

Antimicrobial Stewardship: Intervention to Reduce Rates of *Clostridium difficile* Infection

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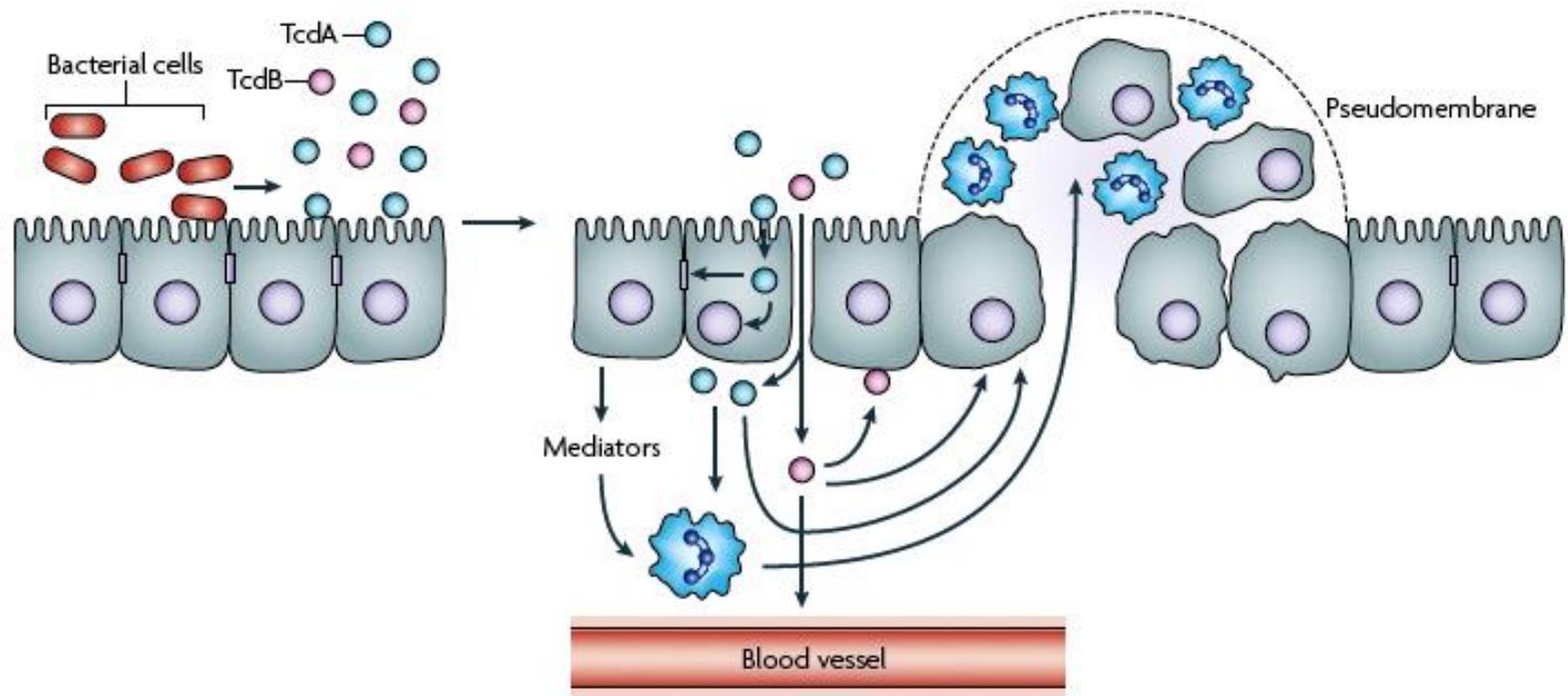
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Antimicrobial Stewardship and CDI

- Background
- Role of diagnostic testing
- Evidence that modification of antimicrobial use lowers rates
- UC Davis Experience with program implementation

Clostridium difficile Infection

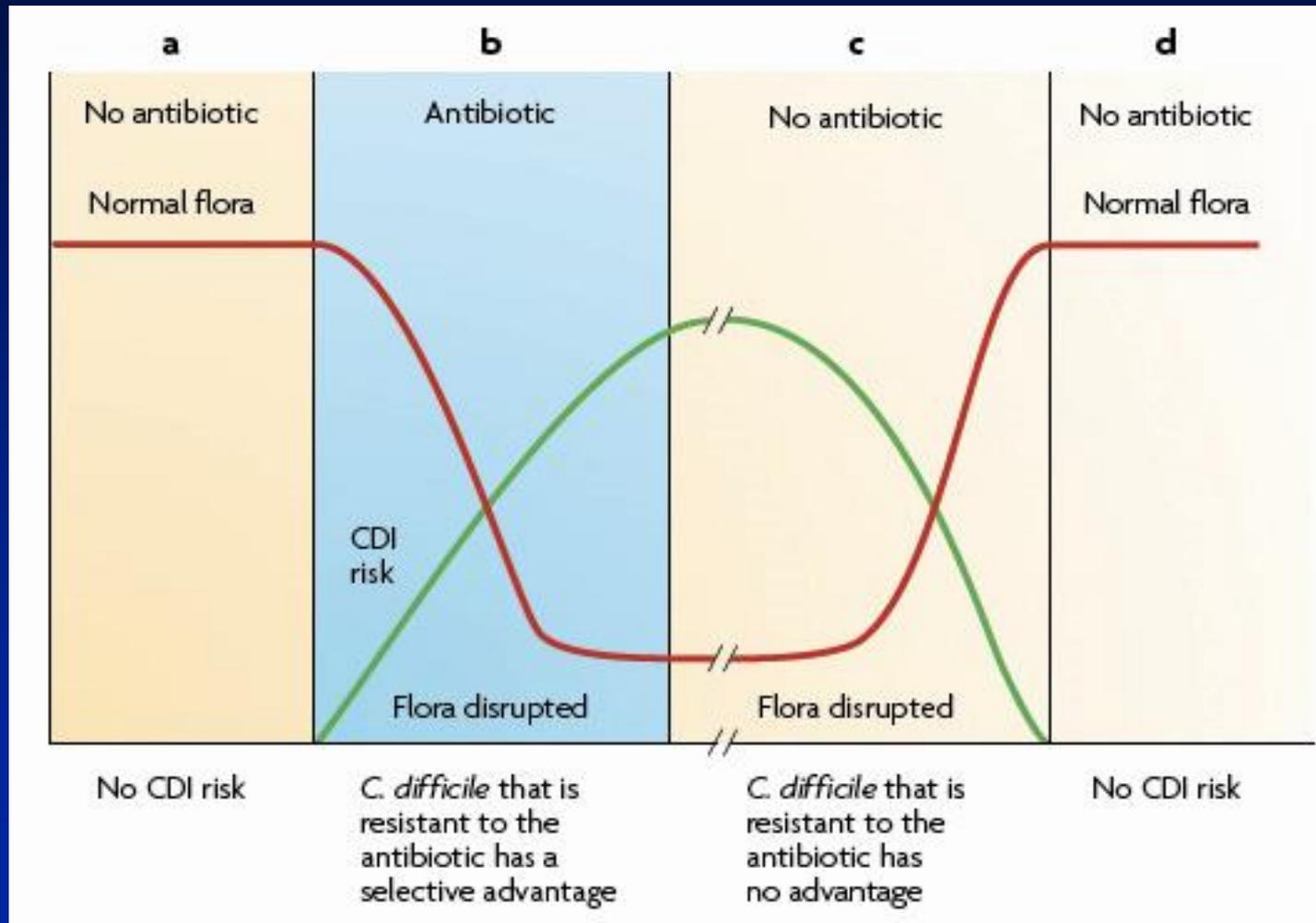
Pathogenesis



Host Protection Against CDI Occurs at Two Levels

- **Normal microbiota** prevent establishment of *C. difficile* colonization of the GI tract
- **Antibodies**, serum (and mucosal?) prevent CDI if colonization occurs
 - Antibodies are probably first acquired in infancy

Clostridium difficile Infection



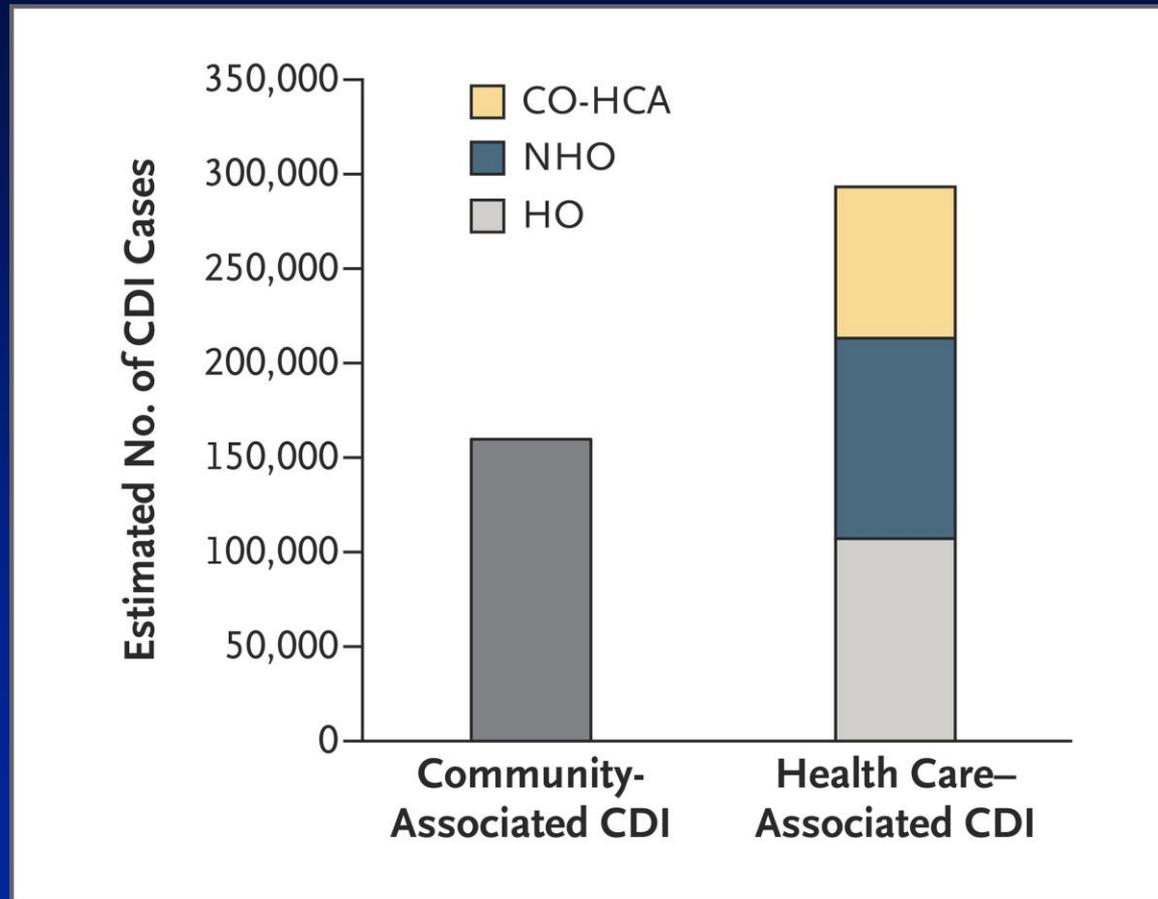
Community Associated (CA) CDI

- 989 CA-CDI cases identified in 8 population-based EIP sites (CA, CO, CT, MD, MN, NY, OR, and TN)
- No inpatient overnight stay within 12 weeks
- 41% had high-level outpatient healthcare exposure (surgery, dialysis, ER visit, inpatient visit not overnight stay)
- 41% had low-level outpatient healthcare exposure (Dr. or dentist office, pharmacy)

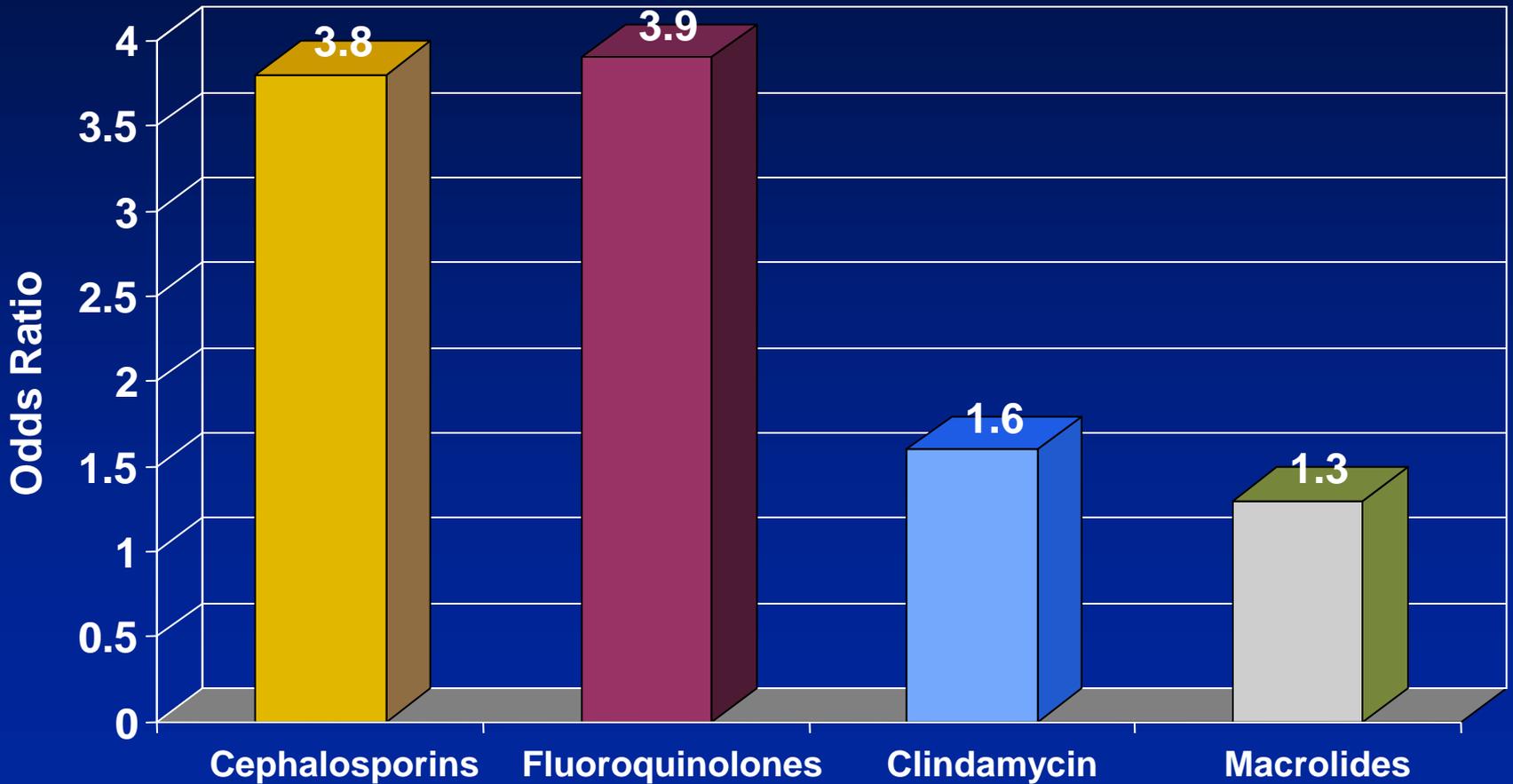
Community Associated (CA) CDI

- Only 18% CA-CDI patients had no health-care exposure in the prior 12 weeks.
- Infant <1 yr ($p<.04$) and CDI patient in home ($p<.05$) were risk factors in the low-level exposure group.
- PPI use in patients w/antimicrobials (26%) was not different than in patients w/o antibiotics (31%, $p=.07$)
- Antimicrobials were used by 68% of healthcare exposed patients compared to 43% with no healthcare exposure ($p<.01$)
 - Importance of healthcare exposure to antibiotic use
 - Most for upper respiratory infection (35%).

Estimated U.S. Burden of *Clostridium difficile* Infection (CDI), According to the Location of Stool Collection and Inpatient Health Care Exposure, 2011



Antibiotic Class and Risk of Hospital-Acquired CDI



Loo VG, et al. *N Engl J Med.* 2005;353:2442-2449.

Clostridium difficile Infection

Diagnostic Testing – Summary

- Must have clinical syndrome before testing
- No clear answer on optimal testing
 - Is PCR too sensitive? – picks up colonized patients
 - Is EIA not sensitive enough for use?
 - Is strain typing considered helpful?
 - What is the role of biomarkers like fecal lactoferrin?
(Still not clear but associated with persistent diarrhea)

Median Post/Pre Ratios of Incident CDI: Switch vs. Non-switch to NAAT

State	Switch Median Ratio (No. month-pairs)	Non-switch Median Ratio (No. month-pairs)	Median Test p-value	Relative % Increase due to NAAT
CA	1.52 (14)	1.0 (56)	0.09	52%
CO	1.43 (24)	1.0 (161)	0.0002	43%
GA	1.67 (50)	1.0 (149)	< 0.0001	67%

Diagnosis of CDI

- 6522 inpatient episodes of CDI evaluated with multiple CDI laboratory tests
- By univariate analysis patients who were CCA positive had a higher 30-day mortality than those who were toxigenic culture positive and CCA negative (72/435 [16.6%] vs 20/207 [9.7%], $p=0.044$) and those who were negative by both tests (503/5880 [8.6%], $p<0.001$)

Multivariate Analysis of 30-day Mortality

Variable	Odds Ratio (95% CI)	P value
Cytotoxin Assay positive vs both Toxigenic Culture and Cytotoxin Assay negative	1.61 (1.12–2.31)	0.0101
WBC $>15 \times 10^9/L$	1.94 (1.52–2.47)	<0.0001
$>50\%$ rise in serum creatinine	2.25 (1.69–2.99)	<0.0001
Serum albumin <20 g/L	2.72 (1.90–3.91)	<0.0001

Diagnosis of CDI

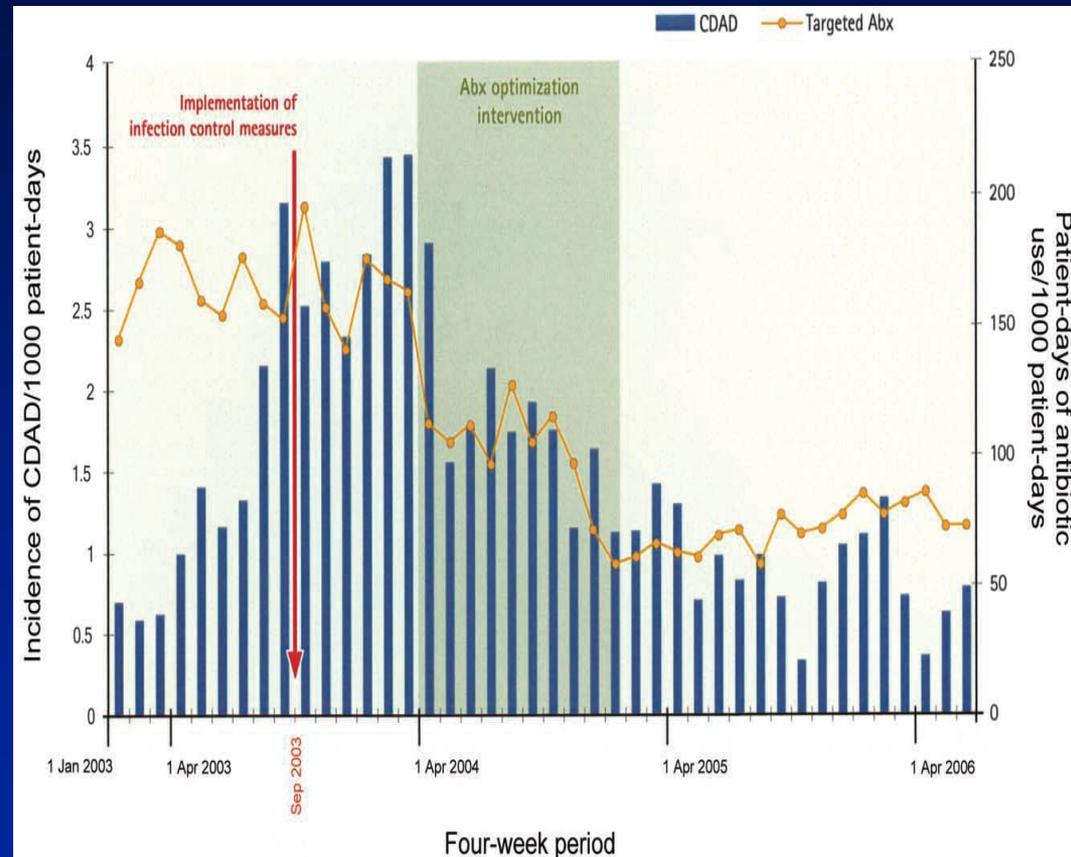
Dog Identifying *C. difficile* in Patients

- 2 year old beagle
- 300 patients (30 with CDI)
- Initially trained by smelling cultures
- Patients: CDI diagnosed by EIA and toxigenic culture
- Dog became excited and sat down when he found a positive



Reduce Risk of CDI Acquisition: Antimicrobial Stewardship

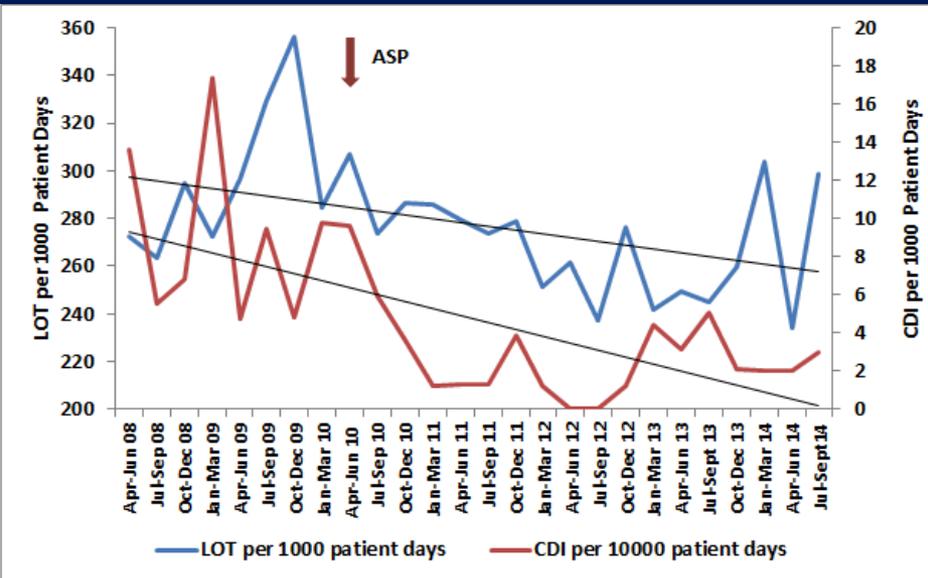
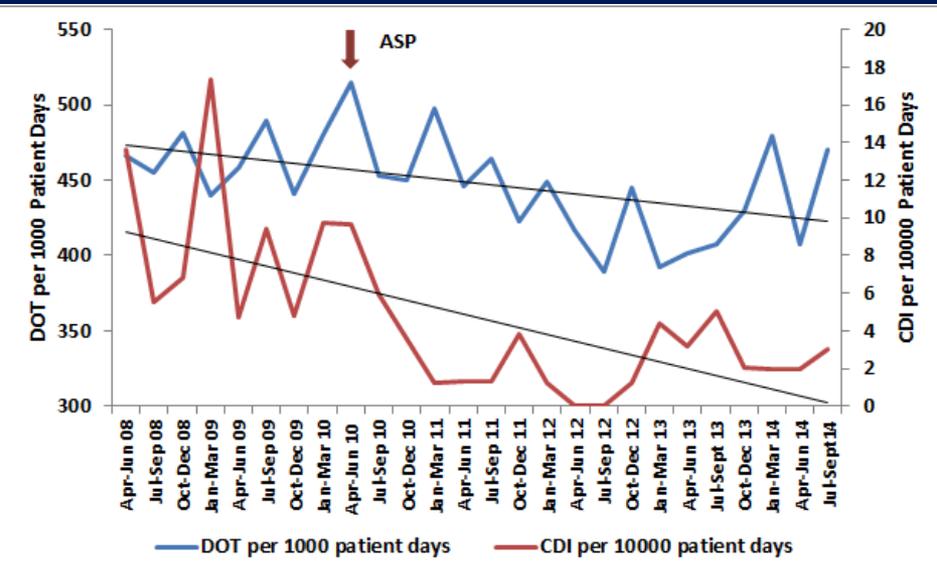
- Reduce use of “high risk” antimicrobials
- Reduce unnecessary antimicrobial use
- Effective in outbreak and non-outbreak settings



Use of Concurrent Antimicrobials and Treatment of CDI

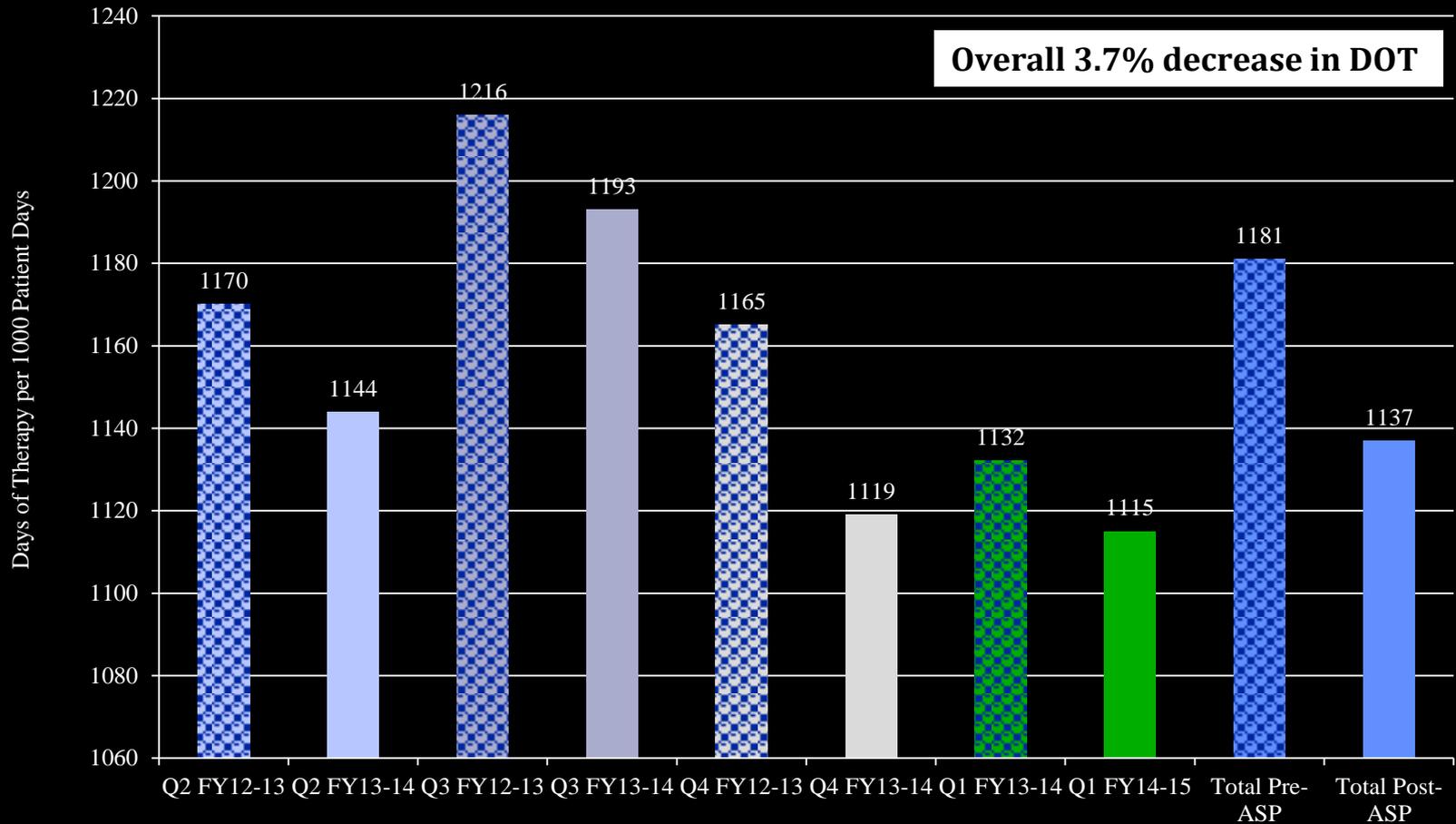
- Phase 2 and 3 trial for fidaxomicin
- 999 patients for cure, 794 for recurrences
- Concurrent antimicrobials in 27.5% of patients
- Lower cure rate (84.4% vs 92.6% $P < 0.001$)
- Longer time to resolution (97 vs 54 hrs $P < 0.001$)
- More recurrences 24.8% vs 17.7% $P = \text{NS}$

UC Davis Children's Hospital: DOT/LOT and CDI rates

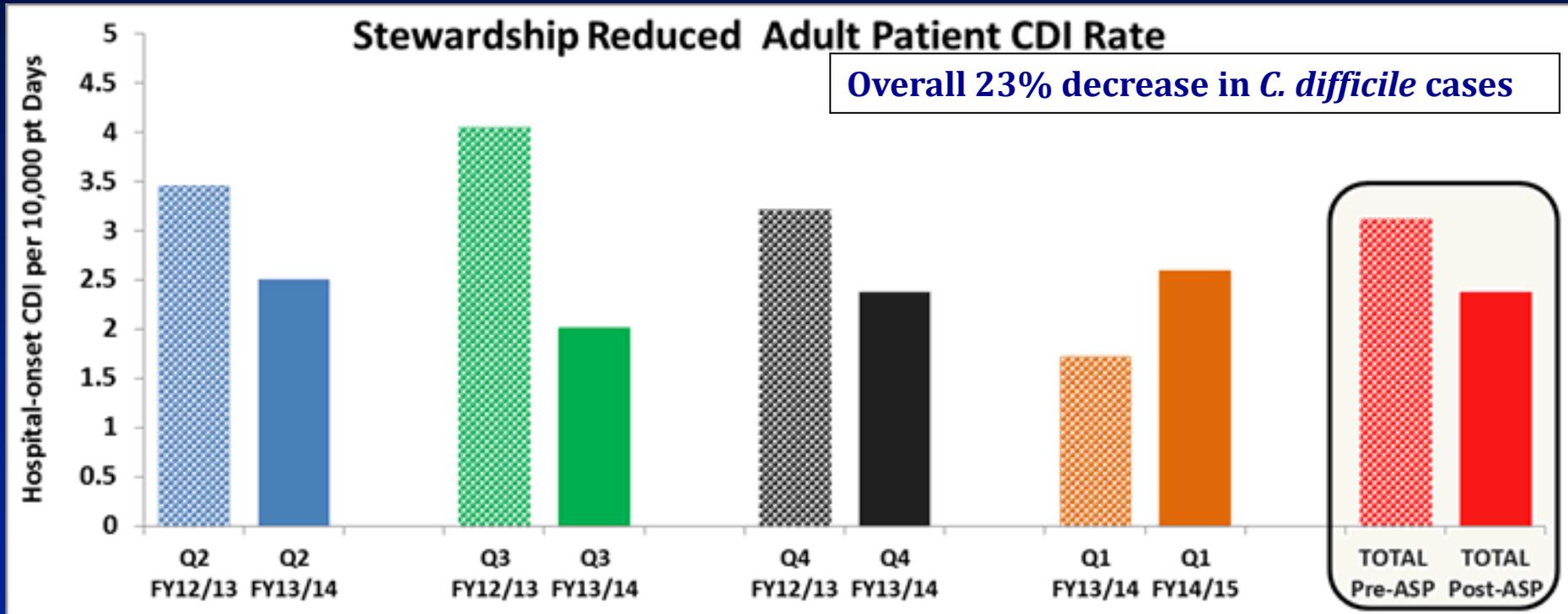


Antimicrobial Stewardship: Implementation of Prospective Audit With Feedback

Adult Inpatient All Antimicrobials Days of Therapy per 1000 Patient Days



Antimicrobial Stewardship: Implementation of Prospective Audit With Feedback



Clostridium difficile Infection

Gram's stain
showing gram
positive rods and
PMNs

