The epidemiology of *Clostridium difficile* infection (CDI) in hospitals, longterm care and the community

J Scott Weese DVM DVSc DipACVIM

CPHAZ
Centre for Public Health and Zoonoses

CANADA RESEARCH CHAIRS CHAIRES DE RECHERCHE DU CANADA

UNIVERSITY of GUELPH
CHANGING LIVES IMPROVING LIFE

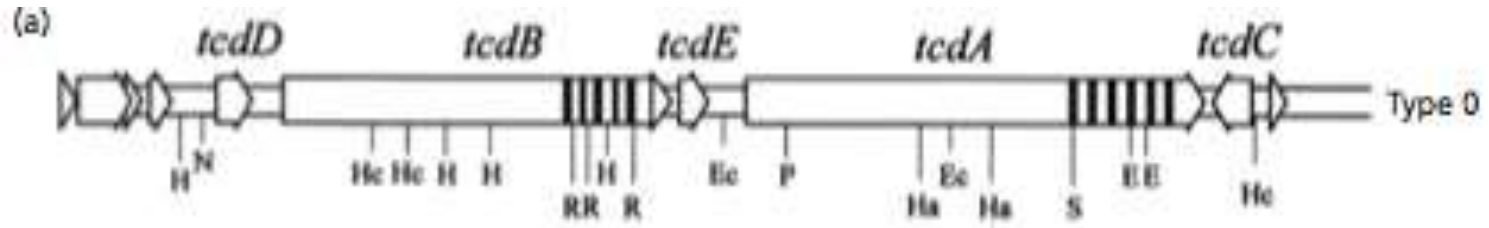
C. difficile

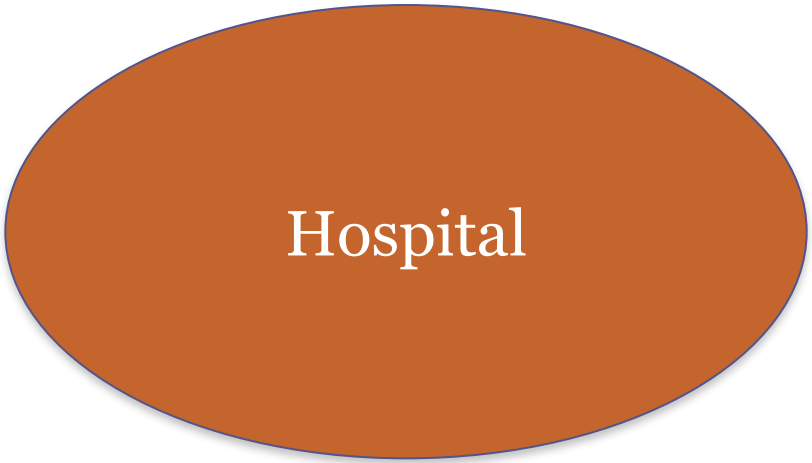
- Gram positive anaerobic sporeforming bacterium first isolated in early 1900's
- Cause of enteric disease in humans and various animal species
- Most commonly diagnosed cause of antimicrobial- and hospital-associated diarrhea in humans

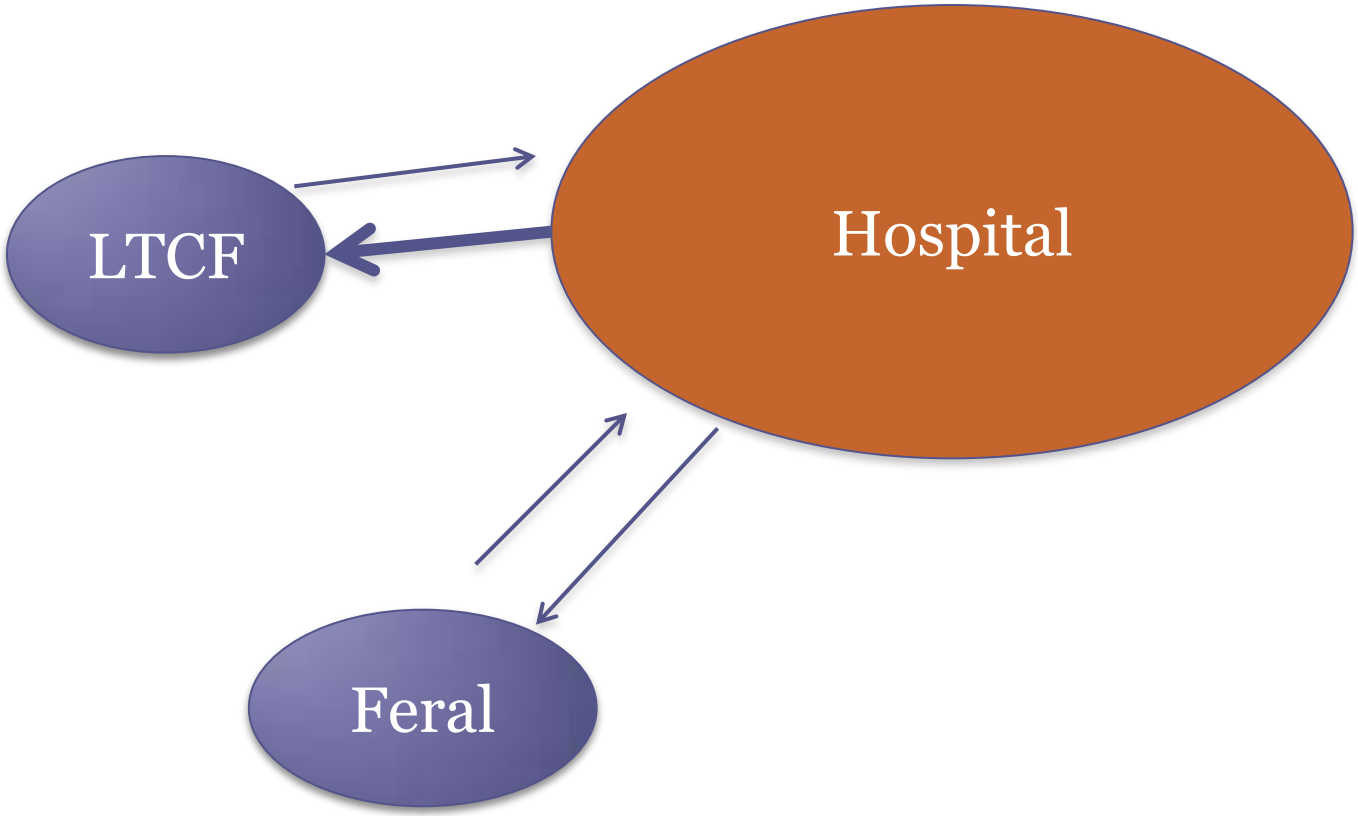
http://jb.asm.org/content/vol191/issue17/cover.dtl

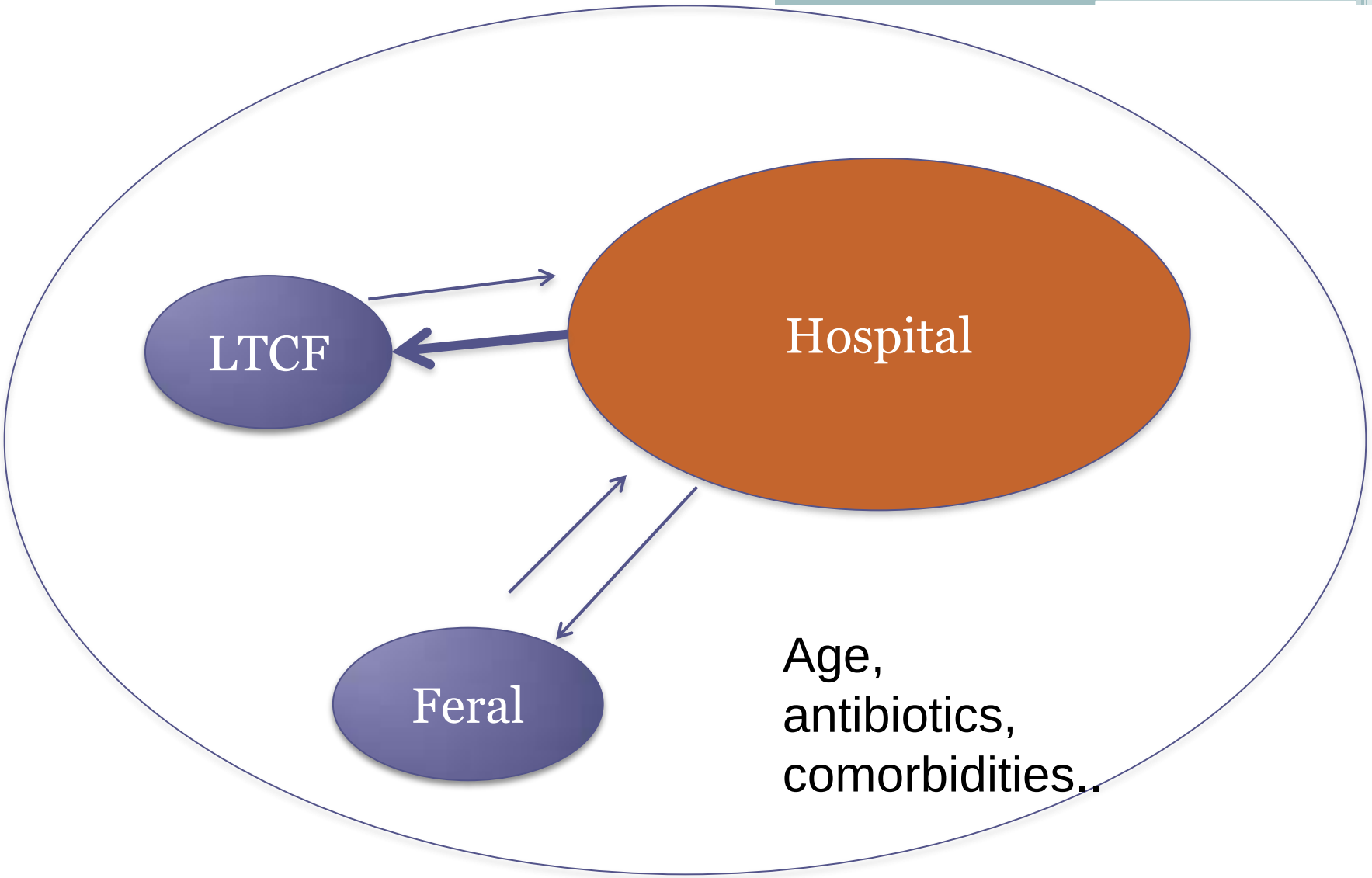
Relevant basics

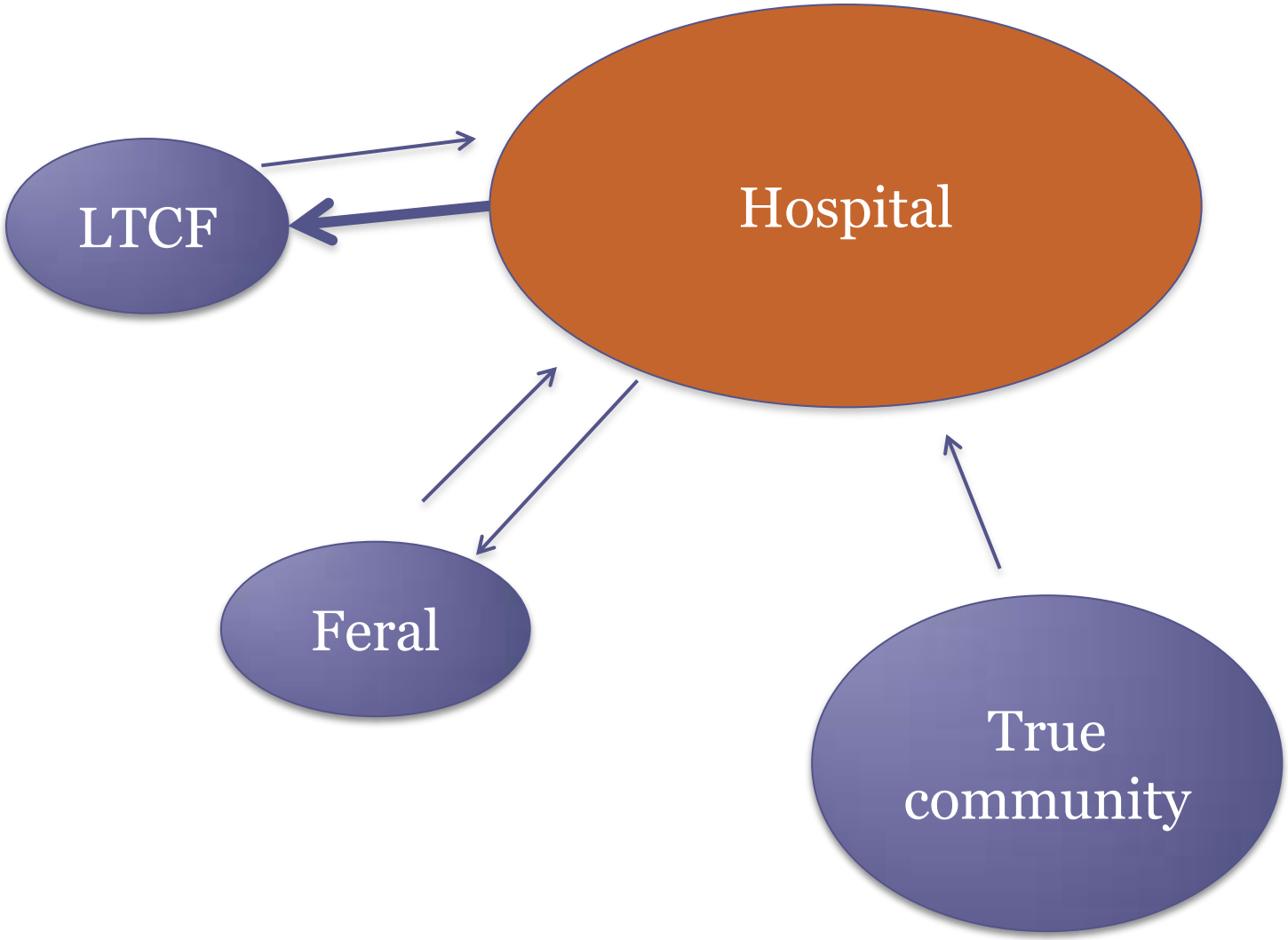
- Three main recognized toxins
  - Toxin A
  - Toxin B
  - CDT (Binary toxin)
    - Varying combinations
  - Likely other toxins

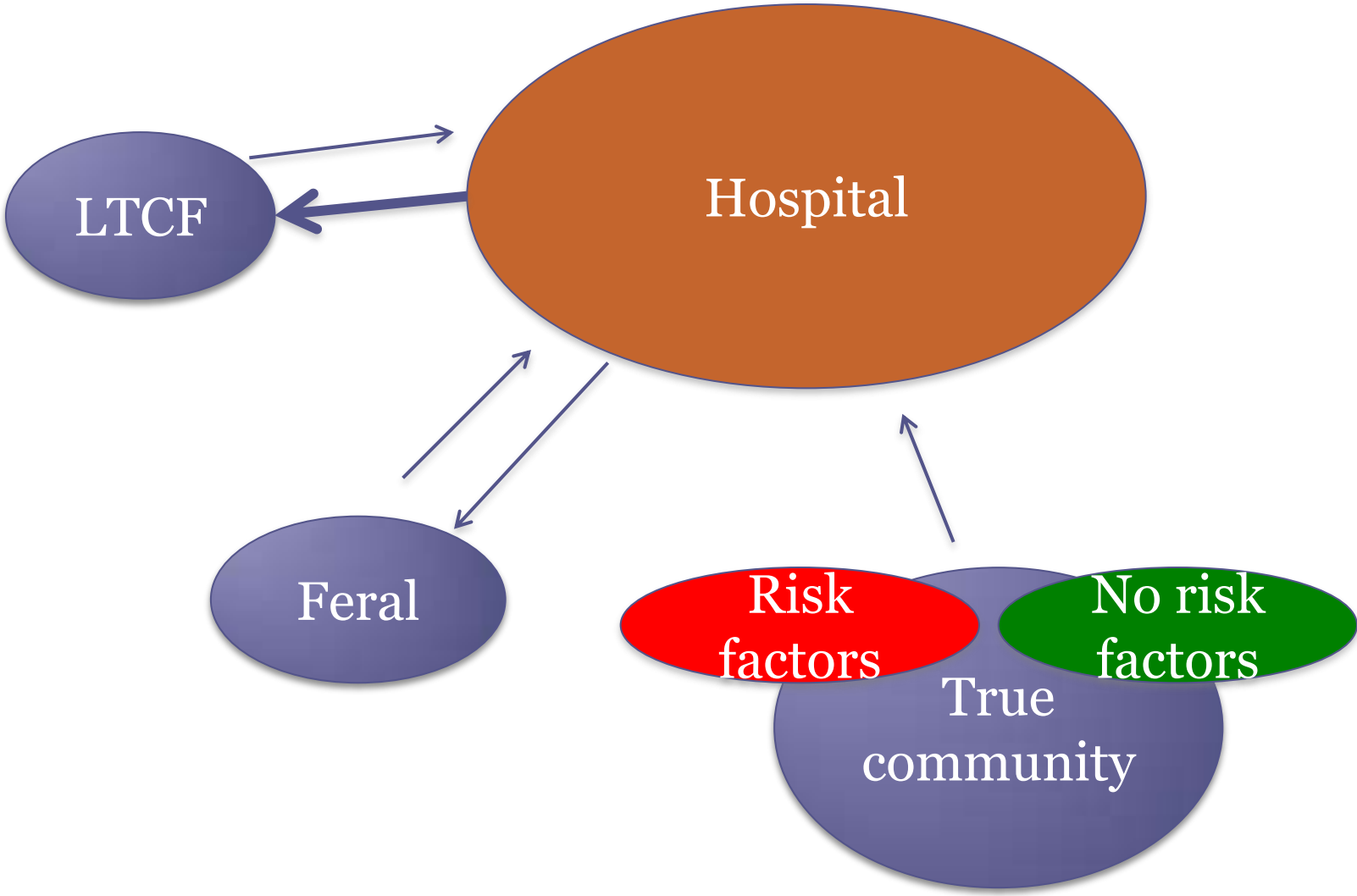



Hospital


LTCF
Hospital
Feral


LTCF
Hospital
Feral
Age,
antibiotics,
comorbidities..


LTCF
Hospital
Feral
True community


LTCF
Hospital
Feral
Risk factors
No risk factors
True community

“Classical CDI”

- >65 y of age
- In hospital or longterm care facility
- Antibiotic exposure
  - +/-Chemotherapeutics, stool softeners…
- Comorbidities

- Overall low severe disease (i.e. ICU stay, colectomy) and mortality rates

Changing Epidemiology

- Increased incidence
  - Lower risk individuals
  - Younger individuals
- Increased severe outcomes
- Increased mortality rates
- Increased relapse rate

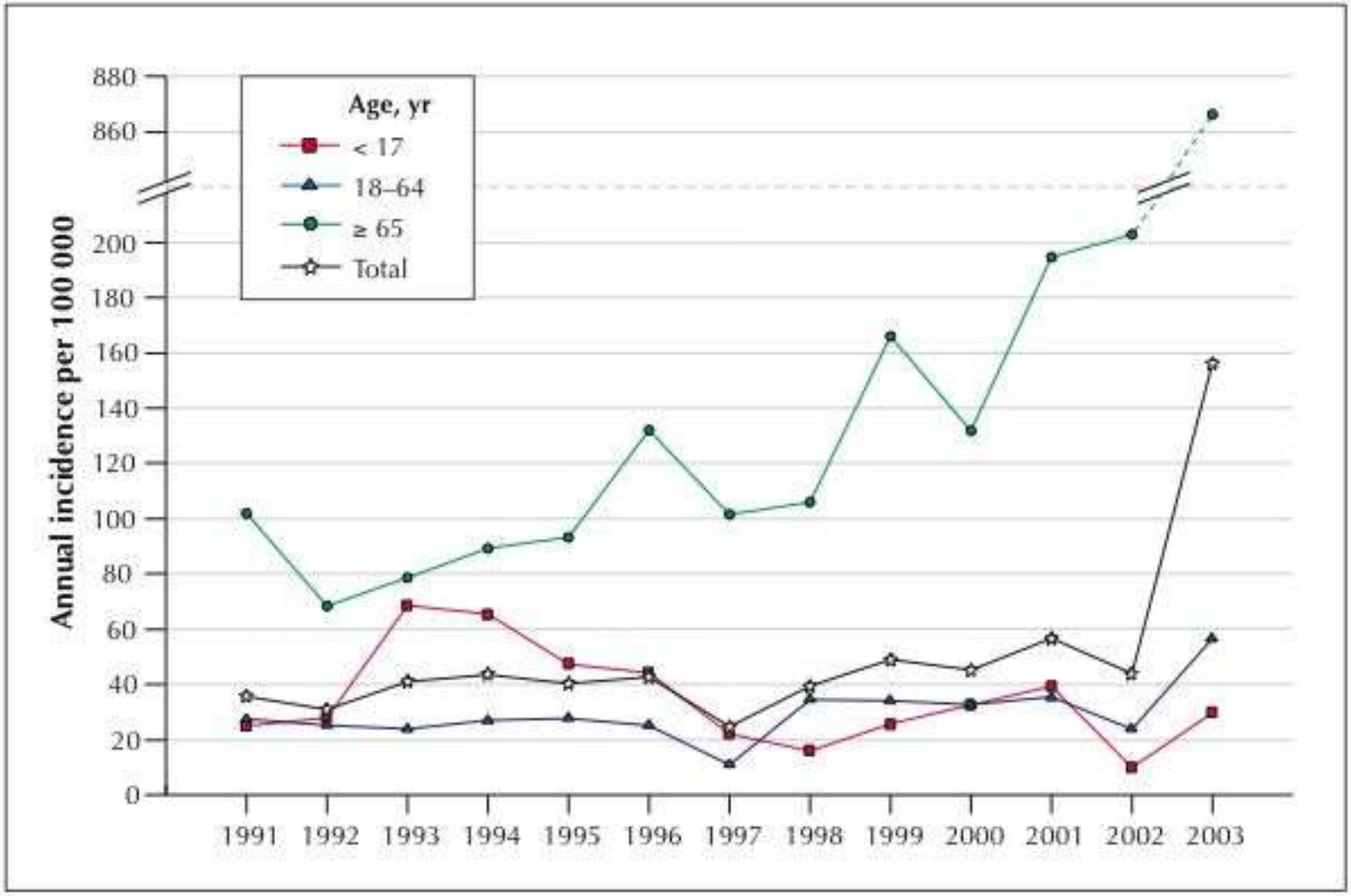


Fig. 1: Annual incidence (per 100 000 population) of *Clostridium difficile*-associated diarrhea (CDAD) in Sherbrooke, Que., 1991–2003.

Pepin et al, CMAJ, 2004.

Clostridium difficile Infections among Hospitalized Children, United States, 1997–2006

Marya D. Zilberberg, Glenn S. Tillotson, and L. Clifford McDonald

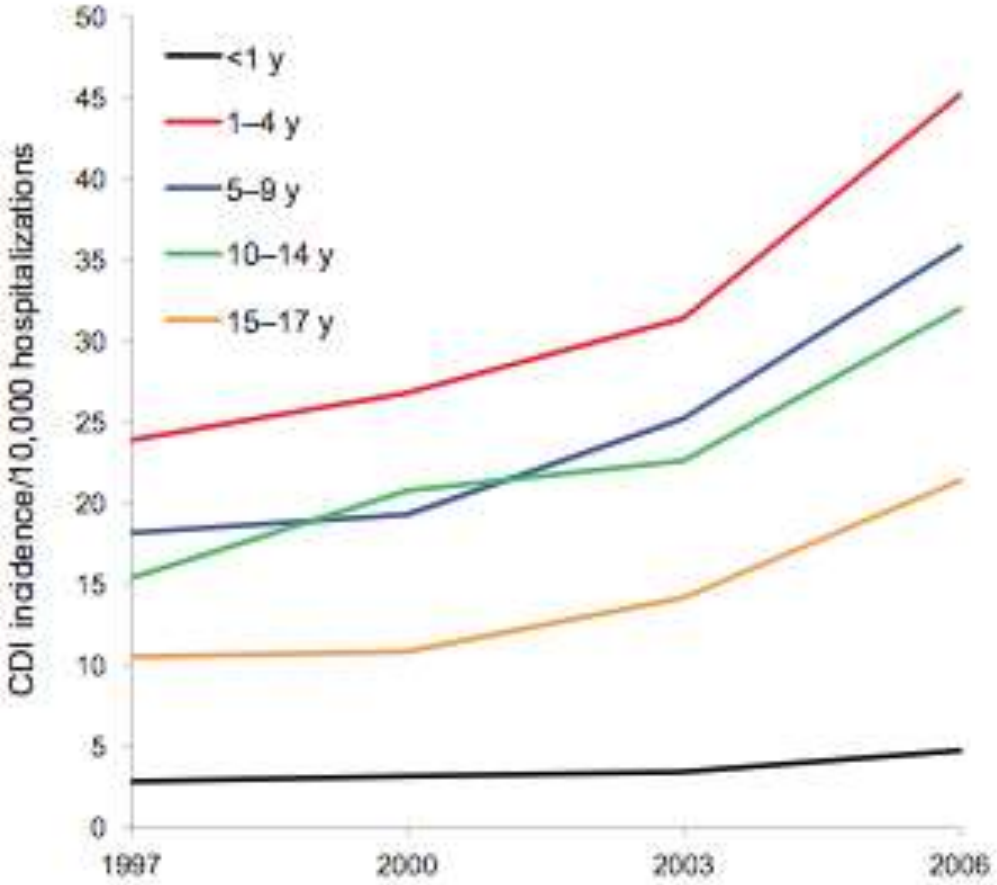


Figure 1. Age-specific incidence of patients with *Clostridium difficile* infection (CDI) per 10,000 hospitalizations, Health Care Utilization Project Kids' and Inpatient Database, United States, 1997–2006.

C. difficile outbreak declared over at Niagara hospital

Death toll from C. diff climbs to 33

By Standard Staff, St. Catharines Standard, Niagara Region, Sun Media

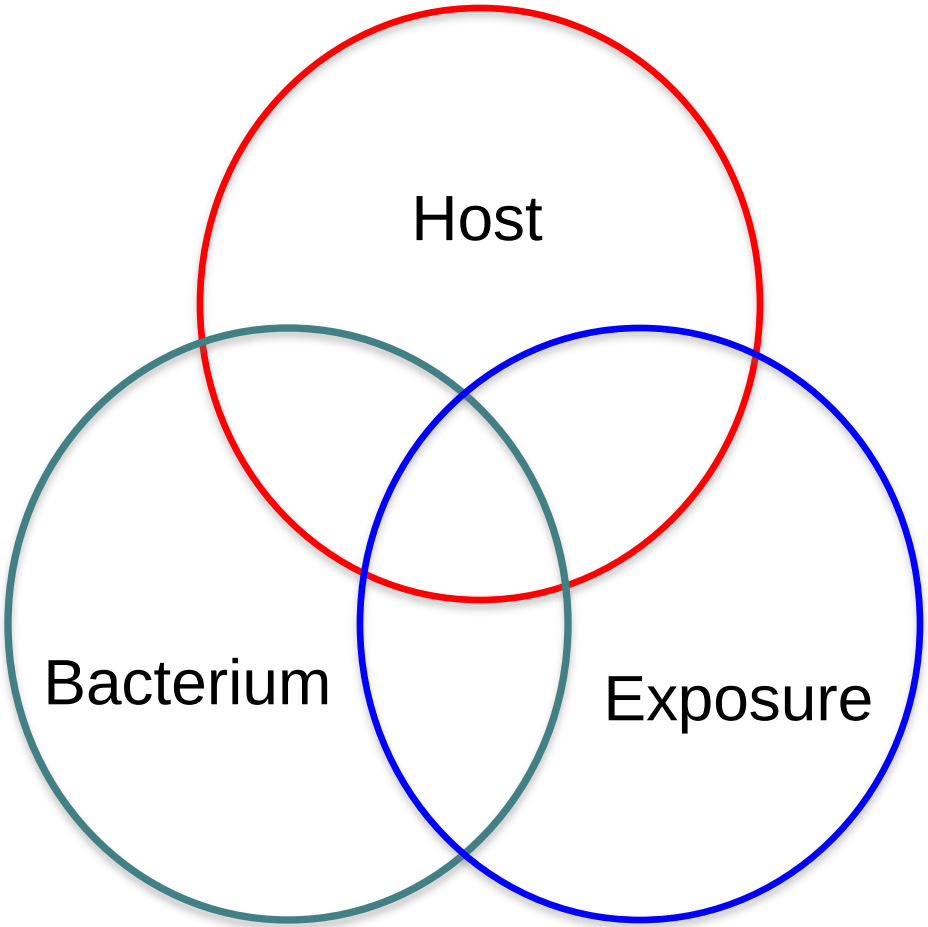
Posted 9 days ago

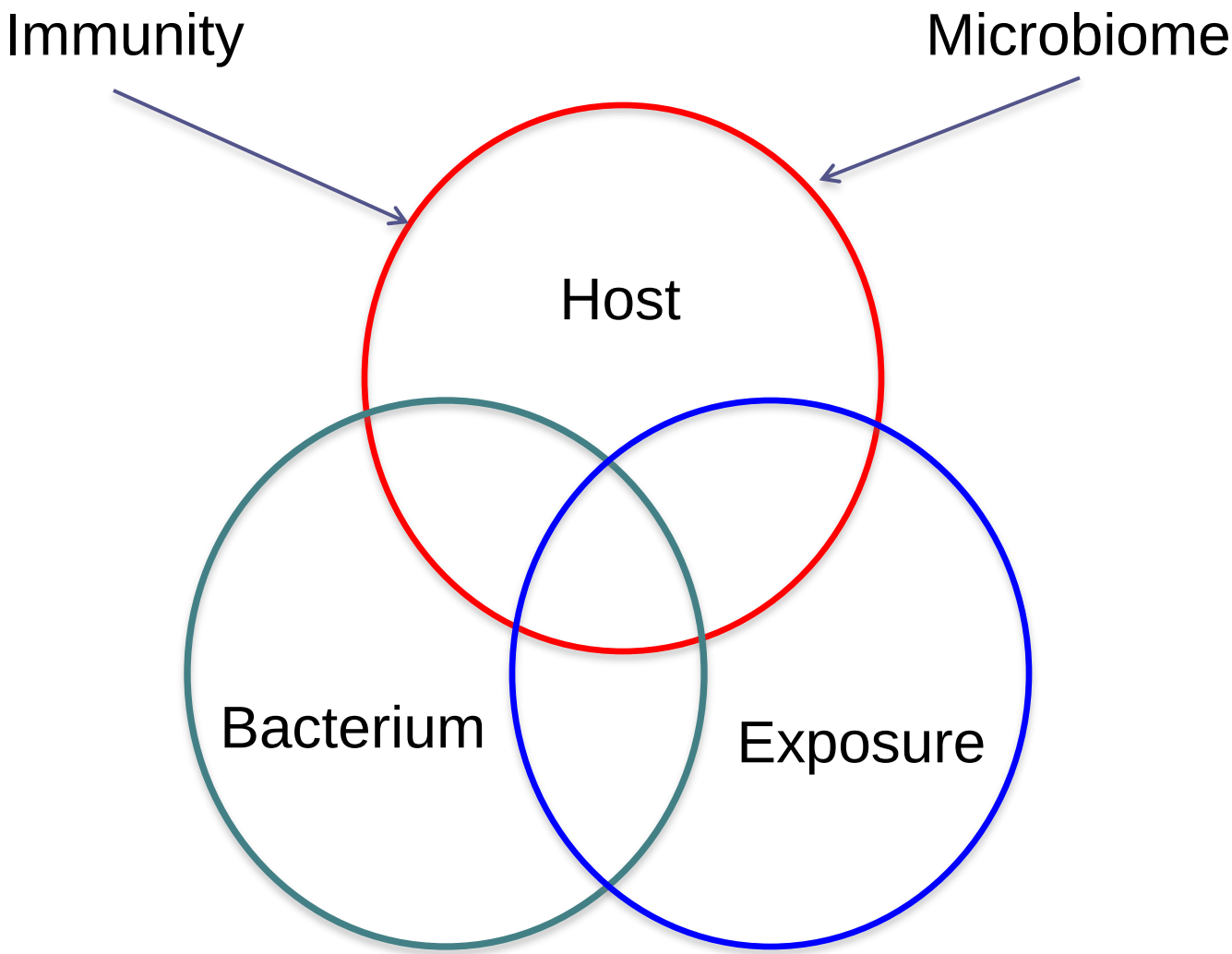
Another Clostridium difficile patient at the St. Catharines General Hospital has died, bringing the death toll from hospital-acquired infections to 33 since the outbreak began May 28.

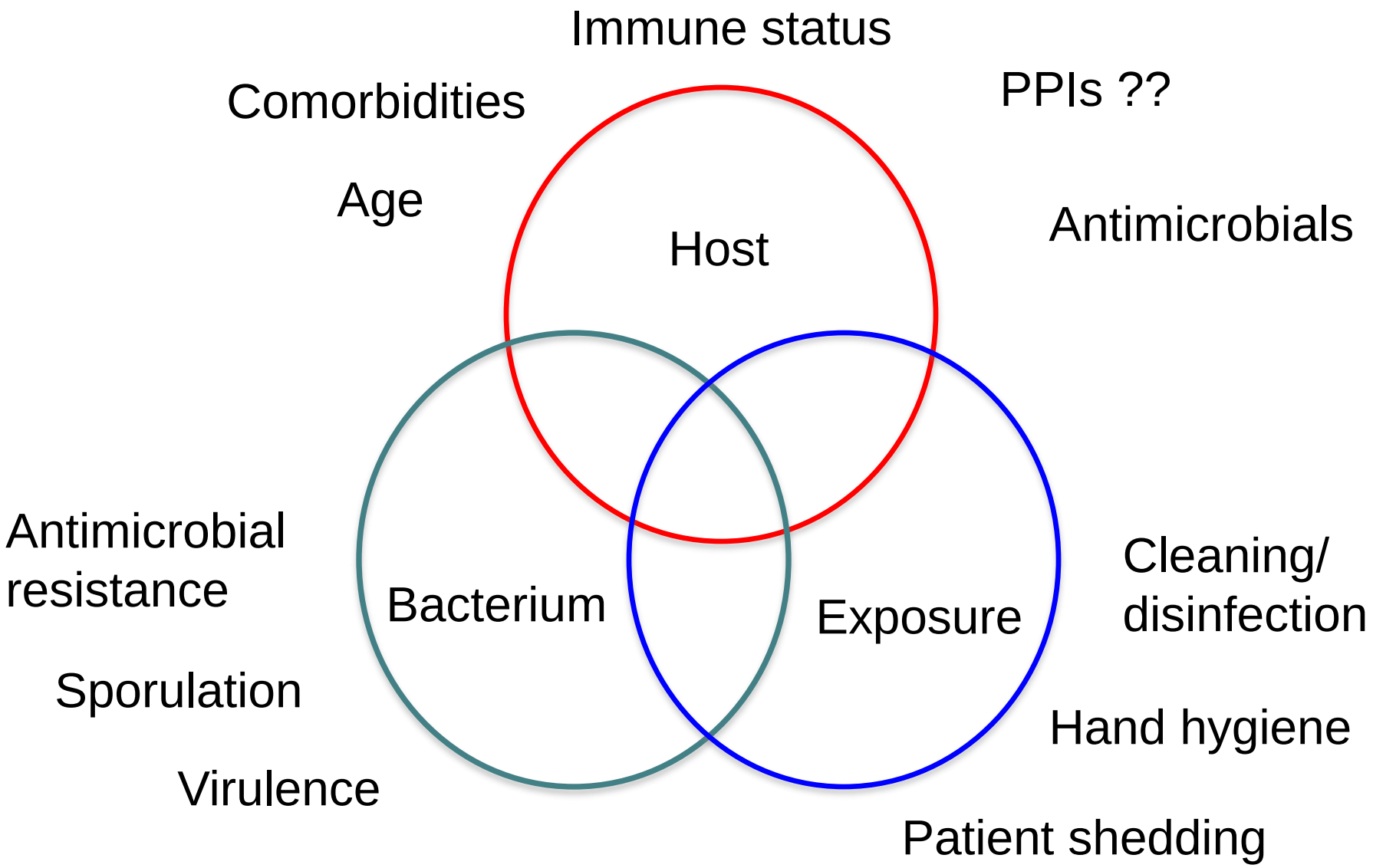
Niagara Health System interim chief of staff Dr. Joanna Hope said the death of the patient — who had several other serious medical problems — is disheartening.

A crowd gathered at a rally in front of the Greater Niagara General Hospital in Niagara Falls, on July 6 2011. (Mike DiBattista, QMI Agency)

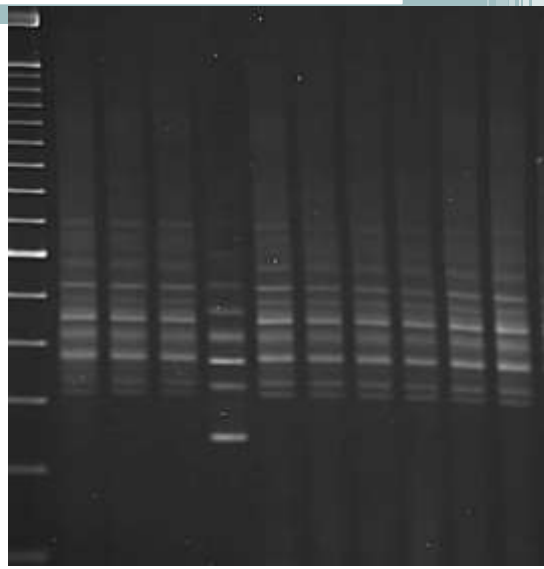
Why??



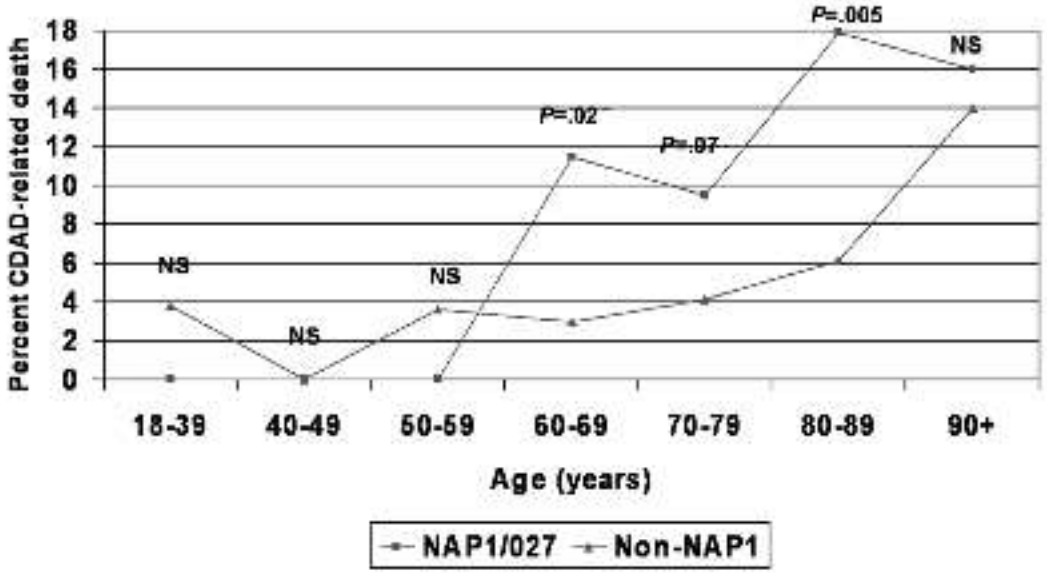

Immunity
Microbiome
Host
Bacterium
Exposure

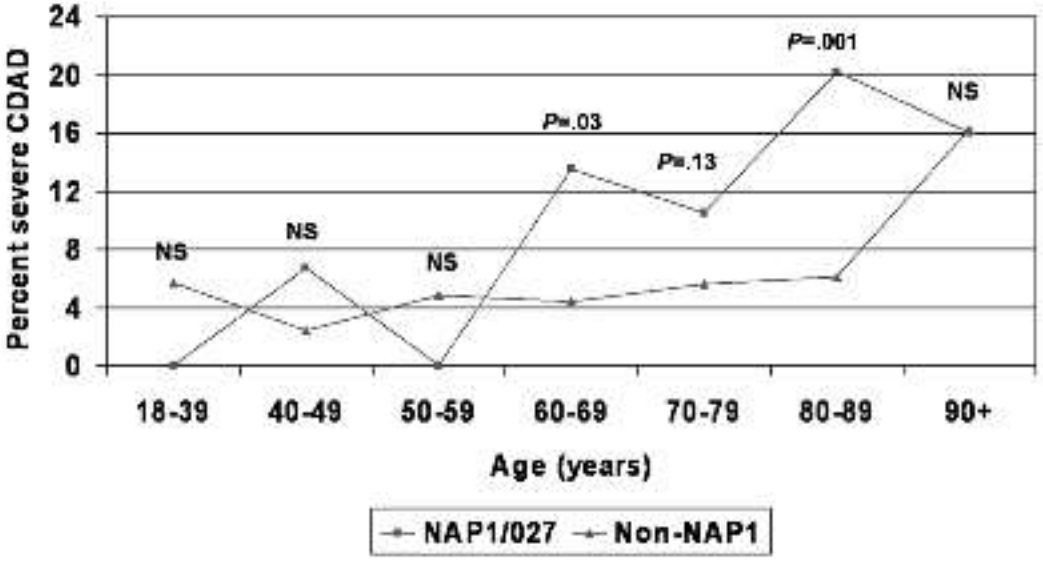

Immune status
Comorbidities
PPIs ??
Age
Antimicrobials
Host
Antimicrobial resistance
Bacterium
Exposure
Cleaning/ disinfection
Sporulation
Hand hygiene
Virulence
Patient shedding

‘Hypervirulent’ (HV) CDI



- **Ribotype 027/toxinotype III**/NAP1
- Ribotype 078/toxintype V/NAP7/8





Miller et al 2011

- Don’t ask if you have ribotype 027/NAP1 in your hospital/LTCF….you do

Characterization of *Clostridium difficile* Strains Isolated from Patients in Ontario, Canada, from 2004 to 2006[▽]

H. Martin,[1] B. Willey,[2] D. E. Low,[2,3] H. R. Staempfli,[1] A. McGeer,[2] P. Boerlin,[4] M. Mulvey,[4] and J. S. Weese[4]*

TABLE 1. Genotypic characteristics of the 21 most common *Clostridium difficile* ribotypes from hospitalized humans in Ontario

Ribotype[a]	Presence of[b]:			*tcdC* deletion size (bp)	*tcdC* alteration type	PFGE type[c]	Toxinotype	No. of regions with ribotype[d]	No. (%) of isolates
	Toxin A	Toxin B	CDT						
W	+	+	−			NAP2	0	7	275 (25.5)
027	+	+	+	18	Δ117	NAP1	III	7	209 (19.4)
N	+	+	+	18	Δ117	NAP1	III	5	71 (6.6)
L	+	+	−			0042	0	6	63 (5.8)
017	−	+	−			0117	VIII	5	58 (5.4)
A	+	+	+			0012	IX	7	37 (3.4)
Y	+	+	+	18	Δ117	0098	III	5	36 (3.3)
S	+	+	−			0076	0	5	28 (2.6)
AD	+	+	+	18	Δ117	NAP1	III	6	27 (2.5)
C**	+	+	−			NAP2	0	6	16 (1.5)
C**	+	+	+			0012	IX	3	10 (0.9)
AK	+	+	−			NAP6	0	7	25 (2.3)
D	+	+	−			NAP2	0	5	21 (1.9)
F	+	+	−			0066	0	6	18 (1.7)
078	+	+	+	39	C184T	NAP8	V	5	17 (1.6)
G	+	+	−			NAP2	0	5	16 (1.5)
V	+	+	−			NAP4	0	5	16 (1.5)
AC	+	+	−			NAP2	0	4	15 (1.4)
H	+	+	−			0077	XII	1	10 (0.9)
R	+	+	−			0046	0	4	10 (0.9)
U	+	+	−			00162	0	4	10 (0.9)
AB	+	+	+			0047	IX	2	10 (0.9)

- Presence of a hypervirulent strain does not mean you have or will have an outbreak

- If you have an institutional outbreak, you almost probably have a ribotype 027/NAP1 outbreak

- If hypervirulent strains are endemic, what drives outbreaks?
  - Antibiotic use practices?
  - Specific subtypes of strains?
  - Breakdowns in cleaning, disinfection and infection control?
  - Supershedders?
  - Influx of highly susceptible patients?
  - Influx of community cases?
  - Bad luck?

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 26, 2013 VOL. 369 NO. 13

Diverse Sources of *C. difficile* Infection Identified on Whole-Genome Sequencing

David W. Eyre, B.M., B.Ch., Madeleine L. Cule, Ph.D., Daniel J. Wilson, D.Phil., David Griffiths, B.Sc., Alison Vaughan, B.Sc., Lily O'Connor, B.Sc., Camilla L.C. Ip, Ph.D., Tanya Golubchik, Ph.D., Elizabeth M. Batty, Ph.D., John M. Finney, B.Sc., David H. Wyllie, Ph.D., Xavier Didelot, D.Phil., Paolo Piazza, Ph.D., Rory Bowden, Ph.D., Kate E. Dingle, Ph.D., Rosalind M. Harding, Ph.D., Derrick W. Crook, M.B., B.Ch., Mark H. Wilcox, M.D., Tim E.A. Peto, D.Phil., and A. Sarah Walker, Ph.D.

Over a 3-year period, 45% of *C. difficile* cases in Oxfordshire were genetically distinct from all previous cases. Genetically diverse sources, in addition to symptomatic patients, play a major part in *C. difficile* transmission. (Funded by the U.K. Clinical Research Collaboration Translational Infection Research Initiative and others.)

The NEW ENGLAND

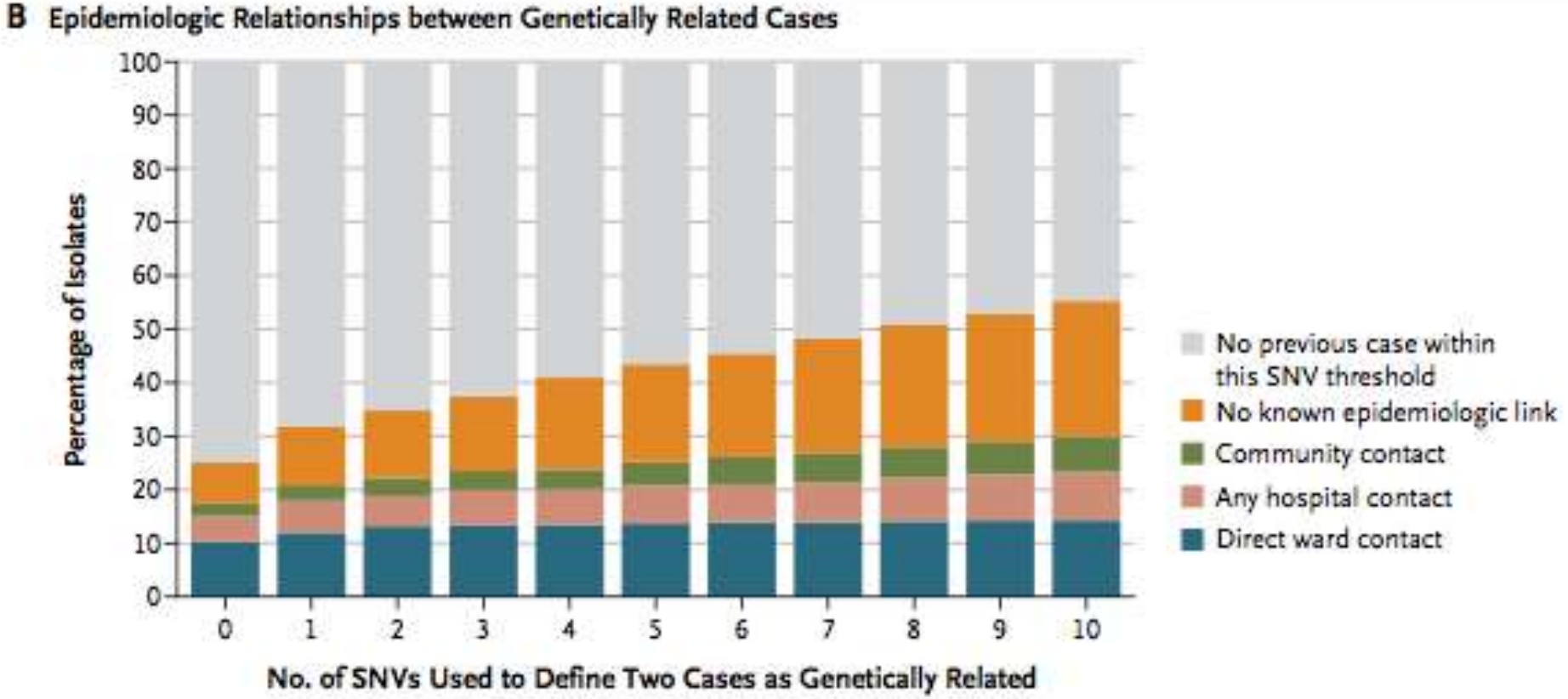


Figure 1. Genetic Variation and Epidemiologic Relationships among 957 Isolates Obtained from Patients with *Clostridium difficile* Infection.

tients, play a major part in *C. difficile* transmission. (Funded by the U.K. Clinical Research Collaboration Translational Infection Research Initiative and others.)

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY OCTOBER 2009, VOL. 30, NO. 10

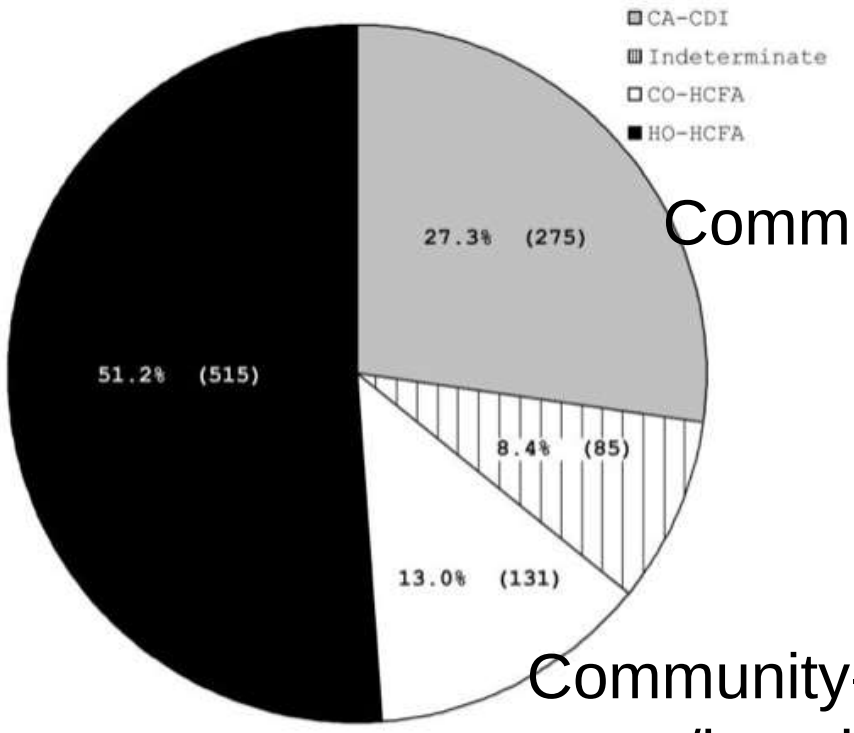
ORIGINAL ARTICLE

Population-Based Surveillance of *Clostridium difficile* Infection in Manitoba, Canada, by Using Interim Surveillance Definitions

Pascal J. Lambert, MSc; Myrna Dyck, MSc; Laura H. Thompson, MSc; Greg W. Hammond, MD, FRCPC

Hospital

Community



Community-onset/hospital associated

FIGURE 1. Percentage of *Clostridium difficile* infection (CDI) cases by surveillance definition. Numbers in parentheses indicate numbers of cases. CA-CDI, community-associated CDI; CO-HCFA, community-onset, healthcare facility–associated CDI; HO-HCFA, healthcare-onset, healthcare facility–associated CDI.

Dig Dis Sci
DOI 10.1007/s10620-013-2848-x

ORIGINAL ARTICLE

Epidemiology of *Clostridium difficile*-Associated Disease (CDAD): A Shift from Hospital-Acquired Infection to Long-Term Care Facility-Based Infection

Shashank Garg · Yusra R. Mirza · Mohit Girotra · Vivek Kumar · Samuel Yoselevitz · Ankur Segon · Sudhir K. Dutta

- Hospital-associated
  - 21%
- Community-associated
  - 33%
- LTCF associated
  - 47%

- Diarrhea as the presenting complaint
  - CA: 29%
  - LTCF: 15%
- Abdominal pain (26%), fever (20%), altered mental status (17%)
- 73% of LTCF admissions on PPIs
  - No apparent medical indication for 24%

Food
Water

Endogenous
microflora

Pet therapy

Visitors

Hospital
environment

HCW hands

Infected/colonized
patient

Food
Water

Endogenous
microflora

Pet therapy

Visitors

Hospital
environment

HCW hands

Infected/colonized
patient

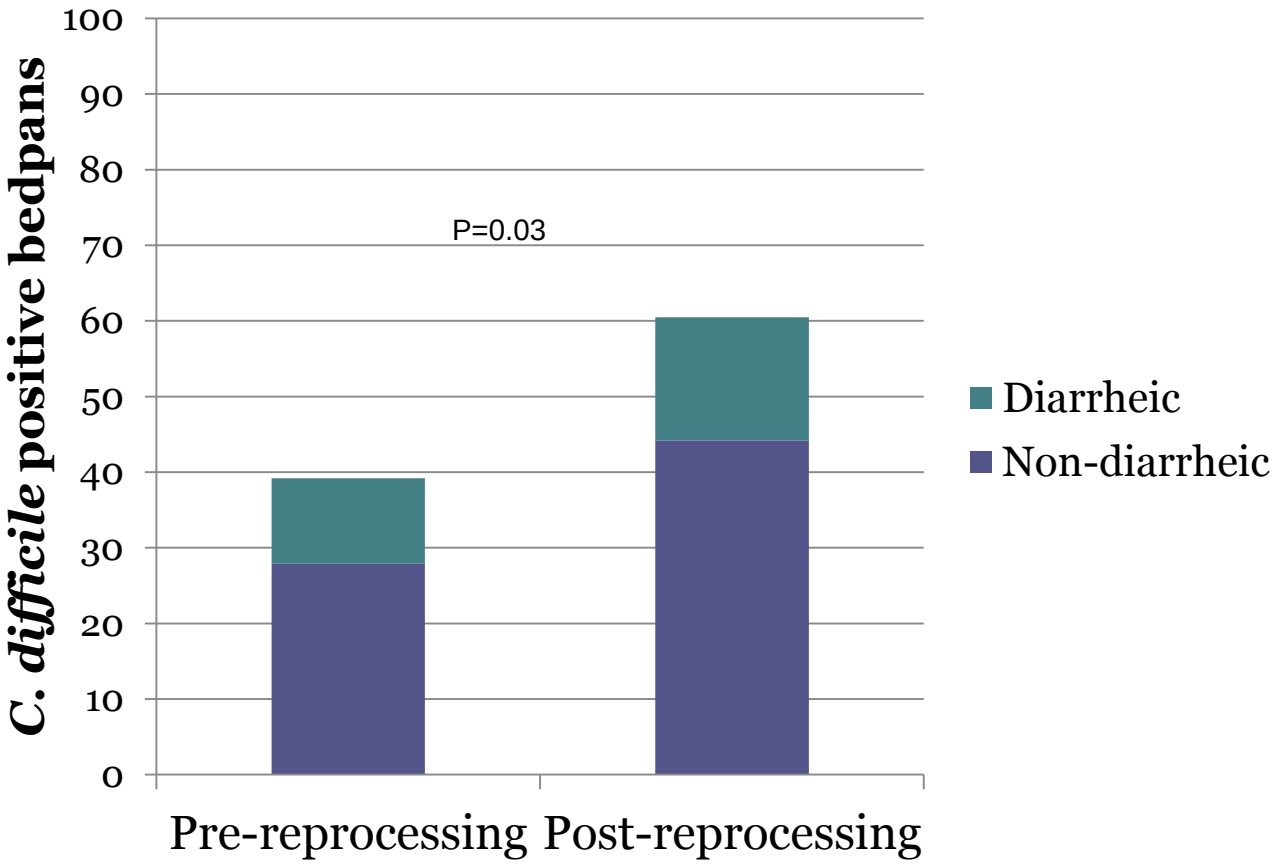
RESEARCH ARTICLE Open Access

A prospective study to examine the epidemiology of methicillin-resistant *Staphylococcus aureus* and *Clostridium difficile* contamination in the general environment of three community hospitals in southern Ontario, Canada

Meredith C Faires[1*], David L Pearl[1], William A Ciccotelli[2,3], Karen Straus[2], Giovanna Zinken[4], Olaf Berke[1,5], Richard J Reid-Smith[1,6] and J Scott Weese[6]

- 2.4% of hospital sites
  - 027: 15.4%
  - 078: 7.7%

- Testing of bedpans pre/post processing
- *C. difficile* isolated from 26% overall



Metcalf et al

What is the role of the hospital environment?


Clean is good
. . . really!!
VIROX
AHP
Johnson Diversey
BUTCHER'S
deb

Long-term care

- Relatively limited information

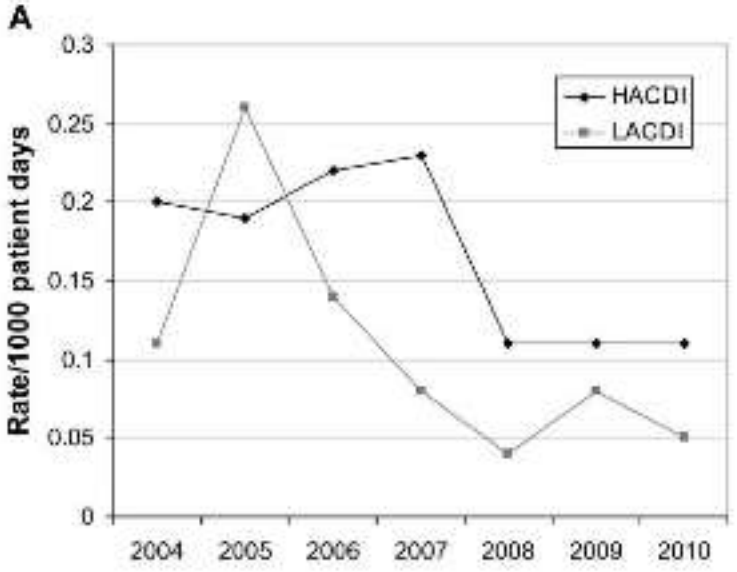
- Clearly….
  - Highly susceptible population
    - Age, antimicrobials, comorbidities…
  - Infection control and hygiene challenges
  - Close contact with acute care facilities

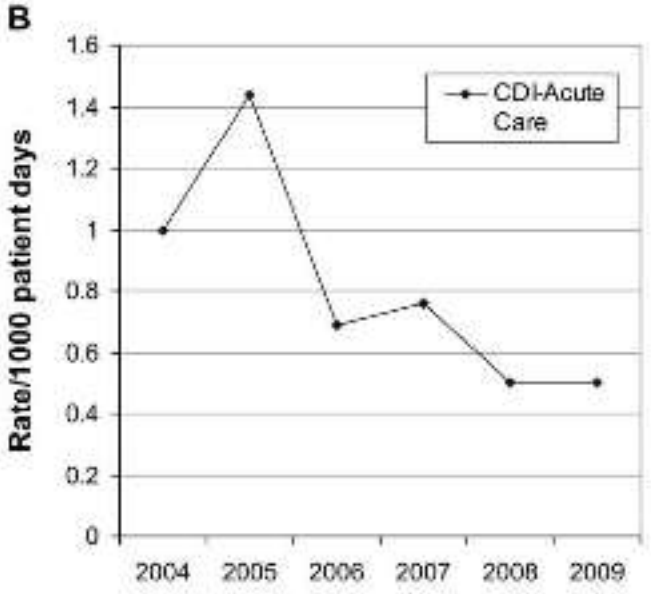
INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY JULY 2011, VOL. 32, NO. 7

ORIGINAL ARTICLE

Clostridium difficile Infection in a Long-Term Care Facility: Hospital-Associated Illness Compared with Long-Term Care–Associated Illness

Jong Hun Kim, MD;[1] Diana Toy, RN;[2] Robert R. Muder, MD[1,2]





LTC

Long Term Care

CDC Home | Search | Health Topics A-Z

MMWR

Weekly

December 2, 2005 / 54(47);1201-1205

Severe *Clostridium difficile*--Associated Disease in Populations Previously at Low Risk --- Four States, 2005

- 2 cases of CA-CDI, one fatal
- Further investigation identified 10 peripartum and 23 CA-CDI cases
  - 24% had no antimicrobial exposure in preceding 3 months
  - Transmission to close contacts identified in 4 cases

- 2005: 7.6/100000 population in Connecticut
  - Females had twice the incidence of males
  - Higher incidence during spring/summer
  - 46% required hospitalization
    - 12% required ICU stay
    - 2% toxic megacolon and colectomy
    - 2% died
  - 25% had no underlying disease of healthcare exposure in preceding 12 months
    - 36% of those had no antimicrobial exposure

MMWR 2008

- Young age
- Potential for severe disease
- Pregnant women?
- Different risk factors
  - Limited or no antimicrobial exposure
  - Proton pump inhibitors (mixed data)
  - Female gender
  - IBD
  - Contact with children <2y of age
- Community transmission

Wilcox et al 2008, Dial et al 2005/2006


5

Toxinotype V *Clostridium difficile* in Humans and Food Animals

Michael A. Jhung,* Angela D. Thompson,* George E. Killgore,* Walter E. Zukowski,† Glenn Songer,‡
Michael Warny,§ Stuart Johnson,†¶ Dale N. Gerding,†¶ L. Clifford McDonald,*
and Brandi M. Limbago*

msnbc

search site | web | MSN Home | Mail

featuring Today Show | Nightly News | Dateline | Meet the Press

Health / Health care

Categories

- U.S. news
- World news
- Politics
- Business
- Sports
- Entertainment
- Health
- Diet and nutrition
- Women's health
- Health care
- Men's health
- Kids and parenting

Tainted meats point to superbug C. diff in food

Study finds gut germ in 40 percent of grocery meats; CDC says not to worry

Joe Raedle / Getty Images file

An Arizona researcher found 40 percent of meat products tested from three national chain stores were contaminated with bacteria normally associated with severe hospital infections. Federal health officials, however, say more study is needed to determine whether C. diff is transmitted through food.

Letters in
Applied Microbiology

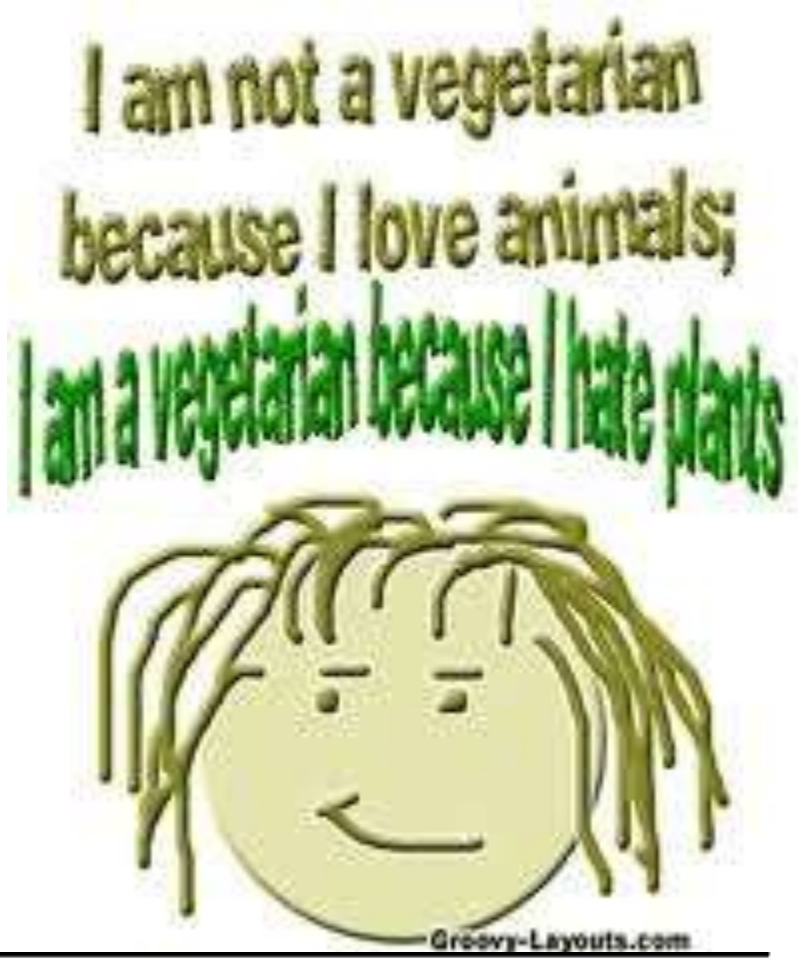
Letters in Applied Microbiology ISSN 0266-8254

NOTE TO THE EDITOR

Clostridium difficile in vegetables, Canada

D.S. Metcalf, M.C. Costa, W.M.V. Dew and J.S.Weese

University of Guelph, Guelph, Ontario, Canada



Clostridium difficile in Ready-to-Eat Salads, Scotland

Marwah M. Bakri, Derek J. Brown,
n P. Butcher, and Alistair D. Sutherland

0 ready-to-eat salads, 3 (7.5%) were positive for
m difficile by PCR. Two isolates were PCR ribo-
(toxin A–, B+), and 1 was PCR ribotype 001. Iso-
e susceptible to vancomycin and metronidazole but
esistant to other antimicrobial drugs. Ready-to-eat
ay be potential sources for virulent *C. difficile*.

Note

Clostridium difficile in seafood and fish

Devon Metcalf [a,*], Brent P. Avery [b], Nicol Janecko [b], Nancy Matic [a], Richard Reid-Smith [b], J. Scott Weese [a]

- *C. difficile* from 44/836 (5.3%) of sites in 26/84 (31%) households (Weese et al 2010)

Ribotype	*n*	Environmental site	Animals (*n*)
027	8	Pet food bowl (3), kitchen sink (2), kitchen sink tap, kitchen floor, toilet	None
078	5	Fridge shelf (2), kitchen sink, kitchen sink tap, toilet	None
L	5	Toilet (2), kitchen sink, kitchen counter, fridge shelf	Canine (1)
001	5	Kitchen sink, fridge shelf, dog food bowl, toilet, fridge shelf	Canine (4), feline (2)
Y	3	Fridge shelf, vacuum contents, kitchen counter	None
V	2	Kitchen sink tap, dog eating area	Feline (1)
AI	2	Kitchen counter, dog food bowl	Canine (2)
C	1	Kitchen counter	Canine (1)
AA	1	Fridge shelf	None
Q	0	None	Canine (2)

Is exposure to *C. difficile* a daily event?

The End

Hospital Visitation Dogs

- *C. difficile* acquisition by
  - 28% of hospital visitation vs 15% controls (P=0.025)
- Risk factors
  - Healthcare contact: OR 2.2 (1.4-3.5)
  - Visitation of children: OR 3.5 (2.4-4.2)
  - Antimicrobial treatment of someone in the house: OR 2.2 (1.3-3.6)
- Nested case-control study
  - Licked patients: OR 2.9 (1.04-8.1)
  - Sat on beds: OR 2.9 (1.1-7.5)
  - Ate feces: OR 0.12 (0.01-0.88)

Lefebvre et al 2008