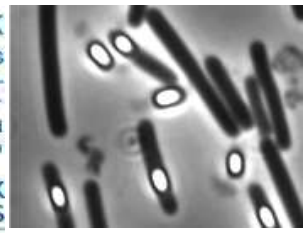

How to eradicate *Clostridium difficile* from the environment ?

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Objectives

- To review the scientific evidence demonstrating that the environment plays an important role in the transmission of *C. difficile*
- To review the current recommended guidelines to reduce the risk of environment-mediated transmission
  - The *in vitro* studies
  - The *in situ* studies
  - The clinical studies
- To discuss new perspectives in disinfection of hospital room surfaces and equipments : No touch methods (NTD)

Burden of *Clostridium difficile* infections

- *C. difficile* is a major nosocomial pathogen

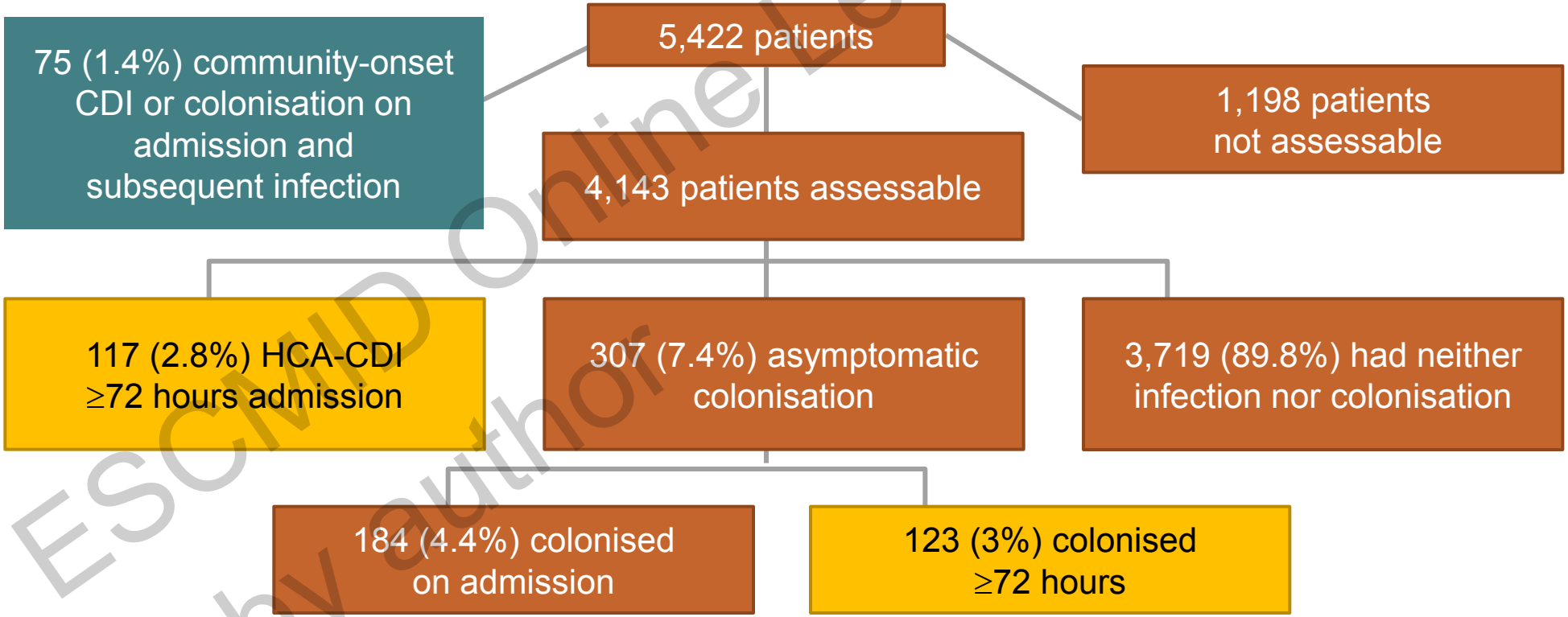
- In a pan-European hospital-based survey:[1]
  - Incidence of CDI : 4.1/10,000 patients-days
  - CDI caused or contributed to death in 9% within 3 months of diagnosis
  - CDI is the 3rd most frequent HAI and CD ranks 1 in the microorganisms responsible for HAI[6]

- CDI patients, when compared with non-infected matched controls:[1–3]
  - Spend on average an extra 7–21 days in hospital
  - Attributable additional cost of €7,147 per case
  - Estimates suggest the potential costs associated with management of CDI in Europe are in the region of €3 billions per year[5]…

1. Bauer et al. Lancet 2011;377:63–73;
2. Vonberg et al. J Hosp Infect 2008;70:15–20;
3. Dubberke et al. Infect Control Hosp Epidemiol 2009;30:57–66;
4. Wilcox et al. J Hosp Infect 1996;34:23–30
5- Kuijper EJ, et al. Clin Microbiol Infect 2006;12 Suppl 6:2–18; 2.
6- Magill S.S.,. New England Journal of Medicine, 2014, Mars , 1198-1208

Acquisition of *C. difficile* is frequent

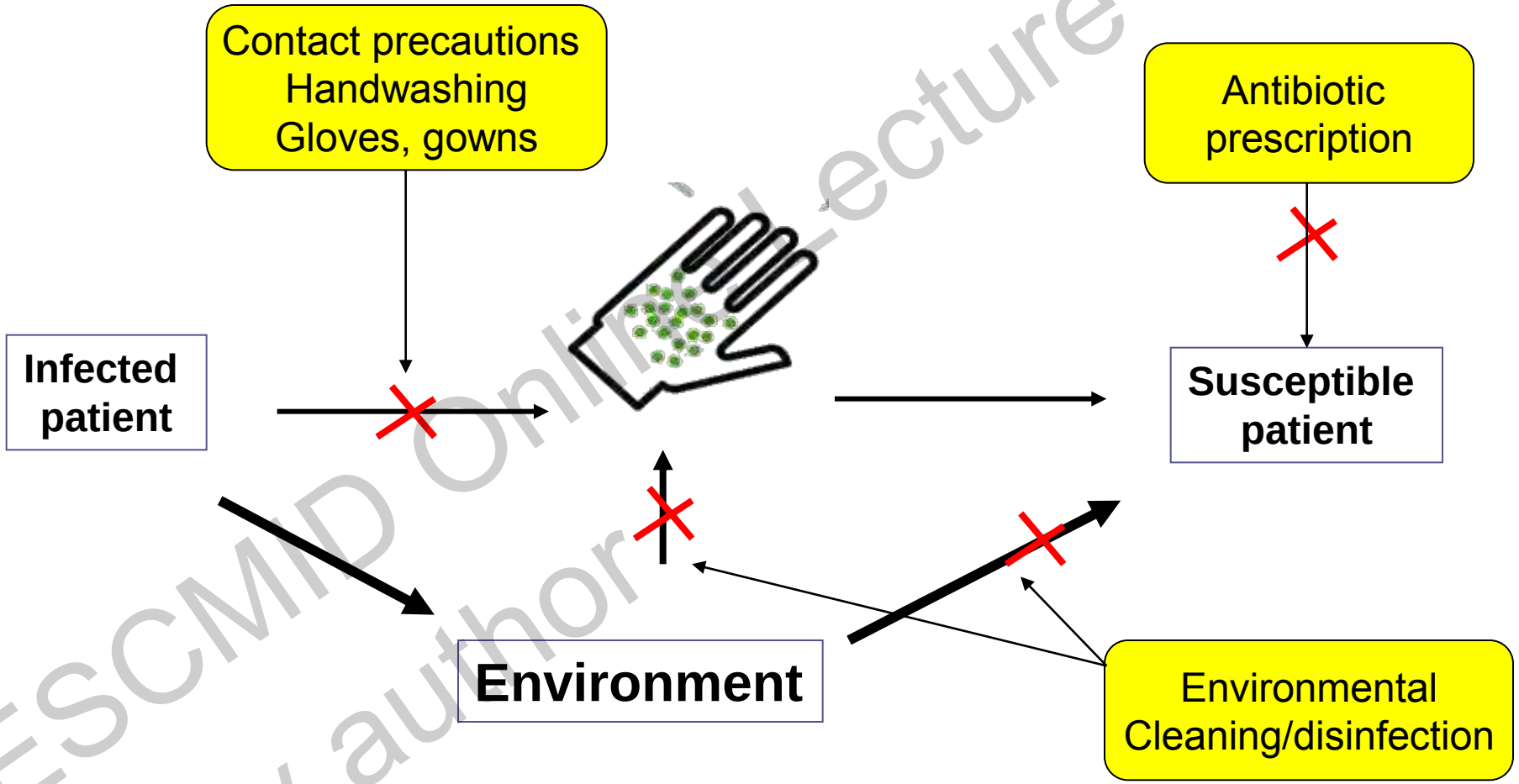
- Prospective multicentre study (6 hospitals in Québec and Ontario in 2006–7)
- Stool specimens taken on admission and every week
- Asymptomatic carriers of *C. difficile* more frequent than symptomatic patients



Loo V. *et al.* N Engl J Med 2011;365:1693–703.

HCA, healthcare acquired

Transmission of *C. difficile*

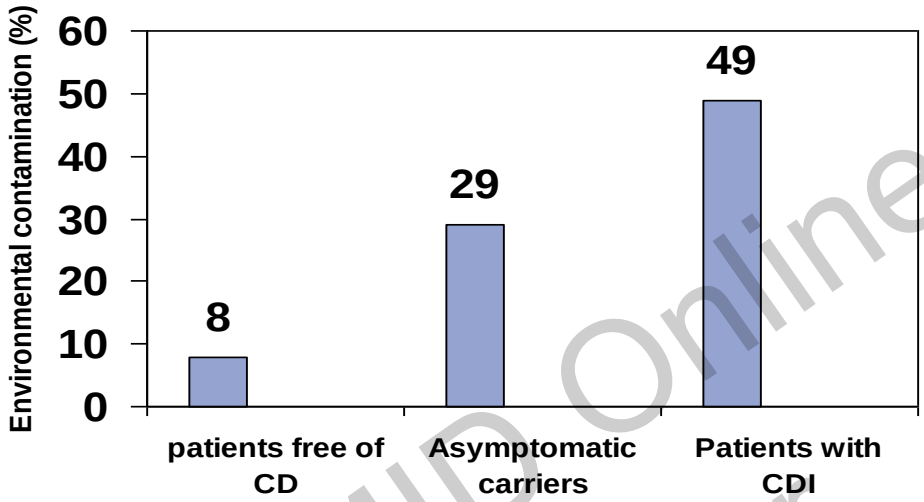


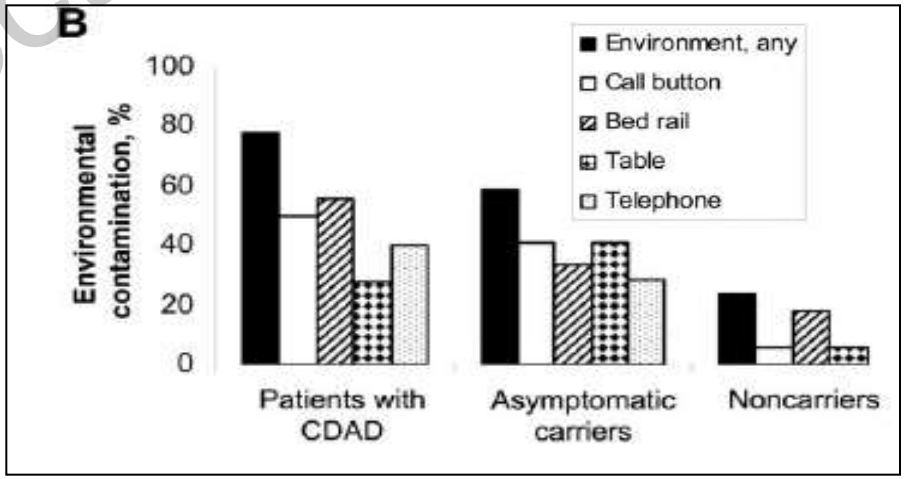
Dubberke ER, ICHE 2008, 29, S81-92
Otter J, et al. ICHE 2011, 32, 687-99

Evidence demonstrating that the environment plays an important role in the transmission of *C. difficile*

Frequency of environmental contamination

- Rates of contamination range from 9.7%[1] to 58%[2]
- CD is also isolated in rooms of patients not colonized or infected with CD[3, 4]





- Aeral dissemination of *C. difficile* spores may in part account for widespread environnemental contamination in areas not occupied by colonized of infected patients[5].
- *C. difficile* has also been isolated from medical devices

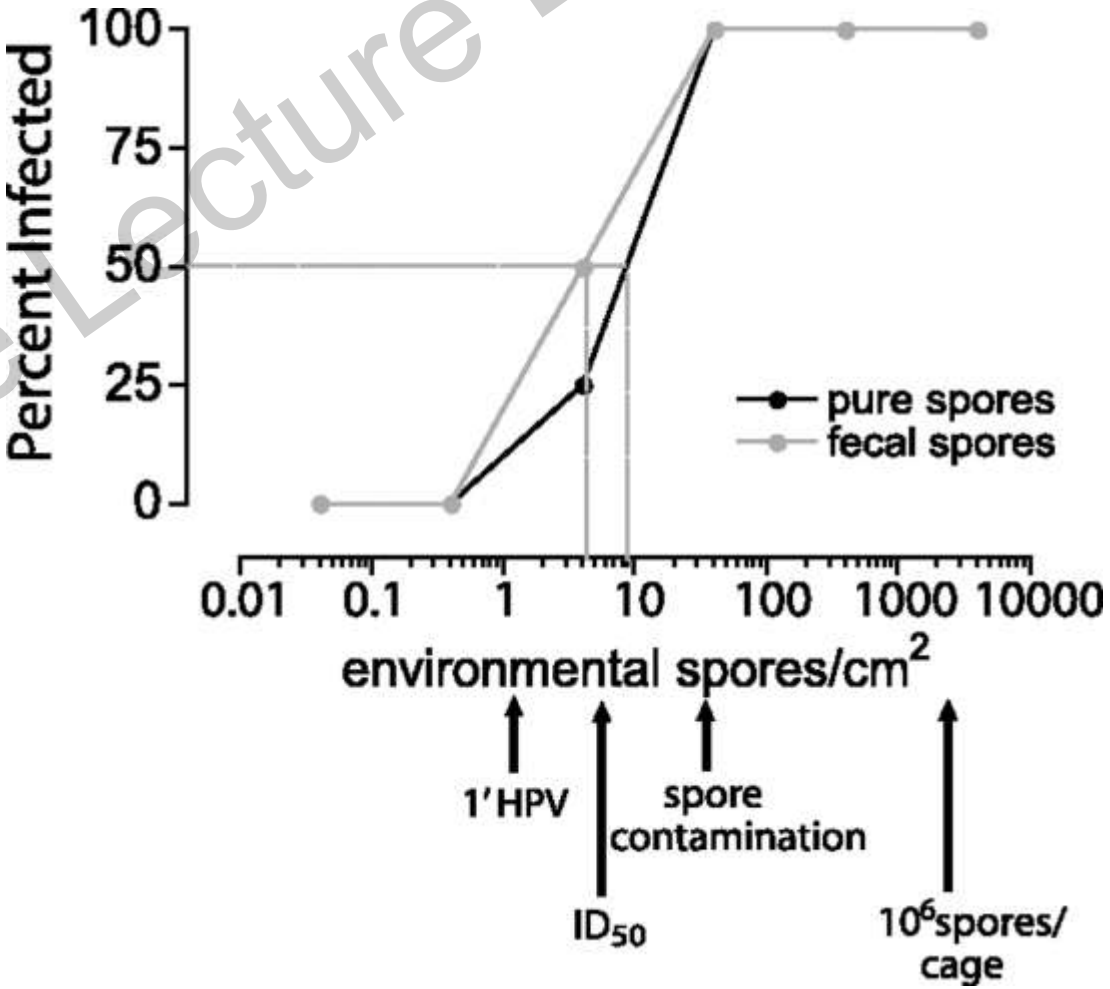
1. Kim et al., JID 1981; 143, 42-50
2. Samore MH et al., Am J Med 1996 100, 32-40
3. McFarland LV, NEJM 1989, 320, 204-201
4. Riggs et al., CID 2007, 45, 992-97
5. Best EL, CID 2010, 50, 1450-7

Review : Otter J et al., AJIC 2013, 41, S6-S11

Level of contamination

- The level of contamination is usually low (< 1 or 2 $\log_{10}$ CFU)[1-2]
- Boyce *et al.* found contamination up to 1300 CFU (sponge technique)[3]
- Transmission experiments in mouse model
  - Infectious dose : 5-10 spores /cm^2

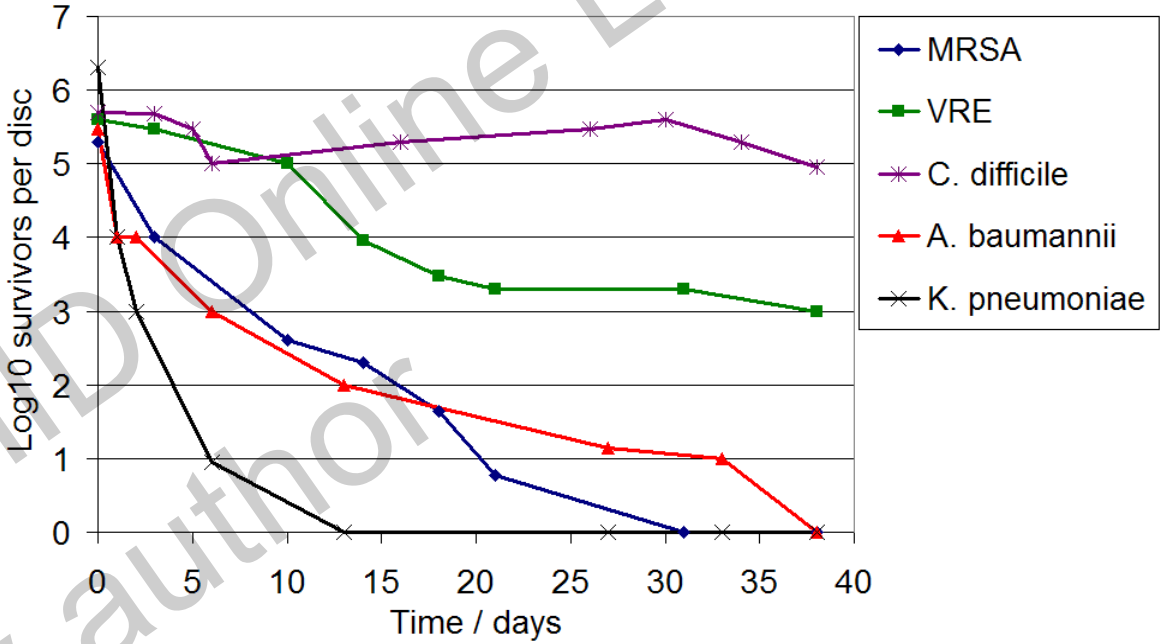
- The frequency of acquisition has been linked with the level of contamination[2]



1. Kim et al., JID 1981; 143, 42-50
2. Samore MH et al., Am J Med 1996 100, 32-40
3. Boyce JM et al., ICHE 2008, 29, 723-29
4. Lawley TD et al., Appl. Environ. Microbiol., 2010

Survival curve

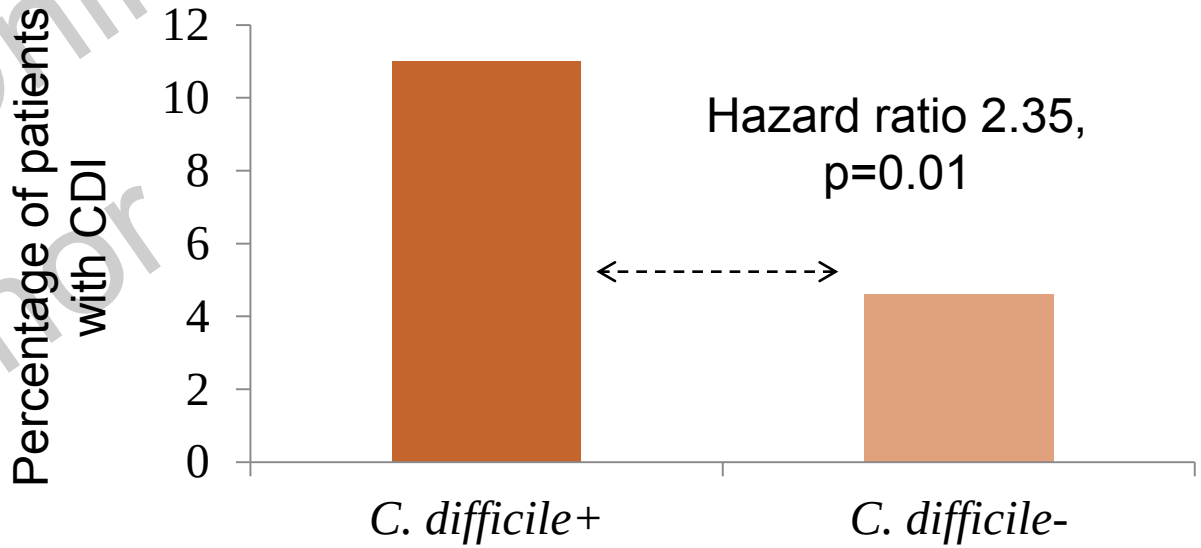
- Vegetative CD survive for only a short time (15 min) on surfaces exposed to room air
- Spores can survive for weeks or months[1, 2]
- Spores are resistant to most commonly used disinfectants (quaternary ammonium compound)
- Exposure to cleaning or disinfectant agent may increase the sporulation rate of *C. difficile*[3]



1- Otter and French. *J Clin Microbiol* 2009;47:205-207
2- Wagenvoort *et al. J Hosp Infect* 2011;77:282-283
3- Fawley WN,. *Infect Control Hosp Epidemiol* 2007;28:920-5

Evidence for environment-mediated transmission

- Being admitted to a room previously occupied by a patient with CDI is a risk factor
  - 18-month retrospective cohort study on an ICU, Ann Arbor, Michigan, USA.
  - 134 cases of *C. difficile* infection occurred 48 hours after ICU admission or with 30 days of discharge in 1,844 patients admitted to the ICU during the study



Shaughnessy et al. Infect Control Hosp Epidemiol 2011;32:201-206
Courtesy of J Otter.

How to reduce the risk of environment-mediated transmission ?

Guidelines are available

Am J Infect Control. 2011 Apr;39(3):239-42. Epub 2011 Mar 3.

Preventing Clostridium difficile infections: an executive summary of the Association for Professionals in Infection Control and Epidemiology's elimination guide.

Rebmann T, Carrico RM, Association for Professionals in Infection Control and Epidemiology.

Institute for Biosecurity, Division of Environmental and Occupational Health, School of Public Health, St. Louis University, MO 63104, USA. rebmannt@slu.edu

Infect Control Hosp Epidemiol. 2010 May;31(5):431-55.

Clinical practice guidelines for Clostridium difficile infection in adults: 2010 update by the society for healthcare epidemiology of America (SHEA) and the infectious diseases society of America (IDSA).

Cohen SH, Gerding DN, Johnson S, Kelly CP, Loo VG, McDonald LC, Pepin J, Wilcox MH; Society for Healthcare Epidemiology of America; Infectious Diseases Society of America.

Department of Internal Medicine, Division of Infectious and Immunologic Diseases, University of California Davis Medical Center, Sacramento, California, USA.

Clin Microbiol Infect. 2008 May;14 Suppl 5:2-20.

Infection control measures to limit the spread of Clostridium difficile.

Vonberg RP, Kuijper EJ, Wilcox MH, Barbut F, Tüll P, Gastmeier P; European C difficile-Infection Control Group; European Centre for Disease Prevention and Control (ECDC), van den Broek PJ, Colville A, Coignard B, Daha T, Debast S, Duerden BI, van den Hof S, van der Kooi T, Maarleveld HJ, Nagy E, Notermans DW, O'Driscoll J, Patel B, Stone S, Wiuff C.

Institute for Medical Microbiology and Hospital Epidemiology, Medical School Hannover, Hannover, Germany. Vonberg.Ralf@MH-Hannover.DE

Infect Control Hosp Epidemiol. 2008 Oct;29 Suppl 1:S81-92.

Strategies to prevent clostridium difficile infections in acute care hospitals.

Dubberke ER, Gerding DN, Classen D, Arias KM, Podgorny K, Anderson DJ, Burstin H, Calfee DP, Coffin SE, Fraser V, Griffin FA, Gross P, Kaye KS, Klompas M, Lo E, Marschall J, Mermel LA, Nicolle L, Pegues DA, Perl TM, Saint S, Salgado CD, Weinstein RA, Wise R, Yokoe DS.

Washington University School of Medicine, St. Louis, Missouri, USA.

Bundle of measures

- Antimicrobial stewardship
- Contact precautions
  - Single room with private toilets facilities
  - Use of gloves and appropriate hand hygiene
  - **Improved room cleaning/disinfection**

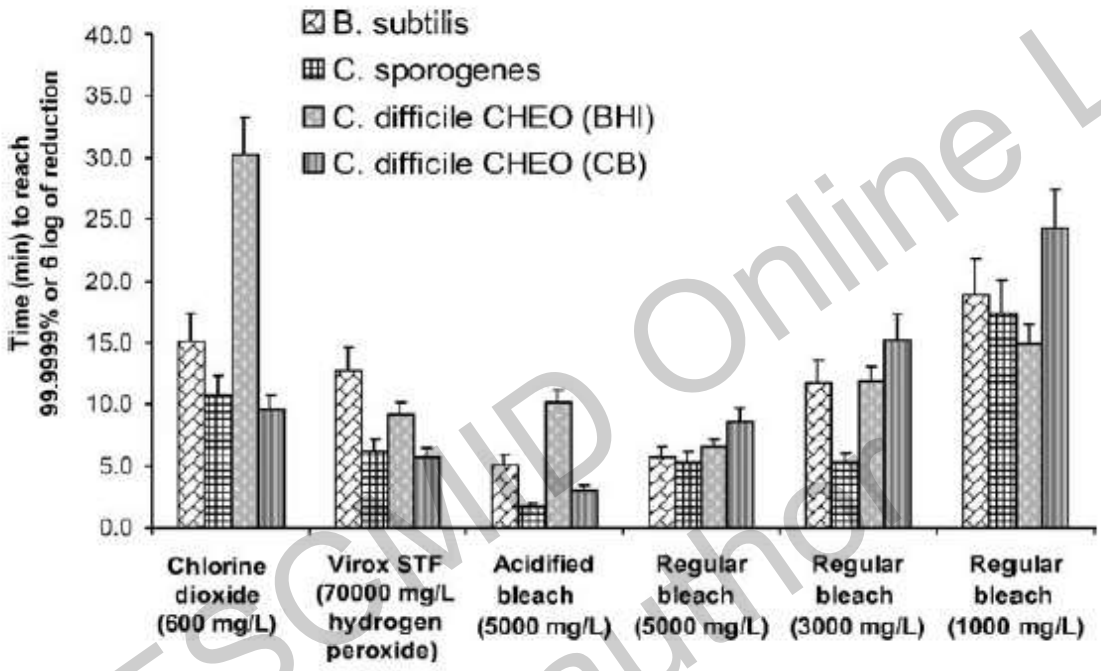
Guidelines

All the guidelines emphasize the need to provide adequate cleaning of all surfaces in the room.

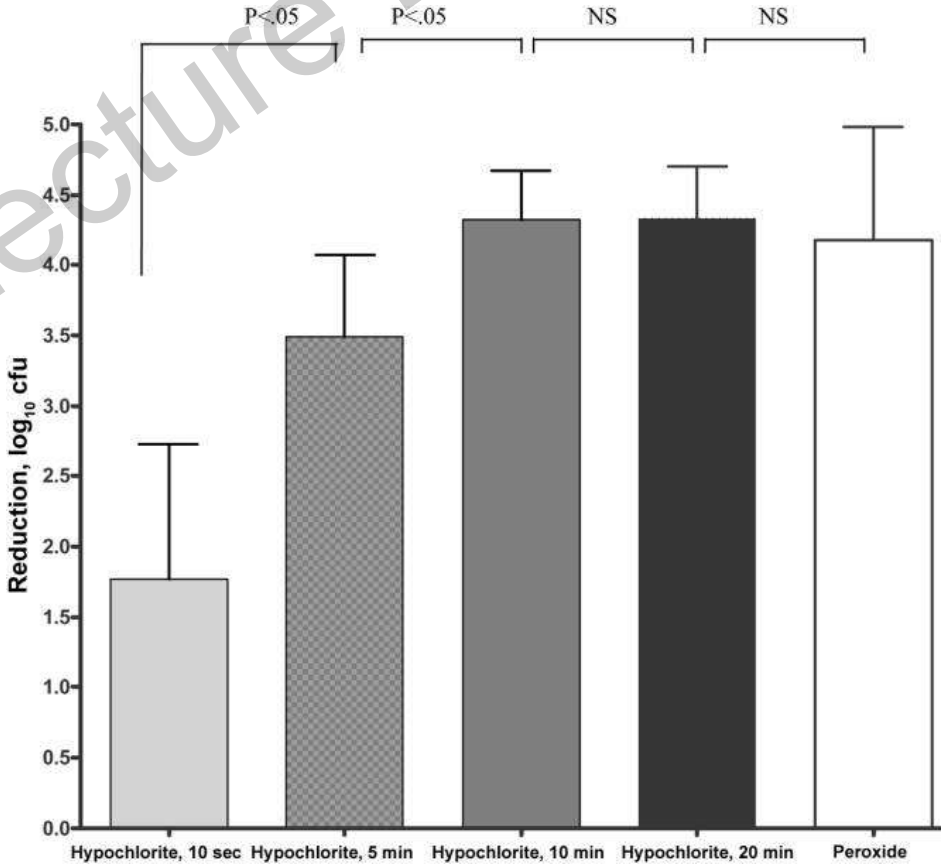
Reference (year)	Scientific Society	Guidelines
Siegel JD, 2012	CDC HICPAC	consistent environmental cleaning and disinfection be used as one of the control measures for *C difficile* and that "**hypochlorite solutions (5,000 ppm)** may be required if transmission continues
Rebmann T, AJIC 2011	APIC	recommends a 1:10 dilution of hypochlorite for use when there is ongoing transmission, but they recommend a contact time of **1 minute** for nonporous surfaces
Cohen SH , ICHE 2010	IDSA, SHEA	using a "chlorine-containing cleaning agent or other sporicidal agent to address environmental contamination in areas with **increased rates of CDI**
Vonberg RP, CMI 2008	ESGCD, ECDC	**Regular environmental disinfection** should be done using sporicidal agent, ideally chlorine containing agent (at least 1000 ppm available chorine) Hospital wards should be cleaned regularly (at least once a day) After discharge of a CDI patient, rooms must be cleaned and disinfected thoroughly
Dubberke ER, ICHE 2008	IDSA, SHEA	"facilities should consider using a 1:10 dilution of sodium hypochlorite (household beach) for environmental disinfection **in outbreak settings and settings of hyperendemicity** in conjunction with other infection prevention and control measures . . .. the beach solution should have a contact time of at least **10 minutes**

In vitro studies of disinfectants

Performance criterion was >6 $\log_{10}$



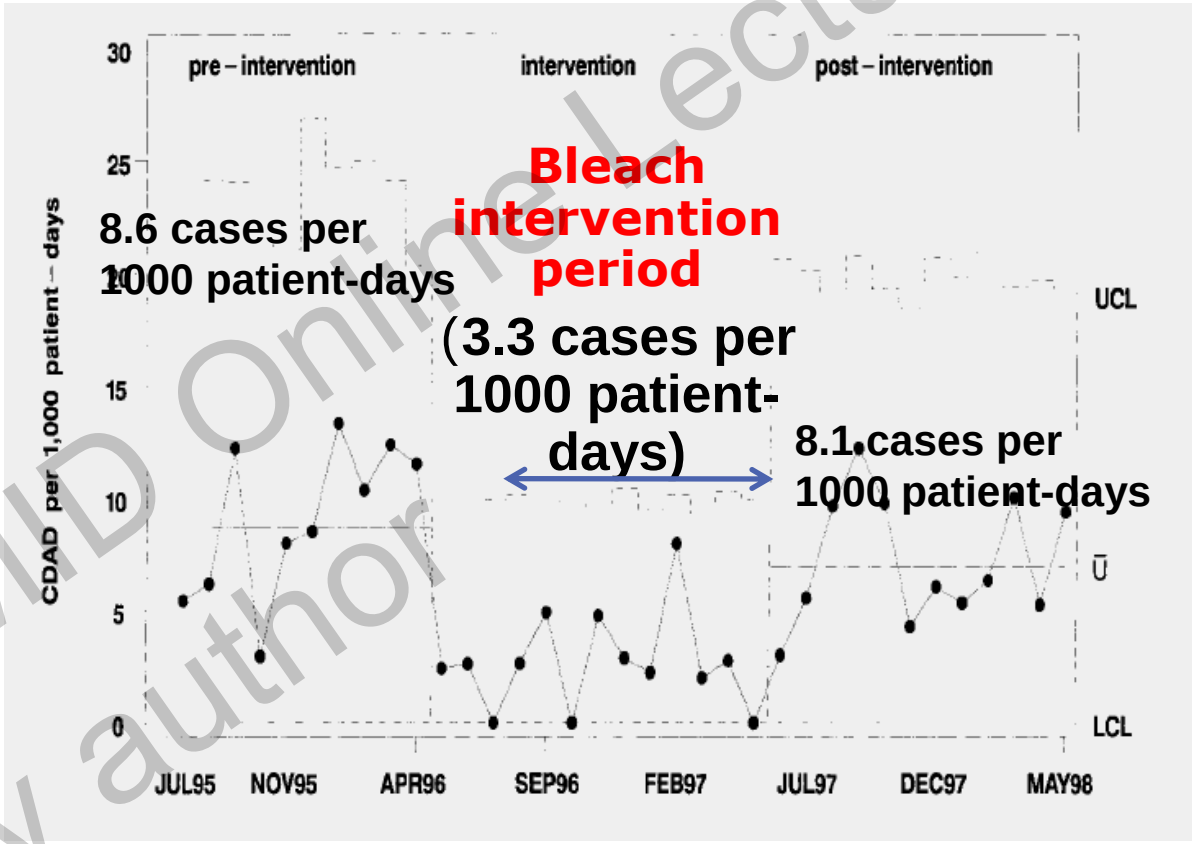
Perez J et al., AJIC 2005, 33,320-25.



Barbut F, ICHE 2009, 30, 207-14

Clinical studies of disinfectants and CDI

- Mayfield *et al.* (2000)[1] showed that switching from QAC to hypochlorite disinfection significantly reduced the incidence of *C. difficile* infection for high risk patients.



1. Mayfield *et al. Clin Infect Dis* 2000;31:995-1000.

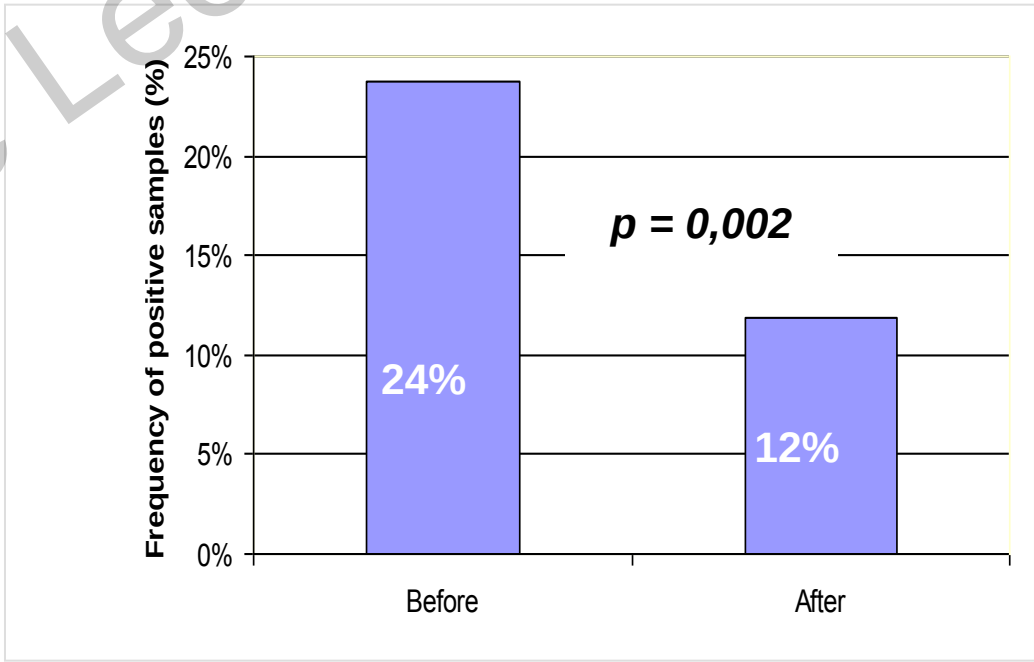
Clinical studies of disinfectants and CDI

Author (year)	Setting	Product	Practice	Monitoring of disinfection	Effect
Kaatz (1988)	Medical ward	Hypochlorite 500 ppm	Terminal disinfect	Surface contamination -21%	Outbreak ended
Mayfield (2000)	BMT and medical ward, ICU	Hypochl. 5,000 ppm	Terminal disinfect	No	Incidence decreased in one ward
Wilcox (2003)	2 medical wards	Hypochl. 1,000 ppm	Terminal disinfect	No decrease¨% of positive cultures	Decrease in one of two wards
McMullen (2007)	Medical and surgical ICU	Hypochl. 5,000 ppm	Ward 1 : Terminal CDI rooms. Ward 2 : all rooms	No	62 % decrease of CDI incidence
Hacek (2010)	3 hospitals	Hypochl. 5,000 ppm	Terminal disinfect.	No	48% decrease in prevalence density of CDI
Orenstein (2011)	Medical ward	Hypochl. (5,500 ppm - wipes)	Terminal and daily disinfect.	ATB bioluminescence	85% decrease HA-CDI

Efficacy of cleaning /disinfection remains sub-optimal

- Many surfaces are poorly cleaned [1, 2]
  - 1119 patient rooms from 23 acute hosp.
  - Transparent, fluorescent dye
  - 49% (35-81%) of surfaces were correclty cleaned

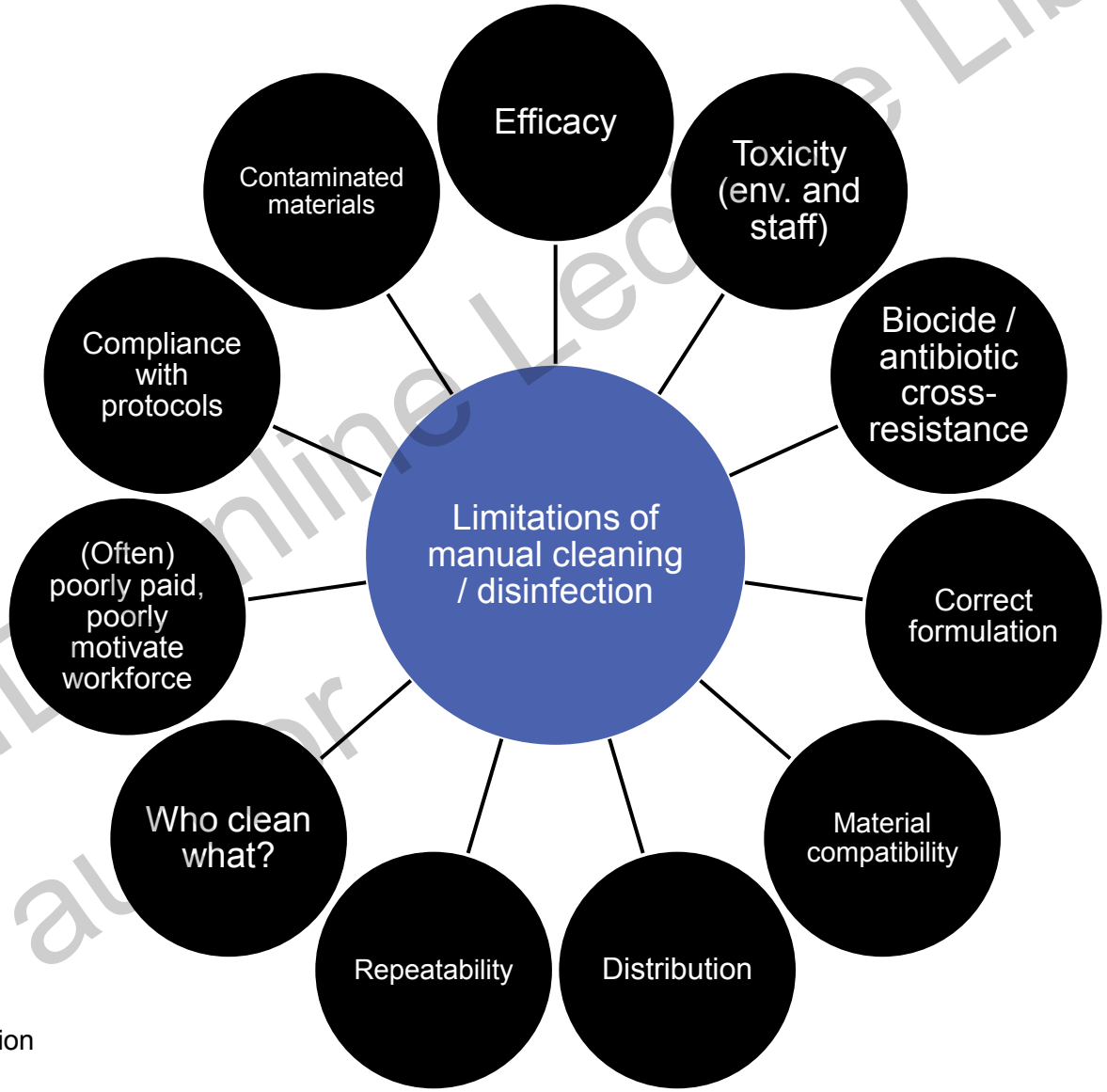
- Many surfaces remain contaminated with *C. difficile* despite terminal disinfection [3]



388 samples (16 rooms)
Relative decontamination : 50%

1- Carling PC,. Infect Control Hosp Epidemiol 2008;29:1-7.
2- Carling PC, JHI, 2008, 68, 39-44
3- Barbut F, ICHE 2009, 30, 207-14

Limitations of manual cleaning/disinfection



1. Otter , personal communication

New perspectives : No touch methods for disinfection (NTD)

No touch methods for disinfection (NTD)

UV lights (UV-C)	Gazeous hydrogen peroxyde
Tru-D Smart (TRU-D., Lumalier corp.) - UV 254 nm - UV sensors to monitor the amount of energy delivered (22,000 µWs/cm² 45 min)	**Glosair (formerly Sterinis)** - Dry mist (8-12µ) : 5% HP, <50 ppm silver cations, < 50 ppm ortho phosporic acid - 6 ml /m^3 - Passive decomposition
IRiS (Medline industry) **SterilRay** (Healty innov.) - mobile, hand-held device - far UV : 185-230 nm	**Steris** - Vaporized HP (35% HP), non condensing - Active catalytic conversion
Pulse Xenon UV, (Xenex Health Care) - Pulse xenon radiation (200-230 nm) - UV sensor	**Bioquell** - Vaporized HP (35% HP), condensing - Active catalytic conversion

1- Nerandzic et al., BMR Inf Dis 2010, 10, 197
2- Anderson DJ *et al,* ICHE 2013, 34, 466-471.

No touch methods for disinfection : advantages

UV	Hydrogene peroxyde
Effective against *C. difficile*, although requires longer exposure (50 min.) Eliminate >2.4 log spores seeded on formica surfaces[1]	Achieves high-level disinfection (>6-log reduction)
HVAC (heating, ventilation, air conditioning) does not need to be disabled and the room does not need to be sealed	Compatible with hospital materials including electronics
No safety and health concerns	Environmentally friendly – degrades to O_2 and water vapour
	Clinical studies (reduce CDI incidence)
Good distribution of UV energy via an automated monitoring system	Does not rely on the operator for distribution, contact time and repeatability Real-time monitoring and feedback and can be validated using BIs* / cycle data

1-Rutala *et al.,* ICHE 2010, 31, 1025-1029
2- Fu TY *et al.,* JHI 2012, 80, 190-205

No touch methods for disinfection: disadvantages

UV	Hydrogene peroxyde
Cleaning must precede disinfection	
Patients or staff should be removed prior to decontamination (cannot be used for daily disinfection)	
Capital equipment cost are substantial Staff time to transport the equipment to the room.	
Sensitive to use parameters (eg wavelength , UV dose delivered)	HPV is hazardous to humans so needs to be contained
Equipment and furniture must be moved away from the walls	Doors must be closed with gaps sealed by tapes
No clinical studies	Disinfection requires 2.5-5 hours

In situ studies with NTD

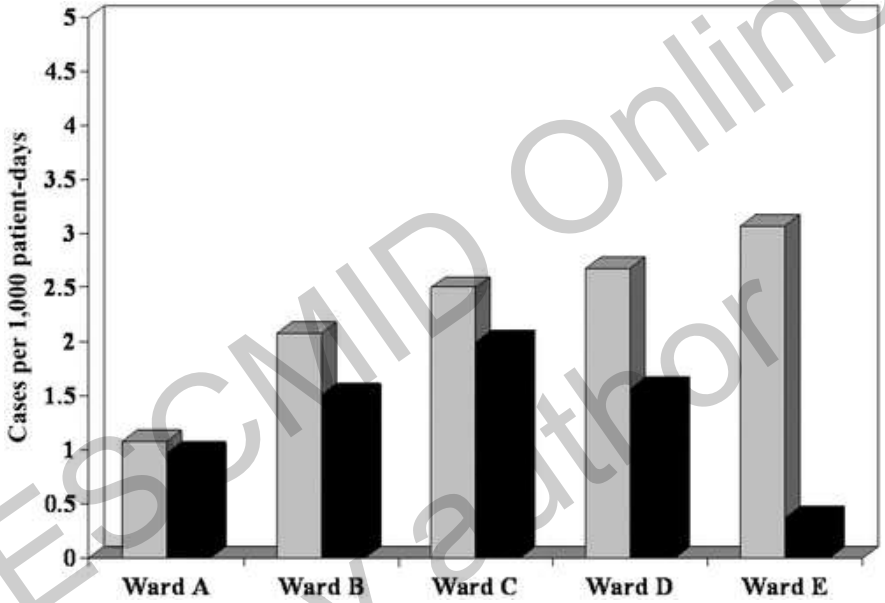
Authors, (year)	Disinfectant	% CD contamination before	% CD contamination after	% reduction
Boyce, (2008)	HPV (Bioquell)	11/43 (26%)	0/37 (0%)	100
Shapey, (2008)	HP dry mist (Glosair)	48/203 (24%)	7/203 (3%)	88
Barbut, (2009)	HP dry mist Hypochlorite	34/180 (19%) 46/194 (24%)	4/180 (2%) 23//194 (12 %)	88 50
Havill, (2012)	UV (Tru-D) HPV (Bioquell)	BI (10^6 *Geobacillus s.)*	100 % of BI grew 1 % of BI grew	2 log reduction >6 log reduction
Fu, (2012)	HP dry mist HPV (Bioquell)	BI (10^6 *Geobacillus s.)*	>90% of BI grew 10% of BI grew	0.6-5.6 log reduction >5.2 log reduction

Shapey et al., JHI 2008, 70, 136-141
Boyce JM, JHI 2007, 67, 50-54.

Barbut F, ICHE 2009, 30, 207-14
Havil NL, ICHE 2012, 35, 507-512
Fu Y et al., JHI 2012, 80; 199-205.

Clinical studies with NTD

- Prospective before-after intervention study.
- Setting : A hospital affected by an epidemic strain of *C. difficile*.
- Intervention : intensive hydrogen peroxide vapor disinfection (Bioquell) (at patient's discharge) in 5 high incidence wards (A–E) followed by hospital-wide disinfection



Nosocomial CDI (incidence /1000 patient days)			
	Pre intervention (June 04-March 05)	Intervention (June 05-March 06)	p
5 wards	2.28	1.28	0.047
Hospital*	1.89	0.88	0.04

*period with epidemic strain

Boyce JM, ICHE 2008, 29, 723-9

Clinical studies with NTD

- 900-bed community teaching hospital (MO, US)
- Retrospective «Before-after » design
- Pre-intervention period (jan. 2007-nov 2008): daily and terminal cleaning with bleach
- Intervention (jan. 2009-dec 2009): daily cleaning with bleach and terminal cleaning with bleach + hydrogene peroxyde (Bioquell)
- No significant changes in rates of compliance to hand hygiene, gowning and gloving

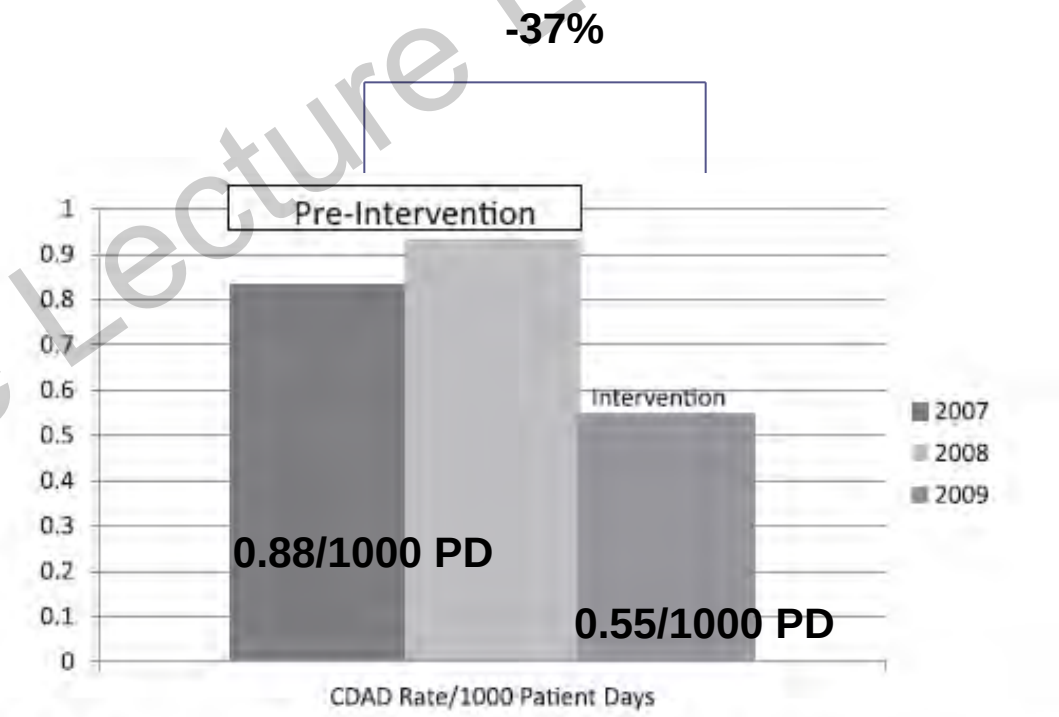


Fig 1. Nosocomial *C difficile*-associated diarrhea rates by year during preintervention and intervention periods.

Manian FA et al., AJIC 2013, 41, 537-41

Conclusion

- Evidence that the environment plays a key role in *C. difficile* transmission
- Cleaning/ disinfection of rooms remains suboptimal and a bundle of measures should be implemented to increase compliance (improved education, monitoring the thoroughness of cleaning (dye, ATP assays, culture) with feedback of performances, use of checklist.
- Evidence that NTD sytems can reduce environmental contamination but their impact on CDI incidence should be evaluated through clinical studies
- Other means for disinfection are emerging : copper or silver surfaces[1], ozone based process[2]

1-Wheeldon IJ *et al*, JAC 2008, 62, 522-5
2 - Zoutman D. *et al.,* AJIC 2011, 39, 873-879

Conclusion

Laboratory demonstration of efficacy (10^3-10^6 reduction)

Demonstration in use bioburden reduction

Demonstration that in use bioburden reduction may be clinically relevant
1- terminal-only use : **reduction of same room transmission**
2-terminal and daily use : **reduction in hand contamination**

Control for other confounding factors : hand hygiene, isolation, antibiotic use
Careful attention to baseline infection rate, trends, sample size consideration

Demonstrate **reduced transmission** via admission-discharge active surveillance testing and clinical incidence

Demonstrate reduced infections

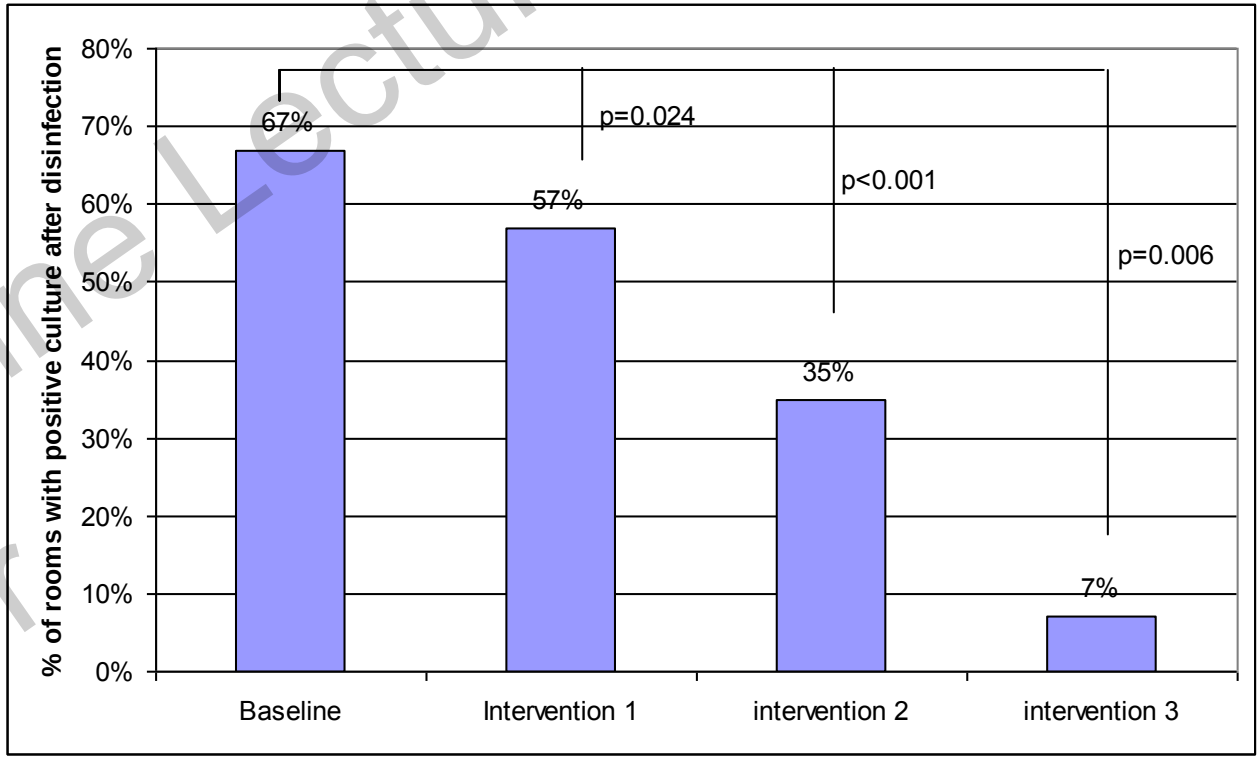
McDonald and Arduino, CID 2013, 56, 36-9

Effects of sequential interventions to improve disinfection of *C. difficile* isolation rooms

- Prospective intervention study (Cleveland, OH, US)
- Bleach for terminal disinfection

- **Intervention 1:** Fluorescent marker to provide monitoring and feedback on thoroughness of cleaning
- **Intervention 2** : UV radiation for CDI room
- **Intervention 3** : Dedicated daily disinfection team (bleach wipe) + process requiring supervisory assessment to clear the room

- Broth enrichment technique using a gauze pad moistened in sterile water (5 high-touch surfaces)



1- Sitzlar B. *et al*, ICHE 2013, 34, 459-465.