

Table S1 Perinatal risk factors and development of IBD in childhood, stratified by age at onset.

	EO-IBD†			P-IBD‡		
Characteristics	Cases (n=62, n (%))	Controls (n=620), n (%)	Fully adjusted OR (95% CI)	Cases (n=102, n (%))	Controls (n=1020), n (%)	Fully adjusted OR (95% CI)
Season of birth						
May-September	31 (50.0)	279 (45.0)	1.25 (0.74-2.12)	45 (44.1)	421 (41.3)	1.16 (0.77-1.76)
October-April	31(50.0)	341 (55.0)	1	57 (55.9)	599 (58.7)	1
Siblings						
No	36(58.1)	343 (55.3)	1.14 (0.65-1.99)	62 (60.8)	535 (52.4)	1.20 (0.76-1.90)
Yes	26 (41.9)	277 (46.7)	1	40 (39.2)	485 (47.6)	1
Multiple births						
1	61 (98.4)	610 (98.4)	1	98 (96.1)	997 (97.8)	1
≥2	1 (1.61)	10 (1.6)	0.89 (0.09-9.19)	4 (3.9)	23 (2.3)	1.68 (0.49-5.76)
Birth weight						
≥2500	58(93.6)	590 (95.2)	1	96 (94.1)	973 (95.4)	1
<2500	4 (6.5)	30 (4.8)	1.23 (0.31-4.96)	6 (5.9)	47 (4.6)	1.00 (0.25-4.05)
Gestational age, weeks						
≤ 35	2 (3.2)	12 (1.9)	1.35 (0.18-9.93)	5 (5.0)	35 (3.5)	1.41 (0.32-6.27)
≥36	60 (96.8)	606 (98.1)	1	96 (95.1)	980 (96.5)	1
Apgar score						

≥7	57 (91.9)	583 (94.0)	1	97 (95.1)	959 (94.2)	1
≤6	5 (8.1)	37 (6.0)	1.28 (0.46-3.50)	5 (4.9)	59 (5.8)	0.73 (0.27-2.00)
Maternal age, years						
< 25	5 (8.7)	54 (8.7)	0.86 (0.30-2.45)	17 (16.7)	142 (13.9)	1.00 (0.55-1.85)
25-29	19 (30.7)	178 (28.7)	1	45 (44.1)	369 (36.2)	1
30-34	23 (37.1)	245 (39.5)	0.99 (0.51-1.91)	27 (26.5)	341 (33.4)	0.68 (0.40- 1.14)
35-39	11 (17.7)	124 (20.0)	0.95 (0.42-2.14)	11 (10.8)	149 (14.6)	0.62 (0.30-1.28)
≥ 40	4 (6.5)	19 (3.1)	2.43 (0.70-8.36)	2 (2.0)	19 (1.9)	0.98 (0.22-4.46)
Maternal education						
University	6 (9.7)	105 (17.1)	0.63 (0.24-1.68)	10 (9.8)	91 (8.9)	1.40 (0.65-3.04)
High school	36 (58.1)	290 (47.1)	1.37 (0.77-2.44)	50 (49.3)	475 (46.7)	1.15 (0.74-1.81)
Primary/middle school	20 (35.3)	221 (35.9)	1	42 (41.8)	452 (44.4)	1

†Age at diagnosis <10 years

‡ Age at diagnosis 10-17 years

Fully adjusted: sex, year of birth, season of birth; having older siblings; number of births; birth weight; gestational age; Apgar scores at 1 minute; maternal age; and mother's formal education at the moment of birth.

Table S2 Risk of perinatal characteristics in the development of Crohn's disease and UC.

Characteristics	Crohn's Disease			Ulcerative Colitis		
	Cases (n=83, n (%))	Controls (n=830), n (%)	Adj2 OR (95% CI)	Cases (n=63, n (%))	Controls (n=630), n (%)	Fully adjusted OR (95% CI)
Season of birth						
May-September	35 (42.17)	338 (40.7)	1.14 (0.71-1.82)	31 (49.21)	282 (44.8)	1.31 (0.77-2.22)
October-April	48 (57.83)	492 (59.3)	1	32 (50.79)	348 (55.2)	1
Siblings						
No	45 (54.22)	458 (55.2)	1.86 (0.52-1.40)	41 (65.08)	324 (51.4)	1.79 (0.99-3.22)
Yes	38 (45.78)	372 (44.8)	1	22 (34.92)	306 (48.6)	1
Multiple births						
1	79 (95.18)	818 (98.5)	1	79 (95.18)	612 (97.1)	1
≥2	4 (4.82)	12 (1.5)	2.18 (0.51-9.32)	1 (1.59)	18 (2.9)	1.58 (0.18-13.95)
Birth weight						
≥2500	74 (89.32)	795 (95.8)	1	63 (100.00)	595 (94.4)	1
<2500	9 (10.84)	35 (4.2)	2.01 (0.66-6.18)	0	35 (5.6)	-
Gestational age						
≤35	6 (7.23)	19 (2.3)	1.53 (0.37-6.42)	0	23 (3.7)	-
≥36	77 (92.77)	806 (97.7)	1	62 (100.00)	605 (96.3)	1

Apgar						
≥7	77 (92.77)	792 (95.4)	1	60 (95.24)	582 (92.7)	1
≤ 6	6 (7.23)	38 (4.6)	1.33 (0.52-3.38)	3 (4.76)	46 (7.3)	0.80 (0.22-2.86)
Maternal age						
< 25	11 (13.25)	95 (11.5)	1.08 (0.52-2.25)	7 (11.11)	79 (12.5)	0.66 (0.27-1.62)
25-29	33 (39.76)	281 (33.9)	1	25 (39.68)	203 (32.2)	1
30-34	19 (22.89)	297 (35.8)	0.48 (0.26-0.89)	24 (38.10)	221 (35.1)	1.07 (0.57-2.01)
35-39	15 (18.07)	133 (16.0)	0.80 (0.39-1.61)	6 (9.52)	114 (18.1)	0.62 (0.23-1.64)
≥ 40	5 (6.02)	24 (2.9)	1.46 (0.49-4.35)	1 (1.59)	13 (2.1)	1.05 (0.13-8.84)
Maternal education						
University	11 (13.25)	106 (12.8)	1.56 (0.70-3.52)	4 (6.35)	79 (12.5)	0.56 (0.18-1.70)
High school	46 (55.42)	396 (47.9)	1.61 (0.94-2.74)	34 (53.97)	282 (44.8)	1.22 (0.70-2.14)
Primary/middle school	26 (31.33)	324 (39.2)	1	25 (39.68)	269 (42.7)	1

Fully adjusted: sex, year of birth, season of birth; having older siblings; number of births; birth weight; gestational age; Apgar scores at 1 minute; maternal age; and mother's formal education at the moment of birth.

Table S3. Frequency of antibiotic prescriptions stratified by type of active ingredient and antibiotic spectrum, among IBD cases and controls.

ANTIBIOTIC ATC CODE (Active ingredient)	Antibiotic type	Spectrum (broad/narrow)	IBD			All per type of antibiotic
			Controls	Cases	All	
J01CA04 (amoxicillin)	penicillin	Broad	278	53	331	399
			44.6	42.4		
J01CR02 (moxicillin and beta-lactamase inhibitor)		Narrow	56	12	68	
			9.0	9.6		
J01DA06 (cefuroxime)	cephalosporin	Broad	5	0	5	
0.8			0			
J01DA08-DC04 (cefactor)		Broad	95	30	125	
			15.2	24.0		
J01DA11 (ceftazidime)		Broad	5	1	6	
			0.8	0.8		
J01DA23 (cefixime)		Broad	25	0	25	
			4.0	0		
J01DA33 (Cefpodoxime)		Broad	1	0	1	
			0.2	0		
J01DA39 (ceftibuten)		Broad	14	1	15	
			2.2	0.8		
J01DA41 (cefprozil)		Broad	1	0	1	
			0.2	0		
J01DC02 (cefuroxime)	Broad	1	0	1		
		0.2	0			
					193	

J01DD08 (cefixime)		Broad	1	0	1	
			0.2	0		
J01DD13 (cefpodoxime)		Broad	2	1	3	
			0.3	0.8		
J01DD14 (Ceftibuten)		Broad	8	2	10	
			1.3	1.6		
J01EA01 (trimethoprim)	sulfonamide	Broad	1	0	1	
			0.2	0		
J01EE01 (Sulfamethoxazole and trimethoprim)		Broad	2	1	3	4
			0.3	0.8		
J01FA01 (erythromycin)	macrolide	Narrow	5	0	5	
			0.8	0		
J01FA06 (roxithromycin)		Narrow	1	0	1	
			0.2	0		
J01FA07 (josamycin)		Broad	17	1	18	
			2.7	0.8		
J01FA09 (clarithromycin)		Narrow	62	4	66	
			9.9	3.2		
J01FA10 (azithromycin)		Narrow	35	5	40	
			5.6	4		
J01FA11 (miocamycin)		Narrow	3	1	4	
			0.5	0.8		
J01FA12 (rokitamycin)		Narrow	3	0	3	137
			0.5	0		
J01GB03 (gentamicin)	aminoglycoside	Broad	0	10	10	
			0	8		
J01GB07 (netilmicin)		Broad	1	3	4	14
			0.2	2.4		
J01MA01 (ofloxacin)	quinolone	Broad	1	0	1	
			0.2	0		
						1

J01XX01 (fosfomycin)	other	Broad	1	0	1	1
			0.2	0		
Total			624	125	749	

Table S4 Risk of developing VEO-IBD (1-5 years) after antibiotic exposure in the first 6 and 12 months of life.

	VEO-IBD (n = 19) n (%)	Controls (n = 190), n (%)	Adj 2 OR (95% CI)
Antibiotic prescription in the first 6 months of life			
No	11 (57.9)	155 (81.6)	1
Yes	8 (42.1)	35 (18.4)	4.56 (1.48-14.02)
1†	3 (15.8)	25 (13.2)	2.02 (0.49-8.40)
2-3†	3 (15.8)	9 (4.7)	9.32 (1.62-53.60)
≥4†	2 (10.5)	1 (0.5)	25.63 (1.34-490.46)
Antibiotic prescription in the first 12 months of life			
No	5 (26.3)	108 (56.8)	1
Yes	14 (73.7)	82 (43.2)	4.54 (1.47-14.02)
1†	5 (26.3)	45 (23.7)	3.42 (0.77-15.27)
2-3†	3 (15.8)	28 (14.7)	2.30 (0.47-11.18)
≥4†	6 (31.6)	9 (4.7)	87.07 (8.43-899.78)

†Reference group: not exposed to antibiotics

Adj2: sex, year of birth, season of birth; having older siblings; number of births; birth weight; gestational age; Apgar scores at 1 minute; maternal age; and mother's formal education at the moment of birth