

**Effects of dietary fibers or probiotics on functional constipation symptoms and roles of gut microbiota: a double-blinded randomized placebo trial**

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**Table S1. Changes of Constipation symptoms over the intervention by group <sup>a</sup>.**

Symptom	Placebo	Group A	<i>P</i> <sup>b</sup>	Group B	<i>P</i> <sup>b</sup>	Group C	<i>P</i> <sup>b</sup>	Group D	<i>P</i> <sup>b</sup>
BMF									
Week 1-week 0	1.07 ± 2.85	0.77 ± 2.40	0.672	1.35 ± 1.99	0.220	1.18 ± 2.59	0.210	0.88 ± 1.76	0.805
Week 2-week 0	2.04 ± 3.01	1.95 ± 2.53	0.721	1.89 ± 2.40	0.640	2.01 ± 2.29	0.520	1.68 ± 2.21	0.903
Week 3-week 0	2.29 ± 2.24	2.20 ± 2.28	0.831	2.53 ± 2.40	0.786	2.16 ± 2.18	0.814	1.90 ± 1.79	0.632
Week 4-week 0	2.24 ± 2.78	1.97 ± 2.41	0.925	2.40 ± 2.53	0.408	2.29 ± 2.04	0.395	2.02 ± 2.30	0.853
BSS									
Week 2-week 0	0.51 ± 1.43	0.86 ± 1.23	0.196	0.53 ± 1.37	0.519	0.98 ± 1.07	0.051	0.86 ± 1.59	0.176
Week 4-week 0	0.35 ± 1.51	0.96 ± 1.43	0.056	0.96 ± 1.50	0.037	0.94 ± 1.41	0.058	1.04 ± 1.67	0.042
DDS									
Week 2-week 0	-0.73 ± 0.95	-0.72 ± 1.03	0.904	-1.06 ± 0.99	0.108	-0.74 ± 0.97	0.890	-0.80 ± 1.03	0.750
Week 4-week 0	-0.33 ± 1.12	-0.33 ± 0.90	0.994	-0.55 ± 1.14	0.428	-0.43 ± 0.95	0.787	-0.14 ± 0.99	0.330

Data are mean ± SD

<sup>a</sup> n= 50 for each group with the following exceptions: week 1 (group C: n = 49, placebo: n = 49), week 2 (group B: n = 49, group C: n = 47, placebo: n = 48), week 3 (group A: n = 49, group B: n = 49, group C: n = 47, placebo: n = 48), week 4 (group A: n = 49, group B: n = 49, group C: n = 47, placebo: n = 48).

<sup>b</sup> Wilcoxon rank-sum test was used for comparing changes from baseline to each visit time between each intervention group and placebo.

BMF, bowel movement frequency; BSS, Bristol stool scale score; DDS, Defecation difficulty score.

**Table S2. Changes in biochemical parameters**

Biochemical Variable	Overall (n = 242)	Group A (n = 48)	Group B (n = 49)	Group C (n = 47)	Group D (n = 50)	Placebo (n = 48)	P Value		
							Group	Time	Time × Group
GLU (mmol/L)							0.013	0.361	0.459
Week 0	5.01 (4.75, 5.54)	5.08 (4.78, 5.69)	5.02 (4.70, 5.32)	4.97 (4.83, 5.26)	5.03 (4.80, 5.60)	5.00 (4.68, 6.01)			
Week 4	5.04 (4.69, 5.52)	5.19 (4.72, 5.46)	5.00 (4.68, 5.35)	4.89 (4.64, 5.40)	5.08 (4.77, 5.66)	5.01 (4.66, 5.82)			
△	-0.04 (-0.29, 0.25)	-0.02 (-0.28, 0.33)	-0.03 (-0.26, 0.25)	-0.13 (-0.33, 0.07)	-0.03 (-0.25, 0.47)	-0.14 (-0.33, 0.13)			
TC (mmol/L)							0.266	0.138	0.665
Week 0	4.67 ± 0.95	4.90 ± 0.85	4.55 ± 0.97	4.62 ± 0.86	4.64 ± 0.89	4.64 ± 1.16			
Week 4	4.72 ± 0.94	4.92 ± 0.84	4.57 ± 1.00	4.66 ± 0.88	4.66 ± 0.86	4.81 ± 1.08			
△	0.05 ± 0.56	0.02 ± 0.56	0.02 ± 0.52	0.05 ± 0.50	0.02 ± 0.60	0.17 ± 0.60			
TG (mmol/L)							0.323	0.024	0.995
Week 0	1.09 (0.77, 1.46)	1.06 (0.86, 1.56)	1.08 (0.71, 1.29)	1.14 (0.71, 1.35)	1.21 (0.78, 1.86)	1.05 (0.75, 1.48)			
Week 4	1.18 (0.90, 1.69)	1.14 (0.93, 1.56)	1.13 (0.89, 1.54)	1.24 (0.93, 1.71)	1.35 (0.92, 2.04)	1.14 (0.81, 1.77)			
△	0.09 (-0.13, 0.30)	0.03 (-0.17, 0.19)	0.05 (-0.13, 0.34)	0.13 (-0.09, 0.33)	0.15 (-0.16, 0.35)	0.13 (-0.10, 0.28)			
HDL-C (mmol/L)							0.827	0.055	0.672
Week 0	1.31 (1.11, 1.53)	1.35 (1.12, 1.59)	1.32 (1.16, 1.59)	1.34 (1.11, 1.42)	1.29 (1.08, 1.46)	1.29 (1.13, 1.52)			
Week 4	1.33 (1.13, 1.55)	1.38 (1.10, 1.49)	1.33 (1.18, 1.57)	1.31 (1.17, 1.49)	1.31 (1.08, 1.57)	1.38 (1.18, 1.54)			
△	0.01 (-0.07, 0.09)	-0.01 (-0.06, 0.07)	-0.02 (-0.10, 0.09)	0.00 (-0.08, 0.08)	0.03 (-0.04, 0.09)	0.02 (-0.06, 0.10)			
LDL-C (mmol/L)							0.305	0.057	0.792
Week 0	2.85 ± 0.82	3.04 ± 0.76	2.73 ± 0.85	2.81 ± 0.74	2.84 ± 0.80	2.83 ± 0.93			
Week 4	2.91 ± 0.79	3.08 ± 0.70	2.78 ± 0.82	2.86 ± 0.76	2.85 ± 0.75	2.97 ± 0.91			
△	0.06 ± 0.47	0.04 ± 0.47	0.05 ± 0.46	0.05 ± 0.44	0.01 ± 0.51	0.13 ± 0.48			

Data were mean ± SD and median (interquartile range) for normal or non-normal distribution variable.

GLU, glucose; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein cholesterol; TC, cholesterol; TG, triglyceride.

P values were determined by generalized estimating equations, adjusted for age, sex.

△ Changes from week 0 to week 4.

**Table S3. Adverse events recorded in the study.**

Adverse Event	Group A	Group B	Group C	Group D	Placebo
Slight dizziness	0	0	1	0	0
Acute gastroenteritis	0	0	0	0	1
Stomachache	1	0	1	1	0
Bloating	1	2	2	1	0
Farting increasing	1	2	1	1	0
Diarrhea	0	2	0	1	0
Tenesmus	2	1	0	0	0
Appetite decreased	0	0	0	1	2
Hemorrhoids aggravated	0	0	0	1	0

Data are the numbers of events

**Table S4. The difference and ratio of relative genus abundance between intervention groups and the placebo group.**

Genera	Group A		Group B		Group C		Group D	
	Q value <sup>a</sup>	ratio <sup>b</sup>	Q value <sup>a</sup>	ratio <sup>b</sup>	Q value <sup>a</sup>	ratio <sup>b</sup>	Q value <sup>a</sup>	ratio <sup>b</sup>
<b>Week 0</b>								
g Adlercreutzia	0.9844	0.5597	0.9859	0.5410	0.9626	0.6152	0.9852	0.3654
g Agathobacter	0.9869	1.3577	0.9672	0.7122	0.9642	0.7730	0.9868	0.9697
g Akkermansia	0.9656	2.2021	0.9787	2.9946	0.8044	2.9953	0.8788	2.6512
g Alistipes	0.9721	0.8109	0.9831	0.8039	0.9827	0.7553	0.9868	0.9895
g Allisonella	0.9783	0.7273	0.9405	0.9796	0.8959	0.4743	0.9122	0.4364
g Anaerostipes	0.9590	0.7188	0.9861	0.5940	0.9826	0.6149	0.9871	0.6220
g Anaerotruncus	0.9828	0.5714	0.9763	0.5598	0.9810	0.6957	0.9853	0.6400
g Bacteroides	0.9716	1.1160	0.9804	1.0865	0.9849	1.0204	0.9837	1.0327
g Barnesiella	0.9859	0.9294	0.9814	0.9215	0.9732	0.5748	0.9856	0.9519
g Bifidobacterium	0.8844	1.4011	0.9376	1.8328	0.9518	1.0820	0.9324	1.7412
g Bilophila	0.9830	1.0432	0.9858	0.8163	0.9648	1.3977	0.9740	0.8474
g Blautia	0.9761	0.7225	0.9680	0.7956	0.9829	1.0347	0.9776	0.7338
g Butyricicoccus	0.8655	1.0065	0.8044	1.0083	0.9034	0.9347	0.8561	1.1945
g Butyricimonas	0.9558	1.9231	0.9841	1.4485	0.9873	1.1237	0.9652	1.6000
g CAG-352	0.9839	0.7787	0.9841	1.2820	0.8950	1.2373	0.9855	0.3436
g CAG-56	0.9552	0.5204	0.8044	0.2949	0.9708	0.5111	0.9077	0.5192
g Christensenellaceae R-7 group	0.9523	2.5538	0.8044	3.4361	0.8044	3.5104	0.9428	2.7077
g Clostridium innocuum group	0.9802	0.5000	0.9453	2.2857	0.8876	2.9565	0.9481	1.9200
g Clostridium sensu stricto 1	0.9856	0.4481	0.9470	1.3115	0.9799	4.5902	0.9610	1.9410
g Colidextribacter	0.9762	1.0394	0.9537	0.6479	0.8908	1.1092	0.9680	0.8164
g Collinsella	0.9779	1.0609	0.9694	1.0825	0.9688	1.9138	0.9673	0.8450
g Coprobacter	0.9750	3.0588	0.9393	7.8367	0.9797	4.1739	0.9813	0.6494
g Coprococcus	0.9788	0.8500	0.9761	1.4265	0.9698	1.6859	0.9820	1.2510
g Desulfovibrio	0.9661	1.5294	0.9836	0.8759	0.8044	2.4184	0.9697	1.1068
g Dialister	0.8708	1.7904	0.8044	1.3600	0.8044	1.8234	0.8044	1.3377
g Dorea	0.9542	1.0000	0.9827	0.7731	0.9810	0.8423	0.9620	0.9815
g Eggerthella	0.9818	0.8000	0.9392	2.6122	0.9843	3.2696	0.9847	1.0880
g Eisenbergiella	0.8871	1.8125	0.9754	2.9388	0.9866	1.6957	0.9829	2.2200
g Erysipelatoclostridium	0.9302	7.0000	0.8044	11.7551	0.8044	20.8696	0.8170	9.6000
g Erysipelotrichaceae UCG-003	0.9848	0.8612	0.9595	0.8109	0.9809	1.0185	0.9461	1.1208
g Escherichia-Shigella	0.9651	0.4694	0.8192	0.2818	0.9850	0.5960	0.9746	0.5154
g Eubacterium eligens group	0.9708	1.3780	0.9830	0.9103	0.9852	0.9620	0.9870	1.1403
g Eubacterium hallii group	0.9757	0.5000	0.9832	0.5671	0.9632	0.7864	0.9844	0.5902

g Eubacterium oxidoreducens group	0.9098	1.8000	0.9790	1.1265	0.9459	0.8870	0.9814	1.3440
g Eubacterium ruminantium group	0.9816	1.6099	0.9615	0.5921	0.9805	1.2556	0.9844	0.7279
g Eubacterium siraeum group	0.9218	10.2647	0.9653	5.8487	0.9661	1.3811	0.9798	1.2988
g Eubacterium ventriosum group	0.9777	1.0844	0.9487	0.6743	0.9689	1.9921	0.9646	1.0535
g Eubacterium xylanophilum group	0.9802	1.2222	0.9849	0.5079	0.9627	1.7005	0.9807	0.7644
g Faecalibacterium	0.9856	0.9846	0.9727	1.1537	0.9859	0.9628	0.9786	0.9814
g Family XIII AD3011 group	0.9669	2.0769	0.9663	2.2606	0.9628	3.6120	0.8317	2.4369
g Family XIII UCG-001	0.9866	1.3636	0.9853	0.8905	0.9849	1.2806	0.9827	0.9164
g Flavonifractor	0.9709	1.2513	0.8295	1.1367	0.9663	1.5847	0.8900	1.8379
g Fusicatenibacter	0.9804	0.7588	0.9610	1.1234	0.9851	0.7754	0.9572	1.7036
g Fusobacterium	0.9842	22.1364	0.9754	3.6735	0.9426	13.6601	0.9841	10.2109
g GCA-900066575	0.9756	1.3333	0.9827	3.9184	0.9354	2.0870	0.9836	1.6000
g Haemophilus	0.9823	1.6000	0.9325	1.7455	0.9804	0.7779	0.9796	2.1469
g Holdemanella	0.9840	0.8919	0.9806	0.1589	0.9864	0.6204	0.9676	1.8162
g Holdemania	0.9773	2.2857	0.9529	2.7988	0.9817	1.3416	0.9830	1.2343
g Hungatella	0.9863	2.1304	0.9741	1.6610	0.8970	1.4064	0.9854	5.9687
g Intestinibacter	0.9792	1.1053	0.9633	1.2288	0.9858	1.5469	0.9873	0.9684
g Intestinimonas	0.9864	1.7500	0.9832	1.8367	0.9590	2.3478	0.9870	1.0800
g Klebsiella	0.9076	0.5422	0.9734	8.0610	0.9744	3.4322	0.9704	1.7928
g Lachnoclostridium	0.9871	0.7980	0.9855	1.0576	0.9756	1.1989	0.9841	1.0070
g Lachnospira	0.9362	1.2202	0.9867	0.9288	0.9849	0.9840	0.9844	1.0806
g Lachnospiraceae FCS020 group	0.9836	0.8000	0.9874	1.1755	0.9223	2.0870	0.9538	1.3440
g Lachnospiraceae NC2004 group	0.9859	0.6000	0.9811	0.5224	0.9549	1.5304	0.9802	0.5120
g Lachnospiraceae ND3007 group	0.9615	1.6271	0.8044	1.8596	0.9408	1.6271	0.8542	1.6434
g Lachnospiraceae NK4A136 group	0.9809	1.3677	0.9819	0.8988	0.9865	1.1009	0.9827	1.3097
g Lachnospiraceae UCG-001	0.9054	1.7200	0.8559	1.7371	0.8322	2.1426	0.9747	1.1904
g Lachnospiraceae UCG-004	0.9701	1.1502	0.9847	1.1604	0.9777	1.1196	0.9852	1.0136
g Lachnospiraceae UCG-010	0.9869	0.9412	0.9589	0.6242	0.9853	0.7059	0.9798	0.8188
g Lactobacillus	0.8044	5.7778	0.8044	6.1224	0.8961	4.7246	0.8044	5.0400
g Marvinbryantia	0.9828	1.4375	0.9837	0.7959	0.9612	1.8913	0.9863	0.9600
g Megamonas	0.9640	0.9231	0.8059	0.1613	0.9826	0.6691	0.9640	0.5515
g Megasphaera	0.9842	0.8161	0.9831	0.6535	0.9840	1.8051	0.9868	1.3440
g Monoglobus	0.9652	0.4781	0.9414	0.5591	0.9242	0.4462	0.9777	0.5091
g NK4A214 group	0.9655	1.9495	0.9502	1.6806	0.9544	1.9003	0.9357	2.9813
g norank f Christensenellaceae	0.9853	0.8182	0.9871	1.2468	0.9674	1.5178	0.9860	0.7855
g norank f Coriobacteriales Incertae Sedis	0.9779	0.7778	0.9782	0.9796	0.9017	3.2464	0.9610	0.7467
g norank f Eubacterium coprostanoligenes group	0.9796	0.9311	0.9565	1.0342	0.9740	0.7989	0.9544	1.3172
g norank f Lachnospiraceae	0.9684	0.7455	0.9106	0.7124	0.9378	0.6261	0.9853	0.9076

g norank f Muribaculaceae	0.8044	2.0435	0.9764	1.8953	0.8044	9.3913	0.8044	8.3478
g norank f norank o Clostridia UCG-014	0.9861	1.0486	0.9859	0.9415	0.9852	1.4800	0.9870	1.4213
g norank f norank o Clostridia vadinBB60 group	0.9783	1.5000	0.9805	1.3605	0.9822	0.9275	0.9738	2.7200
g norank f norank o RF39	0.9606	2.4706	0.9851	0.9104	0.9760	1.0312	0.9504	0.9713
g norank f norank o Rhodospirillales	0.9289	6.5128	0.9567	3.8430	0.9813	0.8027	0.9628	2.6831
g norank f Oscillospiraceae	0.9870	1.0392	0.9722	1.1525	0.9653	1.4936	0.9865	1.2612
g norank f Ruminococcaceae	0.9845	1.1241	0.9398	1.7345	0.9408	3.3501	0.9836	1.6710
g norank f UCG-010	0.9237	1.7353	0.9867	1.9016	0.9808	1.3504	0.8044	3.7553
g Odoribacter	0.9380	1.4848	0.9717	1.3655	0.9853	1.1067	0.8618	1.8764
g Oscillibacter	0.9675	1.0398	0.9695	0.8850	0.9489	1.1680	0.9851	0.8236
g Oscillospira	0.9774	0.7000	0.9614	0.4898	0.9858	1.1478	0.9829	1.0560
g Oxalobacter	0.9505	1.6364	0.9806	0.4453	0.9827	0.9486	0.9695	1.3091
g Paludicola	0.9612	2.7500	0.9588	3.6735	0.9865	1.8261	0.9830	1.6800
g Parabacteroides	0.8044	1.1810	0.9477	1.3621	0.8044	1.2919	0.8632	1.1246
g Paraprevotella	0.9850	4.1458	0.9870	1.4082	0.9854	1.4348	0.8850	3.4400
g Parasutterella	0.9850	1.2163	0.9873	1.1636	0.9819	1.5463	0.9658	1.1739
g Peptococcus	0.9552	1.5000	0.9824	0.7347	0.9664	2.6087	0.8962	2.1600
g Phascolarctobacterium	0.8044	0.4761	0.8044	0.5381	0.9642	0.8231	0.9474	0.6270
g Prevotella	0.9663	0.4926	0.9856	0.7197	0.9856	0.4446	0.9815	0.6365
g Pyramidobacter	0.9810	1.2500	0.9537	40.6531	0.8044	13.5652	0.8044	26.8800
g Romboutsia	0.8248	1.6055	0.8044	2.1839	0.9851	2.1635	0.9698	1.5325
g Roseburia	0.9811	1.3447	0.9838	1.0589	0.9722	1.2983	0.9816	1.3429
g Ruminococcus	0.9853	1.2198	0.9533	1.3184	0.9571	1.4777	0.9838	1.1198
g Ruminococcus gnavreuii group	0.9849	0.8000	0.9827	0.7401	0.9871	1.1362	0.9820	0.7893
g Ruminococcus gnavus group	0.9714	1.0083	0.9579	3.4893	0.9828	1.8369	0.9802	0.7855
g Ruminococcus torques group	0.9341	0.7753	0.9802	0.9128	0.9589	1.1858	0.9690	1.2170
g Senegalimassilia	0.9868	1.7895	0.9869	1.1343	0.9869	0.8787	0.9853	0.8084
g Streptococcus	0.9869	1.7500	0.9818	1.8101	0.9872	1.0548	0.9763	1.0643
g Subdoligranulum	0.9640	1.1241	0.9801	1.0444	0.8044	1.6776	0.9825	0.9358
g Sutterella	0.9694	1.3160	0.9844	1.0945	0.9801	0.7736	0.9744	1.6947
g Terrisporobacter	0.9776	0.6667	0.8053	3.0694	0.9872	0.6957	0.9832	1.6000
g Turicibacter	0.9510	1.2000	0.9329	1.0776	0.9607	2.1913	0.8044	2.3040
g Tyzzerella	0.9862	0.9474	0.9798	1.7916	0.9824	1.8398	0.9600	0.9095
g UBA1819	0.9809	0.8140	0.9270	1.4124	0.9699	1.9656	0.9350	1.8084
g UCG-002	0.9652	1.2900	0.9473	1.5720	0.9772	1.2449	0.9852	1.2534
g UCG-003	0.8044	2.0859	0.8733	1.7712	0.9474	1.6074	0.9708	1.5079
g UCG-005	0.9631	2.4706	0.9505	1.8295	0.9734	1.5090	0.9489	2.9976
g unclassified c Clostridia	0.9360	2.1406	0.9207	1.5000	0.9656	2.0217	0.9491	1.6650

g unclassified f Enterobacteriaceae	0.9849	0.0565	0.9864	0.0866	0.9850	0.1846	0.9609	0.0330
g unclassified f Lachnospiraceae	0.9691	1.0718	0.9850	0.8987	0.9338	1.2385	0.9868	0.9326
g unclassified f Oscillospiraceae	0.8106	1.6757	0.9775	1.2179	0.8044	2.0024	0.9824	1.3232
g unclassified f Peptostreptococcaceae	0.9577	2.3333	0.9822	1.9592	0.9514	2.7826	0.9604	2.5600
g unclassified f Ruminococcaceae	0.9663	5.3250	0.8044	3.1837	0.9501	2.0087	0.9226	2.7120
g unclassified k norank d Bacteria	0.9790	1.2979	0.9685	0.8337	0.9855	1.2877	0.9771	0.8374
g unclassified o Bacteroidales	0.9418	1.8333	0.9773	0.7347	0.9657	1.9130	0.9811	1.4400
g unclassified o Oscillospirales	0.9855	1.0000	0.9849	1.0340	0.9694	1.6812	0.9867	1.0133
g unclassified p Firmicutes	0.9807	0.8667	0.9851	1.0449	0.9737	0.9739	0.9840	1.0240
g Veillonella	0.9744	12.7429	0.8863	15.9534	0.9853	6.1714	0.9575	2.5234
g Victivallis	0.9620	2.0000	0.9480	2.2391	0.8551	2.0373	0.9529	1.1429
<b>Week 2</b>								
g Adlercreutzia	0.9031	0.6909	0.8808	0.8547	0.8944	1.0844	0.7591	0.5082
g Agathobacter	0.9227	0.8151	0.8241	0.7266	0.8067	0.7753	0.9121	0.8956
g Akkermansia	0.8379	1.7729	0.7860	0.9576	0.8939	2.0049	0.9179	1.0840
g Alistipes	0.6988	0.5663	0.3144	0.3473	0.5885	0.4851	0.5953	0.5073
g Allisonella	0.8569	1.6596	0.9044	1.8367	0.7801	2.3478	0.8365	1.3200
g Anaerostipes	0.4709	1.5603	0.5706	1.8866	0.8210	1.3527	0.7723	3.1689
g Anaerotruncus	0.7969	0.2723	0.8160	0.5224	0.8764	0.4174	0.8126	0.3840
g Bacteroides	0.8982	0.9544	0.7678	1.2243	0.8624	1.1315	0.8341	1.1096
g Barnesiella	0.8938	0.7660	0.8138	0.5078	0.8101	0.5519	0.9115	0.8387
g Bifidobacterium	0.3144	1.5345	0.7998	1.0468	0.7048	0.9500	0.7906	0.9736
g Bilophila	0.9208	0.7810	0.8773	0.5629	0.9168	0.8310	0.8807	0.5777
g Blautia	0.7948	0.6916	0.8046	0.8591	0.7355	0.7136	0.8030	0.8080
g Butyricoccus	0.8812	0.9188	0.9134	1.0817	0.9186	1.1361	0.9087	0.9563
g Butyricimonas	0.9141	1.4247	0.5678	0.6318	0.7380	0.6887	0.8758	0.8736
g CAG-352	0.8644	0.6119	0.9154	0.7009	0.8270	2.1094	0.9176	0.6869
g CAG-56	0.9261	0.8824	0.6071	0.4780	0.9225	0.7680	0.9193	0.9600
g Christensenellaceae R-7 group	0.6085	2.3262	0.9216	1.0918	0.8378	0.9457	0.9215	1.7267
g Clostridium innocuum group	0.6033	0.8824	0.4884	0.6318	0.4697	1.1315	0.7099	0.6869
g Clostridium sensu stricto 1	0.8247	0.6302	0.9039	0.8913	0.8075	0.8790	0.8464	0.8389
g Colidextribacter	0.9103	0.7130	0.9119	0.8933	0.8636	0.7022	0.8949	0.8091
g Collinsella	0.7643	1.3432	0.9161	0.8075	0.8680	1.1909	0.9090	0.9287
g Coprobacter	0.8614	1.1593	0.7812	0.8649	0.7891	0.3948	0.9088	0.3373
g Coprococcus	0.9157	0.7852	0.8939	0.8854	0.8543	0.8453	0.9134	0.8875
g Desulfovibrio	0.9077	1.3860	0.8733	1.0076	0.8787	2.4149	0.9232	0.9600
g Dialister	0.7698	1.6394	0.6659	1.8767	0.7410	2.5300	0.6070	1.7381
g Dorea	0.8043	1.0595	0.8436	1.0254	0.6774	0.9557	0.9052	1.6508



g Eggerthella	0.8716	0.9532	0.7931	3.2653	0.9035	0.9739	0.9229	1.4080
g Eisenbergiella	0.8077	0.7748	0.9252	1.3849	0.9109	0.5757	0.8746	0.8607
g Erysipelatoclostridium	0.9021	1.1348	0.7459	1.3061	0.8952	1.3913	0.8799	1.8133
g Erysipelotrichaceae UCG-003	0.7099	0.6183	0.8045	1.4667	0.8421	1.1450	0.8126	1.4115
g Escherichia-Shigella	0.8168	1.6005	0.8947	1.1366	0.9072	2.2092	0.7645	0.7706
g Eubacterium eligens group	0.5806	1.5277	0.7753	1.5110	0.9259	1.2779	0.8153	1.1152
g Eubacterium hallii group	0.8973	1.1113	0.8731	1.1222	0.8636	1.2274	0.8954	1.1549
g Eubacterium oxidoreducens group	0.5607	2.6553	0.7786	2.0571	0.9044	0.8348	0.8086	2.1120
g Eubacterium ruminantium group	0.7495	1.8435	0.8941	0.2407	0.7782	1.4945	0.7387	1.6759
g Eubacterium siraeum group	0.8750	1.2359	0.9157	0.6247	0.9065	0.4083	0.9241	0.9183
g Eubacterium ventriosum group	0.8113	1.4515	0.8157	0.8844	0.8568	1.2899	0.9215	1.0978
g Eubacterium xylanophilum group	0.8502	1.4776	0.9090	1.0630	0.7656	2.2202	0.9116	0.6536
g Faecalibacterium	0.7790	1.1204	0.8160	1.3088	0.8938	1.0337	0.8255	1.0453
g Family XIII AD3011 group	0.8931	1.1605	0.9138	1.0241	0.9051	0.6166	0.8798	1.2218
g Family XIII UCG-001	0.8435	0.9011	0.8868	0.8643	0.8365	0.8593	0.8931	0.4518
g Flavonifractor	0.8403	0.5184	0.9000	0.7920	0.9125	0.4980	0.9130	0.5515
g Fusicatenibacter	0.4866	1.4676	0.7273	1.5088	0.8428	0.8300	0.6780	1.2856
g Fusobacterium	0.9238	1.7935	0.9083	0.9676	0.8707	20.8696	0.9121	1.3815
g GCA-900066575	0.7054	2.9362	0.8057	1.9592	0.8631	1.3043	0.8807	1.3200
g Haemophilus	0.9127	1.1835	0.8519	2.1881	0.8886	1.0532	0.5991	1.0766
g Holdemanella	0.7844	1.4209	0.9130	0.8518	0.9030	1.0888	0.8460	2.2122
g Holdemania	0.8723	0.8754	0.9092	0.8397	0.8140	1.3416	0.7655	0.1371
g Hungatella	0.7889	0.4057	0.8809	0.3892	0.8104	0.2144	0.8499	0.2499
g Intestinibacter	0.9036	0.7629	0.8288	1.1566	0.8605	1.0058	0.8863	1.1913
g Intestinimonas	0.9236	1.0213	0.8607	0.5714	0.7945	1.8261	0.8600	0.6400
g Klebsiella	0.7648	0.1406	0.8016	3.0598	0.9171	0.9731	0.9188	0.5501
g Lachnoclostridium	0.8924	1.1856	0.8079	2.0643	0.9031	1.5372	0.9099	1.1054
g Lachnospira	0.7610	1.3868	0.7561	2.0327	0.8096	1.3456	0.7516	1.5211
g Lachnospiraceae FCS020 group	0.7687	0.5106	0.9173	1.5673	0.8429	2.0870	0.9027	1.5360
g Lachnospiraceae NC2004 group	0.8035	1.9404	0.8540	1.3714	0.9092	0.8348	0.8612	1.3440
g Lachnospiraceae ND3007 group	0.8641	1.5985	0.5841	1.5333	0.5971	1.8299	0.7619	1.6417
g Lachnospiraceae NK4A136 group	0.8980	1.2185	0.7894	0.7566	0.9198	1.1307	0.7831	0.7525
g Lachnospiraceae UCG-001	0.9067	0.8151	0.8002	1.7237	0.7159	1.3645	0.8350	0.8308
g Lachnospiraceae UCG-004	0.8512	0.8671	0.7061	1.2031	0.9264	0.8229	0.9227	0.8408
g Lachnospiraceae UCG-010	0.9054	1.0093	0.8107	0.8989	0.8881	0.9575	0.8589	0.6438
g Lactobacillus	0.8001	8.2530	0.6428	7.5455	0.8166	3.9201	0.8650	4.7481
g Marvinbryantia	0.8031	1.3050	0.9255	0.7619	0.9155	0.5797	0.8739	1.0667
g Megamonas	0.7619	0.6555	0.7303	0.4710	0.9106	0.6219	0.8054	0.5535

g Megasphaera	0.8156	0.7375	0.7936	0.3240	0.9187	0.8080	0.8425	0.9867
g Monoglobus	0.8831	1.3878	0.8111	2.0670	0.8545	0.9886	0.8376	2.8754
g NK4A214 group	0.8996	1.3240	0.9004	1.1335	0.8562	1.5280	0.8117	1.5360
g norank f Christensenellaceae	0.9101	0.9362	0.9029	0.9796	0.8322	0.5217	0.8113	0.4800
g norank f Coriobacteriales Incertae Sedis	0.7717	3.9049	0.8133	1.1525	0.7667	5.4015	0.8542	1.8635
g norank f Eubacterium coprostanoligenes group	0.9259	1.0275	0.9232	1.0246	0.8388	0.6232	0.8162	0.6630
g norank f Lachnospiraceae	0.8160	1.0750	0.9154	0.9796	0.8274	0.9886	0.8133	0.6400
g norank f Muribaculaceae	0.8078	2.2307	0.8146	0.6702	0.6096	8.4577	0.4888	9.6253
g norank f norank o Clostridia UCG-014	0.8078	0.7703	0.9015	0.4377	0.8943	0.5140	0.9114	0.7598
g norank f norank o Clostridia vadinBB60 group	0.9156	0.5419	0.7306	0.2599	0.6958	0.1917	0.8140	0.6073
g norank f norank o RF39	0.7529	2.6944	0.9151	1.0630	0.8789	1.5097	0.7434	2.0834
g norank f norank o Rhodospirillales	0.8066	2.3607	0.6852	5.1067	0.8986	0.7014	0.7262	0.8656
g norank f Oscillospiraceae	0.4755	0.6950	0.7517	0.8707	0.7805	0.6957	0.3852	0.5733
g norank f Ruminococcaceae	0.8169	1.7508	0.8139	0.8918	0.8621	1.0056	0.5626	0.6090
g norank f UCG-010	0.8116	1.6368	0.7552	0.5636	0.8636	0.6861	0.8964	1.4071
g Odoribacter	0.8874	1.1830	0.6581	0.4980	0.8147	0.8783	0.8463	0.9040
g Oscillibacter	0.8017	0.6547	0.7700	0.7577	0.7636	0.9721	0.5425	0.6195
g Oscillospira	0.9217	1.2766	0.9257	1.2245	0.9131	0.8696	0.5951	0.1600
g Oxalobacter	0.7390	1.9574	0.7947	0.7347	0.7524	0.3478	0.8968	0.6400
g Paludicola	0.7939	1.6049	0.8999	4.1983	0.8117	1.6398	0.8809	1.0971
g Parabacteroides	0.3144	2.6112	0.8818	1.3840	0.7210	1.5375	0.9168	0.9794
g Paraprevotella	0.9187	0.6396	0.8815	0.9499	0.9091	0.6746	0.6053	2.4533
g Parasutterella	0.8039	1.4628	0.8153	1.2026	0.8168	1.6375	0.6490	1.5744
g Peptococcus	0.7825	3.4723	0.7956	0.3918	0.8699	1.2522	0.9106	1.1520
g Phascolarctobacterium	0.8427	1.0770	0.7667	0.8623	0.8026	1.1069	0.7823	0.6389
g Prevotella	0.9072	0.7115	0.8938	0.7004	0.8371	0.7482	0.8730	0.9112
g Pyramidobacter	0.5084	0.0056	0.8307	0.4046	0.9055	0.0567	0.7872	0.0991
g Romboutsia	0.9139	0.7557	0.8752	1.2080	0.8901	0.7393	0.9237	0.8222
g Roseburia	0.8996	1.0649	0.9094	1.1276	0.8976	0.8663	0.8653	1.2478
g Ruminococcus	0.7408	2.1138	0.8884	1.6906	0.9007	1.4238	0.8006	1.7937
g Ruminococcus gauvreauii group	0.9160	0.8511	0.8284	0.4082	0.9052	0.6087	0.8033	1.1400
g Ruminococcus gnavus group	0.7174	0.3965	0.8746	1.0660	0.8769	1.3565	0.9017	0.6325
g Ruminococcus torques group	0.3144	0.3696	0.6974	0.7201	0.6841	0.7573	0.7870	0.6287
g Senegalimassilia	0.8602	5.5830	0.8939	0.7837	0.9232	1.0435	0.9177	0.4480
g Streptococcus	0.9044	0.8279	0.7350	1.5881	0.9225	0.6877	0.8572	0.8000
g Subdoligranulum	0.7860	1.2805	0.9010	1.0721	0.8791	1.2162	0.8865	1.1432
g Sutterella	0.9227	0.9180	0.8892	0.7155	0.8613	0.8153	0.9054	0.9954
g Terrisporobacter	0.8858	2.2979	0.6232	4.8980	0.4199	7.5652	0.6440	3.8400

g Turicibacter	0.8799	0.9483	0.9239	1.6793	0.9242	0.7453	0.9193	0.6857
g Tyzzerella	0.9093	1.2584	0.7923	0.8397	0.8408	2.6273	0.8196	0.9600
g UBA1819	0.8494	0.4750	0.6073	0.9568	0.6887	0.3883	0.7758	0.6140
g UCG-002	0.9115	0.9257	0.8092	0.7473	0.8747	0.7067	0.9154	0.9775
g UCG-003	0.8907	1.0145	0.9239	1.0612	0.8447	1.0365	0.8544	1.2640
g UCG-005	0.8252	2.6072	0.8669	0.8283	0.9101	1.0689	0.8745	2.0488
g unclassified c Clostridia	0.5385	1.5840	0.8144	1.2995	0.7871	1.1287	0.8867	1.0384
g unclassified f Enterobacteriaceae	0.9136	1.4209	0.7480	2.2786	0.8423	3.7883	0.8797	4.5287
g unclassified f Lachnospiraceae	0.8933	1.1098	0.9241	1.1562	0.8953	1.0489	0.8051	0.8918
g unclassified f Oscillospiraceae	0.9034	0.8000	0.8666	0.6857	0.9085	0.6435	0.8558	0.9600
g unclassified f Peptostreptococcaceae	0.8060	2.5532	0.9039	0.9796	0.8137	0.2609	0.8583	2.1600
g unclassified f Ruminococcaceae	0.8574	1.3495	0.8305	1.2070	0.8198	0.8571	0.8925	1.4057
g unclassified k norank d Bacteria	0.6300	1.7317	0.8950	1.4481	0.9152	1.1342	0.8127	1.4609
g unclassified o Bacteroidales	0.9132	0.8298	0.8268	0.6735	0.8952	0.7174	0.9131	0.6600
g unclassified o Oscillospirales	0.9181	1.3617	0.8373	2.1769	0.8130	2.4348	0.9057	1.2800
g unclassified p Firmicutes	0.7898	1.2998	0.7379	0.9796	0.7999	1.5178	0.9212	0.7855
g Veillonella	0.9132	0.5971	0.8151	2.2455	0.8404	1.5090	0.8431	0.5465
g Victivallis	0.9210	0.9719	0.7910	0.3318	0.8835	0.3871	0.8858	0.3406
<b>Week 4</b>								
g Adlercreutzia	0.9817	0.4201	0.9843	0.4562	0.9804	0.4193	0.9777	0.7978
g Agathobacter	0.9835	1.1571	0.9027	0.4189	0.8268	0.4315	0.9834	0.6534
g Akkermansia	0.9056	1.1706	0.9808	1.2965	0.9623	0.4972	0.5064	1.8522
g Alistipes	0.9311	0.5199	0.8985	0.4994	0.9054	0.5320	0.9612	0.5931
g Allisonella	0.9393	1.6667	0.9795	0.6531	0.9298	3.1304	0.9813	2.2400
g Anaerostipes	0.9809	1.0000	0.6507	1.7652	0.9799	1.3390	0.9845	0.9841
g Anaerotruncus	0.9565	0.6364	0.8895	0.5788	0.9554	0.8063	0.9806	1.3527
g Bacteroides	0.9761	1.0666	0.9132	1.2259	0.9586	1.1350	0.9767	1.1707
g Barnesiella	0.9827	0.6325	0.9716	0.4647	0.9414	0.4183	0.9824	0.5965
g Bifidobacterium	0.3689	2.5166	0.7490	2.2321	0.6012	2.8489	0.9474	1.8327
g Bilophila	0.9635	0.6842	0.9739	0.8404	0.9471	0.7359	0.9849	0.8893
g Blautia	0.9365	0.7712	0.9584	1.1820	0.9748	1.2740	0.7117	0.7409
g Butyricicoccus	0.9341	1.3794	0.3455	1.7282	0.9712	1.0265	0.9779	0.9860
g Butyricimonas	0.9528	1.4566	0.9497	0.8210	0.9843	1.0616	0.9236	1.5982
g CAG-352	0.9801	1.3721	0.9809	0.5183	0.9669	1.6684	0.9839	0.8763
g CAG-56	0.9772	1.0152	0.9296	0.7421	0.7684	0.3399	0.9761	0.7855
g Christensenellaceae R-7 group	0.9362	1.8755	0.9693	1.0646	0.9842	1.1892	0.9838	2.0251
g Clostridium innocuum group	0.3807	0.0000	0.9736	2.5714	0.9228	6.9130	0.9724	3.4800
g Clostridium sensu stricto 1	0.9685	1.0306	0.9802	0.9839	0.9573	1.2303	0.9767	1.7230

g Colidextribacter	0.9420	0.9866	0.8784	0.8284	0.7785	0.6793	0.9723	0.9729
g Collinsella	0.9846	0.7243	0.9536	0.4800	0.9837	0.6639	0.9097	0.5135
g Coprobacter	0.9767	1.5532	0.9785	1.5215	0.9718	4.1739	0.9671	1.9609
g Coprococcus	0.9800	1.2824	0.9838	1.0199	0.9801	1.0619	0.9814	1.0758
g Desulfovibrio	0.9814	0.5524	0.9821	0.5480	0.9826	0.7516	0.9786	0.5975
g Dialister	0.8920	2.0962	0.4045	1.8016	0.6232	1.6699	0.5317	1.4058
g Dorea	0.9793	0.9046	0.9828	1.0634	0.9618	0.8890	0.9794	0.9379
g Eggerthella	0.9678	1.4167	0.9658	1.4694	0.9581	0.9565	0.9842	2.0400
g Eisenbergiella	0.9808	1.1429	0.9407	1.3994	0.9400	2.9814	0.9848	1.8514
g Erysipelatoclostridium	0.9802	1.7000	0.9791	0.6367	0.9771	1.3043	0.9831	1.3440
g Erysipelotrichaceae UCG-003	0.9773	1.1480	0.9847	1.1246	0.9766	0.7534	0.9647	1.4206
g Escherichia-Shigella	0.8896	0.4193	0.9773	0.6593	0.9685	0.6258	0.9765	1.9000
g Eubacterium eligens group	0.9026	1.3227	0.9685	0.9024	0.9803	0.9006	0.9742	1.2248
g Eubacterium hallii group	0.9785	0.7352	0.9512	0.9995	0.9705	1.1901	0.9848	0.8662
g Eubacterium oxidoreducens group	0.9628	1.3556	0.9334	0.4789	0.7716	0.4406	0.9601	0.8320
g Eubacterium ruminantium group	0.9282	1.1168	0.9824	0.4433	0.9418	0.8454	0.8890	1.0791
g Eubacterium siraeum group	0.9772	0.9041	0.9847	0.8521	0.9757	0.2144	0.9757	0.5260
g Eubacterium ventriosum group	0.9239	0.7454	0.8981	0.5639	0.8716	1.2245	0.9603	0.6731
g Eubacterium xylanophilum group	0.9677	0.8667	0.9845	0.9959	0.9642	1.4087	0.9701	1.2480
g Faecalibacterium	0.9569	1.1676	0.9754	0.9891	0.9608	1.1980	0.9831	1.0251
g Family XIII AD3011 group	0.9814	0.7333	0.9284	0.4898	0.9770	0.8348	0.9634	1.2800
g Family XIII UCG-001	0.9653	0.6897	0.9566	0.6080	0.8835	0.3958	0.9324	0.5297
g Flavonifractor	0.9706	1.2179	0.9812	1.0726	0.9827	0.9910	0.9805	1.0941
g Fusicatenibacter	0.8828	1.5350	0.9697	1.3498	0.9702	1.2739	0.9822	1.0242
g Fusobacterium	0.9847	1.9202	0.9848	0.5140	0.9303	1.9441	0.9831	0.6607
g GCA-900066575	0.9728	1.1818	0.9846	1.1577	0.9846	0.6640	0.9840	0.9600
g Haemophilus	0.8974	1.0857	0.9600	1.2035	0.9706	0.5292	0.9604	1.0354
g Holdemanella	0.9806	1.2424	0.9699	1.0093	0.9839	1.1067	0.9684	1.6291
g Holdemania	0.9130	0.4706	0.3767	0.1152	0.4079	0.1841	0.9239	0.7341
g Hungatella	0.9724	1.9000	0.9728	0.3918	0.9672	0.6000	0.9813	0.3600
g Intestinibacter	0.9824	1.0714	0.9542	1.9125	0.9766	1.0683	0.9644	1.4057
g Intestinimonas	0.9706	0.6111	0.9842	0.7075	0.9799	0.6377	0.9699	0.8533
g Klebsiella	0.9694	0.1620	0.9837	2.4904	0.8628	1.9988	0.9783	1.7375
g Lachnoclostridium	0.9808	1.0100	0.9838	1.1833	0.9678	1.5757	0.9786	1.0080
g Lachnospira	0.9498	0.8937	0.9763	0.8487	0.9845	0.8723	0.8911	0.4912
g Lachnospiraceae FCS020 group	0.4107	4.5000	0.9111	2.6939	0.3743	3.6522	0.9317	2.5200
g Lachnospiraceae NC2004 group	0.9798	0.8824	0.9789	1.1525	0.9837	0.7673	0.9627	1.4118
g Lachnospiraceae ND3007 group	0.9745	1.7724	0.9418	1.3380	0.7308	1.4677	0.9707	1.1317

g Lachnospiraceae NK4A136 group	0.9832	0.5409	0.9738	0.6469	0.9766	0.6256	0.9541	0.6199
g Lachnospiraceae UCG-001	0.9641	0.5862	0.9693	1.5268	0.9802	1.0147	0.9780	0.5363
g Lachnospiraceae UCG-004	0.8732	1.0567	0.9626	1.0352	0.9642	1.1089	0.9821	1.0546
g Lachnospiraceae UCG-010	0.9814	1.0217	0.9809	0.6282	0.9437	0.7032	0.9771	0.9496
g Lactobacillus	0.6546	3.8791	0.3722	1.8408	0.9732	1.6398	0.9759	0.8545
g Marvinbryantia	0.9637	1.6154	0.8537	0.5275	0.9755	0.8027	0.5866	0.5169
g Megamonas	0.8856	0.4123	0.8252	0.3981	0.9807	1.2052	0.9732	1.1722
g Megasphaera	0.9252	0.5085	0.8926	0.4770	0.9742	0.7053	0.9401	0.1896
g Monoglobus	0.9744	0.7417	0.9033	1.1386	0.9209	1.0473	0.9524	0.8892
g NK4A214 group	0.9824	0.9807	0.9643	1.1498	0.9824	1.5874	0.9522	1.1564
g norank f Christensenellaceae	0.9677	0.3125	0.9662	0.3061	0.9817	0.5217	0.9790	0.7200
g norank f Coriobacteriales Incertae Sedis	0.7529	2.4615	0.9792	1.8085	0.6450	3.3712	0.8913	3.9877
g norank f Eubacterium coprostanoligenes group	0.9438	1.4016	0.9732	1.0233	0.9625	1.2573	0.9697	1.0846
g norank f Lachnospiraceae	0.9732	1.4000	0.8594	1.7633	0.9654	0.8812	0.9548	1.8347
g norank f Muribaculaceae	0.7296	3.3396	0.9329	1.8483	0.4871	9.0369	0.5284	4.7638
g norank f norank o Clostridia UCG-014	0.9807	1.0484	0.9830	0.5823	0.9811	0.6853	0.9834	1.1188
g norank f norank o Clostridia vadinBB60 group	0.9683	1.2308	0.9427	1.3187	0.9787	0.5619	0.9075	2.3631
g norank f norank o RF39	0.9803	1.7600	0.9692	1.1951	0.9722	1.0643	0.9324	2.4576
g norank f norank o Rhodospirillales	0.9177	3.4091	0.9215	3.1614	0.9467	0.4506	0.9561	0.9818
g norank f Oscillospiraceae	0.9757	0.6782	0.9713	0.7319	0.9836	0.6237	0.9827	0.6069
g norank f Ruminococcaceae	0.9843	1.0913	0.9407	0.9381	0.9709	1.1759	0.4113	0.5816
g norank f UCG-010	0.9565	1.9111	0.9804	1.7415	0.9732	1.4841	0.9377	3.3707
g Odoribacter	0.5609	2.0323	0.9701	1.2535	0.9341	1.4474	0.9251	1.5381
g Oscillibacter	0.9293	0.6245	0.9848	0.9383	0.9695	0.8145	0.9681	0.7008
g Oscillospira	0.9157	0.2500	0.9706	0.5510	0.8538	0.1957	0.9517	0.6600
g Oxalobacter	0.9787	0.5000	0.9351	0.1959	0.9788	1.0435	0.9752	1.1520
g Paludicola	0.8262	2.5000	0.9536	3.9184	0.9210	2.7826	0.8612	1.7600
g Parabacteroides	0.3113	1.9521	0.9256	0.9496	0.9367	1.1784	0.9577	0.8120
g Paraprevotella	0.9628	0.8506	0.9776	1.0021	0.9617	1.4033	0.4123	2.9241
g Parasutterella	0.9577	1.5233	0.9096	1.7194	0.9627	1.5207	0.9247	1.4037
g Peptococcus	0.9715	2.2857	0.9789	2.3790	0.9832	1.7888	0.9790	1.9200
g Phascolarctobacterium	0.7379	0.5950	0.8987	0.7359	0.8480	0.9199	0.9480	0.9094
g Prevotella	0.9847	0.7594	0.9801	0.7856	0.9737	0.6375	0.9835	0.7899
g Pyramidobacter	0.9126	0.1765	0.9821	1.0948	0.9460	2.9463	0.9493	0.3953
g Romboutsia	0.9647	0.8233	0.9421	0.7892	0.8963	0.5715	0.9738	2.0693
g Roseburia	0.9525	1.0224	0.9303	1.3559	0.9658	1.0449	0.9726	0.8485
g Ruminococcus	0.9800	1.0557	0.9823	1.1501	0.9610	1.2347	0.9748	1.2095
g Ruminococcus gauvreauii group	0.7477	1.5510	0.8712	0.9596	0.9807	0.7879	0.9312	1.4106

g Ruminococcus gnavus group	0.9636	0.8571	0.9230	3.0243	0.8506	2.2360	0.9789	0.5486
g Ruminococcus torques group	0.0704	0.3241	0.8664	0.7347	0.9313	0.8510	0.9452	0.7663
g Senegalimassilia	0.9356	5.0000	0.9793	2.2041	0.9503	2.3478	0.9740	1.4400
g Streptococcus	0.9700	1.0428	0.9273	0.9482	0.9748	0.8928	0.9651	0.8933
g Subdoligranulum	0.9795	1.0969	0.9828	0.8220	0.9666	0.9939	0.9841	0.8486
g Sutterella	0.9658	0.9882	0.9777	0.7796	0.9805	0.8889	0.9718	0.6369
g Terrisporobacter	0.9764	1.7742	0.9836	1.3272	0.9340	0.2020	0.9595	1.2387
g Turicibacter	0.9690	1.0968	0.9617	1.1060	0.9837	1.5484	0.9122	3.1587
g Tyzzerella	0.9691	1.1205	0.9796	1.2510	0.9805	2.3510	0.9091	0.6477
g UBA1819	0.9279	0.5702	0.9783	1.0226	0.9817	0.5767	0.9773	0.7747
g UCG-002	0.9559	1.0661	0.9710	0.9796	0.9842	0.9031	0.9743	1.3825
g UCG-003	0.9800	1.0298	0.9825	1.0607	0.9203	0.8258	0.9799	1.1158
g UCG-005	0.9595	1.6466	0.9829	0.9311	0.9702	1.0693	0.9838	1.5061
g unclassified c Clostridia	0.9379	0.9588	0.9782	0.9969	0.9649	0.4972	0.9811	0.7398
g unclassified f Enterobacteriaceae	0.9772	1.1148	0.9771	1.7665	0.9575	2.7541	0.9824	1.0859
g unclassified f Lachnospiraceae	0.9786	1.0803	0.9786	1.0297	0.9764	0.7775	0.9812	0.9776
g unclassified f Oscillospiraceae	0.9841	1.0676	0.9298	0.6486	0.8134	0.5076	0.9821	1.5438
g unclassified f Peptostreptococcaceae	0.9624	0.9286	0.9221	2.0991	0.9790	0.9689	0.8313	2.3314
g unclassified f Ruminococcaceae	0.9542	1.5980	0.9819	1.0564	0.9759	0.6036	0.9240	1.8918
g unclassified k norank d Bacteria	0.9675	1.0000	0.9810	0.8802	0.9810	0.7108	0.9648	1.2939
g unclassified o Bacteroidales	0.9803	1.5161	0.9723	0.6320	0.9785	0.5722	0.9832	1.2697
g unclassified o Oscillospirales	0.9777	0.6585	0.9807	0.7646	0.9756	0.4072	0.9265	1.1239
g unclassified p Firmicutes	0.9753	1.9375	0.9839	2.5102	0.9845	0.8478	0.9802	1.3200
g Veillonella	0.7818	2.1064	0.7657	4.0017	0.9596	2.3645	0.9472	1.7668
g Victivallis	0.9709	0.9032	0.9831	0.5688	0.9846	0.7069	0.9830	0.6813

<sup>a</sup>The difference in the relative genus abundance between any intervention group and the placebo group was tested by using Wilcoxon rank-sum test. FDR-adjusted *P* values (Q value) were presented.

<sup>b</sup>The ratio of mean relative genus abundance between interventions group and the placebo group.

**Table S5. Partial correlation between the 4-week change in *Bifidobacterium* abundance and changes in constipation symptoms by group.**

Bacterial genera	Group	r			P value			FDR P value		
		BMF	BSS	DSS	BMF	BSS	DSS	BMF	BSS	DSS
g__Bifidobacterium	A	-0.124	-0.057	0.031	0.411	0.705	0.840	0.832	0.840	0.840
	B	0.133	-0.219	-0.050	0.379	0.145	0.743	0.832	0.832	0.840
	C	0.110	-0.041	-0.108	0.476	0.792	0.485	0.832	0.840	0.832
	D	-0.138	0.058	0.198	0.350	0.695	0.177	0.832	0.840	0.832

Partial spearman correlation was used adjusted for age and gender. BMF: bowel movements per week; BSS: Bristol stool scale score; DDS: degree of defecation straining.

**Table S6: Partial correlations between changes of continuously changed bacterial genera abundance and changes in constipation symptoms.**

Group	Bacterial genera	r			P value			FDR P value		
		BMF	BSS	DSS	BMF	BSS	DSS	BMF	BSS	DSS
A	g__Odoribacter	0.104	-0.234	0.078	0.493	0.118	0.607	0.874	0.708	0.910
	G__UCG-002	-0.083	-0.298	0.107	0.583	<b>0.044</b>	0.479	0.874	0.708	0.910
	g__Eisenbergiella	-0.011	-0.072	0.000	0.944	0.633	0.999	0.950	0.865	0.999
	g__Megamonas	0.044	-0.064	-0.032	0.773	0.673	0.835	0.950	0.865	0.945
B	g__Escherichia-Shigella	-0.230	-0.169	-0.106	0.125	0.262	0.483	0.561	0.770	0.910
	g__Anaerostipes	0.207	-0.008	-0.021	0.168	0.960	0.891	0.604	0.960	0.945
	g__Roseburia	-0.136	-0.009	0.081	0.368	0.952	0.594	0.874	0.960	0.910
	g__NK4A214_group	0.069	0.016	-0.020	0.651	0.914	0.893	0.901	0.960	0.945
C	g__Anaerostipes	0.383	0.015	-0.169	<b>0.010</b>	0.925	0.274	0.183	0.960	0.910
	g__Ruminococcus_gnavus_group	0.258	0.169	0.200	0.091	0.273	0.192	0.561	0.770	0.910
	g__norank_f__norank_o__RF39	-0.014	-0.204	-0.038	0.928	0.185	0.808	0.950	0.770	0.945
D	g__Erysipelatoclostridium	-0.112	0.153	-0.106	0.447	0.300	0.473	0.874	0.770	0.910
	g__norank_f__norank_o__RF39	-0.138	-0.092	0.162	0.350	0.534	0.270	0.874	0.859	0.910
	g__Lachnospiraceae_ND3007_group	0.105	0.247	0.026	0.476	0.090	0.862	0.874	0.708	0.945

Partial spearman correlation was used adjusted for age and gender. Bold *P* value denoted that the correlation was significant. BMF, bowel movements frequency; BSS, Bristol stool scale score; DDS, degree of defecation straining.



**Table S7 The top 10 KEGG pathways and top 10 modules based on PICSRUSt-2 functional profiling from the constantly changed genera.**

Group	Pathway level2		Module	
	Description	Mean abundance	Description	Mean abundance
A	Global and overview maps	60008	Citrate cycle (TCA cycle, Krebs cycle)	858
	Carbohydrate metabolism	16300	Reductive citrate cycle (Arnon-Buchanan cycle)	777
	Amino acid metabolism	10594	Glycolysis (Embden-Meyerhof pathway), glucose => pyruvate	712
	Metabolism of cofactors and vitamins	6579	Histidine biosynthesis, PRPP => histidine	687
	Membrane transport	5694	Citrate cycle, second carbon oxidation, 2-oxoglutarate => oxaloacetate	675
	Energy metabolism	5410	Inosine monophosphate biosynthesis, PRPP + glutamine => IMP	640
	Translation	5129	Pentose phosphate pathway (Pentose phosphate cycle)	516
	Replication and repair	4296	Cobalamin biosynthesis, cobinamide => cobalamin	513
	Nucleotide metabolism	3579	C5 isoprenoid biosynthesis, non-mevalonate pathway	513
	Cellular community - prokaryotes	3024	Shikimate pathway, phosphoenolpyruvate + erythrose-4P => chorismate	512
B	Global and overview maps	59113	Glycolysis (Embden-Meyerhof pathway), glucose => pyruvate	979
	Carbohydrate metabolism	15334	F-type ATPase, prokaryotes and chloroplasts	736
	Amino acid metabolism	9499	Gluconeogenesis, oxaloacetate => fructose-6P	700
	Energy metabolism	6269	Histidine biosynthesis, PRPP => histidine	607
	Metabolism of cofactors and vitamins	6152	Reductive pentose phosphate cycle (Calvin cycle)	576
	Membrane transport	6102	Inosine monophosphate biosynthesis, PRPP + glutamine => IMP	540
	Translation	4773	Reductive citrate cycle (Arnon-Buchanan cycle)	514
	Replication and repair	4204	Pentose phosphate pathway (Pentose phosphate cycle)	512
	Signal transduction	4178	Uridine monophosphate biosynthesis, glutamine (+ PRPP) => UMP	500
	Nucleotide metabolism	3745	Shikimate pathway, phosphoenolpyruvate + erythrose-4P => chorismate	497
C	Global and overview maps	11409	Glycolysis (Embden-Meyerhof pathway), glucose => pyruvate	229
	Carbohydrate metabolism	3743	Gluconeogenesis, oxaloacetate => fructose-6P	165
	Amino acid metabolism	1634	Reductive pentose phosphate cycle (Calvin cycle)	156
	Energy metabolism	1236	Reductive pentose phosphate cycle, glyceraldehyde-3P => ribulose-5P	136
	Membrane transport	1204	F-type ATPase, prokaryotes and chloroplasts	130
	Metabolism of cofactors and vitamins	995	Formaldehyde assimilation, ribulose monophosphate pathway	120
	Translation	774	Pentose phosphate pathway (Pentose phosphate cycle)	108
	Replication and repair	680	Histidine biosynthesis, PRPP => histidine	96
	Nucleotide metabolism	635	Shikimate pathway, phosphoenolpyruvate + erythrose-4P => chorismate	92
	Lipid metabolism	547	Reductive citrate cycle (Arnon-Buchanan cycle)	90

D	Global and overview maps	3807	Glycolysis (Embden-Meyerhof pathway), glucose => pyruvate	68
	Carbohydrate metabolism	979	Inosine monophosphate biosynthesis, PRPP + glutamine => IMP	47
	Amino acid metabolism	636	Gluconeogenesis, oxaloacetate => fructose-6P	44
	Translation	387	Pentose phosphate pathway (Pentose phosphate cycle)	42
	Energy metabolism	371	F-type ATPase, prokaryotes and chloroplasts	41
	Membrane transport	369	Lysine biosynthesis, succinyl-DAP pathway, aspartate => lysine	41
	Metabolism of cofactors and vitamins	361	Glycolysis, core module involving three-carbon compounds	39
	Replication and repair	338	Uridine monophosphate biosynthesis, glutamine (+ PRPP) => UMP	39
	Nucleotide metabolism	278	Shikimate pathway, phosphoenolpyruvate + erythrose-4P => chorismate	37
Signal transduction	231	Reductive pentose phosphate cycle (Calvin cycle)	36	

For each intervention group, the constant changing genera from the soft clustering analysis were used to formulate the ASV's abundant tables. Based on the tables, PICRUST2 software package (version v2.2.0-b) was used to predict the abundance enriched in the Kyoto Encyclopedia of Genes and Genomes (KEGG) module and pathways to infer microbial functional content, respectively.

**Table S8. The top10 KEGG pathways and top10 modules based on PICSRUSt-2 functional profiling for the differential genera predicting responsiveness.**

Constipation symptoms	Group	Pathway level2		Module	
		Description	Mean abundance	Description	Mean abundance
BMF increase > 1	A	Global and overview maps	4698	Glycolysis (Embden-Meyerhof pathway), glucose => pyruvate	75
		Carbohydrate metabolism	1094	Inosine monophosphate biosynthesis, PRPP + glutamine => IMP	51
		Amino acid metabolism	819	Citrate cycle (TCA cycle, Krebs cycle)	50
		Metabolism of cofactors and vitamins	516	Gluconeogenesis, oxaloacetate => fructose-6P	49
		Energy metabolism	474	Reductive citrate cycle (Arnon-Buchanan cycle)	49
		Translation	411	NADH:quinone oxidoreductase, prokaryotes	48
		Replication and repair	348	Histidine biosynthesis, PRPP => histidine	48
		Membrane transport	347	Uridine monophosphate biosynthesis, glutamine (+ PRPP) => UMP	48
		Glycan biosynthesis and metabolism	298	Shikimate pathway, phosphoenolpyruvate + erythrose-4P => chorismate	45
		Nucleotide metabolism	287	Lysine biosynthesis, succinyl-DAP pathway, aspartate => lysine	44
	B	Aging	295	Reductive citrate cycle (Arnon-Buchanan cycle)	857
		Amino acid metabolism	7554	Citrate cycle (TCA cycle, Krebs cycle)	764
		Biosynthesis of other secondary metabolites	1335	Citrate cycle, second carbon oxidation, 2-oxoglutarate => oxaloacetate	723
		Cancer: overview	304	Heme biosynthesis, plants and bacteria, glutamate => heme	500
		Cancer: specific types	96	Histidine biosynthesis, PRPP => histidine	448
		Carbohydrate metabolism	7442	Inosine monophosphate biosynthesis, PRPP + glutamine => IMP	431
		Cardiovascular disease	177	Fumarate reductase, prokaryotes	429
		Cell growth and death	778	Lysine biosynthesis, succinyl-DAP pathway, aspartate => lysine	373
		Cell motility	279	Arginine biosynthesis, glutamate => acetylcitrulline => arginine	357
		Aging	295	Glycolysis (Embden-Meyerhof pathway), glucose => pyruvate	345
	C	Global and overview maps	6045	Glycolysis (Embden-Meyerhof pathway), glucose => pyruvate	93
		Carbohydrate metabolism	1504	Reductive citrate cycle (Arnon-Buchanan cycle)	83
		Amino acid metabolism	1103	Citrate cycle (TCA cycle, Krebs cycle)	69
		Energy metabolism	664	Gluconeogenesis, oxaloacetate => fructose-6P	68
		Metabolism of cofactors and vitamins	655	Inosine monophosphate biosynthesis, PRPP + glutamine => IMP	68
		Translation	523	Histidine biosynthesis, PRPP => histidine	61
		Replication and repair	481	Citrate cycle, second carbon oxidation, 2-oxoglutarate => oxaloacetate	61
		Nucleotide metabolism	442	Uridine monophosphate biosynthesis, glutamine (+ PRPP) => UMP	58

	D	Membrane transport	341	Glycolysis, core module involving three-carbon compounds	54
		Signal transduction	329	F-type ATPase, prokaryotes and chloroplasts	52
		Global and overview maps	15418	Glycolysis (Embden-Meyerhof pathway), glucose => pyruvate	250
		Carbohydrate metabolism	3249	F-type ATPase, prokaryotes and chloroplasts	247
		Amino acid metabolism	2794	Uridine monophosphate biosynthesis, glutamine (+ PRPP) => UMP	191
		Metabolism of cofactors and vitamins	1650	Histidine biosynthesis, PRPP => histidine	188
		Energy metabolism	1514	Gluconeogenesis, oxaloacetate => fructose-6P	162
		Translation	1427	Inosine monophosphate biosynthesis, PRPP + glutamine => IMP	159
		Replication and repair	1218	C5 isoprenoid biosynthesis, non-mevalonate pathway	158
		Nucleotide metabolism	1107	Lysine biosynthesis, succinyl-DAP pathway, aspartate => lysine	156
		Cell motility	1045	Shikimate pathway, phosphoenolpyruvate + erythrose-4P => chorismate	156
		Signal transduction	1040	Lysine biosynthesis, DAP aminotransferase pathway, aspartate => lysine	144
BSS increase >1	Group A	Global and overview maps	8966	Heme biosynthesis, plants and bacteria, glutamate => heme	119
		Carbohydrate metabolism	1766	Reductive citrate cycle (Arnon-Buchanan cycle)	115
		Amino acid metabolism	1625	Cobalamin biosynthesis, cobinamide => cobalamin	110
		Metabolism of cofactors and vitamins	1280	Citrate cycle (TCA cycle, Krebs cycle)	106
		Energy metabolism	933	Citrate cycle, second carbon oxidation, 2-oxoglutarate => oxaloacetate	104
		Translation	814	Glycolysis (Embden-Meyerhof pathway), glucose => pyruvate	97
		Membrane transport	768	Histidine biosynthesis, PRPP => histidine	95
		Replication and repair	685	Inosine monophosphate biosynthesis, PRPP + glutamine => IMP	92
		Nucleotide metabolism	638	Methionine biosynthesis, aspartate => homoserine => methionine	90
	Cellular community - prokaryotes	443	3-Hydroxypropionate bi-cycle	90	
	Group B	None	None		
	Group C	Global and overview maps	16926	Reductive citrate cycle (Arnon-Buchanan cycle)	310
		Carbohydrate metabolism	3847	Glycolysis (Embden-Meyerhof pathway), glucose => pyruvate	277
		Amino acid metabolism	2997	Citrate cycle (TCA cycle, Krebs cycle)	267
		Metabolism of cofactors and vitamins	1914	Citrate cycle, second carbon oxidation, 2-oxoglutarate => oxaloacetate	263
		Energy metabolism	1719	NADH:quinone oxidoreductase, prokaryotes	228
		Translation	1696	Inosine monophosphate biosynthesis, PRPP + glutamine => IMP	222
		Replication and repair	1408	Uridine monophosphate biosynthesis, glutamine (+ PRPP) => UMP	195
		Glycan biosynthesis and metabolism	1218	Gluconeogenesis, oxaloacetate => fructose-6P	181

	Group D	Nucleotide metabolism	1194	Incomplete reductive citrate cycle, acetyl-CoA => oxoglutarate	177
		Lipid metabolism	860	KDO2-lipid A biosynthesis, Raetz pathway, non-LpxL-LpxM type	171
		Global and overview maps	2023	Glycolysis (Embden-Meyerhof pathway), glucose => pyruvate	31
		Carbohydrate metabolism	429	Histidine biosynthesis, PRPP => histidine	25
		Amino acid metabolism	367	Gluconeogenesis, oxaloacetate => fructose-6P	23
		Metabolism of cofactors and vitamins	240	Inosine monophosphate biosynthesis, PRPP + glutamine => IMP	21
		Energy metabolism	206	Lysine biosynthesis, succinyl-DAP pathway, aspartate => lysine	21
		Translation	190	Reductive citrate cycle (Arnon-Buchanan cycle)	20
		Replication and repair	159	Uridine monophosphate biosynthesis, glutamine (+ PRPP) => UMP	20
		Membrane transport	154	Lysine biosynthesis, DAP aminotransferase pathway, aspartate => lysine	19
		Nucleotide metabolism	143	F-type ATPase, prokaryotes and chloroplasts	18
		Cellular community - prokaryotes	113	Shikimate pathway, phosphoenolpyruvate + erythrose-4P => chorismate	18
		DDS decrease >1	Group A	Global and overview maps	39750
Carbohydrate metabolism	9642			Gluconeogenesis, oxaloacetate => fructose-6P	456
Amino acid metabolism	6630			Lysine biosynthesis, succinyl-DAP pathway, aspartate => lysine	449
Membrane transport	4677			F-type ATPase, prokaryotes and chloroplasts	415
Metabolism of cofactors and vitamins	4264			Shikimate pathway, phosphoenolpyruvate + erythrose-4P => chorismate	393
Energy metabolism	4144			Lysine biosynthesis, DAP aminotransferase pathway, aspartate => lysine	390
Translation	3130			Histidine biosynthesis, PRPP => histidine	370
Nucleotide metabolism	2641			Inosine monophosphate biosynthesis, PRPP + glutamine => IMP	366
Replication and repair	2625			Glycolysis, core module involving three-carbon compounds	353
Signal transduction	2207			Uridine monophosphate biosynthesis, glutamine (+ PRPP) => UMP	351
Group B	Global and overview maps		1294	Glycolysis (Embden-Meyerhof pathway), glucose => pyruvate	17
	Carbohydrate metabolism		349	Reductive citrate cycle (Arnon-Buchanan cycle)	17
	Amino acid metabolism		244	Dicarboxylate-hydroxybutyrate cycle	15
	Energy metabolism		129	Gluconeogenesis, oxaloacetate => fructose-6P	12
	Metabolism of cofactors and vitamins		114	Citrate cycle (TCA cycle, Krebs cycle)	12
	Translation		103	Lysine biosynthesis, succinyl-DAP pathway, aspartate => lysine	12
	Membrane transport		102	Histidine biosynthesis, PRPP => histidine	12
	Cellular community - prokaryotes		94	Inosine monophosphate biosynthesis, PRPP + glutamine => IMP	12
	Signal transduction		93	Methionine biosynthesis, aspartate => homoserine => methionine	11

		Replication and repair	91	Shikimate pathway, phosphoenolpyruvate + erythrose-4P => chorismate	11
Group C		Global and overview maps	151634	Glycolysis (Embden-Meyerhof pathway), glucose => pyruvate	2209
		Carbohydrate metabolism	38916	F-type ATPase, prokaryotes and chloroplasts	1751
		Amino acid metabolism	25304	Histidine biosynthesis, PRPP => histidine	1616
		Metabolism of cofactors and vitamins	16928	Gluconeogenesis, oxaloacetate => fructose-6P	1562
		Membrane transport	16066	Inosine monophosphate biosynthesis, PRPP + glutamine => IMP	1478
		Energy metabolism	14995	Shikimate pathway, phosphoenolpyruvate + erythrose-4P => chorismate	1414
		Translation	12408	Citrate cycle (TCA cycle, Krebs cycle)	1378
		Replication and repair	10519	Lysine biosynthesis, succinyl-DAP pathway, aspartate => lysine	1343
		Nucleotide metabolism	9444	Reductive citrate cycle (Arnon-Buchanan cycle)	1328
		Signal transduction	8730	Uridine monophosphate biosynthesis, glutamine (+ PRPP) => UMP	1320
Group D		Global and overview maps	14851	Reductive citrate cycle (Arnon-Buchanan cycle)	219
		Carbohydrate metabolism	4318	Citrate cycle (TCA cycle, Krebs cycle)	214
		Amino acid metabolism	2913	Glycolysis (Embden-Meyerhof pathway), glucose => pyruvate	203
		Energy metabolism	1504	V/A-type ATPase, prokaryotes	184
		Membrane transport	1340	Pyruvate oxidation, pyruvate => acetyl-CoA	184
		Metabolism of cofactors and vitamins	1219	Citrate cycle, second carbon oxidation, 2-oxoglutarate => oxaloacetate	158
		Signal transduction	1193	Histidine biosynthesis, PRPP => histidine	138
		Translation	1016	Gluconeogenesis, oxaloacetate => fructose-6P	137
		Replication and repair	998	Inosine monophosphate biosynthesis, PRPP + glutamine => IMP	136
		Cellular community - prokaryotes	955	Dicarboxylate-hydroxybutyrate cycle	131

For each intervention group, the genera from the top 10 in each model with significant difference between the responders and the non-responders were used to formulate the ASV's abundant tables. Based on the tables, PICRUST2 software package (version v2.2.0-b) was used to predict the abundance enriched in the Kyoto Encyclopedia of Genes and Genomes (KEGG) module and pathways.

**Table S9 Dietary and lifestyle counselling materials**

1. Core recommendations of dietary guidelines for the general population
(a) Eat a variety of foods, cereal based (b) Be active to maintain a healthy body weight (c) Eat plenty of vegetables, fruits, dairy, and soybeans (d) Enjoy fish, poultry, eggs, and lean meats in moderate amounts (e) Limit table salt, cooking oil, added sugar, and alcohol (f) Develop healthy eating habits, avoid food waste
2. Increase water intake Keep water intake between 1.5 and 2.0 L/d.
3. Regular exercise Exercise 30~60 min/occasion, at least two times/week.
4. Keep a good bowel habit Try defecation right after getting up in the morning or within two hours after breakfast. The squat defecation position would make defecation easier. In addition, try to avoid interruption by factors unrelated to defecation when going to the toilet and keep a good defecation habit.
5. Basic knowledge of prebiotics and probiotics. Prebiotics are substances that can be selectively utilized by host microorganisms to bring health benefits, with dietary fiber being the most common one. The water-holding capacity of dietary fiber increases the faecal volume. Its fermentability increases the faecal weight and stimulates defecation by optimizing the microflora, thereby relieving constipation. Dietary fiber promotes the growth of intestinal probiotics to facilitate the maintain of intestinal immune function. Probiotics are live microorganisms that, when ingested in adequate amounts, confer health benefits on the host. The functions of probiotics include maintaining the normal intestinal flora and inhibiting pathogenic bacteria, improving and maintaining the intestinal function, involved in the nutrient metabolism of the body, regulating the immune system function, regulating endocrine system, and neuropsychiatric health.

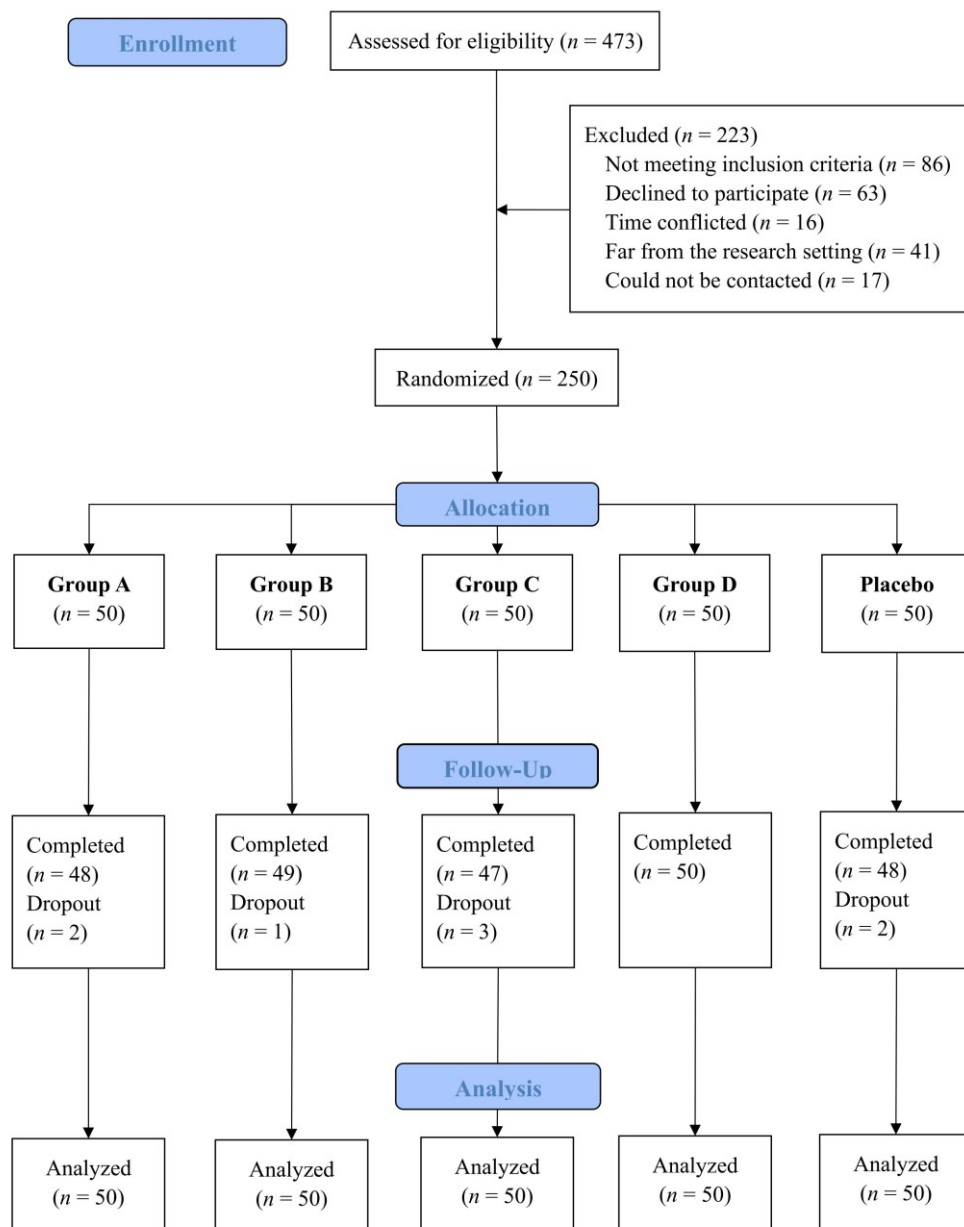
**Table S10 Assessment and analyses details of gut microbiota**

Content	Description
16S rRNA sequencing	DNA was extracted from stool samples (200 mg) using QIAamp DNA Stool Mini Kit (Qiagen, Hilden, Germany) following the manufacturer's instructions, with additional homogenized steps in a bead beater (FastPrep, Thermo Electron Co, Boston, Massachusetts, USA). The V3-V4 hypervariable regions of the bacteria 16S rRNA gene were amplified with primers 338F (5'-ACTCCTACGGGAGGCAGCAG-3') and 806R (5'-GGACTACHVGGGTWTCTAAT-3') by thermocycler PCR system (GeneAmp 9700, ABI, USA). The purified amplicons were pooled in equimolar and paired-end sequenced ( $2 \times 300$ ) using an Illumina MiSeq platform (Illumina, San Diego, California, USA) according to the standard protocols by Majorbio Bio-Pharm Technology Co. Ltd. (Shanghai, China).
Soft clustering and functional annotation	To identify changing trends of gut microbiota in each intervention group over three stages (week 0, 2, and 4), soft clustering analysis was used for its accuracy and robustness to noise and less information loss using the fuzzy c-means algorithm with time-course data by applying the R package " <i>Mfuzz</i> " <sup>1,2</sup> . For each group over the three stages, several clusters were identified, including continuous increase, continuous decrease, increase-decrease, decrease-increase, and no obvious change with selected parameters (minimum SD = 0, membership value = 0.65, and c optimal = 8). For each intervention group, the mean abundance values of genera that fit the continuous increase or decrease clusters were subsequently used to calculate log <sub>2</sub> fold changes from week 0 to week 2 or 4 per predefined research interests. Herein the log <sub>2</sub> fold changes of genera were presented only if they were exclusively identified in the intervention groups but not in the placebo group. For each intervention group, the constant changing genera from the soft clustering analysis were used to formulate ASV's abundant tables. Based on the tables, PICRUSt2 (version v2.2.0-b) was used to predict the abundance enriched in the Kyoto Encyclopedia of Genes and Genomes (KEGG) module and pathways to infer microbial functional content, respectively. The correlations between the changes in continuously increased/decreased bacterial genera and the changes in constipation symptoms (BMF, BSS, DDS) were analyzed by spearman partial rank correlation. Age and sex-adjusted mean general change levels of particular interest were presented by the relief level of constipation symptom, using general linear model in the R package "emmeans".



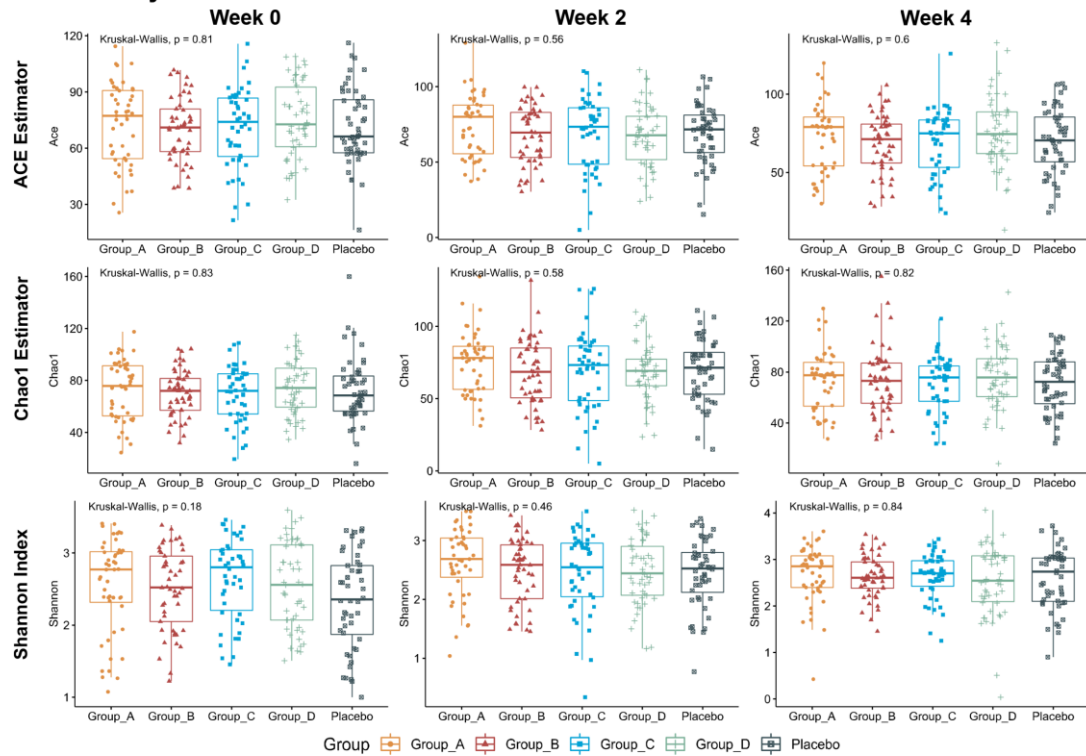
<p>Random forest models and functional annotation</p>	<p>In order to explore the predictive performance of microbiota profiles in responders and non-responders in each intervention group, we defined responders for three scenarios: 1) <math>\geq 1</math> increase in BMF; 2) <math>\geq 1</math> increase in BSS score; 3) <math>\geq 1</math> decrease in DDS. Random forests analysis was used to determine genus-level gut microbiota patterns predicting responders using the R package “<i>caret</i>”. After removing the variable with the variance of 0, 75% of the samples were randomly selected as the training set and the hold-out set was used to evaluate classification accuracy with 500 repetitions. We calculated the area under the receiver operating characteristics curve (AUC) with the cross-validation error with 10000 bootstraps for confidence intervals using the R package “<i>pROC</i>”. The differences between responders and non-responders for the top 10 genera in each model were compared using Wilcoxon signed-rank test. For each intervention group, the genera from the top 10 in each model with significant differences between the responders and the non-responders were used to formulate KEGG module and pathways.</p>
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1. Kumar L, M EF. Mfuzz: a software package for soft clustering of microarray data. *Bioinformatics* 2007;2(1):5-7. doi: 10.6026/97320630002005 [published Online First: 20070520]
2. Futschik ME, Carlisle B. Noise-robust soft clustering of gene expression time-course data. *J Bioinform Comput Biol* 2005;3(4):965-88. doi: 10.1142/s0219720005001375

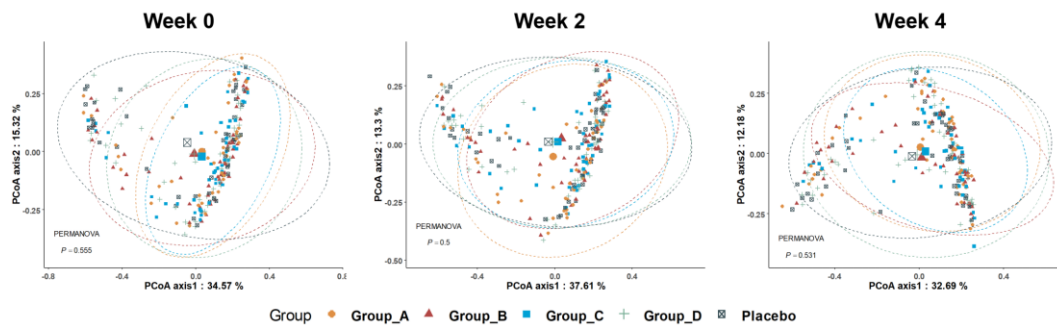


**Figure S1 Study flow.**

## A $\alpha$ -diversity



## B PCoA on Genus level



**Figure S2. Microbiota diversity in each stage by group.**

A,  $\alpha$ -Diversity at genus level estimated by Ace, Chao 1, and Shannon estimator. B, PCoA score plots with  $P$  values for PERMANOVA (Permutational multivariate analysis of variance) based on Bray-Curtis distance at genus level.