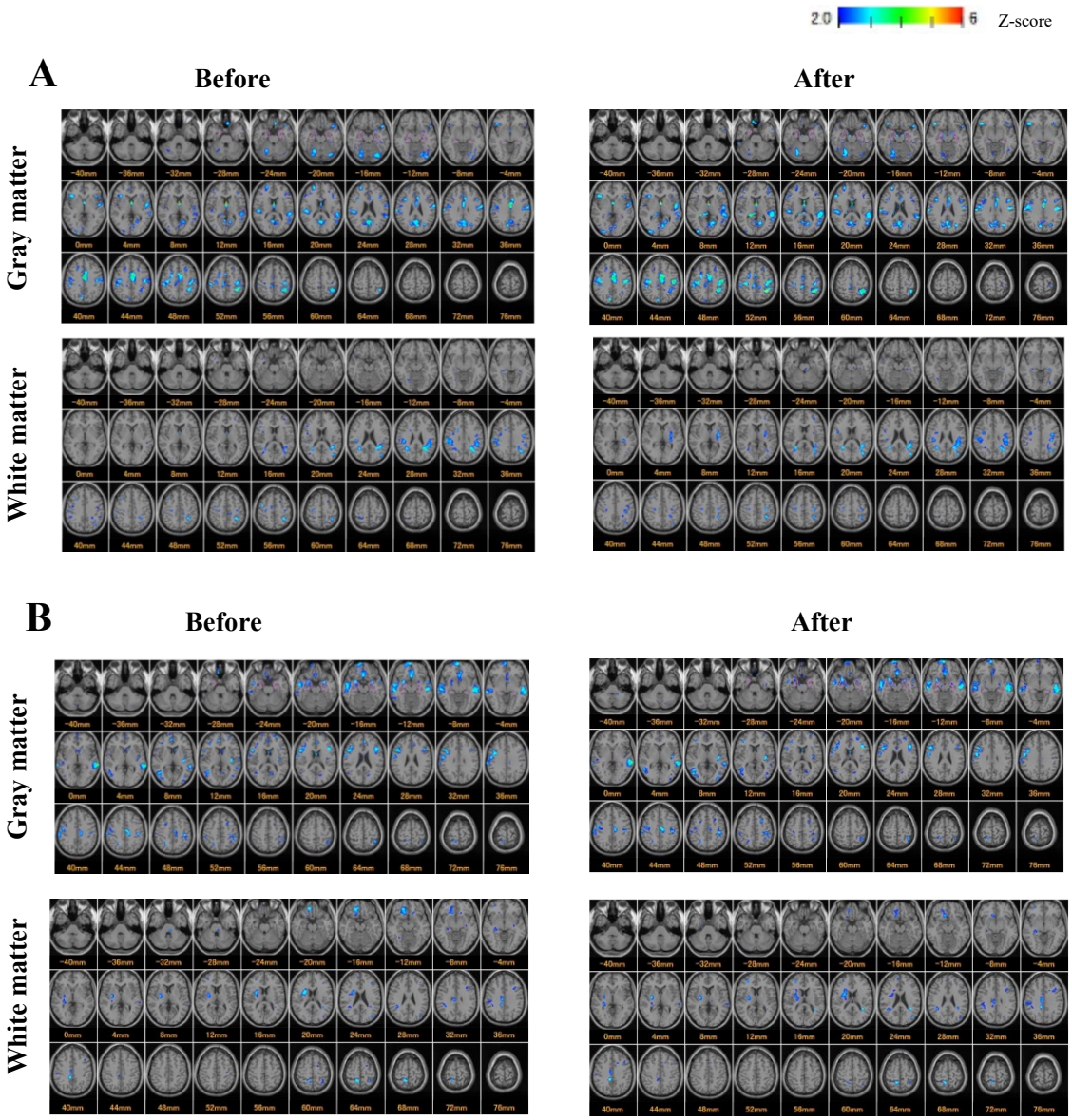
Supplementary Material

Effect of Probiotic *Bifidobacterium breve* in Improving Cognitive Function and Preventing Brain Atrophy in Older Patients with Suspected Mild Cognitive Impairment: Results of a 24-Week Randomized, Double-Blind, Placebo-Controlled Trial



Supplementary Figure 1. Examples of a subject's gray and white matter transition regions demonstrated in the color-coded voxels in the placebo group (A) and probiotic group (B). The top 12 images show gray matter, and bottom 12 images show white matter in the horizontal plane for an individual in each group. The color from blue to red indicates increased degree of gray and white matter.

Supplementary Table 1. Changes of blood parameters during the intervention period

	Visit 1 (week 0)			Visit 2 (Week 8)			Visit 3 (Week 16)			Visit 4 (Week 24)		
	Probiotics	Placebo	p	Probiotics	Placebo	p	Probiotics	Placebo		Probiotics	Placebo	p
ALP (units/L)	242.3 (77.6)	259.6 (121)	0.084	233.6 (78.3)	256.5 (116.8)	0.075	233.4 (82.9)	257.2 (130.8)	0.142	236.2 (76.6)	261.4 (124.1)	0.129
AST (units/L)	24 (8.7)	29.4 (15.2)	0.396	25.4 (9.3)	26.6 (12.2)	0.396	26.2 (9.4)	26.3 (12.4)	0.566	26.2 (8.5)	30.9 (28)	0.596
ALT (units/L)	17.3 (9)	23.3 (18.2)	0.753	18.7 (11.3)	18.5 (10.4)	0.751	19.5 (11.7)	18.5 (10.7)	0.713	18.9 (10.2)	25.8 (46.3)	0.787
LDH (units/L)	198.6 (35.9)	203.4 (35)	0.374	201.2 (34.5)	201 (38.6)	0.225	206.4 (36.6)	199.8 (38.6)	0.259	204.2 (29.9)	205.9 (36.5)	0.211
γ-GTP (units/L)	35.6 (34)	33.7 (34.7)	0.025	37.1 (35.3)	34.8 (55.5)	0.567	37.6 (42.9)	37.5 (68.7)	0.937	36.9 (31.8)	40.5 (59.9)	0.250
Total-Bil (mg/dL)	0.7 (0.2)	0.7 (0.3)	0.033	0.8 (0.3)	0.7 (0.3)	0.943	0.8 (0.3)	0.8 (0.3)	0.648	0.8 (0.2)	0.8 (0.3)	0.304
TP (g/dL)	7.1 (0.5)	7.1 (0.4)	0.482	7.1 (0.7)	7 (0.4)	0.971	7.1 (0.6)	7 (0.4)	0.361	7.1 (0.8)	7.1 (0.4)	0.795
Alb (g/dL)	4.2 (0.3)	4.2 (0.3)	0.775	4.2 (0.3)	4.1 (0.3)	0.796	4.2 (0.3)	4.1 (0.3)	0.990	4.2 (0.3)	4.2 (0.3)	0.699
A/G	1.5 (0.3)	1.4 (0.3)	0.886	1.5 (0.3)	1.5 (0.3)	0.774	1.5 (0.3)	1.5 (0.3)	0.670	1.5 (0.3)	1.5 (0.3)	0.493
BUN (mg/dL)	19.3 (6)	18.6 (4.9)	0.755	19.2 (6.8)	18.2 (4.3)	0.308	18.9 (5.5)	18.3 (5.3)	0.392	19 (7.9)	18.1 (5.3)	0.856
Creatinine (mg/dL)	0.8 (0.4)	0.8 (0.3)	0.396	0.8 (0.4)	0.8 (0.3)	0.246	0.8 (0.3)	0.8 (0.3)	0.241	0.9 (0.4)	0.8 (0.3)	0.831
e-GFR (ml/min)	65.4 (18)	63.9 (18.1)	0.080	63.8 (18.2)	62 (17.1)	0.548	64 (18.1)	64.2 (19.7)	0.409	64.4 (20.9)	62.1 (16.8)	0.850
Blood-glucose (mg/dL)	115.3 (29.6)	116.3 (28.5)	0.524	113.4 (28)	116.9 (30)	0.320	119.7 (34.8)	112.2 (29.1)	0.550	115.6 (30.1)	116.5 (34.3)	0.522
Uric acid (mg/dL)	5.2 (1.3)	5.4 (1.2)	0.260	5.2 (1.3)	5.4 (1.2)	0.107	5.3 (1.5)	5.4 (1.2)	0.136	5.3 (1.3)	5.4 (1.1)	0.681
Lipase (U/L)	42.1 (20.3)	44.3 (16.9)	0.305	44.5 (29.5)	42.4 (14.6)	0.606	41.4 (22.2)	44 (19)	0.631	41.1 (24)	41.9 (13.8)	0.964
Amylase (U/L)	101.4 (42.2)	109.2 (64.1)	0.784	103.9 (59.8)	101.6 (52.2)	0.740	99.7 (46.2)	106.7 (65.4)	0.725	106 (64.9)	109.3 (81.2)	0.682
Fe (μg/dL)	83.3 (27.5)	88.9 (32.8)	0.455	87.8 (32.7)	83.7 (31.6)	0.834	87.9 (35.6)	86.9 (32.3)	0.521	84 (30.4)	94.1 (31.1)	0.819
ferritin (ng/ml)	143.9 (136.4)	172 (150.2)	0.819	145.6 (137.1)	165.4 (155.5)	0.341	159.4 (161.4)	179.3 (162.1)	0.285	162 (159.1)	176 (154.1)	0.701
HDL-Cholesterol (mg/dL)	66.1 (19.6)	62.8 (15.8)	0.473	66.1 (20.5)	61.4 (15)	0.510	65.5 (19.5)	61.7 (16.8)	0.752	66.6 (20.9)	63.2 (16.8)	0.666
LDL-Cholesterol (mg/dL)	112.4 (27.5)	108.4 (27.6)	0.460	109.3 (28.7)	105.7 (25)	0.478	108.9 (28.1)	105.2 (26.8)	0.819	109.1 (29.3)	104.8 (29.4)	0.537
LDL/HDL	1.9 (0.7)	1.8 (0.7)	0.522	1.8 (0.7)	1.8 (0.6)	0.628	1.8 (0.7)	1.8 (0.7)	0.521	1.8 (0.7)	1.8 (0.6)	0.818
Triglyceride (mg/dL)	152.6 (75.6)	130.4 (66.6)	0.341	141.5 (83.5)	132 (60)	0.171	139.4 (70.6)	132.2 (69.6)	0.280	146 (75.1)	122.4 (67.3)	0.347
HbA1c (%)	5.8 (0.5)	5.9 (0.7)	0.456	5.8 (0.5)	5.8 (0.7)	0.480	5.9 (0.6)	5.8 (0.7)	0.482	5.9 (0.7)	5.8 (0.6)	0.446
hsCRP (mg/l)	1156.4 (1595.5)	1916.6 (5205.6)	0.915	1568.3 (3324.8)	1673.4 (3522.4)	0.923	2405.1 (5918.9)	3079.9 (7170.6)	0.946	4950.5 (19402.3)	1115.9 (1426.8)	0.729

Values are indicated as mean (SD). p values are by Student's t test for inter-group differences.

Supplementary Table 2. Correlation of Cognitive Test Scores with VSRAD Scores

	VOI Z-score		GM extent		VOI extent		Ratio	
	ρ	p	ρ	p	ρ	p	ρ	p
ADAS-cog total score	0.254	0.016	0.283	0.007	0.281	0.008	0.213	0.045
Word recall	0.227	0.033	0.253	0.017	0.233	0.028	0.177	0.098
Spoken language ability	NA	NA	NA	NA	NA	NA	NA	NA
Comprehension of spoken language	NA	NA	NA	NA	NA	NA	NA	NA
Word-finding difficulty	-0.061	0.571	0.126	0.238	-0.022	0.839	-0.050	0.639
Following commands	0.121	0.258	0.139	0.195	0.129	0.228	0.092	0.393
Naming	-0.181	0.09	-0.004	0.969	-0.164	0.125	-0.164	0.125
Constructions	-0.104	0.332	0.028	0.795	-0.082	0.446	-0.099	0.356
Ideational praxis	0.129	0.228	0.124	0.247	0.206	0.053	0.182	0.087
Orientation	0.397	0.000	0.384	0.000	0.399	0.000	0.336	0.001
Word recognition	0.113	0.293	-0.012	0.913	0.107	0.317	0.091	0.395
Recall of test instructions	-0.055	0.61	-0.111	0.3	-0.080	0.459	-0.079	0.459
MMSE total score	-0.172	0.107	-0.146	0.172	-0.213	0.045	-0.200	0.061
Orientation in time	-0.269	0.011	-0.258	0.015	-0.256	0.016	-0.228	0.032
Orientation in place	0.012	0.912	-0.006	0.952	-0.037	0.733	-0.050	0.644
Registration	0.073	0.499	-0.100	0.353	0.064	0.549	0.087	0.416
Serial-7 s	0.127	0.235	0.015	0.889	0.101	0.344	0.112	0.296
Recall	-0.238	0.024	-0.051	0.632	-0.255	0.016	-0.262	0.013
Naming	NA	NA	NA	NA	NA	NA	NA	NA
Repetition	-0.059	0.584	-0.042	0.693	-0.057	0.594	-0.041	0.7
Three-stage command	0.006	0.955	0.047	0.659	0.002	0.983	-0.016	0.881
Reading	0.145	0.174	-0.120	0.261	0.120	0.261	0.131	0.222
Writing	0.073	0.499	0.106	0.325	0.066	0.536	0.024	0.825
Construction	0.003	0.974	-0.048	0.652	0.015	0.892	0.053	0.619
mMMSE total score	-0.212	0.046	-0.103	0.339	-0.246	0.02	-0.245	0.021

Correlation (ρ and p) are by Spearman analysis at baseline.

VSRAD, Voxel-based Specific Regional Analysis System for Alzheimer's Disease; VOI, volume of interest; GM, gray matter atrophy in the whole brain; Ratio, VOI extent/GM extent.

Supplementary Table 3. Subgroup Analysis of Gut Microbiota by Baseline MMSE Scores

	MMSE ≥ 25		MMSE < 25			
	Median (IQR)		Median (IQR)		p	qe
Phylum						
Actinobacteria	2.04	(0.56-6.63)	0.7	(0.29-3.27)	0.006	0.067
Bacteroidetes	37.32	(27.21-44.99)	37.31	(29.94-46.46)	0.492	0.950
Firmicutes	55.24	(44.53-61.36)	50.79	(46.08-64.19)	0.825	0.974
Proteobacteria	2.73	(1.39-6.85)	2.97	(1.15-6.7)	0.936	0.974
Fusobacteria	0	(0-0.34)	0	(0-0.01)	0.067	0.400
Verrucomicrobia	0	(0-0.11)	0	(0-0.05)	0.633	0.950
Genus						
Bifidobacterium	1.87	(0.4-6.49)	0.55	(0.18-3.15)	0.006	0.182
Bacteroides	29.58	(14.71-39.79)	22.57	(13.18-33.46)	0.105	0.677
Parabacteroides	1.68	(0.58-2.78)	1.28	(0.6-2.31)	0.407	0.843
Prevotella	0	(0-0.03)	0	(0-14.83)	0.009	0.182
Rikenellaceae|g__	0.8	(0.02-1.5)	0.69	(0.13-1.81)	0.537	0.908
f__S24-7|g__	0	(0-0)	0	(0-0.03)	0.152	0.677
[Barnesiellaceae]|g__	0	(0-0.23)	0	(0-0.61)	0.200	0.677
Paraprevotella	0	(0-0)	0	(0-0)	0.237	0.677
[Prevotella]	0	(0-0)	0	(0-0)	0.198	0.677
Bacillus	0	(0-0)	0	(0-0.24)	0.190	0.677
Lactobacillales|f__|g__	0	(0-0)	0	(0-0)	0.385	0.843
Enterococcus	0	(0-0.04)	0	(0-0)	0.653	0.908
Lactobacillus	0.03	(0-0.47)	0.04	(0-0.6)	0.889	0.962
Leuconostocaceae|g__	0	(0-0)	0	(0-0)	0.205	0.677
Streptococcus	2.31	(0.6-5.69)	1.87	(0.2-6.37)	0.405	0.843
Turicibacter	0	(0-0.17)	0	(0-0.21)	0.827	0.962
Clostridiales|__|__	0.38	(0.08-1.01)	0.48	(0.2-1.43)	0.283	0.773
Clostridiales|f__|g__	0.12	(0-0.43)	0.19	(0-0.53)	0.592	0.908
Christensenellaceae|g__	0	(0-0.11)	0	(0-0.21)	0.817	0.962
Clostridiaceae|g__	0	(0-0.19)	0.11	(0-0.9)	0.007	0.182
Clostridium	0.26	(0.04-0.62)	0.23	(0-0.54)	0.346	0.843
Lachnospiraceae|__	0.88	(0.3-1.56)	1.14	(0.58-1.73)	0.175	0.677
Lachnospiraceae|g__	3.67	(2.12-4.81)	3.4	(2.33-5.21)	0.753	0.949
Anaerostipes	0.12	(0-0.29)	0.08	(0-0.32)	0.657	0.908
Blautia	4.5	(3.2-6.22)	3.54	(2.59-5.43)	0.194	0.677
Coprococcus	2.01	(0.76-3.46)	1.45	(0.95-3.17)	0.936	0.962
Dorea	0.51	(0.19-0.98)	0.54	(0.28-0.74)	0.946	0.962
Epulopiscium	0	(0-0)	0	(0-0)	0.608	0.908
Lachnobacterium	0	(0-0)	0	(0-0)	0.370	0.843
Lachnospira	1.39	(0.39-2.56)	1.59	(0.53-2.64)	0.627	0.908
Roseburia	3.1	(1.04-6.07)	3.44	(0.66-6.08)	0.913	0.962
[*Ruminococcus*]	1.4	(0.74-2.47)	1.81	(0.87-3.3)	0.321	0.839

Ruminococcaceae|__	0.29	(0-1.14)	0.38	(0.07-1.05)	0.851	0.962
Ruminococcaceae|g__	0.57	(0.23-1.16)	0.88	(0.46-2.04)	0.044	0.532
Faecalibacterium	7.23	(3.54-13.35)	9.65	(4.03-14.51)	0.229	0.677
Gemmiger	0.37	(0-1.65)	0.24	(0-1.22)	0.382	0.843
Oscillospira	0.62	(0.36-1.12)	0.55	(0.28-1.15)	0.650	0.908
Ruminococcus	3.47	(0.16-6.91)	1.97	(0.27-5.91)	0.591	0.908
Acidaminococcus	0	(0-0.07)	0	(0-0.02)	0.706	0.942
Dialister	0	(0-0.52)	0	(0-0.76)	0.580	0.908
Megamonas	0	(0-0)	0	(0-0)	0.656	0.908
Megasphaera	0	(0-0)	0	(0-0)	0.597	0.908
Mitsuokella	0	(0-0)	0	(0-0)	0.933	0.962
Phascolarctobacterium	0.18	(0-0.58)	0.38	(0.06-0.73)	0.041	0.532
Veillonella	0.05	(0-0.43)	0	(0-0.18)	0.186	0.677
Erysipelotrichaceae|__	0.04	(0-0.25)	0	(0-0.15)	0.189	0.677
Erysipelotrichaceae|g__	0	(0-0.03)	0	(0-0.34)	0.137	0.677
Catenibacterium	0	(0-0)	0	(0-0)	0.666	0.908
[*Eubacterium*]	0.03	(0-0.63)	0.06	(0-0.54)	0.433	0.865
Fusobacterium	0	(0-0.34)	0	(0-0)	0.060	0.539
o__RF32|f__|g__	0	(0-0)	0	(0-0)	0.995	0.995
Sutterella	0.83	(0.18-1.53)	0.66	(0.06-1.35)	0.558	0.908
Bilophila	0.06	(0-0.2)	0.08	(0-0.15)	0.867	0.962
Enterobacteriaceae|__	0	(0-0.33)	0	(0-0.08)	0.849	0.962
Citrobacter	0	(0-0)	0	(0-0)	0.063	0.539
Escherichia	0.05	(0-0.41)	0.09	(0-0.41)	0.770	0.949
Klebsiella	0	(0-0.11)	0	(0-0.03)	0.775	0.949
Serratia	0	(0-0)	0	(0-0)	0.219	0.677
Haemophilus	0	(0-0.2)	0	(0-0.11)	0.762	0.949
Akkermansia	0	(0-0.11)	0	(0-0.05)	0.602	0.908

Data are indicated as mean (interquartile range, IQR) of relative abundance. P value, intergroup difference (Wilcoxon rank sum test). Q value is a p value that has been adjusted for the False Discovery Rate (FDR).

Supplementary Table 4. Gut Microbiota composition

	Probiotic						Placebo					
	Baseline		Week 24				Baseline		Week 24			
	Median (IQR)		Median (IQR)		p	q	Median (IQR)		Median (IQR)		p	q
Phylum												
Actinobacteria	1.82	(0.47-4.31)	2.08	(0.48-4.39)	0.418	0.746	1.44	(0.35-4.88)	1.69	(0.38-6.32)	0.611	1.000
Bacteroidetes	38.94	(32.95-44.68)	39.28	(31.5-47.14)	0.836	0.746	37.17	(26.01-47.07)	36.78	(29.93-43.66)	0.596	1.000
Firmicutes	53.59	(44.48-59.83)	49.67	(40.31-58.45)	0.441	0.455	55.53	(45.85-64.57)	51.39	(43.94-59.82)	0.083	1.000
Proteobacteria	2.97	(1.15-8.5)	2.62	(1.26-6.99)	0.891	0.746	2.94	(1.25-6.04)	2.71	(1.41-6.63)	0.355	1.000
Fusobacteria	0	(0-0.43)	0	(0-0.33)	0.686	0.746	0	(0-0.03)	0	(0-0)	0.463	1.000
Verrucomicrobia	0	(0-0.16)	0	(0-0.13)	0.396	0.746	0	(0-0.07)	0	(0-0)	0.399	1.000
Genus												
Bifidobacterium	1.51	(0.34-4.1)	1.99	(0.38-4.14)	0.467	0.948	1.33	(0.2-4.72)	1.58	(0.25-5.65)	0.358	1.000
Bacteroides	29.59	(20.07-37.86)	29.3	(22.27-38.18)	0.961	0.948	22.83	(7.53-32.98)	25.11	(15.41-33.63)	0.538	1.000
Parabacteroides	1.68	(0.45-2.98)	1.52	(0.19-2.71)	0.904	0.948	1.2	(0.44-1.84)	1.54	(0.79-2.5)	0.152	1.000
Prevotella	0	(0-3.03)	0	(0-0.88)	0.824	1.000	0	(0-2.4)	0	(0-6.8)	1.000	1.000
Rikenellaceae|g__	1.18	(0.19-2.02)	0.74	(0.13-2.52)	0.946	0.948	0.42	(0.06-1.38)	0.5	(0.07-1.8)	0.484	1.000
f__S24-7|g__	0	(0-0)	0	(0-0)	0.791	0.948	0	(0-0)	0	(0-0)	0.726	1.000
[Barnesiellaceae]|g__	0	(0-0.79)	0	(0-0.33)	0.779	0.948	0	(0-0.2)	0	(0-0.11)	0.636	1.000
Paraprevotella	0	(0-0)	0	(0-0)	0.430	0.948	0	(0-0)	0	(0-0)	0.678	1.000
[Prevotella]	0	(0-0)	0	(0-0)	0.625	0.948	0	(0-0)	0	(0-0)	0.500	1.000
Bacillus	0	(0-0.15)	0	(0-0.24)	1.000	0.948	0	(0-0.24)	0	(0-0.18)	0.625	1.000
Lactobacillales|f__|g__	0	(0-0)	0	(0-0)	0.375	0.948	0	(0-0)	0	(0-0)	0.438	1.000
Enterococcus	0	(0-0.03)	0	(0-0)	0.441	0.986	0	(0-0)	0	(0-0)	0.953	1.000
Lactobacillus	0	(0-0.45)	0	(0-0.3)	0.987	0.948	0.04	(0-0.81)	0.05	(0-0.82)	0.691	1.000
Leuconostocaceae|g__	0	(0-0)	0	(0-0)	1.000	0.986	0	(0-0)	0	(0-0)	0.938	1.000
Streptococcus	3.1	(0.59-6.06)	3.56	(0.31-6.34)	0.611	0.948	2.55	(0.34-7.47)	1.06	(0.16-4.76)	0.114	1.000
Turicibacter	0	(0-0.09)	0	(0-0.11)	0.779	0.948	0	(0-0.27)	0	(0-0.16)	0.612	1.000
Clostridiales|__|__	0.44	(0.17-0.97)	0.34	(0.11-0.97)	0.851	0.948	0.49	(0.12-1.51)	0.53	(0.11-1.38)	0.670	1.000
Clostridiales|f__|g__	0.16	(0-0.37)	0.14	(0-0.35)	0.911	0.948	0.12	(0-0.63)	0.2	(0-0.79)	0.689	1.000
Christensenellaceae|g__	0	(0-0.13)	0	(0-0.21)	0.410	0.948	0	(0-0.15)	0	(0-0.14)	0.432	1.000

Clostridiaceae|g__	0	(0-0.21)	0	(0-0.17)	0.723	0.948	0	(0-0.83)	0.05	(0-0.58)	0.680	1.000
Clostridium	0.28	(0.07-0.59)	0.17	(0.06-0.44)	0.182	0.948	0.26	(0-0.55)	0.15	(0-0.4)	0.239	1.000
Lachnospiraceae|__	1.11	(0.41-1.71)	0.95	(0.52-1.29)	0.979	0.948	1.01	(0.51-1.67)	1.06	(0.44-1.51)	0.766	1.000
Lachnospiraceae|g__	3.67	(2.24-5.02)	3.11	(2.02-5.36)	0.353	0.948	3.94	(2.37-5.16)	3.21	(2.26-4.77)	0.516	1.000
Anaerostipes	0.08	(0-0.31)	0.14	(0-0.35)	0.585	0.948	0.11	(0-0.27)	0.13	(0-0.33)	0.348	1.000
Blautia	4.5	(3.24-6.67)	4.67	(2.92-7.59)	0.528	0.948	3.93	(2.54-5.64)	3.53	(2.31-5.3)	0.456	1.000
Coprococcus	2.49	(0.8-3.49)	1.91	(0.6-3.15)	0.281	0.948	1.89	(1.02-3.21)	1.58	(1.07-2.48)	0.465	1.000
Dorea	0.54	(0.26-0.77)	0.51	(0.17-1.01)	0.914	0.948	0.48	(0.19-0.86)	0.51	(0.24-1.28)	0.295	1.000
Epulopiscium	0	(0-0)	0	(0-0)	0.203	0.948	0	(0-0)	0	(0-0)	0.688	1.000
Lachnobacterium	0	(0-0)	0	(0-0)	0.750	0.948	0	(0-0)	0	(0-0)	0.523	1.000
Lachnospira	0.88	(0.39-2.04)	0.66	(0.16-2)	0.572	0.948	1.49	(0.63-3.11)	1.21	(0.02-2.13)	0.090	1.000
Roseburia	2.64	(0.82-5.71)	2.47	(0.59-5.97)	0.647	0.948	3.89	(1.4-6.31)	2.17	(0.6-5.86)	0.101	1.000
[Ruminococcus]	1.95	(1.1-3.61)	1.58	(0.78-3.34)	0.992	0.948	1.31	(0.67-2.22)	1.44	(0.71-2.52)	0.304	1.000
Ruminococcaceae|__	0.26	(0-0.91)	0.3	(0-1.11)	0.607	0.966	0.49	(0.08-1.16)	0.6	(0.08-1.27)	0.863	1.000
Ruminococcaceae|g__	0.81	(0.26-1.5)	0.56	(0.25-1.18)	0.336	0.948	0.6	(0.29-1.32)	0.66	(0.2-1.36)	0.560	1.000
Faecalibacterium	6.63	(1.88-12.86)	7.92	(1.68-12.65)	0.528	0.948	9.67	(6.46-14.59)	7.43	(4.28-13.62)	0.377	1.000
Gemmiger	0	(0-1.1)	0	(0-1.06)	0.791	0.948	0.53	(0-1.5)	0.68	(0-1.49)	0.544	1.000
Oscillospira	0.64	(0.3-1.16)	0.59	(0.21-1.39)	0.783	0.948	0.53	(0.31-1.1)	0.63	(0.24-1.38)	0.579	1.000
Ruminococcus	3.05	(0.27-6.32)	1.53	(0.23-3.61)	0.159	0.966	2.42	(0.18-6.58)	2.75	(0.17-6.18)	0.870	1.000
Acidaminococcus	0	(0-0.25)	0	(0-0.31)	0.958	0.948	0	(0-0)	0	(0-0)	0.799	1.000
Dialister	0.09	(0-1.03)	0	(0-0.99)	0.840	0.948	0	(0-0.42)	0	(0-0.52)	0.822	1.000
Megamonas	0	(0-0)	0	(0-0)	0.846	1.000	0	(0-0)	0	(0-0)	1.000	1.000
Megasphaera	0	(0-0)	0	(0-0)	0.761	0.948	0	(0-0)	0	(0-0)	0.733	1.000
Mitsuokella	0	(0-0)	0	(0-0)	1.000	0.948	0	(0-0)	0	(0-0)	0.813	1.000
Phascolarctobacterium	0.23	(0-0.59)	0.16	(0-0.58)	0.929	0.948	0.21	(0-0.59)	0.24	(0-0.61)	0.576	1.000
Veillonella	0	(0-0.2)	0	(0-0.17)	0.893	0.948	0.09	(0-0.52)	0.02	(0-0.46)	0.765	1.000
Erysipelotrichaceae|__	0.04	(0-0.22)	0	(0-0.24)	0.870	0.948	0	(0-0.13)	0	(0-0.12)	0.811	1.000
Erysipelotrichaceae|g__	0	(0-0)	0	(0-0)	0.893	0.966	0	(0-0.45)	0	(0-0.2)	0.902	1.000
Catenibacterium	0	(0-0)	0	(0-0)	0.641	0.948	0	(0-0)	0	(0-0)	0.720	1.000
[Eubacterium]	0.02	(0-0.2)	0	(0-0.27)	0.830	0.948	0.02	(0-0.57)	0.06	(0-0.7)	0.680	1.000
Fusobacterium	0	(0-0.43)	0	(0-0.33)	0.749	0.948	0	(0-0)	0	(0-0)	0.610	1.000

o__RF32|f__|g__	0	(0-0)	0	(0-0)	0.563	0.948	0	(0-0)	0	(0-0)	0.688	1.000
Sutterella	1.01	(0-1.5)	0.76	(0.04-1.35)	0.345	0.948	0.75	(0.03-1.25)	0.92	(0.26-1.96)	0.308	1.000
Bilophila	0.07	(0-0.19)	0	(0-0.19)	1.000	0.948	0.07	(0-0.15)	0.06	(0-0.19)	0.720	1.000
Enterobacteriaceae|__	0	(0-0.16)	0	(0-0.69)	0.839	0.966	0	(0-0.16)	0	(0-0.22)	0.895	1.000
Citrobacter	0	(0-0)	0	(0-0)	0.734	0.948	0	(0-0)	0	(0-0)	0.641	1.000
Escherichia	0.09	(0-0.45)	0	(0-0.16)	0.219	0.948	0	(0-0.41)	0.13	(0-0.75)	0.328	1.000
Klebsiella	0	(0-0)	0	(0-0)	0.325	0.948	0	(0-0.12)	0	(0-0.28)	0.417	1.000
Serratia	0	(0-0)	0	(0-0)	0.813	0.948	0	(0-0)	0	(0-0)	0.820	1.000
Haemophilus	0	(0-0.09)	0	(0-0.06)	0.634	0.948	0.04	(0-0.24)	0	(0-0.11)	0.027	1.000
Akkermansia	0	(0-0.16)	0	(0-0.13)	0.396	0.948	0	(0-0.07)	0	(0-0)	0.474	1.000

Data are indicated as mean (interquartile range, IQR) of relative abundance. P value, intergroup difference (Wilcoxon rank sum test). Q value is a p value that has been adjusted for the False Discovery Rate (FDR).