@EmoryGastroHep
©Emory 2025

Emory Faculty Retroflexions:
New Clinical Evidence in Clostridioides difficile Management

Alarica Dietzen, MD MPH in Discussion with Tanvi Dhere, MD

Background

The most recent 2021 ACG clinical guideline regarding treatment of primary *Clostridioides difficile* (Cdiff) (Kelly et al, 2021) indicated that vancomycin, fidaxomicin, or metronidazole should be used first-line treatment (tx) for Cdiff infection (CDI). Antibiotic (ABX) choice should be based on infection severity.

- The crude overall incidence rate of CDI in 2022 was 116.1 cases per 100,000 persons, with a higher incidence of community-associated cases versus healthcare-associated cases (CDC, 2024).

2021 ACG Guidelines Regarding FMT

Previously, the ACG recommended Fecal Microbiota Transplantation (FMT) **ONLY** for 1) cases of severe and fulminant CDI refractory to standard ABX therapy and 2) as adjunct therapy for patients w/recurrent CDI (Kelly et al, 2021). Per the 2021 ACG Guidelines,

- In pt's w/ severe or fulminant CDI, consider FMT if poor clinical response to 48-72h of ABX tx (*strong recommendation, low quality of evidence*).
- In pt's w/ recurrent CDI, treat with appropriate ABX. FMT can be delivered via colonoscopy or capsules to decrease risk of further recurrence (*strong recommendation, moderate quality of evidence).*

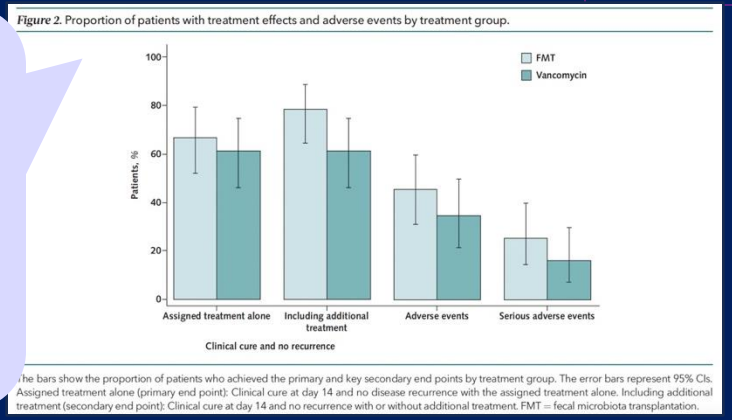
Kelly CR, Fischer M, Allegretti JR, et al. ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of Clostridioides difficile Infections [published correction appears in Am J Gastroenterol 2022 Feb 1;117(2):358.] Am J Gastroenterol. 2021;116(6):1124-1147.

New Clinical Evidence: RCT Investigating FMT for Primary CDI (2025)

A **new RCT** from Norway by Juul et al (2025) was recently published that studied FMT as tx for primary CDI.

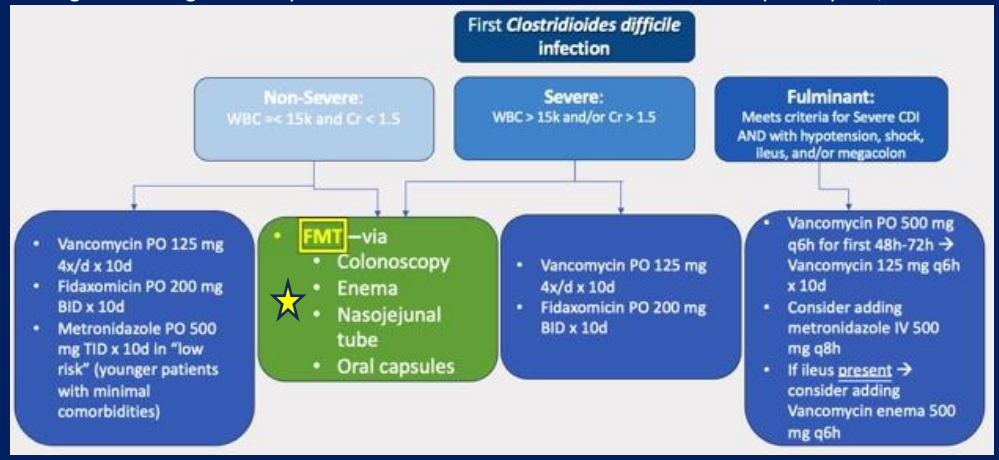
- Study design: 100 patients with primary CDI were divided into 2 groups—group 1 received FMT as primary tx (n=51) and group 2 received standard of care vancomycin (n=49).
  - ***End-points***: 1) clinical cure at day 14 and no recurrence within 60 days; 2) clinical cure at day 14 *with or w/o additional tx* (ABX, FMT) & no recurrence within 60 days.
- Patient Population: Median age 70-71 years. 63% of patients in FMT cohort were female vs. 53% in vancomycin cohort.
  - 71% of the FMT cohort had community-acquired CDI vs. 55% of the vancomycin cohort. All patients had *non-severe or severe CDI*.
  - *Exclusion criteria*: IBS-D, severely immunodeficient, microscopic colitis, IBD, and/or fulminant CDI; pregnant or nursing women; status post-colectomy ileostomy or -colostomy, had received > 1 dose of an ABX for CDI or ABX for other infections, in ICU
- Intervention: A) one 50g FMT enema was administered within 24h of randomization or B) 125 mg of oral vancomycin was given 4x/day for 10 days
- Results: FMT found to be non-inferior to vancomycin for primary CDI. 67% of the FMT cohort vs. 61% of the vancomycin cohort achieved clinical cure w/o recurrence.

Dr. Dhere: "FMT for recurrent CDI has proven to be safe, cost-effective, and successful in terms of clearance of CDI as well as improving quality of life. The use of FMT for primary CDI is an attractive option given that 25% of patients will develop recurrence after an initial episode of CDI."



Key Points & Future Directions

- However, further research needed directly comparing fidaxomicin versus FMT for primary CDI and determine optimal protocol and route of FMT instillation (Juul et al, 2025).
- If further research provides additional evidence of the efficacy of **FMT**, future treatment algorithms might be adapted to include **FMT** for non-severe and severe primary CDI, such as



Key Points: Further research is needed before implementing FMT for primary non-severe and severe CDI tx. The non-inferior nature of FMT in this trial is promising, but it should be noted that 21% of FMT patients required secondary treatment vs. 8% of vancomycin patients. However, there was no significant difference in adverse events between the 2 groups.

Dr. Dhere: "Additional research including assessing cost-effectiveness and improvement in quality of life in using FMT for primary CDI is warranted."

Juul FE, Bretthauer M, Johnsen PH, et al. Fecal Microbiota Transplantation Versus Vancomycin for Primary *Clostridioides difficile* Infection : A Randomized Controlled Trial. *Ann Intern Med*. 2025;178(7):940-947. doi:10.7326/ANNALS-24-03285

Centers for Disease Control and Prevention. 2024. Emerging Infections Program, Healthcare-Associated Infections – Community Interface Surveillance Report, Clostridioides difficile infection (CDI), 2022.