Clostridioides difficile
Playbook
Antimicrobial Stewardship and Environmental Cleaning Task Force (AMSEC) of Rhode Island
February 2022
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Guiding Principles

**Consistency:** Coordinate statewide efforts to reduce healthcare-associated infections by engaging providers, executive administrators, and stakeholders.

**Prevention:** Rhode Island has consistently ranked in the bottom 5% of the US for *Clostridioides difficile* infection (CDI) since 2013.

**Minimize Morbidity and Mortality:** Crude 30-day, all-cause mortality rate is 10.6% for the initial CDI episode and 8.3% for the first recurrence.

**Minimize Cost:** *C. difficile* infections cost up to $4.8 billion each year in excess healthcare costs for acute care facilities alone.
Purpose
The CDC has designated Clostridioides difficile as an **urgent** global threat, calling it an “**immediate public health threat that requires urgent and aggressive action**.”

- US Department of Health and Human Services, CDC; 2019.
Five states with highest laboratory-diagnosed CDI cases, by SIR:

- New Hampshire: 0.79
- West Virginia: 0.77
- Wyoming: 0.67
- Massachusetts: 0.67
- Wisconsin: 0.65

Rhode Island’s SIR was 0.61, with a ranking of 43/51 (based on all 50 states and D.C.).

This report, summarized by state, is based on 2020 data published in 2021, and uses the 2015 Baseline and risk-adjusted models. HAI data summarized at the hospital-level are published on the Hospital Compare website. For detailed HAI-specific information regarding the current national baseline and risk adjustments, please see the SIR Guide.

### KEY DATA POINTS

- **29%**
  - Rhode Island ACHs reported a significant decrease in CDIs between 2019 and 2020.

- **20%**
  - Among the 10 ACHs in Rhode Island with enough data to calculate an SIR, 20% had an SIR significantly higher (worse) than 0.52, the value of the national SIR.
Acknowledgements

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Rhode Island Department of Health, Center for Acute Infectious Diseases and center for Public Health Information Staff
Myths
<table>
<thead>
<tr>
<th>Myth</th>
<th>Fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Only adults older than 65 get CDI.</td>
<td>One third of all CDI occur in people younger than 65.</td>
</tr>
<tr>
<td>CDI only occurs in hospitals.</td>
<td>Approximately 45% of cases are community acquired, although past exposure to hospitals or healthcare settings increases the risk to about 90%. Healthcare-associated CDI is more deadly.</td>
</tr>
<tr>
<td>CDI is unavoidable in healthcare settings.</td>
<td>It is possible and necessary to eliminate hospital-acquired infections, and many hospitals have succeeded in doing so.</td>
</tr>
<tr>
<td>Fecal microbiota transplantation (FMT) is a treatment of last resort.</td>
<td>FMT is indicated after a second recurrence (third episode) and can be considered after the first recurrence of more severe CDI.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Myth</th>
<th>Fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>A confirmatory test is needed to say that a CDI is cured.</td>
<td>Since <em>C. difficile</em> bacteria remain in the stool, even after symptoms have stopped, retesting is NOT recommended.</td>
</tr>
<tr>
<td>Antibiotics do not have side effects.</td>
<td>Antibiotic use is the primary risk factor for CDI.</td>
</tr>
<tr>
<td><em>Clostridium difficile</em> is different from <em>Clostridioides difficile</em>.</td>
<td>In 2016, <em>Clostridium difficile</em> was assigned to a new genus. The bacteria is now classified as <em>Clostridioides difficile</em>.</td>
</tr>
</tbody>
</table>

Plan
How Do We Implement Change?

Identification of Trends

• Late specimen collection
• Inappropriate testing
• Knowledge deficit
• True antimicrobial-associated

Plan-Do-Study-Act (PDSA)

• Led to development of different tools
Diarrhea Differential: Other Causes

- Antibiotics (10–20% of cases)
- Lactose intolerance
- Laxatives
- Traveler's diarrhea
- Pancreatic insufficiency
- Alcohol intoxication
- Irritable Bowel Syndrome (IBS)
- Inflammatory Bowel Disease (IBD)
- Celiac disease
- Other bacterial, viral, or parasitic infections and toxins (Norovirus, Shigella, Salmonella)

What symptoms make CDI less likely?
- No response to oral vancomycin
- Long duration of symptoms prior to testing/diagnosis
- Diarrhea that resolves in 24-48 hours
**Mini Root Cause Analysis (RCA) Tool**

**Why:** There are many different causes of diarrhea.

**Use:** The Mini RCA CDI tool is used when someone submits a specimen for testing inappropriately. It can be embedded into the hospital’s EMR.

This allows for a conversation to occur, but also gives the individual insight as to why the specimen was sent.

This two-way communication identifies knowledge deficits on either side, which can then be the focus for educational efforts.

### Sample Mini RCA CDI Process Improvement Discovery Tool

<table>
<thead>
<tr>
<th>Process</th>
<th>Yes/No</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Within 24 hours prior to stool collection, the patient...</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Had less than three unexpected and unexplained stools?</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Received a laxative or enema?</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Received lactulose, tube feedings or IV contrast?</strong></td>
<td></td>
</tr>
<tr>
<td><strong>The patient had NONE of the following:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Risk factors for CDI (antibiotics in prior 60 days; PPI more than three days in the week prior to stool collection)?</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Symptoms of CDI: abdominal pain, elevated WBC, temperature higher than 38° C?</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Status</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Was the patient known to be a carrier (prior positive test result)?</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Specimen quality</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Was the stool specimen submitted formed stool?</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Comments:</strong></td>
<td></td>
</tr>
</tbody>
</table>
Once a nurse completes an RCA form, they receive a $1 gift card and a *Did You Know?* card.

**Did You Know?**

Up to 15% of healthy adult patients are colonized with *C. diff*!

Make sure that the patient has **risk factors** for *C. diff* before testing:

- ✔ More than three loose/watery stools in a 24-hour period
- ✔ Specimen is loose/watery (not formed or semi-formed)
- ✔ No recent history of a positive *C. diff* test result (Patients can remain colonized for months!)
- ✔ No recent laxatives (including Colace and Senna)

Colonization is different than infection. When patients are colonized, they have no true signs/symptoms and should **NOT** be tested or treated.

Questions? Call Infection Prevention: ____________________________
Colonization with *C. difficile*

- Positive test, but asymptomatic
  - Patients may remain positive for months after symptoms have resolved.
- Found in 3.4% – 8.1% of patients upon admission
- Risk of over-diagnosis/overtreatment if not differentiated from active CDI
  - **Financial risks:** increased hospital stay, increased costs and resource utilization
  - **Clinical risks:** unnecessary use of antibacterials, risk of antibacterial-resistant *C. difficile*
- Mitigation strategies
  - Proper use and interpretation of diagnostic tests for CDI (**diagnostic stewardship**)
  - Minimize frequency and duration of high-risk antibacterial therapy and number of agents prescribed (**antibiotic stewardship**)

Testing
Testing Summary

• Test only if suspected CDI: acute onset diarrhea, risk factors, symptoms.

• Samples should be unformed stool that takes the shape of the container.

• Recommend two-step testing:
  1. PCR Test: either GDH or NAAT
  2. EIA toxin test to confirm active CDI

• Do not conclude results until both testing steps are complete.

• Patients should be placed on infection control precautions if suspected CDI.
When to Suspect an Active CDI

• Acute onset diarrhea (three or more loose stools in past 24 hours)
  • No recent laxative or enema use
  • No recent lactulose, tube feedings, or IV contrast
  • Consider other causes of diarrhea based on the patient's clinical presentation.

• Risk Factors for CDI

• Signs and Symptoms
  • Elevated white blood cell count
  • Abdominal pain
  • Temperature higher than 38°C

• No recent history of a positive C. diff test result (see Colonization)
## Risk Factors for *C. difficile*

<table>
<thead>
<tr>
<th>Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>65 or older</td>
</tr>
<tr>
<td>Antibiotic use in the past 60 days</td>
</tr>
<tr>
<td>Recent hospital or nursing home stay</td>
</tr>
<tr>
<td>Immunocompromised host (likely to be colonized)</td>
</tr>
<tr>
<td>Previous <em>C. difficile</em> infection</td>
</tr>
<tr>
<td>(Most recurrences happen within two to four weeks of completing course of anti-CDI therapy.)</td>
</tr>
</tbody>
</table>

Considerations for CDI Testing

Clinical Considerations

• Assess for appropriateness of testing: implement diagnostic stewardship program that is either staffed in real time or automated in the EHR.

• Discontinue laxatives, wait at least 48 hours before testing if still symptomatic.

• Once a patient has a positive CDI test result, do not repeat testing to detect cure as tests may remain positive for six or more weeks.

Laboratory Considerations

• Implement laboratory procedures to ensure testing of only appropriate specimens (e.g., **unformed stool that take the shape of the container**) for *C. difficile* or its toxins.

• Report test results IMMEDIATELY to clinical care providers and infection control personnel through reliable means (e.g., a laboratory alert system).
## Diagnostic Tests for CDI

<table>
<thead>
<tr>
<th>Test type</th>
<th>Substance detected</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxigenic culture (TC)</td>
<td><em>C. difficile</em> vegetative cells or spores</td>
<td>High</td>
<td>Low</td>
<td>Limited diagnostic use (reference method and epidemiologic tool)</td>
</tr>
<tr>
<td>Cell culture cytotoxicity neutralization assay (CCNA)</td>
<td>Free toxins in the stool</td>
<td>High</td>
<td>High</td>
<td>Limited diagnostic use (reference method)</td>
</tr>
<tr>
<td>Glutamate dehydrogenase (GDH)</td>
<td><em>C. difficile</em> common antigen (GDH is an essential enzyme produced by all <em>C. difficile</em> isolates)</td>
<td>High</td>
<td>Low</td>
<td>Used diagnostically as a screening test; antigen is present in both toxigenic and non-toxigenic strains, so results must be confirmed with another test that detects the toxin genes</td>
</tr>
<tr>
<td>Toxin A and B enzyme immunoassays (EIAs)</td>
<td>Free toxins A+B</td>
<td>Low</td>
<td>Moderate</td>
<td>With clinical data, diagnostic of CDI; inferior sensitivities compared with reference standards (100-1000pg of toxin must be present, can lead to false negative)</td>
</tr>
<tr>
<td>Nucleic acid amplification tests (NAATs)</td>
<td><em>C. difficile</em> nucleic acid (toxin genes)</td>
<td>High</td>
<td>Moderate</td>
<td>Specific for toxigenic strains; not for active toxin protein production and can detect asymptomatic carriers; thus, should only be used in patients with acute disease (three or more loose stools in 24 hours)</td>
</tr>
</tbody>
</table>

Statewide Strategy: Consider Two-Step Testing

Critical step in testing

**MUST have clinical suspicion for CDI**
- Acute onset diarrhea (≥3 loose stools in past 24 hours)
- Risk factors for CDI (e.g., antibiotic use in past 60 days, hospitalization, advanced age)
- Signs & Symptoms: elevated WBC, abdominal pain, T > 38°C
- No recent history of a (+) C. diff test
- No recent laxative use

Place patient on Infection Control Precautions and start treatment.

Laboratory should report results one step at a time, but note "IN PROGRESS" once first step of test is complete. See following slide for examples.

First Step (PCR)
- Collect LOOSE/UNFORMED stool specimen
- GDH or NAAT

2nd Step
- EIA toxin test
- STOP: patient unlikely to have acute CDI
- Complete two-step testing in 24 hours (Per CDC/NHSN)

Note: If PCR result is positive, put patient on infection control precautions.

Treat CDI infection
- Likely colonization (don’t treat)
AMSEC Suggested Approach

Sample lab results (Lifespan)

Why are there two testing steps?

- PCR tests are specific for toxigenic strains but do not test for active toxin production. PCR tests cannot differentiate between actively infected and colonized patients, which may result in unnecessary treatment.
- The EIA toxin test detects the presence of free toxins in the body and, in combination with a positive PCR test, confirms an active CDI.
- No test can stand alone. Consideration of clinical judgment is important.
Treatment
Treatment Considerations

• **Discontinue** antimicrobial therapy with the inciting agent(s) as soon as possible, as this may influence the risk of CDI recurrence.
  - *Strong recommendation, moderate quality of evidence*

• **Empiric Therapy**: Antibiotic therapy for CDI should be started empirically for situations where a substantial delay (more than 48 hours) in laboratory confirmation is expected, or for fulminant CDI.
  - *Weak recommendation, low quality of evidence*

## Classification of CDI

<table>
<thead>
<tr>
<th>Classification</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-severe</td>
<td>Leukocytosis with a white blood cell count of (&lt;15000 \text{ cells/mL}) \textit{and} serum creatinine (\leq 1.5 \text{ mg/dL})</td>
</tr>
<tr>
<td>Severe</td>
<td>Leukocytosis with a white blood cell count of (\geq 15000 \text{ cells/mL}) \textit{or} serum creatinine (&gt;1.5 \text{ mg/dL})</td>
</tr>
</tbody>
</table>
| Fulminant      | \textit{IDSA}: hypotension or shock, ileus, megacolon  
\textit{ACG}: criteria for severe infection plus hypotension or shock, ileus, megacolon |

IDSA Guidelines
## IDSA Treatment: Initial Episodes

<table>
<thead>
<tr>
<th>Classification</th>
<th>Recommended Treatment (Strength of Recommendation / Quality of Evidence)</th>
<th>Alternative Treatment (Strength of Recommendation / Quality of Evidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial CDI episode, non-severe</td>
<td><strong>Fidaxomicin</strong> 200 mg orally twice daily for 10 days (Conditional/Moderate)</td>
<td><strong>Vancomycin</strong> 125 mg orally four times daily for 10 days <em>(Strong/High)</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>OR</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Metronidazole</strong> 500 mg orally three times daily for 10-14 days <em>(Weak/High)</em></td>
</tr>
<tr>
<td>Initial CDI episode, severe</td>
<td><strong>Fidaxomicin</strong> 200 mg orally twice daily for 10 days (Conditional/Moderate)</td>
<td><strong>Vancomycin</strong> 125 mg orally four times daily for 10 days <em>(Strong/High)</em></td>
</tr>
<tr>
<td>Fulminant CDI</td>
<td><strong>Vancomycin</strong> 500 mg four times daily by mouth or by nasogastric tube <em>(Strong/Moderate)</em></td>
<td>AND</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Metronidazole</strong> 500 mg IV every 8 hours, particularly if ileus is present <em>(Strong/Moderate)</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Consider adding rectal vancomycin instillation</strong> if ileus is present <em>(Weak/Low)</em></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Classification</th>
<th>Recommended Treatment</th>
<th>Alternative Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Fidaxomicin</strong> 200 mg orally twice daily for 10 days OR twice daily for 5 days, followed by once every other day for 20 days <em>(Conditional/Moderate)</em></td>
<td><strong>Vancomycin in a tapered and pulsed regimen <em>(Weak/Low)</em></strong>&lt;br&gt;Example: 125 mg four times daily for 10-14 days, twice daily for 7 days, once daily for 7 days, and then every 2 or 3 days for 2-8 weeks OR <strong>Vancomycin</strong> 125 mg orally four times daily for 10 days <em>(Weak/Low)</em></td>
</tr>
<tr>
<td>First CDI recurrence</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Fidaxomicin</strong> 200 mg orally twice daily for 10 days OR twice daily for 5 days, followed by once every other day for 20 days <em>(Weak/Low)</em> OR **Vancomycin in a tapered and pulsed regimen <em>(Weak/Low)</em> OR <strong>Vancomycin</strong> 125 mg four times daily for 10 days, followed by rifaximin 400 mg three times daily for 20 days <em>(Weak/Low)</em> OR <strong>Fecal microbiota transplantation</strong> after appropriate treatment for at least two recurrences <em>(Strong/Moderate)</em></td>
<td></td>
</tr>
</tbody>
</table>

Bezlotoxumab (BEZ)

- BEZ is a human monoclonal antibody that binds to one of two exotoxins produced by *C. diff* (toxin B) and prevents it from entering the GI cell layer, preventing colonic cell damage.
- In patients with **recurrent CDI within the last six months**, BEZ is suggested as a **co-intervention** along with standard-of-care antibiotics. *(Conditional recommendation, very low certainty of evidence)*
  - Limited data on the use of BEZ in patients receiving fidaxomicin
  - Caution in patients with congestive heart failure
- BEZ may also be considered in primary CDI patients with risk factors for CDI recurrence (older age, immunocompromised, severe CDI).
- **Dosing**: BEZ 10 mg/kg IV once during administration of standard-of-care antibiotics
ACG Guidelines
## ACG Treatment: Initial Episodes

<table>
<thead>
<tr>
<th>Classification</th>
<th>Recommended Treatment (Strength of Recommendation/Quality of Evidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial CDI episode, non-severe</td>
<td><strong>Vancomycin</strong> 125 mg orally four times daily for 10 days <em>(Strong/Low)</em></td>
</tr>
<tr>
<td></td>
<td><strong>OR</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Fidaxomicin</strong> 200 mg orally twice daily for 10 days <em>(Strong/Moderate)</em></td>
</tr>
<tr>
<td></td>
<td><strong>OR</strong></td>
</tr>
<tr>
<td></td>
<td>**Low-risk patients: Metronidazole 500 mg orally three times daily for 10 days <em>(Strong/Moderate)</em></td>
</tr>
<tr>
<td>Initial CDI episode, severe</td>
<td><strong>Vancomycin</strong> 125 mg orally four times daily for 10 days <em>(Strong/Low)</em></td>
</tr>
<tr>
<td></td>
<td><strong>OR</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Fidaxomicin</strong> 200 mg orally twice daily for 10 days <em>(Conditional/Very Low)</em></td>
</tr>
<tr>
<td></td>
<td>• Limited data in patients with fulminant CDI and life-threatening illness</td>
</tr>
<tr>
<td>Fulminant CDI</td>
<td><strong>Adequate volume resuscitation</strong></td>
</tr>
<tr>
<td></td>
<td><strong>AND</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Vancomycin</strong> 500 mg orally four times daily for the first 48-72 hours <em>(Strong/Very Low)</em></td>
</tr>
<tr>
<td></td>
<td>±</td>
</tr>
<tr>
<td></td>
<td><strong>Vancomycin enemas</strong> 500 mg orally every 6 hours may be beneficial if ileus <em>(Conditional/Very Low)</em></td>
</tr>
<tr>
<td></td>
<td>±</td>
</tr>
<tr>
<td></td>
<td><strong>Metronidazole</strong> 500 mg intravenously every 8 hours may be beneficial if paralytic ileus <em>(Conditional/Very Low)</em></td>
</tr>
</tbody>
</table>

Fulminant: Surgical Therapy

• Total colectomy with an end ileostomy and a stapled rectal stump

OR

• Diverting loop ileostomy with colonic lavage and intraluminal vancomycin

• Consider clinical circumstances, the patient’s estimated tolerance to surgery, and the surgeon’s best judgment.

May be considered for patients with severe and fulminant CDI refractory to antibiotic therapy, particularly when patients are poor surgical candidates

- Strong recommendation, low quality of evidence
## ACG Treatment: Recurrent Episodes

<table>
<thead>
<tr>
<th>Initial Treatment Course Used</th>
<th>Recommended Treatment (Strength of Recommendation/Quality of Evidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fidaxomicin, vancomycin, or metronidazole</td>
<td>Vancomycin in a tapered and pulsed regimen (Strong/Very Low)</td>
</tr>
<tr>
<td>Vancomycin or metronidazole</td>
<td><strong>Fidaxomicin</strong> 200 mg orally twice daily for 10 days (Strong/Moderate)</td>
</tr>
</tbody>
</table>

FMT for Prevention of Recurrence

- Recommended for patients experiencing their second or further CDI recurrence to prevent further recurrences (Strong recommendation, moderate quality of evidence)

- Methods of Delivery
  - Recommended through colonoscopy or capsules (Strong recommendation, moderate quality of evidence)
  - If other methods unavailable, suggest delivery by enema (Conditional recommendation, low quality of evidence)

- Repeat FMT for patients experiencing a recurrence of CDI within eight weeks of an initial FMT
  - Conditional recommendation, very low quality of evidence

Suppressive and Prophylactic Vancomycin

- Long-term suppressive oral vancomycin may be used to prevent further recurrences in patients with recurrent CDI who meet at least one of the following (Conditional recommendation, very low quality of evidence):
  - Are not candidates for FMT
  - Have relapsed after FMT
  - Require ongoing or frequent courses of antibiotics

- **Suggested dose:** 125 mg orally once daily, may be increased to two or three times daily to control symptoms of loose stools

- Oral vancomycin prophylaxis may be considered during subsequent systemic antibiotic use in patients with a history of CDI who are at high risk of recurrence (Conditional recommendation, low quality of evidence)

Bezlotoxumab can be considered for prevention of CDI recurrence in patients who are at high risk of recurrence.

**Recommended Patient Population:** 65 or older with at least one of the following additional risk factors:

- Second episode of CDI within the past six months
- Immunocompromised
- Severe CDI
  - *Conditional recommendation, moderate quality of evidence*

- Caution in patients with severe underlying cardiovascular comorbidities
- Not recommended for patients with a history of heart failure

Antisecretory Therapy

• Also known as therapy with **proton pump inhibitors** (ex. lansoprazole, omeprazole, pantoprazole, etc.) or **histamine-2 receptor antagonists** (ex. famotidine)

• ACG suggests against discontinuation of antisecretory therapy in patients with CDI, provided there is an appropriate indication for their use (**Strong recommendation, very low quality of evidence**)

• Assess patients for appropriateness of therapy.
  • Observational studies proposed an increased risk of CDI in patients with gastric acid suppression, although confounding variables may be to blame.

Special Populations

• **Pregnant, Peripartum, Breastfeeding:** Recommend the use of vancomycin as first-line therapy for treatment of CDI.

• **Immunocompromised:** Recommend the use of vancomycin or fidaxomicin as first-line therapy for treatment of CDI.

Inflammatory Bowel Disease (IBD)

• Recommend CDI testing in patients with IBD presenting with an acute flare associated with diarrhea.
  • Strong recommendation, low quality of evidence

• Suggest vancomycin 125 mg orally 4 times a day for a minimum of 14 days in patients with IBD and CDI.
  • Strong recommendation, very low quality of evidence

• Consider FMT for recurrent CDI in patients with IBD.
  • Strong recommendation, very low quality of evidence

• Immunosuppressive IBD therapy should not be held during anti-CDI therapy in the setting of disease flare, and escalation of therapy may be considered if there is no symptomatic improvement with treatment of CDI
Probiotics

- **Proposed Mechanism:** colonization/normalization of intestinal microbiota, competitive exclusion of pathogens, immune and metabolic modulation
- Although high-quality evidence is lacking, the idea of probiotics is appealing to patients. As dietary supplements, probiotics are not strictly regulated by the FDA.
- **ACG Guidelines:** Recommend **AGAINST** the use of probiotics for both primary and secondary prevention of CDI.
  - Primary Prevention: *Conditional recommendation against use, moderate quality of evidence*
  - Secondary Prevention: *Strong recommendation against use, very low quality of evidence*

*Note: Some studies have found that probiotics impede normal recolonization of the colon after antibiotic use*

Guideline Comparison
<table>
<thead>
<tr>
<th>Clinical Definition</th>
<th>IDSA/SHEA Guidelines June 2021</th>
<th>ACG Guidelines May 2021</th>
</tr>
</thead>
</table>
| **Initial episode, non-severe**         | **Preferred:** Fidaxomicin 200 mg orally twice daily for 10 days  
  *(Conditional/Moderate)* | Vancomycin 125 mg orally four times daily for 10 days  
  *(Strong/Low)*  
  **OR**  
  Fidaxomicin 200 mg orally twice daily for 10 days  
  *(Strong/Moderate)*  
  **OR**  
  Metronidazole for low-risk patients: 500 mg orally three times daily for 10-14 days  
  *(Strong/Moderate)* |
|                                         | Alternative: Vancomycin 125 mg orally four times daily for 10 days  
  *(Strong/Low)* |  
  **OR**  
  Fidaxomicin 200 mg orally twice daily for 10 days  
  *(Strong/Moderate)*  
  **OR**  
  Metronidazole for low-risk patients: 500 mg orally three times daily for 10-14 days  
  *(Strong/Moderate)* |
|                                         | Alternative if above regimen unavailable: Metronidazole 500 mg orally three times daily for 10-14 days  
  *(Weak/High)* |  
  **OR**  
  Fidaxomicin 200 mg orally twice daily for 10 days  
  *(Strong/Moderate)*  
  **OR**  
  Metronidazole for low-risk patients: 500 mg orally three times daily for 10-14 days  
  *(Strong/Moderate)* |
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<th>IDSA/SHEA Guidelines June 2021 (Strength of Recommendation/Quality of Evidence)</th>
<th>ACG Guidelines May 2021 (Strength of Recommendation/Quality of Evidence)</th>
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</table>
| Initial episode, severe | Preferred: **Fidaxomicin** 200 mg orally twice daily for 10 days (*Conditional/Moderate*)  
Alternative: **Vancomycin** 125 mg orally four times daily for 10 days (*Strong/High*) | **Vancomycin** 125 mg orally four times daily for 10 days (*Strong/Low*)  
**OR**  
**Fidaxomicin** 200 mg orally twice daily for 10 days (*Conditional/Very Low*)  
*Note: Limited data in patients with fulminant CDI and life-threatening illness* |
<table>
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<tr>
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<tbody>
<tr>
<td>First Recurrence</td>
<td>Preferred: <strong>Fidaxomicin</strong> 200 mg orally twice daily for 10 days OR twice daily for 5 days followed by every other day for 20 days <em>(Conditional/Moderate)</em>&lt;br&gt;&lt;br&gt;Alternative: <strong>Vancomycin</strong> in a tapered and pulsed regimen OR if metronidazole was used for the initial episode: 125 mg orally four times daily for 10 days <em>(Conditional/Low)</em></td>
<td>Vancomycin a tapered and pulsed regimen after an initial course of fidaxomicin, vancomycin, or metronidazole <em>(Strong/Very Low)</em>&lt;br&gt;&lt;br&gt;OR&lt;br&gt;&lt;br&gt;Fidaxomicin after an initial course of vancomycin or metronidazole <em>(Conditional/Moderate)</em>&lt;br&gt;&lt;br&gt;Vancomycin a tapered and pulsed regimen after an initial course of fidaxomicin, vancomycin, or metronidazole <em>(Strong/Very Low)</em>&lt;br&gt;&lt;br&gt;OR&lt;br&gt;&lt;br&gt;Fidaxomicin after an initial course of vancomycin or metronidazole <em>(Conditional/Moderate)</em></td>
</tr>
<tr>
<td>Second or Subsequent Recurrence</td>
<td><strong>Fidaxomicin</strong> 200 mg twice daily for 10 days, OR twice daily for 5 days, followed by once every other day for 20 days <em>(Weak/Low)</em> OR&lt;br&lt;br&gt;<strong>Vancomycin in a tapered and pulsed regimen</strong> <em>(Weak/Low)</em> OR&lt;br&lt;br&gt;<strong>Vancomycin</strong> 125 mg orally four times daily for 10 days followed by <strong>rifaximin</strong> 400 mg three times daily for 20 days <em>(Weak/Low)</em> OR&lt;br&lt;br&gt;<strong>FMT</strong> if appropriate antibiotic treatment for 2 prior recurrences <em>(Conditional/Low)</em></td>
<td><strong>FMT</strong> to prevent further recurrences in patients experiencing their second or further recurrence <em>(Strong/Moderate)</em>&lt;br&lt;br&gt;<strong>Vancomycin prophylaxis</strong> <em>(Suggested dose: 125 mg orally daily)</em> for patients who are not candidates for FMT or who relapsed after FMT <em>(Conditional/Very Low)</em>, or who require ongoing or frequent courses of antibiotics <em>(Conditional/Low)</em></td>
</tr>
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<td>Clinical Definition</td>
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<tr>
<td><strong>Fulminant CDI</strong></td>
<td><strong>Vancomycin</strong> 500 mg orally or by nasogastric tube four times daily <em>(Strong/Moderate)</em>&lt;br&gt;<strong>Consider adding rectal vancomycin</strong> 500 mg four times daily if ileus present <em>(Weak/Low)</em>&lt;br&gt;<strong>Consider adding metronidazole</strong> 500 mg IV every 8 hours, particularly if ileus is present <em>(Strong/Moderate)</em></td>
<td><strong>Adequate volume resuscitation AND</strong>&lt;br&gt;<strong>Vancomycin</strong> 500 mg orally every 6 hours for the first 48-72 hours <em>(Strong/Very Low)</em>&lt;br&gt;<strong>Consider adding rectal vancomycin</strong> 500 mg every 6 hours if ileus present <em>(Conditional/Very Low)</em>&lt;br&gt;<strong>Consider adding metronidazole</strong> 500 mg IV every 8 hours, particularly in cases of paralytic ileus <em>(Conditional/Very Low)</em>&lt;br&gt;<strong>FMT</strong> for patients refractory to antibiotics, particularly if poor surgical candidates</td>
</tr>
<tr>
<td>Clinical Definition</td>
<td>IDSA/SHEA Guidelines June 2021 <em>(Strength of Recommendation/Quality of Evidence)</em></td>
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</tbody>
</table>
| **Use of Bezlotoxumab for prevention of CDI recurrence** | Recommended in patients with CDI recurrence within the last 6 months *(Conditional/Very Low)* | Recommended in patients age 65 or older and with at least one risk factor of recurrence:  
- Severe CDI  
- Second CDI episode within past 6 months  
- Immunocompromised *(Conditional/Moderate)* |
| Dose: 10 mg/kg IV once during administration of standard of care antibiotics | In settings where logistics are not an issue, patients with primary CDI and risk factors for CDI recurrence (age ≥ 65 years, immunocompromised, severe CDI) may benefit. | Caution in patients with a history of heart failure or severe underlying cardiovascular comorbidities. |
|                     | Data in combination with idaxomycin are limited. | |
Infection Control and Prevention
Core Prevention Strategies

1. Isolate and initiate contact precautions for suspected or confirmed CDI.

2. Perform environmental cleaning to prevent CDI.
   - Use of sporicidal agents (EPA List K agents)
   - Supplemental: no-touch technologies for disinfection (UV light)

3. Develop infrastructure to support CDI prevention.

4. Engage the facility’s Antimicrobial Stewardship Program (AMS).

Isolate and Initiate Contact Precautions

- Create ED nurse-driven protocols (versus inpatient) to facilitate rapid isolation of patients with suspected or confirmed CDI for earlier detection and ordering of samples.

- Ensure rapid evaluation by healthcare personnel and infection prevention.

- Place symptomatic patients on contact precautions and in a single-patient room with a dedicated toilet. (Cohort like patients if single-patient rooms are not available.)

- Adhere to recommended hand hygiene practices.

- Use dedicated patient-care equipment (blood pressure cuffs, stethoscopes).

- Implement daily patient bathing or showering with soap and water.

- When transferring patients: Notify receiving wards/facilities about the patient’s CDI status so contact precautions are maintained at the patient’s new location.

Perform Environmental Cleaning

- Create daily and terminal cleaning protocols and checklists for patient-care areas and equipment.

- Perform daily cleaning of CDI patient rooms using a *C. difficile* sporicidal agent (EPA List K agent).

- Perform terminal cleaning after CDI patient transfer/discharge with a *C. difficile* sporicidal agent (EPA List K agent).

- Clean additional areas that are contaminated during transient visits by patients with suspected or confirmed CDI (Radiology, Emergency Departments, Physical Therapy) with a *C. difficile* sporicidal agent (EPA List K agent).

- Clean and disinfect the patient-care environment (including immediate vicinity around CDI patient and high-touch surfaces) at least once daily, including toilets.

- Clean and disinfect all shared equipment prior to use with another patient (wheelchairs, gurneys).

Develop Infrastructure

- Incorporate reduction of CDI into the facility healthcare-associated infection prevention program. Include a multidisciplinary team to identify and implement strategies and to follow results of the interventions.

- Monitor facility CDI rates, and target units with highest incidence of CDI for evaluation and intervention.

- Educate and train healthcare personnel on prevention practices for CDI.

- Routinely audit prevention and precautionary practices, such as adherence to hand hygiene and contact precautions, and adequacy of room cleaning.

- Provide CDI rates to senior leadership, clinical providers, laboratory personnel, environmental services, and other stakeholders.

Engage the Facility's AMS Program

1. Develop facility-specific treatment recommendations for common infections that include first and second-line antibiotics.

2. Evaluate antibiotic treatment of conditions that commonly lead to high-risk antibiotic use, such as asymptomatic bacteriuria and common infections such as urinary tract infections and community-acquired pneumonia, to minimize the use of high-risk antibiotics.

3. Ensure that patients receive the shortest effective duration of antibiotic therapy.

4. Include inpatient antibiotic duration when determining post-discharge antibiotic duration.

Handwashing
Healthcare Personnel Precautions and Hand Hygiene

- Healthcare personnel must wear gloves and gowns on entry to a CDI patient room and while caring for patients with CDI.

- In routine or endemic settings, perform hand hygiene before and after contact with a patient with CDI and after removing gloves. Use either soap and water or an alcohol-based hand hygiene product (at least 70% isopropyl alcohol).

- In CDI outbreaks or hyperendemic (sustained high rates) settings, perform hand hygiene with soap and water instead of alcohol-based hand hygiene products before and after caring for a patient with CDI, given the increased efficacy of spore removal with soap and water.

- Handwashing with soap and water is preferred if there is direct contact with feces or an area where fecal contamination is likely (the perineal region).

How Good Are Handwashing Techniques?

• A study conducted in two non-profit hospitals assessed the handwashing activities of 90 RNs, LPNs, and nursing aides on general medical-surgical units.

• The quality of hand washes was rated according to Feldman’s Criteria.

• The study results showed that the hand washing by nursing personnel in these medical-surgical units was infrequently and poorly performed.

### When to Perform Hand Hygiene

<table>
<thead>
<tr>
<th>Before having direct contact with patients</th>
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<tbody>
<tr>
<td>After contact with blood, body fluids or secretions, mucous membranes, non-intact skin, or wound dressings</td>
</tr>
<tr>
<td>After contact with a patient’s intact skin (e.g., when taking a pulse or blood pressure or lifting a patient)</td>
</tr>
<tr>
<td>If hands will be moving from a contaminated-body site to a clean-body site during patient care</td>
</tr>
<tr>
<td>After contact with inanimate objects (including medical equipment) in the immediate vicinity of the patient</td>
</tr>
<tr>
<td>After removing gloves</td>
</tr>
</tbody>
</table>

Handwashing Tip and Tricks

- **Handwashing**: After applying soap, rub hands together vigorously for at least 15 seconds, covering all surfaces of the hands and fingers. Other entities have recommended at least 20 seconds; however, either time is acceptable.

- **Artificial Nails**: Do not wear artificial fingernails or extenders if duties include direct contact with patients at high risk for infection and associated adverse outcomes (those in ICUs or operating rooms).
  - Develop an organizational policy on the wearing of non-natural nails by healthcare personnel who have direct contact with patients outside of the groups specified above.

World Health Organization
Handwashing Video
Handwashing Versus Hand Sanitizer

• Wash hands with soap and water if contact with spores (e.g., *C. difficile* or *Bacillus anthracis*) is likely to have occurred. The physical action of washing and rinsing hands under such circumstances is recommended because alcohols, chlorhexidine, iodophors, and other antiseptic agents have poor activity against spores.

• However, early experimental data suggest that, even using soap and water, the removal of *C. diff* spores is more challenging than the removal or inactivation of other common pathogens.

Pediatrics
CDI Testing in Children

• Testing for CDI should never be routinely recommended for neonates and infants younger than 12 months with diarrhea due to high asymptomatic colonization in this age group.

  • Though asymptomatic colonization decreases with age, routinely performing CDI testing in children 1-2 years of age with diarrhea is NOT recommended unless other infectious or noninfectious causes have been excluded.

• Testing for CDI in children age two or older is recommended for patients with prolonged or worsening diarrhea and risk factors.

Non-Severe: Treatment of Initial Episode (Pediatrics)

• Metronidazole 7.5 mg/kg/dose orally 3 or 4 times daily for 10 days (max dose 500 mg)
  • Weak recommendation, low quality of evidence

OR

• Vancomycin 10 mg/kg/dose orally 4 times daily for 10 days (max dose 125 mg)
  • Weak recommendation, low quality of evidence

Severe/Fulminant: Treatment of Initial Episode (Pediatrics)

- Vancomycin 10 mg/kg/dose orally or rectally 4 times daily for 10 days (max dose 500 mg)
  - *Strong recommendation, moderate quality of evidence*

  With or without

- Metronidazole 10 mg/kg/dose IV 3 times daily for 10 days (max dose 500 mg)
  - Consider addition in cases associated with critical illness.
  - *Weak recommendation, low quality of evidence*

Treatment of First Recurrence (Non-Severe, Pediatric)

• Metronidazole 7.5 mg/kg/dose orally 3 or 4 times daily for 10 days (max dose 500 mg)
  • Weak recommendation, low quality of evidence

  OR

• Vancomycin 10 mg/kg/dose orally 4 times daily for 10 days (max dose 125 mg)
  • Weak recommendation, low quality of evidence

Treatment of Second or Subsequent Recurrence (Pediatrics)

- Vancomycin 10 mg/kg/dose orally 4 times daily for 10-14 days, then 10 mg/kg/dose orally 2 times daily for a week, then 10 mg/kg/dose once daily for a week, then 10 mg/kg/dose every 2 or 3 days for 2-8 weeks (max dose 125 mg)
  - *Weak recommendation, low quality of evidence*
  - OR
- Vancomycin 10 mg/kg/dose orally 4 times daily for 10 days (max dose 500 mg), followed by rifaximin for 20 days:
  - children younger than 12: 15-30 mg/kg/day in divided doses 3 times daily (max dose 400 mg)
  - Children 12 or older: 400 mg 3 times daily
  - *Weak recommendation, low quality of evidence*
  - OR
- Fecal microbiota transplantation
  - *Weak recommendation, very low quality of evidence*

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Staff and Patient Resources
Staff Education

- Fact Sheet
- Handwashing Training
- Frequently Asked Questions For Clinicians
- *Clostridioides Difficile* Educational Video
• What is C. diff?

• Patient Education Handout

• Understanding C. Diff Educational Video
US Antibiotic Awareness Week (USAAW)

- Annual one-week observance that gives participating organizations an opportunity to increase awareness of the threat of antibiotic resistance and correct antibiotic use

- *Be Antibiotics Aware* is a CDC educational initiative that complements USAAW

- [CDC Partner Toolkit](#)
Be Antibiotics Aware CDC Toolkit

Instagram Animations (MP4)

Facebook/Twitter Animations (gif)

Infographics

Public Service Announcements

Videos for Social Media

Web Images

ANTIBIOTICS AREN'T ALWAYS THE ANSWER

What is antibiotic-resistant bacteria?

Public Service Announcements

Community Antibiotic Prescriptions per 1,000 Population by State - 2019

(revised methodology)
Clean Hands Count Campaign (CDC)

• The **Clean Hands** World Hand Hygiene Day – May 5

• **Count campaign** aims to:
  • Improve healthcare provider adherence to CDC hand hygiene [recommendations](www.cdc.gov/HandHygiene)
  • Address the myths and misperceptions about hand hygiene
  • Empower patients to play a role in their care by asking or reminding healthcare providers to clean their hands