

The background consists of a dark blue gradient with several overlapping geometric shapes. On the left, there is a vertical rectangular bar. On the right, there is a large circle. These shapes are in lighter shades of blue, creating a layered effect.

Clostridium difficile: A Pathogen of the Nineties

Tom Riley

Editorial

Clostridium difficile: A Pathogen of the Nineties

T. V. Riley

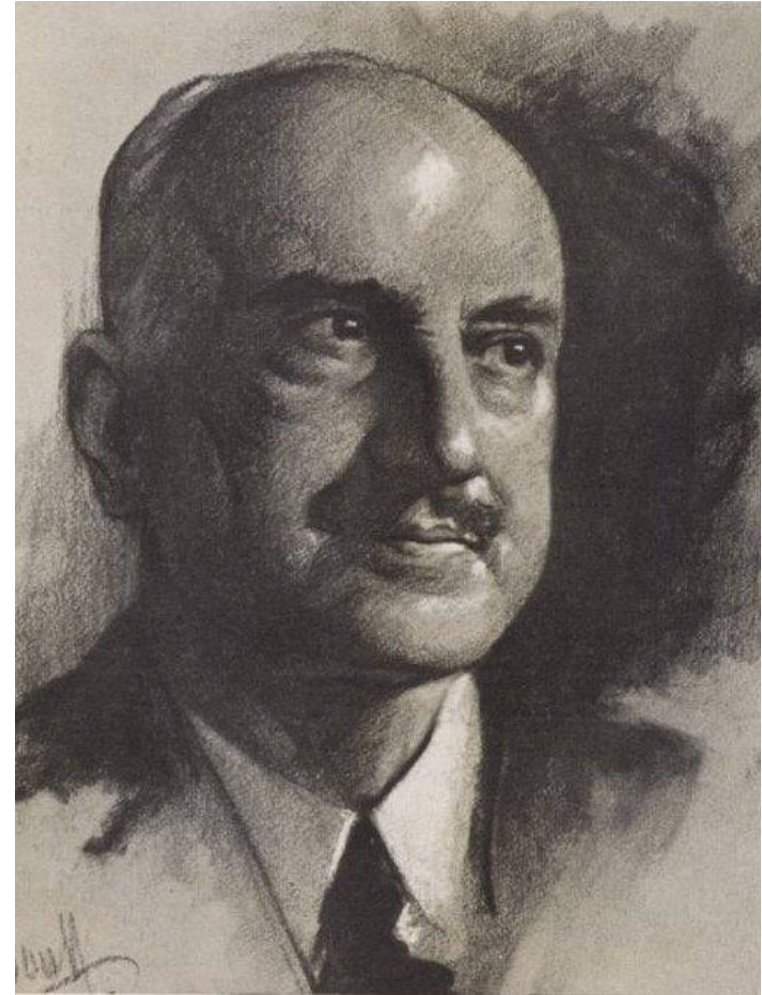
T. V. Riley
Department of Microbiology, The University of Western
Australia, Nedlands, Western Australia, Australia

Topics mentioned in 1998

- Hospital-acquired infection
- Antimicrobials inciting *C. difficile* disease
 - Clindamycin
 - Cephalosporins
- Community-acquired infection
- Reservoirs/exogenous sources
- Outbreaks (not actually mentioned at all – my bad!)
- Costs

George Santayana
(1863 – 1952) was a
philosopher, essayist,
poet and novelist.

**“Those who cannot
remember the past
are condemned to
repeat it”**





ANNALS

of Internal Medicine

OCTOBER 1974 • VOLUME 81 • NUMBER 4

Published Monthly by the American College of Physicians

Clindamycin-Associated Colitis

A Prospective Study

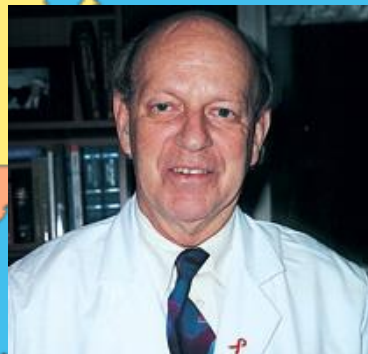
FRANCIS J. TEDESCO, M.D., ROBERT W. BARTON, M.D., and DAVID H. ALPERS, M.D.,
St. Louis, Missouri

A prospective study of 200 consecutive patients receiving clindamycin (Cleocin HCl®*) for various reasons showed a 21% incidence of diarrhea and a 10% incidence of pseudomembranous colitis.

**ETIOLOGY OF
ANTIMICROBIAL-AGENT-ASSOCIATED
COLITIS**

W. LANCE GEORGE VERA L. SUTTER
ELLIE J. C. GOLDSTEIN SHELLY L. LUDWIG
SYDNEY M. FINEGOLD

THE LANCET, APRIL 15, 1978



Not
Douglas
Burden!



**Identification of Clostridium
difficile as a cause of
pseudomembranous colitis**

BRITISH MEDICAL JOURNAL

Department of Microbiology, Birmingham Children's Hospital,
Birmingham

R H GEORGE, MB, MRCPATH, consultant microbiologist
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Departments of Microbiology and Surgery, General Hospital,
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FRANCES DIMOCK, FIMLS, research technician
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Y ARABI, FRCS, senior registrar
N SHINAGAWA, MD, senior registrar
M R B KEIGHLEY, MS, FRCS, consultant surgeon and senior lecturer
J ALEXANDER-WILLIAMS, MD, FRCS, consultant surgeon
D W BURDON, MB, MRCPATH, consultant microbiologist

**Clindamycin-Induced Enterocolitis in Hamsters as a Model of
Pseudomembranous Colitis in Patients**

TE-WEN CHANG,^{†*} JOHN G. BARTLETT,¹ SHERWOOD L. GORBACH² AND
ANDREW B. ONDERDONK¹

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Received for publication 16 November 1977

INFECTION AND IMMUNITY, May 1978, p. 526-529



**CLOSTRIDIUM DIFFICILE AND THE
ETIOLOGY OF PSEUDOMEMBRANOUS
COLITIS**

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THE LANCET, MAY 20, 1978

A couple of important notes

CDAD - *Clostridium difficile*
associated diarrhoea

became

CDI - *Clostridium difficile*
infection

Clostridium difficile

became

Clostridioides difficile



Anaerobe 40 (2016) 95–99

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journal homepage: www.elsevier.com/locate/anaerobe

Clostridium difficile

Reclassification of *Clostridium difficile* as *Clostridioides difficile* (Hall and O'Toole 1935) Prévot 1938

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Anaerobe 52 (2018) 125–126

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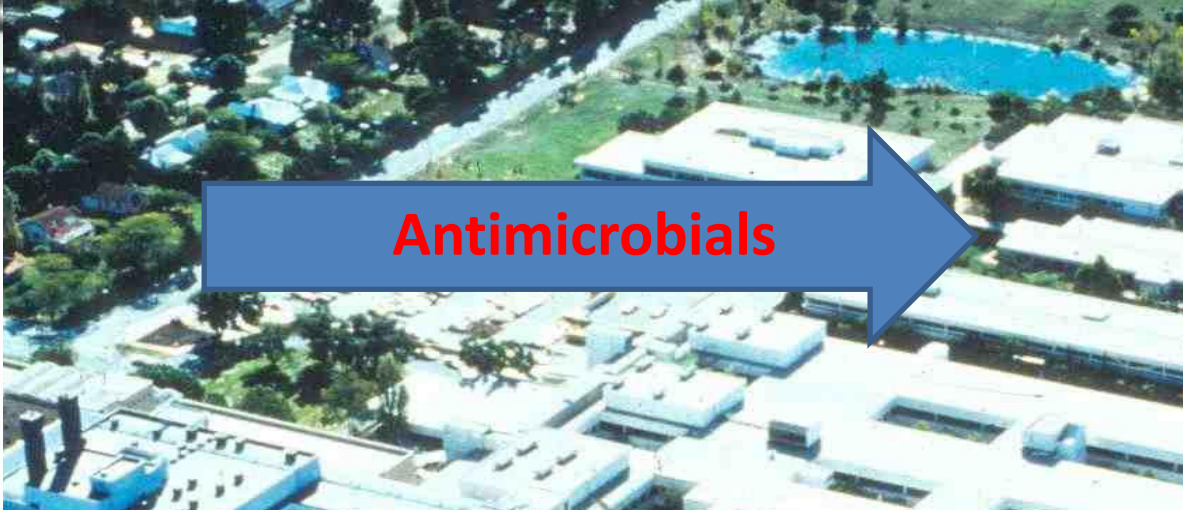
journal homepage: www.elsevier.com/locate/anaerobe

Short communication

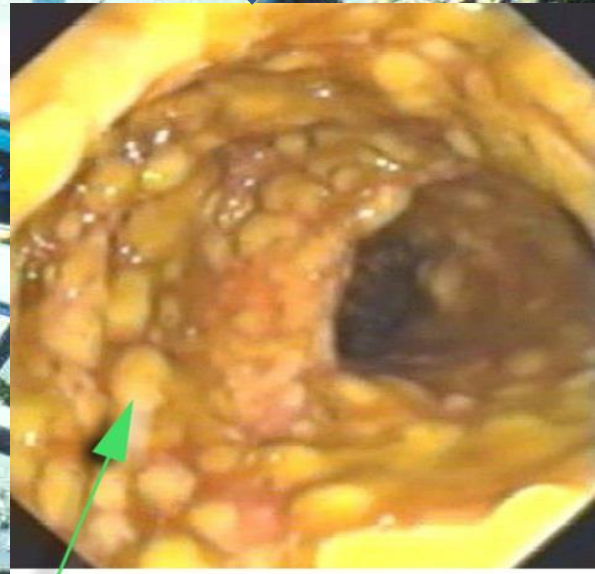
Clostridium difficile and *Clostridioides difficile*: Two validly published and correct names

Aharon Oren ^a, Maja Rupnik ^{b,c,*}

^a Department of Plant and Environmental Sciences, The Alexander Silberman Institute of Life Sciences, The Hebrew University of Jerusalem, Edmond J. Safra Campus, Jerusalem, 9190401, Israel
^b National Laboratory for Health, Environment and Food, NLZOH, Maribor, Slovenia
^c University of Maribor, Faculty of Medicine, Maribor, Slovenia



Antimicrobials



Community-acquired infection

Several recent studies, including that of Hirschhorn et al. [10], have focused on CDAD in the community or general practice [15, 16]. In the first of these studies, *Clostridium difficile* or its cytotoxin was found in 16 (5.5%) of 288 stool samples from patients with diarrhoeal illness consulting their general practitioners and was the most common enteric pathogen detected [15]. Most patients had only mild to moderate diarrhoea; however, in the majority of cases the diarrhoea was protracted. In a later study a larger group of 580 specimens was investigated following a campaign to educate general practitioners about CDAD [16]. There were 75 positive samples (10.7%) from 61 patients and *Clostridium difficile* was the second most frequent enteric pathogen following *Campylobacter* spp.

DIARRHEAL DISEASE DUE TO *CLOSTRIDIUM DIFFICILE* IN GENERAL PRACTICE

THOMAS V. RILEY,* FRANCES WETHERALL,† JACINTA BOWMAN,*
JILLIAN MOGYOROSY† AND CLAYTON L. GOLLEDGE‡

*Department of Microbiology, University of Western Australia and Sir Charles Gairdner Hospital, Queen Elizabeth II Medical Centre, Nedlands,

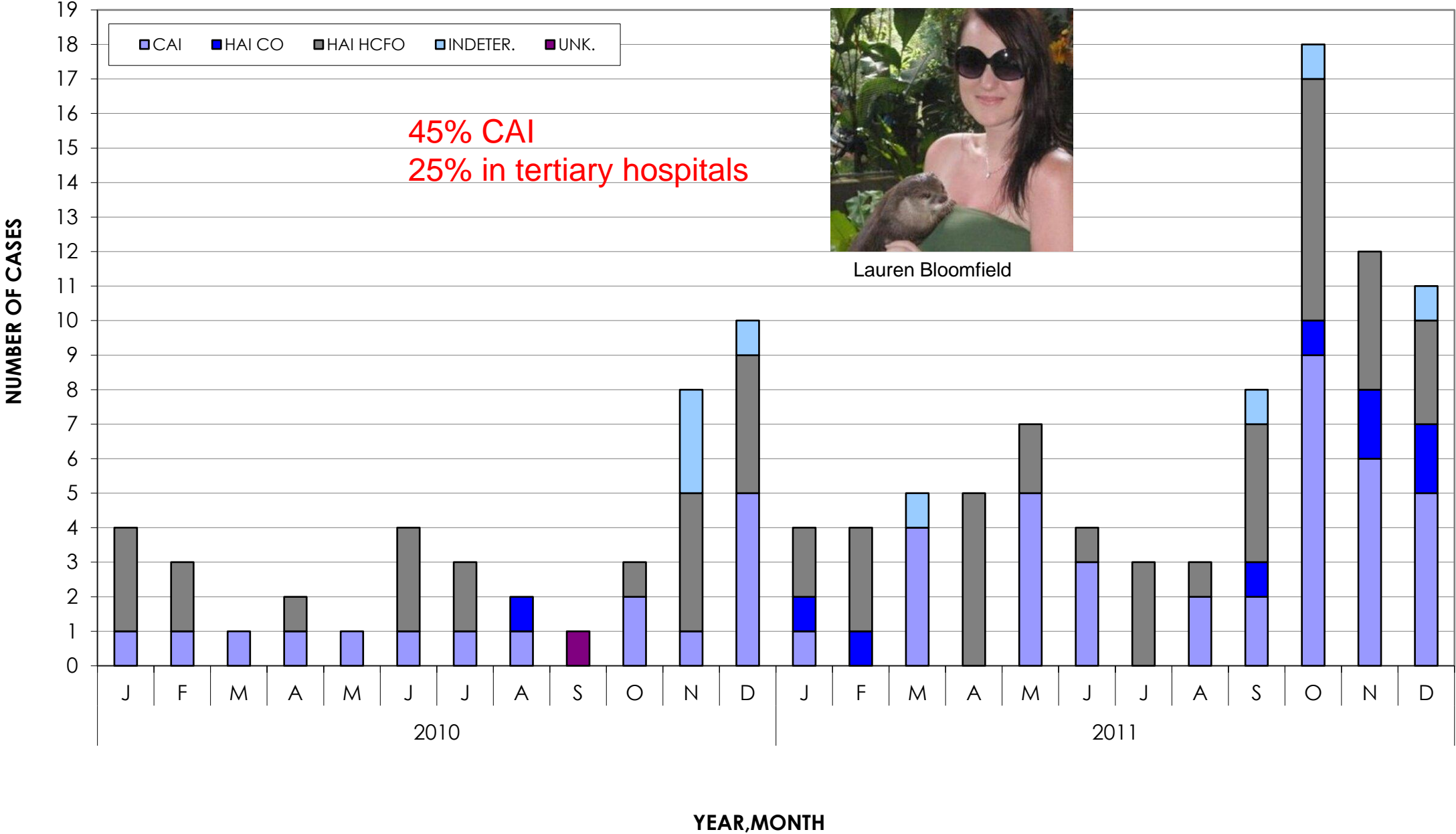
†Clinipath Laboratories, Wembley, ‡Department of Microbiology, Fremantle Hospital, Fremantle, Western Australia

Community-Acquired *Clostridium difficile*-Associated Diarrhea. THOMAS V. RILEY, MARGARET COOPER, BRYAN BELL, AND CLAYTON L. GOLLEDGE. From the National Centre for Epidemiology and Population Health, The Australian National University, Canberra, Australian Capital Territory; and the Epidemiology and Health Statistics Section, Health Department of Western Australia, East Perth, and Western Diagnostic Pathology, Myaree, Western Australia, Australia

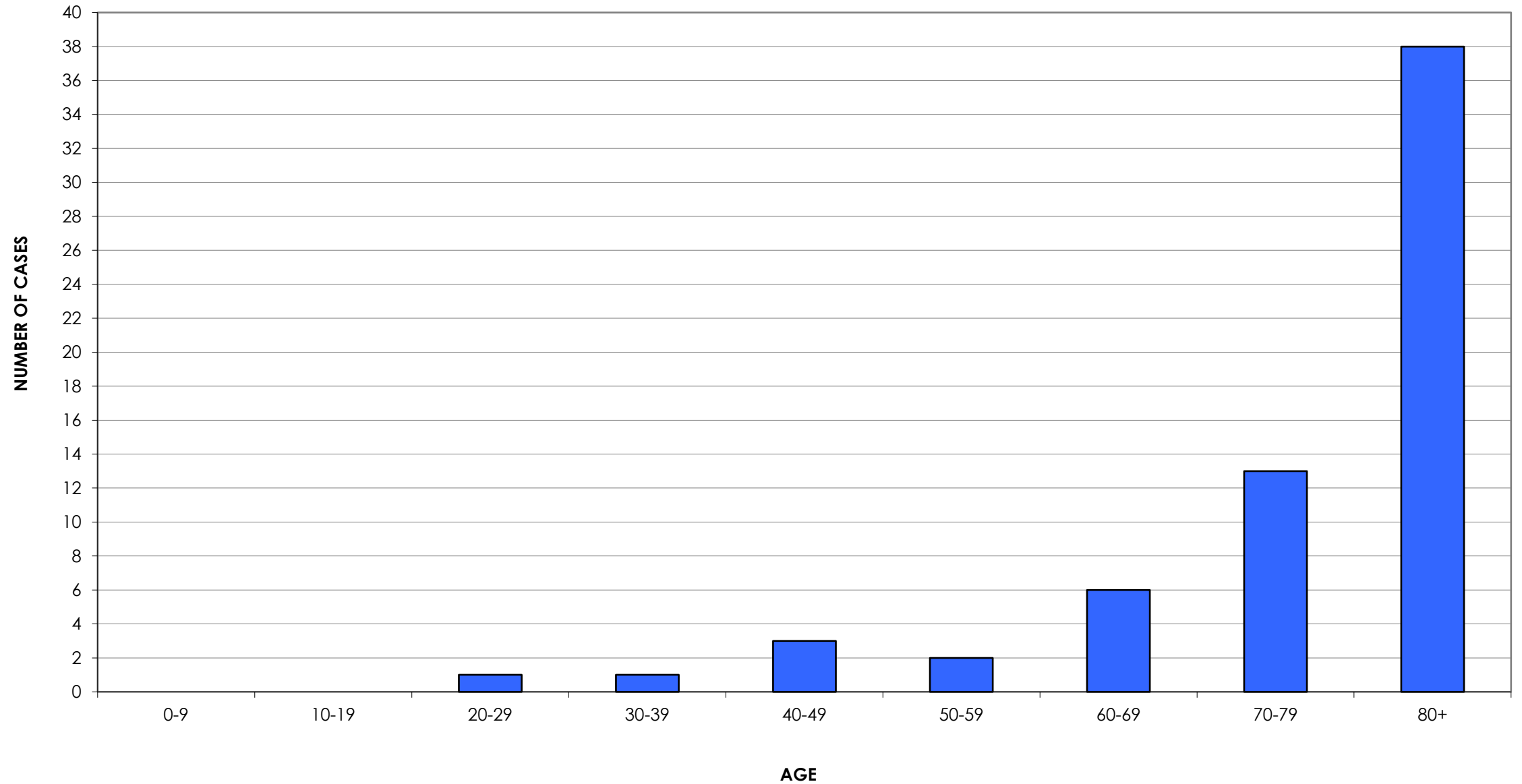
Clinical Infectious Diseases 1995;20(Suppl 2):S263-5
© 1995 by The University of Chicago. All rights reserved.
1058-4838/95/2006-0080\$02.00

This clearly meant that there were sources/reservoirs of *C. difficile* in the community.

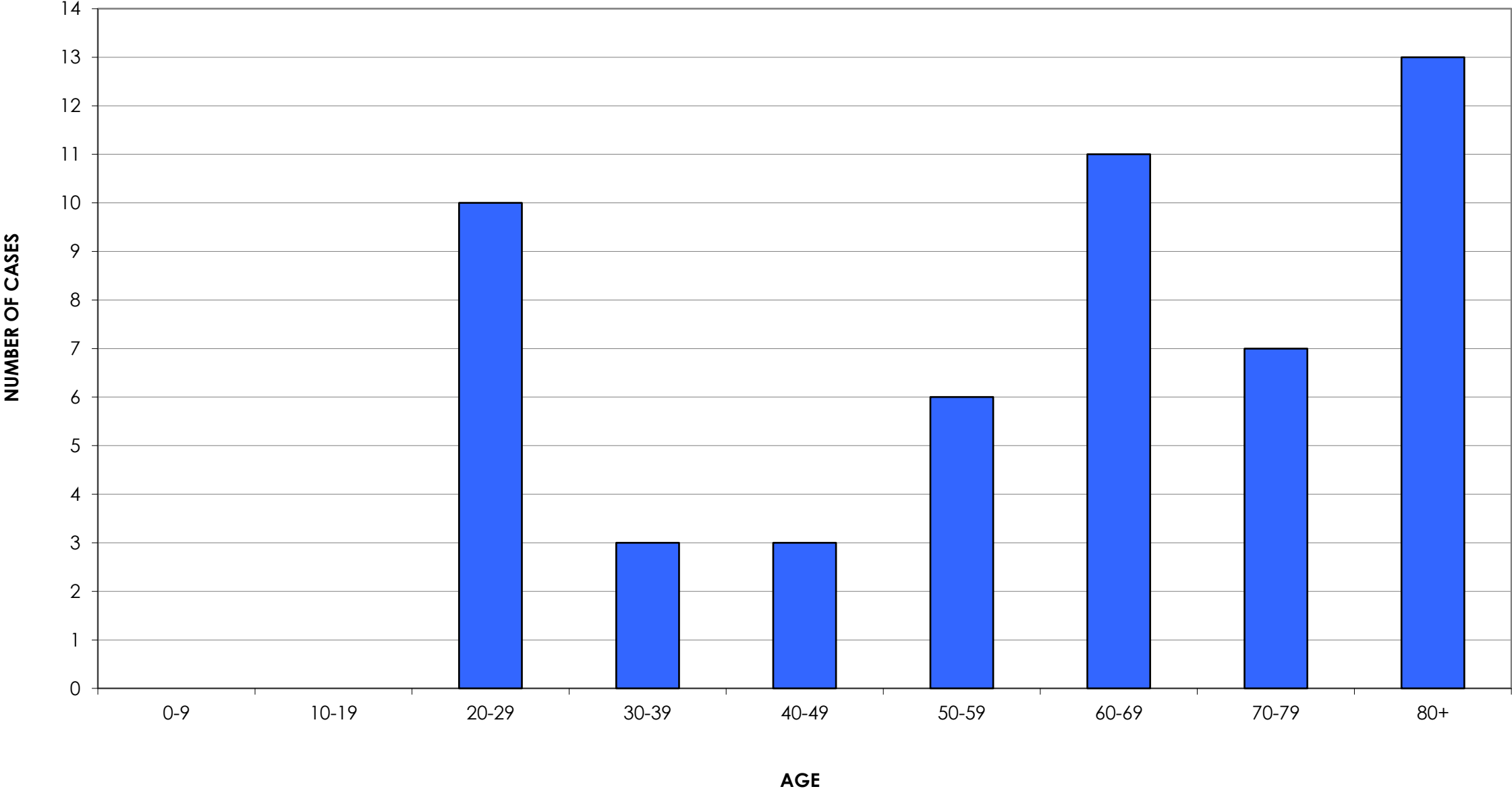
CDI CASES IDENTIFIED AT METRO NON-TERTIARY HOSPITALS 2010-2011



HA-CDI - MNT HOSPITALS - PATIENT DEMOGRAPHICS



CA-CDI CASES - MNT HOSPITALS - PATIENT DEMOGRAPHICS



Reservoirs/exogenous sources

The human intestinal tract is probably the most important reservoir of infection.

WRONG!



Epidemiol. Infect. (1991), **107**, 659–665
Printed in Great Britain

659

Gastrointestinal carriage of *Clostridium difficile* in cats and dogs attending veterinary clinics

T. V. RILEY, J. E. ADAMS, G. L. O'NEILL AND R. A. BOWMAN

*Department of Microbiology, University of Western Australia and
Sir Charles Gairdner Hospital, Queen Elizabeth II Medical Centre,
Nedlands 6009, Western Australia*

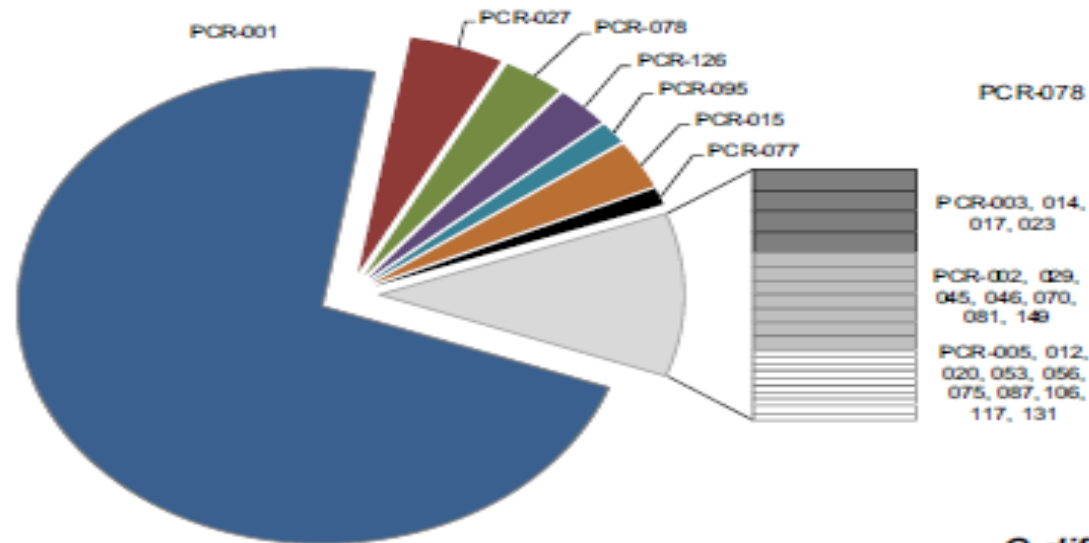
Cats and dogs being treated at two veterinary clinics were investigated for gastrointestinal carriage of *Clostridium difficile* using selective solid and enrichment media. Thirty-two (39·5 %) of 81 stool samples yielded *C. difficile*. There were significant differences in isolation rates between clinics, 61·0 % of animals being positive at one clinic compared to 17·5 % at the other (Chi-square, $P < 0\cdot005$). Of 29 animals receiving antibiotics, 15 (52·0 %) harboured *C. difficile* while 11 (23·9 %) of 46 animals not receiving antibiotics were positive (Chi-square, $P < 0\cdot01$). There was no difference in carriage rate between cats (38·1 %) and dogs (40·0 %).



C. difficile in people

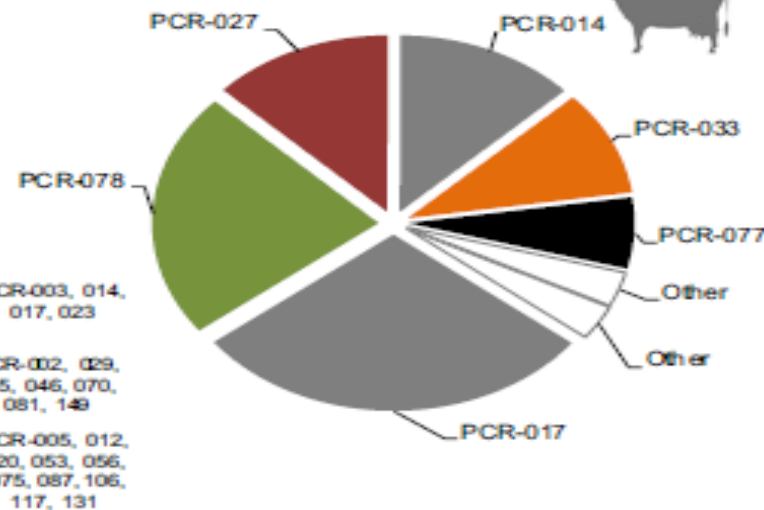


Hospitals, Germany



C. difficile in calves at the farm, 102 farms, Canada

May-September 2004



C. difficile in foods North America

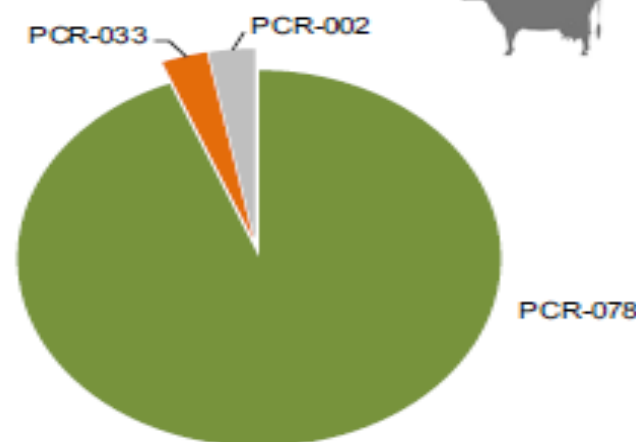
BEEF meats



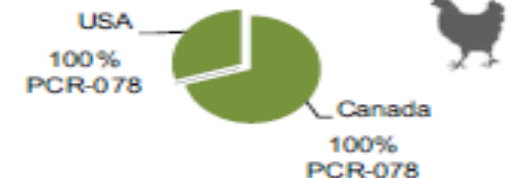
PORK meats



C. difficile in calves shipped to a single farm, USA



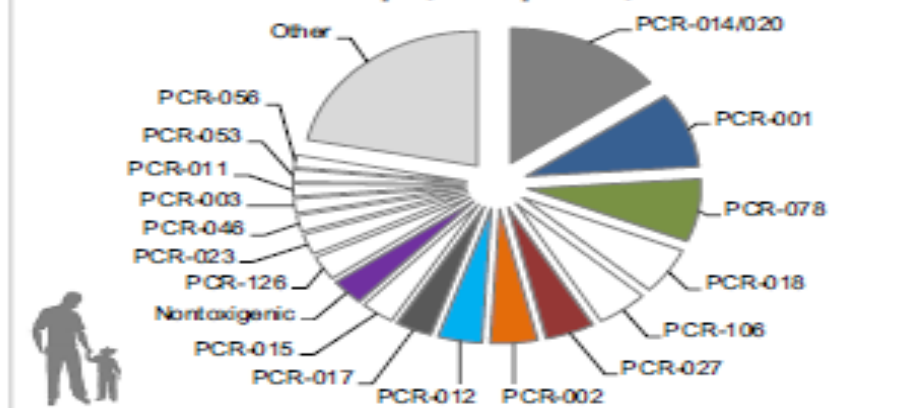
POULTRY meats



Seafood & vegetables



C. difficile in Europe, hospitals, 34 countries



Gardening centres

~30% of samples positive for *C. difficile*

Some obvious like animal manures

Some less obvious like compost/mulch

But expired vegetables from large stores going into compost/mulch



Su-Chen Lim

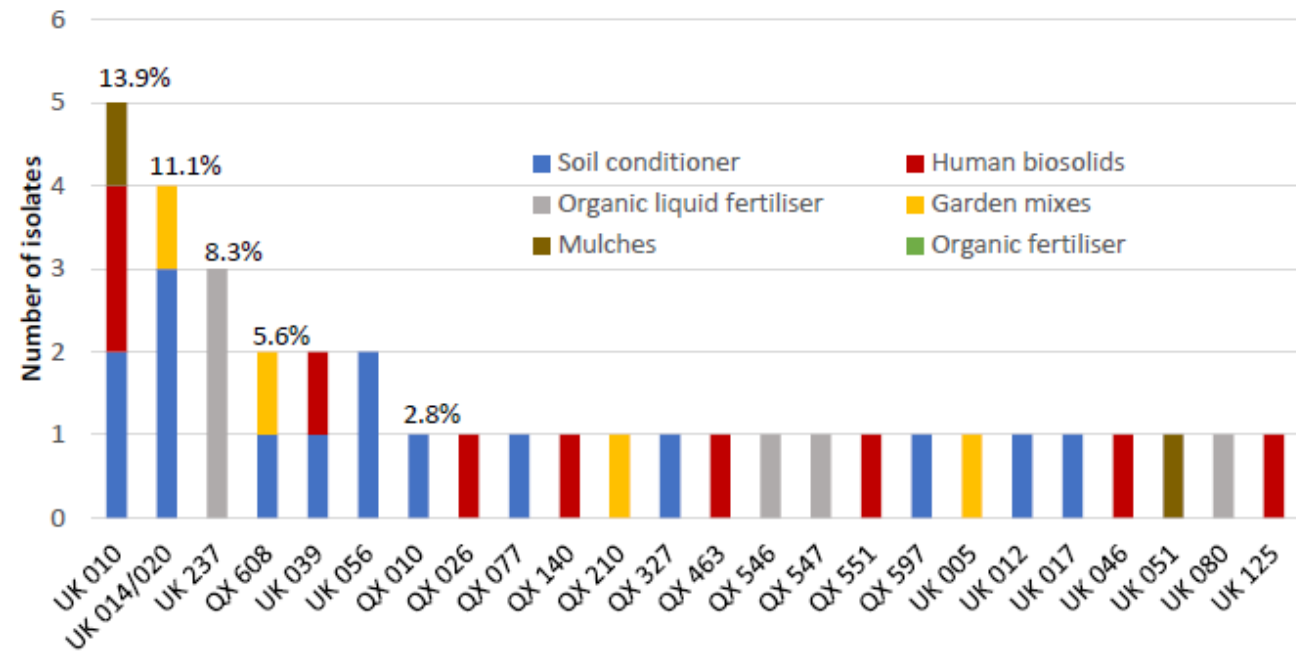
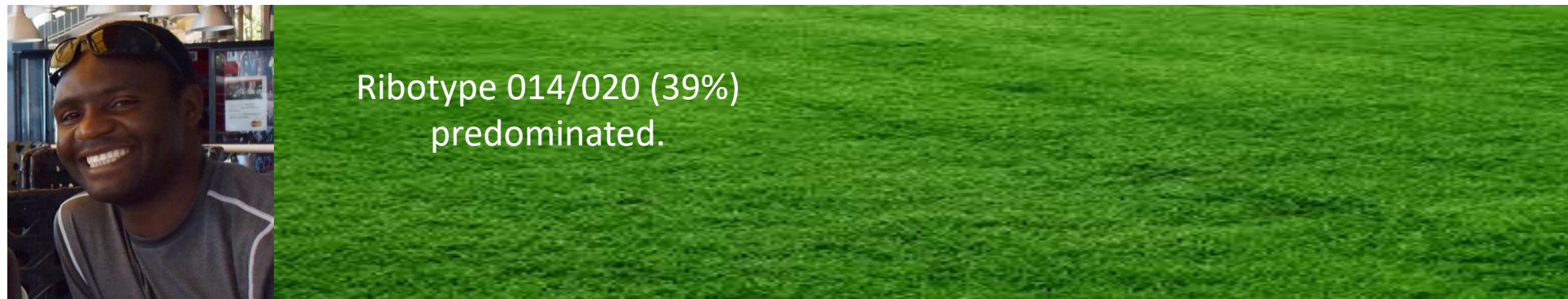


Figure 1. PCR ribotype of *C. difficile* isolates in gardening products

Variable	Variable categories	<i>C. difficile</i> number isolated (%)	Univariable model	Covariate Odds ratios (95% CI)*	
			Odds ratios (95% CI)†	Sampling site	<i>P</i> value‡
Age‡	Old lawn (n = 113)	53 (47)	Referent		
	New lawn (n = 198)	129 (65)	2.11 (1.32–3.4)	2.30 (1.16–4.57)	0.015#
Area	Extra-large (n = 85)	53 (62)	Referent		
	Large (n = 53)	26 (49)	0.58 (0.28–1.16)	0.49 (0.16–1.49)	0.7
	Medium (n = 101)	60 (59)	0.88 (0.49–1.59)	1.02 (0.42–2.51)	0.7
	Small (n = 72)	43 (60)	0.89 (0.47–1.71)	0.88 (0.32–2.43)	0.7
Location	North (n = 161)	98 (60.9)	Referent		
	South (n = 150)	84 (56)	1.22 (0.78–1.92)	1.25 (0.61–2.59)	0.99
Season	Autumn (n = 224)	135 (60.3)	Referent		
	Winter (n = 87)	47 (54)	0.77 (0.47–1.28)	0.67 (0.28–1.62)	0.52

Table 1. The relationship between the prevalence of *C. difficile* in lawn and the age of the lawn, its size, sampling site, location, postcode, and season in Perth.





Community- and healthcare-associated infections in females in WA, by age group, 2010 – 2014

Age group	CAI n (%)	HAI HCFO n (%)	OR (CI ₉₅)
2 - 19 years	29 (43.9)	37 (56.1)	0.92 (0.48 – 1.76)
20 - 39 years	109 (67.2)	53 (32.7)	1.90 (1.19 – 3.05)
40 - 59 years	100 (39.3)	154 (60.6)	1.13 (0.77 – 1.67)
60 - 79 years	141 (31.8)	303 (68.2)	1.18 (0.88 – 1.58)
80+ years	116 (27.9)	300 (72.1)	0.86 (0.61 – 1.21)
Total	495 (57.0)	847 (52.8)	1.09 (0.93 – 1.30)



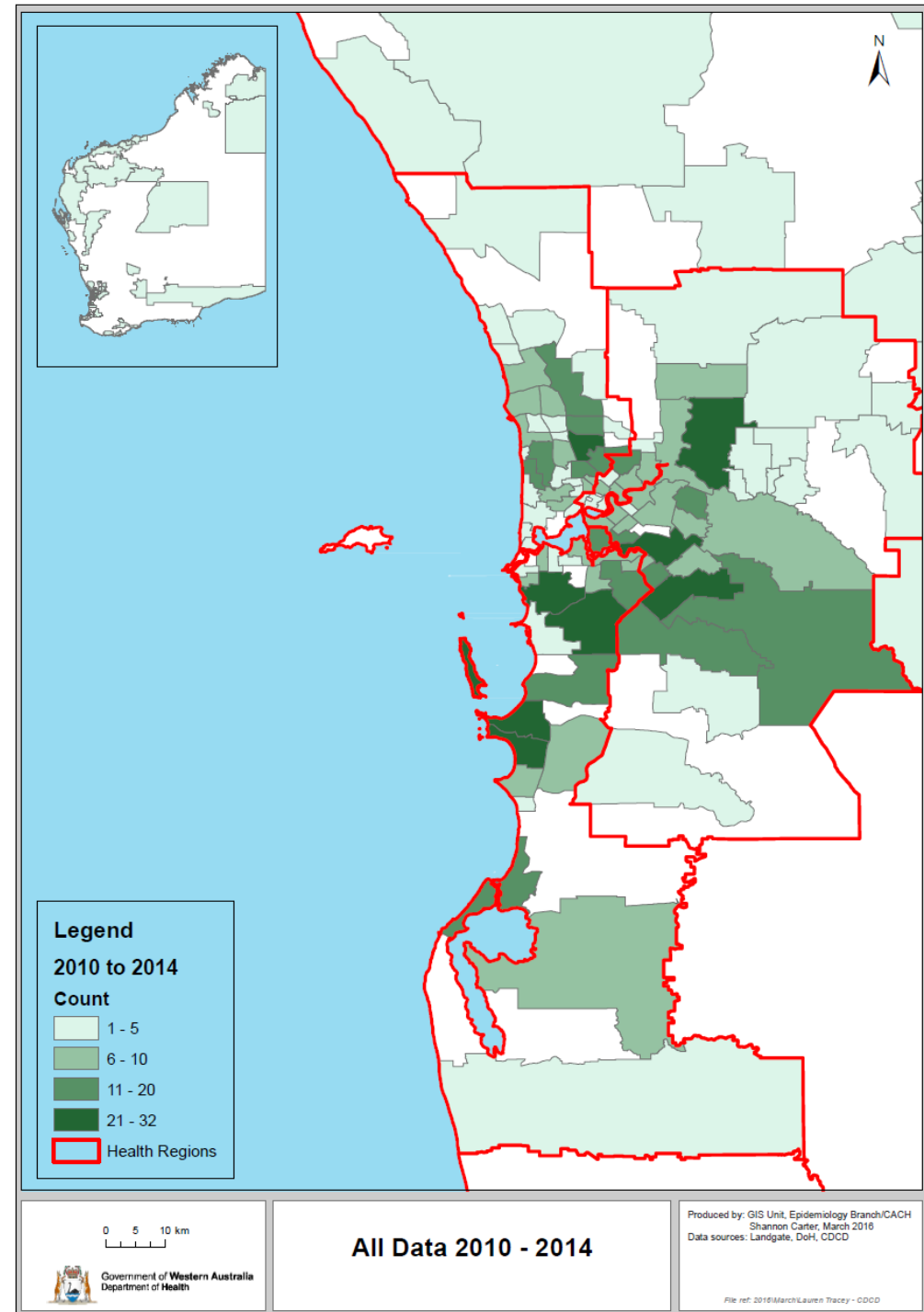
Lauren Bloomfield

New lawn in Perth is significantly more likely to grow *C. difficile* than old lawn.

New suburbs of Perth have significantly higher rates of CA-CDI than older suburbs.

Maybe confounded by young families.

Many antimicrobials consumed in the community.



Outbreaks

Several small outbreaks reported from hospitals in USA and UK – usually a single ward and a single strain, although typing in those days was not good.

Nothing major until the early 2000s in North America (South East Canada and North East USA) when an apparently new strain of *C. difficile* (RT 027) emerged in hospital patients.

Moved to UK and then to Europe causing several outbreaks with high mortality.

Management and control of a large outbreak of diarrhoea due to *Clostridium difficile*

**T. D. I. Cartmill, H. Panigrahi, M. A. Worsley, D. C. McCann,
C. N. Nice and E. Keith**

Departments of Microbiology and Infection Control, North Manchester General Hospital, Crumpsall, Manchester M8 6RB, UK

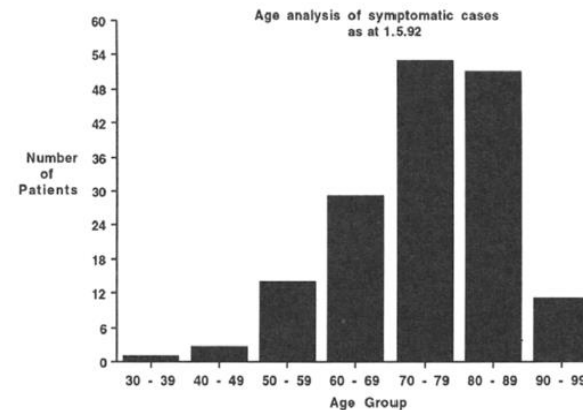


Figure 1. Age distribution of 175 patients with symptomatic disease due to *Clostridium difficile*.

Clearly a hospital outbreak. Over 75% of patients had received a cephalosporin. Strain retrospectively ribotyped as RT 001, the predominant strain circulating in UK at the time.

ORIGINAL ARTICLE

A Predominantly Clonal Multi-Institutional Outbreak of *Clostridium difficile*—Associated Diarrhea with High Morbidity and Mortality

Vivian G. Loo, M.D., Louise Poirier, M.D., Mark A. Miller, M.D.,
Matthew Oughton, M.D., Michael D. Libman, M.D., Sophie Michaud, M.D., M.P.H.,
Anne-Marie Bourgault, M.D., Tuyen Nguyen, M.D., Charles Frenette, M.D.,
Mirabelle Kelly, M.D., Anne Vibien, M.D., Paul Brassard, M.D., Susan Fenn, M.L.T.,
Ken Dewar, Ph.D., Thomas J. Hudson, M.D., Ruth Horn, M.D., Pierre René, M.D.,
Yury Monczak, Ph.D., and André Dascal, M.D.

Quebec Province: Cases in 2004 – 7004, deaths 1270

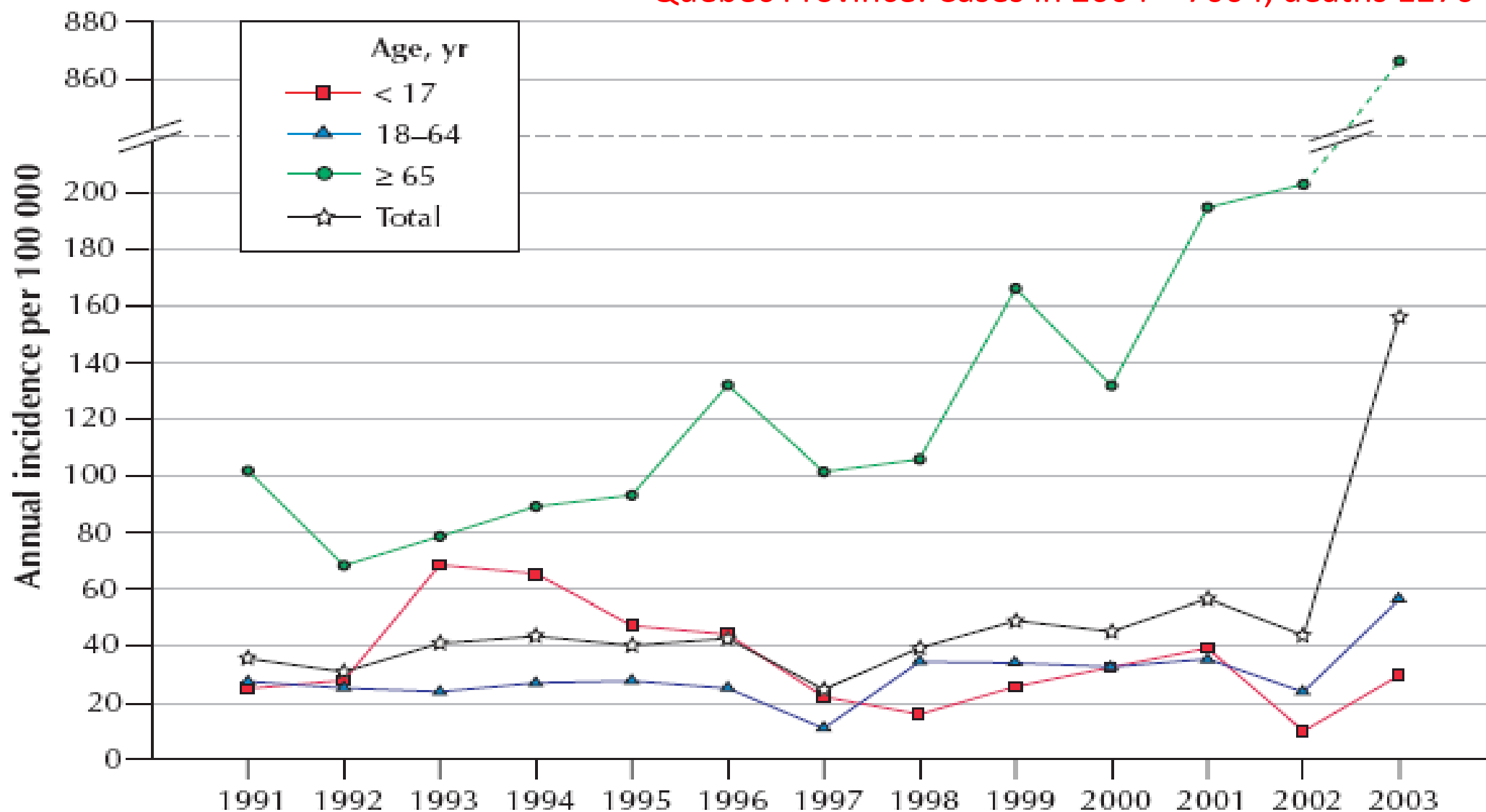


Fig. 1: Annual incidence (per 100 000 population) of *Clostridium difficile*-associated diarrhea (CDAD) in Sherbrooke, Que., 1991–2003.

Superbug kills war hero who survived three years as a PoW

By **Luke Salkeld**

THE family of a distinguished war veteran have criticised the hospital where he was infected by a killer bug.

Major Sam Weller – who survived three years as a prisoner of war – died after catching *Clostridium Difficile* following an operation on his hip. Yesterday, his relatives said he had been let down by the country he fought for.

Major Weller, 88, had surgery at Gloucestershire Royal Hospital but he developed an infection and was given a course of antibiotics.

Weeks later he died and an inquest was told the medicine had left him more vulnerable to catching the superbug.

Yesterday, his family criticised the hospital treatment he received and standards of

2,247

ALMOST 56,000 vulnerable and elderly patients have been infected with *C. Diff* in the past year.

Between January and March alone, 15,592 caught the bug – an astonishing 22 per cent rise on the previous three months.

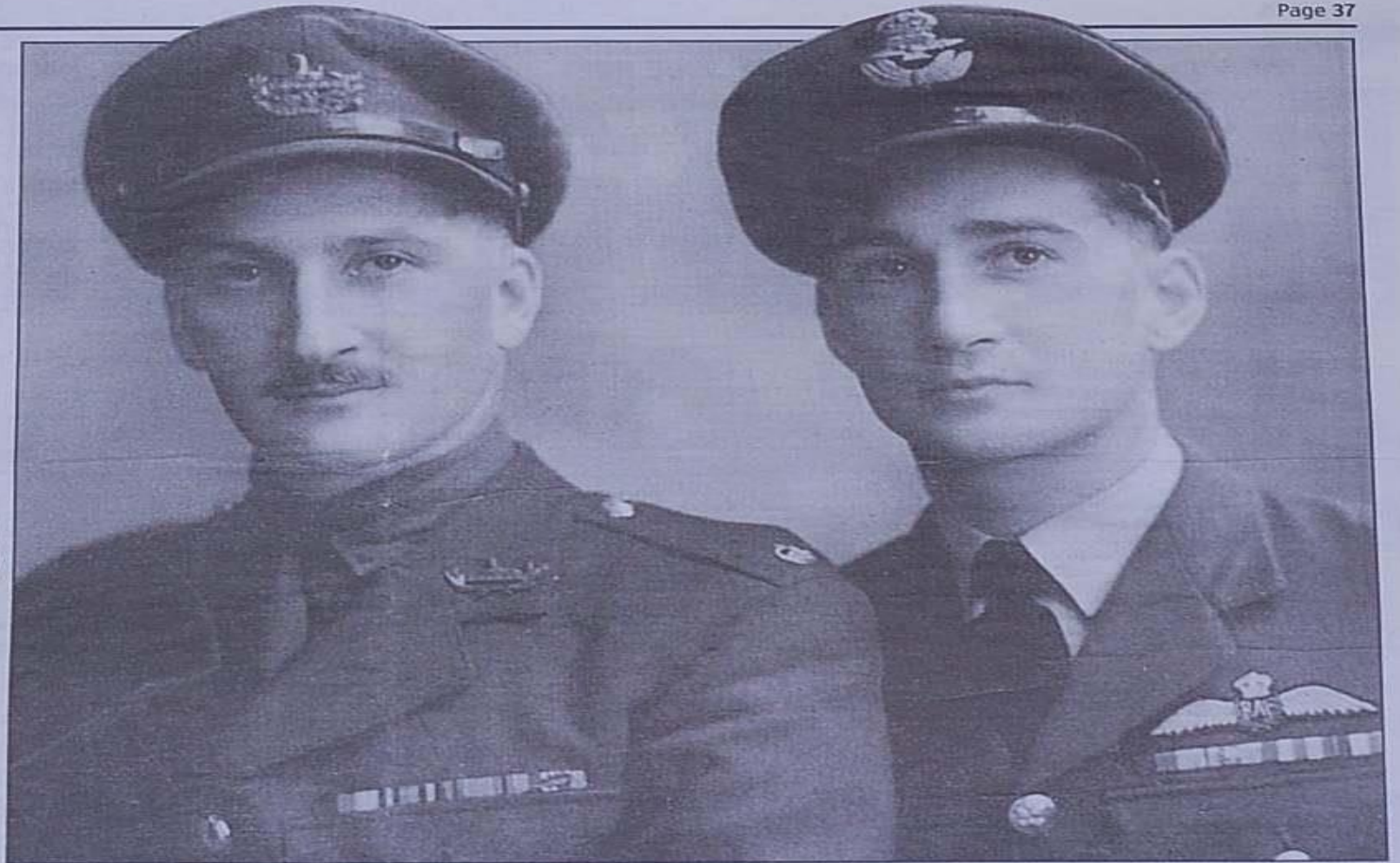
C. Diff, which is spread by dirty hands and bedding, is a bigger killer than MRSA. It claimed 2,247 lives in 2005 – a 69 per cent rise on the previous year.

It exists naturally in the

stomachs of many healthy adults, where it is kept under control by 'friendly' bacteria.

Problems start if the balance of bacteria is disturbed, perhaps as a result of taking antibiotics for another infection.

Once the 'friendly' bacteria are killed off, the *C. Diff* is able to multiply and produce the toxins which cause diarrhoea and, in the worst cases, a fatal infection of the abdomen.

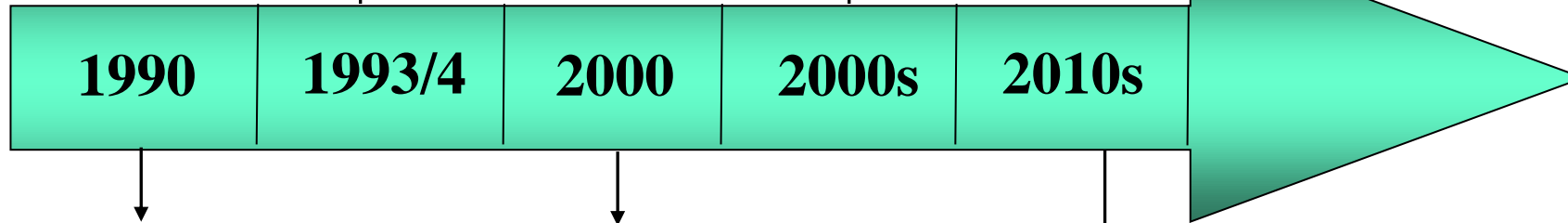
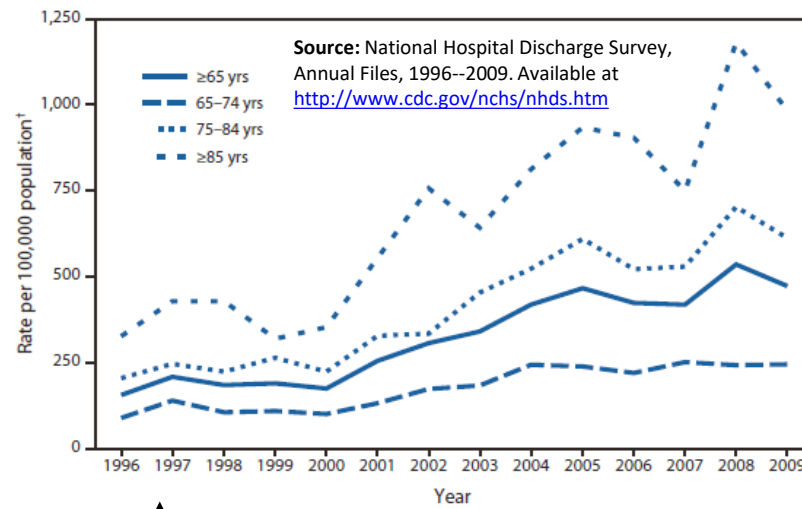


Fearless officer: Major Sam Weller, left, who was decorated for his bravery, is pictured with his brother Tony in 1947



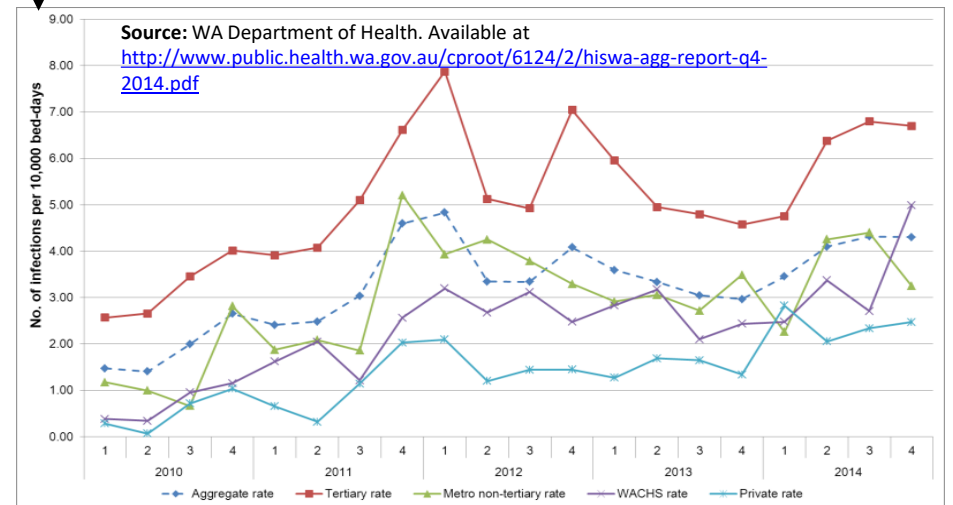


Ribotype 027 mutates to FQ resistance in 2 places independently (He *et al.* 2013)



Ceftiofur licensed for animal use in North America

Ceftiofur licensed for animal use in Australia



Emergence and spread of predominantly community-onset *Clostridium difficile* PCR ribotype 244 infection in Australia, 2010 to 2012

D W Eyre (david.eyre@ndm.ox.ac.uk)^{1,2,3}, **L Tracey**^{3,4}, **B Elliott**⁵, **C Slimings**⁴, **P G Huntington**⁶, **R L Stuart**⁷, **T M Korman**⁷, **G Kotsiou**⁶, **R McCann**⁴, **D Griffiths**¹, **W N Fawley**⁸, **P Armstrong**⁴, **K E Dingle**¹, **A S Walker**^{1,2}, **T E Peto**^{1,2}, **D W Crook**^{1,2}, **M H Wilcox**⁸, **T V Riley**^{5,9}

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7. Monash Infectious Diseases and Monash University, Clayton, Australia

8. Department of Microbiology, Old Medical School, Leeds Teaching Hospitals NHS Trust and University of Leeds, Leeds General Infirmary, Leeds, United Kingdom

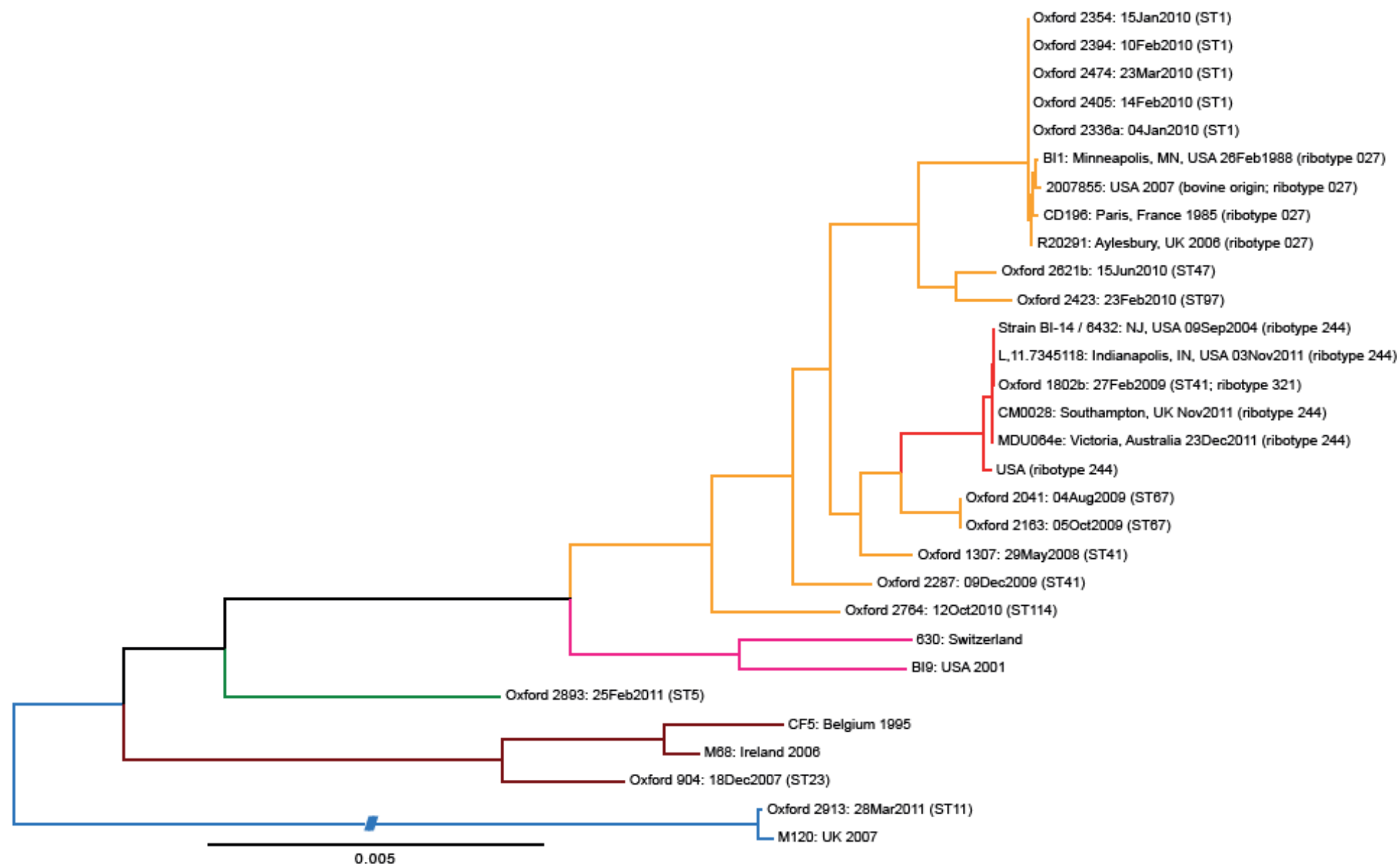
9. Microbiology and Infectious Diseases, PathWest Laboratory Medicine, Nedlands, Australia

Citation style for this article:

Eyre DW, Tracey L, Elliott B, Slimings C, Huntington PG, Stuart RL, Korman TM, Kotsiou G, McCann R, Griffiths D, Fawley WN, Armstrong P, Dingle KE, Walker AS, Peto TE, Crook DW, Wilcox MH, Riley TV. Emergence and spread of predominantly community-onset *Clostridium difficile* PCR ribotype 244 infection in Australia, 2010 to 2012. *Euro Surveill.* 2015;20(10):pii=21059. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21059>

FIGURE 4

Phylogenetic relationship of outbreak ribotype 244 lineage, Western Australia, October 2011–September 2012, to global *Clostridium difficile* diversity



C. difficile RT 244 Australia 2020/22



Substitutions per site: 10 

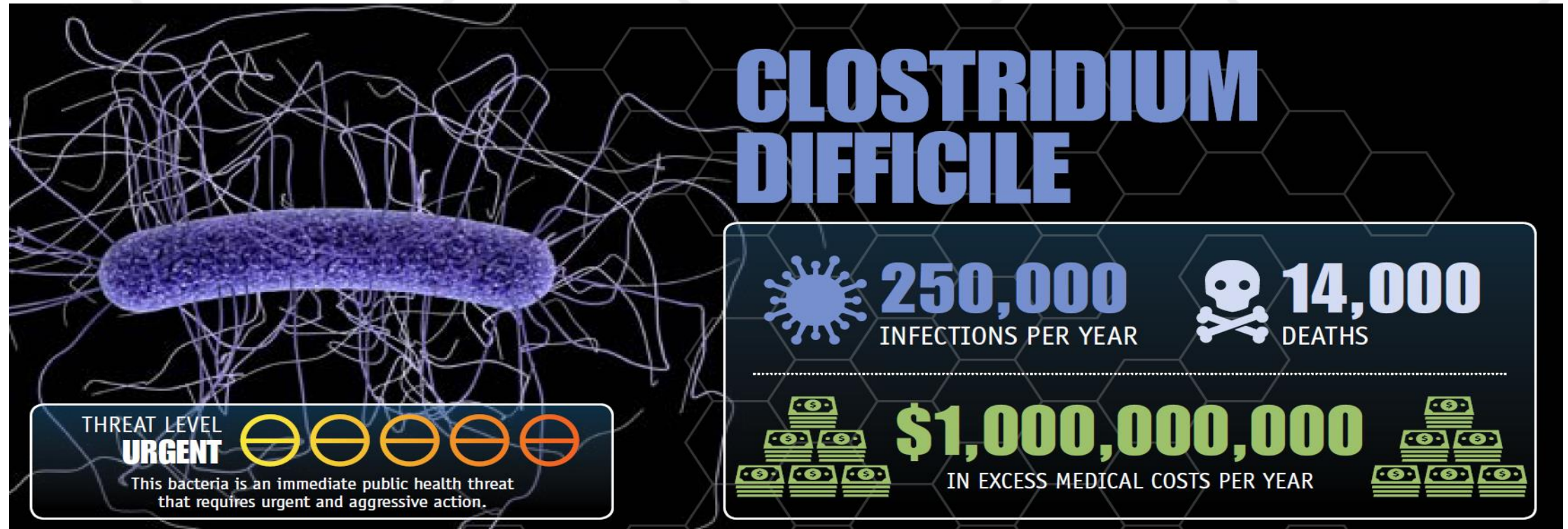
C. difficile RT 244 Australia 2020/22

[illegible]

Urgent Threats

Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States. Atlanta: CDC, 2013. Available at www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf

- *Clostridium difficile*
- Carbapenem-resistant Enterobacteriaceae (CRE)
- Drug-resistant *Neisseria gonorrhoeae*



Clostridium difficile (*C. difficile*) causes life-threatening diarrhea. These infections mostly occur in people who have had both recent medical care and antibiotics. Often, *C. difficile* infections occur in hospitalized or recently hospitalized patients.

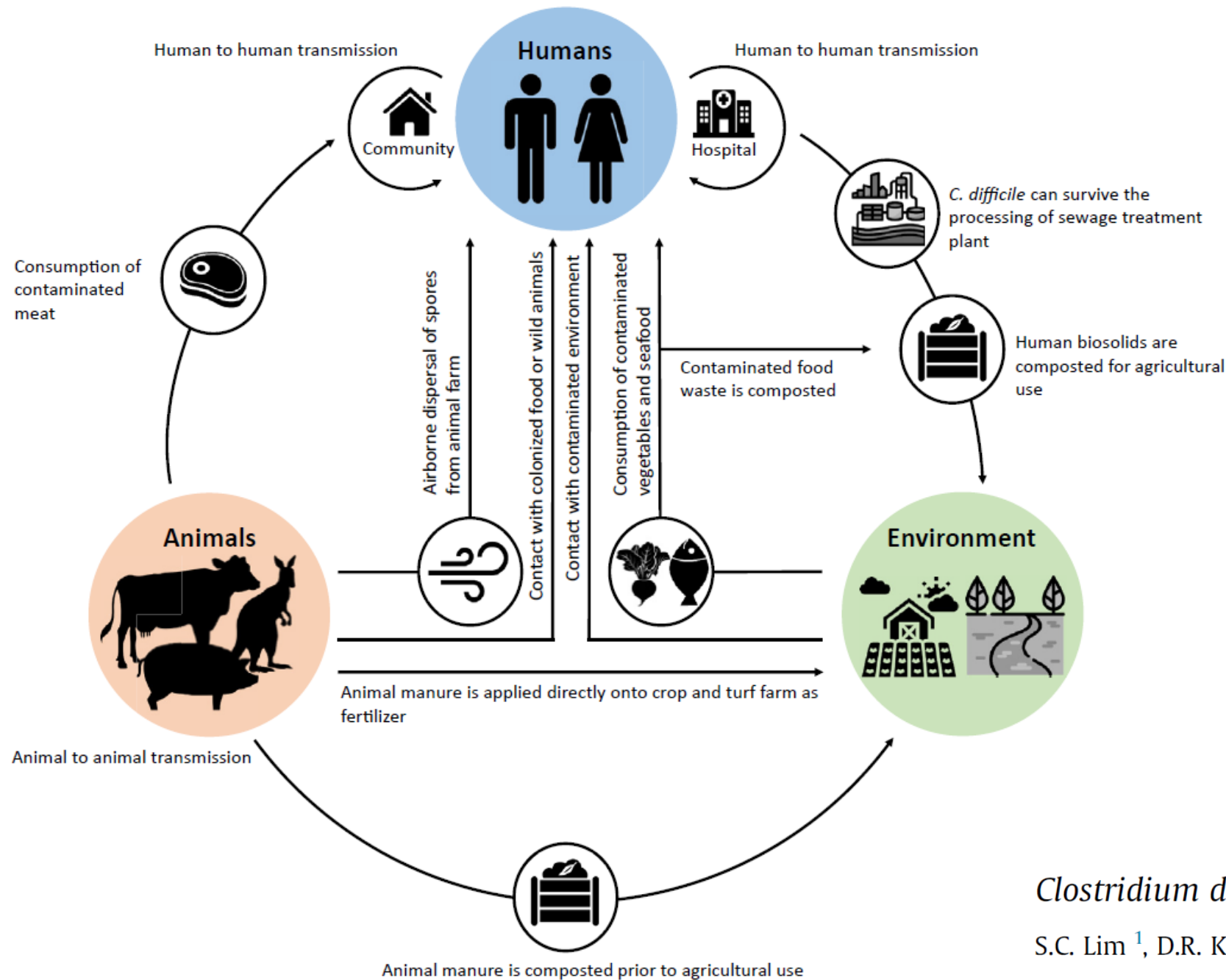


Fig. 2. Transmission of *Clostridium difficile*.

Clostridium difficile and One Health

S.C. Lim ¹, D.R. Knight ², T.V. Riley ^{1, 2, 3, 4, *}

Clin Microbiol Infect 2020;26:857

Lessons from Australia

CDI not a hospital issue anymore, it's a public health issue.

Many sources of *C. difficile* other than other patients.

Food important? (good evidence still lacking) or other factors more important (such as gardens/lawn in WA).

Each jurisdiction will need to look in its own back yard!

Anywhere there is animal manure there is a problem.

Antimicrobials in production animals are driving this problem.

Requires a One Health approach.