

## *Clostridium difficile* (*C. diff*) Infection

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# What is a Clinical Pathway?

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An evidence-based guideline that decreases unnecessary variation and helps promote safe, effective, and consistent patient care.

# Objectives of Pathway

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- Standardize testing for suspected *C. difficile* infection
- Standardize treatment for first-time and recurrent *C. difficile* infections based on severity of disease

# Why is the Pathway Necessary?

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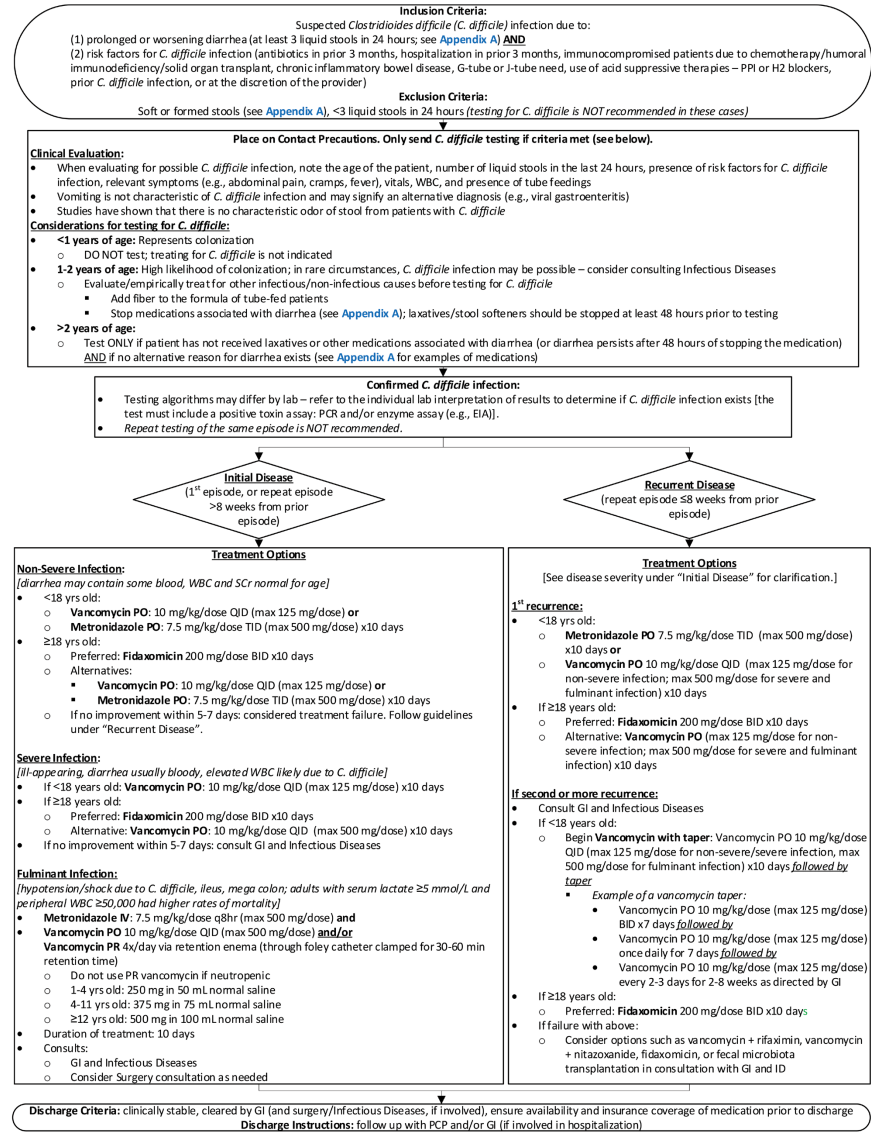


- *C. difficile* (*C. diff*) infection is becoming more common in children
- There is a wide range of clinical presentations and it may be difficult to distinguish diarrhea from *C. diff* infection from other etiologies
- The diagnosis of *C. diff* infection is based on both clinical and laboratory findings as colonization can occur.
- Management of *C. diff* depends on severity and recurrence of disease
  - With recurrence there is increased likelihood of side-effects and possible resistance. Thus, alternative recommendations are given.
- Complications from infection are more rare in children than adults, but can include pseudomembranous colitis, toxic megacolon, intestinal perforation, shock, and hypotension. They are rarely fatal.

**CLINICAL PATHWAY:**  
Suspected *Clostridioides difficile* (*C. difficile*) Infection Evaluation and Management

THIS PATHWAY  
SERVES AS A GUIDE  
AND DOES NOT  
REPLACE CLINICAL  
JUDGMENT.

This is the *C. difficile* Infection Pathway. We will be reviewing it in the following slides.



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**Inclusion Criteria:**

Suspected *Clostridioides difficile* (*C. difficile*) infection due to:

- (1) prolonged or worsening diarrhea (at least 3 liquid stools in 24 hours; see [Appendix A](#)) **AND**
- (2) risk factors for *C. difficile* infection (antibiotics in prior 3 months, hospitalization in prior 3 months, immunocompromised patients due to chemotherapy/humoral immunodeficiency/solid organ transplant, chronic inflammatory bowel disease, G-tube or J-tube need, use of acid suppressive therapies – PPI or H2 blockers, prior *C. difficile* infection, or at the discretion of the provider)

**Exclusion Criteria:**

Soft or formed stools (see [Appendix A](#)), <3 liquid stools in 24 hours (*testing for C. difficile is NOT recommended in these cases*)

1-2 years of age: High likelihood of colonization; in rare circumstances, *C. difficile* infection may be possible – consider consulting Infectious Diseases

- o Evaluate/empirically treat for other infectious/non-infectious causes before testing for *C. difficile*
  - Add fiber to the formula of tube-fed patients
  - Stop medications associated with diarrhea (see [Appendix A](#)); laxatives/stool softeners should be stopped at least 48 hours prior to testing

Other medications associated with diarrhea (or diarrhea persists after 48 hours of stopping the medication) (see [Appendix A](#) for examples of medications)

**Confirmed *C. difficile* infection:**  
To the individual lab interpretation of results to determine if *C. difficile* infection exists (the R and/or enzyme assay (e.g., EIA)).  
*Testing is not recommended.*

**Recurrent Disease**  
(repeat episode ≥8 weeks from prior episode)

**Treatment Options**

[See disease severity under "Initial Disease" for clarification.]

- 1<sup>st</sup> recurrence:**
- <18 yrs old:
    - o **Metronidazole PO** 7.5 mg/kg/dose TID (max 500 mg/dose) x10 days
    - o **Vancomycin PO** 10 mg/kg/dose QID (max 125 mg/dose for non-severe infection; max 500 mg/dose for severe and fulminant infection) x10 days
  - If ≥18 years old:
    - o Preferred: **Fidaxomicin** 200 mg/dose BID x10 days
    - o Alternative: **Vancomycin PO** (max 125 mg/dose for non-severe infection; max 500 mg/dose for severe and fulminant infection) x10 days
- If second or more recurrence:**
- Consult GI and Infectious Diseases
  - If <18 years old:
    - o Begin **Vancomycin with taper**: Vancomycin PO 10 mg/kg/dose QID (max 125 mg/dose for non-severe/severe infection, max 500 mg/dose for fulminant infection) x10 days *followed by taper*
      - *Example of a vancomycin taper:*
        - Vancomycin PO 10 mg/kg/dose (max 125 mg/dose) BID x7 days *followed by*
        - Vancomycin PO 10 mg/kg/dose (max 125 mg/dose) once daily for 7 days *followed by*
        - Vancomycin PO 10 mg/kg/dose (max 125 mg/dose) every 2-3 days for 2-8 weeks as directed by GI
  - If ≥18 years old:
    - o Preferred: **Fidaxomicin** 200 mg/dose BID x10 days
  - If failure with above:
    - o Consider options such as vancomycin + rifaximin, vancomycin + nitazoxanide, fidaxomicin, or fecal microbiota transplantation in consultation with GI and ID

Infectious Diseases, if involved, ensure availability and insurance coverage of medication prior to discharge  
follow up with PCP and/or GI (if involved in hospitalization)

• *C. diff* infection should only be considered if there is diarrhea (which is defined as at least 3 liquid stools in 24 hours) AND there are specific risk factors for infection.

- It is important to distinguish *C. diff* from other causes of acute-onset diarrhea. Risk factors that increases the likelihood of *C. diff* are listed here. They include prior antibiotic exposure, hospitalization, immunocompromised state, inflammatory bowel disease, use of a feeding tube, or acid suppressive therapies.
- Provider discretion can also allow for a patient to be included on this pathway, as community acquisition is possible without any prior risk factors, particularly with highly virulent strains.

**CLINICAL PATHWAY:**  
**Suspected *Clostridioides difficile* (*C. difficile*) Infection Evaluation and Management**  
**Appendix A: Bristol Stool Chart and Medications That Can Cause Diarrhea**

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

**CLINICAL PATHWAY:**  
**Suspected *Clostridioides difficile* (*C. difficile*) Infection Evaluation and Management**

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

**Bowel Consistency – Bristol Stool Chart**

FORMED	1		Separate hard lumps, like nuts (hard to pass)
	2		Sausage-shaped but lumpy
	3		Like a sausage but with cracks on its surface
SOFT	4		Like a sausage or snake, smooth and soft
	5		Soft blobs with clear-cut edges
LIQUID	6		Fluffy pieces with ragged edges, a mushy stool
	7		Watery, no solid pieces, entirely liquid

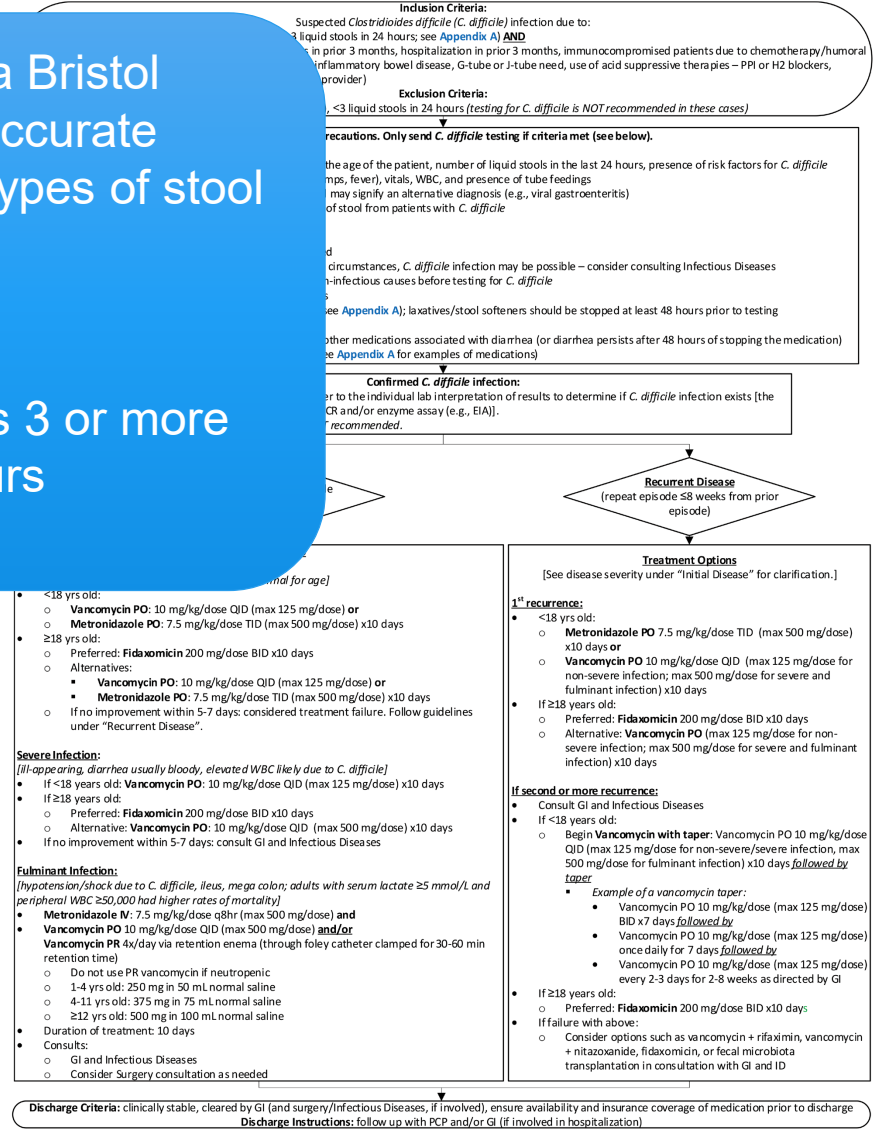


Appendix A includes a Bristol Stool Chart to allow accurate assessment of what types of stool would be considered liquid/diarrhea.

Diarrhea is defined as 3 or more liquid stools in 24 hours

**Examples of Medications That Can Cause Diarrhea**

- Laxatives:
  - Lactulose, bisacodyl, magnesium citrate, docusate, Go-lytely, Senna, polyethylene glycol, sorbitol, etc.
- Enemas and suppositories
- Others:
  - Kayexalate
  - Colchicine
  - Octreotide
  - Metformin and other diabetic medications
  - Antibiotics
  - Antineoplastics
  - Magnesium containing antacids





**Place on Contact Precautions. Only send *C. difficile* testing if criteria met (see below).**

**Clinical Evaluation:**

- When evaluating for possible *C. difficile* infection, note the age of the patient, number of liquid stools in the last 24 hours, presence of risk factors for *C. difficile* infection, relevant symptoms (e.g., abdominal pain, cramps, fever), vitals, WBC, and presence of tube feedings
- Vomiting is not characteristic of *C. difficile* infection and may signify an alternative diagnosis (e.g., viral gastroenteritis)
- Studies have shown that there is no characteristic odor of stool from patients with *C. difficile*

**Considerations for testing for *C. difficile*:**

- **<1 years of age:** Represents colonization
  - DO NOT test; treating for *C. difficile* is not indicated
- **1-2 years of age:** High likelihood of colonization; in rare circumstances, *C. difficile* infection may be possible – consider consulting Infectious Diseases
  - Evaluate/empirically treat for other infectious/non-infectious causes before testing for *C. difficile*
    - Add fiber to the formula of tube-fed patients
    - Stop medications associated with diarrhea (see [Appendix A](#)); laxatives/stool softeners should be stopped at least 48 hours prior to testing
- **>2 years of age:**
  - Test ONLY if patient has not received laxatives or other medications associated with diarrhea (or diarrhea persists after 48 hours of stopping the medication) AND if no alternative reason for diarrhea exists (see [Appendix A](#) for examples of medications)

If *C. diff* infection is suspected, place on Brown Contact precautions immediately to avoid potential spread. Waiting for results (if testing was sent) is not recommended,

<p><i>[diarrhea may contain some blood, WBC and SCr normal for age.]</i></p> <ul style="list-style-type: none"> <li>• &lt;18 yrs old:                     <ul style="list-style-type: none"> <li>○ <b>Vancomycin PO:</b> 10 mg/kg/dose QID (max 125 mg/dose) or</li> <li>○ <b>Metronidazole PO:</b> 7.5 mg/kg/dose TID (max 500 mg/dose) x10 days</li> </ul> </li> <li>• ≥18 yrs old:                     <ul style="list-style-type: none"> <li>○ Preferred: <b>Fidaxomicin</b> 200 mg/dose BID x10 days</li> <li>○ Alternatives:                             <ul style="list-style-type: none"> <li>▪ <b>Vancomycin PO:</b> 10 mg/kg/dose QID (max 125 mg/dose) or</li> <li>▪ <b>Metronidazole PO:</b> 7.5 mg/kg/dose TID (max 500 mg/dose) x10 days</li> </ul> </li> <li>○ If no improvement within 5-7 days: considered treatment failure. Follow guidelines under "Recurrent Disease".</li> </ul> </li> </ul> <p><b>Severe Infection:</b> <i>[ill-appearing, diarrhea usually bloody, elevated WBC likely due to C. difficile]</i></p> <ul style="list-style-type: none"> <li>• If &lt;18 years old: <b>Vancomycin PO:</b> 10 mg/kg/dose QID (max 125 mg/dose) x10 days</li> <li>• If ≥18 years old:             <ul style="list-style-type: none"> <li>○ Preferred: <b>Fidaxomicin</b> 200 mg/dose BID x10 days</li> <li>○ Alternative: <b>Vancomycin PO:</b> 10 mg/kg/dose QID (max 500 mg/dose) x10 days</li> </ul> </li> <li>• If no improvement within 5-7 days: consult GI and Infectious Diseases</li> </ul> <p><b>Fulminant Infection:</b> <i>[hypotension/shock due to C. difficile, ileus, mega colon; adults with serum lactate ≥5 mmol/L and peripheral WBC ≥50,000 had higher rates of mortality]</i></p> <ul style="list-style-type: none"> <li>• <b>Metronidazole IV:</b> 7.5 mg/kg/dose q8hr (max 500 mg/dose) and</li> <li>• <b>Vancomycin PO</b> 10 mg/kg/dose QID (max 500 mg/dose) and/or</li> <li>• <b>Vancomycin PR</b> 4x/day via retention enema (through foley catheter clamped for 30-60 min retention time)             <ul style="list-style-type: none"> <li>○ Do not use PR vancomycin if neutropenic</li> <li>○ 1-4 yrs old: 250 mg in 50 mL normal saline</li> <li>○ 4-11 yrs old: 375 mg in 75 mL normal saline</li> <li>○ ≥12 yrs old: 500 mg in 100 mL normal saline</li> </ul> </li> <li>• Duration of treatment: 10 days</li> <li>• Consults:             <ul style="list-style-type: none"> <li>○ GI and Infectious Diseases</li> <li>○ Consider Surgery consultation as needed</li> </ul> </li> </ul>	<p><i>[see disease severity order - Initial Disease - for clarification.]</i></p> <p><b>1<sup>st</sup> recurrence:</b></p> <ul style="list-style-type: none"> <li>• &lt;18 yrs old:             <ul style="list-style-type: none"> <li>○ <b>Metronidazole PO</b> 7.5 mg/kg/dose TID (max 500 mg/dose) x10 days or</li> <li>○ <b>Vancomycin PO</b> 10 mg/kg/dose QID (max 125 mg/dose for non-severe infection; max 500 mg/dose for severe and fulminant infection) x10 days</li> </ul> </li> <li>• If ≥18 years old:             <ul style="list-style-type: none"> <li>○ Preferred: <b>Fidaxomicin</b> 200 mg/dose BID x10 days</li> <li>○ Alternative: <b>Vancomycin PO</b> (max 125 mg/dose for non-severe infection; max 500 mg/dose for severe and fulminant infection) x10 days</li> </ul> </li> </ul> <p><b>If second or more recurrence:</b></p> <ul style="list-style-type: none"> <li>• Consult GI and Infectious Diseases</li> <li>• If &lt;18 years old:             <ul style="list-style-type: none"> <li>○ Begin <b>Vancomycin with taper:</b> Vancomycin PO 10 mg/kg/dose QID (max 125 mg/dose for non-severe/severe infection, max 500 mg/dose for fulminant infection) x10 days <i>followed by taper</i> <ul style="list-style-type: none"> <li>▪ <i>Example of a vancomycin taper:</i> <ul style="list-style-type: none"> <li>• Vancomycin PO 10 mg/kg/dose (max 125 mg/dose) BID x7 days <i>followed by</i></li> <li>• Vancomycin PO 10 mg/kg/dose (max 125 mg/dose) once daily for 7 days <i>followed by</i></li> <li>• Vancomycin PO 10 mg/kg/dose (max 125 mg/dose) every 2-3 days for 2-8 weeks as directed by GI</li> </ul> </li> </ul> </li> </ul> </li> <li>• If ≥18 years old:             <ul style="list-style-type: none"> <li>○ Preferred: <b>Fidaxomicin</b> 200 mg/dose BID x10 days</li> </ul> </li> <li>• If failure with above:             <ul style="list-style-type: none"> <li>○ Consider options such as vancomycin + rifaximin, vancomycin + nitazoxanide, fidaxomicin, or fecal microbiota transplantation in consultation with GI and ID</li> </ul> </li> </ul>
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**Discharge Criteria:** clinically stable, cleared by GI (and surgery/Infectious Diseases, if involved), ensure availability and insurance coverage of medication prior to discharge  
**Discharge Instructions:** follow up with PCP and/or GI (if involved in hospitalization)







**Place on Contact Precautions. Only send *C. difficile* testing if criteria met (see below).**

**Clinical Evaluation:**

- When evaluating for possible *C. difficile* infection, note the age of the patient, number of liquid stools in the last 24 hours, presence of risk factors for *C. difficile* infection, relevant symptoms (e.g., abdominal pain, cramps, fever), vitals, WBC, and presence of tube feedings
- Vomiting is not characteristic of *C. difficile* infection and may signify an alternative diagnosis (e.g., viral gastroenteritis)
- Studies have shown that there is no characteristic odor of stool from patients with *C. difficile*

**Considerations for testing for *C. difficile*:**

- **<1 years of age:** Represents colonization
  - DO NOT test; treating for *C. difficile* is not indicated
- **1-2 years of age:** High likelihood of colonization; in rare circumstances, *C. difficile* infection may be possible – consider consulting Infectious Diseases
  - Evaluate/empirically treat for other infectious/non-infectious causes before testing for *C. difficile*
    - Add fiber to the formula of tube-fed patients
    - Stop medications associated with diarrhea (see [Appendix A](#)); laxatives/stool softeners should be stopped at least 48 hours prior to testing
- **>2 years of age:**
  - Test ONLY if patient has not received laxatives or other medications associated with diarrhea (or diarrhea persists after 48 hours of stopping the medication) AND if no alternative reason for diarrhea exists (see [Appendix A](#) for examples of medications)

- Consider the following when *C. diff* infection is suspected.
- Note patient risk factors for infection.
- Vomiting and “characteristic” stool odor does not signify that a *C. diff* infection is present.

<p><i>[diarrhea may contain some blood, WBC and S/Cr normal for age]</i></p> <ul style="list-style-type: none"> <li>• &lt;18 yrs old:                     <ul style="list-style-type: none"> <li>○ <b>Vancomycin PO:</b> 10 mg/kg/dose QID (max 125 mg/dose) or</li> <li>○ <b>Metronidazole PO:</b> 7.5 mg/kg/dose TID (max 500 mg/dose) x10 days</li> </ul> </li> <li>• ≥18 yrs old:                     <ul style="list-style-type: none"> <li>○ Preferred: <b>Fidaxomicin</b> 200 mg/dose BID x10 days</li> <li>○ Alternatives:                             <ul style="list-style-type: none"> <li>▪ <b>Vancomycin PO:</b> 10 mg/kg/dose QID (max 125 mg/dose) or</li> <li>▪ <b>Metronidazole PO:</b> 7.5 mg/kg/dose TID (max 500 mg/dose) x10 days</li> </ul> </li> <li>○ If no improvement within 5-7 days: considered treatment failure. Follow guidelines under “Recurrent Disease”.</li> </ul> </li> </ul> <p><b>Severe Infection:</b> <i>[ill-appearing, diarrhea usually bloody, elevated WBC likely due to C. difficile]</i></p> <ul style="list-style-type: none"> <li>• If &lt;18 years old: <b>Vancomycin PO:</b> 10 mg/kg/dose QID (max 125 mg/dose) x10 days</li> <li>• If ≥18 years old:             <ul style="list-style-type: none"> <li>○ Preferred: <b>Fidaxomicin</b> 200 mg/dose BID x10 days</li> <li>○ Alternative: <b>Vancomycin PO:</b> 10 mg/kg/dose QID (max 500 mg/dose) x10 days</li> </ul> </li> <li>• If no improvement within 5-7 days: consult GI and Infectious Diseases</li> </ul> <p><b>Fulminant Infection:</b> <i>[hypotension/shock due to C. difficile, ileus, mega colon; adults with serum lactate ≥5 mmol/L and peripheral WBC ≥50,000 had higher rates of mortality]</i></p> <ul style="list-style-type: none"> <li>• <b>Metronidazole IV:</b> 7.5 mg/kg/dose q8hr (max 500 mg/dose) and</li> <li>• <b>Vancomycin PO</b> 10 mg/kg/dose QID (max 500 mg/dose) and/or</li> <li>• <b>Vancomycin PR</b> 4x/day via retention enema (through foley catheter clamped for 30-60 min retention time)             <ul style="list-style-type: none"> <li>○ Do not use PR vancomycin if neutropenic</li> <li>○ 1-4 yrs old: 250 mg in 50 mL normal saline</li> <li>○ 4-11 yrs old: 375 mg in 75 mL normal saline</li> <li>○ ≥12 yrs old: 500 mg in 100 mL normal saline</li> </ul> </li> <li>• Duration of treatment: 10 days</li> <li>• Consults:             <ul style="list-style-type: none"> <li>○ GI and Infectious Diseases</li> <li>○ Consider Surgery consultation as needed</li> </ul> </li> </ul>	<p><i>[see disease severity order - Initial Disease - for clarification.]</i></p> <p><b>1<sup>st</sup> recurrence:</b></p> <ul style="list-style-type: none"> <li>• &lt;18 yrs old:             <ul style="list-style-type: none"> <li>○ <b>Metronidazole PO</b> 7.5 mg/kg/dose TID (max 500 mg/dose) x10 days or</li> <li>○ <b>Vancomycin PO</b> 10 mg/kg/dose QID (max 125 mg/dose for non-severe infection; max 500 mg/dose for severe and fulminant infection) x10 days</li> </ul> </li> <li>• If ≥18 years old:             <ul style="list-style-type: none"> <li>○ Preferred: <b>Fidaxomicin</b> 200 mg/dose BID x10 days</li> <li>○ Alternative: <b>Vancomycin PO</b> (max 125 mg/dose for non-severe infection; max 500 mg/dose for severe and fulminant infection) x10 days</li> </ul> </li> </ul> <p><b>If second or more recurrence:</b></p> <ul style="list-style-type: none"> <li>• Consult GI and Infectious Diseases</li> <li>• If &lt;18 years old:             <ul style="list-style-type: none"> <li>○ Begin <b>Vancomycin with taper:</b> Vancomycin PO 10 mg/kg/dose QID (max 125 mg/dose for non-severe/severe infection, max 500 mg/dose for fulminant infection) x10 days <i>followed by taper</i> <ul style="list-style-type: none"> <li>▪ <i>Example of a vancomycin taper:</i> <ul style="list-style-type: none"> <li>• Vancomycin PO 10 mg/kg/dose (max 125 mg/dose) BID x7 days <i>followed by</i></li> <li>• Vancomycin PO 10 mg/kg/dose (max 125 mg/dose) once daily for 7 days <i>followed by</i></li> <li>• Vancomycin PO 10 mg/kg/dose (max 125 mg/dose) every 2-3 days for 2-8 weeks as directed by GI</li> </ul> </li> </ul> </li> </ul> </li> <li>• If ≥18 years old:             <ul style="list-style-type: none"> <li>○ Preferred: <b>Fidaxomicin</b> 200 mg/dose BID x10 days</li> </ul> </li> <li>• If failure with above:             <ul style="list-style-type: none"> <li>○ Consider options such as vancomycin + rifaximin, vancomycin + nitazoxanide, fidaxomicin, or fecal microbiota transplantation in consultation with GI and ID</li> </ul> </li> </ul>
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**Discharge Criteria:** clinically stable, cleared by GI (and surgery/Infectious Diseases, if involved), ensure availability and insurance coverage of medication prior to discharge  
**Discharge Instructions:** follow up with PCP and/or GI (if involved in hospitalization)

Place on Contact Precautions. Only send *C. difficile* testing if criteria met (see below).

**Clinical Evaluation:**

- When evaluating for possible *C. difficile* infection, note the age of the patient, number of liquid stools in the last 24 hours, presence of risk factors for *C. difficile* infection, relevant symptoms (e.g., abdominal pain, cramps, fever), vitals, WBC, and presence of tube feedings
- Vomiting is not characteristic of *C. difficile* infection and may signify an alternative diagnosis (e.g., viral gastroenteritis)
- Studies have shown that there is no characteristic odor of stool from patients with *C. difficile*

**Considerations for testing for *C. difficile*:**

- **<1 years of age:** Represents colonization
  - DO NOT test; treating for *C. difficile* is not indicated
- **1-2 years of age:** High likelihood of colonization; in rare circumstances, *C. difficile* infection may be possible – consider consulting Infectious Diseases
  - Evaluate/empirically treat for other infectious/non-infectious causes before testing for *C. difficile*
    - Add fiber to the formula of tube-fed patients
    - Stop medications associated with diarrhea (see [Appendix A](#)); laxatives/stool softeners should be stopped at least 48 hours prior to testing
- **>2 years of age:**
  - Test ONLY if patient has not received laxatives or other medications associated with diarrhea (or diarrhea persists after 48 hours of stopping the medication) AND if no alternative reason for diarrhea exists (see [Appendix A](#) for examples of medications)



- There are specific criteria for testing.
- Asymptomatic intestinal colonization with *C. difficile* is very common in children less than 2 years of age.
- In those <1 year of age, up to 50% of healthy infants are colonized.
- For those 1-2 years of age, it is rare that *C. difficile* infection is present. Consult ID to help determine if testing is appropriate.
- It is important to evaluate for other causes for diarrhea. Appendix A lists medications that can cause diarrhea.

**Examples of Medications That Can Cause Diarrhea**

- Laxatives:
  - Lactulose, bisacodyl, magnesium citrate, docusate, Go-lytely, Senna, polyethylene glycol, sorbitol, etc.
- Enemas and suppositories
- Others:
  - Kayexalate
  - Colchicine
  - Octreotide
  - Metformin and other diabetic medications
  - Antibiotics
  - Antineoplastics
  - Magnesium containing antacids

Place on Contact Precautions. Only send *C. difficile* testing if criteria met (see below).

**Clinical Evaluation:**

- When evaluating for possible *C. difficile* infection, note the age of the patient, number of liquid stools in the last 24 hours, presence of risk factors for *C. difficile* infection, relevant symptoms (e.g., abdominal pain, cramps, fever), vitals, WBC, and presence of tube feedings
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  - Evaluate/empirically treat for other infectious/non-infectious causes before testing for *C. difficile*
    - Add fiber to the formula of tube-fed patients
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- **>2 years of age:**
  - Test ONLY if patient has not received laxatives or other medications associated with diarrhea (or diarrhea persists after 48 hours of stopping the medication) AND if no alternative reason for diarrhea exists (see [Appendix A](#) for examples of medications)



- For those that are over 2 years of age, colonization rates drop.
- It is important to consider potential alternative causes of diarrhea prior to testing for *C. difficile* infection.

**Examples of Medications That Can Cause Diarrhea**

- Laxatives:
  - Lactulose, bisacodyl, magnesium citrate, docusate, Go-lytely, Senna, polyethylene glycol, sorbitol, etc.
- Enemas and suppositories
- Others:
  - Kayexalate
  - Colchicine
  - Octreotide
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  - Antibiotics
  - Antineoplastics
  - Magnesium containing antacids



**Confirmed *C. difficile* infection:**

- Testing algorithms may differ by lab – refer to the individual lab interpretation of results to determine if *C. difficile* infection exists [the test must include a positive toxin assay: PCR and/or enzyme assay (e.g., EIA)].
- Repeat testing of the same episode is NOT recommended.

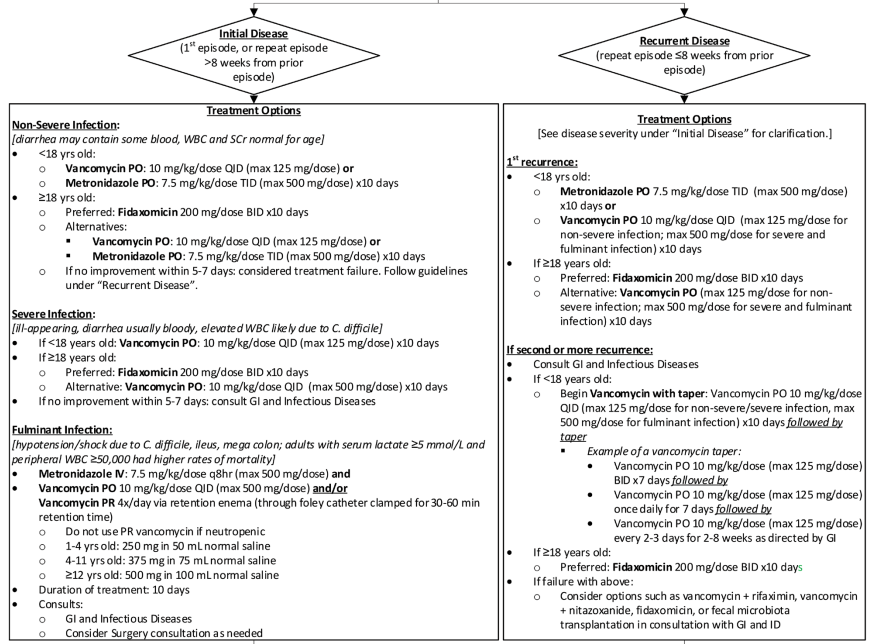
- Testing algorithms for *C. difficile* differ by the lab. The test will include a positive toxin assay.
- Each lab will interpret their results.
- Note that repeat testing of the same episode is not recommended. There is a high risk for false-positive results. In addition, the lab will not process another stool sample for *C. diff* if it was sent within 14 days of a previously positive test.
  - However, if there is a recurrence of symptoms following successful treatment (and diarrhea has stopped), then repeat testing is indicated.

**Initial Disease Criteria:**

- Vomiting is not characteristic of *C. difficile* infection and may signify an alternative diagnosis (e.g., viral gastroenteritis)
- Studies have shown that there is no characteristic odor of stool from patients with *C. difficile*
- **Considerations for testing for *C. difficile*:**
  - DO NOT test; testing for *C. difficile* is not indicated
  - **<1 years of age:** Represents colonization
  - **1-2 years of age:** High likelihood of colonization; in rare circumstances, *C. difficile* infection may be possible – consider consulting Infectious Diseases
  - Evaluate/empirically treat for other infectious/non-infectious causes before testing for *C. difficile*
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- **>2 years of age:**
  - Test ONLY if patient has not received laxatives or other medications associated with diarrhea (or diarrhea persists after 48 hours of stopping the medication) AND if no alternative reason for diarrhea exists (see Appendix A for examples of medications)

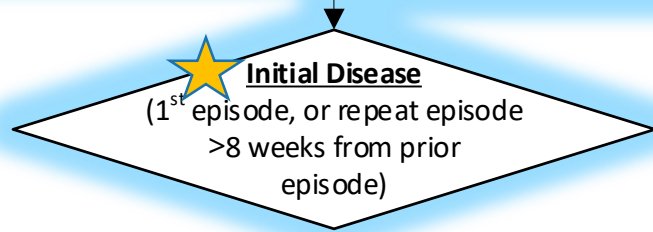
**Confirmed *C. difficile* infection:**

- Testing algorithms may differ by lab – refer to the individual lab interpretation of results to determine if *C. difficile* infection exists [the test must include a positive toxin assay: PCR and/or enzyme assay (e.g., EIA)].
- Repeat testing of the same episode is NOT recommended.



**Confirmed *C. difficile* infection:**

- Testing algorithms may differ by lab – refer to the individual lab interpretation of results to determine if *C. difficile* infection exists [the test must include a positive toxin assay: PCR and/or enzyme assay (e.g., EIA)].
- Repeat testing of the same episode is NOT recommended.



**Recurrent Disease**  
(repeat episode ≤8 weeks from prior  
episode)

**Clinical Evaluation:**

- When evaluating for possible *C. difficile* infection, note the age of the patient, number of liquid stools in the last 24 hours, presence of risk factors for *C. difficile* infection, relevant symptoms (e.g., abdominal pain, cramps, fever), vitals, WBC, and presence of tube feedings
- Vomiting is not characteristic of *C. difficile* infection and may signify an alternative diagnosis (e.g., viral gastroenteritis)
- Studies have shown that there is no characteristic odor of stool from patients with *C. difficile*

**Considerations for testing for *C. difficile*:**

- <1 years of age: Represents colonization
- DO NOT test; treating for *C. difficile* is not indicated
- 1-2 years of age: High likelihood of colonization; in rare cases, may be associated with *C. difficile* infection
- Evaluate/empirically treat for other infectious diseases
  - Add fiber to the formula
  - Stop medications
- >2 years of age:
  - Test ONLY if patient has not received laxatives (see [Laxative Use in Children](#))
  - AND if no alternative reason for diarrhea exists (see [Diarrhea in Children](#))

- Treatment varies by how many episodes of *C. difficile* infection the patient has had.
- “Initial disease” are patients who are experiencing their first infection, or it is a repeat episode that happened more than 8 weeks after a prior episode (these do not represent “recurrent” disease).
- “Recurrent disease” are patients who are experiencing a repeat infection 8 or less weeks apart from another prior infection.

**Confirmed *C. difficile* infection:**

- Testing algorithms may differ by lab – refer to the individual lab interpretation of results to determine if *C. difficile* infection exists [the test must include a positive toxin assay: PCR and/or enzyme assay (e.g., EIA)].
- Repeat testing of the same episode is NOT recommended.

**Initial Disease**  
(1<sup>st</sup> episode, or repeat episode  
>8 weeks from prior  
episode)

**Recurrent Disease**  
(repeat episode ≤8 weeks from prior  
episode)

**Treatment Options**

Under “Initial Disease” for clarification.]

**Vancomycin** 7.5 mg/kg/dose TID (max 500 mg/dose)

**Fidaxomicin** 10 mg/kg/dose QID (max 125 mg/dose for non-severe infection; max 500 mg/dose for severe and fulminant infection) x10 days

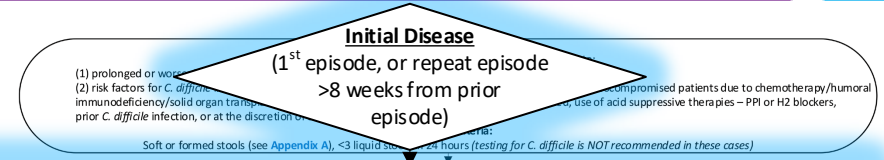
**Vancomycin** 200 mg/dose BID x10 days

**Vancomycin PO** (max 125 mg/dose for non-severe infection; max 500 mg/dose for severe and fulminant infection) x10 days

**Discharge Criteria:** clinically stable, cleared by GI (and surgery/Infectious Diseases, if involved), ensure availability and insurance coverage of medication prior to discharge

**Discharge Instructions:** follow up with PCP and/or GI (if involved in hospitalization)

Treatment is further divided by severity of infection. Definitions for each category are provided.



**Treatment Options**

**Non-Severe Infection:**

*[diarrhea may contain some blood, WBC and Scr normal for age]*

- <18 yrs old:
  - **Vancomycin PO:** 10 mg/kg/dose QID (max 125 mg/dose) **or**
  - **Metronidazole PO:** 7.5 mg/kg/dose TID (max 500 mg/dose) x10 days
- ≥18 yrs old:
  - Preferred: **Fidaxomicin** 200 mg/dose BID x10 days
  - Alternatives:
    - **Vancomycin PO:** 10 mg/kg/dose QID (max 125 mg/dose) **or**
    - **Metronidazole PO:** 7.5 mg/kg/dose TID (max 500 mg/dose) x10 days
  - If no improvement within 5-7 days: considered treatment failure. Follow guidelines under “Recurrent Disease”.

**Severe Infection:**

*[ill-appearing, diarrhea usually bloody, elevated WBC likely due to *C. difficile*]*

- If <18 years old: **Vancomycin PO:** 10 mg/kg/dose QID (max 125 mg/dose) x10 days
- If ≥18 years old:
  - Preferred: **Fidaxomicin** 200 mg/dose BID x10 days
  - Alternative: **Vancomycin PO:** 10 mg/kg/dose QID (max 500 mg/dose) x10 days
- If no improvement within 5-7 days: consult GI and Infectious Diseases

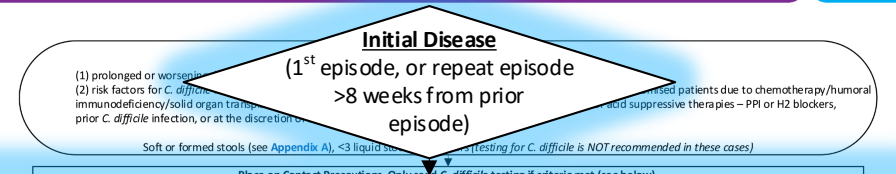
**Fulminant Infection:**

*[hypotension/shock due to *C. difficile*, ileus, mega colon; adults with serum lactate ≥5 mmol/L and peripheral WBC ≥50,000 had higher rates of mortality]*

- **Metronidazole IV:** 7.5 mg/kg/dose q8hr (max 500 mg/dose) **and**
- **Vancomycin PO** 10 mg/kg/dose QID (max 500 mg/dose) **and/or**  
**Vancomycin PR** 4x/day via retention enema (through foley catheter clamped for 30-60 min retention time)
  - Do not use PR vancomycin if neutropenic
  - 1-4 yrs old: 250 mg in 50 mL normal saline
  - 4-11 yrs old: 375 mg in 75 mL normal saline
  - ≥12 yrs old: 500 mg in 100 mL normal saline
- Duration of treatment: 10 days
- Consults:
  - GI and Infectious Diseases
  - Consider Surgery consultation as needed

## Non-severe and severe infection:

- Vancomycin or metronidazole can be used as first line agents for those less than 18 years of age.
  - Some studies have shown vancomycin PO to be superior to metronidazole PO.
  - As such, although metronidazole can be used in non-severe infection, it is not preferred for severe infections.
- Updated 2021 IDSA guidelines (for adults with *C. difficile* infection) recommend fidaxomicin as a first line agent for those 18 years and older.
  - In this age group, fidaxomicin has been shown to have superior outcomes than PO vancomycin.
- Duration of treatment is typically 10 days based on available randomized trials.



**Treatment Options**

**Non-Severe Infection:**  
*[diarrhea may contain some blood, WBC and SCr normal for age]*

- <18 yrs old:
  - **Vancomycin PO:** 10 mg/kg/dose QID (max 125 mg/dose) **or**
  - **Metronidazole PO:** 7.5 mg/kg/dose TID (max 500 mg/dose) x10 days
- ≥18 yrs old:
  - Preferred: **Fidaxomicin** 200 mg/dose BID x10 days
  - Alternatives:
    - **Vancomycin PO:** 10 mg/kg/dose QID (max 125 mg/dose) **or**
    - **Metronidazole PO:** 7.5 mg/kg/dose TID (max 500 mg/dose) x10 days
  - If no improvement within 5-7 days: considered treatment failure. Follow guidelines under “Recurrent Disease”.

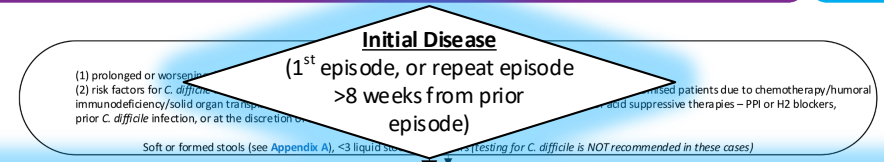
**Severe Infection:**  
*[ill-appearing, diarrhea usually bloody, elevated WBC likely due to C. difficile]*

- If <18 years old: **Vancomycin PO:** 10 mg/kg/dose QID (max 125 mg/dose) x10 days
- If ≥18 years old:
  - Preferred: **Fidaxomicin** 200 mg/dose BID x10 days
  - Alternative: **Vancomycin PO:** 10 mg/kg/dose QID (max 500 mg/dose) x10 days
- If no improvement within 5-7 days: consult GI and Infectious Diseases

**Fulminant Infection:**  
*[hypotension/shock due to C. difficile, ileus, mega colon; adults with serum lactate ≥5 mmol/L and peripheral WBC ≥50,000 had higher rates of mortality]*

- **Metronidazole IV:** 7.5 mg/kg/dose q8hr (max 500 mg/dose) **and**
- **Vancomycin PO** 10 mg/kg/dose QID (max 500 mg/dose) **and/or**  
**Vancomycin PR** 4x/day via retention enema (through foley catheter clamped for 30-60 min retention time)
  - Do not use PR vancomycin if neutropenic
  - 1-4 yrs old: 250 mg in 50 mL normal saline
  - 4-11 yrs old: 375 mg in 75 mL normal saline
  - ≥12 yrs old: 500 mg in 100 mL normal saline
- Duration of treatment: 10 days
- Consults:
  - GI and Infectious Diseases
  - Consider Surgery consultation as needed





**Treatment Options**

**Non-Severe Infection:**

*[diarrhea may contain some blood, WBC and SCr normal for age]*

- <18 yrs old:
  - **Vancomycin PO:** 10 mg/kg/dose QID (max 125 mg/dose) **or**
  - **Metronidazole PO:** 7.5 mg/kg/dose TID (max 500 mg/dose) x10 days
- ≥18 yrs old:
  - Preferred: **Fidaxomicin** 200 mg/dose BID x10 days
  - Alternatives:
    - **Vancomycin PO:** 10 mg/kg/dose QID (max 125 mg/dose) **or**
    - **Metronidazole PO:** 7.5 mg/kg/dose TID (max 500 mg/dose) x10 days
  - If no improvement within 5-7 days: considered treatment failure. Follow guidelines under “Recurrent Disease”.

**Severe Infection:**

*[ill-appearing, diarrhea usually bloody, elevated WBC likely due to *C. difficile*]*

- If <18 years old: **Vancomycin PO:** 10 mg/kg/dose QID (max 125 mg/dose) x10 days
- If ≥18 years old:
  - Preferred: **Fidaxomicin** 200 mg/dose BID x10 days
  - Alternative: **Vancomycin PO:** 10 mg/kg/dose QID (max 500 mg/dose) x10 days
- If no improvement within 5-7 days: consult GI and Infectious Diseases

**Fulminant Infection:**

*[hypotension/shock due to *C. difficile*, ileus, mega colon; adults with serum lactate ≥5 mmol/L and peripheral WBC ≥50,000 had higher rates of mortality]*

- **Metronidazole IV:** 7.5 mg/kg/dose q8hr (max 500 mg/dose) **and**
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  - Do not use PR vancomycin if neutropenic
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  - 4-11 yrs old: 375 mg in 75 mL normal saline
  - ≥12 yrs old: 500 mg in 100 mL normal saline
- Duration of treatment: 10 days
- Consults:
  - GI and Infectious Diseases
  - Consider Surgery consultation as needed



**Fulminant infection:**

- IDSA guidelines recommend vancomycin PO and/or PR as well as metronidazole IV. Addition of metronidazole IV is important to achieve therapeutic concentrations in an inflamed colon.
- A high lactate or WBC is associated with a high mortality and may be a candidate for surgical intervention.



**Recurrent Disease**  
(repeat episode ≤8 weeks from prior episode)

(1) prolonged or worsening diarrhea (at least 3 unformed stools per day) for ≥2 days  
(2) risk factors for *C. difficile* infection (antibiotics in prior 2 months, immunocompromised patients due to chemotherapy/humoral immunodeficiency/solid organ transplant, chronic inflammatory bowel disease, use of acid suppressive therapies – PPI or H2 blockers, prior *C. difficile* infection, or at the discretion of the provider)

Exclusion criteria:

**Treatment Options**

[See disease severity under “Initial Disease” for clarification.]

**1<sup>st</sup> recurrence:**

- <18 yrs old:
  - **Metronidazole PO** 7.5 mg/kg/dose TID (max 500 mg/dose) x10 days **or**
  - **Vancomycin PO** 10 mg/kg/dose QID (max 125 mg/dose for non-severe infection; max 500 mg/dose for severe and fulminant infection) x10 days
- If ≥18 years old:
  - Preferred: **Fidaxomicin** 200 mg/dose BID x10 days
  - Alternative: **Vancomycin PO** (max 125 mg/dose for non-severe infection; max 500 mg/dose for severe and fulminant infection) x10 days

**If second or more recurrence:**

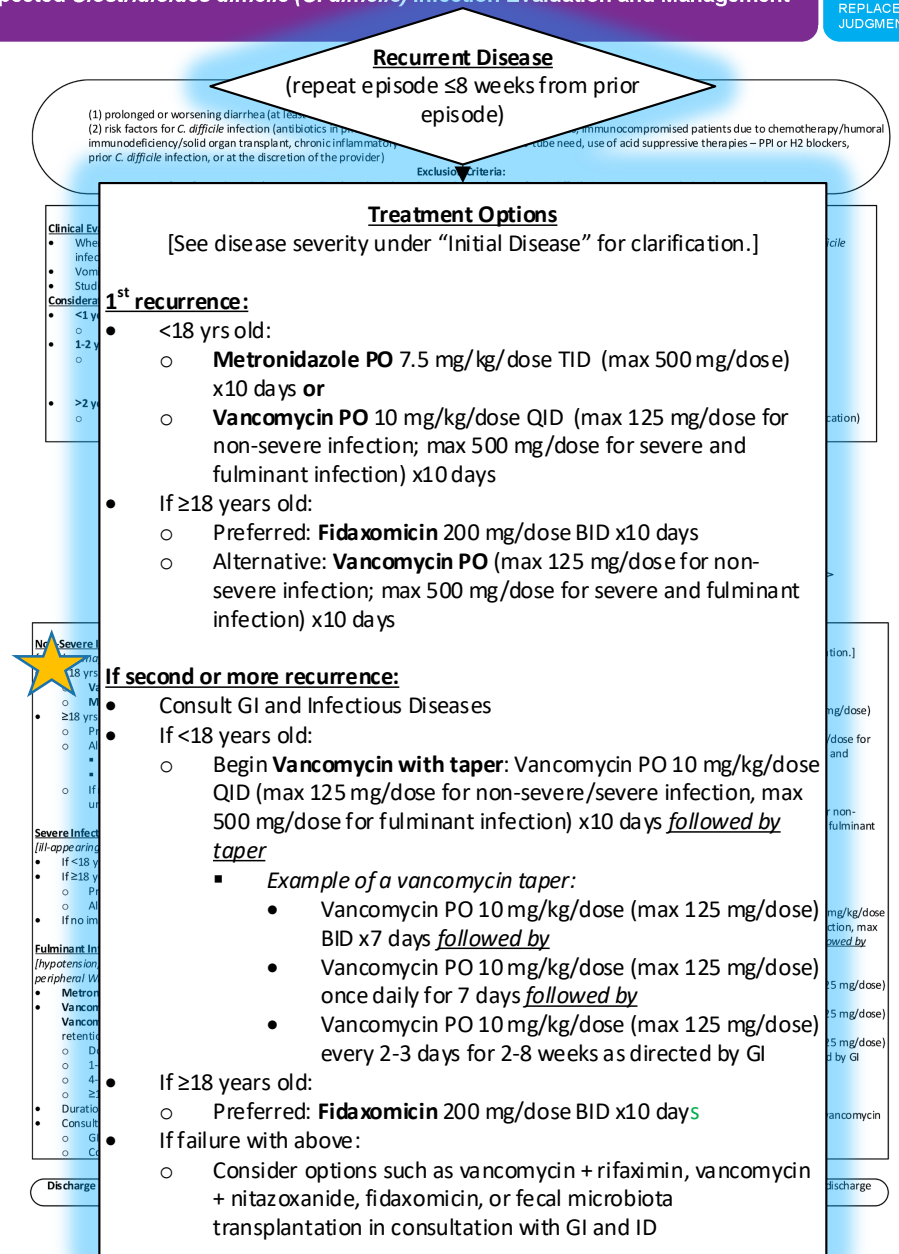
- Consult GI and Infectious Diseases
- If <18 years old:
  - Begin **Vancomycin with taper**: Vancomycin PO 10 mg/kg/dose QID (max 125 mg/dose for non-severe/severe infection, max 500 mg/dose for fulminant infection) x10 days ***followed by taper***
    - **Example of a vancomycin taper:**
      - Vancomycin PO 10 mg/kg/dose (max 125 mg/dose) BID x7 days ***followed by***
      - Vancomycin PO 10 mg/kg/dose (max 125 mg/dose) once daily for 7 days ***followed by***
      - Vancomycin PO 10 mg/kg/dose (max 125 mg/dose) every 2-3 days for 2-8 weeks as directed by GI
- If ≥18 years old:
  - Preferred: **Fidaxomicin** 200 mg/dose BID x10 days
- If failure with above:
  - Consider options such as vancomycin + rifaximin, vancomycin + nitazoxanide, fidaxomicin, or fecal microbiota transplantation in consultation with GI and ID

1<sup>st</sup> Recurrence:

- 1<sup>st</sup> recurrence of an episode can be treated with oral vancomycin (or oral metronidazole, particularly if it was not used for the initial episode)
  - At this time, there is little data to support vancomycin over metronidazole. The IDSA recommends either for the younger population.
- Fidaxomicin remains a preferred option for those who are 18 years of age and older.

## 2<sup>nd</sup> or more Recurrence:

- For second or more recurrences, vancomycin should be given in a tapered regimen. The goal of a tapered regimen is that vegetative forms will be controlled by restoring the normal microbiota.
- Metronidazole is not recommended as studies in adults have showed response rates are inferior to vancomycin and prolonged use can potentially cause neurotoxicity.
- Again, fidaxomicin is recommended for the older patients.
- If there is failure after these management plans, other options can be considered in consultation with GI and ID.
  - Current robust studies evaluating the benefit of fecal microbiota transplantation in pediatrics are lacking, although it has shown good results in adults. Case reports have shown that it could be effective in treating recurrent infections.



**Discharge Criteria:** clinically stable, cleared by GI (and surgery/Infectious Diseases, if involved), ensure availability and insurance coverage of medication prior to discharge

**Discharge Instructions:** follow up with PCP and/or GI (if involved in hospitalization)

When considering discharge, providers should ensure any discharge medications are ordered and available prior to discharge as PO vancomycin in particular is difficult to find on an outpatient basis.

- Consider bedside delivery when possible

**Inclusion Criteria:**  
Suspected *Clostridioides difficile* (*C. difficile*) infection due to:  
(1) prolonged or worsening diarrhea (at least 3 liquid stools in 24 hours; see Appendix A) AND  
(2) risk factors for *C. difficile* infection (antibiotics in prior 3 months, hospitalization in prior 3 months, immunocompromised patients due to chemotherapy/humoral immunodeficiency, recent contact with nursing home, contact with a health care facility, contact with a long-term care facility, contact with a hospital, contact with a dialysis center, contact with a laboratory, contact with a pharmacy, contact with a transfusion center, contact with a surgical center, contact with a transplant center, contact with a dialysis center, contact with a laboratory, contact with a pharmacy, contact with a transfusion center, contact with a surgical center, contact with a transplant center)

**Clinical Evaluation:**

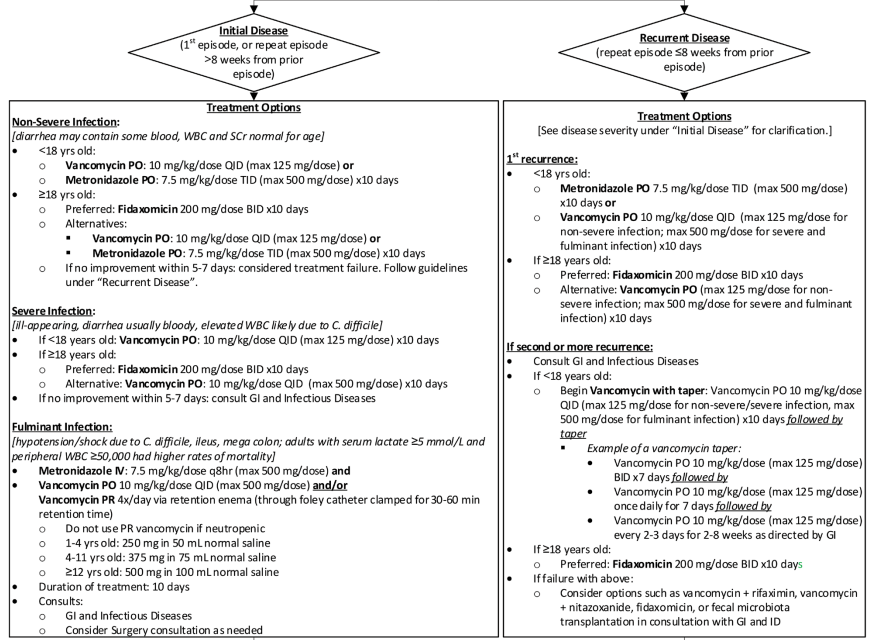
- When evaluating for possible *C. difficile* infection, note the age of the patient, number of liquid stools in the last 24 hours, presence of risk factors for *C. difficile* infection, relevant symptoms (e.g., abdominal pain, cramps, fever), vitals, WBC, and presence of tube feedings
- Vomiting is not characteristic of *C. difficile* infection and may signify an alternative diagnosis (e.g., viral gastroenteritis)
- Studies have shown that there is no characteristic odor of stool from patients with *C. difficile*

**Considerations for testing for *C. difficile*:**

- <1 years of age: Represents colonization
  - DO NOT test; treating for *C. difficile* is not indicated
- 1-2 years of age: High likelihood of colonization; in rare circumstances, *C. difficile* infection may be possible – consider consulting Infectious Diseases
  - Evaluate/empirically treat for other infectious/non-infectious causes before testing for *C. difficile*
    - Add fiber to the formula of tube-fed patients
    - Stop medications associated with diarrhea (see Appendix A); laxatives/stool softeners should be stopped at least 48 hours prior to testing
- >2 years of age:
  - Test ONLY if patient has not received laxatives or other medications associated with diarrhea (or diarrhea persists after 48 hours of stopping the medication) AND if no alternative reason for diarrhea exists (see Appendix A for examples of medications)

**Confirmed *C. difficile* infection:**

- Testing algorithms may differ by lab – refer to the individual lab interpretation of results to determine if *C. difficile* infection exists [the test must include a positive toxin assay: PCR and/or enzyme assay (e.g., EIA)].
- Repeat testing of the same episode is NOT recommended.



# Review of Key Points

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- Testing for *C. diff* infection is appropriate for patients over the age of 1 year with 3 or more episodes of liquid stool in 24 hours, plus risk factors for *C. diff* infection
  - Follow guidelines for children aged 1-2 years.
- *C. diff* testing interpretation depends on the lab.
- Treatment of *C. diff* is based on the number of previous infections and the severity of infection.
- Vancomycin PO can be difficult to obtain on an outpatient basis, providers should ensure medication is available in hand prior to discharge home.

# Quality Metrics

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- Percentage of patients with order set usage
- Percentage of patients with appropriate testing for diagnosis of *C. difficile* infection
- Percentage of patients receiving recommended antibiotics based on severity
- Average duration of treatment
- Average length of stay
- Percentage of patients with relapses within 30 days
- Percentage of patients who required medication escalation
- Percentage of patients who required escalation to fecal microbiota transplantation

# References



- [Clinical Practice Guidelines for \*Clostridium difficile\* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America \(IDSA\) and Society for Healthcare Epidemiology of America \(SHEA\)](#). *Clin Infect Dis*. 2018.
- Kimberlin DW, Banerjee R, Barnett ED, Lynfield R, Sawyer MH. “*Clostridioides difficile*”. *Red Book: 2024-2027 Report of the Committee on Infectious Diseases*. 2024.
- Surawicz CM, Brandt LJ, Binion DG, Ananthakrishnan AN, Cury SR, Gilligan PH, McFarland LV, Mellow M, Zuckerbraun BS. [Guidelines for Diagnosis, Treatment, and Prevention for \*Clostridium difficile\* Infections](#). *Am J Gastroenterol*. 2013; 108:478-498
- Schutze GE, Willoughby RE; Committee on Infectious Diseases; American Academy of Pediatrics. [Clostridium difficile infection in infants and children](#). *Pediatrics*. 2013; 131:196-200.

# Pathway Contacts

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- Peter Townsend, MD
  - CT Children's Gastroenterology Division
- Grace Hong, APRN
  - Infectious Disease and Immunology Division
- Jennifer Giroto, PharmD, BCPPS, BCIDP
  - Antimicrobial Stewardship Program

# Thank You!



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## **About Connecticut Children's Pathways Program**

Clinical pathways guide the management of patients to optimize consistent use of evidence-based practice. Clinical pathways have been shown to improve guideline adherence and quality outcomes, while decreasing length of stay and cost. Here at Connecticut Children's, our Clinical Pathways Program aims to deliver evidence-based, high value care to the greatest number of children in a diversity of patient settings.

These pathways serve as a guide for providers and do not replace clinical judgment.