C.difficile Associated Disease: A Financial Burden Analysis

Dr. Ralf-Peter Vongerg, Hanover Medical School

A Webber Training Teleclass

C. difficile-associated diseases: A financial burden analysis

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Hannover Medical School

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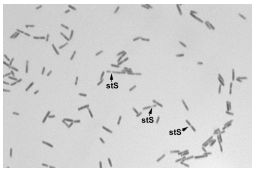
PART #1

Epidemiology of *C. difficile*-associated disease (CDAD)

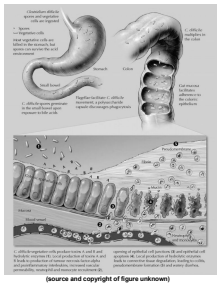
Clostridium difficile (CD)

- Gram positive rod
- anaerobic growth
- sub-terminal spores (stS)
- toxin production
  - toxin A (enterotoxin)
  - toxin B (cytotoxin)
- part of the normal gut flora



C. difficile-associated disease (CDAD)

- following antibiotic therapy
- numerous substances are CDAD-associated
- mild to severe diarrhea
- abdominal pain
- pseudomembranous colitis
- toxic megacolon
- ileus
- relapses occur frequently



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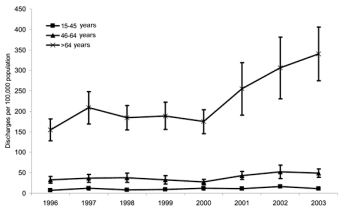
CDAD-associated antibiotics

- broad spectrum penicillins
- 3rd generation cephalosporins
- clindamycin
- fluorquinolones
- others

CDAD in the US (1996 – 2003)



Rates of US short-stay hospital discharges with *C. difficile* listed as any diagnosis.

McDonald Emerg.Infect.Dis. 2006; 12: 409

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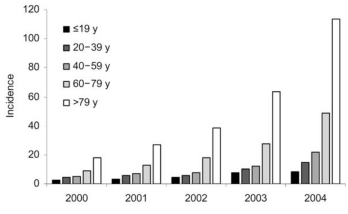
CDAD in Germany (2000 – 2004)



Incidence of Clostridium difficile–associated disease
per 100,000 inpatients upon discharge from hospitals in Germany.

Vonberg Emerg.Infect.Dis. 2007; 13: 179

A new and hypervirulent CD strain

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 8, 2005 VOL. 353 NO. 23

An Epidemic, Toxin Gene–Variant Strain of *Clostridium difficile*

L. Clifford McDonald, M.D., George E. Killgore, Dr.P.H., Angela Thompson, M.M.Sc., Robert C. Owens, Jr., Pharm.D., Sophia V. Kazakova, M.D., M.P.H., Ph.D., Susan P. Sambol, M.T., Stuart Johnson, M.D., and Dale N. Gerding, M.D.

McDonald N.Eng.J.Med. 2005; 353: 2433

A new and hypervirulent CD strain

- **toxinotype III**
- **North American PFGE type 1 (NAP1)**
- **PCR-ribotype 027**

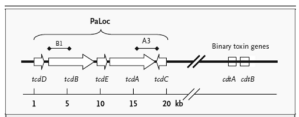
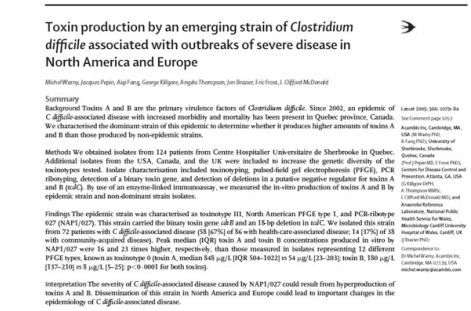


Figure 1. **Major Genes in the Pathogenicity Locus (PaLoc) of *Clostridium difficile* and Relation to the Genes for Binary Toxin.**

McDonald N.Eng.J.Med. 2005; 353: 2433

A new and hypervirulent CD strain



Toxin production by an emerging strain of *Clostridium difficile* associated with outbreaks of severe disease in North America and Europe

Michel Warny, Jacques Pepin, Alaji Fang, George Killgore, Angela Thompson, Jon Brazier, Eric Frost, L. Clifford McDonald

Summary

Background Toxins A and B are the primary virulence factors of *Clostridium difficile*. Since 2002, an epidemic of *C difficile*-associated disease with increased morbidity and mortality has been present in Quebec province, Canada. We characterised the dominant strain of this epidemic to determine whether it produces higher amounts of toxins A and B than those produced by non-epidemic strains.

Methods We obtained isolates from 124 patients from Centre Hospitalier Univ-ersitaire de Sherbrooke in Quebec. Additional isolates from the USA, Canada, and the UK were included to increase the genetic diversity of the toxinotypes tested. Isolate characterisation included toxinotyping, pulsed-field gel electrophoresis (PFGE), PCR ribotyping, detection of a binary toxin gene, and detection of deletions in a putative negative regulator for toxins A and B (tcdC). By use of an enzyme-linked immunoassay, we measured the in-vitro production of toxins A and B by epidemic strain and non-dominant strain isolates.

Findings The epidemic strain was characterised as toxinotype III, North American PFGE type 1, and PCR-ribotype 027 (NAP1/027). This strain carried the binary toxin gene *cdtB* and an 18-bp deletion in *tcdC*. We isolated this strain from 72 patients with *C difficile*-associated disease (58 [67%] of 86 with health-care-associated disease; 14 [17%] of 38 with community-acquired disease). Peak median (IQR) toxin A and toxin B concentrations produced in vitro by NAP1/027 were 16 and 23 times higher, respectively, than those measured in isolates representing 12 different PFGE types, known as toxinotype 0 (toxin A, median 8·45 μg/L [IQR 5·04–10·22] *vs* 54 μg/L [23–203]; toxin B, 150 μg/L [137–210] *vs* 5 μg/L [5–25]; p<0·0001 for both toxins).

Interpretation The severity of *C difficile*-associated disease caused by NAP1/027 could result from hyperproduction of toxins A and B. Dissemination of this strain in North America and Europe could lead to important changes in the epidemiology of *C difficile*-associated disease.

Lancet 2005; 366: 1079–84

See Comment page 1051
Acambis Inc, Cambridge, MA, USA (M Warny PhD, A Fang PhD); University of Sherbrooke, Sherbrooke, Quebec, Canada (Prof J Pepin MD, E Frost PhD); Centers for Disease Control and Prevention, Atlanta, GA, USA (G Killgore DrPH, A Thompson MMSc, L Clifford McDonald MD); and Anaerobe Reference Laboratory, National Public Health Service for Wales, Microbiology Cardiff University Hospital of Wales, Cardiff, UK (J Brazier PhD)
Correspondence to:
Dr Michel Warny, Acambis Inc, Cambridge, MA 02139, USA
michel.warny@acambis.com

Warny Lancet 2005; 366:1079

A new and hypervirulent CD strain

- **toxin production ⇧**
  - **toxin A peak: ~ 16-fold**
  - **toxin B peak: ~ 23-fold**
- **18-bp *tcdC* deletion**
- **binary toxin**

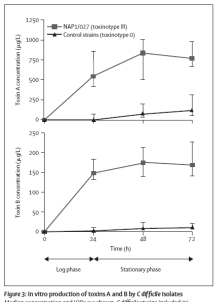


Figure 3: **In vitro production of toxins A and B by *C difficile* isolates**
Median concentration and IQRs are shown. *C difficile* strains included 25 toxinotype 0 and 15 NAP1/027 strains (toxinotype III) from various locations.

Warny Lancet 2005; 366:1079

PART #2

Financial burden of CDAD

A) in Hannover Medical School
B) in other health care settings

C.difficile Associated Disease: A Financial Burden Analysis

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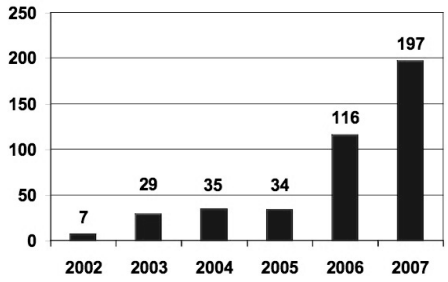
Hannover Medical School

Hannover Medical School

- tertiary care university hospital
- 1,419 beds, 75 wards, 18 medical departments
- total # of patients per year
  - inpatients: 53,000
  - outpatients: 323,300
- total # of transplantations per year
  - bone marrow TX: 200
  - solid organ TX: 440 (thereof 100 lung TX)

CDAD in Hannover Medical School



CDAD in Hannover Medical School

Journal of Hospital Infection (2008) 70, 15–20
Available online at www.sciencedirect.com
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www.elsevierhealth.com/journals/jhin

Costs of nosocomial *Clostridium difficile*-associated diarrhoea

R.-P. Vonberg [a,*], C. Reichardt [a], M. Behnke [b], F. Schwab [b], S. Zindler [c], P. Gastmeier [a]

[a] *Institute for Medical Microbiology and Hospital Epidemiology, Medical School Hannover, Hannover, Germany*
[b] *Institute for Hygiene and Environmental Medicine, Charité – University Medicine Berlin, Berlin, Germany*
[c] *Financial Controlling, Medical School Hannover, Hannover, Germany*

Aim of the present study

To determine the excess costs for patients who acquire nosocomial CDAD during stay in Hannover Medical School.

Methods

- matched case-control study (ratio 1:3)
- matching criteria
  - severity of underlying disease
  - time at risk

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Definition of a CDAD case

- inpatient of Hannover Medical School between January 1st and December 31st 2006
- onset of CDAD symptoms (diarrhea) >72 hours after admission to the hospital
- detection of CD in stool samples by either
  - positive toxin A / toxin B ELISA or
  - culturing of a toxin-producing CD strain

Definition of a control patient

- inpatient in our facility in the same year
- diagnosis related group (DRG) must exactly match the corresponding CDAD case
- length of hospital stay (LOS) ≥ CDAD case
- at no time any signs or symptoms of CDAD
- Charlson co-morbidity index ± 1

Charlson co-morbidity index

Pergamon

J Clin Epidemiol Vol. 45, No. 11, pp. 1245-1251, 1994
0895-4356(94)00080-8

0895-4356/94 $7.00 + 0.00

VALIDATION OF A COMBINED COMORBIDITY INDEX

MARY CHARLSON,[1,2]* TED P. SZATROWSKI,[1,2] JANEY PETERSON[1,2] and JEFFREY GOLD[3]
[1]Clinical Epidemiology Unit, Department of Medicine, [2]Research Methodology Core, Cornell Arthritis and Musculoskeletal Disease Centre, Hospital for Special Surgery and [3]Department of Surgery, Cornell University Medical College, New York, NY 10021, U.S.A.

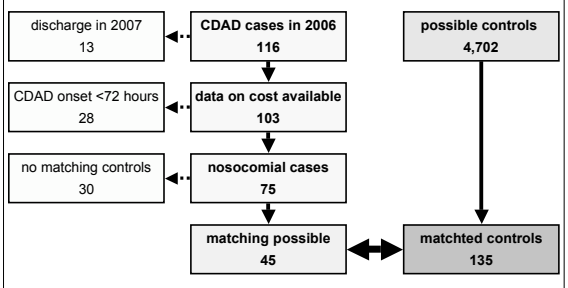
(Received 12 April 1994)

Abstract—The basic objective of this paper is to evaluate an age-comorbidity index in a cohort of patients who were originally enrolled in a prospective study to identify risk factors for peri-operative complications. Two-hundred and twenty-six patients were enrolled in the study. The participants were patients with hypertension or diabetes who underwent elective surgery between 1982 and 1985 and who survived to discharge. Two-hundred and eighteen patients survived until discharge. These patients were followed for at least five years post-operatively. The estimated relative risk of death for each comorbidity rank was 1.4 and for each decade of age was 1.4. When age and comorbidity were modelled as a combined age-comorbidity score, the estimated relative risk for each combined age-comorbidity unit was 1.45. Thus, the estimated relative risk of death from an increase of one in the comorbidity score proved approximately equal to that from an additional decade of age. The combined age-comorbidity score may be useful in some longitudinal studies to estimate relative risk of death from prognostic clinical covariates.

Charlson co-morbidity index

- first published 1980 by Mary E. Charlson as a marker for the mortality of breast cancer
- modified and validated for determining the mortality risk of additional diseases
- takes into account
  - underlying diseases (DRGs and ICD-10 codes)
  - surgical procedures (OP codes) during stay
  - age of the patient

Results: Case finding



Results: Matching

	cases (n = 45)	controls (n = 135)	p-value
male gender (%)	24 (53.3%)	85 (63.0%)	0,292
age (median; years)	56	57	0,930
days before CDAD onset CDAD (median)	15	---	---
length of hospital stay (median; days)	27	20	0,006
length of ICU stay (median; days)	3	1	0,463
Charlson co-morbidity index	4	4	0,902

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Results: Overall costs for the hospital

180 patients

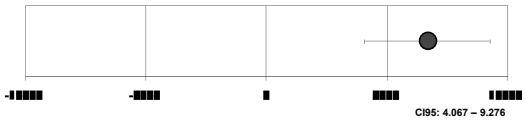
(45 cases & 135 controls)

€ 8,793,460

Results: cases vs. controls

	Fälle (n = 45)	Kontrollen (n = 135)
cost per patient (€)	53,995	47,138

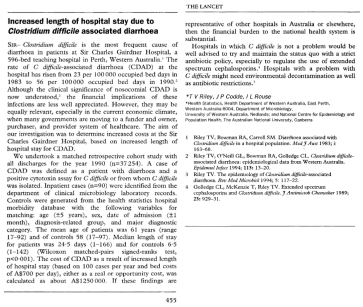
7,147 € excess costs* of CDAD cases (*significant difference) !



Results: cost vs. re-imbursement

	Fälle (n = 45)	Kontrollen (n = 135)
cost per patient (€)	53,995	47,138
re-imbursement per patient (€)	47,888	45,734
financial loss per patient (€)	6,107	1,404
financial loss per patient day (€)	165	51

Riley 1995



Increased length of hospital stay due to *Clostridium difficile* associated diarrhoea

Sir– *Clostridium difficile* is the most frequent cause of diarrhoea in patients at Sir Charles Gairdner Hospital, a 596-bed teaching hospital in Perth, Western Australia.[1] The rate of *C difficile*-associated diarrhoea (CDAD) at the hospital has risen from 23 per 100 000 occupied bed days in 1983 to 96 per 100 000 occupied bed days in 1990.[2] Although the clinical significance of nosocomial CDAD is now understood,[3] the financial implications of these infections are less well appreciated. However, they may be equally relevant, especially in the current economic climate, when many governments are moving to a funder and owner, purchaser, and provider system of healthcare. The aim of our investigation was to determine increased costs at the Sir Charles Gairdner Hospital, based on increased length of hospital stay for CDAD.

We undertook a matched retrospective cohort study with all discharges for the year 1990 (n=37 254). A case of CDAD was defined as a patient with diarrhoea and a positive cytotoxin assay for *C difficile* or from whom *C difficile* was isolated. Inpatient cases (n=90) were identified from the department of clinical microbiology laboratory records. Controls were generated from the health statistics hospital morbidity database with the following variables for matching: age (±5 years), sex, date of admission (±1 month), diagnosis-related group, and major diagnostic category. The mean age of patients was 61 years (range 17–92) and of controls 58 (17–97). Median length of stay for patients was 24·5 days (1–166) and for controls 6·5 (1–142) (Wilcoxon matched-pairs signed-ranks test, p<0·001). The cost of CDAD as a result of increased length of hospital stay (based on 100 cases per year and bed costs of A$700 per day), either as a real or opportunity cost, was calculated as about A$1 250 000. If these findings are

THE LANCET

representative of other hospitals in Australia or elsewhere, then the financial burden to the national health system is substantial.

Hospitals in which *C difficile* is not a problem would be well advised to try and maintain the status quo with a strict antibiotic policy, especially to regulate the use of extended spectrum cephalosporins.[4] Hospitals with a problem with *C difficile* might need environmental decontamination as well as antibiotic restrictions.[1]

T V Riley, J P Coddle, I L Rouse

Health Statistics, Health Department of Western Australia, East Perth, Western Australia 6004, Department of Microbiology, University of Western Australia, Nedlands, and National Centre for Epidemiology and Population Health, The Australian National University, Canberra

1 Riley TV, Bowman RA, Carroll SM. Diarrhoea associated with *Clostridium difficile* in a hospital population. *Med J Aust* 1983; i: 103–06.

2 Riley TV, O'Neill GL, Bowman RA, Golledge CL. *Clostridium difficile*-associated diarrhoea: preliminary national data from Western Australia. *Epidemiol Infect* 1994; 113: 15–20.

3 Riley TV. The epidemiology of *Clostridium difficile*-associated diarrhoea. *Rev Med Microbiol* 1994; 5: 117–25.

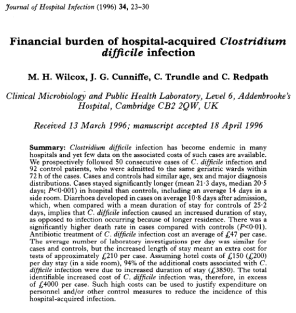
4 Golledge CL, McKenzie T, Riley TV. Expanded spectrum cephalosporins and *Clostridium difficile*. *J Antimicrob Chemother* 1995; 25: 929–31.

455

Riley 1995

- **teaching hospital, Perth, Australia**
- **retrospective matched cohort study (1990)**
- **n = 90 CDAD cases**
- **n = ? control patients (n.m.)**
- **mean LOS (day) cases = 24.5 vs. controls = 6.5**
- **costs attributable to CDAD: A$ 12,600**

Wilcox 1996



Journal of Hospital Infection (1996) **34**, 23–30

Financial burden of hospital-acquired *Clostridium difficile* infection

M. H. Wilcox, J. G. Cunniffe, C. Trundle and C. Redpath

Clinical Microbiology and Public Health Laboratory, Level 6, Addenbrooke's Hospital, Cambridge CB2 2QW, UK

Received 13 March 1996; manuscript accepted 18 April 1996

Summary: *Clostridium difficile* infection has become endemic in many hospitals and yet few data on the associated costs of such cases are available. We prospectively followed 50 consecutive cases of *C. difficile* infection and 92 control patients, who were admitted to the same geriatric wards within 72 h of the cases. Cases and controls had similar age, sex and major diagnosis distributions. Cases stayed significantly longer (mean 21·3 days, median 20·5 days; $P<0·001$) in hospital than controls, including an average 14 days in a side room. Diarrhoea developed in cases on average 10·8 days after admission, which, when compared with a mean duration of stay for controls of 23·2 days, implies that *C. difficile* infection caused an increased duration of stay, as opposed to infection occurring because of longer residence. There was a significantly higher death rate in cases compared with controls ($P<0·01$). Antibiotic treatment of *C. difficile* infection cost an average of £47 per case. The average number of laboratory investigations per day was similar for cases and controls, but the increased length of stay meant an extra cost for tests of approximately £210 per case. Assuming hotel costs of £150 (£200 per day stay (in a side room), 94% of the additional costs associated with *C. difficile* infection were due to increased duration of stay (£3850). The total identifiable increased cost of *C. difficile* infection was, therefore, in excess of £4000 per case. Such high costs can be used to justify expenditure on personnel and/or other control measures to reduce the incidence of this hospital-acquired infection.

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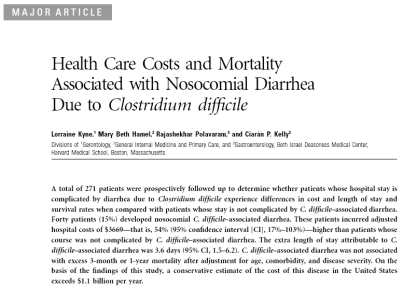
Wilcox 1996

- university hospital, Cambridge, UK
- matched case-control study (12/94 – 06/95)
- n = 50 CDAD cases
- n = 92 control patients
- mean LOS (day) cases = 46.5 vs. controls = 25.2
- costs attributable to CDAD: £ 4,107

Kyne 2002



MAJOR ARTICLE

Health Care Costs and Mortality Associated with Nosocomial Diarrhea Due to *Clostridium difficile*

Lorraine Kyne,[1] Mary Beth Hamel,[2] Rajashekhar Polavaram,[3] and Ciarán P. Kelly[3]

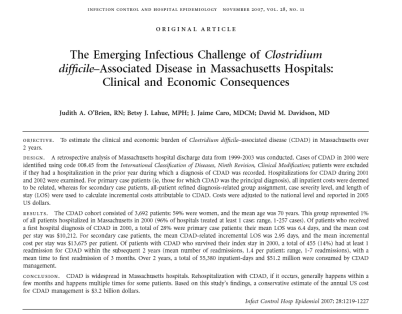
Divisions of [1]Gerontology, [2]General Internal Medicine and Primary Care, and [3]Gastroenterology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts

A total of 271 patients were prospectively followed up to determine whether patients whose hospital stay is complicated by diarrhea due to *Clostridium difficile* experience differences in cost and length of stay and survival rates when compared with patients whose stay is not complicated by *C. difficile*–associated diarrhea. Forty patients (15%) developed nosocomial *C. difficile*–associated diarrhea. These patients incurred adjusted hospital costs of $3669—that is, 54% (95% confidence interval [CI], 17%–103%)—higher than patients whose course was not complicated by *C. difficile*–associated diarrhea. The extra length of stay attributable to *C. difficile*–associated diarrhea was 3.6 days (95% CI, 1.5–6.2). *C. difficile*–associated diarrhea was not associated with excess 3-month or 1-year mortality after adjustment for age, comorbidity, and disease severity. On the basis of the findings of this study, a conservative estimate of the cost of this disease in the United States exceeds $1.1 billion per year.

Kyne 2002

- university hospital, Boston, US
- prospective cohort study (01/98 – 05/98)
- n = 40 CDAD cases
- n = 224 control patients
- median LOS (day) cases = 12 vs. controls = 5
- costs attributable to CDAD: US$ 3,669

O´Brien 2007



INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY NOVEMBER 2007, VOL. 28, NO. 11

ORIGINAL ARTICLE

The Emerging Infectious Challenge of *Clostridium difficile*–Associated Disease in Massachusetts Hospitals: Clinical and Economic Consequences

Judith A. O'Brien, RN; Betsy J. Lahue, MPH; J. Jaime Caro, MDCM; David M. Davidson, MD

OBJECTIVE. To estimate the clinical and economic burden of *Clostridium difficile*–associated disease (CDAD) in Massachusetts over 2 years.

DESIGN. A retrospective analysis of Massachusetts hospital discharge data from 1999-2003 was conducted. Cases of CDAD in 2000 were identified using code 008.45 from the *International Classification of Diseases, Ninth Revision, Clinical Modification*; patients were excluded if they had a hospitalization in the prior year during which a diagnosis of CDAD was recorded. Hospitalizations for CDAD during 2001 and 2002 were examined. For primary case patients (ie, those for which CDAD was the principal diagnosis), all inpatient costs were deemed to be related, whereas for secondary case patients, all-patient refined diagnosis-related group assignment, case severity level, and length of stay (LOS) were used to calculate incremental costs attributable to CDAD. Costs were adjusted to the national level and reported in 2005 US dollars.

RESULTS. The CDAD cohort consisted of 3,692 patients; 59% were women, and the mean age was 70 years. This group represented 1% of all patients hospitalized in Massachusetts in 2000 (96% of hospitals treated at least 1 case; range, 1–257 cases). Of patients who received a first hospital diagnosis of CDAD in 2000, a total of 28% were primary case patients their mean LOS was 6.4 days, and the mean cost per stay was $10,212. For secondary case patients, the mean CDAD-related incremental LOS was 2.95 days, and the mean incremental cost per stay was $13,675 per patient. Of patients with CDAD who survived their index stay in 2000, a total of 455 (14%) had at least 1 readmission for CDAD within the subsequent 2 years (mean number of readmissions, 1.4 per patient; range, 1–7 readmissions), with a mean time to first readmission of 3 months. Over 2 years, a total of 55,380 inpatient-days and $51.2 million were consumed by CDAD management.

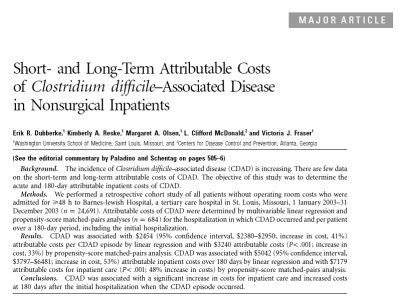
CONCLUSION. CDAD is widespread in Massachusetts hospitals. Rehospitalization with CDAD, if it occurs, generally happens within a few months and happens multiple times for some patients. Based on this study's findings, a conservative estimate of the annual US cost for CDAD management is $3.2 billion dollars.

Infect Control Hosp Epidemiol 2007; 28:1219-1227

O´Brien 2007

- 77 acute care hospitals, Massachusetts, US
- retrospective cohort study (2000)
- n = 3,692 CDAD cases
- n ~ 450,000 control patients
- mean LOS (day) cases = 13 vs. controls = n.m.
- costs attributable to CDAD: US$ 12,705

Dubberke 2008



MAJOR ARTICLE

Short- and Long-Term Attributable Costs of *Clostridium difficile*–Associated Disease in Nonsurgical Inpatients

Erik R. Dubberke,[1] Kimberly A. Reske,[1] Margaret A. Olsen,[1] L. Clifford McDonald,[2] and Victoria J. Fraser[1]

[1]Washington University School of Medicine, Saint Louis, Missouri; and [2]Centers for Disease Control and Prevention, Atlanta, Georgia

(See the editorial commentary by Paladino and Schentag on pages 505–6)

Background. The incidence of *Clostridium difficile*–associated disease (CDAD) is increasing. There are few data on the short-term and long-term attributable costs of CDAD. The objective of this study was to determine the acute and 180-day attributable inpatient costs of CDAD.

Methods. We performed a retrospective cohort study of all patients without operating room costs who were admitted for ≥48 h to Barnes-Jewish Hospital, a tertiary care hospital in St. Louis, Missouri, 1 January 2003–31 December 2003 (*n* = 24,691). Attributable costs of CDAD were determined by multivariable linear regression and propensity-score matched-pairs analyses (*n* = 684) for the hospitalization in which CDAD occurred and per patient over a 180-day period, including the initial hospitalization.

Results. CDAD was associated with $2454 (95% confidence interval, $2380–$2950; increase in cost, 41%) attributable costs per CDAD episode by linear regression and with $3240 attributable costs (*P* < .001; increase in cost, 33%) by propensity-score matched-pairs analysis. CDAD was associated with $5042 (95% confidence interval, $3797–$6481; increase in cost, 53%) attributable inpatient costs over 180 days by linear regression and with $7179 attributable costs for inpatient care (*P* < .001; 48% increase in costs) by propensity-score matched-pairs analysis.

Conclusions. CDAD was associated with a significant increase in costs for inpatient care and increased costs at 180 days after the initial hospitalization when the CDAD episode occurred.

C.difficile Associated Disease: A Financial Burden Analysis

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Dubberke 2008

- tertiary care hospital, St. Louis, US
- retrospective cohort study (01/03 – 12/03)
- n = 439 CDAD cases
- n = 24,252 control patients
- median LOS (day) cases = 10 vs. controls = 4
- costs attributable to CDAD: US$ 9,085

Dubberke Clin.Infect.Dis. 2008; 46: 497

Financial burden of CDAD

	excess cost of CDAD cases	= US$ (in study year)
Riley 1995	A$ 12,600	9,366
Wilcox 1996	£ 4,107	6,393
Kyne 2002	US$ 3,669	3,669
O´Brien 2007	US$ 12,705	12,705
Dubberke 2008	US$ 9,085	9,085
Vonberg 2008	€ 7.147	8,283

Suggested reading

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY JANUARY 2009, VOL. 30, NO. 1

REVIEW ARTICLE

Review of Current Literature on the Economic Burden of *Clostridium difficile* Infection

Erik R. Dubberke, MD; Albert I. Wertheimer, PhD, MBA

Clostridium difficile is well recognized as the most common infectious cause of healthcare-associated diarrhea. Since 2000, this pathogen has demonstrated an increased propensity to cause more frequent and virulent illness that is often refractory to treatment. An analysis by the Centers for Disease Control and Prevention revealed that, in the United States, the number of patients discharged from hospitals who received the *International Classification of Diseases, Ninth Revision* discharge diagnosis code for *C. difficile* infection (CDI) more than doubled from 2000 to 2003. Unpublished data indicate that this trend has continued and that more than 250,000 US hospitalizations were associated with CDI in 2005. A previously uncommon hypervirulent strain of *C. difficile* is thought to contribute, in part, to the dramatic increase in the incidence and severity of the infection. Although the economic impact of the disease is believed to be profound and is expected to increase, data on the costs associated with CDI are scarce. To more completely assess its economic burden, we performed a review of available literature that reported costs associated with the infection.

Infect Control Hosp Epidemiol 2009; 30:57-66

Dubberke Inf.Control.Hosp.Epi. 2009; 30: 57

PART #3

Infection control for the prevention of CDAD

ECDC guidance document

European Centre for Disease Prevention and Control

"Basic Guideline"

ECDC guidance document

Infection control measures to limit the spread of *Clostridium difficile*

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Vonberg Clin.Microbiol.Infect. 2008; 14: 2

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Categories of recommendation

IA Strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies.

IB Strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies and a strong theoretical rationale.

II Suggested for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale.

? Unresolved issue. Practices for which insufficient evidence or no consensus regarding efficacy exists.

screening | surveillance | education of staff | isolation procedures | hand hygiene | protective clothing | environmental cleaning | medical devices | antimicrobial treatment | nosocomial outbreaks

1. **Promptly perform tests for CD toxins (± the bacterium) in stool specimens in each case of nosocomial diarrhea and for individuals who are admitted with diarrhea acquired outside the hospital. Stop repeated testing of diarrheal stool samples as soon as CD has been diagnosed. Only when a recurrence of CDAD is suspected, repeat the CD testing and exclude other potential causes of diarrhea.** — IB
2. **Perform tests for CD or its toxins only on diarrheal (unformed) stool specimens, unless ileus is present. Testing of stool specimens from asymptomatic patients is not recommended.** — IB
3. **Do not perform a 'test of cure' after treatment.** — IA
4. **Fecal samples from all CDAD cases, and especially patients (a) with severe CDAD (e.g., leading to admission to intensive care unit, undergoing colectomy, or fatal cases), or (b) in an outbreak situation, should be stored so that typing can be performed, if necessary, retrospectively.** — IB

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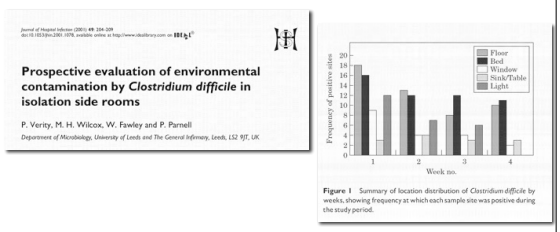
1. **Ensure routine surveillance of CDAD should be carried out routinely in hospitals.** — IB
2. **Determine the unit-specific baseline incidence of CDAD by reviewing results of fecal toxin tests or CD cultures.** — IB
3. **Define a threshold incidence or frequency of CDAD that would trigger implementation of additional control interventions.** — IB
4. **Ensure appropriate and prompt diagnostic testing of patients with an acute diarrheal illness not otherwise explained (especially with diarrhea associated with antimicrobial therapy).** — IB
5. **Be alert for changes in the rate, complications (including recurrences) or severity of CDAD that may indicate the introduction of new strain(s).** — ?

screening | surveillance | education of staff | isolation procedures | hand hygiene | protective clothing | environmental cleaning | medical devices | antimicrobial treatment | nosocomial outbreaks

1. **Everyone who enters a patient's room / environment, including healthcare workers and visitors, should be educated about the clinical features, transmission and epidemiology of CDAD.** — IA

Contamination of the patient's room



Prospective evaluation of environmental contamination by *Clostridium difficile* in isolation side rooms

P. Verity, M. H. Wilcox, W. Fawley and P. Parnell

Department of Microbiology, University of Leeds and The General Infirmary, Leeds, LS2 9JT, UK.

Figure 1 Summary of location distribution of *Clostridium difficile* by weeks, showing frequency at which each sample site was positive during the study period.

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1. Patients with CDAD represent a source for pathogen spread to others and should be isolated in single rooms whenever possible. **IB**
2. A designated toilet or commode (transportable toilet) for CDAD patients should be provided. **IB**
3. If isolation in single rooms is not possible, isolation in cohorts should be undertaken. If there is a lack of capacity, then consideration should be given to using a designated ward or unit for cohort isolation. **IB**
4. Cohorted patients should be managed by designated staff to minimize the risk of cross-infection to other patients. **IB**
5. Isolation precautions may be discontinued 48 h after symptomatic CDAD has resolved and bowel movements have returned to normal. **II**

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1. Besides the use of gloves, meticulous hand washing with soap and water is recommended for all staff after contact with body substances, or following any other potential contamination of hands when caring for known CDAD patients. The physical action of rubbing and rinsing is the only way to remove spores from hands. Washing of hands using water and soap is also recommended after the removal of gloves or aprons used during contact with individual patients. **IB**
2. There is no recommendation for the use of a soap that contains antiseptic substances. **?**
3. Alcohol-based hand rub should not be the only hand hygiene measure when caring for suspected or proven CD positive patients. **IB**

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Alcohol does not kill bacterial spores

650 INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY July 2005

REDUCTION IN NOSOCOMIAL TRANSMISSION OF DRUG-RESISTANT BACTERIA AFTER INTRODUCTION OF AN ALCOHOL-BASED HANDRUB

TABLE 2
CHANGE IN RATES OF NOSOCOMIAL ISOLATES OF DRUG-RESISTANT BACTERIA FOLLOWING IMPLEMENTATION OF THE ALCOHOL-BASED HANDRUB

	1998	1999	2000	Mean 3-Year Rate per 10,000 Patient Care–Days	2001*	2002	2003	Mean 3-Year Rate per 10,000 Patient Care–Days	P†
No. of patient care–days	92,583	87,888	84,960		81,329	83,877	83,115		
No. of new, nosocomial isolates for inpatients									
Staphylococcus aureus	66	99	59	8.44	61	52	44	6.32	.005
VRE	40	37	38	4.33	26	17	18	2.46	.001
Clostridium difficile	24	32	30	3.24	30	28	20	3.38	.78

VRE = vancomycin-resistant *Enterococcus*.
*Alcohol-based handrub implemented.
†P value of change in rate.

no alcohol → alcohol

Gordin Inf.Control.Hosp.Epi. 2005; 26: 650

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1. Healthcare workers should wear gloves for contact with a CDAD patient; this includes contact with body substances, and / or potentially contaminated environment (including the immediate vicinity of the patient). **IB**
2. Gowns or aprons should always be used for managing patients who have diarrhea. **IB**

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1. Regular environmental disinfection of rooms of CDAD patients should be done using sporocidal agents, ideally chlorine-containing agents (at least 1,000 p.p.m. available chlorine). The choice of cleaning regimen will depend on local policy. **IB**
2. Hospital wards should be cleaned regularly (at least once a day), concentrating on frequently touched surfaces. **IB**
3. Cleaning staff should be notified immediately when environmental fecal soiling has occurred. Cleaning needs to be done as soon as possible. **IB**
4. Toilets and items such as commodes and bed pans, which are likely to be fecally contaminated, are important sources of CD spores and must therefore be cleaned scrupulously. Cleaned commodes and bed pans should be stored under dry conditions. **IB**
5. After discharge of a CDAD patient, rooms must be cleaned and disinfected thoroughly. **IB**

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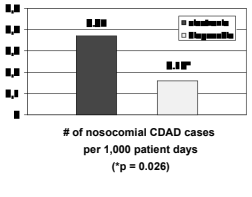
Use of different types of thermometers

494 INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY July 1998

A RANDOMIZED CROSSOVER STUDY OF DISPOSABLE THERMOMETERS FOR PREVENTION OF *CLOSTRIDIUM DIFFICILE* AND OTHER NOSOCOMIAL INFECTIONS



# of nosocomial CDAD cases per 1,000 patient days (*p = 0.026)

Gordin Inf.Control.Hosp.Epi. 1998; 19: 494

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1. **Medical devices such as blood pressure cuffs should be dedicated to a single patient.** IB
2. **All equipment should carefully be cleaned and disinfected using a sporocidal agent immediately after use on a CDAD case.** IB
3. **Thermometers should not be shared and use of electronic thermometers with disposable sheaths should be avoided.** IA
4. **The use of disposable materials should be considered whenever possible.** IB

ESCMID CD treatment guideline

European Society for Clinical Microbiology and Infectious Diseases (ESCMID) Guidance Document of *Clostridium difficile* infection (CDI) diagnosis and treatment: Treatment Guideline

Martijn P. Bauer, Ed J. Kuijper, Jaap T. van Dissel. On behalf of the CDI Guidance Document Executive Committee: Martijn Bauer, Emilio Bouza, Lars Burman, Jaap van Dissel, Anne Gilleece, Benoit Guery, Michel Delmée, Ed Kuijper, Zoltán Maszárovics, Andreas Widmer, Mark Wilcox

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Final version (October 2008)

Submitted to Clin.Microbiol.Infect.

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1. **Stop any (non-CD) antimicrobial treatment in a patient with CDAD as soon as possible.** IA

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1. **Infection control staff should always be informed when there is an increased number or severity of CDAD cases.** IB
2. **All hygiene measures should be reinforced in case of a CDAD outbreak.** IB
3. **Review the standard of environmental cleaning to ensure high quality and frequency of decontamination. If possible, implement a designated and well-educated cleaning team especially for the rooms of CDAD patients.** II
4. **Perform good antibiotic stewardship. Antimicrobial prescribing (frequency, duration, and types of agents) should be reviewed as soon as possible, with emphasis on avoiding the use of high-risk agents (e.g. cephalosporins, fluoroquinolones and clindamycin) in at-risk patients. Use these agents only when medically needed.** IB
5. **Fecal samples from all CDAD cases should be stored, so that they can be cultured, either locally or in a reference laboratory, and typing can performed, if necessary, retrospectively.** IB

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6. **In order to elucidate the epidemiology of CD, isolates from infected patients should ideally be compared by molecular methods.** II
7. **Implement interim policies for patient admissions, placement, and staffing as needed to prevent CD transmission.** IB
8. **For details on isolation procedures and dedicated nursing staff, please refer to the recommendations on isolation procedures.**
9. **When transmission continues despite the assignment of dedicated staff, close the unit or facility to new admissions.** IB
10. **When transmission continues despite all of the above measures (e.g. re-opened unit), vacate the unit for intensive environmental cleaning to eliminate all potential environmental reservoirs of CD.** II

Summary: CDAD …

- **… is a common nosocomial complication.**
- **… is a high economic burden for hospitals.**
- **… may be dangerous for affected patients.**
- **… requires appropriate infection control.**

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