

AGA clinical practice guideline on fecal microbiota–based therapies for select gastrointestinal diseases.

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Overview

Guideline Objective

To present clinical recommendations on the use of fecal microbiota–based therapies in adults with recurrent *Clostridioides difficile* infection (CDI) and conventional fecal microbiota transplant (FMT) in severe to fulminant CDI in the hospital setting, irritable bowel diseases (IBDs) (i.e., Crohn's disease ulcerative colitis, and pouchitis), and irritable bowel syndrome (IBS) based on the best available evidence

Patient Population

Adults with recurrent CDI or severe to fulminant CDI, IBD, and IBS

Recommendations

Recommendation Statements

Question 1. In immunocompetent adults with recurrent *Clostridioides difficile* (*C difficile*) infection (CDI) should fecal microbiota–based therapies be used?

Recommendation 1. In immunocompetent adults with recurrent CDI, the AGA suggests the use of fecal microbiota–based therapies upon completion of standard of care antibiotics over no fecal microbiota–based therapies. (**Conditional recommendation; Low certainty evidence**)

Implementation Considerations: The following considerations are specific to immunocompetent adult patients with nonsevere, nonfulminant recurrent CDI in the outpatient setting.

- *Diagnosis of recurrent CDI:*
 - A CDI diagnosis requires acute-onset, clinically significant, new-onset diarrhea (e.g., 3 or more unformed stools in 24 hours) and highly sensitive (nucleic acid amplification or glutamate dehydrogenase) in combination with highly specific (toxin enzyme immunoassay) testing plus improvement of diarrhea with *C difficile*–directed antibiotics. A positive nucleic acid amplification test alone in the appropriate clinical context is also reasonable for making a CDI diagnosis.
 - Recurrent CDI is typically defined as clinically significant diarrhea with a confirmatory positive test within 8 weeks of completing antibiotics for CDI.
 - In patients who develop recurrent diarrhea after treatment for CDI, it is important to consider not only CDI recurrence, but also alternative diagnoses, especially if there are atypical symptoms, such as diarrhea alternating with constipation or no response in diarrheal symptoms to treatment with vancomycin or fidaxomicin.
- *When to consider fecal microbiota–based therapies:*
 - Fecal microbiota–based therapies include conventional fecal microbiota transplant (FMT), fecal microbiota live-jslm and fecal microbiota spores live-brpk.

- Prevention with fecal microbiota–based therapies can be considered in patients after the second recurrence (third episode) of CDI or in select patients at high risk of either recurrent CDI or a morbid CDI recurrence. Select use includes patients who have recovered from severe, fulminant, or particularly treatment-refractory CDI and patients with significant comorbidities.
- Careful consideration before proceeding with fecal microbiota–based therapies is recommended in patients who require frequent antibiotics or long-term antibiotic prophylaxis, because ongoing antibiotics may diminish the efficacy of such therapy.
- *How to administer fecal microbiota–based therapies:*
 - Fecal microbiota–based therapies should be given upon completion of a course of standard of care antibiotics for recurrent CDI. The fecal microbiota–based therapies are to prevent recurrence, not for CDI treatment.
 - Suppressive anti-CDI antibiotics (e.g., vancomycin) should be used to bridge standard of care antibiotics until fecal microbiota–based therapies are given.
 - Ideally, antibiotics for CDI should be stopped 1–3 days before conventional FMT to allow adequate time for antibiotics to wash out of the system. If a bowel purge is given, FMT can be given 1 day after stopping antibiotics. If no bowel purge is given, 3 days off antibiotics is recommended to allow clearance of oral antibiotics. Rarely, patients will recur rapidly (within 1–2 days of stopping CDI antibiotics), this risk needs to be considered when determining an individual treatment window. When administering fecal microbiota spores live-brpk and fecal microbiota live-jslm, refer to the manufacturer package insert for instructions.
 - Conventional FMT should be performed with appropriately screened donor stool.
 - Conventional FMT can be delivered via multiple routes. There is insufficient evidence to recommend a specific route.
- *Alternatives to fecal microbiota–based therapies:* A vancomycin taper, tapered-pulsed fidaxomicin, or bezlotoxumab are reasonable alternative therapies to prevent recurrent CDI in patients who are not interested in fecal microbiota–based therapies.

Question 2. In immunocompromised adults with recurrent CDI, should fecal microbiota–based therapies be used?

Recommendation 2.

- In mildly or moderately immunocompromised adults with recurrent CDI, the AGA suggests the use of conventional FMT upon completion of standard of care antibiotics over no FMT. (**Conditional recommendation; Very low certainty of evidence**)
- In severely immunocompromised adults with recurrent CDI, the AGA suggests against the use of fecal microbiota–based therapies upon completion of standard of care antibiotics over no fecal microbiota–based therapies. (**Conditional recommendation; Very low certainty of evidence**)

Implementation Considerations: The following considerations are specific to immunocompromised adult patients with nonsevere, nonfulminant recurrent CDI in the outpatient setting. "Severely immunocompromised" includes patients receiving active cytotoxic therapy for solid tumors and hematologic malignancies, patients who have received chimeric antigen receptor T-cell therapy or hematopoietic cell transplant (only when neutropenic), any neutropenia, patients with severe primary immunodeficiency, patients with advanced or untreated HIV infection (CD4 counts $<200/\text{mm}^3$, AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV). Mildly or moderately immunocompromised adults are patients who are immunocompromised but do not meet our definition of "severe."

- The implementation considerations for the use of fecal microbiota–based therapies in immunocompetent adults with recurrent CDI can be used in the mildly or moderately immunocompetent population, with the exception of using fecal microbiota spores live-brpk or fecal microbiota live-jslm. There is insufficient evidence to recommend fecal microbiota spores live-brpk or fecal microbiota live-jslm in immunocompromised adult patients with recurrent CDI.
- Conventional FMT should be performed with appropriately screened donor stool and special testing may be necessary.

Question 3. In adults hospitalized with severe or fulminant CDI, should conventional FMT be used?

Recommendation 3. In adults hospitalized with severe or fulminant CDI not responding to antimicrobial therapy, the AGA suggests the use of conventional FMT over no FMT.
(**Conditional recommendation; Very low certainty of evidence**)

Implementation Considerations: The following considerations are specific to adult patients in the hospital with severe or fulminant CDI refractory to standard of care antibiotics.

- *What is severe or fulminant CDI:*
 - Severe CDI is defined as patients with CDI and a leukocyte count $\geq 15 \times 10^9$ cells/L and/or creatinine ≥ 1.5 mg/dL.
 - Fulminant CDI presents as severe disease with shock, ileus, or megacolon.
- *When to consider conventional FMT:*
 - Patients with severe or fulminant CDI require multidisciplinary care including critical care, surgery, gastroenterology, and infectious disease.
 - FMT should be considered in hospitalized patients not responding to standard of care antibiotics, generally within 2–5 days after initiating CDI treatment.
 - FMT is not advised in patients with a bowel perforation, obstruction, or those who are severely immunocompromised.
- *How to administer conventional FMT:*
 - FMT should be performed with appropriately screened donor stool. There is no evidence for using the U.S. Food and Drug Administration (FDA)-approved fecal microbiota-based therapies as adjuvant treatment in severe or fulminant CDI.
 - A bowel purge before FMT may not be feasible or safe. In these cases, FMT should be performed without a bowel preparation.
 - First dose of FMT should be delivered via colonoscopy or flexible sigmoidoscopy. Colonoscopy allows the provider to confirm the diagnosis and determine CDI severity. There is insufficient evidence in severe or fulminant CDI for FMT via enema or capsules. Administration of FMT via nasoenteric tube is discouraged, given the increased risk of fecal aspiration.
- *Follow-up after initial FMT:*

- Treatment response can be assessed by means of monitoring stool output, white blood cell count, and C-reactive protein.
- Most patients with severe or fulminant CDI will need repeat FMT. The exact timing (generally every 3–5 days) should be based on the patient's response to treatment, local protocols, and multidisciplinary care. The route of repeated FMT dosing will depend on local expertise and treatment response.
- Anti-CDI antibiotics may need to be continued after FMT. Most published reports resume anti-CDI antibiotics or continue anti-CDI antibiotics when administering FMT.
- After resolution of colitis, suppressive vancomycin should be continued at discharge and a final fecal microbiota–based therapy performed as an outpatient to prevent CDI recurrence. This treatment for prevention of recurrence can be administered via colonoscopy, capsule, or enema.
- *Alternatives to FMT:* Cases of severe CDI not responding to antibiotics, or fulminant CDI, are often considered for colectomy.

Question 4. In adults with ulcerative colitis (UC) should conventional FMT be used?

Recommendation 4. In adults with UC, the AGA suggests against the use of conventional FMT, except in the context of clinical trials. (**Conditional recommendation; Very low certainty of evidence**)

Implementation Considerations:

- Conventional FMT can reasonably be used in the context of clinical trials and potentially outside a clinical trial in cases of expanded access when no comparable or satisfactory alternative therapy options are available.
- The recommendation is specific to the use of conventional FMT for the treatment of UC. For patients with recurrent, severe, or fulminant CDI in the settings of UC, refer to the Recommendations of Questions 1–3.

Question 5. In adults with Crohn's disease (CD), should conventional FMT be used?

Recommendation 5. In adults with CD, the AGA suggests against the use of conventional FMT, except in the context of a clinical trial. (**Conditional recommendation; Very low certainty of evidence**)

Implementation Considerations: The recommendation is specific to the use of conventional FMT for the treatment of CD. For patients with recurrent, severe, or fulminant CDI in the settings of CD, refer to the Recommendations of Questions 1–3.

Question 6. In adults with pouchitis, should conventional FMT be used?

Recommendation 6. In adults with pouchitis, the AGA suggests against the use of conventional FMT, except in the context of clinical trial. (**Conditional recommendation; Very low certainty of evidence**)

Implementation Considerations: The recommendation is specific to the use of conventional FMT for the treatment of pouchitis. For patients with recurrent, severe, or fulminant CDI in the settings of pouchitis, refer to the Recommendations of Questions 1–3.

Question 7. In adults with irritable bowel syndrome, should conventional FMT be used?

Recommendation 7. In adults with irritable bowel syndrome, the AGA suggests against the use of conventional FMT, except in the context of clinical trials. (**Conditional recommendation; Very low certainty of evidence**)

Implementation Considerations: The recommendation is specific to the use of conventional FMT for the treatment of irritable bowel syndrome. For patients with recurrent, severe, or fulminant CDI in the settings of irritable bowel syndrome, refer to the Recommendations of Questions 1–3.

Evidence Rating Scheme

Interpretation of the Certainty in Evidence of Effects Using the Grading of Recommendations Assessments, Development and Evaluation (GRADE) Framework

Certainty Level	Interpretation
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Recommendation Rating Scheme

Interpretation of Strong and Conditional Recommendations Using the GRADE Framework

Implications	Strong Recommendation	Conditional Recommendation
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the intervention. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Different choices will be appropriate for individual patients consistent with his or her values and preferences. Use shared decision-making. Decision aids may be useful in helping patients make decisions

		consistent with their individual risks, values, and preferences.
For policy makers	The recommendation can be adapted as policy or performance measure in most situations.	Performance measures should assess whether decision making is appropriate.

Note: Strong recommendations are indicated by statements that lead with 'we recommend' and conditional recommendations are indicated by statements that lead with 'we suggest.'

Related Content

Supporting Documents

- [Supplemental Document.](#)
- [Fecal Microbiota Transplantation for the Treatment of Recurrent *Clostridioides difficile* \(*Clostridium difficile*\) \(Review\); 2023 Apr 25.](#)
- [Fecal Transplantation for Treatment of Inflammatory Bowel Disease \(Review\); 2023 Apr 25.](#)
- [The AGA Institute Process for Developing Clinical Practice Guidelines Part One: Grading the Evidence; 2013 Apr 1.](#)

Implementation Tools

- [Clinical Decision Support Tool: Use of Fecal Microbiota-Based Therapies in Adults With GI Disorders; 2024.](#)
- [Spotlight: Use of Fecal Microbiota-Based Therapies in Adults With Select GI Disorders; 2024.](#)

Patient Education

- [Fecal Microbiota Transplantation \(FMT\).](#)
- [Fecal Microbiota Transplantation \(FMT\): Frequently Asked Questions.](#)

- *Clostridioides difficile* (*C. diff*).

Note: This patient information is intended to help patients better understand their health and their diagnosed disorders. Patients and their representatives should still consult with a licensed health care professional for evaluation of treatment options as well as answers to their personal medical questions.

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TRUST Scorecard

Composition of Guideline Development Group (GDG)

Multidisciplinary GDG Members

No

Methodologist Involvement

Yes

Incorporation of Patient and Public Perspective



Systematic Review of Evidence

Literature Search



Study Selection



Evidence Synthesis



Foundations for Recommendations

Strength of Evidence Grade



Description of Benefits and Harms of Recommendations



Summary of Evidence Supporting Recommendations



Strength of Recommendations Rating



Clear Articulation of Recommendations



Funding Source

Yes

Disclosure and Management of Financial Conflicts of Interests



External Review



Updating

