threats in the United States, 2019.

C Difficile and Quality of Life

- Survey of adults hospitalized with *C difficile* between July 2019 – March 2020
  - Completed two separate quality of life surveys
  - Compared to the general population, *C difficile* patients scored significantly lower on:
    - Physical health
    - Mental health
  - Lower scores associated with
    - Recurrent illness
    - Severe illness
    - Additional stool episodes/day

Han Z et al ICHE 2021;Oct 7:1-6 online ahead of print

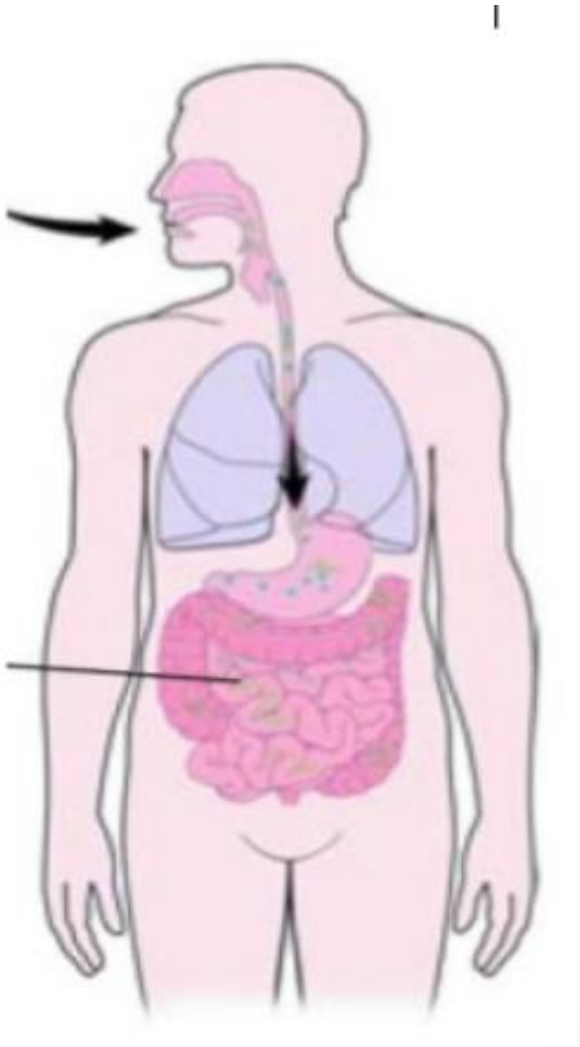
Risk Factors

- Advanced age
- Hospital exposure & length of stay
- Irritable bowel disease
- Immunocompromised patients
- End-stage renal disease
- End-stage liver disease
- Antibiotic use
- Proton pump inhibitor use

McDonald et al CID 2018;66(7):e1-48

Pathophysiology

1) Exposure to *C difficile* spore
2) Disruption of normal flora
3) Inadequate immune response



McDonald et al CID 2018;66(7):e1-48

Exposure to *C difficile*

- *C difficile* is particularly challenging to control spread given that it is a spore-forming organism
  - Resistant to alcohol-based hand sanitizers
  - Recommended to wash hands with soap and water in an effort to reduce spore transmission by healthcare workers

Dubberke ER et al ICHE 2015;35(S2):48-65

Pathophysiology

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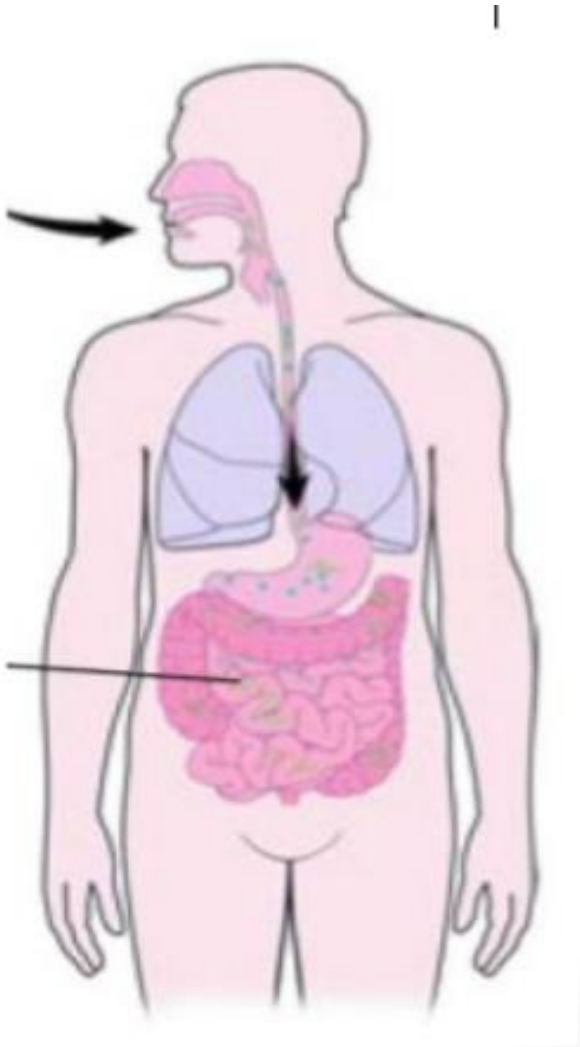
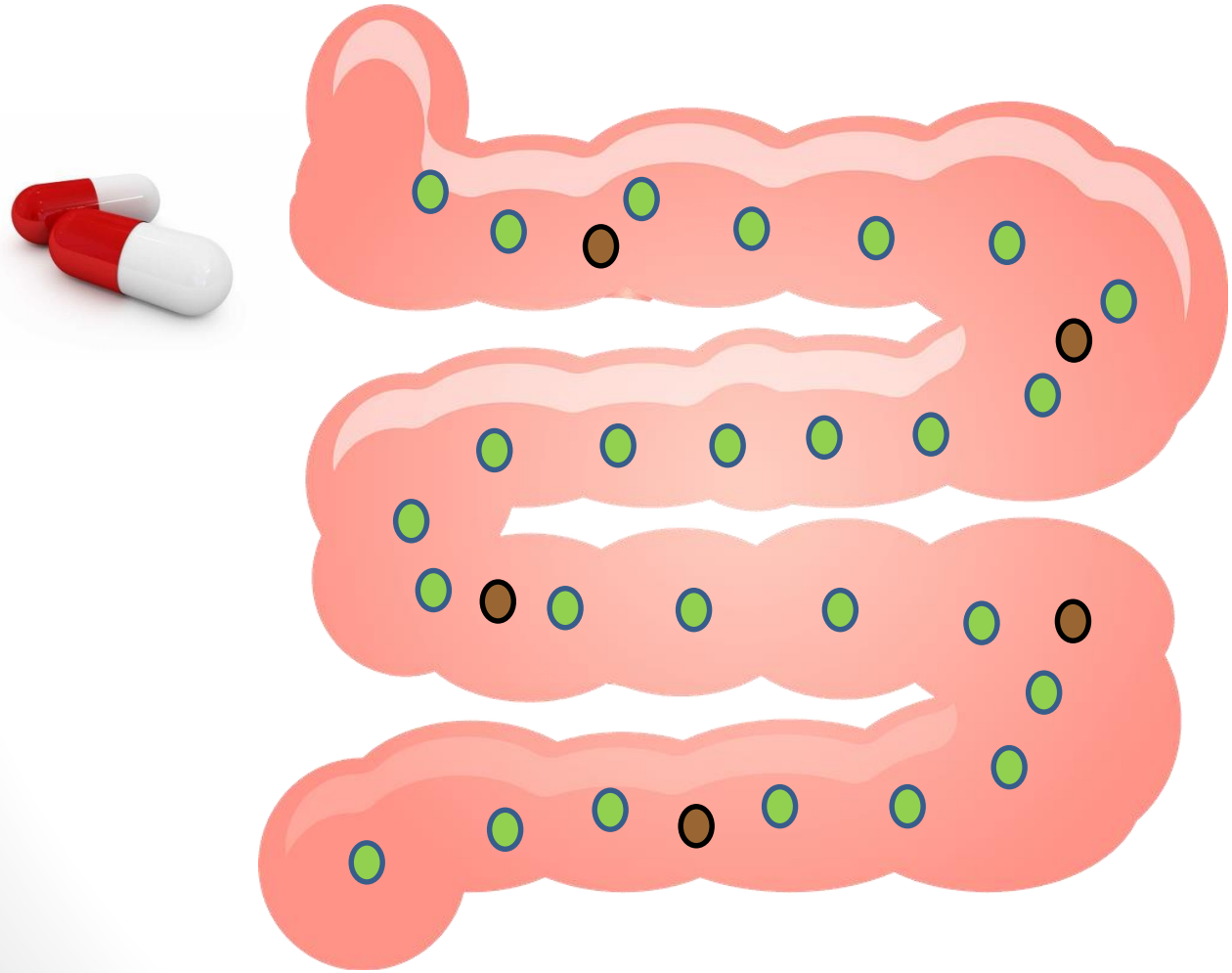


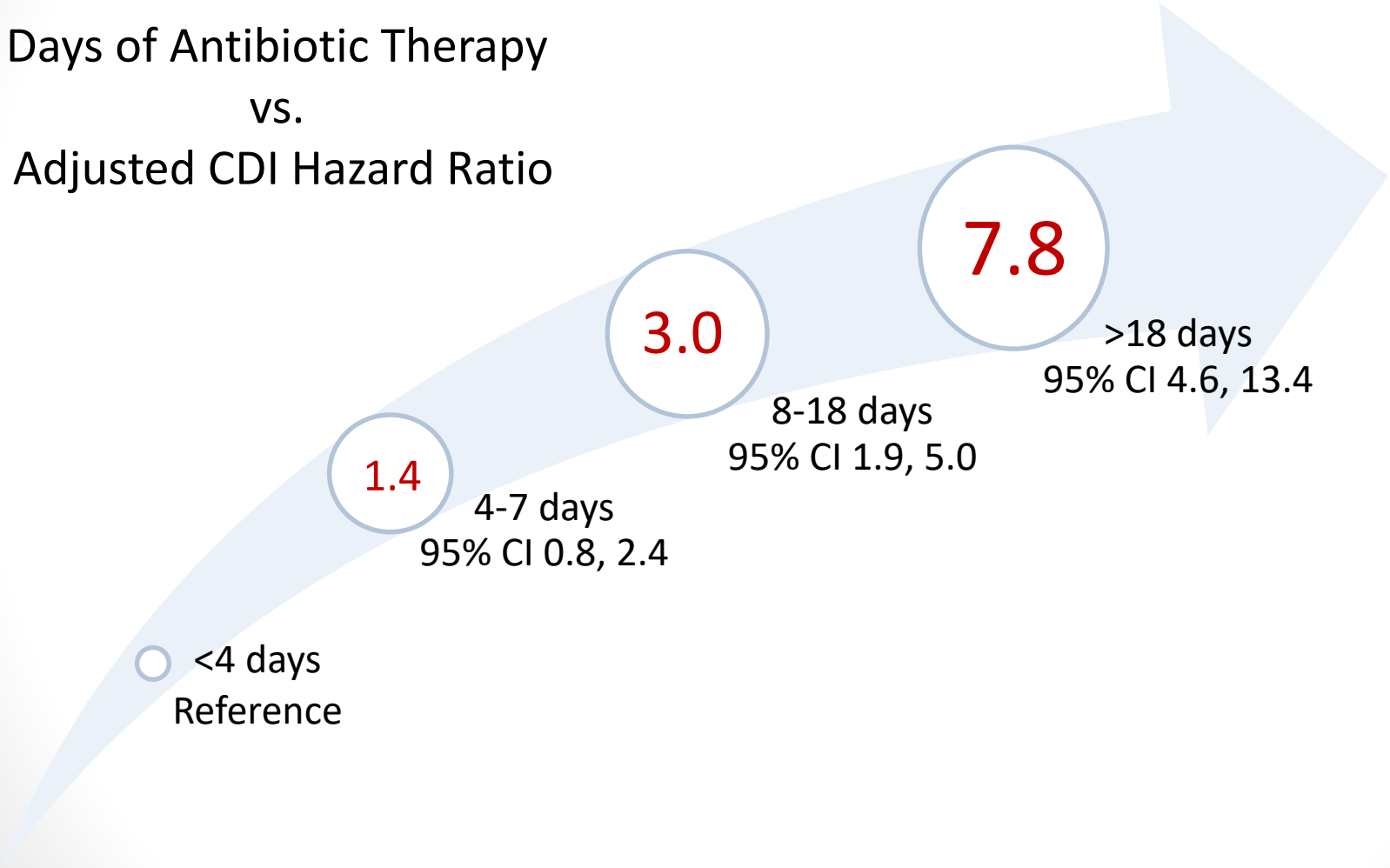
McDonald et al CID 2018;66(7):e1-48

Disruption of normal flora



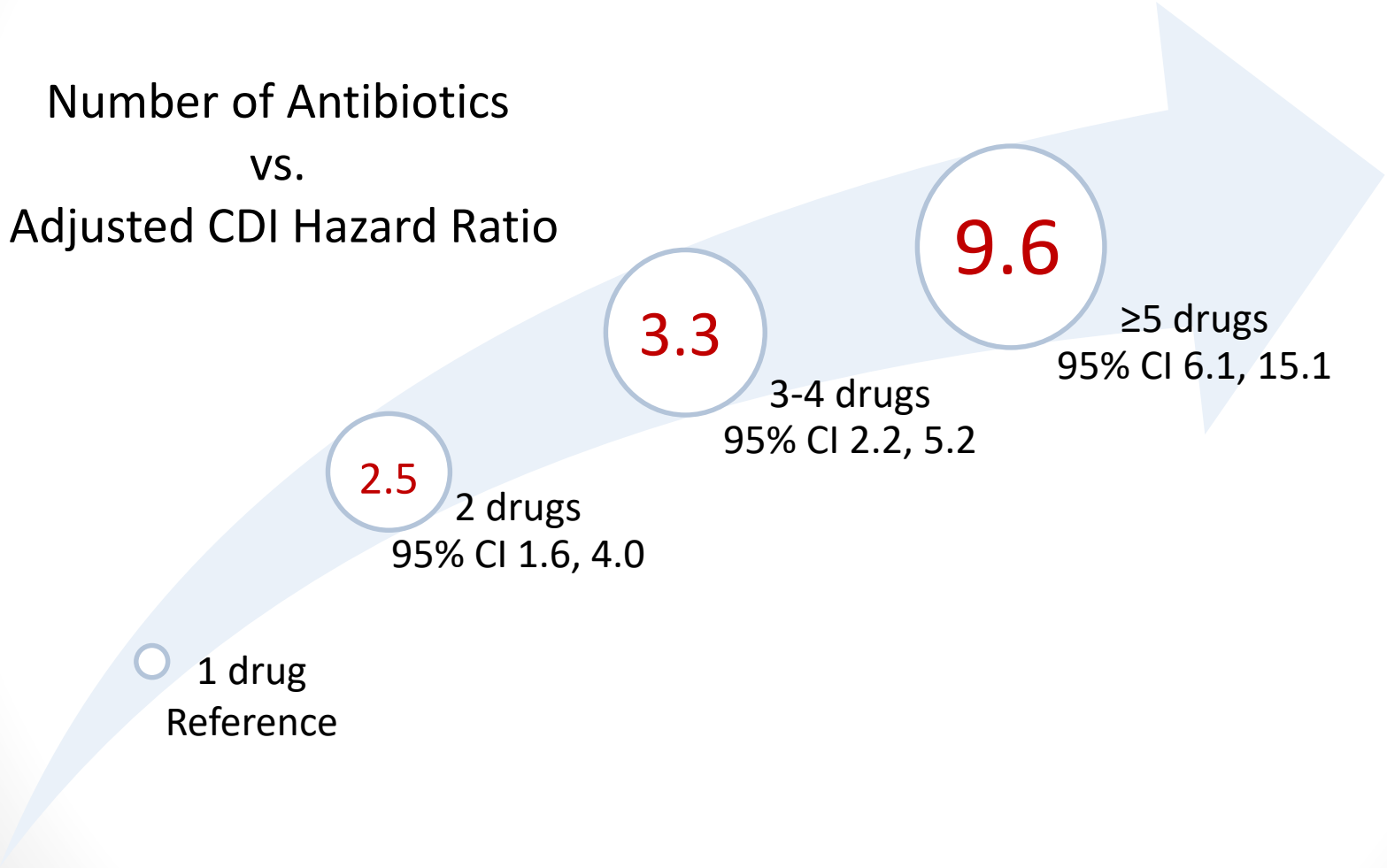
Cumulative ABX exposure risk

Days of Antibiotic Therapy
vs.
Adjusted CDI Hazard Ratio



Stevens V et al. CID 2011;53(1):42-48.

Cumulative ABX exposure risk



Stevens V et al. CID 2011;53(1):42-48.

Antibiotic Exposure Risk

Antibiotic	CDI Adjusted Hazard Ratio (95% CI)
Fluoroquinolones	4.0 (2.7, 5.9)
Aminoglycosides	0.9 (0.3, 3.0)
Clindamycin	1.9 (0.8, 4.4)
3rd/4th Generation Cephalosporins	3.1 (1.9, 5.2)
1st/2nd Generation Cephalosporins	2.4 (1.4, 4.1)
Penicillins	1.9 (0.9, 4.0)

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Fluoroquinolones

Stevens V et al. CID 2011;53(1):42-48.

Fluoroquinolone Restriction

- Multicenter, quasi-experimental study at 4 adult hospitals in Texas in two phases
  - Phase 1: Provider Education
  - Phase 2: Quinolone Restrictions

Restrictions Criteria for Community-acquired Pneumonia Patients
Severe beta-lactam allergy (ex. Anaphylaxis)
Received cephalosporin in the last 3 months
Positive *S pneumoniae* culture with isolate resistant to ceftriaxone

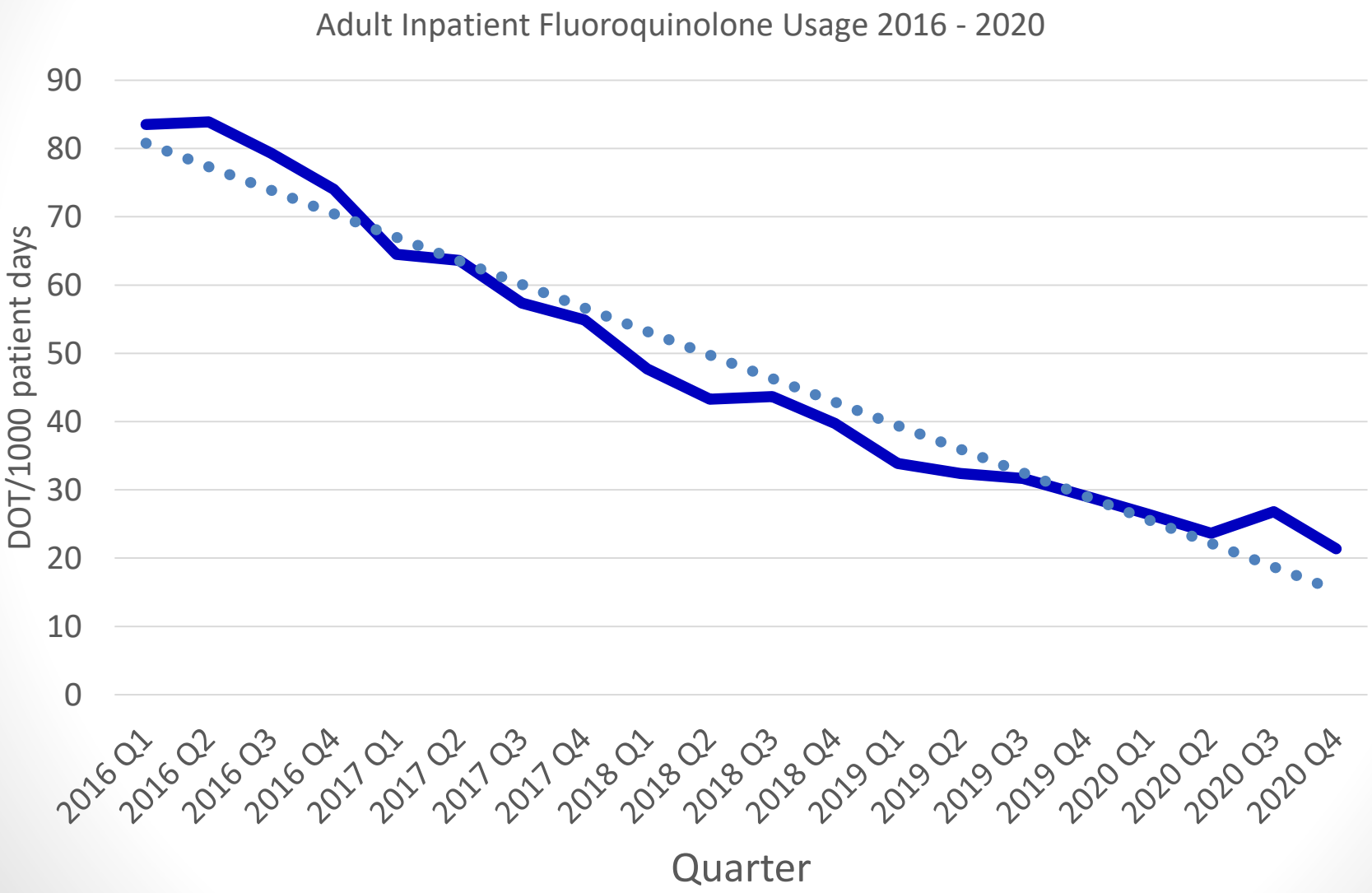
Shea KM et al Antimicrob Agents Chemother 2017;61(6):e00125-17

Fluoroquinolone Restriction

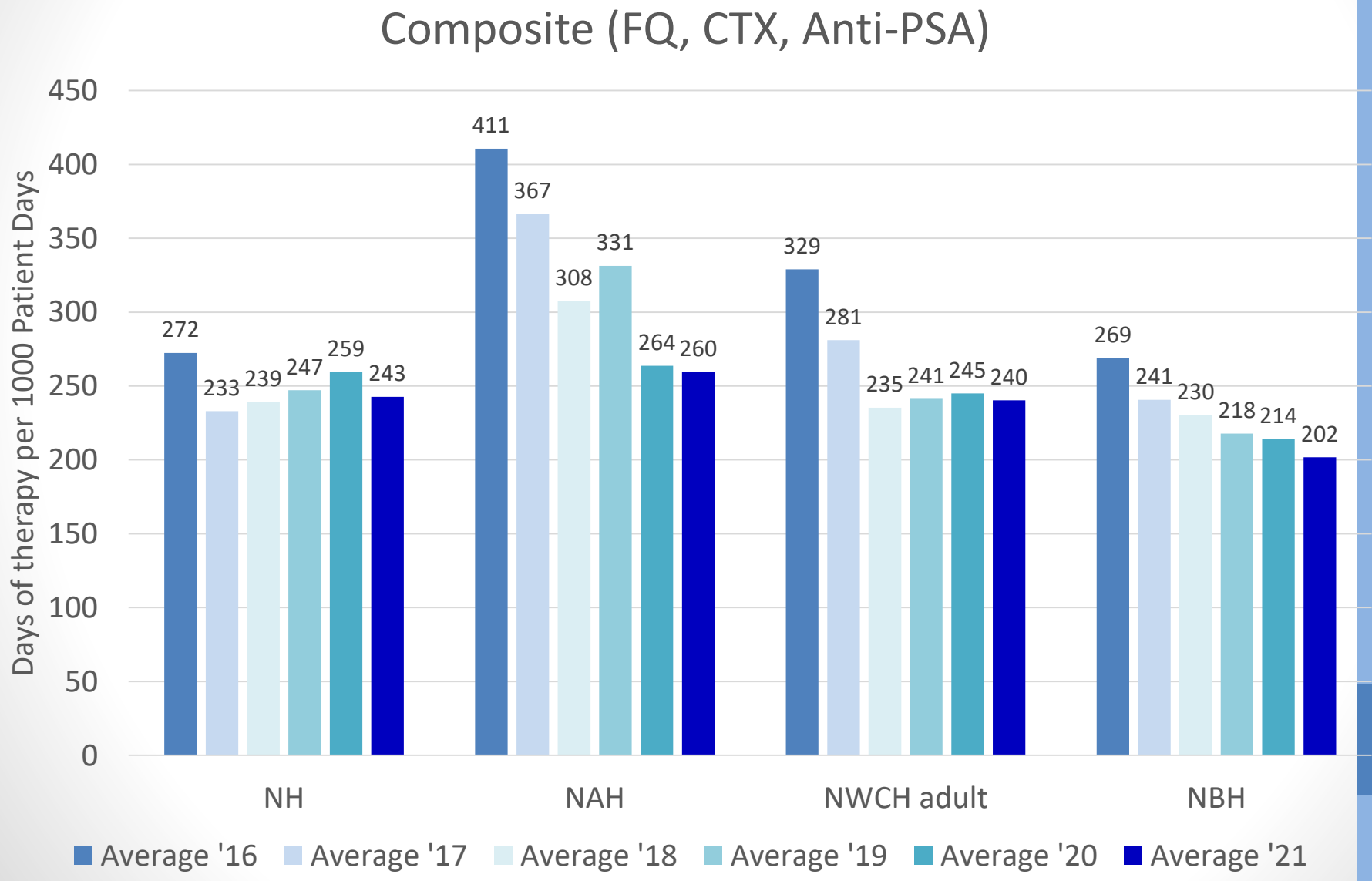
	Days of Therapy per 1000 Patient Days	CDI Cases per 10,000 Patient Days
Pre-intervention	41.0	4.0
Phase 1: Provider Education	↓ 21.5	↓ 3.4
Phase 2: Quinolone Restriction	↓ 4.8	↓ 2.2

Shea KM et al Antimicrob Agents Chemother 2017;61(6):e00125-17

Fluoroquinolones at Norton



C difficile Drivers at Norton



Lower Risk Antibiotics

- Penicillins
- First generation cephalosporins
- Tetracyclines
- Nitrofurantoin
- Metronidazole
- Aminoglycosides
- Vancomycin

Stevens V et al. CID 2011;53(1):42-48.
Brown KA et al. CID 2021;72(4):836-44

Testing for *C difficile*

- Only test patients with clinically significant diarrhea
- At Norton we use a 2-step testing algorithm
  1. PCR (more sensitive, less specific to active disease)
  2. Toxin assay (less sensitive, more specific to active disease)

Test Results	Interpretation
PCR negative	Patient does not have CDI
PCR positive, toxin negative	Patient may be colonized or have active disease
PCR positive, toxin positive	Patient has CDI

McDonald et al CID 2018;66(7):e1-48

Treating *C difficile*

Occurrence	Treatment
First episode	• Oral vancomycin • Oral fidaxomicin Alternative: oral metronidazole in non-severe illness
Second episode	• Prolonged taper/pulse vancomycin • Oral fidaxomicin
Third or subsequent	• Prolonged taper/pulse vancomycin • Oral fidaxomicin • Fecal microbiota transplantation (FMT)
Adjunctive therapy	• Bezlotoxumab in high risk recurrent illness
Fulminant Disease	• High dose oral vancomycin + rectal vancomycin + IV metronidazole (particularly if ileus is present)

Johnson S, CID 2021;73(5):e1029-44

Kelly C, Am J Gastroenterol 2021;116(6):1124-1147

Questions?

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