Open Forum Infectious Diseases

MAJOR ARTICLE

Clinician Management Preferences for *Clostridioides difficile* Infection in Adults: A 2024 Emerging Infections Network Survey

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Background. The 2021 Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) guidelines for *Clostridioides difficile* infection (CDI) introduced new recommendations for managing initial and recurrent CDI. Since then, new microbiome-based therapies for preventing recurrent CDI have become available. We surveyed infectious diseases (ID) clinicians to understand their experiences, practices, and challenges in CDI management.

Methods. An electronic survey was distributed to members of the IDSA Emerging Infections Network in May 2024, targeting ID physicians and healthcare professionals in the United States who manage adult CDI. The survey assessed treatment preferences, clinical practices, and barriers to accessing and prescribing CDI therapies.

Results. Of the 500 respondents who reported treating CDI in the past year, 83% (417/500) indicated that vancomycin was their most frequently prescribed agent for initial, nonfulminant CDI. Additionally, 72% (357/498) reported that their institutional guidelines recommended vancomycin as the first-line agent. The most common barrier to fidaxomicin use was challenges with outpatient insurance coverage (82% [408/496]). Bezlotoxumab was available to 74% (370/500) of respondents, though 33% (165/497) indicated they do not use bezlotoxumab routinely. Most clinicians (87% [437/500]) had previously recommended fecal microbiota transplantation (FMT) for recurrent CDI, though only 48% (239/500) had current access to FMT using donor stool. Fecal microbiota live-jslm was available to 36% (179/500), and fecal microbiota spores live-brpk was available to 30% (150/500).

Conclusions. Significant barriers, including high costs, insurance challenges, and limited availability of CDI therapies, impact clinical decision-making and adherence to guideline recommendations.

Keywords. CDI; *Clostridioides difficile* infection; guidelines; infectious diseases clinicians; survey.

The Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) updated guidelines for managing *Clostridioides difficile* infection (CDI) in 2021, introducing key conditional recommendations for both fidaxomicin and bezlotoxumab. Notably, the updated guidelines preferred fidaxomicin over vancomycin for initial and recurrent CDI episodes based on data showing that fidaxomicin is associated with lower recurrence rates [1–5]. However, vancomycin remains an acceptable alternative, particularly when the higher cost of fidaxomicin limits its use. Additionally, a recommendation was introduced for bezlotoxumab as an adjunctive therapy to reduce CDI recurrence risk in patients with a CDI episode in the last 6 months [1]. In the absence of logistical barriers, bezlotoxumab was also recommended for patients with primary CDI who have other risk factors for recurrence. Since the release of the IDSA/SHEA guidelines, the US Food and Drug Administration (FDA) approval of fecal microbiota live-jslm (Rebyota) and fecal microbiota spores live-brpk (Vowst) has added new microbiome-based therapies as options for prevention of recurrent CDI [6, 7].

The adoption of guideline recommendations by infectious diseases (ID) clinicians and the utilization of newer therapies remain unclear. Fidaxomicin remains significantly more expensive than vancomycin, often requiring prior authorizations and leading to higher out-of-pocket costs for patients [8, 9]. Similarly, bezlotoxumab is a costly medication, and use may be limited by the logistics of scheduling outpatient infusions during standard-of-care antimicrobial therapy [10]. Access to traditional fecal microbiota transplantation (FMT) decreased during the coronavirus disease 2019 (COVID-19) pandemic [11], and the high costs or logistical challenges of newer therapies— fecal microbiota live-jslm and fecal microbiota spores live-brpk—may limit accessibility [12, 13].

Received 06 May 2025; editorial decision 02 June 2025; published online 17 June 2025
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https://doi.org/10.1093/ofid/ofaf335

CDI remains a significant cause of morbidity and mortality [14–16]. Understanding current clinician practices and preferences as well as barriers to adopting guidelines and new therapies is important for improving access and optimizing CDI management. To explore these issues, we surveyed ID clinicians regarding their experiences and challenges in managing CDI.

METHODS

We developed an electronic survey focused on the management of CDI in adults. This survey was distributed through the IDSA Emerging Infections Network (EIN), an ID community provider–based network supported by the Centers for Disease Control and Prevention [17]. The survey link was emailed 3 times in May 2024 to both physician and healthcare professional (eg, pharmacists and advanced practice providers) EIN members who practice adult ID in the US. Pediatric ID clinicians were excluded as an EIN survey on management of CDI in children was being concurrently developed. An EIN survey on CDI management in adults was last distributed in 2012 [18], prior to the release of the 2017 and 2021 IDSA/SHEA guidelines.

The initial question asked members to estimate the number of patients with CDI they treated over the past 12 months. Respondents who treated zero CDI patients were allowed to opt out of answering further questions. Subsequent questions focused on management preferences for initial and recurrent nonfulminant CDI, including how clinicians define recurrent CDI when deciding on treatment. Additional questions explored factors and barriers related to use of fidaxomicin, bezlotoxumab, FMT, and microbiome-based therapies. The survey utilized single- and multiple-choice answer selections. Free-text fields were provided for additional comments. The full survey instrument is provided in the Supplementary Data. Representative free-text comments were selected to illustrate common themes identified in responses and were not edited or paraphrased.

Not all respondents answered every question, so denominators varied. Data were analyzed using descriptive statistics.

RESULTS

Response Rate and Practice Characteristics

The survey response rate was 36% (577/1618). The majority of respondents were ID physicians (88% [509/577]), and the most common practice setting was academic/university (38% [222/577]). Respondents most commonly reported seeing between 10 and 20 patients with CDI in the past 12 months (34% [196/577]). Complete geographical distributions, years of experience after terminal ID training, and practice characteristics of respondents are detailed in Table 1. Of the 577 respondents, 500 reported caring for at least 1 patient with CDI in the prior 12 months and completed the full survey.

Table 1. Characteristics of Survey Respondents (N = 577)

Characteristic	No. (%)
Region[a]	
US: New England	51 (9)
US: Mid-Atlantic	80 (14)
US: East North Central	83 (14)
US: West North Central	68 (12)
US: South Atlantic	104 (18)
US: East South Central	22 (4)
US: West South Central	44 (8)
US: Mountain	29 (5)
US: Pacific	91 (16)
Canada and Puerto Rico	5 (0.9)
Experience after terminal ID training, y	
<5	104 (18)
5–14	194 (34)
15–24	110 (19)
≥25	169 (29)
Primary hospital type	
Community	154 (27)
Non-university teaching	135 (23)
University	222 (38)
Veterans Affairs Hospital or Department of Defense	36 (6)
City/county	26 (5)
Outpatient only	4 (0.7)
Member type	
Infectious diseases physician	509 (88)
Healthcare professional (APP, PharmD)	68 (12)
No. of patients treated for CDI in past year	
None	77 (13)
<10	127 (22)
10–20	196 (34)
21–30	91 (16)
>30	86 (15)

Abbreviations: APP, advanced practice provider; CDI, *Clostridioides difficile* infection; ID, infectious diseases; US, United States.

[a]Regions defined by US Census Bureau regions and divisions of the United States.

Management of Initial, Nonfulminant CDI Episodes

Eighty-three percent (417/500) of ID clinicians selected vancomycin as the most frequently prescribed antibiotic for initial, nonfulminant CDI (Table 2). When asked to disregard formulary restrictions and insurance/financial considerations, 68% (339/499) preferred fidaxomicin. Additionally, 72% (357/498) reported that their healthcare facility's institutional guidelines recommend vancomycin as the first-line agent. Representative free-text comments are presented in Table 3. Multiple respondents wrote that their institutional guidelines also recommend fidaxomicin as first-line therapy when patients have high risk for recurrence.

Management of Recurrent CDI

For treatment purposes, 57% (283/495) of respondents defined recurrent CDI as an episode within 8 weeks of the initial episode and 29% (145/495) defined it as an episode within 6 months (Table 2).

Table 2. Treatment Preferences, Barriers, and Availability of Therapies for Management of *Clostridioides difficile* Infection, May 2024 Emerging Infections Network Member Responses to Survey Questions[a]

Survey Items and Responses	No. (%)
Reported treatment in usual practice for an initial episode of nonfulminant[b] CDI (n = 500)	
Metronidazole (PO)	3 (0.6)
Vancomycin (PO)	417 (83)
Fidaxomicin	80 (16)
Preferred treatment regardless of formulary or patient insurance/financial considerations for an initial episode of nonfulminant CDI (n = 499)	
Metronidazole (PO)	2 (0.4)
Vancomycin (PO)	158 (32)
Fidaxomicin	339 (68)
Recommend agent per respondents' healthcare facility's institutional guidelines for an initial episode of nonfulminant CDI (n = 498)	
Metronidazole (PO)	1 (0.2)
Vancomycin (PO)	357 (72)
Fidaxomicin	78 (16)
Not sure	44 (9)
No institutional guidelines	10 (2)
Respondents' definition of recurrent CDI when deciding on treatment (n = 495)	
CDI episode occurring within 8 wk after the initial episode	283 (57)
CDI episode occurring within 6 mo after the initial episode	145 (29)
CDI episode occurring within 1 y after the initial episode	60 (12)
CDI episode occurring >1 y after the initial episode	7 (1)
Reported treatment in usual practice for a first recurrence of nonfulminant CDI if a standard 10-d course of vancomycin was used for the initial episode (n = 499)	
Metronidazole (PO)	1 (0.2)
Vancomycin (PO), 10-d course	59 (12)
Vancomycin (PO), tapered-pulsed regimen	188 (38)
Fidaxomicin, 10-d course	227 (45)
Fidaxomicin, extended or tapered-pulsed regimens	24 (5)
Treatment options respondents would consider for a second recurrence of nonfulminant CDI (n = 489)[c]	
Metronidazole (PO)	3 (0.6)
Vancomycin (PO), 10-d course	33 (7)
Vancomycin (PO), tapered-pulsed regimen	299 (61)
Fidaxomicin, 10-d course	209 (43)
Fidaxomicin, extended or tapered-pulsed regimens	199 (41)
Vancomycin (PO) followed by rifaximin chaser	18 (4)
Patient factors that would influence respondents to use fidaxomicin rather than other agents for nonfulminant CDI (n = 500)[c]	
Recurrent CDI	418 (84)
Immunocompromised	319 (64)
Age >65 y	266 (53)
Severe CDI on presentation	198 (40)
Concomitant systemic antibiotics	134 (27)
Inflammatory bowel disease	106 (21)
No factors selected	40 (8)
Barriers that prevent respondents from prescribing/recommending fidaxomicin (n = 496)[c]	
No barriers	47 (9)
Challenges with insurance coverage for outpatients (eg, prior authorization, high copays)	408 (82)
Restricted inpatient availability (eg, nonformulary or high inpatient costs)	231 (47)
Patient already on oral vancomycin and unclear benefit of switching therapy	189 (38)
Circumstances that would influence respondents to use bezlotoxumab (n = 497)[c]	
Initial, nonfulminant or fulminant disease	9 (2)
Recurrent infection, first recurrence	135 (27)
Recurrent infection, ≥2 recurrences	297 (60)
Immunocompromised host, any episode	223 (45)
Age >65 y, any episode	138 (28)
I do not prescribe or recommend bezlotoxumab routinely	165 (33)
Have respondents previously recommended FMT (n = 500)[c]	
No, not available	50 (10)
No, would not recommend	10 (2)
Yes, for acute fulminant disease	80 (16)
Yes, for recurrent infection[d]	437 (87)
CDI therapies available to respondents' patients (n = 500)[c,e]	
Bezlotoxumab	370 (74)
FMT using donor stool	239 (48)
Fecal microbiota live-jslm	179 (36)
Fecal microbiota spores live-brpk	150 (30)
None selected	59 (12)

Abbreviations: CDI, *Clostridioides difficile* infection; FMT, fecal microbiota transplantation; PO, per os.

[a]Number of respondents varied by question.

[b]Nonfulminant CDI: infection without associated hypotension, shock, ileus, or megacolon.

[c]Respondents could select all that apply; percentage may add to >100%.

[d]There were 418 responses to follow-up question on what number of CDI recurrences respondents have recommended FMT; 35 (8%) recommended FMT after 1 recurrence, 236 (57%) after 2 recurrences, and 147 (35%) after 3 recurrences.

[e]Forty-one (8%) respondents selected all 4 therapies, 96 (19%) selected 3 therapies, 182 (36%) selected 2 therapies, and 122 (24%) selected 1 therapy.

When treating a first recurrence of CDI after a 10-day course of vancomycin for the initial episode, 45% (227/499) of respondents selected a 10-day course of fidaxomicin as the most frequently prescribed regimen, while 38% (188/499) selected a tapered-pulsed regimen of vancomycin (Table 2). Less commonly selected regimens included repeating a 10-day course of vancomycin (12% [59/499]) or using an extended or tapered-pulsed regimen of fidaxomicin (5% [24/499]).

For a second recurrence of CDI, respondents were asked to select all regimens they would consider (Table 2). The most common choice was a tapered-pulsed regimen of vancomycin (61% [299/489]), followed by a 10-day course of fidaxomicin (43% [209/489]) and extended or tapered-pulsed regimens of fidaxomicin (41% [199/489]).

Experience With Fidaxomicin

Recurrent CDI (84% [418/500]), immunocompromised status (64% [319/500]), and age >65 years (53% [266/500]) were the most common factors influencing respondents to choose fidaxomicin over other agents for nonfulminant CDI episodes (Table 2). The most common barrier to prescribing or

Table 3. Select Free-Text Responses

Component of CDI Management	Representative Comments
Reported practices, preferences, and healthcare facility institutional guidelines for treatment of initial, nonfulminant CDI	• "Fidaxomicin is recommended based on patient-specific risk factors (age, recurrent CDI, immunosuppression and concomitant abx) and pending insurance coverage. If pt doesn't meet criteria or can't afford, we use po vanco up-front" • "Fidaxomicin is restricted to ID and GI. Pharmacy prefers us to use vancomycin, but I push for fidaxomicin if multiple risk factors for recurrence, not quickly responding to vanc, etc" • "My patient population is admitted for hematologic/oncologic malignancies and includes HSCT. Therefore, if *C. difficile* infection is confirmed, fidaxomicin is preferred. Our guidelines list oral vancomycin and fidaxomicin as recommended agents"
Barriers to prescribing or recommending fidaxomicin	• "High costs (copays or out-of-pocket) for patients remains a significant barrier to fidaxomicin use; many insurance companies still do not have fidaxomicin on a low-cost tier. There is a wide range of variability in insurance coverage, making it difficult to even predict the potential patient copay for fidaxomicin" • "Cost or just suspected cost/red tape about fidaxomicin often leads to preferential use of oral vancomycin" • "I think that the emphasis on fidaxomicin by IDSA in guidelines is financially irresponsible. It is hard to get for patients, which delays care" • "No challenges at VA. Many insurance challenges at academic affiliate"
Use and availability of bezlotoxumab and microbiome-based therapies	• "Every time I've tried to arrange bezlo outpatient it has been a fail due to insurance coverage, patient residing in SNF, etc" • "I have prescribed bezlo in patients at risk for recurrence, but do not frequently do so now because of lack of availability and resource limitations at my institution" • "Commercially available FMT products are crazy expensive" • "I cover a lot of rural community hospitals and while I'd like to consider Vowst/Rebyota more often, patients would have to travel to far-away academic centers in most cases to get these agents, which is a considerable barrier" • "There is no IDSA guideline update to reflect newer therapies like Rebyota or Vowst so we're still struggling with the place in therapy for these"

Abbreviations: CDI, *Clostridioides difficile* infection; FMT, fecal microbiota transplantation; GI, gastroenterology; HSCT, hematopoietic stem cell transplant; ID, infectious diseases; IDSA, Infectious Diseases Society of America; PO, per os; SNF, skilled nursing facility; VA, Veterans Affairs.

recommending fidaxomicin was challenges with insurance coverage for outpatients (eg, prior authorizations or high copays; 82% [408/496]) followed by restricted inpatient availability (eg, nonformulary or high inpatient costs; 47% [231/496]). Few respondents (9% [47/496]) reported no barriers to using fidaxomicin. Clinicians working at city or county facilities had the lowest proportion reporting no barriers to fidaxomicin use (2/22; Supplementary Table 1). In free-text comments, multiple respondents wrote about their challenges with insurance coverage and the high cost of fidaxomicin (Table 3).

Experience With Bezlotoxumab and Microbiome-Based Therapies

Bezlotoxumab was available to 74% (370/500) of respondents; however, 33% (165/497) indicated that they do not prescribe or recommend bezlotoxumab routinely (Table 2). Clinicians working at city or county facilities had the lowest proportion of bezlotoxumab availability (41% [9/22]; Supplementary Table 2). The most frequently selected circumstances for using bezlotoxumab as adjunctive therapy were second or subsequent recurrences of CDI (60% [297/497]) and immunocompromised status (45% [223/497]) (Table 2). In free-text comments, multiple respondents noted logistical challenges of coordinating bezlotoxumab infusions (Table 3).

Eighty-seven percent (437/500) of respondents have previously recommended FMT using donor stool for recurrent CDI, with most (57% [236/418]) recommending FMT after at least 2 recurrences. However, FMT using donor stool was currently available to 48% (239/500) of respondents (Table 2). Only 2% (10/500) indicated they would not recommend FMT, and 10% (50/500) of respondents reported never recommending FMT due to lack of availability. Additionally, 16% (80/500) have recommended FMT for acute fulminant disease.

Fecal microbiota live-jslm was available to 36% of respondents (179/500), and fecal microbiota spores live-brpk was available to 30% (150/500). Only 8% (41/500) indicated that bezlotoxumab, FMT using donor stool, fecal microbiota live-jslm, and fecal microbiota spores live-brpk were all available for their patients. Availability of microbiome-based therapies by practice setting is presented in Supplementary Tables 3–5. In free-text comments, respondents noted that high costs and lack of availability interfere with their use of microbiome-based therapies (Table 3).

DISCUSSION

Three years after the 2021 IDSA/SHEA guidelines update, significant barriers to recommended therapies were reported by the ID community. Notably, we found that ID clinicians in the US primarily use oral vancomycin for initial episodes of CDI in their routine practice. This aligns with the findings of Dubberke et al, who reported that vancomycin was the most frequently prescribed agent for CDI in the year following the guidelines update [19]. Despite these findings, two-thirds of respondents in our survey indicated a preference for fidaxomicin over vancomycin if there were no insurance or cost barriers. By directly surveying a large national sample of ID clinicians, our

study provides insights into the reasons behind the substantial gap between preference and practice.

ID providers reported that the most common barrier to fidaxomicin use is outpatient insurance coverage. Previous studies have shed light on insurance hurdles when prescribing fidaxomicin, including only 1.1% of Medicare patients having coverage for fidaxomicin in a low-cost tier status without a need for prior authorization [9]. In addition, single-center studies have showed wide variation in fidaxomicin copays [20, 21]. In free-text comments, respondents noted that the time required to navigate prior authorizations and high patient copays is prohibitive and delays care. The second most common barrier to fidaxomicin use was restricted inpatient availability. In our survey, the majority of institutional guidelines continue to recommend vancomycin as the first-line agent for initial CDI episodes with higher acquisition costs of fidaxomicin being one potential barrier. The common restriction of inpatient fidaxomicin availability highlights discordance between IDSA guideline recommendations and local practice adoption. Notably, the American College of Gastroenterology (ACG) guidelines consider vancomycin and fidaxomicin as acceptable first-line options [22], which may contribute to variation in clinical practice and institutional guideline development.

ID providers reported limited adoption of bezlotoxumab despite a recommendation for use by both IDSA/SHEA and ACG guidelines [1, 22]. Access was a significant barrier, with more than a quarter of all respondents reporting that bezlotoxumab was unavailable to their patients, and providers from city or county healthcare facilities reporting lower availability. Logistical challenges also likely play a significant role in limiting bezlotoxumab utilization. Since bezlotoxumab is administered intravenously during standard-of-care therapy, obtaining prior authorizations and coordinating outpatient infusions often need to occur within a narrow treatment window. Recently, the manufacturer announced it would discontinue production of bezlotoxumab as of 31 January 2025, <10 years after FDA approval. The reasons behind discontinuation have not been publicized, and the availability of this therapy is likely to be exhausted in the near future [23].

Fecal microbiota transplantation has emerged as a cornerstone for preventing CDI recurrences, with 87% of respondents having recommended it. This aligns with IDSA/SHEA guidelines, which include a strong recommendation for FMT in patients with multiple recurrences [24]. However, less than half of respondents in our survey currently have access to FMT for their patients. Potential reasons for limited accessibility include the disruption in production from donor stool banks, such as OpenBiome, caused by the COVID-19 pandemic and prior updates to the FDA enforcement policy around FMT [25–27]. More recently, OpenBiome announced it would cease distribution of investigational FMT products [28]. The low availability reported by ID clinicians in our survey may reflect the ongoing challenges in restoring pathways for FMT product access.

Two new microbiome-based therapies, fecal microbiota live-jslm and fecal microbiota spores live-brpk, were approved by the FDA based on phase 3 clinical trials demonstrating their safety and efficacy in preventing recurrent CDI [29, 30]. In our survey, availability of these therapies was limited, with 36% and 30% of respondents reporting access to fecal microbiota live-jslm and fecal microbiota spores live-brpk, respectively. This limited availability is understandable given their recent release and potential high costs, with fecal microbiota live-jslm priced at $9000 and fecal microbiota spores live-brpk at $17 500 per course [12, 13]. Additionally, while fecal microbiota spores live-brpk is available as a prescription, fecal microbiota live-jslm requires administration via rectal suspension by a healthcare provider, posing another logistical barrier. These therapies have not been directly studied against conventional FMT using donor stool from stool banks and have yet to be incorporated into guidelines [22].

Our study has several limitations. Survey length limitations restricted exploration of the full spectrum of CDI management. Additionally, EIN members with a particular interest in CDI may have been more likely to respond, introducing response bias. Generalizability may be further limited by the overrepresentation of ID clinicians from university settings, who may have more access to certain resources, such as pharmacy transition-of-care teams, outpatient infusion centers, or gastroenterology specialists able to perform conventional FMT. While our survey focused on ID clinicians, future surveys of gastroenterologists and other specialties could provide valuable insights given their key roles in CDI management. Our question about institutional guidelines did not include the option to select both vancomycin and fidaxomicin as first-line agents, a limitation indicated by several respondents in free-text comments who noted that both are recommended depending on patient risk factors for recurrence. Last, this survey was distributed >6 months prior to the announcements regarding discontinuation of bezlotoxumab production and OpenBiome's cessation of donor stool distribution, both of which will impact ID clinician practices.

This survey provides an updated and widescale investigation into ID clinicians' use of, access, and barriers to CDI therapies. High upfront costs of guideline-recommended therapies continue to shape clinical decision-making. Recent economic modeling suggests that fidaxomicin is not cost-effective compared to vancomycin at its current price point, unless the price is substantially reduced [31]. Observational real-world data have shown that total postindex hospitalization costs are similar between fidaxomicin- and vancomycin-treated patients, though these analyses reflect healthcare system costs rather than patient out-of-pocket expenses [19]. Prior cost-effectiveness studies showed mixed results depending on the assumptions about

drug pricing, recurrence rates, and target populations [32–34]. The price point at which newer microbiome-based therapies would become cost-effective on a population level remains unclear. Importantly, the clinical benefits that individual patients experience from optimized treatments and reduced recurrence risk are difficult to quantify in purely economic terms. Insights from practicing ID clinicians, as demonstrated in this survey, can be essential in guiding efforts to improve access and promote the sustainable use of CDI therapies.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Acknowledgments. The authors thank Clifford McDonald, MD, Alice Y. Guh MD, MPH, and Erik R. Dubberke, MD, MSPH, for their feedback on the survey questions.

Patient consent. This study did not include factors necessitating patient consent.

Financial support. This work was funded by the Centers for Diseases Control and Prevention (cooperative agreement number 5, grant number NU50CK000574 to P. M. P. and S. E. B.).

Potential conflicts of interest. All authors: No reported conflicts of interest.

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