Supplementary Online Content

Costello SP, Hughes PA, Waters O, et al. Effect of fecal microbiota transplantation on 8-week remission in patients with ulcerative colitis: a randomized clinical trial. *JAMA*. doi:10.1001/jama.2018.20046

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Donor Screening Criteria

Medical interview (exclusions)
Age: <18 or >65
Antimicrobial therapy or probiotics in the past 6 months
Active medical illness or symptoms
Any medications (other than oral contraceptive pill)
International travel in last 1 months to areas at high risk of travelers' diarrhea
High risk sexual activity (unprotected sex in last 1 month outside of a monogamous relationship)
Illicit drug use
Known HIV or viral hepatitis exposure in the last 12 months
Incarceration or a history of incarceration.
Medical history and Examination (exclusions)
Any gastrointestinal disorder
Obesity (BMI>30), hypertension, type 2 diabetes and dyslipidaemia
Malnutrition (BMI <18)
Autoimmune disease
Atopic disease
Depression
Infection with HIV, Syphilis, Hepatitis B or C
Malignancy
Chronic pain syndromes, neurologic or neurodevelopmental disorders

eTable 1. Donor Screening Criteria (Continued)

Blood screening
Full blood count
Electrolytes, Urea and Creatinine
Liver function tests
Human T-cell lymphotropic virus 1 and 2 serology
Epstein Barr Virus IgM and IgG
Cytomegalovirus IgM and IgG
Syphilis (Rapid plasma reagin)
Strongyloides stercoralis, *Entamoeba histolytica*, *Helicobacter pylori* serology
Hepatitis A virus IgM
Hepatitis B surface antigen and core antibody, Hepatitis C virus antibody
HIV PCR
Fasting lipids and Blood sugar level
C-Reactive Protein and Erythrocyte Sedimentation Rate
Stool screening Microscopy
and Culture *Clostridium*
difficle toxin PCR
Egg, cysts and parasites (including Cryptosporidium spp., Giardia spp., *Dientamoeba*
fragilis and *Entamoeba histolytica* PCR)

eTable 2. 12-Month Clinical Follow-up of Ulcerative Colitis Patients

		Number(%)	
Remission definition	Randomized Group	Remission 12-month assessment	Remission and no UC symptoms since donor FMT
Clinical and endoscopic remission[a]	dFMT	11/26 (42)	4/26 (7)
	aFMT[b]	10/17 (58)	5/17 (29)
	Combined	21/43 (49)	9/43 (21)
Clinical remission[c]	dFMT	18/29 (62)	5/29 (17)
	aFMT[b]	9/20 (45)	4/20 (20)
	Combined	27/49 (55)	9/49 (18)
Endoscopic remission[d]	dFMT	4/26 (15)	1/26 (4)
	aFMT[b]	4/17 (23)	3/17 (18)
	Combined	8/43 (19)	4/43 (9)
Clinical and endoscopic remission at week 8 in donor FMT group (n=12)[a]		5/12 (42)	3/12 (25)

Abbreviations: UC, ulcerative colitis; FMT, fecal microbiota transplantation; dFMT, donor fecal microbiota transplantation; aFMT, autologous fecal microbiota transplantation

[a] Clinical and endoscopic remission was defined as a Total Mayo score ≤ 2 and endoscopic Mayo score ≤ 1)

[b] Due to aFMT patients crossing over at 8 weeks, 72 of 73 study patients had received donor FMT after 8-week time point.

[c] Clinical remission, was defined as a Simple Clinical Colitis Activity Index score ≤ 2

[d] Endoscopic remission was defined as an Endoscopic Mayo score equal to 0.

eTable 3. Patient Survey of Perception and Acceptability of FMT Prior to Undergoing FMT

Question	Number (% of responders)					No response
	Impossible	Not likely	Unsure	Quite likely	Very likely	
Do you believe that FMT is likely to help with your symptoms? (n=69)	0 (0)	0(0)	25 (36)	36 (52)	8 (12)	4
Do you consider that FMT is likely to be safe? (n=69)	0(0)	0(0)	10 (14)	45 (65)	14 (20)	4
Do you consider that5-ASA medication (e.g. sulfasalazine, mesalazine) is likelyto be safe? (n=69)	6 (9)	7 (10)	18 (26)	26 (38)	12 (17)	4
Do you consider that steroid medication(e.g. prednisolone) is likely to be safe? (n=69)	9 (13)	33 (48)	13 (19)	12 (17)	2 (3)	4
Do you consider that thiopurine medication (e.g. azathioprine/ 6-Mercaptopurine) is likely to be safe?	3 (4)	31 (46)	22 (32)	10 (15)	2 (3)	5
Do you consider that methotrexate medication is likely to be safe? (n=67)	3 (4)	20 (30)	41 (61)	3 (4)	0(0)	6
Do you consider that anti-TNF medication (e.g. infliximab/adalimumab) is likely to be safe? (n=68)	6 (9)	12 (18)	45 (66)	5 (7)	0(0)	5
Do you consider that surgical removal of the colon is likely to be safe? (n=69)	3 (4)	32 (46)	24 (35)	10 (14)	0(0)	4

Abbreviations: FMT, fecal microbiota transplantation; 5-ASA, 5-aminosalicylate; TNF, tumor necrosis factor alpha

eTable 3. Patient Survey of Perception and Acceptability of FMT Prior to Undergoing FMT (Continued)

Question	Number (% of responders)			No Response
	Yes	No	Unsure	
Do you believe FMT as carried out in this study would be seen as acceptable by the general Australian population? (n=66)	29 (44)	9 (14)	28 (42)	7
Do you believe FMT as carried out in this study would be seen as acceptable by patients with ulcerative colitis (n=68)	65 (96)	0(0)	3 (4)	5
Do you have any cultural or religious concerns about receiving fecal material from another person? (n=69)	0(0)	65 (94)	3 (4)	5
Do you have any concerns about discussion FMT with friends or family? (n=63)	19 (30)	44 (70)	0(0)	10

Abbreviations: FMT, fecal microbiota transplantation

eTable 4. Patient Perception and Acceptability of FMT 12 Months Following Donor FMT

Question	Number (% of responders)					No response
	Not at all	Yes (at all)	Yes a little	Yes a lot	Unsure	
Do you believe that FMT helped with your symptoms at least temporarily? (n=61)	17 (28)	38 (62)	17 (28)	21 (34)	6 (10)	12
	Increased	Decreased	The same	Unsure	Not applicable	No response
Has your medication requirement decreased or increased in the 12 months since FMT? (n=60)	10 (17)	18 (30)	30 (50)	2 (3)	0(0)	13
Has the amount of steroid medication changed in the 12 months post FMT compared to the 12 months prior? (n=60)	7 (12)	25 (42)	12 (20)	2 (3)	14 (23)	13
	Impossible	Not likely	Unsure	Quite Likely	Very likely	No response
Do you consider that FMT is likely to be safe? (n=60)	0	0	12 (20)	19 (32)	29 (48)	13

Abbreviations: FMT, fecal microbiota transplantation

eTable 4. Patient Survey of Perception and Acceptability of FMT 12 Months Following FMT (Continued)

Question	Number (% of responders)			No response
	Yes	No	Unsure	
Do you believe FMT as carried out in this study would be seen as acceptable by the general Australian population? (n=59)	30 (52)	8 (14)	21 (36)	14
Do you believe FMT as carried out in this study would be acceptable to patients with ulcerative colitis? (n=60)	57 (95)	0	3 (5)	13
Do you have any cultural or religious concerns about receiving fecal material from another person? If yes, what are your concerns? (n=57)	1 (2)	56 (98)		16
Do you have any concerns about discussing FNT with friends or family? (n=60)	5 (8)	55 (92)		13
Have you required hospitalization in the 12 months after FMT? (n=61)	18 (30)	43 (70)		12
Did you require surgery (colectomy) for your Ulcerative colitis since your FMT (n=69)	9 (13)	60 (87)		4

Abbreviations: FMT, fecal microbiota transplantation

eTable 5. Correlation of Immune Cell Populations With Baseline Total Mayo Score, Change in Total Mayo Score, and Donor Fecal Microbiota Transplantation Treatment Effect

Immune cell population	Flow cytometry marker	Baseline Total Mayo Score		Mayo Change from Baseline to week8		Donor FMT treatment		Donor FMT adjusted for total Mayo score	
		Est [95% CI]	***P* Value**	**Est [95% CI]**	***P* Value**	**Est [95% CI]**	**P Value**	**Est [95% CI]**	***P* Value**
Lamina Propria Mononuclear Cells									
γδ T cell	CD3+ gamma delta T +	-0.17 [-0.65 to 0.31]	.48	-0.3 [-1 to 0.41]	.42	-0.51 [-1.2 to 0.19]	.16	-0.49 [-1.2 to 0.27]	.21
Natural killer cell	CD19/CD20-CD16/CD56+	-0.5 [-0.91 to -0.099]	.02	-0.39 [-0.84 to 0.05]	.11	0.022 [-0.74 to 0.78]	.95	-0.25 [-1.1 to 0.57]	.55
Natural Killer T cell	CD3+ NKT +	-0.21 [-0.66 to 0.25]	.36	-0.43 [-1 to 0.15]	.18	-0.43 [-1.1 to 0.23]	.2	-0.47 [-1.2 to 0.26]	.21
Memory T cell	CD3+ve CD45RO+ve	0.34 [-0.16 to 0.83]	.18	0.18 [-0.61 to 0.97]	.66	-0.21 [-0.65 to 0.23]	.35	0.05 [-0.4 to 0.5]	.83
B cells	CD19+/CD20+ CD45RO-	0.46 [0.057 to 0.87]	.03	0.67 [0.13 to 1.2]	.03	-0.053 [-0.82 to 0.71]	.89	0.37 [-0.35 to 1.1]	.31

Abbreviations: FMT, fecal microbiota transplantation

eTable 5. Correlation of Immune Cell Populations With Baseline Total Mayo Score, Change in Total Mayo Score, and Donor Fecal Microbiota Transplantation Treatment Effect (Continued)

Immune cell population	Flow cytometry marker	Baseline Total Mayo Score		Mayo Change from Baseline to week8		Donor FMT treatment		Donor FMT adjusted for total Mayo score	
		Est [95% CI]	***P* Value**	**Est [95% CI]**	***P* Value**	**Est [95% CI]**	***P* Value**	**Est [95% CI]**	***P* Value**
Lamina Propria Mononuclear Cells									
Macrophage	Lineage- HLA-DR+ CD33+ SSC+	0.26 [-0.26 to 0.77]	.33	-0.00032 [-0.61 to 0.61]	1	-0.36 [-0.9 to 0.19]	.20	-0.22 [-0.84 to 0.41]	.49
Dendritic	Lineage- HLA-DR+ CD11c+ CD33+ve	0.43 [0.042 to 0.82]	.03	0.36 [-0.08 to 0.81]	.13	-0.14 [-0.76 to 0.47]	.64	0.24 [-0.41 to 0.9]	.46
Helper T cell	cd4 scc+	0.11 [-0.34 to 0.57]	.62	-0.8 [-1.4 to -0.19]	.03	-0.17 [-0.63 to 0.29]	.47	-0.31 [-0.8 to 0.18]	.22
Cytotoxic T cell	cd8 scc+	-0.28 [-0.75 to 0.19]	.24	-0.62 [-1.2 to -0.026]	.08	-0.32 [-1.2 to 0.54]	.46	-0.37 [-1.3 to 0.53]	.42
$T_{REGULATORY}$ cell	cd4 scc+ CD25+FOXP3+	0.45 [-0.13 to1]	.13	1.1 [0.27 to2]	.03	-0.21 [-0.73 to 0.3]	.41	-0.056 [-0.59 to 0.48]	.84

Abbreviations: FMT, fecal microbiota transplantation

eTable 5. Correlation of Immune Cell Populations With Baseline Total Mayo Score, Change in Total Mayo Score, and Donor Fecal Microbiota Transplantation Treatment Effect (Continued)

Immune cell population	Flow cytometry marker	Baseline Total Mayo Score		Mayo Change from Baseline to week 8		Donor FMT treatment		Donor FMT adjusted for total Mayo score	
		Est [95% CI]	***P* Value**	**Est [95% CI]**	***P* Value**	**Est [95% CI]**	**P Value**	**Est [95% CI]**	***P* Value**
Peripheral Blood Mononuclear cells									
Gut homing T_{HELPER} cell (blood)	CD4+ CD8- CD45RO+ β_7+	-0.057 [-0.45 to 0.34]	.78	0.01 [-0.57 to 0.59]	.97	0.47 [0.053 to 0.88]	.03	0.45 [0.0088 to 0.89]	.05
Gut homing $T_{REGULATORY}$ cell (blood)	CD4+ CD8- CD45RO β_7+ CD25+ FOXP3+	0.029 [-0.7 to 0.76]	.94	0.41 [-0.58 to 1.4]	.44	-0.12 [-0.6 to 0.36]	.61	-0.056 [-0.56 to 0.45]	.83

Abbreviations: FMT, fecal microbiota transplantation

eTable 6. Microbial Diversity Comparisons

Comparison of Diversity (number of operational taxonomic units)	**Odds ratio (95%CI)**	***P* value**
Baseline UC patients vs individual stool donors	0.65 (0.53 to0.80)	<.001
Pooled donor stool vs individual donor stool	1.89 (1.44 to 2.48)	<.001
UC patients week 4 dFMT vs aFMT	1.35 (1.11 to 1.64)	.002
UC patients week 8 dFMT vs aFMT	1.31 (1.08 to 1.60)	.006
UC Patients at 12-months following open label donor FMT vs baseline	1.17 (1.10 to 1.24)	<.001
UC Patients at 4 weeks following aFMT vs baseline	0.92 (0.89 to 0.96)	<.001
UC Patients at 8 weeks following aFMT vs baseline	0.94 (0.90 to0.98)	.001
UC patients 12-months aFMT vs dFMT [a]	0.98 (0.80 to 1.20)	.82

Abbreviations: UC, ulcerative colitis; dFMT, donor fecal microbiota transplantation; aFMT, autologous fecal microbiota transplantation

a. 34 of 35 participants randomized to the autologous FMT group subsequently received donor FMT at week8

eTable 7. Organisms Associated With a Change in Abundance Following Donor Fecal Microbiota Transplantation (FMT) as Compared to Autologous FMT at Weeks 4 and 8 (cut off $p \leq .01$ at weeks 4 and 8)

Species	Family	Phylum	Week 4 Log change abundance β [95%CI]	Week 4 *P* Value	Week 8 log change abundance β [95%CI]	Week 8 *P* Value
Association with increased abundance following donor FMT						
Peptococcus niger	Peptococcaceae 1	Firmicutes	4.95 [3.18 to 6.73]	<.001	4.6 [2.86 to 6.34]	<.001
Faecalicoccus pleomorphus	Erysipelotrichaceae	Firmicutes	3.77 [2.17 to 5.37]	<.001	3.07 [1.47 to 4.68]	<.001
Olsenella sp.	Coriobacteriaceae	Actinobacteria	3.07 [1.96 to 4.17]	<.001	2.41 [1.33 to 3.49]	<.001
Acidaminococcus intestini	Acidaminococcaceae	Firmicutes	1.76 [0.73 to 2.8]	<.001	2.27 [1.23 to 3.31]	<.001
Senegalimassilia anaerobia	Coriobacteriaceae	Actinobacteria	1.9 [0.88 to 2.92]	<.001	2.03 [1.02 to 3.04]	<.001
Prevotella copri	Prevotellaceae	Bacteroidetes	2.16 [1.01 to 3.32]	<.001	2.03 [0.86 to 3.2]	<.001
Methanobrevibacter smithii	Methanobacteriaceae	Euryarchaeota	1.78 [0.57 to 3]	.004	1.65 [0.44 to 2.86]	.008
Clostridium methylpentosum	Ruminococcaceae	Firmicutes	2.03 [0.95 to 3.11]	<.001	1.57 [0.49 to 2.66]	.004
Alistipes indistinctus	Rikenellaceae	Bacteroidetes	1.58 [0.67 to 2.5]	<.001	1.49 [0.58 to 2.4]	.001
Slackia isoflavoniconvertens	Coriobacteriaceae	Actinobacteria	1.44 [0.55 to 2.32]	.002	1.44 [0.54 to 2.33]	.002
Odoribacter splanchnicus strain	Porphyromonadaceae	Bacteroidetes	1.18 [0.38 to 1.97]	.004	1.07 [0.26 to 1.87]	.009
Association with reduced abundance following donor FMT						
Anaerostipes caccae	Lachnospiraceae	Firmicutes	-2.78 [-4.36 to -1.21]	<.001	-2.53 [-4.23 to -0.84]	.003
Gordonibacter pamelaeae	Coriobacteriaceae	Actinobacteria	-1.46 [-2.37 to -0.54]	.002	-1.7 [-2.65 to -0.76]	<.001
Clostridium aldenense	Lachnospiraceae	Firmicutes	-1.38 [-2.31 to -0.45]	.004	-1.4 [-2.36 to -0.44]	.004

Abbreviation: FMT, Fecal microbiota transplantation

eTable 8. Log Change From Baseline Abundance Following Donor Fecal Microbiota Transplantation at Weeks 4, 8, and 12 Months in the Species Listed in eTable 7

Species	Family	Phylum	Week 4 log change abundance [95%CI]	Week 4 *P* Value	Week 8 log change abundance [95%CI]	Week 8 *P* Value	12-month log change abundance [95%CI]	12-month *P* Value
Positive Associations (increase in species following donor FMT)								
Peptococcusniger	Peptococcaceae	Firmicutes	4.05 [2.76 to 5.34]	<.001	3.79 [2.57 to 5]	<0.001	4.05 [2.49 to 5.6]	<.001
Faecalicoccus pleomorphus	Erysipelotrichaceae	Firmicutes	3.22 [2.07 to 4.38]	<.001	2.37 [1.23 to 3.5]	<0.001	1.93 [0.48 to 3.39]	.009
Olsenella sp.	Coriobacteriaceae	Actinobacteria	2.17 [1.38 to 2.96]	<.001	1.59 [0.81 to 2.36]	<0.001	1.22 [0.24 to 2.19]	.01
Acidaminococcus intestini	Acidaminococcaceae	Firmicutes	1.06 [0.34 to 1.79]	.004	1.1 [0.38 to 1.83]	0.003	1.19 [0.24 to 2.15]	.01
Senegalimassiliaanaerobia	Coriobacteriaceae	Actinobacteria	1.62 [0.9 to 2.34]	<.001	1.69 [0.95 to 2.42]	<0.001	0.71 [-0.21 to 1.64]	.13
Prevotella copri	Prevotellaceae	Bacteroidetes	1.69 [0.88 to 2.51]	<.001	2.08 [1.26 to 2.91]	<0.001	1.99 [0.89 to 3.1]	<.001
Methanobrevibacter smithii	Methanobacteriaceae	Euryarchaeota	1.32 [0.46 to 2.17]	.002	1.03 [0.18 to 1.88]	0.02	0.46 [-0.67 to 1.58]	.43
Clostridium methylpentosum	Ruminococcaceae	Firmicutes	0.87 [0.1 to 1.64]	.03	0.83 [0.05 to 1.61]	0.04	1.14 [0.15 to 2.12]	.02
Alistipesindistinctus	Rikenellaceae	Bacteroidetes	0.93 [0.29 to 1.58]	.004	0.68 [0.04 to 1.31]	0.04	1.29 [0.45 to 2.12]	.002
Slackia isoflavoniconvertens	Coriobacteriaceae	Actinobacteria	0.8 [0.17 to 1.42]	.01	0.79 [0.15 to 1.43]	0.01	0.73 [-0.13 to 1.59]	.10
Odoribacter splanchnicus	Porphyromonadaceae	Bacteroidetes	0.29 [-0.27 to 0.85]	.31	0.52 [-0.04 to 1.08]	0.07	0.91 [0.19 to 1.63]	.01

Abbreviation: FMT, fecal microbiota transplantation

eTable 8. Log Change From Baseline Abundance Following Donor Fecal Microbiota Transplantation at Weeks 4, 8, and 12 Months in the Species Listed in eTable 7 (Continued)

Species	Family	Phylum	Week 4 log change abundance [95%CI]	Week 4 *P* Value	Week 8 log change abundance [95%CI]	Week 8 *P* Value	12-month log change abundance [95%CI]	12-month *P* Value
Negative Associations (decrease in species following donor FMT)								
Anaerostipescaccae	Lachnospiraceae	Firmicutes	-2.24 [-3.47 to -1.01]	<.001	-2.43 [-3.74 to -1.11]	<0.001	1.98 [0.69 to 3.26]	.003
Gordonibacterpamelaeae	Coriobacteriaceae	Actinobacteria	-0.99 [-1.65 to -0.33]	.003	-1.39 [-2.08 to -0.7]	<0.001	-0.28 [-1.18 to 0.62]	.54
Clostridiumaldenense	Lachnospiraceae	Firmicutes	-0.9 [-1.59 to -0.21]	.01	-1.15 [-1.86 to -0.44]	0.002	1.01 [0.21 to 1.82]	.01

Abbreviation: FMT, fecal microbiota transplantation

eTable 9. Organisms Whose Change in Abundance (A) Was Associated With Change in Total Mayo Score and (B) Differed by Treatment

Species	Family	Phylum	Total Mayo score Change[a] [95%CI]	*P* Value	Treatment difference log change[b] [95%CI]	*P* Value
Species associated with Mayo score decrease(diseaseimprovement)						
Anaerofilum pentosovorans	Ruminococcaceae	Firmicutes	-1.08 [-1.51 to-0.64]	<.001	1.41 [0.51 to2.32]	.002
Bacteroides coprophilus	Bacteroidaceae	Bacteroidetes	-0.89 [-1.23 to-0.55]	<.001	2.84 [0.14 to5.53]	.04
Clostridium methylpentosum	Ruminococcaceae	Firmicutes	-0.63 [-1.1 to-0.15]	.01	1.84 [0.97 to2.72]	<.001
Acidaminococcus intestini	Acidaminococcaceae	Firmicutes	-0.55 [-1.01 to-0.08]	.03	1.93 [1.14 to2.73]	<.001
Senegalimassilia anaerobia	Coriobacteriaceae	Actinobacteria	-0.51 [-1.01 to-0.01]	.05	1.84 [0.97 to2.72]	<.001
Species associated with Mayo score increase (disease deterioration)						
Fusicatenibacter saccharivorans[c]	Lachnospiraceae	Firmicutes	0.58 [0.07 to1.09]	.03	-0.67 [-1.11 to-0.23]	.003
Paraprevotellaxylaniphila[d]	Prevotellaceae	Bacteroidetes	0.5 [0.11 to0.89]	.02	0.83 [0.04 to1.63]	.04

[a] Total Mayo change was defined as the change in total Mayo score per standard deviation in log abundance of organism (cut off $p \leq .05$).
[b] Treatment difference log change was defined as organisms associated with a change in abundance following donor fecal microbiota transplantation as compared to autologous fecal microbiota transplantation at weeks 4 and 8 (cut off $p \leq 0.05$).
[c] Treatment caused *Fusicatenibacter saccharivorans* to decrease and thereby it was associated with a higher Mayo score.
[d] Only *Paraprevotella xylaniphila* was associated in the incorrect direction, ie it increased after treatment and was positively associated with Mayo score change.

eTable 10. Change in Short Chain Fatty Acids Levels From Baseline at Weeks 4 and 8 in Donorand Autologous FMTGroups

Short Chain fatty acid	Autologous FMT		Donor FMT		Treatment effect *P* value
	Week 4 vs 0 % baseline [95% CI]	Week 8 vs 0 % baseline [95% CI]	Week 4 vs 0 % baseline [95% CI]	Week 8 vs 0 % baseline [95% CI]	
Acetate	114.0 [89.6 to 145.1]	88.8 [70.0 to 112.5]	98.5 [77.7 to 124.8]	107.4 [85.3 to135.0]	.75
Propionate	126.7 [96.6 to 166.0]	104.2 [79.8 to 136.1]	130.1 [98.4 to 171.9]	147.8 [112.5 to 194.2]	.34
Butyrate	134.1 [99.3 to 181.0]	99.0 [73.7 to 132.9]	86.4 [64.3 to 116.1]	97.8 [73.5 to130.2]	.47
Iso-Butyrate	142.3 [108.2 to 187.1]	107.7 [82.2 to 140.9]	93.7 [70.9 to 123.9]	115.0 [87.6 to150.9]	.11
valerate	90.3 [64.3 to 126.9]	81.6 [58.4 to 114.2]	119.3 [85.5 to 166.6]	142.9 [103.2 to 197.8]	.41
Iso-Valerate	136.8 [102.2 to 182.9]	95.8 [72.0 to 127.6]	93.7 [69.5 to 126.3]	113.1 [84.5 to151.3]	.46
Caproate	108.7 [79.8 to 148.1]	89.3 [65.9 to 121.1]	125.9 [91.8 to 172.7]	111.8 [82.1 to152.3]	.51

Abbreviations: FMT, fecal microbiota transplantation

eTable 11. Associations Between Total Mayo Score at Baseline and Change in Mayo Score With Short Chain Fatty Acid Levels (at Baseline and Change, Respectively)

	Baseline Mayo		**Mayo Change**	
	Est [95% CI]	***P* Value**	**Est [95% CI]**	***P* Value**
Acetate	-0.015 [-0.45 to 0.42]	.95	-0.23 [-1.3 to0.83]	.67
Propionate	-0.0092 [-0.36 to 0.35]	.96	-0.19 [-0.98 to0.6]	.64
Butyrate	-0.036 [-0.38 to 0.3]	.83	-0.14 [-1 to0.75]	.75
Iso-butyrate	0.024 [-0.35 to 0.39]	.90	-0.42 [-1.3 to0.5]	.38
Valerate	-0.078 [-0.42 to 0.26]	.65	-0.39 [-1.3 to0.55]	.42
Iso-valerate	0.027 [-0.34 to 0.4]	.88	-0.48 [-1.3 to0.37]	.27
Caproate	-0.13 [-0.57 to 0.31]	.55	-0.48 [-1.6 to0.65]	.41

eTable 12. Mean Change in Mayo Score for the Two Treatment Groups for Each Baseline Factor, and the Linear Mixed Effects Regression Estimated *P* Value for the Pairwise Interaction[a]

		Mayo scoreChange		Interaction
		Autologous FMT	Donor FMT	LME *P* value
Sex	Male	-1.2 (2.0)	-3.4 (2.6)	.79
	Female	-1.2 (2.4)	-3.7 (2.4)	
Age at diagnosis (years)	Younger	-1.4 (2.1)	-3.6 (2.5)	.77
	Older	-1.1 (2.3)	-3.4 (2.6)	
Age at randomization (years)	Younger	-1.9 (2.0)	-3.8 (2.4)	.12
	Older	-0.5 (2.1)	-3.3 (2.7)	
Duration of disease (years)	Shorter	-1.6 (1.7)	-3.2 (2.9)	.1
	Longer	-0.9 (2.5)	-3.8 (2.1)	
Diseaseextent	Pancolitis	-0.8 (2.0)	-3.7 (2.5)	.34
	Left sided	-1.5 (2.2)	-3.4 (2.6)	
Oralsteroids	No	-1.6 (1.9)	-3.1 (2.3)	.01
	Yes	-0.5 (2.5)	-5.7 (2.5)	
5-ASA oral	No	-1.3 (2.4)	-2.2 (1.7)	.34
	Yes	-1.2 (2.1)	-3.7 (2.6)	
5-ASA topical	No	-1.2 (2.2)	-3.5 (2.5)	.99
	Yes	-1.4 (1.8)	-3.7 (2.7)	
Immunomodulator	No	-1.5 (2.1)	-3.5 (2.9)	.61
	Yes	-0.9 (2.2)	-3.5 (1.9)	
Biologics	No	-1.1 (2.0)	-3.5 (2.6)	.97
	Yes	-2.0 (3.2)	-4.0 (1.0)	

Abbreviations: LME, linear mixed effects model; 5-ASA, 5-aminosalicylate

[a] For presentation of means (SD) continuous predictors are divided by their population median scores.

eTable 12. Mean Change in Mayo Score for the Two Treatment Groups for Each Baseline Factor, and the Linear Mixed Effects Regression Estimated *P* Value for the Pairwise Interaction (Continued)[a]

		Mayo scoreChange	**Interaction**	**Mayo Change**
	Level	**Autologous FMT**	**Donor FMT**	**LME *P*value**
CRP (mg / L)	Low	-1.5 (1.9)	-3.4 (2.1)	.35
	High	-0.9 (2.4)	-3.6 (2.9)	
WBC (x10^9 /L)	Low	-1.7 (2.0)	-3.6 (2.2)	.97
	High	-1.0 (2.2)	-3.3 (3.1)	
Calprotectin (mg/kg)	Low	-1.4 (1.9)	-3.2 (2.4)	.23
	High	-1.1 (2.3)	-3.9 (2.7)	
Protein (g)	Low	-1.0 (1.9)	-3.5 (2.8)	.25
	High	-1.4 (2.4)	-3.6 (2.2)	
Carbohydrate(g)	Low	-1.2 (2.3)	-3.4 (3.0)	.49
	High	-1.3 (1.9)	-3.6 (2.0)	
Total fat (g)	Low	-1.1 (2.4)	-3.5 (2.8)	.43
	High	-1.3 (1.9)	-3.6 (2.2)	
Saturated fat(g)	Low	-1.4 (2.6)	-3.6 (2.8)	.26
	High	-1.1 (1.7)	-3.4 (2.2)	
Sugars (g)	Low	-1.4 (2.4)	-3.8 (3.1)	.91
	High	-1.1 (1.8)	-3.2 (1.9)	
Starch (g)	Low	-0.7 (1.9)	-3.9 (3.0)	.47
	High	-1.9 (2.2)	-3.2 (2.1)	
Fiber (g)	Low	-1.1 (1.8)	-3.5 (2.8)	.63
	High	-1.3 (2.4)	-3.6 (2.2)	

Abbreviations: LME, linear mixed effects model; CRP, C-reactive protein; WBC, white blood cell; g, grams; mg, milligrams; kg, kilogram; L, litre

[a] For presentation of means (SD) continuous predictors are divided by their population median scores.

eTable 12. Mean Change in Mayo Score for the Two Treatment Groups for Each Baseline Factor, and the Linear Mixed Effects Regression Estimated *P* Value for the Pairwise Interaction (Continued)[a]

		Mayo Change	**Interaction**	**Mayo Change**
	Level	**Autologous FMT**	**Donor FMT**	**LME *P* value**
Calcium (mg)	Low	-1.1 (1.7)	-3.3 (2.7)	.16
	High	-1.4 (2.6)	-3.7 (2.4)	
Iron (g)	Low	-0.9 (1.4)	-3.3 (2.8)	.87
	High	-1.5 (2.7)	-3.7 (2.2)	
Energy (kj)	Low	-1.4 (2.2)	-3.2 (3.1)	.25
	High	-1.1 (2.1)	-3.8 (1.9)	
Emulsifier	Low	-0.8 (1.9)	-3.7 (3.0)	.45
	High	-1.9 (2.3)	-3.3 (1.9)	
Sulphate	Low	-1.4 (2.2)	-4.1 (3.0)	.38
	High	-1.0 (2.1)	-2.9 (1.8)	

Abbreviations: LME, linear mixed effects model; g, grams; kj, kilojoules

[a] For presentation of means (SD) continuous predictors are divided by their population median scores.

eTable 13. Mean Blood Measures at Baseline and Week 8 and the Comparison in the Change Over Time Between Treatment Groups

	Mean (%)				
	Autologous FMT		**Donor FMT**		
	Week 0	**Week 8**	**Week 0**	**Week 8**	***P* Value**
Haemoglobin(g/L)	142.1 (17.6)	141 (21.6)	137.2 (16.9)	138.1 (15.7)	.55
Creatinine (umol/L)	74.9 (18.1)	75.9 (18.2)	74.2 (14.5)	75.3 (14.9)	.52
Bilirubin (umol/L)	14.7 (9.3)	13.4 (8)	13.9 (7.2)	13.9 (6)	.43
Alkaline Phosphatase (U/L)	76.8 (29.2)	80.7 (59.3)	80.8 (26.3)	84.8 (35.7)	.72
Alanine Aminotransferase (U/L)	23.7 (9)	30 (19.7)	25.1 (13.3)	32.6 (43.5)	.73
White Blood Cells (x10*9/L)	7.7 (2.4)	7.2 (2.6)	6.6 (2.3)	6.2 (1.9)	.42
Neutrophils (x10*9/L)	6.5 (8.7)	6.5 (10.9)	4.2 (1.8)	3.9 (1.7)	.54
C-Reactive Protein (mg/L)	6.8 (8.5)	7.4 (10.4)	6.5 (8.3)	5 (8.3)	.38

Abbreviations: FMT, fecal microbiota transplantation; g, grams; L, liter

eTable 14. 12-Month Adverse Events

	Number(%)
Adverse effects	(n = 61)
Worsening colitis	13 (21)
- Colectomy	9 (15)
- No Colectomy	4 (7)
Weightgain	13 (21)
Weight loss	8 (13)
Fecal incontinence	2 (3)
Infections	
- Influenza	2 (3)
- *Clostridium difficile* infection	2(3)
- Sinusitis	1 (2)
- Pneumonia	1 (2)
- Wisdom tooth infection	1 (2)
- Respiratory virus	1 (2)
Immune related	
- Psoriatic arthritis	2 (3)
- Crohn's disease	1 (2)
- Enteropathic arthritis	1 (2)
- Allergic reaction toinfliximab	1 (2)
Dermatitis	1 (2)
Backpain	1 (2)
Skin petichiae	1 (2)
Urinary hesitancy	1 (2)
Asthma	1 (2)
Diverticulitis	1 (2)
Oesophageal dysmotility	1 (2)

eTable 15. Fecal Calprotectin Level Relative to Baseline at Week 4 and Week 8 (Log Transformed)

		% of baseline fecal calprotectin [95%CI]	***P* Value**
Donor FMT	Week 4	47.0 [23.3,94.6]	.03
	Week 8	44.1 [22.4,87.2]	.02
Placebo FMT	Week 4	81.8 [41.2,162.2]	.56
	Week 8	35.5 [18.3,69.1]	.002

Abbreviations: FMT, fecal microbiota transplantation

eTable 16. Baseline and Week 8 Data for Patients Randomized to Autologous Fecal Microbiota Transplantation

			Visit 1 (week0)		Visit 2 (week8)		Week 8					
Study Participant	Sex	Disease extent	Left endoscopic Mayo score	Total Mayo score	Left endoscopic Mayo score	Total Mayo score	Primary end point	Clinical remission	Clinical response	Endoscopic remission	Medications (Studyentry)	Colecomy by week 8
1	Male	Pancolitis	2	6	2	7	No	No	No	No	Prednisolone, Mesalazine	No
4	Female	Pancolitis	2	9	2	9	No	No	No	No	Prednisolone, 6-mercaptopurine	No
6	Female	Pancolitis	3	8	3	8	No	No	No	No	Mesalazine, Azathioprine	No
7	Male	Left sided	2	7	2	7	No	No	No	No	Prednisolone, Mesalazine	No
9	Female	Pancolitis	2	9	2	9	No	No	No	No	Prednisolone, Mesalazine, methotrexate	No
10	Female	Left sided	2	5	2	5	No	No	No	No	Budesonide	No
11	Male	Pancolitis	2	7	2	7	No	No	No	No	Sulfasalazine	No
14	Female	Left sided	2	7	1	4	No	No	Yes	No	Sulfasalazine, Mesalazine (topical), Azathioprine	No
19	Male	Left sided	2	4	1	3	No	No	No	No	Azathioprine	No
21	Female	Left sided	2	6	2	9	No	No	No	No	Prednisolone, Mesalazine, Azathioprine	No

eTable 16. Baseline and Week 8 Data for Patients Randomized to Autologous Fecal Microbiota Transplantation (Continued)

			Visit 1 (week0)		Visit 2 (week8)		Week 8					
Study Participant	Sex	Disease extent	Left endoscopic Mayo score	Total Mayo score	Left endoscopic Mayo score	Total Mayo score	Primary end point	Clinical remission	Clinical response	Endoscopic remission	Medications (Studyentry)	Colecomy by week 8
22	Male	Left sided	2	7	2	7	No	No	No	No	Mesalazine, Mesalazine (topical)	No
23	Male	Pancolitis	2	8	2	7	No	No	No	No	Mesalazine	No
25	Female	Left sided	2	9	2	7	No	No	No	No	Mesalazine, Mesalazine (topical)	No
27	Male	Pancolitis	2	6	1	7	No	No	No	No	Mesalazine, Mesalazine (topical), 6-mercapropurine	No
28	Male	Left sided	3	10	2	9	No	No	No	No	Azathioprine	No
30	Male	Left sided	2	6	1	2	Yes	Yes	Yes	No	Mesalazine, Mesalazine (topical)	No
35	Male	Left sided	2	6	2	7	No	No	No	No	Budesonide, Topicalsteroid	No
37	Male	Pancolitis	2	7	2	4	No	Yes	Yes	No	Mesalazine	No
38	Female	Pancolitis	2	9	n/a	n/a	No	No	No	No	Azathioprine	No
39	Female	Left sided	2	8	1	3	No	No	No	No	Prednisolone, Mesalazine	No
43	Female	Pancolitis	3	10	2	4	No	Yes	Yes	No	Azathioprine, Infliximab	No

eTable 16. Baseline and Week 8 Data for Patients Randomized to Autologous Fecal Microbiota Transplantation (Continued)

			Visit 1 (week0)		Visit 2 (week8)		Week 8					
Study Participant	Sex	Disease extent	Left endoscopic Mayo score	Total Mayo score	Left endoscopic Mayo score	Total Mayo score	Primary end point	Clinical remission	Clinical response	Endoscopic remission	Medications (Study entry)	Colecomy by week 8
44	Male	Left side	3	10	3	9	No	No	No	No	Prednisolone, 6-mercaptopurine	No
45	Male	Left side	3	8	2	4	No	No	Yes	No	Mesalazine	No
46	Male	Pancolitis	2	5	2	3	No	Yes	No	No	Mesalazine	No
49	Female	Left side	2	5	0	2	Yes	No	Yes	No	Mesalazine, Azathioprine, Infliximab	No
51	Male	Pancolitis	2	5	2	4	No	Yes	No	No	Prednisolone	No
52	Male	Left side	3	10	3	10	No	No	No	No	Mesalazine, Mesalazine (topical)	No
55	Female	Left side	3	10	3	8	No	No	No	No	Mesalazine, Mesalazine (topical), Azathioprine	No
57	Female	Left side	3	10	3	10	No	No	No	No	Mesalazine	No
59	Female	Pancolitis	2	6	3	7	No	No	No	No	Prednisolone	No
61	Male	Left side	2	7	1	2	Yes	Yes	Yes	No	Nil	No
62	Male	Left side	2	4	1	3	No	No	No	No	Mesalazine	No

eTable 16. Baseline and Week 8 Data for Patients Randomized to Autologous Fecal Microbiota Transplantation (Continued)

			Visit 1 (week0)		Visit 2 (week8)		Week 8					
Study Participant	Sex	Disease extent	Left endoscopic Mayo score	Total Mayo score	Left endoscopic Mayo score	Total Mayo score	Primary end point	Clinical remission	Clinical response	Endoscopic remission	Medications (Study entry)	Colecomy by week 8
64	Male	Left sided	2	7	2	8	No	No	No	No	Mesalazine, Budesonide, Azathioprine, Vedolizumab	No
70	Male	Left sided	2	8	1	3	No	No	Yes	No	Prednisolone Mesalazine	No
72	Female	Left sided	3	10	3	10	No	No	No	No	Mesalazine, Azathioprine, Infliximab	No

eTable 17. Baseline and Week 8 Data for Patients Randomized to Donor Fecal Microbiota Transplantation

			Visit 1 (week0)		Visit 2 (week8)		Week 8					
Study Participant	Sex	Disease extent	Left endoscopic Mayo score	Total Mayo score	Left endoscopic Mayo score	Total Mayo score	Primary end point	Clinical remission	Clinical response	Endoscopic remission	Medications (Studyentry)	Colecomy by week 8
2	Male	Left sided	2	7	1	4	No	Yes	Yes	No	Sulfasalzine, Azathioprine	No
3	Male	Pancolitis	2	7	1	5	No	No	No	No	Mesalazine, Mesalazine (topical), Methotrexate	No
5	Female	Left sided	3	8	1	4	No	Yes	Yes	No	Mesalazine, Azathioprine	No
8	Male	Left sided	2	7	1	3	No	Yes	Yes	No	Sulfasalazine	No
12	Female	Pancolitis	3	10	n/a	n/a	No	No	No	No	Prednisolone, Sulfasalazine, Mesalazine (topical), Azathioprine	Yes
13	Male	Pancolitis	2	8	1	3	No	Yes	Yes	No	Mesalazine, Azathioprine	No
15	Female	Left sided	2	7	1	2	Yes	No	Yes	No	Mesalazine, Mesalazine (topical)	No
16	Male	Left sided	2	7	2	5	No	Yes	No	No	Mesalazine, Mesalazine (topical)	No

eTable 17. Baseline and Week 8 Data for Patients Randomized to Donor Fecal Microbiota Transplantation (Continued)

			Visit 1 (week0)		Visit 2 (week8)		Week 8					
Study Participant	Sex	Disease extent	Left endoscopic Mayo score	Total Mayo score	Left endoscopic Mayo score	Total Mayo score	Primary end point	Clinical remission	Clinical response	Endoscopic remission	Medications (Study entry)	Colecomy by week 8
17	Female	Left sided	2	8	n/a	n/a	No	No	No	No	Mesalazine, Mesalazine (topical)	No
18	Male	Pancolitis	2	7	0	0	Yes	Yes	Yes	Yes	Mesalazine	No
20	Female	Left sided	2	5	1	4	No	No	No	No	Mesalazine	No
24	Male	Pancolitis	2	8	0	0	Yes	Yes	Yes	Yes	Mesalazine	No
26	Female	Left sided	3	9	1	2	Yes	Yes	Yes	No	Prednisolone, Sulfasalazine	No
29	Male	Pancolitis	2	6	2	6	No	No	No	No	Nil	No
31	Female	Left sided	3	7	2	5	No	Yes	No	No	Mesalazine (topical), Methotrexate	No
32	Male	Left sided	2	6	2	9	No	No	No	No	Sulfasalazine	No
33	Male	Left sided	2	7	1	3	No	No	Yes	No	Mesalazine, Mesalazine (topical)	No
34	Female	Pancolitis	2	7	2	6	No	No	No	No	Mesalazine	No
36	Male	Left sided	2	8	2	7	No	No	No	No	Mesalazine. 6-mercaptopurine	No

eTable 17. Baseline and Week 8 Data for Patients Randomized to Donor Fecal Microbiota Transplantation (Continued)

			Visit 1 (week0)		Visit 2 (week8)		Week 8					
Study Participant	Sex	Disease extent	Left endoscopic Mayo score	Total Mayo score	Left endoscopic Mayo score	Total Mayo score	Primary end point	Clinical remission	Clinical response	Endoscopic remission	Medications (Study entry)	Colecomy by week 8
40	Female	Left side	2	8	0	0	No	No	No	No	Prednisolone, Sulfasalazine, Mesalazine (topical)	No
41	Male	Pancolitis	2	4	1	2	Yes	No	No	No	Mesalazine	No
42	Female	Left side	3	9	1	3	No	Yes	Yes	No	Sulfasalazine, Mesalazine (topical)	No
47	Male	Left sided	2	4	0	0	Yes	Yes	Yes	Yes	Sulfasalazine	No
48	Male	Pancolitis	3	9	1	2	Yes	No	Yes	No	Prednisolone, Mesalazine, Azathioprine	No
50	Male	Left sided	1	4	0	0	Yes	Yes	Yes	Yes	Mesalazine, Azathioprine	No
53	Female	Left sided	2	7	1	2	Yes	Yes	Yes	No	Mesalazine, Mesalazine (topical), Vedolizumab	No
54	Female	Left sided	2	6	1	4	No	No	No	No	Mesalazine, Azathioprine	No
56	Male	Pancolitis	2	7	2	6	No	No	No	No	Mesalazine, Azathioprine	No
58	Female	Left sided	3	9	2	6	No	No	Yes	No	Nil	No

eTable 17. Baseline and Week 8 Data for Patients Randomized to Donor Fecal Microbiota Transplantation (Continued)

			Visit 1 (week0)		Visit 2 (week8)		Week 8					
Study Participant	Sex	Disease extent	Left endoscopic Mayo score	Total Mayo score	Left endoscopic Mayo score	Total Mayo score	Primary end point	Clinical remission	Clinical response	Endoscopic remission	Medications (Study entry)	Colecomy by week 8
60	Female	Pancolitis	3	10	2	5	No	No	Yes	No	Prednisolone, Mesalazine, Azathioprine	No
63	Female	Left sided	2	6	2	7	No	No	No	No	Mesalazine, Mesalazine (topical)	No
65	Male	Pancolitis	3	10	2	6	No	Yes	Yes	No	Mesalazine	No
66	Male	Left side	2	7	1	1	Yes	Yes	Yes	No	Prednisolone, Mesalazine, 6-mercaptopurine	No
67	Male	Pancolitis	2	7	1	2	Yes	Yes	Yes	No	Mesalazine, Mesalazine (topical)	No
68	Female	Left side	3	8	2	4	No	Yes	Yes	No	Infliximab	No
69	Female	Left side	3	10	n/a	n/a	No	No	No	No	Prednisolone	No
71	Female	Pancolitis	2	4	1	1	Yes	Yes	Yes	No	Mesalazine, Azathioprine, Infliximab	No
73	Male	Pancolitis	2	7	2	5	No	No	No	No	Mesalazine	No

eTable 18. 12-Month Data for Patients Randomized to Autologous Fecal Microbiota Transplantation

Study Participant	Sex	Left endoscopic Mayo	Total Mayo	Clinical and endoscopic remission	Clinical remission	Endoscopic remission	Medications (12 months)	Months taking corticosteroid	Symptoms free for 12 months	Colectomy by 12 months
1	Male	n/a	n/a	n/a	n/a	n/a	Unknown	Unknown	No	No
4	Female	n/a	n/a	n/a	n/a	n/a	Nil	0	No	Yes
6	Female	0	1	Yes	Yes	Yes	Azathioprine	0	Yes	No
7	Male	2	9	No	No	No	Prednisolone, Mesalazine	11	No	No
9	Female	n/a	n/a	n/a	No	n/a	Prednisolone, Mesalazine	12	No	No
10	Female	1	1	Yes	Yes	No	Mesalazine	0	Yes	No
11	Male	n/a	n/a	n/a	n/a	n/a	Infliximab, Methotrexate	2	No	Yes
14	Female	n/a	n/a	n/a	n/a	n/a	Unknown	Unknown	Yes	No
19	Male	1	2	Yes	Yes	No	Azathioprine	3	No	No
21	Female	3	7	No	No	No	Prednisolone, Mesalazine, Azathioprine	6	No	No
22	Male	n/a	n/a	n/a	No	n/a	Mesalazine, Mesalazine (topical)	0	Yes	No
23	Male	n/a	n/a	n/a	n/a	n/a	Unknown	Unknown	No	Yes
25	Female	1	2	Yes	Yes	No	Mesalazine	0	No	No
27	Male	1	2	Yes	Yes	No	Mesalazine, 6-mercapropurine	3	No	No
28	Male	n/a	n/a	n/a	n/a	n/a	Nil	0	No	No
30	Male	2	5	No	Yes	No	Mesalazine, Mesalazine (topical)	0	No	No
35	Male	1	2	Yes	Yes	No	Budesonide	0	Yes	No

eTable 18. 12-Month Datafor Patients Randomized to Autologous Fecal Microbiota Transplantation(Continued)

Study Participant	Sex	Left endoscopic Mayo	Total Mayo	Clinical and endoscopic remission	Clinical remission	Endoscopic remission	Medications (12 months)	Months taking corticosteroid	Symptoms free for 12 months	Colectomy by 12 months
37	Male	n/a	n/a	n/a	n/a	n/a	Unknown	Unknown	No	No
38	Female	n/a	n/a	n/a	n/a	n/a	Unknown	Unknown	No	No
39	Female	1	2	Yes	Yes	No	Azathioprine	3	No	No
43	Female	2	7	No	No	No	100mg Azathioprine	0	No	No
44	Male	n/a	n/a	n/a	n/a	n/a	Nil	0	No	Yes
45	Male	0	0	Yes	Yes	Yes	Azathioprine	0	Yes	No
46	Male	2	7	No	No	No	Mesalazine, Vedolizumab	3	No	No
49	Female	0	2	Yes	n/a	Yes	Unknown	Unknown	No	No
51	Male	2	7	No	No	No	Infliximab	0	No	No
52	Male	n/a	n/a	n/a	No	n/a	mesalazine (topical)	0	No	No
55	Female	n/a	n/a	n/a	No	n/a	Mesalazine, Infliximab	0	No	No
57	Female	3	9	No	No	No	Mesalazine	2	No	No
59	Female	n/a	n/a	n/a	n/a	n/a	Unknown	Unknown	No	Yes
61	Male	n/a	n/a	n/a	n/a	n/a	Unknown	Unknown	No	No
62	62	n/a	n/a	n/a	No	n/a	Prednisolone, Mesalazine, Azathioprine, Infliximab	3	No	No
64	64	n/a	n/a	n/a	n/a	n/a	Nil	0	No	Yes
70	70	0	0	Yes	n/a	Yes	Nil	0	Yes	No
72	72	n/a	n/a	n/a	n/a	n/a	Mesalazine, Azathioprine, Infliximab	0	Yes	No

eTable 19. 12-Month Data for Patients Randomized to Donor Fecal Microbiota Transplantation

Study Participant	Sex	Left endoscopic Mayo	Total Mayo	Clinical and endoscopic remission	Clinical remission	Endoscopic remission	Medications (12 months)	Months taking corticosteroid	Symptoms free for 12 months	Colectomy by 12 months
2	Male	0	0	Yes	Yes	Yes	Azathioprine	0	Yes	No
3	Male	n/a	n/a	n/a	n/a	n/a	Mesalazine, Infliximab	3	No	No
5	Female	2	7	No	No	No	Mesalazine, Mesalazine (topical), Azathioprine	2	No	No
8	Male	2	4	No	No	No	Sulfasalazine, Infliximab	4	No	No
12	Female	n/a	n/a	n/a	n/a	n/a	Prednisolone, Sulfasalazine, Mesalazine (topical)	10	No	Yes
13	Male	n/a	n/a	n/a	Yes	n/a	Mesalazine, Azathioprine	0	No	No
15	Female	n/a	n/a	n/a	No	n/a	Mesalazine	0	No	No
16	Male	3	10	No	No	No	Unknown	Unknown	No	No
17	Female	n/a	n/a	n/a	n/a	n/a	Mesalazine (topical)	8	No	Yes
18	Male	1	2	Yes	Yes	No	Mesalazine	0	Yes	No
20	Female	0	0	Yes	Yes	Yes	Mesalazine (topical)	0	No	No
24	Male	2	5	No	No	No	Mesalazine	0	Yes	No
26	Female	1	3	No	No	No	Prednisolone, Mesalazine	10	No	No
29	Male	n/a	n/a	n/a	n/a	n/a	Vedolizumab	4	No	No

eTable 19. 12-Month Data for Patients Randomized to Donor Fecal Microbiota Transplantation (Continued)

Study Participant	Sex	Left endoscopic Mayo	Total Mayo	Clinical and endoscopic remission	Clinical remission	Endoscopic remission	Medications (12 months)	Months taking corticosteroid	Symptoms free for 12 months	Colectomy by 12 months
31	Female	2	4	No	Yes	No	Mesalazine (topical), Methotrexate	0	Yes	No
32	Male	1	6	No	No	No	Sulfasalazine, Vedolizumab	Unknown	No	No
33	Male	n/a	n/a	n/a	n/a	n/a	Mesalazine, Mesalazine (topical)	1	No	No
34	Female	2	3	No	Yes	No	Mesalazine	Unknown	No	No
36	Male	n/a	n/a	n/a	No	n/a	Prednisolone, Mesalazine. 6-mercaptopurine, Vedolizumab	12	No	No
40	Female	n/a	n/a	n/a	Yes	n/a	Sulfasalazine	2	No	No
41	Male	1	2	Yes	Yes	No	Mesalazine	0	Yes	No
42	Female	3	7	No	Yes	No	Sulfasalazine	0	No	No
47	Male	1	2	Yes	Yes	No	Sulfasalazine	0	No	No
48	Male	1	1	Yes	Yes	No	Azathioprine	6	No	No
50	Male	n/a	n/a	n/a	Yes	n/a	Unknown	Unknown	No	No
53	Female	n/a	n/a	n/a	n/a	n/a	Nil	0	No	Yes
54	Female	0	0	Yes	Yes	Yes	Mesalazine, Azathioprine	2	No	No
56	Male	1	3	No	No	No	Unknown	Unknown	No	No
58	Female	1	4	No	Yes	No	Unknown	Unknown	No	No
60	Female	0	0	Yes	No	Yes	Mesalazine, Azathioprine	2	No	No

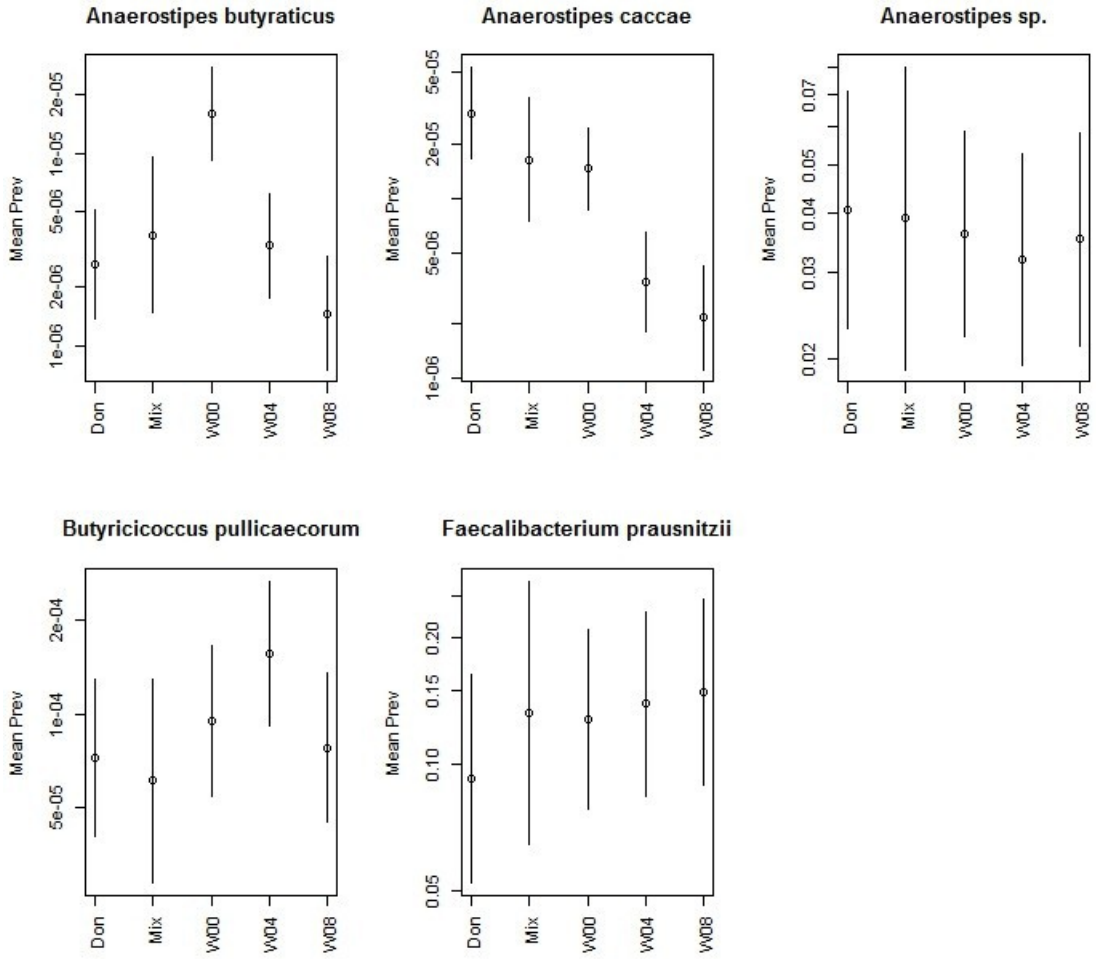
eTable 19. 12-Month Data for Patients Randomized to Donor Fecal Microbiota Transplantation (Continued)

Study Participan	Sex	Left endoscopic Mayo	Total Mayo score	Clinical and endoscopic remission	Clinical remission	Endoscopic remission	Medications (12 months)	Months taking	Symptoms free for 12 months	Colectomy by 12 months
63	Female	1	1	Yes	No	No	Mesalazine, Mesalazine (topical)	Unknown	No	No
65	Male	2	6	No	Yes	No	Mesalazine	0	No	No
66	Male	1	3	No	No	No	Mesalazine, 6-mercaptopurine	0	No	No
67	Male	2	7	No	No	No	Mesalazine, Adalimumab	2	No	No
68	Female	1	2	Yes	Yes	No	Infliximab	0	No	No
69	Female	n/a	n/a	n/a	Yes	n/a	Vedolizumab	4	No	No
71	Female	1	2	Yes	Yes	No	Infliximab	0	Yes	No
73	Male	2	6	No	No	No	Mesalazine	1	Yes	No

eTable 20. Change Due to Treatment in Butyrate Producing Species and Genera

Species	**Family**	**Phylum**	**Treatment difference log change abundance Week 4 [95%CI]**	**Week 4 *P* Value**	**Treatment difference log change abundance Week 8 [95%CI]**	**Week 8 *P* Value**
Anaerostipescaccae	Lachnospiraceae	Firmicutes	-2.78 [-4.36 to -1.21]	.0005	-2.53 [-4.23 to -0.84]	.003
Butyricicoccus pullicaecorum	Ruminococcaceae	Firmicutes	0.95 [-0.13 to 2.03]	.09	-0.45 [-1.55 to0.65]	.42
Roseburiainulinivorans	Lachnospiraceae	Firmicutes	0.54 [-0.41 to1.48]	.27	-0.36 [-1.3 to0.59]	.46
Anaerostipes butyraticus	Lachnospiraceae	Firmicutes	-1.26 [-4 to1.47]	.37	-5.11 [-8.12 to-2.1]	<.001
Roseburia.intestinalis	Lachnospiraceae	Firmicutes	-0.3 [-1.02 to0.41]	.4	-0.27 [-0.98 to0.44]	.46
Faecalibacterium prausnitzii	Ruminococcaceae	Firmicutes	0.16 [-0.22 to 0.54]	.41	-0.06 [-0.45 to0.32]	.74
Anaerostipessp.	Lachnospiraceae	Firmicutes	-0.12 [-0.59 to0.35]	.62	-0.13 [-0.6 to0.35]	.60

eFigure. Butyrate Producing Bacteria Prevalence in Donors (Individual and Pooled) and Patients Prior to, Then 4 and 8 Weeks After Donor Fecal Microbiota Transplantation



eAppendix 1. Bacterial Analysis Methods

There were 228 fecal samples available from 72 patients enrolled in the study and 72 fecal samples available from donors (53 individual donor and 19 pooled batches). Stool from patients and individual donors was frozen without additive at –80°C. Stool swabs were stored for up to 8 weeks at -20°C prior to transfer to –80°C. Stool from the donor batches was frozen at -80°C with 65% saline and 10% glycerol.

We extracted bacterial DNA from the samples using the MoBio PowerMag Microbial DNA Isolation kit (MoBio Laboratories, Carlsbad, CA, USA) following the manufacturer's protocol. All stool samples were extracted and processed in duplicate. Amplicon library preparation was performed using a modified dual-index PCR approach.[1] The first-step primers (515F, 806R), which were modified by the inclusion of a phaser to increase heterogeneity in the sequencing run,[2] amplified the V4-V5 hypervariable region of the 16S rRNA gene and the second set (i5, i7) added the indexed barcodes to enable multiplexing of our large number of samples.[1] The library was pooled at equi-molar concentrations and run on an Illumina HiSeq2500 Rapid instrument using 2 x 250 bp paired end chemistry (Ramaciotti Centre for Genomics, University of New South Wales). The median number of reads per sample was 143k (thousand) (IQR, 111k-196k). Samples with total read count <10k were excluded.

eAppendix 2. Bioinformatics

Raw sequencing data was processed using a combination of both in-house and open source software. The bioinformatic pipeline utilised USEARCH algorithms[3] which included merging, quality-filtering, partitioning/de-replicating and clustering into operational taxonomic units (OTUs) at 97% similarity. Representative sequences from each OTU were classified in two ways: via the RDP Naïve Bayesian Classifier and by finding the closest match in a set of curated reference sequences (RDP 16S Training Set + RefSeq 16S).[4] The use of two independent classification techniques improves confidence in the taxonomic assignments.

eAppendix 3. Flow Cytometry

Lamina Propria Mononuclear Cell isolation: Colonic mucosal biopsies were incubated twice in Hepes buffered HBSS supplemented with 1mM EDTA and 1mM DTT (Sigma) for 10 minutes at 37°C under slow rotation, with the suspension strained (100μM) between incubations. Residual tissue was incubated in Hepes buffered Ca^{2+}/Mg^{2+} free HBSS for 10 minutes at 37°C under slow rotation and strained (100μM). Residual tissue was minced and incubated in complete media (RPMI 1640 [Gibco, Germany] supplemented with fetal calf serum, glutamax and penicillin / streptomycin, Collagenase D [1mg/ml, Roche], DNAse1 [0.5mg/ml, Sigma] and Dispase [3mg/ml, Roche]). Collagenase D (Roche, NSW, Australia), 0.5mg/ml DNAse1 (Sigma) and 3mg/mL Dispase (Roche) for 20 minutes twice with supernatant removal from centrifugation (300*g*, 5minutes) after each incubation. Residual suspensions were sequentially strained (100μM followed by 40μM), with the supernatant centrifuged (300*g*, 5min), resuspended, stained with trypan blue to determine viability and cell number as previously described.[5-7]

Cell staining: 0.5 x 10^6 F_c blocked cells (BD Biosciences, NSW, Australia) were stained for viability (FVD eFlour450, eBioscience) and the following anti-human monoclonal antibody panels (BD Bioscience unless otherwise stated): a) HLADR-APC, CD11C-FITC, Lin (CD3, CD14, CD16, CD19, CD34, CD56 all APC-Cy7, CD33-PerCP Cy5.5), b) CD3-APC, CD45RO-PerCPCy5.5, CD19-APCCy7, CD20-APCCy7, CD16-PE, CD56-PE, Vα24jα-FITC (eBioscience), c) CD3-APC, CD8-FITC, CD45RO-PerCP Cy5.5, γδT-PE (eBioscience). For T_{REG}, cells were stained with CD4-APC Cy7, CD8-PE, CD45RO PerCP Cy5.5, CD25 PE Cy7, β7-FITC, followed by fixation and permeabilization (Transcription buffer staining set, eBioscience) and staining with FOXP3-APC (eBioscience). The following gating strategy wasusedtoidentifycellpopulations: Macrophages(lin-ve/HLADR/CD33+ve), dendritic cells (lin –ve HLADR+/CD33+/CD11c+), T_{HELPER} (CD4+ CD8-), $T_{CYTOTOXIC}$ (CD8+ CD4-), $T_{REGULATORY}$(CD4+/CD8-/CD25+/FOXP3+),B(CD3-,CD19+CD20+),NaturalKiller(CD3-/CD16+/CD56+/CD45RO-), Natural Killer T (CD3+/NKT+), γδ T (CD3+/γδT+) in LPMC, and gut homing T_{HELPER} (CD4+/CD8-/CD45RO+/β_7+) and gut homing $T_{REGULATORY}$ (CD4+/CD8-/CD45RO+/β_7+/CD25+/FOXP3+) were determined in PBMC. 20,000 events / tube were analysed on a FACSCanto II (BD Biosciences) and proportions of live singlets were determined using FlowJo (Tree Star, OR, USA) as previously described.[5-7]

eAppendix 4. Statistical Analysis

Microbiome Diversity

Microbiome diversity was defined as the fraction of unique species present at an assessment out of all species present at any analysis in any sample. Logistic mixed effects regressions were used to compare between treatment groups with donor stool and stool mix samples. Outcome was the presence of a species in a particular sample. Fixed effects included sample origin (donor vs mix vs treated patient vs untreated patient) and total sample count (log-transformed). Three non-nested random effects were included; patient identifier, donor batch, and the microbiome species identifier. To assess the effect of treatment a separate model was contrasted with only post baseline samples included as outcome. This model was identical to the previous except that the fixed effects were baseline prevalence (logit transformed), treatment allocation, assessment time (week 4 vs week 8), the pairwise treatment-assessment time interaction, and total sample count (log-transformed).

Associations between both baseline diversity and change in diversity, and change in Mayo score were assessed as before (re associations with baseline factors). A two-stage approach was taken, first the mean diversity was estimated using the logistic mixed effects models previously described in this section. These diversity estimates were then included in the models of total Mayo score as fixed effects.

Microbiome Abundance

Associations between changes in biome species abundance with total Mayo score were modelled in a similar manner. For each sample the mean proportion of total counts was calculated, and subsequently for individuals with samples at both week 4 and 8 averaged to estimate baseline and post randomization prevalence estimates. The change in prevalence was then included in linear mixed effects models of total Mayo

score. A false discovery rate (FDR) analysis was performed to provide evidence of associations beyond what would be expected due to multiple testing, with the FDR being compared with the same analysis repeated, but with outcome (total Mayo score) permuted between individuals.

The change in abundance by treatment group and assessment time were assessed using a negative binomial mixed effects regression for each microbiome species. Fixed effects included treatment allocation, assessment time (baseline, week 4, week 8, and 12-months) and their pairwise interaction. Nested random intercepts per patient and assessment were included in the model, with total sample count (log transformed) included as an offset. Due to the large variation in abundance across species, from highly abundant to mostly absent, a zero-inflation term was included in the model and Akaike's information criteria was used to determine whether this improved model fit per species.

Fecalshort chain fatty acid & calprotectin

The estimate of treatment effect on calprotectin and short chain fatty acids (SCFAs), which had an extra assessment at week 4, was similarly modelled with however both week 4 and week 8 assessments as outcome. Baseline values, treatment group, assessment time (week 4 v week 8), and the pairwise interaction between time and treatment were included as fixed effects. In addition to the batch and site random intercepts, within-individual randomintercepts were included nestedwithinsite. After inspection of the distribution of the residuals, these analyses were performed on log transformed calprotectin, SFCA measures and immunological markers, with results converted back to the original scale.

Associations between estimated change in SCFA and week 8 Mayo score were assessed by including the estimated change in SCFA as a fixed effect in the mixed effects regression models with week 8 Mayo score as outcome. Individual level SCFA change scores were estimated using linear mixed effects regressions adjusting for baseline levels and treatment, with random intercepts per batch, individual and site, with individual level effects nested within site.

eAppendix 5. Patient Perception of Faecal Transplantation for Ulcerative Colitis Questionnaire

Government of South Australia
SA Health

Name: **DOB:** **Date:**

Patient Perception of Faecal Transplantation for Ulcerative Colitis Questionnaire

Prior to faecal transplantation- Please circle the most appropriate answer

1. Do you believe that faecal transplantation is likely to help with your symptoms?

Impossible Not likely Unsure Quite likely Very likely

2. Have you considered faecal transplantation for ulcerative colitis previously?

Yes I have considered it I have heard of it, but not considered it

I have never heard of it before

3.1 Do you consider that faecal transplantation is likely to be safe?

Impossible Not likely Unsure Quite likely Very likely

Please explain why

3.2 Do you consider that 5-ASA medication (e.g. sulphasalazine, mesalazine) is likely to be safe?

Impossible Not likely Unsure Quite likely Very likely

3.3 Do you consider that steroid medication (e.g. prednisolone) is likely to be safe?

Impossible Not likely Unsure Quite likely Very likely

3.4 Do you consider that thiopurine medication (e.g. azathioprine/ 6-MP) is likely to be safe?

Impossible Not likely Unsure Quite likely Very likely

3.5 Do you consider that methotrexate medication is likely to be safe?

Impossible Not likely Unsure Quite likely Very likely

3.6 Do you consider that anti-TNF medication (e.g. infliximab (Remicade)/ adalimumab (Humira)) is likely to be safe?

Impossible Not likely Unsure Quite likely Very likely

3.7 Do you consider that surgical removal of the colon is likely to be safe?

Impossible Not likely Unsure Quite likely Very likely

4. Do you believe faecal transplantation as carried out in this study would be seen as acceptable by

1) The general Australian population? Yes No Unsure
2) Patients with ulcerative colitis? Yes No Unsure

5. Do you have any cultural or religious concerns about receiving faecal material from another person?

Yes No Unsure

If yes, what are your concerns?

6. How would you compare faecal transplantation to traditional medical treatments of ulcerative colitis?

a) How do you compare the acceptability of these treatments?

7. How would you compare faecal transplantation to other treatments such as probiotics?

a) How do you compare the acceptability of these treatments

8. Do you have any concerns about discussing faecal transplant with friends or family?

If so why?

Government of South Australia
SA Health

Name: DOB: Date:

Patient perception of faecal transplantation for ulcerative colitis questionnaire

12 months post faecal transplantation – Please circle the most appropriate answer

1. Do you believe that faecal transplantation helped with your symptoms at least temporarily?

Not at all, Yes a little, Yes a lot Unsure (Circle)

If you had symptom improvement how long did this last?

2. Has your medication requirement decreased or increased in the 12 months since faecal transplant? (Circle) Decreased Increased The same

What are you now taking?

For how many months were you taking steroid (eg prednisolone) in the 12 months after faecal transplant?

Has the amount of steroid medication changed in the 12 months post faecal transplant compared to the 12 months prior? (circle)

Increased Decreased Stayed the same

3. How many flares of disease did you have in the 12 months after faecal transplant?

If you had flares of disease, for how many months were you symptomatic in the 12 months after faecal transplant?

Have you required hospitalisation in the 12 months after faecal transplant?

Yes (how many times:) No

4. Did you require surgery (colectomy) for your Ulcerative colitis since your faecal transplant

Yes (date:) No

4. Do you consider that faecal transplantation is likely to be safe?

Impossible Not likely Unsure Quite likely Very likely

5. How would you compare faecal transplantation to traditional medical treatments of ulcerative colitis?

a) How do you compare the acceptability of thesetreatments?

b) How do you compare the effectiveness of thesetreatments?

6. How would you compare faecal transplantation to other treatments such as probiotics?

a) How do you compare the acceptability of thesetreatments?

b) How do you compare the effectiveness of thesetreatments?

7. Do you believe faecal transplantation as carried out in this study would be seen as acceptable by

1) The general Australian population? Yes No Unsure
2) Patients with ulcerative colitis? Yes No Unsure

8. Do you have any cultural or religious concerns about receiving faecal material from another person? If yes, what are your concerns?

9 . Do you have any concerns about discussing faecal transplant with friends or family?

If sowhy?

10. If you had your time in the study again would you like any aspects of the faecal transplant process to be done differently?

If yes please elaborate

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