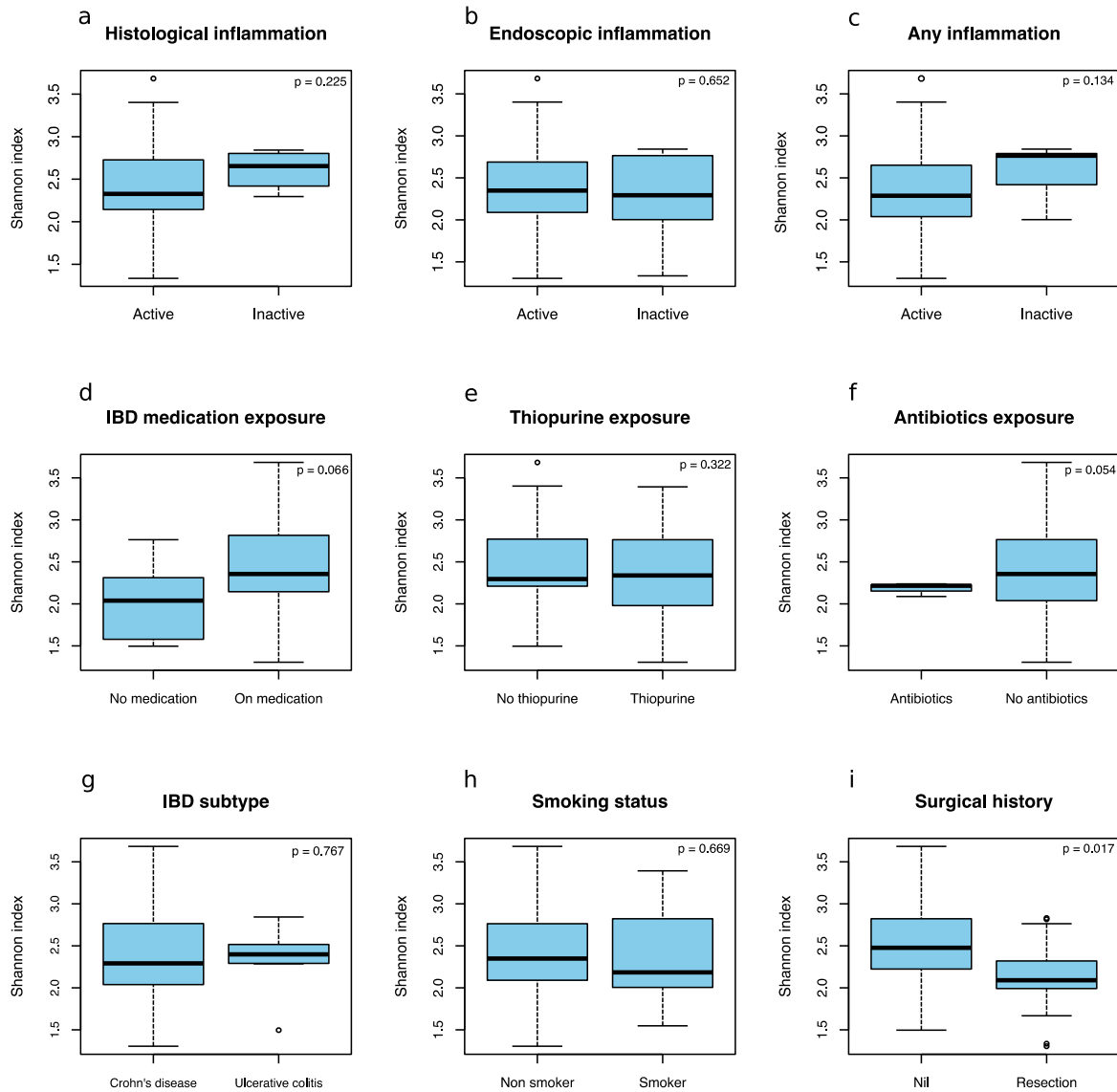


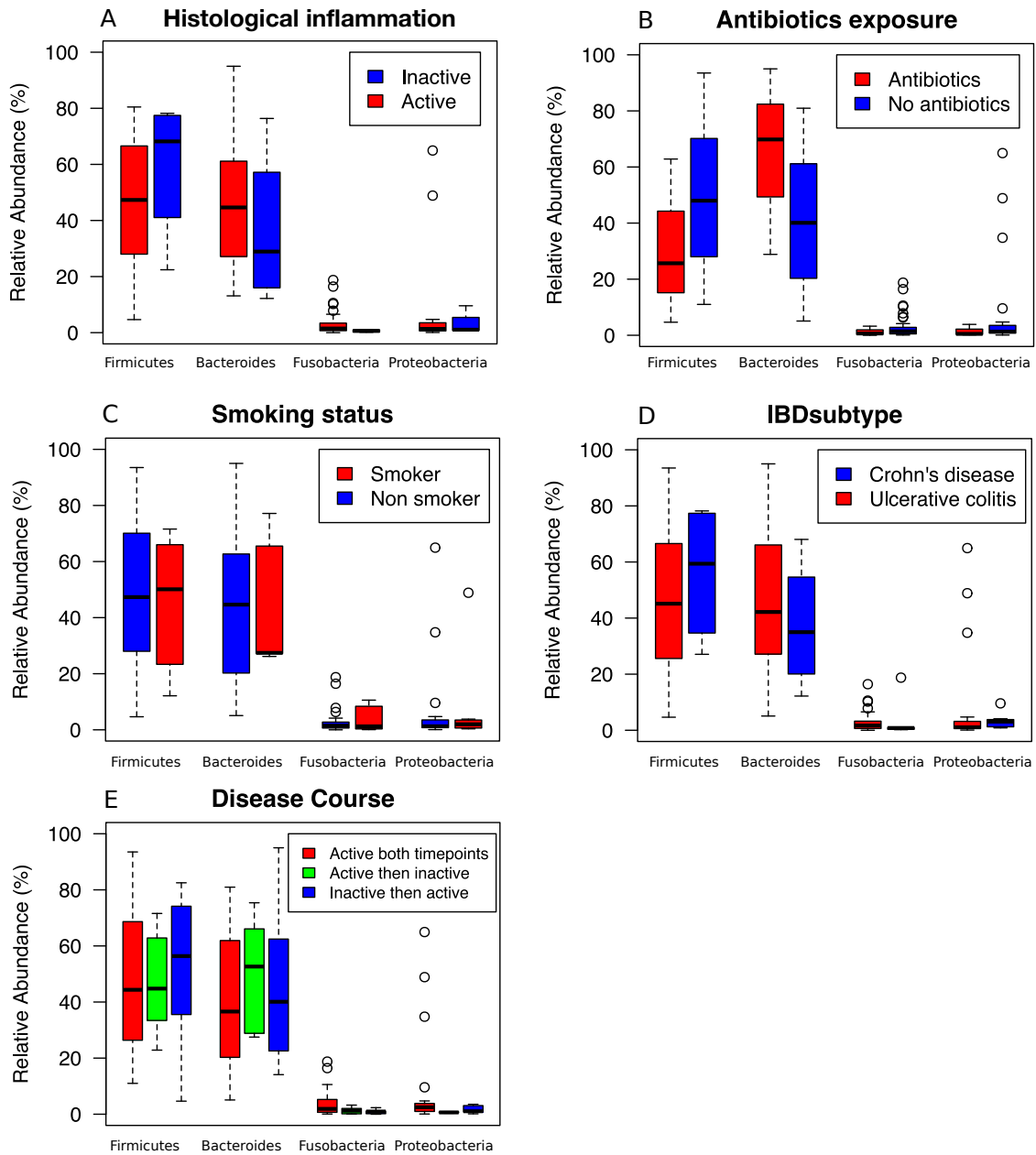
Supplementary Figure 1

Alpha diversity of samples (Shannon diversity indices). Comparisons between inflammation presence ((a) histologically confirmed; (b) endoscopic; (c) any inflammation), medication exposure ((d) IBD medications; (e) thiopurine; (f) antibiotics); (g) IBD subtype; (h) smoking status; (i) surgical history.



Supplementary Figure 2

Relative abundance of the predominant bacterial phyla in samples according to A) the presence or absence of histologically confirmed inflammation; B) antibiotic exposure; C) smoking status; D) IBD subtype; and E) disease course.



Supplementary Figure 3

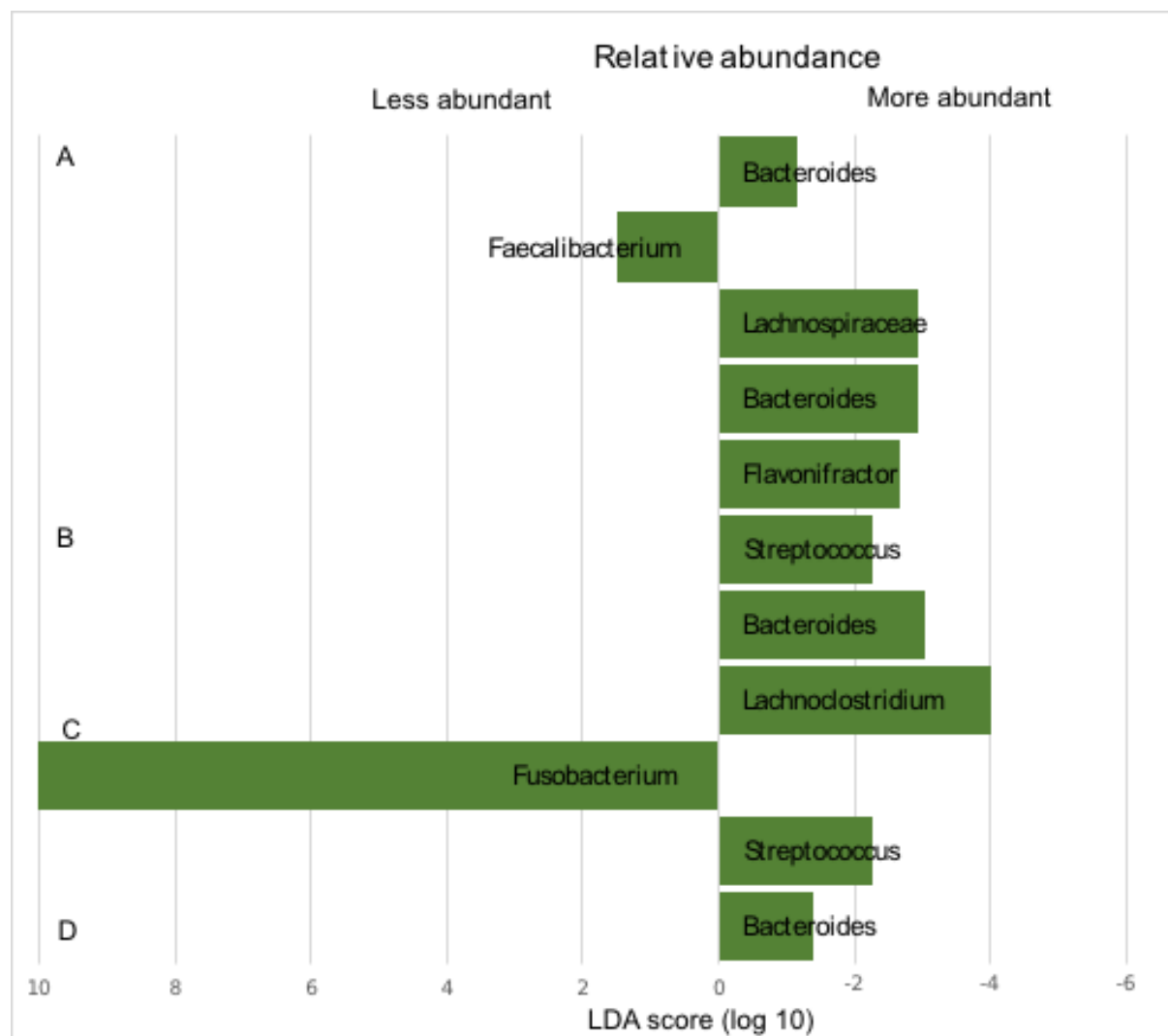
Relative abundances of inferred metagenomes, calculated using PICRUSt.



Supplementary Figure 4

Bacteria with significantly different relative abundances. Determined by LDA (linear discriminant analysis) score cut-off of >1.0 , Kruskal-Wallis test <0.05 . More/less abundant means that a particular bacteria genus contributes significantly higher/lower percentage composition to the microbiome with respect to different clinical data.

A: Samples from patients with ulcerative colitis versus Crohn's disease (here bacteroides are significantly more abundant in samples from patients with ulcerative colitis versus Crohn's disease);
B: Samples taken in the presence of active inflammation versus those initially active and subsequently inactive;
C: Samples taken in the presence of active inflammation versus those initially inactive and subsequently active;
D: Samples exposed to antibiotics versus those not exposed to antibiotics.



Supplementary Table 1

Clinical information concerning the subjects. Montreal classification (for CD: behaviour B1= inflammatory, B2=stricturing, B3= penetrating, location L1= ileal, L2=colonic, L3= ileal and colonic, L4= upper GI; for UC severity S1=mild, S2=moderate, S3=severe; extent E1=proctitis, E2= rectum to splenic flexure, E3= pancolitis)

Sample name	Sex	IBD subtype	Montreal classification	Sample location	Previous surgery	Endoscopic activity	Histological activity	Time between procedures (years)	Disease Length (years)	Smoking status	IBD medications	Antibiotics
1a	Male	CD	B2, L3	Transverse colon	Nil	Active	NA		5	Non smoker	Infliximab, prednisone	No antibiotics
1b	Male	CD	B2, L3	Caecum	Nil	Active	Active	1.9	3	Non smoker	Nil	No antibiotics
2a	Male	CD	B3, L3	Ascending colon	Resection	Inactive	NA		15.4	Non smoker	Azathioprine	No antibiotics
2b	Male	CD	B3, L3	Caecum	Resection	Active	NA	0.4	15.7	Non smoker	Azathioprine	No antibiotics
2c	Male	CD	B3, L3	Caecum	Resection	Active	NA		16.6	Non smoker	Azathioprine	No antibiotics
2d	Male	CD	B3, L3	Terminal ileum	Resection	Inactive	Active	0.7	17.2	Non smoker	Azathioprine	No antibiotics
3a	Female	CD	B1, L4	Terminal ileum	Nil	Active	Active		4.3	Smoker	Azathioprine	No antibiotics
3b	Female	CD	B1, L4		Nil	Active	Active	1.3	5.5	Smoker	Azathioprine	No antibiotics
4a	Male	CD	B3, L3	Colon	Colectomy	Active	Active		16.6	Non smoker	Sirolimus	No antibiotics
4b	Male	CD	B3, L3	Colon	Nil	Active	Active	1	15.6	Non smoker	Adalimumab	No antibiotics
5a	Male	CD	B1, L3	Rectum	Nil	Active	Active		30.6	Smoker	Abatacept	No antibiotics
5b	Male	CD	B1, L3	Rectum	Nil	Active	Active	0.8	31.4	Smoker	Nil	No antibiotics
6a	Female	UC	S3, E3	Rectum	Nil	Active	Active		40.1	Non smoker	Nil	No antibiotics

6b	Female	UC	S3, E3	Rectum	Nil	Inactive	Active	2.1	42.2	Non smoker	Infliximab	No antibiotics
8a	Female	CD	B1p, L1	Terminal ileum	Resection	Inactive	Active		19.4	Non smoker	Nil	No antibiotics
8b	Female	CD	B1p, L1	Caecum	Resection	Inactive	NA	4.8	24.3	Non smoker	Nil	No antibiotics
9a	Female	CD	B1, L3	Sigmoid colon	Nil	Active	Inactive		1.8	Non smoker	Adalimumab	No antibiotics
9b	Female	CD	B1, L3	Terminal ileum	Nil	Inactive	Active	5.9	7.7	Non smoker	Nil	No antibiotics
10a	Male	CD	B2, L3	Ascending colon	Resection	Active	NA		7.5	Non smoker	Adalimumab	No antibiotics
10b	Male	CD	B2, L3		Resection	Active	Active	1.6	9.1	Non smoker	Adalimumab	No antibiotics
11a	Female	CD	B2, L1	Caecum	Nil	Inactive	Active		3.5	Smoker	Infliximab	No antibiotics
11b	Female	CD	B2, L1	Terminal ileum	Resection	Active	NA	4	7.5	Smoker	Nil	No antibiotics
12a	Male	CD	B2p, L3	Sigmoid colon	Nil	Active	Active		9.9	Smoker	Nil	No antibiotics
12b	Male	CD	B2p, L3	Terminal ileum	Nil	Active	Active	5.8	15.7	Smoker	Azathioprine	No antibiotics
14a	Female	CD	B2, L1	Terminal ileum	Resection	Active	Active		14	Non smoker	Azathioprine, adalimumab	Antibiotics
14b	Female	CD	B2, L1	Rectum	Resection	Inactive	Inactive	0.6	14.6	Non smoker	Nil	No antibiotics
15a	Female	CD	B2, L1	Terminal ileum	Resection	Inactive	Active		12.7	Non smoker	Nil	Antibiotics
15b	Female	CD	B2, L1	Terminal ileum	Resection	Active	Active	1.7	14.4	Non smoker	Nil	No antibiotics
16a	Female	CD	B2p, L3	Ascending colon	Nil	Active	Active		5.5	Non smoker	Adalimumab	Antibiotics

16b	Female	CD	B2p, L3	Terminal ileum	Resection	Active	Active	1.9	7.3	Non smoker	Adalimumab	No antibiotics
17a	Male	UC	S1, E3	Ascending colon	Nil	Active	Active		0	Non smoker	Nil	No antibiotics
17b	Male	UC	S1, E3	Ascending colon	Nil	Active	Active	3.4	3.4	Non smoker	6-mercaptopurine, prednisone	No antibiotics
18a	Male	CD	B2, L3 L4	Caecum	Nil	Inactive	NA		8.7	Non smoker	Azathioprine	No antibiotics
18b	Male	CD	B2, L3 L4	Caecum	Resection	Inactive	Active	0.8	9.5	Non smoker		No antibiotics
19a	Female	UC	S1, E3	Caecum	Nil	Inactive	Inactive		8.2	Non smoker	Mesalazine	No antibiotics
19b	Female	UC	S1, E3	Caecum	Nil	Active	Active	1.7	19.9	Non smoker	Mesalazine	No antibiotics
24a	Female	CD	B2, L2	Terminal ileum	Nil	Inactive	Active		25.5	Non smoker	Azathioprine	No antibiotics
24b	Female	CD	B3, L2	Terminal ileum	Nil	Active	Active	3.3	22.2	Non smoker	Azathioprine	No antibiotics
25a	Female	CD	B1, L2	Caecum	Nil	Active	Active		3.9	Non smoker	Nil	No antibiotics
25b	Female	CD	B2, L2	Transverse colon	Nil	Active	Active	4.7	8.6	Non smoker	Azathioprine, prednisone	No antibiotics
26a	Female	UC	S2, E2	Ascending colon	Nil	Active	Active		12.6	Non smoker	Mesalazine	No antibiotics
26b	Female	UC	S3, E2	Terminal ileum	Nil	Inactive	Inactive	2.9	15.4	Non smoker	Mesalazine	No antibiotics

Supplementary Table 2

Intra-sample microbial diversity comparisons (alpha diversity) in relation to inflammation, disease type, smoking status, disease duration, exposure to IBD medications and previous intestinal surgery. SD is the Shannon diversity index. Not all samples were included in this analysis as one sample had only 329 sequences, and histopathology reports were only available for 33 samples.

Comparison	Group 1	N=	Group 2	N=	Mean SD Group 1	Mean SD Group 2	P value (ANOVA)
Histologically confirmed inflammation	Active inflammation	29	No inflammation	4	2.423	2.634	0.225
Disease type	Crohn's disease	33	Ulcerative colitis	8	2.379	2.343	0.767
Smoking	Active smokers	8	Non smokers	33	2.370	2.372	0.669
Disease duration	>4 years	35	<4 years	6	2.384	2.299	0.825
Treatment effect	On treatment	34	No treatment	7	2.446	2.011	0.066
Surgery	Previous surgery	15	No previous surgery	26	2.083	2.510	0.017

Supplementary Table 3

Differences in relative abundance of bacterial taxa based on clinical subtypes (metastats). Phylogenetic placement given by Silva reference database. OTUs included if overall relative abundance >0.1%. P values were adjusted using the Benjamini-Hochberg method.

Subset compared	Base group mean (%)	p-value	adjusted p-value	log2fold change	Taxonomic classification (OTU number)	
Crohn's disease and ulcerative colitis	8.99	0.033	0.1648	-1.16	Bacteroides (OTU 1)	
	3.39	0.011	0.1177	1.5	Faecalibacterium (OTU 2)	
	4.584	0.04	0.1691	-2.28	Lachnospiraceae (OTU 10)	
	0.0793	0.011	0.1177	-3.89	Lachnoclostridium (OTU 17)	
	0.2733	0.032	0.1648	-2.47	Lachnoclostridium (OTU 19)	
	0.1234	0.03	0.1648	-2.83	Lachnoclostridium (OTU 21)	
	0	0.029	0.1648		Parasutterella (OTU 24)	
	0	0.002	0.0824		Lachnospiraceae (OTU 26)	
	0.1146	0.015	0.1177	-2.95	Bacteroides (OTU 29)	
	0	0.003	0.0824		Parabacteroides (OTU 33)	
	0.097	0.014	0.1177	-2.66	Flavonifractor (OTU 34)	
	0	0.005	0.0916		Phascolarctobacterium (OTU 40)	
	0.0264	0.036	0.1648	-3.19	Lachnoclostridium (OTU 49)	
Active-inactive and active-active		0.025				
	0.5289	3	0.3479	-2.37	Streptococcus (OTU 5)	
		0.001				
	0.1528	8	0.1017	-3.05	Bacteroides (OTU 14)	
	0.0588	0.004	0.1087	-4	Lachnoclostridium (OTU 21)	
	0.011					
	0.094	7	0.2145	-1.86	Streptococcus (OTU 44)	
	0.476	0.031	0.4258	-2.52	Streptococcus (OTU 5)	
Inactive-active and active-active	8.5949	0.006	0.1648	10.11	Fusobacterium (OTU 7)	
	0.141	0.023	0.4212	-2.27	Streptococcus (OTU 32)	
	0	0.003	0.1648		Tyzzarella_4 (OTU 59)	
No antibiotics and antibiotics	16.0623	0.000	1	0.0074	-1.38	Bacteroides (OTU 1)