

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Previous Studies of Inflammatory Bowel Disease (IBD) and Risk of Psychiatric Outcome in Childhood-Onset IBD, Adult-Onset IBD and Mixed IBD Patients (Both Childhood- and Adult-Onset)

Study	Country, study period (population)	Number of IBD patients	Age at IBD onset, years	Age at the end of follow-up, years	Psychiatric outcome, number (%)	Psychiatric outcome: Relative risk estimate (95% CI)	Assessment / Diagnosis criteria	Time of follow-up, years	Patient years of follow-up in IBD patients	Incidence per 1000 person-years (95%CI)	Time of follow-up, up to 18 yrs/over 18 yrs
Childhood-onset IBD											
Loftus, 2011	USA, 2000-2006 (CD patients)	CD: 2144	Range 0-18 Mean 11.8	-	Depression: 118 (5.5) Anxiety: 81 (3.8)	Depression: 1.7 (1.4-2.3) Anxiety: 2.3 (1.7-3.2)	Register data/ICD-9 CM	-	-	Depression: 26.9 Anxiety: 18.1	yes/no
Virta, 2014	Finland, 2006-2010, (IBD patients)	IBD: 248	Range 6-16 Median (IQR) 12 (10-13)	Median ^a 14	Antidepressants: 8 (3.2) ADHD drugs: 2 (0.8)	Antidepressants: 2.7 (1.1-6.7) ^a ADHD drugs: NS	Register data/Dispensed prescriptions	Median (IQR) 2.1 (1.5-3.0)	-	-	yes/no
Our study	Sweden, 1973-2013 (UC, CD, IBD-U patients)	IBD: 6464 (UC: 3228 CD: 2536 IBD-U: 700)	Median (IQR) 14 (11-16)	Median (IQR) 23 (18-29)	Any psychiatric disorders: 1,117 (17.3) Suicide attempts: 117 (1.8) Specific psychiatric disorders: see results	Any psychiatric disorders: 1.6 (1.5-1.7) Suicide attempts: 1.4 (1.2-1.7) Specific psychiatric disorders: see results	Register data/ICD-8, ICD-9, ICD-10, ADHD medicine prescription	Median (IQR) 9 (4-15)	Any psychiatric disorders: 65,503 Suicide attempts: 71,147	Any psychiatric disorders: 17.1 Suicide attempts: 1.6 Specific psychiatric disorders: see results	yes/yes
Adult-onset IBD and mixed IBD patients											
Persson, 1996	Sweden, 1955-1990 (IBD patients)	UC: 1547 CD: 1251	0-60+	-	Completed suicide UC:5 CD:9	Completed suicide UC: 0.8 (0.3-1.8) CD: 1.9 (0.9-3.0)	Register data/ICD-6 to 9	>15	-	-	NA
Jess, 2002	Denmark, 1962-1997 (IBD patients)	CD: 374	0-80+	-	Completed suicide: 1 (0.0)	Completed suicide: NS	Register data/ICD-10	Median (Range)	6,569	Completed suicide: 0.15	NA

Study	Country, study period (population)	Number of IBD patients	Age at IBD onset, years	Age at the end of follow-up, years	Psychiatric outcome, number (%)	Psychiatric outcome: Relative risk estimate (95% CI)	Assessment / Diagnosis criteria	Time of follow-up, years	Patient years of follow-up in IBD patients	Incidence per 1000 person-years (95%CI)	Time of follow-up, up to 18 yrs/over 18 yrs
) 17 (1-36)			
Jess, 2006	USA, 1940–2004 (IBD patients)	UC: 378 CD: 314	Median UC: 33.3 CD: 28.9	-	Completed suicide: UC: 1 (0.0) CD: 0 (0.0)	Completed suicide: NS	Register data/ICD	Median (Range) 14 (0-58)	11,307	-	NA
Walker, 2008	Canada, USA, New Zealand, 2002-2004 (IBD patients)	IBD: 351	Mean (SD) 36.5 (14.5)	Range 19-81 Mean (SD) 43 (14)	<u>Mood disorder</u> ^a Major Depression: 32 (9.1) ^m /95 (27.2) ^l Bipolar disorder: 4 (1.1) ^m /6 (1.7) ^l <u>Anxiety disorder</u> ^a Panic: 13 (3.7) ^m /28 (8.0) ^l Agoraphobia: 2 (0.6) ^m /4 (1.1) ^l Social anxiety: 9 (2.6) ^m /21 (6.0) ^l	<u>Mood disorder</u> Major Depression: NS ^m /2.2 (1.6-2.9) ^l Bipolar disorder: NS ^m /NS ^l <u>Anxiety disorder</u> Panic: NS ^m /NS ^l Agoraphobia: NS ^m /NS ^l Social anxiety: NS ^m /0.5 (0.3-0.8) ^l	CIDI interview /DSM-IV	2	NA	NA	NA
Eaton, 2010	Denmark 1977-2006 (patients with bipolar disorder and schizophrenia)	UC: 54 CD: 38	-	-	Bipolar disorder: UC: 31 ^c /23 ^d CD: 16 ^c /22 ^d Schizophrenia: UC: 28 ^c /35 ^d CD: 11 ^c /28 ^d	Bipolar disorder: UC: 1.8 ^c /NS ^d CD: 1.9 ^c /1.8 ^d Schizophrenia: UC: NS ^c /NS ^d CD: NS ^c /1.7 ^d	Register data/ICD-8, ICD-10	>5yr	NA	NA	NA
Gradus, 2010	Denmark, 1981-2006 (completed suicide cases)	UC: 897 CD: 445	-	15-90	NA	Completed suicide: UC: 1.7 (1.3-2.1) CD: 1.6 (1.1-2.3)	Register data/ICD-8, ICD-10	NA	NA	NA	NA

Study	Country, study period (population)	Number of IBD patients	Age at IBD onset, years	Age at the end of follow-up, years	Psychiatric outcome, number (%)	Psychiatric outcome: Relative risk estimate (95% CI)	Assessment / Diagnosis criteria	Time of follow-up, years	Patient years of follow-up in IBD patients	Incidence per 1000 person-years (95%CI)	Time of follow-up, up to 18 yrs/over 18 yrs
Goodhand, 2012	UK, 2008-2011 (IBD patients)	UC: 103 CD: 101	Mean (SD) UC: 27.3 (1.2) CD: 28.6 (13.1)	Range 18-75 Mean (SD) 42 (14)	NA	Symptoms of depression and anxiety: NA	HADS scale/score	NA	NA	NA	NA
Jess, 2013	Denmark, 1982-2010 (IBD patients)	UC: 36080 CD: 15362	Range 0-80+ Median UC: 45.2 CD: 36.3	-	Completed suicide UC: 81 (0.2) CD: 32 (0.2)	Completed suicide: UC: 1.3 (1.1-1.5) CD: NS	Register data/ICD-8, ICD-10	>10	-	-	NA
Bernstein, 2019	Canada, 1989-2012 (IBD patients)	IBD: 5346	Range 18-65+ Mean (SD) 43 (17)	-	-	Depression: 1.4 (1.3-1.5) Anxiety disorder: 1.4 (1.3-1.5) Bipolar disorder: 1.8 (1.4-2.3) Schizophrenia: 1.6 (0.9-2.8)	Register data/ICD-9, ICD-10	Median (IQR) 10.4 (5.0-16.4)	-	Depression: 18.6 (95% CI, 14.2-24.3) Anxiety disorder: 25.0 (95% CI, 19.6-32.0) Bipolar disorder: 3.80 (95% CI, 2.29-6.30) Schizophrenia : 4.6 (95% CI, 3.1-6.8)	NA

a, Values calculated with use of numbers provided in the manuscript; ADHD, Attention-deficit hyperactivity disorder; c, Concurrent risk within the first 4 complete years following date of onset of the autoimmune disease. CD, Crohn's Disease; CI, Confidence Interval; CIDI, The Comprehensive International Diagnostic Interview; d, Delayed risk \geq 5 years after date of onset of the autoimmune disease; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders 4th Edition; HADS, Hospital Anxiety and Depression Scale; IBD, inflammatory bowel disease; IBD-U, inflammatory bowel disease unclassified; ICD, International Classification of Diseases; IQR, interquartile range; l, The lifetime prevalence rates of psychiatric disorders for the IBD cohort; m, The 12-month prevalence rates of psychiatric disorders for the IBD cohort; NA=Not applicable; NS, Not Statistically Significant; UC, Ulcerative colitis; -, information not available.

eTable 2. *International Classification of Diseases (ICD) Codes Defining Inflammatory Bowel Disease (IBD)*

	ICD-8	ICD-9	ICD-10
	1969-1986	1987-1996	1997-
Ulcerative colitis (UC)	563,10 ; 563,99 ; 569,02	556	K51
Crohn's disease (CD)	563,00	555	K50
IBD unclassified (IBD-U)	UC+CD	UC+CD	UC + CD, or K52.3

eTable 3. ICD Codes Used to Define Different Psychiatric Disorders and Suicide Attempts in the Study

Psychiatric outcome	ICD-8 (1969-1986)	ICD-9 (1987-1996)	ICD-10 (1997-)
Primary outcomes:			
Any psychiatric disorders	Any code from specific categories of psychiatric disorders	Any code from specific categories of psychiatric disorders	Any code from specific categories of psychiatric disorders
Suicide attempts	E950-E959	E950-E959	X60-X84
Secondary outcomes, specific categories of psychiatric disorders:			
Psychotic disorders	295, 297-299;	295, 297, 298;	F20-F29
Mood disorders	296, 300.40;	296, 300E, 311	F30-F39
Anxiety disorders	300.00-300.30,300.50-300.99, 307;	300, 300A-300D, 300F-300X, 308-309	F40-F45, F48
Eating disorders		307B, 307F;	F50
Substance misuse	291, 303, 304;	291, 303, 304, 305A, 305X	F10-F19
Behavioral disorders	-	-	F91
Attention-deficit hyperactivity disorder	-	314	F90
Autism spectrum disorders	-	299A	F84.0, F84.1, F84.5, F84.8, F84.9
Intellectual disability	310-315;	317-319	F70-F79
Personality disorders	301	301	F60-F62, F69

Abbreviations: ICD, International Classification of Diseases

eTable 4. Extraintestinal Manifestations and Primary Sclerosing Cholangitis in Patients with Inflammatory Bowel Disease (IBD) As defined by *ICD-9* and *ICD-10* Codes

Complication	ICD-9	ICD-10
	1987-1996	1997-
Primary sclerosing cholangitis	576B	K83.0
Extra-intestinal manifestations		
Erythema nodosum	695C	L52
Pyoderma gangrenosum	-	L88
Sweet syndrome	-	L98.2
Iridocyclitis	364	H20
Arthropathy in Crohn's disease	713B	M07.4
Arthropathy in Ulcerative colitis	713B	M07.5
Other defined arthropathy in gastrointestinal disorders	-	M07.6
Juvenile arthritis in Crohn's disease	-	M09.1
Juvenile arthritis in Ulcerative colitis	-	M09.2
Bechterew's disease	720A	M45
Spondylarthritis, inflammatory NOD	720C, 720W, 720X	M460, M461, M468, M469
Arthritis NOD	-	M139, M255

eTable 5. Surgery Codes Included in the Definitions of “Inflammatory Bowel Disease-Related Bowel Surgery and Perianal Surgery” (Since 1964)

Classification of surgical procedures	6th revision	7th revision
Colectomy		
1) Subtotal colectomy with end ileostomy		
Colectomy and ileostomy with closure of the rectum	4651	JFH10
Laparoscopic colectomy and ileostomy		JFH11
Other colectomy		JFH96
2) Colectomy with IRA (ileorectal anastomosis)		
Colectomy with ileorectal anastomosis	4650	JFH00
Laparoscopic colectomy with ileorectal anastomosis		JFH01
Ileorectal anastomosis		JFC40
Laparoscopic ileorectal anastomosis		JFC41
Closure of enterostomy with anastomosis to the rectum		JFG29
Closure of enterostomy with anastomosis to the colon		JFG26
3) Partial colectomies		
Right-sided colectomy	4641	JFB30, JFB31
Resection of the colon transversum	4643	JGB40, JFB41
Left-sided colectomy	4640	JFB43, JFB44
Resection of the sigmoid colon	4644	JFB46, JFB47
Other colon resection	4649	JFB50, JFB51
4) Proctocolectomy with IPAA (ileal pouch-anal anastomosis)		
Colectomy, rectal mucosectomy and ileoanal anastomosis <i>without</i> ileostomy.		JFH30
Colectomy, rectal mucosectomy and ileoanal anastomosis <i>and</i> ileostomy.		JFH33
Mucosectomy and ileoanal anastomosis after previous colectomy.	4654	JGB50
Extirpation of rectum or making of an ileoanal anastomosis after previous colectomy.		JGB60
5) Continent ileostomy at time of colectomy		
Proctocolectomy with continent ileostomy, Kock	4653	JFH40
Converting a conventional ileostomy to a continent ileostomy		JFG60
6) Proctocolectomy		
Proctocolectomy with ileostomy	4652	JFH20
7) Other bowel surgery		
Strictureplasty to the small bowel		JFA60
Strictureplasty to the colon		JFA63
Closure the small intestinal fistula		JFA76
Closure of the fistula of the colon		JFA86
Colonic and/or small bowel resection	4630, 4631, 4640-4649	JFB
Formation of the stoma		JFF
Operations on the intestinal stoma or reservoir		JFG
Other operation of the small bowel and/or colon	4660-4668, 4700-4739, 4790-4798	JFW96
Other laparoscopic operation of the small bowel and/or colon		JFW97
Rectal resection	4820-4828	JGB

Classification of surgical procedures	6th revision	7th revision
Colectomy		
8) Perianal surgery		
Perianal incision and drainage	4900	JHA00
Dilatation of the anal sphincter	4960	JHD00
Lay open or excision of perianal fistula	4920, 4922-4924	JHD20
Partial lay open or excision of perianal fistula (including seton placement)	4970-4971	JHD30
Completion lay open or excision of perianal fistula		JHD33
Excision of perianal fistula with advancement flap		JHD50
Occlusion of perianal fistula with collagen plug		JHD60
Occlusion of perianal fistula with fibrin glue		JHD63
Other anal or perianal surgery (e.g. examination under anesthesia)	4999	JHW96

eTable 6. Hazard Ratios of Primary and Secondary Psychiatric Outcomes Diagnosed Before and After 18th Birthday in the Cohort of Patients With Childhood Onset (<18 Years) Stratified by type of IBD Diagnosis—Patients With IBD Compared With Matched General Population Reference Individuals

	Before 18th birthday				After 18th birthday (follow-up starts after 18 years of age)			
	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value
	Inflammatory bowel disease	Reference individuals			Inflammatory bowel disease	Reference individuals		
Primary outcomes:								
Any psychiatric disorders	507/24,053 (21.1)	12,772/1,241,875 (10.3)	2.1 (2.0-2.3)	<.001	610/64,114 (9.5)	25,266/3,351,707 (7.5)	1.3 (1.2-1.4)	<.001
Suicide attempts	27/25,275 (1.1)	1,337/1,264,821 (1.1)	1.0 (0.7-1.6)	0.82	90/71,050 (1.3)	2,998/3,566,910 (0.8)	1.5 (1.2-1.9)	<.001
Secondary outcomes:								
Psychotic disorders	4/25,330 (0.2)	149/1,267,365 (0.1)	1.2 (0.5-3.3)	0.69	27/71,711 (0.4)	1366/3,588,044 (0.4)	1.0 (0.7-1.5)	0.97
Mood disorders	122/25,096 (4.9)	2,989/1,263,193 (2.4)	2.1 (1.8-2.5)	<.001	305/69,328 (4.4)	1,1031/3,521,471 (3.1)	1.4 (1.3-1.6)	<.001
Anxiety disorders	288/24,578 (11.7)	4,024/1,260,776 (3.2)	3.9 (3.4-4.3)	<.001	385/67,674 (5.7)	14,736/3,496,221 (4.2)	1.4 (1.2-1.5)	<.001
Eating disorders	48/25,223 (1.9)	1076/1,265,689 (0.9)	2.3 (1.7-3.0)	<.001	34/71,234 (0.5)	1,467/3,579,842 (0.4)	1.2 (0.8-1.7)	0.35
Substance misuse	54/25,260 (2.1)	3051/1,262,702 (2.4)	0.9 (0.7-1.1)	0.33	196/70,114 (2.8)	8,628/3,520,636 (2.5)	1.1 (1.0-1.3)	0.07
Personality disorders	3/25,332 (0.1)	96/1,267,400 (0.1)	1.6 (0.5-5.0)	0.44	67/71,530 (0.9)	2,425/3,584,173 (0.7)	1.4 (1.1-1.8)	0.009
Behavioral disorders	14/25,289 (0.6)	508/1,266,413 (0.4)	1.4 (0.8-2.4)	0.21	2/71,775 (0.0)	102/3,593,024 (0.0)	1.0 (0.2-4.0)	0.99

	Before 18th birthday				After 18th birthday (follow-up starts after 18 years of age)			
	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value
	Inflammatory bowel disease	Reference individuals			Inflammatory bowel disease	Reference individuals		
Attention-deficit hyperactivity disorder	83/25,155 (3.3)	3,627/1,258,793 (2.9)	1.1 (0.9-1.4)	0.22	90/71,036 (1.3)	3641/3,557,316 (1.0)	1.2 (1.0-1.5)	0.040
Autism spectrum disorders	34/25,238 (1.3)	1,126/1,264,942 (0.9)	1.5 (1.1-2.1)	0.017	38/71,483 (0.5)	1496/3,582,601 (0.4)	1.3 (0.9-1.8)	0.13
Intellectual disability	20/25,257 (0.8)	641/1,265,603 (0.5)	1.6 (1.0-2.5)	0.045	9/71,593 (0.1)	570/3,588,292 (0.2)	0.8 (0.4-1.5)	0.48

eTable 7. Hazard Ratios of Primary and Secondary Psychiatric Outcomes Diagnosed Before and After 18th Birthday in the Cohort of Patients With Childhood Onset (<18 Years) Stratified by Type of IBD Diagnosis—Patients With IBD Compared With Matched General Population Reference Individuals

	Ulcerative colitis				Crohn's Disease				IBD-unclassified			
	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value
	Patients	Population			Patients	Population			Patients	Population		
Before 18th birthday												
Primary outcomes:												
Any psychiatric disorders	205/ 12,950 (15.8)	6,060/ 661,224 (9.2)	1.8 (1.5-2.0)	<.001	229/ 8,804 (26.0)	5270/ 460,147 (11.5)	2.4 (2.1-2.7)	<.001	73/ 2,299 (31.7)	1,442/ 120,504 (12.0)	2.8 (2.2-3.6)	<.001
Suicide attempts	14/ 13,441 (1.0)	669/ 672,356 (1.0)	1.0 (0.6-1.9)	0.89	8/ 9,398 (0.9)	544/ 469,523 (1.2)	0.7 (0.3-1.6)	0.39	5/ 2,436 (2.1)	124/ 122,942 (1.0)	2.7 (1.1-6.7)	0.031
Secondary outcomes,:												
Psychotic disorders	1/ 13,467 (0.1)	78/ 673,635 (0.1)	0.6 (0.1-4.5)	0.63	2/ 9,415 (0.2)	60/ 470,548 (0.1)	1.4 (0.3-5.9)	0.63	1/ 2,448 (0.4)	11/ 123,182 (0.1)	4.2 (0.5 - 32.8)	0.17
Mood disorders	51/ 13,378 (3.8)	1,511/ 671,484 (2.3)	1.7 (1.3-2.3)	<.001	57/ 9,286 (6.1)	1,163/ 468,930 (2.5)	2.5 (1.9-3.3)	<.0001	14/ 2,432 (5.8)	315/ 122,779 (2.6)	2.3 (1.4-4.0)	<.001
Anxiety disorders	100/ 13,223 (7.6)	1,901/ 670,410 (2.8)	2.7 (2.2-3.4)	<.001	138/ 9,016 (15.3)	1,650/ 467,888 (3.5)	4.6 (3.9-5.5)	<.0001	50/ 2,339 (21.4)	473/ 122,479 (3.9)	6.0 (4.5-8.1)	<.001
Eating disorders	18/ 13,424 (1.3)	544/ 672,761 (0.8)	1.6 (1.0-2.6)	0.040	22/ 9,359 (2.4)	437/ 469,907 (0.9)	2.6 (1.7-4.0)	<.0001	8/ 2,440 (3.3)	95/ 123,021 (0.8)	4.4 (2.1-9.1)	<.001
Substance misuse	29/ 13,434 (2.2)	1422/ 671,448 (2.1)	1.0 (0.7-1.4)	1.00	20/ 9,385 (2.1)	1,297/ 468,557 (2.8)	0.8 (0.5-1.2)	0.23	5/ 2,441 (2.0)	332/ 122,698 (2.7)	0.8 (0.3-1.9)	0.57
Personality disorders	2/ 13,467 (0.1)	42/ 673,657 (0.1)	2.6 (0.6 - 11.0)	0.18	1/ 9,415 (0.1)	41/ 470,570 (0.1)	1.1 (0.2-8.2)	0.91	0/ 2,450 (0.0)	13/ 123,173 (0.1)	-	0.99
Behavioral disorders	3/ 13,458	252/ 673,165	0.6	0.38	9/ 9,382	198/ 470,191	2.3	<.05	2/ 2,449	58/ 123,057	1.8	0.43

	Ulcerative colitis				Crohn's Disease				IBD-unclassified			
	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value
	Patients	Population			Patients	Population			Patients	Population		
	(0.2)	(0.4)	(0.2-1.9)		(1.0)	(0.4)	(1.2-4.6)		(0.8)	(0.5)	(0.4-7.3)	
Attention-deficit hyperactivity disorder	45/ 13,354	1,669/ 669,556	1.4	0.042	32/ 9,362	1523/ 467,000	1.1	0.74	6/ 2,439	435/ 122,236	0.7	0.31
	(3.4)	(2.5)	(1.0-1.8)		(3.4)	(3.3)	(0.7-1.5)		(2.5)	(3.6)	(0.3-1.5)	
Autism spectrum disorders	22/ 13,397	532/ 672,411	2.1	<.001	10/ 9,397	475/ 469,584	1.0	0.91	2/ 2,444	119/ 122,947	0.9	0.83
	(1.6)	(0.8)	(1.4-3.2)		(1.1)	(1.0)	(0.6-1.9)		(0.8)	(1.0)	(0.2-3.5)	
Intellectual disability	10/13,424	309/ 672,727	1.7	0.12	5/ 9,391	261/ 469,875	1.0	0.93	5/ 2,442	71/ 123,002	3.4	<.001
	(0.7)	(0.5)	(0.9-3.1)		(0.5)	(0.6)	(0.4-2.3)		(2.0)	(0.6)	(1.4-8.5)	
After 18th birthday (follow-up starts after 18 years of age)												
Primary outcomes:												
Any psychiatric disorders	318/ 34,951	13,440/ 1,805,548	1.2	<.001	240/ 23,398	9,422/ 1,234,544	1.4	<.0001	52/ 5,765	2,404/ 311,615	1.2	0.21
	(9.1)	(7.4)	(1.1-1.4)		(10.3)	(7.6)	(1.2-1.5)		(9.0)	(7.7)	(0.9-1.6)	
Suicide attempts	40/ 38,199	1,647/ 1,918,618	1.2	0.20	39/ 26,279	1091/ 1,315,553	1.8	<.001	11/ 6,572	260/ 332,739	2.1	0.013
	(1.0)	(0.9)	(0.9-1.7)		(1.5)	(0.8)	(1.3-2.5)		(1.7)	(0.8)	(1.2-3.9)	
Secondary outcomes:												
Psychotic disorders	13/ 38,551	735/ 1,930,432	0.9	0.65	13/ 26,459	512/ 1,323,026	1.3	0.35	1/ 6,701	119/ 334,585	0.4	0.38
	(0.3)	(0.4)	(0.5-1.5)		(0.5)	(0.4)	(0.7-2.3)		(0.1)	(0.4)	(0.1-3.0)	
Mood disorders	160/ 37,311	5,909/ 1,893,727	1.4	<.001	113/ 25,600	4,092/ 1,299,312	1.4	<.001	32/ 6,417	1030/ 328,432	1.6	0.007
	(4.3)	(3.1)	(1.2-1.6)		(4.4)	(3.1)	(1.2-1.7)		(5.0)	(3.1)	(1.1-2.3)	
Anxiety disorders	204/ 36,816	7,976/ 1,880,492	1.3	<.001	151/ 24,725	5,416/ 1,290,005	1.5	<.0001	30/ 6,133	1344/ 325,724	1.2	0.32
	(5.5)	(4.2)	(1.1-1.5)		(6.1)	(4.2)	(1.2-1.7)		(4.9)	(4.1)	(0.8-1.7)	
Eating disorders	16/ 38,360	772/ 1,926,160	1.0	0.87	15/ 26,250	546/ 1319763	1.4	0.20	3/ 6,624	149/ 333,919	1.1	0.92
	(0.4)	(0.4)	(0.6-1.7)		(0.6)	(0.4)	(0.8-2.3)		(0.5)	(0.4)	(0.3-3.3)	
Substance misuse	101/ 37,751	4,559/ 1,895,517	1.1	0.29	84/ 25,808	3,230/ 1297044	1.3	0.015	11/ 6,555	839/ 328,075	0.6	0.15
	(2.7)	(2.4)	(0.9-1.4)		(3.3)	(2.5)	(1.1-1.6)		(1.7)	(2.6)	(0.4-1.2)	

	Ulcerative colitis				Crohn's Disease				IBD-unclassified			
	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value
	Patients	Population			Patients	Population			Patients	Population		
Personality disorders	37/ 38,442	1,328/ 1,928,298	1.4	0.045	21/ 26,426	890/ 1,321,690	1.2	0.45	9/ 6,662	207/ 334,185	2.1	0.026
	(1.0)	(0.7)	(1.0-1.9)		(0.8)	(0.7)	(0.8-1.8)		(1.4)	(0.6)	(1.1-4.2)	
Behavioral disorders	2/ 38,616	61/ 1,933,128	1.7	0.48	0/ 26,452	28/ 1,324,913	-	0.99	0/ 6,707	13/ 334,983	-	0.99
	(0.1)	(0.0)	(0.4-6.8)		(0.0)	(0.0)			(0.0)	(0.0)		
Attention-deficit hyperactivity disorder	41/ 38,191	1,898/ 1,915,383	1.1	0.57	39/ 26,210	1,429/ 1,310,602	1.4	0.05	10/ 6,635	314/ 331,331	1.6	0.14
	(1.1)	(1.0)	(0.8-1.5)		(1.5)	(1.1)			(1.5)	(0.9)	(0.9-3.0)	
Autism spectrum disorders	17/ 38,398	776/ 1,927,827	1.1	0.68	15/ 26,409	590/ 1,320,745	1.3	0.34	6/ 6,676	130/ 334,028	2.3	0.046
	(0.4)	(0.4)	(0.7-1.8)		(0.6)	(0.4)	(0.8-2.1)		(0.9)	(0.4)	(1.0-5.2)	
Intellectual disability	4/ 38,481	305/ 1,930,599	0.7	0.40	3/ 26,480	207/ 1,323,140	0.7	0.59	2/ 6,633	58/ 334,553	1.7	0.48
	(0.1)	(0.2)	(0.2-1.8)		(0.1)	(0.2)	(0.2-2.3)		(0.3)	(0.2)	(0.4-6.8)	

eTable 8. Hazard Ratio of Primary and Secondary Psychiatric Outcomes in the Cohort of Patients With Childhood Onset (<18 Years) Stratified by Time After Cohort Entry (Diagnosis of Inflammatory Bowel Disease or Respected Date in Reference Individuals)—IBD Compared With Matched General Population Reference Individuals

	Time after cohort entry											
	<1 year				1 to 4 years				>5 years			
	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value
	Patients	Population			Patients	Population			Patients	Population		
Primary outcomes:												
Any psychiatric disorders	204/ 6,230 (32.7)	3,030/ 316,062 (9.6)	3.5 (3.0-4.0)	<.001	339/ 27,332 (12.4)	12,385/ 1,407,739 (8.8)	1.5 (1.3-1.6)	<.001	574/ 64,454 (8.9)	22,629/ 3,357,992 (6.7)	1.3 (1.2-1.5)	<.001
Suicide attempts	10/ 6,336 (1.6)	482/ 316,590 (1.5)	1.3 (0.5-3.1)	0.60	28/ 28,749 (1.0)	1,229/ 1437573 (0.9)	1.1 (0.8-1.7)	0.50	79/ 71,059 (1.1)	2,624/ 3,567,067 (0.7)	1.5 (1.2-1.9)	<.001
Secondary outcomes:												
Psychotic disorders	2/ 6,346 (0.3)	30/ 317,467 (0.1)	3.3 (0.8 - 13.9)	0.10	5/ 28,820 (0.2)	289/ 1,441,336 (0.2)	0.9 (0.4-2.1)	0.75	24/ 71,703 (0.3)	1,196/ 3,587,692 (0.3)	1.0 (0.7-1.5)	0.96
Mood disorders	41/ 6,324 (6.5)	586/ 317,224 (1.8)	3.5 (2.6-4.8)	<.001	106/ 28,449 (3.7)	3,524/ 1,433,827 (2.5)	1.5 (1.3-1.8)	<.001	280/ 69,402 (4.0)	9,912/ 3,521,947 (2.8)	1.4 (1.3-1.6)	<.001
Anxiety disorders	130/ 6,267 (20.7)	814/ 317,114 (2.6)	8.2 (6.8-9.9)	<.001	190/ 27,961 (6.8)	4,726/ 1,431,072 (3.3)	2.1 (1.8-2.5)	<.001	353/ 67,766 (5.2)	13,223/ 3,496,636 (3.8)	1.4 (1.3-1.5)	<.001
Eating disorders	16/ 6,339 (2.5)	249/ 317,373 (0.8)	3.2 (2.0-5.4)	<.001	36/ 28,706 (1.3)	942/ 1,439,228 (0.7)	1.9 (1.4-2.7)	<.001	30/ 71,267 (0.4)	1,352/ 3,580,870 (0.4)	1.1 (0.8-1.6)	0.53
Substance misuse	8/ 6,344 (1.3)	704/ 317,158 (2.2)	0.6 (0.3-1.1)	0.11	68/ 28,696 (2.4)	3,686/ 1,432,553 (2.6)	0.9 (0.7-1.2)	0.49	174/ 70,118 (2.5)	7,292/ 3,520,078 (2.1)	1.2 (1.0-1.4)	0.018
Personality disorders	1/ 6,347 (0.2)	25/ 317,470 (0.1)	2.0 (0.3 - 14.8)	0.50	10/ 28,813 (0.3)	436/ 1,441,146 (0.3)	1.1 (0.6-2.2)	0.66	59/ 71,505 (0.8)	2,060/ 3,583,053 (0.6)	1.4 (1.1-1.9)	0.007
Behavioral disorders	4/ 6,346	89/ 317,441	2.2	0.11	7/ 28,813	302/ 1,441,017	1.2	0.71	5/ 71,799	219/ 3,594,015	1.2	0.72

	Time after cohort entry											
	<1 year				1 to 4 years			>5 years				
	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value
	Patients	Population			Patients	Population			Patients	Population		
	(0.6)	(0.3)	(0.8-6.1)		(0.2)	(0.2)	(0.5-2.4)		(0.1)	(0.1)	(0.5-2.8)	
ADHD	11/ 6,342	749/ 317,128	0.7	0.31	65/ 28,679	2,599/ 1,434,566	1.3	0.07	97/ 71,163	3,921/ 3,562,199	1.2	0.031
	(1.7)	(2.4)	(0.4-1.3)		(2.3)	(1.8)	(1.0-1.6)		(1.4)	(1.1)	(1.0-1.5)	
Autism spectrum disorders	7/ 6,343	179/ 317,399	2.0	0.08	28/ 28,760	949/ 1,439,588	1.5	0.041	37/ 71,520	1,494/ 3,584,001	1.2	0.18
	(1.1)	(0.6)	(0.9-4.2)		(1.0)	(0.7)	(1.0-2.2)		(0.5)	(0.4)	(0.9-1.7)	
Intellectual disability	2/ 6,346	137/ 317,409	0.7	0.66	10/ 28,807	526/ 1,440,254	1.0	0.88	17/ 71,665	549/ 3,588,846	1.6	0.07
	(0.3)	(0.4)	(0.2-2.9)		(0.3)	(0.4)	(0.5-1.8)		(0.2)	(0.2)	(1.0-2.5)	

eTable 9. Hazard Ratio of the First Ever Event of Any Psychiatric Disorders in the Cohort of Patients With Childhood Onset (<18 Years)—IBD Compared With Matched General Population Reference Individuals

	Any psychiatric disorders				Suicide attempts			
	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value
	Inflammatory bowel disease	Reference individuals			Inflammatory bowel disease	Reference individuals		
Sex								
Males	543/37,515 (14.5)	19,403/1,932,856 (10.0)	1.5 (1.3-1.6)	<.001	39/40,354 (1.0)	1,731/2,024,216 (0.9)	1.2 (0.9-1.6)	0.30
Females	574/27,988 (20.5)	18,641/1,463,491 (12.7)	1.7 (1.5-1.8)	<.001	78/30,793 (2.5)	2,604/1,546,195 (1.7)	1.5 (1.2-1.9)	<.001
Age of cohort entry								
< 6 years	66/3,657 (18.0)	1554/196,681 (7.9)	2.4 (1.9-3.1)	<.001	3/3,992 (0.8)	125/203,602 (0.6)	1.3 (0.4-4.0)	0.69
< 10 years	224/12,795 (17.5)	6118/667,339 (9.2)	2.0 (1.7-2.3)	<.001	21/13,996 (1.5)	587/696,553 (0.8)	1.8 (1.2-2.8)	0.009
< 15 years	710/42,340 (16.8)	23449/2,208,489 (10.6)	1.6 (1.5-1.8)	<.001	70/46,076 (1.5)	2,468/2,319,533 (1.1)	1.5 (1.2-1.9)	0.002
< 17 years	993/57,486 (17.3)	33285/3,006,887 (11.1)	1.6 (1.5-1.7)	<.001	100/62,672 (1.6)	3,702/3,161,679 (1.2)	1.4 (1.1-1.7)	0.002
ICD classification at the time of cohort entry								
ICD-8 (1973-1986)	30/4,951 (6.1)	1,228/250,610 (4.9)	1.3 (0.9-1.8)	0.21	0/5,230 (0.0)	127/259,969 (0.5)	-	0.98
ICD-9 (1987-1996)	261/24,787 (10.5)	9,206/1,272,733 (7.2)	1.5 (1.3-1.7)	<.001	47/26,424 (1.8)	1,207/1,331,816 (0.9)	2.0 (1.5-2.6)	<.001
ICD-10 (1997-2013)	826/35,765 (23.1)	2,7610/1,873,004 (14.7)	1.6 (1.5-1.7)	<.001	70/39,493 (1.8)	3,001/1,978,626 (1.5)	1.2 (0.9-1.5)	0.14
Source of data at the time of cohort entry								
Inpatient register (prior to 2002)	574/20,931 (27.4)	18,455/1,103,965 (16.7)	1.7 (1.5-1.8)	<.001	40/23,216 (1.7)	1,875/1,161,475 (1.6)	1.1 (0.8-1.5)	0.73
In-and out-patient (since 2002)	543/44,572 (12.2)	19,589/2,292,381 (8.5)	1.4 (1.3-1.6)	<.001	77/47,932 (1.6)	2,460/2,408,936 (1.0)	1.6 (1.3-2.0)	<.001
Complications during follow-up								
Extra intestinal manifestation	166/7,622 (21.8)	4,478/399,447 (11.2)	2.0 (1.7-2.4)	<.001	16/8,485 (1.9)	549/420,346 (1.3)	1.5 (0.9-2.5)	0.10

	Any psychiatric disorders				Suicide attempts			
	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value	No. of Outcomes /No. of Accumulated Person-Years (Incidence Rate/1000 Person-Years)		Hazard Ratio (95%CI)	P Value
	Inflammatory bowel disease	Reference individuals			Inflammatory bowel disease	Reference individuals		
Primary sclerosing cholangitis	102/6,297 (16.2)	3,424/330,010 (10.4)	1.6 (1.3-1.9)	<.001	10/6,888 (1.5)	363/347,166 (1.0)	1.3 (0.7-2.5)	0.42
IBD Surgery								
Bowel surgery	208/13,020 (16.0)	5,924/677,888 (8.7)	1.9 (1.6-2.2)	<.001	27/14,238 (1.9)	748/711,565 (1.1)	1.8 (1.2-2.7)	<.001
Perianal surgery	145/7,617 (19.0)	3,983/402,131 (9.9)	2.0 (1.7-2.4)	<.001	17/8,502 (2.0)	457/422,517 (1.1)	1.8 (1.1-3.0)	0.019
Parental psychiatric history	24/ 260 (9.2)	746/16,796 (44.4)	3.4 (1.7-6.7)	<.001	2/ 315 (6.3)	49/18,591 (2.6)	-	0.99