Clinical Pathways

Clostridium difficile (C. diff)

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Connecticut Children's

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What is a Clinical Pathway?

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

Objectives of Pathway

- To create a systematic way to manage *C. difficile*
- To determine the proper management of *C. difficile* based upon individual patient history

Why is Pathway Necessary?

- *C. difficile (C.diff)* is a significant infection that is becoming more common in children.
- Most episodes can be treated with initial empiric first line therapies, however, some patients should receive a pre-emptive escalation of therapy.
- Management of recurrent infection differs from management of first time infection
  - With recurrence there is increased likelihood of side-effects and possible resistance making alternative therapies recommended.
- The pathway is designed to ensure proper treatment is employed for the use of patients presenting with *C. diff* associated infection.

2019 Updates: *C. difficile* testing

There is now stepwise testing for C. difficile

Positive *C. difficile* PCR reflexes to *C. difficile* Ag/Toxin EIA test. For all positive *C. difficile* Gene with a negative or positive NAP1 result, the following comment will be attached to end of result:

"Positive PCR may represent colonization, infection must be confirmed with GDH/EIA Antigen/Toxin test. Confirmatory testing will be reported within approximately 24 hours of PCR."

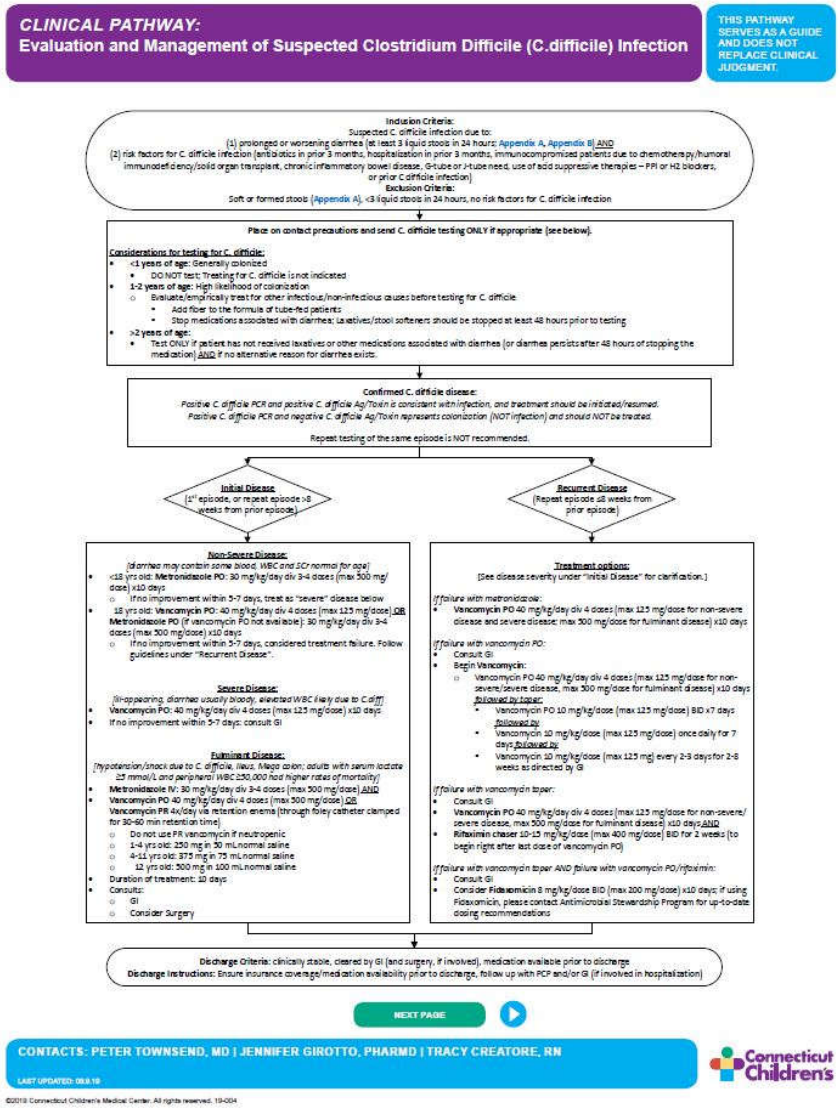
For positive or negative antigen and negative *C. difficile* toxin, the following comment will be attached to the end of the *C. difficile* Ag/Toxin EIA test results:

"Suggestive of colonization and should not be treated without clinical correlation"

For positive or negative *C. difficile* antigen and positive *C. difficile* toxin, the following comment will be attached to the end of the *C. difficile* Ag/Toxin EIA test results:

"Consistent with infection"

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



CLINICAL PATHWAY:
Evaluation and Management of Suspected Clostridium Difficile (C.difficile) Infection

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

Inclusion Criteria:
Suspected C. difficile infection due to:
(1) prolonged or worsening diarrhea (at least 3 liquid stools in 24 hours; Appendix A, Appendix B) 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, or prior C difficile infection)
Exclusion Criteria:
Soft or formed stools (Appendix A), <3 liquid stools in 24 hours, no risk factors for C. difficile infection

Place on contact precautions and send C. difficile testing ONLY if appropriate (see below).

Considerations for testing for C. difficile:
- **<1 years of age:** Generally colonized
  - DO NOT test: Treating for C. difficile is not indicated
- **1-2 years of age:** High likelihood of colonization
  - 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; 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.

Confirmed C. difficile disease:
Positive C difficile PCR and positive C. difficile Ag/Toxin is consistent with infection, and treatment should be initiated/resumed.
Positive C. difficile PCR and negative C. difficile Ag/Toxin represents colonization (NOT infection) and should NOT be treated.

Repeat testing of the same episode is NOT recommended.

Initial Disease
(1st episode, or repeat episode >8 weeks from prior episode)

Recurrent Disease
(Repeat episode ≤8 weeks from prior episode)

Non-Severe Disease:
(diarrhea may contain some blood, WBC and SCr normal for age)
- <18 yrs old: **Metronidazole PO:** 30 mg/kg/day div 3-4 doses (max 500 mg/dose) x10 days
  - If no improvement within 5-7 days, treat as "severe" disease below
- ≥18 yrs old: **Vancomycin PO:** 40 mg/kg/day div 4 doses (max 125 mg/dose) OR **Metronidazole PO** (if vancomycin PO not available): 30 mg/kg/day div 3-4 doses (max 500 mg/dose) x10 days
  - If no improvement within 5-7 days, considered treatment failure. Follow guidelines under "Recurrent Disease".

Severe Disease:
(Ill-appearing, diarrhea usually bloody, elevated WBC likely due to C.diff)
- **Vancomycin PO:** 40 mg/kg/day div 4 doses (max 125 mg/dose) x10 days
- If no improvement within 5-7 days: consult GI

Fulminant Disease:
(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:** 30 mg/kg/day div 3-4 doses (max 500 mg/dose) AND
- **Vancomycin PO** 40 mg/kg/day div 4 doses (max 500 mg/dose) 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
  - Consider Surgery

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

If failure with metronidazole:
- **Vancomycin PO** 40 mg/kg/day div 4 doses (max 125 mg/dose for non-severe disease and severe disease; max 500 mg/dose for fulminant disease) x10 days

If failure with vancomycin PO:
- Consult GI
- Begin **Vancomycin:**
  - Vancomycin PO 40 mg/kg/day div 4 doses (max 125 mg/dose for non-severe/severe disease, max 500 mg/dose for fulminant disease) x10 days *followed by taper:*
    - Vancomycin PO 10 mg/kg/dose (max 125 mg/dose) BID x7 days *followed by*
    - Vancomycin 10 mg/kg/dose (max 125 mg/dose) once daily for 7 days *followed by:*
    - Vancomycin 10 mg/kg/dose (max 125 mg) every 2-3 days for 2-8 weeks as directed by GI

If failure with vancomycin taper:
- Consult GI
- **Vancomycin** PO 40 mg/kg/day div 4 doses (max 125 mg/dose for non-severe/severe disease, max 500 mg/dose for fulminant disease) x10 days AND
- **Rifaximin chaser** 10-15 mg/kg/dose (max 400 mg/dose) BID for 2 weeks (to begin right after last dose of vancomycin PO)

If failure with vancomycin taper AND failure with vancomycin PO/rifaximin:
- Consult GI
- Consider **Fidaxomicin** 8 mg/kg/dose BID (max 200 mg/dose) x10 days; if using Fidaxomicin, please contact Antimicrobial Stewardship Program for up-to-date dosing recommendations

Discharge Criteria: clinically stable, cleared by GI (and surgery, if involved), medication available prior to discharge
Discharge Instructions: Ensure insurance coverage/medication availability prior to discharge, follow up with PCP and/or GI (if involved in hospitalization)

NEXT PAGE

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THIS PATHWAY SERVES AS A GUIDE AND DOES NOT [illegible] CLINICAL

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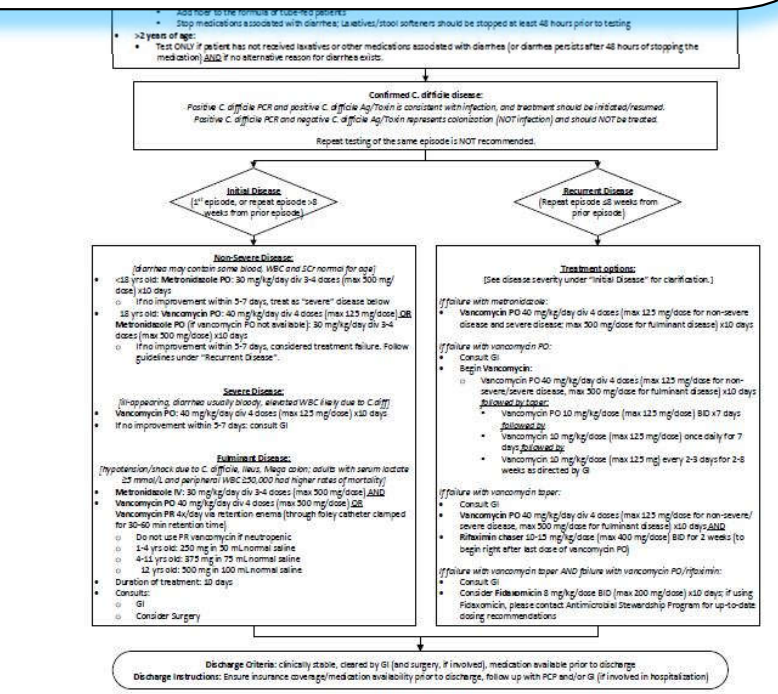
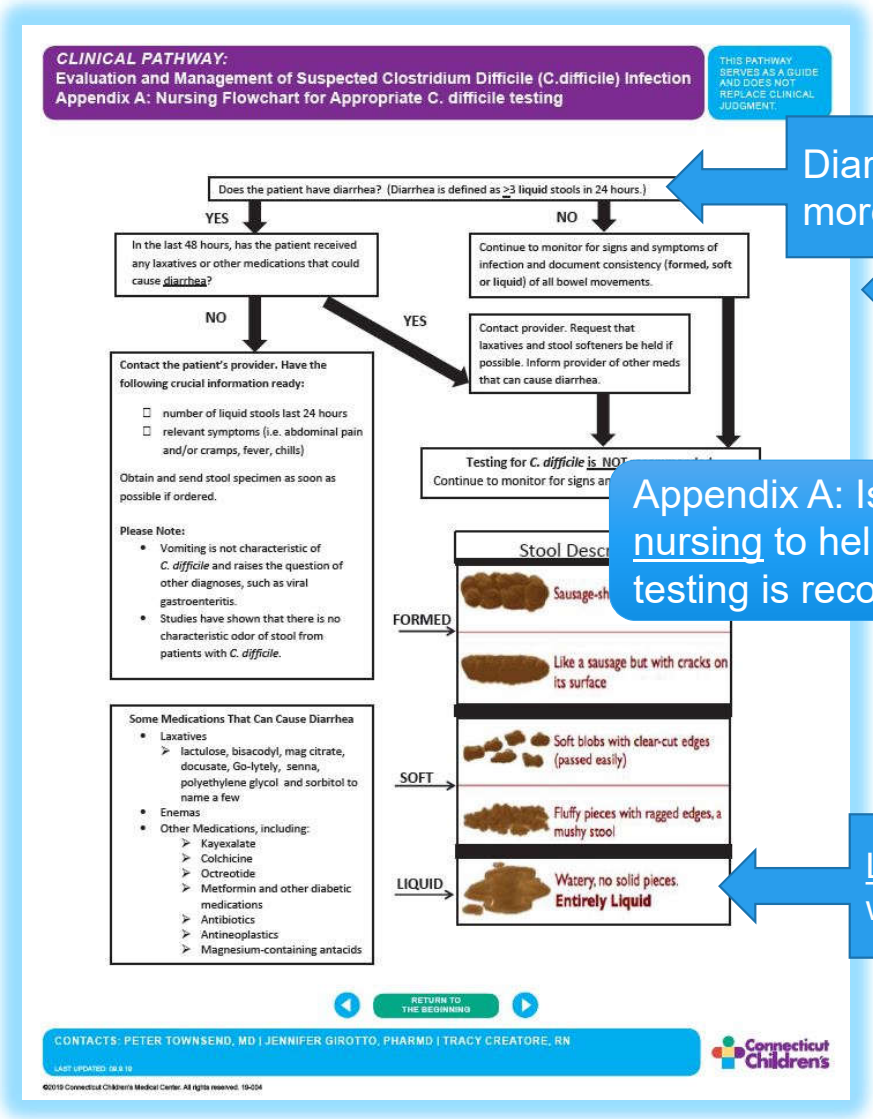
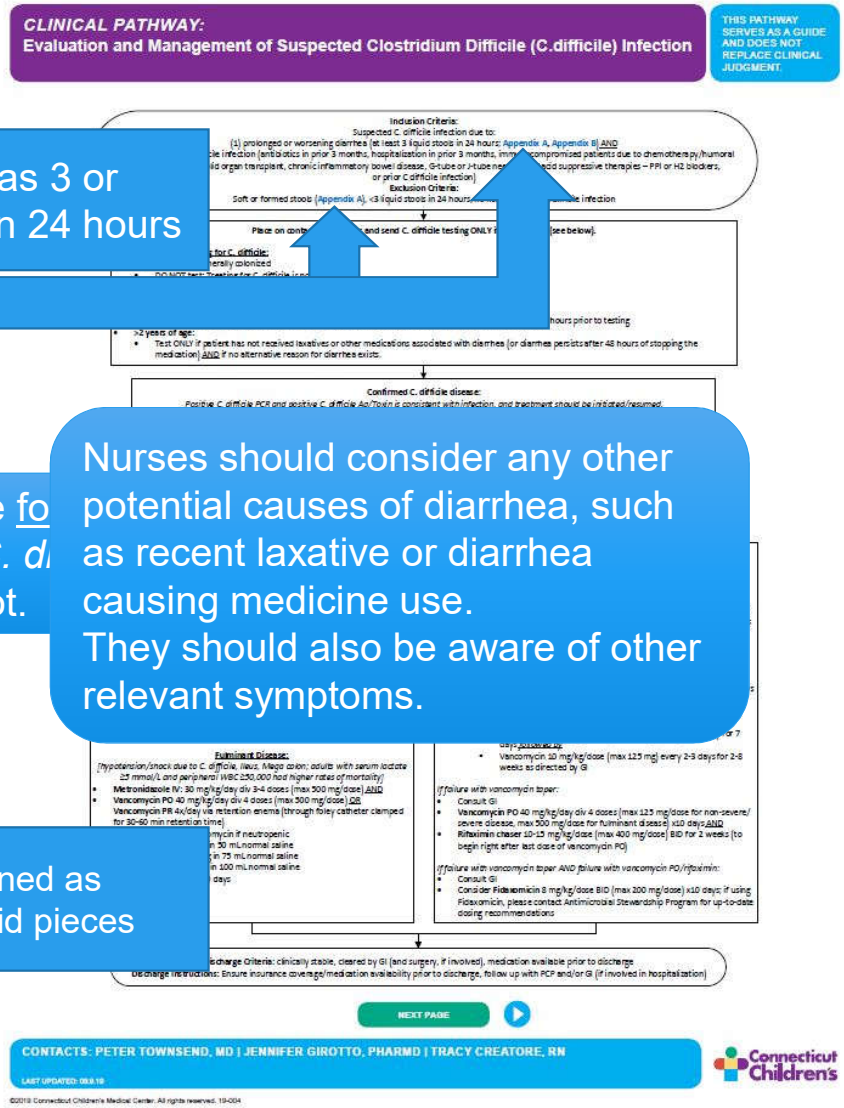
(1) prolonged or worsening diarrhea (at least 3 liquid stools in 24 hours; **Appendix A**, **Appendix B**) AND
(2) risk factors for C. difficile infection (antibiotics in prior 3 months, hospitalization in prior 3 months, immunocompromised patients due to chemotherapy/humoral immunodeficiency/solid organ transplant, chronic inflammatory bowel disease, G-tube or J-tube need, use of acid suppressive therapies – PPI or H2 blockers, or prior C difficile infection)
Exclusion Criteria:
Soft or formed stools (**Appendix A**), <3 liquid stools in 24 hours, no risk factors for C. difficile infection

C. diff infection should be considered in patients with prolonged and worsening diarrhea
AND
Risk factors for *C. diff* infection.

C. diff infection causes frequent liquid stools. So children with soft or formed stool, less than 3 stools in 24 hours, or with no risk factors for infection are excluded from the pathway





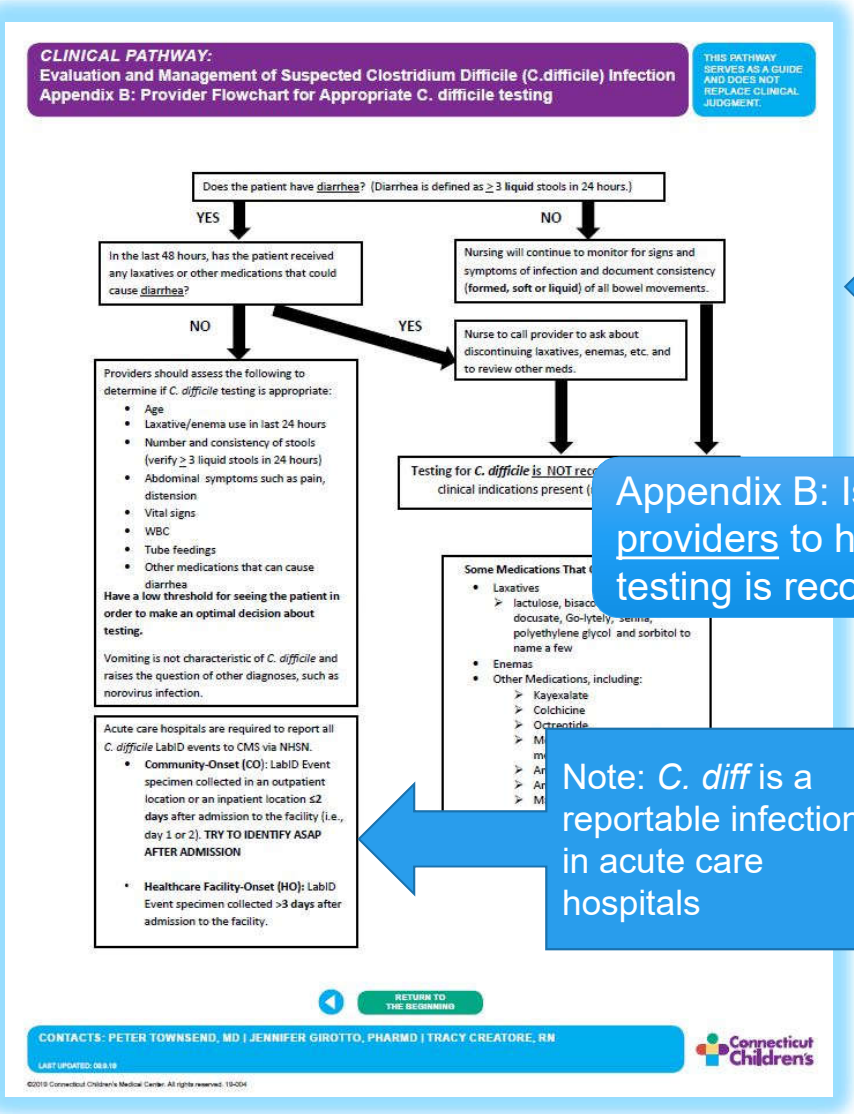


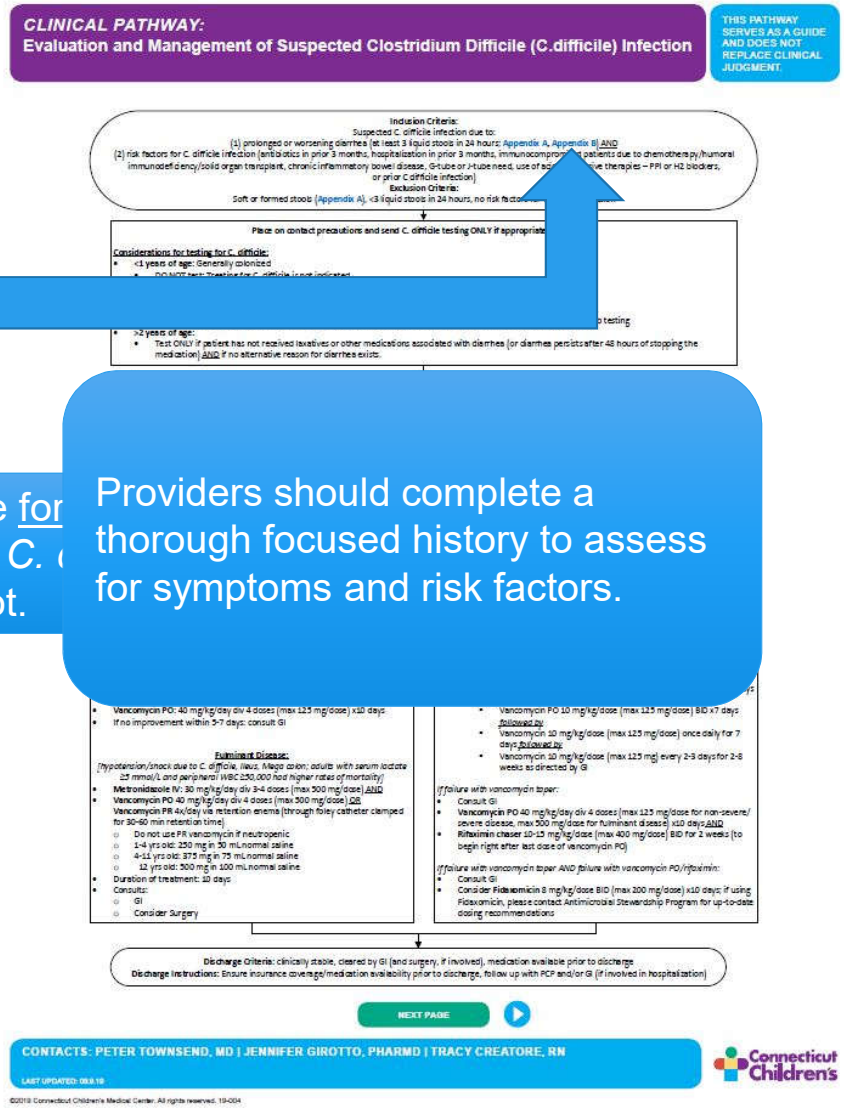
Diarrhea is defined as 3 or more Liquid stools in 24 hours

Appendix A: Is a decision tree fo nursing to help determine if *C. d* testing is recommended or not.

Nurses should consider any other potential causes of diarrhea, such as recent laxative or diarrhea causing medicine use.
They should also be aware of other relevant symptoms.

Liquid stool is defined as watery with no solid pieces





Appendix B: Is a decision tree for providers to help determine if *C.* testing is recommended or not.

Providers should complete a thorough focused history to assess for symptoms and risk factors.

Note: *C. diff* is a reportable infection in acute care hospitals

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Place on contact precautions and send C. difficile testing ONLY if appropriate (see below).

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- **1-2 years of age:** High likelihood of colonization
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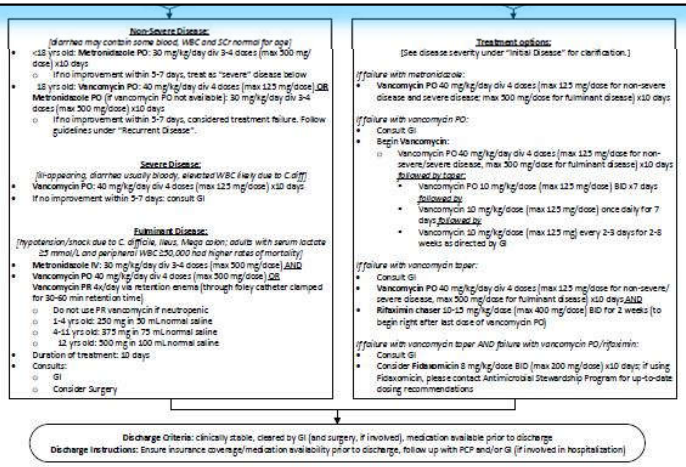
    - Add fiber to the formula of tube-fed patients
    - Stop medications associated with diarrhea; Laxatives/stool softeners should be stopped at least 48 hours prior to testing
- **>2 years of age:**
  - Test ONLY if patient has not received laxatives or other medications associated with diarrhea (or diarrhea persists after 48 hours of stopping the medication) AND if no alternative reason for diarrhea exists.

Age is another factor to take into account when considering testing for *C. diff*.

DO NOT test in patients less than 1 year of age.



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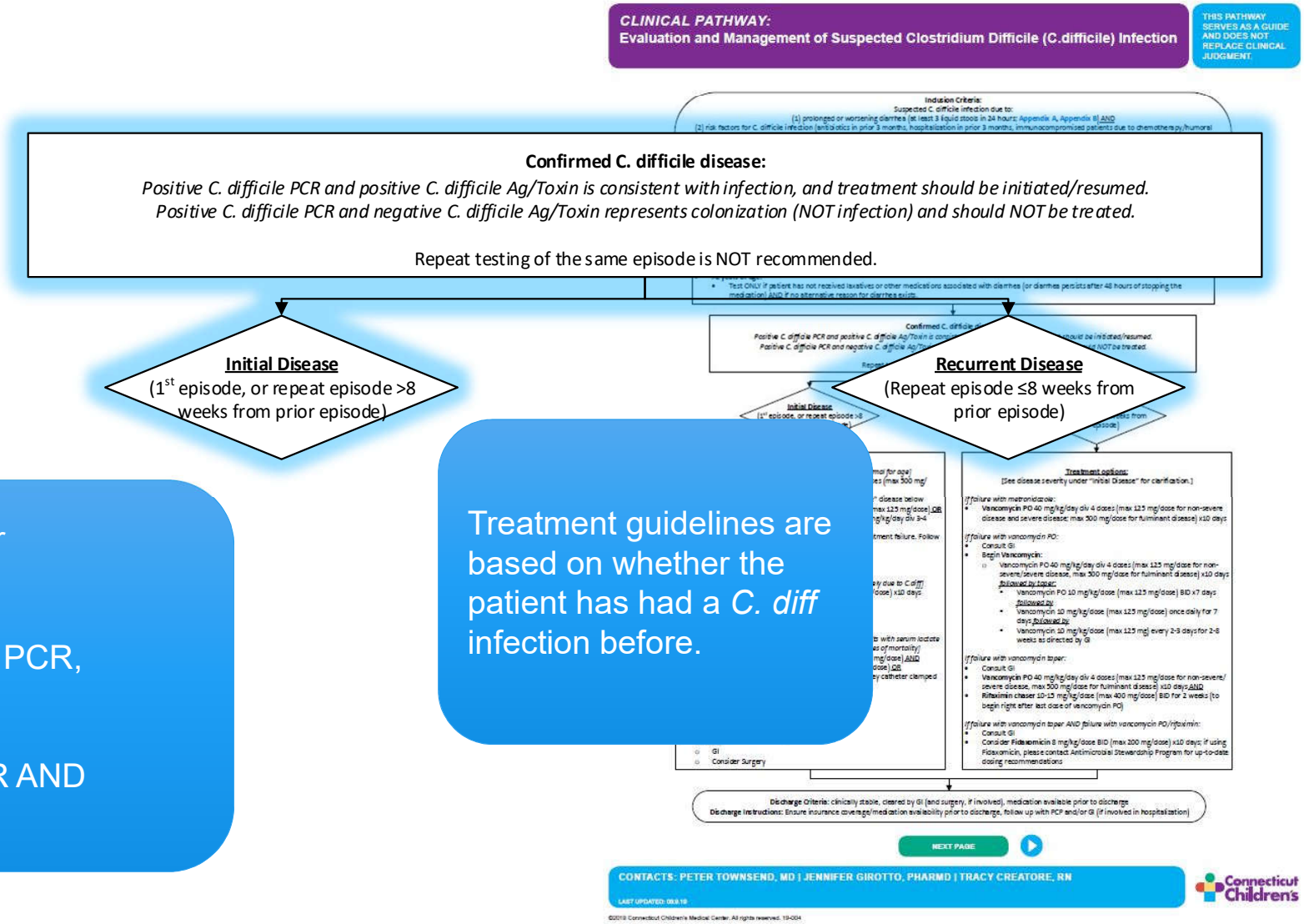
Is it *C. diff* infection, or colonization?

Colonization: Positive PCR, negative Ag/Toxin

Infection: Postive PCR AND Postive Ag/ Toxin

Treatment guidelines are based on whether the patient has had a *C. diff* infection before.



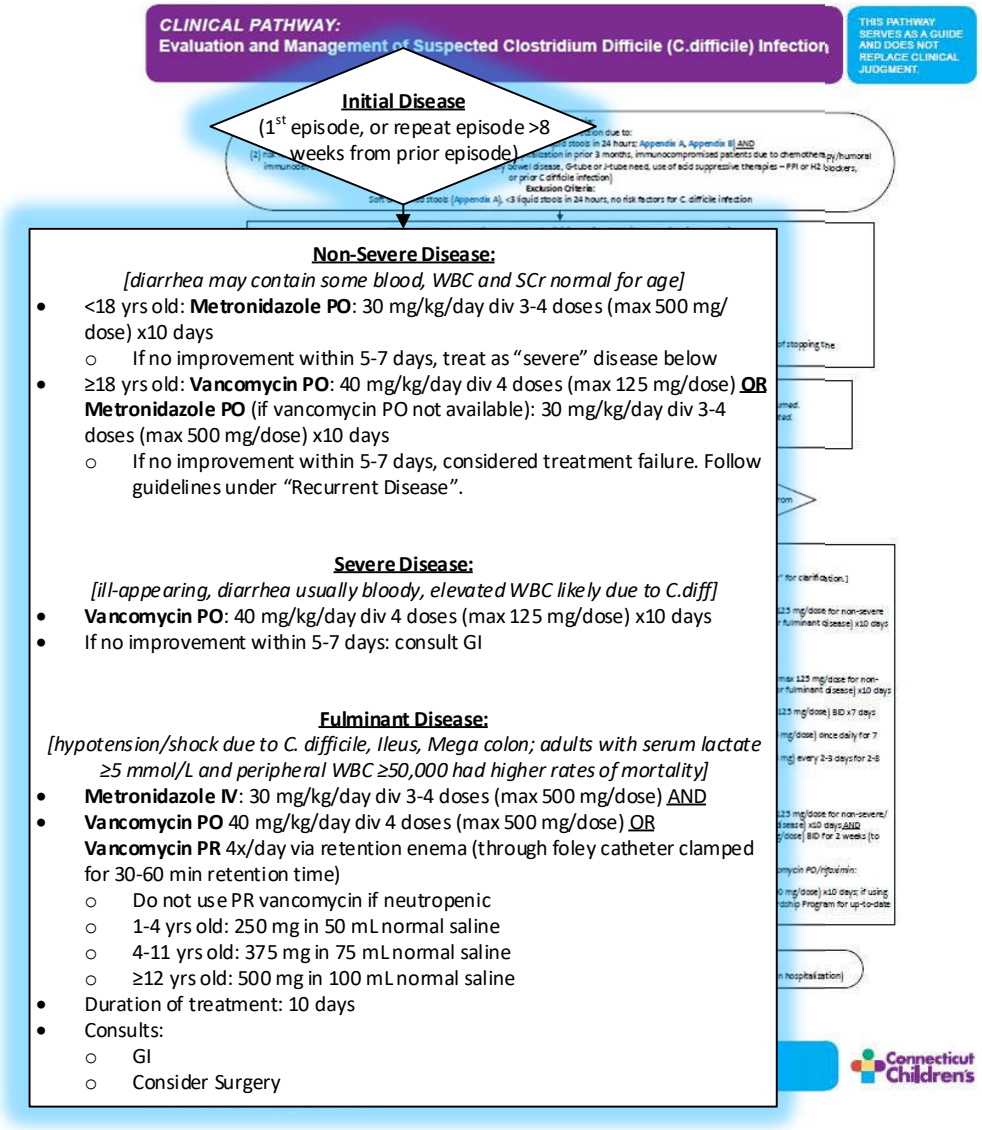
Disease Severity:

Non-severe: Patients with normal WBC and Serum Creatinine

Severe: ill appearing patient, with elevated WBC (thought due to *C. diff*)

Fulminant Disease: Patients with hypotension/shock, ileus, mega colon.

- Adult patients with elevated serum lactates and WBC >50,000 have the highest rate of mortality



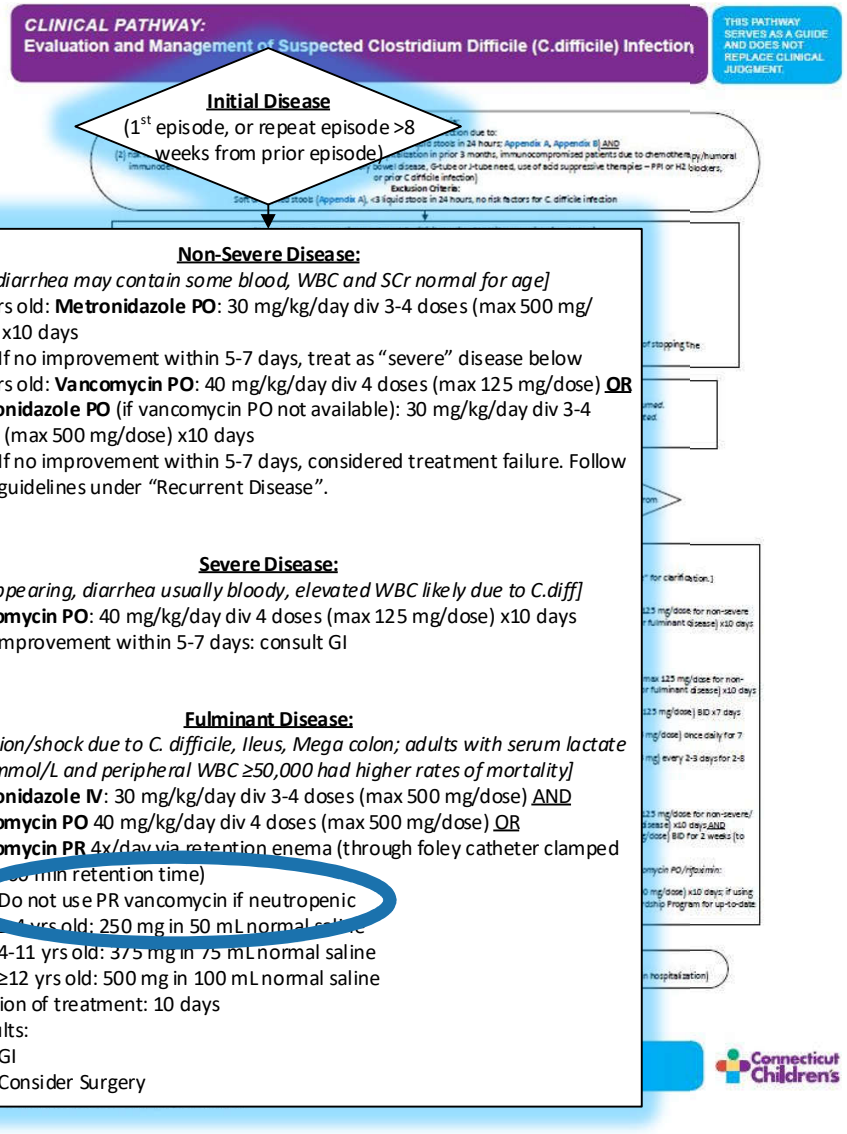
Uncomplicated first time infections are treated with PO Metronidazole or PO Vancomycin if 18 years or older

First line for ill-appearing patients or those with no improvement after

Adults with high serum lactate and/or very high WBC have the highest rate of mortality. Have a low threshold to consult Surgery

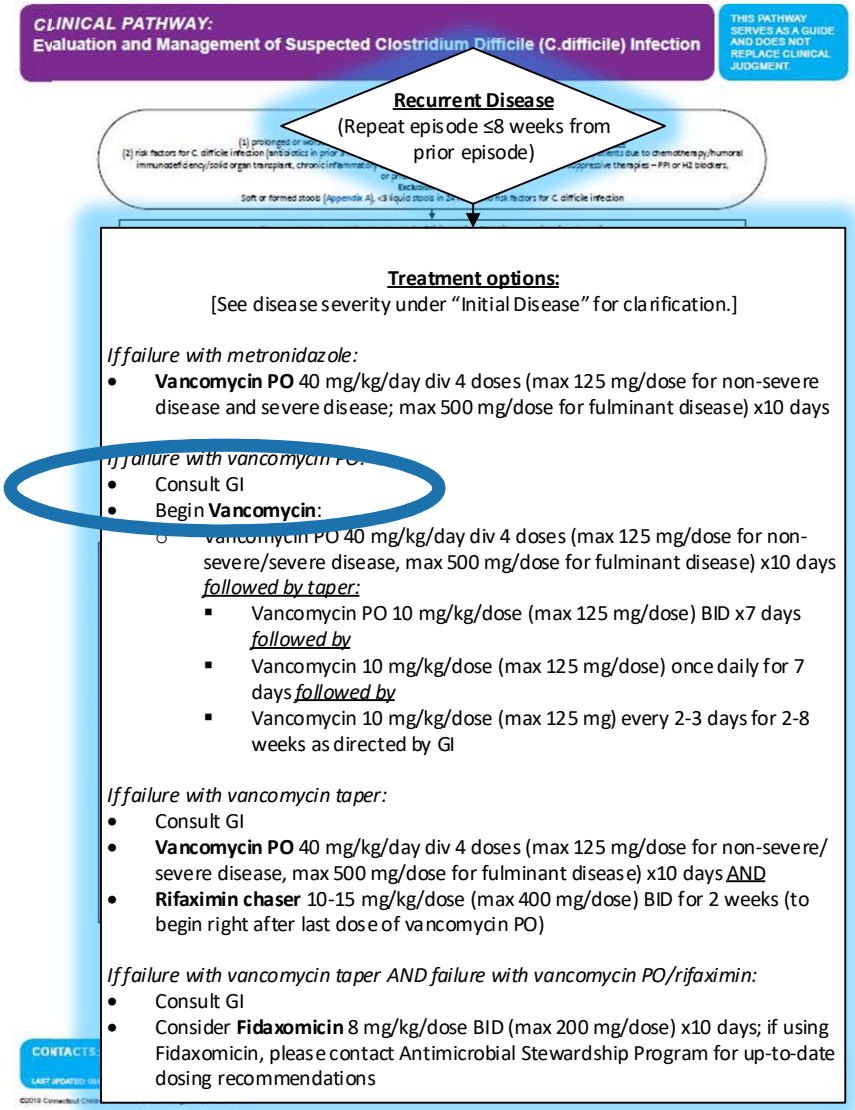
AND
PO vs PR Vancomycin

Consult GI and consider Surgery and/or ID consults



In patients with recurrent disease PO Vancomycin will be the first line treatment.

GI should be consulted for any patient who has failed PO Vancomycin therapy.



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(Repeat episode ≤8 weeks from prior episode)

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

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If failure with vancomycin PO:

- Consult GI
- Begin **Vancomycin**:
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If failure with vancomycin taper:

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- Consult GI
- Consider **Fidaxomicin** 8 mg/kg/dose BID (max 200 mg/dose) x10 days; if using Fidaxomicin, please contact Antimicrobial Stewardship Program for up-to-date dosing recommendations

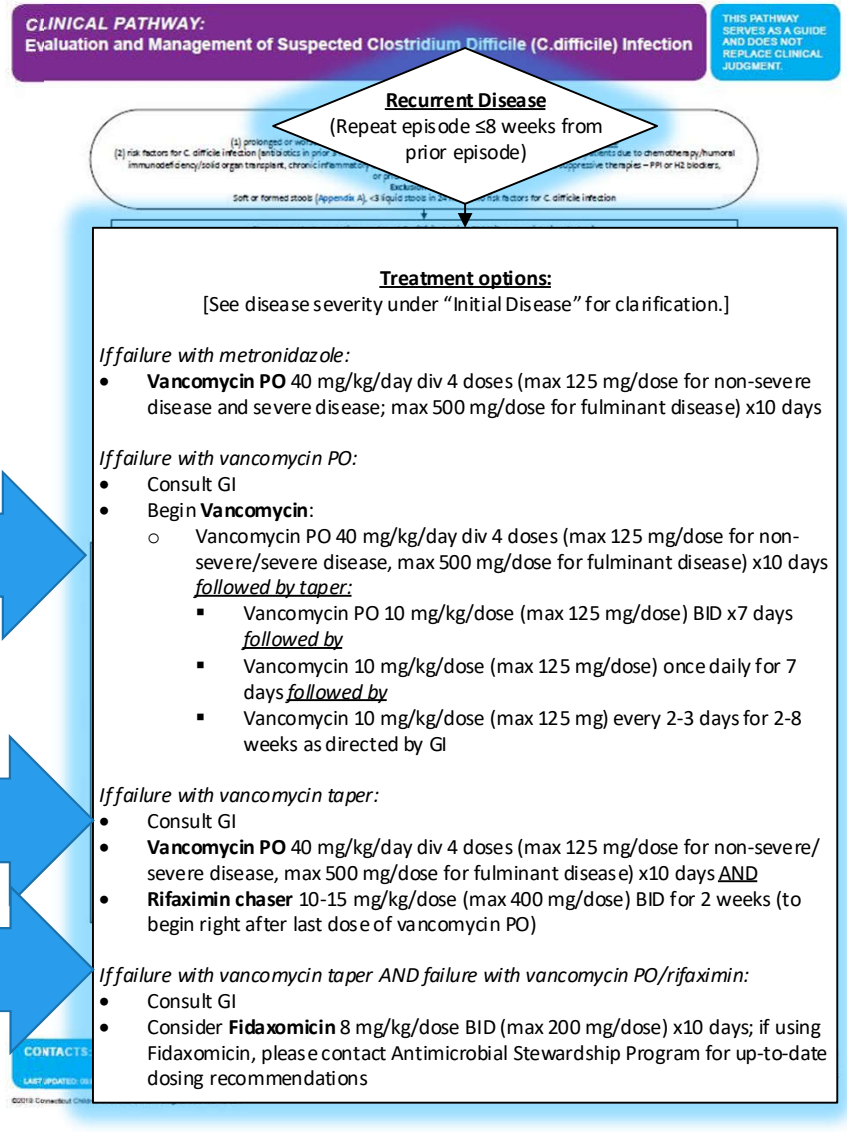
CONTACTS:

Reminder: GI should be involved with any patient who has failed PO Vancomycin. May also consider ID consult at any point.

Patients who have failed PO Vancomycin therapy start another course of PO Vancomycin followed by a 4-8 week taper.

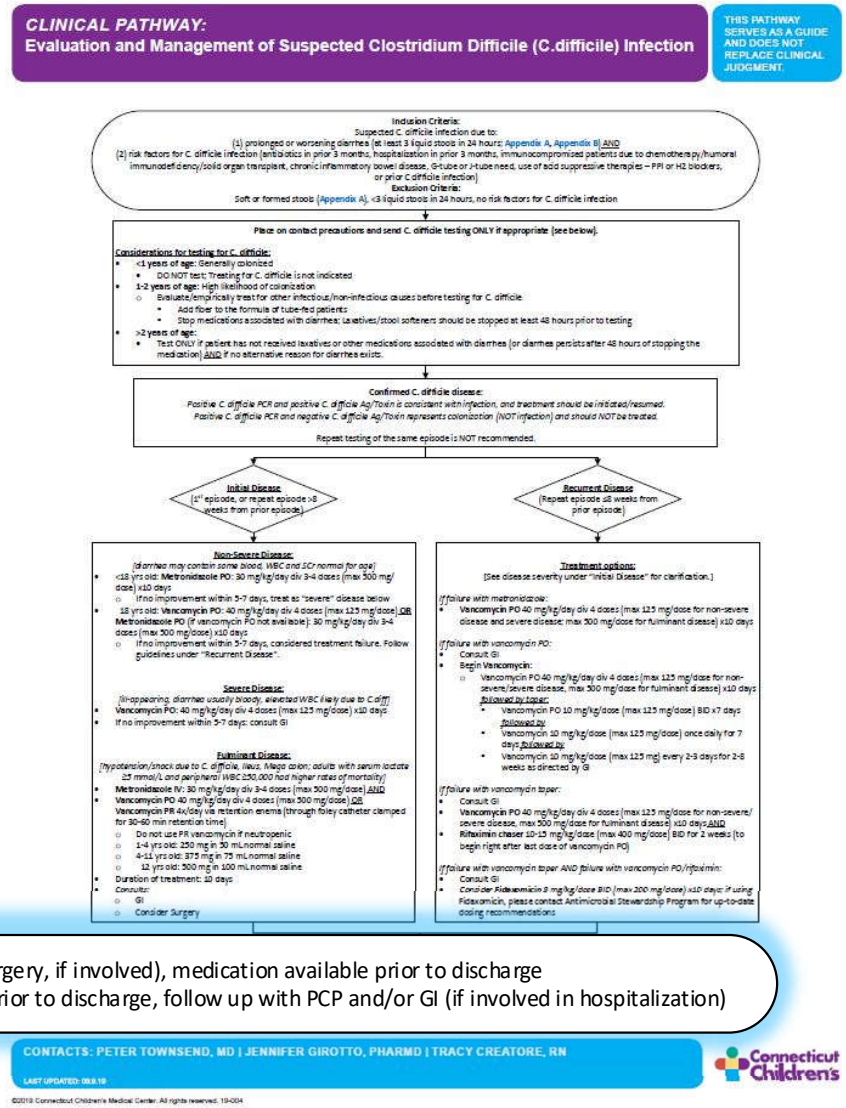
If the Vancomycin taper fails patients will do

If there is failure of all of the above treatments consider Fidaxomicin under the guidance of the Antimicrobial Stewardship Program



When considering discharge, providers should ensure any discharge medications are ordered and available prior to discharge.

- Consider bedside delivery when possible



Review of Key Points

- 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 has two components the PCR and the Ag/Toxin. Both must be positive for it to be a treatable *C. diff* infection.
- Treatment of *C. diff* is based on the number of previous infections and the type of previous treatments
- GI should be consulted for any patient with Fulminant infection, or with any patient who has failed PO Vancomycin therapy
- 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

- 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
- Percentage of patients with relapses within 30 days
- Percentage of patients who required medication escalation
- Percentage of patients who required escalation to stool transplant

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. [Epub ahead of print].
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- 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

- Jennifer Girotto, PharmD, BCPPS
  - Antimicrobial Stewardship Program
- Peter Townsend, MD
  - Pediatric Gastroenterology
- Tracy Creatore, RN, BSN, CIC
  - Epidemiology Nurse with Infection Prevention Department

Thank You!

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 judgement

This Educational Module was edited by:

Abby Theriaque, APRN

Educational Module Specialist