# EPIDEMIOLOGY AND PREVENTION OF *CLOSTRIDIUM DIFFICILE* INFECTION (CDI)

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# DISCLOSURES

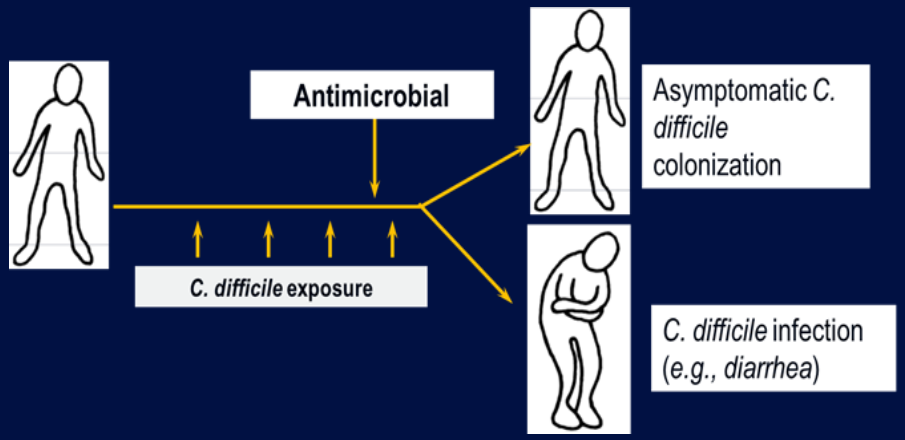
- Relevant financial disclosures
  - **Clorox (consultation within past 3 years)**
  - **ASP (speaker)**
  - **Grants:  CDC, NIH, CMS, Merck, Pfizer**
- Thanks for slides
  - **Dale Gerding, MD**
  - **Cliff McDonald, MD**

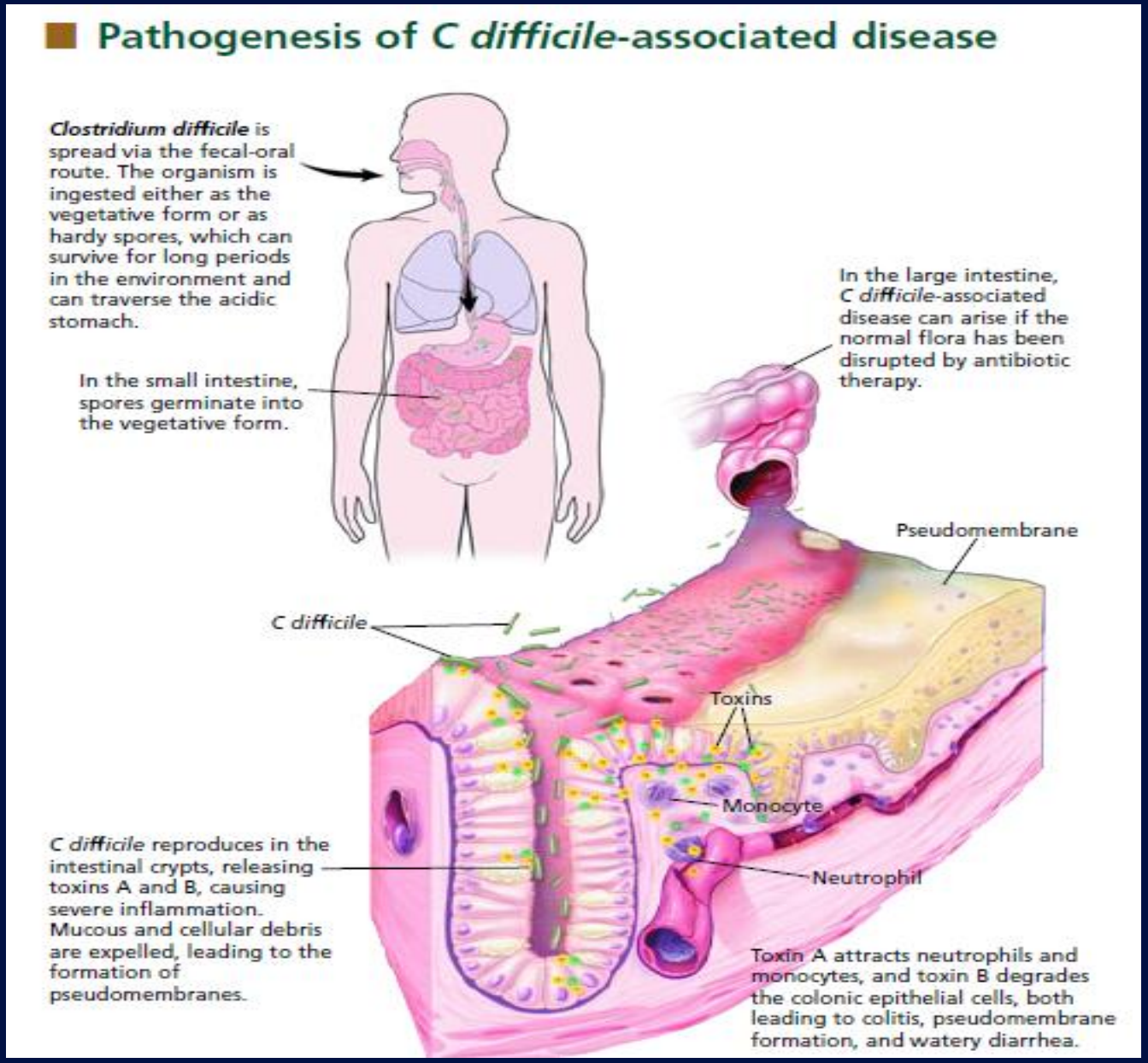
# LECTURE OBJECTIVES

- Describe the microbiology of *C. difficile*
- Describe the pathophysiology of *C. difficile* infection (CDI)
- Describe the epidemiology of CDI
- Describe the methods of preventing CDI
  - **Antibiotic stewardship**
  - **Hand hygiene and barrier precautions (Contact Precautions)**
  - **Environmental disinfection**

# *CLOSTRIDIUM DIFFICILE*
# MICROBIOLOGY

- Anaerobic bacterium
- Forms spores that persist
- Colonizes human GI tract
- Fecal-oral spread
- Toxins produce colitis
  - Diarrhea
  - More severe disease; death
- 2-steps to infection
  - Antibiotics result in vulnerability
  - New acquisition via transmission
- CDI due to BI/NAP1/027 carries high mortality and management remains problematic

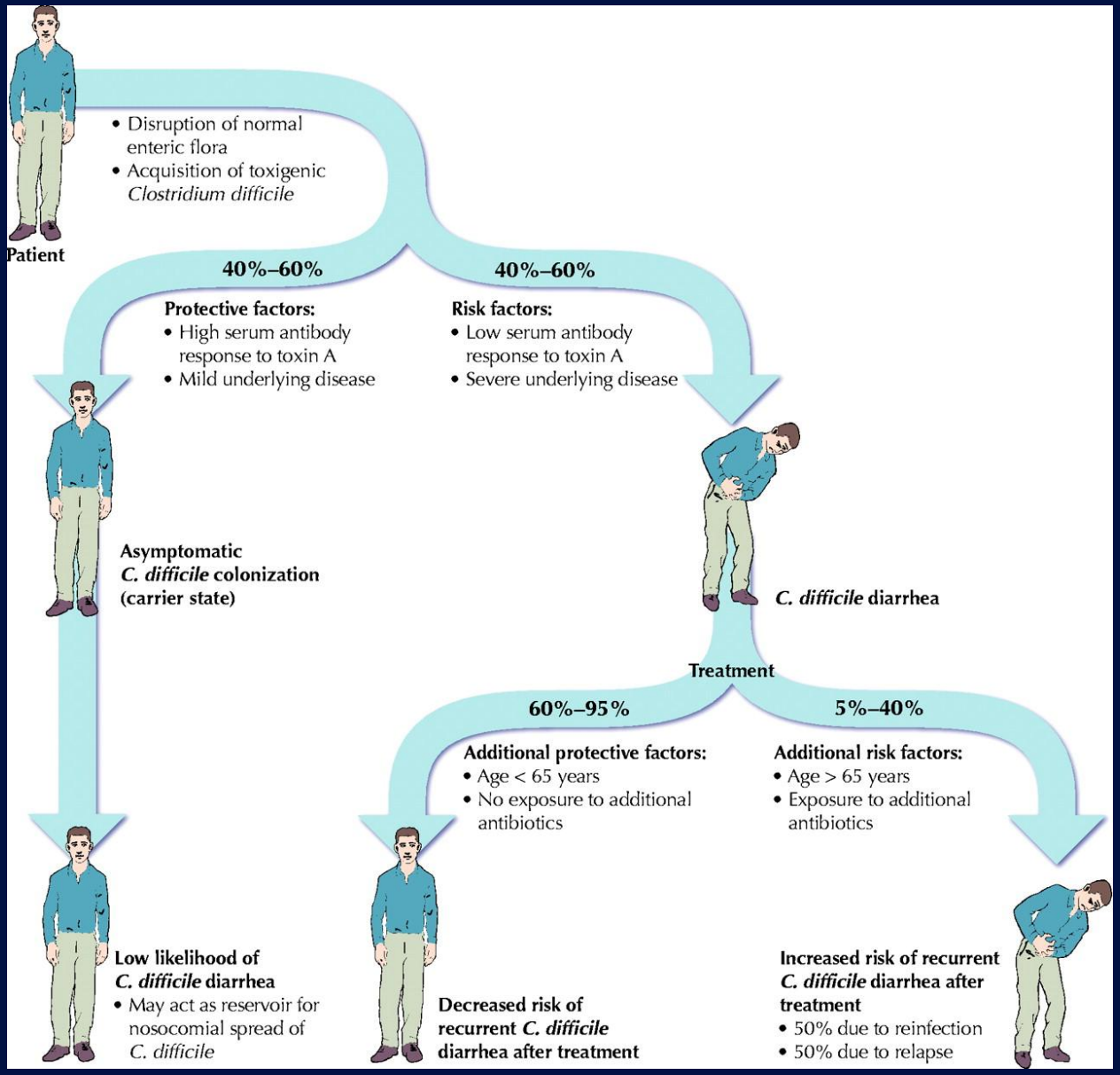




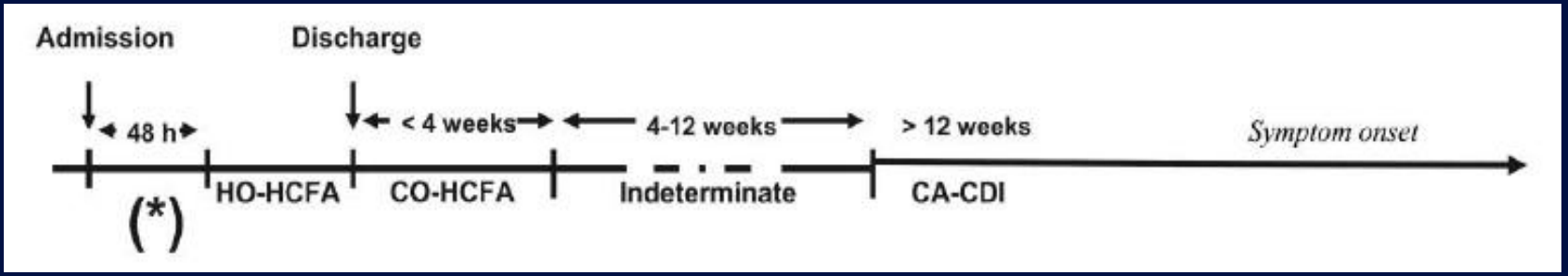

Sunenshine RH, McDonald LC. Cleve Clin J Med 2006;73:187-197

# IMPORTANT HOST DEFENSE AND RISK FACTORS FOR CDI

- Host Defenses
  - **Intact/undisturbed lower intestinal microbiota**
    - **Intact appendix?**
  - **Infancy**
  - **Humoral immune response**
  - **Stomach acid?**
    - **Spores are acid resistant**
- Risk Factors
  - **Medications that disrupt microbiota**
    - **Antibiotics**
    - **PPIs?**
  - **Older age**
  - **Immunosuppressants**
  - **Inflammatory bowel disease**
  - **Tube feedings**
  - **Factors increasing acquisition**
    - **Contaminated hospital environment**


Patient
• Disruption of normal enteric flora
• Acquisition of toxigenic *Clostridium difficile*
40%–60%
Protective factors:
• High serum antibody response to toxin A
• Mild underlying disease
40%–60%
Risk factors:
• Low serum antibody response to toxin A
• Severe underlying disease
Asymptomatic *C. difficile* colonization (carrier state)
*C. difficile* diarrhea
Treatment
60%–95%
Additional protective factors:
• Age < 65 years
• No exposure to additional antibiotics
5%–40%
Additional risk factors:
• Age > 65 years
• Exposure to additional antibiotics
Low likelihood of *C. difficile* diarrhea
• May act as reservoir for nosocomial spread of *C. difficile*
Decreased risk of recurrent *C. difficile* diarrhea after treatment
Increased risk of recurrent *C. difficile* diarrhea after treatment
• 50% due to reinfection
• 50% due to relapse

# DEFINITIONS

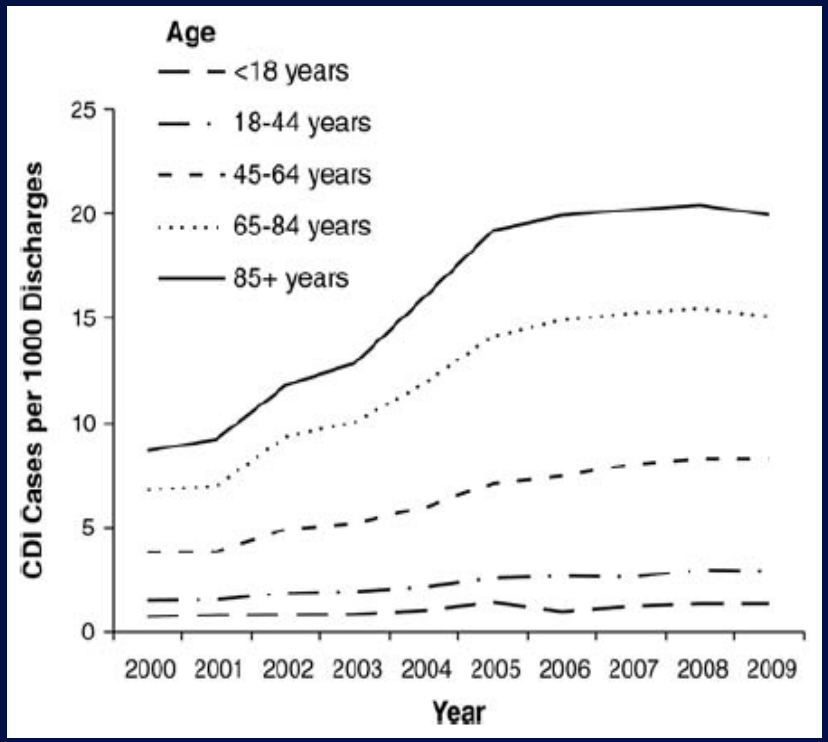



- HO-HCFA: Healthcare facility-onset, healthcare facility-associated CDI
- CO-HCFA: Community onset, healthcare facility-associated disease
- CA-CDI: Community-associated CDI

Cohen SH, et al. ICHEZ 2010;31:431-455

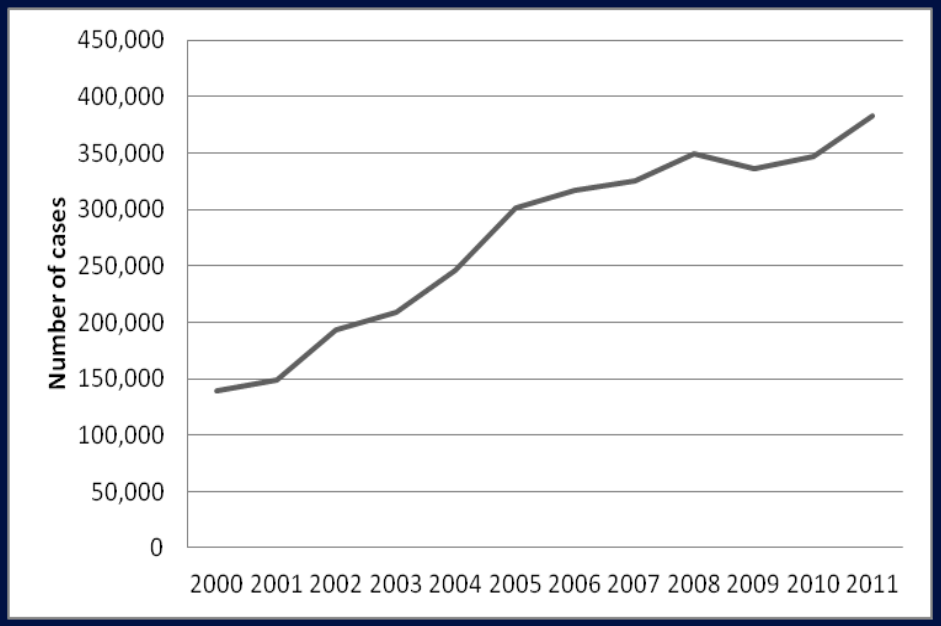
# *CLOSTRIDIUM DIFFICILE*
# EPIDEMIOLOGY

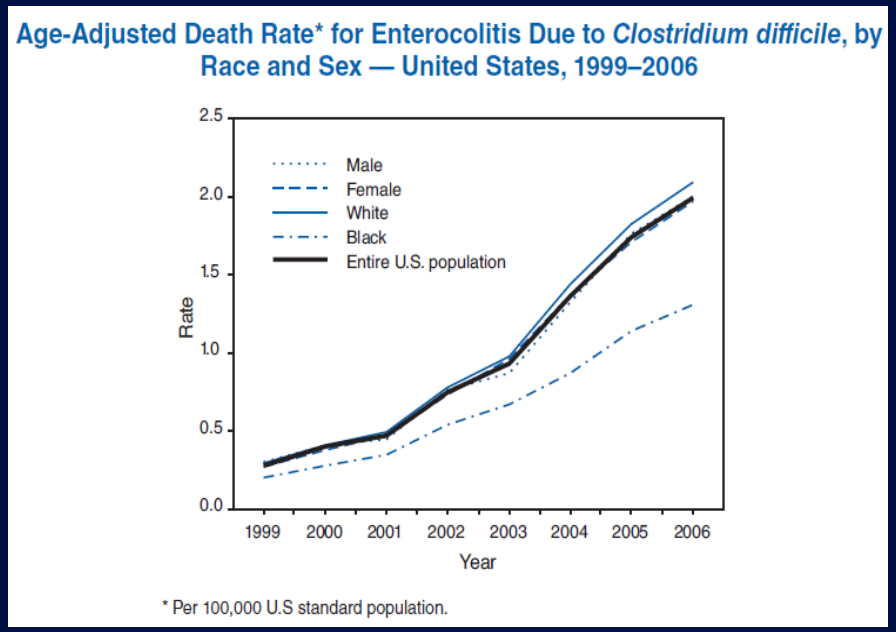
- Increasing prevalence & incidence
- Introduction from community to hospital
- Age a major risk factor for severe disease
- CDI now the most common healthcare associated pathogen




Lessa FC, et al. Clin Infect Dis 2012;55(S2):S65-70

# *C. difficile*: INCREASING INCIDENCE AND DEATH RATE



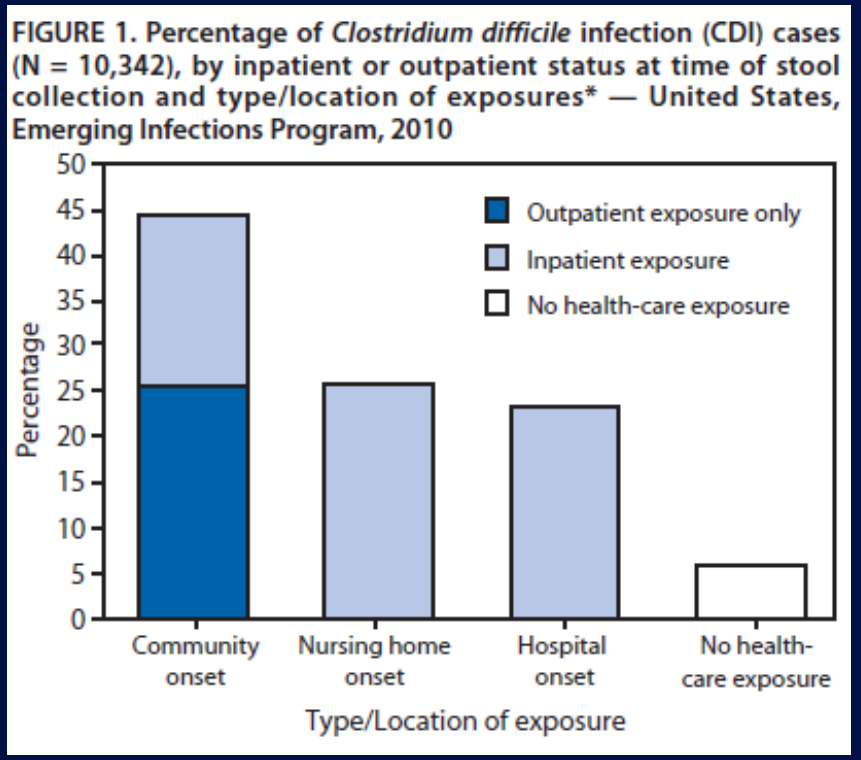




AHRQ HCUP data CDC.

MMWR 2009;58:505

# CDI LARGELY HEALTHCARE RELATED; BUT MOST DEVELOP SYMPTOMS OUTSIDE HOSPITALS

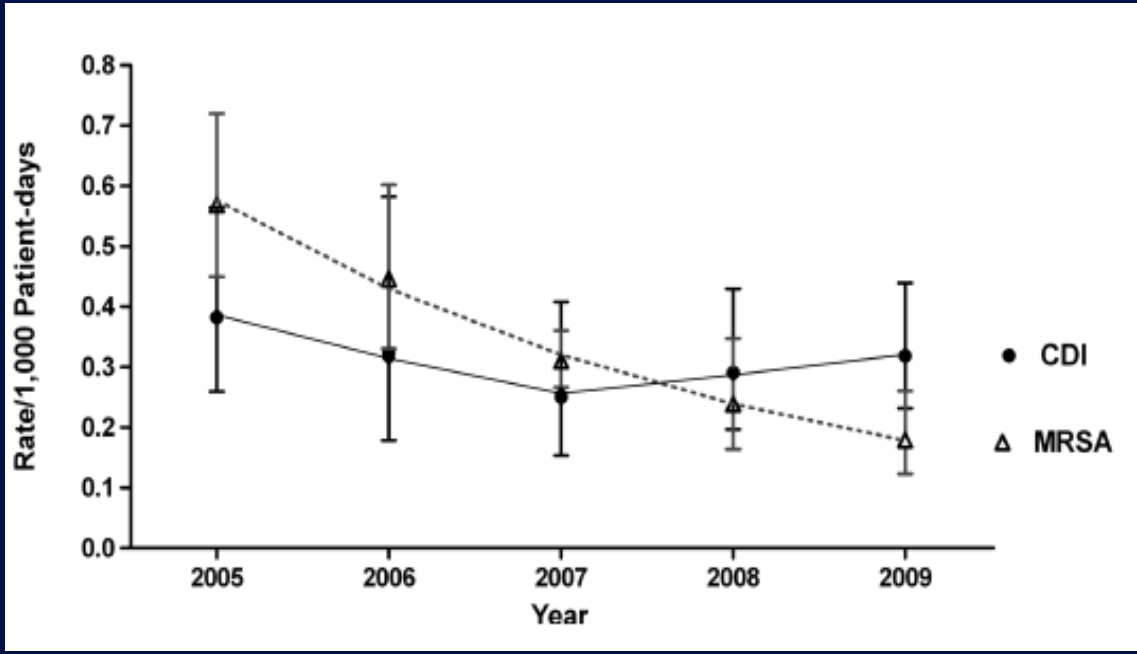
- 94% healthcare related
- 75% of these outside hospitals
  - **Nursing home patients**
  - **Patients in community**
    - **Outpatient exposures**
    - **Only recent inpatient exposure**
- 25% hospital inpatients
- Post-discharge CDI common
  - **Most potent antibiotics used in hospitals**
  - **Lasting effect on patients**




CDC. MMWR 2012;61:1-6

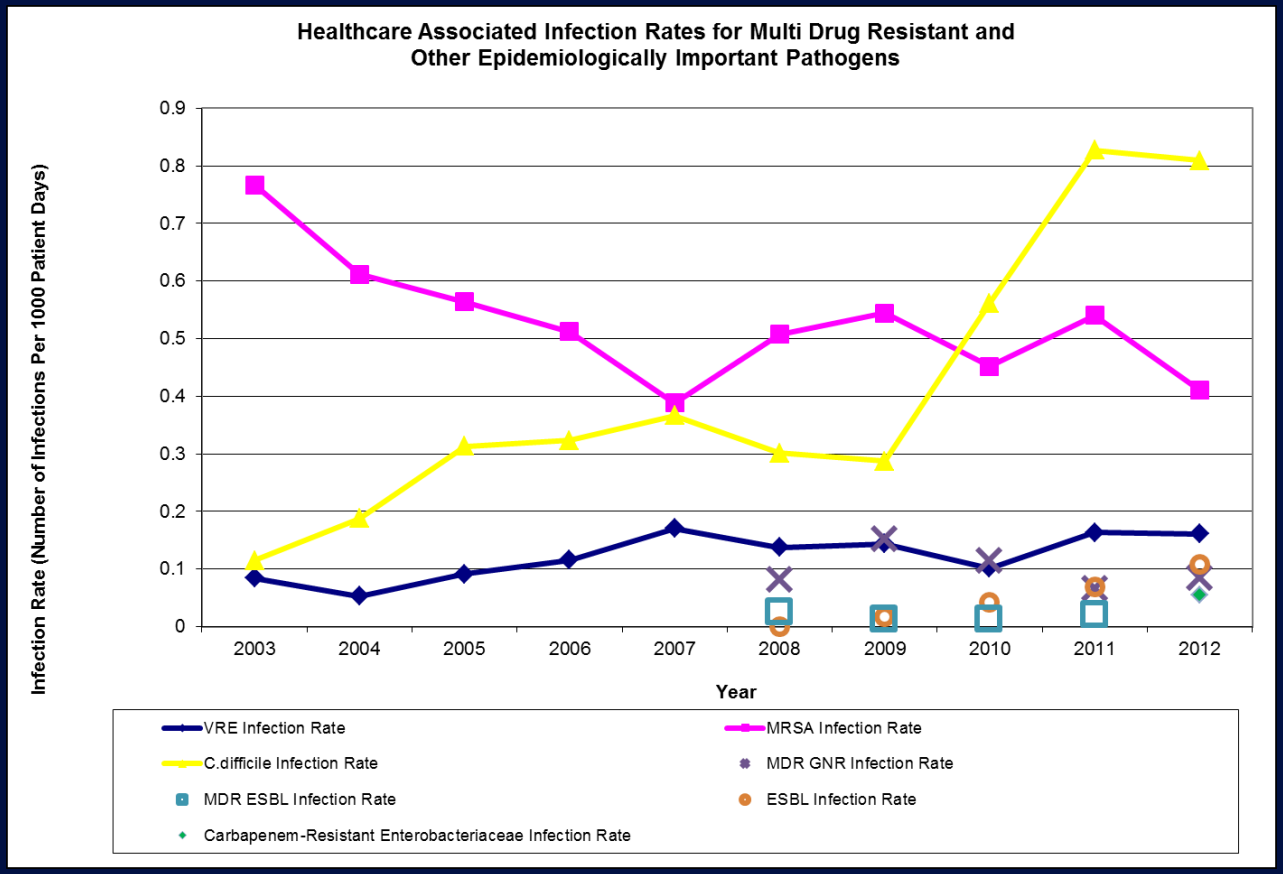
# CDI NOW THE MOST COMMON HEALTHCARE-ASSOCIATED PATHOGEN

- Analysis of 10 community hospitals, 2005-2009, in the Duke DICON system



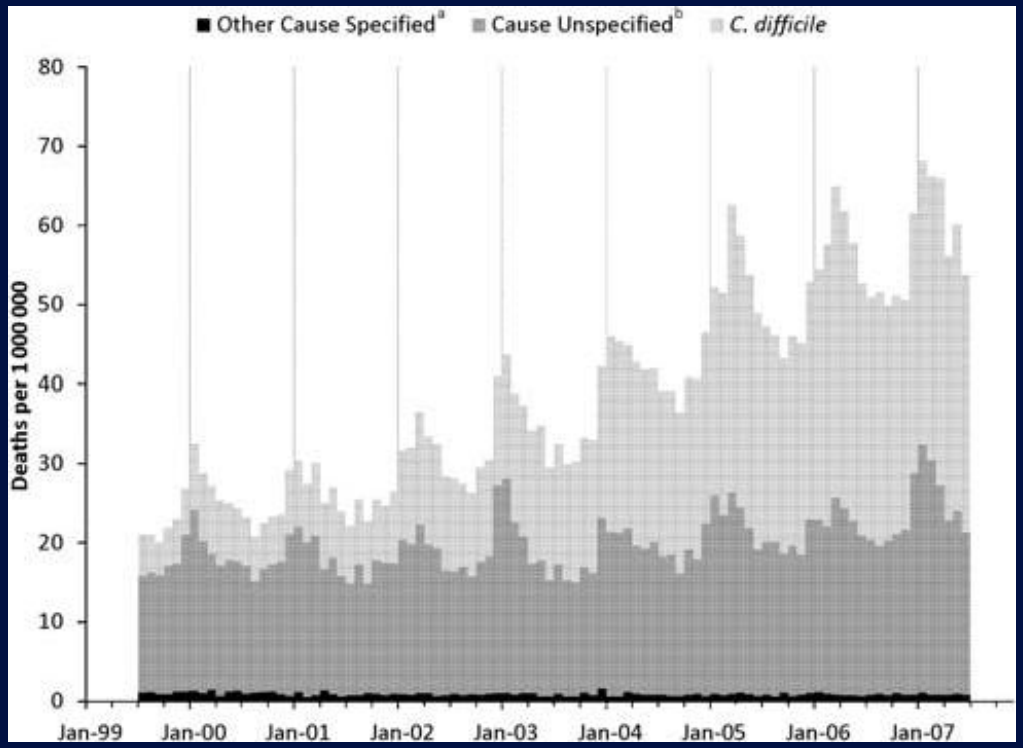

Miller BA, et al. ICHE 2011;32:387-390

# UNC RATES OF MULTIDRUG RESISTANT PATHOGENS, 2003-2012



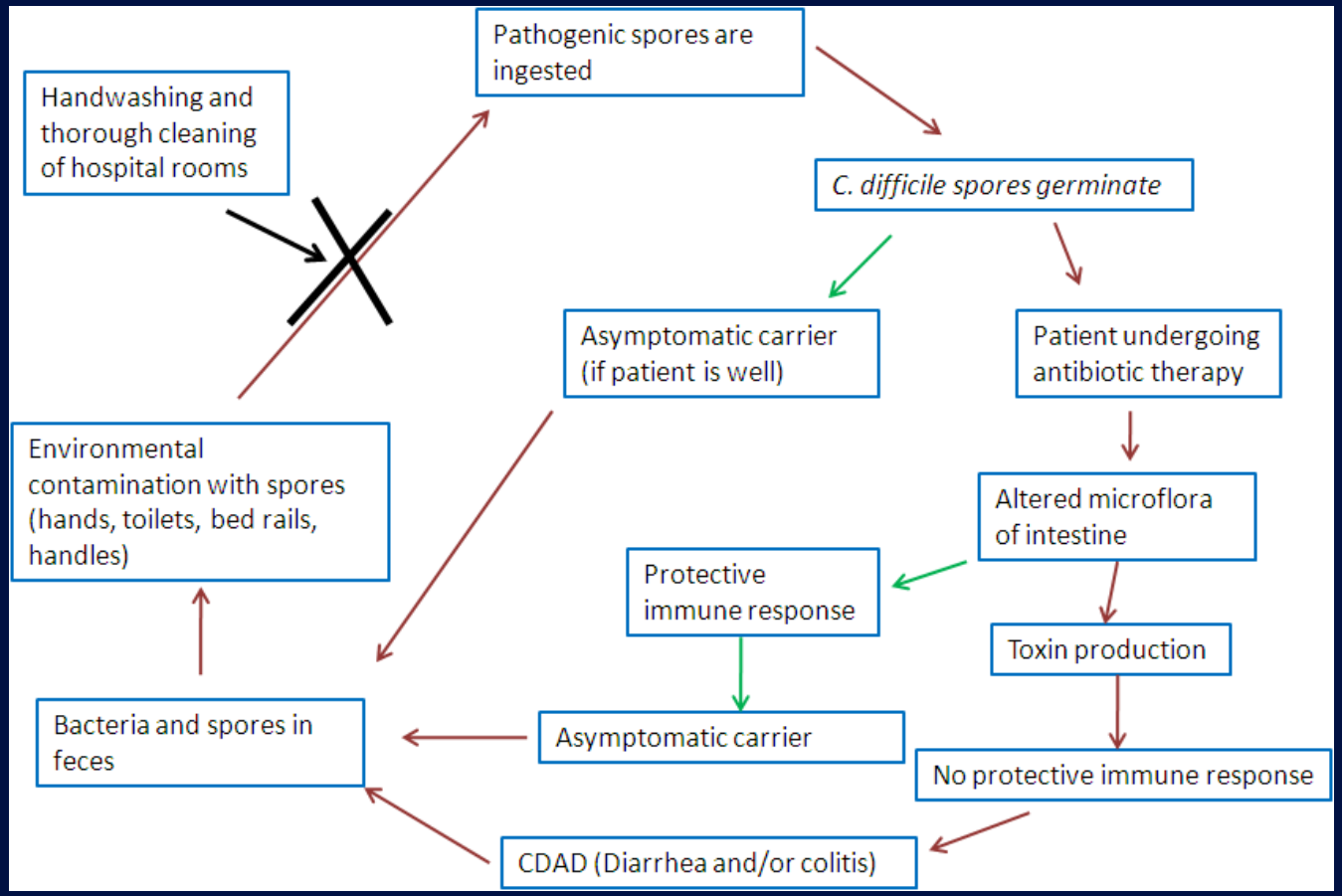
# Increasing CDI Severity

- Outbreaks of severe CDI in US, Canada, Ireland, England, Netherlands, France, Germany
- Sherbrooke, Quebec, Canada, outbreak, 2003
  - 16.7% attributable mortality
- St. Louis, endemic, 2003
  - 5.7% attributable mortality
  - 2.2 times more likely readmitted
  - 1.6 times more likely discharged to nursing home




Pépin J, et al. Can Med Assoc J. 2005; Dubberke ER, et al. CID. 2008; Dubberke EID 2008; Hall. CID. 2012

# *C. difficile* PATHOGENESIS




CDC

# Summary of Assay Performance

| Assay | Sensitivity to detect *C. difficile* | Specificity for CDI | Storage | Turn-around |
|---|---|---|---|---|
| Toxin EIA | ++ | +++ | Refrigerate / freeze | Hours |
| GDH EIA | +++ | ++ | | Hours |
| Cytotoxicity | ++ | ++++ | Refrigerate / freeze | Days |
| NAAT | +++ | ++ | | Hours |
| Culture | ++++ | ++ | | Days |

# Diagnostics Available

| Test | Advantage(s) | Disadvantage(s) |
|---|---|---|
| **Toxin testing** | | |
| Toxin Enzyme immunoassay (EIA) | Rapid, simple, inexpensive, specific for CDI | Least sensitive method, assay variability, strain prevalence may impact sensitivity |
| Tissue culture cytotoxicity | More sensitive than toxin EIA, biologically active toxin, specific for CDI | Labor intensive; requires 24–48 hours for a final result, special equipment; |
| **Organism identification** | | |
| Glutamate dehydro-genase (GDH) EIA | Rapid, sensitive | Not specific for CDI, toxin testing required to verify diagnosis; may not be 100% sensitive (screening test) |
| Nucleic acid amplification tests (NAAT) | Rapid, sensitive, detects presence of toxin gene | Cost, special equipment, not specific for CDI |
| Stool culture | Most sensitive test available when performed appropriately | Confirm toxin production; labor-intensive; requires 48–96 hours for results, not specific for CDI |

# Current CDI Treatment by Infection Severity and Recurrence

| Organism | Antibiotic | Dose | Alternatives |
|---|---|---|---|
| *C. difficile* (mild to moderate) | Metronidazole | 500 mg po tid X 10-14d | Vancomycin 125 mg po qid X 10-14d |
| *C. difficile* (severe) | Vancomycin | 125 mg po qid X 10-14d | Fidaxomicin 200 mg po bid X 10d |
| *C. difficile* (severe complicated or fulminant) | Vancomycin + Metronidazole | 500 mg po qid X 10-14d<br>500 mg iv tid X 10-14d | Tigecycline 50 mg iv bid X 10-21d in place of metronidazole or vancomycin<br>Additional vancomycin via rectal retention enema, 500 mg in 100 ml NS q 6h if complete ileus present<br>Colectomy or Ileostomy |
| *C. difficile* (first recurrence) | Same as primary CDI based on severity of disease | | Fidaxomicin 200 mg po bid X 10d<br>Fecal Transplant |
| *C. difficile* (>1 recurrence) | Vancomycin taper | 125 mg po qid X 10d, then 125 mg po bid X 7d, then 125 mg po qd X 7d, then 125 mg po qod or q3d X 14-28d, then stop | Vancomycin 125 mg po qid X 10d followed by rifaximin 400 mg po bid X 14d,<br>Fidaxomicin 200 mg po bid X 10d<br>Fecal Transplant |

Adapted from Cohen S et al Infect Cont Hosp Epidemiol 2010;31:431-55.

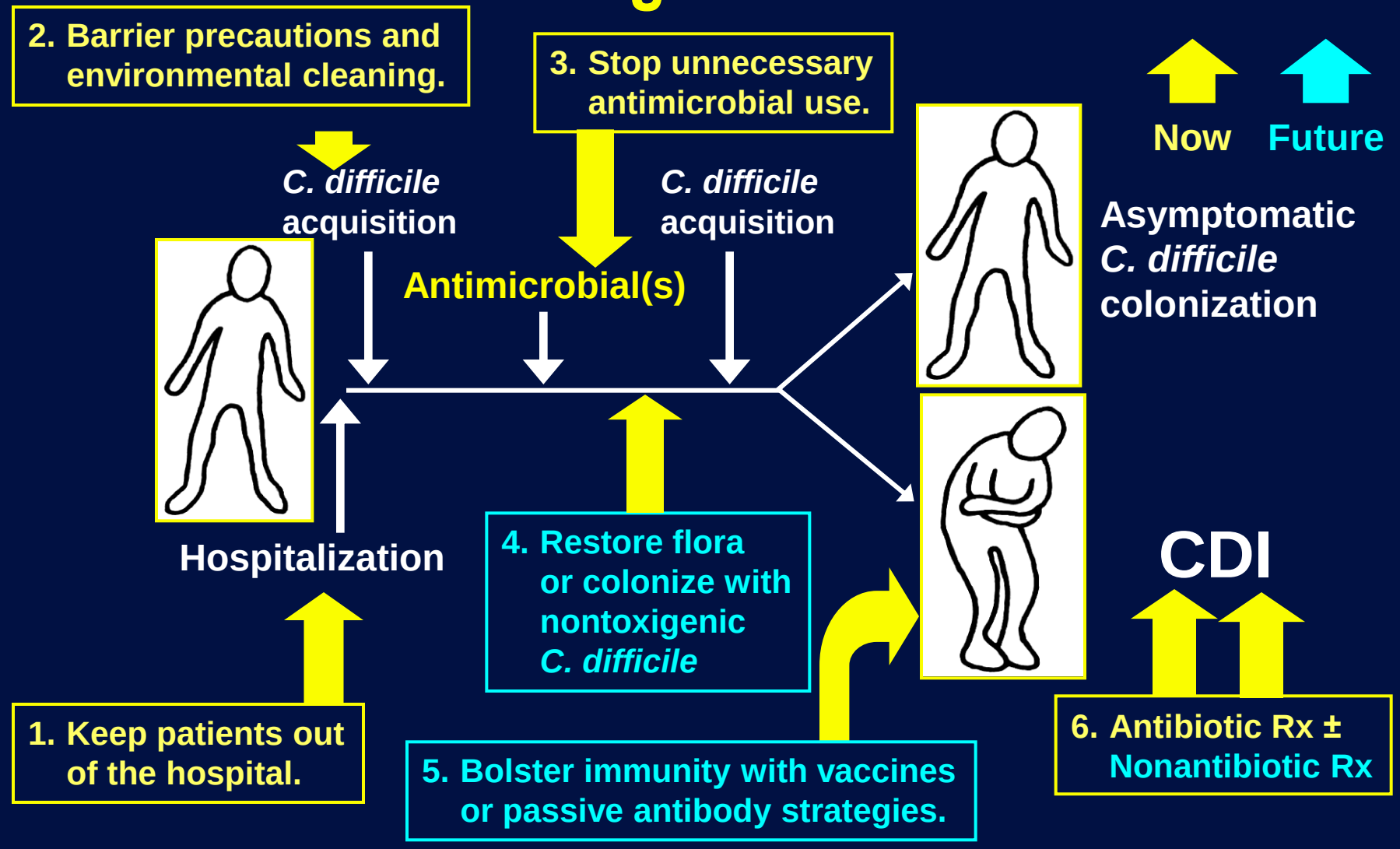
# Decreasing Order of Resistance of Microorganisms to Disinfectants/Sterilants

**Most Resistant**

**Most Susceptible**

Prions
Bacterial spores (*C. difficile*)
Protozoal oocysts
Helminth eggs
Mycobacteria
Small, non-enveloped viruses (norovirus)
Protozoal cysts
Fungal spores
Gram-negative bacilli (*Acinetobacter*)
Vegetative fungi and algae
Large, non-enveloped viruses'
Gram-positive bacteria (MRSA, VRE)
Enveloped viruses

# Sites of Attack for Prevention and Management of CDI




Gerding and Johnson Clin Infect Dis. 2010;51:1306-13

# ANTIBIOTIC STEWARDSHIP

- Encourage appropriate antibiotic use which includes:
  - **Avoiding antimicrobial exposure if the patient does not have a condition for which antibiotics are indicated**
  - **When possible select an antibiotic associated with a lower risk of CDI**
  - **Avoid the use of multiple antibiotics**
  - **Practice de-escalation or streamlining**
  - **Treat infections for the minimum of time consistent with proper therapy**

**Strategies to Prevent CDI Infections in Acute Care Hospitals: Draft SHEA Guideline, 2013**

# INFECTION CONTROL MEASURES TO PREVENT TRANSMISSION OF *C. difficile*

| Variable | Strength of recommendation |
|---|---|
| Hand hygiene | A-II |
| Contact precautions | |
| Glove use | A-I |
| Gowns | B-III |
| Use of private rooms or cohorting | C-III |
| Environmental cleaning, disinfection, or use of disposables | |
| Disinfection of patient rooms and environmental surfaces | B-II |
| Disinfection of equipment between uses for patients | C-III |
| Elimination of use of rectal thermometers | B-II |
| Use of hypochlorite (1,000 ppm available chlorine) for disinfection | B-II |

Cohen SH, et al. ICHE 2010;31:431-455

# HAND HYGIENE

- Perform hand hygiene before and after entering the room; use soap and water or an alcohol-based hand hygiene product (routine or endemic settings)
- Perform hand hygiene with soap and water preferentially instead of alcohol hand hygiene products after caring for a patient with CDI in outbreak or hyper-endemic settings

Strategies to Prevent CDI Infections in Acute Care Hospitals: Draft SHEA Guideline, 2013

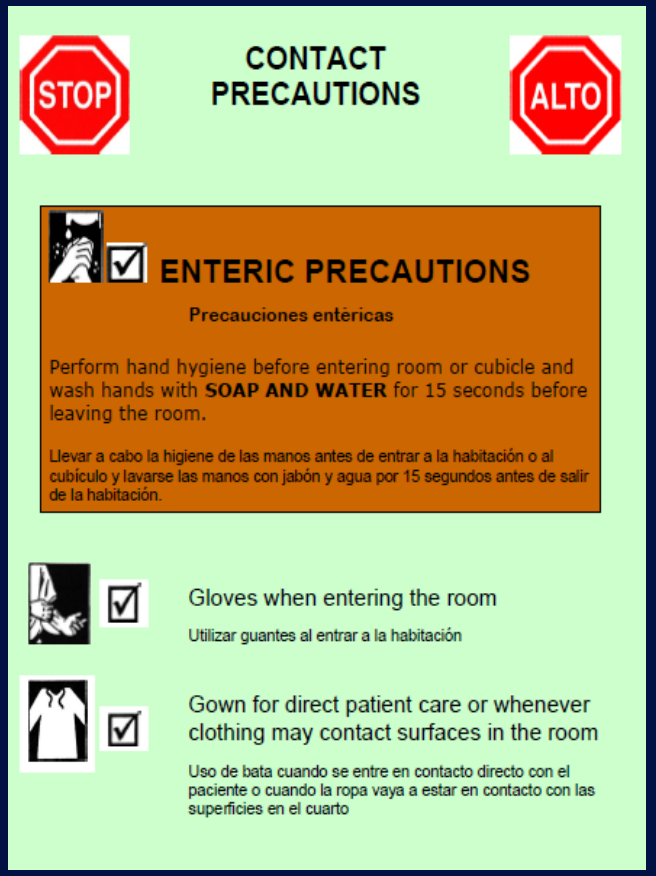
# BARRIER PRECAUTIONS

- Avoid use of electronic thermometers
- Use dedicated patient care items and equipment
- If equipment must be shared; clean and disinfect between patients
- Use full barrier precautions (gowns and gloves) for contact with CDI patients and for contact with their environment (i.e., Contact Precautions)
- Place patient with CDI in a private room, if available; give isolation preference to patients with fecal incontinence if room availability is limited

**Strategies to Prevent CDI Infections in Acute Care Hospitals: Draft SHEA Guideline, 2013**

# UNC ISOLATION SIGN FOR PATIENTS WITH *C. difficile*

- Use term contact-enteric precautions
- Requires gloves and gown when entering room
- Recommends hand hygiene with soap and water (instead of alcohol based antiseptic)
- Information in English and Spanish
- Also use with norovirus and rotavirus



# EFFICACY OF ALCOHOL AS A HAND HYGIENE AGENT AGAINST *C. difficile*

TABLE 1. Mean *Clostridium difficile* Colony Counts after Different Hand Hygiene Interventions According to the Whole-Hand Protocol

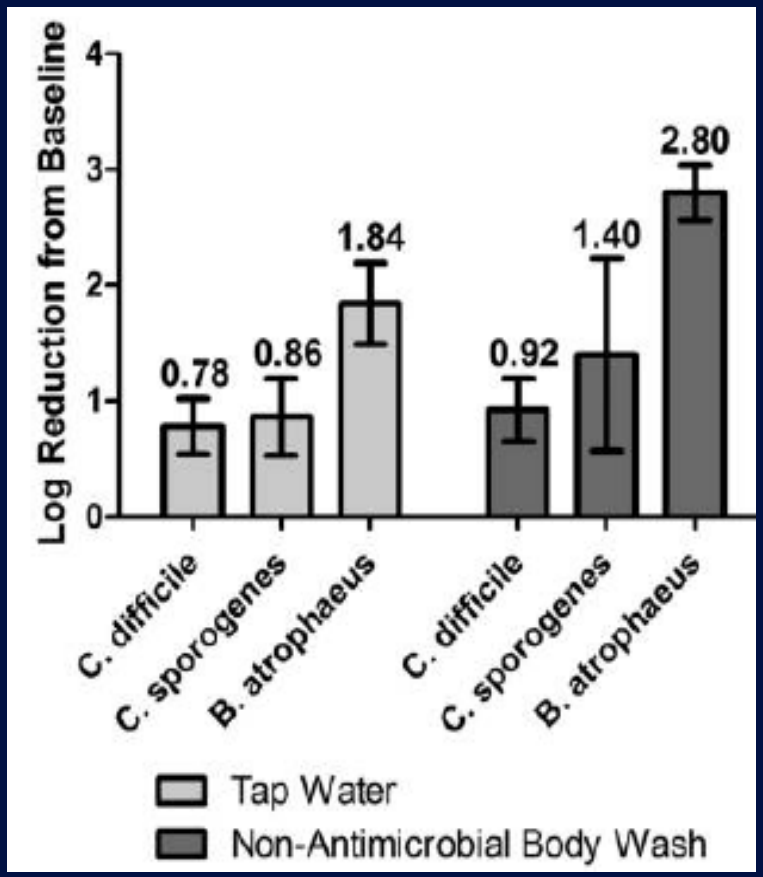
| Intervention | Mean count (95% CI), $\log_{10}$ CFU/mL |
|---|---|
| Warm water and plain soap | 1.99 (1.80–2.09) |
| Cold water and plain soap | 1.90 (1.58–2.22) |
| Warm water and antibacterial soap | 2.31 (2.04–2.58) |
| Antiseptic hand wipe | 3.25 (3.04–3.45) |
| Alcohol-based handrub | 3.74 (3.40–4.07) |
| No intervention | 3.82 (3.54–4.10) |

- Probability of heavy contamination (TNTC) following different HH interventions: warm water and plain soap = 0, cold water and plain soap = 0, warm water and antibacterial soap = 0, antiseptic hand wipe = 0.05, alcohol-based handrub = 0.43, and no hand hygiene = 1

Oughton MT, et al. ICHE 2009;30:939-944

# HAND HYGIENE TO REMOVE OR INACTIVATE *C. difficile*

- Study design: Human challenge study
  - **15 second exposure followed by 15 second rinse**
- *C. difficile* less easy to remove than *C. sorogenes* or *B. atropheus*
- Best product for removal of *C. difficile* was peracetic acid and surfactant formulation (next slide)




Edmonds SL, et al. ICHE 2013;34:302-305

# EFFICACY OF DIFFERENT HAND HYGIENE AGENTS AGAINST C. difficile

| Test product | No. of samples tested | $Log_{10}$ cfu/mL reduction | Standard deviation | $P^a$ |
|---|---|---|---|---|
| Tap water | 18 | 0.76 | 0.11 | N/A |
| 4% chlorhexidine gluconate hand wash | 18 | 0.77 | 0.11 | >.05 |
| Nonantimicrobial hand wash | 6 | 0.78 | 0.16 | >.05 |
| Nonantimicrobial body wash | 18 | 0.86 | 0.22 | >.05 |
| 0.5% bleach and surfactant prototype | 6 | 0.98 | 0.13 | >.05 |
| 0.3% triclosan hand wash | 6 | 0.99 | 0.13 | >.05 |
| 8% hydrogen peroxide and surfactant prototype | 6 | 0.99 | 0.72 | >.05 |
| Peracetic acid wipe | 6 | 1.08 | 0.29 | >.05 |
| Sodium tetraborate decahydrate powder | 6 | 1.18[b] | 0.31 | <.05 |
| Ink and stain remover | 12 | 1.21[b] | 0.22 | <.001 |
| Ink and stain remover with brush | 6 | 1.47[b] | 0.10 | <.0001 |
| Peracetic acid and surfactant prototype | 6 | 1.51[b] | 0.42 | <.0001 |

# PHYSICAL REMOVAL VERSUS CHEMICAL INACTIVATION

TABLE 2. Effectiveness of Different Wipe and Spray Methods as Measured by Reduction in Bacterial Count and Drying Time

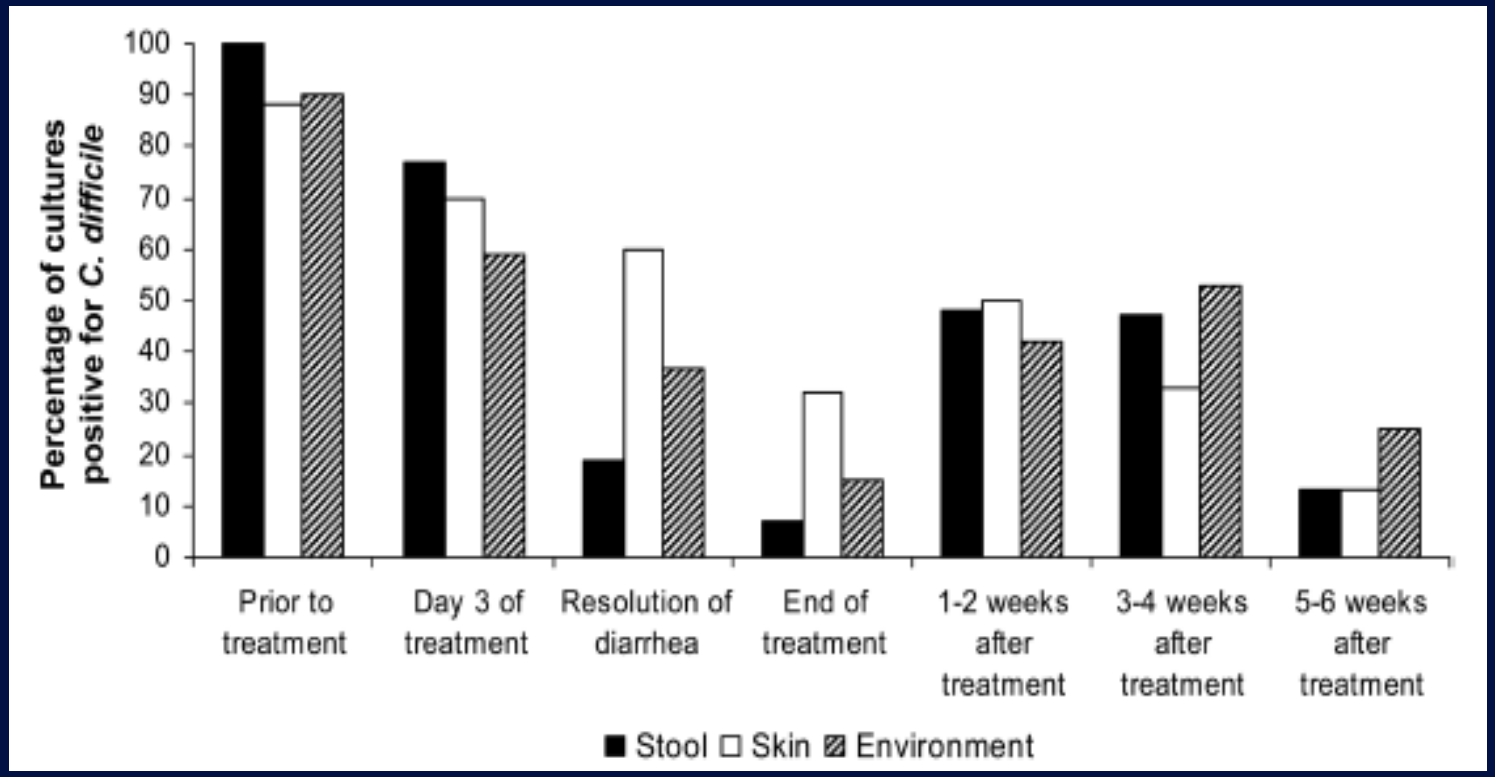
| | Wipe and/or spray method | | | | | |
|---|---|---|---|---|---|---|
| Product | Saturated cloth[a] | Spray (10 s) and wipe | Spray, wipe, spray (1 min), wipe | Disposable pop-up wipes | Spray, wipe, spray, air dry | Spray and air dry |
| Ecolab QC-53, detergent | | | | | | |
| Reduction | 3.38 (1.61–5.16) | 3.28 (2.18–4.38) | 4.02 (3.68–4.35) | NT | 2.90 (1.34–4.45) | <2.00 (1.78–2.21) |
| Drying time, min:s | 2:09 | 4:18 | 3:34 | NT | 24:26 | 28:11 |
| Ecolab A456-II | | | | | | |
| Reduction | 3.14 (2.01–4.27) | 2.98 (1.92–4.04) | 4.18 (3.46–4.90) | NT | 2.90 (1.52–4.27) | <2.00 (1.78–2.21) |
| Drying time, min:s | 2:26 | 6:18 | 4:44 | NT | 24:00 | 30:14 |
| 1 : 10 Bleach | | | | | | |
| Reduction | 3.90 (2.87–4.92) | 4.48 (4.26–4.69) | 4.48 (4.26–4.69) | NT | 4.48 (4.26–4.69) | 3.44 (1.65–5.22) |
| Drying time, min:s | 1:45 | 5:18 | 5:21 | NT | 51:08 | 39:40 |
| Kimtech One-Step Germicidal Wipe | | | | | | |
| Reduction | NT | NT | NT | 4.18 (4.18–4.18) | NT | NT |
| Drying time, min:s | NT | NT | NT | 4:06 | NT | NT |
| Clorox Germicidal Wipe | | | | | | |
| Reduction | NT | NT | NT | 3.98 (3.23–4.72) | NT | NT |
| Drying time, min:s | NT | NT | NT | 1:47 | NT | NT |
| Clorox #9255–41–1 and 3 | | | | | | |
| Reduction | NT | 6.14 (6.14–6.14) | NT | NT | NT | 5.96 (5.22–6.70) |
| Drying time, min:s | NT | 2:49 | NT | NT | NT | 40:14 |

Rutala WA, Gergen MF, Weber DJ. ICHE 2012;33:1255-58

# DISCONTINUING ISOLATION

- CDC currently recommends contact precautions for the duration of illness when care for patients with CDI.
  - **Some experts recommend continuing contact precautions for at least 48 hours after diarrhea resolves**
- At this time data do NOT exist to support extending isolation as a measure to decrease CDI incidence.

# PERCENT OF STOOL, SKIN, AND ENVIRONMENT CULTURES POSITIVE FOR *C. difficile*




Skin (chest and abdomen) and environment (bed rail, bedside table, call button, toilet seat)

Sethi AK, et al. ICHE 2010;31:21-27

# ENVIRONMENTAL DISINFECTION

- Perform environmental decontamination of rooms housing patients with CDI with sodium hypochlorite (household beach) diluted 1:10 with water, or an EPA-registered sporicidal product in an outbreak or hyper-endemic setting including:
  - **Furnishing such as bed tables, commodes, and bedrails**
  - **Patient care equipment such as stethoscopes and BP cuffs**
  - **Surfaces such as door knobs and IV infusion pumps**
- When possible dedicate non-critical patient care items such as BP cuffs, stethoscopes and thermometers to a single CDI patient

**Strategies to Prevent CDI Infections in Acute Care Hospitals: Draft SHEA Guideline, 2013**

# DISINFECTANTS

## No measurable activity (1 *C. difficile* strain, J9; spores at 20 min)

- Vesphene (phenolic)
- 70% isopropyl alcohol
- 95% ethanol
- 3% hydrogen peroxide
- Clorox disinfecting spray (65% ethanol, 0.6% QUAT)
- Lysol II disinfecting spray (79% ethanol, 0.1% QUAT)
- TBQ (0.06% QUAT); QUAT may increase sporulation capacity- (Lancet 2000;356:1324)
- Novaplus (10% povidone iodine)
- Accel (0.5% hydrogen peroxide)

**Rutala W, Weber D, et al ICHE 2006**

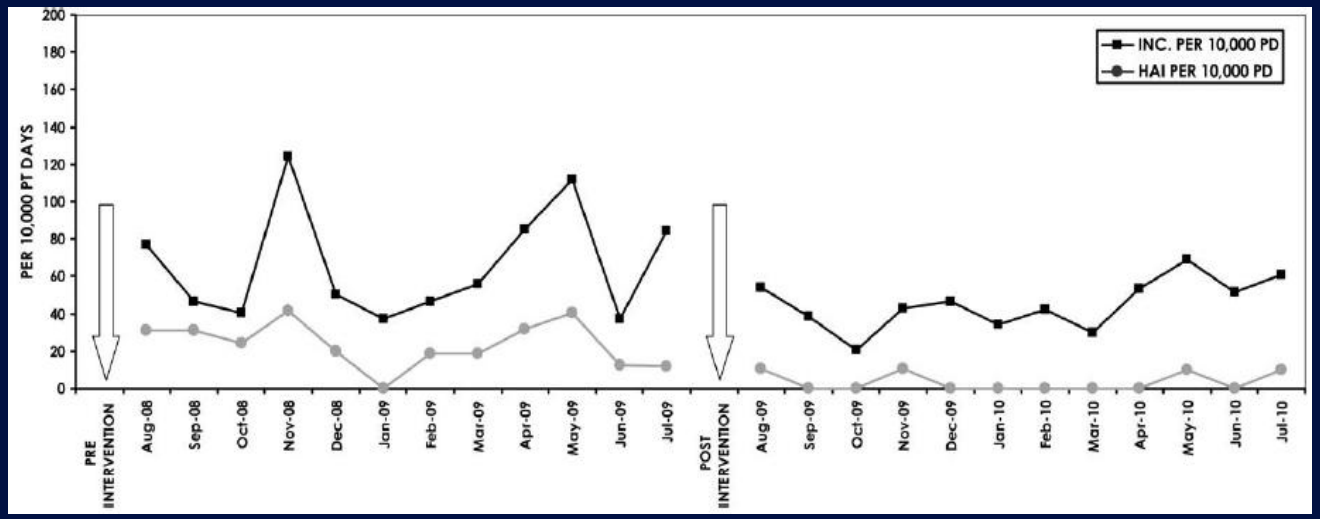
# DISINFECTANTS

## *C. difficile* spores at 10 and 20 min

- ~4 $\log_{10}$ reduction (3 *C. difficile* strains including BI-9)
  - **Clorox, 1:10, ~6,000 ppm chlorine (but not 1:50, ~1,200 ppm)**
  - **Clorox Clean-up, ~19,100 ppm chlorine**
  - **Tilex, ~25,000 ppm chlorine**

# REDUCTION IN CDI INCIDENCE WITH ENHANCED ROOM DISINFECTION

- Before-after study of CDI incident rates in two hyperendemic wards at a 1,249 bed hospital
- Intervention: Change from cleaning rooms with QUAT to bleach wipes (0.55% Cl) for both routine and terminal disinfection
- Results
  - CDI incidence dropped from 24.2 to 3.6 cases per 10,000 pt-days (p<0.001)

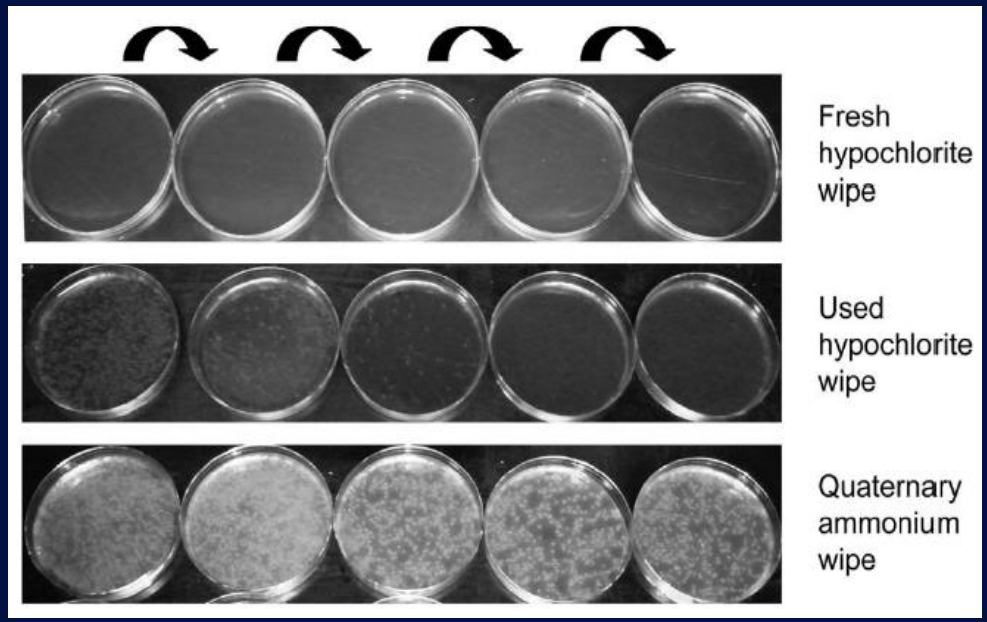



Orenstein R, et al
ICHE 2011;32:1137

# TRANSFER OF C. DIFFICILE SPORES BY NONSPORICIDAL WIPES AND IMPROPERLY USED HYPOCHLORITE WIPES

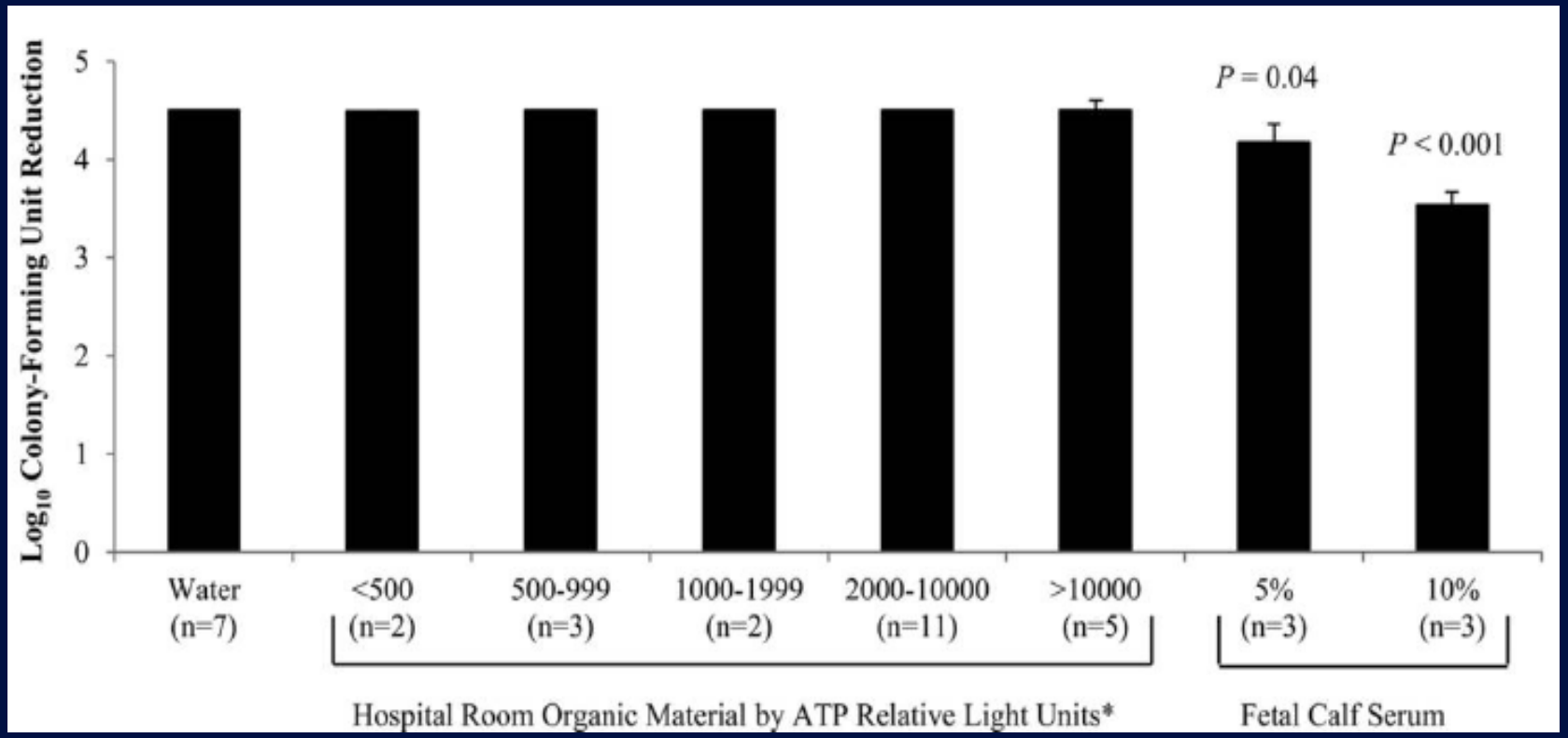
- Study design: *In vitro* study that assessed efficacy of different wipes in killing of *C. difficile* spores (5-$\log_{10}$)
  - Fresh hypochlorite wipes
  - Used hypochlorite wipes
  - Quaternary ammonium wipes
- Results (4$^{th}$ transfer)
  - Quat had no efficacy (3-$\log_{10}$ spores)
  - Fresh hypochlorite worked
  - Used hypochlorite transferred spores in lower concentration (0.4-$\log_{10}$ spores)

**Practice + Product = Perfection**



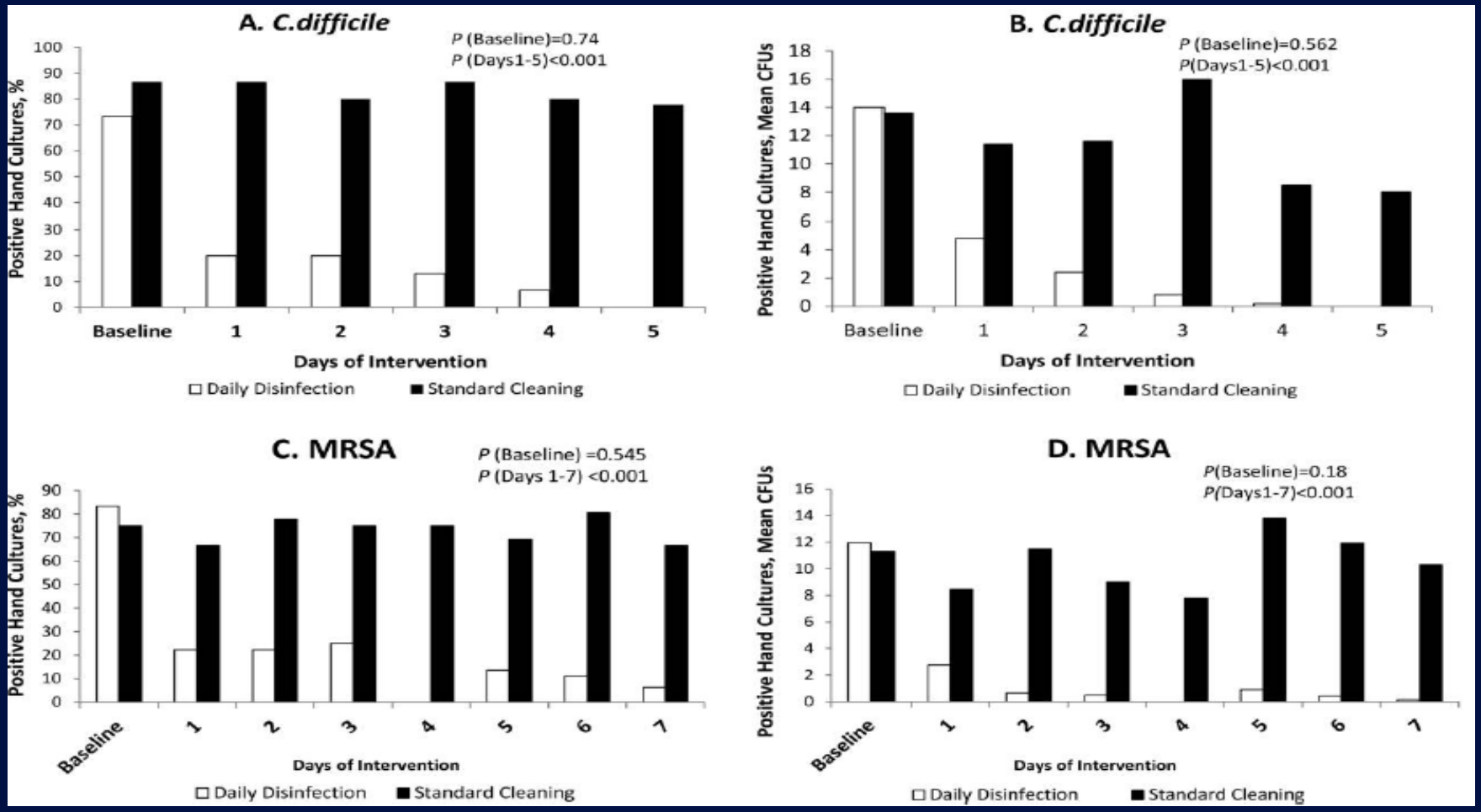

Cadnum JL, et al. ICHE 2013;34:441-2

# EFFECT OF ORGANIC MATERIAL ON HYPOCHLORITE KILLING OF *C. DIFFICILE* SPORES




Zhang A, et al. ICHE 2013;34:1106-1108

# EFFECT OF DAILY CLEANING VERSUS ONLY WHEN SOILED ON CONTAMINATION OF HCP HANDS




Kundrapu S, et al. ICHE 2012;33:1039-1042

# MISCELLANEOUS

- Perform CDI testing only on unformed diarrheal stools
- Do not place patients at high risk for CDI on prophylactic antimicrobial CDI therapy
- Do not treat or attempt to decolonize asymptomatic CDI carriers
- Do not conduct repeat testing for *C. difficile* if a patient has had a positive stool of *C. difficile* unless symptoms resolved with treatment and then returned after treatment discontinued

**Strategies to Prevent CDI Infections in Acute Care Hospitals: Draft SHEA Guideline, 2013**

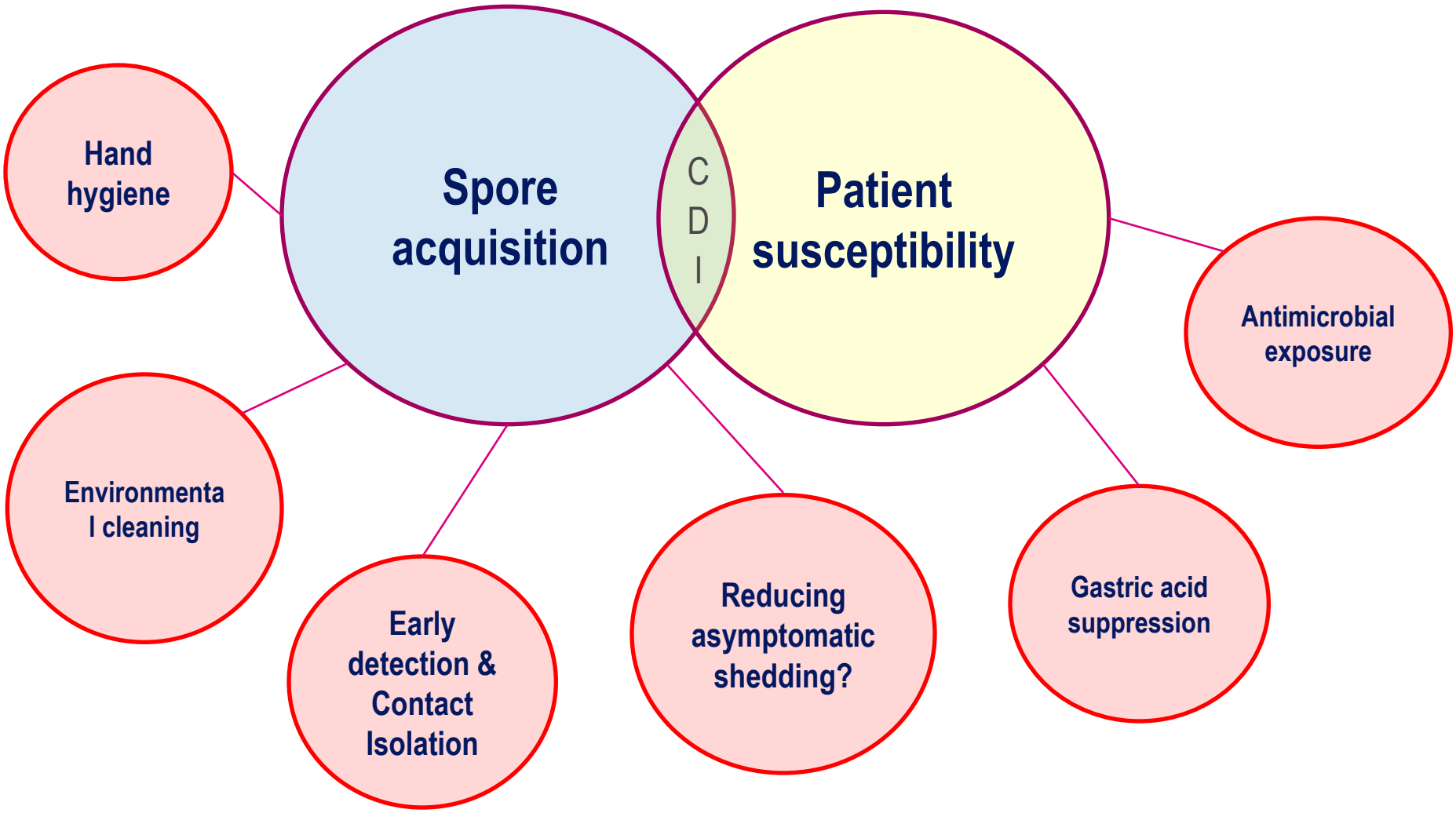
# SPECIAL APPROACHES FOR PREVENTING CDI

- Intensify the assessment of compliance with process measures
  - **Compliance with hand hygiene**
  - **Compliance with Contact Precautions**
  - **If compliance inadequate, institute corrective actions**
- Perform hand hygiene with soap and water
- Empirically place patients with diarrhea on Contact Precautions (remove isolation if test for *C. difficile* is negative)
- Create a unit specific check list for room disinfection
- Monitor the effectiveness of room cleaning (e.g., fluorescent dye)
- Consider routine environmental decontamination with sodium hypochlorite or an EPA-registered sporicidal agent

**UNC routine measures are in yellow**

**Strategies to Prevent CDI Infections in Acute Care Hospitals: Draft SHEA Guideline, 2013**

# Preventing CDI



# 6 STEPS TO PREVENT HOSPITAL-ONSET CDI

- Prescribe and use antibiotics carefully
- Focus on an early and reliable diagnosis
- Isolate patients immediately
- Wear gloves and gowns for all contact with patient and the patient care environment
- Assure adequate cleaning and disinfection of the patient care environment; use an EPA-registered C. difficile sporicidal disinfectant
- Notify facilities upon patient transfer

**Source: http://www.cdc.gov/VitalSigns/Hai/StoppingCdifficile/**

# CONCLUSIONS

- *C. difficile* is now the most common healthcare-associated pathogen in the United States
  - Increasing incidence and prevalence
- *C. difficile* colitis is a serious disease especially in older adults with frequent morbidity and substantial mortality
- Preventing includes the following:
  - Antibiotic stewardship
  - Proper infection control (contact precautions, hand hygiene, surface disinfection)

# THANK YOU!!