

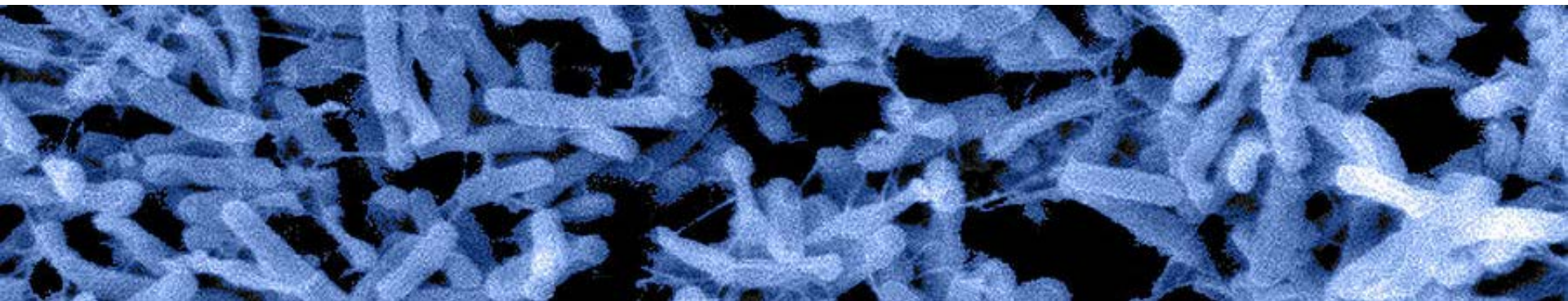


Community-Associated *C. difficile* Infection: Think Outside the Hospital

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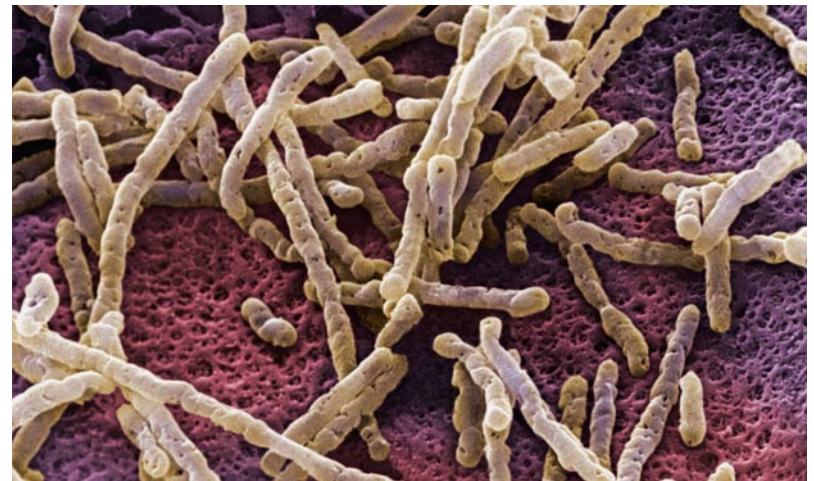
May 1, 2018



Clostridium difficile

Clostridium difficile

- ***Clostridium difficile* (*C. diff*)**
 - Anaerobic
 - Gram positive
 - Spore forming
 - Toxin-producing
- Ubiquitous in soil and the environment
- *C. diff* infection (CDI) is most common health care-associated infection (HAI) in US
- Transmitted through the fecal-oral route



Spectrum of Disease

CDI symptoms can range from asymptomatic colonization to life-threatening



Risk Factors

Antimicrobial exposure 

Acquisition of *C. difficile* 

Advanced age

Underlying illness

Immunosuppression

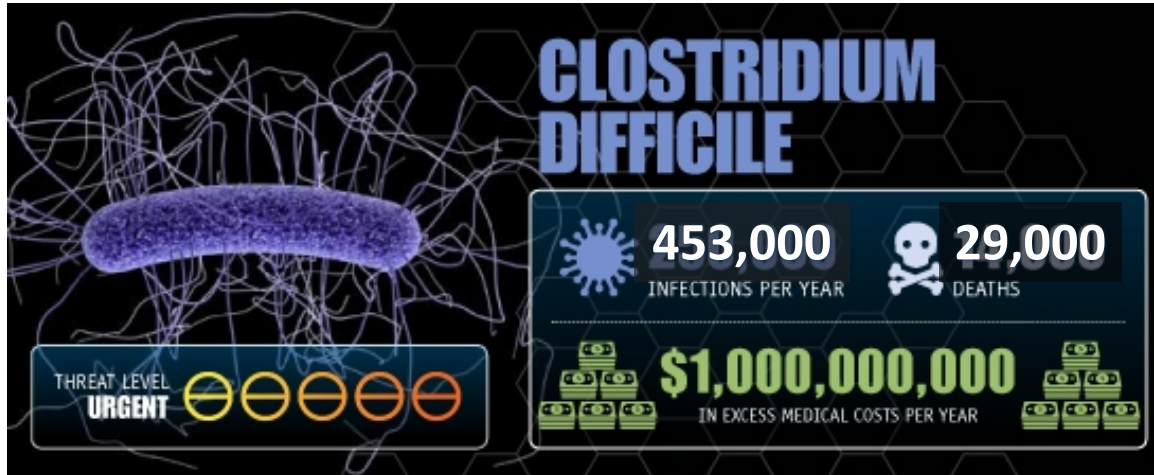
Gastric acid suppression

Use of nasogastric or gastrostomy feeding tubes

Use of proton-pump inhibitors (PPIs)

“Threat level: urgent”

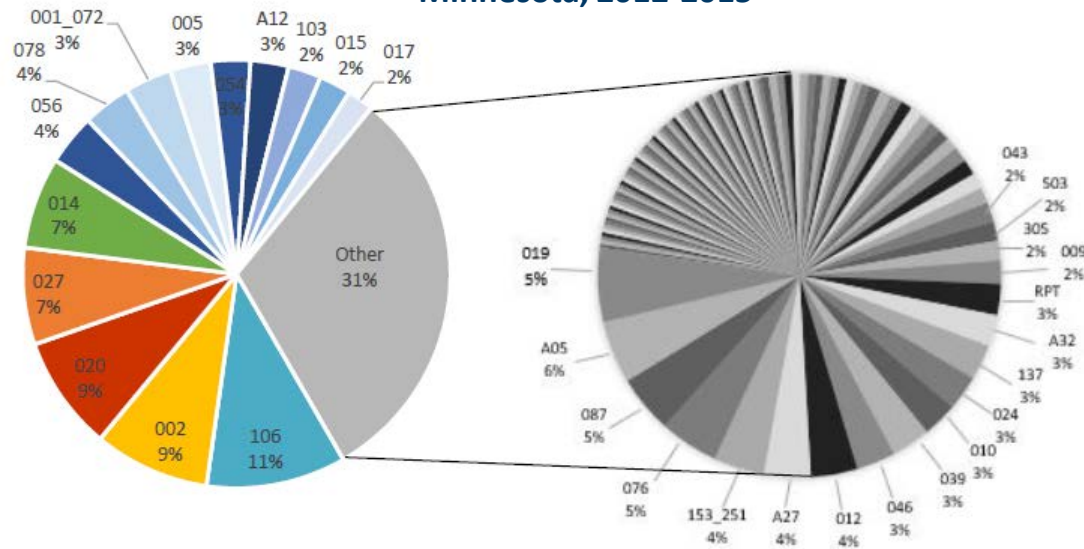
- An estimated 453,000 cases occur in the US every year, resulting in 29,000 deaths
- Causes \$1 billion in excess medical costs per year



Genetic diversity

- *C. difficile* is an extremely diverse bacteria, with hundreds of ribotypes currently identified




Percent of *C. difficile* Ribotypes Among All Submitted Isolates, Minnesota, 2012-2015



New IDSA guidelines were released in early 2018

Clinical Infectious Diseases

IDSA GUIDELINE

Clinical Practice Guidelines for *Clostridium difficile*
Infection in Adults and Children: 2017 Update by the
Infectious Diseases Society of America (IDSA) and Society
for Healthcare Epidemiology of America (SHEA)

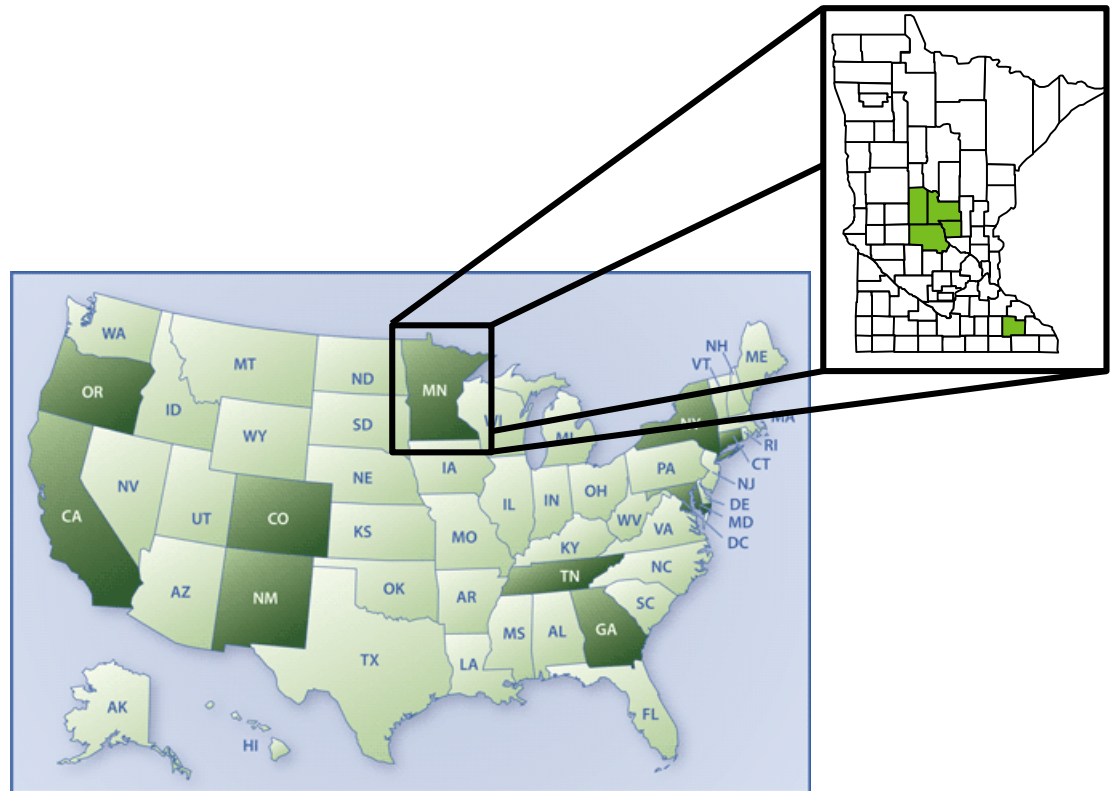
L. Clifford McDonald,¹ Dale N. Gerding,² Stuart Johnson,^{2,3} Johan S. Bakken,⁴ Karen C. Carroll,⁵ Susan E. Coffin,⁶ Erik R. Dubberke,⁷
Kevin W. Garey,⁸ Carolyn V. Gould,¹ Ciaran Kelly,⁹ Vivian Loo,¹⁰ Julia Shaklee Sammons,⁶ Thomas J. Sandora,¹¹ and Mark H. Wilcox¹²



Minnesota Department of Health CDI Surveillance

CDI Sentinel Surveillance

- One of 10 sites participating in the CDC Emerging Infections Program (EIP)
- MDH has been conducting active, population-based surveillance in four counties since 2009, with a fifth added in 2012
 - Total population: ~400,000



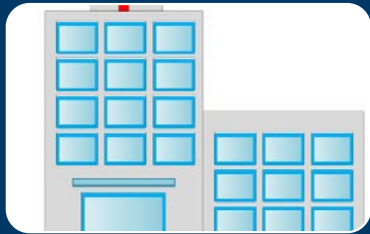


CDI Surveillance Methods

- **CDI surveillance team reviews outpatient and hospital medical records for the 12 weeks prior to the positive stool**
- **Cases with no overnight hospitalization or LTCF stay (community-associated or CA-CDI) are contacted for an interview**
 - **MDH is only state that interviews cases**

Epidemiological Classifications

CDI cases are defined by onset and exposure:



Healthcare associated (HA)

- Overnight hospitalization or LTCF stay in previous 12 weeks



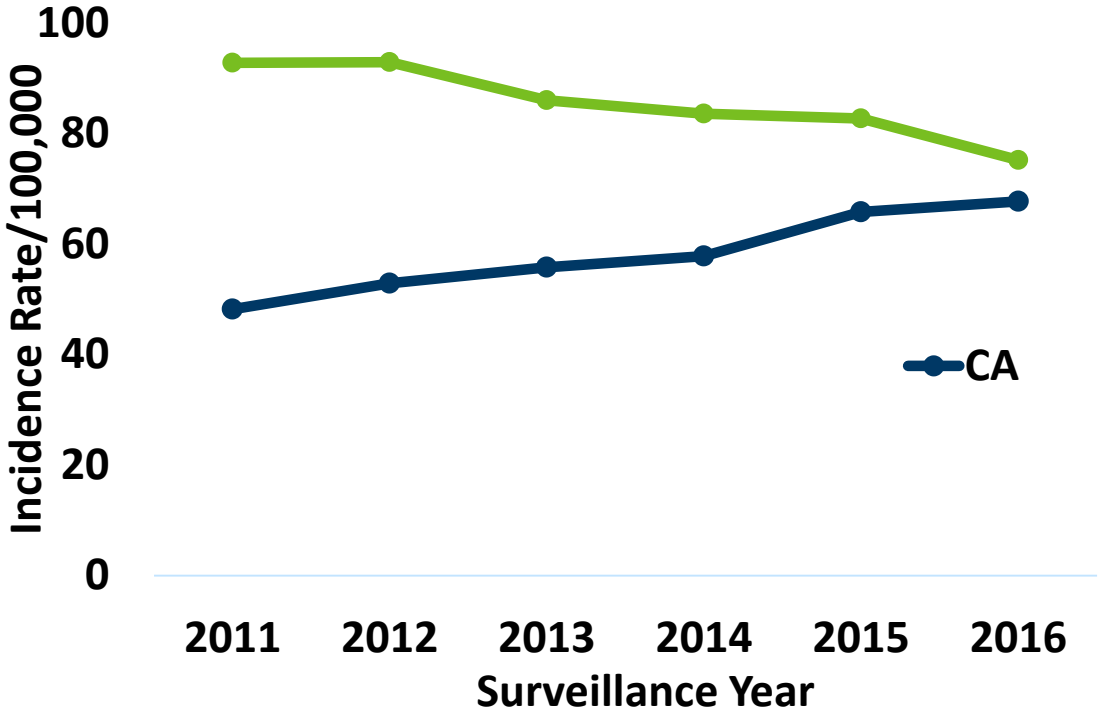
Community associated (CA)

- No overnight hospitalization or LTCF stay



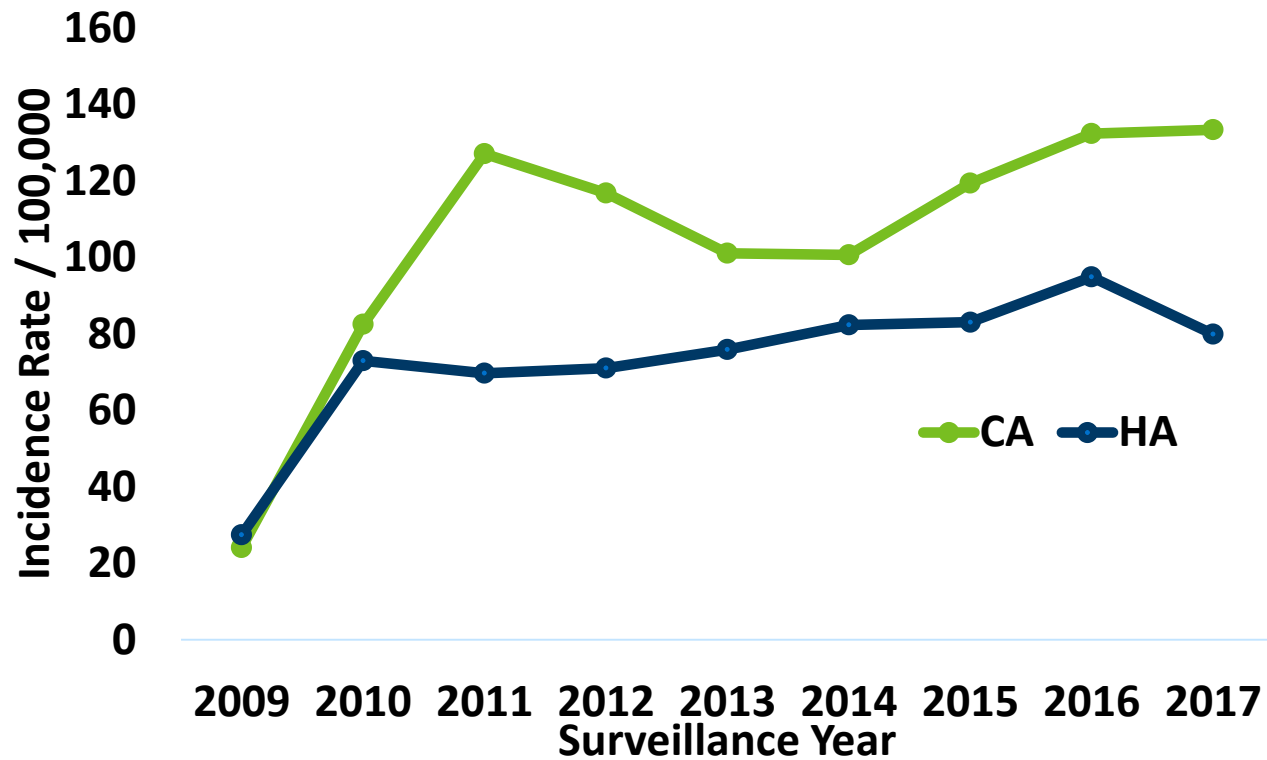
Community-Associated CDI: A Growing Problem

National CDI Incidence Rates



The gap between healthcare-associated and community-associated CDI incidence has closed in recent years

Minnesota CDI Incidence Rates



- In general, CA-CDI cases are

Female

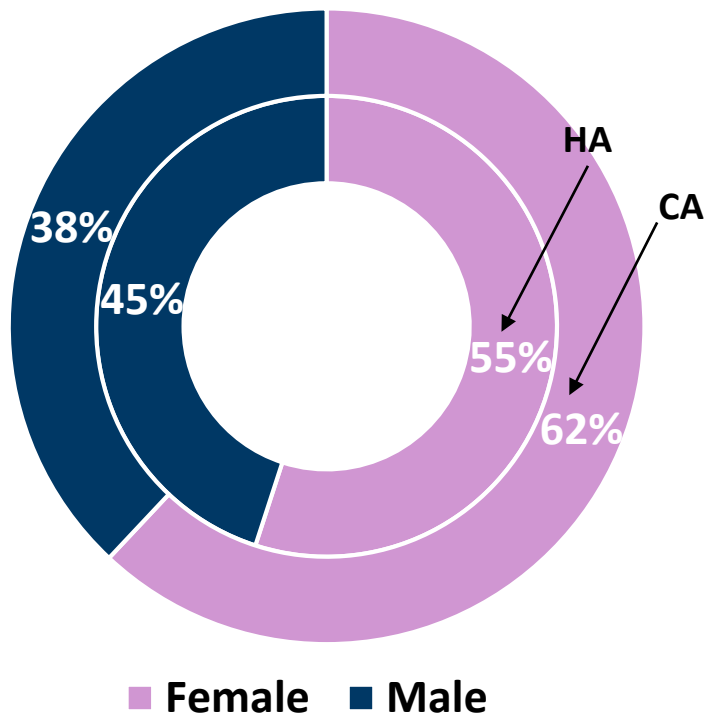
Younger

Healthier

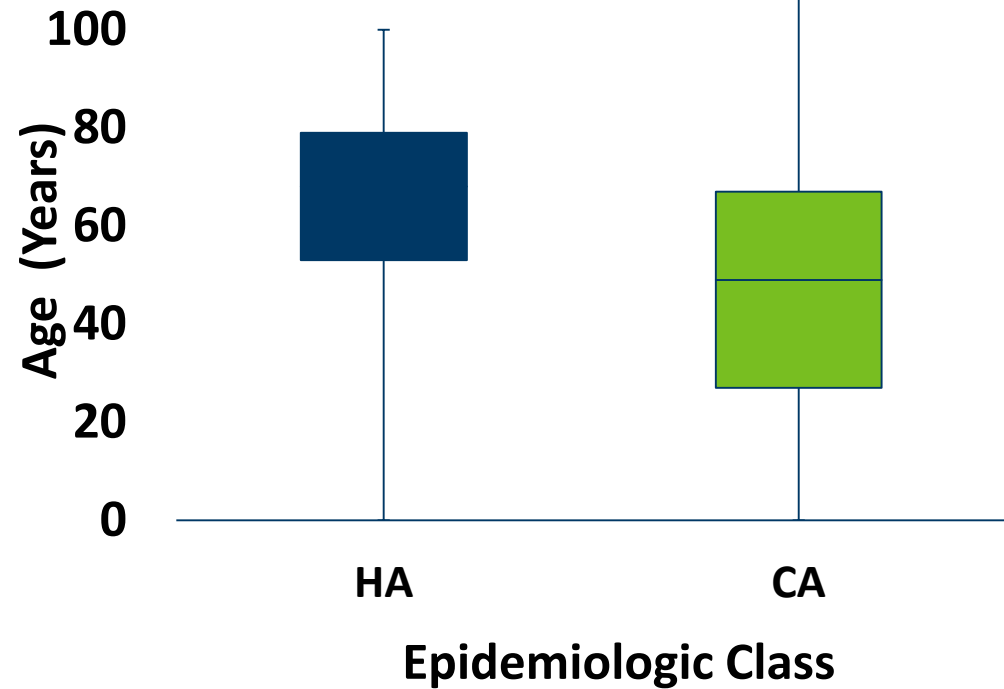
than HA-CDI cases

Minnesota CDI Demographics

Gender

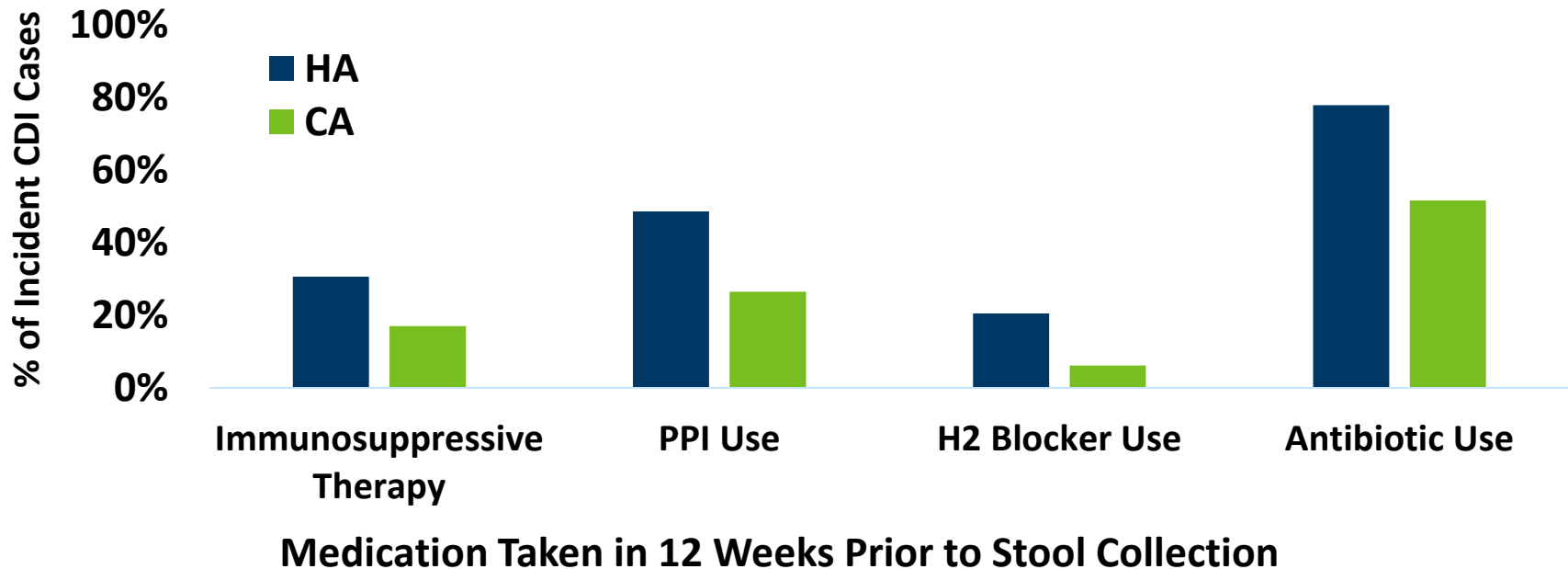


Age Distribution



Medications Taken by Minnesota CA-CDI Cases

CA-CDI cases are less likely to take antibiotics, proton pump inhibitors (PPIs), H2 blockers, and immunosuppressive therapy



Case-control study

- From 2014-2015, MDH participated in a case-control study to identify risk factors for CA-CDI
- 62% of cases reported antibiotic use in the prior 12 weeks, compared to 10% of controls
- The most common antibiotics received were:
 - Beta-lactam or beta-lactamase inhibitor combinations (18%)
 - Clindamycin (12%)
 - Fluoroquinolone (11%)
 - Cephalosporin (8%)

- **The most common indications for antimicrobial use included:**
 - **Ear, sinus, or upper respiratory tract infection (22%)**
 - **Skin infection (19%)**
 - **Dental surgery (16%)**
 - **Urinary tract infection treatment (12%)**
 - **Bronchitis or pneumonia (9%)**

Case-control study: final results

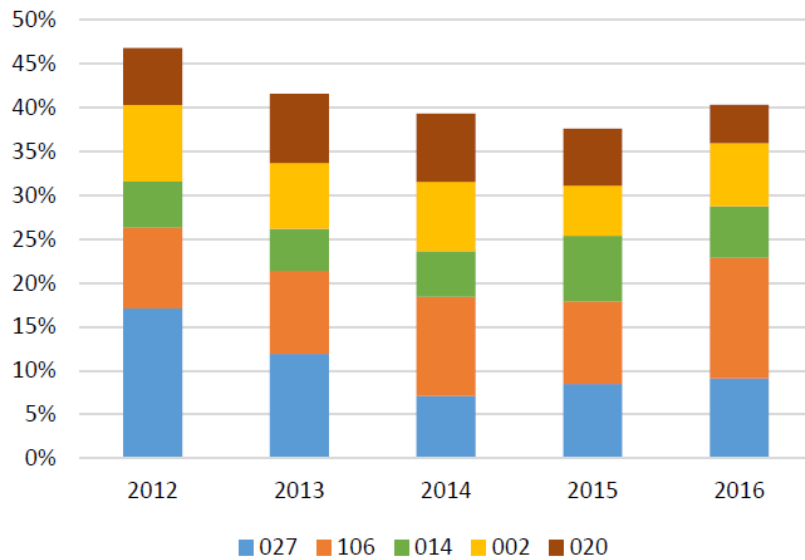
After running multi-variate analyses, multiple antibiotics were found to be independently significant

Antibiotic use

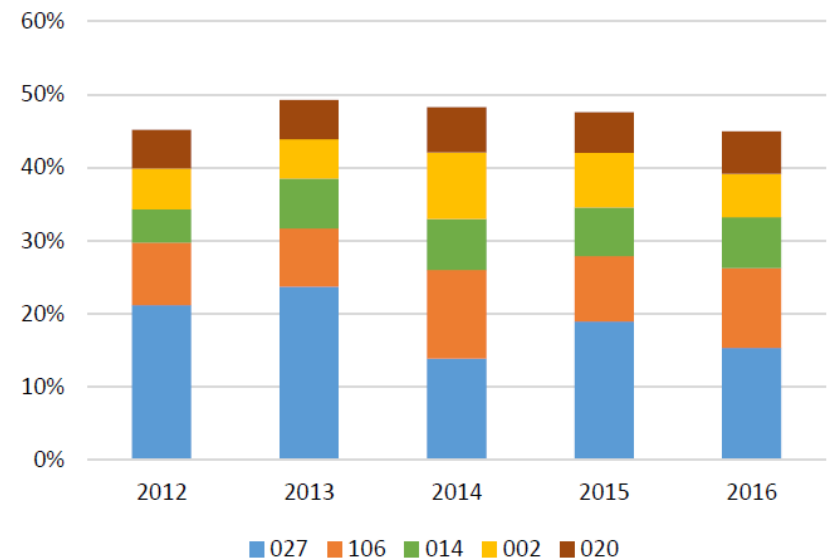
- Cephalosporin
- Clindamycin
- Fluoroquinolone
- Beta-lactam / beta-lactamase inhibitor combination

Genetic diversity

Top 5 Ribotypes Among Community-Associated CDI



Top 5 Ribotypes Among Healthcare-Associated CDI





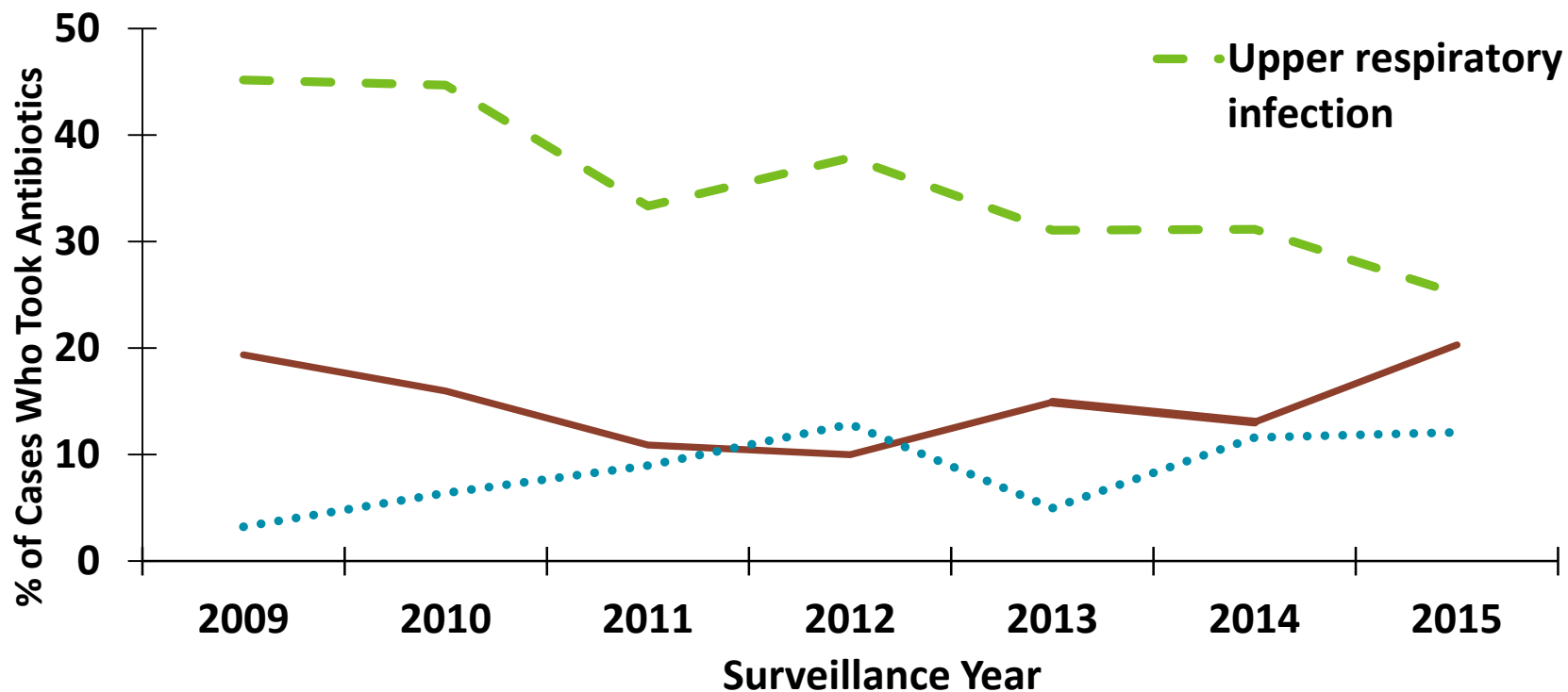
Severity and outcomes

- **Despite being generally less severe than HA-CDI, CA-CDI still can be severe**
 - **26% hospitalized**
 - **5% admitted to ICU**
 - **3% toxic megacolon**
 - **2% death**
- **20% treatment failure**
- **28% had recurrent CDI**



Antibiotics Used for Dental Procedures in CA-CDI Cases

Indications for Antibiotic Prescriptions Reported by CA-CDI Cases During Interview, 2009-2015





Antibiotic Prescriptions in Dentistry

- **Dentists not considered a key stakeholder**
- **Dentists prescribe ~10% of antibiotics in outpatient settings**
 - **Over 24 million prescriptions in 2013**
 - **Treatment of oral infections**
 - **Prophylaxis during invasive procedures**



Antibiotic Prescriptions in Dentistry

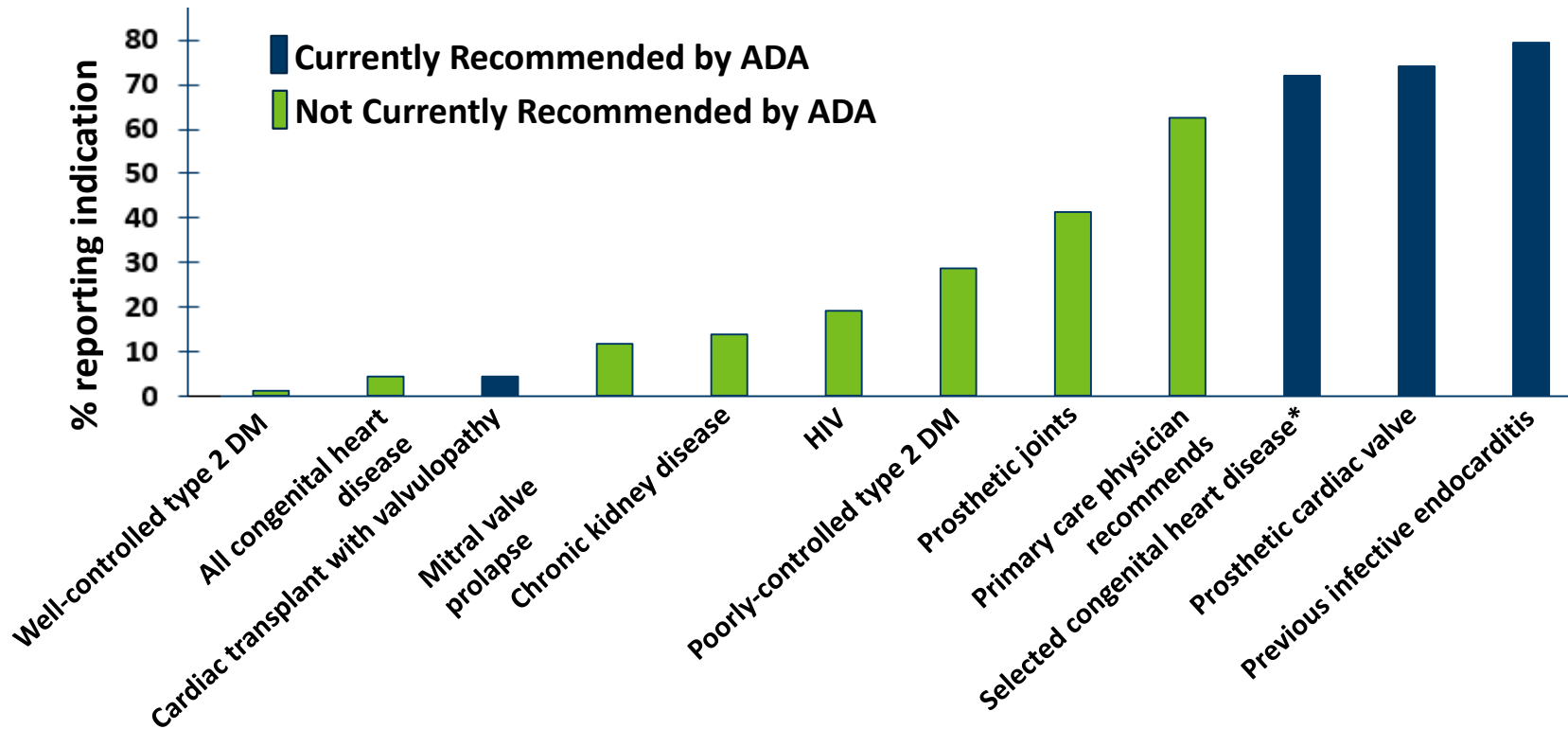
- **Antibiotics are indicated to treat oral infections**
 - **Tooth abscesses**
- **Recommendations for prophylaxis exist for two groups of patients**
 - **Heart conditions that may predispose them to infective endocarditis**
 - **Prosthetic joints and may be at risk for developing infection at the site of prosthetic**



2015 Survey of Minnesota Dentists

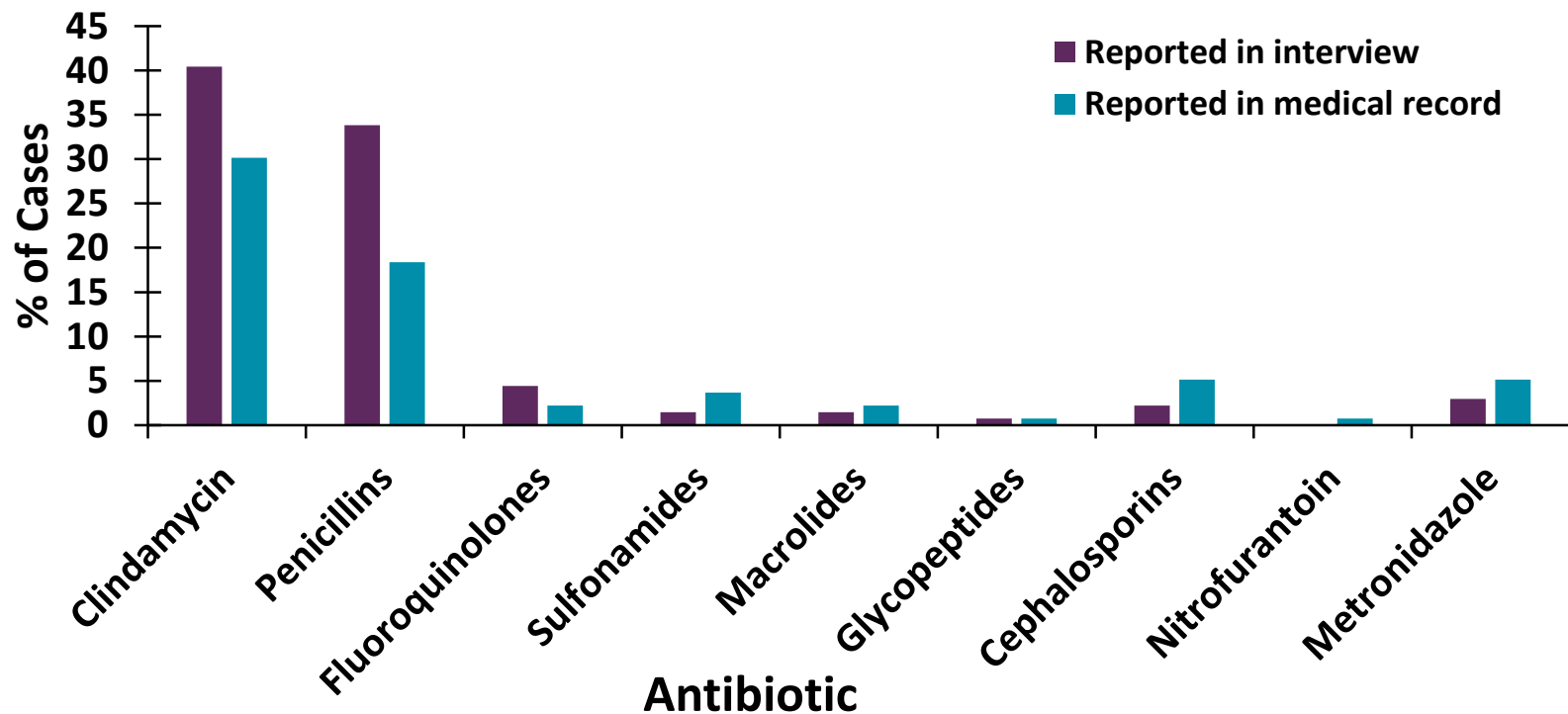
- **Dentists were asked for which scenarios they would prescribe antibiotics:**
 - **Prophylaxis for patients with high risk conditions (84%)**
 - **Localized swelling (70%)**
 - **Gum pain (38%)**
 - **Precautionary (38%)**
 - **Legal concerns (24%)**
- **Less than half reported a concern for adverse drug effects, antibiotic resistance, or *C. diff* as factors that influenced their prescribing decisions.**

High Risk Conditions Reported as Warranting Antibiotic Prophylaxis Before Invasive Dental Procedures



- **Of CA-CDI cases who reported antibiotic use in the 12 weeks before diagnosis, 136 (15%) CA-CDI reported being prescribed antibiotics for a dental procedure**
 - **116 (85%) were prescribed antibiotics only for dental reasons**
 - **46 (34%) reported antibiotics in the interview that were not documented in the medical record**

Antibiotics Taken by CA-CDI cases for a Dental Procedure in 12 Weeks Prior to Diagnosis



Antibiotics Taken by CA-CDI Cases for a Dental Procedure

	Dental Antibiotics n (%) n=136	Non-Dental Antibiotics n (%) n=790	P-value
Clindamycin	68 (50)	78 (10)	0.001
Cephalosporins	10 (7)	237 (30)	0.001
Fluoroquinolones	8 (6)	153 (19)	0.001

*Antibiotic reported in interview or recorded in medical record



Dental Antibiotic Prescribing Practices (n=76)


- In July 2015, MDH began collecting dental antibiotic indications and prescriber information in the interview
- 76 CA-CDI cases with dental antibiotic use
- To date, the top indications are:
 - Tooth infection/abscess (43%)
 - Oral surgery prophylaxis (35%)
 - Dental cleaning prophylaxis (13%)



Dental Antibiotic Prescribing Practices (n=76)

- **51 (67%)** of these cases were prescribed antibiotics by dentists
- **4 (3%)** cases reported heart conditions
 - **1** with valve replacement 15 years ago
- **4 (3%)** cases reported having joint replacements

Making Waves



OCT 7, 2017 @ 1:23 PM 4,812

[The Little Black Book of Billionaire Secrets](#)

Taking Prophylactic Antibiotics Before Dental Procedures Is Rarely Necessary And Can Make You Sick

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Dentists to Blame for Increasing C Diff Cases?

OCTOBER 08, 2017



- **Antibiotics prescribed by dentists are contributing to CDI**
 - Recent study showed dental prescribing increased by 62%
- **Dentists most often prescribed antibiotics for tooth abscesses or prophylaxis before invasive procedures**
- **Generally not recommended for dental cleaning or oral surgery**

- **CA-CDI cases prescribed antibiotics for dental procedures were older and more likely to receive clindamycin**
 - **National data show dentists prescribe more penicillins than clindamycin**
 - **7x more likely to develop CDI if taking any antibiotic**
 - **20x more likely to develop CDI if taking clindamycin**



Recommendations

- **Dentists need to be included in antibiotic stewardship programs**
- **Dentists should consider the risk for CDI and other potential complications of antibiotic use**
- **Clarification and consistency between associations regarding dental prophylaxis for joint replacement recommendations**
- **More research needed to quantify risks of adverse events associated with invasive dental procedures with or without antibiotic prophylaxis**



Antibiotic Prescribing in Pediatric *Clostridium difficile* Cases

- **60-70% of healthy newborns are colonized with *C. diff***
 - Rate decreases with age
 - Carriage rates being similar to adult population at one year
- **As with adult CDI, pediatric CDI rates are increasing**
- **Pediatric CDI shares some risk factors with adult CDI, including healthcare exposure, PPI use, and antibiotic use**
- **71% of pediatric cases are CA-CDI**

Demographics

- 8% of MN CDI cases were pediatric
- 367 had medical records available for antibiotic prescribing data abstraction
- 47% of pediatric cases were female
- 80% were CA

Variable	n (%)
Female	175 (47)
White	271 (91)
Median Age (IQR)	5 (2-11)
Epidemiological Class	
CA	295 (80)
CO-HCFA	57 (15)
HCFO	15 (4)
Underlying Conditions	
None	272 (74)

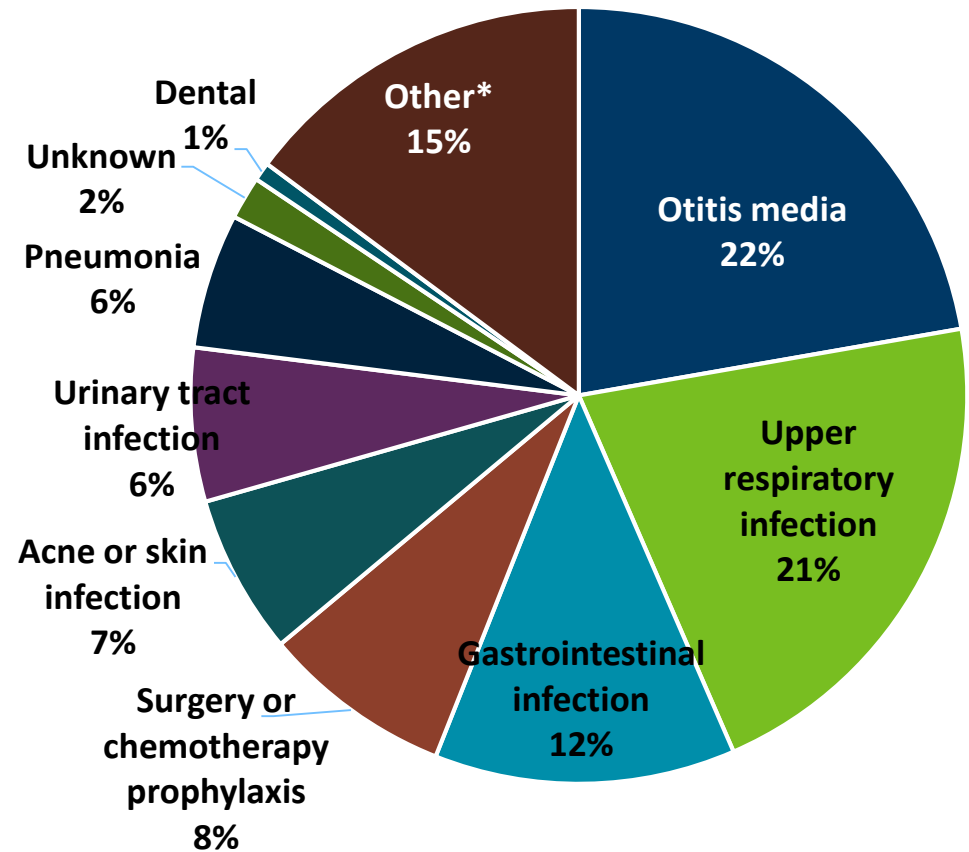
Pediatric Antibiotic Prescriptions

- Among these, 209 (57%) pediatric cases received 393 prescriptions in the 12 weeks prior to developing CDI
 - 50 (14%) cases were prescribed ≥ 3 antibiotics
- The median time between prescription end date and CDI diagnosis was 13 days
- Most (73%) of antibiotics were prescribed in an outpatient setting

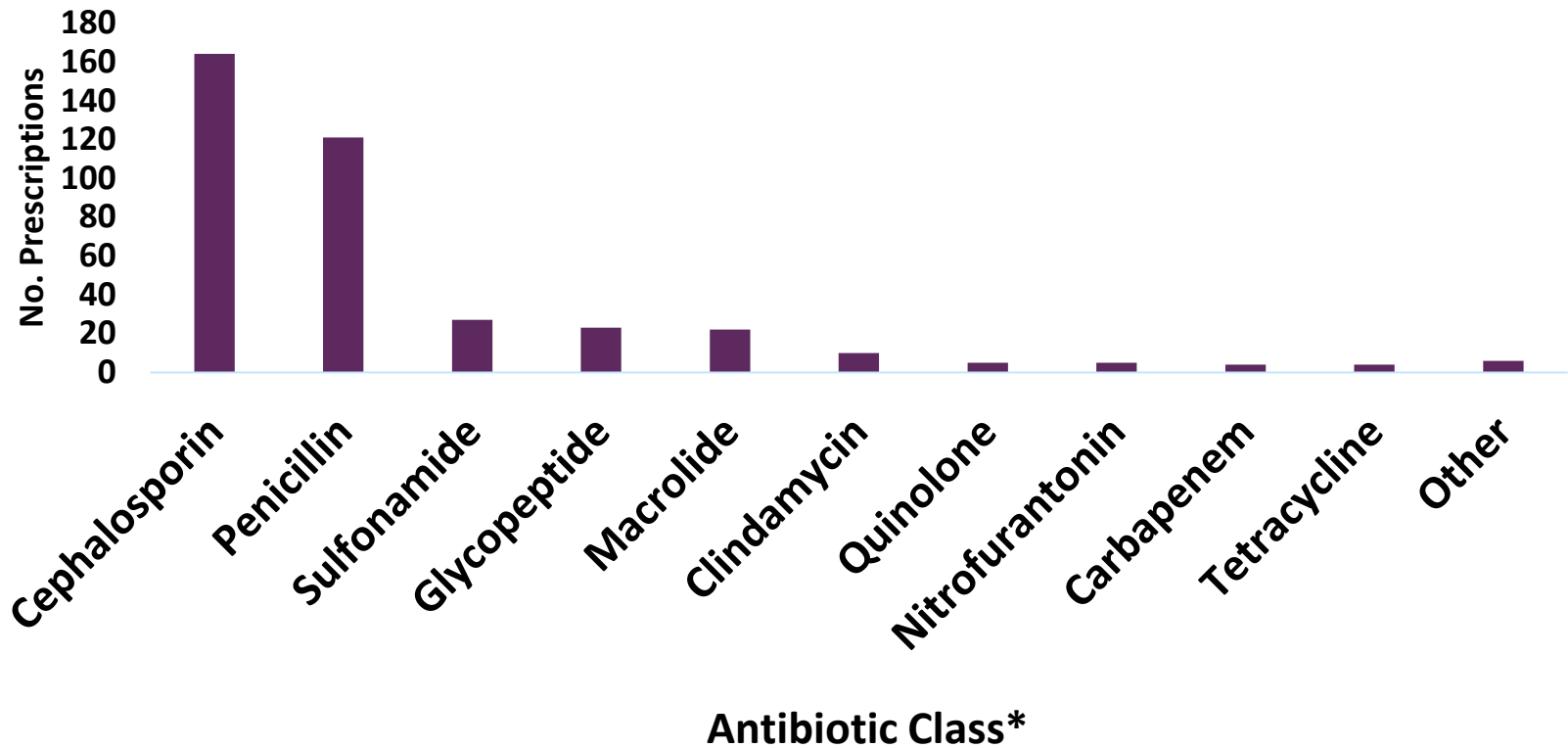
Variable	n(%)
No. Antibiotic Prescriptions	393
No. Cases Prescribed Antibiotics	209 (57)
1	103 (28)
2	56 (15)
3+	50 (14)
Median days between last antibiotic dose and CDI diagnosis* (IQR)	13 (3-40)
Prescriber Location	
Outpatient	282 (73)
Hospital	74 (19)
ED	31 (8)

Antibiotic Indications

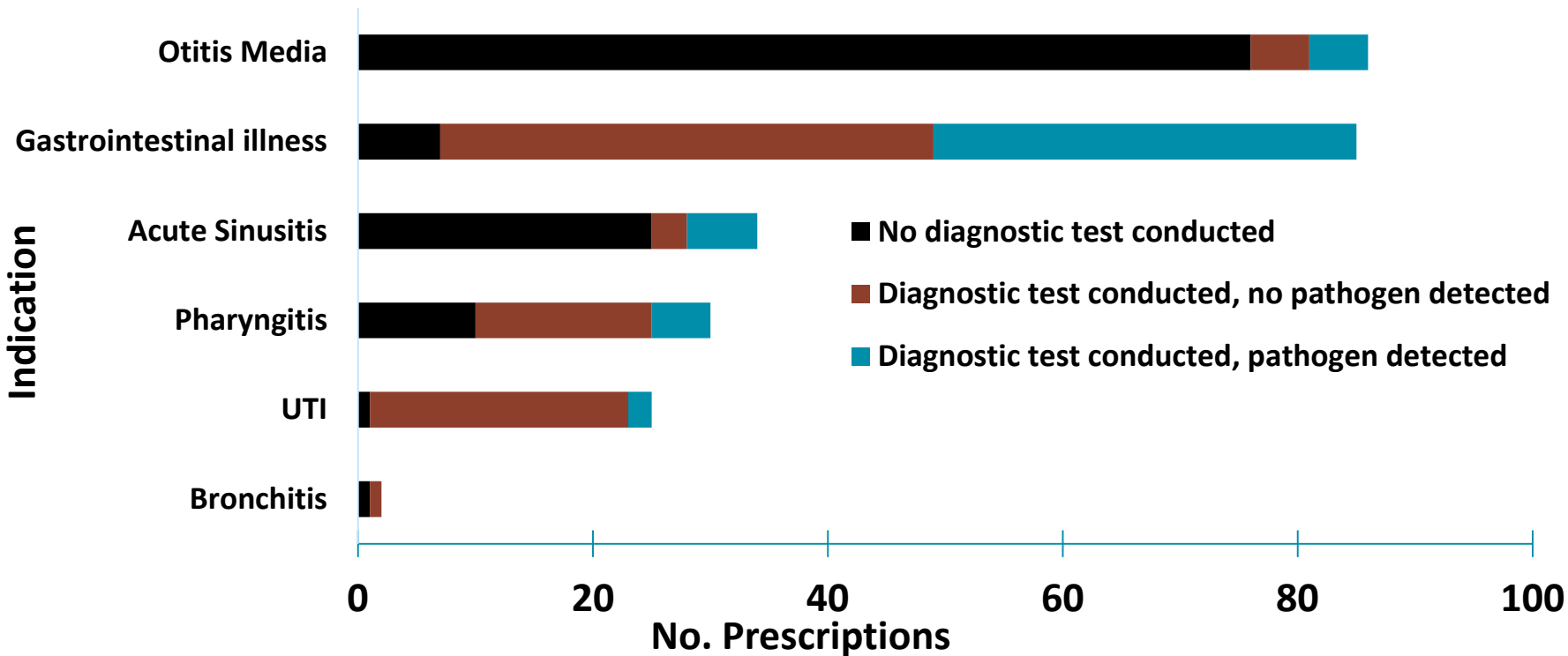
- Antibiotics were prescribed most frequently for:
 - Otitis media (22%)
 - URIs (21%)
 - Gastrointestinal infection (12%)



Antibiotics Prescribed to Pediatric CDI Cases in the 12 Weeks Prior to CDI Diagnosis



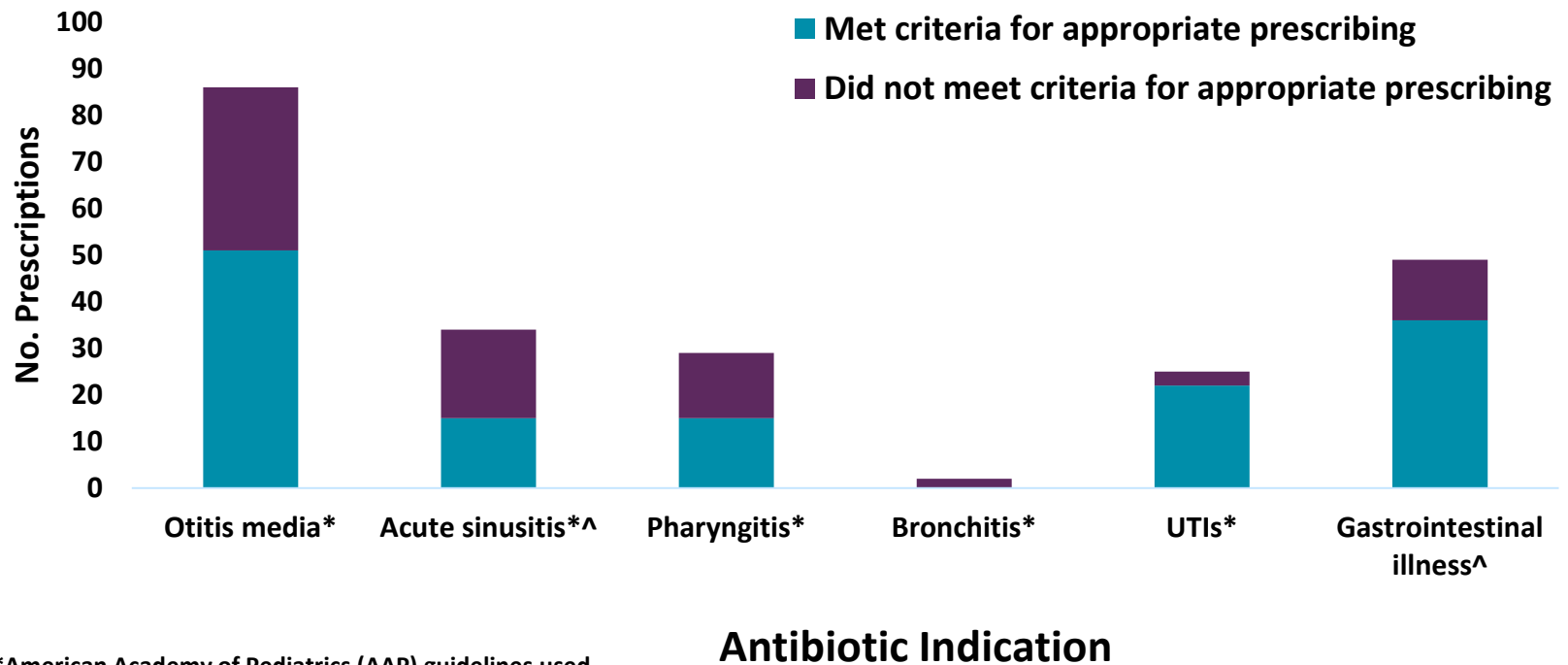
Diagnostic Tests Conducted at Time of Antibiotic Prescription



Impact of Diagnostics

- **For antibiotics that were prescribed prior to testing results being available, once test results were received:**
 - 11% were changed
 - 27% were discontinued
 - 59% were continued

Appropriateness of Antibiotics Prescribed to Pediatric CDI Cases



*American Academy of Pediatrics (AAP) guidelines used

^Infectious Disease Society of America (IDSA) guidelines used

Conclusions

- **Outpatient clinics and EDs remain a major source of antibiotic prescriptions among pediatric CDI cases**
- **Diagnostic stewardship is important**
 - **Potentially narrow the antibiotic spectrum**
 - **Discontinue unnecessary antibiotics**
- **Enhanced prevention efforts focusing on URI antimicrobial stewardship in pediatric outpatient settings are needed to reduce pediatric CDI**

Tying it All Together

- **Antimicrobial stewardship is important in all healthcare settings and for all prescribers**
- **Even young, otherwise healthy patients can contract CDI**

- **Follow national guidelines for prescribing antibiotics**
- **When appropriate, conduct diagnostic tests to identify a pathogen**
 - **Let the results of diagnostic tests impact antibiotic prescribing**
- **Ask patients about antibiotics or conditions possibly not listed in their medical record**
 - **Dental visits and medications taken for dental reasons**

Practical Steps

- **When prescribing antibiotics, warn patients about adverse effects, like CDI**
 - Encourage them to reach out to you if symptoms develop
- **Consider using CDI rates as a measure of antimicrobial stewardship in your facility**
- **Benchmark antimicrobial use at your facility to identify areas for improvement**



Acknowledgements

MDH

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Thank you!