ARS TOSCANA
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antibiotico-resistenza: sconfiggiamola insieme!

Convegno

Antimicrobico-resistenza: cure e ambiente

Firenze, 6 -7 giugno 2019

Istituto Stensen, viale Don Minzoni n. 25/C, Firenze

La sorveglianza nel CD

Nicola Petrosillo, MD, FESCMID

Istituto Nazionale per le Malattie Infettive «Lazzaro Spallanzani», IRCCS - Roma

cdiff awareness
cdifffoundation.org

MULTA CORDA UNA CAUSA
Istituto di Ricovero e Cura a Carattere Scientifico
LAZZARO SPALLANZANI

Competing interests disclosure

- Honorary as speaker for MSD, Pfizer, B&D, Gilead, GSK, J &J , Angelini, Zambon, 3M, Accelerate, Shionogi, Takeda.

- Honorary as member of scientific board for Pfizer, MSD, B&D.

- **Clostridium difficile was first described in 1935 in the resident flora of healthy neonates.**

- **Corresponding to the difficulty of cultivating the bacteria, it was initially termed Bacillus difficilis.**

- **More than 3 decades later, the relation between pseudomembranous colitis and C difficile was revealed, especially after clindamycin treatment.**

- **During the past 20 years this gram-positive and spore-forming bacterium has been identified as the most common cause of antibiotic-associated diarrhea in industrialized countries.**

Hall IC and O'Toole ER. Am J Dis Chil 1935; 49:390-42
Cohen E et al. JAMA 1973; 223:1379-80

Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals

2011–2012

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

- **In 2011–2012, 29 EU/EEA Member States and Croatia participated in the first EU-wide, ECDC-coordinated point prevalence survey (PPS) of healthcare-associated infections (HAIs) and antimicrobial use in acute care hospitals.**

- **231 459 patients from 947 hospitals were included in the final European sample for analysis.**

•The prevalence of patients with at least one HAI in acute care hospitals in the PPS sample was 6.0% (country range 2.3%–10.8%).

•Of a total of 15 000 reported HAIs, the most frequently reported HAI types were
-respiratory tract infections (pneumonia 19.4% and lower respiratory tract 4.1%),
-surgical site infections (19.6%),
-urinary tract infections (19.0%),
-bloodstream infections (10.7%) and
-gastro-intestinal infections (7.7%), with Clostridium difficile infections accounting for 48% of the latter.

Figure 3. *Clostridium difficile* infections and other gastro-intestinal infections (excluding hepatitis) as a percentage of all HAIs, by country, ECDC PPS 2011–2012

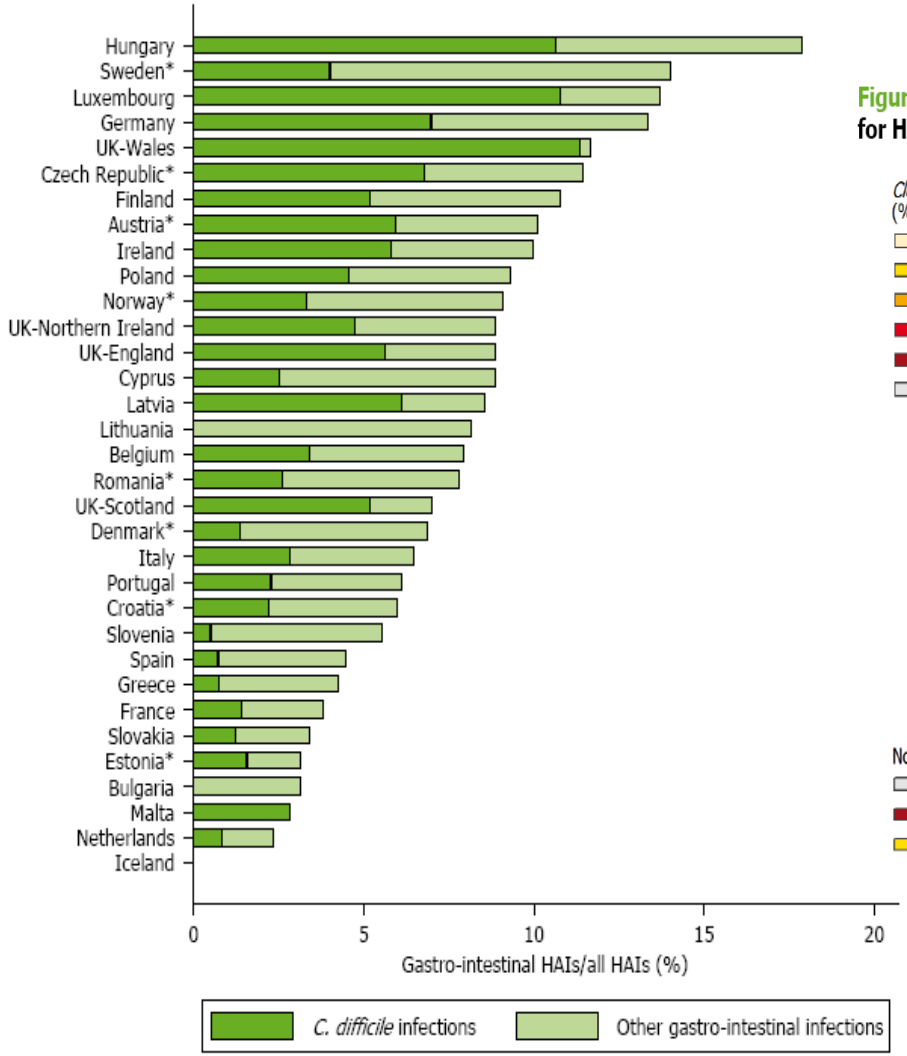
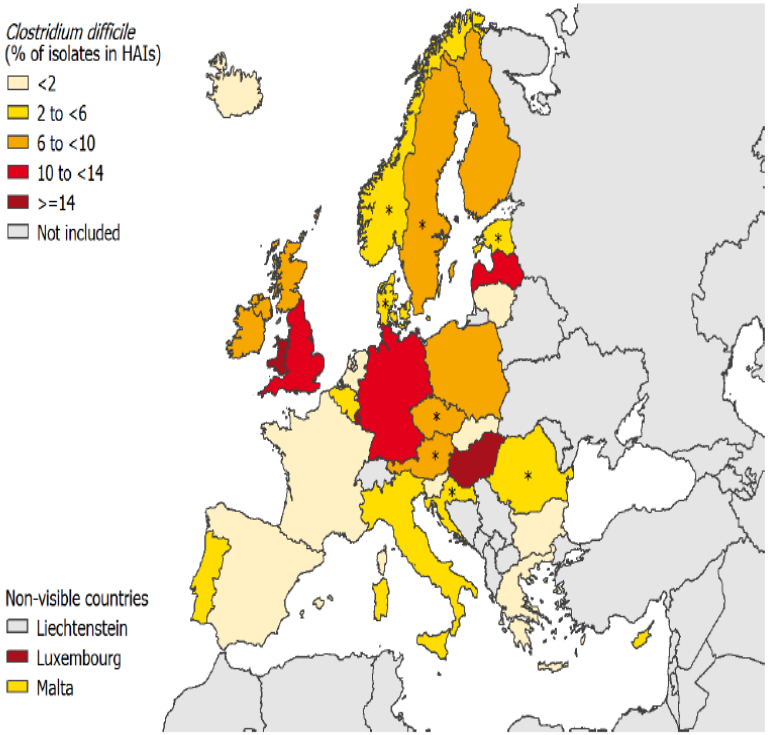


Figure 42. Relative frequency of *Clostridium difficile* as a percentage of all microorganisms reported for HAIs, by country (n=548 isolates), ECDC PPS 2011–2012



ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Prevalence of healthcare-associated infections, estimated incidence and composite antimicrobial resistance index in acute care hospitals and long-term care facilities: results from two European point prevalence surveys, 2016 to 2017

- **HAI PPS and antimicrobial use in the European Union and European Economic Area (EU/EEA) from 2016 to 2017 included 310,755 patients from 1,209 acute care hospitals (ACH) in 28 countries and 117,138 residents from 2,221 long-term care facilities (LTCF) in 23 countries.**

- **6.5% patients in ACH and 3.9% residents in LTCF had at least one HAI.**

- **On any given day, 98,166 patients in ACH and 129,940 residents in LTCF had an HAI.**

- **HAI episodes per year were estimated at 8.9 million, including 4.5 million in ACH and 4.4 million in LTCF; 3.8 million patients acquired an HAI each year in ACH.**

- **Antimicrobial resistance (AMR) to selected AMR markers was 31.6%**

Suetens C et al. Euro Surveill. 2018 Nov;23(46)

Prevalence of healthcare-associated infections, estimated incidence and composite antimicrobial resistance index in acute care hospitals and long-term care facilities: results from two European point prevalence surveys, 2016 to 2017

The most frequently reported types of HAI were
•respiratory tract infections (21.4% pneumonia and 4.3% other lower respiratory tract infections),
•urinary tract infections (18.9%),
•surgical site infections (18.4%),
•bloodstream infections (10.8%) and
•gastro-intestinal infections (8.9%), with *C. difficile* infections accounting for 44.6% of the latter or 4.9% of all HAI.

Twenty-three per cent of HAI were present on admission. One third of HAI on admission were surgical site infections.

Suetens C et al Euro Surveill 2018;23(46):pii=1800516

Underdiagnosis of *Clostridium difficile* across Europe: the European, multicentre, prospective, biannual, point-prevalence study of *Clostridium difficile* infection in hospitalised patients with diarrhoea (EUCLID)

- **482 participating hospitals across 20 European countries.**

- **During the study period, participating hospitals reported a mean of 65·8 tests (country range 4·6–223·3) for C difficile infection per 10 000 patient-bed days and a mean of 7·0 cases (country range 0·7–28·7) of C difficile infection per 10,000 patient-bed days.**

- **Only two-fifths of hospitals reported using optimum methods for testing of C difficile infection.**

Davies KA et al. Lancet Infect Dis 2014;14:1208-19

Underdiagnosis of *Clostridium difficile* across Europe: the European, multicentre, prospective, biannual, point-prevalence study of *Clostridium difficile* infection in hospitalised patients with diarrhoea (EUCLID)

- **Across all 482 European hospitals on the two sampling days, 148 (23%) of 641 samples positive for C difficile infection (as determined by the national laboratory) were not diagnosed by participating hospitals because of an absence of clinical suspicion, equating to about**

74 missed diagnoses per day

Davies KA et al. Lancet Infect Dis 2014;14:1208-19

CDI surveillance

A recommended case definition for surveillance requires

(1) the presence of diarrhea or evidence of megacolon or severe ileus and

(2) either a positive laboratory diagnostic test result or evidence of pseudomembranes demonstrated by endoscopy or histopathology.

McDonald LC et al. Clin Infect Dis 2018;66(7):e1–e48

- **An incident case is defined as a new primary episode of symptom onset (i.e., no episode of symptom onset with positive result within the previous 8 weeks) and positive assay result (eg, toxin enzyme immunoassay [EIA] or nucleic acid amplification test [NAAT]).**

- **A recurrent case is defined as an episode of symptom onset and positive assay result following an episode with positive assay result in the previous 2–8 weeks.**

Clostridium difficile recurrence definitions in studies assessing prediction scores of recurrences.
Définition d'une récidive d'infection à Clostridium difficile *dans les études ayant évalué les scores de prédiction clinique des récidives.*

Year/First author/Ref.	Definition
2009/Hu MY/34	A new episode of diarrhea confirmed by a positive stool *C. difficile* toxin assay, after resolution of the initial *C.difficile* infection (CDI) episode for at least 2 days and after discontinuation of therapy with metronidazole or vancomycin.
2012/Eyre DW/2	Definition not given.
2014/Zilberberg MD/35	A repeat positive toxin within 42 days following the end of the initial CDI treatment.
2014/D'Agostino RB/37	Definition not given. Patients who were cured were subsequently followed for 28 days for an assessment of recurrence.
2015/LaBarbera FD/38	Confirmed presence of *C. difficile* toxin via polymerase chain reaction after complete resolution of diarrhea for a minimum of 6 months and the completion of antibiotic therapy.
2017/Viswesh V/39	Recurrence was defined as (1) a documented positive result on an enzyme immunoassay or PCR test for *C. difficile* antigen and toxin or (2) a documented return of CDAD symptoms and subsequent CDAD treatment.

Petrosillo N. Med Mal Infect 2018; 48(1): 18-22

Risk factors for recurrence in patients with *Clostridium difficile* infection due to 027 and non-027 ribotypes

M. Falcone [1,*], G. Tiseo [2], F. Iraci [3], G. Raponi [3], P. Goldoni [3], D. Delle Rose [4], I. Santino [5], P. Carfagna [6], R. Murri [7], M. Fantoni [7], C. Fontana [8], M. Sanguinetti [9], A. Farcomeni [3], G. Antonelli [10], A. Aceti [11], C. Mastroianni [3], M. Andreoni [4], R. Cauda [7], N. Petrosillo [12], M. Venditti [3]

Clin Microbiol Infect 2018 Jun 28

- **From January to December 2014, 717 episodes of CDI were observed.**
- **CDI incidence was 4.2 cases/10,000 patient-days during the study period.**

Table 3
Multivariate analysis of risk factors for recurrence among patients with 027 *Clostridium difficile* infection (CDI)

	Multivariate analysis			
	sHR	95.0%CI		p value
		Lower	Upper	
Therapy for first CDI (*vancomycin as reference variable*):				
Metronidazole monotherapy versus vancomycin monotherapy	2.380	1.549	3.650	**<0.001**
Metronidazole + vancomycin versus vancomycin monotherapy	0.349	0.105	1.150	0.084
Any immunosuppressive therapy	3.116	1.906	5.090	**<0.001**

Statistical significant variables ($p \leq 0.05$) were highlighted in bold. sHR, subdistributional hazard ratio.

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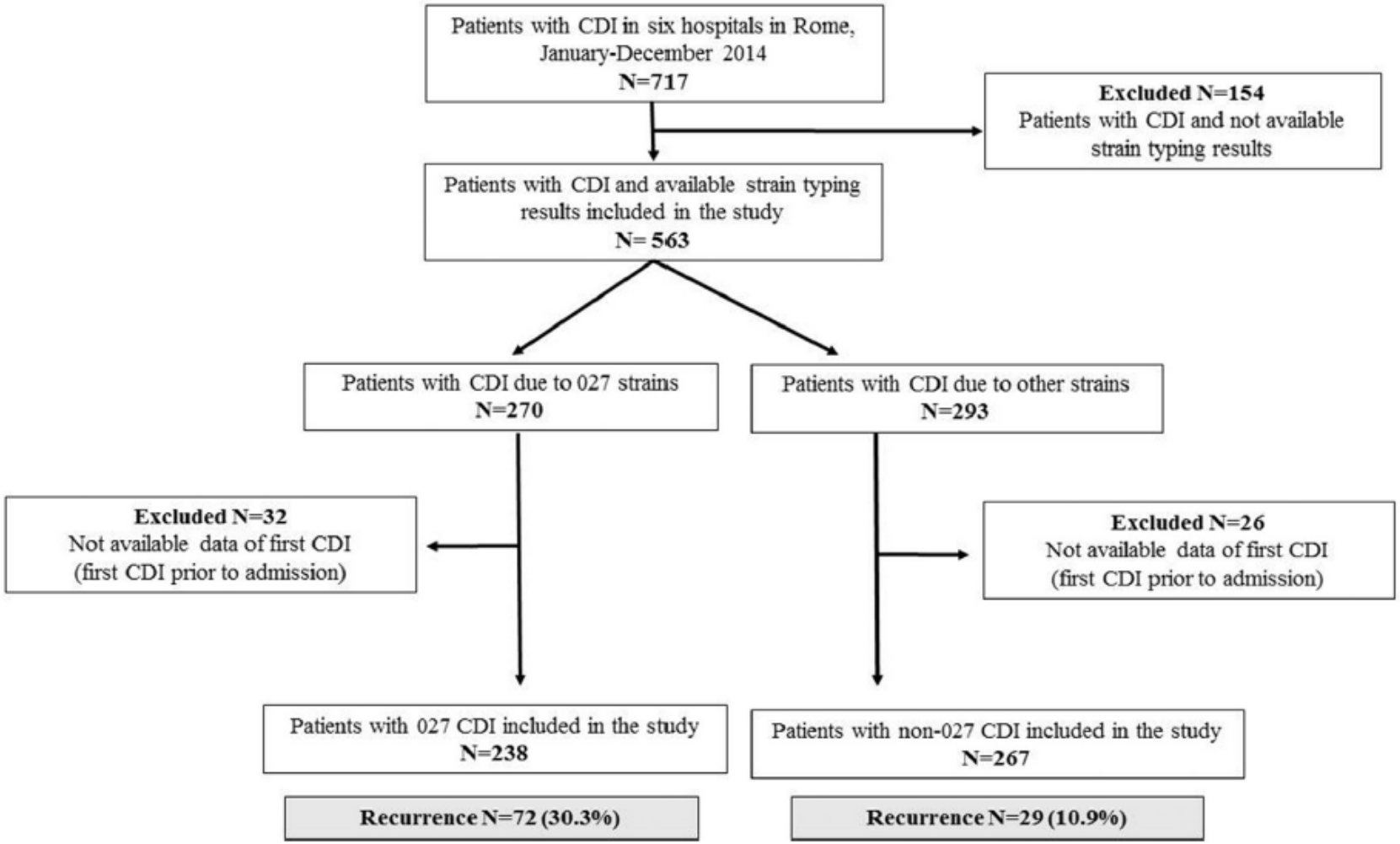
Clin Microbiol Infect 2018 Jun 28



Clostridium difficile Infection Control and Prevention

Clinical Infectious Diseases

IDSA GUIDELINE

Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA)

L. Clifford McDonald,[1] Dale N. Gerding,[2] Stuart Johnson,[2,3] Johan S. Bakken,[4] Karen C. Carroll,[5] Susan E. Coffin,[6] Erik R. Dubberke,[7] Kevin W. Garey,[8] Carolyn V. Gould,[1] Ciaran Kelly,[9] Vivian Loo,[10] Julia Shaklee Sammons,[6] Thomas J. Sandora,[11] and Mark H. Wilcox[12]

Clinical Infectious Diseases® 2018;66(7):987–94

The minimum surveillance that should be performed by all healthcare facilities is tracking of healthcare facility–onset (HO) cases, which will allow for detection of elevated rates or an outbreak within the facility.

I.How are CDI cases best defined?

Recommendation

1. To increase comparability between clinical settings, use available standardized case definitions for surveillance of

(1)healthcare facility-onset (HO) CDI;
(2)community-onset, healthcare facility–associated (CO-HCFA) CDI; and
(3)community-associated (CA) CDI

(good practice recommendation).

II. What is the minimal surveillance recommendation for institutions with limited resources?

Recommendation

1.At a minimum, conduct surveillance for HO-CDI in all in- patient healthcare facilities to detect elevated rates or out- breaks of CDI within the facility

(weak recommendation, low quality of evidence).

III. What is the best way to express CDI incidence and rates?

Recommendation

1. Express the rate of HO-CDI as the number of cases per 10 000 patient-days. Express the CO-HCFA prevalence rate as the number of cases per 1000 patient admissions *(good practice recommendation)*.

IV. How should CDI surveillance be approached in settings of high endemic rates or outbreaks?

Recommendation

1. Stratify data by patient location to target control measures when CDI incidence is above national and/or facility reduction goals or if an outbreak is noted *(weak recommendation, low quality of evidence)*.

E’ possibile utilizzare la sindrome diarroica nella sorveglianza di Cdif?

Diarrea e ricovero in ospedale

Diarrea acquisita in comunità: diarrea insorta prima del ricovero e comunque da meno di 48 dal ricovero stesso, in assenza dei fattori di esposizione a procedure assistenziali (vedi dopo)

Diarrea associata all'assistenza insorta in comunità: inizio dei sintomi in comunità e comunque < 48h dal ricovero, in presenza dei seguenti fattori di esposizione a procedure assistenziali:

- ospedalizzazione (compresi i ricoveri in strutture protette) nei 3 mesi precedenti,
- procedure assistenziali (dialisi, DH, day surgery, etc…) nei tre mesi precedenti,
- attività lavorativa associata all'assistenza sanitaria.

Diarrea acquisita in ospedale: inizio della diarrea e dei sintomi associati ≥48 ore dal ricovero.

RF IRCCS – dati personali

Definizione di **risultato diagnostico positivo** per infezione da C difficile.

•Antigene GDH positivo + tossine A/B positive (EIA) ovvero

•Antigene GDH positivo + tossine A/B negative (EIA) + PCR positive per TdcB ovvero

•PCR positiva per TdcB + tossina A/B positiva (EIA)

- **Durante il periodo dello studio, sono stati ricoverati 7329 pazienti; di questi 603 (8,2%) avevano o riferivano una diarrea al momento del ricovero ovvero avevano sviluppato una diarrea durante il ricovero.**

- **111 pazienti sono stati esclusi dall'analisi per risoluzione della diarrea entro 24 ore dal ricovero senza terapia anti Clostridium difficile e un paziente ha rifiutato di entrare nello studio.**

- **Sono stati pertanto analizzati i dati di 491 (6,7%) pazienti con diarrea.**

RF IRCCS – dati personali

Diarrea ad esordio in comunità.

- **284/491 pazienti (57,8%) riferivano diarrea al momento del ricovero in ospedale o entro le 48 dall'inizio del ricovero;**

- **141 (49,6%) venivano classificate come diarree comunitarie e**

- **143 (51,4%) come diarree associate a procedure assistenziali con esordio in comunità.**

RF IRRCS-dati personali

Diarrea ad esordio in comunità.

- **Nel gruppo delle diarree comunitarie, il test per C difficile è stato richiesto dai clinici nel 64,5% dei casi (91/141), ed in questi è risultato positivo in 12 casi (13,1%);**

- **nei 50 casi in cui il test per C difficile non è stato richiesto dai clinici, il test su aliquote residue di feci è risultato positivo in 4 casi (8%).**

Diarrea ad esordio in comunità.

- **Nel gruppo delle diarree associate all'assistenza insorte in comunità, il test per C difficile è stato chiesto nell'84,6% dei casi (121) ed in questi è risultato positivo nel 53,7% dei casi (65).**

- **Nei 22 casi in cui il test per C difficile non è stato chiesto, il test su aliquote di campione fecale è risultato positivo in 1 caso (4,5%).**

RF IRRCS-dati personali

Diarrea ad esordio in ospedale (>=48 ore dal ricovero)

- **L'incidenza di diarrea insorta dopo 48h dal ricovero è stata di 18,1 casi (207/114513) per 10.000 giorni ricovero.**

- **In 171 dei 207 casi considerati (82,6%) è stato richiesto il test per C difficile che è risultato positivo in 34 casi (19,9%);**

- **nei 36 casi in cui non è stato richiesto, il test è risultato positivo (utilizzando aliquote di campione di feci) in 2 casi (5,5%).**

- **L'incidenza di infezione da C difficile è stata di 3,1 infezioni (36/114513 giornate di degenza) per 10.000 giorni ricovero.**

RF IRRCS-dati personali

In totale,

- **la positività per infezione da C difficile è stata del 24% (118/491) tra i pazienti che presentavano diarrea ad esordio comunitario od ospedaliero;**

- **nelle diarree comunitarie senza fattori di rischio associate a procedure assistenziali è stata dell'11,3% (16/141),**

- **in quelle con fattori di rischio per procedure assistenziali (sia ad esordio comunitario che ospedaliero) è stata del 29,1% (102/350).**

RF IRRCS-dati personali

Sottodiagnosi di infezione da C difficile

sui 108 campioni di feci per i quali il test per C difficile non era stato richiesto su feci diarroiche, il laboratorio è stato in grado, su aliquote residue di feci, di identificare l'infezione da C difficile in 7 casi (6,4%)

- **4 nel gruppo delle diarree comunitarie (4/50=8%),**
- **1 nel gruppo delle diarree ad insorgenza comunitaria-associate a procedure assistenziali (1/22= 4,5%) e**
- **2 (2/36=5,5%) casi nel gruppo delle diarree ad insorgenza nosocomiale.**

Il tasso di sottodiagnosi equivale ad 1,42 casi ogni 100 pazienti con diarrea ricoverati in ospedale, inclusi quelli con insorgenza comunitaria o ospedaliera.

RF IRRCS-dati personali

Sottodiagnosi di infezione da C difficile

•nel gruppo delle diarree comunitarie senza fattori di rischio associati all'assistenza, se non fosse stata eseguita l'analisi dei campioni residui si sarebbero perse **2,8 diagnosi di infezione da C difficile ogni 100 pazienti con diarrea**;

•nel gruppo delle diarree comunitarie con fattori di rischio associati all'assistenza si sarebbero perse **0,7 infezioni ogni 100 pazienti con diarrea**, e nel gruppo delle diarree ad insorgenza ospedaliera **1 infezione ogni 100 pazienti con diarrea.**

In definitiva, nel gruppo di pazienti con diarrea per i quali non è stato chiesto il test per C difficile, l'NNT (Number needed to test) è di 15,4 test per rilevare una infezione da C difficile.

RF IRRCS-dati personali

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Clinical Infectious Diseases® 2018;66(7):987–94

INFECTION PREVENTION AND CONTROL

Isolation Measures for Patients With CDI

XIII. Should private rooms and/or dedicated toilet facilities be used for isolated patients with CDI?

Recommendations

1. Accommodate patients with CDI in a private room with a dedicated toilet to decrease transmission to other patients. If there is a limited number of private single rooms, prioritize patients with stool incontinence for placement in private rooms *(strong recommendation, moderate quality of evidence).*
2. If cohorting is required, it is recommended to cohort patients infected or colonized with the same organism(s)—that is, do not cohort patients with CDI who are discordant for other multidrug-resistant organisms such as methicillin-resistant *Staphylococcus aureus* or vancomycin-resistant *Enterococcus (strong recommendation, moderate quality of evidence).*

XIV. Should gloves and gowns be worn while caring for isolated CDI patients?

Recommendation

1. Healthcare personnel must use gloves *(strong recommendation, high quality of evidence)* and gowns *(strong recommendation, moderate quality of evidence)* on entry to a room of a patient with CDI and while caring for patients with CDI.

XIX. Should noncritical devices or equipment be dedicated to or specially cleaned after being used on the isolated patient with CDI?

Recommendation

1. Use disposable patient equipment when possible and ensure that reusable equipment is thoroughly cleaned and disinfected, preferentially with a sporicidal disinfectant that is equipment compatible *(strong recommendation, moderate quality of evidence)*.

XV. When should isolation be implemented?

Recommendation

1. Patients with suspected CDI should be placed on preemptive contact precautions pending the *C. difficile* test results if test results cannot be obtained on the same day *(strong recommendation, moderate quality of evidence)*.

XVI. How long should isolation be continued?

Recommendations

1. Continue contact precautions for at least 48 hours after diarrhea has resolved *(weak recommendation, low quality of evidence)*.
2. Prolong contact precautions until discharge if CDI rates remain high despite implementation of standard infection control measures against CDI *(weak recommendation, low quality of evidence)*.

XXIV. Should asymptomatic carriers of *C. difficile* be identified and isolated if positive?

Recommendation

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

Guidance document for prevention of *Clostridium difficile* infection in acute healthcare settings

Sarah Tschudin-Sutter, MD MSc, Ed J. Kuijper, PhD, Ana Durovic, Maria J.G.T. Vehreschild, MD, Frédéric Barbut, PhD, Catherine Eckert, PhD, Fidelma Fitzpatrick, MD, Markus Hell, MD, Torbjörn Norén, MD, Jean O'Driscoll, MB, John Coia, MD, Petra Gastmeier, MD, Lutz von Müller, MD, Mark H. Wilcox, MD PhD, Andreas F. Widmer, MD MSc, Franz Allerberger, Oliver A. Cornely, Michel Delmée, Bente Olesen, MD PhD, Johan van Broeck

Clin Microb Infect 2018

Does screening for C. difficile identify colonised/carrier patients at increased or decreased risk of developing C. difficile infection?

Recommendation for outbreak and endemic settings

4. We do not recommend screening for *C. difficile* to identify colonised/carrier patients as a way of altering the risk of developing CDI in either colonized subjects or other patients and thus reducing CDI-rates (conditional recommendation, low level of evidence in the endemic setting).

To screen or not to screen?

Risk Factors for Clostridium difficile Isolation in Inflammatory Bowel Disease: A Prospective Study.

They prospectively recruited consecutive IBD patients presenting to their outpatient clinic between April 2015 and February 2016.

A rectal swab was performed from which toxigenic culture and PCR analysis for the presence of toxin and fluorescent PCR ribotyping were performed. The primary outcome of interest was isolation of toxigenic C. difficile.

Micic D et al. Dig Dis Sci 2018;63:1016-1024

- **190 patients including 137 (72%) with Crohn's disease and 53 (28%) with ulcerative colitis. At the time of enrollment, 69 (36%) had clinically active disease.**

- **Sixteen (8.4%) patients had toxigenic C. difficile isolated on rectal swab at enrollment and four (2.1%) patients had non-toxigenic C. difficile cultured.**

- **Mixed infection with more than one toxigenic isolate was present in 5/16 (31.3%) individuals.**

- **C. difficile isolation at the time of presentation was not associated with a subsequent disease relapse over a 6-month period in CD (p = 0.557) or UC (p = 0.131).**

Micic D et al. Dig Dis Sci 2018;63:1016-1024

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

Barker AK et al. *Infect Control Hosp Epidemiol* 2018;39:177–185

Aim: evaluate the clinical effectiveness of CD screening at admission on the rate of hospital-onset CDI.
Before-and-after trial

All 5,357 patients admitted to the BMT and general medicine wards from January 2014 to February 2017 were included in the study.
All BMT patients were screened within 48 hours of admission. Colonized patients, as defined by a C. difficile–positive PCR stool result, were placed under contact precautions for the duration of their hospital stay.

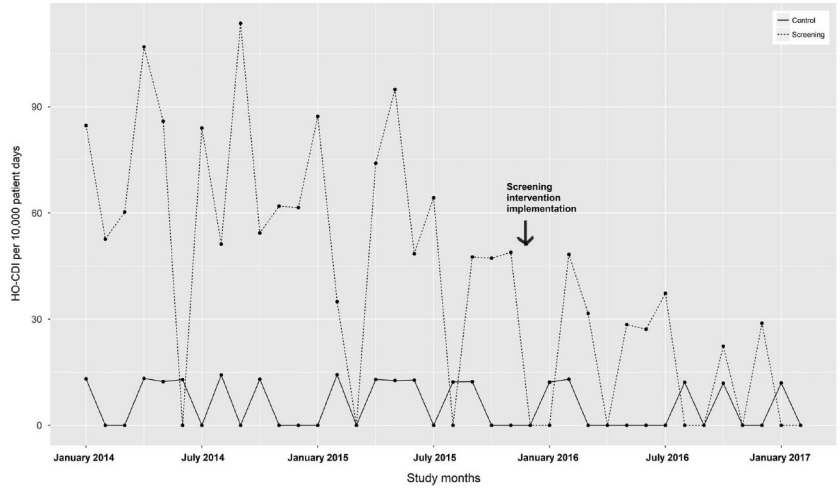


FIGURE 2. Hospital-onset *Clostridium difficile* infection (CDI) rates pre- and post-intervention.

Interventions to Reduce the Incidence of Hospital-Onset *Clostridium difficile* Infection: An Agent-Based Modeling Approach to Evaluate Clinical Effectiveness in Adult Acute Care Hospitals

Clin Infect Dis 2018;66(8):1192-1203.

Anna K. Barker,[1] Oguzhan Alagoz,[1,2] and Nasia Safdar[3,4]

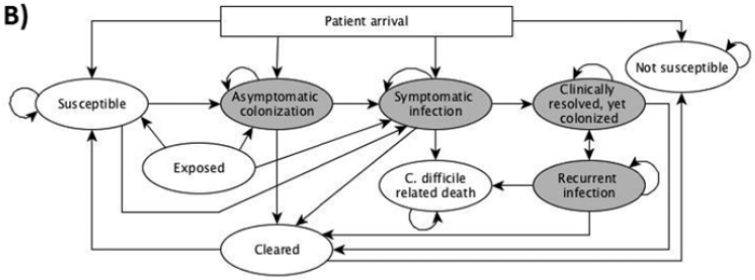
- **Agent-based model of *C* dif transmission in a 200-bed adult hospital.**
- **Model→ environmental component and 4 distinct agent types: patients, visitors, nurses and physicians.**

- **9 single interventions and 8 multiple-intervention bundles→ effectiveness to reduce HO-CDI and asymptomatics *C* dif colonization**

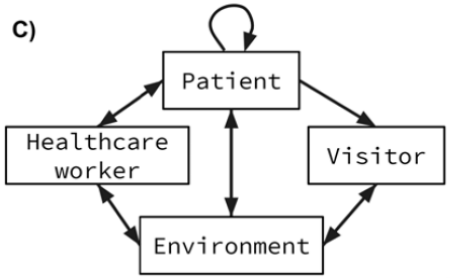
A)

$$P = \begin{array}{c} \\ Cleared \\ Susceptible \\ Exposed \\ Colonized \\ Infected \\ Recolonized \\ Recurrence \\ Death \\ Nonsusceptible \end{array} \begin{array}{c} \begin{array}{ccccccccc} Cleared & Susceptible & Exposed & Colonized & Infected & Recolonized & Recurrence & Death & Nonsusceptible \end{array} \\ \begin{pmatrix} 0 & p_{1,2} & 0 & 0 & 0 & 0 & 0 & 0 & p_{1,9} \\ 0 & p_{2,2} & 0 & p_{2,4} & p_{2,5} & 0 & 0 & 0 & 0 \\ 0 & p_{3,2} & 0 & p_{3,4} & p_{3,5} & 0 & 0 & 0 & 0 \\ p_{4,1} & 0 & 0 & p_{4,4} & p_{4,5} & 0 & 0 & 0 & 0 \\ p_{5,1} & 0 & 0 & 0 & p_{5,5} & p_{5,6} & 0 & p_{5,8} & 0 \\ p_{6,1} & 0 & 0 & 0 & 0 & p_{6,6} & p_{6,7} & 0 & 0 \\ p_{7,1} & 0 & 0 & 0 & 0 & p_{7,6} & p_{7,7} & p_{7,8} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix} \end{array}$$

B)



C)



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Clin Infect Dis 2018;66(8):1192-1203.

Anna K. Barker,[1] Oguzhan Alagoz,[1,2] and Nasia Safdar[3,4]

- **Daily cleaning with sporicidal disinfectant and *C. difficile* screening at admission were the most effective single-intervention strategies, reducing HO-CDI by 68.9% and 35.7%, respectively (both *P* < .001).**
- **Combining these interventions into a 2-intervention bundle reduced HO-CDI by 82.3% and asymptomatic hospital-onset colonization by 90.6% (both, *P* < .001).**
- **Adding patient hand hygiene to healthcare worker hand hygiene reduced HO-CDI rates an additional 7.9%.**
- **Visitor hand hygiene and contact precaution interventions did not reduce HO-CDI, compared with baseline.**
- **Excluding those strategies, healthcare worker contact precautions were the least effective intervention at reducing hospital-onset colonization and infection.**

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

- **Population-based prospective cohort study at 2 university hospitals in Denmark, screening all patients for toxigenic C difficile in the intestine upon admittance,from October 1, 2012, to January 31, 2013.**

- **Screening results were blinded to patients, staff, and researchers.**

- **Patients were followed during their hospital stay by daily registration of wards and patient rooms.**

- **The primary outcomes were rate of C difficile infection in exposed and unexposed patients and factors associated with transmission.**

Blixt T et al. Gastroenterology 2017;152:1031–1041

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

- **C difficile infection was found in 2.6% of the unexposed and 4.6% of the exposed patients in the room, and the odds of C difficile infection were higher in patients sharing a room with an asymptomatic carrier than in patients without this exposure (OR, 1.79; 95% CI, 1.162.76).**

- **Amount of exposure correlated with risk of C difficile infection, from 2.2% in the lowest quartile to 4.2% in the highest quartile of exposed patients (P = .026).**

Blixt T et al. Gastroenterology 2017;152:1031–1041

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

- **Patients admitted to the Mayo Clinic unit for HSCT or chemotherapy for hematologic malignancy were screened for CDI starting in 2010 as part of an infection control surveillance program.**

- **Stools collected within 3 days of admission were tested for toxigenic *C difficile* by polymerase chain reaction (GeneXpert).**

- **1,090 total admissions to the HSCT unit from December 2012-December 2013.**

- **A total of 470 patients (43%) met criteria for screening (HSCT patients or receiving chemotherapy for hematologic malignancy) and did not have diarrhea and were able to provide a formed stool sample for *C difficile* testing.**

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

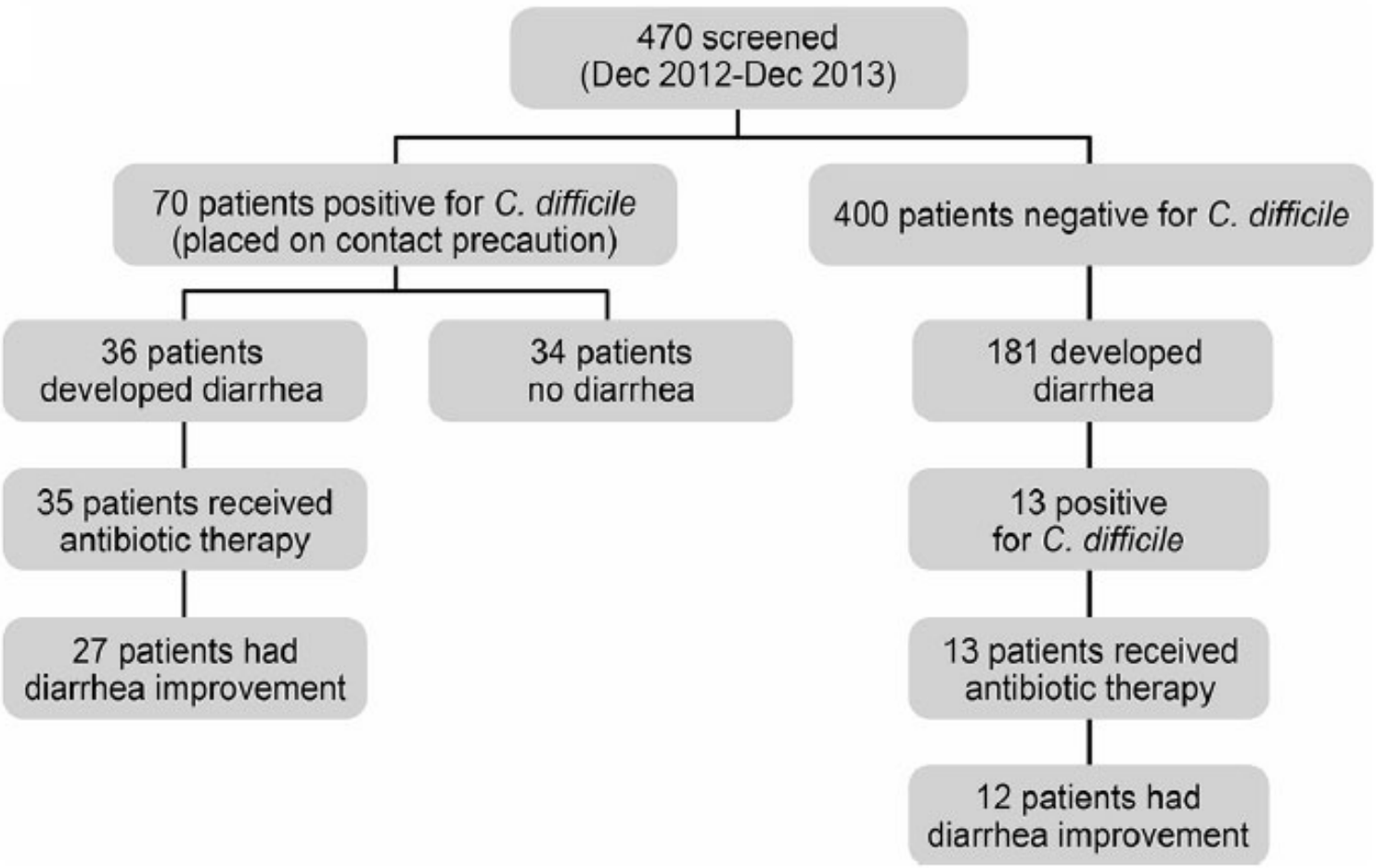
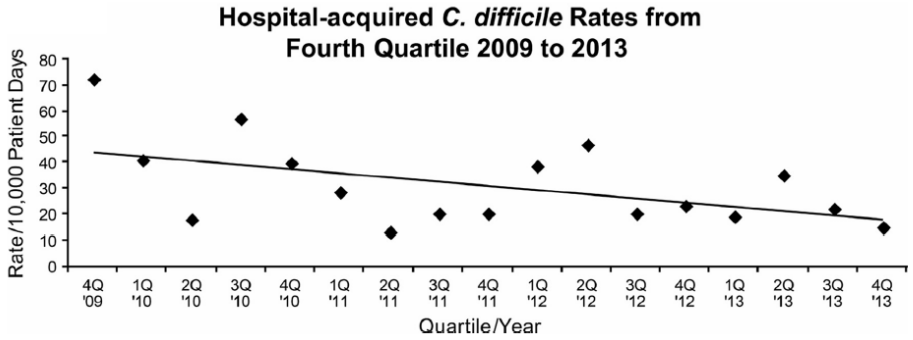


Fig 1. Flow chart describing *Clostridium difficile* (*C. difficile*) testing and antibiotic response during hospitalization.



←colonized patients were placed in contact isolation

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

Transmission of *Clostridium difficile* from asymptomatically colonized or infected long-term care facility residents

Aim: To test the hypothesis that LTCF residents with CDI or asymptomatic carriage of toxigenic strains are an important source of transmission in the LTCF and in the hospital during acute-care admissions.

A 6-month cohort study with identification of transmission events was conducted based on tracking of patient movement combined with restriction endonuclease analysis (REA) and whole-genome sequencing (WGS).

Donskey CJ et al. Infect Control Hosp Epidemiol 2018; 39: 909-16

Transmission of *Clostridium difficile* from asymptomatically colonized or infected long-term care facility residents

29 LTCF residents identified as asymptomatic carriers of toxigenic C. difficile based on every other week perirectal screening and 37 healthcare facility-associated CDI cases

Of the 37 CDI cases, 7 (18.9%) were linked to LTCF residents with LTCF-associated CDI or asymptomatic carriage, including 3 of 26 hospital-associated CDI cases (11.5%) and 4 of 11 LTCF-associated cases (36.4%).

Of the 7 transmissions linked to LTCF residents, 5 (71.4%) were linked to asymptomatic carriers versus 2 (28.6%) to CDI cases, and all involved transmission of epidemic BI/NAP1/027 strains.

Donskey CJ et al. Infect Control Hosp Epidemiol 2018; 39: 909-16

Transmission of *Clostridium difficile* from asymptomatically colonized or infected long-term care facility residents

LTCF residents with asymptomatic carriage of C. difficile or CDI contribute to transmission both in the LTCF and in the affiliated hospital during acute-care admissions.

Donskey CJ et al. Infect Control Hosp Epidemiol 2018; 39: 909-16

Clostridium difficile Screening for Colonization During an Outbreak Setting

Clinical Infectious Diseases® 2018;

Katherine Linsenmeyer,[1,2] William O'Brien,[1] Stephen M. Brecher,[1,3]
Judith Strymish,[1,3] Alexandra Rochman,[1] Kamal Itani,[1,2] and Kalpana Gupta[1,2]

In response to frequent *C. difficile* outbreaks on the surgical service, a quality improvement initiative identifying and isolating *C. difficile* carriers was implemented to:

(1)compare rates of HA-CDI before and after implementation of isolation for asymptomatic carriers,

(2) evaluate the prevalence of and risk factors for *C. difficile* carriage, and

(3) determine the association between carriage and subsequent development of symptomatic CDI.

Clostridium difficile Screening for Colonization During an Outbreak Setting

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- **773 patients→ 24 (3.1%) were asymptomatic *C. difficile* carriers.**
- **Symptomatic CDI within 90 days of admission occurred in 15 of 773 patients (1.9%): 7 (29%) of 24 asymptomatic *C. difficile* carriers compared with 8 (1%) of 749 with negative results at admission ($P < .05$).**
- **In the multivariate analysis controlling for antimicrobial use, *C. difficile* carriage was the only factor independently associated with the development of HA-CDI, with a >25-fold increased risk among patients who were carriers at admission (OR, 26.1; 95% CI, 7.4–92.1).**

Asymptomatic carriers were then placed on contact isolation, similar to standard precautions for symptomatic patients with CDI.

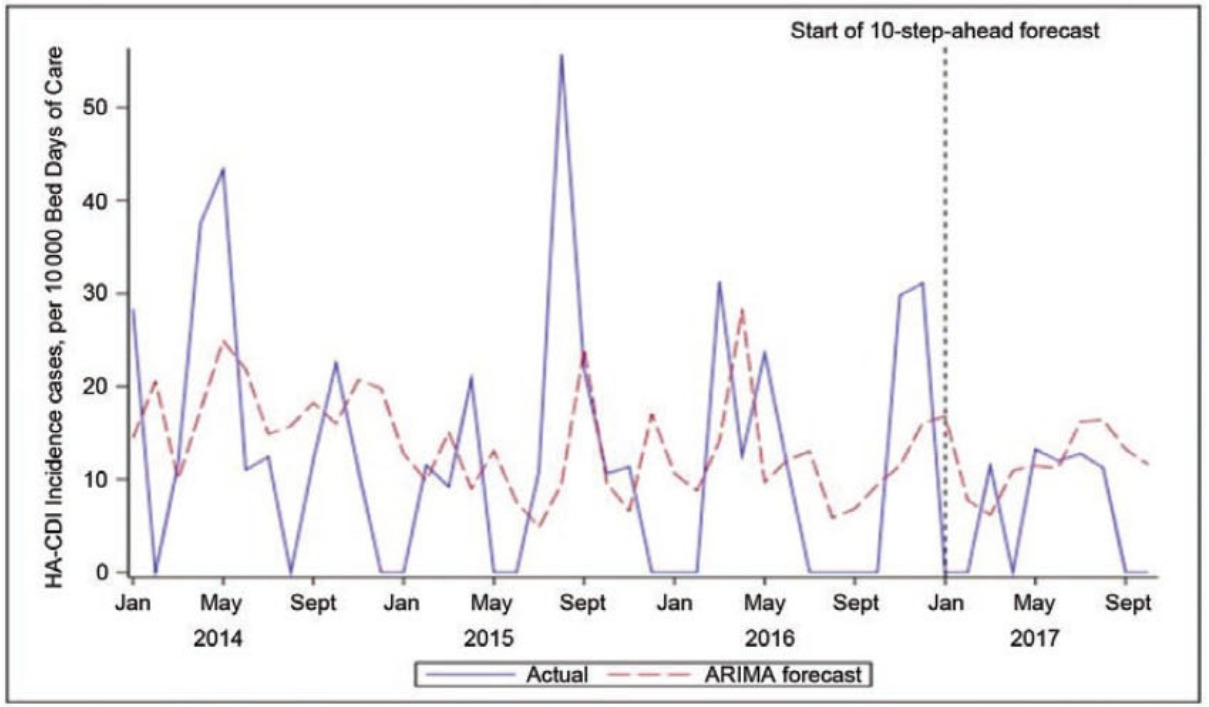

Figure 1. Observed versus forecasted hospital-acquired *Clostridium difficile* (HA-CDI) incidence rates (per 10 000 bed-days of care), with forecasts based on an autoregressive integrated moving average (ARIMA) model. Abbreviations: Jan, January; Sept, September.

Linsenmeyer K et al. Clin Infect Dis 2018

When to discontinue isolation?

- **IDSA/SHEA guidelines → with Solomon wisdom, they suggest to continue precautions for at least 48 after diarrhea ends, or prolong contact precautions until discharge in settings with high CDI rates despite implementation on infection control measures against CDI. (**McDonald LC et al. Clin Infect Dis. 2018 Feb 15)

- **However, Clostridium difficile stool detection is high up to 4 weeks post-treatment (**Sethi AK et al. Infect Control Hosp Epidemiol 2010; 31:21–7)**.**

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

Barker AK et al. *Infect Control Hosp Epidemiol* 2018;39:177–185

- **Healthcare worker contact precautions were the least effective intervention at reducing hospital-onset colonization and infection.**
- **In this study, paradoxically, daily cleaning with sporicidal disinfectant significantly reduced hospital onset-CDI by 68.9%.**
- **Can we hypothesize that the failure of contact precautions as single intervention depended on its duration?**

I'll tell you

my opinion.

Take home messages

- **Asymptomatic CD carriage is a topic of relevant interest and perspective**
- **CD screening is currently not recommended routinely, mainly due to uncertainty with regards to the appropriate management of asymptomatic carriers.**
- **However data are accumulating in certain settings and epidemiological conditions on its value.**
- **Discontinuing isolation should not be based only on the resolution of diarrhea, but also on the setting and infection control practices.**