Clostridium difficile Infection (CDI) Prevention Primer

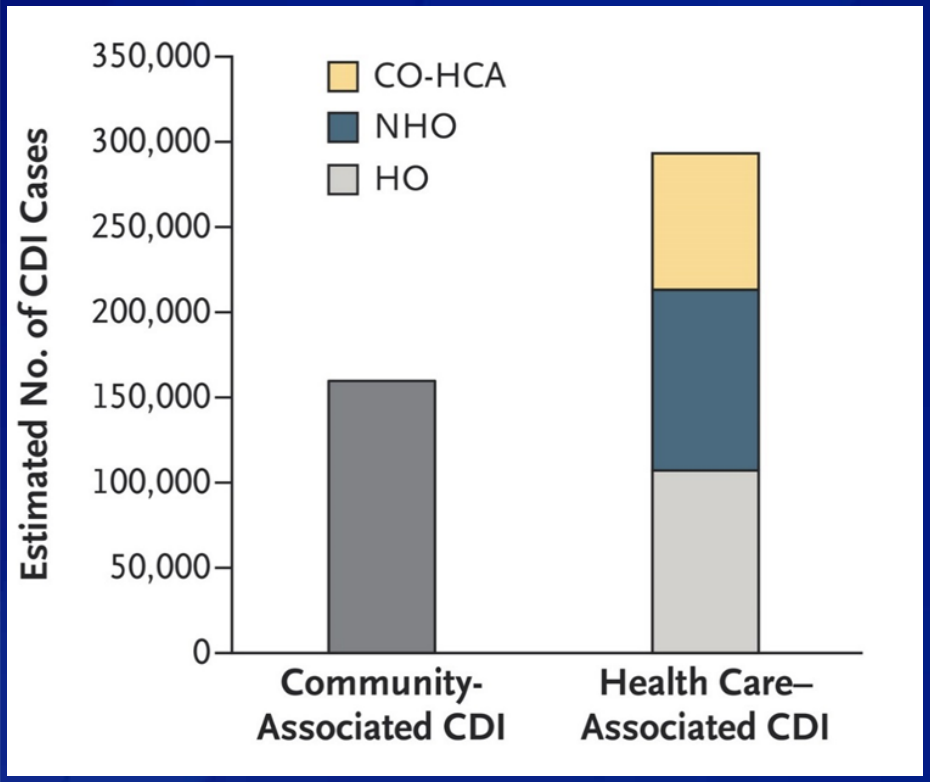
Last reviewed 03/04/16. Disclaimer: The findings and conclusions in this presentation are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Outline

- **Background on *Clostridium difficile* Infection (CDI)**
  - Burden
  - Pathogenesis
  - Epidemiology
- **General Infrastructure for CDI Prevention**
- **Basic Practices and Special Approaches for CDI Prevention**
- **Implementing a Practical Approach to CDI Prevention**
- **Resources and References**

Background:
Burden, Pathogenesis, Epidemiology

Estimated Annual U.S. Burden



Estimated U.S. Burden of CDI, According to the Location of Stool Collection and Inpatient Health Care Exposure, 2011.

- **453,000 CDI cases[1]**
  - **293,000 healthcare-associated**
    - **107,000 hospital-onset**
    - **104,000 nursing home-onset**
    - **81,000 community-onset, healthcare-facility associated**
  - **160,000 community-associated**
    - **82% associated with outpatient healthcare exposure**

Overall, 94% of CDI cases related to healthcare

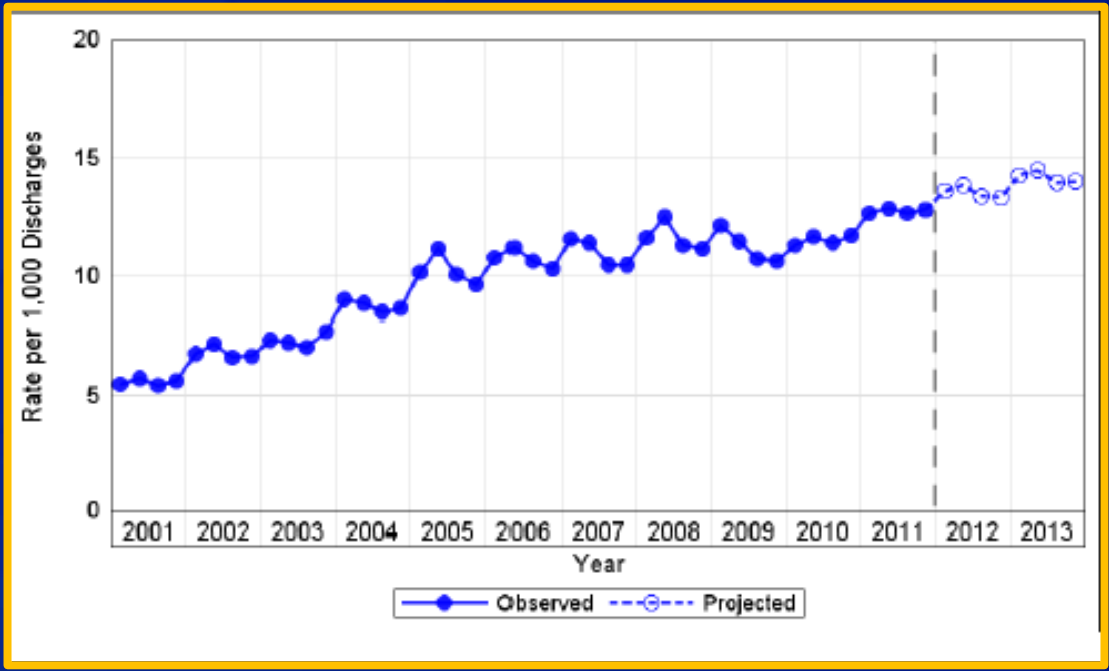
- **29,000 deaths**
- **$4.8 billion in excess healthcare costs[2]**

CO-HCA: Community onset healthcare-associated
NHO: Nursing home onset
HO: Hospital onset

1. Lessa et al. N Engl J Med 2015; 372(9):825-834.
2. Dubberke et al. Clin Infect Dis 2012; 55:S88-92.

Healthcare Burden

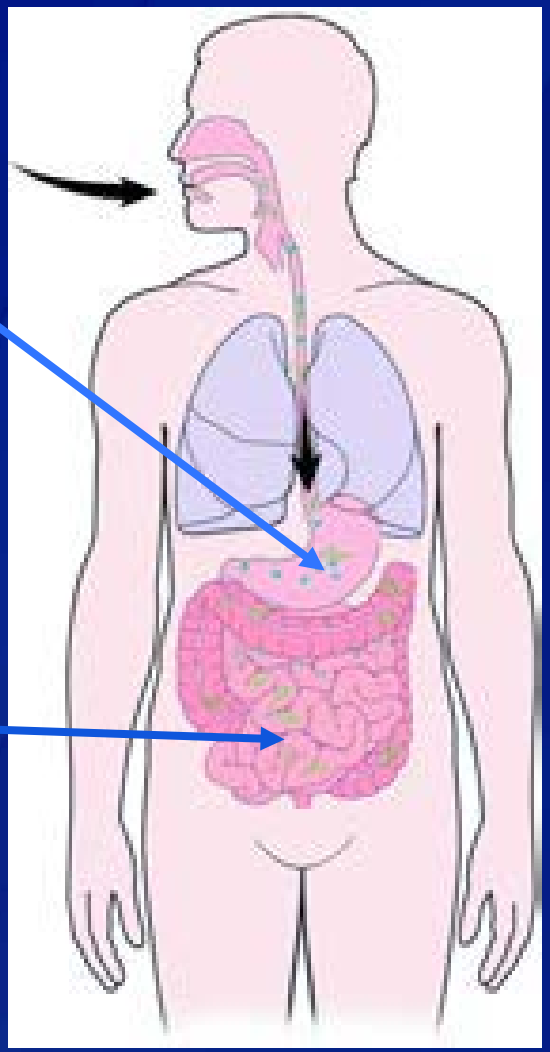
- ***C. difficile* most commonly reported pathogen in 2011 multistate prevalence survey of healthcare-associated infections (HAI)[1]**
  - 12.1% of 452 HAIs caused by CDI
  - Rates of CDI per 1,000 discharges have risen through 2013[2]



1. Magill et al. N Engl J Med 2014; 370:1198-1208.
2. Steiner et al. HCUP Projections Report 2014-01.

Pathogenesis of CDI

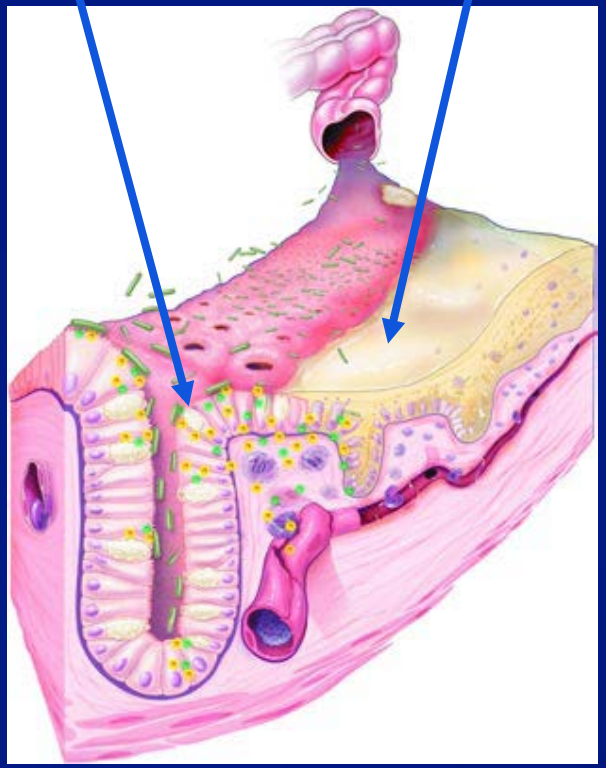
1. CDI spores survive in the environment for long periods of time. Following ingestion, they traverse the acidic environment of the stomach.



2. Spores germinate within the intestine.

3. Altered lower intestine flora (due to antimicrobial use) allows proliferation of *C. difficile* in colon.

4. Toxin A & B Production leads to colon damage +/- pseudomembrane.



Sunenshine & McDonald Cleve Clin J Med 2006; 73(2):187-197.

Epidemiology: Epidemic Strain

- **BI/NAP1/027, toxinotype III**
- **First emerged in 2000[1]**
- **Associated with healthcare[2]**
- **More resistant to fluoroquinolones[3]**
- **Greater virulence**
  - Associated with more severe disease and mortality[4]
  - Increased toxin A and B production[4,5]
  - Polymorphisms in binding domain of toxin B[5]

1. McDonald et al. N Engl J Med 2005; 353(23):2433-2441.
2. See et al. Clin Infect Dis 2014; 58(10):1394-1400.
3. Pepin et al. Clin Infect Dis 2005; 41(9):1254–1260.
4. Stabler et al. J Med Micro 2008; 57(6):771-775.
5. Warny et al. Lancet 2005; 366(9491):1079-1084.

Epidemiology: Host Factors

Advanced age

- Incidence higher among females, whites, and persons > 65 years[1]
- Death more common in persons > 65 years (5x greater risk)[2]

Underlying illness and medical history

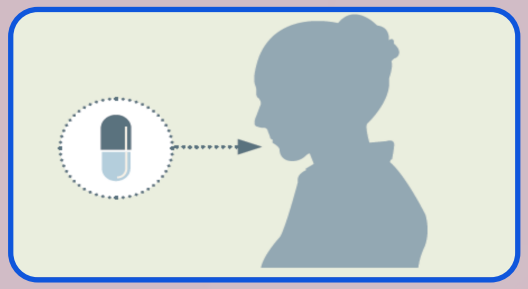
- 79% of 7421 patients with CDI had a comorbid condition[2]
- 38% of 585 patients with NAP1 strain had ED visit in previous 12 weeks[2]
- Tube feeds[3]

Immunosuppression

- Inflammatory bowel disease[2]
- Immune-suppressive treatment[2]
- Hematological malignancy/stem cell transplant (15-25x greater risk)[4]

1. Lessa et al. N Engl J Med 2015; 372(9):825-834.
2. See et al. Clin Infect Dis 2014; 58(10):1394-1400.
3. Bliss et al. Ann Intern Med 1998; 129:1012-1019.
4. Kombuj et al. Infect Control Hosp Epidemiol 2016; 37:8-15.

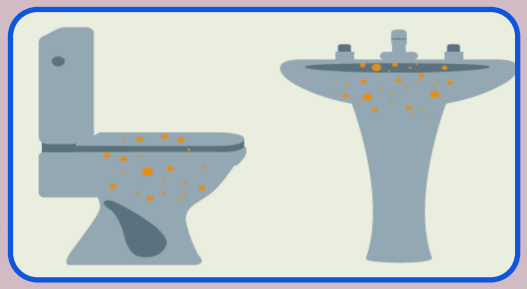
Epidemiology: Modifiable Risk Factors



Exposure to antibiotics

High Risk:

- Fluoroquinolones [1]
- 3rd and 4th generation cephalosporins, clindamycin, carbapenems[2]



Exposure to *C. difficile* spores

- Spores can remain viable for months[3]
- Contamination is increased in rooms of patients with active CDI [4,5]
- Hands of patients and personnel are easily contaminated[5]

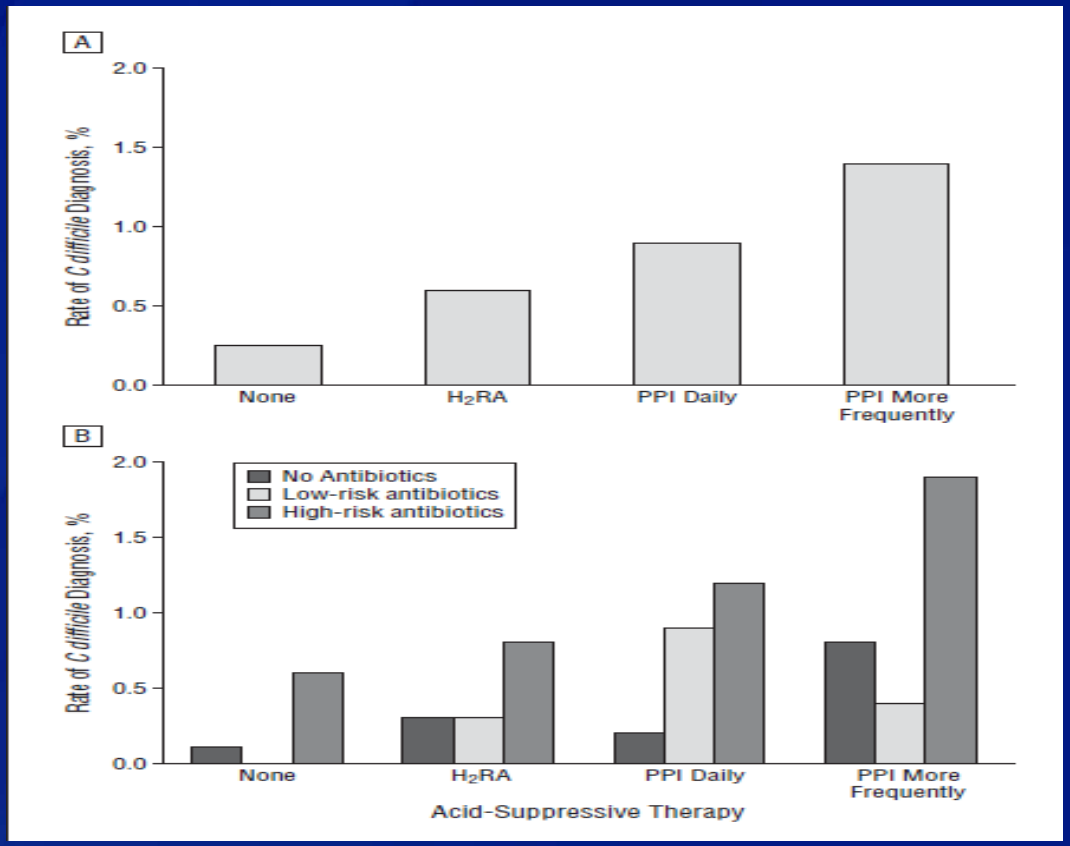
Gastric acid suppression

- Data, though inconsistent, implicate proton pump inhibitor (PPI) use[1,4,6,7]
- More study is needed to link restriction of PPI use with decreased CDI incidence[8]

1. Pepin et al. Clin Infect Dis 2005; 41(9):1254–1260.
2. Hensgens et al. J Antimicrob Chemother 2012; 67(3):742-748.
3. Weber & Rutala. Infect Control Hosp Epidemiol 2011; 32: 207-209.
4. Dubberke et al. Am J Infect Control 2007; 35:315-318.
5. Shaugnessy et al. Infect Control Hosp Epidemiol 2011; 32;201-206.
6. Linney et al. Can J Hosp Pharm 2010; 63(1):31–37.
7. Buendgens et al. J Crit Care 2014; 696:e11-15.
8. Dubberke et al. Infect Control Hosp Epidemiol 2014; 35(6):628-645.

Gastric Acid Suppression and CDI Risk

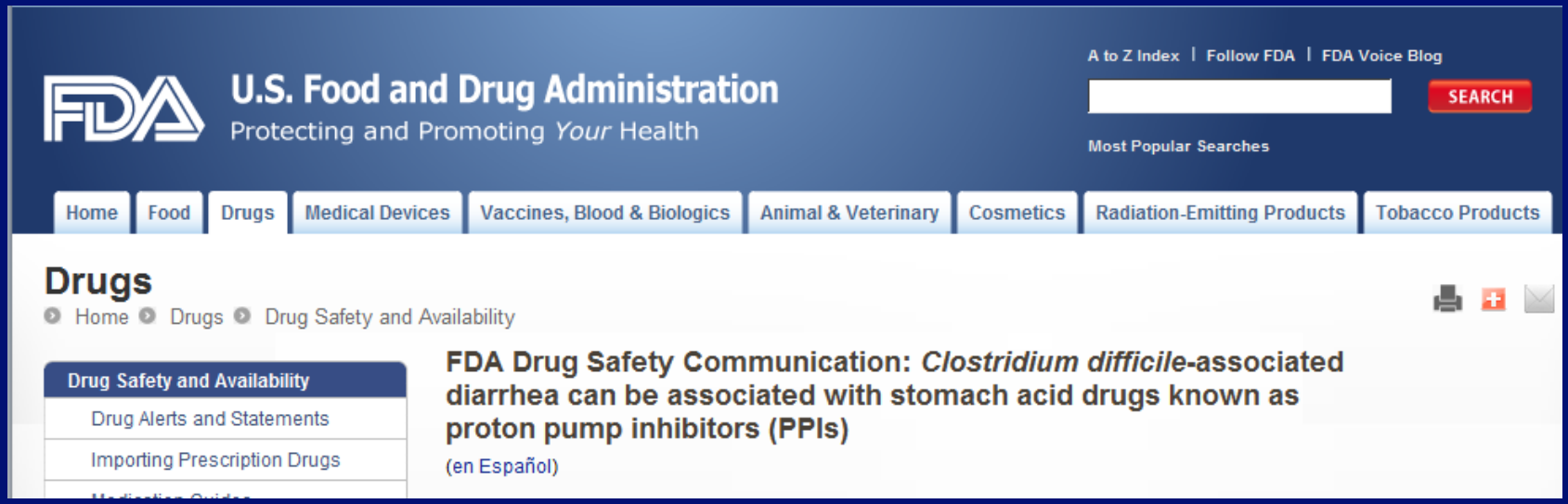
Dose Response and Interactions with Antibiotics



Howell et al. Arch Intern Med 2010; 170(9):784-790.

Use of Proton Pump Inhibitors (PPI) and CDI

February 8 , 2012 – FDA warning on PPI Use



Stevens et al. Pharmacoepidemiol Drug Safety 2011; 20:1035-1042.

Defining Outbreaks and Hyperendemic CDI

- **What is an outbreak?**
  - Increase in CDI that is greater than expected by chance alone
  - Can be facility-wide, unit specific, or occurring within the community

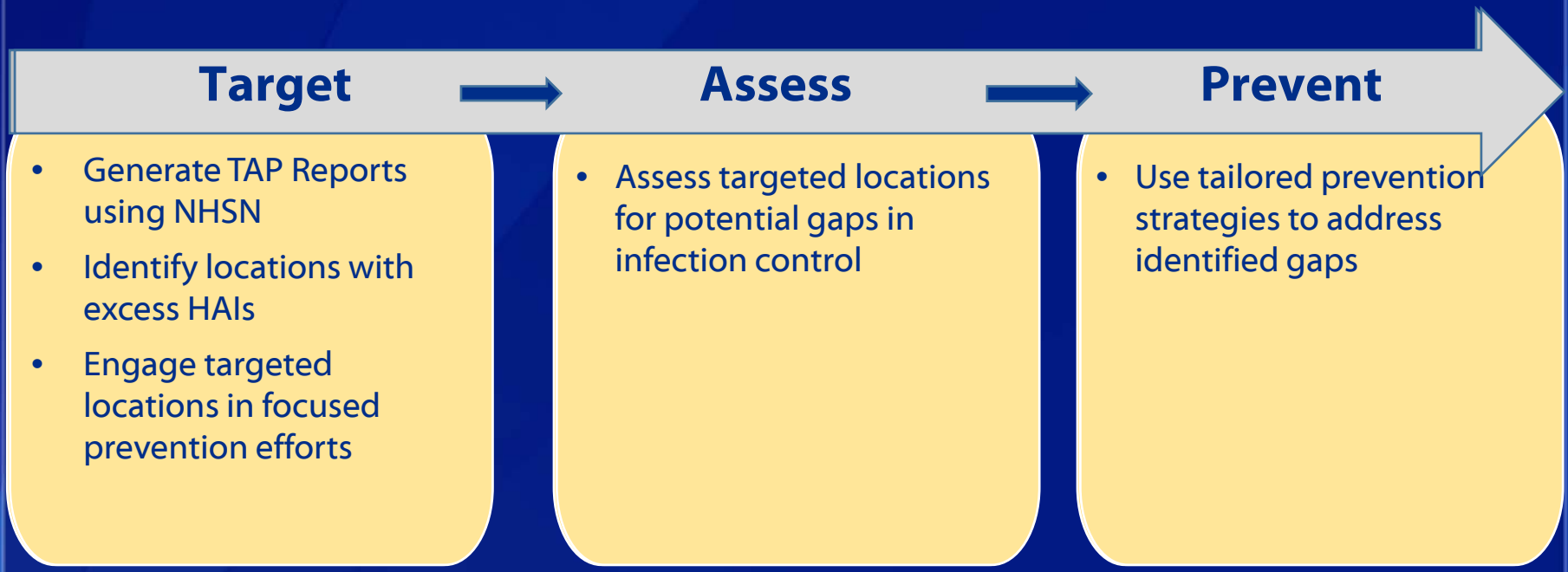
- **What is hyperendemicity?**
  - Persistently high rates of CDI compared to past rates or compared to similar facilities/units
  - Example: Excess infections above a prevention goal as indicated by the Cumulative Attributable Difference (CAD) metric in an NHSN Targeted Assessment for Prevention (TAP) report

Dubberke et al. Infect Control Hosp Epidemiol 2014;35(6):628-645.

www.cdc.gov/hai/prevent/tap.html

Data for Action

Using the CDC Targeted Assessment for Prevention (TAP) Strategy

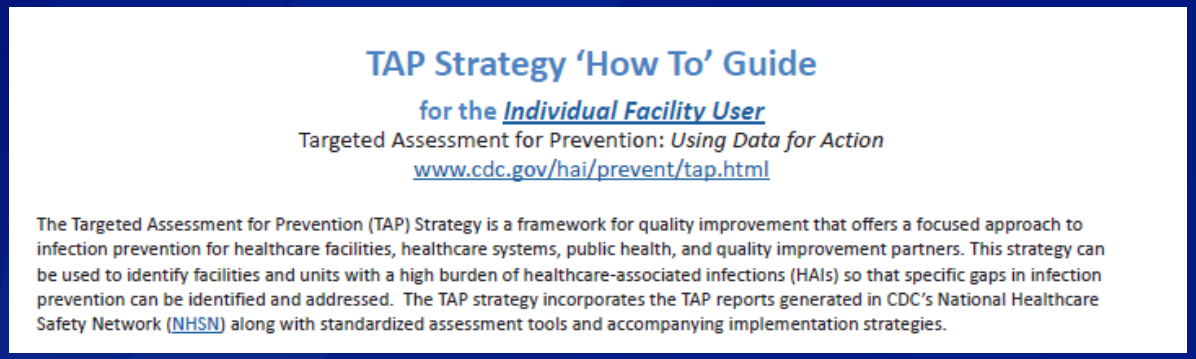


An elevated CDI CAD on a hospital's TAP report can identify the need to initiate an infection prevention assessment. In many cases, a specific unit or units in the hospital account for the majority of cases.

www.cdc.gov/hai/prevent/tap.html

Target Units or Facilities with Excess Infections

Identify facilities or units with opportunities for improvement using a TAP Report generated in the National Healthcare Safety Network (NHSN).



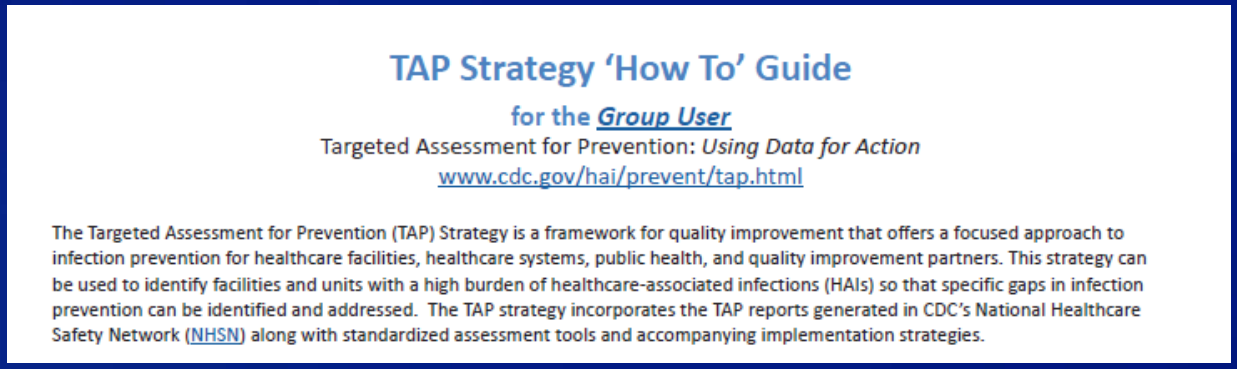
TAP Strategy 'How To' Guide

for the ***Individual Facility User***

Targeted Assessment for Prevention: *Using Data for Action*

www.cdc.gov/hai/prevent/tap.html

The Targeted Assessment for Prevention (TAP) Strategy is a framework for quality improvement that offers a focused approach to infection prevention for healthcare facilities, healthcare systems, public health, and quality improvement partners. This strategy can be used to identify facilities and units with a high burden of healthcare-associated infections (HAIs) so that specific gaps in infection prevention can be identified and addressed. The TAP strategy incorporates the TAP reports generated in CDC's National Healthcare Safety Network (NHSN) along with standardized assessment tools and accompanying implementation strategies.



TAP Strategy 'How To' Guide

for the ***Group User***

Targeted Assessment for Prevention: *Using Data for Action*

www.cdc.gov/hai/prevent/tap.html

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www.cdc.gov/hai/prevent/tap.html

Assess Infection Prevention Practices

- **Assess policies and practices related to CDI prevention**
  - Leadership
  - Training, auditing/feedback
  - Antibiotic stewardship
  - Early detection and isolation
  - Appropriate testing practices
  - Contact Precautions/hand hygiene
  - Environmental cleaning

II. Antibiotic Stewardship for CDI Prevention	Response Choices	Comments (and/or "As Evidenced By")
1. Does your facility review appropriateness of antibiotics prescribed for treatment of other conditions (e.g., UTI) for patients with new or recent CDI diagnosis?	◯Yes ◯No ◯Unk	
2. Does your facility educate providers about the risk of CDI with antibiotics?	◯Yes ◯No ◯Unk	
3. Does your facility educate patients/family members about the risk of CDI with antibiotics?	◯Yes ◯No ◯Unk	
Does your facility monitor the use of the following antibiotics that are high-risk for CDI:		
4. Fluoroquinolones	◯Yes ◯No ◯Unk	
5. 3rd/4th generation cephalosporins?	◯Yes ◯No ◯Unk	
Does your facility use strategies to reduce the use of the following antibiotics that are high-risk for CDI:		
6. Fluoroquinolones	◯Yes ◯No ◯Unk	
7. 3rd/4th generation cephalosporins?	◯Yes ◯No ◯Unk	

Prevent Infections with Tailored Measures

II. Antibiotic Stewardship

Example Resources	Websites
Get Smart for Healthcare – Implementation Resources Resources to assist in the implementation of hospital antibiotic stewardship programs, including guidelines, assessment tools, conceptual models, and a sample inter-facility infection control transfer form, from CDC	http://www.cdc.gov/getsmart/healthcare/implementation.html
Get Smart for Healthcare – Stewardship Program Examples Links to hospital stewardship programs at various hospitals, success stories, and an interactive collection of charts and maps summarizing national and subnational data on antimicrobial use and resistance (Resistance Map), from CDC	http://www.cdc.gov/getsmart/healthcare/programs.html
Get Smart for Healthcare - Checklist for Core Elements of Hospital Antibiotic Stewardship Programs A checklist to evaluate hospital antibiotic stewardship programs, from CDC	Checklist for Core Elements of Hospital Antibiotic Stewardship Programs | Get Smart for Healthcare | CDC
Antimicrobial Stewardship Toolkit Best practices from an Antimicrobial Stewardship Collaborative, from the Greater New York Hospital Association and the United Hospital Fund	http://www.shea-online.org/Portals/0/GNYHA_Antimicrobial_Stewardship_Toolkit_FINALv2%20Dec2011.pdf
Toolkit for Reduction of Clostridium difficile Infections Through Antimicrobial Stewardship: Possible Methods for Evaluating Antibiotic Use Table of possible metrics to use for measurement and evaluation of antibiotic use, from the Agency for Healthcare Research and Quality (AHRQ)	http://www.ahrq.gov/professionals/quality-patient-safety/patient-safety-resources/resources/cdifftoolkit/cdiffl2tools2c.html

III. Early Detection and Isolation, Appropriate Testing

Example Resources	Websites
Algorithms for Prevention and Management of *Clostridium difficile* Infections in Long-term Care Facilities Decision-making strategies for enhancing early recognition, testing, and isolation of patients with CDI in long-term care facilities, from the Minnesota Department of Public Health	http://www.health.state.mn.us/divs/idepc/diseases/cdiff/hcp/ltcalgorithms.pdf
***C. difficile* Infection Change Package: Preventing *C. difficile* Transmission and Infection** Compilation of tools, including algorithms for testing and diarrhea decision trees that align with appropriate isolation and testing guidelines (pgs. 12, 13), from the Health Research & Educational Trust (HRET), American Hospital Association (AHA), and Partnership for Patients	http://www.hret-hen.org/topics/cdi/13-14/2014-CDIChangePackage508.pdf
Bristol Stool Form Scale Scale tool that provides an objective way to differentiate between various types of stool forms and recognize diarrhea, from the National Institutes of Health (NIH)	http://bowelcontrol.nih.gov/bristol.aspx

General Infrastructure for CDI Prevention

Leadership

- **Need to understand organizational culture and change it when it hinders performance[1]**
- **Direct evidence linking leadership to infection rates is limited but consistent themes have been identified[2]**

Leadership traits that may assist in preventing infections[3]:

Proactive, positive, visible

Supportive of change

Clear responsibilities

Clear policies

Leadership traits that may be associated with risk[2]:

Reactive

Laissez faire management style

Failure to assign responsibility and maintain accountability

Wide span of control

1. De Bono et al. J Hosp Infect 2014; 86:1-6
2. Griffiths et al. J Hosp Infect 2009; 73:1-14
3. Sinkowitz-Cochran et al. Am J Infect Control 2012; 40:138-143

Capacity

Capacity may be affected by complex management issues

Low Nurse Staffing Ratios

- Nurse to patient staffing ratios inversely associated with healthcare-associated infections (UTI and SSI).[1]

High Occupancy

- Inpatient wards with occupancy rates of 80-90% had CDI rates 56% higher than during baseline occupancy rates (0-69%).[2]

Feeling Overwhelmed

- Stress and chaos associated with poorer infection prevention practices.[3]

Strong leadership at the unit level and above is likely a prerequisite for infection prevention improvements[4]

1. Cimiotti et al. Am J Infect Control 2012; 40:486-490.
2. Ahyow et al. Infect Control Hosp Epidemiol 2013; 34:1062-1069.
3. Sinkowitz-Cochran et al. Am J Infect Control 2012; 40:138-143.
4. Griffiths et al. J Hosp Infect 2009; 73:1-14.

Competency

Healthcare personnel education and competencies are foundational to successful performance

Hand Hygiene

- Appropriate selection and use of products

Patient Placement

- Knowledge of signs and symptoms to initiate transmission-based precautions

Personal Protective Equipment

- Appropriate selection of PPE
- Procedures to don, doff, and dispose of PPE

Patient Transport

- Appropriate interventions for transport
- Notification of receiving caregivers within and outside of facility upon transfer

Carrico et al. Am J Infect Control 2008; 36:691-701.

Sustainable Quality Improvement

Participants in The Institute for Healthcare Improvement 100,000 Lives Campaign believed that data feedback, buy in, hardwiring (incorporation into daily activities), and leadership support were essential to sustainability.

Sinkowitz-Cochran et al. Infect Control Hosp Epidemiol 2012; 33:135-143.

General Infrastructure

Surveillance and Ongoing Measurement

Process and outcome measures should be collected using ongoing, longitudinal methods with regular feedback to healthcare personnel.[1]

Process Measures	• Prospective, actionable, useful for feedback about unit implementation of prevention measures[2] • Examples include: * Appropriate Isolation * Hand hygiene and PPE adherence
Outcome Measures	• Useful to target assessments and prevention measures • Examples include: * Hospital-onset CDI * Community-onset, healthcare facility-associated CDI

1. Dubberke et al. Infect Control Hosp Epidemiol 2014; 35(6):628-645.

2. Berhe et al. Am J Infect Control 2006, 34(8): 537-539.

Basic Practices and Special Approaches for CDI Prevention

Overview

- Basic practices are prevention measures that should be in place at all times.
- Facilities should consider adopting some or all of the special approaches whenever ongoing opportunities for improvement are identified or as indicated by risk assessment.

Basic Practices	Special Approaches
❑ Appropriate use of antimicrobials	❑ Antimicrobial stewardship program
❑ Hand hygiene per CDC/WHO recommendations ▪ Measure healthcare personnel adherence	❑ Hand hygiene with soap and water after glove removal following care of CDI patients ▪ Intensify measurement of adherence
❑ Contact Precautions for CDI patients ▪ Measure healthcare personnel adherence	❑ Presumptive Contact Precautions while laboratory results are pending ❑ Prolonged duration of Contact Precautions ▪ Intensify measurement of adherence
❑ Cleaning and disinfection of equipment and environment	❑ Use of EPA-approved sporicidal disinfectant ❑ Assess adequacy of room cleaning
❑ Laboratory-based alert system for immediate notification to IP and clinical personnel of newly diagnosed CDI patients	
❑ CDI surveillance, analysis, and reporting	
❑ Educate healthcare personnel, patients, and families	

Dubberke et al. Infect Control Hosp Epidemiol 2014; 35(6):628-645.

Antimicrobial Stewardship

Antimicrobial Stewardship

Exposure to any antimicrobial is the single most important risk factor for *C. difficile* infection (CDI).

- **Antibiotic exposure has lasting impact on the microbiome.**
  - Risk of CDI is elevated (7-10 fold) during and in the 3 months following antimicrobial therapy[1,2]
  - 85-90% of CDI occurs within 30 days of antimicrobial exposure[1]
- **Target high risk antibiotics for CDI prevention**
  - Fluoroquinolones[3]
  - 3rd/4th generation cephalosporins, carbapenems[2]

1. Chang et al. Infect Control Hosp Epidemiol 2007; 28(8):926–931.
2. Hensgens et al. J Antimicrob Chemother 2012; 67(3):742-748.
3. Hsu et al. Am J Gastroenterol 2010; 105(11):2327–2339.

Seven Core Elements of Antimicrobial Stewardship

1. Leadership Commitment

Dedicating necessary human, financial, technological resources

2. Accountability

Appointing a single leader (physician or pharmacist) responsible for program outcomes

3. Drug Expertise

A single dedicated pharmacist with responsibility to improve antibiotic use

4. Tracking

Monitoring antibiotic prescribing and resistance patterns

5. Reporting

Feedback of information on antibiotic use and resistance to frontline providers

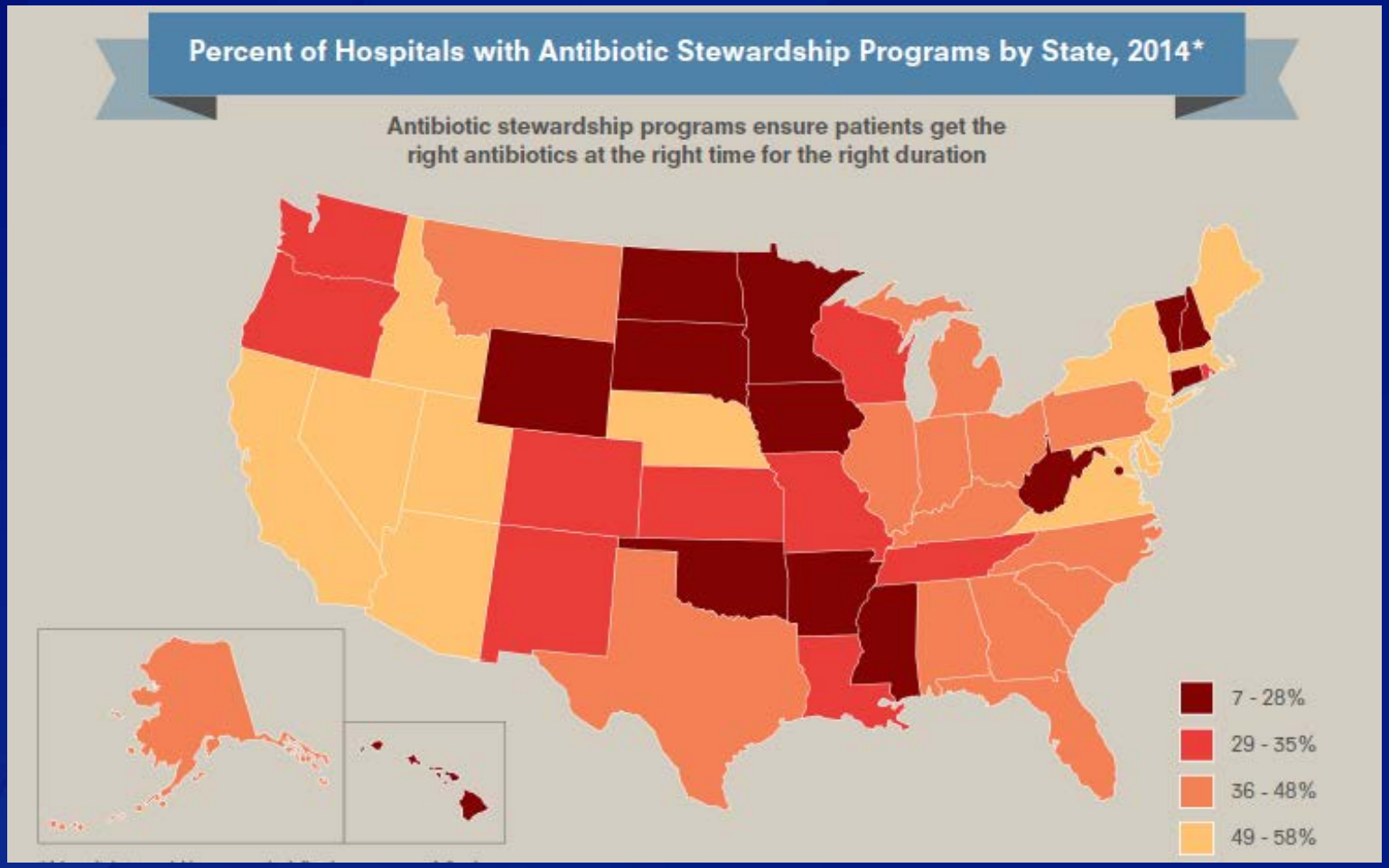
6. Education

Ongoing education of clinicians about resistance and optimal prescribing

7. Action

Implementing at least one recommended action

http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html



Currently 39% (1,642/4,184) of U.S. hospitals have an antibiotic stewardship program with all 7 core elements.

The national goal is 100% of hospitals by 2020.

http://www.cdc.gov/getsmart/healthcare/evidence.html

Leaders Committed to Antibiotic Stewardship

Consider making your organization's commitment to Antibiotic Stewardship public on the CDC Website.

Examples:

- **Hospital Corporation of America** has committed to continue current collaborations with CDC about this issue, develop and implement new clinical decision support and real-time antibiogram tracking to rapidly respond to lab results, catch bug-drug mismatches, implement strategy to prevent health-care associated infections in adult intensive care unit patients, and strengthen national efforts to identify and report cases of antibiotic resistance.

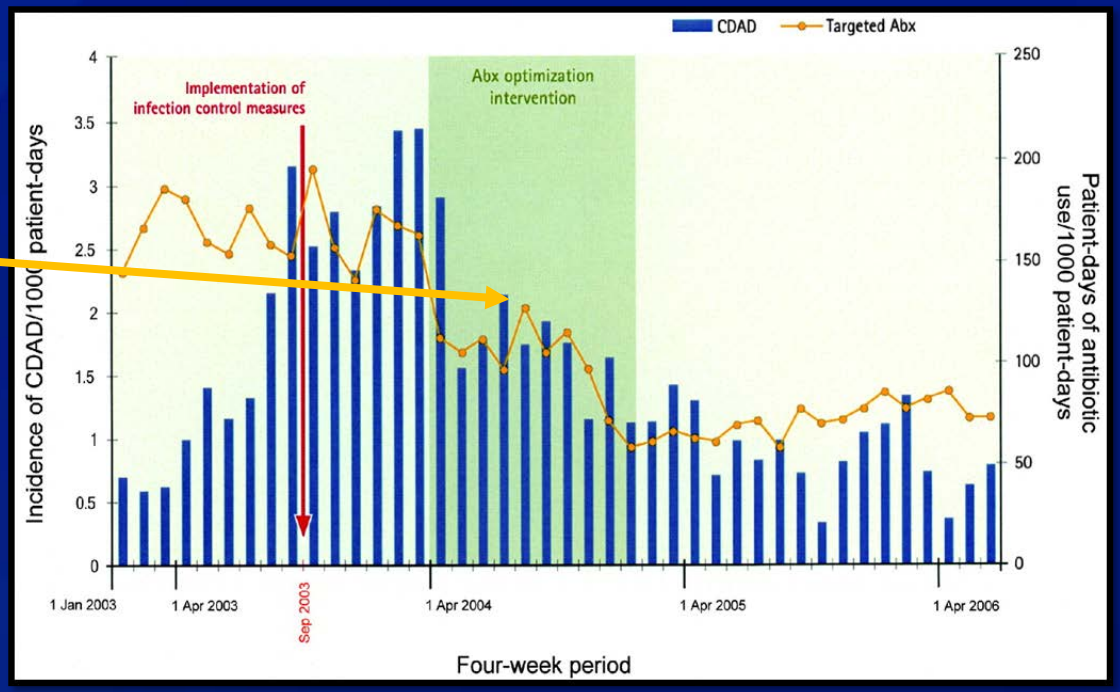
- **The Joint Commission** has committed to include stewardship as part of onsite surveys.

Full instructions on submitting a commitment are available at:
http://www.cdc.gov/drugresistance/federal-engagement-in-ar/stewardship-commitment/index.html

Stewardship Approach: Feedback

Non-restrictive feedback resulted in statistically significant reductions in incident CDI.

Reductions in CDI attained through antimicrobial stewardship surpassed those attained through infection control measures.



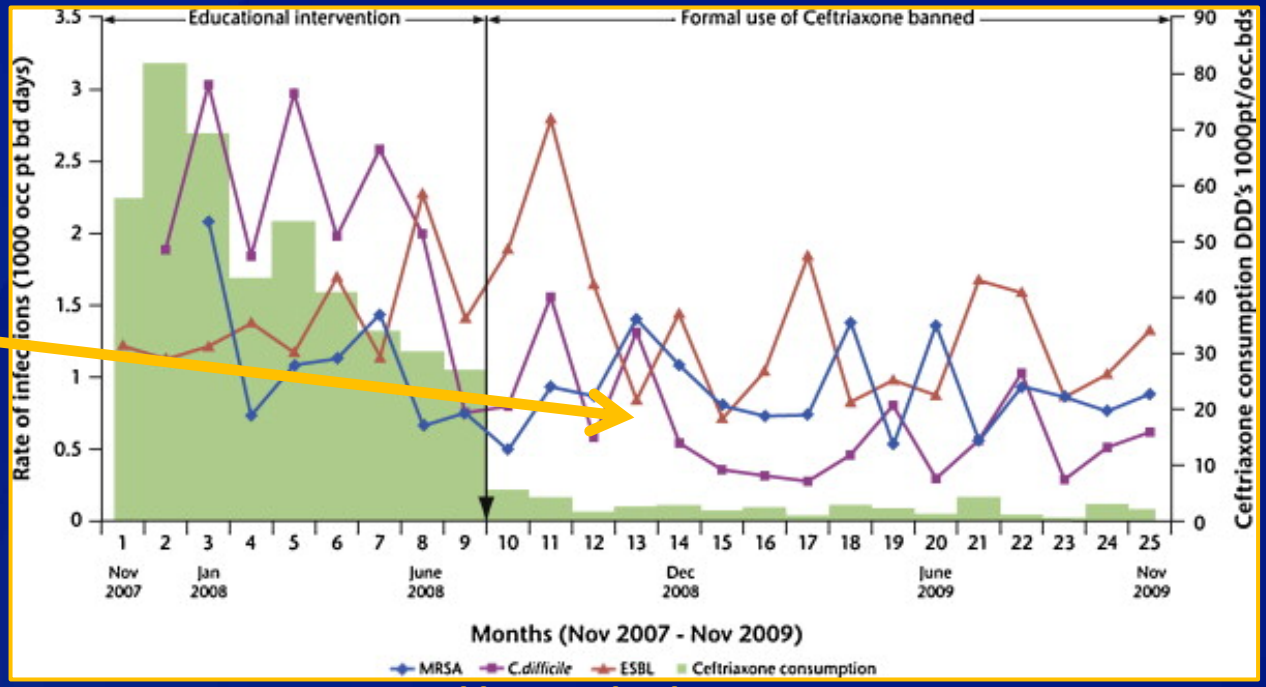
Tertiary Hospital in Quebec, 2003-2006

Valiquette et al. Clin Infect Dis 2007; 45:S112-121.

Stewardship Approach: Restriction

Restricting the use of ceftriaxone was associated with reduced rates of CDI.

Formal restriction implemented



District general hospital; Glasgow, UK, 2007-2009

Fig. 1 Hospital-acquired methicillin-resistant *Staphylococcus aureus* (MRSA), *Clostridium difficile* and extended-spectrum β-lactamase (ESBL)-producing coliform rates following a restrictive antibiotic policy in a district general hospital over 2 years. pt/occ.bds, patient-occupied bed-days; DDDs, defined daily doses.

Dancer et al. Intl J Antimicrob Agents 2013; 41(2):137-142.

Early Detection and Isolation

Early Detection and Isolation

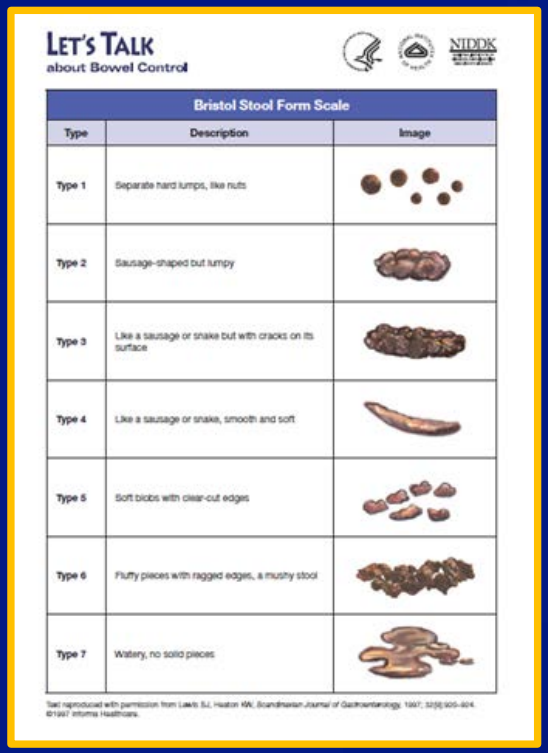
1) Focus testing on patients with clinically significant diarrhea,[1,2] ***without other identified causes***

- ≧ 3 liquid bowel movements (type 7)

  in 24 hours
- Stool conforms to shape of container

2) Utilize presumptive Contact Precautions*

until infectious causes are ruled out



The Bristol Stool Chart assists in objectively identifying stool characteristics[2]

**presumptive use of Contact Precautions is a special approach*

1. Dubberke et al. Infect Control Hosp Epidemiol 2014; 35(6):628-645.
2. Peterson & Robicsek. Ann Intern Med 2009; 151(3):176-179.

Patient and Family Education

Educate

- Patient education at the time of isolation is a critical intervention to reduce stress and anxiety[1]
- Patient educational background may influence the preferred mode of education[2]

Engage

- 94 of 100 patients believed that information about their infection would help them make choices that resulted in better care[2]

Empower

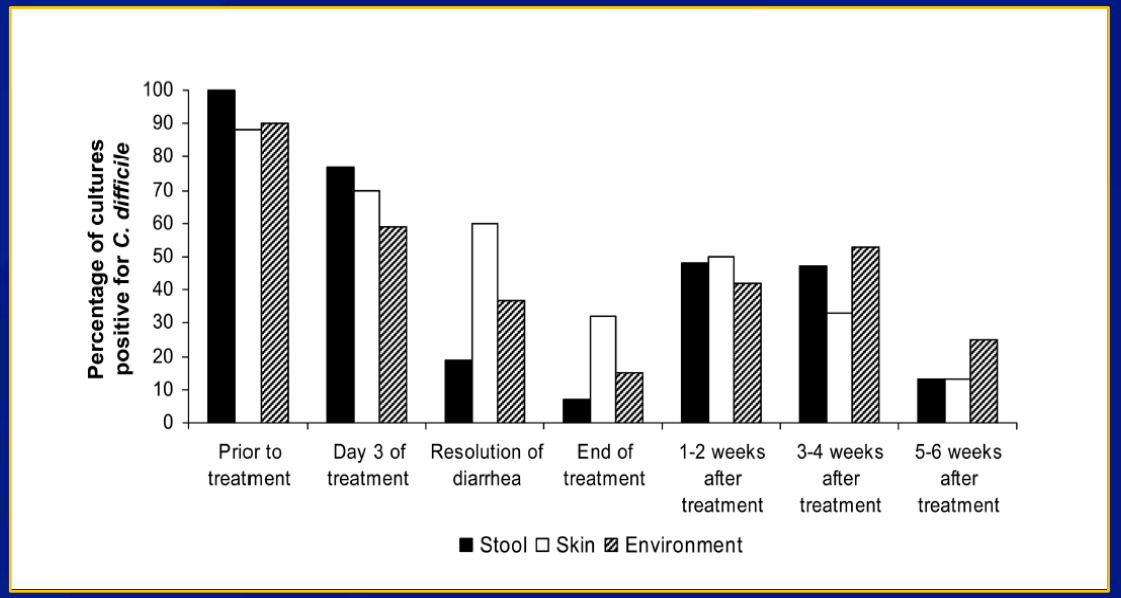
- Patients more likely to speak up to ensure adherence with hand hygiene if explicitly empowered to do so by healthcare personnel[3]

1. Abad et al. J Hosp Infect 2010; 76:97-102.
2. Gudnadottir et al. Am J Infect Control 2013; 41(11):955-958.
3. McGuckin & Govedin J Hosp Infect 2013; 84:191-199.

Contact Precautions and Hand Hygiene

Contact Precautions (CP)

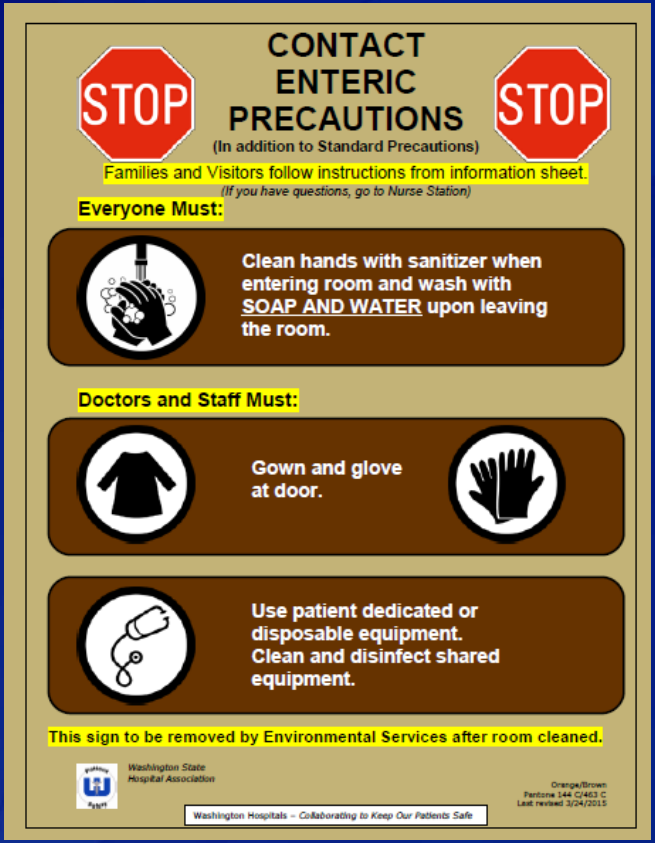
- Contamination of the environment is highest prior to treatment[1]
- **Presumptive CP**, while CDI test results are pending, may be used as a special approach whenever indicated by risk assessement[2]



- Patients who have been treated may have asymptomatic shedding[3]
- **Prolonging the duration of CP** until discharge is a special approach based on evidence of continued shedding of spores after diarrhea resolves (especially up to 4 weeks after treatment ends)[2]

1. Bobulsky et al. Clin Infect Dis 2008; 46(3):447-450
2. Dubberke et al. Infect Control Hosp Epidemiol 2014; 35(6):628-645
3. Sethi et al. Infect Control Hosp Epidemiol 2010: 31(1):21-27

Contact Precautions



Isolation Precaution Signage: http://www.wsha.org/quality-safety/projects/standardization/

- Don gown and gloves upon room entry[1]
- Use disposable or dedicated patient care equipment[1,2]
  - Electronic thermometers have been associated with transmission
- Communicate Contact Precautions[2,3]
  - at room entrance
  - at handoff
  - during transfers

1. CDC Guideline for Isolation Precautions: http://www.cdc.gov/hicpac/2007IP/2007ip_appendA.html
2. Dubberke et al. Infect Control Hosp Epidemiol 2014; 35(6):628-645
3. Hsu et al. Am J Gastroenterol 2010; 105(11):2327–2339

Cohorting of CDI Patients

- Private rooms are preferred for patients with fecal incontinence[1]
- Cohorting of patients[1,2]
  - Cohort patients with same multidrug-resistant organisms only
  - Ensure healthcare personnel follow appropriate isolation practices when moving between patients
    - Perform hand hygiene when donning or doffing PPE
    - Gloves and gowns must be changed and HH performed between each patient

1. Dubberke et al. Infect Control Hosp Epidemiol 2014; 35(6):628-645.
2. CDC Guideline for Isolation Precautions: http://www.cdc.gov/hicpac/2007IP/2007ip_appendA.htm

Elements of a Multi-Modal Program to Improve Hand Hygiene

A robust, ongoing hand hygiene program should be in place

Program Component	Action Item
Ongoing monitoring of HAI incidence	Setting specific feedback about incident CDI
Administrative support and leadership	Clear policies and messages about hand hygiene
Multidisciplinary team	Members of administration, clinical leaders, and front line staff collaboration to increase adherence
Ensure accessibility of supplies	Point of care hand hygiene should be within arms reach of healthcare personnel
Reinforce behavior and accountability	Contests, incentives, recognition tickets, notice letters, personnel action
Provision of reminders	Posters, just-in-time training, inclusion in checklists
Ongoing monitoring of adherence and feedback on compliance	Direct observation, product use monitoring, real-time feedback, monthly posting on adherence,

Pincock et al. Am J Infect Control 2012; 40:S18-27.

Hand Hygiene and Care of the Patient with CDI

- **Hand hygiene** policies should promote preferential use of alcohol-based hand rub (ABHR) over soap and water in all clinical situations except when hands are visibly soiled (e.g., blood, body fluids) or after caring for a patient with known or suspected *C. difficile* or norovirus during an outbreak or if endemic rates are high.

- Strict adherence to **glove use** is the most effective means of preventing hand contamination with *C. difficile* spores[1]
  - Spores not killed by ABHR and may be difficult to remove even with thorough hand washing [2,3]
  - Although there have been no studies demonstrating a decrease in CDI infection with use of soap and water as opposed to ABHR[4], because ABHR is not effective against spores, facilities may consider routine use of soap and water after glove removal during care of patients with *C. difficile* infection even absent an outbreak.

- **Measuring compliance** is a basic practice and critical to success
  - Ensure technique is good and re-educate if lapses identified

1. Riggs et al. Clin Infect Dis 2007; 45(8):992-998.
2. Isaacson et al. Am J Infect Control 2015; 43:530-532.
3. Oughton et al. Infect Control Hosp Epidemiol 2009; 30(10):939-944.
4. Boyce et al. Infect Control Hosp Epidemiol 2006; 27(5):479-483.

Soap and Water vs. Alcohol Hand Rub

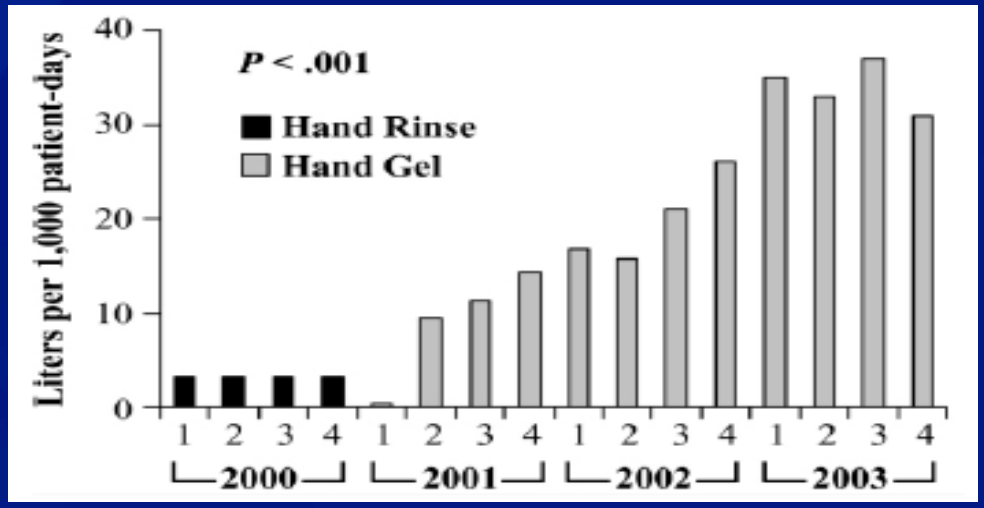
Interventions compared		Mean log reduction (95% CI), $\log_{10}$ CFU/mL
Intervention 1	Intervention 2	
Warm water and plain soap	No hand hygiene	2.14 (1.74–2.54)
Warm water and plain soap	Alcohol-based handrub	2.08 (1.69–2.47)
Cold water and plain soap	No hand hygiene	1.88 (1.48–2.28)
Cold water and plain soap	Alcohol-based handrub	1.82 (1.43–2.22)
Warm water and plain soap	Antiseptic hand wipe	1.57 (1.18–1.96)
Warm water and antibacterial soap	No hand hygiene	1.51 (1.12–1.91)
Warm water and antibacterial soap	Alcohol-based handrub	1.46 (1.06–1.85)
Cold water and plain soap	Antiseptic hand wipe	1.31 (0.92–1.71)
Warm water and antibacterial soap	Antiseptic hand wipe	0.94 (0.55–1.34)
Warm water and plain soap	Warm water and antibacterial soap	0.63 (0.23–1.02)
Antiseptic hand wipe	No hand hygiene	0.57 (0.17–0.96)
Antiseptic hand wipe	Alcohol-based handrub	0.51 (0.12–0.91)
Cold water and plain soap	Warm water and antibacterial soap	0.37 (−0.03 to 0.76)
Warm water and plain soap	Cold water and plain soap	0.26 (−0.14 to 0.66)
Alcohol-based handrub	No hand hygiene	0.06 (−0.34 to 0.45)

Oughton et al. Infect Control Hosp Epidemiol 2009; 30(10):939-944.

ABHR and CDI Rates

Data from 2000-2003 show no association between alcohol-based hand rub (ABHR) use and increase in CDI rates

Figure 1. Use of alcohol hand rub by healthcare workers; Liters per 1,000 patient-days, per quarter 2000-2003



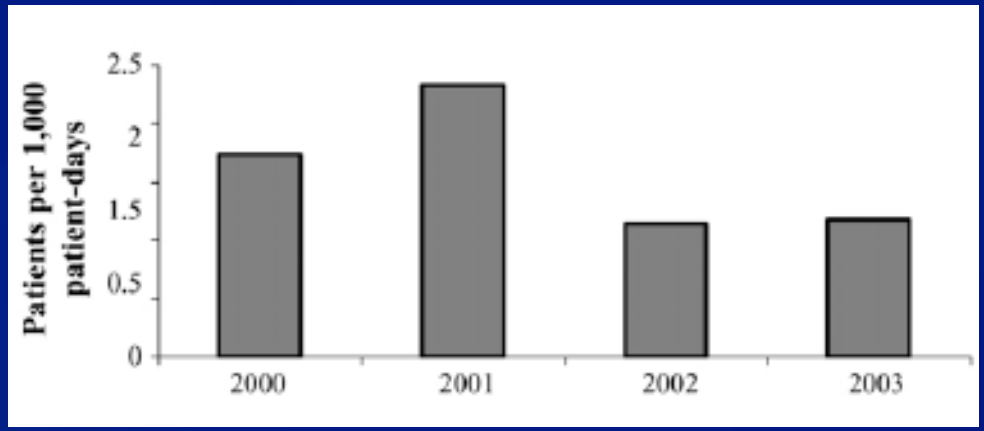


Figure 2. Number of patients with 1 or more tests positive for *C. difficile* toxin per 1,000 patient-days, 2000-2003

Boyce et al. Infect Control Hosp Epidemiol 2006; 27(5):479-483.

Importance of Gloves

Since spores may be difficult to remove from hands even with hand washing, strict adherence to glove use, and Contact Precautions in general, should be emphasized for preventing *C. difficile* transmission via the hands of healthcare personnel.

Johnson et al. Am J Med 1990; 88(2):137-140.

Importance of Gloving

- Environmental contamination may be increased during outbreaks and in locations with hyperendemicity[1]
- Glove use is most effective means of preventing contamination of the hands of HCPs with *C. difficile* spores from symptomatic patients
- Universal gloving is a special approach for use when indicated by risk assessment[2]

1. Riggs et al. Clin Infect Dis 2007; 45(8):992-998.
2. Dubberke et al. Infect Control Hosp Epidemiol 2014; 35(6):628-645.

Remember Patient Hands!

A randomized trial of soap and water wash versus alcohol hand rub shows soap and water are more effective at removal of *C. difficile* spores on patient hands.

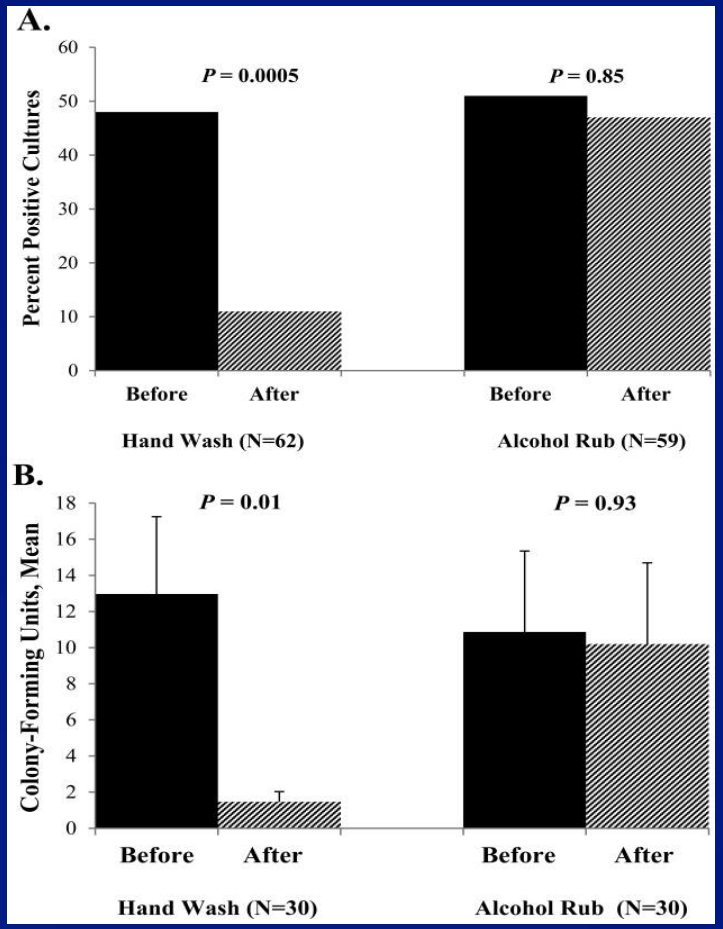


Figure 1: Percent of patient hands with positive *Clostridium difficile* cultures.

Kundrapu et al. Infect Control Hosp Epidemiol 2014; 35:204.

Environmental Cleaning and Disinfection

Key Principles

- There is no substitute for meticulous cleaning[1,2,3]
- Cleaning reduces spores in the environment[2]
- Disinfectants with a sporicidal claim inactivate spores[2]
- Monitoring and feedback optimize performance[1]
- Policies should clearly define who is responsible for cleaning and disinfecting environmental surfaces and equipment[4]

Cleaning	**The removal of organic debris using vigorous wiping and or scrubbing until all visible soil is removed[1]**
Disinfection	**Removal or inactivation of some or all pathogens on inanimate objects[1]**

1. Carling Am J Infect Control 2013; 41:S20-25.
2. Rutala et al. Infect Control Hosp Epidemiol 2012; 33(12):1255-1258.
3. CDC Guidelines for Environmental Control in Healthcare Facilities: http://www.cdc.gov/hicpac/pdf/guidelines/eic_in_HCF_03.pdf
4. CDC Guidelines for Disinfection and Sterilization in Healthcare Facilities: http://www.cdc.gov/hicpac/pdf/guidelines/Disinfection_Nov_2008.pdf

Mitigating Risks Through Environmental Cleaning and Disinfection

High touch items

- **Facilities must ensure adequate cleaning of[1,2] high touch surfaces in the patient environment.**
- **Examples:**
  - Bed rails
  - Restroom hand rails
  - Bed side tables
  - See CDC checklist for full list*

Disinfectant preparation

- **Facilities must ensure proper preparation and use of disinfectants[3]. Including appropriate:**
  - Dilution
  - Storage
  - Application
  - Contact Time

Proper use of disinfectants

- **Factors that influence disinfectant effectiveness[3]:**
  - Porosity of surface
  - Crevices or ridges
- **Facilities must ensure cross contamination is avoided**

1. Dubberke et al. Infect Control Hosp Epidemiol 2014; 35(6):628-645.
2. CDC Options for Evaluating Environmental Cleaning: http://www.cdc.gov/hai/toolkits/Evaluating-Environmental-Cleaning.html
3. CDC Guidelines for Environmental Control in Healthcare Facilities: http://www.cdc.gov/hicpac/pdf/guidelines/eic_in_HCF_03.pdf

Environmental Contamination

- Patients with asymptomatic carriage may be an important source of environmental contamination[1]
- Patients that have been treated may continue to shed spores[2]

In a cross sectional survey of 6 facilities[3]:

- NAP1 strain recovered at each facility
- All rooms housing a CDI patient yielded positive cultures for *C. difficile*
- 4/12 (33%) of rooms without a CDI patient yielded positive cultures for *C. difficile*

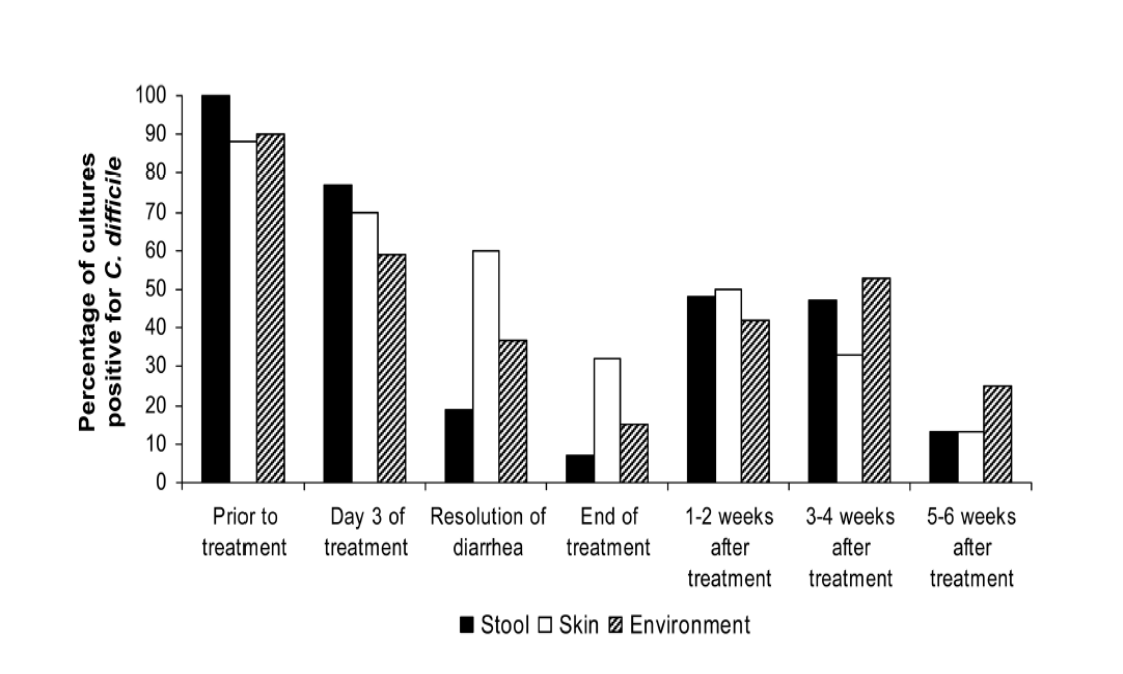


Figure from Sethi, 2010

1. Riggs et al. Clin Infect Dis 2007; 45(8):992-98.
2. Sethi et al. Infect Control Hosp Epidemiol 2010; 31:21-27.

Dubberke et al. Am J Infect Control 2007; 35:315-318.

Spore Removal

- Meticulous cleaning with any cleaner/disinfectant reduces the number of spores in the environment[1]
- However, greater reduction and inactivation of spores is achieved when a sporicidal agent is used[1]
- Removal of spores influenced by contact time (duration of wetness) and texture of surface being cleaned[2]

Technique	Reduction in Spores	Dry Time
Wiping with any disinfectant	> 2.9 $\log_{10}$	2-6 minutes
Spraying (no wipe) with sporicide	3.4 $\log_{10}$	28-40 minutes
Wiping with sporicide	3.9 $\log_{10}$	2-6 minutes

1. Rutala et al. Infect Control Hosp Epidemiol 2012; 33(12):1255-1258. 2. Gonzalez et al. Am J Infect Control 2015; 43:1331-1335.

EPA-Approved Disinfectants Effective Against *C. difficile*

- Before-after intervention studies demonstrated benefit of sporicidal disinfectants in units with high endemic CDI rates[1]
- Environmental contamination indirectly increases risk of cross contamination, likely via the hands of healthcare personnel[2]

When using sporicidal disinfectants[1]:

- Avoid toxicity to patients and environmental services staff
- Avoid damage to equipment
- Ensure method to communicate when sporicidal disinfectants should be used

A current list of EPA-approved disinfectants with sporicidal claim is available at:
http://www.epa.gov/pesticide-registration/list-k-epas-registered-antimicrobial-products-effective-against-clostridium

1. Dubberke et al. Infect Control Hosp Epidemiol 2014; 35(6):628-645. 2. Wilcox et al. J Hosp Infect 2003; 54(2):109-114.

Inactivation of *C. difficile* Spores

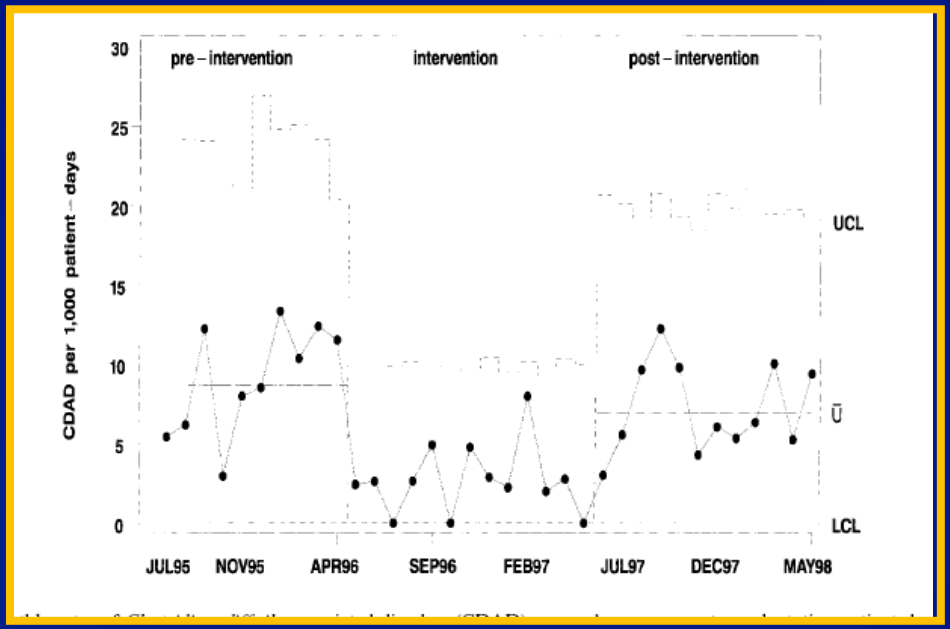
Sporicidal disinfectants most effective in reducing CDI when endemic rates are high.

Bone Marrow Transplant Unit
CDI Rates/ 1000 pt. days:

- Pre intervention: **8.6**
- Intervention: **3.3**
- Post-intervention: **8.1**

No reduction:

- Neurosurgical ICU: **3.0**
- General medical ward: **1.3**

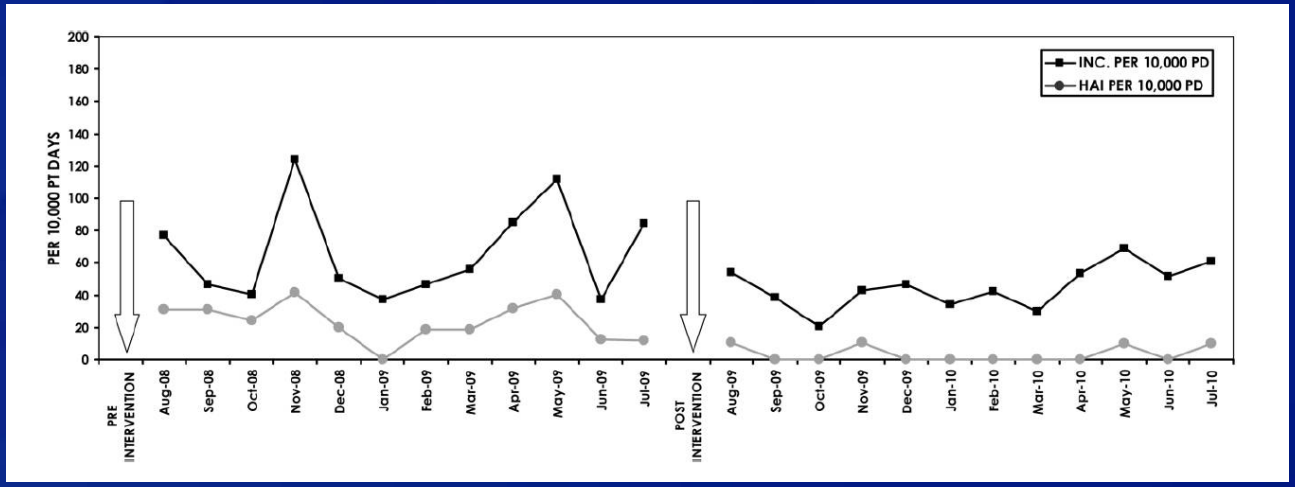


CDI rates in bone marrow transplant unit

Mayfield et al. Clin Infect Dis 2003; 31(4):995–1000.

Reducing CDI Using a Sporicidal Wipe for Cleaning

- Before/after study in two high-risk medical wards
- Intervention:
  - **Daily** and **terminal** cleaning of **all** rooms with ATP monitoring before/after (similar pass rate)
  - Quaternary ammonium compound before
  - Hypochlorite wipes with 10 minute contact time after
- **Results: 24.2 to 3.6 cases per 10,000 patient-days (85% decline)**

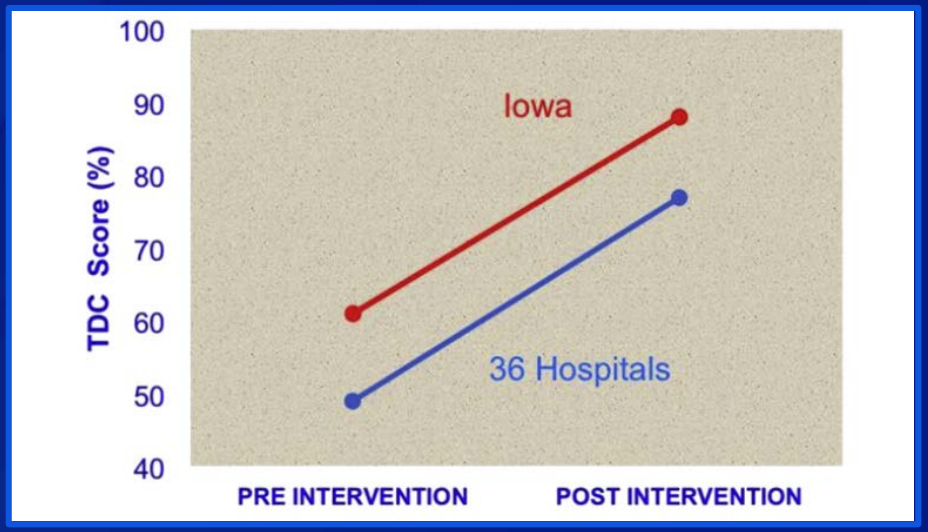


Orenstein et al. Infect Control Hosp Epidemiol 2011; 32:1137-1139.

Evaluating Cleanliness

Objective assessment of cleaning assists in optimizing performance[1,2]

- Monitoring of surfaces using florescent gel resulted in significant improvements in cleaning
- Educational interventions with environmental services staff resulted in sustained improvement



Terminal Disinfection and Cleaning

1. Carling. Am J Infect Control 2013; 41:S21-25.
2. CDC Options for Evaluating Environmental Cleaning: http://www.cdc.gov/hai/toolkits/Evaluating-Environmental-Cleaning.html

Methods of Evaluating Cleanliness

Evaluating Patient Zone Environmental Cleaning

Method	Ease of Use	Identifies Pathogens	Accuracy	Useful for Teaching	Use in Programmatic Monitoring
Direct observation	Low	No	Variable	Yes	Difficult
Culture swab	High	Yes	High	No	No
Agar culture system	Moderate	Possible	Moderate	No	Possible*
Fluorescent system	High	No	High	Yes	Yes
ATP Bioluminescence	High	No	Variable	Yes	Possible*

* Measures cleanliness at that moment but NOT the process of cleaning

Carling. Am J Infect Control 2013; 41:S21-25.

Using ATP Bioluminescence To Evaluate Cleanliness

Facilities using Adenosine Triphosphate (ATP) bioluminescence to monitor cleaning should carefully consider the range and diversity of results[1]

Researchers, using a convenience sample of 500 surfaces, determined[2]:

- 378 (76%) surfaces had fluorescent marker removed
- 225 (45%) had ATP bioluminescence measurement indicating cleanliness
- 384 (77%) had aerobic colony counts indicating cleanliness

Method	Pro	Con
Fluorescent Gel	Easy to apply – Stable in Environment Removal accurately signifies cleaning[3] Evaluates cleaning process[3] Effective training tool for ES staff[3]	Requires application before cleaning and reassessment after cleaning
ATP Bioluminescence	Ease of use Evaluates current cleanliness[3] Effective training tool for ES staff	Does not evaluate cleaning process[3] ATP failures may not correlate with fluorescent gel or CFU counts[3,4] Disinfectants may confound results[4] Facility and surface specific benchmarks may be needed[3,4,5] Specificity ~ 57%[4]

1. Moore et al. Am J Infect Control 2010; 38:617-622.
2. Boyce et al. Infect Control Hosp Epidemiol 2011; 32(12):1187-1193.
3. Carling Am J Infect Control 2013; 41:S21-25.
4. Mulvey et al. J Hosp Infect 2011; 77:25-30.
5. Shama & Malik Int J Hyg Env 2013; 216:115-125.

Ultraviolet Light and Hydrogen Peroxide Fogging

- **Data currently insufficient to recommend inclusion of these methods in a CDI prevention program**[1]

- Standard room cleaning and disinfection found to be suboptimal when UV disinfection was used[2]
  - Consistent cleaning attributed to 2 interventions:
    - Dedicated team
    - Supervisory housekeeping staff or IP staff checked rooms post cleaning

Effectiveness of no-touch disinfection technologies in preventing CDI requires further evaluation.[2]

1. Dubberke et al. Infect Control Hosp Epidemiol 2014; 35(6):628-645.
2. Sitzlar et al. Infect Control Hosp Epidemiol 2013; 34:459-465.

Appropriate Testing and Laboratory Practices

Guidance from the American Society for Microbiology

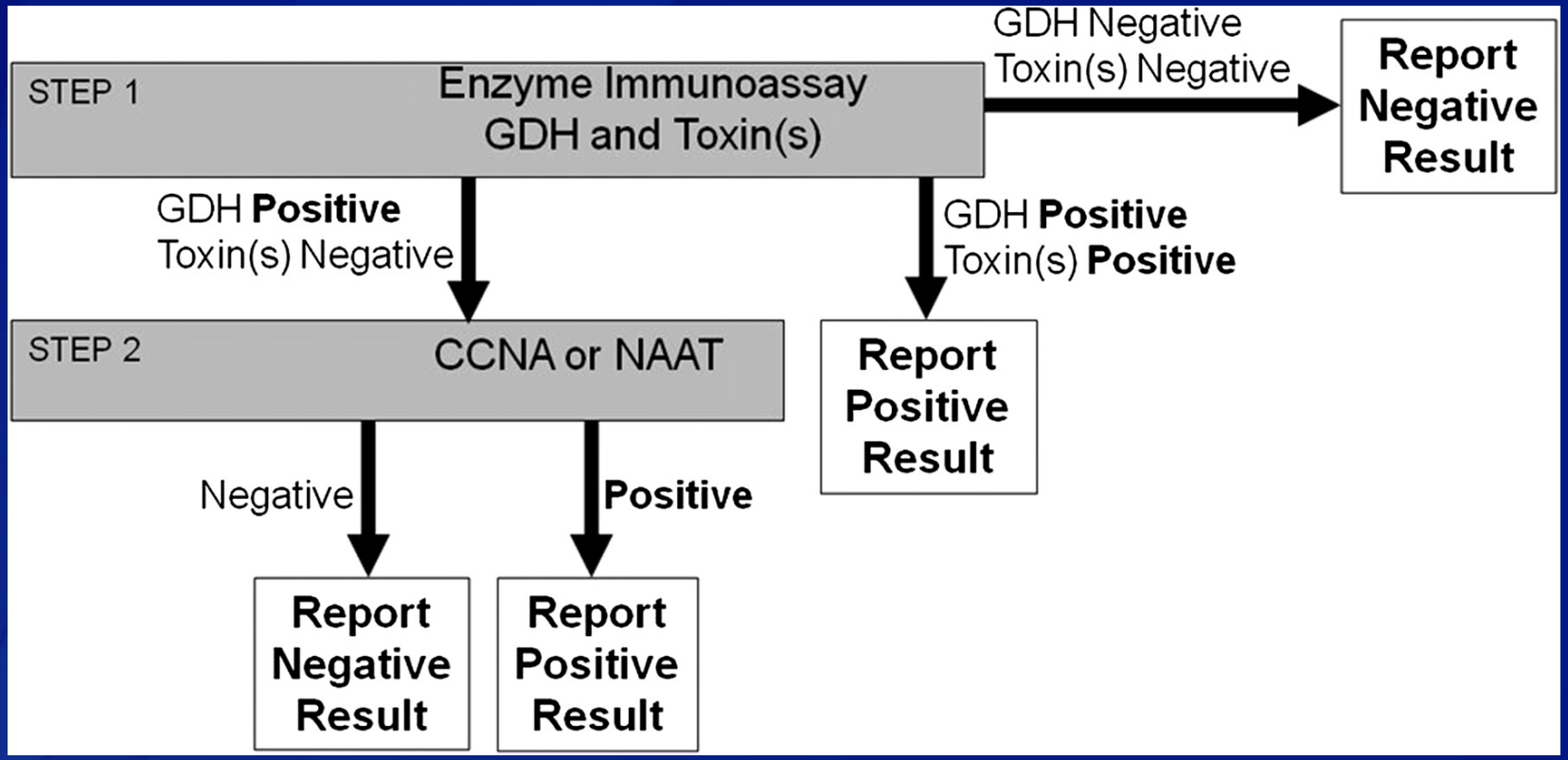
- Toxin A/B enzyme immunoassays have low sensitivity and should not be used as stand alone tests.[1]
- Highly sensitive screening tests like glutamate dehydrogenase antigen assays (GDH) should have positive results confirmed.
- Nucleic acid amplification that detects *C. difficile* toxin genes may be used as a stand alone test.
- Repeat testing, testing of formed stool, and testing for cure should be avoided.[2]

Regardless of testing method, ensure appropriate testing to optimizing test performance!

1. Am Soc Microbiol, 2010.

2. Dubberke et al. Infect Control Hosp Epidemiol 2014; 35 (6):628-645.

Typical Diagnostic Algorithm for Detection of Toxigenic *C. difficile* in Stool



Kufelnicka & Kirn. Clin Infect Dis 2011; 52:1451-457.

Understanding Predictive Value

True prevalence in the population tested for *C. difficile* greatly impacts predictive value of diagnostic tests

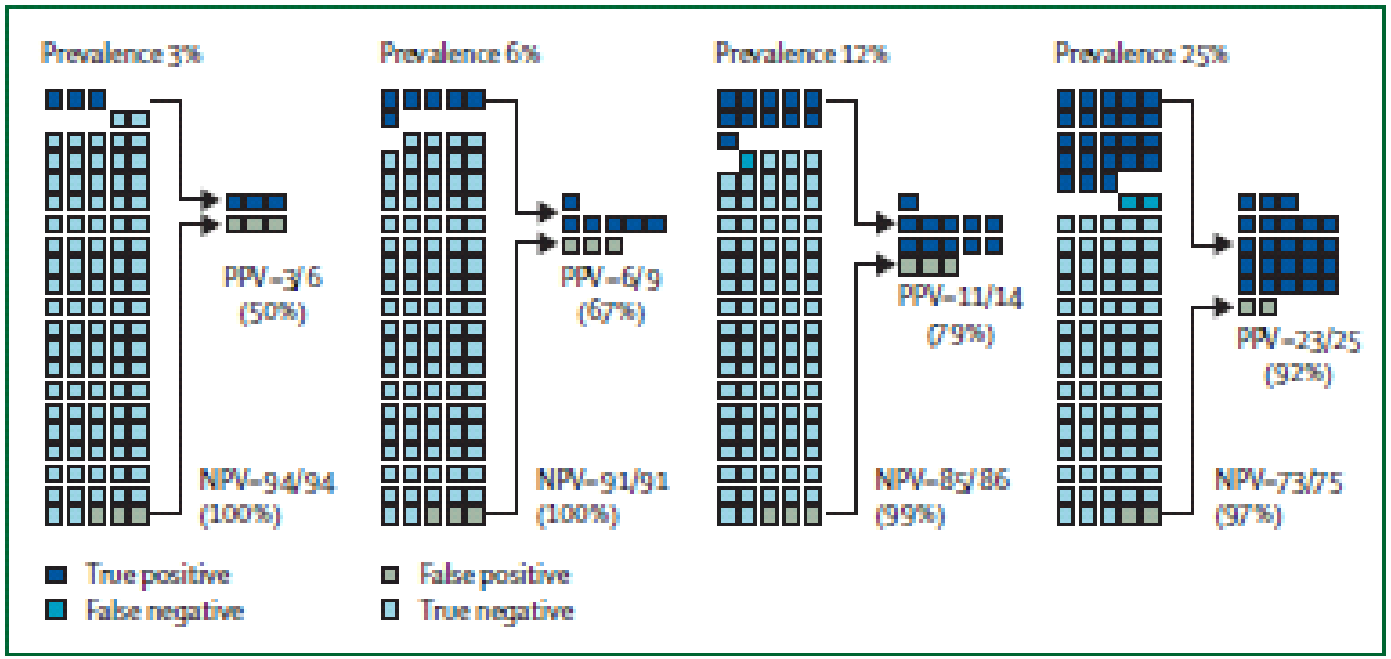


Figure 1: Effect of varying prevalence on the PPV and NPV of a theoretical *Clostridium difficile* toxin assay with a sensitivity of 92% and a specificity of 97%

NPV=negative predictive value. PPV=positive predictive value.

Planche et al. Lancet Infect Dis 2008; 8: 777–784.

Repeat Testing

- **Testing with a low sensitivity test and repeat testing are not recommended**[1]
  - Results in increased false positive results
  - Pseudo-outbreaks related to false positives and repeated testing have been identified[2,3]

Table 2. **Model of Results for Toxigenic *Clostridium difficile* Detection When Testing Is Repeated***

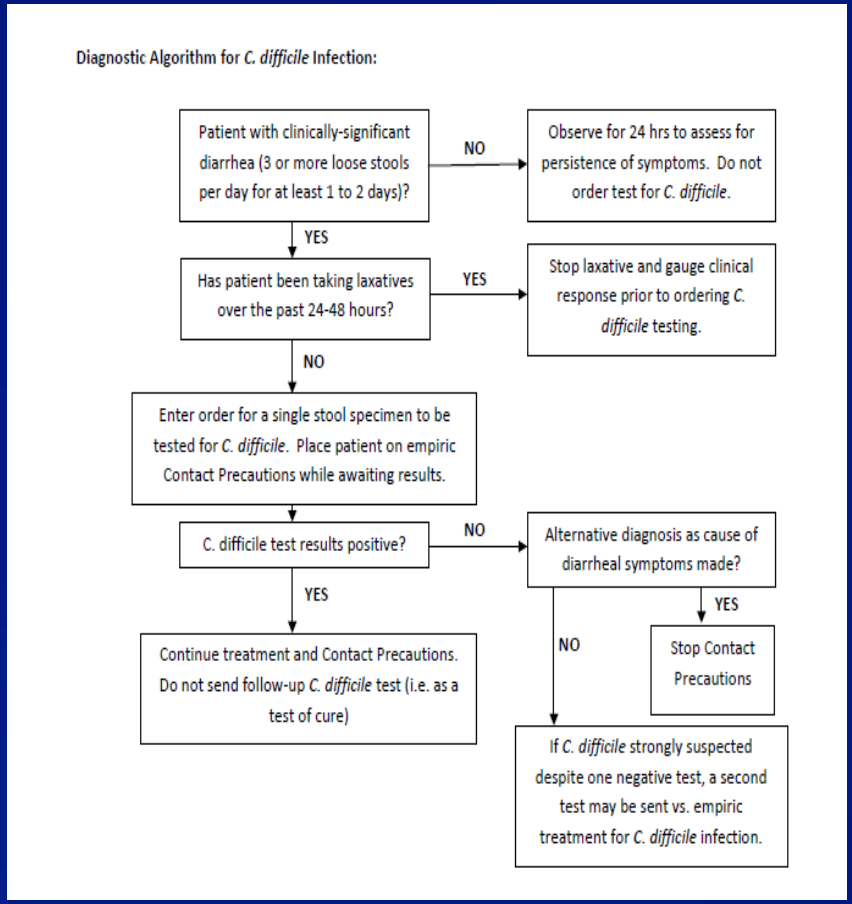
Test Sequence	EIA						qPCR					
	Tested, *n*	True Positive, *n*	PPV	False Positive, *n*	Undetected Disease, *n*	Remaining Negative Results, *n*	Tested, *n*	True Positive, *n*	PPV	False Positive, *n*	Undetected Disease, *n*	Remaining Negative Results, *n*
First	1000	73	0.75	24	27	903	1000	93	0.78	26	7	881
Second	903	18	0.45	22	9	863	881	7	0.23	23	0	851
Third	863	7	0.25	21	2	835	–	–		–	–	
Fourth	835	1	0.05	20	1	814	–	–		–	–	
Fifth	814	1	0.05	20	0	793	–	–		–	–	
Total		100†		107				100‡		49		

EIA = enzyme immunoassay; PPV = positive predictive value; qPCR = quantitative real-time polymerase chain reaction.
* In this model, there are 1000 tested participants and *C. difficile* prevalence in the test population is 10%. Patients with negative results have tests repeated sufficiently to ensure that all true-positive results are captured. Assumptions for EIA: sensitivity = 73.3%; specificity = 97.6%; and test performance does not change when repeated (6). Assumptions for qPCR: sensitivity = 93.3%; specificity = 97.4%; and test performance does not change when repeated (6).
† Overall PPV = 0.48.
‡ Overall PPV = 0.67.

1. Dubberke et al. Infect Control Hosp Epidemiol 2014; 35(6):628-645.
2. Litvin et al. Infect Control Hosp Epidemiol 2009; 30:1166-1171.
3. Peterson et al. Ann Intern Med 2009; 151(3):176-179.

Guidance for Appropriate Testing

- Tools that guide clinical decision making, such as algorithms, can assist in ensuring appropriate testing



Example of a CDI decision tool from Vanderbilt University Medical Center

1. Dubberke et al. Infect Control Hosp Epidemiol 2014; 35(6):628-645.
2. Vanderbilt University Medical Center: http://www.mc.vanderbilt.edu/documents/infectioncontrol/files/Guidance%20for%20Providers%20FINAL%202011.pdf

NHSN CDI Risk Adjusted SIR Accounts for More Sensitive Testing

Variables from Final Model to be included for Risk Adjustment in SIR Calculation

Factor	Description
Intercept	
Facility Bed Size	> 245
	101-245
	≤ 100
Teaching Type	Major
	Graduate
	Limited & Non
CDI Test Type	NAAT (PCR)
	EIA
	All Other
Prevalence	Continuous (no CO-HCFA)

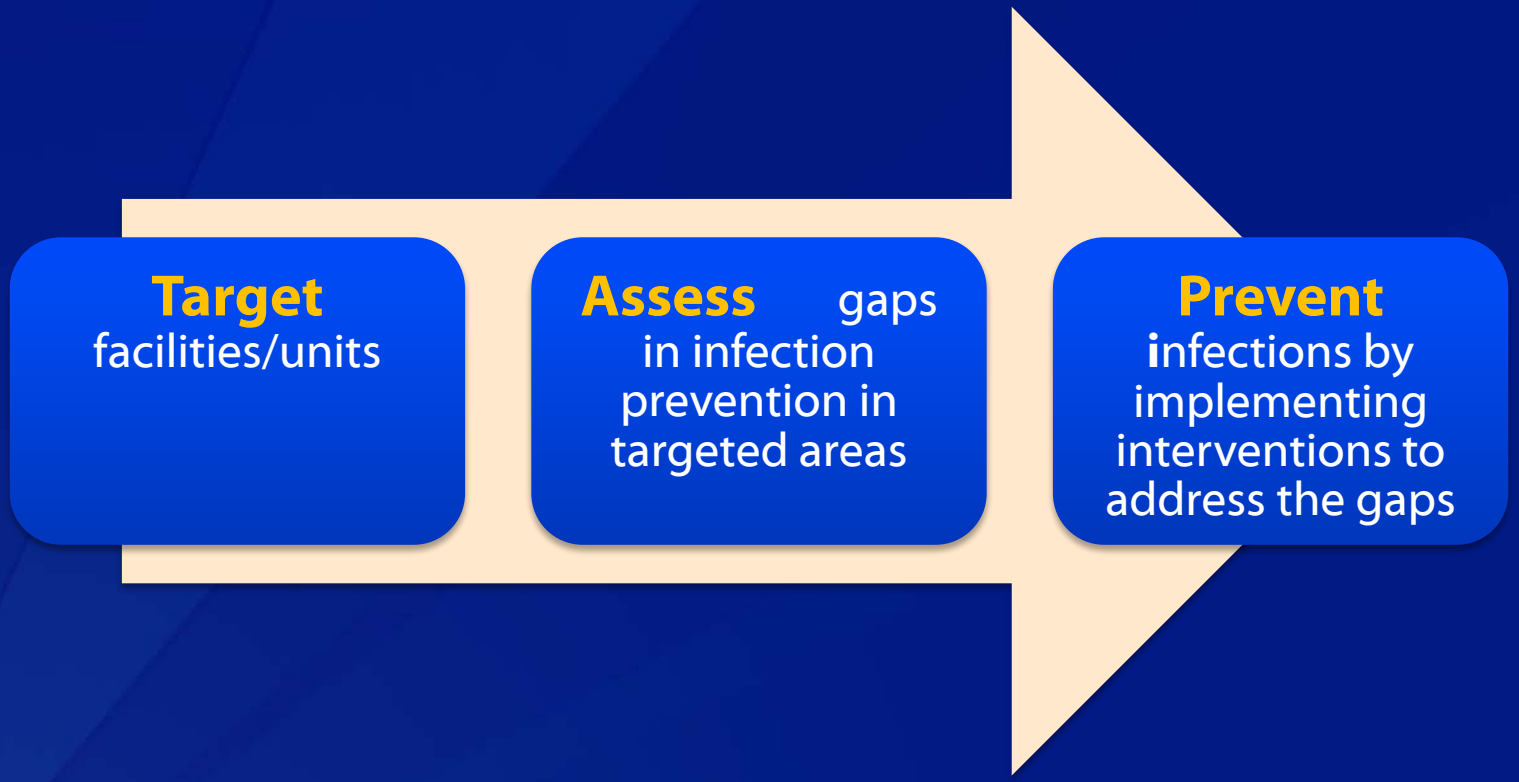
Data Sources and Submission

- CDI test type, facility bed size, and teaching type are collected on the required Annual Facility Survey

http://www.cdc.gov/nhsn/PDFs/mrsa-cdi/RiskAdjustment-MRSA-CDI.pdf

Implementing a Practical Approach to CDI Prevention

Targeted Assessment for Prevention (TAP) Strategy



CDI TAP reports available in NHSN

Work ongoing to use CO-CDI and other data sources to identify CDI cases from nursing homes and other community sources

www.cdc.gov/hai/prevent/tap.html

CDI Risk Assessment

- Conduct a risk assessment annually and whenever CDI goals are not met[1]
  - Use CDC's Targeted Assessment for Prevention (TAP) Strategy
  - Pairing the results of a CDI facility assessment with the CDI Implementation Tool allows facilities to implement infection prevention strategies that most directly meet their needs.

II. Antibiotic Stewardship
Example Resources
Get Smart for Healthcare – Implementation Resources Resources to assist in the implementation of hospital antibiotic stewardship programs, including guidelines, assessment tools, conceptual models, and a sample inter-facility infection control transfer form, from CDC
Get Smart for Healthcare – Stewardship Program Examples Links to hospital stewardship programs at various hospitals, success stories, and an interactive collection of charts and maps summarizing national and subnational data on antimicrobial use and resistance (Resistance Map), from CDC
Get Smart for Healthcare - Checklist for Core Elements of Hospital Antibiotic Stewardship Programs A checklist to evaluate hospital antibiotic stewardship programs, from CDC
Antimicrobial Stewardship Toolkit Best practices from an Antimicrobial Stewardship Collaborative, from the Greater New York Hospital Association and the United Hospital Fund

Dubberke et al. Infect Control Hosp Epidemiol 2014; 35(6):628-645.

www.cdc.gov/hai/prevent/tap.html

CDI Case Review

- Review each CDI case (e.g., root cause analysis)
- Examine temporal and spatial relationships between cases to determine units at risk for transmission due to community-onset or hospital-onset CDI cases.

The CDI Implementation Tool includes a template for CDI Case Review

FEEDBACK
NHSN Resources for MDRO and *C. difficile* Infection Module Protocols and training for National Healthcare Safety Network and the collection of CDI incidence data for reporting and feedback, from CDC
CDI Cause Analysis Worksheet for reviewing CDI cases and adherence to facility policies and practices, including antibiotic review log, from the Massachusetts Coalition for the Prevention of Medical Errors

Dubberke et al. Infect Control Hosp Epidemiol 2014; 35(6):628-645.

www.cdc.gov/hai/prevent/tap.html

A Coordinated Response

A coordinated response is more effective than independent efforts[1]

Partners in Prevention:

The state and local health department and other state partners can assist and provide opportunities to extend efforts across the continuum of care

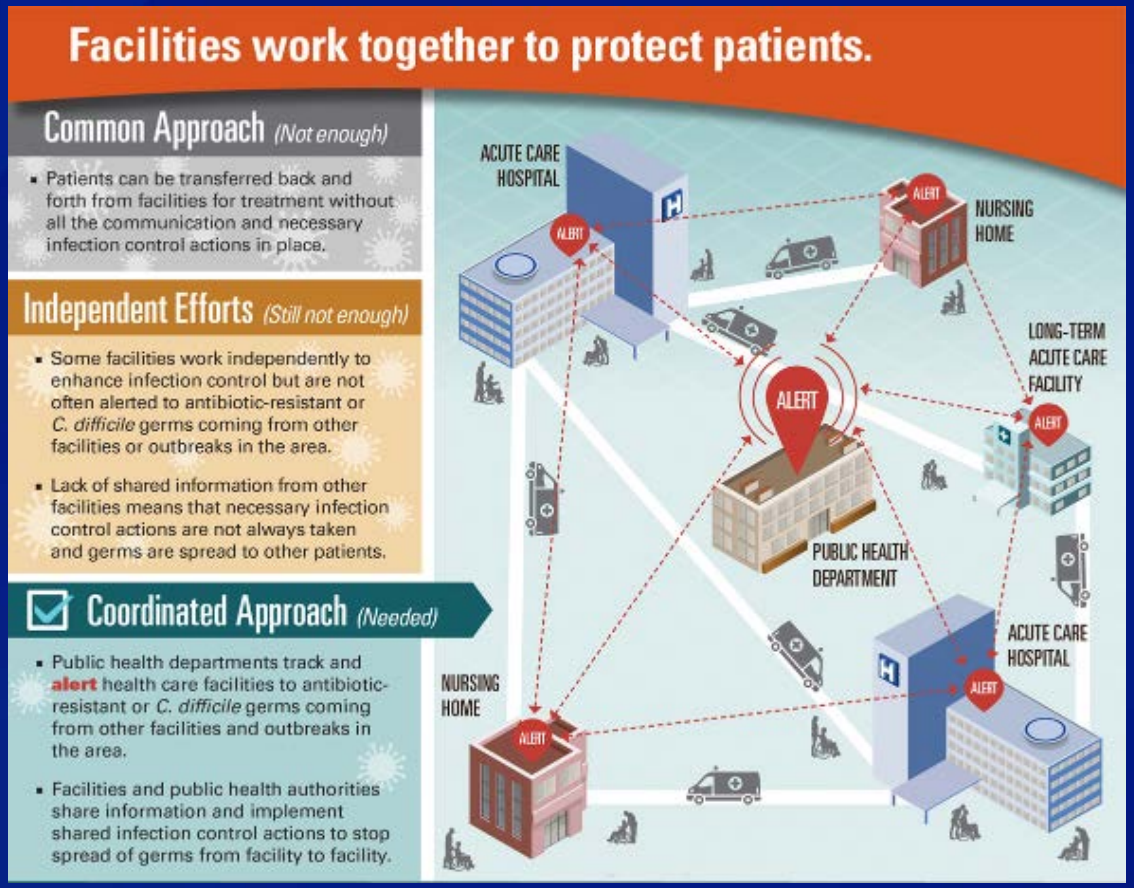


Figure from CDC Vitals Signs: http://www.cdc.gov/vitalsigns/stop-spread/index.html

1. Slayton et al. MMWR 2015; 64(30): 826-831.

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A practical guidance document for the laboratory detection of toxigenic *Clostridium difficile* infection. American Society of Microbiology Web site. http://www.asm.org/images/pdf/Clinical/clostridiumdifficile9-21.pdf Published September 21, 2010. Accessed February 24, 2016.

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Bliss D.Z., Johnson S., Savik L., Clabots C.R., Willard K., Gerding D.N. (1998). Acquisition of *Clostridium difficile* and *Clostridium difficile* associated disease in hospitalized patients receiving tube feeding. *Ann Intern Med, 129,* 1011-1019.

Bobulsky G.S., Al-Nassir W.N., Riggs M.M., Sethi A.K., & Donskey C.J. (2008). *Clostridium difficile* skin contamination in patients with *C. difficile*-associated disease. *Clin Infect Dis, 46(3),* 447-450.

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Buendgens L., Bruensing J., Matthes M., et al. (2014). Administration of proton pump inhibitors in critically ill patients is associated with increased risk of developing *Clostridium difficile*-associated diarrhea. *J Crit Care, 696*, e11-15.

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