Observational Study

Absence of a Consistent Gut or Oral Microbial Signature in Fibromyalgia Under Strictly Controlled Clinical Conditions: A Multi-Compartment 16S rRNA Analysis

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Background: Fibromyalgia (FM) has been increasingly studied in the context of gut-brain-immune interactions, and several reports have suggested an association between FM and alterations in gut or oral microbial communities. However, prior studies have often suffered from heterogeneous comorbidities, inconsistent sampling procedures, and limited control for environmental factors, making it unclear whether FM is associated with a reproducible, site-independent microbial signature.

Objectives: To determine whether women with FM exhibit consistent alterations in gut or oral microbiota when evaluated under strictly standardized physiological, clinical, and environmental conditions.

Study Design: A prospective, observational, case-control study.

Setting: The Department of Pain Medicine and Department of Medical Microbiology at Gazi University, Türkiye.

Methods: The patient selection comprised 31 women (16 with FM; 15 healthy controls) who met rigorous inclusion and exclusion criteria, minimizing confounding from diet, metabolic disease, medications, hormonal status, and recent infections. No therapeutic intervention was performed; all patients provided paired oral mucosal and fecal samples during the follicular phase of the menstrual cycle. Sequencing of 16S rRNA V3-V4was performed on DNA extracted from all samples. Alpha and beta diversity metrics, taxonomic profiles, and differential abundance analyses (including LEfSe with FDR correction) were compared between groups. The clinical severity of FM was assessed using scores on the visual analog scale (VAS), Widespread Pain Index (WPI), and Symptom Severity Scale (SSS).

Results: No statistically significant differences were observed between FM patients and controls in fecal or oral alpha diversity (Shannon, Simpson, Chao1, Observed OTU indices, all $P > 0.05$). Beta diversity analyses (Bray-Curtis PERMANOVA) revealed no between-group separation in either compartment (fecal $R^2 = 0.032$, $P = 0.529$; oral $R^2 = 0.032$, $P = 0.464$). Both groups displayed preserved core microbial communities in the gut, dominated by Firmicutes and Bacteroidota and, in the oral cavity, Streptococcus-enriched profiles. Minor genus-level variations were detected, but none remained significant after FDR correction. Cross-site analyses confirmed the expected ecological divergence between oral and fecal habitats but identified no FM-specific microbial pattern. Post hoc sensitivity analysis indicated that the study was powered to detect only moderate effect sizes ($R^2 \geq 0.11$), suggesting that subtle differences might have remained undetected.

Limitations: A modest sample size, a lack of quantitative dietary assessment, and reliance on 16S rRNA sequencing limited the detection of subtle or functional microbial alterations. Additionally, the cross-sectional design precludes causal inference.

Conclusions: Under highly controlled sampling and exclusion conditions, FM was not associated with detectable alterations in the diversity or composition of gut or oral microbes. These findings suggest that previously reported dysbiosis may reflect comorbidity-driven or phenotype-specific variation rather than a universal microbial hallmark. Larger, multi-omic and phenotype-stratified studies are needed to clarify functional host-microbiome interactions in FM.

Key words: Fibromyalgia, gut microbiome, oral microbiome, 16S rRNA sequencing, chronic pain, mucosal ecosystems, alpha diversity, beta diversity, dysbiosis, nociplastic pain, microbiota composition, microbial ecology

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Fibromyalgia (FM) is a prevalent nociplastic pain syndrome characterized by widespread musculoskeletal pain, fatigue, cognitive dysfunction, and multisystem symptoms (1,2). Despite its clinical burden, the underlying biological mechanisms of FM remain insufficiently defined, and no validated biomarker for them has been established (2). Increasing evidence highlights the gut-brain axis as a central integrative framework involving microbial metabolites, immune signaling, and neuroendocrine pathways, all of which overlap with proposed FM pathophysiology (3,4).

Multiple studies have reported reduced microbial richness, shifts in β-diversity, and alterations in short-chain fatty acid (SCFA)–producing taxa, including families such as Lachnospiraceae and Ruminococcaceae, in individuals with FM or chronic widespread pain (3,5). Extensive population-based analyses have similarly identified decreased alpha diversity and specific taxonomic depletions in persons with chronic widespread pain, independent of demographic or dietary factors (5). However, findings across cohorts remain inconsistent, partly due to heterogeneous diets, medication use, comorbid gastrointestinal disorders, geographic variability, and differences in sequencing or preprocessing methodologies. These discrepancies complicate efforts to define a reproducible microbiome signature for FM.

In contrast, the oral microbiome has received limited attention in FM research, despite its known role in systemic inflammation, mucosal immunity, and modulation of chronic disease (3,6). Prior evidence indicates that women with FM may exhibit altered oral microbial profiles, including increased periopathogenic taxa such as Prevotella denticola and Solobacterium moorei, particularly in the context of impaired oral health (4). Yet these findings originate from small, clinically heterogeneous populations, and no study has examined oral and gut microbiota concurrently under standardized conditions.

Notably, no previous research has simultaneously characterized both oral and fecal microbiota in FM while controlling rigorously for confounding factors such as diet, hormonal phase, medication exposure, smoking, metabolic disease, or recent antibiotic use. Given the ecological divergence between the oral cavity and gut, dual-site assessment may clarify whether FM exerts a broad microbiome effect or whether reported alterations are site-specific or secondary to comorbid conditions.

Accordingly, this prospective study aimed to compare oral and fecal microbial diversity, community structure, and taxonomic composition in women with FM and age-matched healthy controls, using standardized 16S rRNA sequencing. Secondary analyses evaluated differentially abundant taxa and cross-site ecological patterns to determine whether FM was associated with consistent or habitat-specific microbial alterations.

Methods

Study Design and Patients

This prospective observational study was conducted between August 2024 and August 2025 at the Department of Pain Medicine at Gazi University, Türkiye. Thirty-one women participated in the study, including 16 patients diagnosed with fibromyalgia (FM) according to the 2016 American College of Rheumatology (ACR) criteria and 15 age-matched healthy controls without chronic pain or systemic disease. Patients were recruited via outpatient pain and neurology clinics as well as community announcements.

All procedures were approved by the Gazi University Clinical Research Ethics Committee (Approval No: 11.12.2023-976), and written informed consent was obtained from each patient in accordance with the Declaration of Helsinki.

Inclusion and Exclusion Criteria

Eligible patients were women aged 18-65 years who could provide both oral and fecal samples and

comply with the study procedures. Exclusion criteria were strictly applied to minimize confounding from dietary, metabolic, hormonal, inflammatory, and pharmacological factors. Individuals were excluded if they had used antibiotics or probiotics within 4 weeks of the recruitment period; had diabetes mellitus, malignancy, or gastrointestinal or autoimmune disease; were pregnant or lactating; smoked regularly; had recently instated major dietary changes; used corticosteroids, immunosuppressants, or daily medications for chronic conditions; had major psychiatric disorders; exhibited abnormal stool consistency (Bristol Stool Form Scale); or were unable to provide a fecal sample. Patients with recent infection, elevated inflammatory markers, or known food allergies were also excluded.

Sample Collection Procedures

To minimize behavioral and hormonal variability, all samples were collected in the morning, within 2 hours after awakening, during the follicular phase of each patient's menstrual cycle. Patients received standardized written and verbal sampling instructions.

Oral mucosal samples were obtained at the research center by trained investigators using sterile nylon-flocked swabs, which were rubbed along the buccal mucosa for at least 30 seconds. Swabs were immediately placed into an RNA/DNA stabilization buffer and stored at -80° C.

Fecal samples were self-collected at home, using sterile DNA-free containers provided in the sampling kits. Patients avoided contamination with urine and collected approximately a pea-sized portion of stool. Samples were frozen at -80° C immediately after collection or refrigerated at 4° C if immediate freezing was not possible. They were then delivered to the laboratory within 6 hours. Upon receipt, all specimens were transferred to -80° C for long-term storage.

Clinical Assessments

Demographic data were obtained from all patients. The FM symptom burden was evaluated using the visual analog scale (VAS), Widespread Pain Index (WPI), and Symptom Severity Scale (SSS), as defined by the 2016 ACR criteria.

DNA Extraction and Sequencing

Microbial DNA was extracted from oral and fecal samples using the High Pure PCR Template Preparation Kit (Roche®) following the manufacturer's protocol. Negative extraction controls were processed in parallel to monitor contamination. DNA concentration and purity were assessed using spectrophotometry and Qubit fluorometry (Thermo Fisher Scientific).

The V3-V4 region of the 16S rRNA gene was amplified using primers 341F and 806R with sample-specific barcodes. Amplicons were purified using magnetic bead-based cleanup, quantified fluorometrically, pooled at equimolar concentrations, and sequenced on the MiSeq platform (Illumina Inc.) (2 × 250 bp paired-end), including a 10% PhiX control.

Bioinformatics and Data Processing

Raw reads were demultiplexed, trimmed, and quality-filtered prior to merging using FLASH v1.2.11 (Johns Hopkins University Center for Computational Biology) (7). Chimeric sequences were removed via VSEARCH (Edgar) against the SILVA reference database (8). Amplicon sequence variants (ASVs) were generated using the DADA2 (Callahan et al) pipeline implemented in QIIME 2 v2023.9 (Boylen et al). Taxonomic classification was performed using the SILVA database for 16S rRNA sequences.

Sequence depth normalization was achieved by rarefying samples to the minimum read count (20,000 reads/sample). Diversity metrics, phylogenetic analyses, and community structure visualizations were conducted in QIIME 2 and R v4.3.1 (The R Foundation).

Statistical Analysis

Alpha diversity was assessed using the observed OTU, Chao1 richness, and Shannon's and Simpson's diversity, Pielou's evenness, and Good's coverage indices. Beta diversity was evaluated using Bray-Curtis, Jaccard, unweighted UniFrac, and weighted UniFrac distance matrices, visualized through PCA and PCoA.

Group differences in community structure were tested via PERMANOVA, using the Adonis function with 999 permutations, implemented in the vegan package in R (The R Foundation). Homogeneity of multivariate dispersion was examined using PERMDISP to ensure that significant findings were not driven by unequal variances. Additional ecological comparisons were performed using the ANOSIM, MRPP, and SIMPER functions. Differentially abundant taxa were identified through LEfSe (The Huttenhower Foundation, Harvard T. H. Chan School of Public Health) with the Benjamini-Hochberg FDR correction. Correlation analyses (Spearman) and redundancy analyses (CCA, db-RDA) were conducted to explore relationships between microbial variation and clinical variables.

No formal a priori power analysis could be performed, due to the lack of established effect-size estimates for dual-site microbiome comparisons in cases of FM. Instead, a post hoc sensitivity analysis was conducted using the observed PERMANOVA effect size. Given the sample size (n = 31; 16 FM and 15 controls) and the standard permutation-based framework (α = 0.05, 999 permutations), the study had 80% power to detect moderate effect sizes ($R^2 \geq 0.11$) in beta diversity. Subtler or more minor microbial differences may have remained undetectable.

Results

A total of 67 individuals were screened; 31 women met the eligibility criteria and completed all study procedures, comprising 16 patients with FM and 15 healthy controls (Fig. 1). The mean age did not differ significantly between groups (45.67 ± 11.33 years in controls vs. 47.81 ± 11.37 years in the FM group; *P* = 0.603). Symptom severity among FM patients indicated a clinically meaningful disease burden, with mean VAS, WPI, and SSS scores of 7.75 ± 1.24, 14.44 ± 2.10, and 9.38 ± 1.96, respectively.

Analysis of fecal microbiota revealed no statistically significant differences in alpha diversity between the FM and control groups (Fig. 2). The Shannon and Simpson indices showed a nonsignificant trend toward reduced diversity in the FM group (*P* = 0.078 and *P* = 0.060, respectively), whereas Chao1 richness and observed-OTU score were comparable across groups (both *P* = 0.192). Beta diversity assessed using Bray-Curtis PERMANOVA demonstrated no significant between-group separation ($R^2 = 0.032$; *P* = 0.529), a finding further supported by the PCoA plot in which samples from both groups displayed substantial overlap (Fig. 3).

Taxonomic profiling showed that Firmicutes and Bacteroidota were the dominant phyla in both groups, and at the genus level, Faecalibacterium and Segatella were most abundant in both FM and control patients. Although minor variations in relative abundance were observed, none of the taxa remained significant after correction for multiple testing, and heat map visualizations indicated pronounced inter-individual variability without FM-specific clustering. A genus-level heat map illustrating these distributions is provided in the Supplementary Materials (Suppl. Fig. X), as is a stacked bar plot summarizing the top 30 genera (Suppl. Fig. Y).

Similarly, the LEfSe (The Huttenhower Foundation, Harvard T. H. Chan School of Public Health) analysis did

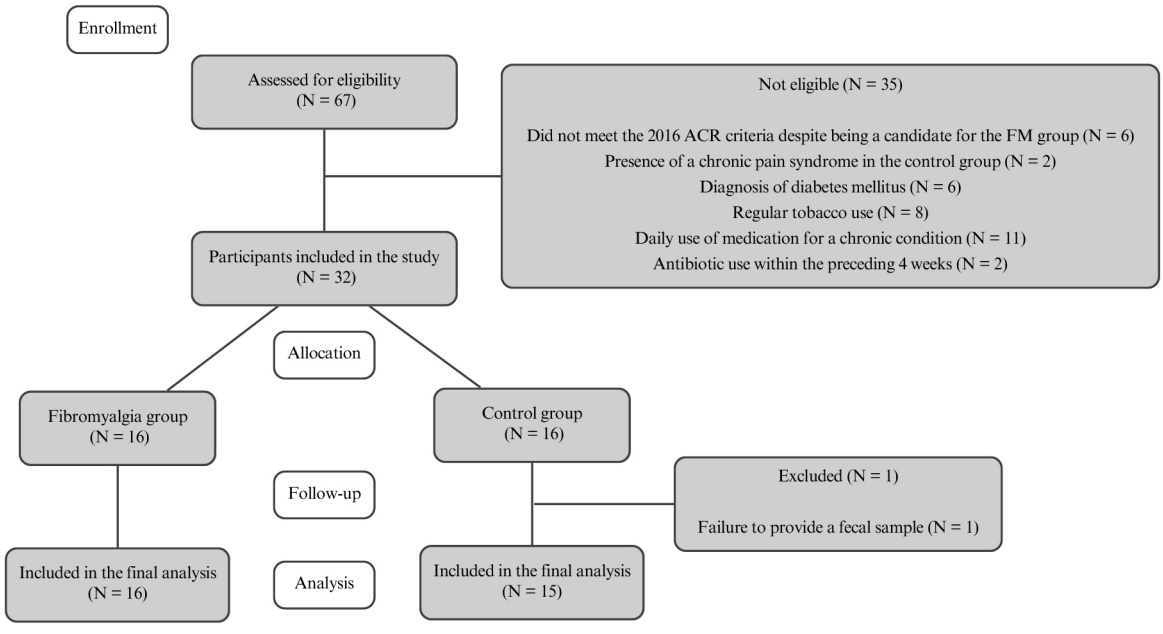


Fig. 1. *Study flowchart.*
Flow diagram showing patient screening, exclusion criteria, and final enrollment of 31 women (16 with FM and 15 healthy controls), who completed all study procedures and provided fecal and oral microbiota samples.

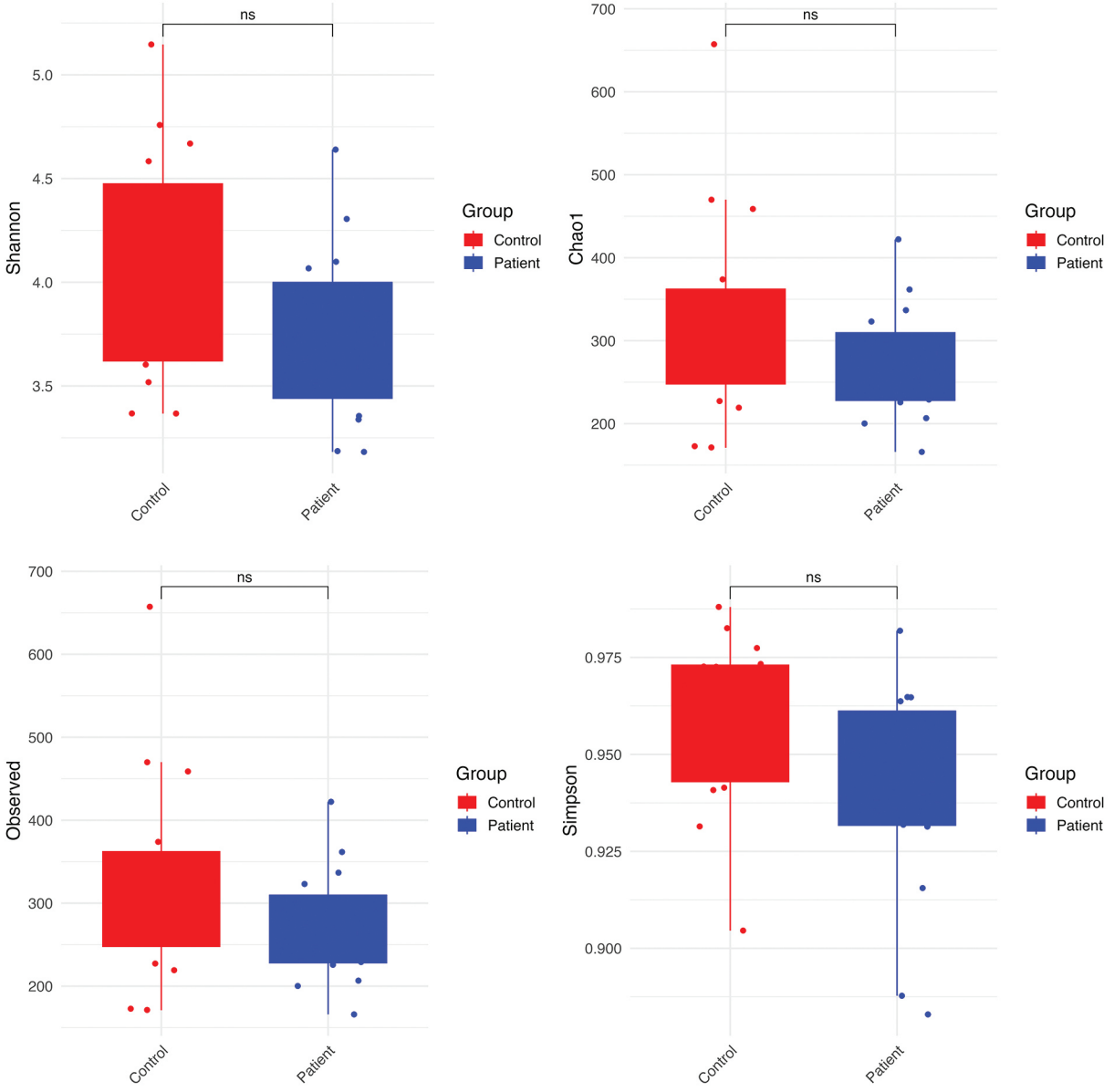


Fig. 2. *Fecal alpha diversity in FM and control patients.*
Composite panel displaying Shannon, Simpson, Chao1, and observed-OTU indices for fecal samples. All indices showed comparable distributions between groups, with no statistically significant differences, indicating preserved microbial richness and evenness in FM.

not identify taxa that remained statistically significant after FDR correction, although several low-abundance genera and families displayed differential trends between the groups (Fig. 4). In a result consistent with that finding, the LDA bar plot demonstrated that the majority of the taxa contributing to group differences were relatively enriched in controls, with only isolated taxa showing higher abundance in FM patients (Fig. 5).

Oral microbiota analysis likewise revealed no significant differences between the groups. Alpha diversity metrics, including Shannon (P = 0.470), Simpson (P = 0.358), Chao1 (P = 0.874), and observed OTUs (P = 0.874) were comparable across groups. Beta diversity analysis also showed no evidence of group-level sepa-

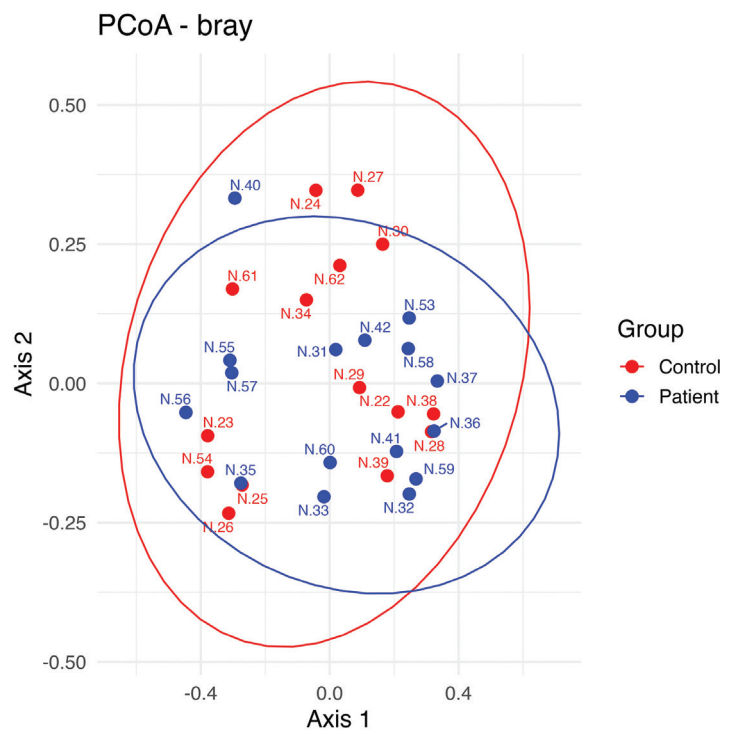


Fig. 3. *Beta diversity analysis based on Bray-Curtis dissimilarity. Principal coordinates analysis (PCoA) plot showing overlapping ordination patterns between FM and control patiets, consistent with the absence of significant between-group separation as confirmed by PERMANOVA ($R^2 = 0.032$; $P = 0.529$).*

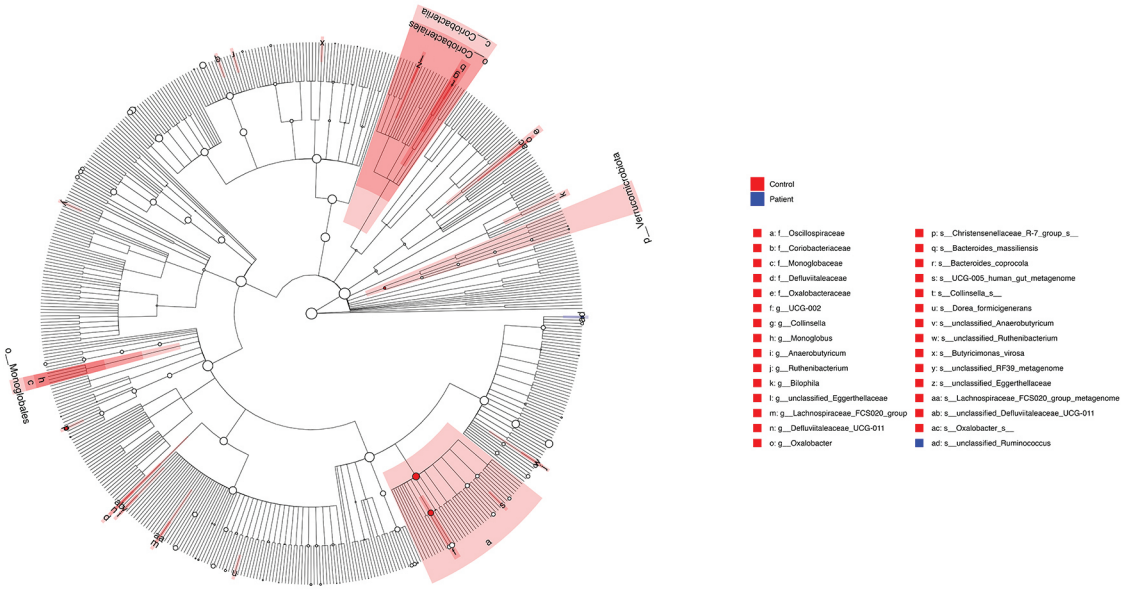


Fig. 4. *LEfSe cladogram of differentially enriched taxa between groups. Circular cladogram illustrating phylogenetic relationships of taxa differentially enriched in FM or control patients. Red highlights indicate taxa enriched in controls, and blue highlights indicate taxa enriched in the FM group. No taxa remained significant after the FDR correction.*

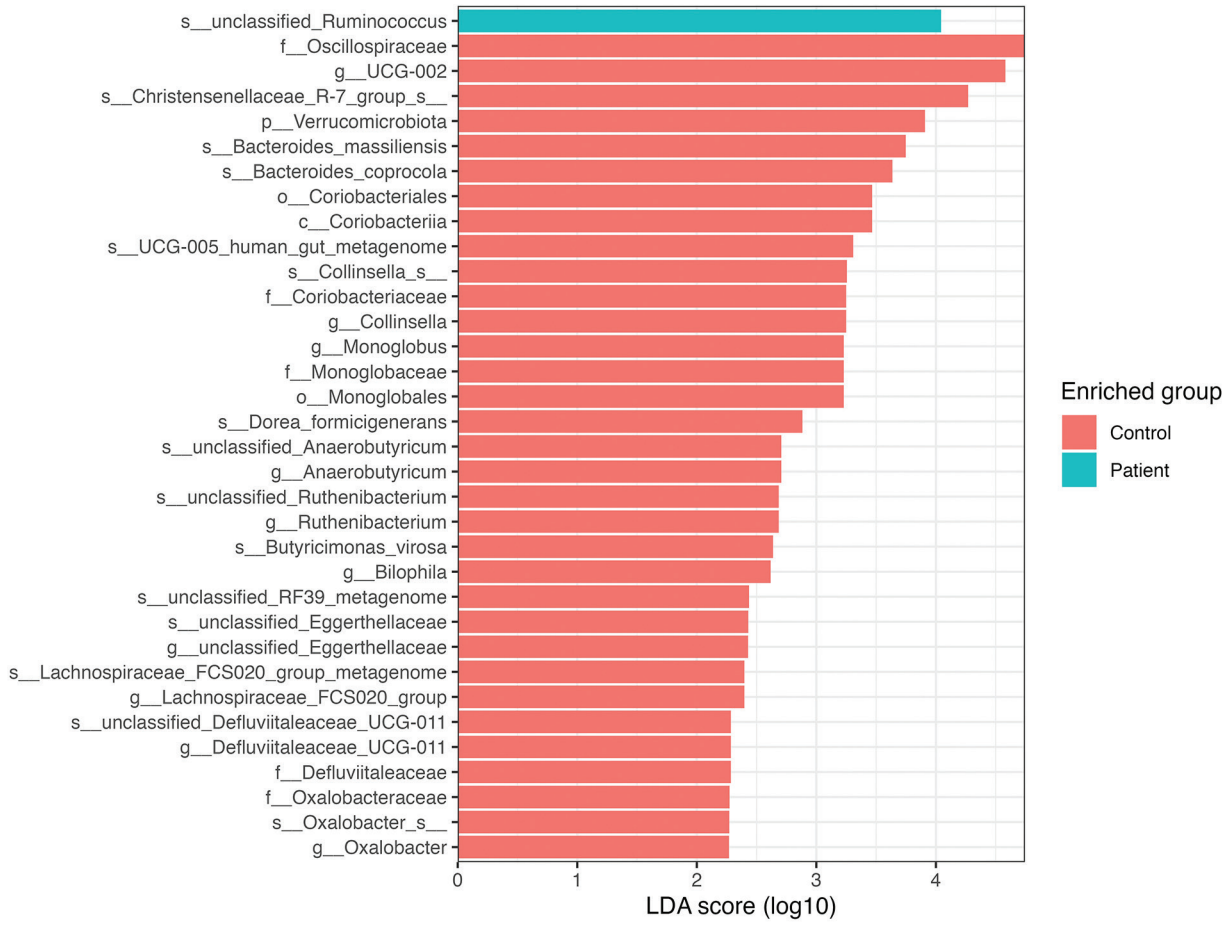


Fig. 5. *Linear discriminant analysis (LDA) scores of differentially abundant taxa.*

ration (Bray-Curtis $R^2 = 0.032$; $P = 0.464$), and ordination plots demonstrated overlapping distributions. The oral microbial communities of both groups were dominated by typical facultative anaerobes, with Streptococcus being the predominant genus in FM (44.88%) and control patients (32.61%) alike, followed by Haemophilus, Prevotella, and Veillonella. Although modest interindividual differences in taxonomic composition were observed, neither pairwise comparisons nor LEfSe (The Huttenhower Foundation, Harvard T. H. Chan School of Public Health) analysis identified taxa that remained significant after multiple-testing correction.

Cross-site comparisons confirmed the expected ecological divergence between oral and fecal microbiota: fecal samples exhibited substantially higher richness and were dominated by strict anaerobes, whereas oral samples showed lower diversity and were enriched in facultative anaerobes. Despite these intrinsic ecological differences between sites, no FM-associated microbial alterations were observed in either compartment.

Discussion

This study offers one of the most methodologically rigorous evaluations of the FM-affected microbiome to date, providing greater control over confounding factors than the existing literature. Unlike previous work that has examined only a single biological compartment, our investigation simultaneously assessed both the fecal and oral microbiota within the same individuals, enabling a multi-compartment analysis of mucosal ecosystems and allowing us to determine whether FM was associated with a systemic microbial signature. By applying stringent exclusion criteria, including the removal of patients who had used antibiotics or probiotics recently or who had gastrointestinal comorbidities, acute infections, chronic inflammatory diseases,

or metabolic disorders, we were able to isolate the FM phenotype on a biologically "clean" background. This approach directly addresses a primary source of inconsistency in prior studies and provides robust evidence that, under well-controlled clinical and environmental conditions, FM does not exhibit a reproducible taxonomic alteration in either gut or oral microbial communities. These findings help clarify the origins of heterogeneity in the FM microbiome literature and establish a high-quality reference framework for future research, particularly for studies aiming to disentangle disease-specific biological signals from context-driven microbial variability.

Previous research has identified a range of potential gut microbial alterations in FM and chronic widespread pain, including decreased alpha diversity, reduced butyrate-producing taxa, and shifts in β-diversity (3,5,9). However, as emphasized by Minerbi and Fitzcharles, many of these findings originate from heterogeneous populations with substantial confounding from comorbid gastrointestinal conditions, psychotropic medication use, metabolic disease, and dietary variation (5,10). Minerbi and Fitzcharles's review argued that the reproducibility crisis in FM microbiome studies stemmed largely from inadequate control of variables in host environments, making it challenging to distinguish disease-specific microbial signals from context-driven fluctuations (10). The stability observed in our cohort, recruited under some of the most stringent exclusion criteria in the FM microbiome literature, supports this interpretation and indicates that FM itself may not uniformly perturb gut microbial composition.

While this study employed one of the most stringently controlled designs in the literature on FM microbiomes, the absence of statistically significant compositional differences should be interpreted with appropriate caution. Our findings indicate that, under the specific methodological conditions used, no reproducible taxonomic signature was detectable across either the oral or fecal microbiota. However, this does not necessarily imply that microbiome-related alterations are universally absent from cases of FM. Instead, more minor, context-dependent, or functionally relevant shifts, particularly those influenced by diet, mucosal immunity, medication exposure, stress physiology, or metabolic state, may fall below the resolution of 16S rRNA profiling or the statistical power of the present sample. Accordingly, the results support the view that FM does not exhibit a robust or uniform microbial pattern. Still, they do not exclude the possibility of phenotype-specific or functionally driven dysregulation.

Although the sample size was comparable to those of prior exploratory microbiome studies, the sensitivity analysis indicated that the study was powered to detect only moderate differences in community structure ($R^2 \geq 0.11$). More minor or more nuanced alterations—particularly those driven by low-abundance taxa or functionally relevant pathways—may therefore not have been captured. Accordingly, the absence of statistically significant differences should not be interpreted as definitive evidence of a completely preserved microbial profile in FM.

However, the absence of compositional differences does not rule out underlying biological relevance. Recent Mendelian randomization analyses suggest that specific gut genera, including Ruminococcus and Coprococcus, may exert upstream causal influences on FM risk independent of environmental confounders (11). This finding raises the significant possibility that FM-related microbial alterations may be subtle, pathway-specific, or metabolically driven rather than changes that manifest as broad shifts in overall community structure. In this context, our null results provide meaningful evidence that taxonomy alone may be insufficient to capture relevant host–microbiome interactions in FM.

It is also important to acknowledge methodological constraints related to the differential abundance analysis. Although LefSe (The Huttenhower Foundation, Harvard T. H. Chan School of Public Health) is widely used in exploratory microbiome research, the method is known to be sensitive to data sparsity, nonnormal distributions, and unequal group sizes, potentially leading to inflated false-positive or false-negative findings. Recent benchmarking studies have demonstrated that LEfSe (The Huttenhower Foundation, Harvard T. H. Chan School of Public Health) may lack robustness compared with more compositionality-aware approaches such as ANCOM-II, ALDEx2 (Bioconductor), or DESeq2 (Bioconductor) (12,13). Accordingly, the absence of significant taxa after FDR correction in the present study should be interpreted in light of these limitations, as subtle but biologically relevant differences may remain undetectable. Future studies integrating alternative differential abundance methods and multi-omics platforms will be essential to clarify functional pathway-level alterations beyond the taxonomic structure.

A similar interpretation applies to the oral microbi-

ome. Earlier work had suggested increased periopathogenic taxa there in cases of FM; however, more advanced metatranscriptomic analyses indicate that functional disturbances, such as upregulation of sulfur-reducing or proteolytic pathways, may be more relevant than compositional differences (3). This principle was demonstrated by Erdrich et al, who showed that oral microbial activity differed between FM patients and controls despite minimal taxonomic divergence (3). Our findings of preserved oral microbial structure under tightly controlled conditions are therefore consistent with the hypothesis that functional dysregulation may precede or overshadow structural taxonomic shifts.

Taken together, these observations support a broader conceptual model: FM may not involve a unified dysbiotic signature but instead reflect phenotype-specific, environment-modulated, or immune-metabolic alterations within the microbial community. The multidimensional gut-brain-immune model proposed by Watai et al highlights mechanistic pathways through which microbial metabolites and neuroimmune crosstalk may influence nociceptive amplification without requiring overt microbial imbalance (14). This framework aligns with clinical observations that FM symptoms fluctuate with stress, diet, sleep patterns, and hormonal variation, all of which can modulate microbial metabolism and mucosal immune signaling.

Our findings, therefore, have 2 key implications for future research. First, microbiome-directed interventions may benefit only specific FM subgroups, particularly those with gastrointestinal comorbidities, metabolic abnormalities, or heightened inflammatory tone. Second, future studies should incorporate multi-omics approaches, including metatranscriptomics, metabolomics, and proteomics, to identify functional microbial signatures that may be biologically meaningful yet remain undetectable through 16S rRNA profiling alone.

Despite its contributions, this study has several limitations. The modest sample size limited the ability to detect subtle microbial differences, as the study had adequate power only for moderate effect sizes ($R^2 \geq 0.11$). Smaller compositional or functionally meaningful shifts may therefore have remained undetected. The cross-sectional design prevents causal inference and precludes the evaluation of temporal microbiome dynamics in FM. Although recent antibiotic, probiotic, and acute inflammatory exposures were rigorously excluded, other determinants of microbial composition, such as diet, physical activity, sleep quality, and chronic analgesic or psychotropic medication use, could not be fully quantified or controlled.

The study did not include a standardized or quantitative dietary assessment. Because diet is a significant determinant of gut microbial composition, the lack of detailed nutritional data limits our ability to fully account for interindividual dietary variability. Future studies that incorporate structured dietary monitoring will help better isolate disease-related microbial signals.

Furthermore, 16S rRNA sequencing restricts taxonomic resolution at the species level and does not permit the direct assessment of microbial functional pathways relevant to nociplastic pain mechanisms. Finally, the single-center, all-female sample limits generalizability.

Nevertheless, the present study possesses essential strengths. It provides one of the few parallel evaluations of both fecal and oral microbiota within the same FM patients, enabling a multi-compartment assessment of mucosal ecosystems. The strict exclusion criteria minimized major confounders known to influence microbial composition, thereby enhancing internal validity. The analytical strategy incorporated alpha and beta diversity metrics, taxonomic profiling, and differential abundance analysis based on LefSe (The Huttenhower Foundation, Harvard T. H. Chan School of Public Health), the last of which was supported by rigorous FDR correction. The combined use of PERMANOVA and PCoA further strengthened the robustness of the beta-diversity results. Collectively, these strengths enhance confidence in the absence of a consistent microbiome signature in FM and contribute high-quality negative evidence to a field characterized by methodological heterogeneity.

Conclusions

In conclusion, this study represents one of the most comprehensively controlled evaluations of both gut and oral microbiota in FM to date. Under tightly standardized physiological and environmental conditions, no consistent taxonomic differences were identified between FM patients and healthy controls. These findings suggest that previously reported dysbiosis may reflect contextual or phenotype-specific influences rather than a universal microbial hallmark of FM. Nevertheless, the possibility of subtle or functionally meaningful microbial alterations cannot be excluded. Future studies incorporating larger cohorts, multi-omics approaches, and detailed phenotypic stratification will be essential to clarify the role of host–microbiome interactions in nociplastic pain conditions.

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Author Contributions

GC: contributed to study conception and design, patient recruitment, clinical data collection, and manuscript drafting and served as the corresponding author.

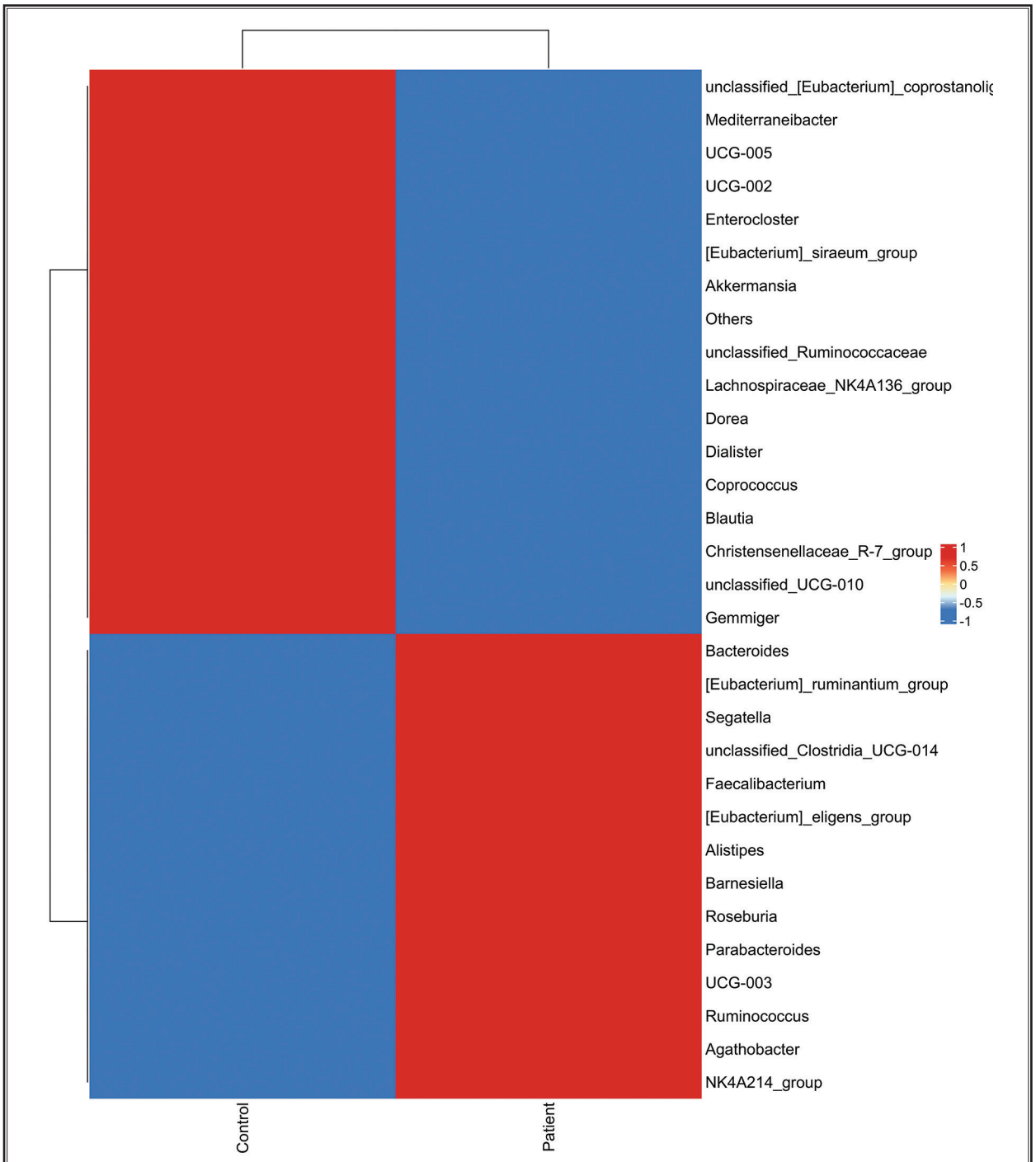
EY: contributed to the clinical evaluation and coordination of sample collection.

NI: contributed to the clinical evaluation, supervision of sample collection, and critical manuscript review.

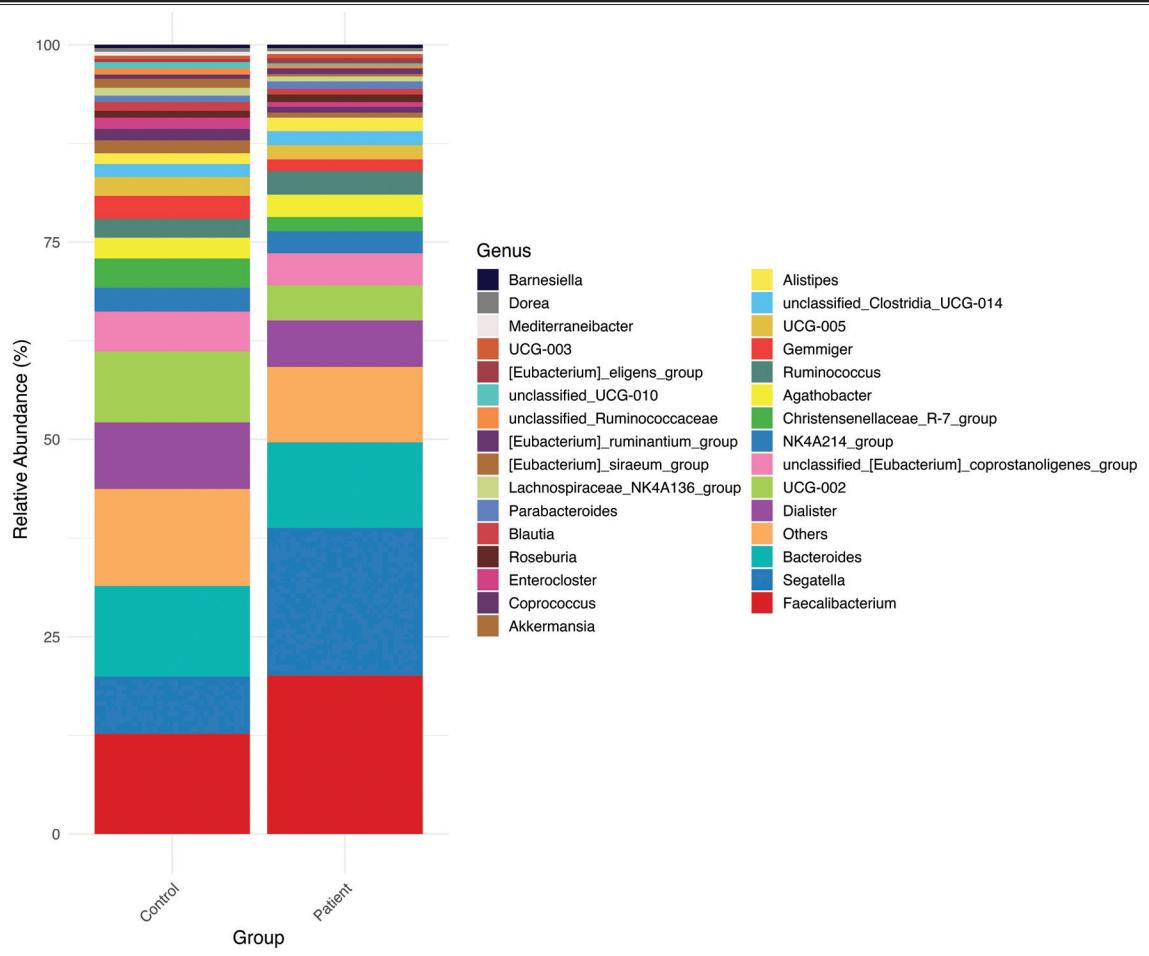
AMY: supervised the bioinformatics workflow, performed data validation, and contributed to manuscript revision.

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Supplementary Fig. X. ***Genus-level heat map of fecal microbiota.***
Heat map showing Z-score–normalized relative abundances of predominant genera across FM and control patients. The plot demonstrates high interindividual variability and no coherent clustering or group-specific distribution pattern.



Supplementary Fig. Y. ***Stacked bar plot of the top 30 fecal genera.***
Relative abundance bar plot illustrating the 30 most abundant fecal genera in FM and control patients. Both groups displayed broadly similar compositional profiles, with no consistent shifts in dominant taxa.
Bar plot presenting LDA effect size scores for taxa contributing to group differences. Most taxa with elevated LDA values were enriched in controls, while only isolated taxa showed relative enrichment in the FM group. None retained significance after multiple testing corrections.