Supplementary methods

Lactate

Fifty mg of freeze dried feces was suspended in 800 µl distilled water, and the suspension was incubated at 65° C during 20 minutes. Impurities were removed and fecal lactate was determined in extracts according to the manufacturer's instruction.

Short-chain fatty acids/branch-chain fatty acids

SCFA/BCFA were measured in diethyl ether extracts by gas chromatography using a TRACE^{TM} 7890A flame ionization detector (FID) gas chromatograph and a Zerbon ZB-Was capillary column were used. Nitrogen was used as the carrier gas. Internal standard and orthophosphoric acid (16M) were added to 75 mg of freeze-dried samples. The internal standard was used to correct the losses that occur during handling, extraction and quantification of the samples while the orthophosphoric acid was used to reduce the dissociation constant of the acids, so that it separates from the rest of the sample into the ether phase. The mixture was extracted three times with 1.5 ml of diethyl ether, centrifuged and the supernatant collected. External standards were used for calibration (185.8 µmol/l acetic, 144.4 µmol/l propionic, 97.3 µmol/l isobutyric, 114.1 µmol/l butyric, 87 µmol/l isovaleric, 83.4 µmol/l valeric, 52.6 µmol/l isocaproic, 76.5 µmol/l caproic, 65.7 µmol/l heptanoic, 53.1 µmol/l octanoic, Sigma-Aldrich, UK). All samples coming from the same patient were analyzed at the same run to minimize intra-assay error. An external quality control sample of a mixture of feces samples was run at the beginning of the run and at the end to assure the repeatability of the assay and the intra-assay between the runs.

DNA extraction

Fifty mg of freeze dried feces was suspended in 250 µl of 4M guanidine thiocyanate (Sigma-Aldrich, UK), 0.1M Tris-Cl (pH 7.5) and 40 µl of N-lauroyl sarcosine 10% (Sigma-Aldrich, UK) buffer. After that, 500 µl 5% N-lauroylsarcosine in 0.1 M phosphate buffer (pH 8) was added, and the sample was incubated at 70˚C for 1 hour. Sterile zirconium beads (0.1 mm, BioSpec, USA) were added and the bacterial cells were lysed three times for 60 seconds with a bead beater. Polyvinylpyrrolidone (Sigma-Aldrich, UK) (15 mg) was added to the sample, which was vortexed and centrifuged for 3 min at 15,000 g at 4˚C. The supernatant was collected and the pellet was washed three times with 400 µl TENP (50 mM Tris (pH 8), 20 mM EDTA (pH 8), 100 mM NaCl, 1% polyvinylpolypyrrolidone) and centrifuged for 3 min at 15,000 g and 4˚C each time. Nucleic acids were precipitated by the addition of isopropanol v/v for 10 m room temperature, and centrifuged 5 min at 15,000 g. The pellet was suspended in 225 µl 0.1M phosphate buffer (pH 8) and 25 µl 5M potassium acetate (Sigma-Aldrich, UK) and the sample was left in a fridge overnight. The next day, samples were centrifuged at 15,000 g and 4˚C for 30 minutes, and 5 µl RNAse (10 mg/ml) was added to the supernatant (Sigma-Aldrich, UK). The mixture was incubated at 37˚C for 45 min. SDS 10% (25 µl) and proteinase K (12.5 µl) were added and this mixture was incubated at 45˚C for 2 hours. Afterwards, the DNA was precipitated by the addition of 54 µl sodium acetate (Sigma-Aldrich, UK) and 1 ml of 100% ethanol stored at -20˚C. DNA was recovered after centrifugation at 15,000 g for 15 minutes, washing with 70% ethanol (stored at -20˚C), dried, and suspended in Tris-EDTA buffer.

Bioinformatics

Microbiota composition was analyzed using operational taxonomic units (OTUs) obtained from the 16S rRNA sequencing data and clustered at a level of 97% similarity. OTUs were generated from the raw data using a modified version of the VSEARCH pipeline (https://github.com/torognes/vsearch/wiki/VSEARCH-pipeline) (1). The paired fastq files were merged together and quality filtering was performed with a fastq_maxee (maximum expected error value for merged sequences) parameter of 0.5. Sequences longer than 275bp and shorter than 225bp were filtered out. The files were then combined, dereplicated, and all singleton sequences were removed. Sequences were preclustered at 98%, and chimeras were identified and removed from the dataset using the VSEARCH implementation of the UCHIME de-novo algorithm (2). A secondary chimera detection and removal step was carried out, this time using the UCHIME reference-based method and the 'Gold' ChimeraSlayer reference dataset (3). OTUs were then generated by clustering the remaining sequences at 97%. OTUs were taxonomically classified to genus level using the assignTaxonomy function in the dada2 R package (4).

Data analysis and statistics

For microbiota analysis, non-metric multidimensional scaling (NMDS) ordination was carried out using the phyloseq package in R (5) and permutation ANOVA was performed using the adonis function in the R vegan package (6). These methods used Bray-Curtis distance matrices as input.

Generalized linear mixed models were used to identify relationships between disease characteristics and microbial diversity measures; each model was generated using one variable of interest and the subject's age as explanatory variables with the subject ID included as a random effect. The general linear mixed model analysis was carried out using the lme4 package in R (7). Correlation tests were performed using the cor.test function in R for unpaired data and using the rmcorr function when analyzing repeated measures. Statistics were performed using SPSS version 21 (SPSS, IBM, Armonk) and R version 3.4.3.

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Supplementary Table 1. Differences in relative abundance between IF patients and healthy controls for all samples at OTU level

OTU	p-value	adjusted p-value	Differences in mean log relative abundance
OTU_114_Genus_Faecalibacterium	1.24E-21	2.48E-19	-5.376
OTU_60_Genus_Anaerostipes	1.61E-15	1.61E-13	-4.834
OTU_183_Genus_[Eubacterium] ventriosum group	1.62E-13	1.08E-11	-3.921
OTU_122_Genus_Lachnospiraceae ND3007 group	1.28E-12	6.38E-11	-4.533
OTU_123_Genus_Erysipelotrichaceae UCG-003	2.47E-12	9.88E-11	-3.932
OTU_106_Genus_[Eubacterium] hallii group	9.19E-12	3.06E-10	-3.839
OTU_31_Genus_Faecalibacterium	7.80E-11	2.23E-09	-5.758
OTU_83_Genus_Ruminococcus 1	2.96E-10	7.41E-09	-4.240
OTU_108_Genus_Fusicatenibacter	5.15E-10	1.14E-08	-3.521
OTU_67_Genus_Collinsella	6.07E-10	1.21E-08	-4.688
OTU_48_Genus_Blautia	1.21E-09	1.88E-08	-3.414
OTU_154_Genus_Incertae Sedis	1.26E-09	1.88E-08	-3.659
OTU_57_Genus_Subdoligranulum	1.28E-09	1.88E-08	-4.403
OTU_129_Genus_Lachnospiraceae NC2004 group	1.32E-09	1.88E-08	-3.642
OTU_98_Genus_Lachnospiraceae NK4A136 group	1.56E-09	2.06E-08	-4.216
OTU_204_Genus_Ruminiclostridium	1.65E-09	2.06E-08	-3.983
OTU_63_Genus_Lachnoclostridium	2.58E-09	3.03E-08	-3.677
OTU_55_Genus_Blautia	6.57E-09	7.02E-08	-4.166
OTU_347_Genus_Lachnoclostridium	6.66E-09	7.02E-08	-2.972
OTU_179_Genus_Coprococcus 1	9.14E-09	9.14E-08	-3.053
OTU_191_Genus_Lachnospiraceae UCG-008	1.05E-08	9.95E-08	-3.536
OTU_220_Family_Lachnospiraceae	1.21E-08	1.10E-07	-4.571
OTU_167_Genus_Ruminococcus 1	3.31E-08	2.81E-07	-3.704
OTU_140_Genus_Ruminococcaceae NK4A214 group	3.37E-08	2.81E-07	-3.843
OTU_251_Genus_Ruminiclostridium 9	3.62E-08	2.89E-07	-2.591
OTU_97_Genus_Dorea	5.01E-08	3.86E-07	-3.643
OTU_86_Genus_Parasutterella	7.56E-08	5.60E-07	-3.617
OTU_200_Genus_Roseburia	1.09E-07	7.78E-07	-2.959
OTU_33_Genus_Pseudobutyrivibrio	1.31E-07	9.05E-07	-3.859
OTU_89_Genus_Lachnospira	1.46E-07	9.75E-07	-3.909

OTU_124_Genus_[Ruminococcus] gauvreauii group	2.35E-07	1.52E-06	-3.283
OTU_197_Genus_Enterorhabdus	2.48E-07	1.55E-06	-2.429
OTU_228_Genus_Lachnoclostridium	2.63E-07	1.59E-06	-3.166
OTU_121_Genus_Dorea	3.94E-07	2.32E-06	-3.683
OTU_113_Genus_Lachnoclostridium	4.23E-07	2.42E-06	-4.277
OTU_670_Genus_Alistipes	4.40E-07	2.44E-06	-2.529
OTU_290_Genus_Collinsella	4.78E-07	2.58E-06	-2.608
OTU_41_Genus_Subdoligranulum	5.91E-07	3.11E-06	-3.274
OTU_162_Genus_[Eubacterium] hallii group	9.25E-07	4.74E-06	-3.759
OTU_85_Genus_Lachnospiraceae NK4A136 group	1.07E-06	5.35E-06	-4.381
OTU_65_Genus_Ruminococcaceae UCG-002	1.32E-06	6.43E-06	-3.808
OTU_297_Genus_Lachnospiraceae UCG-001	1.68E-06	8.02E-06	-2.685
OTU_59_Genus_Barnesiella	1.74E-06	8.07E-06	-2.904
OTU_153_Genus_Lachnospiraceae FCS020 group	2.25E-06	1.02E-05	-2.686
OTU_73_Genus_Coprococcus 3	3.22E-06	1.43E-05	-3.335
OTU_943_Class_Bacteroidetes VC2.1 Bac22	3.84E-06	1.67E-05	-2.422
OTU_42_Genus_Ruminococcus 2	4.13E-06	1.76E-05	-4.088
OTU_286_Family_Clostridiales vadinBB60 group	5.17E-06	2.15E-05	-2.397
OTU_272_Genus_Ruminococcaceae UCG-005	5.32E-06	2.17E-05	-2.276
OTU_102_Genus_Odoribacter	5.83E-06	2.33E-05	-3.728
OTU_82_Genus_Bacteroides	7.78E-06	3.05E-05	-3.502
OTU_78_Genus_Blautia	8.43E-06	3.24E-05	-2.958
OTU_77_Genus_Ruminococcaceae UCG-002	9.43E-06	3.56E-05	-2.811
OTU_74_Genus_Ruminococcaceae UCG-002	1.00E-05	3.68E-05	-3.636
OTU_159_Class_Bacteroidetes VC2.1 Bac22	1.01E-05	3.68E-05	-2.458
OTU_40_Genus_Phascolarctobacterium	1.07E-05	3.81E-05	-3.787
OTU_262_Genus_Ruminococcus 1	1.15E-05	4.02E-05	-2.474
OTU_120_Genus_Ruminiclostridium 6	1.32E-05	4.54E-05	-2.262
OTU_116_Genus_Ruminococcaceae UCG-005	1.53E-05	5.20E-05	-2.697
OTU_13_Genus_Bacteroides	1.62E-05	5.41E-05	-3.985
OTU_252_Genus_Gordonibacter	2.46E-05	8.07E-05	-2.392
OTU_119_Genus_Ruminococcus 1	2.53E-05	8.07E-05	-2.973
OTU_146_Genus_Intestinibacter	2.54E-05	8.07E-05	-2.337

OTU_239_Genus_Terrisporobacter	2.96E-05	9.25E-05	-2.204
OTU_185_Genus_Senegalimassilia	3.28E-05	1.01E-04	-2.386
OTU_110_Genus_Alistipes	3.38E-05	1.02E-04	-2.868
OTU_194_Genus_Butyricimonas	3.72E-05	1.11E-04	-2.619
OTU_201_Family_Lachnospiraceae	4.07E-05	1.20E-04	-2.742
OTU_142_Genus_[Eubacterium] coprostanoligenes group	4.34E-05	1.26E-04	-2.874
OTU_1049_Genus_Lachnospiraceae NC2004 group	4.57E-05	1.30E-04	-2.221
OTU_75_Family_Ruminococcaceae	4.62E-05	1.30E-04	-2.726
OTU_26_Genus_Blautia	5.64E-05	1.57E-04	-3.538
OTU_327_Genus_Lachnospiraceae NC2004 group	5.88E-05	1.59E-04	-2.168
OTU_100_Genus_Coprococcus 2	5.94E-05	1.59E-04	-2.666
OTU_189_Genus_Ruminococcaceae UCG-013	5.94E-05	1.59E-04	-1.963
OTU_221_Genus_Alistipes	6.08E-05	1.60E-04	-1.906
OTU_71_Genus_Blautia	6.46E-05	1.68E-04	-3.997
OTU_324_Genus_Ruminiclostridium 9	6.83E-05	1.75E-04	-2.231
OTU_14_Genus_Staphylococcus	8.67E-05	2.19E-04	4.025
OTU_145_Genus_Bacteroides	9.58E-05	2.39E-04	-2.573
OTU_68_Genus_Ruminococcaceae UCG-005	1.24E-04	3.06E-04	-3.264
OTU_203_Genus_Ruminiclostridium 6	1.63E-04	3.98E-04	-2.068
OTU_173_Genus_Lachnospiraceae NK4A136 group	1.70E-04	4.10E-04	-1.718
OTU_205_Genus_Alistipes	1.80E-04	4.28E-04	-2.029
OTU_125_Genus_Ruminococcaceae UCG-003	2.15E-04	5.06E-04	-2.768
OTU_64_Genus_Ruminococcus 1	2.90E-04	6.74E-04	-3.283
OTU_49_Genus_Roseburia	2.95E-04	6.77E-04	-3.480
OTU_105_Genus_Lachnospiraceae UCG-003	3.91E-04	8.83E-04	-2.160
OTU_152_Genus_Christensenellaceae R-7 group	3.93E-04	8.83E-04	-2.732
OTU_32_Genus_Bacteroides	4.22E-04	9.38E-04	-2.767
OTU_180_Family_Coriobacteriaceae	4.64E-04	1.02E-03	-1.553
OTU_24_Genus_Bifidobacterium	5.24E-04	1.14E-03	-2.802
OTU_56_Genus_Alistipes	6.25E-04	1.33E-03	-3.169
OTU_259_Genus_Ruminococcus 1	6.26E-04	1.33E-03	-1.943
OTU_235_Genus_Lachnospiraceae NK4A136 group	6.47E-04	1.36E-03	-2.154
OTU_3_Genus_Cronobacter	6.96E-04	1.45E-03	3.795

OTU_109_Genus_Anaerostipes	7.27E-04	1.50E-03	-1.813
OTU_70_Genus_Bacteroides	8.72E-04	1.78E-03	-2.301
OTU_93_Genus_Blautia	9.98E-04	2.02E-03	-2.403
OTU_186_Genus_Ruminococcaceae UCG-010	1.05E-03	2.10E-03	-1.729
OTU_229_Genus_Clostridium sensu stricto 1	1.32E-03	2.61E-03	-1.674
OTU_50_Genus_Christensenellaceae R-7 group	1.34E-03	2.63E-03	-2.491
OTU_23_Genus_Alistipes	1.67E-03	3.24E-03	-3.356
OTU_215_Genus_Erysipelatoclostridium	1.68E-03	3.24E-03	-1.661
OTU_198_Genus_Anaerotruncus	1.77E-03	3.37E-03	-1.530
OTU_275_Family_Lachnospiraceae	1.81E-03	3.42E-03	-1.297
OTU_169_Genus_Ruminococcus 1	1.87E-03	3.50E-03	-1.233
OTU_250_Genus_Oscillibacter	2.43E-03	4.50E-03	-1.806
OTU_134_Genus_Ruminococcaceae UCG-005	2.49E-03	4.57E-03	-1.818
OTU_187_Genus_[Eubacterium] ruminantium group	2.60E-03	4.72E-03	-1.633
OTU_39_Genus_Alistipes	3.11E-03	5.60E-03	-2.431
OTU_28_Genus_Bacteroides	3.20E-03	5.72E-03	-2.897
OTU_170_Genus_Ruminococcaceae UCG-014	3.58E-03	6.31E-03	-1.586
OTU_1_Genus_Escherichia-Shigella	3.59E-03	6.31E-03	3.354
OTU_10_Family_Bacteroidales S24-7 group	4.34E-03	7.55E-03	-2.184
OTU_99_Genus_Bacteroides	4.41E-03	7.56E-03	-1.356
OTU_112_Genus_Ruminiclostridium 5	4.43E-03	7.56E-03	-2.129
OTU_66_Genus_Paraprevotella	4.64E-03	7.86E-03	-1.504
OTU_90_Genus_Thalassospira	5.66E-03	9.51E-03	-1.398
OTU_148_Family_Ruminococcaceae	5.89E-03	9.79E-03	-1.704
OTU_6_Genus_Haemophilus	5.92E-03	9.79E-03	-1.610
OTU_133_Genus_Bacteroides	6.21E-03	1.02E-02	-2.676
OTU_104_Genus_Ruminiclostridium 5	6.47E-03	1.05E-02	-1.977
OTU_132_Genus_Desulfovibrio	8.69E-03	1.39E-02	-1.789
OTU_144_Genus_Ruminococcaceae UCG-004	8.70E-03	1.39E-02	-2.046
OTU_12_Genus_Bacteroides	1.06E-02	1.68E-02	-2.674
OTU_25_Genus_Streptococcus	1.09E-02	1.71E-02	-2.331
OTU_230_Genus_Coprobacter	1.12E-02	1.75E-02	-1.378
OTU_47_Genus_Dialister	1.16E-02	1.80E-02	-1.992

OTU_160_Genus_Paraprevotella	1.33E-02	2.04E-02	-1.693
OTU_44_Genus_[Eubacterium] coprostanoligenes group	1.35E-02	2.05E-02	-1.540
OTU_80_Family_Lachnospiraceae	1.38E-02	2.10E-02	-1.952
OTU_1064_Genus_Sutterella	1.40E-02	2.11E-02	-1.577
OTU_208_Genus_Ruminiclostridium	1.52E-02	2.27E-02	-1.556
OTU_118_Genus_Butyrivibrio	1.72E-02	2.54E-02	-1.063
OTU_168_Genus_Bacteroides	1.86E-02	2.73E-02	-0.995
OTU_111_Genus_[Eubacterium] coprostanoligenes group	1.87E-02	2.73E-02	-1.624
OTU_91_Genus_Sutterella	1.89E-02	2.74E-02	-2.317
OTU_188_Family_Ruminococcaceae	2.05E-02	2.95E-02	-1.264
OTU_255_Genus_Ruminiclostridium 5	2.11E-02	3.02E-02	-1.419
OTU_69_Family_Ruminococcaceae	2.24E-02	3.17E-02	-1.931
OTU_177_Genus_Bacteroides	2.30E-02	3.23E-02	-1.207
OTU_92_Genus_Bilophila	2.42E-02	3.38E-02	-1.929
OTU_135_Genus_Lachnoclostridium	2.47E-02	3.43E-02	-1.478
OTU_190_Family_Christensenellaceae	2.59E-02	3.57E-02	-1.033
OTU_234_Genus_Coprococcus 2	2.82E-02	3.87E-02	-1.241
OTU_151_Family_Corynebacteriaceae	2.89E-02	3.94E-02	-0.773
OTU_127_Genus_Prevotellaceae NK3B31 group	3.00E-02	4.06E-02	-1.016
OTU_62_Genus_Parabacteroides	3.49E-02	4.69E-02	-1.754
OTU_95_Genus_[Eubacterium] oxidoreducens group	3.89E-02	5.19E-02	-1.626
OTU_58_Genus_Parabacteroides	4.98E-02	6.60E-02	-1.871
OTU_126_Genus_Eggerthella	5.71E-02	7.52E-02	-1.398
OTU_695_Genus_Bacteroides	6.07E-02	7.94E-02	-1.274
OTU_81_Genus_Paraprevotella	7.01E-02	9.11E-02	-1.226
OTU_163_Genus_Blautia	7.38E-02	9.52E-02	-0.726
OTU_94_Genus_Clostridium sensu stricto 1	9.18E-02	1.18E-01	-1.195
OTU_87_Genus_[Eubacterium] coprostanoligenes group	9.73E-02	1.24E-01	-1.257
OTU_37_Genus_Lachnoclostridium	9.92E-02	1.26E-01	-1.279
OTU_107_Genus_Lachnoclostridium	1.05E-01	1.33E-01	-1.056
OTU_5_Genus_Akkermansia	1.18E-01	1.47E-01	-1.416
OTU_137_Genus_Lachnospiraceae UCG-008	1.40E-01	1.74E-01	-0.863
OTU_72_Genus_Phascolarctobacterium	1.42E-01	1.75E-01	-0.951

OTU_27_Genus_Neisseria	1.43E-01	1.76E-01	0.825
OTU_61_Genus_Clostridium sensu stricto 1	1.45E-01	1.77E-01	1.093
OTU_52_Genus_Peptoclostridium	1.51E-01	1.83E-01	-1.132
OTU_143_Genus_Thalassospira	1.68E-01	2.03E-01	-0.697
OTU_156_Genus_Ruminiclostridium 9	2.09E-01	2.51E-01	-0.740
OTU_2_Genus_Pseudomonas	2.15E-01	2.56E-01	1.032
OTU_7_Genus_Prevotella 9	2.33E-01	2.76E-01	-0.944
OTU_96_Genus_Streptococcus	2.83E-01	3.33E-01	0.584
OTU_51_Genus_Flavonifractor	3.17E-01	3.70E-01	-0.909
OTU_18_Genus_Lactobacillus	3.19E-01	3.70E-01	0.959
OTU_29_Family_Lachnospiraceae	3.52E-01	4.07E-01	0.479
OTU_171_Genus_Staphylococcus	4.27E-01	4.90E-01	0.452
OTU_19_Genus_Tyzzerella 4	4.33E-01	4.95E-01	-0.693
OTU_606_Genus_Akkermansia	4.49E-01	5.11E-01	-0.514
OTU_8_Genus_Morganella	4.73E-01	5.34E-01	0.555
OTU_150_Family_Veillonellaceae	4.93E-01	5.54E-01	0.428
OTU_22_Genus_Lachnoclostridium	5.00E-01	5.59E-01	0.649
OTU_34_Genus_Veillonella	5.28E-01	5.86E-01	0.433
OTU_225_Genus_Actinomyces	5.40E-01	5.96E-01	-0.307
OTU_43_Family_Lachnospiraceae	6.16E-01	6.77E-01	-0.413
OTU_9_Genus_Veillonella	6.20E-01	6.78E-01	-0.409
OTU_4_Genus_Lactobacillus	6.24E-01	6.78E-01	0.392
OTU_136_Genus_Ruminiclostridium 5	6.67E-01	7.18E-01	-0.273
OTU_244_Genus_Blautia	6.68E-01	7.18E-01	-0.254
OTU_20_Genus_Aeromonas	6.74E-01	7.18E-01	0.336
OTU_158_Genus_Peptoniphilus	6.78E-01	7.18E-01	-0.231
OTU_30_Genus_Hungatella	6.79E-01	7.18E-01	-0.441
OTU_17_Genus_Lactobacillus	6.95E-01	7.31E-01	0.317
OTU_84_Genus_Lachnoclostridium	7.59E-01	7.95E-01	-0.248
OTU_212_Genus_Hafnia	8.13E-01	8.46E-01	-0.133
OTU_16_Genus_Lachnoclostridium	8.27E-01	8.57E-01	0.212
OTU_139_Genus_Stenotrophomonas	8.36E-01	8.62E-01	0.112
OTU_117_Genus_Epulopiscium	9.05E-01	9.28E-01	0.068

OTU_54_Genus_Proteus	9.34E-01	9.53E-01	0.056
OTU_103_Genus_Clostridium sensu stricto 1	9.43E-01	9.57E-01	0.046
OTU_45_Genus_Lachnoclostridium	9.68E-01	9.78E-01	0.035
OTU_182_Genus_Incertae Sedis	9.80E-01	9.85E-01	-0.015
OTU_79_Genus_Alkaliphilus	9.93E-01	9.93E-01	-0.006

Legend: A positive mean log relative abundance means that the abundance is higher in IF patients, a negative mean log relative abundance means that the abundance is higher in the healthy controls

Abbreviations: IF, intestinal failure.

Supplementary Table 2. Differences in relative abundance between IF patients and healthy controls for all samples at family level

Family	**p-value**	**adjusted p-value**	**Differences in mean log relative abundance**
Clostridiales vadinBB60 group	4.10E-08	5.08E-06	-3.155
Coriobacteriaceae	4.74E-07	2.94E-05	-3.676
Ruminococcaceae	6.34E-06	2.62E-04	-3.754
Acidaminococcaceae	8.82E-06	2.73E-04	-3.667
Family XIII	1.54E-05	3.82E-04	-1.995
Alcaligenaceae	2.90E-05	5.99E-04	-3.991
Enterobacteriaceae	6.03E-05	1.07E-03	4.116
Staphylococcaceae	7.09E-05	1.07E-03	3.771
Christensenellaceae	7.73E-05	1.07E-03	-2.571
Victivallaceae	9.51E-05	1.18E-03	-1.722
Clostridium sp. CAG:306	1.41E-04	1.59E-03	-1.439
Defluviitaleaceae	1.54E-04	1.59E-03	-1.523
Erysipelotrichaceae	1.77E-04	1.59E-03	-2.727
Bacteroidales S24-7 group	1.79E-04	1.59E-03	-3.019
Bifidobacteriaceae	5.10E-04	4.22E-03	-2.771
Rikenellaceae	1.44E-03	1.11E-02	-2.816
Porphyromonadaceae	1.58E-03	1.15E-02	-2.584
Mitochondria	1.71E-03	1.18E-02	-0.889
Lachnospiraceae	1.91E-03	1.25E-02	-2.346
Bacteroidaceae	2.12E-03	1.32E-02	-2.913
Rhodospirillaceae	2.63E-03	1.55E-02	-2.088
Thermoanaerobacteraceae	8.75E-03	4.93E-02	-0.774
Pasteurellaceae	1.01E-02	5.29E-02	-1.480
Desulfovibrionaceae	1.02E-02	5.29E-02	-2.108
env.OPS 17	1.79E-02	6.39E-02	-0.646
Synergistaceae	2.18E-02	6.39E-02	-0.682
Anaeroplasmataceae	2.50E-02	6.39E-02	-0.721
Prevotellaceae	2.52E-02	6.39E-02	-1.668
Rhizobiaceae	2.60E-02	6.39E-02	-0.619
Caldicoprobacteraceae	2.90E-02	6.39E-02	-0.581
Dictyoglomaceae	3.16E-02	6.39E-02	-0.619

Alcanivoracaceae	3.55E-02	6.39E-02	-0.575
Alicyclobacillaceae	3.55E-02	6.39E-02	-0.575
Bartonellaceae	3.55E-02	6.39E-02	-0.575
Bdellovibrionaceae	3.55E-02	6.39E-02	-0.575
Bogoriellaceae	3.55E-02	6.39E-02	-0.575
Brevibacteriaceae	3.55E-02	6.39E-02	-0.575
Brucellaceae	3.55E-02	6.39E-02	-0.575
BVA18	3.55E-02	6.39E-02	-0.575
Cytophagaceae	3.55E-02	6.39E-02	-0.575
Family III	3.55E-02	6.39E-02	-0.575
Gemmatimonadaceae	3.55E-02	6.39E-02	-0.575
Geodermatophilaceae	3.55E-02	6.39E-02	-0.575
Halieaceae	3.55E-02	6.39E-02	-0.575
Hydrogenophilaceae	3.55E-02	6.39E-02	-0.575
Hyphomicrobiaceae	3.55E-02	6.39E-02	-0.575
Hyphomonadaceae	3.55E-02	6.39E-02	-0.575
Iamiaceae	3.55E-02	6.39E-02	-0.575
KD3-10	3.55E-02	6.39E-02	-0.575
Methylobacteriaceae	3.55E-02	6.39E-02	-0.575
Methylophilaceae	3.55E-02	6.39E-02	-0.575
Microbacteriaceae	3.55E-02	6.39E-02	-0.575
Mycoplasmataceae	3.55E-02	6.39E-02	-0.575
Nannocystaceae	3.55E-02	6.39E-02	-0.575
Nitrospiraceae	3.55E-02	6.39E-02	-0.575
Oceanospirillaceae	3.55E-02	6.39E-02	-0.575
Oligoflexaceae	3.55E-02	6.39E-02	-0.575
Parachlamydiaceae	3.55E-02	6.39E-02	-0.575
Phycisphaeraceae	3.55E-02	6.39E-02	-0.575
Pseudonocardiaceae	3.55E-02	6.39E-02	-0.575
Rhodobacteraceae	3.55E-02	6.39E-02	-0.575
Rhodocyclaceae	3.55E-02	6.39E-02	-0.575
Rhodospirillales Incertae Sedis	3.55E-02	6.39E-02	-0.575
SM2D12	3.55E-02	6.39E-02	-0.575

Spirochaetaceae	3.55E-02	6.39E-02	-0.575
Spongiibacteraceae	3.55E-02	6.39E-02	-0.575
Succinivibrionaceae	3.55E-02	6.39E-02	-0.575
TM146	3.55E-02	6.39E-02	-0.575
Vulgatibacteraceae	3.55E-02	6.39E-02	-0.575
Planctomycetaceae	3.73E-02	6.61E-02	-0.540
Peptococcaceae	4.39E-02	7.66E-02	-0.802
FamilyI	4.47E-02	7.69E-02	-0.540
Cardiobacteriaceae	4.66E-02	7.81E-02	-0.525
CFT112H7	4.66E-02	7.81E-02	-0.525
1174-901-12	4.75E-02	7.85E-02	-0.525
Dermacoccaceae	5.26E-02	8.58E-02	-0.525
Nitrospinaceae	5.85E-02	9.42E-02	-0.524
Methanobacteriaceae	6.36E-02	1.01E-01	-0.545
Holophagaceae	7.05E-02	1.07E-01	-0.496
Nitrosomonadaceae	7.05E-02	1.07E-01	-0.496
Family XI	7.15E-02	1.07E-01	1.086
NS9 marine group	7.15E-02	1.07E-01	-0.476
Unknown Family	7.15E-02	1.07E-01	-0.476
Leptospiraceae	7.34E-02	1.08E-01	-0.496
Micromonosporaceae	7.38E-02	1.08E-01	-0.476
Methylocystaceae	7.47E-02	1.08E-01	-0.496
Sphingobacteriaceae	8.07E-02	1.15E-01	-0.496
Deferribacteraceae	8.68E-02	1.22E-01	-0.460
Syntrophorhabdaceae	8.76E-02	1.22E-01	-0.476
Neisseriaceae	8.92E-02	1.23E-01	1.003
Verrucomicrobiaceae	1.21E-01	1.65E-01	-1.392
Peptostreptococcaceae	1.38E-01	1.86E-01	-1.058
Pseudomonadaceae	1.47E-01	1.96E-01	1.206
Caulobacteraceae	1.61E-01	2.10E-01	-0.368
Sporichthyaceae	1.61E-01	2.10E-01	-0.377
Lactobacillaceae	1.87E-01	2.41E-01	1.376
Aerococcaceae	1.90E-01	2.43E-01	-0.376

Fusobacteriaceae	1.98E-01	2.49E-01	0.598
Chitinophagaceae	1.99E-01	2.49E-01	-0.357
Campylobacteraceae	2.00E-01	2.49E-01	-0.442
Acetobacteraceae	2.28E-01	2.80E-01	-0.361
Bradyrhizobiaceae	2.45E-01	2.98E-01	-0.303
Bacillaceae	2.63E-01	3.17E-01	-0.320
Nocardiaceae	2.70E-01	3.23E-01	-0.389
Oxalobacteraceae	3.28E-01	3.87E-01	-0.323
Streptococcaceae	3.57E-01	4.17E-01	-0.563
Eubacteriaceae	3.81E-01	4.42E-01	-0.487
Leptotrichiaceae	4.78E-01	5.48E-01	0.315
Comamonadaceae	4.99E-01	5.67E-01	-0.191
Sphingomonadaceae	5.03E-01	5.67E-01	-0.180
Xanthomonadaceae	5.18E-01	5.79E-01	0.376
Micrococcaceae	5.47E-01	6.06E-01	-0.232
Clostridiaceae 1	5.87E-01	6.44E-01	-0.434
Burkholderiaceae	5.99E-01	6.52E-01	-0.225
Moraxellaceae	6.10E-01	6.55E-01	0.207
Carnobacteriaceae	6.12E-01	6.55E-01	-0.187
Corynebacteriaceae	6.43E-01	6.82E-01	-0.208
Aeromonadaceae	6.59E-01	6.93E-01	0.353
Veillonellaceae	7.04E-01	7.34E-01	-0.266
Actinomycetaceae	7.56E-01	7.82E-01	0.160
Leuconostocaceae	8.77E-01	8.99E-01	0.103
Flavobacteriaceae	8.91E-01	9.06E-01	0.052
Clostridiaceae 2	9.87E-01	9.87E-01	0.010
Paenibacillaceae	9.87E-01	9.87E-01	0.007

Legend: A positive mean log relative abundance means that the abundance is higher in IF patients, a negative mean log relative abundance means that the abundance is higher in the healthy controls.

Abbreviations: IF, intestinal failure.

Supplementary Table 3. Concentration of SCFA and lactate for IF patients and healthy controls at first sample collection per g wet feces

Per g wet feces	**n**	**Patients with IF**	**n**	**Healthy controls**	**p-value**
		n = 15		**n = 25**	
SCFA	14[1]		21[1]		
Acetic acid (C2), µmol/g		32.1 (20.1 – 66.2)		172 (130 – 222)	p < 0.001
Acetic acid (C2), %		14.8 (8.94 – 21.8)		37.9 (34.2 - 43.6)	p < 0.001
Propionic acid (C3), µmol/g		1.23 (0.19 – 6.50)		31.4 (28.7 – 51.4)	p < 0.001
Propionic acid (C3), %		0.61 (0.11 – 1.85)		7.80 (5.70 – 10.7)	p < 0.001
Butyric acid (C4), µmol/g		0.31 (0.18 – 2.06)		29.9 (22.6 – 36.9)	p < 0.001
Butyric acid (C4), %		0.17 (0.06 – 1.23)		6.63 (3.39 – 7.98)	p < 0.001
Valeric acid (C5), µmol/g		0.05 (0.01 – 0.97)		2.35 (1.11 – 4.82)	p < 0.001
Valeric acid (C5), %		0.03 (0.00 – 0.13)		0.67 (0.19 – 1.08)	p < 0.001
Caproic acid (C6), µmol/g		0.10 (0.02 – 0.17)		0.36 (0.24 – 2.86)	p < 0.001
Caproic acid (C6), %		0.02 (0.01 – 0.12)		0.08 (0.04 – 0.75)	p = 0.037
Heptanoic acid (C7), µmol/g		0.12 (0.02 – 0.23)		0.04 (0.02 – 0.11)	p = 0.273
Heptanoic acid (C7), %		0.03 (0.01 – 0.14)		0.01 (0.00 – 0.03)	p = 0.040
Octanoic acid (C8), µmol/g		0.02 (0.00 – 0.11)		0.09 (0.02 – 0.23)	p = 0.089
Octanoic acid (C8), %		0.01 (0.00 – 0.11)		0.01 (0.00 – 0.06)	p = 0.713
Total, µmol/g		34.6 (25.1 – 75.7)		255 (199 – 367)	p < 0.001
Iso-butyric acid (iC4), µmol/g		0.09 (0.202 – 0.84)		4.27 (2.27 – 5.85)	p < 0.001
Iso-butyric acid (iC4), %		0.08 (0.01 – 0.18)		1.06 (0.51 – 1.24)	p < 0.001
Iso-valeric acid (iC5), µmol/g		0.15 (0.03 – 0.78)		3.88 (2.10 – 5.92)	p < 0.001
Iso-valeric acid (iC5), %		0.08 (0.01 – 0.15)		0.96 (0.45 – 1.28)	p < 0.001
Iso-caproic acid (iC6), µmol/g		0.07 (0.05 – 0.23)		0.22 (0.13 – 0.28)	p = 0.027
Iso-caproic acid (iC6), %		0.04 (0.01 – 0.09)		0.04 (0.03 – 0.06)	p = 0.553
D-lactate, µg/g	8	185 (81 - 1358)	20[2]	53 (38 – 84)	p = 0.002
L-lactate, µg/g	8	168 (90 - 682)	20[2]	93 (41 - 150)	p = 0.055
Total lactate, µg/g	8	351 (157 – 2134)	20[2]	159 (92 – 207)	p = 0.007
% D-lactate	8	48 (42 – 57)	20[2]	34 (21 – 56)	p = 0.070

Legend: Values shown ad median (IQR) or n (%) unless stated otherwise. [1] For one patient and for 4 healthy controls, water content was not known at the first sample, [2] the same applies for 5 healthy controls regarding the water content of their lactate samples.

Abbreviations: IF, intestinal failure; IQR, SCFA, short-chain fatty acids.

Supplementary Table 4. Fecal water content, concentration of SCFA, lactate, and number of 16S rRNA gene copies for IF patients and healthy controls at last sample

	n	Patients with IF	n	Healthy controls	p-value
		n = 15		**n = 25**	
Fecal water content (%)	13	83.3 (75.0 – 85.7)	25	65 (62-74)	p = 0.062
SCFA (per g dry feces)	14		25		
Acetic acid (C2), µmol/g		265 (156 – 457)		323 (266-370)	p = 0.176
Acetic acid (C2), %		90.1 (73.8 – 93.6)		67.6 (64.7-61.3)	p = 0.016
Propionic acid (C3), µmol/g		15.0 (4.45 – 38.7)		64.0 (47.5-85.1)	p < 0.001
Propionic acid (C3), %		4.79 (2.30 – 10.7)		13.7 (10.6-18.8)	p = 0.005
Butyric acid (C4), µmol/g		13.5 (0.39 – 52.4)		54.3 (36.6-71.0)	p = 0.001
Butyric acid (C4), %		3.91 (0.17 – 10.4)		11.6 (5.60-14.9)	p = 0.010
Valeric acid (C5), µmol/g		1.64 (0.17 – 5.01)		4.94 (2.04-9.56)	p = 0.010
Valeric acid (C5), %		0.38 (0.08 – 1.39)		1.39 (0.36-2.26)	p = 0.118
Caproic acid (C6), µmol/g		0.46 (0.35 – 0.55)		0.51 (0.26-3.72)	p = 0.071
Caproic acid (C6), %		0.14 (0.08 – 0.34)		0.12 (0.08-0.78)	p = 0.965
Heptanoic acid (C7), µmol/g		0.21 (0.05 – 0.71)		0.07 (0.04-0.17)	p = 0.141
Heptanoic acid (C7), %		0.08 (0.01 – 0.20)		0.01 (0.00-0.05)	p = 0.076
Octanoic acid (C8), µmol/g		0.47 (0.06 – 1.60)		0.17 (0.04-0.34)	p = 0.166
Octanoic acid (C8), %		0.26 (0.01 – 0.56)		0.01 (0.01-0.08)	p = 0.020
Total, µmol/g		288 (188 – 529)		472 (397-592)	p = 0.019
Iso-butyric acid (iC4), µmol/g		0.19 (0.41 – 5.66)		6.40 (3.73-10.2)	p = 0.006
Iso-butyric acid (iC4), %		0.49 (0.13 – 1.97)		1.42 (0.92-2.17)	p = 0.125
Iso-valeric acid (iC5), µmol/g		1.47 (0.41 – 6.42)		6.27 (3.48-10.2)	p = 0.013
Iso-valeric acid (iC5), %		0.46 (0.12 – 2.26)		1.18 (0.82-14.9)	p = 0.216
Iso-caproic acid (iC6), µmol/g		0.27 (0.13 – 1.03)		0.35 (0.26-0.48)	p = 0.784
Iso-caproic acid (iC6), %		0.08 (0.04 – 0.25)		0.07 (0.05-0.09)	p = 0.460
D-lactate, µg/g dry feces	9	298 (172 – 1577)	24	79 (58-156)	p < 0.001
L-lactate, µg/g dry feces	9	287 (210 – 1985)	24	211 (102-257)	p = 0.018
Total lactate, µg/g dry feces	9	518 (383 – 3750)	24	256 (193-376)	p < 0.001
% D-lactate per g dry feces	9	42 (34 – 57)	24	33 (19-50)	p = 0.121
Log of 16S rRNA gene copy number per g dry feces (IQR, range)	14	10.8 (10.1 – 11.0, 9.41 – 11.10)	25	11.1 (10.9-11.3, 10.7-11.7)	p = 0.001

Log of 16S rRNA gene copy number per g wet feces (IQR, range)	13	9.90 (9.48 – 10.5, 8.42 – 11.06)	25	3.82 (3.33-4.37, 2.6-18.4)	p = 0.001

Legend: Values shown ad median (IQR) or n (%) unless stated otherwise.

Abbreviations: IF, intestinal failure; IQR, interquartile range; SCFA, short-chain fatty acids.

Supplementary Table 5. Differences in relative abundance between surgical IF and functional IF patients for all samples at OTU level

OTU	p-value	adjusted p-value	Differences in mean log relative abundance
OTU_210_Genus_Lactobacillus	3.06E-05	3.06E-03	-1.506
OTU_22_Genus_Lachnoclostridium	3.76E-05	3.06E-03	3.763
OTU_18_Genus_Lactobacillus	4.59E-05	3.06E-03	-2.409
OTU_126_Genus_Eggerthella	7.76E-05	3.40E-03	2.684
OTU_255_Genus_Ruminiclostridium 5	8.51E-05	3.40E-03	1.816
OTU_84_Genus_Lachnoclostridium	1.06E-04	3.53E-03	3.108
OTU_164_Genus_Capnocytophaga	2.35E-04	6.51E-03	-1.000
OTU_6_Genus_Haemophilus	2.60E-04	6.51E-03	2.272
OTU_121_Genus_Dorea	3.68E-04	7.62E-03	2.161
OTU_51_Genus_Flavonifractor	3.81E-04	7.62E-03	2.924
OTU_56_Genus_Alistipes	5.05E-04	8.65E-03	2.486
OTU_45_Genus_Lachnoclostridium	5.19E-04	8.65E-03	2.944
OTU_166_Genus_Lactobacillus	6.29E-04	9.68E-03	-1.146
OTU_96_Genus_Streptococcus	7.12E-04	9.77E-03	1.694
OTU_46_Genus_Prevotella 7	7.50E-04	9.77E-03	-1.503
OTU_21_Genus_Anaeroglobus	7.81E-04	9.77E-03	-1.849
OTU_30_Genus_Hungatella	8.75E-04	1.03E-02	2.913
OTU_54_Genus_Proteus	9.72E-04	1.08E-02	-1.120
OTU_94_Genus_Clostridium sensu stricto 1	1.07E-03	1.12E-02	2.042
OTU_69_Family_Ruminococcaceae	1.27E-03	1.27E-02	2.074
OTU_34_Genus_Veillonella	1.37E-03	1.30E-02	-1.651
OTU_36_Genus_Megasphaera	1.50E-03	1.36E-02	-2.076
OTU_103_Genus_Clostridium sensu stricto 1	1.72E-03	1.50E-02	2.346
OTU_12_Genus_Bacteroides	2.10E-03	1.75E-02	2.752
OTU_38_Genus_Lactobacillus	2.41E-03	1.85E-02	-1.511
OTU_115_Genus_Selenomonas 3	2.41E-03	1.85E-02	-1.206
OTU_17_Genus_Lactobacillus	2.71E-03	1.95E-02	-1.708
OTU_80_Family_Lachnospiraceae	2.73E-03	1.95E-02	2.312
OTU_3_Genus_Cronobacter	3.02E-03	1.99E-02	-2.372
OTU_277_Genus_Xanthomonas	3.06E-03	1.99E-02	-0.916

OTU_268_Genus_Holdemanella	3.09E-03	1.99E-02	-0.869
OTU_128_Genus_Peptoclostridium	3.21E-03	2.00E-02	-1.232
OTU_207_Genus_Allisonella	3.68E-03	2.23E-02	-0.871
OTU_88_Family_CFT112H7	3.81E-03	2.24E-02	-1.263
OTU_226_Genus_Slackia	3.98E-03	2.27E-02	-0.849
OTU_212_Genus_Hafnia	4.98E-03	2.77E-02	-0.723
OTU_161_Genus_Neisseria	5.84E-03	3.03E-02	-0.654
OTU_90_Genus_Thalassospira	5.94E-03	3.03E-02	-0.738
OTU_58_Genus_Parabacteroides	5.95E-03	3.03E-02	2.257
OTU_147_Genus_Bergeyella	6.06E-03	3.03E-02	-0.649
OTU_175_Genus_Comamonas	6.79E-03	3.14E-02	-0.635
OTU_133_Genus_Bacteroides	6.86E-03	3.14E-02	2.064
OTU_71_Genus_Blautia	6.88E-03	3.14E-02	1.909
OTU_26_Genus_Blautia	7.09E-03	3.14E-02	1.779
OTU_92_Genus_Bilophila	7.18E-03	3.14E-02	1.856
OTU_19_Genus_Tyzzerella 4	7.22E-03	3.14E-02	2.235
OTU_93_Genus_Blautia	7.72E-03	3.29E-02	1.446
OTU_138_Genus_Gemella	8.39E-03	3.50E-02	1.227
OTU_16_Genus_Lachnoclostridium	8.56E-03	3.50E-02	2.370
OTU_97_Genus_Dorea	9.25E-03	3.70E-02	1.282
OTU_4_Genus_Lactobacillus	9.50E-03	3.72E-02	-1.470
OTU_98_Genus_Lachnospiraceae NK4A136 group	1.16E-02	4.37E-02	1.391
OTU_695_Genus_Bacteroides	1.16E-02	4.37E-02	1.552
OTU_113_Genus_Lachnoclostridium	1.45E-02	5.22E-02	1.651
OTU_171_Genus_Staphylococcus	1.46E-02	5.22E-02	1.022
OTU_204_Genus_Ruminiclostridium	1.49E-02	5.22E-02	1.298
OTU_215_Genus_Erysipelatoclostridium	1.50E-02	5.22E-02	1.362
OTU_182_Genus_Incertae Sedis	1.51E-02	5.22E-02	1.195
OTU_199_Genus_Anaerostipes	1.56E-02	5.29E-02	1.319
OTU_165_Genus_Campylobacter	1.60E-02	5.34E-02	-0.985
OTU_101_Genus_Thalassospira	1.64E-02	5.39E-02	-0.674
OTU_67_Genus_Collinsella	1.67E-02	5.39E-02	1.280
OTU_130_Genus_Acidaminococcus	1.73E-02	5.48E-02	-0.682

OTU_86_Genus_Parasutterella	1.75E-02	5.48E-02	-0.993
OTU_152_Genus_Christensenellaceae R-7 group	1.78E-02	5.49E-02	1.268
OTU_191_Genus_Lachnospiraceae UCG-008	1.85E-02	5.61E-02	0.924
OTU_85_Genus_Lachnospiraceae NK4A136 group	2.00E-02	5.96E-02	1.505
OTU_49_Genus_Roseburia	2.03E-02	5.97E-02	1.533
OTU_52_Genus_Peptoclostridium	2.13E-02	6.18E-02	1.643
OTU_75_Family_Ruminococcaceae	2.52E-02	7.19E-02	1.249
OTU_74_Genus_Ruminococcaceae UCG-002	2.58E-02	7.28E-02	1.327
OTU_23_Genus_Alistipes	3.00E-02	8.34E-02	1.717
OTU_62_Genus_Parabacteroides	3.08E-02	8.43E-02	1.487
OTU_125_Genus_Ruminococcaceae UCG-003	3.50E-02	9.45E-02	1.194
OTU_20_Genus_Aeromonas	3.75E-02	1.00E-01	-0.672
OTU_5_Genus_Akkermansia	4.09E-02	1.07E-01	1.411
OTU_14_Genus_Staphylococcus	4.10E-02	1.07E-01	1.637
OTU_82_Genus_Bacteroides	4.20E-02	1.08E-01	1.119
OTU_33_Genus_Pseudobutyrivibrio	4.54E-02	1.14E-01	1.016
OTU_157_Genus_Veillonella	4.55E-02	1.14E-01	1.038
OTU_55_Genus_Blautia	4.84E-02	1.20E-01	0.951
OTU_40_Genus_Phascolarctobacterium	5.74E-02	1.40E-01	-0.621
OTU_15_Genus_Tyzzerella	5.88E-02	1.42E-01	1.188
OTU_31_Genus_Faecalibacterium	6.75E-02	1.61E-01	0.876
OTU_145_Genus_Bacteroides	6.97E-02	1.64E-01	-0.641
OTU_230_Genus_Coprobacter	7.37E-02	1.71E-01	0.815
OTU_201_Family_Lachnospiraceae	7.43E-02	1.71E-01	0.872
OTU_205_Genus_Alistipes	7.71E-02	1.75E-01	0.837
OTU_83_Genus_Ruminococcus 1	7.81E-02	1.75E-01	0.900
OTU_220_Family_Lachnospiraceae	7.89E-02	1.75E-01	1.001
OTU_2_Genus_Pseudomonas	8.03E-02	1.76E-01	-1.258
OTU_114_Genus_Faecalibacterium	9.13E-02	1.99E-01	0.733
OTU_106_Genus_[Eubacterium] hallii group	9.33E-02	2.01E-01	0.754
OTU_65_Genus_Ruminococcaceae UCG-002	1.01E-01	2.15E-01	0.827
OTU_29_Family_Lachnospiraceae	1.07E-01	2.26E-01	1.251
OTU_240_Genus_Tyzzerella	1.12E-01	2.34E-01	0.723

OTU_13_Genus_Bacteroides	1.21E-01	2.50E-01	1.046
OTU_64_Genus_Ruminococcus 1	1.23E-01	2.51E-01	0.692
OTU_193_Genus_Erysipelatoclostridium	1.27E-01	2.57E-01	0.801
OTU_116_Genus_Ruminococcaceae UCG-005	1.36E-01	2.71E-01	0.757
OTU_68_Genus_Ruminococcaceae UCG-005	1.37E-01	2.71E-01	0.897
OTU_235_Genus_Lachnospiraceae NK4A136 group	1.45E-01	2.84E-01	0.668
OTU_261_Genus_Desulfovibrio	1.48E-01	2.86E-01	-0.474
OTU_42_Genus_Ruminococcus 2	1.49E-01	2.86E-01	0.799
OTU_148_Family_Ruminococcaceae	1.58E-01	3.00E-01	0.596
OTU_194_Genus_Butyricimonas	1.60E-01	3.01E-01	0.618
OTU_135_Genus_Lachnoclostridium	1.65E-01	3.06E-01	0.717
OTU_112_Genus_Ruminiclostridium 5	1.65E-01	3.06E-01	0.690
OTU_39_Genus_Alistipes	1.68E-01	3.06E-01	0.928
OTU_108_Genus_Fusicatenibacter	1.68E-01	3.06E-01	0.687
OTU_141_Genus_Neisseria	1.72E-01	3.09E-01	-0.480
OTU_76_Genus_Anaeroglobus	1.84E-01	3.29E-01	-0.483
OTU_225_Genus_Actinomyces	1.97E-01	3.49E-01	0.527
OTU_946_Genus_Veillonella	2.01E-01	3.52E-01	-0.436
OTU_37_Genus_Lachnoclostridium	2.03E-01	3.52E-01	0.645
OTU_144_Genus_Ruminococcaceae UCG-004	2.05E-01	3.54E-01	0.654
OTU_8_Genus_Morganella	2.11E-01	3.59E-01	1.105
OTU_28_Genus_Bacteroides	2.12E-01	3.59E-01	0.925
OTU_99_Genus_Bacteroides	2.35E-01	3.93E-01	-0.475
OTU_119_Genus_Ruminococcus 1	2.36E-01	3.93E-01	0.468
OTU_89_Genus_Lachnospira	2.39E-01	3.95E-01	0.764
OTU_63_Genus_Lachnoclostridium	2.41E-01	3.95E-01	0.740
OTU_208_Genus_Ruminiclostridium	2.78E-01	4.48E-01	0.473
OTU_143_Genus_Thalassospira	2.81E-01	4.48E-01	0.499
OTU_24_Genus_Bifidobacterium	2.82E-01	4.48E-01	-0.565
OTU_276_Genus_Finegoldia	2.84E-01	4.48E-01	-0.398
OTU_91_Genus_Sutterella	2.85E-01	4.48E-01	0.755
OTU_110_Genus_Alistipes	3.08E-01	4.81E-01	0.464
OTU_195_Genus_Campylobacter	3.10E-01	4.81E-01	-0.307

OTU_104_Genus_Ruminiclostridium 5	3.15E-01	4.85E-01	0.452
OTU_73_Genus_Coprococcus 3	3.31E-01	5.06E-01	0.431
OTU_48_Genus_Blautia	3.36E-01	5.08E-01	0.352
OTU_763_Genus_Veillonella	3.38E-01	5.08E-01	-0.427
OTU_305_Genus_Lachnoanaerobaculum	3.44E-01	5.13E-01	-0.323
OTU_102_Genus_Odoribacter	3.46E-01	5.13E-01	0.552
OTU_7_Genus_Prevotella 9	3.50E-01	5.14E-01	0.453
OTU_59_Genus_Barnesiella	3.57E-01	5.21E-01	0.501
OTU_943_Class_Bacteroidetes VC2.1 Bac22	3.69E-01	5.35E-01	-0.323
OTU_302_Genus_Peptostreptococcus	3.75E-01	5.39E-01	0.336
OTU_181_Genus_Dielma	3.80E-01	5.43E-01	0.398
OTU_41_Genus_Subdoligranulum	3.85E-01	5.46E-01	0.488
OTU_248_Genus_Johnsonella	3.89E-01	5.47E-01	0.315
OTU_25_Genus_Streptococcus	3.96E-01	5.54E-01	0.606
OTU_44_Genus_[Eubacterium] coprostanoligenes group	3.99E-01	5.54E-01	0.348
OTU_244_Genus_Blautia	4.01E-01	5.54E-01	0.427
OTU_57_Genus_Subdoligranulum	4.08E-01	5.59E-01	0.374
OTU_231_Genus_Leuconostoc	4.21E-01	5.68E-01	0.452
OTU_11_Genus_Rikenella	4.22E-01	5.68E-01	0.555
OTU_142_Genus_[Eubacterium] coprostanoligenes group	4.23E-01	5.68E-01	0.369
OTU_140_Genus_Ruminococcaceae NK4A214 group	4.48E-01	5.94E-01	0.371
OTU_154_Genus_Incertae Sedis	4.48E-01	5.94E-01	0.309
OTU_43_Family_Lachnospiraceae	4.72E-01	6.20E-01	0.393
OTU_150_Family_Veillonellaceae	4.75E-01	6.20E-01	0.344
OTU_27_Genus_Neisseria	4.79E-01	6.22E-01	-0.326
OTU_9_Genus_Veillonella	4.95E-01	6.39E-01	-0.499
OTU_159_Class_Bacteroidetes VC2.1 Bac22	5.24E-01	6.72E-01	0.306
OTU_160_Genus_Paraprevotella	5.34E-01	6.80E-01	0.254
OTU_87_Genus_[Eubacterium] coprostanoligenes group	5.51E-01	6.97E-01	-0.256
OTU_72_Genus_Phascolarctobacterium	5.60E-01	7.05E-01	0.274
OTU_137_Genus_Lachnospiraceae UCG-008	5.67E-01	7.05E-01	0.219
OTU_100_Genus_Coprococcus 2	5.67E-01	7.05E-01	0.255
OTU_131_Genus_Blautia	5.73E-01	7.08E-01	0.221

OTU_247_Family_Coriobacteriaceae	5.91E-01	7.25E-01	0.219
OTU_78_Genus_Blautia	5.94E-01	7.25E-01	0.261
OTU_149_Genus_Lactococcus	6.21E-01	7.53E-01	-0.217
OTU_60_Genus_Anaerostipes	6.37E-01	7.64E-01	0.235
OTU_196_Genus_Ruminococcaceae NK4A214 group	6.38E-01	7.64E-01	-0.160
OTU_206_Genus_Varibaculum	6.45E-01	7.66E-01	-0.151
OTU_32_Genus_Bacteroides	6.48E-01	7.66E-01	0.297
OTU_10_Family_Bacteroidales S24-7 group	6.90E-01	8.09E-01	0.235
OTU_155_Genus_Enterorhabdus	6.92E-01	8.09E-01	0.188
OTU_184_Genus_Anaerosporobacter	7.20E-01	8.37E-01	-0.119
OTU_1_Genus_Escherichia-Shigella	7.26E-01	8.40E-01	0.320
OTU_35_Genus_Aggregatibacter	7.33E-01	8.43E-01	0.166
OTU_158_Genus_Peptoniphilus	7.43E-01	8.47E-01	-0.132
OTU_398_Genus_Ruminococcaceae UCG-014	7.50E-01	8.47E-01	-0.144
OTU_47_Genus_Dialister	7.51E-01	8.47E-01	-0.197
OTU_347_Genus_Lachnoclostridium	7.54E-01	8.47E-01	-0.124
OTU_107_Genus_Lachnoclostridium	7.67E-01	8.57E-01	0.126
OTU_172_Family_Ruminococcaceae	7.75E-01	8.59E-01	-0.108
OTU_61_Genus_Clostridium sensu stricto 1	7.77E-01	8.59E-01	0.218
OTU_117_Genus_Epulopiscium	8.06E-01	8.86E-01	-0.094
OTU_53_Genus_Fusobacterium	8.20E-01	8.92E-01	-0.162
OTU_162_Genus_[Eubacterium] hallii group	8.21E-01	8.92E-01	-0.087
OTU_136_Genus_Ruminiclostridium 5	8.26E-01	8.93E-01	-0.085
OTU_209_Genus_Victivallis	8.41E-01	9.04E-01	0.086
OTU_216_Genus_Alistipes	8.46E-01	9.04E-01	0.078
OTU_227_Genus_Lachnospira	8.59E-01	9.14E-01	0.071
OTU_79_Genus_Alkaliphilus	8.69E-01	9.20E-01	-0.068
OTU_1064_Genus_Sutterella	8.79E-01	9.23E-01	0.068
OTU_606_Genus_Akkermansia	8.82E-01	9.23E-01	0.068
OTU_81_Genus_Paraprevotella	8.86E-01	9.23E-01	0.068
OTU_167_Genus_Ruminococcus 1	8.96E-01	9.28E-01	0.049
OTU_156_Genus_Ruminiclostridium 9	9.04E-01	9.31E-01	0.055
OTU_139_Genus_Stenotrophomonas	9.10E-01	9.31E-01	-0.042

OTU_218_Family_Lachnospiraceae	9.13E-01	9.31E-01	0.046
OTU_50_Genus_Christensenellaceae R-7 group	9.17E-01	9.31E-01	0.039
OTU_224_Order_Gastranaerophilales	9.25E-01	9.34E-01	-0.032
OTU_213_Order_Gastranaerophilales	9.84E-01	9.87E-01	0.008
OTU_95_Genus_[Eubacterium] oxidoreducens group	9.87E-01	9.87E-01	0.008

Legend: A positive mean log relative abundance means that the abundance is higher in functional IF patients, a negative mean log relative abundance means that the abundance is higher in surgical IF patients.

Abbreviations: IF, intestinal failure.

Supplementary Table 6. Differences in relative abundance between functional and surgical IF patients for all samples at family level

Family	**p-value**	**adjusted p-value**	**Differences in mean log relative abundance**
Erysipelotrichaceae	7,85E-06	6,94E-04	2.462
Lachnospiraceae	1.12E-05	6.94E-04	2.511
Ruminococcaceae	3.89E-05	1.28E-03	2.200
Coriobacteriaceae	5.07E-05	1.28E-03	1.998
Lactobacillaceae	5.16E-05	1.28E-03	-2.942
Mitochondria	6.41E-04	1.33E-02	-0.636
Aerococcaceae	7.70E-04	1.36E-02	-0.566
Pasteurellaceae	1.01E-03	1.57E-02	2.067
Clostridiaceae 1	1.50E-03	1.93E-02	2.402
Desulfovibrionaceae	1.88E-03	1.93E-02	2.005
NS9 marine group	2.27E-03	1.93E-02	-0.496
Flavobacteriaceae	2.40E-03	1.93E-02	-0.887
Family XIII	2.83E-03	1.93E-02	1.124
Methylocystaceae	2.94E-03	1.93E-02	-0.489
Rikenellaceae	3.07E-03	1.93E-02	2.417
Sphingobacteriaceae	3.08E-03	1.93E-02	-0.489
KD3-10	3.16E-03	1.93E-02	-0.489
Spirochaetaceae	3.19E-03	1.93E-02	-0.532
Acetobacteraceae	3.37E-03	1.93E-02	-0.533
Nitrospiraceae	3.39E-03	1.93E-02	-0.489
Alcanivoracaceae	3.43E-03	1.93E-02	-0.489
Bogoriellaceae	3.43E-03	1.93E-02	-0.489
CFT112H7	3.71E-03	1.94E-02	-1.267
Methylobacteriaceae	3.75E-03	1.94E-02	-0.489
Planctomycetaceae	4.50E-03	2.07E-02	-0.436
Dictyoglomaceae	4.68E-03	2.07E-02	-0.462
Iamiaceae	4.68E-03	2.07E-02	-0.462
Rhizobiaceae	4.68E-03	2.07E-02	-0.462

Paenibacillaceae	5.18E-03	2.21E-02	-0.561
Porphyromonadaceae	5.80E-03	2.33E-02	1.899
Pseudonocardiaceae	5.96E-03	2.33E-02	-0.429
Cardiobacteriaceae	6.01E-03	2.33E-02	-0.479
Caldicoprobacteraceae	6.64E-03	2.37E-02	-0.429
Microbacteriaceae	6.65E-03	2.37E-02	-0.426
Streptococcaceae	6.68E-03	2.37E-02	1.495
Bacteroidaceae	7.44E-03	2.39E-02	2.060
BVA18	8.29E-03	2.39E-02	-0.409
Gemmatimonadaceae	8.29E-03	2.39E-02	-0.409
Hyphomicrobiaceae	8.29E-03	2.39E-02	-0.409
Oceanospirillaceae	8.29E-03	2.39E-02	-0.409
Oligoflexaceae	8.29E-03	2.39E-02	-0.409
SM2D12	8.29E-03	2.39E-02	-0.409
TM146	8.29E-03	2.39E-02	-0.409
env.OPS 17	8.98E-03	2.53E-02	-0.453
Synergistaceae	9.98E-03	2.70E-02	-0.499
Caulobacteraceae	1.00E-02	2.70E-02	-0.369
Halieaceae	1.12E-02	2.78E-02	-0.396
Hyphomonadaceae	1.12E-02	2.78E-02	-0.396
Nannocystaceae	1.12E-02	2.78E-02	-0.396
Peptostreptococcaceae	1.14E-02	2.78E-02	1.736
Staphylococcaceae	1.15E-02	2.78E-02	1.831
Anaeroplasmataceae	1.25E-02	2.93E-02	-0.426
Micromonosporaceae	1.35E-02	2.93E-02	-0.396
Holophagaceae	1.35E-02	2.93E-02	-0.409
Bradyrhizobiaceae	1.42E-02	2.93E-02	-0.409
Unknown Family	1.46E-02	2.93E-02	-0.397
Cytophagaceae	1.47E-02	2.93E-02	-0.385
Phycisphaeraceae	1.47E-02	2.93E-02	-0.385
Vulgatibacteraceae	1.47E-02	2.93E-02	-0.385
Leptospiraceae	1.48E-02	2.93E-02	-0.409
Nitrospinaceae	1.48E-02	2.93E-02	-0.409

Brevibacteriaceae	1.49E-02	2.93E-02	-0.409
Geodermatophilaceae	1.49E-02	2.93E-02	-0.409
Actinomycetaceae	1.59E-02	3.06E-02	1.008
Parachlamydiaceae	1.60E-02	3.06E-02	-0.409
Thermoanaerobacteraceae	1.63E-02	3.06E-02	-0.409
Family III	1.84E-02	3.32E-02	-0.376
Spongiibacteraceae	1.84E-02	3.32E-02	-0.376
Family XI	1.85E-02	3.32E-02	1.158
Succinivibrionaceae	1.94E-02	3.40E-02	-0.416
Syntrophorhabdaceae	1.95E-02	3.40E-02	-0.396
Dermacoccaceae	1.98E-02	3.41E-02	-0.393
Deferribacteraceae	2.18E-02	3.70E-02	-0.352
Bartonellaceae	2.34E-02	3.92E-02	-0.396
Rhodocyclaceae	2.67E-02	4.41E-02	-0.363
1174-901-12	2.95E-02	4.82E-02	-0.363
Rhodospirillales Incertae Sedis	3.59E-02	5.78E-02	-0.343
Aeromonadaceae	3.66E-02	5.81E-02	-0.676
Clostridium sp. CAG:306	3.79E-02	5.94E-02	-0.432
Verrucomicrobiaceae	3.87E-02	5.99E-02	1.413
FamilyI	3.91E-02	5.99E-02	-0.407
Christensenellaceae	4.16E-02	6.20E-02	0.937
Bdellovibrionaceae	4.20E-02	6.20E-02	-0.333
Hydrogenophilaceae	4.20E-02	6.20E-02	-0.333
Nitrosomonadaceae	4.80E-02	7.00E-02	-0.343
Campylobacteraceae	5.39E-02	7.77E-02	-0.868
Methylophilaceae	5.75E-02	8.19E-02	-0.327
Moraxellaceae	5.96E-02	8.40E-02	-0.494
Pseudomonadaceae	6.28E-02	8.74E-02	-1.333
Brucellaceae	6.41E-02	8.82E-02	-0.357
Methanobacteriaceae	6.61E-02	9.00E-02	-0.300
Mycoplasmataceae	7.15E-02	9.64E-02	-0.301
Chitinophagaceae	9.07E-02	1.21E-01	-0.297
Rhodobacteraceae	1.00E-01	1.32E-01	-0.333

Nocardiaceae	1.14E-01	1.48E-01	-0.347
Micrococcaceae	1.90E-01	2.45E-01	0.420
Oxalobacteraceae	2.58E-01	3.29E-01	-0.264
Bacillaceae	2.71E-01	3.43E-01	-0.208
Bifidobacteriaceae	2.83E-01	3.54E-01	-0.555
Xanthomonadaceae	2.94E-01	3.65E-01	-0.451
Alicyclobacillaceae	3.04E-01	3.73E-01	-0.181
Burkholderiaceae	3.17E-01	3.83E-01	0.313
Sporichthyaceae	3.18E-01	3.83E-01	-0.178
Peptococcaceae	3.49E-01	4.16E-01	0.328
Clostridiales vadinBB60 group	3.65E-01	4.31E-01	0.394
Neisseriaceae	3.79E-01	4.43E-01	-0.418
Corynebacteriaceae	3.94E-01	4.57E-01	0.301
Veillonellaceae	4.24E-01	4.84E-01	-0.496
Leuconostocaceae	4.25E-01	4.84E-01	0.447
Sphingomonadaceae	4.62E-01	5.21E-01	-0.127
Defluviitaleaceae	5.14E-01	5.74E-01	-0.158
Comamonadaceae	5.25E-01	5.81E-01	-0.199
Bacteroidales S24-7 group	5.88E-01	6.45E-01	0.315
Carnobacteriaceae	7.02E-01	7.63E-01	-0.125
Eubacteriaceae	7.09E-01	7.64E-01	-0.132
Prevotellaceae	7.24E-01	7.68E-01	-0.173
Victivallaceae	7.28E-01	7.68E-01	0.149
Fusobacteriaceae	7.31E-01	7.68E-01	-0.242
Enterobacteriaceae	7.80E-01	8.13E-01	-0.196
Clostridiaceae 2	8.62E-01	8.91E-01	-0.072
Leptotrichiaceae	9.27E-01	9.50E-01	0.039
Acidaminococcaceae	9.56E-01	9.68E-01	0.027
Rhodospirillaceae	9.61E-01	9.68E-01	0.025
Alcaligenaceae	9.77E-01	9.77E-01	0.021

Legend: A positive mean log relative abundance means that the abundance is higher in functional IF patients, a negative mean log relative abundance means that the abundance is higher in the surgical IF patients.

Abbreviations: IF, intestinal failure.

Supplementary Table 7. Concentration of SCFA and lactate for surgical IF and functional IF patients at first sample collection per g dry feces

Per g dry feces	**n**	**Surgical IF (n = 8)**	**n**	**Functional IF (n = 7)**	**p-value**
SCFA	8		7		
Acetic acid (C2), µmol/g		226 (153-340)		86.8 (78.1-616)	0.613
Acetic acid (C2), %		94.0 (90.2-96.8)		83.4 (76.0-91.8)	**0.014**
Propionic acid (C3), µmol/g		8.68 (0.84-17.6)		5.47 (3.24-155)	0.536
Propionic acid (C3), %		2.66 (0.47-4.49)		5.79 (3.64-15.0)	**0.040**
Butyric acid (C4), µmol/g		1.57 (1.16-2.69)		5.18 (0.92-78.5)	0.281
Butyric acid (C4), %		0.75 (0.58-0.91)		4.10 (1.85-6.12)	0.072
Valeric acid (C5), µmol/g		0.19 (0.09-0.29)		5.66 (0.17-8.01)	0.189
Valeric acid (C5), %		0.08 (0.04-0.13)		0.65 (0.18-0.92)	**0.002**
Caproic acid (C6), µmol/g		0.44 (0.33-0.48)		0.52 (0.33-0.80)	0.536
Caproic acid (C6), %		0.18 (0.08-0.25)		0.35 (0.06-0.61)	0.536
Heptanoic acid (C7), µmol/g		0.68 (0.28-0.90)		0.71 (0.44-0.87)	0.955
Heptanoic acid (C7), %		0.27 (0.08-0.47)		0.50 (0.14-0.76)	0.281
Octanoic acid (C8), µmol/g		0.37 (0.06-0.98)		0.00 (0.00-0.18)	0.054
Octanoic acid (C8), %		0.20 (0.02-0.42)		0.00 (0.00-0.20)	0.094
Total, µmol/g		245 (173-362)		103 (89.1-917)	0.613
Iso-butyric acid (iC4), µmol/g		0.40 (0.21-1.78)		2.32 (0.09-9.37)	0.336
Iso-butyric acid (iC4), %		0.19 (0.12-0.47)		1.00 (0.15-1.78)	0.072
Iso-valeric acid (iC5), µmol/g		0.86 (0.28-1.19)		2.26 (0.11-6.05)	0.336
Iso-valeric acid (iC5), %		0.34 (0.14-0.48)		0.73 (0.14-1.94)	0.189
Iso-caproic acid (iC6), µmol/g		0.40 (0.21-0.63)		0.89 (0.10-1.42)	0.397
Iso-caproic acid (iC6), %		0.17 (0.10-0.29)		0.21 (0.05-0.86)	0.694
D-lactate, µg/g	5	2052 (1427-9042)	3	298 (189-*)	0.143
L-lactate, µg/g	5	2525 (1276-8152)	3	287 (220-*)	0.143
Total lactate, µg/g	5	4578 (2702-17193)	3	518 (476-*)	0.143
% D-lactate	5	0.51 (0.43-0.62)	3	0.44 (0.40-*)	0.571

Legend: Values shown ad median (IQR) or n (%) unless stated otherwise. * Due to the number of patients it was not possible to calculate an IQR.

Abbreviations: IF, intestinal failure; IQR, SCFA, short-chain fatty acids.

Supplementary Table 8. General linear mixed model for clinical variables and % of short-chain fatty acids

%	**c2**		**c3**		**ic4**		**c4**		**ic5**		**c5**	
	β	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**
Nutrition												
Duration of PN (y)	-0.55	0.669/0.807	0.16	0.817/0.844	0.07	0.417/0.807	0.06	0.911/0.911	0.11	0.295/0.729	-0.26	0.094/0.618
Type of nutrition												
PN only	NA	0.069/0.143	NA	0.369/0.440	NA	0.065/0.143	NA	0.054/0.143	NA	0.065/0.143	NA	0.002/**0.016**
PN+tube feeding	-3.48		1.29		0.36		0.18		0.50		0.07	
PN+oral nutrition±tubefeeding	-0.38		0.355		0.08		0.70		-0.06		0.37	
Tubefeeding/oral nutrition	-18.4		7.70		1.46		7.88		1.58		1.24	
PN dependency (% of total energy intake)	0.17	0.017/0.106	-0.066	0.133/0.242	-0.01	0.024/0.119	-0.06	0.059/0.174	-0.01	0.031/0.119	-0.01	0.003/**0.049**
Calories of PN divided by REE (%)	8.87	0.057/0.227	-2.86	0.317/0.393	-0.56	0.115/0.265	-3.33	0.085/0.241	-0.57	0.171/0.298	-0.38	0.068/0.227
Oral nutrition (no/yes)	-1.78	0.699/0.774	1.21	0.670/0.769	0.28	0.440/0.593	2.03	0.294/0.492	0.13	0.746/0.797	0.35	0.083/0.427
Oral/enteral fiber intake per kg (g/kg)	-24.7	0.100/0.259	18.7	0.031/0.158	1.92	0.085/0.251	5.78	0.381/0.651	2.71	0.036/0.161	0.58	0.379/0.651
Tube feeding (no/yes)	-3.88	0.480/0.640	2.06	0.516/0.640	0.45	0.262/0.527	0.55	0.804/0.859	0.54	0.260/0.527	0.10	0.707/0.811
Tube feeding type												
Polymeric	NA	0.949/0.990	NA	0.857/0.990	NA	0.838/0.990	NA	0.751/0.990	NA	0.848/0.990	NA	0.571/0.931
Semi-elemental	2.68		-3.27		-0.35		-2.48		-0.49		-0.39	
Elemental	-2.33		-3.81		0.25		2.12		0.17		1.47	
Mode of tube feeding												
Continuous	NA	0.530/0.876	NA	0.795/0.957	NA	0.899/0.957	NA	0.267/0.786	NA	0.926/0.957	NA	0.357/0.786
Bolus	-5.27		1.64		0.28		3.17		0.29		0.55	
Both	-12.5		3.96		0.14		6.80		0.22		-0.01	

Gastro-intestinal characteristics												
Whole bowel in situ (no/yes)	-1.31	0.862/0.950	0.36	0.926/0.957	0.09	0.861/0.950	2.51	0.385/0.615	-0.24	0.694/0.906	0.02	0.985/0.985
Remaining small bowel length (cm)	0.10	0.481/0.842	-0.05	0.496/0.842	-0.10	0.292/0.796	-0.01	0.880/0.989	-0.01	0.563/0.872	0.00	0.989/0.989
Ileocecal valve in situ (no/yes)	-0.71	0.923/0.950	-0.31	0.937/0.950	0.18	0.710/0.852	2.03	0.476/0.771	-0.28	0.638/0.824	1.56	0.058/0.180
Partial or total colectomy (no/yes)	7.20	0.288/0.461	-1.88	0.593/0.716	-0.69	0.097/0.376	-2.75	0.293/0.461	-0.67	0.204/0.460	-0.96	0.276/0.461
Growth												
BMI SDS	-2.00	0.460/0.852	0.88	0.615/0.852	-0.10	0.666/0.852	0.02	0.983/0.983	-0.04	0.876/0.970	0.01	0.962/0.983
Height-for-age SDS < -2 (no/yes)	-13.2	0.322/0.704	3.65	0.600/0.750	1.23	0.154/0.478	6.68	0.194/0.502	1.20	0.260/0.619	1.26	0.454/0.704
Growing outside target height range (no/yes)	-6.91	0.608/0.797	0.89	0.899/0.929	0.60	0.458/0.797	4.37	0.394/0.797	0.55	0.593/0.797	1.01	0.566/0.797
Medication use (no/yes)												
Proton pump inhibitor	16.5	0.008/**0.035**	-8.98	0.004/**0.025**	-1.20	0.002/**0.016**	-2.47	0.340/0.499	-1.67	<0.001/**0.007**	-0.34	0.226/0.427
Motility agents	15.0	0.019/**0.063**	-7.72	0.024/**0.068**	-0.89	0.035/**0.081**	-5.34	0.037/**0.081**	-1.36	0.007/**0.039**	-0.18	0.668/0.828
Cholestyramine	-6.99	0.206/0.426	1.59	0.604/0.693	0.31	0.480/0.620	0.81	0.728/0.806	0.64	0.199/0.426	1.33	<0.001/**<0.001**
Ursochol	15.6	0.053/0.150	-7.04	0.130/0.288	-1.37	0.024/0.083	-2.73	0.414/0.755	-1.65	0.020/**0.083**	-2.12	<0.001/**<0.001**
Treatment of bacterial overgrowth	-3.40	0.723/0.833	3.65	0.461/0.696	-0.25	0.693/0.833	-4.50	0.217/0.597	0.10	0.901/0.931	-0.90	0.458/0.696
Antibiotics at sample*	13.0	0.003/**0.019**	-7.37	0.004/**0.020**	-0.75	0.024/**0.069**	-4.39	0.018/**0.056**	-1.10	0.004/**<0.001**	-0.32	0.123/0.238
Antibiotics between samples	14.0	<0.001/**0.001**	-7.25	0.003/**0.013**	-1.19	<0.001/**0.001**	-4.60	0.005/**0.018**	-1.43	<0.001/**<0.001**	-0.41	0.010/**0.028**
Line sepsis (no/yes)**	14.8	0.007/**0.071**	-5.07	0.143/0.371	-1.15	0.010/0.078	-4.08	0.084/0.344	-1.39	0.005/**0.071**	-0.72	0.002/**0.067**

Supplementary Table 8 continued. General linear mixed model for clinical variables and % of short-chain fatty acids and branched-chain fatty acids

%	**ic6**		**c6**		**c7**		**c8**	
	β	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**
Nutrition								
Duration of PN (y)	-0.01	0.717/0.807	-0.01	0.651/0.807	0.09	0.120/0.618	0.26	0.385/0.676
Type of nutrition								
PN only	NA	0.757/0.757	NA	0.689/0.712	NA	0.262/0.338	NA	0.399/0.283
PN+tube feeding	-0.04		0.07		0.45		2.44	
PN+oral nutrition±tubefeeding	0.03		-0.01		-0.18		0.11	
Tubefeeding/oral nutrition	-0.08		0.08		-0.12		0.08	
PN dependency (% of total energy intake)	0.00	0.842/0.877	-0.01	0.075/0.175	0.00	0.905/0.905	-0.02	0.234/0.242
Calories of PN divided by REE (%)	0.02	0.714/0.738	-0.11	0.072/0.227	0.11	0.674/0.720	-1.64	0.213/0.287
Oral nutrition (no/yes)	0.00	0.998/0.998	-0.03	0.649/0.769	-0.41	0.141/0.463	-1.11	0.404/0.574
Oral/enteral fiber intake per kg (g/kg)	-0.02	0.894/0.920	-0.12	0.519/0.699	-0.61	0.474/0.668	-2.21	0.609/0.764
Tube feeding (no/yes)	-0.05	0.440/0.640	0.07	0.321/0.586	0.24	0.404/0.640	1.61	0.258/0.527
Tube feeding type								
Polymeric	NA	0.829/0.990	NA	0.251/0.698	NA	0.916/0.990	NA	0.379/0.781
Semi-elemental	-0.07		-0.01		0.13		4.09	
Elemental	-0.03		0.33		0.30		-0.22	
Mode of tube feeding								
Continuous	NA	0.701/0.945	NA	0.034/0.527	NA	0.584/0.876	NA	0.366/0.786
Bolus	-0.03		-0.31		0.25		-3.17	
Both	0.05		-0.23		-0.28		-3.27	
Gastro-intestinal characteristics								
Whole bowel in situ (no/yes)	0.02	0.741/0.919	-0.04	0.701/0.906	-0.26	0.410/0.615	-1.92	0.255/0.514

Remaining small bowel length (cm)	-0.01	0.212/0.795	-0.01	0.117/0.605	0.01	0.334/0.796	-0.05	0.085/0.605
Ileocecal valve in situ (no/yes)	0.14	0.055/0.180	0.06	0.569/0.802	-0.28	0.424/0.771	-3.61	0.032/0.140
Partial or total colectomy (no/yes)	-0.12	0.026/0.272	-0.11	0.274/0.461	0.40	0.160/0.450	-0.62	0.686/0.733
Growth								
BMI SDS	-0.02	0.590/0.852	0.02	0.629/0.852	0.11	0.505/0.852	-0.60	0.443/0.852
Height-for-age SDS < -2 (no/yes)	-0.06	0.653/0.750	0.29	0.096/0.331	-0.15	0.806/0.843	-1.32	0.671/0.750
Growing outside target height range (no/yes)	-0.06	0.623/0.797	0.34	0.056/0.351	0.24	0.665/0.797	-1.58	0.609/0.797
Medication use (no/yes)								
Proton pump inhibitor	0.03	0.648/0.744	-0.07	0.372/0.501	0.18	0.526/0.627	-2.14	0.145/0.326
Motility agents	-0.02	0.716/0.854	0.01	0.952/1.000	0.72	0.008/0.620	-0.48	0.768/0.882
Cholestyramine	-0.13	0.023/0.101	0.13	0.078/0.241	0.21	0.464/0.620	1.98	0.153/0.365
Ursochol	0.01	0.922/0.974	-0.25	0.037/0.116	-0.14	0.755/0.923	-0.54	0.804/0.923
Treatment of bacterial overgrowth	-0.12	0.167/0.597	0.11	0.417/0.696	-0.12	0.772/0.850	6.86	<0.001/**0.004**
Antibiotics at sample[1]	-0.01	0.818/0.967	0.02	0.723/0.934	0.52	0.045/**0.095**	1.17	0.361/0.567
Antibiotics between samples	-0.02	0.762/0.844	0.02	0.661/0.844	0.41	0.162/0.314	0.80	0.527/0.779
Line sepsis (no/yes)[2]	-0.05	0.514/0.613	-0.11	0.106/0.364	0.15	0.686/0.759	-1.31	0.430/0.522

Legend: [1] Due to bacterial overgrowth, line sepsis or another cause. [2] with a range of two months before and 2 months after sample collection.
A positive beta coefficient means that the two variables are positively associated, a negative coefficient means that they are negatively associated. For categorical variables the beta coefficients of all categories relative to the first category are mentioned; positive coefficients means that it is more positively associated with higher values of the response variable than the first category.
Abbreviations: BMI, body mass index; PN, parenteral nutrition; REE, resting energy expenditure; SDS, standard deviation score.

Supplementary Table 9. General linear mixed model for clinical variables and absolute values of short-chain fatty acids

Absolute values	**c2**		**c3**		**ic4**		**c4**		**ic5**		**c5**	
	β	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**
Nutrition												
Duration of PN (y)	-20.2	0.230/0.688	-4.63	0.146/0.646	-0.19	0.483/0.807	-3.72	0.067/0.618	-0.08	0.791/0.844	-0.49	0.048/0.618
Type of nutrition												
PN only	NA	0.191/0.283	NA	0.085/0.155	NA	0.006/**0.031**	NA	0.005/**0.031**	NA	0.015/**0.065**	NA	0.006/**0.031**
PN+tube feeding	-15.1		-23.5		-1.24		-14.9		-0.84		-0.96	
PN+oral nutrition±tubefeeding	-80.7		-5.63		-0.06		3.95		6.05		0.50	
Tubefeeding/oral nutrition	-36.4		36.2		5.44		30.9		-0.85		3.53	
PN dependency (% of total energy intake)	0.94	0.292/0.411	-0.20	0.361/0.465	-0.03	0.062/0.174	-0.11	0.375/0.465	-0.04	0.037/0.128	-0.02	0.079/0.175
Calories of PN divided by REE (%)	77.2	0.179/0.298	-15.5	0.270/0.363	-2.25	0.059/0.227	-8.57	0.309/0.393	-2.62	0.052/0.227	-1.25	0.128/0.265
Oral nutrition (no/yes)	15.14	0.792/0.818	18.6	0.272/0.492	2.27	0.080/0.427	16.5	0.075/0.427	2.07	0.182/0.463	1.08	0.186/0.463
Oral/enteral fiber intake per kg (g/kg)	-126	0.399/0.651	98.7	<0.001/**0.004**	8.25	0.003/**0.030**	32.3	0.089/0.251	11.1	0.002/**0.026**	1.82	0.474/0.668
Tube feeding (no/yes)	-121	0.072/0.386	-12.2	0.426/0.640	-0.42	0.754/0.835	-10.5	0.249/0.527	0.22	0.885/0.887	-0.95	0.342/0.589
Tube feeding type												
Polymeric	NA	0.765/0.990	NA	0.121/0.552	NA	0.270/0.698	NA	0.191/0.591	NA	0.367/0.781	NA	0.012/0.103
Semi-elemental	-32.5		-38.5		-3.21		-18.7		-3.90		-1.966	
Elemental	50.9		-30.0		-0.16		8.12		-1.38		2.20	
Mode of tube feeding												
Continuous	NA	0.887/0.957	NA	0.161/0.786	NA	0.380/0.786	NA	0.235/0.786	NA	0.412/0.799	NA	0.593/0.876
Bolus	29.5		14.0		1.53		8.10		1.87		-0.58	

Both	31.4		31.3		2.24		20.0		2.76		-1.37	
Gastro-intestinal characteristics												
Whole bowel in situ (no/yes)	225	0.010/**0.044**	35.6	0.035/0.109	3.27	0.023/**0.078**	29.5	0.006/**0.031**	1.91	0.251/0.514	4.39	<0.001/**0.002**
Remaining small bowel length (cm)	2.17	0.045/0.605	-0.09	0.722/0.973	-0.10	0.684/0.964	0.04	0.768/0.989	-0.01	0.941/0.989	0.01	0.231/0.795
Ileocecal valve in situ (no/yes)	47.9	0.615/0.824	32.9	0.068/0.192	2.65	0.090/0.232	25.6	0.022/0.113	0.66	0.714/0.852	4.04	0.001/**0.021**
Partial or total colectomy (no/yes)	-47.0	0.602/0.716	-8.07	0.624/0.716	-1.60	0.248/0.461	-11.6	0.297/0.461	-0.95	0.530/0.716	-2.48	0.048/0.372
Growth												
BMI SDS	32.7	0.310/0.852	12.2	0.134/0.852	0.57	0.417/0.852	5.37	0.222/0.852	0.37	0.660/0.852	0.36	0.409/0.852
Height-for-age SDS < -2 (no/yes)	73.3	0.677/0.750	18.7	0.576/0.750	4.83	0.090/0.331	37.3	0.091/0.331	4.12	0.192/0.502	4.31	0.096/0.331
Growing outside target height range (no/yes)	-36.3	0.832/0.929	0.91	0.977/0.977	2.04	0.406/0.797	25.8	0.235/0.797	1.16	0.668/0.797	2.76	0.280/0.797
Medication use (no/yes)												
Proton pump inhibitor	99.7	0.147/0.326	-16.9	0.280/0.434	-2.54	0.053/0.151	-3.59	0.707/0.782	-3.29	0.021/**0.078**	-0.95	0.354/0.499
Motility agents	-108	0.196/0.289	-38.3	0.012/**0.048**	-3.64	0.004/**0.034**	-22.6	0.032/**0.081**	-4.49	0.001/**0.012**	-1.92	0.130/0.211
Cholestyramine	-72.3	0.266/0.485	-2.75	0.856/0.856	1.03	0.474/0.620	-5.88	0.528/0.647	1.47	0.338/0.551	3.00	0.015/**0.095**
Ursochol	95.9	0.343/0.664	-15.2	0.516/0.836	-3.59	0.086/0.223	1.45	0.917/0.974	-3.19	0.175/0.362	-5.57	<0.001/**0.003**
Treatment of bacterial overgrowth	-141	0.246/0.597	-16.0	0.494/0.696	-2.42	0.222/0.597	-23.9	0.114/0.597	-1.91	0.382/0.696	-2.41	0.182/0.597
Antibiotics at sample[1]	-115	0.031/**0.081**	-46.5	<0.001/**0.002**	-3.46	0.002/**0.016**	-18.73	0.017/**0.056**	-4.61	<0.001/**0.002**	-2.23	0.004/**0.019**
Antibiotics between samples	-48.2	0.310/0.534	-48.3	<0.001/**0.001**	-4.66	<0.001/**<0.001**	-18.8	0.006/**0.018**	-6.33	<0.001/**<0.001**	-2.33	<0.001/**0.002**
Line sepsis (no/yes)[2]	112	0.089/0.344	4.17	0.818/0.846	-1.60	0.313/0.555	5.51	0.588/0.675	-1.95	0.295/0.555	-1.54	0.125/0.371

Supplementary Table 9 continued. General linear mixed model for clinical variables and absolute values of short-chain fatty acids and branched-chain fatty acids

Absolute values	**ic6**		**c6**		**c7**		**c8**		**total**	
	β	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**
Nutrition										
Duration of PN (y)	-0.02	0.723/0.807	-0.03	0.343/0.759	0.37	0.095/0.618	0.46	0.244/0.688	-25.5	0.175/0.676
Type of nutrition										
PN only	NA	0.110/0.190	NA	0.029/0.095	NA	0.616/0.658	NA	0.186/0.283	NA	0.080/0.154
PN+tube feeding	-0.40		-0.11		1.25		4.00		-173	
PN+oral nutrition±tubefeeding	0.22		-0.10		-0.68		-0.70		-52.1	
Tubefeeding/oral nutrition	-0.23		0.65		0.35		0.85		68.0	
PN dependency (% of total energy intake)	0.01	0.415/0.476	-0.01	0.016/0.106	-0.01	0.849/0.877	-0.04	0.140/0.242	0.29	0.776/0.859
Calories of PN divided by REE (%)	0.13	0.535/0.624	-0.38	0.021/0.213	0.08	0.943/0.943	-2.69	0.148/0.287	37.1	0.573/0.634
Oral nutrition (no/yes)	0.27	0.194/0.463	0.22	0.183/0.463	-0.97	0.407/0.574	-2.39	0.216/0.478	70.7	0.302/0.492
Oral/enteral fiber intake per kg (g/kg)	-0.15	0.676/0.788	-0.46	0.385/0.651	-1.49	0.686/0.788	-1.79	0.765/0.847	16.85	0.920/0.920
Tube feeding (no/yes)	-0.54	0.016/0.349	0.11	0.512/0.640	0.85	0.474/0.640	3.03	0.138/0.474	-134	0.075/0.386
Tube feeding type										
Polymeric	NA	0.531/0.915	NA	0.007/0.103	NA	0.990/0.990	NA	0.368/0.781	NA	0.403/0.781
Semi-elemental	-0.22		-0.07		-0.22		5.12		-135	
Elemental	-0.10		1.04		0.23		-1.08		13.9	
Mode of tube feeding										

Continuous	NA	0.120/0.786	NA	0.099/0.786	NA	0.540/0.876	NA	0.373/0.786	NA	0.518/0.876
Bolus	0.12		-0.50		1.63		-3.35		62.4	
Both	0.33		-0.34		-0.42		-4.40		98.2	
Gastro-intestinal characteristics										
Whole bowel in situ (no/yes)	0.62	0.006/**0.031**	0.39	0.018/**0.069**	-0.77	0.553/0.780	-3.82	0.079/0.204	273	0.004/**0.030**
Remaining small bowel length (cm)	0.01	0.655/0.964	-0.01	0.157/0.694	0.02	0.316/0.796	-0.04	0.268/0.796	2.16	0.075/0.605
Ileocecal valve in situ (no/yes)	0.53	0.051/0.180	0.170	0.410/0.771	-1.05	0.462/0.771	-6.73	0.002/**0.037**	110	0.300/0.715
Partial or total colectomy (no/yes)	-0.39	0.068/0.376	-0.27	0.085/0.376	1.78	0.119/0.410	1.31	0.522/0.716	-59.8	0.560/0.716
Growth										
BMI SDS	0.03	0.859/0.970	0.10	0.336/0.852	0.37	0.581/0.852	-0.73	0.535/0.852	34.5	0.324/0.852
Height-for-age SDS < -2 (no/yes)	-0.11	0.816/0.843	1.44	<0.001/**<0.001**	0.20	0.935/0.935	-2.13	0.621/0.750	168	0.406/0.704
Growing outside target height range (no/yes)	-0.27	0.535/0.797	1.02	<0.001/**0.011**	0.33	0.890/0.929	-2.37	0.572/0.797	31.8	0.869/0.929
Medication use (no/yes)										
Proton pump inhibitor	0.25	0.255/0.427	-0.29	0.080/0.207	0.96	0.417/0.538	-2.52	0.213/0.427	56.9	0.468/0.581
Motility agents	-0.288	0.215/0.303	-0.31	0.062/0.112	2.61	0.020/**0.063**	0.42	0.848/0.939	-167	0.074/0.128
Cholestyramine	-0.38	0.071/0.241	0.31	0.093/0.241	1.20	0.313/0.540	4.60	0.012/**0.095**	-58.7	0.426/0.620
Ursochol	-0.11	0.743/0.923	-0.93	0.121/0.288	-1.32	0.475/0.817	-0.23	0.942/0.974	65.9	0.566/0.836
Treatment of bacterial overgrowth	-0.47	0.135/0.597	0.07	0.795/0.850	-0.91	0.593/0.800	8.79	0.001/**0.008**	-178	0.194/0.597
Antibiotics at sample[1]	-0.02	0.936/0.967	-0.03	0.874/0.967	1.63	0.134/0.244	2.31	0.204/0.351	-152	0.013/**0.051**
Antibiotics between samples	0.16	0.476/0.777	-0.03	0.847/0.906	1.42	0.245/0.447	1.28	0.511/0.778	-78.2	0.158/0.314
Line sepsis (no/yes)[2]	0.10	0.710/0.759	-0.28	0.246/0.537	0.00	1.000/1.000	-2.95	0.240/0.537	111	0.143/0.371

Legend: [1] Due to bacterial overgrowth, line sepsis or another cause. [2] with a range of two months before and 2 months after sample collection. A positive beta coefficient means that the two variables are positively associated, a negative coefficient means that they are negatively associated. For categorical variables the beta coefficients of all categories relative to the first category are mentioned; positive coefficients means that it is more positively associated with higher values of the response variable than the first category.

Abbreviations: BMI, body mass index; PN, parenteral nutrition; REE, resting energy expenditure; SDS, standard deviation score.

Supplementary Table 10. General linear mixed model for clinical variables and lactate and number of 16S rRNA gene copies

	L lactate		**D lactate**		**Total lactate**		**% D lactate**		**Log of 16S rRNA gene copy number per g dry feces**		**Log of 16S rRNA gene copy number per g wet feces**	
	β	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**	**β**	**p-value unadjusted/ adjusted**
Nutrition												
Duration of PN (y)	17.5	0.546/0.807	17.0	0.531/0.807	-12.7	0.700/0.807	-0.01	0.469/0.807	0.03	0.517/0.807	4.12	0.710/0.807
Type of nutrition												
PN only	NA	0.238/0.320	NA	0.140/0.229	NA	0.067/0.143	NA	0.353/0.437	NA	0.031/**0.095**	NA	0.542/0.600
PN+tube feeding	-125		-284		0.00		0.03		0.53		-62.0	
PN+oral nutrition±tubefeeding	-148		-102		329		0.05		0.56		-97.3	
Tubefeeding/oral nutrition	-456		-333		-85.9		0.08		0.55		-115	
PN dependency (% of total energy intake)	5.31	0.008/**0.086**	3.59	0.027/0.119	4.27	0.188/0.291	-0.01	0.141/0.242	-0.01	0.074/0.175	0.71	0.399/0.476
Calories of PN divided by REE (%)	308	0.016/0.213	204	0.051/0.227	220	0.186/0.298	-0.04	0.116/0.265	-0.21	0.250/0.352	34.0	0.544/0.624
Oral nutrition (no/yes)	-185	0.191/0.463	-62.8	0.622/0.769	146	0.399/0.574	0.04	0.139/0.463	0.20	0.300/0.492	-72.2	0.232/0.480
Oral/enteral fiber intake per kg (g/kg)	-488	0.189/0.451	-371	0.212/0.469	-1045	0.085/0.251	0.01	0.862/0.920	0.34	0.446/0.668	-167	0.300/0.621
Tube feeding (no/yes)	25.8	0.887/0.887	-274	0.023/0.349	-365	0.113/0.474	0.03	0.239/0.527	0.37	0.041/0.349	-64.3	0.272/0.527
Tube feeding type												
Polymeric	NA	0.155/0.552	NA	0.980/0.990	NA	0.137/0.552	NA	0.979/0.990	NA	0.676/0.990	NA	0.476/0.869
Semi-elemental	551		56.3		-312		0.01		-0.26		100	
Elemental	96.0		46.2		-460		0.01		-0.02		6.78	
Mode of tube feeding												
Continuous	NA	0.140/0.786	NA	0.775/0.957	NA	0.020/0.527	NA	0.679/0.945	NA	0.960/0.960	NA	0.369/0.786
Bolus	298		106		295		0.03		-0.04		-73.2	
Both	301		68.9		554		0.01		-0.07		-71.3	
Gastro-intestinal characteristics												

Whole bowel in situ (no/yes)	-139	0.394/0.615	133	0.266/0.514	-31.5	0.864/0.950	-0.01	0.889/0.950	0.18	0.417/0.615	98.6	0.108/0.259
Remaining small bowel length (cm)	-0.25	0.962/0.989	3.24	0.452/0.842	5.94	0.433/0.842	0.01	0.443/0.842	-0.01	0.845/0.989	-1.16	0.099/0.605
Ileocecal valve in situ (no/yes)	-115	0.497/0.771	111	0.433/0.771	155	0.371/0.771	-0.01	0.813/0.901	-0.06	0.810/0.901	4.45	0.950/0.950
Partial or total colectomy (no/yes)	78.3	0.659/0.729	-5.50	0.974/0.974	345	0.093/0.376	0.03	0.208/0.460	-0.05	0.811/0.838	-80.7	0.136/0.420
Growth												
BMI SDS	66.3	0.502/0.852	123	0.116/0.852	-91.7	0.423/0.852	-0.01	0.687/0.852	0.01	0.960/0.983	42.0	0.212/0.852
Height-for-age SDS < -2 (no/yes)	-222	0.349/0.704	-77.6	0.665/0.750	-379	0.057/0.331	0.04	0.447/0.704	0.32	0.423/0.704	-69.6	0.587/0.750
Growing outside target height range (no/yes)	-222	0.349/0.797	-77.6	0.665/0.797	-379	0.057/0.351	0.04	0.447/0.797	0.26	0.448/0.797	-89.6	0.444/0.797
Medication use (no/yes)												
Proton pump inhibitor	286	0.023/**0.078**	294	0.007/**0.035**	409	0.001/**0.015**	-0.01	0.732/0.782	-0.22	0.244/0.427	-1.75	0.976/0.991
Motility agents	461	0.003/**0.034**	316	0.052/0.100	0.00	1.000/1.000	-0.01	0.983/1.000	-0.46	0.012/**0.048**	-69.3	0.232/0.312
Cholestyramine	-216	0.086/0.241	-261	0.023/0.101	-428	0.005/**0.047**	0.03	0.236/0.457	0.04	0.818/0.845	51.3	0.363/0.563
Ursochol	483	0.015/**0.080**	666	0.024/**0.083**	0.00	1.000/1.000	0.01	0.779/0.923	-0.12	0.669/0.902	-43.4	0.639/0.900
Treatment of bacterial overgrowth	-239	0.278/0.615	-221	0.189/0.597	-348	0.084/0.597	-0.01	0.723/0.833	-0.01	0.988/0.988	91.9	0.250/0.597
Antibiotics at sample[1]	112	0.471/0.696	-3.54	0.977/0.977	-286	0.041/**0.095**	-0.01	0.977/0.934	-0.16	0.366/0.567	14.7	0.787/0.967
Antibiotics between samples	41.5	0.752/0.844	14.0	0.911/0.941	354	0.028/**0.073**	0.01	0.989/0.989	-0.11	0.553/0.780	-33.0	0.608/0.819
Line sepsis (no/yes)[2]	267	0.335/0.555	496	0.060/0.309	348	0.402/0.562	0.05	0.340/0.555	0.21	0.368/0.562	-56.4	0.506/0.613

Legend: [1]Due to bacterial overgrowth, line sepsis or another cause. [2] with a range of two months before and 2 months after sample collection.
A positive beta coefficient means that the two variables are positively associated, a negative coefficient means that they are negatively associated. For categorical variables the beta coefficients of all categories relative to the first category are mentioned; positive coefficients means that it is more positively associated with higher values of the response variable than the first category.
Abbreviations: BMI, body mass index; PN, parenteral nutrition; REE, resting energy expenditure; SDS, standard deviation score.

Supplementary Table 11. Clinical variables associated with OTUs

Variable	**OTUs**	**Adjusted p-value**	**β coefficient*** **		
Nutrition					
Duration of PN (y)	No significant associations with OTUs				
Type of nutrition (PN only (NA), PN+tube feeding, PN+oral nutrition±tubefeeding, tubefeeding/oral nutrition)	OTU_86_Genus_Parasutterella	<0.001	-0.039	-0.822	4.037
	OTU_13_Genus_Bacteroides	<0.001	-1.323	0.232	4.360
	OTU_32_Genus_Bacteroides	<0.001	-0.689	-0.543	4.114
	OTU_59_Genus_Barnesiella	<0.001	-0.660	0.056	3.759
	OTU_347_Genus_Lachnoclostridium	<0.001	0.287	0.275	3.069
	OTU_88_Family_CFT112H7	<0.001	-0.370	-0.943	3.720
	OTU_128_Genus_Peptoclostridium	<0.001	-0.029	-0.819	3.599
	OTU_102_Genus_Odoribacter	<0.001	-0.601	0.341	3.787
	OTU_49_Genus_Roseburia	0.001	-2.051	-0.558	2.650
	OTU_57_Genus_Subdoligranulum	0.001	-0.475	-0.399	2.618
	OTU_55_Genus_Blautia	0.001	-0.752	-0.145	2.443
	OTU_205_Genus_Alistipes	0.001	-0.554	0.073	2.574
	OTU_63_Genus_Lachnoclostridium	0.001	-0.953	-0.338	3.084
	OTU_67_Genus_Collinsella	0.001	-1.356	-0.973	1.981
	OTU_268_Genus_Holdemanella	0.002	0.575	0.052	2.509
	OTU_23_Genus_Alistipes	0.002	-1.687	0.475	3.181
	OTU_220_Family_Lachnospiraceae	0.002	-0.395	0.483	2.974
	OTU_33_Genus_Pseudobutyrivibrio	0.003	-0.889	-0.536	2.790
	OTU_60_Genus_Anaerostipes	0.004	-0.569	0.273	2.853
	OTU_108_Genus_Fusicatenibacter	0.006	-0.955	0.147	2.356
	OTU_943_Class_Bacteroidetes VC2.1 Bac22	0.011	0.713	1.465	2.245
	OTU_10_Family_Bacteroidales S24-7 group	0.012	0.041	0.217	2.827
	OTU_12_Genus_Bacteroides	0.018	-2.147	0.095	2.735
	OTU_133_Genus_Bacteroides	0.019	-1.825	0.063	2.624
	OTU_207_Genus_Allisonella	0.020	0.135	-0.219	2.207
	OTU_230_Genus_Coprobacter	0.021	-0.629	0.689	1.610
	OTU_226_Genus_Slackia	0.021	0.174	-0.178	2.172
	OTU_28_Genus_Bacteroides	0.021	0.472	2.489	4.141
	OTU_155_Genus_Enterorhabdus	0.023	0.133	0.322	2.297
	OTU_82_Genus_Bacteroides	0.023	-0.770	1.046	1.829
	OTU_116_Genus_Ruminococcaceae UCG-005	0.024	-0.683	-0.139	1.870
	OTU_106_Genus_[Eubacterium] hallii group	0.025	-0.400	0.455	1.901
	OTU_62_Genus_Parabacteroides	0.028	-0.966	1.488	1.518
	OTU_209_Genus_Victivallis	0.029	0.191	0.311	2.100

	OTU_159_Class_Bacteroidetes VC2.1 Bac22	0.030	-0.221	0.066	2.081
	OTU_85_Genus_Lachnospiraceae NK4A136 group	0.030	-1.318	-0.311	2.033
	OTU_39_Genus_Alistipes	0.030	-1.002	1.391	1.989
	OTU_213_Order_Gastranaerophilales	0.030	0.225	0.322	1.859
	OTU_99_Genus_Bacteroides	0.030	-0.586	-0.472	2.204
	OTU_43_Family_Lachnospiraceae	0.030	0.669	-0.622	-2.032
	OTU_191_Genus_Lachnospiraceae UCG-008	0.030	-1.000	-0.226	0.858
	OTU_75_Family_Ruminococcaceae	0.039	-0.685	0.399	1.976
	OTU_74_Genus_Ruminococcaceae UCG-002	0.039	-0.406	0.137	2.699
	OTU_44_Genus_[Eubacterium] coprostanoligenes group	0.055	-0.213	0.167	1.751
	OTU_130_Genus_Acidaminococcus	0.055	0.260	0.224	2.077
	OTU_26_Genus_Blautia	0.055	-1.156	-0.067	2.564
	OTU_93_Genus_Blautia	0.059	-0.815	0.379	1.920
	OTU_184_Genus_Anaerosporobacter	0.059	0.432	1.246	0.431
	OTU_19_Genus_Tyzzerella 4	0.061	-3.313	-1.131	-1.395
	OTU_1_Genus_Escherichia-Shigella	0.065	-1.521	-0.886	-4.733
	OTU_196_Genus_Ruminococcaceae NK4A214 group	0.065	0.229	0.330	1.324
	OTU_96_Genus_Streptococcus	0.068	-1.460	0.335	-1.359
	OTU_41_Genus_Subdoligranulum	0.070	0.062	0.158	2.403
	OTU_89_Genus_Lachnospira	0.070	-1.673	-1.202	0.999
	OTU_42_Genus_Ruminococcus 2	0.071	0.248	-0.185	2.284
	OTU_48_Genus_Blautia	0.071	-0.542	-0.204	1.374
	OTU_78_Genus_Blautia	0.072	0.391	1.314	1.330
	OTU_14_Genus_Staphylococcus	0.079	-0.550	-0.307	-3.509
	OTU_113_Genus_Lachnoclostridium	0.083	-1.459	-0.317	1.293
	OTU_154_Genus_Incertae Sedis	0.085	-0.072	0.241	1.436
	OTU_29_Family_Lachnospiraceae	0.088	-2.486	-1.142	0.479
	OTU_114_Genus_Faecalibacterium	0.098	-0.547	0.113	1.334
	OTU_194_Genus_Butyricimonas	0.098	-0.553	-0.062	1.169
	OTU_695_Genus_Bacteroides	0.098	-1.039	0.417	1.723
	OTU_261_Genus_Desulfovibrio	0.098	-0.210	0.402	1.721
	OTU_204_Genus_Ruminiclostridium	0.098	-0.743	0.038	1.508
	OTU_94_Genus_Clostridium sensu stricto 1	0.098	-1.738	-1.118	-1.070
	OTU_61_Genus_Clostridium sensu stricto 1	0.099	-1.716	0.015	-2.036
Calories of PN divided by REE (%)	OTU_86_Genus_Parasutterella	0.001	-2.627		
	OTU_88_Family_CFT112H7	0.001	-2.768		
	OTU_128_Genus_Peptoclostridium	0.001	-2.539		
	OTU_347_Genus_Lachnoclostridium	0.004	-1.402		
	OTU_268_Genus_Holdemanella	0.004	-1.487		

	OTU_32_Genus_Bacteroides	0.004	-1.969		
	OTU_59_Genus_Barnesiella	0.015	-1.764		
	OTU_13_Genus_Bacteroides	0.020	-2.180		
	OTU_207_Genus_Allisonella	0.022	-1.344		
	OTU_226_Genus_Slackia	0.022	-1.310		
	OTU_7_Genus_Prevotella 9	0.022	1.361		
	OTU_44_Genus_[Eubacterium] coprostanoligenes group	0.024	-1.172		
	OTU_57_Genus_Subdoligranulum	0.026	-1.208		
	OTU_55_Genus_Blautia	0.034	-1.336		
	OTU_1_Genus_Escherichia-Shigella	0.034	2.777		
	OTU_213_Order_Gastranaerophilales	0.034	-1.024		
	OTU_196_Genus_Ruminococcaceae NK4A214 group	0.038	-0.700		
	OTU_102_Genus_Odoribacter	0.042	-1.735		
	OTU_130_Genus_Acidaminococcus	0.044	-1.103		
	OTU_231_Genus_Leuconostoc	0.044	-1.504		
	OTU_10_Family_Bacteroidales S24-7 group	0.047	-1.426		
	OTU_60_Genus_Anaerostipes	0.047	-1.354		
	OTU_220_Family_Lachnospiraceae	0.054	-1.289		
	OTU_99_Genus_Bacteroides	0.054	-1.452		
	OTU_943_Class_Bacteroidetes VC2.1 Bac22	0.054	-1.131		
	OTU_28_Genus_Bacteroides	0.054	-2.040		
	OTU_63_Genus_Lachnoclostridium	0.059	-1.385		
	OTU_209_Genus_Victivallis	0.065	-1.129		
	OTU_33_Genus_Pseudobutyrivibrio	0.081	-1.355		
	OTU_61_Genus_Clostridium sensu stricto 1	0.082	1.611		
	OTU_205_Genus_Alistipes	0.084	-1.129		
	OTU_155_Genus_Enterorhabdus	0.087	-1.237		
	OTU_90_Genus_Thalassospira	0.092	-0.900		
	OTU_72_Genus_Phascolarctobacterium	0.099	0.946		
PN dependency (% of total energy intake)	OTU_347_Genus_Lachnoclostridium	0.009	-0.022		
	OTU_86_Genus_Parasutterella	0.012	-0.033		
	OTU_88_Family_CFT112H7	0.051	-0.029		
	OTU_128_Genus_Peptoclostridium	0.051	-0.028		
	OTU_32_Genus_Bacteroides	0.051	-0.026		
	OTU_59_Genus_Barnesiella	0.051	-0.024		
	OTU_943_Class_Bacteroidetes VC2.1 Bac22	0.051	-0.019		
	OTU_7_Genus_Prevotella 9	0.052	0.019		
	OTU_213_Order_Gastranaerophilales	0.052	-0.015		
	OTU_196_Genus_Ruminococcaceae NK4A214 group	0.057	-0.011		

	OTU_268_Genus_Holdemanella	0.058	-0.017		
	OTU_57_Genus_Subdoligranulum	0.058	-0.017		
	OTU_130_Genus_Acidaminococcus	0.058	-0.018		
	OTU_10_Family_Bacteroidales S24-7 group	0.058	-0.020		
	OTU_209_Genus_Victivallis	0.058	-0.016		
	OTU_155_Genus_Enterorhabdus	0.058	-0.018		
	OTU_13_Genus_Bacteroides	0.070	-0.026		
	OTU_207_Genus_Allisonella	0.070	-0.018		
	OTU_226_Genus_Slackia	0.070	-0.017		
	OTU_61_Genus_Clostridium sensu stricto 1	0.070	0.027		
	OTU_18_Genus_Lactobacillus	0.070	-0.029		
	OTU_220_Family_Lachnospiraceae	0.074	-0.019		
	OTU_44_Genus_[Eubacterium] coprostanoligenes group	0.075	-0.015		
	OTU_55_Genus_Blautia	0.075	-0.018		
	OTU_1_Genus_Escherichia-Shigella	0.075	0.037		
	OTU_102_Genus_Odoribacter	0.075	-0.023		
	OTU_42_Genus_Ruminococcus 2	0.075	-0.019		
	OTU_22_Genus_Lachnoclostridium	0.091	0.024		
	OTU_159_Class_Bacteroidetes VC2.1 Bac22	0.095	-0.016		
	OTU_90_Genus_Thalassospira	0.096	-0.015		
	OTU_14_Genus_Staphylococcus	0.096	0.026		
Oral nutrition (no/yes)	OTU_62_Genus_Parabacteroides	0.003	2.591		
	OTU_13_Genus_Bacteroides	0.015	2.465		
	OTU_220_Family_Lachnospiraceae	0.032	1.699		
	OTU_28_Genus_Bacteroides	0.032	2.861		
	OTU_59_Genus_Barnesiella	0.047	1.777		
	OTU_55_Genus_Blautia	0.048	1.354		
	OTU_102_Genus_Odoribacter	0.048	1.913		
	OTU_23_Genus_Alistipes	0.048	2.431		
	OTU_75_Family_Ruminococcaceae	0.048	1.519		
	OTU_133_Genus_Bacteroides	0.048	2.304		
	OTU_78_Genus_Blautia	0.058	1.058		
	OTU_49_Genus_Roseburia	0.058	2.054		
	OTU_82_Genus_Bacteroides	0.058	1.459		
	OTU_12_Genus_Bacteroides	0.061	2.382		
	OTU_347_Genus_Lachnoclostridium	0.068	1.090		
	OTU_943_Class_Bacteroidetes VC2.1 Bac22	0.068	1.146		
	OTU_60_Genus_Anaerostipes	0.068	1.426		
	OTU_106_Genus_[Eubacterium] hallii group	0.068	1.135		

	OTU_108_Genus_Fusicatenibacter	0.068	1.479		
	OTU_39_Genus_Alistipes	0.068	1.887		
	OTU_230_Genus_Coprobacter	0.068	1.120		
	OTU_191_Genus_Lachnospiraceae UCG-008	0.068	0.938		
	OTU_181_Genus_Dielma	0.068	0.954		
	OTU_695_Genus_Bacteroides	0.073	1.576		
	OTU_113_Genus_Lachnoclostridium	0.073	1.545		
	OTU_32_Genus_Bacteroides	0.076	1.474		
	OTU_63_Genus_Lachnoclostridium	0.086	1.384		
	OTU_80_Family_Lachnospiraceae	0.086	1.556		
	OTU_43_Family_Lachnospiraceae	0.089	-1.162		
	OTU_171_Genus_Staphylococcus	0.094	1.077		
Oral/enteral fiber intake per kg	OTU_99_Genus_Bacteroides	<0.001	8.300		
	OTU_207_Genus_Allisonella	<0.001	6.414		
	OTU_226_Genus_Slackia	<0.001	6.303		
	OTU_128_Genus_Peptoclostridium	<0.001	8.984		
	OTU_86_Genus_Parasutterella	<0.001	8.507		
	OTU_130_Genus_Acidaminococcus	<0.001	5.682		
	OTU_88_Family_CFT112H7	<0.001	9.088		
	OTU_34_Genus_Veillonella	<0.001	10.627		
	OTU_90_Genus_Thalassospira	<0.001	4.698		
	OTU_268_Genus_Holdemanella	<0.001	5.162		
	OTU_261_Genus_Desulfovibrio	<0.001	4.263		
	OTU_145_Genus_Bacteroides	0.001	4.980		
	OTU_32_Genus_Bacteroides	0.001	6.469		
	OTU_943_Class_Bacteroidetes VC2.1 Bac22	0.001	3.751		
	OTU_59_Genus_Barnesiella	0.002	5.800		
	OTU_347_Genus_Lachnoclostridium	0.004	4.316		
	OTU_101_Genus_Thalassospira	0.005	3.647		
	OTU_102_Genus_Odoribacter	0.014	4.483		
	OTU_13_Genus_Bacteroides	0.018	5.070		
	OTU_57_Genus_Subdoligranulum	0.018	3.786		
	OTU_156_Genus_Ruminiclostridium 9	0.046	3.251		
	OTU_220_Family_Lachnospiraceae	0.061	4.044		
Tube feeding (no/yes)	No significant associations with OTUs				
Tube feeding type (polymeric, semi-elemental, elemental)	OTU_34_Genus_Veillonella	0.006	-0.013	3.921	
	OTU_56_Genus_Alistipes	0.006	-0.564	2.826	
	OTU_159_Class_Bacteroidetes VC2.1 Bac22	0.006	-0.422	2.771	
	OTU_80_Family_Lachnospiraceae	0.006	-0.490	2.573	

	OTU_155_Genus_Enterorhabdus	0.006	0.087	3.358	
	OTU_230_Genus_Coprobacter	0.006	-4.501	-6.141	
	OTU_209_Genus_Victivallis	0.012	-0.482	2.471	
	OTU_10_Family_Bacteroidales S24-7 group	0.016	-0.611	3.237	
	OTU_213_Order_Gastranaerophilales	0.017	-0.425	2.029	
	OTU_116_Genus_Ruminococcaceae UCG-005	0.021	-0.806	2.434	
	OTU_88_Family_CFT112H7	0.023	0.148	1.981	
	OTU_99_Genus_Bacteroides	0.023	0.712	3.450	
	OTU_128_Genus_Peptoclostridium	0.023	-0.027	2.805	
	OTU_152_Genus_Christensenellaceae R-7 group	0.023	-0.221	1.982	
	OTU_41_Genus_Subdoligranulum	0.023	0.265	2.541	
	OTU_114_Genus_Faecalibacterium	0.023	-3.254	-3.878	
	OTU_82_Genus_Bacteroides	0.023	-3.702	-4.499	
	OTU_194_Genus_Butyricimonas	0.023	0.013	2.707	
	OTU_65_Genus_Ruminococcaceae UCG-002	0.023	-0.205	2.222	
	OTU_154_Genus_Incertae Sedis	0.023	-3.786	-4.561	
	OTU_140_Genus_Ruminococcaceae NK4A214 group	0.023	-1.457	1.320	
	OTU_205_Genus_Alistipes	0.023	0.123	2.794	
	OTU_268_Genus_Holdemanella	0.027	-2.103	-2.938	
	OTU_31_Genus_Faecalibacterium	0.030	0.180	3.159	
	OTU_695_Genus_Bacteroides	0.031	-1.588	1.343	
	OTU_207_Genus_Allisonella	0.037	-2.332	-2.782	
	OTU_226_Genus_Slackia	0.038	-1.399	2.612	
	OTU_231_Genus_Leuconostoc	0.038	-2.282	-2.713	
	OTU_86_Genus_Parasutterella	0.040	-3.292	-3.854	
	OTU_78_Genus_Blautia	0.040	-0.192	1.619	
	OTU_44_Genus_[Eubacterium] coprostanoligenes group	0.040	-0.427	1.774	
	OTU_305_Genus_Lachnoanaerobaculum	0.081	2.069	-0.624	
	OTU_131_Genus_Blautia	0.086	-0.457	1.625	
	OTU_28_Genus_Bacteroides	0.086	-3.392	1.233	
	OTU_261_Genus_Desulfovibrio	0.089	-2.144	0.441	
	OTU_49_Genus_Roseburia	0.089	-1.745	-2.045	
	OTU_83_Genus_Ruminococcus 1	0.093	-0.108	2.232	
	OTU_145_Genus_Bacteroides	0.093	-1.688	-2.763	
	OTU_156_Genus_Ruminiclostridium 9	0.094	-1.691	-2.165	
	OTU_85_Genus_Lachnospiraceae NK4A136 group	0.095	0.459	2.486	
	OTU_130_Genus_Acidaminococcus	0.098	-0.554	2.102	
	OTU_62_Genus_Parabacteroides	0.098	-1.913	-2.148	
	OTU_73_Genus_Coprococcus 3	0.099	1.306	0.197	

	OTU_23_Genus_Alistipes	0.099	-2.307	0.361	
	OTU_133_Genus_Bacteroides	0.099	-2.628	0.936	
	OTU_72_Genus_Phascolarctobacterium	0.099	0.046	2.304	
Mode of tube feeding (continuous, bolus, both)	OTU_261_Genus_Desulfovibrio	<0.001	5.055	-0.236	
	OTU_145_Genus_Bacteroides	<0.001	6.643	0.466	
	OTU_156_Genus_Ruminiclostridium 9	<0.001	4.449	-0.888	
	OTU_87_Genus_[Eubacterium] coprostanoligenes group	0.005	2.579	-0.422	
	OTU_244_Genus_Blautia	0.011	3.717	-0.350	
	OTU_34_Genus_Veillonella	0.057	2.630	4.133	
	OTU_90_Genus_Thalassospira	0.068	0.295	2.167	
	OTU_88_Family_CFT112H7	0.083	6.236	3.487	
	OTU_99_Genus_Bacteroides	0.095	5.544	1.837	
Gastro-intestinal characteristics					
Whole bowel in situ (no/yes)	OTU_56_Genus_Alistipes	<0.001	3.128		
	OTU_80_Family_Lachnospiraceae	<0.001	3.102		
	OTU_58_Genus_Parabacteroides	<0.001	3.013		
	OTU_84_Genus_Lachnoclostridium	<0.001	4.302		
	OTU_12_Genus_Bacteroides	0.002	3.470		
	OTU_152_Genus_Christensenellaceae R-7 group	0.002	1.752		
	OTU_121_Genus_Dorea	0.003	2.351		
	OTU_98_Genus_Lachnospiraceae NK4A136 group	0.003	1.811		
	OTU_695_Genus_Bacteroides	0.004	2.192		
	OTU_199_Genus_Anaerostipes	0.004	1.895		
	OTU_75_Family_Ruminococcaceae	0.004	1.833		
	OTU_93_Genus_Blautia	0.004	2.117		
	OTU_133_Genus_Bacteroides	0.004	2.740		
	OTU_113_Genus_Lachnoclostridium	0.005	2.099		
	OTU_204_Genus_Ruminiclostridium	0.005	1.788		
	OTU_62_Genus_Parabacteroides	0.007	2.075		
	OTU_49_Genus_Roseburia	0.007	2.687		
	OTU_30_Genus_Hungatella	0.008	3.897		
	OTU_45_Genus_Lachnoclostridium	0.015	3.275		
	OTU_97_Genus_Dorea	0.017	1.381		
	OTU_55_Genus_Blautia	0.019	1.487		
	OTU_23_Genus_Alistipes	0.019	2.584		
	OTU_85_Genus_Lachnospiraceae NK4A136 group	0.020	1.893		
	OTU_92_Genus_Bilophila	0.022	1.993		
	OTU_171_Genus_Staphylococcus	0.024	1.375		
	OTU_205_Genus_Alistipes	0.027	1.572		

	OTU_191_Genus_Lachnospiraceae UCG-008	0.034	0.996		
	OTU_15_Genus_Tyzzerella	0.038	1.559		
	OTU_5_Genus_Akkermansia	0.038	1.633		
	OTU_126_Genus_Eggerthella	0.038	2.785		
	OTU_6_Genus_Haemophilus	0.048	1.813		
	OTU_230_Genus_Coprobacter	0.048	1.544		
	OTU_19_Genus_Tyzzerella 4	0.049	2.933		
	OTU_215_Genus_Erysipelatoclostridium	0.049	1.641		
	OTU_82_Genus_Bacteroides	0.058	1.966		
	OTU_83_Genus_Ruminococcus 1	0.058	1.193		
	OTU_16_Genus_Lachnoclostridium	0.069	3.204		
	OTU_22_Genus_Lachnoclostridium	0.074	3.698		
	OTU_71_Genus_Blautia	0.074	1.947		
	OTU_201_Family_Lachnospiraceae	0.081	1.168		
	OTU_52_Genus_Peptoclostridium	0.091	1.994		
	OTU_94_Genus_Clostridium sensu stricto 1	0.098	1.810		
Ileocecal valve in situ (no/yes)	OTU_135_Genus_Lachnoclostridium	0.023	1.903		
	OTU_152_Genus_Christensenellaceae R-7 group	0.030	1.726		
	OTU_93_Genus_Blautia	0.030	2.151		
	OTU_92_Genus_Bilophila	0.030	2.467		
	OTU_126_Genus_Eggerthella	0.030	3.025		
	OTU_69_Family_Ruminococcaceae	0.030	2.490		
	OTU_144_Genus_Ruminococcaceae UCG-004	0.030	1.743		
	OTU_45_Genus_Lachnoclostridium	0.030	3.647		
	OTU_49_Genus_Roseburia	0.030	2.738		
	OTU_82_Genus_Bacteroides	0.031	2.185		
	OTU_85_Genus_Lachnospiraceae NK4A136 group	0.031	2.198		
	OTU_12_Genus_Bacteroides	0.031	3.168		
	OTU_84_Genus_Lachnoclostridium	0.031	3.470		
	OTU_15_Genus_Tyzzerella	0.031	1.941		
	OTU_208_Genus_Ruminiclostridium	0.031	1.856		
	OTU_23_Genus_Alistipes	0.031	2.753		
	OTU_133_Genus_Bacteroides	0.041	2.683		
	OTU_62_Genus_Parabacteroides	0.046	2.078		
	OTU_199_Genus_Anaerostipes	0.049	1.624		
	OTU_244_Genus_Blautia	0.049	1.845		
	OTU_33_Genus_Pseudobutyrivibrio	0.051	1.887		
	OTU_56_Genus_Alistipes	0.052	2.348		
	OTU_695_Genus_Bacteroides	0.058	1.951		

	OTU_58_Genus_Parabacteroides	0.059	2.364		
	OTU_74_Genus_Ruminococcaceae UCG-002	0.065	1.910		
	OTU_26_Genus_Blautia	0.065	2.203		
	OTU_191_Genus_Lachnospiraceae UCG-008	0.068	1.061		
	OTU_98_Genus_Lachnospiraceae NK4A136 group	0.072	1.551		
	OTU_13_Genus_Bacteroides	0.073	2.189		
	OTU_71_Genus_Blautia	0.091	2.081		
Partial or total colectomy (no/yes)	No significant associations with OTUs				
Remaining small bowel length (cm)	No significant associations with OTUs				
Growth					
BMI (SDS)	OTU_212_Genus_Hafnia	0.078	-0.654		
Height-for-age SDS < -2 (no/yes)	OTU_155_Genus_Enterorhabdus	<0.001	4.046		
	OTU_10_Family_Bacteroidales S24-7 group	<0.001	4.717		
	OTU_159_Class_Bacteroidetes VC2.1 Bac22	<0.001	4.359		
	OTU_209_Genus_Victivallis	<0.001	3.551		
	OTU_213_Order_Gastranaerophilales	<0.001	2.947		
	OTU_41_Genus_Subdoligranulum	0.001	4.128		
	OTU_116_Genus_Ruminococcaceae UCG-005	0.001	3.641		
	OTU_114_Genus_Faecalibacterium	0.001	3.107		
	OTU_31_Genus_Faecalibacterium	0.001	3.502		
	OTU_140_Genus_Ruminococcaceae NK4A214 group	0.001	3.032		
	OTU_230_Genus_Coprobacter	0.001	3.393		
	OTU_154_Genus_Incertae Sedis	0.002	2.554		
	OTU_65_Genus_Ruminococcaceae UCG-002	0.002	3.303		
	OTU_194_Genus_Butyricimonas	0.003	2.669		
	OTU_131_Genus_Blautia	0.005	2.287		
	OTU_44_Genus_[Eubacterium] coprostanoligenes group	0.005	2.808		
	OTU_42_Genus_Ruminococcus 2	0.008	3.666		
	OTU_83_Genus_Ruminococcus 1	0.010	3.101		
	OTU_55_Genus_Blautia	0.011	3.268		
	OTU_247_Family_Coriobacteriaceae	0.014	2.539		
	OTU_74_Genus_Ruminococcaceae UCG-002	0.023	3.946		
	OTU_205_Genus_Alistipes	0.027	3.046		
	OTU_196_Genus_Ruminococcaceae NK4A214 group	0.027	1.603		
	OTU_82_Genus_Bacteroides	0.027	4.087		
	OTU_1_Genus_Escherichia-Shigella	0.038	-6.610		
	OTU_73_Genus_Coprococcus 3	0.040	2.301		
	OTU_85_Genus_Lachnospiraceae NK4A136 group	0.057	3.773		
	OTU_78_Genus_Blautia	0.067	2.014		

	OTU_125_Genus_Ruminococcaceae UCG-003	0.088	2.769		
	OTU_231_Genus_Leuconostoc	0.088	2.978		
	OTU_106_Genus_[Eubacterium] hallii group	0.092	2.128		
Growing outside target height range (no/yes)	OTU_155_Genus_Enterorhabdus	<0.001	-0.547		
	OTU_10_Family_Bacteroidales S24-7 group	<0.001	-0.862		
	OTU_159_Class_Bacteroidetes VC2.1 Bac22	<0.001	-1.086		
	OTU_209_Genus_Victivallis	<0.001	-0.561		
	OTU_41_Genus_Subdoligranulum	<0.001	-2.196		
	OTU_213_Order_Gastranaerophilales	<0.001	-0.581		
	OTU_116_Genus_Ruminococcaceae UCG-005	0.001	-1.475		
	OTU_8_Genus_Morganella	0.002	7.298		
	OTU_114_Genus_Faecalibacterium	0.004	0.455		
	OTU_157_Genus_Veillonella	0.004	3.589		
	OTU_140_Genus_Ruminococcaceae NK4A214 group	0.004	-0.693		
	OTU_31_Genus_Faecalibacterium	0.004	-0.092		
	OTU_230_Genus_Coprobacter	0.005	0.342		
	OTU_154_Genus_Incertae Sedis	0.006	-0.487		
	OTU_65_Genus_Ruminococcaceae UCG-002	0.008	-0.450		
	OTU_194_Genus_Butyricimonas	0.011	-0.189		
	OTU_55_Genus_Blautia	0.014	-1.376		
	OTU_205_Genus_Alistipes	0.017	-1.823		
	OTU_131_Genus_Blautia	0.017	-0.279		
	OTU_44_Genus_[Eubacterium] coprostanoligenes group	0.021	0.089		
	OTU_42_Genus_Ruminococcus 2	0.022	-0.671		
	OTU_83_Genus_Ruminococcus 1	0.024	-0.812		
	OTU_247_Family_Coriobacteriaceae	0.038	-0.485		
	OTU_196_Genus_Ruminococcaceae NK4A214 group	0.057	-0.554		
	OTU_398_Genus_Ruminococcaceae UCG-014	0.057	-2.758		
	OTU_74_Genus_Ruminococcaceae UCG-002	0.062	-0.739		
	OTU_100_Genus_Coprococcus 2	0.078	-1.911		
	OTU_1_Genus_Escherichia-Shigella	0.085	2.001		
	OTU_82_Genus_Bacteroides	0.085	0.430		
Medication					
Proton pump inhibitor (no/yes)	OTU_226_Genus_Slackia	0.002	-2.362		
	OTU_207_Genus_Allisonella	0.002	-2.476		
	OTU_99_Genus_Bacteroides	0.008	-3.260		
	OTU_86_Genus_Parasutterella	0.015	-2.752		
	OTU_347_Genus_Lachnoclostridium	0.024	-1.504		
	OTU_18_Genus_Lactobacillus	0.024	-2.783		

	OTU_128_Genus_Peptoclostridium	0.024	-2.429		
	OTU_88_Family_CFT112H7	0.030	-2.495		
	OTU_59_Genus_Barnesiella	0.041	-1.995		
	OTU_57_Genus_Subdoligranulum	0.049	-1.198		
	OTU_130_Genus_Acidaminococcus	0.052	-1.404		
	OTU_162_Genus_[Eubacterium] hallii group	0.058	-1.022		
	OTU_1_Genus_Escherichia-Shigella	0.083	3.128		
Motility agents (no/yes)	No significant associations with OTUs				
Cholestyramine (no/yes)	OTU_155_Genus_Enterorhabdus	0.004	1.898		
	OTU_149_Genus_Lactococcus	0.004	2.065		
	OTU_128_Genus_Peptoclostridium	0.004	2.763		
	OTU_86_Genus_Parasutterella	0.004	2.871		
	OTU_88_Family_CFT112H7	0.004	3.018		
	OTU_209_Genus_Victivallis	0.005	1.645		
	OTU_213_Order_Gastranaerophilales	0.005	1.394		
	OTU_205_Genus_Alistipes	0.009	1.957		
	OTU_32_Genus_Bacteroides	0.010	4.475		
	OTU_268_Genus_Holdemanella	0.011	1.541		
	OTU_10_Family_Bacteroidales S24-7 group	0.016	2.074		
	OTU_102_Genus_Odoribacter	0.036	3.071		
	OTU_277_Genus_Xanthomonas	0.050	1.214		
	OTU_207_Genus_Allisonella	0.050	1.343		
	OTU_226_Genus_Slackia	0.050	1.308		
	OTU_55_Genus_Blautia	0.065	1.866		
	OTU_139_Genus_Stenotrophomonas	0.071	1.058		
	OTU_49_Genus_Roseburia	0.076	2.605		
	OTU_220_Family_Lachnospiraceae	0.076	1.890		
	OTU_164_Genus_Capnocytophaga	0.076	0.915		
	OTU_99_Genus_Bacteroides	0.076	1.496		
	OTU_44_Genus_[Eubacterium] coprostanoligenes group	0.079	1.262		
	OTU_159_Class_Bacteroidetes VC2.1 Bac22	0.097	1.346		
	OTU_196_Genus_Ruminococcaceae NK4A214 group	0.097	0.641		
	OTU_130_Genus_Acidaminococcus	0.097	1.032		
	OTU_67_Genus_Collinsella	0.097	1.068		
Ursochol (no/yes)	OTU_155_Genus_Enterorhabdus	<0.001	-5.720		
	OTU_209_Genus_Victivallis	<0.001	-4.915		
	OTU_149_Genus_Lactococcus	<0.001	-4.514		
	OTU_213_Order_Gastranaerophilales	<0.001	-3.974		
	OTU_10_Family_Bacteroidales S24-7 group	<0.001	-6.477		

	OTU_44_Genus_[Eubacterium] coprostanoligenes group	<0.001	-4.108		
	OTU_68_Genus_Ruminococcaceae UCG-005	<0.001	-4.866		
	OTU_82_Genus_Bacteroides	0.011	-3.635		
	OTU_606_Genus_Akkermansia	0.011	2.075		
	OTU_125_Genus_Ruminococcaceae UCG-003	0.018	-3.921		
	OTU_159_Class_Bacteroidetes VC2.1 Bac22	0.021	-3.218		
	OTU_25_Genus_Streptococcus	0.063	3.819		
	OTU_126_Genus_Eggerthella	0.063	-3.246		
	OTU_102_Genus_Odoribacter	0.073	-3.850		
	OTU_42_Genus_Ruminococcus 2	0.097	-3.344		
Treatment of bacterial overgrowth (no/yes)	OTU_210_Genus_Lactobacillus	0.010	3.482		
	OTU_277_Genus_Xanthomonas	0.072	1.922		
	OTU_4_Genus_Lactobacillus	0.072	5.051		
	OTU_40_Genus_Phascolarctobacterium	0.092	2.072		
Antibiotics at sample (no/yes)[1]	OTU_946_Genus_Veillonella	0.024	-1.515		
	OTU_244_Genus_Blautia	0.043	-1.640		
	OTU_240_Genus_Tyzzerella	0.043	-1.192		
Antibiotics between samples (no/yes)	OTU_29_Family_Lachnospiraceae	0.015	-2.551		
	OTU_71_Genus_Blautia	0.015	-2.301		
	OTU_92_Genus_Bilophila	0.015	-2.327		
	OTU_220_Family_Lachnospiraceae	0.054	-1.703		
	OTU_96_Genus_Streptococcus	0.054	1.381		
	OTU_244_Genus_Blautia	0.055	-1.505		
	OTU_207_Genus_Allisonella	0.055	-1.164		
	OTU_226_Genus_Slackia	0.055	-1.133		
	OTU_99_Genus_Bacteroides	0.073	-1.416		
	OTU_137_Genus_Lachnospiraceae UCG-008	0.079	-0.891		
	OTU_204_Genus_Ruminiclostridium	0.094	-1.238		
	OTU_148_Family_Ruminococcaceae	0.094	-0.944		
	OTU_23_Genus_Alistipes	0.094	-1.927		
Line sepsis[2]	No significant associations with OTUs				

Legend: [1] Due to bacterial overgrowth, line sepsis or another cause. [2] with a range of two months before and 2 months after sample collection.

For categorical variables, the first group mentioned in the variable column is assigned as baseline. The beta coefficient mentioned is the coefficient of the second group, the second beta coefficient is the coefficient of the third group and the third coefficient is the coefficient of the fourth group.

Abbreviations: BMI, body mass index; PN, parenteral nutrition; REE, resting energy expenditure; SDS, standard deviation score.

Supplementary Table 12. Permutation ANOVA for the relation between disease characteristics and microbiota community structure (β diversity) taking into account multiple samples per patient

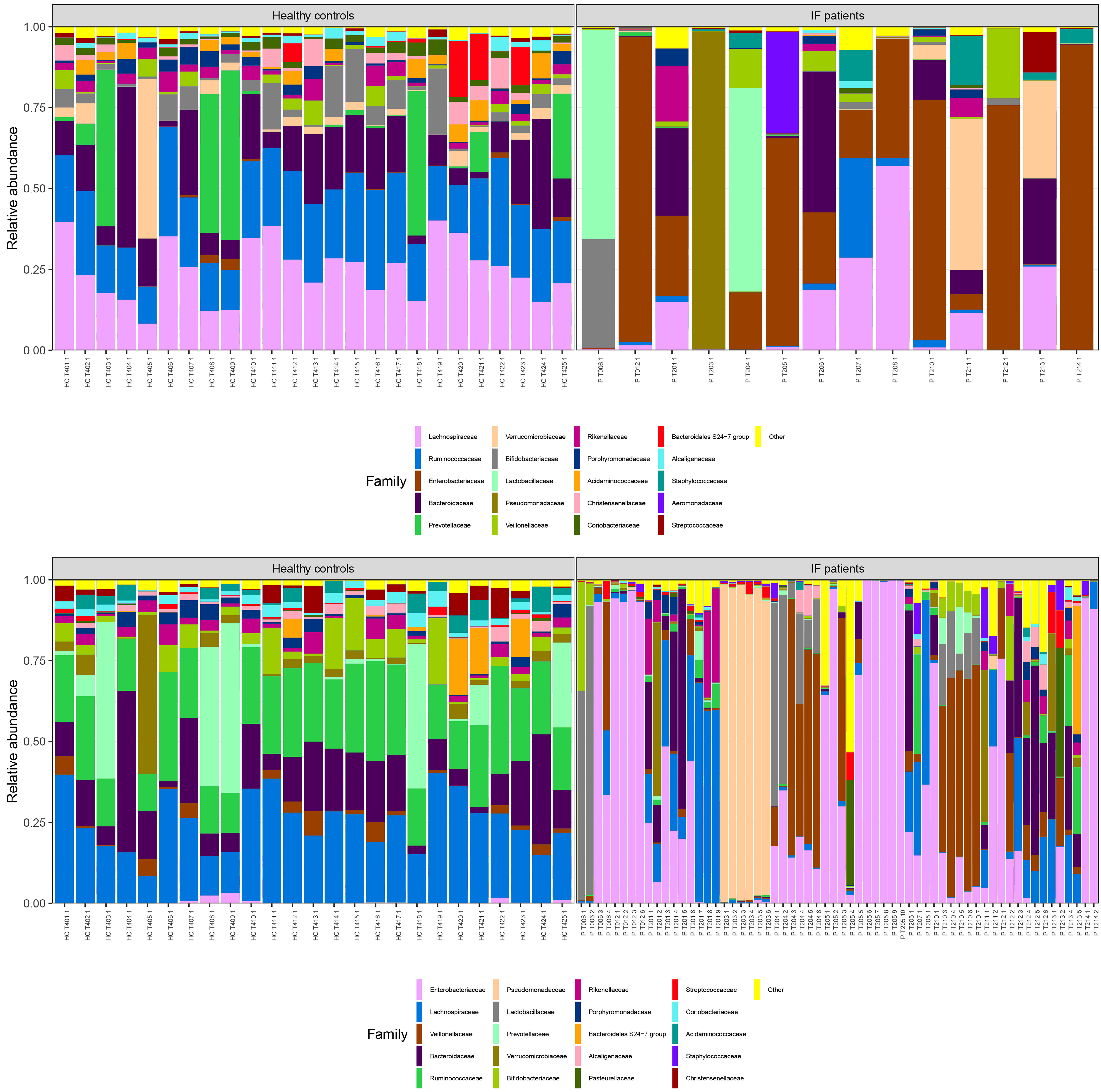
Variable	**R^2**	**p-value**
Nutrition		
Duration of PN (y)	0.06	0.005
Type of nutrition (PN, PN±tubefeeding, PN+oral nutrition±tube feeding, tube feeding/oral nutrition)	0.15	0.039
PN dependency (% of total energy intake)	0.06	0.005
Calories of PN divided by REE (%)	0.05	0.004
Oral nutrition (no/yes)	0.04	0.522
Fiber intake per kg (g/kg)	0.05	0.011
Tube feeding (no/yes)	0.07	0.221
Tube feeding type (polymeric, semi-elemental, elemental)	0.11	0.339

Mode of tube feeding (continuous, bolus, both)	0.09	0.474
Growth		
BMI (SDS)	0.03	0.965
Height-for-age SDS < -2	0.03	1.000
Growing outside target height range (no/yes)	0.04	1.000
Gastro-intestinal characteristics		
Whole small bowel in situ (no/yes)	0.06	1.000
Remaining small bowel length (cm)	0.06	1.000
Ileocecal valve in situ (no/yes)	0.08	1.000
Partial or total colectomy (no/yes)	0.07	0.308
Medication		

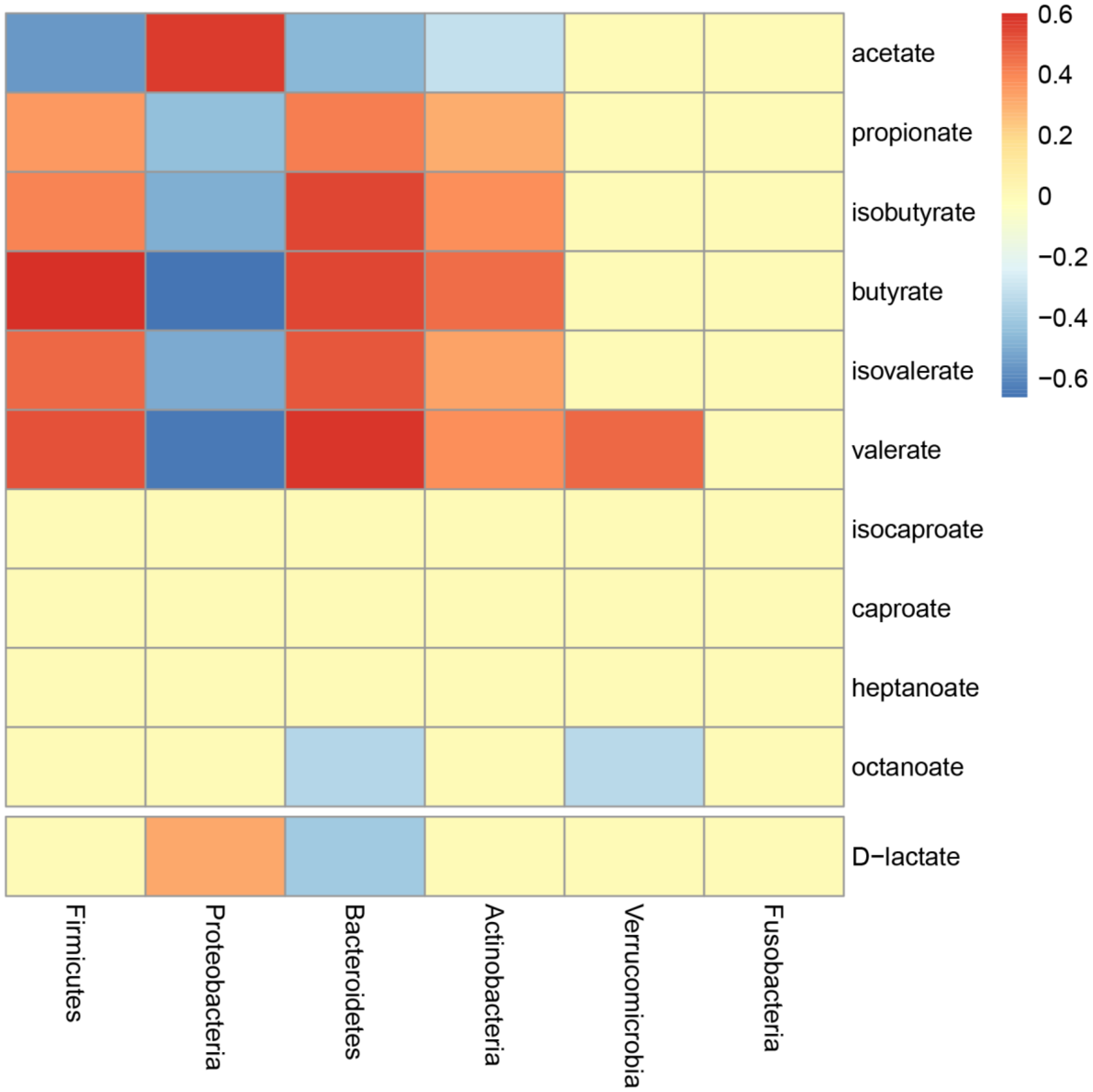
Proton pump inhibitor (no/yes)	0.07	0.209
Motility agents (no/yes)	0.08	0.098
Cholestyramine (no/yes)	0.04	0.869
Ursochol (no/yes)	0.02	0.673
Antibiotics at sample (no/yes)*	0.05	0.005
Antibiotics between samples (no/yes)	0.04	0.020
Line sepsis**	0.02	0.134

Legend: *Due to bacterial overgrowth, line sepsis or another cause. **with a range of two mo before and 2 mo after sample collection

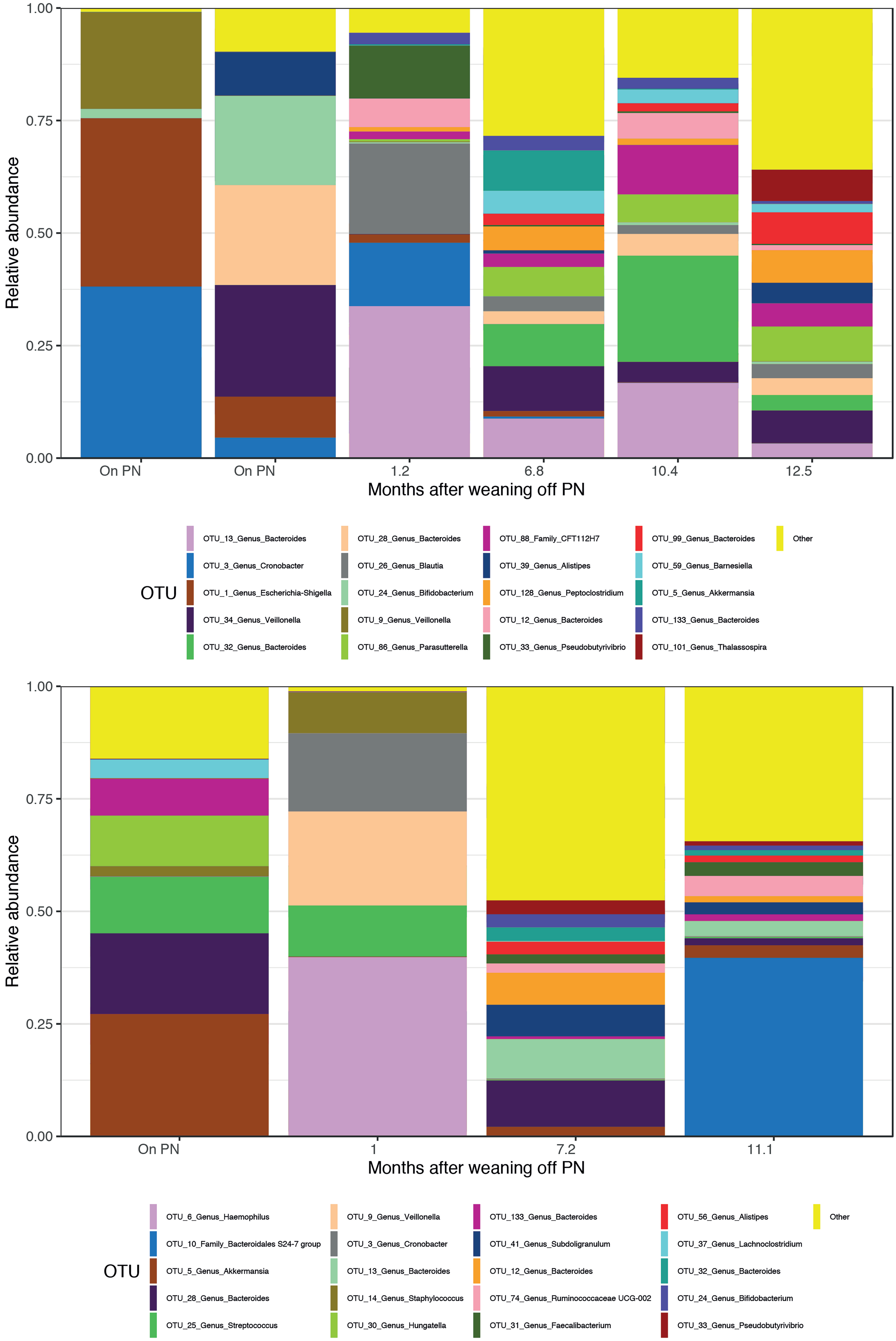
Abbreviations: BMI, body mass index; PN, parenteral nutrition; REE, resting energy expenditure; SDS, standard deviation score.



Supplementary Figure 1. Taxonomic composition of microbiota of healthy controls (left) and pediatric IF patients (right) at family level at first sample (above) and for all samples (below).



Supplementary Figure 2. Heatmap of correlations between the main 6 phyla of the gut microbiota and short-chain fatty acids and D-lactate (both per gram dry feces).



Supplementary Figure 3. Example of longitudinal changes at operational taxonomic unit (OTU) level for two patients during the study period. Both patients were stable on parenteral nutrition during this time. The patient on the upper part had surgical IF, whereas the patient below had functional IF.