Thus,

Body mass index changes after fecal microbiota transplantation for recurrent *Clostridioides difficile* infection

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Abstract

Background: Fecal microbiota transplantation (FMT) is a successful therapy for *Clostridioides difficile* infection (CDI). FMT from overweight donors is speculated to influence the recipient's body mass index (BMI) after administration for CDI.

Objectives: We investigated changes in the recipient's BMI after FMT in relation to the donor's BMI.

Design: We conducted a retrospective cohort study involving patients who underwent FMT for recurrent CDI at Mayo Clinic between 2012 and 2019.

Methods: We analyzed demographic and donor data for patients undergoing FMT at Mayo Clinic (2012–2019). Recipient BMI (pre- and post-FMT) and donor BMI were extracted from medical records. Mixed-effects linear regression was used to evaluate the impact of donor BMI, donor BMI category, recipient baseline BMI, time before and after FMT, and interactions between these variables on overall BMI change and BMI change per month. Kaplan-Meier curves were used to assess BMI changes (\geq 5 units) based on the last recorded post-FMT BMI. Results: We analyzed data from 401 patients with recorded BMI measurements before and after FMT. The median age of the recipients at the time of FMT was 59.1 years (interguartile range (IQR): 40.5–70.1 years), with 61.6% being female. The median BMI for recipients prior to FMT was 26.7 kg/m² (IQR: 22.7–31.6 kg/m²), while the median BMI of the donors was 24.5 kg/m² [IQR: 23.9–27.5 kg/m²]. Stool from donors with a normal BMI was used for 58.2% of recipients, while 41.8% received stool from pre-obese donors. Donor BMI data were missing for 3.2% of recipients. Donor BMI was not significantly associated with changes in recipient BMI; for each 1-unit increase in donor BMI, a 0.01-unit monthly increase was observed (95% confidence interval: -0.0003, 0.02; p = 0.11). The log-rank test for BMI increases ($\geq +5$) and decreases (≤ -5) revealed no significant differences among the donor BMI groups (Chi-squared = 4.4, p=0.1 for increases, Chi-squared = 2, p=0.4 for decreases).

Conclusion: The lack of impact of donor BMI on BMI changes post-FMT suggests that these changes are more dependent on the recipient's metabolic profile. Prospective, controlled trials are required to analyze these results more comprehensively.

Plain language summary

Exploring the impact of fecal transplant on body weight: does the donor's BMI matter?

Why was the study conducted?

This study aimed to determine whether fecal microbiota transplantation (FMT), a treatment mainly used for Clostridioides difficile infection (CDI), could affect body mass index (BMI) in patients. The primary question explored was whether the BMI of the donor had an impact on the recipient's BMI after FMT. Researchers aimed to investigate this relationship due to concerns that stool from overweight donors might affect weight outcomes in recipients.

Original Research

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What did the researchers do?

Researchers analyzed medical records from 401 patients who underwent FMT at the Mayo Clinic between 2012 and 2019. They compared BMI changes in recipients before and after FMT and examined whether these changes were influenced by the BMI of the stool donors. The study used statistical models and survival analyses to evaluate BMI changes over time.

What did the researchers find?

The researchers found no significant relationship between donor BMI and changes in recipient BMI after FMT. Most recipients experienced minimal weight changes after FMT, with any increases likely reflecting recovery from weight loss caused by the infection rather than donor-related factors. For example, donors with higher BMIs did not lead to noticeable weight gain in recipients.

What do the findings mean?

These findings suggest that post-FMT BMI changes are more dependent on the recipient's own health and recovery from CDI than on the BMI of the stool donor. This highlights the need for further research, particularly through long-term and controlled studies, to confirm these results and refine donor selection guidelines.

Keywords: body mass index, Clostridioides difficile, fecal microbiota transplant

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Introduction

The human microbiome plays a crucial role in gut health, immune function, and metabolic regulation.1 Disruptions in microbiota balance can contribute to various diseases, including obesity and gastrointestinal infections such as Clostridioides difficile infection (CDI). CDI often results in severe abdominal pain, watery diarrhea, significant weight loss, and hypoalbuminemia due to impaired nutrient absorption and inflammation. Recurrence of infection is common and remains a major challenge in reducing overall incidence.²⁻⁷ Fecal microbiota transplantation (FMT) has emerged as an effective treatment for recurrent CDI, demonstrating high success rates in restoring gut microbial diversity and preventing infection recurrence.⁶ However, the impact of FMT extends beyond infection control and may influence the recipient's metabolic profile.

Patients recovering from CDI frequently undergo significant weight fluctuations. During the acute phase of CDI, patients typically suffer from diarrhea and colitis, leading to substantial weight loss due to dehydration, malabsorption, and reduced oral intake secondary to gastrointestinal symptoms. In the recovery phase, weight gain is generally observed as patients' gastrointestinal function begins to normalize.^{8,9} Obesity and metabolic syndrome are significant considerations in donor selection for FMT, with the best practice of excluding donors with a body mass index (BMI) over 30 kg/m² or those with metabolic syndrome.¹⁰ This recommendation stems from concerns raised by case reports of weight gain in recipients after receiving FMT from overweight donors and animal studies.^{11,12}

More extensive research is needed to substantiate donor selection guidelines and understand the mechanisms underlying microbiota-driven weight changes. To better understand the impact of donor BMI on weight changes post-FMT for recurrent CDI, our study examined the relationship between the donor BMI and the change in the recipient's BMI after FMT. Our primary objective was to determine whether stool donor BMI affects recipient BMI changes following FMT for recurrent CDI. The secondary objective was to evaluate changes in BMI in patients undergoing FMT for recurrent CDI over a 1-year follow-up period. We hypothesized that donor BMI would have no significant effect on recipient BMI changes (H0), with an alternative hypothesis (H1) suggesting that higher donor BMI may contribute to increased recipient BMI. Understanding

these dynamics could inform donor selection guidelines and clarify the role of microbiota in weight changes.

Methods

A retrospective chart review was conducted, and patients were selected consecutively from the electronic medical records of all individuals who underwent FMT for recurrent CDI at the Mayo Clinic between August 2012 and August 2019.

Demographic data, comorbidities, pre- and post-FMT BMI, along with the corresponding donor BMI, were obtained from electronic medical records and a prospectively maintained FMT database. Predictors included baseline recipient BMI, donor BMI, and time between FMT and BMI measurement pre- and post-FMT.¹³ The Charlson Comorbidity Index was included to describe the prevalence of comorbid illnesses in the recipients, as higher comorbidity scores could potentially impact recovery and weight regain. Recipients lacking BMI measurements within 1 year before or after FMT for recurrent CDI were excluded from the analysis. Data from 13 patients were not assessed for the relationship between donor BMI and recipient BMI post-FMT because their stool donors lacked BMI recordings.

Donor and recipient BMIs (kg/m²) were classified using the World Health Organization (WHO) criteria: underweight <18.5, normal 18.5-24.9, preobese 25–29.9, obese class I 30–34.9, obese class II 35–39.9, and obese class III \ge 40.¹⁴ Pre-recipient BMI was defined as the most recent BMI measurement within the year preceding the FMT. Weight group changes post-FMT were described as increasing or decreasing in BMI range according to the WHO classification. The association between recipient BMI changes post-FMT and donor BMI was investigated. Potential confounders in our study included diet, medication use, physical activity, and CDI severity. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.¹⁵

Statistical methods

Medians and IQRs were reported for continuous variables, while frequencies and percentages were

used for discrete variables. Part of the statistical analyses was conducted using JMP version 16.2 (SAS Institute Inc., Cary, NC). To evaluate the relationship between recipient BMI changes post-FMT and donor BMI, we employed mixedeffects linear regression models using R statistical software version 3.6.2.16 This approach was chosen due to the hierarchical and longitudinal nature of the dataset, where each recipient had multiple BMI measurements over varying time intervals. Mixed-effects models account for both fixed effects (e.g., donor BMI, baseline recipient BMI, the time interval between FMT administration, and BMI recordings pre- and post-FMT) and random effects (e.g., inter-patient variability), ensuring robust estimates. Random intercept and slope terms were included to account for individual-level variability in BMI trajectories over time. This modeling approach allowed us to assess the direct effects of key predictors and their interactions on BMI changes while accounting for repeated measurements within individuals.

We conducted multiple iterations of mixed-effects linear regression models, consecutively including predictors and their interaction terms to examine the influence of donor BMI, donor BMI category, recipient baseline BMI, time before FMT (time from the baseline BMI measurement to the FMT procedure), time after FMT (time between FMT and subsequent BMI measurements), interactions between donor BMI and time after FMT, and interactions between baseline recipient BMI and time before FMT on BMI change and BMI change per month (Supplemental Table 1). The models were compared using the Akaike Information Criterion, Bayesian Information Criterion, and log-likelihood.

We also performed log-rank analysis and created Kaplan–Meier (KM) curves for a \geq 5 increase or decrease in final BMI value post-FMT from baseline BMI stratified by donor BMI category.

Results

Recipient characteristics

The sample size for this study was determined based on the availability of patients who underwent FMT for recurrent CDI at our institution between 2012 and 2019. A total of 980 patients were identified, with 401 patients meeting the inclusion criteria of having complete BMI data pre- and post-FMT (Table 1). A study flow diagram is represented in Figure 1. At the time of FMT, the median recipient age was 59.1 years (IQR: 40.5–70.1), and 61.6% of recipients were female. The median time from the pre-FMT BMI measurement to FMT was 24.7 days (IQR: 4.6– 77.5 days). The median Charlson Comorbidity Index was 1 (IQR 0–2). The median pre-FMT recipient BMI was 26.7 kg/m² (IQR 22.7–31.6, range 14.6–59.2). Table 2 details the distribution of BMI across weight categories.

Donor characteristics

Eighteen unique donors were identified, with BMI information unavailable for 2 of them in the included dataset. Donors had a median BMI of 24.5 kg/m² (range: 20.9–29.6). Stool from donors with a normal BMI was used for 58.2% of the recipients, while 41.8% received stool from preobese donors. No donors fell into obesity Class I, II, or III BMI categories.

Recipient BMI changes post-FMT

Among 401 recipients pre-FMT, the largest proportion fell into the normal BMI category (35.4%), followed by pre-obese (27.9%) and obese categories (17.7% in class I, 7.7% in class II, and 7.0% in class III) with a small percentage classified as underweight (4.2%; Table 2). Recipients were stratified by their initial BMI to examine baseline BMI effects. In our dataset, the median number of follow-up measurements per patient was 5 (IQR: 2–10). Supplemental Figure 6 illustrates the distribution of follow-up measurements, highlighting variability in monitoring frequency.

The median time interval between FMT administration and the first follow-up BMI measurement (as well as between consecutive BMI measurements) was 8.9 days (IQR: 1.2–35 days) and a mean of 29.3 days (standard deviation (SD): ± 47.2), indicating significant variability in the timing of follow-up assessments across patients (Supplemental Figure 3). The overall median time to follow-up, accounting for all follow-up measurements post-FMT for each participant, was 151.61 (IQR: 69.9–260.2) days with a mean of 164.1 (SD: ± 108) days. Supplemental Figure 5 presents the distribution of BMI measurements over time, stratified according to WHO BMI Table 1. Patient summaries.

Study Population Characteristics	Overall (<i>N</i> =401)			
Sex				
Female	247 (61.6%)			
Male	154 (38.4%)			
Age at FMT				
Median (Q1, Q3)	59.1 (40.5, 70.1)			
Donor BMI				
N-missing	13			
Median (<i>Q</i> 1, <i>Q</i> 3)	24.5 (23.9, 27.5)			
BMI, body mass index: FMT, fecal microbiota transplantation.				

classifications. Figure 2 represents the BMI distribution captured in the dataset at monthly intervals during the study period.

Post-FMT, 299 patients (74.6%) maintained their initial weight category, 42 patients (10.5%) moved to a lower weight category, and 60 patients (14.9%) moved to a higher one. Most underweight recipients (70.6%) remained in their weight category, while 23.5% transitioned to normal BMI, and 5.9% moved up three weight categories to obese class I BMI.

For recipients with a normal BMI, 81% maintained their category, 13.4% shifted to the preobese category, and 5.6% decreased to the underweight BMI category. For pre-obese recipients, 70.5% stayed in their category, 18.8% progressed to obese class I, and 10.7% moved down to normal BMI. In the obese class I BMI group, 71.8% maintained their weight group, 12.7% increased to obese class II, and 15.5% decreased to pre-obese BMI.

In patients with obese class II BMI, 58.1% maintained their weight category, 19.4% progressed to obese class III BMI, 16.1% moved down to obese class I, and 6.5% decreased by two categories to pre-obese. Finally, 85.7% of patients within the obese class III BMI category maintained their weight group and 14.3% decreased to obese class II. Supplemental Figure 1 illustrates BMI changes observed over time.

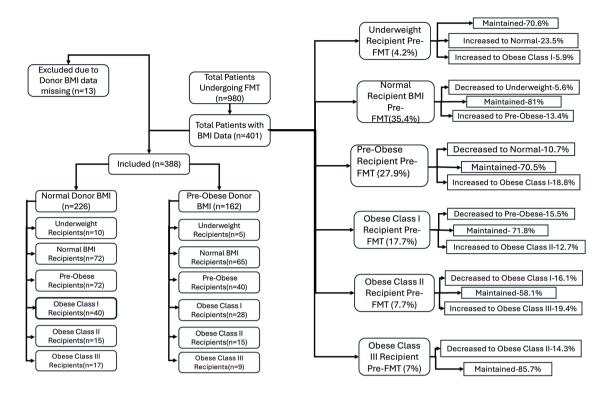


Figure 1. Flowchart of recipient and donor BMI categories and post-FMT BMI changes. BMI, body mass index; FMT, fecal microbiota transplantation.

Recipient BMI before FMT	Underweight (<i>n</i> = 17)	Normal (<i>n</i> = 142)	Pre-obese (<i>n</i> = 112)	Obese class I (n=71)	Obese class II (n=31)	Obese class III (<i>n</i> = 28)	
Recipient BMI after FMT							
Underweight	12 (70.6%)	8 (5.6%)	0	0	0	0	
Normal	4 (23.5%)	115 (81.0%)	12 (10.7%)	0	0	0	
Pre-obese	0	19 (13.4%)	79 (70.5%)	11 (15.5%)	2 (6.5%)	0	
Obese Class I	1 (5.9%)	0	21 (18.8%)	51 (71.8%)	5 (16.1%)	0	
Obese Class II	0	0	0	9 (12.7%)	18 (58.1%)	4 (14.3%)	
Obese Class III	0	0	0	0	6 (19.4%)	24 (85.7%)	

BMI, body mass index; FMT, fecal microbiota transplantation.

Shading intensity represents the percentage of transitions, with darker shades indicating higher transition frequencies between pre-FMT and post-FMT BMI categories.

Impact of donor BMI on recipient BMI following FMT

Model comparisons. In our mixed-effects analysis, we conducted multiple iterations to evaluate various factors, including baseline recipient BMI,

donor BMI, donor BMI category, the time interval between the pre-FMT BMI measurement and FMT administration, as well as the time between FMT administration and the subsequent post-FMT BMI measurements (Supplemental Table 1).

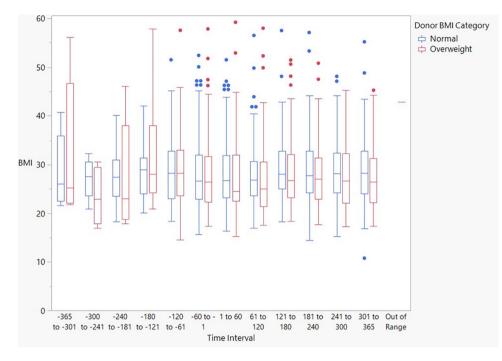


Figure 2. BMI distribution in data at various time intervals. BMI, body mass index.

In addition, we examined the interaction effects between baseline recipient BMI and the time interval prior to FMT administration, as well as between donor BMI and the time elapsed after FMT administration before BMI measurement. The models were built incrementally with variables and interaction terms added sequentially, coefficients for each variable are reported from the models where they were first introduced. The results of all the models are reported in Supplemental Table 1.

A 1-unit increase in donor BMI was associated with a 0.01-unit (-0.0003, 0.02) increase in the recipient's BMI per month; however, this association was not statistically significant (p=0.11). Similarly, an overall decrease of 0.04 (95% CI: -0.12, 0.04) units in BMI for each 1-unit increase in donor BMI was observed, but this relationship also lacked statistical significance (p=0.414). This trend persisted across subsequent models as additional variables were included. Interaction terms with donor BMI and time between FMT administration and the subsequent post-FMT BMI measurements were insignificant (coefficient = 0.00012, p = 0.47) suggesting a time effect. Furthermore, no significant associations were identified between donor BMI categories and

changes in BMI, either every month or overall. For donors with normal BMI, the estimated change in BMI per month was 0.006 units (95% CI: -0.13 to 0.15; p = 0.94), and the overall BMI change was 0.0527 units (95 % CI: -1.03 to 1.13; p=0.93). For pre-obese donors, the estimated change in BMI per month was 0.054 units (95% CI: -0.08 to 0.19; p=0.527), while the overall BMI change was -0.0574 units (95% CI: -1.15 to 1.03; p = 0.93). These findings suggest that neither donor BMI nor donor BMI category significantly influenced changes in recipient BMI over time. Supplemental Figure 2 presents BMI changes observed for different donor BMI values. The time interval between FMT administration and the post-FMT BMI measurement was significantly associated with changes in the recipient's BMI, showing a 0.002 (95%) CI: 0.00089-0.0022)-unit increase per dav (p=0.000049). The time interval between the pre-FMT recipient BMI measurement and FMT administration was not significantly associated with changes in overall BMI or monthly BMI changes. Specifically, there was a 0.00025 (95% CI: -0.00006 to 0.0005)-unit increase in BMI change per month per day (p=0.19) and a 0.0023 (95% CI: -0.00019 to 0.004)-unit increase in overall BMI change per day (p = 0.3).

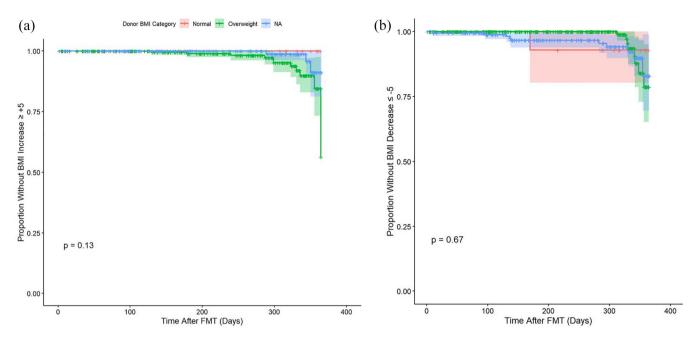


Figure 3. (a) KM curve for a 5-unit increase in recipient BMI last recording from Baseline BMI during the follow-up period. (b) KM curve for a 5-unit decrease in recipient BMI last recording from baseline BMI during the follow-up period. BMI, body mass index; KM, Kaplan-Meier.

Log-rank analysis revealed no significant differences among donor BMI categories (pre-obese, normal, and unknown BMI cohort) in the probability of a 5-unit increase or decrease in the recipient's BMI from baseline during the followup period (Figure 3(a) and (b)). For a 5-unit increase, the Chi-squared value was 4.4 (p=0.1), and for a 5-unit decrease, the Chi-squared value was 2 (p=0.4). We also created a KM curve tracking transitions between different BMI categories during the follow-up period (Supplemental Figure 4).

Baseline BMI was significantly associated with changes in both overall BMI and BMI change per month. Specifically, each 1-unit increase in recipient baseline BMI was associated with a 0.0037 (95% CI: -0.007 to -0.0005)-unit decrease in BMI change per month (p=0.049) and a 0.067 (95% CI: -0.096 to -0.047)-unit decrease in overall BMI (p < 0.00001). Interaction terms with baseline recipient BMI and the time interval between the pre-FMT recipient BMI measurement and FMT administration were insignificant (coefficient = -0.0001, p=0.601). A model with only donor BMI as a variable had the highest log likelihood value (-889.8) indicating the best fit for BMI change per month.

Descriptive analysis. Recipient BMI weight groups post-procedure were further stratified by donor BMI group. This analysis included 388 patients, as 13 were excluded due to missing donor BMI information. Of the 388 patients, 226 received stool from donors with a normal BMI (Table 3). Among these recipients, 10 were underweight, 72 had normal BMI, 72 were pre-obese, 40 were in obese class I, 15 were in obese class II, and 17 were in obese class III. Most of these recipients remained in their weight groups after the procedure (Table 3). In total, 162 out of 388 patients received stool from pre-obese donors (Table 4). Among them, 5 were underweight, 65 had normal BMI, 40 were pre-obese, 28 were in obese class I, 15 belonged to obese class II, and 9 were in obese class III. Like the first group, most recipients maintained their weight group after the procedure.

Discussion

To our knowledge, this is the largest study evaluating weight changes in patients undergoing FMT for recurrent CDI and assessing the impact of donor BMI. Patients who underwent FMT at our institution showed an uptrend in their BMI measurements by 0.05 kg/m^2 per month within a 1-year

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Recipient BMI groups	Underweight (<i>n</i> = 15)	Normal (<i>n</i> = 137)	Pre-obese (<i>n</i> = 112)	Obese class I (<i>n</i> =68)	Obese class II (n=30)	Obese class III (n=26)
Recipient BMI pre-transplant						
Underweight	7 (70.0%)	4 (5.6%)	0	0	0	0
Normal	2 (20.0%)	58 (80.6%)	6 (8.3%)	0	0	0
Pre-obese	0	10 (13.9%)	54 (75.0%)	9 (22.5%)	0	0
Obese Class I	1 (10.0%)	0	12 (16.7%)	27 (67.5%)	3 (20.0%)	0
Obese Class II	0	0	0	4 (10.0%)	9 (60.0%)	2 (11.8%)
Obese Class III	0	0	0	0	3 (20.0%)	15 (88.2%)
Total Recipients	10	72	72	40	15	17

BMI, body mass index.

Shading intensity represents the percentage of transitions, with darker shades indicating higher transition frequencies between pre-FMT and post-FMT BMI categories.

Table 4. BMI weight group changes in recipients with pre-obese BMI donors.

Recipient BMI post-transplant	Underweight	Normal	Pre-obese	Obese class I	Obese class II	Obese class III
Recipient BMI post-transplant						
Underweight	3 (60.0%)	3 (4.6%)	0	0	0	0
Normal	2 (20.0%)	54 (83.1%)	6 (15.0%)	0	0	0
Pre-obese	0	8 (12.3%)	25 (62.5%)	1 (3.6%)	2 (13.3%)	0
Obese Class I	0	0	9 (22.5%)	23 (82.1%)	2 (13.3%)	0
Obese Class II	0	0	0	4 (14.3%)	9 (60.0%)	1 (11.1%)
Obese Class III	0	0	0	0	2 (13.3%)	8 (88.9%)
Total recipients	5	65	40	28	15	9

BMI, body mass index.

Shading intensity represents the percentage of transitions, with darker shades indicating higher transition frequencies between pre-FMT and post-FMT BMI categories.

follow-up period. However, donor BMI did not have any significant influence on this trend. This observation aligns with earlier findings that weight changes following FMT were unrelated to donor BMI. A study by Steevens et al.¹⁷ assessing the influence of donor BMI on recipient weight changes following FMT for recurrent CDI reported no significant association between donor BMI and weight gain after FMT in 30 participants. Another study by Fischer et al. reported no difference in BMI change post-FMT between normal donor BMI, overweight donor BMI, and obese donor BMI groups. Their study included 173 participants. The mean difference in weekly BMI change was 0.002 (95% CI: -0.052 to 0.056; p=0.94) for the normal versus overweight group and 0.04 (95% CI: -0.03 to 0.1; p=0.25) for normal versus obese donor BMI group.¹⁸ In a retrospective follow-up study comparing CDI patients treated with antibiotics and FMT, no significant difference in weight change post-treatment was observed in the two groups with the FMT group showing a weight gain of 2.5 kg and the antibiotic group showing a weight change of

1.3 kg (p=0.51). The average duration of followup was 3.8 years with 80% of patients in both groups showing weight gain with an average weight gain of 1.9 kg.¹⁹

Our study's KM analysis revealed no significant differences among donor BMI categories in the likelihood of a 5-unit BMI increase or decrease during the follow-up period reinforcing the idea that FMT facilitates weight normalization rather than donor-dependent weight gain.

The increase in BMI observed after the procedure may indicate a recovery of weight loss during the diarrheal illness. CDI complications, such as severe diarrhea, weight loss, malnutrition, and hypoalbuminemia, may explain post-FMT weight gain as a return to baseline weight. The time interval between FMT administration and BMI measurements was another significant predictor of BMI changes in our study. Specifically, a 0.0016-unit increase in BMI per dav (p=0.000049) was observed for each additional day post-FMT. This finding suggests that weight recovery continues gradually over time, reflecting the restoration of baseline health.

These results indicate that factors beyond donor BMI, such as microbiota diversity, composition, metabolic activity, or the recipient's baseline metabolic health, may play a more significant role in post-FMT weight outcomes. In our mixed-effects analysis, a significant association of the recipient's baseline BMI with BMI change highlights the influence of the recipient's initial health status on post-FMT outcomes.

These findings contrast with earlier case reports that raised concerns about the potential for FMT to contribute to obesity when stool from overweight donors was used.¹² Monaghan et al. identified that FMT for recurrent CDI is associated with changes in the bile acid-Farnesoid X receptorfibroblast growth factor pathway, which may contribute to weight gain post-FMT. The weight gain did not exceed pre-CDI weight in their cohort.²⁰

In a prospective single-center cohort study conducted by Saha et al., weight gain was reported in 10.3% of patients receiving FMT with a median weight gain of 30 pounds (range: 10–70) during long-term follow-up (median follow-up of 3.7 years). Of note, 23% of the patients reporting weight gain had preexisting obesity.²¹ Another study by Mamo et al. reported weight gain in nearly 50% of participants post-FMT with a median weight change of 5 pounds (IQR: -5 to 10). It is important to note, however, that this study did not collect data on baseline weight pre-FMT, so it is unclear if the weight gain represents an increase above patients' baseline weight or simply a return to their previous weight after weight loss due to CDI.²² However, a study by Smith et al.⁸ reported no significant difference in baseline BMI and BMI measurements at 12 weeks post-FMT for recurrent CDI. In another longterm follow-up study, 53% of participants reported weight gain, and 44% remained the same.²³ The weight changes were not quantitatively reported.

Increased recognition of the association of gut microbiome with pathways influencing weight gain and insulin sensitivity led to the exclusion of obese donors as per current best practice.²⁴

Our findings have important implications for current guidelines that recommend excluding donors with a BMI over 30 due to concerns about the potential transmission of dysbiotic microbiota associated with obesity.²² The absence of a significant relationship between donor BMI and recipient BMI changes in our study suggests that these guidelines may need to be revisited. While the rationale for excluding obese donors is grounded in caution due to potential metabolic risks, our data indicate that the risk may be overstated, at least in the context of changes in BMI.

Limitations

However, it is important to acknowledge the limitations of our study. Given its retrospective nature, we were unable to control confounding factors such as diet, exercise, and concurrent medications, which could influence weight outcomes. In addition, all donors in our study fell within the normal or pre-obese BMI categories, limiting the generalizability of our results and our ability to assess the true impact of obese donors on recipient BMI. The median follow-up time in our study was 151.6 days, allowing us to observe BMI changes during the recovery phase after FMT. This timeframe provides valuable insights into short- to medium-term weight dynamics; however, longer follow-up periods are necessary to fully understand long-term weight changes stratified by donor BMI. This study focuses on BMI changes in FMT recipients without a non-FMT control

group, limiting our ability to directly compare natural BMI trends. Future studies should include a matched non-FMT control cohort to better elucidate the impact of FMT on BMI dynamics.

Conclusion

In conclusion, our study indicates that while FMT effectively manages recurrent CDI, its impact on BMI likely reflects the recovery of weight lost during infection rather than the transfer of donor-specific metabolic traits. These findings contribute to the growing evidence that donor BMI may not play as significant a role in recipient weight outcomes as previously thought. To draw more definitive conclusions, large-scale, prospective studies including a broader range of donor BMI categories and a control group are needed to better understand the long-term metabolic effects of FMT.

Author's note

Data in the study were presented as a poster at the American College of Gastroenterology in 2021.

The Associate Editor of *Therapeutic Advances in Gastroenterology* is the author of this paper; therefore, the peer review process was managed by alternative members of the Board and the submitting Editor was not involved in the decision-making process.

Declarations

Ethics approval and consent to participate

A subset of the dataset consisted of participants from a prior study approved by the Institutional Review Board (IRB) under protocol ID 14-005326. All participants, including those identified through retrospective chart review, were included under a consent waiver.

Consent for publication

No patient images or identifying information were used in this study. All research data were obtained under a consent waiver.

Author contributions

Kanika Sehgal: Conceptualization; Investigation; Methodology; Project administration; Writing – original draft; Writing – review & editing. **Parul Berry:** Formal analysis; Writing – original draft; Writing – review & editing.

Janice Cho: Data curation; Formal analysis; Methodology; Writing – original draft.

George Saffouri: Methodology; Writing – original draft; Writing – review & editing.

Ross A. Dierkhising: Methodology; Software; Supervision; Validation; Writing – original draft.

Eric Battaglioli: Conceptualization; Formal analysis; Methodology; Writing – review & editing.

Purna C. Kashyap: Conceptualization; Methodology; Project administration; Writing – original draft.

Darrell Pardi: Conceptualization; Resources; Software; Supervision; Validation; Writing – review & editing.

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Availability of data and materials

The datasets used and analyzed in this study are available from the corresponding author upon reasonable request.

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Supplemental material

Supplemental material for this article is available online.

References

- Ding G, Yang X, Li Y, et al. Gut microbiota regulates gut homeostasis, mucosal immunity and influences immune-related diseases. *Mol Cell Biochem*. Epub ahead of print July 2024. DOI: 10.1007/s11010-024-05077-y.
- Berry P and Khanna S. Recurrent *Clostridioides* difficile infection: current clinical management and microbiome-based therapies. *BioDrugs* 2023; 37: 757–773.
- 3. Sheitoyan-Pesant C, Abou Chakra CN, Pépin J, et al. Clinical and healthcare burden of multiple recurrences of *Clostridium difficile* infection. *Clin Infect Dis* 2016; 62: 574–580.
- Poylin V, Hawkins AT, Bhama AR, et al. The American Society of colon and rectal surgeons clinical practice guidelines for the management of *Clostridioides difficile* infection. *Dis Colon Rectum* 2021; 64: 650–668.
- Kelly CR, Fischer M, Allegretti JR, et al. ACG clinical guidelines: prevention, diagnosis, and treatment of *Clostridioides difficile* infections. *Am J Gastroenterol* 2021; 116: 1124–1147.
- Peery AF, Kelly CR, Kao D, et al. AGA clinical practice guideline on fecal microbiota-based therapies for select gastrointestinal diseases. *Gastroenterology* 2024; 166: 409–434.
- Lessa FC, Mu Y, Bamberg WM, et al. Burden of *Clostridium difficile* infection in the United States. *N Engl J Med* 2015; 372: 825–834.
- Smith J, Roach B, Hassanzadeh Keshteli A, et al. A275 donor body mass index (BMI) does not impact recipient BMI following fecal microbiota transplantation for recurrent *Clostridium difficile* infection. *J Can Assoc Gastroenterol* 2018; 1: 476–478.
- Omer E and Chhabra G. Impact of *Clostridioides* difficle infection and its therapy on nutritional status. *Curr Gastroenterol Rep* 2022; 24: 99–104.

- Paramsothy S, Borody TJ, Lin E, et al. Donor recruitment for fecal microbiota transplantation. *Inflamm Bowel Dis* 2015; 21: 1600–1606.
- Zoll J, Read MN, Heywood SE, et al. Fecal microbiota transplantation from high caloric-fed donors alters glucose metabolism in recipient mice, independently of adiposity or exercise status. *Am J Physiol Endocrinol Metab* 2020; 319: E203–E216.
- Alang N and Kelly CR. Weight gain after fecal microbiota transplantation. Open Forum Infect Dis 2015; 2: ofv004.
- Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40: 373–383.
- World Health Organisation regional office for Europe. Cut-off for BMI according to WHO Standards. Retrieved February 15, 2025, from, https://gateway.euro.who.int/en/indicators/ mn_survey_19-cut-off-for-bmi-according-to-whostandards/?utm_source=chatgpt.com#id=32083.
- von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007; 370: 1453–1457.
- R Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing, 2019.
- Steevens CD, Roto D and DeCross AJ. Obese stool donors in fecal microbiota transplantation: not associated with recipient weight gain! *Gastroenterology* 2017; 152: S1007–S1008.
- Fischer M, Kao D, Kassam Z, et al. Stool donor body mass index does not affect recipient weight after a single fecal microbiota transplantation for *Clostridium difficile* infection. *Clin Gastroenterol Hepatol* 2018; 16: 1351–1353.
- Jalanka J, Hillamaa A, Satokari R, et al. The longterm effects of faecal microbiota transplantation for gastrointestinal symptoms and general health in patients with recurrent *Clostridium difficile* infection. *Aliment Pharmacol Ther* 2018; 47: 371–379.
- Monaghan T, Mullish BH, Patterson J, et al. Effective fecal microbiota transplantation for recurrent *Clostridioides difficile* infection in humans is associated with increased signalling in the bile acid-farnesoid X receptor-fibroblast growth factor pathway. *Gut Microbes* 2019; 10: 142–148.

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- 21. Saha S, Mara K, Pardi DS, et al. Long-term safety of fecal microbiota transplantation for recurrent *Clostridioides difficile* infection. *Gastroenterology* 2021; 160: 1961–1969.e3.
- 22. Mamo Y, Woodworth MH, Wang T, et al. Durability and long-term clinical outcomes of fecal microbiota transplant treatment in patients with recurrent *Clostridium difficile* infection. *Clin Infect Dis* 2018; 66: 1705–1711.
- Brandt LJ, Aroniadis OC, Mellow M, et al. Long-term follow-up of colonoscopic fecal microbiota transplant for recurrent *Clostridium difficile* infection. *Am J Gastroenterol* 2012; 107: 1079–1087.
- Lee P, Yacyshyn BR and Yacyshyn MB. Gut microbiota and obesity: an opportunity to alter obesity through faecal microbiota transplant (FMT). *Diabetes Obes Metab* 2019; 21: 479–490.