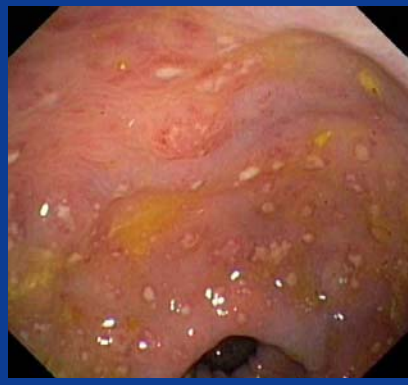
Update on *Clostridium difficile* Infection



Nothing to Disclose

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Division of Healthcare Quality Promotion

The findings and conclusions in this presentation are those of the author and do not necessarily represent the views of the Centers for Disease Control and Prevention

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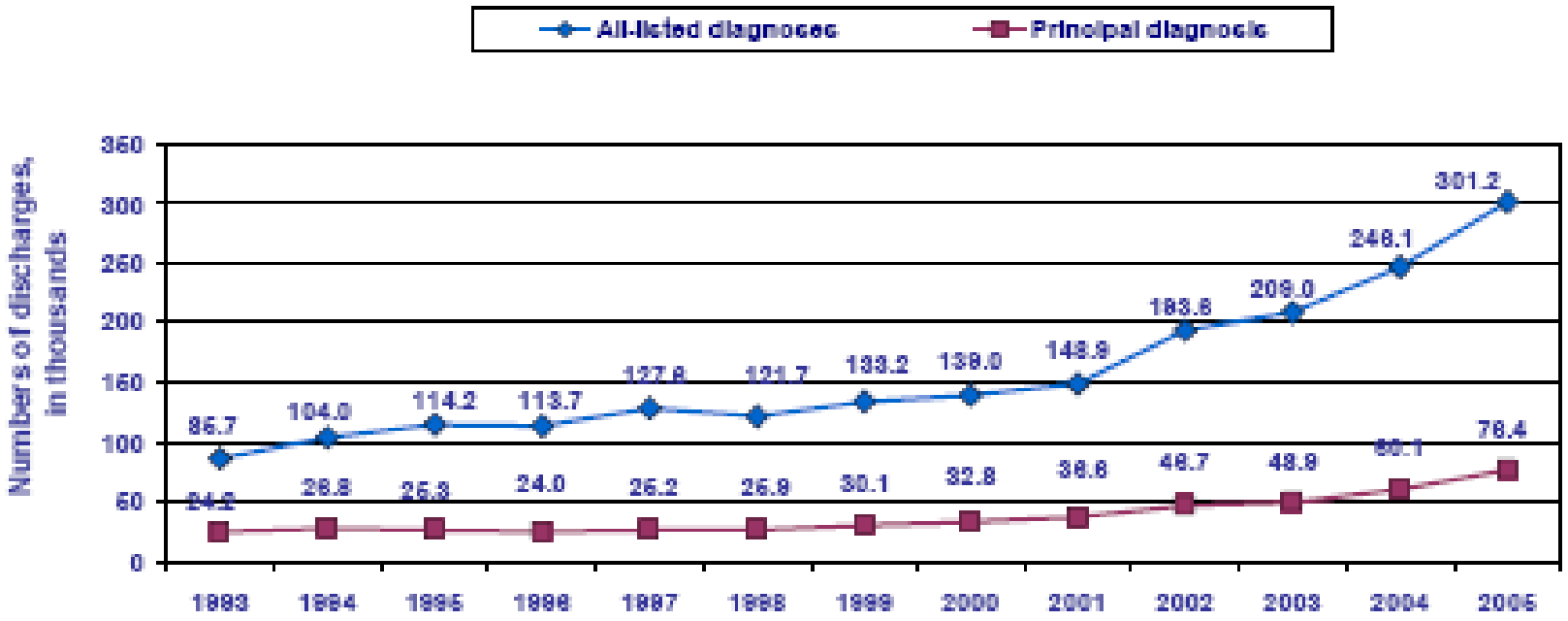
Figure 1. Trends in hospital stays associated with Clostridium difficile-associated disease, 1993-2005

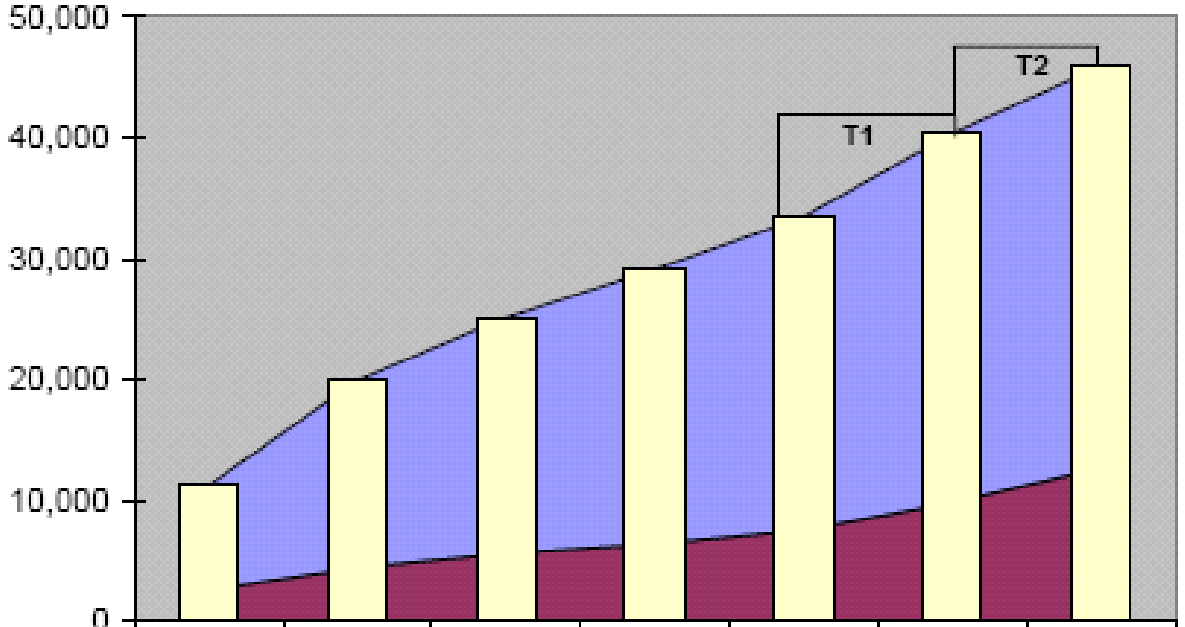


Source: AHRQ, Center for Delivery, Organization, and Markets, Healthcare Cost and Utilization Project, Nationwide Inpatient Sample

Evidence of Continued Increase in 2006
(Premier Inc. Data)

The incidence of CDAD increased from 6.9 to 7.3 cases per 1000 admissions from T1 to T2 (p<0.001).

Total CDAD Hospital Discharges 2000 - 2006



	2000	2001	2002	2003	2004	2005	2006
Secondary CDAD	8,652	15,539	19,527	22,732	25,950	30,576	33,225
Principal CDAD	2,613	4,419	5,630	6,407	7,544	9,829	12,727
All CDAD Discharges	11,265	19,958	25,157	29,139	33,494	40,405	45,952

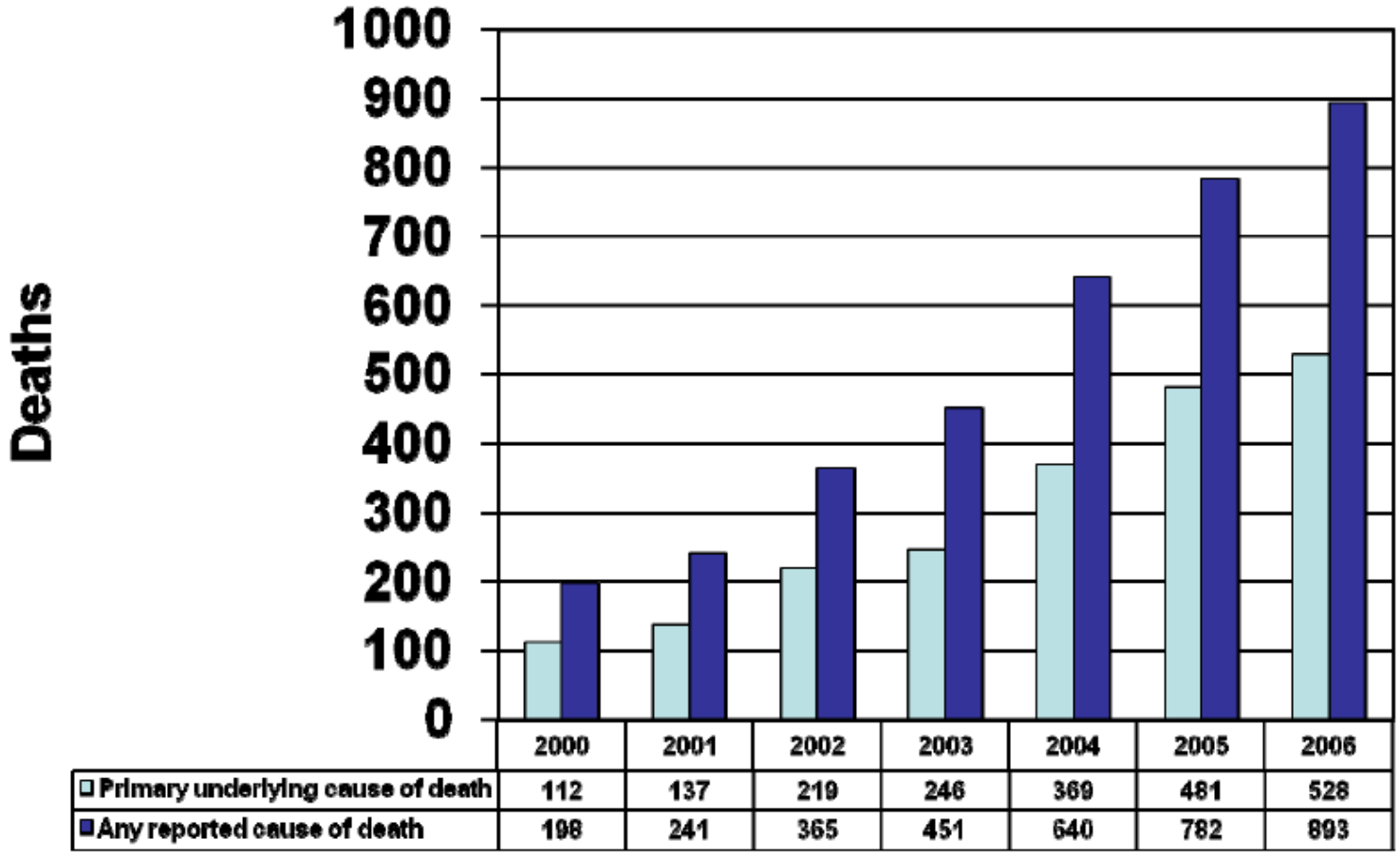
McDonald LC, et al. Presented at the 45th Annual Meeting of the Infectious Diseases Society of America (IDSA), October 4-7, 2007; San Diego, CA.

Public Reporting in Ohio, 2006
Relative importance of long-term care setting

- Approximately 14,100 cases
  - Hospital onset
    - ~5,000 initial cases; 7–8 per 10,000 patient-days
    - ~1,200 recurrent cases; 1–2 per 10,000 patient-days
  - Long-term care facility onset
    - ~4,800 initial cases; 2–3 per 10,000 patient-days
    - ~3,100 recurrent; 1–2 per 10,000 patient-days

Ohio Department of Health. http://www.odh.ohio.gov/alerts/cdiff1.aspx

Figure 3. Enterocolitis due to *C. difficile* Resident Deaths , Ohio, 2000-2006 (ICD-10 A04.7)



	2000	2001	2002	2003	2004	2005	2006
Primary underlying cause of death	112	137	219	246	369	481	528
Any reported cause of death	198	241	365	451	640	782	893

Source: Ohio Vital Statistics Certificates of Death, 2000-2006

Campbell et al. Unpublished data

Public Reporting in Ohio, 2006
Implications for U.S. Public Health

- Ohio
  - 18,200 cases after adjusting for missing data
    - 7,000 in hospitals
    - 11,200 in nursing homes
  - 893 deaths according to death certificates
- Extrapolated to the United States
  - 474,000 cases
    - 182,000 in hospitals
    - 292,000 in nursing homes
  - 23,000 deaths
- These remain underestimates of the total burden of CDI, both in Ohio and the United States

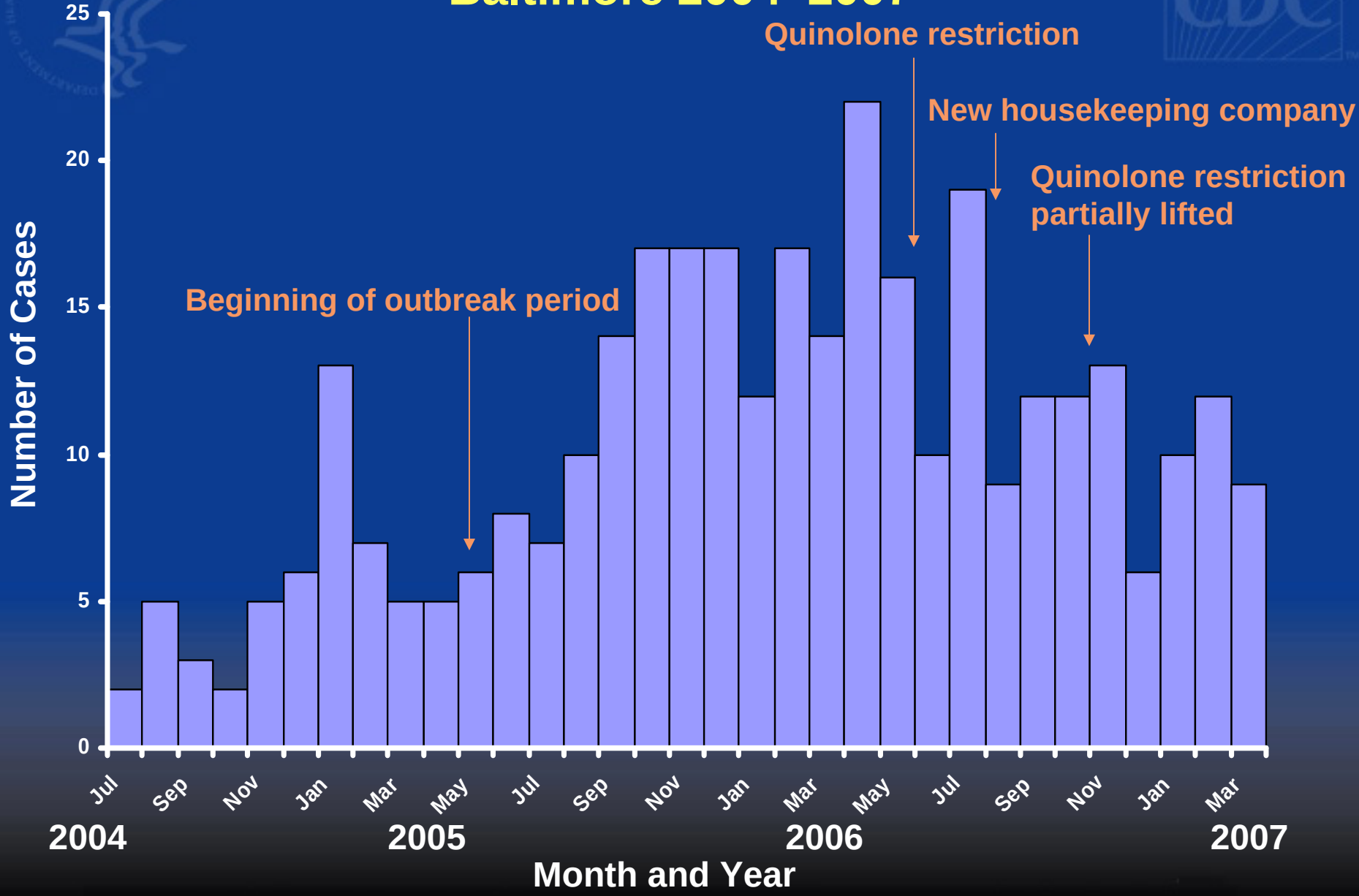
Campbell et al. Unpublished data

Outcomes of CDI in Setting of Endemic Disease

- Excess costs
  - $2,380 to $3,240 per index hospitalization
  - $3,797 to $7,179 inpatient costs over 180 days of follow-up
- Other outcomes
  - 2.8 days attributable excess length of stay
  - 19.3% attributable readmission (180 days)
  - 5.7% attributable mortality (180 days)
  - More likely discharged to long-term care

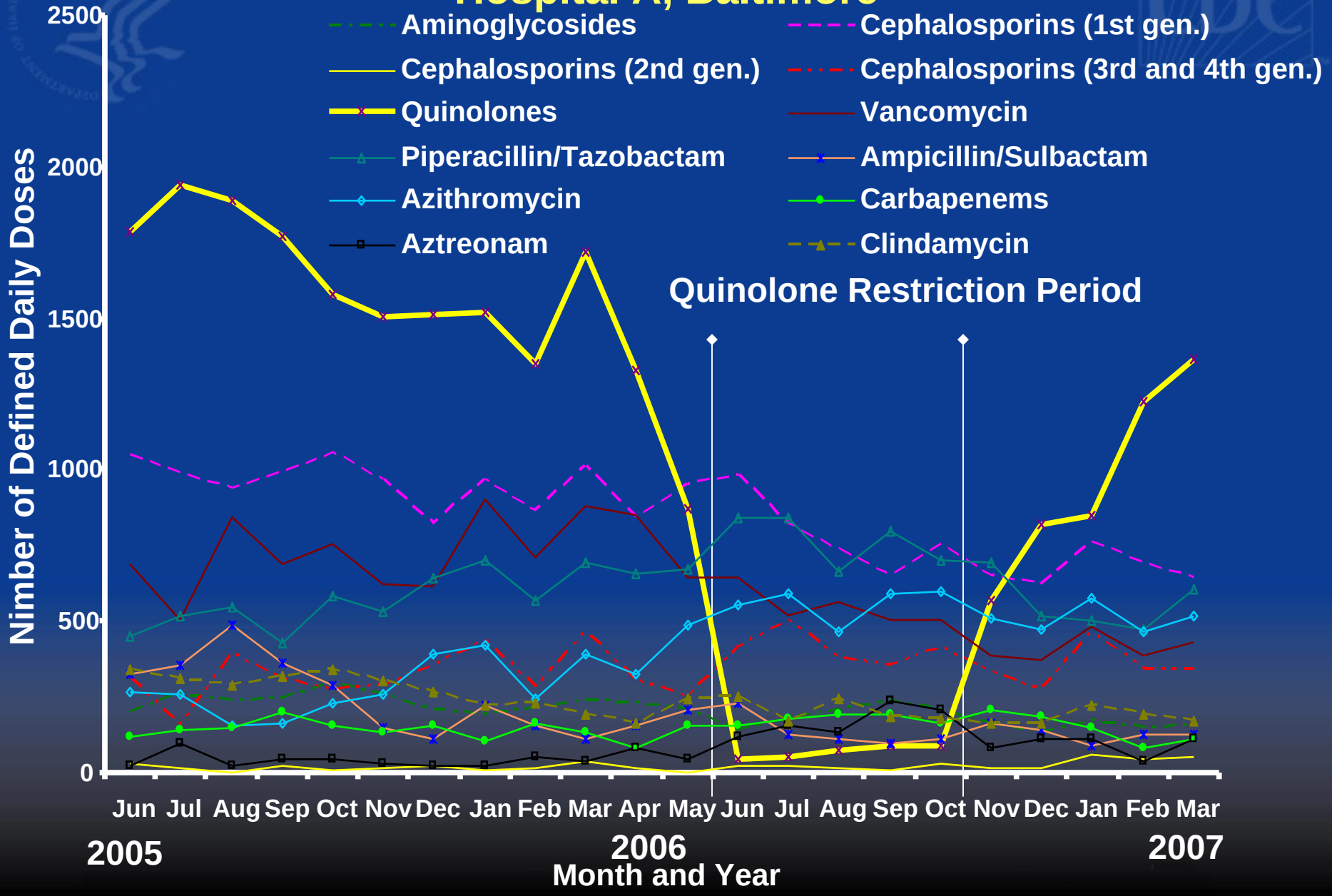
Dubberke ER, et al. *Clin Infect Dis.* 2008;46:497-504.
Dubberke ER, et al. 17th Annual Meeting of The Society for Healthcare Epidemiology of America (SHEA), April 14-17, 2007; Baltimore, MD.
Unpublished data.

Interventions to End an Outbreak, Hospital A, Baltimore 2004–2007



Kallen, et al. 18th Annual Meeting of The Society for Healthcare Epidemiology of America (SHEA), April 6, 2008; Orlando, FL.

Defined Daily Doses of Most Commonly Used Antibiotics, Hospital A, Baltimore



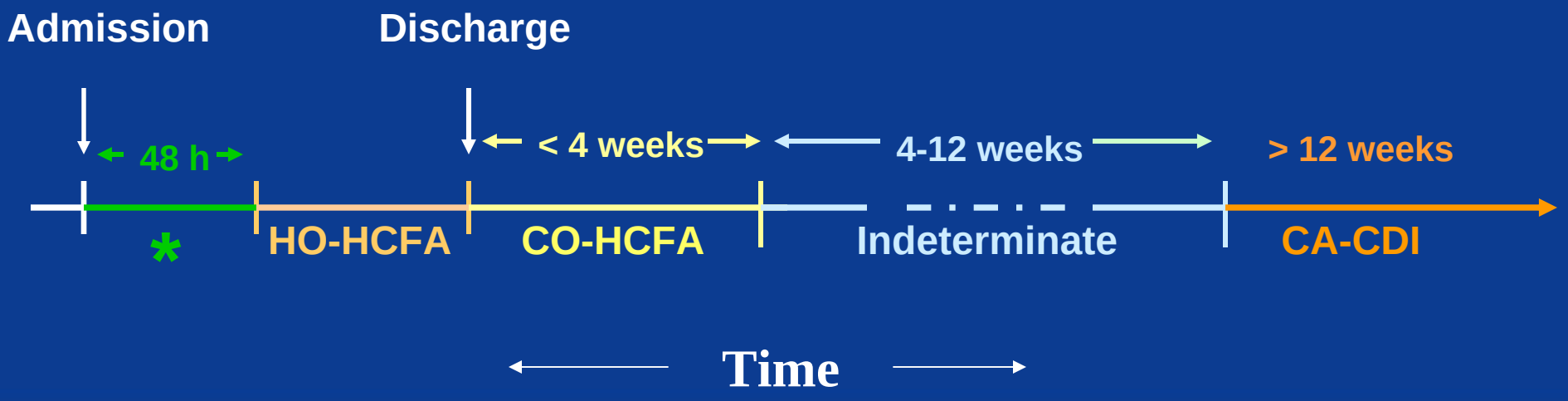
Kallen, et al. 18th Annual Meeting of The Society for Healthcare Epidemiology of America (SHEA), April 6, 2008; Orlando, FL.

Cases of Severe Pregnancy-Associated CDI

- 10 Cases*
  - Only three with prior hospitalization
  - One without antimicrobial exposure
  - Six prepartum, three of four postpartum cases within 1 week of delivery
  - Six required intensive care unit for toxic megacolon
    - Two with evidence of NAP1
  - Five required colectomy
  - Three maternal deaths, three fetal losses

Rouphael NG, et al. *Am J Obstet Gynecol.* 2008; in press.
*Data from Ghai S, Ghai V, Sunderj S. *Obstet Gynecol.* 2007;109(2 Pt2):541-543; and CDC. *Morbid Mortal Wkly Rep*. 2005;54:1201-1205.

Recommendations for Surveillance of *Clostridium difficile* Infection



HO: Hospital (Healthcare) onset
CO-HA: Community Onset Healthcare-associated
CA: Community Associated

* **Depending upon whether patient was discharged within previous 4 weeks, CO-HA vs. CA**

CDAD Surveillance Working Group. *Infect Control Hosp Epidemiol* 2007; 28:140-145

Clostridium difficile–associated Disease (CDAD) cases
N = 1046

Healthcare facility–onset Healthcare facility-associated (HO-HCFA)
N=584 (56%)
(Including 142 with onset in another HCF)

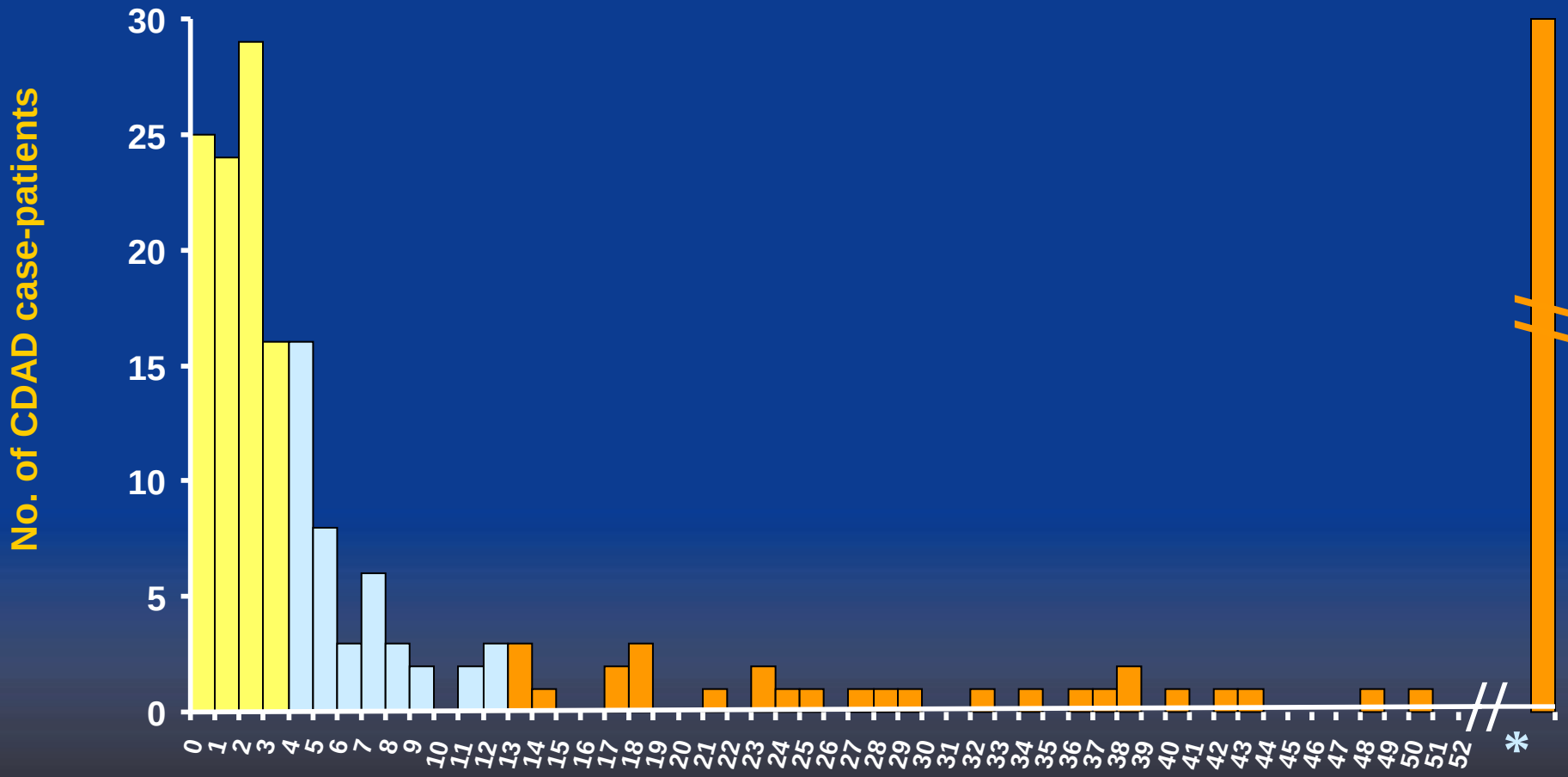
Community Onset
N= 462 (44%)

- **Community Onset Healthcare facility-associated (CO-HCFA)** — **94 (9%)**
- **Indeterminate** — **40 (4%)**
- **Community Associated (CA)** — **208 (20%)**
- **Unknown** — **46 (4%)**
- **Excluded**** — **74 (7%)**

**Excluded:
Prisoner: 8 Out of State:20 Bone Marrow Transplant: 17 Hemodialysis:29

Adapted from Kutty PK, et al. *Infect Control Hosp Epidemiol.* 2008;29:197-202.

Community Onset CDI Relative to Previous Discharge, North Carolina, 2005 (N=348)



* 184 (48%) had a time lapse of more than one year

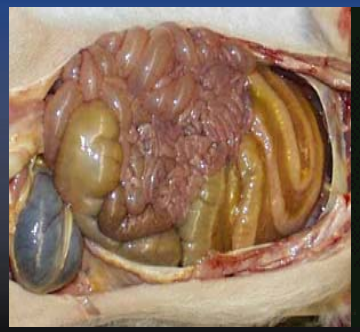
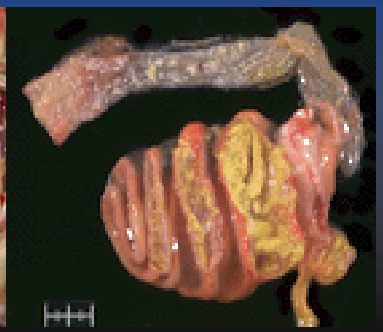
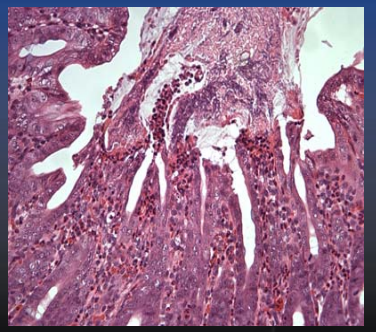
Adapted from Kutty PK, et al. *Infect Control Hosp Epidemiol.* 2008;29:197-202.

Surveillance for Community-Associated *Clostridium difficile* — Connecticut, 2006

Characteristic	No.	(%)
Clinical features		
Abdominal pain (n = 222)	169	(76)
Vomiting (n = 221)	50	(23)
Diarrhea† (n = 236)	227	(96)
Bloody diarrhea (n = 209)	48	(23)
Fever§ (n = 203)	56	(28)
Predisposing risk factors		
Previous health-care exposure (n = 214)	63	(29)
Overnight hospitalization or long-term–care facility stay during preceding >3 to 12 months (n = 222)	34	(15)
Day surgery during preceding 12 months (n = 217)	36	(17)
Underlying medical condition (comorbid condition) (n = 220)	147	(67)
Any antibiotic use during 3 months preceding symptom onset (n = 227)	154	(68)
Clindamycin (n = 121)	19¶	(16)
Fluoroquinolones (n = 121)	42¶	(35)
Other** (n = 121)	54¶	(45)

CDI in Piglets

- < 7 days of age, “scouring from birth”
  - pasty, yellow colonic contents; constipation; obstipation
- Mesocolonic edema; suppurative foci in colonic lamina propria; volcano lesions
- Apparent increase or emergence around the year 2000
- Little evidence to support link to antimicrobial use

Slide courtesy of J. Glenn Songer

Epidemic Animal Strains Share Characteristics with the Human Epidemic Strain

Characteristic	Human Standard Strains	Human Epidemic Strain	Porcine Epidemic Strains	Bovine Strains
Toxinotype	0	III	V	V
PCR ribotype	001 and others	027	078	078
PFGE pattern	<80% related to NAP1	NAP1	NAP7 & NAP8	NAP7
Binary toxin	–	+	+	+
Deletion in *tcdC*	–	18 bp	39 bp	39 bp
TcdC protein	233 aa	65 aa	61 aa	61 aa

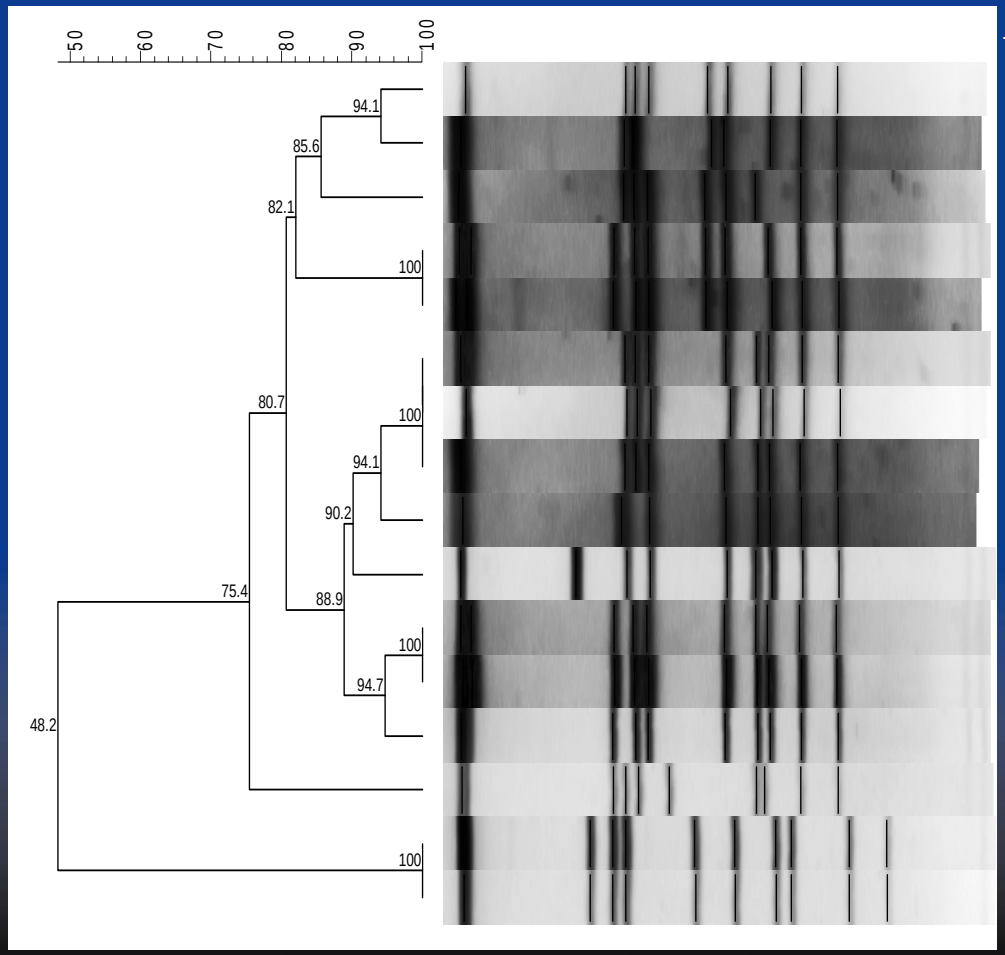
Keel K, et al. *J Clin Microbiol.* 2007;45:1963-1964.

ToxV (BK/NAP7-8/078) Strains; Historically Rare, Recently More Common

Time	Tox V Isolates
Prior to 2001	10/6000
2001-2005	10/600
2006	6/125

Jhung MA, et al. Second International *Clostridium difficile* Symposium, June 6-9, 2007; Maribor, Slovenia.

Human CDAD Caused by Strains Similar to Animal Epidemic Strains, 2001–2006



Source	Toxino type	Binary toxin	*tcdC* deletion
Human	V	+	39 bp
Human	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Human	V	+	39 bp
Hosp Env	V	+	39 bp
Human	V	+	39 bp
Human	V	+	39 bp
Human	V	+	39 bp
Human	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp
Pig	V	+	39 bp

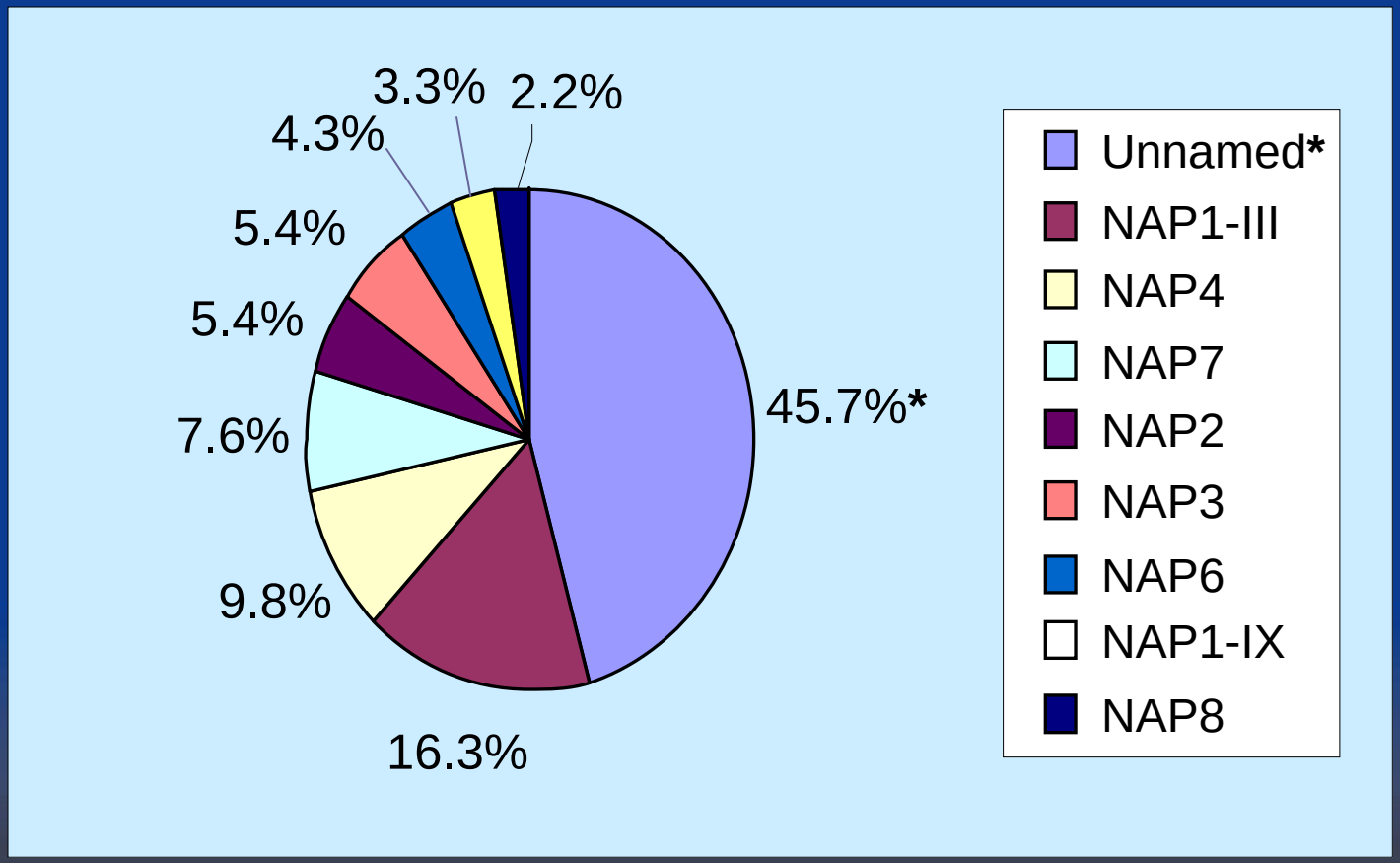
Jhung MA, et al. Second International *Clostridium difficile* Symposium, June 6-9, 2007; Maribor, Slovenia.

Enhanced Surveillance for Strains Causing CDI in Community

- 10 FoodNet sites across the United States, collected over a 3-month period
- *C. difficile* cultured from stool of patients who met community-associated criteria (CA-CDI)
  - *C. difficile* toxin–positive stool specimen collected as an outpatient or within 72 hours of admission
  - No hospitalization in the preceding 3 months
- 92 isolates from nine states submitted to CDC for ID and typing

Limbago BM, et al. Second International *Clostridium difficile* Symposium, June 6-9, 2007; Maribor, Slovenia.

Recognized PFGE Patterns Among CA-CDI Isolates, *N*=92

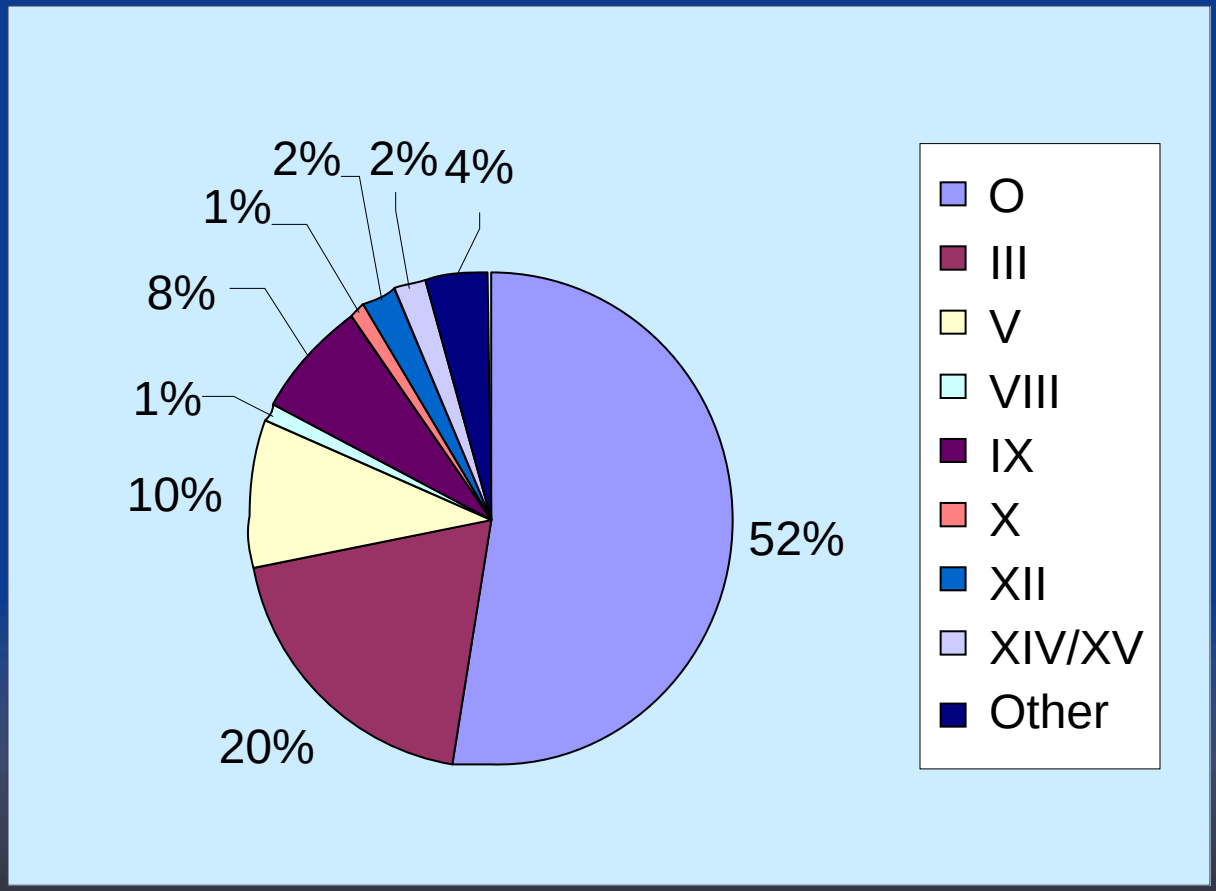


* Unnamed group is composed of 24 unique patterns

PFGE=pulsed field gel electrophoresis.

Limbago BM, et al. Second International *Clostridium difficile* Symposium, June 6-9, 2007; Maribor, Slovenia.

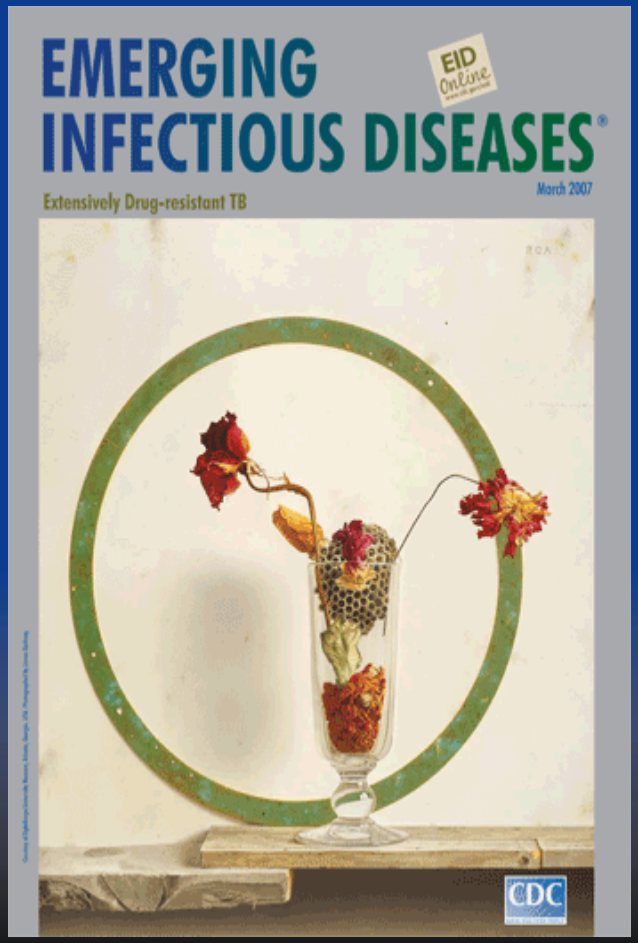
Toxinotypes Represented Among CA-CDI Isolates, *N*=92



Limbago BM, et al. Second International *Clostridium difficile* Symposium, June 6-9, 2007; Maribor, Slovenia.

Clostridium difficile in Retail Ground Meat, Canada

A. Rodriguez-Palacios, H. R. Stämpfli, T. Duffield, and J.S. Weese



March 2007

Summary

- Rates, mortality, and costs associated with CDI continue to increase
- Much of this increase may be due to emergence and spread of BI/NAP1/027
- Disease becoming more notable in previously low-risk populations
- Community-associated disease appears associated with variant toxinotypes
- Ecologic evidence for animal-to-human transmission of toxinotype V strains