

# Assessment and Management of *Clostridioides difficile* Infections (CDI)

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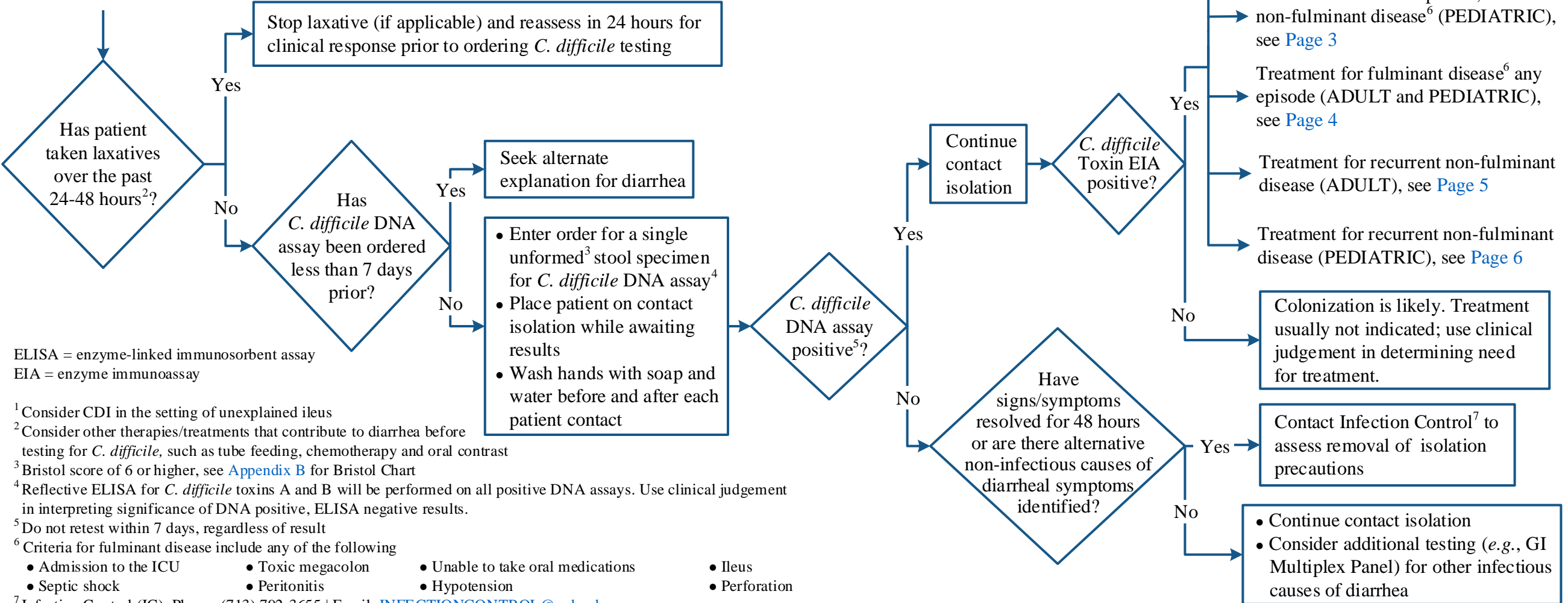
**Note:** Avoid use of unnecessary antibiotics. See [Appendix A: Supportive Care Considerations](#).

## PRESENTATION

## ASSESSMENT

## INTERVENTION

Patient with 3 unformed stools in last 24 hours<sup>1</sup>



ELISA = enzyme-linked immunosorbent assay  
 EIA = enzyme immunoassay

<sup>1</sup> Consider CDI in the setting of unexplained ileus  
<sup>2</sup> Consider other therapies/treatments that contribute to diarrhea before testing for *C. difficile*, such as tube feeding, chemotherapy and oral contrast  
<sup>3</sup> Bristol score of 6 or higher, see [Appendix B](#) for Bristol Chart  
<sup>4</sup> Reflective ELISA for *C. difficile* toxins A and B will be performed on all positive DNA assays. Use clinical judgement in interpreting significance of DNA positive, ELISA negative results.  
<sup>5</sup> Do not retest within 7 days, regardless of result  
<sup>6</sup> Criteria for fulminant disease include any of the following

• Admission to the ICU	• Toxic megacolon	• Unable to take oral medications	• Ileus
• Septic shock	• Peritonitis	• Hypotension	• Perforation

<sup>7</sup> Infection Control (IC): Phone: (713) 792-3655 | Email: [INFECTIONCONTROL@mdanderson.org](mailto:INFECTIONCONTROL@mdanderson.org)

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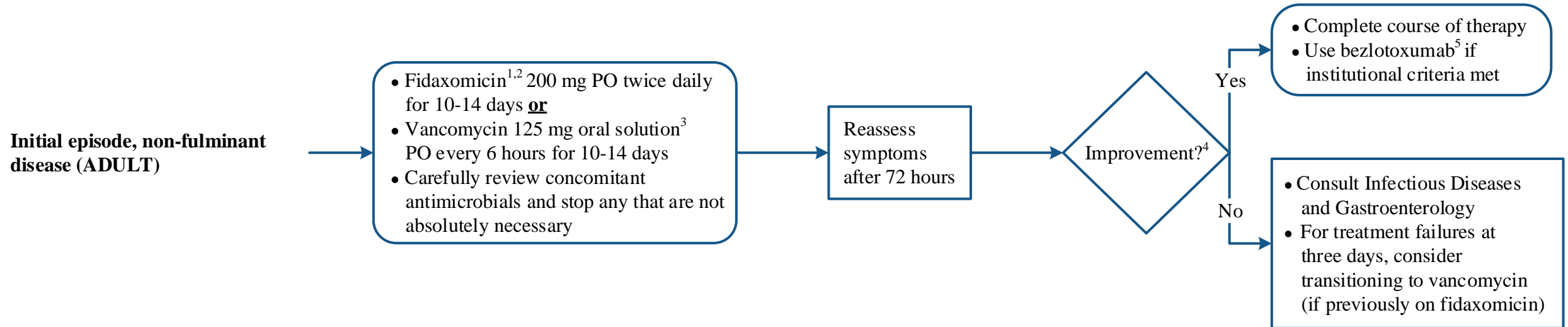
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**Note:** Avoid use of unnecessary antibiotics. See [Appendix A](#): Supportive Care Considerations.

## DISEASE SEVERITY (ADULT)

## TREATMENT

## REASSESSMENT



**Note:** Metronidazole is no longer recommended for treatment of uncomplicated CDI except as an IV adjuvant for fulminant disease or if above agents are not available

<sup>1</sup> Fidaxomicin is preferred over vancomycin for sustained clinical response (fewer recurrences). Consider fidaxomicin if patient is on concomitant systemic antibiotics.

<sup>2</sup> As of April 2022, only the tablet dosage form is available at the inpatient MDACC Pharmacy Formulary. Upon discharge, if fidaxomicin is unobtainable, it is reasonable to complete therapy with vancomycin PO.

<sup>3</sup> May substitute with capsules if oral solution not available

<sup>4</sup> Improvement is defined as a decrease in the number of unformed stools by 50% with hemodynamic stability

<sup>5</sup> Refer to [Appendix C](#) for institutional use criteria

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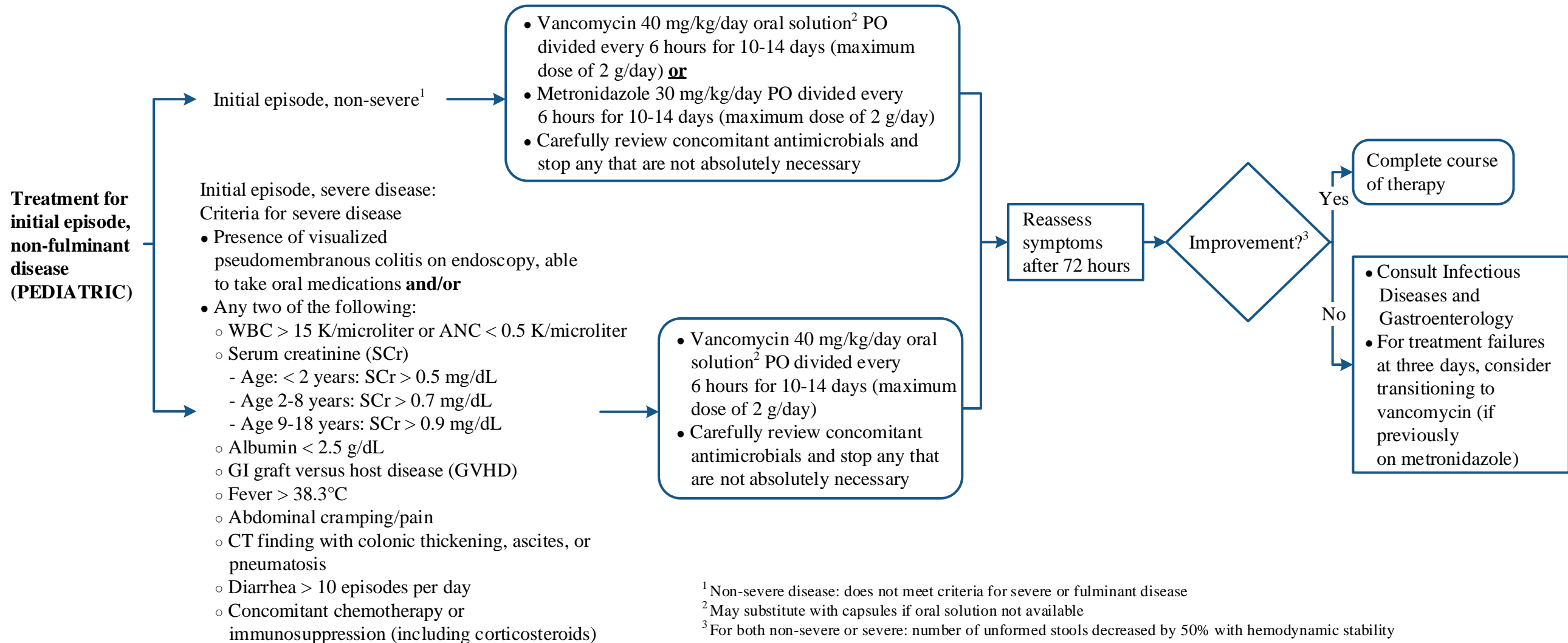
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## DISEASE SEVERITY (PEDIATRIC)

## TREATMENT

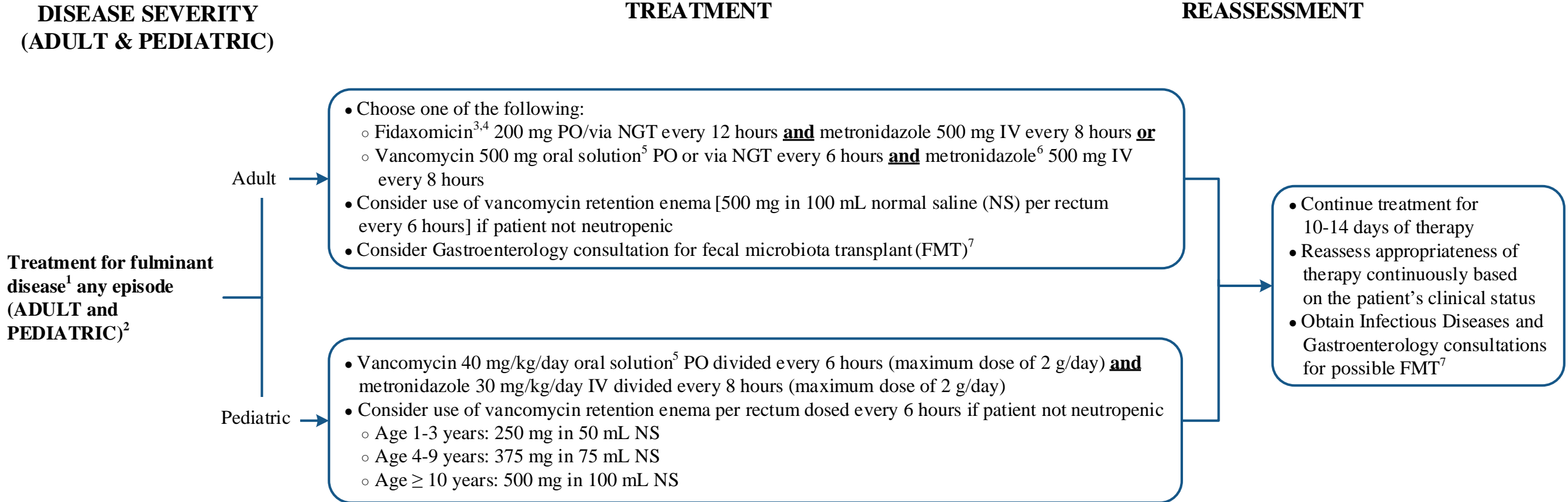
## REASSESSMENT



# Assessment and Management of *Clostridioides difficile* Infections (CDI)

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**Note:** Avoid use of unnecessary antibiotics. See [Appendix A: Supportive Care Considerations](#).



<sup>1</sup> Criteria for fulminant disease include any of the following

- Admission to the ICU
- Toxic megacolon
- Unable to take oral medications
- Ileus
- Septic shock
- Peritonitis
- Hypotension
- Perforation

<sup>2</sup> Consider consulting Surgery, Infectious Diseases, and Gastroenterology

<sup>3</sup> Fidaxomicin is preferred over vancomycin for sustained clinical response (fewer recurrences)

<sup>4</sup> As of April 2022, only the tablet dosage form is available at the inpatient MDACC Pharmacy Formulary. Upon discharge, if fidaxomicin is unobtainable, it is reasonable to complete therapy with vancomycin PO.

<sup>5</sup> May substitute with capsules if oral solution not available

<sup>6</sup> Metronidazole is no longer recommended for treatment of uncomplicated CDI except as an IV adjuvant for fulminant disease or if above agents are not available

<sup>7</sup> Refer to [Appendix D](#) for fecal microbiota transplant indications

# Assessment and Management of *Clostridioides difficile* Infections (CDI)

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**Note:** Avoid use of unnecessary antibiotics. See [Appendix A](#): Supportive Care Considerations.

## RECURRENCE<sup>1</sup> (ADULT)

## TREATMENT

**Treatment for recurrent non-fulminant disease (ADULT):**  
 Diarrhea due to CDI (patient must have completed 10-14 days of effective therapy and have no symptoms for 48 hours after treatment has ended)

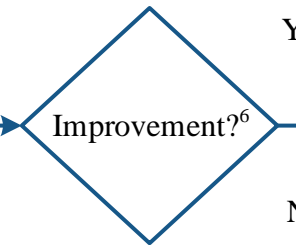
First recurrence

- If metronidazole was used for the initial episode: Vancomycin 125 mg oral solution<sup>2</sup> PO every 6 hours for 10-14 days
  - If vancomycin or metronidazole was used for the initial episode: Fidaxomicin<sup>3,4</sup> 200 mg PO twice daily for 10-14 days
  - If vancomycin or fidaxomicin was used for the first episode: Vancomycin tapering/pulse treatment
    - 125 mg oral solution<sup>2</sup> PO every 6 hours for 14 days, then every 12 hours for 7 days, then once daily for 7 days, then every other day for 4 doses, then every third day for 5 doses, then off
  - Some patients may require chronic suppression thereafter
- Bezlotoxumab:
- For all regimens, use bezlotoxumab<sup>5</sup> if institutional criteria are met and not previously administered

Second and subsequent recurrences

See [Page 7](#)

Reassess symptoms after 72 hours



Consider fecal microbiota transplant (FMT)<sup>7,8</sup> if first two episodes were associated with hospitalization or significant morbidity

Consider Infectious Diseases and Gastroenterology consultations for additional work up and possible FMT<sup>7,8</sup>

<sup>1</sup> Refer to [Appendix E](#) for prevention considerations

<sup>2</sup> May substitute with capsules if oral solution not available

<sup>3</sup> Fidaxomicin is preferred over vancomycin for sustained clinical response (fewer recurrences)

<sup>4</sup> As of April 2022, only the tablet dosage form is available at the inpatient MDACC Pharmacy Formulary. Upon discharge, if fidaxomicin is unobtainable, it is reasonable to complete therapy with vancomycin PO.

<sup>5</sup> Refer to [Appendix C](#) for institutional use criteria

<sup>6</sup> Improvement is defined as a decrease in the number of unformed stools by 50% with hemodynamic stability

<sup>7</sup> Refer to [Appendix D](#) for fecal microbiota transplant indications

<sup>8</sup> Refer to Infectious Disease Clinic at (713) 792-2340 or Gastroenterology at (713) 794-5073

# Assessment and Management of *Clostridioides difficile* Infections (CDI)

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**Note:** Avoid use of unnecessary antibiotics. See [Appendix A: Supportive Care Considerations](#).

## RECURRENCE<sup>1</sup> (PEDIATRIC)

## TREATMENT

### Treatment for recurrent non-fulminant disease (PEDIATRIC)

First recurrence

- If metronidazole or fidaxomicin was used for the initial episode:  
 Vancomycin 40 mg/kg/day oral solution<sup>2</sup> PO divided every 6 hours for 10-14 days
- If vancomycin was used for the initial episode: Fidaxomicin<sup>3</sup>. Weight-based dosing for infants age  $\geq$  6 months to < 18 years: 16 mg/kg/dose PO twice daily for 10-14 days, maximum 200 mg/dose  
 Doses may be rounded as listed below:
  - Weight 4 to < 7 kg: 80 mg PO twice daily
  - Weight 7 to < 9 kg: 120 mg PO twice daily
  - Weight 9 to < 12.5 kg: 160 mg PO twice daily
  - Weight  $\geq$  12.5 kg: 200 mg PO twice daily
- If vancomycin or fidaxomicin was used for the initial episode: Vancomycin tapering/pulse treatment (for age < 18 years):
  - 10 mg/kg/dose oral solution<sup>2</sup> PO every 6 hours for 14 days, then every 12 hours for 7 days, then once daily for 7 days, then every other day for 4 doses, then every third day for 5 doses, then off

Second and subsequent recurrences

See [Page 7](#)

Reassess symptoms after 72 hours

Improvement?<sup>4</sup>

Yes

Consider fecal microbiota transplant (FMT)<sup>5,6</sup> if first two episodes were associated with hospitalization or significant morbidity

No

Consider Infectious Diseases and Gastroenterology consultations for additional work up and possible FMT<sup>5,6</sup>

<sup>1</sup> Refer to [Appendix E](#) for prevention considerations

<sup>2</sup> May substitute with capsules if oral solution not available

<sup>3</sup> As of April 2022, only the tablet dosage form is available at the inpatient MDACC Pharmacy Formulary. Upon discharge, if fidaxomicin is unobtainable, it is reasonable to complete therapy with vancomycin PO.

<sup>4</sup> Improvement is defined as a decrease in the number of unformed stools by 50% with hemodynamic stability

<sup>5</sup> Refer to [Appendix D](#) for fecal microbiota transplant indications

<sup>6</sup> Refer to Infectious Disease Clinic at (713) 792-2340, Pediatric Infectious Disease at (713) 792-6610 or Gastroenterology at (713) 794-5073

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**Note:** Avoid use of unnecessary antibiotics. See [Appendix A: Supportive Care Considerations](#).

## RECURRENCE<sup>1</sup> (ADULT & PEDIATRIC)

## TREATMENT

- If vancomycin or metronidazole was used for the most recent episode: Fidaxomicin<sup>3,4</sup> 200 mg PO twice daily for 10-14 days
- If metronidazole was used for the most recent episode: Vancomycin 125 mg oral solution<sup>5</sup> PO every 6 hours for 10-14 days
- If solid tumor patient or not immunocompromised: Fidaxomicin<sup>3,4,5</sup> 200 mg PO twice daily for 5 days, followed by once every other day for 20 days
- Vancomycin course followed by tapering/pulse treatment:
  - 125 mg oral solution<sup>6</sup> PO every 6 hours for 14 days, then every 12 hours for 7 days, then once daily for 7 days, and then every other day for 4 doses, then every third day for 10-14<sup>7</sup> doses, then off
- For all regimens, use bezlotoxumab<sup>8</sup> if institutional criteria met and not previously administered
- Consider FMT<sup>9,10</sup>

- If vancomycin was used for the most recent episode: Fidaxomicin<sup>4</sup> weight-based dosing for infants age ≥ 6 months to < 18 years: 16 mg/kg/dose PO twice daily for 10 -14 days, maximum 200 mg/dose. Doses may be rounded as listed below:
  - Weight 4 to < 7 kg: 80 mg PO twice daily
  - Weight 7 to < 9 kg: 120 mg PO twice daily
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  - Weight ≥ 12.5 kg: 200 mg twice PO daily
- If vancomycin or fidaxomicin was used for the most recent episode: Vancomycin tapering/pulse treatment (for age < 18 years)
  - 10 mg/kg/dose oral solution<sup>6</sup> PO every 6 hours for 14 days, then every 12 hours for 7 days, then once daily for 7 days, then every other day for 4 doses, then every third day for 10-14<sup>7</sup> doses, then off

Reassess symptoms after 72 hours

Improvement?<sup>11</sup>

Yes

Monitor recurrence<sup>12</sup>

- Consider alternate causes such as post-infectious diarrhea
- Consider FMT<sup>8,9</sup>
- Consider Infectious Disease consultation for recommendations for patients under consideration for chronic suppression therapy

No

Adult →  
 Second and subsequent recurrences<sup>2</sup> →  
 Pediatric →

<sup>1</sup> Refer to [Appendix E](#) for prevention considerations  
<sup>2</sup> Consider Infectious Disease consultation for recurrent CDI  
<sup>3</sup> Fidaxomicin is preferred over vancomycin for sustained clinical response (fewer recurrences).  
<sup>4</sup> As of April 2022, only the tablet dosage form is available at the inpatient MDACC Pharmacy Formulary. Upon discharge, if fidaxomicin is unobtainable, it is reasonable to complete therapy with vancomycin PO.  
<sup>5</sup> Consider extended therapy of fidaxomicin for patients on concomitant systemic antibiotics or age > 60 years  
<sup>6</sup> May substitute with capsules if oral solution not available  
<sup>7</sup> Duration depends on risk of recurrence (e.g., if receiving additional antibiotics, bridge to FMT, awaiting stem cell engraftment, etc.)  
<sup>8</sup> Refer to [Appendix C](#) for institutional use criteria  
<sup>9</sup> Refer to [Appendix D](#) for fecal microbiota transplant indications  
<sup>10</sup> Refer to Infectious Disease Clinic at (713) 792-2340 or Pediatric Infectious Disease at (713) 792-6610 or Gastroenterology at (713) 794-5073  
<sup>11</sup> Improvement is defined as a decrease in the number of unformed stools by 50% with hemodynamic stability  
<sup>12</sup> Consider continuing prophylaxis in selected patients and those awaiting FMT (consult Gastroenterology and Infectious Diseases)

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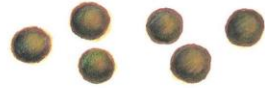






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## APPENDIX A: Supportive Care Considerations

- Clindamycin and fluoroquinolones are associated with the highest risk of CDI. Whenever possible, avoid these agents and all other unnecessary antibiotics, particularly those with anaerobic activity such as ampicillin/sulbactam, piperacillin/tazobactam, and carbapenems.
- Supportive care with hydration, avoidance of anti-motility agents, opiates and bile salts binding agents
- Probiotics are not recommended in cancer patients with CDI. There are no randomized, peer reviewed studies to support the use of probiotics for the prevention or treatment of CDI in cancer patients. Cases of bacteremia (*Lactobacillus*) and fungemia (*Saccharomyces*) have been described in immunosuppressed patients receiving probiotics.
- For patients with a high index of suspicion for severe CDI and negative diagnostic studies, and if not contraindicated, consider diagnostic colonoscopy to examine for pseudomembrane formation. The decision for therapy in these patients is left at the discretion of the treating physician, consider Infectious Diseases consultation.

## APPENDIX B

### THE BRISTOL STOOL FORM SCALE

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

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## APPENDIX C: Institutional Bezlotoxumab Use Criteria (Adults Only)

- Restricted to outpatient use only, with an exception for inpatients with an extended hospitalization that would not allow outpatient administration during concomitant antibacterial treatment for *C. difficile* infection (anti-CDI therapy)
- Must have a positive stool *C. difficile* nucleic acid amplification test **and** a positive toxin by enzyme-linked immunosorbent assay (ELISA)
- Must be receiving concomitant anti-CDI therapy (e.g., vancomycin, fidaxomicin, metronidazole)
- Presence of at least one of the following risk factors for recurrent CDI:
  - Age  $\geq$  60 years
  - At least one prior episode of CDI
  - Compromised immunity: currently receiving immunosuppressants, neutropenia (e.g., ANC  $<$  0.5 K/microliter), and/or lymphopenia (e.g., ALC  $<$  0.2 K/microliter)
  - Clinically severe CDI
    - Presence of visualized pseudomembranous colitis on endoscopy, able to take oral medications **and/or**
    - Any two of the following:
      - Age  $>$  60 years
      - WBC  $>$  15 K/microliter or ANC  $<$  0.5 K/microliter
      - Serum creatinine (SCr)  $>$  1.5 mg/dL
      - Albumin  $<$  2.5 g/dL
      - GI graft versus host disease (GVHD)
      - Fever  $>$  38.3°C
      - Abdominal cramping/pain
      - CT finding with colonic thickening, ascites, or pneumatosis
      - Diarrhea  $>$  10 episodes per day
      - Concomitant chemotherapy or immunosuppression (including corticosteroids)
  - Patient expected to continue non-CDI antibiotics  $\geq$  3 days beyond end of anti-CDI therapy

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## APPENDIX D: Fecal Microbiota Transplant Indications

- Recurrent or relapsing CDI (all CDI must be diagnosed by positive stool test for *C. difficile*):
  - Three or more episodes of mild-to-moderate CDI and failures of a 6-8 week taper with vancomycin with or without an alternative antibiotic (*e.g.*, rifaximin, nitazoxanide, or fidaxomicin)
  - At least two episodes of CDI resulting in hospitalization and associated with significant morbidity
- CDI not responding to standard therapy (vancomycin or fidaxomicin) for at least a week
- Severe (even fulminant CDI) with no response to standard therapy after 48 hours
- Ileus and in patients in whom vancomycin enemas are contraindicated or could cause bowel perforation
- Without severe neutropenia (ANC > 0.5 K/microliter, preferably >1 K/microliter)

## APPENDIX E: Prevention Considerations

- Prolonged courses of perioperative antibiotic prophylaxis beyond a single dose is discouraged except in selected circumstances
- The use of prophylactic antibiotics in patients receiving chemotherapy is discouraged. Exceptions are in patients with neutropenia associated with leukemia and HSCT
- Continued use of antibiotics during therapy for *C. difficile* increases risk of failure and recurrence. Discontinue concomitant antibiotics as soon as possible following diagnosis of *C. difficile*.
- Empiric therapy while awaiting diagnostic testing results is discouraged except in cases of suspected severe CDI (*e.g.*, toxic megacolon, ileus, severe colitis) or when a pseudo membrane is identified on endoscopy.
- Given the high rates of asymptomatic colonization (3-8%), the detection of *C. difficile* nucleic acid test (NAT) by itself is not sufficient to justify specific therapy unless there is a high index of clinical suspicion (*e.g.*, clinically significant diarrhea and no confirmed alternative causes).
  - Routine testing for *C. difficile* infection in children under 2 years of age with diarrhea is not recommended
- Follow infection control measures including:
  - Initiate contact isolation for suspected CDI while awaiting test results
  - Wash hands with soap and water prior to entering and exiting the room. Wear a gown and gloves. The use of hand sanitizer is insufficient to kill *C. difficile* spores.
  - Clean shared patient care items with a hospital approved bleach product, according to manufacturer's instructions
  - Do not re-test for CDI for the sole purpose of removing isolation. Patients who are no longer passing unformed stools will be re-evaluated by an infection preventionist prior to discontinuation of isolation. Only an infection preventionist has the authority to remove patients from isolation.
- Preferably delay chemotherapy until CDI treatment has been completed and diarrhea has resolved
- Consider delaying radiation therapy until GI symptoms have resolved

HSCT = hematopoietic stem cell transplant

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## SUGGESTED READINGS

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## DEVELOPMENT CREDITS

This practice consensus statement algorithm is based on majority opinion of the Infection Control, Infectious Disease, and Pediatrics experts at the University of Texas MD Anderson Cancer Center for the patient population. These experts included:

### Core Development Team Leads

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