

FMT PLUS EXCLUSION DIET IN CROHN'S DISEASE

A 52-Week Randomized, Double-Blind, Sham- Controlled Trial



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DDW2026
Digestive Disease Week®

MAY 2-5, 2026 | CHICAGO, IL

EXHIBIT DATES: MAY 3-5, 2026

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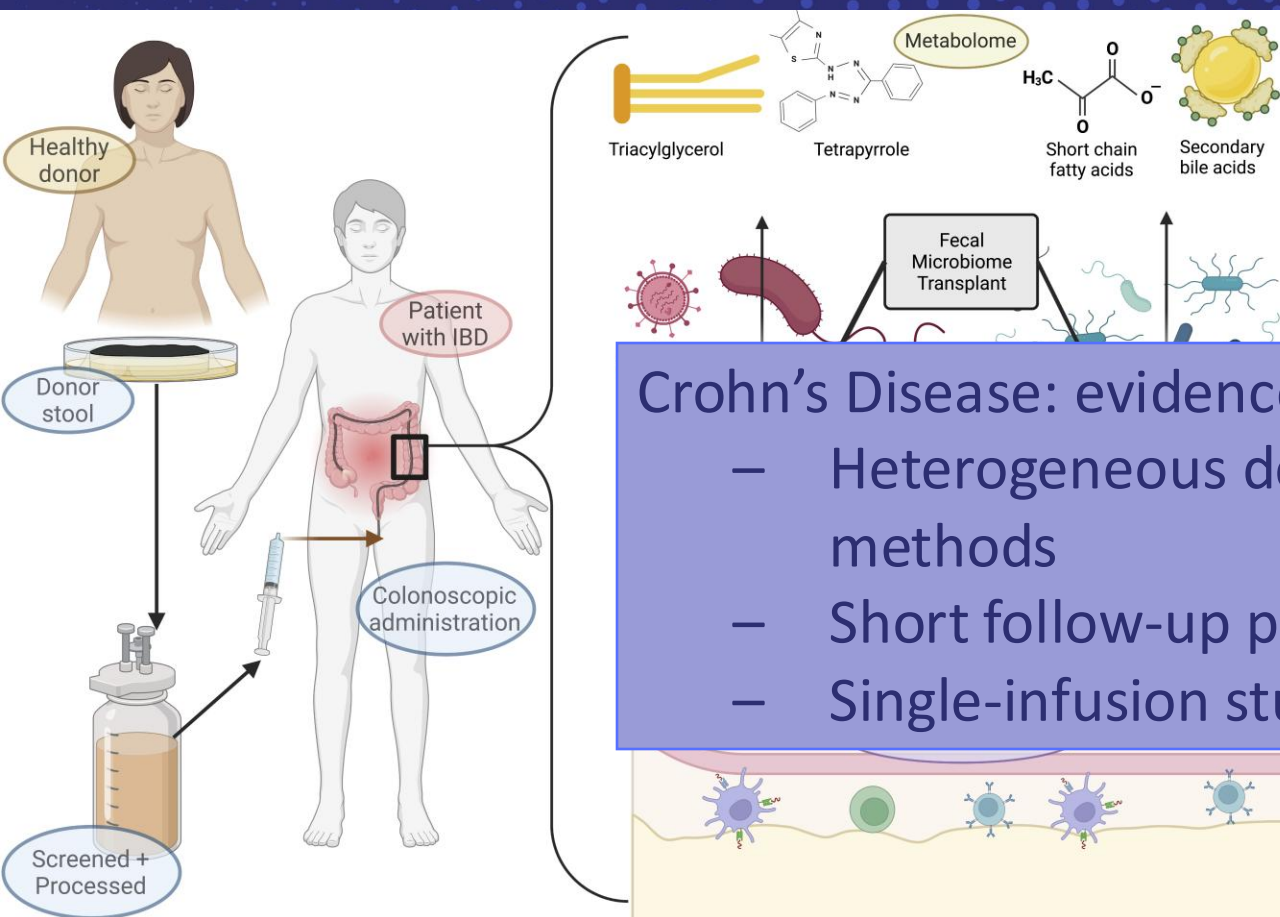
SPEAKER DISCLOSURE

No disclosure

Funding sources

- Indian Council of Medical Research: Center for Advanced Research and Excellence in Intestinal Diseases, awarded to Dr. Vineet Ahuja (grant number: 55/4/11/CARE-ID/2018-NCD-II).
- Ramalingaswami Re-entry Fellowship (BT/HRD/35/02/2006; Sanction Order: BT/RLF/Re-entry/55/2021) awarded to Dr. Tarini Shankar Ghosh by the Department of Biotechnology, Ministry of Science and Technology, Government of India.

FMT IN IBD



Arora U et al. Intest Res. 2024

Crohn's Disease: evidence limited by:

- Heterogeneous delivery methods
- Short follow-up periods
- Single-infusion study designs

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Study

Events Total

Proportion

95%-CI Weight

Wei 2015

0 3

0.00 [0.00; 0.71]

1.8%

Vaughn 2016

10 19

0.53 [0.29; 0.76]

9.9%

Wang 2018

79 139

0.57 [0.48; 0.65]

70.4%

Gutin 2019

1 3

0.33 [0.01; 0.91]

1.8%

Yang 2020

18 27

0.67 [0.46; 0.83]

13.9%

Osaki 2021

1 4

0.25 [0.01; 0.81]

2.3%

195

0.57 [0.49; 0.64]

100.0%

$p = 0.16$

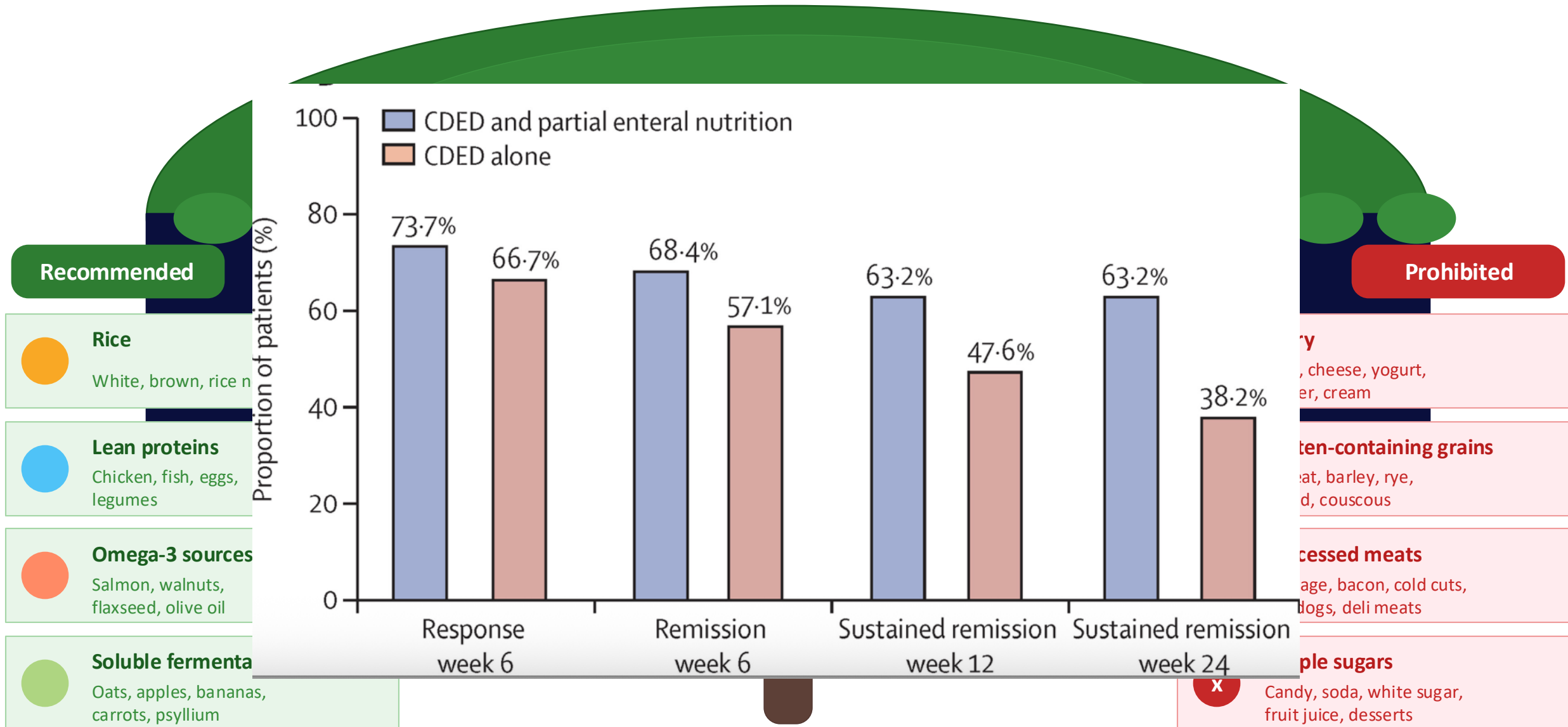
Induction of clinical remission

Zhou S et al. Int J Colorectal Dis. 2023

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Crohn's Disease Exclusion Diet (CDED)



HYPOTHESIS

Combining microbial transfer (FMT) with a microbiome-supportive diet (CDED) would improve clinical, endoscopic, and microbiome outcomes compared with diet alone

- “Seed and Fertilize”

STUDY DESIGN

- Single-centre, double-blind, sham-controlled RCT
- October 2022 – September 2024
- IBD Clinic
- Randomization: 1:1, permuted blocks (n=4)



STUDY CRITERIA

Inclusion criteria

1. Adults (18–70 years)
2. Mild-to-moderate active (CDAI 150–450)
3. Ileal (L1)/Colonic (L2)/ Ileo-colonic (L3) disease
4. Inflammatory (B1) or stricturing (B2) in the absence of prior obstruction
5. Any of SES-CD ≥ 3 , FCP >150 $\mu\text{g/g}$, or radiologic activity
6. Stable immunomodulators (>4 weeks) and biologics (>12 weeks)

Exclusion criteria

1. Proximal disease (L4)
2. Fistulizing disease (B3)
3. Active perianal disease
4. Current hospitalization
5. Pregnancy
6. Prior intestinal surgeries
7. Antibiotic exposure (≤ 2 weeks)

INTERVENTION

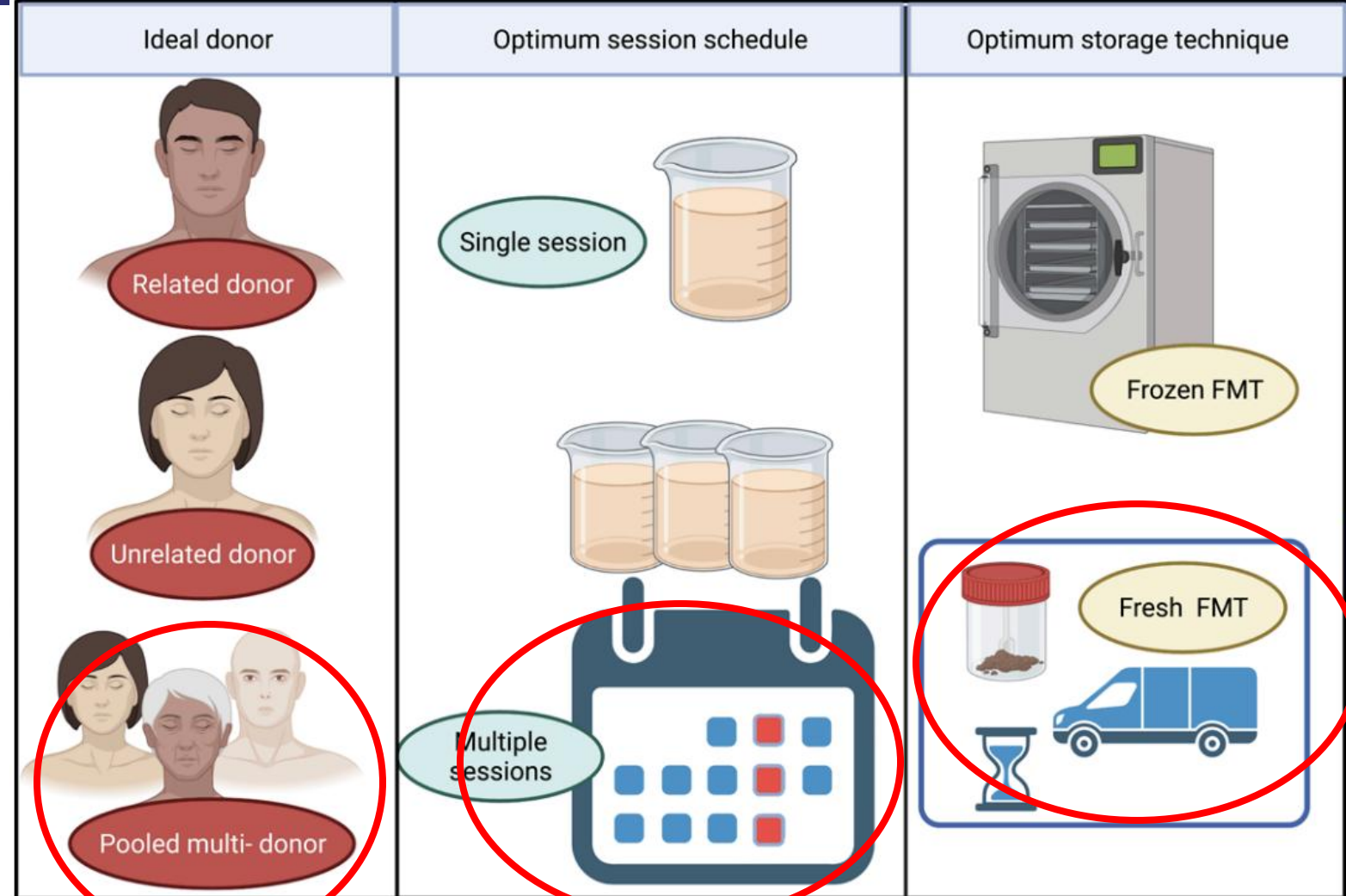
FMT + CDED Group

- Fresh pooled multi-donor FMT (250 mL)
- Donors: Rural North India (high diversity, inter-individual homogeneity)

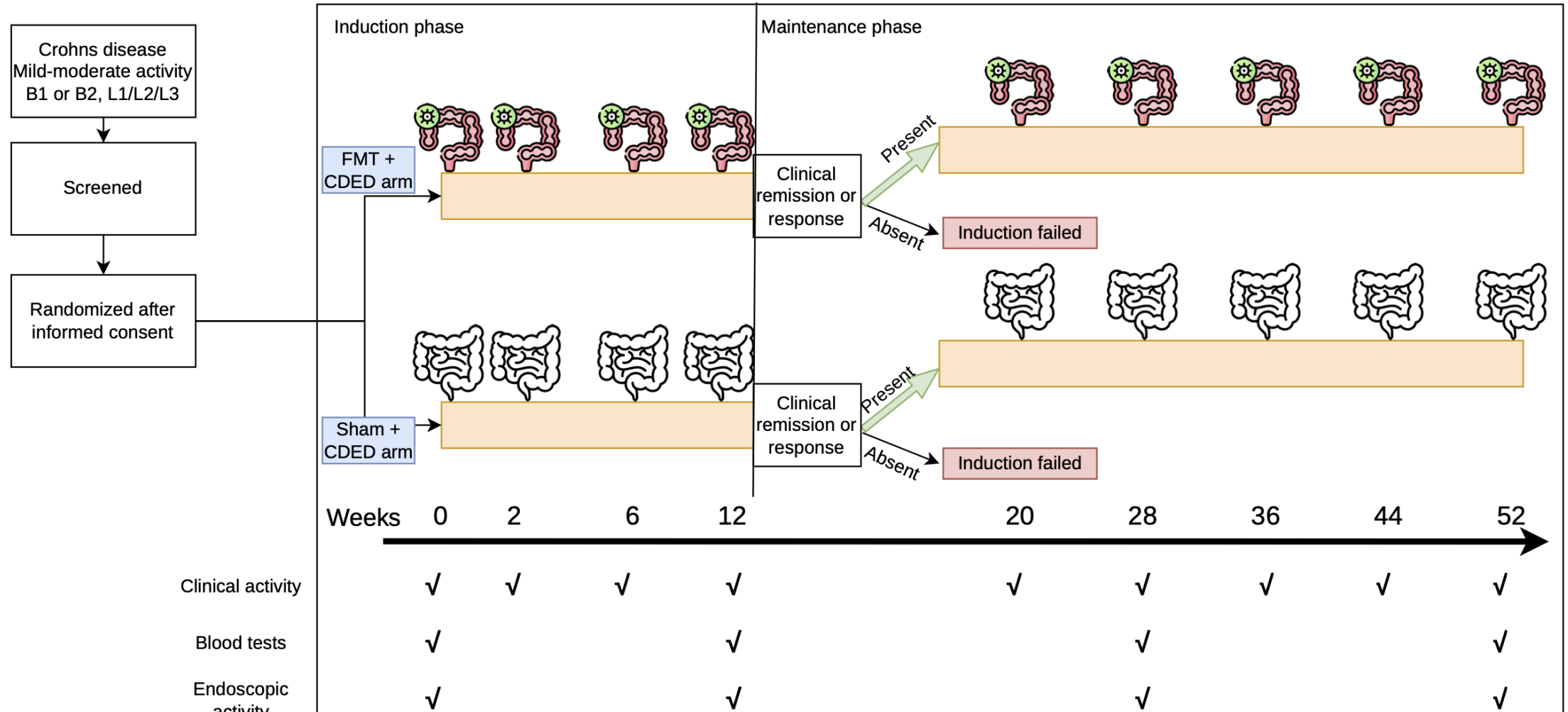
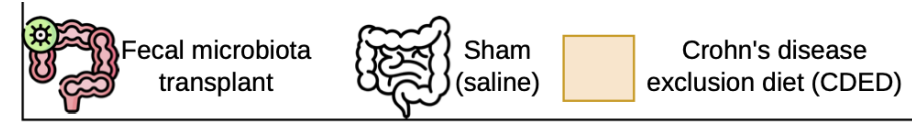
Blinding : Opaque-coated syringes

Instillation was attempted into terminal ileum/cecum, withdrawn to descending colon

Sham + CDED Group: Identical protocol, 250 mL saline



Study design



Dietary adherence: IBD NutriCare app

CO-PRIMARY OUTCOMES

Definitions (STRIDE-II)

- Clinical remission: CDAI <150
- Endoscopic remission: SES-CD 0–2 without ulceration
- Endoscopic response: $\geq 50\%$ SES-CD reduction from baseline

Induction

Clinical
remission

Endoscopic
response

Maintenance

Clinical
remission

Endoscopic
remission

SECONDARY OUTCOMES

Definitions (STRIDE-II)

- Clinical response: ≥ 100 -point CDAI reduction from baseline
- Treatment failure: ≥ 70 -point CDAI increase, need for systemic corticosteroids, or hospitalization

Induction

Clinical response

Endoscopic remission

Treatment failure

Adverse events

Maintenance

Clinical response

Endoscopic response

Treatment failure

Adverse events

MICROBIOME ASSESSMENT

Sample Collection & Sequencing

- Prior to bowel prep, within 2 hours, stored at -80°C
- Whole metagenome sequencing

Microbiome Indices Assessed

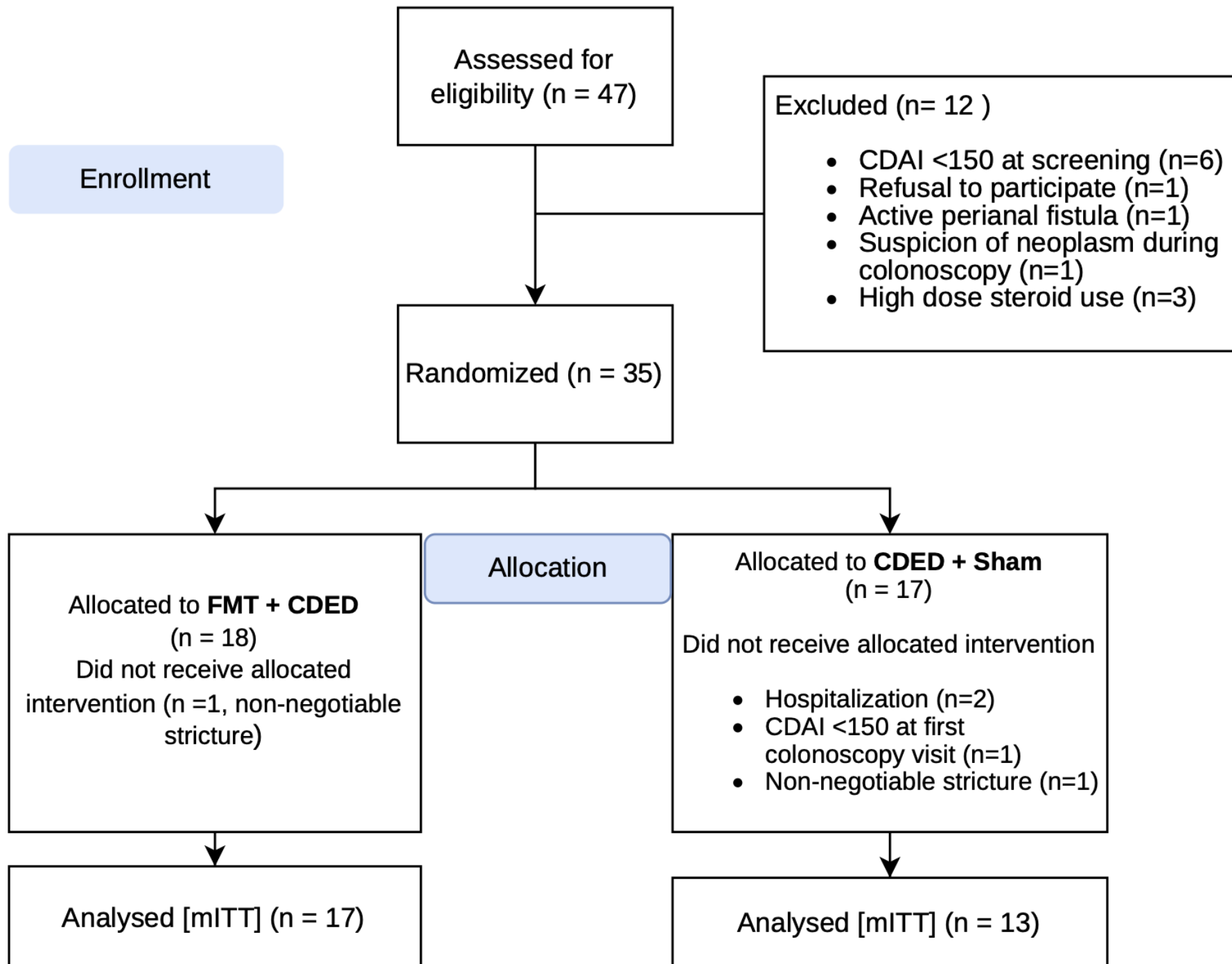
- Shannon (alpha diversity)
- Health indices:
 - HACK top-17 score
 - CGMS
- Dysbiosis score
- Bray-Curtis distance (Beta-diversity)

Engraftment Assessment

- Strain-level transfer: StrainPhlAn4 analysis

STATISTICAL ANALYSIS

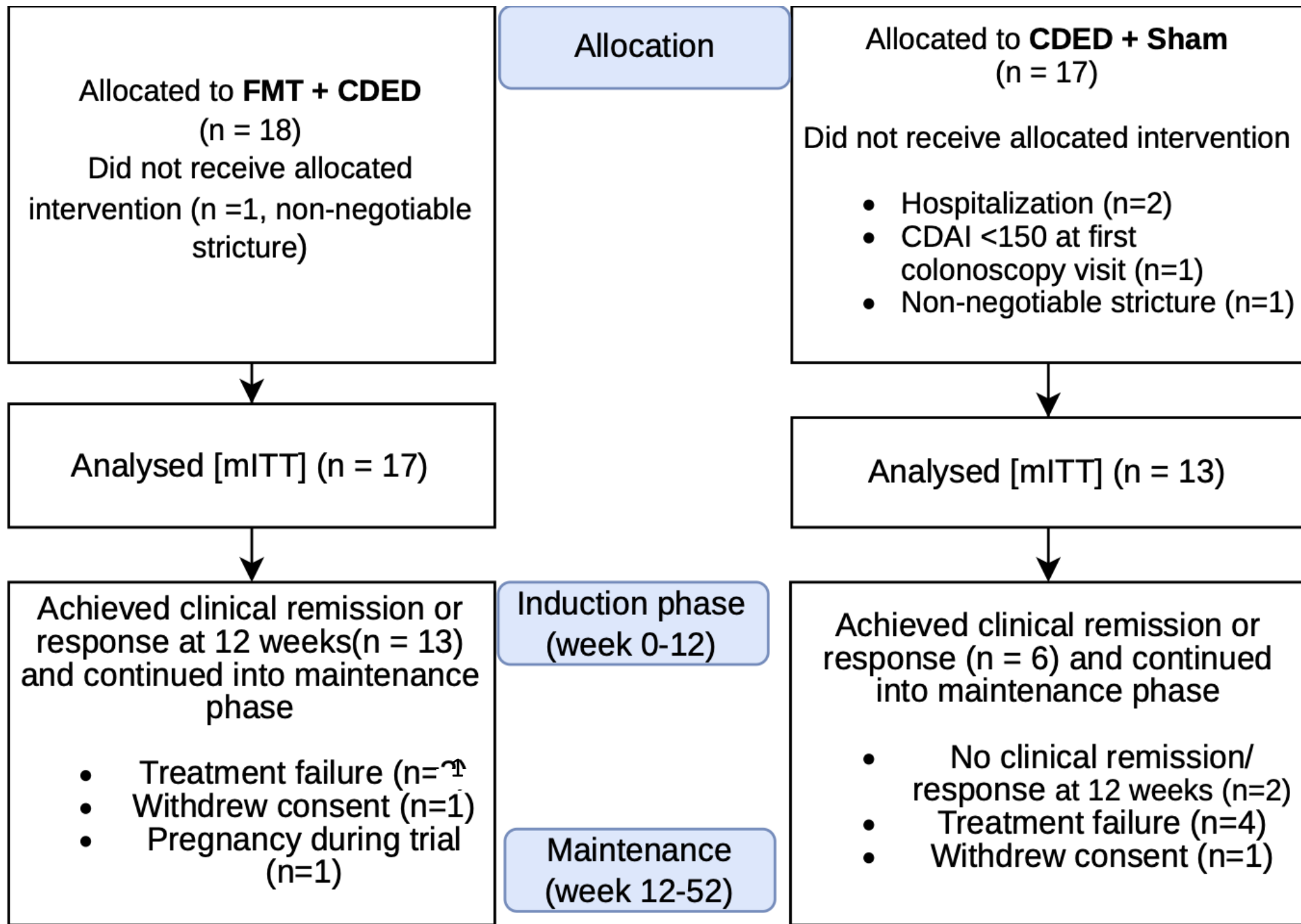
- Modified intention-to-treat (mITT) analysis
- Sample size: planned n=70 (35/arm)
- Two-sided $\alpha=0.05$
- Recruitment stopped early at n=30 in Sep 2024



	FMT+CEDED (n=17)	Sham+CEDED (n=13)
Age (years)	39 ($\pm$ 12)	35 ($\pm$ 11)
Male sex	7 (41%)	8 (62%)
Body Mass Index	21 ($\pm$ 4)	21 ($\pm$ 5)
Residence: Urban	9 (53%)	6 (46%)
Duration of disease (mo)	54 (28–128)	38 (20–120)
Disease location		
L1, n (%)	2 (12%)	2 (15%)
L2, n (%)	9 (53%)	5 (38%)
L3, n (%)	6 (35%)	6 (46%)
Disease behavior		
B1, n (%)	13 (76%)	6 (46%)
B2, n (%)	4 (24%)	7 (54%)
Perianal dis. (inactive)	1 (6%)	2 (15%)

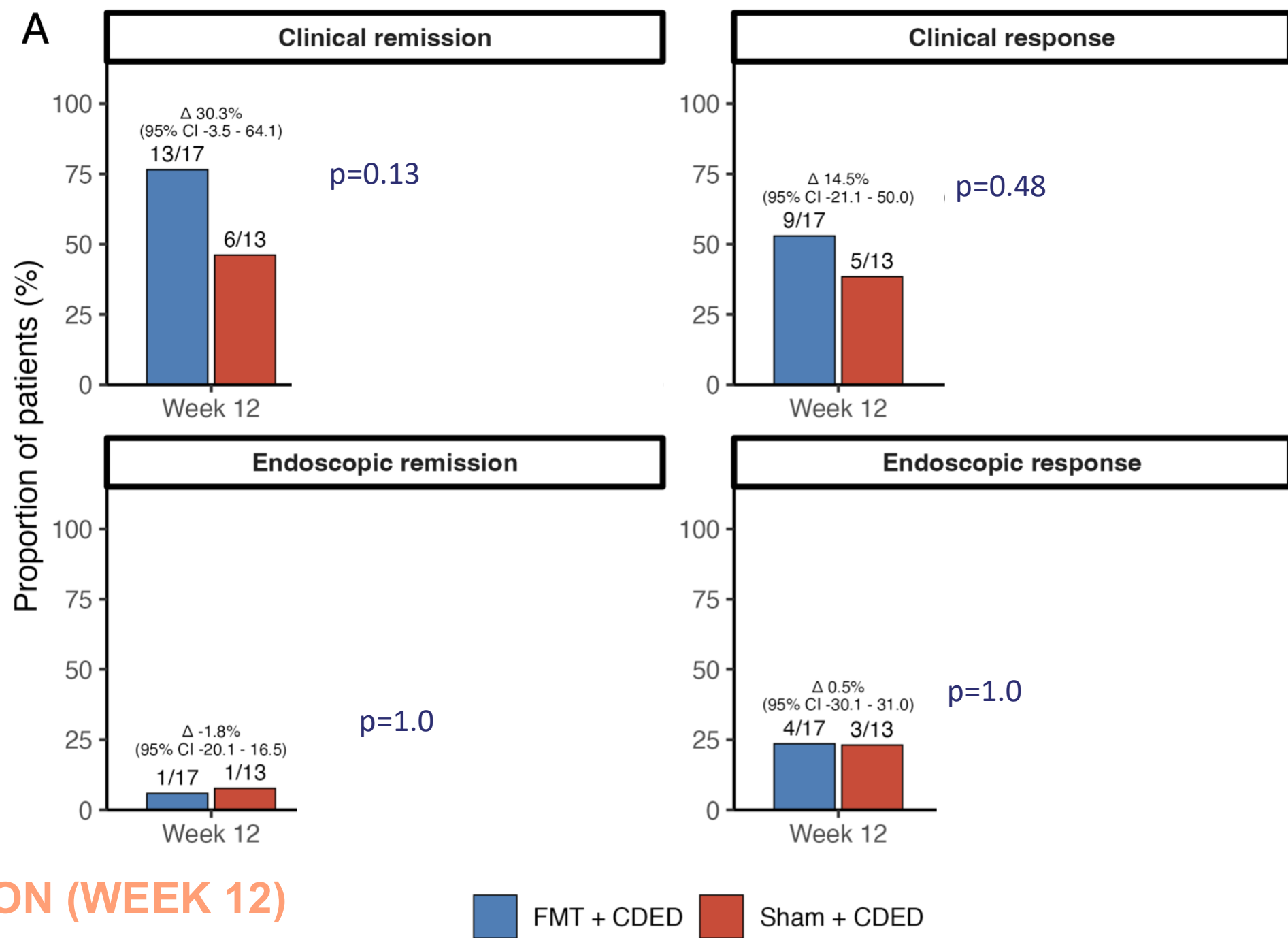
	FMT+CEDED (n=17)	Sham+CEDED (n=13)
CDAI	192 (159–238)	186 (163–252)
SES-CD	14 (11–20)	14 (8–18)
Prior treatment history		
Steroid exposure, n (%)	14 (82%)	10 (77%)
Prior azathioprine use, n (%)	12 (71%)	10 (77%)
Prior methotrexate use, n (%)	3 (18%)	6 (46%)
Any prior biologic use, n (%)	0 (0%)	1 (8%)
Current therapy		
Current steroid use	3 (18%)	2 (15%)
Current azathioprine use	7 (41%)	2 (15%)
Current 6-mercaptopurine use	0 (0%)	1 (8%)
Biochemical markers		
Hemoglobin (g/dL)	11 (±2)	12 (±2)
C-reactive protein (mg/dL)	12 (4–30)	12 (8–34)
Fecal calprotectin (µg/g)	505 (345–901)	314 (224–933)

INDUCTION PHASE



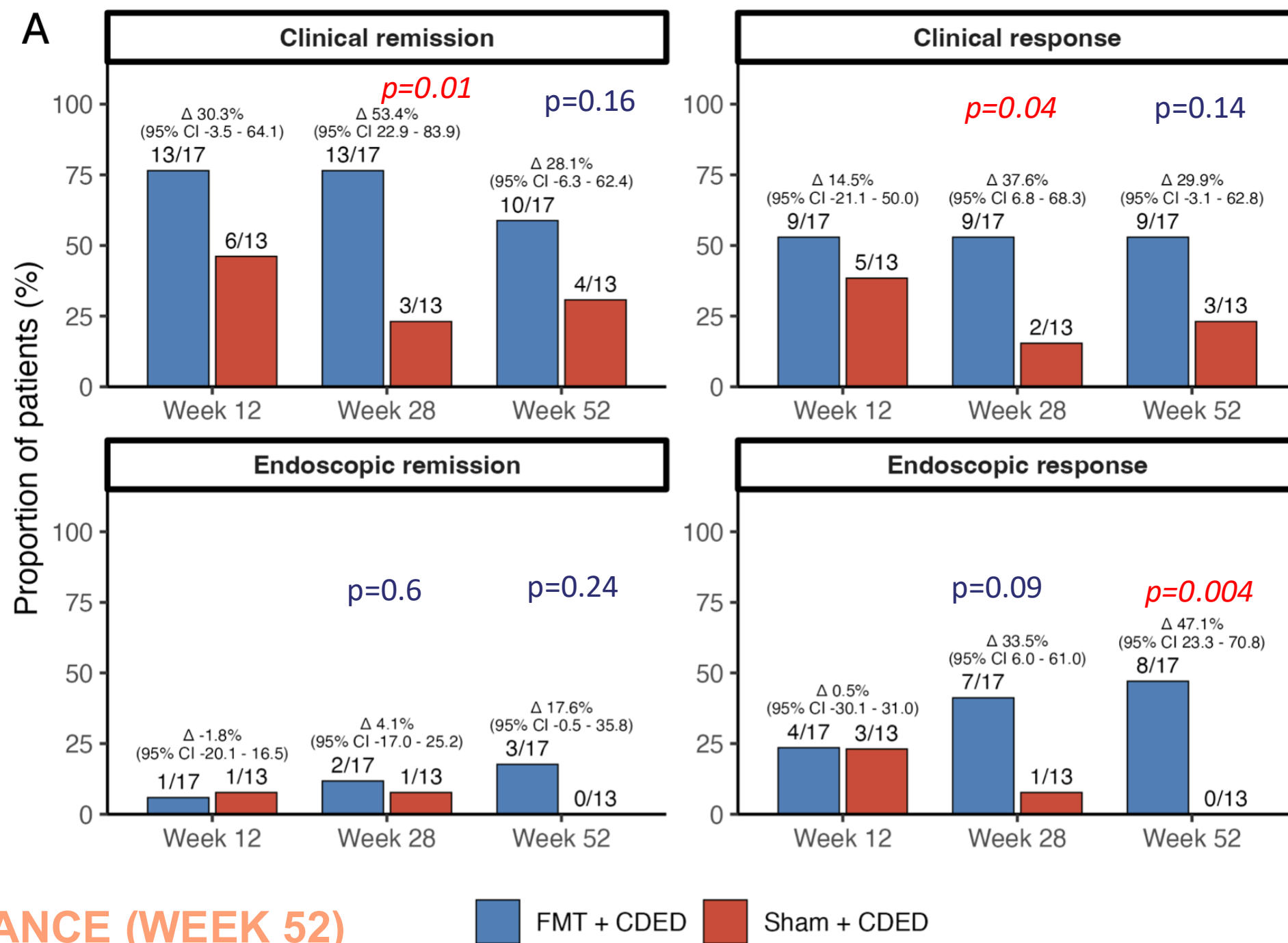
8 patients did not complete induction: treatment failure n=5 (1 in FMT + 4 sham), withdrew consent n=2 (1 each), pregnancy n=1 (FMT)

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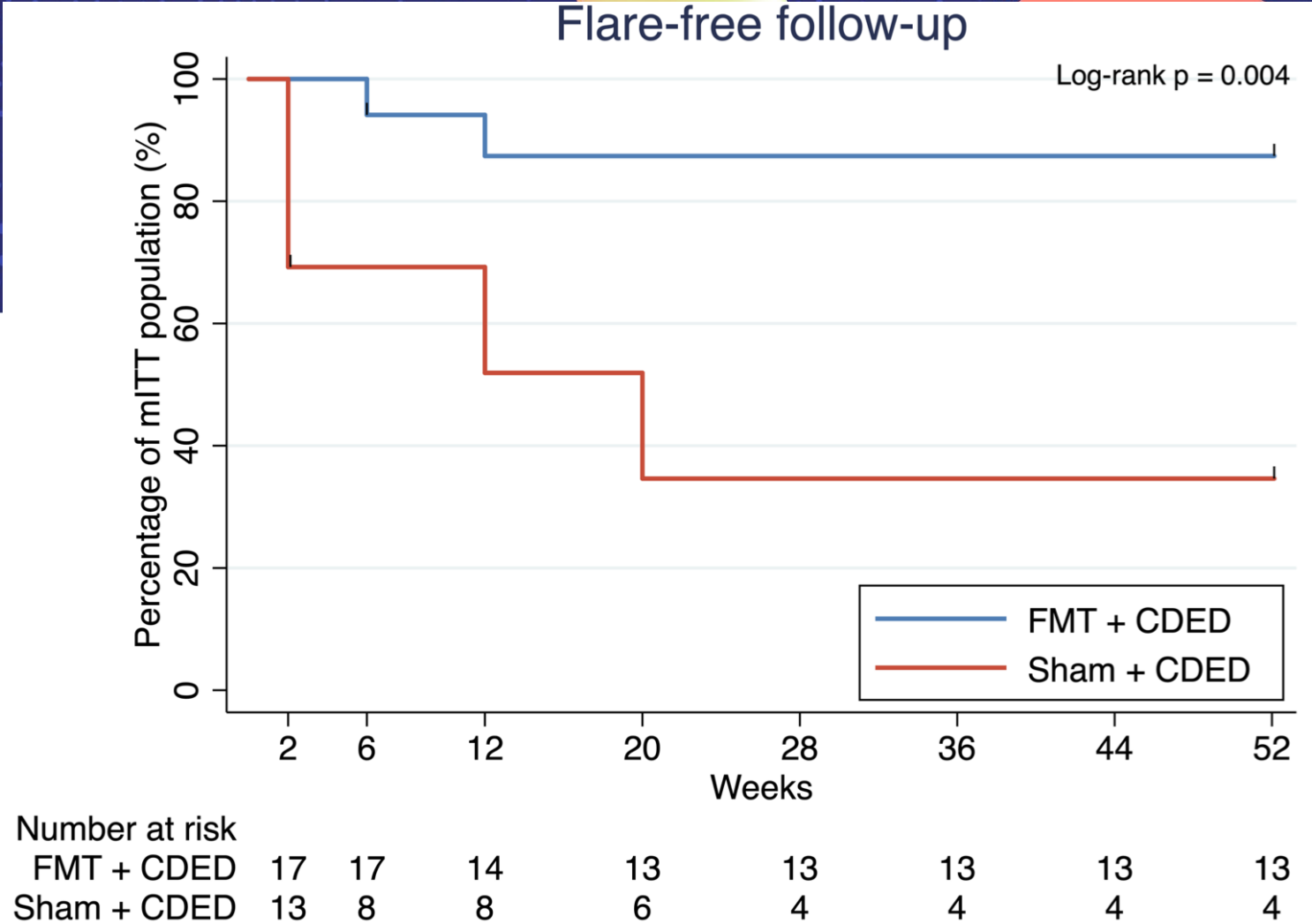
INDUCTION (WEEK 12)

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TREATMENT FAILURE

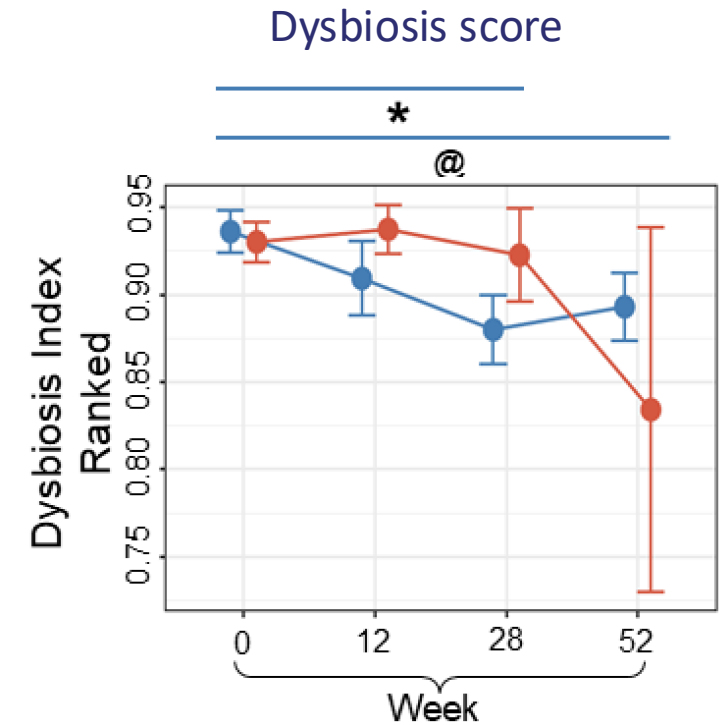
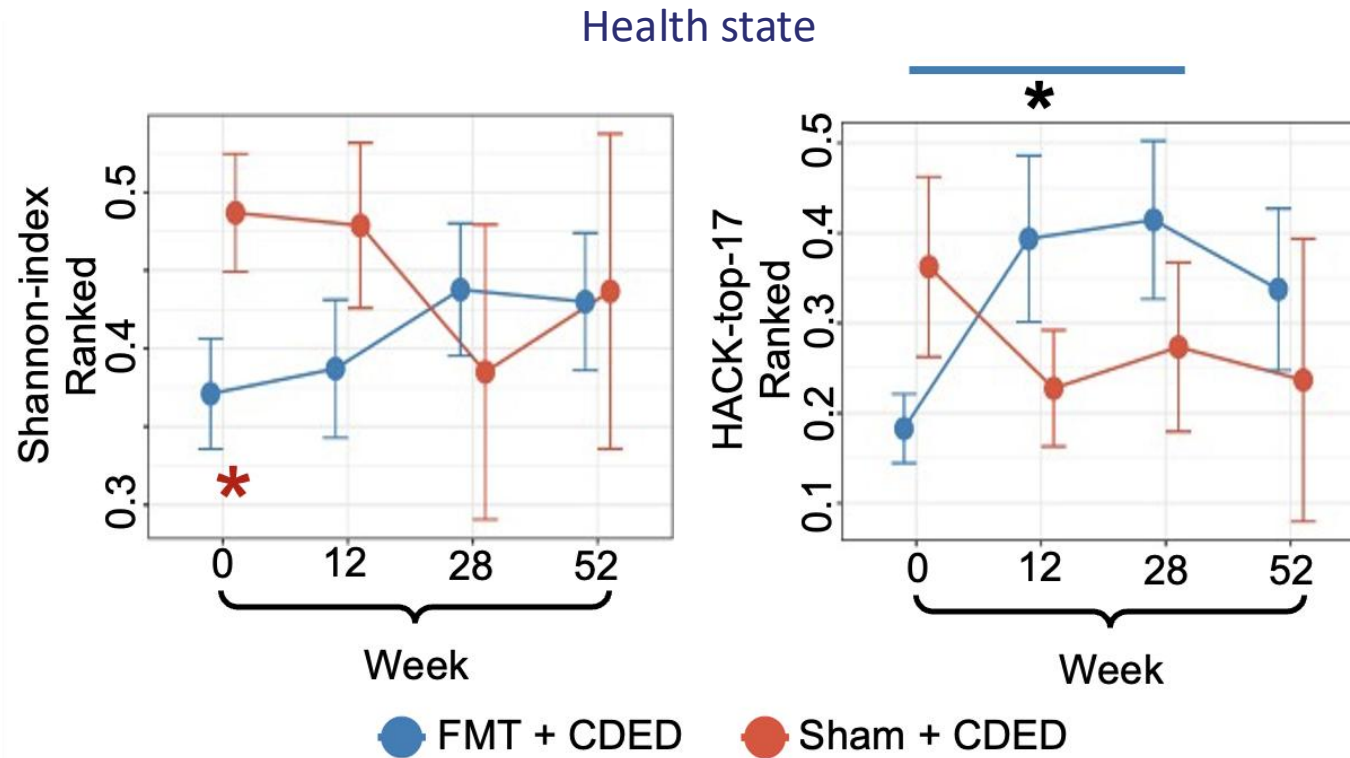
- Lower treatment failure at 28 and 52 weeks ($p=0.03$)
- HR 0.15 (95% CI 0.03–0.70); log-rank $p=0.004$



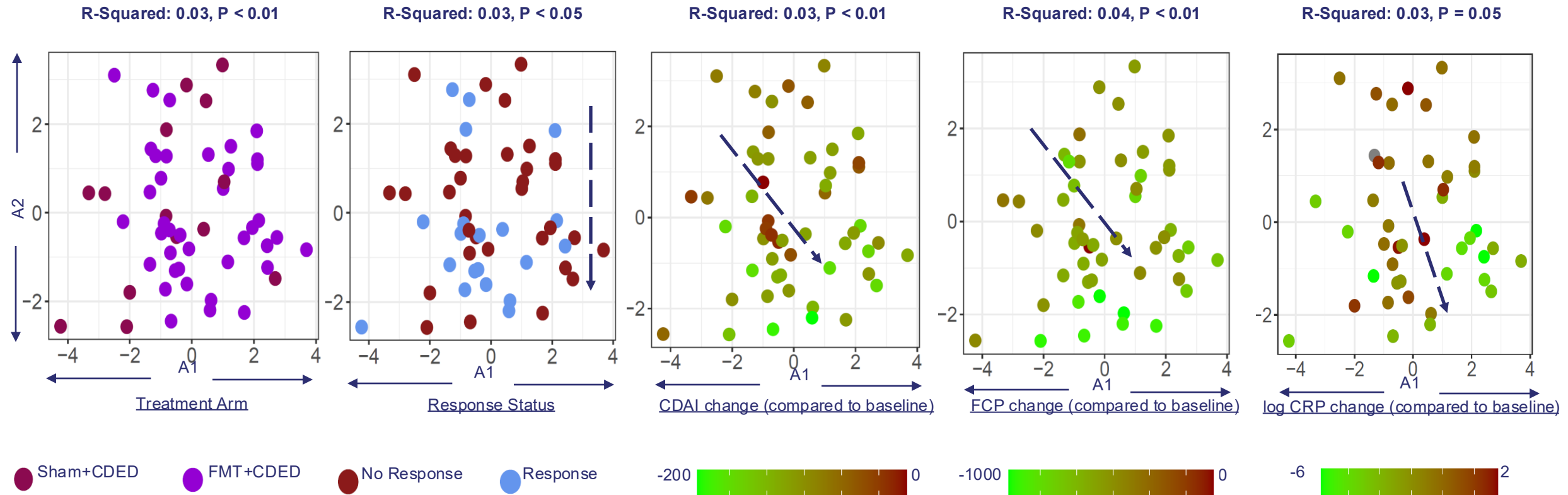
SAFETY PROFILE

	FMT + CDED (n=17)	Sham + CDED (n=13)	p-value
Week 12	4/17 (23.5%)	1/13 (7.7%)	0.34
Week 52	5/17 (29.4%)	2/13 (15.4%)	0.39
Grade ≥ 3 adverse events	1/17 (5.9%) Liver abscess	1/13 (7.7%) High-grade fever	1.00

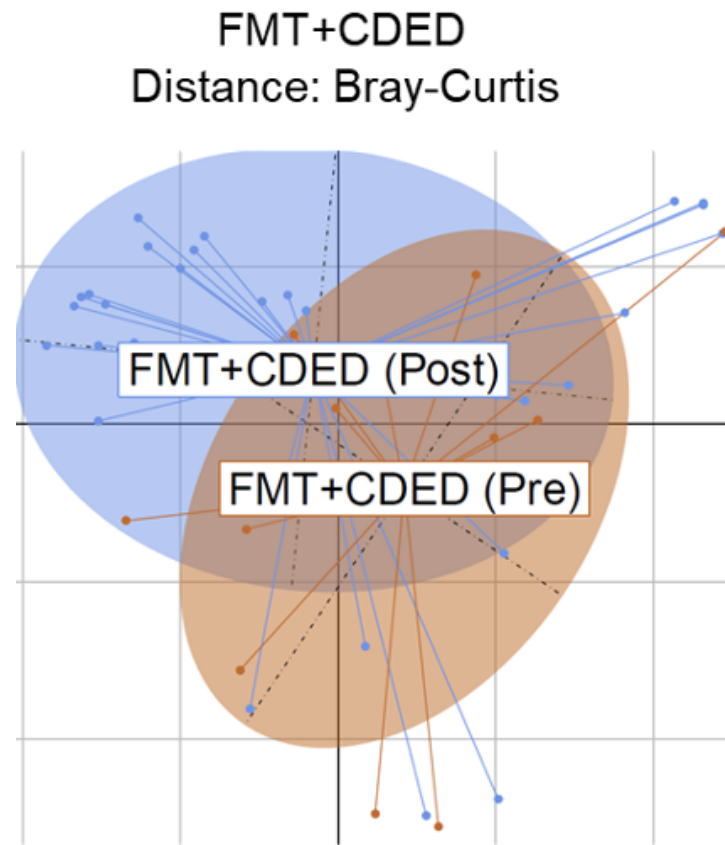
MICROBIOME HEALTH IMPROVES WITH FMT + CDED



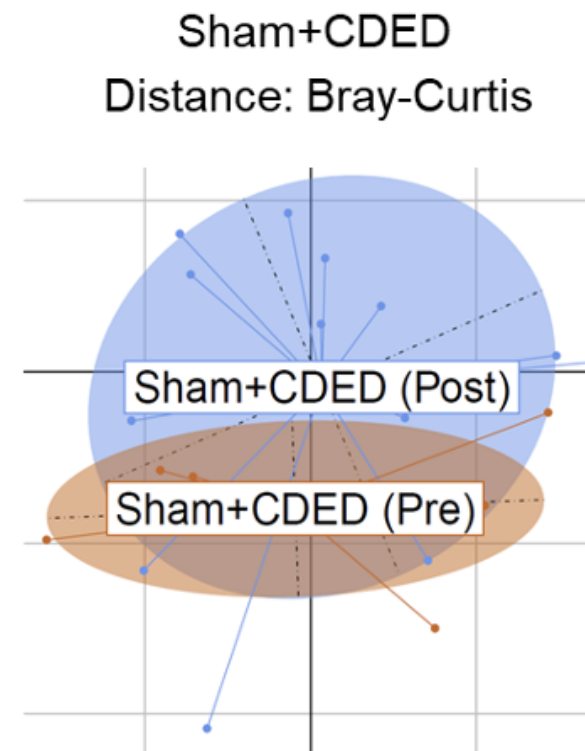
CLINICAL-MICROBIOME CORRELATION



SIGNIFICANT COMPOSITIONAL SHIFTS IN FMT+CDED GROUP



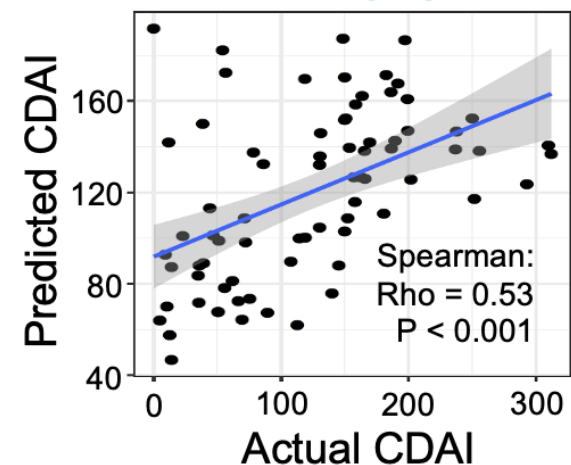
PERMANOVA
R-squared: 0.06, P=0.02



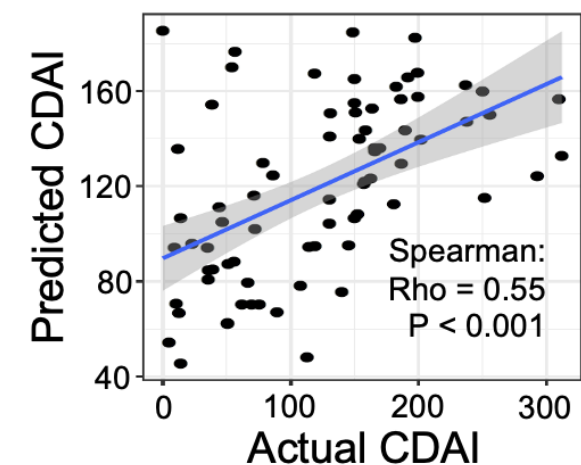
PERMANOVA
R-squared: 0.04, P=0.18

RESPONSE ASSOCIATED TAXA (8)

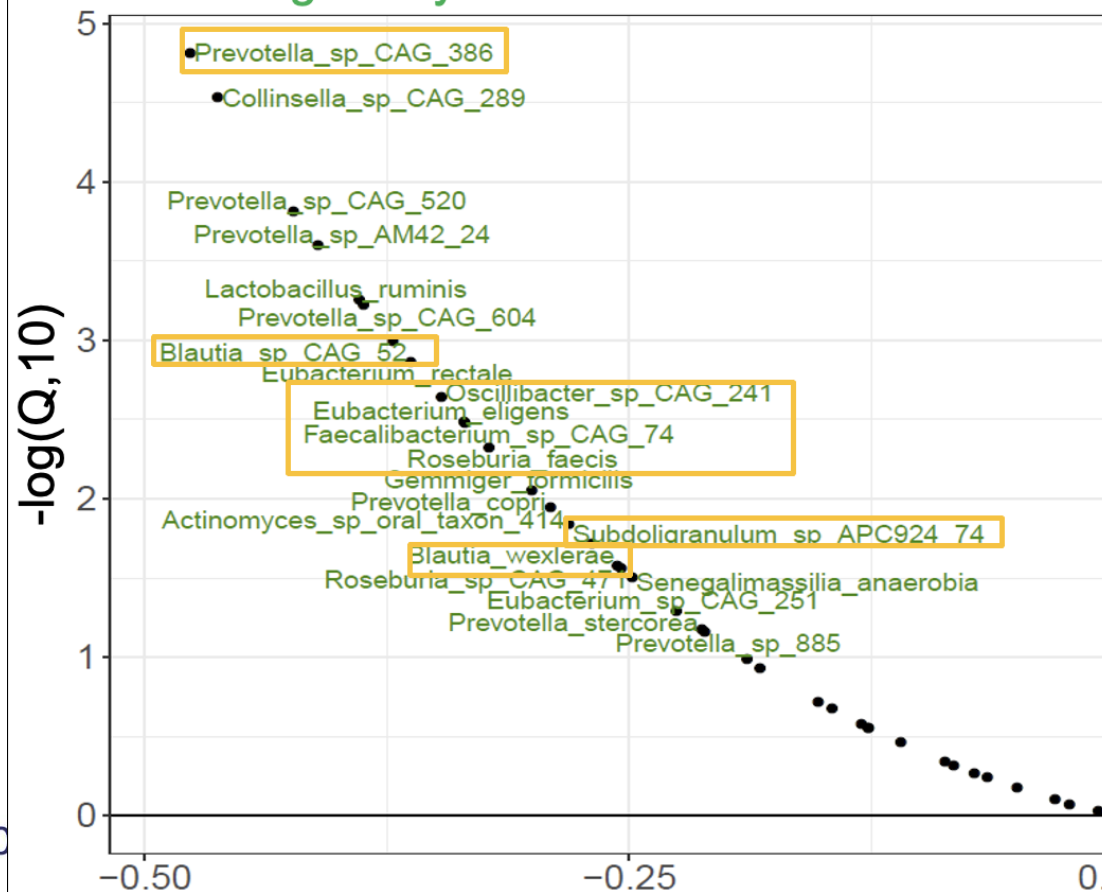
All Taxa



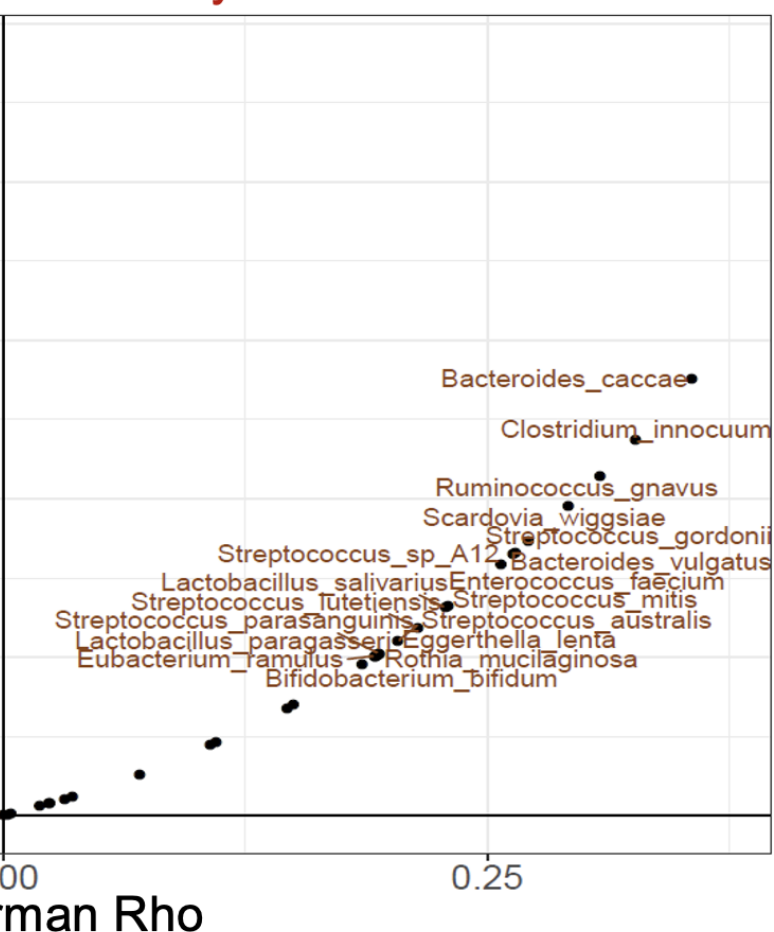
Top Predictor Taxa (N=70)



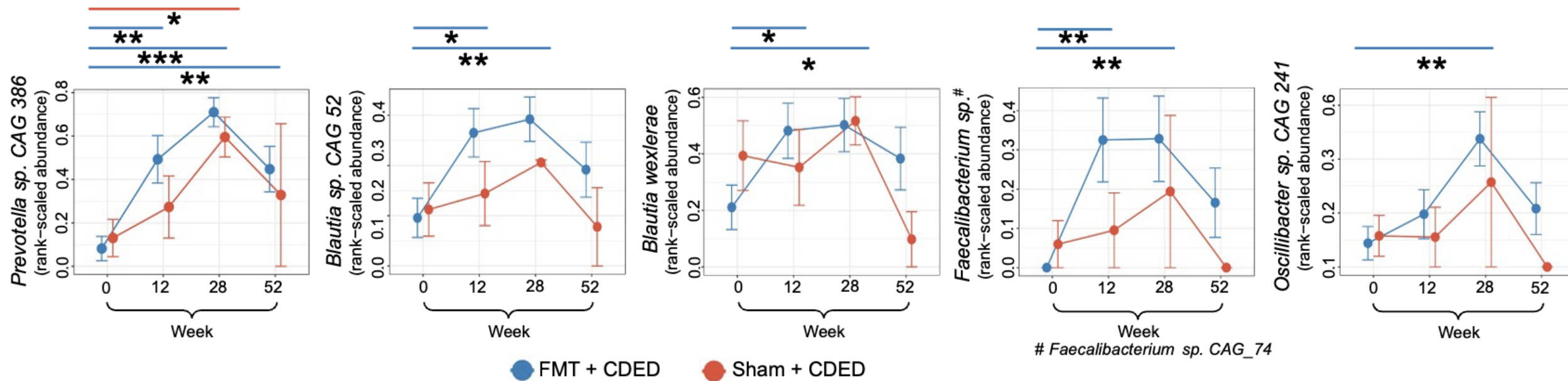
Negatively associated with CDAI



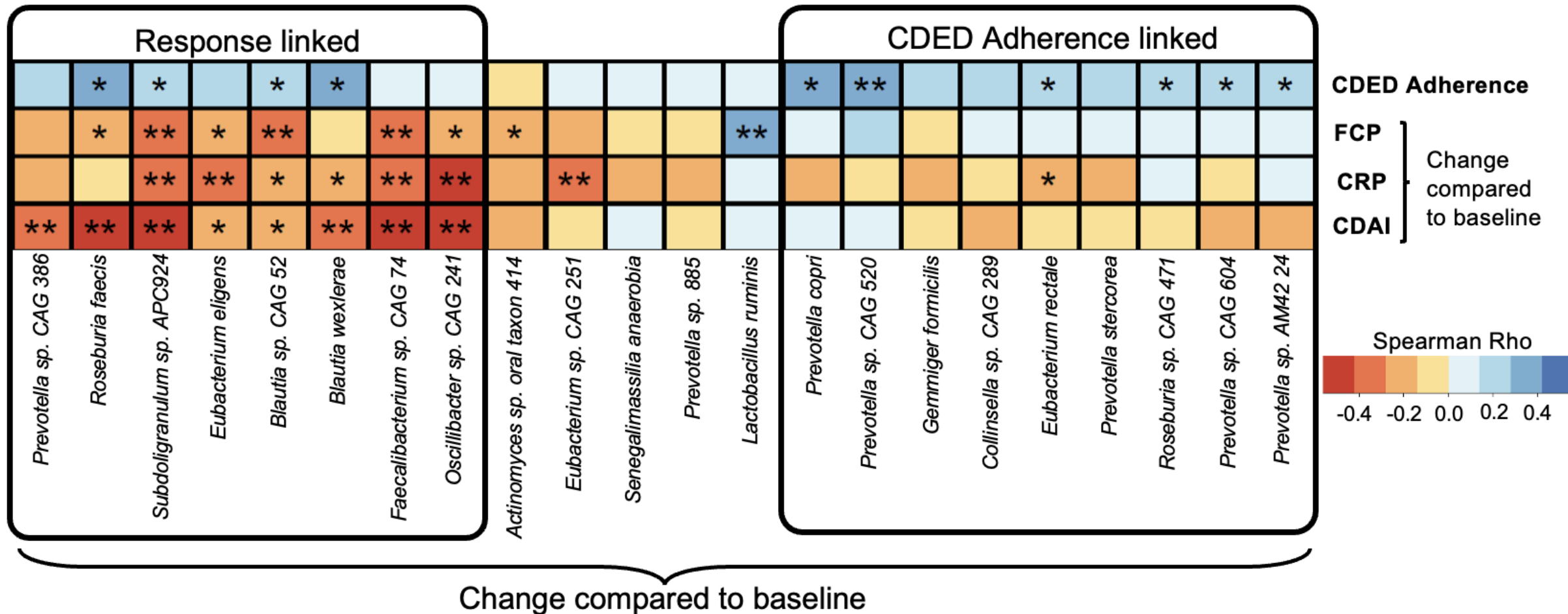
Positively associated with CDAI



RESPONSE ASSOCIATED TAXA

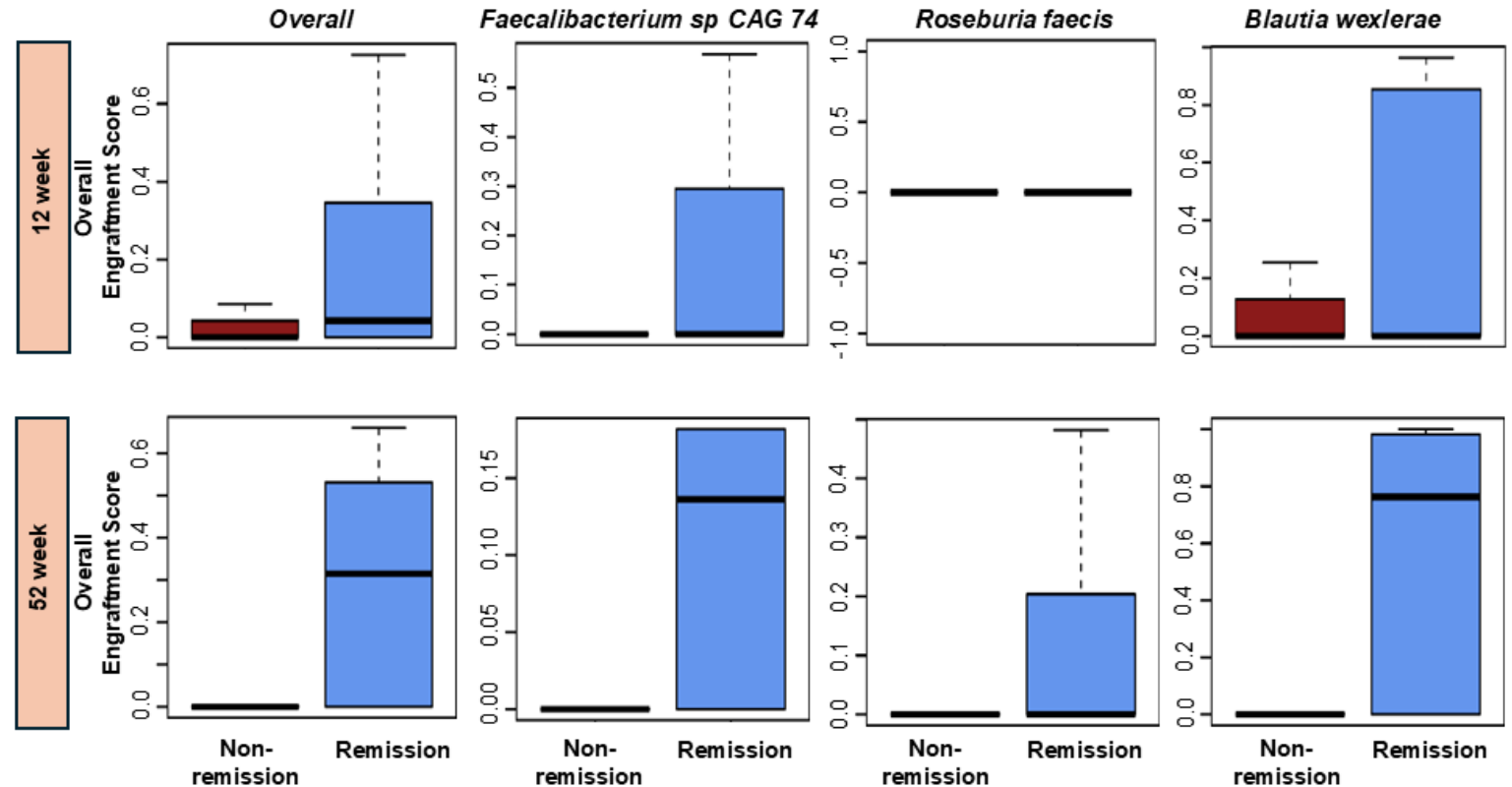


DIET → MICROBIOME → RESPONSE: MEDIATION ANALYSIS



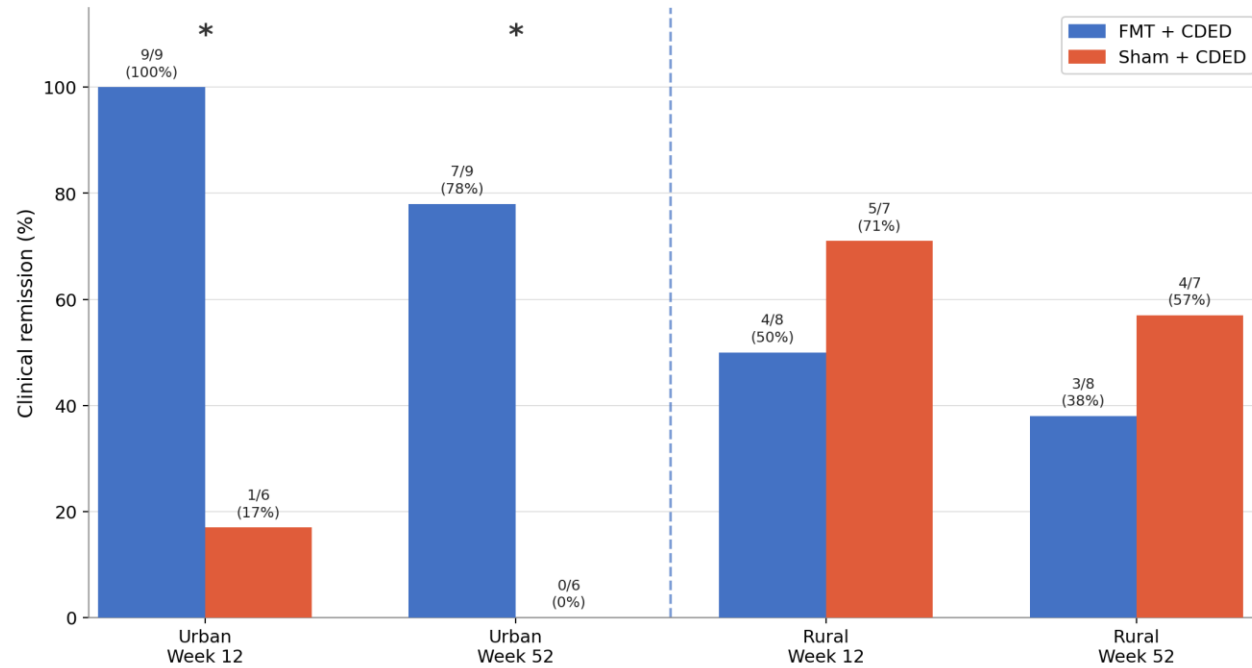
STRAIN-LEVEL TRANSFER

- 16/22 'beneficial' taxa (including 7/8 response-associated) higher prevalence in donors
- Robust strain-level inference - 15 taxa (3 response associated: *Faecalibacterium*, *Roseburia*, *Blautia*)
- Remission - higher donor engraftment scores for all 3 taxa across all post-treatment timepoints

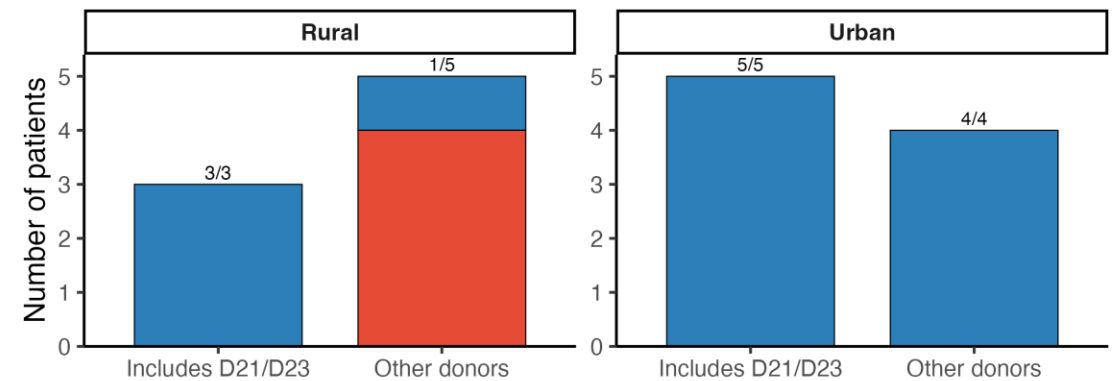


EXPLORATORY SUBGROUP ANALYSES

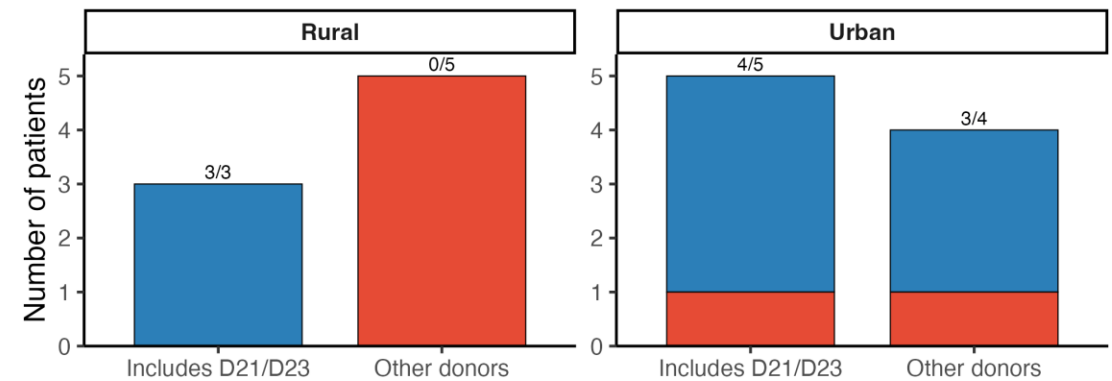
Proportion of patients achieving clinical remission at week 12 and 52, stratified by residence



Clinical remission at Week 12



Clinical remission at Week 52



Clinical remission No remission

DISCUSSION

- First randomized clinical trial to evaluate the combined strategy of microbiome transfer and exclusion diet; Long term follow-up
- Short-term (week 12): Primary endpoints not met
- Long-term (week 52): Superior endoscopic response and maintenance of remission
- FMT + CDED induced health-associated restructuring via convergence of diverse communities and donor-derived strain engraftment of therapeutic anaerobe consortium
- Signal for benefit among:
 - Urban population
 - Select donors (21 and 23)

LIMITATIONS

Early
recruitment
termination

Single-center

Low biologic
exposure

Possible
dietary
confounding

CONCLUSION

- FMT + CDED did not improve short-term remission at 12 weeks
- Superior clinical remission and endoscopic response at one year
- Sustained donor-derived microbiome restructuring toward a health-associated state, not seen with CDED alone
- Multi-modal microbiome manipulation therapies need for larger and more sustained microbiome changes in the resistant IBD microbiomes

GREETINGS

IBD team, AIIMS, Delhi



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