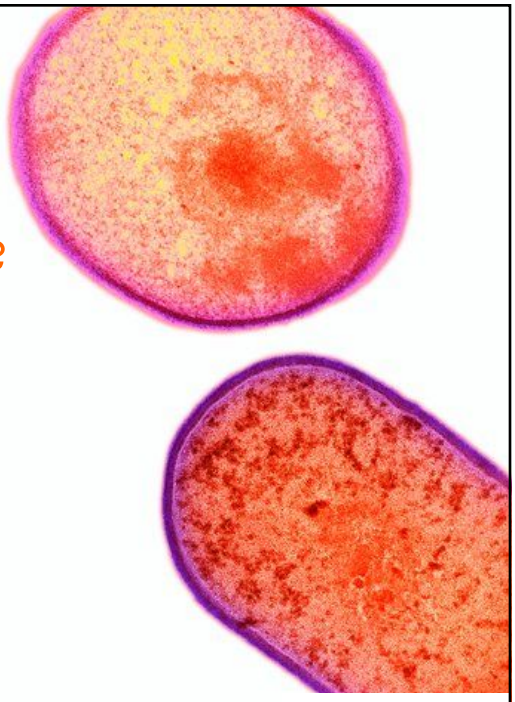
Clostridioides difficile Asymptomatic Carriers: Should We Care About Them?



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Hosted by Paul Webber
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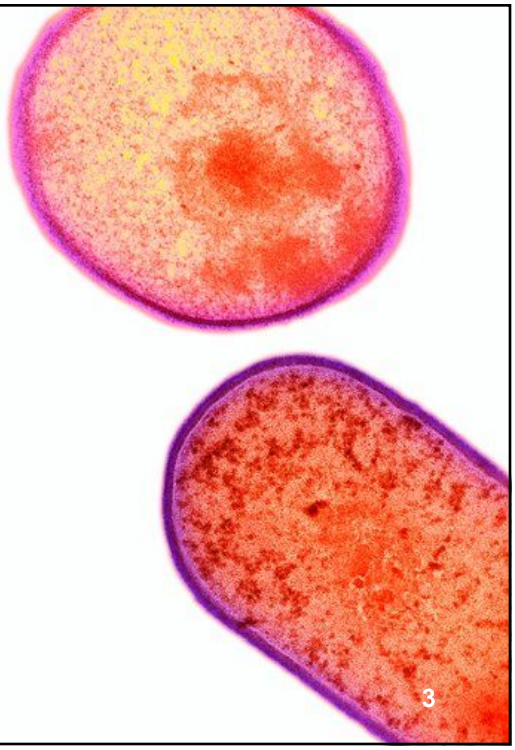
Disclosures

- Research Funding
  - Merck Canada, BD Diagnostics, Canadian Institute for Health Research
- Salary Support from the *Fonds de Recherche en Santé du Québec*

BACKGROUND



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Background

- *C. difficile* infections have become the most frequent cause of healthcare-associated infection in the USA[1-3]
- 500,000 cases per year[2]
- 29,000 deaths[2]
- $4.8 billion in excess medical costs[2]
- One of only 3 microorganisms designated as an "Urgent threat" to the population by CDC[3]

1. Leffler DA et al. N Engl J Med 2015;372:1539-48.
2. Lessa FC, et al. N Engl J Med 2015;372:825-34.
3. CDC ARO report Sept. 16, 2013.

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Evolution of CDI

A small victory

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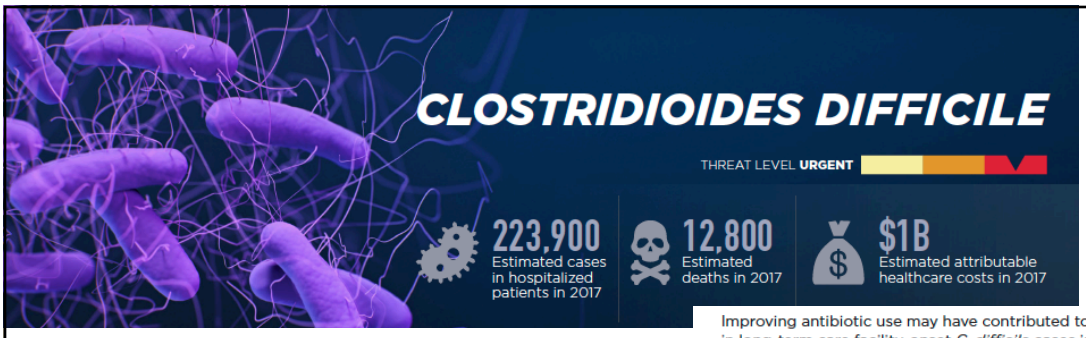
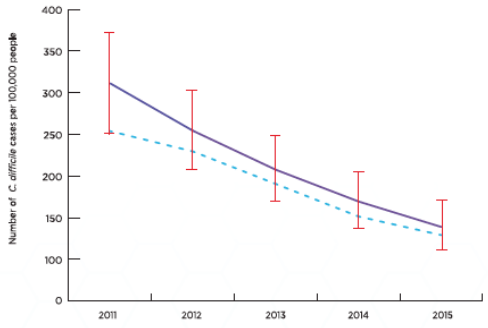


Improving antibiotic use may have contributed to the decrease in long-term care facility-onset *C. difficile* cases in 10 U.S. sites.



Adjusted cases for sex, race, and the percent of cases diagnosed by nucleic acid amplification test.

CDC 2019

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RESEARCH

The evolving epidemiology of *Clostridium difficile* infection in Canadian hospitals during a postepidemic period (2009–2015)

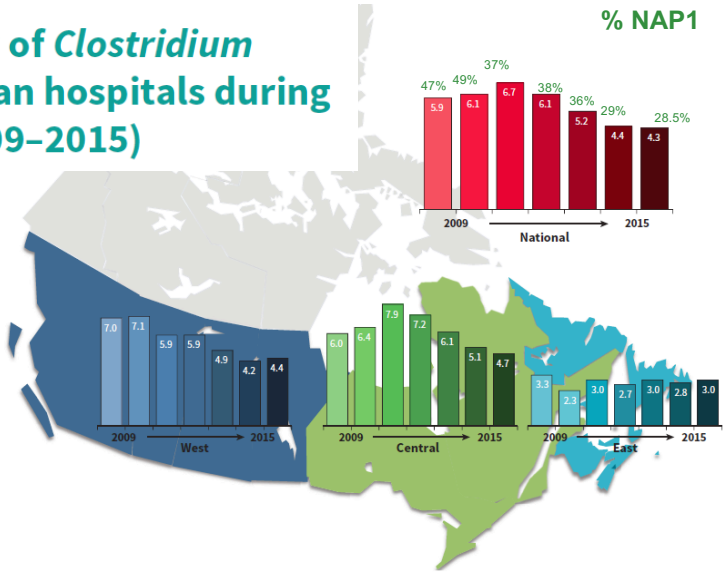

Figure 1: National (not including the territories) and regional rates of health care–associated *Clostridium difficile* infection in adults per 10 000 patient-days from 2009 to 2015. West = British Columbia, Alberta, Saskatchewan and Manitoba; central = Ontario and Quebec; east = Nova Scotia, New Brunswick, Prince Edward Island, and Newfoundland and Labrador.

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Katz K et al. CMAJ. 2018 Jun 25;190(25):E758-E765.

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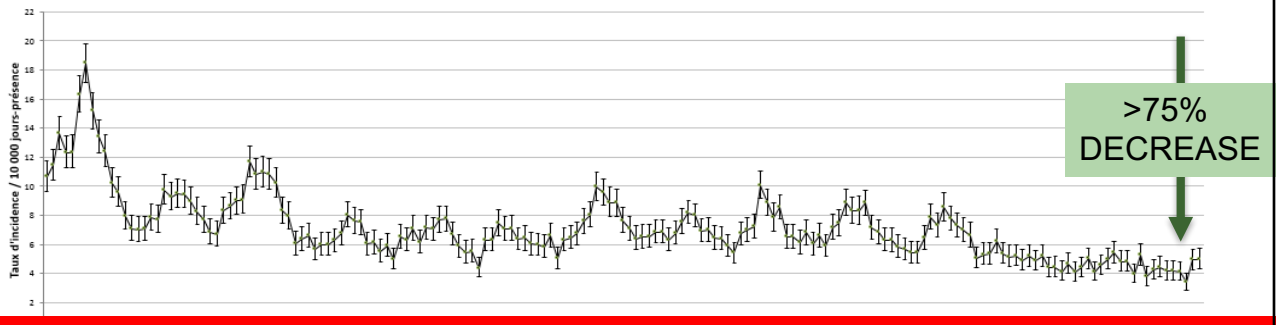
Figure 2 – Évolution des taux d'incidence des DACD nosocomiales (cat. 1a et 1b) pour les installations participantes (N = 94) [1] selon la période administrative, ensemble du Québec, 2004-2005 à 2017-2018 (taux d'incidence par 10 000 jours-présence [I.C. à 95 %])



Why embark in a ACDC screening and isolation program?
We already solved CDI!
No need to improve any further…

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Did we "solve" the CDI issue?

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Because CDI is a HUGE problem still

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Room for improvement

- 13% of U.S. hospitals have CDI rates significantly above average
- Even a decrease of an additional 25%-30% would lead to significant life savings
- How long should we go? Try to eliminate CDI

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https://gis.cdc.gov/grasp/PSA/HAIreport.html

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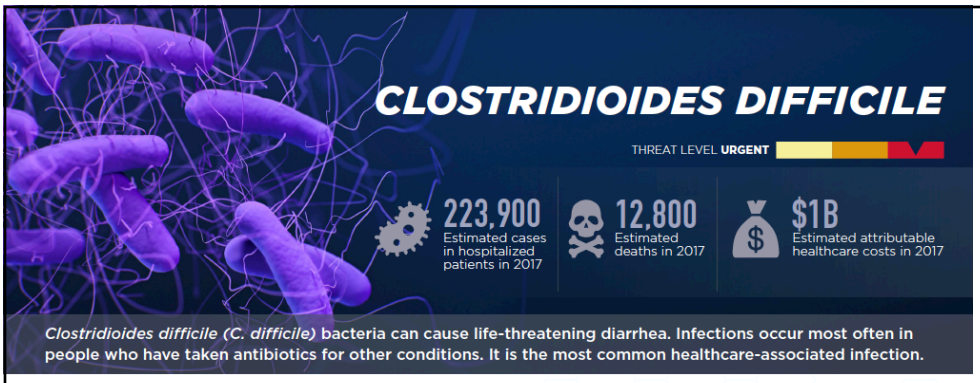


WHAT YOU NEED TO KNOW

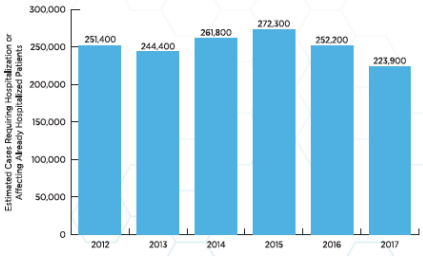
- While healthcare-associated *C. difficile* cases are decreasing, community-associated cases are not.
- Strategies to reduce *C. difficile* infections include improving antibiotic use, infection control, and healthcare facility cleaning and disinfection.
- *C. difficile* infections are more common and tend to be more severe in older patients.

Previously *Clostridium difficile*. Also called *C. diff*. Cost includes hospital-onset cases only.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

CASES OVER TIME

Continued appropriate infection control, antibiotic use, and diagnostic testing are important to maintain decreases in *C. difficile* cases.



CDC 2019

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- *C. difficile* infections burden
- ~~500,000~~ 200,000 cases per year[2]
- ~~29,000~~ 12,000 deaths[2]
- $4.8 billion in excess medical costs[2]

SSI:
157,000 cases;
4700 deaths (3% mortality)

CLABSI:
84,000-203,000 cases;
10,000-25,000 deaths

.

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https://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf
OntheCUSPStopHAI.org

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Prevention of CDI

- Current recommendations relatively unchanged for more than 20 years[1,2]
  - i.e. prior to the onset of the NAP1 epidemic

1. Dubberke ER, et al. Strategies to prevent Clostridium difficile infections: 2014 update. Infect Control Hosp Epidemiol 2014;35 Suppl 2:S48-65.
2. Vonberg RP, et al. Infection control measures to limit the spread of Clostridium difficile. Clin Microbiol Infect 2008;14 Suppl 5:2-20.

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Guidelines

- Measures recommended to prevent CDI
  - **Contact Precautions** for symptomatic patients
    - Only for duration of diarrhea
  - **Hand hygiene**
    - Hand washing in outbreak setting
  - **Environmental cleaning** with chlorine-based agent
  - **Optimization of antimicrobial use**
    - Minimize duration
    - Avoid high-risk drugs

Cohen, S.H., et al., Infect Control Hosp Epidemiol, 2010. **31**(5): p. 431-55.

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Guidelines

- Other Secondary Measures to prevent CDI
  - **Surveillance and feedback** of CDI incidence
  - **No touch disinfection systems**
    - As effective as hypochlorite (not more effective)
    - May be effective in reducing transmission
  - **Educate HCWs, patients and visitors** on how to prevent CDI

Cohen, S.H., et al., Infect Control Hosp Epidemiol, 2010. **31**(5): p. 431-55.
Tschudin-Sutter S et al. Clin Microbiol Infect 2018. 24(10): 1051-1054

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Guidelines

- Ot... Measures to prevent CDI
  - **Educate HCWs, patients and** ... nt CDI

Main Issues

Not based on strong evidence

Flawed: Allow for residual cross-transmission

Cohen, S.H., et al., Infect Control Hosp Epidemiol, 2010. **31**(5): p. 431-55.
Tschudin-Sutter S et al. Clin Microbiol Infect 2018. 24(10): 1051-1054

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Which component is most important?

Infection Control & Hospital Epidemiology (2020), **41**, 52–58
doi:10.1017/ice.2019.290

SHEA

Original Article

Correlation of prevention practices with rates of health care-associated *Clostridioides difficile* infection

Jackson S. Musuuza MBBS, MPH, PhD[1,2], Linda McKinley RN, BSN, MPH, CIC, FAPIC[1], Julie A. Keating PhD[1]
Chidi Obasi MD, PhD[2], Mary Jo Knobloch PhD, MPH[1,2], Christopher Crnich MD, PhD[1,2]
Charlesnika T. Evans PhD, MPH[3,4], Martin E. Evans[5,6]
Eli N. Perencevich MD, MS[7-9]
Katie J. Suda PharmD

Could not identify which component of CDI bundle were associated with lower CDI rates

Survey of 126 hospitals in VA system in the US 2017

Musuuza JS et al. Infect Control Hospit Epidemiol 2020 41(1): 52-58

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Current recommendations

- Current preventive recommendations focus mainly on patients with CDI, but are insufficient to interrupt the dissemination of this microorganism in healthcare settings[1,2]

1. Dubberke ER, et al. Strategies to prevent Clostridium difficile infections: 2014 update. Infect Control Hosp Epidemiol 2014;35 Suppl 2:S48-65.
2. Vonberg RP, et al. Infection control measures to limit the spread of Clostridium difficile. Clin Microbiol Infect 2008;14 Suppl 5:2-20.

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Cross-transmission in Acute Care

Asymptomatic colonization is frequent
during hospitalization in acute care settings

- **9.4%** (54/569) of patients during their hospital stay[1]
- **17%** acquired *C.difficile* during their hospitalization[2]
- **12%** of patients admitted on a geriatric unit[3]
- **8%** (6/76) during their hospital stay[4]
- **21%** (83/399) acquired *C. difficile* during their stay. A third progressed to CDI[5]
- Approximately **10%** after 21 days of hospitalisation[6]

1. Clabots CR. J Infect Dis 1992;166:561-7.
2. Kyne L. N Engl J Med 2000;342:390-7.
3. Rudensky B. Postgrad Med J 1993;69:45-7.
4. Bliss DZ. Ann Intern Med 1998;129:1012-9
5. McFarland LV. N Engl J Med 1989;320:204-10.
6. Loo V et al. N Engl J Med 365;18: 1693-1703

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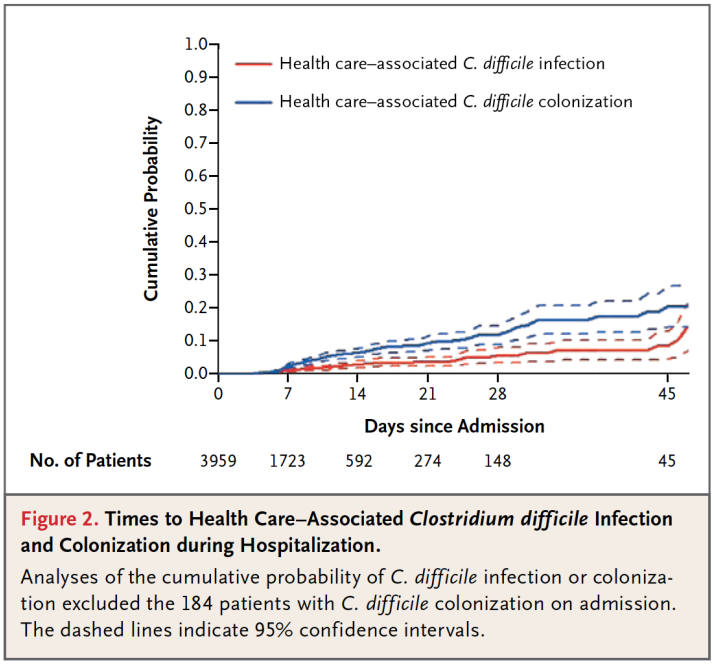
Ongoing Transmission in Quebec Hospitals



Loo V et al. N Engl J Med. 2011 Nov 3;365(18):1693-703.

Figure 2. Times to Health Care–Associated *Clostridium difficile* Infection and Colonization during Hospitalization.

Analyses of the cumulative probability of *C. difficile* infection or colonization excluded the 184 patients with *C. difficile* colonization on admission. The dashed lines indicate 95% confidence intervals.

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Ongoing Transmission in Quebec Hospitals

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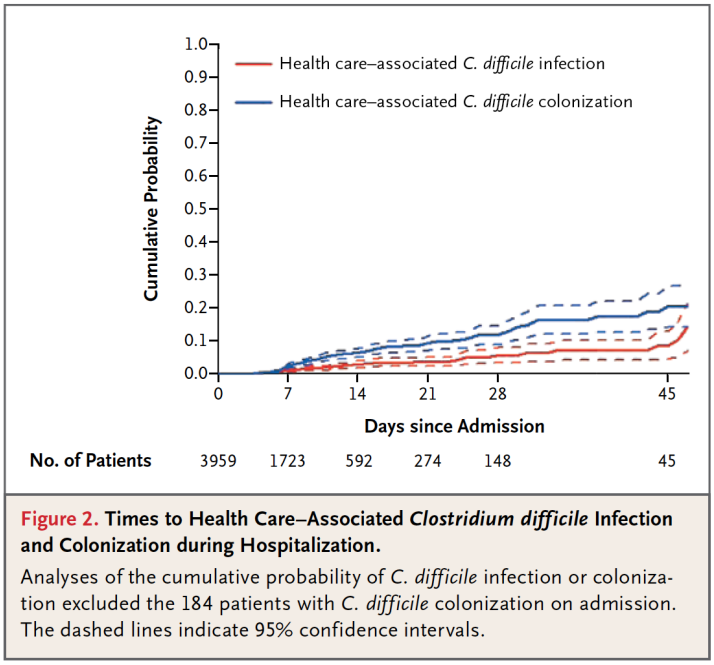

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Ongoing transmission
DESPITE isolation of patients with CDI as per GL

Source of residual transmission?

1. CDI "breakthrough" transmission?
2. Healthcare workers?
3. Food?
4. CD carriers?

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INFECTION CONTROL & HOSPITAL EPIDEMIOLOGY DECEMBER 2016, VOL. 37, NO. 12

ORIGINAL ARTICLE

An Evaluation of Food as a Potential Source for *Clostridium dif* Acquisition in Hospitalized Patients

Jennie H. Kwon, MSCI;[1] Cristina Lanzas, DVM, PhD;[2] Kimberly A. Reske, MPH;[1] Tiffany Hink, BS;[1] Sondra M. Sc
Kerry M. Bommarito, PhD;[1] Carey-Ann D. Burnham, PhD;[3] Erik R. Dubberke, MD, MSPH[1]

TABLE 3. Types of Food Positive for *Clostridium difficile*, by Food Type, for 910 Meals

Food item	Total	*C. difficile*, n (%)
Meat	308	0
Poultry	142	0
Fruit	179	0
Vegetables	455	1 (<1)[a]
Nuts	1	0
Dairy/eggs	210	0
Bread/grains	376	1 (<1)[a]
Other[b]	200	1 (1)[c]

NOT
tha
san
[a]Th
cor
[b]Fo
[c]Ge

STOCHASTIC MODELING: FOOD WOULD BE RESPONSIBLE FOR < 1 NEWLY COLONIZED PATIENT /1,000 ADMS.

2 patients had food + for CD
1 of 2 patients tested for CD at d/c and found negative

Kwon JH et al. Infect Control Hosp Epidemiol 2016;37:1401–1407

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Journal Pre-proof

Matching *Clostridioides difficile* strains obtained from shoe soles of healthcare workers epidemiologically linked to patients and confirmed by whole genome sequencing

Andrea C. Büchler, MD, Melanie Wicki, PhD, Reno Frei, MD, Vladimira Hinic, DVM PhD, Helena M.B. Seth-Smith, PhD, Adrian Egli, MD PhD, Andreas F. Widmer, MD MS

PII: S0195-6701(22)00131-1
DOI: https://doi.org/10.1016/j.jhin.2022.04.016
Reference: YJHIN 6657

To appear in: *Journal of Hospital Infection*

Received Date: 9 March 2022
Accepted Date: 27 April 2022

Unrecognized transmission?

- Observational study, Switzerland single center
- Culture of shoes twice per shift of HCWs caring for patients with C. difficile
- Comparison with patient's C. difficile strain
- RESULT: 17% of HCWs' shoes contaminated with C. difficile
  - 74% strain matching the patient's
  - A longer duration of care associated with greater odds of matching isolates between shoes and patient strain (100 min vs 70 min, p=0.007)

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Buchler AC et al. J Hosp Infect. 2022 May 10;S0195-6701(22)00131-1.

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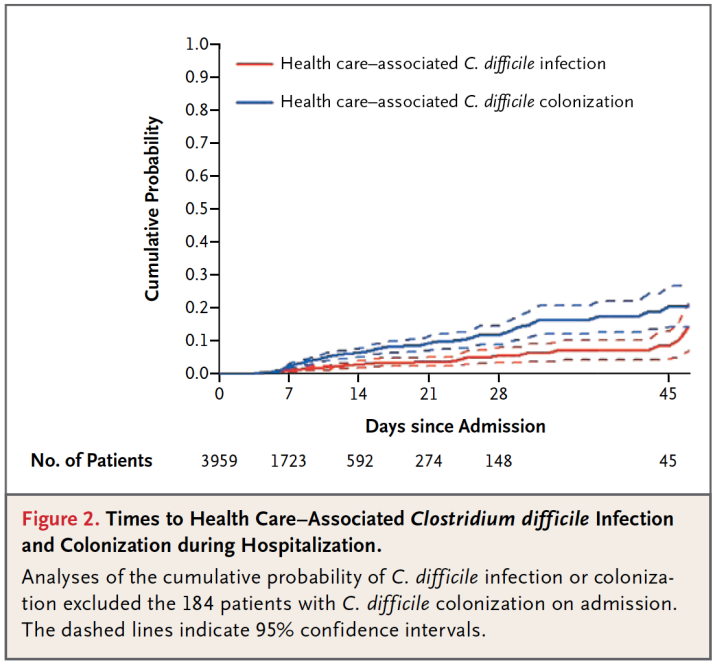
Ongoing Transmission in Quebec Hospitals



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Loo V et al. N Engl J Med. 2011 Nov 3;365(18):1693-703.

Ongoing transmission
DESPITE isolation of patients with CDI as per GL

Source of residual transmission?

1. CDI "breakthrough" transmission? Maybe
2. Healthcare workers? Unlikely
3. Food? Unlikely
4. CD carriers? Possibly

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How numerous are CD-AC?

- A point-prevalence of patients hospitalized in a LTCF during an epidemic showed a very high prevalence (35/73) of asymptomatic carriers and CDAD patients (5/73) (A:S ratio: 7:1)[1]
- A prevalence study of patients hospit. for >7days in a gen. hospital 9 were symptomatic and 51 were asymptomatic (A:S ratio 5:1)[2]
- In a large multicentric study in Quebec, there were 192 CDI cases (75 on admission and 117 after admission) and 307 CD-AC (184 on admission and 123 after admission) (A:S ratio: 1.5:1)[3]

1. Riggs MM, Clin Infect Dis 2007;45:992-8.
2. Johnson S et al. Lancet 1990;336:97-100.
3. Loo V et al. N Engl J Med. 2011 Nov 3;365(18):1693-703

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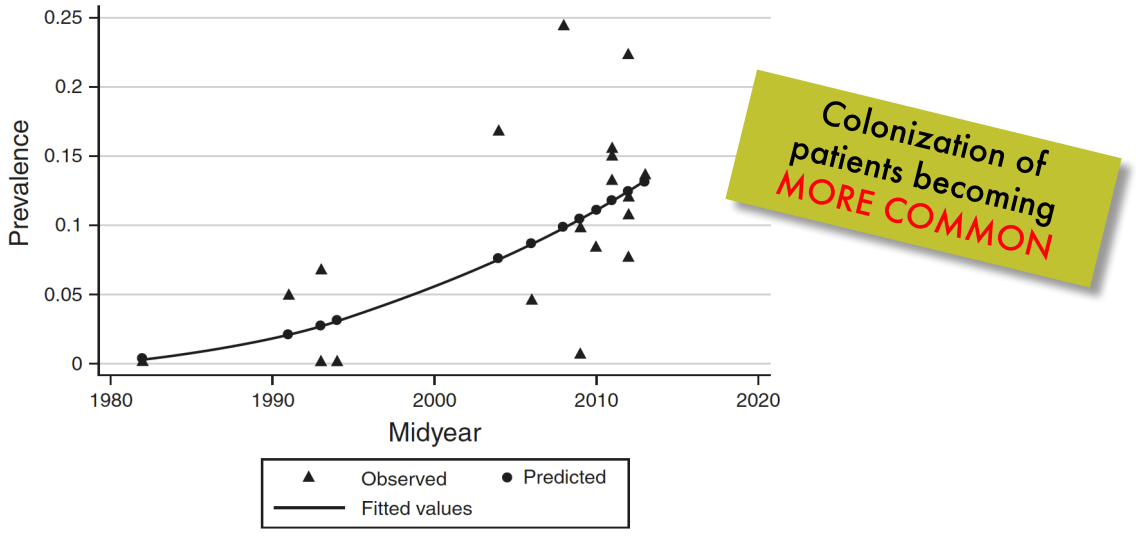

Figure 2. Toxinogenic *C. difficile* colonization trends over time. Observed (triangles) and fitted (circles) prevalence estimates, by study midyear.

Zacharioudakis IM, et al. Am J Gastroenterol **2015**; 110(3): 381-90

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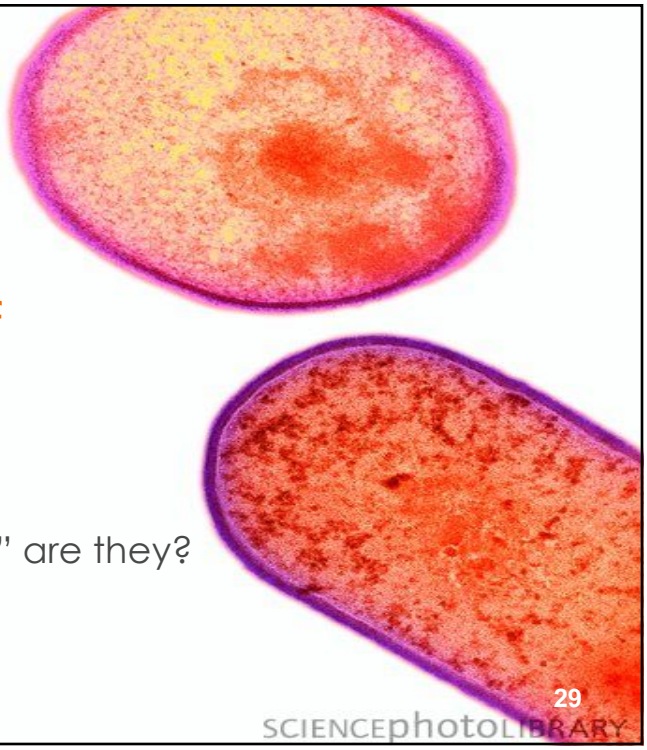

Contagiousness of CDI patients

Just how "contagious" are they?

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Contagiousness of patients with CDI on the day of diagnosis

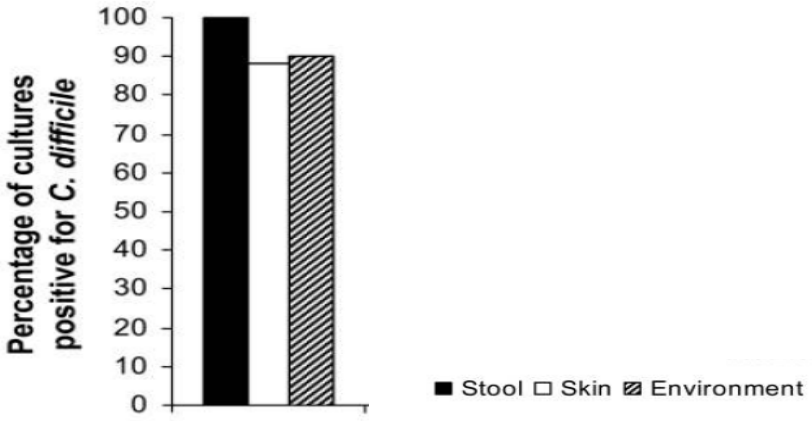

FIGURE 1. Percentage of stool, skin (chest and abdomen), and environmental (bed rail, bedside table, call button, toilet seat) cultures positive for *Clostridium difficile* among 52 patients with *C. difficile* infection. The limit of detection for stool specimens was ~2 $\log_{10}$ colony-forming units/g. The numbers of patients who had samples cultured at each time point were 52 before treatment, 48 on day 3 of treatment, 43 after resolution of diarrhea, 28 at the end of treatment, 22 at 1–2 weeks after treatment, 15 at 3–4 weeks after treatment, and 8 at 5–6 weeks after treatment.

Sethi AK at al. Infect Control Hosp Epidemiol. 2010 Jan;31(1):21-7. doi: 10.1086/649016.

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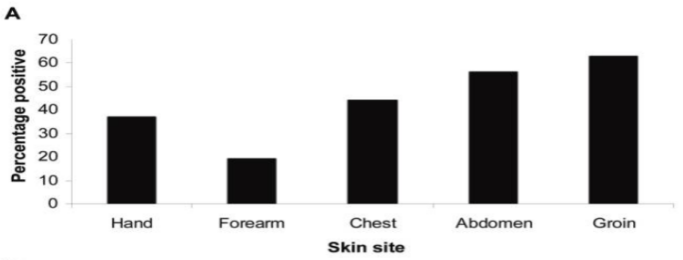
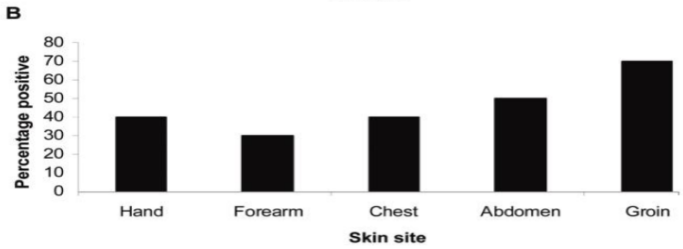
Contagiousness of CDI patients



Skin colonization of CDI patients



Transfer to gloves

Bobulski GS, Clin Infect Dis 2008

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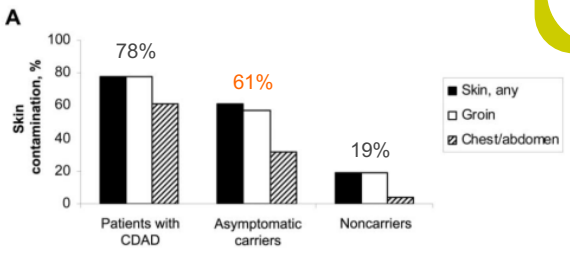
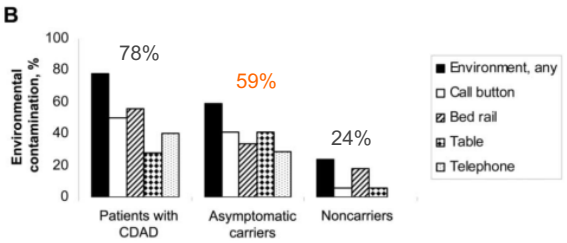
CD-AC are **not** as contagious as CDI patients… but almost!



C. difficile is present on the **SKIN** of asymptomatic carriers



C. difficile in the **IMMEDIATE SURROUNDINGS** of asymptomatic carriers

Figure 1. Percentages of *Clostridium difficile* skin *(A)* and environmental *(B)* contamination among study groups. Samples from skin and environmental surfaces were collected for culture concurrently with stool samples from patients with *C. difficile*–associated disease (CDAD; $n = 18$), asymptomatic fecal carriers ($n = 35$), and noncarriers (i.e., patients with negative stool culture results; $n = 33$). Patients with missing skin ($n = 13$) or environmental ($n = 3$) culture samples were excluded.

Riggs MM. Clin Infect Dis 2007;45:992-8

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C. difficile present on skin of asymptomatic carriers can be transferred to HCWs' hands 30-60% of time
...And an ABHRS won't kill them
Bobulsky GS. *et al*., Clin Infect Dis. 2008; 46(3):447-50
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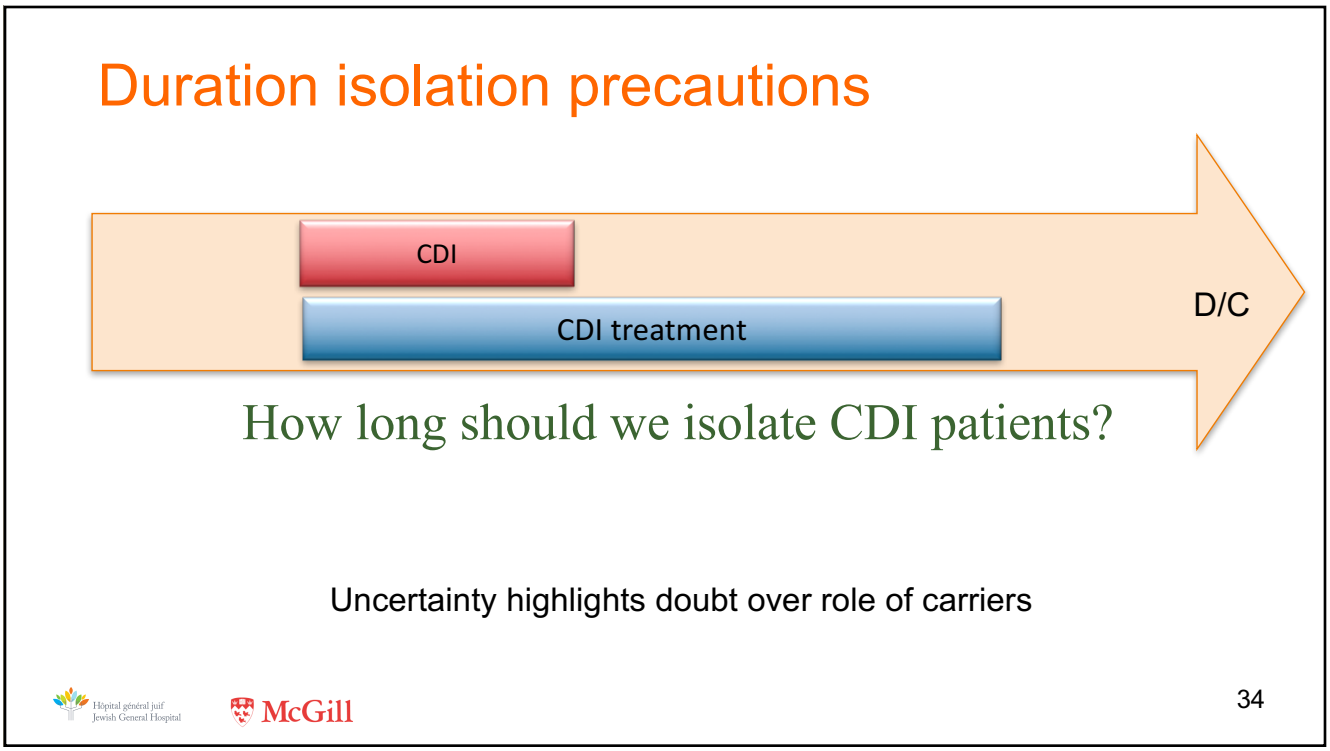
Duration isolation precautions
CDI
CDI treatment
D/C
How long should we isolate CDI patients?
Uncertainty highlights doubt over role of carriers
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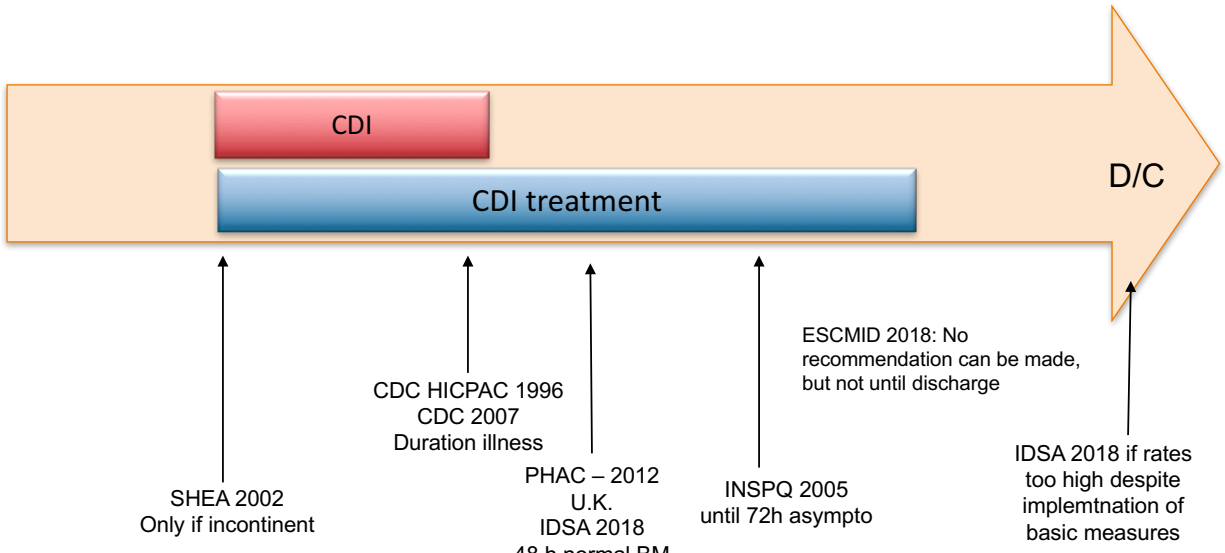
Duration isolation precautions



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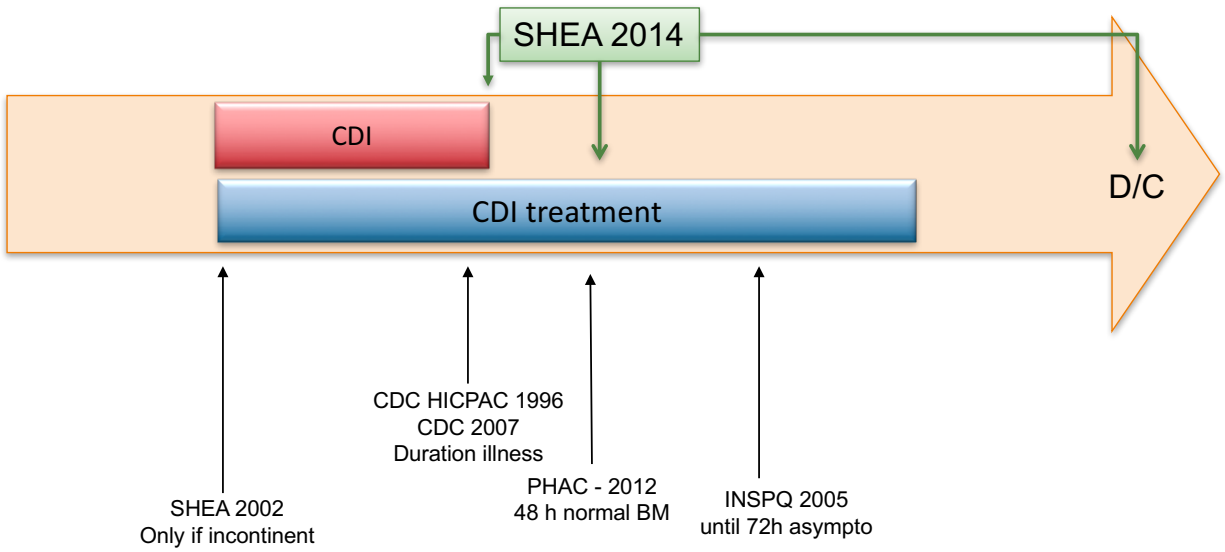
Duration isolation precautions



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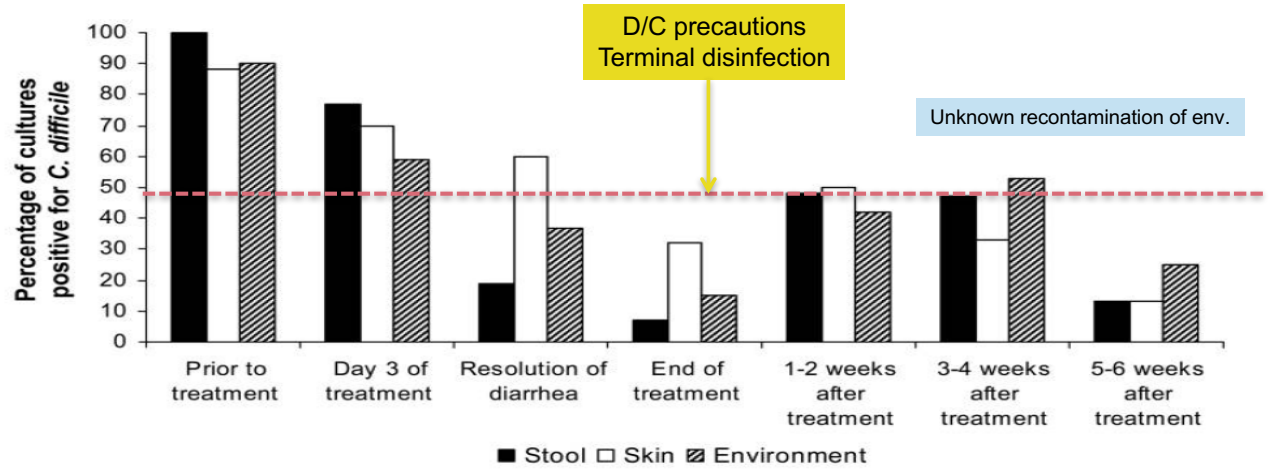

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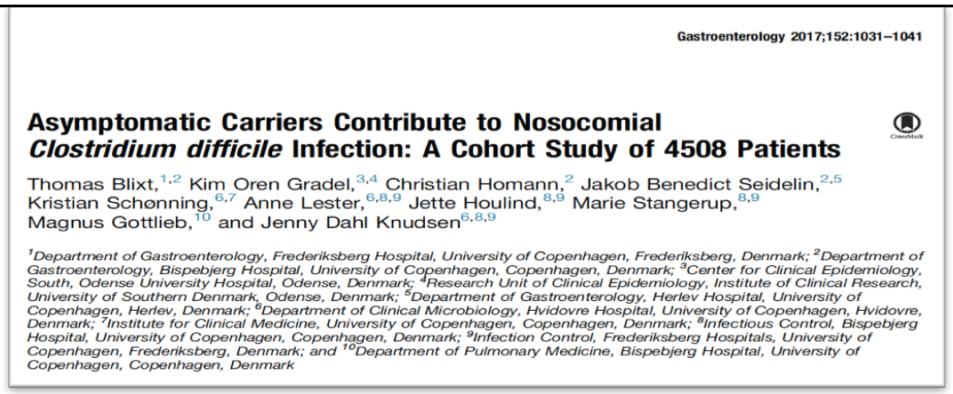

Gastroenterology 2017;152:1031–1041

Asymptomatic Carriers Contribute to Nosocomial *Clostridium difficile* Infection: A Cohort Study of 4508 Patients

Thomas Blixt,[1,2] Kim Oren Gradel,[3,4] Christian Homann,[2] Jakob Benedict Seidelin,[2,5] Kristian Schønning,[6,7] Anne Lester,[6,8,9] Jette Houlind,[8,9] Marie Stangerup,[8,9] Magnus Gottlieb,[10] and Jenny Dahl Knudsen[6,8,9]

[1]Department of Gastroenterology, Frederiksberg Hospital, University of Copenhagen, Frederiksberg, Denmark; [2]Department of Gastroenterology, Bispebjerg Hospital, University of Copenhagen, Copenhagen, Denmark; [3]Center for Clinical Epidemiology, South, Odense University Hospital, Odense, Denmark; [4]Research Unit of Clinical Epidemiology, Institute of Clinical Research, University of Southern Denmark, Odense, Denmark; [5]Department of Gastroenterology, Herlev Hospital, University of Copenhagen, Herlev, Denmark; [6]Department of Clinical Microbiology, Hvidovre Hospital, University of Copenhagen, Hvidovre, Denmark; [7]Institute for Clinical Medicine, University of Copenhagen, Copenhagen, Denmark; [8]Infectious Control, Bispebjerg Hospital, University of Copenhagen, Copenhagen, Denmark; [9]Infection Control, Frederiksberg Hospitals, University of Copenhagen, Frederiksberg, Denmark; and [10]Department of Pulmonary Medicine, Bispebjerg Hospital, University of Copenhagen, Copenhagen, Denmark

C. difficile carriers can cause CDI in other patients

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Blixt T et al. Gastroenterology. 2017 Apr;152(5):1031-1041.

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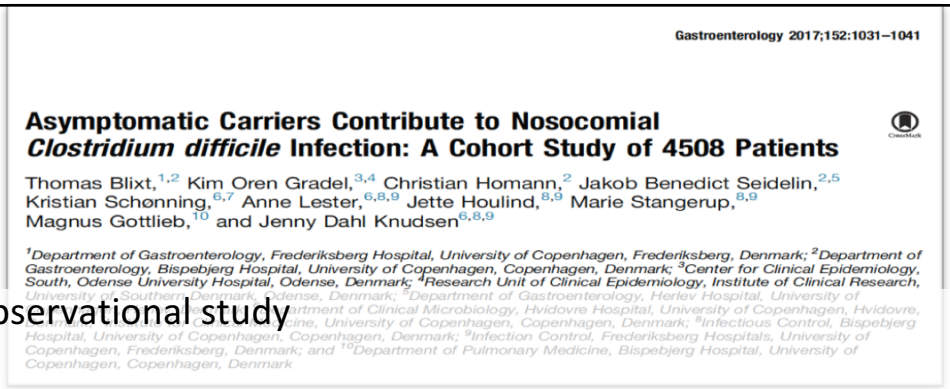

Gastroenterology 2017;152:1031–1041

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- Observational study
- 8 wards in 2 hospitals in Copenhagen
- CDI incidence 2-2.5 per 1,000 patient-days
- Private rooms rare

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Blixt T et al. Gastroenterology. 2017 Apr;152(5):1031-1041.

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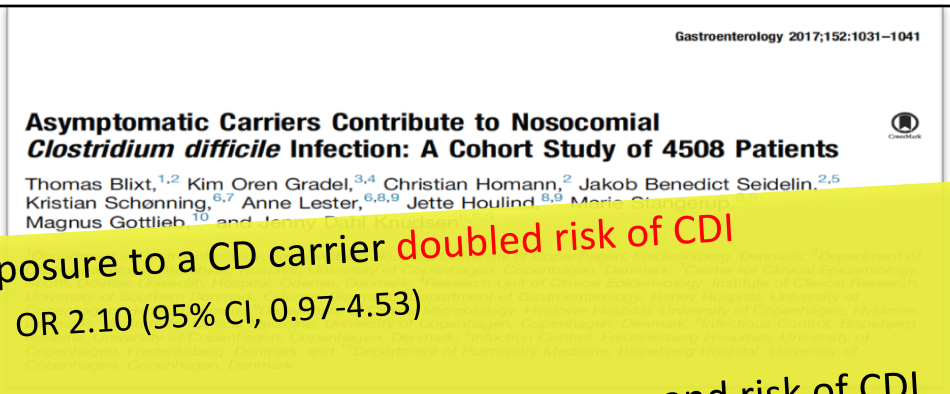

Gastroenterology 2017;152:1031–1041

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- ✓ Exposure to a CD carrier doubled risk of CDI
  - OR 2.10 (95% CI, 0.97-4.53)
- ✓ Association between level of exposure and risk of CDI (no. of carriers and/or Length of stay)

NNTH: 71 (ward level) and 50 (room level)

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Blixt T et al. Gastroenterology. 2017 Apr;152(5):1031-1041.

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Room attribution and risk of CDI

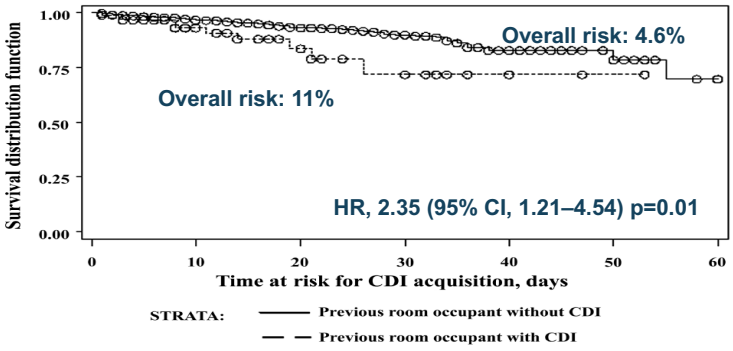

FIGURE 2. Kaplan-Meier curve of *Clostridium difficile* infection (CDI) development. The survival distribution function indicates the absence of the development of CDI. The group with a prior room occupant with CDI was more likely to develop CDI ($P = .008$).

- In ICU, occupying a room of a CDI patient increases risk of CDI two-fold
- Still: 90% of CDI could not be linked to previous CDI case

Shaughnessy MK et al. *Infect Control Hosp Epidemiol* 2011;32(3): 201–206.

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Clinical Infectious Diseases
MAJOR ARTICLE

IDSA Infectious Diseases Society of America hivma hiv medicine association

Clostridium difficile: Investigating Transmission Patterns Between Infected and Colonized Patients Using Whole Genome Sequencing

Ling Yuan Kong,[1] David W. Eyre,[2,3] Jacques Corbeil,[4] Frederic Raymond,[4] A. Sarah Walker,[2] Mark H. Wilcox,[5] Derrick W. Crook,[2,6] Sophie Michaud,[7] Baldwin Toye,[8] Eric Frost,[7] Nandini Dendukuri,[9] Ian Schiller,[10] Anne-Marie Bourgault,[1,11] Andrew Dascal,[12] Matthew Oughton,[12] Yves Longtin,[12] Louise Poirier,[13] Paul Brassard,[10] Nathalie Turgeon,[14] Rodica Gilca,[15] and Vivian G. Loo[1]

[1]Division of Infectious Diseases and Department of Medical Microbiology, McGill University Health Centre, Montréal, Québec, Canada; [2]Nuffield Department of Medicine and [3]National Institute for Health Research Oxford Biomedical Research Centre, John Radcliffe Hospital, United Kingdom; [4]Centre de recherche CHUQ, Université Laval, Québec City, Québec, Canada; [5]Department of Microbiology, Leeds Teaching Hospitals and University of Leeds, and [6]National Infection Service, Public Health England, London, United Kingdom; and [7]Department of Microbiology and Infectiology, Université de Sherbrooke, Québec, [8]Division of Microbiology, Ottawa Hospital, University of Ottawa, Ontario, [9]Technology Assessment Unit and [10]Centre for Outcomes Research, Research Institute, McGill University Health Centre, [11]Department of Microbiology, Centre Hospitalier de l'Université de Montréal, [12]Division of Infectious Diseases, Jewish General Hospital, and [13]Department of Microbiology, Hôpital Maisonneuve-Rosemont, Montréal, [14]Department of Microbiology, Centre Hospitalier Universitaire de Québec, Hôtel-Dieu de Québec, and [15]Québec Institute of Public Health, Québec City, Canada

WGS studies confirm the role of ACDC in some HA-CDI

- Comparing samples from patients with CDI with prior samples from within the cohort by WGS (threshold <2snp)
  - 105 cases (52%) cases linked to a prior sample
    - 65 (62%) linked to both infected and CD carrier
    - 28 (26%) only linked to CDI Case
    - 12 (11%) only linked to CD carrier
  - 96 cases (48%) could not be linked to another patient
    - Over-representation of CD carriers in this population? (ratio colonization/infection: 1.3 : 1)

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Modeling Studies

- Asymptomatic carriers play a role in the dissemination of *C. difficile*, according to modeling experiments
  - Transmission of *C. difficile cannot* be explained solely by symptomatic patients[1]

1. Lanzas C et al. Infect Control Hosp Epidemiol 2011

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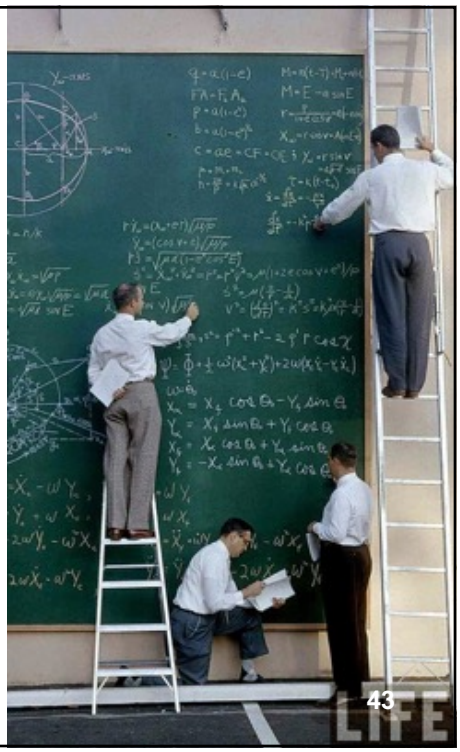

Maghdoori and Moghadas *BMC Infectious Diseases* (2017) 17:384
DOI 10.1186/s12879-017-2494-6

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Assessing the effect of patient screening and isolation on curtailing *Clostridium difficile* infection in hospital settings

Sara Maghdoori* and Seyed M. Moghadas

Rapid detection of colonized patients can significantly affect the prevalence of CDI and its control, especially in the context of asymptomatic carriers and in-ward transmission.

Maghdoori, Mohandas. BMC Infect Dis. 2017 Jun 2;17(1):384.

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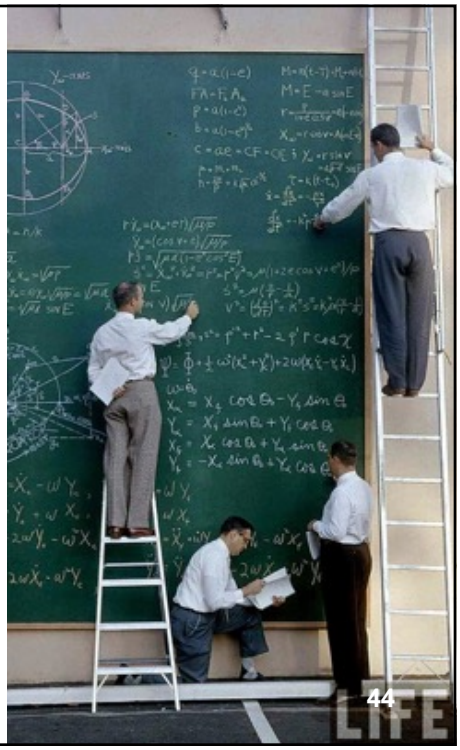

RESEARCH

Quantifying Transmission of *Clostridium difficile* within and outside Healthcare Settings

David P. Durham, Margaret A. Olsen, Erik R. Dubberke, Alison P. Galvani, Jeffrey P. Townsend

Despite lower transmission rates for asymptomatic carriers, this transmission route has a substantial effect on hospital-onset CDI because of the larger reservoir of hospitalized carriers

Durham DP et al. Emerg Infect Dis. 2016 Apr;22(4):608-16.

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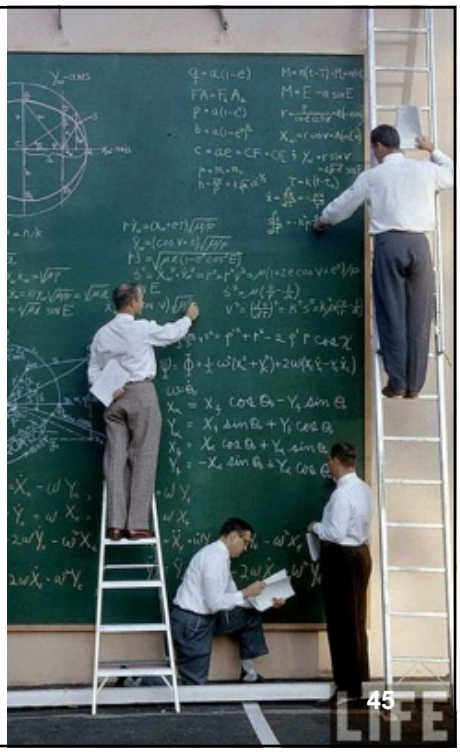

RESEARCH ARTICLE

Isolation of *C. difficile* Carriers Alone and as Part of a Bundle Approach for the Prevention of *Clostridium difficile* Infection (CDI): A Mathematical Model Based on Clinical Study Data

Christos A. Grigoras[1,2], Fainareti N. Zervou[1], Ioannis M. Zacharioudakis[1], Constantinos I. Siettos[2], Eleftherios Mylonakis[1]*

From a baseline CDI incidence of 6.18 per 1,000 admissions, screening of patients at the time of hospital admission with PCR and isolation of those colonized, as a single additive policy to the standard practice, reduced CDI incidence to 4.99 per 1,000 admissions (95% CI, 4.59– 5.42; RR = 19.1%). Applying this policy as part of a bundle approach combined with an antimicrobial stewardship program had effectiveness in reducing CDI incidence. Specifically, CDI incidence reduced to 2.35 per 1,000 admissions (95% CI, 2.07– 2.65; RR = 61.88%) with the addition of an antimicrobial stewardship program.

Grigoras CA. PLoS ONE 11(6): e0156577.

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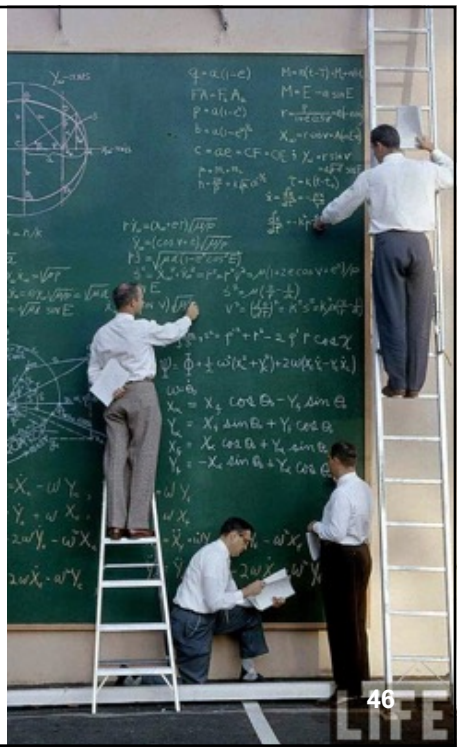

Bull Math Biol (2017) 79:2242–2257
DOI 10.1007/s11538-017-0328-8

Society for Mathematical Biology CrossMark

ORIGINAL ARTICLE

Healthcare-Associated *Clostridium difficile* Infections are Sustained by Disease from the Community

Angus McLure[1] · Archie C. A. Clements[1] · Martyn Kirk[1] · Kathryn Glass[1]

Within-hospital transmission alone is insufficient to sustain endemic conditions in hospitals without the constant importation of colonised individuals. Improved hygiene practices to reduce transmission from symptomatic and asymptomatic individuals and reduced length of stay are most likely to reduce within-hospital transmission and infections;

McLure A. et al. Bull Math Biol. 2017 Aug 3. doi: 10.1007/s11538-017-0328-8.

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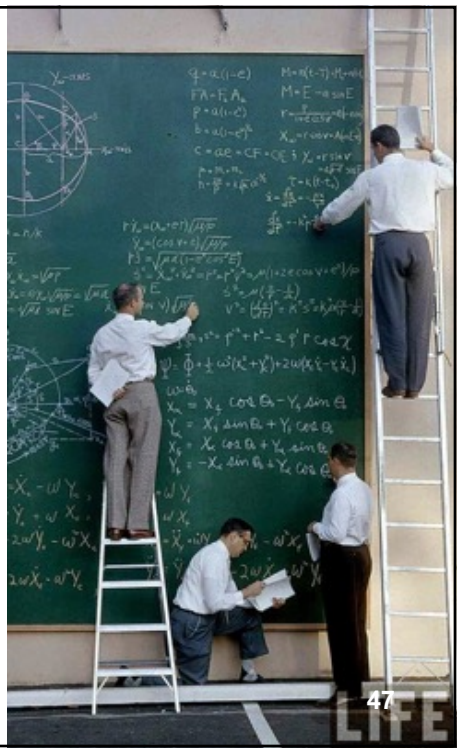

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY AUGUST 2014, VOL. 35, NO. 8

ORIGINAL ARTICLE

Effectiveness of Screening Hospital Admissions to Detect Asymptomatic Carriers of *Clostridium difficile*: A Modeling Evaluation

Cristina Lanzas, PhD;[1] Erik R. Dubberke, MD[2]

On average, testing for asymptomatic carriers reduced the number of new colonizations and HO-CDI cases by 40%-50% and 10%-25%, respectively, compared with the baseline scenario.

1. Lanzas C et al. Infect Control Hosp Epidemiol 2011

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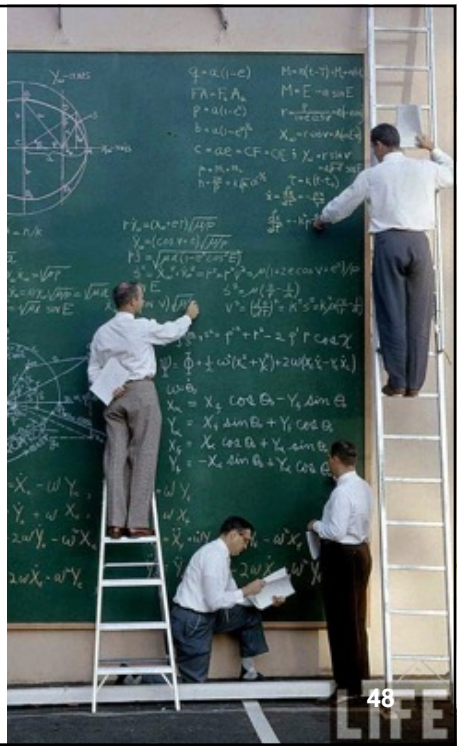

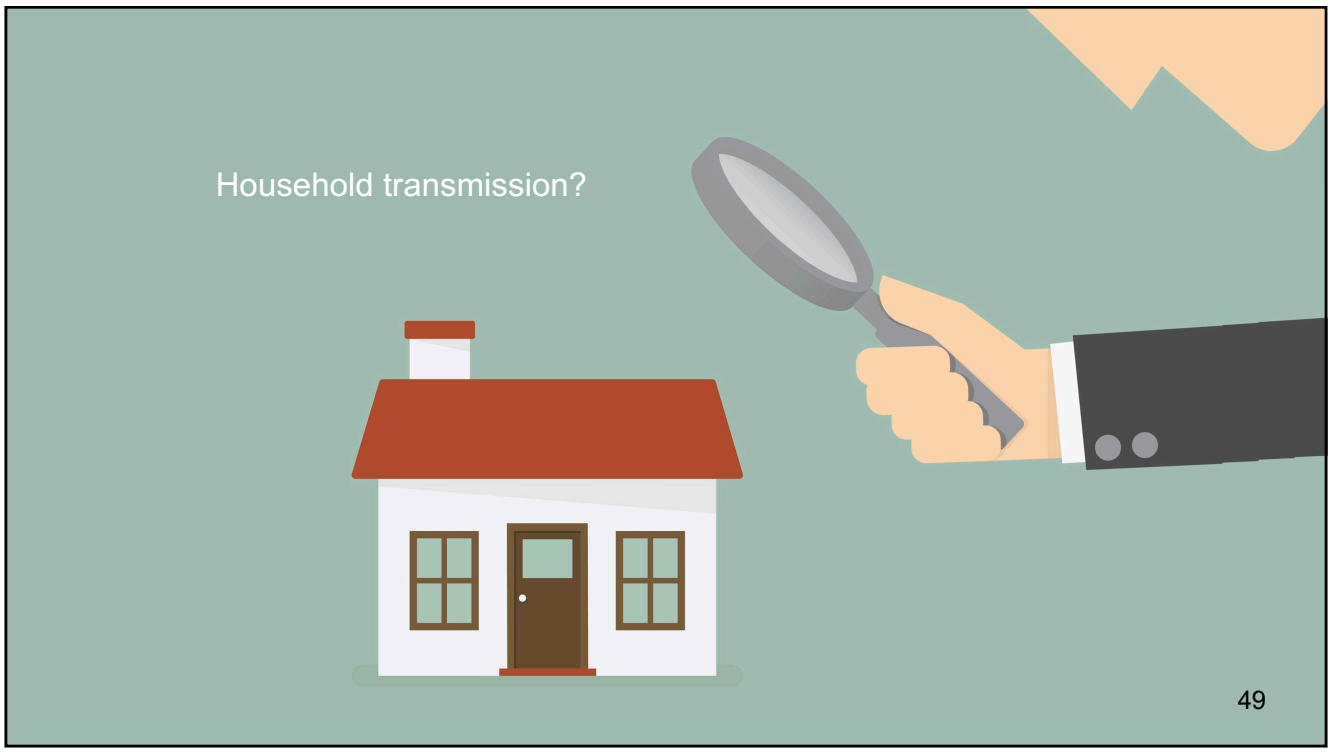

Risk for Asymptomatic Household Transmission of *Clostridioides difficile* Infection Associated with Recently Hospitalized Family Members

Aaron C. Miller, Alan T. Arakkal, Daniel K. Sewell, Alberto M. Segre, Sriram V. Pemmaraju, Philip M. Polgreen; CDC MInD-Healthcare Group

Table 4. Results of regression analysis of incidence rate ratio for *Clostridioides difficile* infection using quasi-Poisson model and 60-day exposure window in study of asymptomatic *C. difficile* transmission among household members, United States*

Variable	IRR (95% CI)
No. days member was hospitalized within 60 d	
0	Referent
1–3	1.30 (1.19–1.41)
4–10	1.46 (1.32–1.62)
11–20	1.79 (1.43–2.23)
21–30	2.17 (1.48–3.18)
>30	2.45 (1.66–3.60)
Age group, y	
0–17	Referent
18–40	1.71 (1.65–1.78)
41–65	2.97 (2.86–3.08)
>65	9.32 (8.92–9.73)
Sex	
M	Referent
F	1.30 (1.28–1.33)
Outpatient antimicrobial drug use within 60 d	
None	Referent
Low-risk drugs	2.69 (2.59–2.79)
High-risk drugs	8.83 (8.63–9.03)
PPI use within 30 d	2.23 (2.15–2.30)
Infant <2 y in family	1.51 (1.44–1.58)

*Models were adjusted for year, month, and family size. Regression models included an offset for number of enrollment months. Because family hospitalization exposure group was followed for 60 days to identify secondary *Clostridioides difficile* infection, the length of their enrollment period is 60 days. For the unexposed group, the length of enrollment was the length of a given month. IRR, incident rate ratio; PPI, proton-pump inhibitor.

Table 3. Number of cases and enrollee-months in each exposure bin for total days of household-hospitalization using a 60-day exposure window in study of asymptomatic *Clostridioides difficile* transmission among household members, United States*

	60-day exposure window		
No. days family members spent hospitalized	No. CDI cases	Total enrollment months	Incidence†
0	160,267	4,980,648,694	3.22
1–3	2,336	52,798,719	4.42
4–10	1,519	27,457,461	5.53
11–20	315	4,338,929	7.26
21–30	107	1,317,610	8.12
>30	106	1,214,792	8.73

*CDI, *Clostridioides difficile* infection.
†Cases per 100,000 enrollment months.

Household members of patients who were hospitalized (but did not develop CDI) are at increased risk of CDI

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Jewish General Hospital McGill

Miller AC et al. Emerg Infect Dis. 2022 May;28(5):932-939.

Detection of carriers

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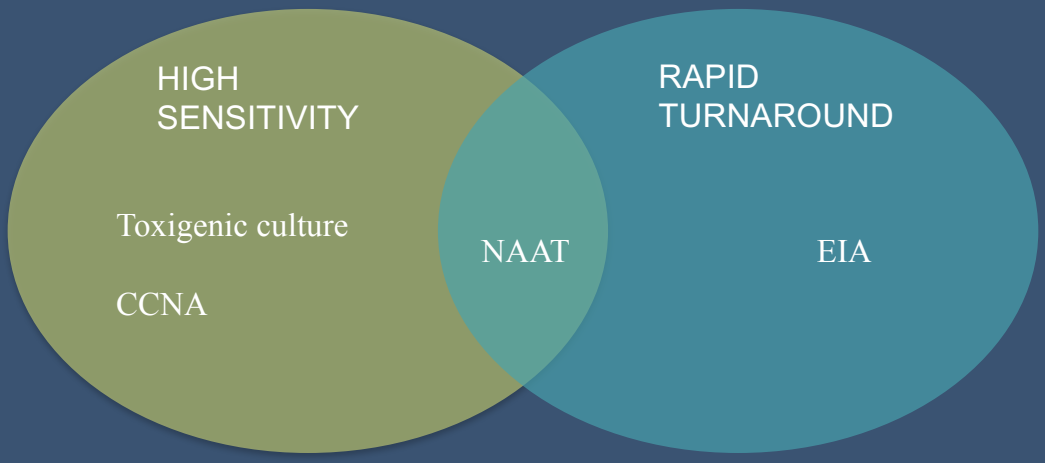

We CAN detect and isolate carriers, not only patients with CDI… and we should seize the opportunity!

REF. Infection Control 101 – control of MRSA, VRE, CRE, C.auris, etc.

Belanger SD et al J Clin Microbiol. 2003 Feb;41(2):730-4.

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Detection of carriers

Journal of Clinical Microbiology®

Detection of *Clostridium difficile* in Feces of Asymptomatic Patients Admitted to the Hospital

Elisabeth M. Terveer,[a] Monique J. T. Crobach,[a] Ingrid M. J. G. Sanders,[a] Margreet C. Vos,[b] Cees M. Verduin,[c] Ed J. Kuijper[a]
Department of Medical Microbiology, Leiden University Medical Center, Leiden, the Netherlands[a]; Department of Medical Microbiology and Infectious Diseases, Erasmus MC University Medical Center, Rotterdam, the Netherlands[b]; Department of Microbiology and Infection Prevention, Amphia Hospital, Breda, the Netherlands[c]

ABSTRACT Recent evidence shows that patients asymptomatically colonized with *Clostridium difficile* may contribute to the transmission of *C. difficile* in health care facilities. Additionally, these patients may have a higher risk of developing *C. difficile* infection. The aim of this study was to compare a commercially available PCR directed to both toxin A and B (*artus C. difficile* QS-RGQ kit CE; Qiagen), an enzyme-linked fluorescent assay to glutamate dehydrogenase (GDH ELFA) (Vidas, bioMérieux), and an in-house-developed PCR to *tcdB*, with (toxigenic) culture of *C. difficile* as the gold standard to detect asymptomatic colonization. Test performances were evaluated in a collection of 765 stool samples obtained from asymptomatic patients at admission to the hospital. The *C. difficile* prevalence in this collection was 5.1%, and 3.1% contained toxigenic *C. difficile*. Compared to *C. difficile* culture, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the *C. difficile* GDH ELFA were 87.2%, 91.2%, 34.7%, and 99.3%, respectively. Compared with results of toxigenic culture, the sensitivity, specificity, PPV, and NPV of the commercially available PCR and the in-house PCR were 95.8%, 93.4%, 31.9%, 99.9%, and 87.5%, 98.8%, 70%, and 99.6%, respectively. We conclude that in a low-prevalence setting of asymptomatically colonized patients, both GDH ELFA and a nucleic acid amplification test can be applied as a first screening test, as they both display a high NPV. However, the low PPV of the tests hinders the use of these assays as stand-alone tests.

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Terveer EM et al. J Clin Microbiol. 2017 Feb;55(2):403-411.

Detection of carriers

Journal of Clinical Microbiology®

Detection of *Clostridium difficile* in Feces ents Admitted to

ch,[a] Ingrid M. J. G. Sanders,[a]
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edical Center, Leiden, the Netherlands[a]; Department MC University Medical Center, Rotterdam, the Prevention, Amphia Hospital, Breda, the

atients asymptomatically colonized with nsmission of *C. difficile* in health care fa- e a higher risk of developing *C. difficile* mpare a commercially available PCR di- *cile* QS-RGQ kit CE; Qiagen), an enzyme- drogenase (GDH ELFA) (Vidas, bioMéri- , with (toxigenic) culture of *C. difficile* as colonization. Test performances were es obtained from asymptomatic patients prevalence in this collection was 5.1%, npared to *C. difficile* culture, the sensitiv-), and negative predictive value (NPV) of %, 34.7%, and 99.3%, respectively. Com- sensitivity, specificity, PPV, and NPV of 93.4%, 31.9%, e that in a low- DH ELFA and a it, as they both se of these as-

TABLE 1 Comparison of various *C. difficile* detection assays in comparison with culture of toxigenic and nontoxigenic *C. difficile* as gold standards

Assay result	No. with toxigenic culture result[a]: Pos	Neg	Sensitivity (% [95% CI])	Specificity (% [95% CI])	PPV (%)	NPV (%)
GDH positive	34	64[b]	87.2 (72.6–95.7)	91.2 (88.9–93.1)	34.7	99.3
GDH negative	5	662				
artus positive	23	49[b]	95.8 (78.9–99.9)	93.4 (91.3–95.1)	31.9	99.9
artus negative	1	691				
In-house positive	21	9[b]	87.5 (67.6–97.3)	98.8 (97.7–99.4)	70	99.6
In-house negative	3	732				

[a]GDH ELFA was compared with *C. difficile* culture, and *artus* PCR and in-house PCR were compared with toxigenic culture. Pos, positive; Neg, negative.
[b]Four of the false-negative sa

GDH →
PCR →

Nasal swabbing for MRSA detection
80-93% sensitivity

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5(2):403-411.

Hand rubbing vs. Hand washing

What is the best way to interrupt dissemination mediated by HCWs' hands?

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A Randomized Trial of Soap and Water Hand Wash Versus Alcohol Hand Rub for Removal of *Clostridium difficile* Spores from Hands of Patients

44 patients CDI or CD-AC
HR with ABHRS
HW with triclosan soap

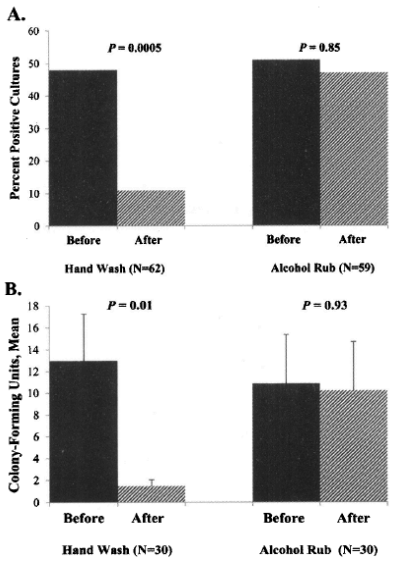

FIGURE 1. Effect of soap and water hand wash versus alcohol hand rub on frequency of hand contamination (*A*) and the mean number of spores recovered (*B*) for patients with *Clostridium difficile* infection or asymptomatic carriage. Error bars show standard error.

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Kundrapu S et al. Infect Control Hosp Epidemiol. 2014 Feb;35(2):204-6.

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Hand washing vs. *C. difficile*

Even **the best** hand hygiene technique **is poorly effective** to remove *C. difficile* from hands!

e.g. ABHRS against E. coli: 3.5 to 5 log reduction

Deschênes P et al. Am J Infect Control. 2017 May 16.

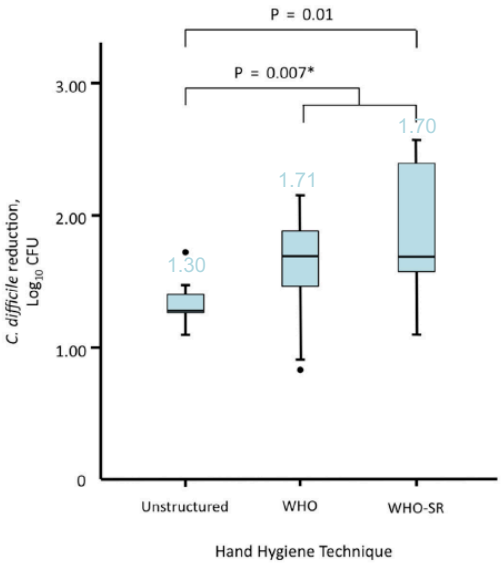

Fig 3. Efficacy of 3 hand hygiene techniques to remove *Clostridium difficile* from artificially contaminated hands. Results are expressed in CFU reduction on a logarithmic scale. The top and bottom of the box plots represent the interquartile ranges, and the horizontal lines represent the median values. The error bars extend to the maximum and minimum values. Outliers are represented by single black dots. *CFU*, colony forming units; *WHO*, World Health Organization; *WHO-SR*, WHO st repeated technique. *Comparison between a structured technique (ie, WHO SR) and an unstructured technique.

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Should we add gloves?

To soap and water or HR ?

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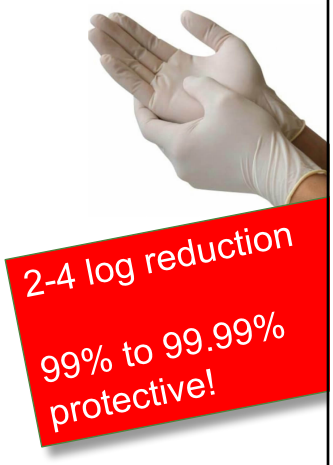
Efficacy of gloves

Summary of Events in Which Concordant Organisms Were Recovered From the Glove Exterior and Health Care Worker's Hand

Event No.	Patient Contact Site	Glove Type	Leak-Test Result (Did Glove Leak?)	Use Time, min	Microorganism	Colony Count on Gloves, cfu*	Colony Count on Hands, cfu*
1	Oral	Vinyl	Yes	10	*Enterobacter cloacae*	2.0×10^5	1.0×10^1
2	Oral	Vinyl	Yes	11	*Acinetobacter calcoaceticus*	1.2×10^5	4.0×10^1
3	Oral	Vinyl	Yes	17	*A calcoaceticus*	6.5×10^2	5.0×10^0
4	Oral	Vinyl	No	11	*A calcoaceticus*	3.0×10^5	2.5×10^2
5	Oral	Vinyl	Yes	6	*A calcoaceticus*	4.2×10^4	1.0×10^1
6	Oral	Vinyl	Yes	7	*A calcoaceticus*, *Enterobacter aerogenes*	. . .†	. . .†
7	Oral	Vinyl	Yes	16	*A calcoaceticus*	5.2×10^3	9.0×10^1
8	Oral	Vinyl	No	15	*Pseudomonas aeruginosa*	2.1×10^3	2.0×10^1
9	Rectal	Vinyl	No	2	*Escherichia coli*	2.0×10^6	2.0×10^1
10	Rectal	Vinyl	No	1	*P aeruginosa*	1.3×10^4	2.0×10^1
11	Oral	Latex	No	6	*A calcoaceticus*	1.5×10^4	1.0×10^1

*cfu indicates colony-forming units.
†Ellipses indicate data not available.



Olsen RJ et al. JAMA. 1993 Jul 21;270(3):350-3.

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Impact of glove use to protect against C. difficile

- Hands of 35 HCWs sampled after caring for C. difficile patient
  - 20/35 (57%) acquired C. difficile on their hands

Glove use	Hand washing	Presence of C. difficile
no	no	7/15 (47%)
no	Regular soap	14/16 (88%)
yes	no	0/4 (0%)

Gloves: the best "hand hygiene" technique?

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McFarland LV et al. N Engl J Med. 1989 Jan 26;320(4):204-10.

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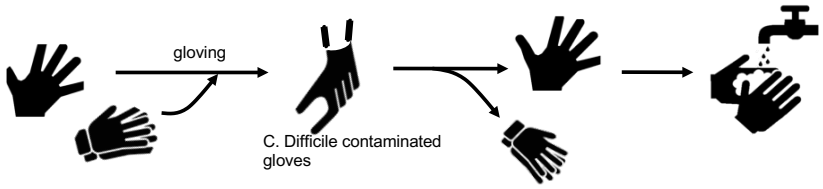
We **NEED** gloves against *C. difficile*!



Standard

	Glove removal		HR or HW		Total
Hand rubbing with ABHRS only	nil	+	0 Log	=	0 Log
Hand washing only	nil	+	1-2 Log	=	1-2 Log
Hand rubbing with ABHRS + gloves	2-4 log	+	0 Log	=	2-4 Log
Hand washing + gloves	2-4 Log	+	1-2 Log	=	3 – 6 Log

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An environmental cleaning bundle and health-care-associated infections in hospitals (REACH): a multicentre, randomised trial

Brett G Mitchell*, Lisa Hall*, Nicole White, Adrian G Barnett, Kate Halton, David L Paterson, Thomas V Riley, Anne Gardner, Katie Page, Alison Farrington, Christian A Gericke, Nicholas Graves

- Multimodal intervention to improve routine cleaning
  - Better product use
  - Improved technique
  - Education
  - Auditing and feedback
  - Communication

Mitchell BG et al. Lancet Infect Dis. 2019 Apr;19(4):410-418.

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associated

er, Katie Page,

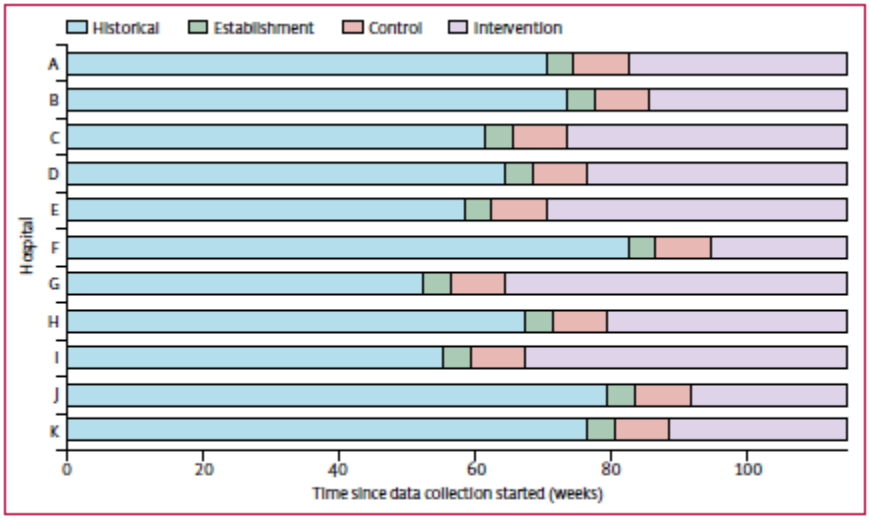

Figure 1: **Trial design**
There was a 4-week establishment period and an 8-week control period for baseline data collection of cleaning audits, context assessment, and staff surveys.

Mitchell BG et al. Lancet Infect Dis. 2019 Apr;19(4):410-418.

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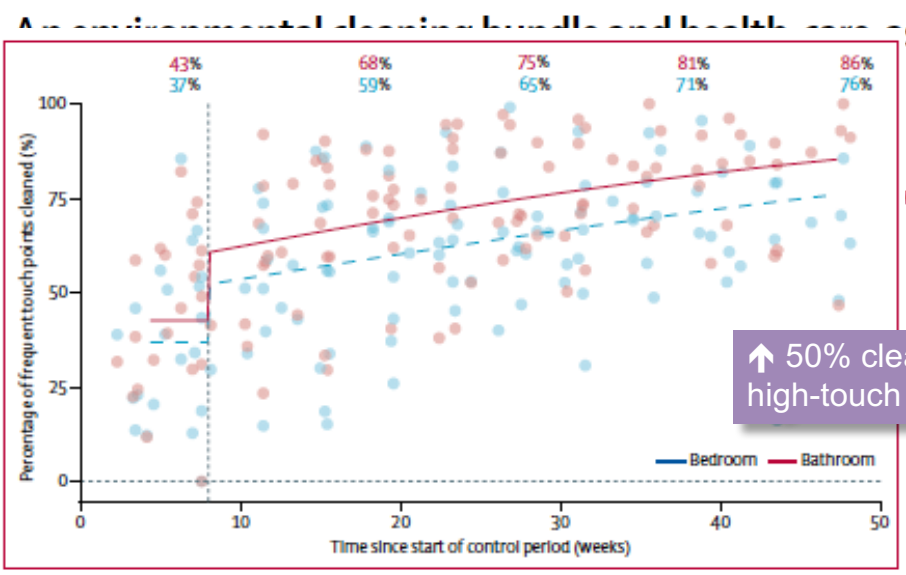

↑ 50% cleaning high-touch surfaces

Figure 4: Percentage of frequent touch points cleaned in patient bathrooms and bedrooms
Percentages are model-based predictions of the outcome. Dotted line shows the start of intervention.

Mitchell BG et al. Lancet Infect Dis. 2019 Apr;19(4):410-418.

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	Pre-intervention	Post-intervention
Infection		
Clostridium difficile infections		
n	968	278
Unadjusted rate per 10 000 OBDs	2·74	2·19
Variance (SE)	0·008 (0·088)	0·017 (0·132)
Staphylococcus aureus bacteraemia		
n	362	109
Unadjusted rate per 10 000 OBDs	1·02	0·86
Variance (SE)	0·003 (0·054)	0·007 (0·082)
Meticillin-susceptible *S aureus* bacteraemia		
n	296	87
Unadjusted rate per 10 000 OBDs	0·84	0·69
Variance (SE)	0·002 (0·049)	0·005 (0·074)
Meticillin-resistant *S aureus* bacteraemia		
n	66	22
Unadjusted rate per 10 000 OBDs	0·19	0·17
Variance (SE)	0·001 (0·023)	0·001 (0·037)
Vancomycin-resistant enterococcus clinical isolates		
n	230	50
Unadjusted rate per 10 000 OBDs	0·65	0·39
Variance (SE)	0·002 (0·043)	0·003 (0·056)
Total OBDs	3 534 439	1 267 134

Unadjusted rates do not account for baseline variation between hospitals or time trends. Pre-intervention includes historical, establishment, and control phases and the first 4 weeks of the intervention phase. Intervention includes from week 5 of the intervention phase until the end of the trial. OBDs=occupied bed-days.

Table 1: Crude rates of health care-associated infections

ental cleaning bundle and health-care-associated

	Estimate (95% CI)	p value
No intervention		
Clostridium difficile infections	−28·8 (−45·9 to −6·4)	0·0163
Staphylococcus aureus bacteraemia*	5·1 (−33·0 to 65·0)	0·8280
Vancomycin-resistant enterococcus clinical isolates	−15·6 (−53·1 to 51·9)	0·5653
With intervention		
Clostridium difficile infections	7·3 (−11·8 to 30·5)	0·4655
S aureus bacteraemia*	−18·1 (−40·2 to 12·0)	0·2180
Vancomycin-resistant enterococcus	−36·9 (−59·0 to −2·8)	0·0340
All infections	−5·8 (−19·8 to 9·4)	0·4246

Per-protocol adjusted results, calculated using a linear trend and a binary switch with a 4-week intervention lag.
*Includes both meticillin-resistant and meticillin-sensitive *S aureus*.

Table 2: Percentage changes in infection rates, by intervention

Mitchell BG et al. Lancet Infect Dis. 2019 Apr;19(4):410-418.

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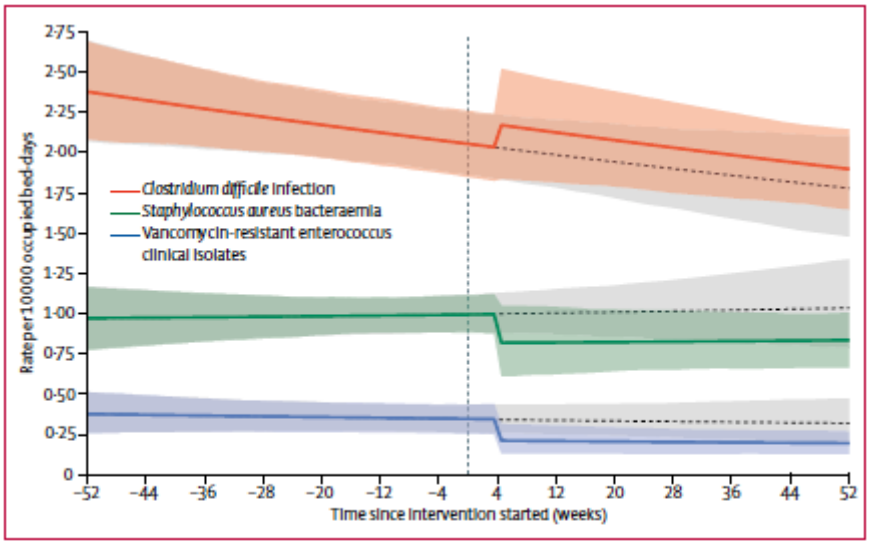

Figure 3: **Estimated changes in health care-associated infection rates before and after the intervention**
Ribbons are 95% prediction intervals. Grey shading shows expected infection rates with no intervention.

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Mitchell BG et al. Lancet Infect Dis. 2019 Apr;19(4):410-418.

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American Journal of Infection Control 47 (2019) 843–845

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Brief Report

Impact of routine use of a spray formulation of bleach on *Clostridium difficile* spore contamination in non-*C difficile* infection rooms

Yilen K. Ng Wong MD [a], Heba Alhmidi MD [a], Thriveen S.C. Mana MS, MNO [a], Jennifer L. Cadnum BS [a], Annette L. Jencson CIC [a], Curtis J. Donskey MD [b,c,*]

[a] *Research Service, Louis Stokes Cleveland Veterans Affairs Medical Center, Cleveland, OH*
[b] *Geriatric Research, Education, and Clinical Center, Louis Stokes Cleveland Veterans Affairs Medical Center, Cleveland, OH*
[c] *Case Western Reserve University School of Medicine, Cleveland, OH*

Impact of universal bleach routine disinfection on *C. difficile* contamination of patient rooms (instead of quaternary ammonium)

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Ng Wong YK et al. Am J Infect Control. 2019 Jul;47(7):843-845.

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[a] Research Service, Louis Stc
[b] Geriatric Research, Educat
[c] Case Western Reserve Uni

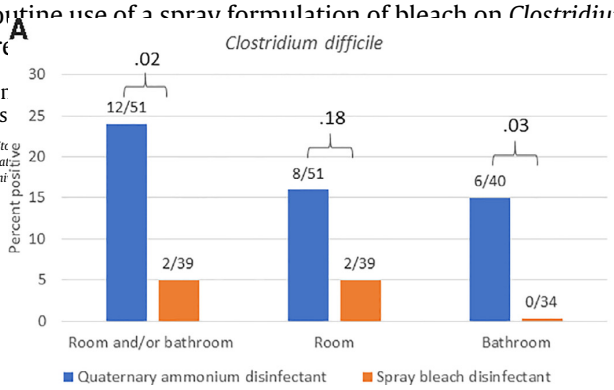

Fig 1. Percentage of non-*Clostridium difficile* infection rooms with positive cultures for *C difficile* (A) or methicillin-resistant *Staphylococcus aureus* (B) after postdischarge cleaning during a period when a quaternary ammonium disinfectant was used versus during a period when a spray bleach disinfectant was used. *CDI*, *C difficile* infection.

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Ng Wong YK et al. Am J Infect Control. 2019 Jul;47(7):843-845.

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Enhanced terminal room disinfection and acquisition and infection caused by multidrug-resistant organisms and *Clostridium difficile* (the Benefits of Enhanced Terminal Room Disinfection study): a cluster-randomised, multicentre, crossover study

Deverick J Anderson, Luke F Chen, David J Weber, Rebekah W Moehring, Sarah S Lewis, Patricia F Triplett, Michael Blocker, Paul Becherer, J Conrad Schwab, Lauren P Knelson, Yuliya Lokhnygina, William A Rutala, Hajime Kanamori, Maria F Gergen, Daniel J Sexton; for the CDC Prevention Epicenters Program

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Anderson et al. Lancet 2017; 389: 805-14

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Effectiveness of targeted enhanced terminal room disinfection on hospital-wide acquisition and infection with multidrug-resistant organisms and *Clostridium difficile*: a secondary analysis of a multicentre cluster randomised controlled trial with crossover design (BETR Disinfection)

Deverick J Anderson, Rebekah W Moehring, David J Weber, Sarah S Lewis, Luke F Chen, J Conrad Schwab, Paul Becherer, Michael Blocker, Patricia F Triplett, Lauren P Knelson, Yuliya Lokhnygina, William A Rutala, Daniel J Sexton, for the CDC Prevention Epicenters Program

- Secondary analysis of main BETR study
- Population-level analysis
- 4 arms of terminal disinfection for carriers of AMR (C.difficile, VRE, MRSA and MDR A. baumannii)

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Anderson DJ et al. Lancet Infect Dis. 2018 Aug;18(8):845-853. 71

Universal sporicidal for terminal cleaning of AMR room

	Standard disinfection period (reference group)	UV period	Bleach period	Bleach and UV period
Clostridium difficile				
Exposed admissions	76 099	84 776	82 193	84 741
Incident cases (%)	375 (0·49%)	389 (0·46%)	362 (0·44%)	389 (0·46%)
Patient days	372 654	426 157	411 471	436 330
Incidence (per 10 000 patient days)	10·1	9·13	8·80	8·92
Risk difference (95% CI)	1 (ref)	0·93 (–0·31 to 2·18)	1·27 (0·005 to 2·53)	1·15 (–0·13 to 2·43)
Relative risk (95% CI); p value	1 (ref)	0·89 (0·80 to 0·99); 0·031	0·91 (0·75 to 1·10); 0·32	0·97 (0·84 to 1·12); 0·68

Significant decrease

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Anderson DJ et al. Lancet Infect Dis. 2018 Aug;18(8):845-853. 72

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NO Significant decrease

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THERE'S MORE THAN P-VALUES TO CONSIDER

Is this difference clinically meaningful?

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Clinical evidence

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Institut Universitaire de Cardiologie et Pneumologie de Québec

- 354-beds Canadian tertiary institution
- Endemic for CDI

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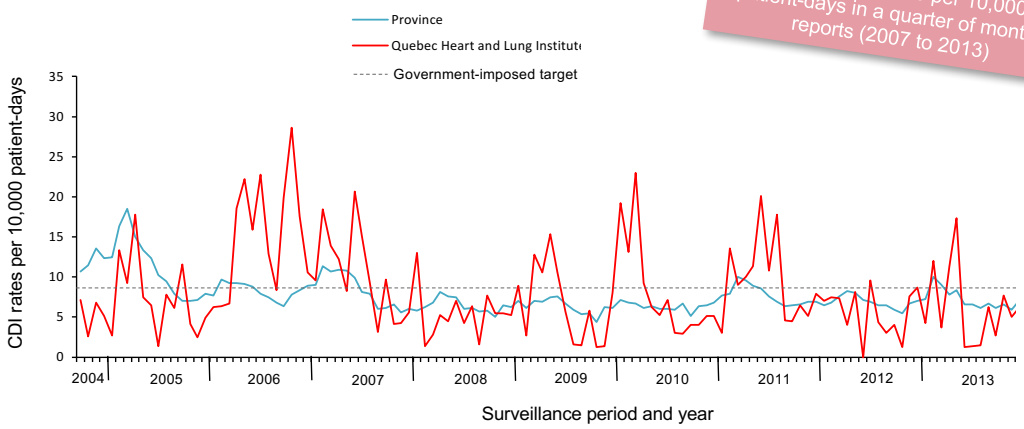
HA-CDI rates, 2004-2013

HA-CDI rates > 9.0 per 10,0000 patient-days in a quarter of monthly reports (2007 to 2013)



Incidence of healthcare-associated *Clostridium difficile* infection (CDI) per 4-week period at the Quebec Heart and Lung Institute and all institutions participating in the provincial CDI surveillance program (n=94).

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Longtin Y et al. JAMA Intern Med. 2016 Jun 1;176(6):796-804.

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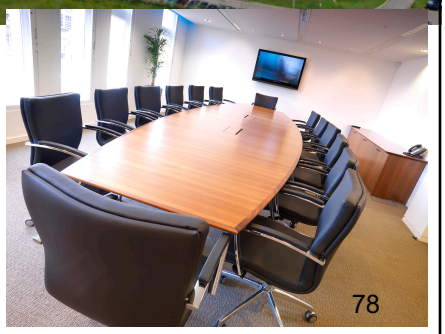
Control of CDI

October 2013

- Review of the literature on the potential role of CD carriers in CDI
- Request from executive committee to implement a strategy to detect and isolate CD-AC
- Creation of a new set of infection control measures for CD carriers



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- Similar to CDI patients with few exceptions:
  - **No isolation gowns**
  - Patients could **share a room** with non-carriers with the privacy curtains drawn
  - Measures discontinued temporarily when **going on exam**

Longtin Y et al. JAMA Intern Med. 2016 Jun 1;176(6):796-804.

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RESULTS

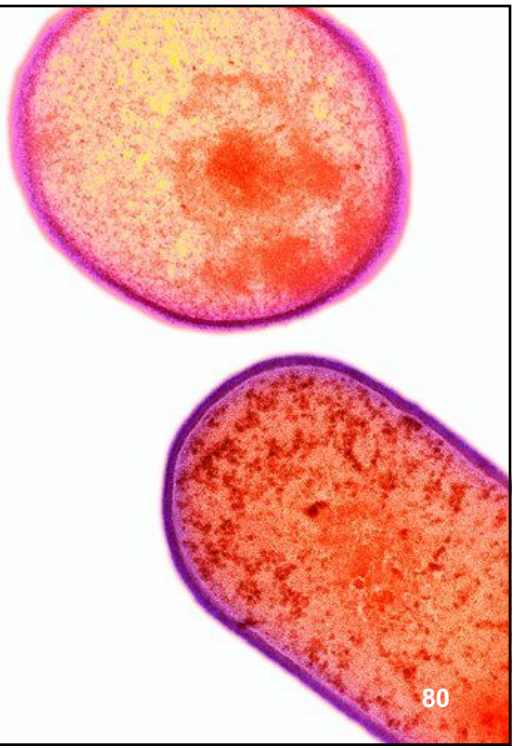

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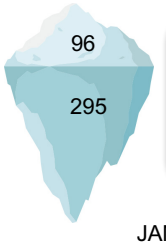
Table 1. Study Characteristics, *Clostridium difficile* Infections, and Complications by Study Period

Variable	Preintervention Period: Epidemic Period From August 22, 2004, to July 21, 2007	Preintervention Period: Postepidemic Period From July 22, 2007, to November 18, 2013	Intervention Period From November 19, 2013, to March 7, 2015	*P* Value[a]
Study periods				
Cumulative duration, mo	35	76	15	NA
4-wk Periods, No.	38	82	17	NA
Admissions, No.	43 783	83 314	18 382	NA
Patient-days, No.	276 072	600 358	127 883	NA
Screening for *C difficile* asymptomatic carriers, No./total No. (%)				
Screened patients[b]	NA	NA	7599/8218 (92.5)	NA
Asymptomatic carriers	NA	NA	368/7599 (4.8)	NA



Every Year
Approx. 295 carriers admitted
Approx. 96 patients with CDI
Ratio 3:1

JAMA Intern Med. 2016 Jun 1;176(6):796-804 81

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Incidence (95% CI) of HA-CDIs per 10 000 patient-days	11.1 (9.9-12.4)	6.9 (6.3-7.6)	3.0 (2.1-4.0)	<.001
Periods above government-imposed target, No./total No. (%)[c]	20/138 (52.6)	20/82 (24.4)	0/17 (0)	.02
Incidence (95% CI) of CDIs associated with ambulatory care per 1000 admissions	0.27 (0.14-0.45)	0.35 (0.23-0.49)	0.54 (0.26-0.93)	.25
Incidence (95% CI) of hospitalized community-acquired CDIs per 1000 admissions	0.75 (0.52-1.03)	0.59 (0.44-0.77)	0.49 (0.22-0.86)	.60

Longtin Y et al. JAMA Intern Med. 2016 Jun 1;176(6):796-804. 82

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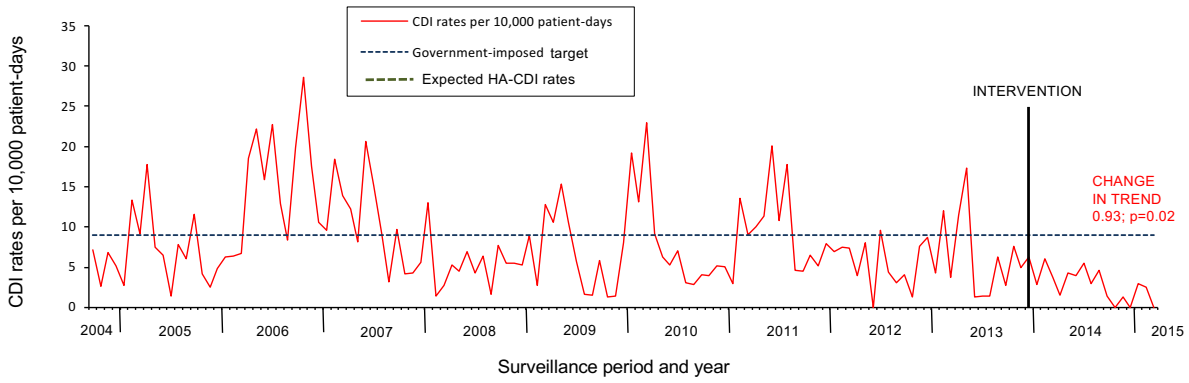

Figure 1. Incidence of healthcare-associated *Clostridium difficile* infection (CDI) per 4-week period according to standardized surveillance definitions, August 2004 - March 2015, Quebec Heart and Lung Institute, Quebec City, Canada. An intervention consisting of screening and isolation of *Clostridium difficile* asymptomatic carriers was introduced on November 19, 2013. The institution is subjected to a government-imposed threshold of 9.0 per 10 000 patient-days (blue dashed line). The expected HA-CDI rate during the intervention using an ARIMA prediction model is presented (dashed green line).

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Longtin Y et al. JAMA Intern Med. 2016 Jun 1;176(6):796-804.

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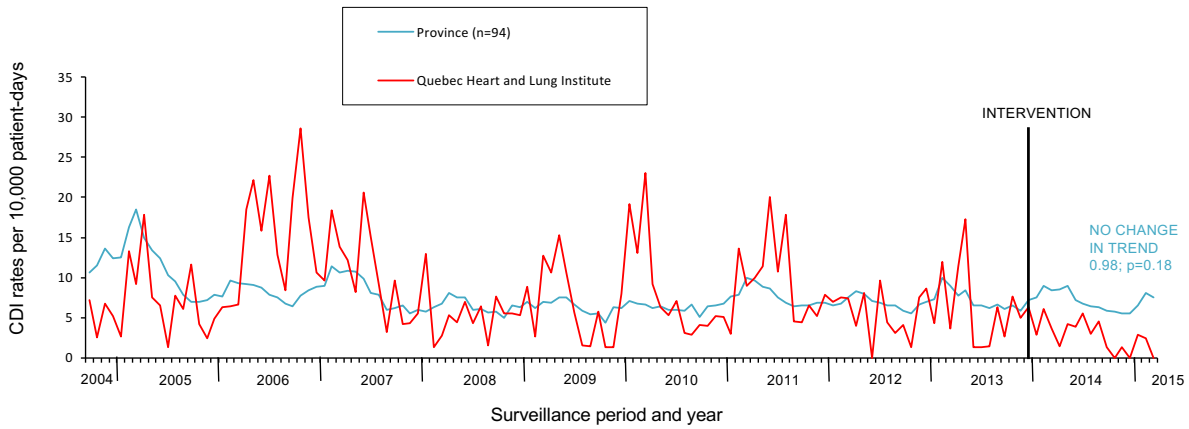

Figure 2. Incidence of healthcare-associated *Clostridium difficile* infection (CDI) per 4-week period at the Quebec Heart and Lung Institute and in 3 control groups: other institutions in Quebec City (n=6); matching academic institutions (n=15); and all institutions participating in the provincial CDI surveillance program (n=94).

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Longtin Y et al. JAMA Intern Med. 2016 Jun 1;176(6):796-804.

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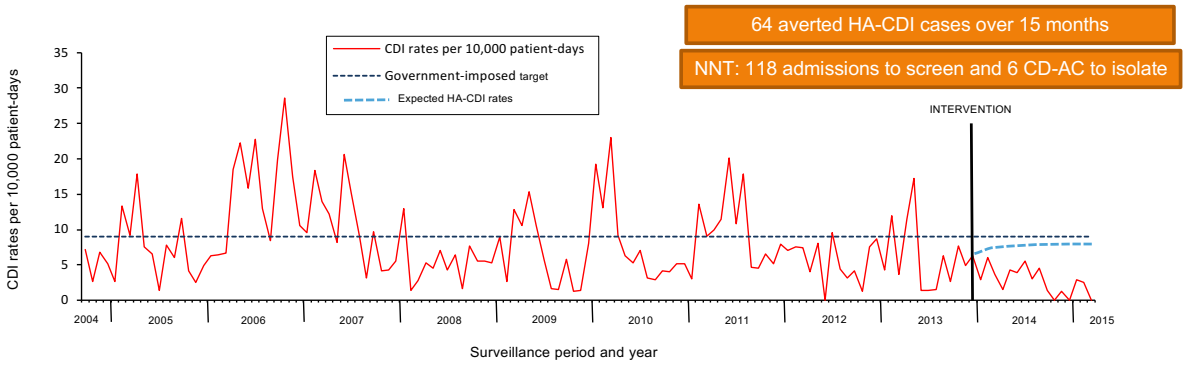
ARIMA modeling



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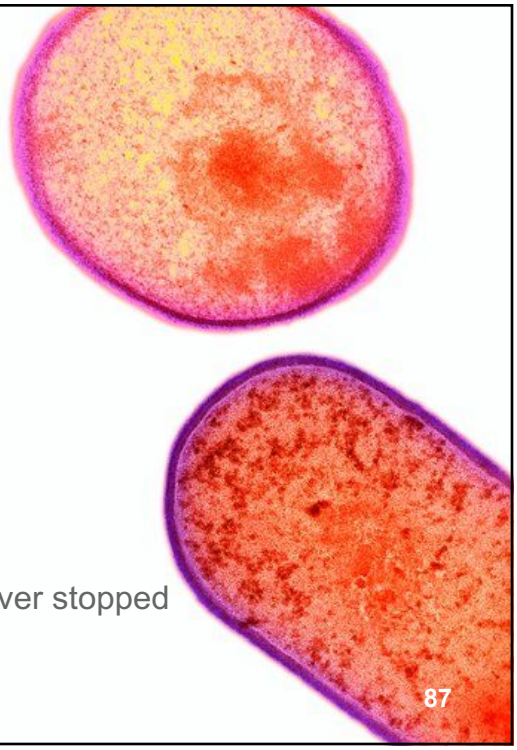

LONG-TERM Follow-up

…The intervention never stopped

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Long-term Impact

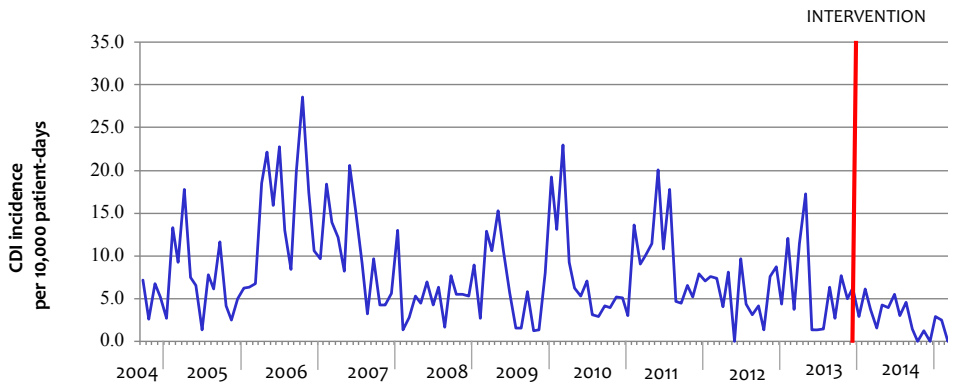

Figure 1. Healthcare-associated CDI incidence, Quebec Hearth and Lung Institute, 2004-2016

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Long-term Impact

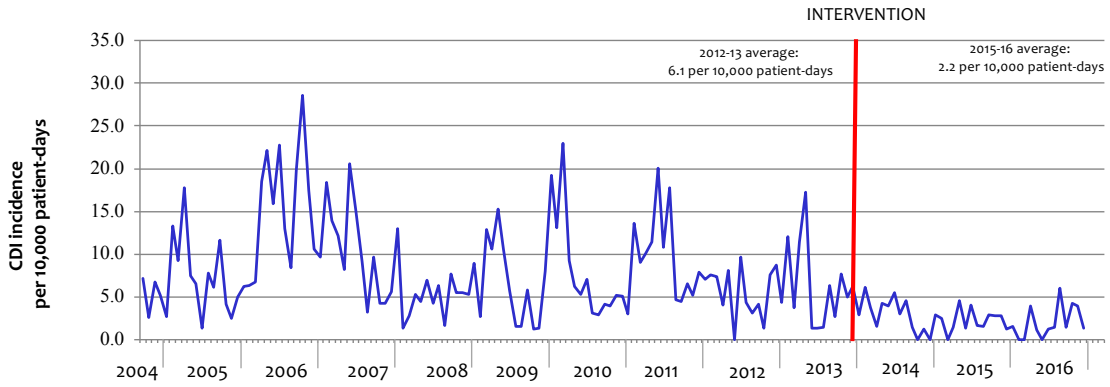

Figure 1. Healthcare-associated CDI incidence, Quebec Hearth and Lung Institute, 2004-2016

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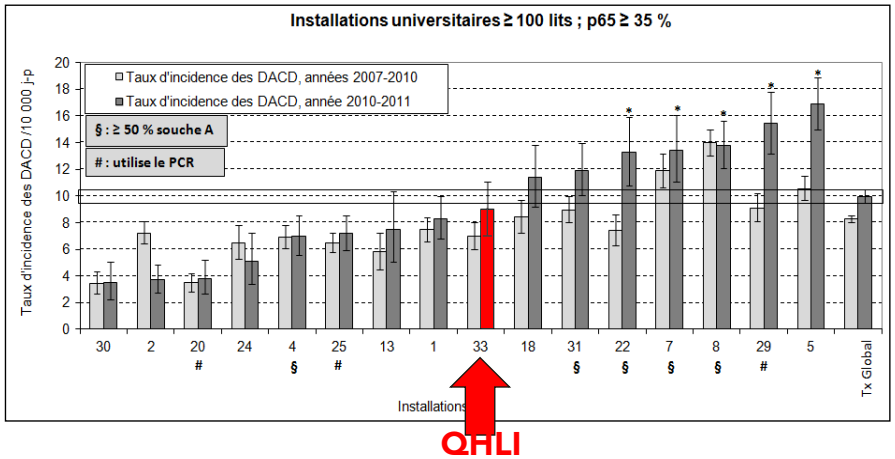
Incidence rate among university hospitals, 2011-2012



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Long-term follow-up

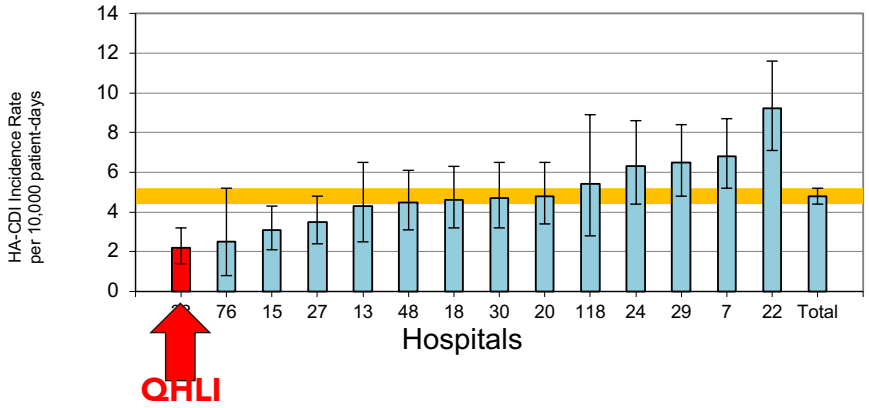

Figure 3. HA-CDI rates of University Hospitals in Quebec, 2015-2016. Red bar represents the HA-CDI incidence rate at the QHLI. Yellow Bar represents the 95% Confidence Interval for the stratum

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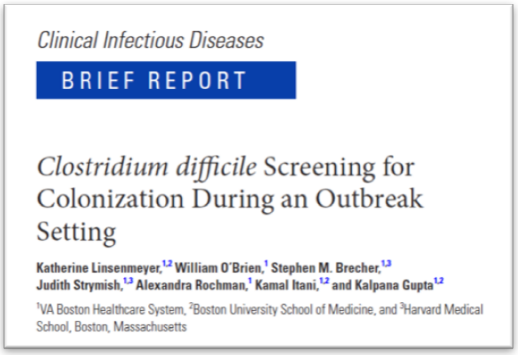

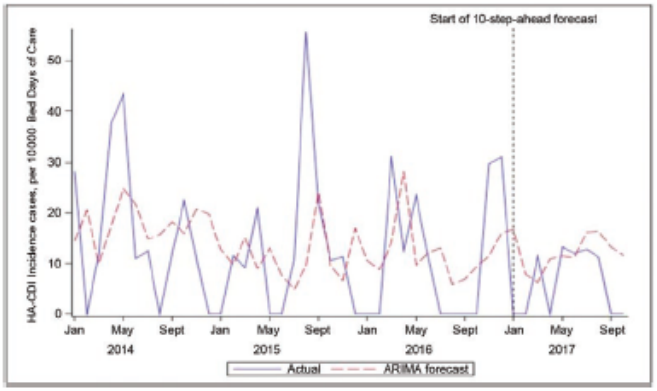

- 1250 patients screened over 12 months
- 3.1% asymptomatic carriers (perirectal swabs)
- Decrease in HA-CDI from 10.9 to 3.0 per 10kpd

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Linsenmeyer K et al. Clin Infect Dis. 2018 May 26. doi: 10.1093/cid/ciy455. [Epub ahead of print]

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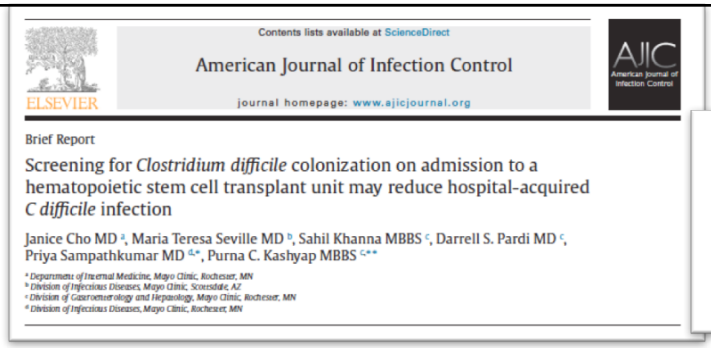

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Brief Report

Screening for *Clostridium difficile* colonization on admission to a hematopoietic stem cell transplant unit may reduce hospital-acquired *C difficile* infection

Janice Cho MD [a], Maria Teresa Seville MD [b], Sahil Khanna MBBS [c], Darrell S. Pardi MD [c], Priya Sampathkumar MD [d,*], Purna C. Kashyap MBBS [c,**]

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[b] Division of Infectious Diseases, Mayo Clinic, Scottsdale, AZ
[c] Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN
[d] Division of Infectious Diseases, Mayo Clinic, Rochester, MN

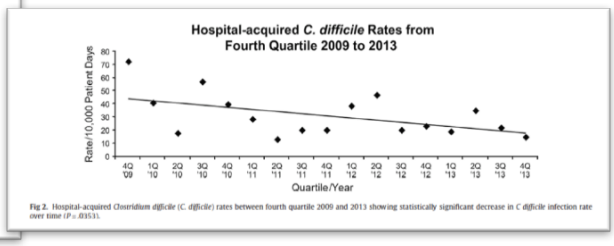

Fig 2. Hospital-acquired *Clostridium difficile* (*C. difficile*) rates between fourth quartile 2009 and 2013 showing statistically significant decrease in *C difficile* infection rate over time ($P = .0353$).

- Screening for CD carriage in HSCT unit
- Program started in 2010 but analyses 2012-2013 only
- 14% carriage rate
- Decrease in HA-CDI (role of screening uncertain – no data prior to screening)

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Cho J et al. Am J Infect Control. 2018 Apr;46(4):459-461.

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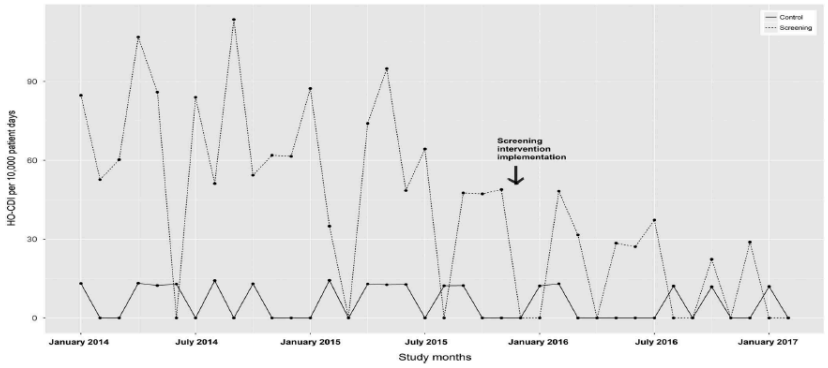
INFECTION CONTROL & HOSPITAL EPIDEMIOLOGY FEBRUARY 2018, VOL. 39, NO. 2

ORIGINAL ARTICLE

Screening for Asymptomatic *Clostridium difficile* Among Bone Marrow Transplant Patients: A Mixed-Methods Study of Intervention Effectiveness and Feasibility

Anna K. Barker, PhD;[1] Benjamin Krasity, MD, PhD;[2] Jackson Musuuza, MBBS, PhD;[3] Nasia Safdar, MD, PhD[3,4]

- Universal admission screening on BMT unit, 2014-2017 (n=5357)



Rates lower post-intervention ...

but

No signifcant change in trend c/w control arm

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PLOS ONE

RESEARCH ARTICLE

Reduced *Clostridioides difficile* infection in a pragmatic stepped-wedge initiative using admission surveillance to detect colonization

Lance R. Peterson[1,2,3]*, Sean O'Grady[4], Mary Keegan[5], Adrienne Fisher[3], Shane Zelencik[3], Bridget Kufner[3], Mona Shah[3], Rachel Lim[3], Donna Schora[2], Sanchita Das[2,3], Kamaljit Singh[1,2,3]

1 Department of Medicine, Division of Infectious Diseases, NorthShore University HealthSystem, Evanston, Illinois, United States of America, 2 Department of Pathology and Laboratory Medicine, Division of Microbiology, NorthShore University HealthSystem, Evanston, Illinois, United States of America, 3 Department of Infection Control, NorthShore University HealthSystem, Evanston, Illinois, United States of America, 4 Chief Clinical Operations Officer, NorthShore University HealthSystem, Evanston, Illinois, United States of America, 5 Department of Nursing, NorthShore University HealthSystem, Evanston, Illinois, United States of America

* lpeterson@northshore.org

Check for updates

- 4 hospitals;
- Targeted screening (pmx of hospit, LTCF resident, previous CDI)
  - 30% admissions screened; 8% CD-AC
- CDI incidence from 5.96 to 4.23 / 10,000 pd (p=0.02)

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Peterson LR et al. PLoS One. 2020 Mar 19;15(3):e0230475 95

Infection Control & Hospital Epidemiology (2020), 1–2
doi:10.1017/ice.2020.428

SHEA

Concise Communication

Universal screening for *Clostridioides difficile* at an urban academic medical center

Maggie Collison MD[1], Cynthia Murillo MASCP, CIC[2], Rachel Marrs DNP, RN, CIC[2], Allison Bartlett MD[3], Vera Tesic MD, MS[4], Kathleen G. Beavis MD[4], Emily Landon MD[1] and Jessica P. Ridgway MD, MS[1]

[1]Section of Infectious Disease, Department of Medicine, University of Chicago, Chicago, Illinois, [2]Department of Infection Control and Prevention, University of Chicago, Chicago, Illinois, [3]Section of Infectious Disease, Department of Pediatrics, University of Chicago, Chicago, Illinois and [4]Department of Pathology, University of Chicago, Chicago, Illinois

Abstract

We implemented universal inpatient *Clostridioides difficile* screening at an 800-bed hospital. Over 3 years, 2,010 of 47,048 screening tests (4.2%) were positive, with significantly higher rates of *C. difficile* colonization on transplant units than medical-surgical units: 5.4% (152 of 2,801) versus 4.3% (880 of 20,564), respectively ($P = .005$). Compliance with screening ranged from 79% to 96%.

(Received 22 May 2020; accepted 9 August 2020)

- Rolling deployment over many months
- Decrease in HA-CDI from 13.3 (12-months pre-intervention) to 5.0 per 10,000 pd (12 month into the intervention)

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Limitations

- Mostly single center trials
- Mostly before-and-after quasi-experimental studies
- Other concomitant interventions
- Multicenter trials with better study design needed!

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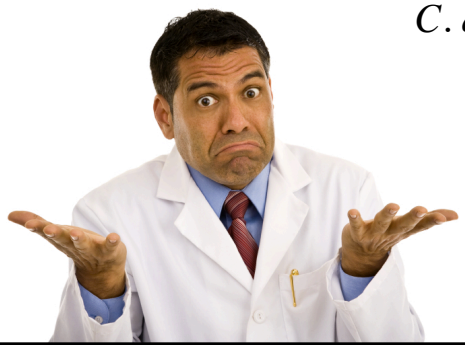
Clinical Infectious Diseases
MAJOR ARTICLE

IDSA Infectious Diseases Society of America hivma hiv medicine association OXFORD

Contribution to *Clostridium Difficile* Transmission of Symptomatic Patients With Toxigenic Strains Who Are Fecal Toxin Negative

Damian P. C. Mawer,[1,a] David W. Eyre,[2,3,a] David Griffiths,[2,3] Warren N. Fawley,[1,4] Jessica S. H. Martin,[5] T. Phuong Quan,[2,3] Timothy E. A. Peto,[2,3] Derrick W. Crook,[2,3,6] A. Sarah Walker,[2,3] and Mark H. Wilcox[1,5]

[1]Department of Microbiology, Leeds Teaching Hospitals NHS Trust; [2]Nuffield Department of Medicine, University of Oxford; [3]National Institute for Health Research Oxford Biomedical Research Centre, University of Oxford; [4]Leeds Regional Microbiology Laboratory, Public Health England; [5]Leeds Institute of Biomedical and Clinical Sciences, University of Leeds; and [6]Public Health England, Colindale, United Kingdom



Patients with diarrhea who are carriers of toxigenic *C. difficile* but without detectable toxin levels : are they contagious?

GDH + but ToxAB -

Mawer DPC et al Clin Infect Dis. 2017 May 1;64(9):1163-1170.

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Clinical Infectious Diseases
MAJOR ARTICLE

Contribution to *Clostridium Difficile* Transmission of Symptomatic Patients With Toxigenic Strains Who Are Fecal Toxin Negative

Damian P. C. Mawer,[1,a] David W. Eyre,[2,3,a] David Griffiths,[2,3] Warren N. Fawley,[1,4] Jessica S. H. Martin,[5] T. Phuong Quan,[2,3] Timothy E. A. Peto,[2,3] Derrick W. Crook,[2,3,6] A. Sarah Walker,[2,3] and Mark H. Wilcox[1,5]

[1]Department of Microbiology, Leeds Teaching Hospitals NHS Trust; [2]Nuffield Department of Medicine, University of Oxford; [3]National Institute for Health Research Oxford Biomedical Research Centre, University of Oxford; [4]Leeds Regional Microbiology Laboratory, Public Health England; [5]Leeds Institute of Biomedical and Clinical Sciences, University of Leeds; and [6]Public Health England, Colindale, United Kingdom

- WGS on all samples of C. difficile detected by GDH
- 2 centres in U.K. over 9-12 months
- Determine the relative contribution of GDH+/ToxAB+ vs. GDH+/ToxAB- in transmission and subsequent CDI

Infect Dis. 2017 May 1;64(9):1163-1170.

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Clinical Infectious Diseases
MAJOR ARTICLE

Contribution to *Clostridium Difficile* Transmission of Symptomatic Patients With Toxigenic Strains Who Are

- Source of new CDI cases
  - GDH+/ Tox + : 10%
  - GDH+/ Tox - : 3%
- But the ratio Tox+:Tox- was approximately 2:1, so the "risk per patient" was almost equivalent

Patients who are GDH+/ Tox- should be isolated

Mawer DPC et al Clin Infect Dis. 2017 May 1;64(9):1163-1170.

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Are guidelines changing?

Asymptomatic Carriers

SHEA The Society for Healthcare Epidemiology of America

Asymptomatically colonized patients who have not had CDI can shed *C. difficile* spores, but the number of spores and degree of contamination is not as great as for patients with active CDI

Dubberke ER, et al. Strategies to prevent Clostridium difficile infections in acute care hospitals: 2014 update. Infect Control Hosp Epidemiol 2014;35 Suppl 2:S48-65.

IDSA

There are insufficient data to recommend screening for asymptomatic carriage and placing asymptomatic carriers on contact precautions (no recommendation).

McDonald LC et al. Clin Infect Dis. 2018 Feb 15. doi: 10.1093/cid/cix1085.

Asymptomatic Carriers

SHEA The Society for Healthcare Epidemiology of America
2010

Routine identification of asymptomatic carriers (patients or healthcare workers) for infection control purposes is not recommended (A-III)

SHEA The Society for Healthcare Epidemiology of America
2014

There are currently no data to support detection or isolation of these asymptomatic patients (Area of controversy).

IDSA
2018

There are insufficient data to recommend screening for asymptomatic carriage and placing asymptomatic carriers on contact precautions (no recommendation).

McDonald LC et al. Clin Infect Dis. 2018 Feb 15. doi: 10.1093/cid/cix1085.

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Asymptomatic Carriers

CDC CENTERS FOR DISEASE CONTROL AND PREVENTION
2018

Supplemental intervention if reduction goals are not reached with baseline strategies:

- Evaluate and test patients at high risk for CDI to detect asymptomatic carriage;
- Isolate patients that test positive, but do not treat in the absence of symptoms

https://www.cdc.gov/hai/prevent/cdi-prevention-strategies.html

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Could it allow primary prevention of CDI?

Risk of CDI

- Non-carriers:
  - QHLI: 6 per 10,000 pd
  - Sheeba: 4.6 per 10,000 pd
- Carriers:
  - QHL I: 67.2 per 10,000 pd (39/5807 hospital-days)
  - Sheeba: 76.7 per 10,000 pd

Meltzer E et al. Clin Microbiol Infect. 2019 Feb 14.

Relative risk of CDI, carriers vs non-carriers (ICU): 9.32 (95% CI, 3.25-26.7)

Worley J et al. Clin Infect Dis. 2021 Oct 5;73(7):e1727-e1736.

…But 10-20 times less frequent than non-carriers so roughly equal contributions between CD carriers and non-carriers to global institutional CDI burden?

C. difficile carriers

- Identifying carriers could lead to strategies to protect CD carriers from progressing to CDI
  - Low hanging fruit: intensive ATB stewardship
  - Potential avenues: Primary prophylaxis, probiotics, vaccination…
  - Detection of carriers is key to this end

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C. difficile carriers

- No prospective study performed so far specifically targetting carriers
- A warning: Vancomycin and flagyl induce dysbiosis

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ATB-induced Dysbiosis

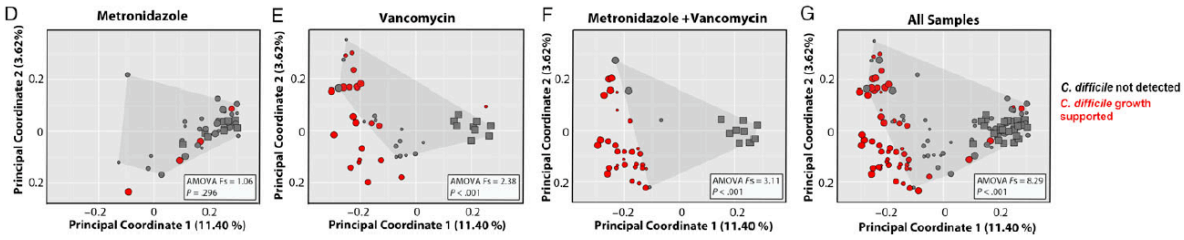

Figure 5. Antibiotic-induced disruptions of microbial communities contribute to *Clostridium difficile* susceptibility. *A–C*, Colon samples were collected from mice 24 hours after *C. difficile* infection and assessed for abundance of individual bacterial operational taxonomic units (large panels). Each stacked bar represents mean microbiota composition of 3 independently housed mice from cohort 1. Small panels in *A–C* represent the fraction of mice found susceptible to *C. difficile* 24 hours after infection in all cohorts (*red bar*; n = 9 mice per time point). *D–G*, Principal coordinate analysis of colon samples from all cohorts 24 hours after infection. Squares represent preantibiotic samples; circles, postantibiotic treatment samples. Circle sizes represent the time point of each posttreatment sample, with large circles representing earliest time points. Analysis of molecular variance (AMOVA) *F* statistics were used to compare samples in which *C. difficile* was not detected (*gray points bounded by shaded region*) with samples that supported *C. difficile* growth (*red points*).

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Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America hivma hiv medicine association OXFORD

Predictors of *Clostridioides difficile* Infection Among Asymptomatic, Colonized Patients: A Retrospective Cohort Study

Dominic Poirier,[1,2] Philippe Gervais,[1,2,3] Margit Fuchs,[4,5] Jean-Francois Roussy,[1,2,3] Bianka Paquet-Bolduc,[3] Sylvie Trottier,[1,2,3] Jean Longtin,[1,2,6] Vivian G. Loo,[7,8] and Yves Longtin[7,9]

[1]Laval University Faculty of Medicine, [2]Infectious Diseases Research Center, Centre Hospitalier Universitaire de Québec, [3]Quebec Heart and Lung Institute, [4]Centre de Recherche sur le Cancer de l'Université Laval, and [5]Centre de Recherche du Centre Hospitalier Universitaire de Québec-Université Laval, [6]Laboratoire de Santé Publique du Québec, Sainte-Anne-de-Bellevue, [7]McGill University, Faculty of Medicine, [8]McGill University Health Centre, and [9]Jewish General Hospital Sir Mortimer B. Davis, Montreal, Canada

- Cross-sectional retrospective study
- Cohort of CD carriers identified at QHLI
- Identify risk factors for progression to CDI
  - Gain insight on pathogenesis
  - Identify patients at greater risk of progression

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Predictors of CDI among CD carriers

- 19,112 patients screened
- 960 CD carriers identified
- 513 (53.4%) enrolled
- 39 (7.6%) developed HO-CDI
  - Median delay between adm. and CDI: 4 days (range, 0-27 d)
  - 5/39 (12.8%) admitted to ICU
  - 1 toxic megacolon, no colectomy
  - 11 deaths within 30 days (case fatality, 28%)
  - Attributable mortality: 7/39 (18%)
- An additional 17 patients without HO-CDI had evidence of CDI following discharge, for an overall CDI risk of 10.9% (56/513)

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Table 3. Factors associated with CDI among *C. difficile* colonized patients (multivariate analysis)

Characteristic	Risk of CDI		
	Adjusted OR	95% CI	P value
Basic demographics			
Age	1.00	0.976-1.024	0.99
Inter-institutional transfer	1.91	0.82-4.43	0.13
Length of stay	1.03	1.01-1.06	0.006
Cirrhosis	5.49	1.56-19.30	0.008
Medication			
Probiotics	2.75	1.07-7.06	0.04
Proton pump inhibitors	1.68	0.76-3.71	0.20
Laxatives	0.36	0.16-0.80	0.01
Opioids	2.78	1.32-5.82	0.007
No. of classes of at-risk antibiotics	1.45	1.05-2.03	0.02
Duration antibiotic treatment	0.998	0.967-1.031	0.93
CDI prophylaxis	0.36	0.04-3.10	0.35

! Risk of acquisition?

Narcotic stewardship?
ATB stewardship?

Risk of CDI

0 ATB: 3.6%
≥ 3 ATB : 13.8%

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Therapeutic Advances in Gastroenterology Meta-analysis

Efficacy of oral vancomycin prophylaxis for prevention of *Clostridioides difficile* infection: a systematic review and meta-analysis

Raseen Tariq, Maryrose Laguio-Vila, Muhammad Waqas Tahir, Robert Orenstein, Darrell S. Pardi and Sahil Khanna

Table 1. Characteristics of included studies.

Study name	Study period	Was prophylaxis for recurrent *versus* primary CDI	Pt population	Abstract *versus* manuscript	Case control *versus* cohort	Dosing	Mean duration of vancomycin	Most recent CDI before initiation of OVP	Definition of CDI	Follow up
Bajrovic and Sims[14]	2010–2015	Rec	All adult inpatients	A	Retro cohort	NA	NA	6 months	NA	6 months
Carignan *et al.*[17]	2003–2011	Rec	All adult inpatients	M	Retro cohort	125 mg QID	7 days	3 months	Standard definition	90 days
Carignan *et al.*[17]	2003–2011	Primary	All adult inpatients	M	Retro cohort	125 mg QID	7 days	3 months	NA	90 days
Gantesky *et al.*[18]	2015–2016	Primary	Allogenic HSCT	M	Retro cohort	125 mg BID	29 days	NA	Standard definition	30 days
O'Connell *et al.*[19]	2013–2016	Rec	All adult inpatients	A	Retro cohort	NA	NA	NA	NA	90 days
Bajrovic and Brizendine[20]	2007–2013	Primary	Lung transplant recipients	A	Retro cohort	NA	NA	NA	NA	1 year
Papic *et al.*[11]	2015–2017	Primary	Pts > 65 inpatient	M	Retro cohort	NA	9 days	NA	NA	3 months
Pereiras *et al.*[21]	2013–2014	Rec	HSCT pts	A	Retro cohort	NA	NA	NA	NA	1 year
Splinter *et al.*[22]	2012–2015	Rec	Renal transplant pts	M	Retro cohort	125 mg BID	19 days	NA	Standard definition	30 days
Van Hise *et al.*[23]	2010–2014	Rec	All adult inpatients	M	Retro cohort	125 mg BID and 250 mg BID	13.7 days	3 years	Standard definition	30 days
Wong and Riska[24]	2011–2014	Rec	All adult inpatients	A	Retro cohort	NA	NA	3 months	NA	30 days
Knight *et al.*[25]	2013–2015	Rec	All adult inpatients	M	Retro cohort	250 mg and 125 mg QID	8.5 days	12 months	Standard definition	12 months
Caroff *et al.*[10]	2009–2015	Rec	All adult inpatients	M	Retro cohort	NA	2.5 days	5 months	Standard definition	90 days
Morrisette *et al.*[26]	2014–2018	Rec	HSCT and hematological malignancy pts	M	Retro cohort	125 mg BID	NA	NA	Standard definition	60 days
Johnson *et al.*[27]	2018–2019	Primary	All adult inpatients	M	Randomized open label prospective	125 mg daily	NA	NA	Standard definition	3 months

A, abstract; BID, two times daily; CDI, *Clostridioides difficile* infection; CI, confidence interval; HSCT, hematopoietic stem cell transplant; M, manuscript; NA, not available; OPV, oral vancomycin prophylaxis; Pt, patient; Rec, recurrent; QID, four times daily standard definition, diarrhea with + stool test for *C. difficile* toxin.

Therapeutic Advances in Gastroenterology Meta-analysis

Efficacy of oral vancomycin prophylaxis for prevention of *Clostridioides difficile* infection: a systematic review and meta-analysis

Raseen Tariq, Maryrose Laguio-Vila, Muhammad Waqas Tahir, Robert Orenstein, Darrell S. Pardi and Sahil Khanna

Ther Adv Gastroenterol
2021, Vol. 14: 1–11
DOI: 10.1177/17562848211994046

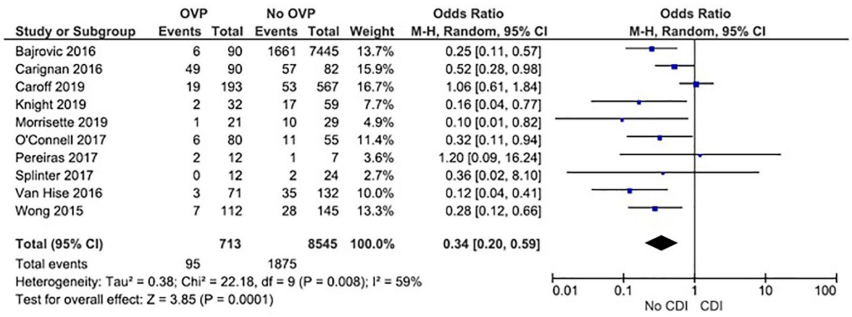

Figure 3. Analysis of studies that evaluated oral vancomycin for recurrent CDI prophylaxis, showing statistically significant decreased risk of CDI.
CDI, *Clostridioides difficile* infection; CI, confidence interval; OPV, oral vancomycin prophylaxis.

Secondary prophylaxis:

- 10 studies, 9258 patients
- CDI: 13.3% vs 21.9%
- (OR, 0.34; 95% CI, 0.20–0.59; $p <$ 0.00001)

Therapeutic Advances in Gastroenterology Meta-analysis

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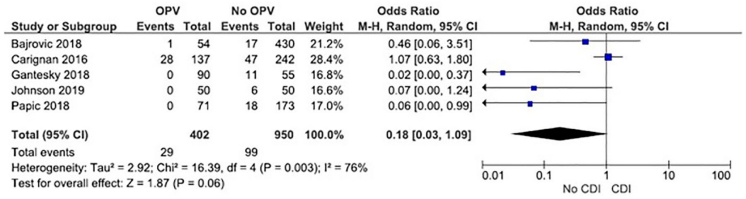

Figure 2. Analysis of studies that evaluated oral vancomycin for primary CDI prophylaxis, showing no prevention benefit.
CDI, *Clostridioides difficile* infection; CI, confidence interval; OPV, oral vancomycin prophylaxis.

Primary prophylaxis:

- 4 studies, 1352 patients
- CDI: 29/402 (7.4%) vs 99/950 (10.4%)
- OR: 0.18, 95% CI, 0.03–1.03; p = 0.06
- Prophylaxis not targeting carriers!
- Short follow-up period (<=90 days in 3 of 4 studies)
- NB Carignan: no primary prophylaxis!

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Tariq R et al. Therap Adv Gastroenterol. 2021 Feb 23;14:1756284821994046.

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Research Agenda

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Unknowns and Research Agenda

- Need high-quality research!
- Generalizability of previous studies?
  - Very pro-infection control hospital, high endemicity, high prevalence of hypervirulent strain
- Best detection methods?
- What is the incidence rate at which it becomes cost-effective?
  - Which population to target?
- Management of *C. difficile* carriers who must receive ATB?
- Where does it fit in relationship with ATB stewardship to control NAP1 ?

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Conclusions

- Optimal approach to prevent CDI remains unknown
- Current strategies = flawed
- Current recommendations based on limited evidence
- Better evidence would be required
  - These are hard to obtain!
- New strategies should be explored

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ANY QUESTIONS?

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www.webbertraining.com/schedulep1.php	
May 25, 2022	*(South Pacific Teleclass)* **PATIENT-FOCUSED ANTIMICROBIAL RESISTANCE SURVEILLANCE: DATA FROM THE GROUND UP** Speaker: **Dr. Paul Turner**, Cambodia Oxford Medical Research Unit, Angkor Hospital for Children, Cambodia
June 8, 2022	**PULLING THE PLUG ON THE SINK DRAIN** Speaker: **Prof. Jean-Yves Maillard**, Cardiff University, Wales
June 28, 2022	*(European Teleclass)* **HOW EFFECTIVE ARE INTERVENTIONS TO IMPROVE CLEANING OF HEALTHCARE ENVIRONMENTS IN LOW-RESOURCED SETTINGS?** Speaker: **Prof. Giorgia Gon**, London School of Hygiene and Tropical Medicine, UK
June 30, 2022	*(FREE Teleclass)* **SHARING KNOWLEDGE: LEARNING FROM THOSE WHO HAVE CHALLENGED THE CIC** Speaker: **Sam MacFarlane**, Public Health Ontario, **Sandra Petersen**,Ottawa Public

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