

METHODS

Data source

This study was based on nationwide Swedish healthcare registers (e.g. the National Patient Register [NPR][1], the Prescribed Drug Register [PDR][2], the Total Population Register[3], the Cause of Death Register[4], and the Swedish Longitudinal Integrated Database for Health Insurance and Labour Market Studies[LISA][5]), the nationwide histopathology cohort ESPRESSO (Epidemiology Strengthened by histoPathology Reports in Sweden)[6], and the Swedish Inflammatory Bowel Disease Registry (SWIBREG)[7].

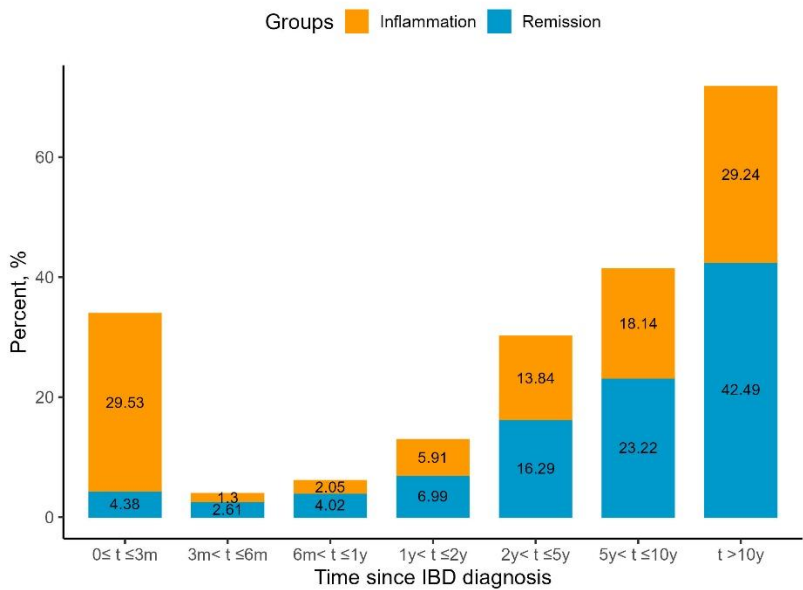
The NPR was founded in 1964 and covers nationwide inpatient care since 1987 and outpatient care since 2001. The PDR covers information on all prescribed drugs dispensed in Sweden since July 2005. Death date was retrieved from the Total Population Register (since 1968, 93% of all deaths in Sweden are reported to this register within 10 days and the remaining 7% within 30 days) and cause of death was identified from the Cause of Death Register (since 1952). The ESPRESSO cohort includes individuals with gastrointestinal biopsies from all 28 pathology departments in Sweden from 1965 to 2017, and each pathology report includes date on biopsy, anatomic location, and morphology (recorded by the adopted Swedish version of the Systematized Nomenclature of Medicine [SNOMED] system). The SWIBREG (since 2005) is a quality register for IBD in Sweden. Educational attainment, which was identified from LISA, is available in > 98% of all individuals aged 25-64 years, with an estimated accuracy for highest attained level of education of 85%.

Covariates

In addition to age at IBD diagnosis, sex, calendar year at index date, and county of residence, we also considered the following covariates. Educational attainment was identified from the Swedish Longitudinal Integrated Database for Health Insurance and Labor Market Studies (available since 1990)[8] with four categories: 0-9 years, 10-12 years, ≥13 years, and “missing”. Country of birth (Nordic [including Sweden, Denmark, Finland, Norway, and Iceland] or others) was identified from the TPR[3]. Number of health care visits between 2 years and 6 months before the index date (0,

1, 2-3, and ≥ 4), a proxy for regular healthcare seeking behavior was retrieved from the NPR. Finally, from the NPR, we also considered comorbidities before the index date, including hypertension, diabetes, obesity, dyslipidemia, chronic kidney disease, and chronic obstructive pulmonary disease/smoking dependence (COPD, a proxy for heavy smoking, only if the patient was diagnosed ≥ 40 years of age).

Except for age at IBD diagnosis, sex, and country of birth, the other covariates were updated at the index date (*i.e.*, time-varying covariates).



Supplementary Figure 1 Distribution of histologic inflammation and remission with time since inflammatory bowel disease diagnosis. IBD: Inflammatory bowel disease.

Supplementary Table 1 International Classification of Disease codes and Systematized Nomenclature of Medicine codes for defining Inflammatory bowel disease

IBD subtypes ¹	ICD-7 (1964-1968)	ICD-8 (1969-1986)	ICD-9 (1987-1996)	ICD-10 (1997-)	SNOMED codes ²
UC	572,20; 578,03	572,21; 563,1; 569,02; 569,04	563,10; 556	K51	D6255 or M41; M42; M43; M44; M463; or M47

CD	572,00; 572,09	563,00	555	K50	D6216 or M41; M42; M43; M44; M463; or M47
IBD-U	UC + CD	UC + CD or 563; 563,0; 563,9; 563,98; 563,99	UC + CD	UC + CD or K523	D6214 or M41; M42; M43; M44; M463; or M47

¹Diagnosis criteria: having either ≥ 2 International Classification of Disease (ICD) codes in the National Patient Register or ≥ 1 ICD code for Inflammatory bowel disease (IBD) and ≥ 1 Systematized Nomenclature of Medicine (SNOMED) code for IBD.

²In SNOMED codes, D codes are the diagnostic codes, D6255 for example was the diagnostic code for UC. Meanwhile, codes starting with "M" (one unspecific SNOMED code) refer to all codes starting with the respective code.

Subtypes of IBD were defined according to the first ICD and SNOMED codes only (*i.e.*, no information after start of follow-up contributed to the subtype definition); in case one individual had one ICD code for IBD and one unspecific SNOMED code (*i.e.*, the "M" code), the IBD subtype was solely determined by the ICD code. CD: Crohn's disease; IBD(-U): Inflammatory bowel disease (unclassified); ICD: International Classification of Disease; SNOMED: Systematized Nomenclature of Medicine; UC: ulcerative colitis.

Supplementary Table 2 International Classification of Disease codes for defining phenotypes of inflammatory bowel disease

Montreal classification	Diagnostic codes
CD location ¹	
Ileal (L1)	K500
Colonic (L2)	K501
Ileocolonic or location not defined (L3/LX)	K508; K509
Perianal disease modifier	Any of the diagnostic codes: K603; K604; K605; K610; K611; K612; K613; K614; K624 OR any of the surgical

procedure codes: JHD20; JHD30; JHD33; JHD50; JHD60; JHD63; JHA00; JHA20; JHW96

UC extent¹

Proctitis (E1)	K512
Left-sided colitis (E2)	K513; K515
Extensive colitis (E3)	K510
Extent not defined (EX)	K514; K518; K519
Primary sclerosing cholangitis	ICD-9 (1987-1996): 576B ICD-10 (1997-): K830
Other extraintestinal manifestations	ICD-9: 695C; 364; 713B; 720A; 720C; 720W; 720X ICD-10: L52; L88; L982; H20; M074; M075; M076 M091; M092; M45; M460; M461; M468; M469; M139; M255

¹The Montreal classification for defining disease phenotypes was available since the use of International Classification of Disease (ICD)-10 in Sweden (1997-). All codes are captured in the Swedish National Patient Register (prospectively recorded in routine clinical practice).

In this study, we categorized Crohn's disease location into two groups: ileal (L1)/ileocolonic (L3)/unknown (LX) or colonic (L2), and categorized ulcerative colitis extent into three groups: proctitis (E1)/left-sided colitis (E2), extensive colitis (E3) or extent not defined (EX).

We restricted our use to ICD-9 and ICD-10 codes since the earlier ICD codes for extraintestinal inflammation are less reliable, particularly for primary sclerosing cholangitis. CD: Crohn's disease; E: Extent; IBD(-U): Inflammatory bowel disease (unclassified); ICD: International Classification of Disease; L: Location; UC: Ulcerative colitis.

Supplementary Table 3 Systematized Nomenclature of Medicine codes for histologic inflammation and remission

SNOMED code	Morphology
M00100	Normal mucosa
M00110	Normal mucosa

M40000	Unspecified inflammation
M40400	Pustulous inflammation, unspecified
M41000	Acute inflammation
M42100	Acute and chronic inflammation
M43000	Chronic inflammation
M43030	Ulcer, chronic inflammation
M42000	Subacute inflammation
M40460	Inflammation with pus
M40700	Inflammation with necrosis
M41700	Inflammation with necrosis, abscess
M41740	Abscess
M44000	Granulomatous inflammation
M44700	Necrotizing granulomatous inflammation
M44900	Necrotizing fibrinous inflammation
M45020	Inflammation with granulation

SNOMED: Systematized Nomenclature of Medicine.

Supplementary Table 4 Inflammatory bowel disease-related surgery

Surgery procedure	Surgeon code (1963-1996)	Surgeon code (1997-)	Apply to subtype of IBD	Exclude colorectal cancer +/- 1 month
Colectomy with ileostomy	4651	JFH10	UC + CD	Colectomy
Laparoscopic colectomy with ileostomy	-	JFH11	UC + CD	Colectomy
Other colectomy	-	JFH96	UC + CD, if with stoma formation code	Colectomy
Formation of a loopileostomy	0054	JFF10	CD	Stoma
Laparoscopic formation of a loopileostomy	-	JFF11	CD	Stoma
Formation of enterostoma	-	JFF13	CD	Stoma

Other formation of stoma on small bowel or colon	0054	JFF96	CD	Stoma
Other laparoscopic formation of stoma on small bowel or colon	-	JFF97	CD	Stoma
Ileocecal resection	4642	JFB20	CD, if with stoma formation code	Ileocecal resection
Laparoscopic ileocecal resection	-	JFB21	CD, if with stoma formation code	Ileocecal resection
Right-sided colectomy	4641	JFB30	CD, if with stoma formation code	Hemi-colectomy
Laparoscopic right-sided colectomy	-	JFB31	CD, if with stoma formation code	Hemi-colectomy

CD: Crohn's disease; IBD: Inflammatory bowel disease; UC: Ulcerative colitis.

Supplementary Table 5 Anatomical Therapeutic Chemical codes for inflammatory bowel disease medications

Medications	ATC code ¹
Immune modulators	
Azathioprine	L04AX01
Mercaptopurine	L01BB02
Methotrexate	L04AX03
Anti-tumor necrosis factor alpha	
Infliximab	L04AB02 (L04AA12 before 2008)
Adalimumab	L04AB04 (L04AA17 before 2008)
Golimumab	L04AB06
Other biologics/small molecules	
Vedolizumab	L04AA33/L04AG05
Ustekinumab	L04AC05
Risankizumab	L04AC18
Mirikizumab	L04AC24
Tofacitinib	L04AA29/L04AF01

Ozanimod	L04AA38/L04AE02
Etrazimod	L04AE05
Filgotinib	L04AA45/L04AF04
Upadacitinib	L04AA44/L04AF03
Systemic corticosteroids	
Betamethasone	H02AB01
Methylprednisolone	H02AB04
Prednisolone	H02AB06
Prednisone	H02AB07
Cortisone	H02AB10
Oral corticosteroids acting locally	
Budesonide	A07EA06

¹Commercial names were also used to identify biologics from SWIBREG: infliximab (Remicade, Remsima, Inflectra, Flixabi, Zessly); adalimumab (Humira, Amgevita, Imraldi, Cyltezo, Hulio, Hyrimoz, Idacio); golimumab (Simponi); vedolizumab (Entyvio); ustekinumab (Stelara); tofacitinib (Xeljanz); ozanimod (Zeposia); filgotinib (Jyseleca); risankizumab (Skyrizi), mirikizumab (Omvo), etrazimod (Velsipity).
ATC: Anatomical Therapeutic Chemical; IBD: inflammatory bowel disease.

Supplementary Table 6 Definitions of outcomes and comorbidities

Outcomes	ICD-8 code	ICD-9 code	ICD-10 code
Overall arrhythmias	A composite outcome including any individual outcomes from 1a-1d		
Atrial fibrillation/flutter	427,92	427D	I48
Bradyarrhythmias	427,20; 427,27; 427,28; 427,29	426A; 426G; 426X	I441; I442; I452; I453; I459; I495
Other supraventricular arrhythmias	427,9	426H; 427A	I456; I471
Ventricular arrhythmias/cardiac arrest	427,91;	427B; 427E;	I460; I461; I469; I470;

	795,99	427F; 798B; 798C	I472; I490; R960
CVD-related comorbidities			
Hypertension	400-404	401-405	I10; I119; I12-I15
Obesity	277	278A; 278B	E65-E66
Diabetes	250	250	E10-E14; O24
Dyslipidemia	279	272	E78
Chronic kidney disease	585; 586; Y29,01	585; 586; V42A; V56	753B; N18; N19; N26; T824; Y841; Q61; Z49; Z992; Z940
Chronic obstructive pulmonary disease (COPD, only if patient diagnosed ≥40 year)/smoking dependence	COPD: 491, 492	COPD: 491, 492, 305B	COPD: J41-J44; Smoking: F17, T65.2, Z71.6, Z72.0

ICD: International Classification of Diseases; COPD: Chronic obstructive pulmonary disease.

Supplementary Table 7 Baseline characteristics of inflammatory bowel disease patients in the cohort of histologic inflammation and histologic remission in 1969–2017

Item	Patients with IBD	Subtypes of IBD		
		CD	UC	IBD-U
No. of patients	61383	17594	40421	3368
Age at IBD diagnosis, years				
Mean ± SD	39.8 ± 18.5	36.5 ± 18.1	41.1 ± 18.3	40.7 ± 20.3
Median (IQR)	37.2 (24.8-53.4)	32.9 (21.8-49.3)	38.9 (26.5-54.7)	37.4 (23.4-56.8)
< 18	6763 (11.0)	2695 (15.3)	3600 (8.9)	468 (13.9)
18-40	26,898 (43.8)	8180 (46.5)	17,382 (43.0)	1336 (39.7)
40-60	17,474 (28.5)	4462 (25.4)	12,155	857 (25.5)

			(30.1)	
≥60	10,248 (16.7)	2257 (12.8)	7284 (18.0)	707 (21.0)
Female	29,271 (47.7)	9048 (51.4)	18,558 (45.9)	1665 (49.4)
Born in Nordic country	57,004 (92.9)	16,191 (92.0)	37,664 (93.2)	3149 (93.5)
Calendar period at IBD diagnosis				
1969-1989	8808 (14.4)	3015 (17.1)	5016 (12.4)	777 (23.1)
1990-2001	19,452 (31.7)	5531 (31.4)	13,428 (33.2)	493 (14.6)
2002-2009	19,296 (31.4)	5375 (30.6)	13,245 (32.8)	676 (20.1)
2010-2017	13,827 (22.5)	3673 (20.9)	8732 (21.6)	1422 (42.2)
Educational attainment				
0-9 years	13,332 (21.7)	3929 (22.3)	8637 (21.4)	766 (22.7)
10-12 years	24,571 (40.0)	6912 (39.3)	16,414 (40.6)	1245 (37.0)
≥ 13 years	14,627 (23.8)	3759 (21.4)	10,193 (25.2)	675 (20.0)
Missing	8853 (14.4)	2994 (17.0)	5177 (12.8)	682 (20.3)
Montreal Classification				
CD at IBD diagnosis				
No location information	-	5685 (32.3)	-	-
L1, L3/LX (Ileal, ileocolonic or location not defined)	-	8998 (51.1)	-	-
L2 (Colonic)	-	2911 (16.6)	-	-
Perianal	-	827 (4.7)	-	-
Montreal Classification				
UC at IBD diagnosis				

No extent information ¹	-	-	10,836 (26.8)	-
E1/E2 (Proctitis, left-sided colitis)	-	-	10,829 (26.8)	-
E3 (Extensive colitis)	-	-	5881 (14.6)	-
EX (Extent not defined)	-	-	12,875 (31.9)	-
Extraintestinal manifestations at IBD diagnosis				
Primary sclerosing cholangitis	488 (0.8)	72 (0.4)	402 (1.0)	14 (0.4)
Other extraintestinal manifestations	1889 (3.1)	687 (3.9)	1031 (2.6)	171 (5.1)

¹No extent information refers to patients who were diagnosed with UC before the introduction of ICD-10 in 1997.

CD: Crohn's disease; IBD(-U): Inflammatory bowel disease (unclassified); IQR: Interquartile range; SD: Standard deviation; UC: Ulcerative colitis.

Supplementary Table 8 2-year risk of arrhythmias in histologic inflammation and histologic remission in patients with inflammatory bowel disease

Outcomes	No. of events (IR, per 10000 person-years)		IR difference (95%CI), per 10000 person-years	HR (95%CI)	
	Histologic inflammation	Histologic remission		Model 1 ¹	Model 2 ²
Arrhythmias	647 (62.0)	382 (47.2)	14.8 (8.0 to 21.5)	1.38 (1.21 to 1.57)	1.35 (1.18 to 1.54)
Atrial fibrillation/flutter	476 (45.6)	273 (33.7)	11.9 (6.1 to 17.6)	1.41 (1.21 to 1.65)	1.38 (1.18 to 1.62)
Bradyarrhythmias	49 (4.7)	34 (4.2)	0.5 (-1.4 to 2.4)	1.10 (0.70 to 1.73)	1.10 (0.69 to 1.74)

Other supraventricular arrhythmias	75 (7.2)	49 (6.0)	1.1 (-1.2 to 3.5)	1.32 (0.91 to 1.92)	1.30 (0.90 to 1.90)
Ventricular arrhythmias/cardiac arrest	131 (12.5)	49 (6.0)	6.5 (3.8 to 9.2)	1.73 (1.23 to 2.44)	1.73 (1.22 to 2.44)

¹ Adjusted for age at IBD diagnosis, sex, and calendar year at index date.

²Further adjusted for county of residence, educational attainment, country of birth, number of health care visits, hypertension, diabetes, obesity, dyslipidemia, chronic kidney disease, and COPD.

CI: confidence interval; HR: hazard ratio; IR: incidence rate.

Supplementary Table 9 2-year risk of arrhythmias in histologic inflammation and histologic remission in patients with Crohn's disease, ulcerative colitis, and inflammatory bowel disease unclassified

Outcomes	No. of events (IR, IR per 10,000 person- years)		IR difference (95% CIs), per 10,000 person- years	HR (95% CIs)	
				Model 1 ¹	Model 2 ²
	Histologic inflammation	Histologic remission			
Patients with CD					
Arrhythmias	150 (57.4)	110 (48.7)	8.8 (-4.2 to 21.7)	1.32 (1.02-1.70)	1.28 (0.99-1.66)
Atrial fibrillation/flutter	112 (42.8)	76 (33.6)	9.3 (-1.7 to 20.2)	1.48 (1.09-2.00)	1.41 (1.03-1.91)
Bradyarrhythmias	8 (3.1)	10 (4.4)	-1.4 (-4.8 to 2.1)	0.63 (0.24-1.67)	0.63 (0.23-1.71)
Other supraventricular arrhythmias	20 (7.6)	16 (7.1)	0.6 (-4.2 to 5.4)	1.18 (0.60-2.31)	1.22 (0.62-2.41)

Ventricular arrhythmias/ca rdiac arrest	30 (11.5)	16 (7.1)	4.4 (-1.0 to 9.8)	1.28 (0.68- 2.41)	1.26 (0.66- 2.39)	
Patients with UC						
Arrhythmias	465 (64.2)	250 (46.2)	18.1 (9.9- 26.2)	1.45 (1.24- 1.71)	1.42 (1.21- 1.67)	
Atrial fibrillation/flut ter	342 (47.2)	183 (33.8)	13.4 (6.4- 20.4)	1.45 (1.20- 1.75)	1.42 (1.18- 1.72)	
Bradyarrhythm ias	38 (5.2)	22 (4.0)	1.2 (-1.2 to 3.6)	1.35 (0.78- 2.33)	1.32 (0.76- 2.30)	
Other supraventricula r arrhythmias	52 (7.2)	29 (5.3)	1.8 (-0.9 to 4.6)	1.47 (0.92- 2.34)	1.42 (0.88- 2.27)	
Ventricular arrhythmias/ca rdiac arrest	93 (12.8)	30 (5.5)	7.3 (4.0- 10.6)	1.92 (1.25- 2.96)	1.90 (1.23- 2.93)	
Patients with IBD-U						
Arrhythmias	32 (55.0)	22 (53.5)	1.5 (-27.9 to 30.9)	1.01 (0.57- 1.82)	0.97 (0.54- 1.77)	
Atrial fibrillation/flut ter	22 (37.8)	14 (34.0)	3.8 (-20.0 to 27.6)	0.94 (0.46- 1.93)	0.90 (0.43- 1.88)	
Bradyarrhythm ias	3 (5.1)	≤ 2	NA	NA	NA	
Other supraventricula r arrhythmias	3 (5.1)	4 (9.7)	-4.5 (-15.7 to 6.6)	0.81 (0.18- 3.69)	0.83 (0.16- 4.40)	
Ventricular arrhythmias/ca rdiac arrest	8 (13.7)	3 (7.3)	6.4 (-6.1 to 19.0)	2.34 (0.59- 9.34)	2.82 (0.50- 15.88)	

¹Adjusted for age at Inflammatory bowel disease diagnosis, sex, and calendar year at index date.

²Further adjusted for county of residence, educational attainment, country of birth, number of health care visits, hypertension, diabetes, obesity, dyslipidemia, chronic kidney disease, and COPD.

CI: Confidence interval; HR: Hazard ratio; IR: Incidence rate; NA: Not available.

Supplementary Table 10 Subgroup analyses for 2-year risk of arrhythmias in histologic inflammation and histologic remission in patients with Inflammatory bowel disease

Outcomes	No. of events (IR, IR		per 10000 person-years)	difference (95% CIs),	HR (95% CIs)	
	Histolog ic inflamm ation	Histol ogic remiss ion	per 10000 person-years		Model 1 ¹	Model 2 ²
Sex						
Male	396 (70.3)	232 (55.0)	15.3 (5.4-25.2)	(5.4-1.62)	1.37 (1.16-1.60)	1.35 (1.14-1.60)
Female	251 (52.3)	150 (38.7)	13.5 (4.5-22.5)	(4.5-1.71)	1.38 (1.12-1.68)	1.36 (1.10-1.68)
Age at IBD diagnosis, years						
< 18	12 (9.3)	8 (7.8)	1.5 (-6.1 to 9.0)	(-6.1 to 3.36)	1.35 (0.55-3.36)	1.30 (0.52-3.25)
18-40	77 (15.6)	84 (22.0)	-6.4 (-12.2 to -0.6)	(-12.2 to 1.32)	0.96 (0.70-1.32)	0.93 (0.67-1.27)
40-60	199 (68.1)	152 (59.3)	8.7 (-4.6 to 22.1)	(-4.6 to 1.85)	1.49 (1.20-1.85)	1.50 (1.21-1.87)
≥ 60	359	138	79.3 (34.2-	(34.2-	1.46 (1.19-	1.41 (1.15-

	(284.0)	(204.8)	124.3)	1.78)	1.73)
Age at index date, years					
< 18	5 (8.2)	≤ 2	NA	2.77 (0.32- 23.79)	2.79 (0.32- 23.93)
18-40	25 (6.4)	21 (8.1)	-1.6 (-5.9 to 2.6)	0.78 (0.43- 1.41)	0.72 (0.40- 1.31)
40-60	136 (36.0)	99 (30.0)	6.0 (-2.4 to 14.5)	1.35 (1.04- 1.76)	1.36 (1.04- 1.78)
≥ 60	481 (222.1)	261 (143.6)	78.4 (52.0- 104.9)	1.42 (1.22- 1.66)	1.38 (1.18- 1.62)

Calendar period at
IBD diagnosis

1969-1989	129 (49.7)	93 (56.8)	-7.1 (-21.5 to 7.3)	1.23 (0.93- 1.63)	1.21 (0.91- 1.60)
1990-2001	229 (58.7)	145 (46.4)	12.2 (1.5- 22.9)	1.29 (1.03- 1.61)	1.30 (1.04- 1.63)
2002-2009	188 (72.0)	101 (41.4)	30.6 (17.5- 43.7)	1.53 (1.19- 1.97)	1.45 (1.12- 1.87)
2010-2017	101 (76.6)	43 (48.6)	28.0 (7.1- 48.8)	1.24 (0.86- 1.77)	1.25 (0.87- 1.79)

Calendar period at
index date

1969-1989	20 (30.0)	3 (16.4)	13.6 (-9.1 to 36.3)	1.28 (0.37- 4.39)	1.19 (0.34- 4.21)
1990-2001	157 (51.2)	33 (26.1)	25.1 (13.1- 37.1)	1.67 (1.14- 2.45)	1.75 (1.19- 2.57)
2002-2009	221 (67.6)	124 (46.8)	20.8 (8.6- 32.9)	1.36 (1.09- 1.70)	1.29 (1.03- 1.62)
2010-2021	249 (72.6)	222 (55.7)	17.0 (5.4- 28.6)	1.33 (1.10- 1.60)	1.29 (1.07- 1.55)

IBD duration, years

0	218 (83.8)	14 (41.6)	42.2 (66.6)	(17.7- 2.30)	1.33 (0.77- 2.32)	1.34 (0.77- 2.32)
1-5	156 (50.8)	105 (38.3)	12.5 (23.3)	(1.7- 1.57)	1.22 (0.95- 1.53)	1.18 (0.92- 1.53)
> 5	273 (57.4)	263 (52.5)	4.8 (14.2)	(-4.5 to 1.52)	1.28 (1.08- 1.52)	1.27 (1.07- 1.52)

Educational attainment

0-9 years	248 (111.4)	130 (83.9)	27.5 (47.5)	(7.5- 1.61)	1.29 (1.04- 1.63)	1.30 (1.04- 1.63)
10-12 years	225 (50.8)	147 (41.6)	9.3 (18.7)	(-0.2 to 1.74)	1.41 (1.13- 1.73)	1.39 (1.12- 1.73)
≥ 13 years	115 (42.7)	97 (37.5)	5.2 (15.9)	(-5.6 to 1.60)	1.21 (0.92- 1.52)	1.15 (0.87- 1.52)
Missing	59 (54.4)	8 (19.3)	35.1 (54.4)	(15.8- 4.01)	1.89 (0.89- 3.87)	1.81 (0.85- 3.87)

Number of healthcare visits

0	235 (50.7)	99 (36.6)	14.0 (23.7)	(4.3- 1.75)	1.37 (1.07- 1.73)	1.35 (1.06- 1.73)
1	93 (45.3)	76 (43.4)	1.8 (15.2)	(-11.6 to 1.39)	1.01 (0.74- 1.36)	0.99 (0.72- 1.36)
2-3	133 (70.7)	79 (46.0)	24.7 (40.5)	(9.0- 2.08)	1.55 (1.16- 2.04)	1.52 (1.14- 2.04)
≥ 4	186 (100.0)	128 (66.8)	33.2 (51.6)	(14.7- 1.84)	1.46 (1.17- 1.85)	1.48 (1.18- 1.85)

Hypertension

No	444 (45.6)	259 (35.0)	10.6 (16.6)	(4.5- 1.57)	1.34 (1.14- 1.55)	1.32 (1.12- 1.55)
Yes	203	123	114.2	(63.4- 1.47	1.47 (1.16- 1.43	1.43 (1.13- 1.43

	(291.3)	(177.1)	165.1)		1.85)	1.80)
Dyslipidemia						
No	600 (58.5)	344 (43.7)	14.8 21.4)	(8.2-	1.38 (1.20-	1.35 (1.17-
Yes	47 (278.5)	38 (184.6)	93.9 (-5.0 to 192.8)	1.37 (0.89-	1.36 (0.88-	
Diabetes						
No	551 (55.1)	336 (43.6)	11.5 18.1)	(5.0-	1.33 (1.16-	1.30 (1.13-
Yes	96 (223.4)	46 (123.3)	100.1 (43.0-	1.74 (1.22-	1.83 (1.28-	
Obesity						
No	626 (60.8)	368 (46.3)	14.5 21.2)	(7.8-	1.37 (1.20-	1.34 (1.17-
Yes	21 (155.9)	14 (101.0)	54.9 (-30.2 to 140.0)	1.89 (0.95-	1.92 (0.96-	
Chronic kidney diseases						
No	615 (59.5)	368 (46.0)	13.5 20.1)	(6.8-	1.35 (1.18-	1.33 (1.16-
Yes	32 (351.1)	14 (163.9)	187.2 (38.4-	2.25 (1.19-	2.35 (1.23-	
COPD						
No	597 (58.0)	357 (44.7)	13.3 19.9)	(6.7-	1.36 (1.19-	1.35 (1.17-
Yes	50 (347.9)	25 (250.0)	97.9 (-39.6 to 235.4)	1.22 (0.75-	1.26 (0.77-	

¹Adjusted for age at IBD diagnosis, sex, and calendar year at index date.

²Further adjusted for county of residence, educational attainment, country of birth, number of health care visits, hypertension, diabetes, obesity, dyslipidemia, chronic kidney disease, and COPD.

IBD: Inflammatory bowel disease; CI: Confidence interval; HR: Hazard ratio; IR: Incidence rate; NA: Not available.

Supplementary Table 11 2-year risk of arrhythmias in histologic inflammation and histologic remission in patients with Inflammatory bowel disease, stratified by the phenotypes of the Montreal Classification

Item			No. of events (IR, per 10000 person-years)		IR difference (95%CI), per 10000 person-years		HR (95%CI)	
			Histologic inflammation	Histologic remission			Model 1 ¹	Model 2 ²
IBD								
Primary	sclerosing	≤ 2	6 (63.9)		NA		0.21 (0.02-1.80)	0.17 (0.01-2.64)
Other	extraintestinal	21 (103.0)	12 (65.2)		37.8 (-19.7 to 95.3)		1.45 (0.70-3.00)	1.51 (0.73-3.13)
CD								
No location information			62 (53.5)	54 (64.8)	-11.3 (-33.1 to 10.5)		1.15 (0.78-1.69)	1.12 (0.76-1.65)
L1, L3/LX	(Ileal, ileocolonic or location not defined)	68 (62.4)	42 (40.7)		21.7 (2.4-41.0)		1.41 (0.95-2.09)	1.33 (0.89-1.99)
L2 (Colonic)			20 (54.9)	14 (35.3)	19.6 (-10.8 to 49.9)		1.65 (0.79-3.44)	1.65 (0.78-3.44)
Perianal			4 (37.3)	≤ 2	NA		NA	NA
Primary	sclerosing	≤ 2		≤ 2	NA		NA	NA
Other	extraintestinal	4 (56.3)	4 (53.3)		2.9 (-73.1 to 78.9)		NA	NA
UC								
No extent information ³			180 (57.0)	100 (49.3)	7.7 (-5.1 to 20.5)		1.43 (1.10-1.84)	1.41 (1.09-1.83)

E1/E2 (Proctitis, left-sided colitis)	85 (66.8)	43 (40.8)	26.0 (7.3-44.7)	1.51 (1.03-2.21)	1.46 (0.99-2.15)
E3 (Extensive colitis)	59 (64.9)	35 (43.5)	21.4 (-0.6 to 43.3)	1.54 (1.00-2.36)	1.47 (0.94-2.29)
EX (Extent not defined)	141 (74.2)	72 (47.1)	27.1 (10.7-43.5)	1.38 (1.03-1.85)	1.36 (1.01-1.83)
Primary sclerosing cholangitis	≤ 2	4 (48.5)	NA	NA	NA
Other extraintestinal manifestations	14 (121.0)	8 (83.3)	37.8 (-48.0 to 123.5)	1.47 (0.59-3.70)	NA

¹Adjusted for age at Inflammatory bowel disease diagnosis, sex, and calendar year at index date.

²Further adjusted for county of residence, educational attainment, country of birth, number of health care visits, hypertension, diabetes, obesity, dyslipidemia, chronic kidney disease, and COPD.

³No extent information refers to patients who were diagnosed with UC before the introduction of ICD-10 in 1997.

CD: Crohn's disease; CI: Confidence interval; E: Extent; HR: Hazard ratio; IR: Incident rate; L: Location; NA: Not available; UC: Ulcerative colitis; IBD: Inflammatory bowel disease.

Supplementary Table 12 5-year risk of arrhythmias in histologic inflammation and histologic remission in patients with Inflammatory bowel disease

Outcomes	No. of events (IR, per 10000 person-years)		IR difference (95% CIs), per 10000 person-years	HR (95% CIs)	
	Histologic inflammation	Histologic remission		Model 1 ¹	Model 2 ²
Arrhythmias	653 (61.9)	804 (49.9)	12.0 (6.1-17.9)	1.44 (1.29-1.60)	1.38 (1.24-1.54)

Atrial fibrillation/flutter	478 (45.3)	585 (36.2)	9.1 (4.0-14.1)	1.47 (1.30-1.67)	1.42 (1.24-1.61)
Bradyarrhythmias	49 (4.6)	86 (5.3)	-0.7 (-2.4 to 1.0)	0.89 (0.62-1.29)	0.88 (0.61-1.28)
Other supraventricular arrhythmias	77 (7.3)	97 (6.0)	1.3 (-0.7 to 3.3)	1.43 (1.05-1.96)	1.40 (1.02-1.92)
Ventricular arrhythmias/cardioid arrest	133 (12.6)	118 (7.3)	5.3 (2.8-7.8)	1.60 (1.23-2.09)	1.55 (1.19-2.02)

¹Adjusted for age at Inflammatory bowel disease diagnosis, sex, and calendar year at index date.

²Further adjusted for county of residence, educational attainment, country of birth, number of health care visits, hypertension, diabetes, obesity, dyslipidemia, chronic kidney disease, and COPD.

CI: Confidence interval; HR: Hazard ratio; IR: Incidence rate.

Supplementary Table 13 2-year risk of arrhythmias in histologic inflammation and histologic remission in patients with inflammatory bowel disease

Outcomes	No. of events (IR, per 10,000 person-years)		IR difference (95% CIs), per 10,000 person-years	HR (95% CIs)	
	Histologic inflammation	Histologic remission		Model 1 ¹	Model 2 ²
Arrhythmias	366 (66.6)	382 (47.2)	19.3 (11.0-27.6)	1.51 (1.30-1.76)	1.46 (1.25-1.70)
Atrial fibrillation/flutter	269 (48.9)	273 (33.7)	15.2 (8.1-22.2)	1.56 (1.31-1.86)	1.51 (1.27-1.80)
Bradyarrhythmias	24 (4.4)	34 (4.2)	0.2 (-2.1 to 2.4)	1.04 (0.60-1.79)	1.04 (0.60-1.80)
Other supraventricular arrhythmias	38 (6.9)	49 (6.0)	0.9 (-1.9 to 3.6)	1.33 (0.86-2.06)	1.31 (0.84-2.03)

Ventricular arrhythmias/cardiac arrest	80 (14.5)	49 (6.0)	8.5 (4.9-12.1)	1.99 (1.37-2.90)	1.92 (1.31-2.80)
--	-----------	----------	----------------	------------------	------------------

¹Adjusted for age at Inflammatory bowel disease diagnosis, sex, and calendar year at index date.

² Further adjusted for county of residence, educational attainment, country of birth, number of health care visits, hypertension, diabetes, obesity, dyslipidemia, chronic kidney disease, and COPD.

A histologic inflammation period was considered present six months following the biopsy date. CI: Confidence interval; HR: Hazard ratio; IR: Incidence rate.

Supplementary Table 14 2-year risk of arrhythmias in histologic inflammation and histologic remission during periods of clinically quiescent inflammatory bowel disease

Outcomes	No. of events (IR, per 10000 person-years)		IR (95% CIs), per 10000 person-years	HR (95% CIs)			
	Histologic inflammation	Histologic remission		Model 1 ¹		Model 2 ²	
Arrhythmias	299 (42.9)	226 (38.8)	4.1 (-2.9 to 11.1)	1.16 (1.00-1.35)		1.16 (1.00-1.36)	
Atrial fibrillation/flutter	231 (32.9)	165 (28.1)	4.8 (-1.2 to 10.9)	1.21 (1.02-1.44)		1.22 (1.02-1.45)	
Bradyarrhythmias	31 (4.4)	17 (2.9)	1.5 (-0.6 to 3.6)	1.03 (0.64-1.64)		0.99 (0.62-1.60)	
Other supraventricular arrhythmias	29 (4.2)	33 (5.7)	-1.5 (-4.0 to 1.0)	0.99 (0.63-1.56)		0.99 (0.63-1.57)	
Ventricular	62 (8.9)	29 (5.0)	3.9 (1.1-6.8)	1.41 (0.97-2.04)		1.44 (0.99-2.08)	

arrhythmias/car

2.05)

2.10)

diac arrest

¹Adjusted for age at Inflammatory bowel disease diagnosis, sex, and calendar year at index date.

²Further adjusted for county of residence, educational attainment, country of birth, number of health care visits, hypertension, diabetes, obesity, dyslipidemia, chronic kidney disease, and COPD.

CI: Confidence interval; HR: Hazard ratio; IR: Incidence rate.

Supplementary Table 15 Sensitivity analyses of the 2-year arrhythmias risk in histologic inflammation and histologic remission in patients with inflammatory bowel disease, after excluding the first 3 months or 1 year after inflammatory bowel disease diagnosis

Outcomes	After excluding the first 3 months after IBD diagnosis			After excluding the first 1 year after IBD diagnosis		
	No. of events (IR, per 10000 person-years)		HR (95%CI)	No. of events (IR, per 10000 person-years)		HR (95%CI)
	Histologic inflammation	Histologic remission		Histologic inflammation	Histologic remission	
Arrhythmias	540 (56.0)	377 (46.8)	1.26 (1.10-1.44)	394 (53.9)	364 (45.8)	1.26 (1.08-1.45)
Atrial fibrillation/flutter	392 (40.6)	268 (33.2)	1.28 (1.08-1.50)	285 (39.0)	259 (32.6)	1.29 (1.08-1.54)
Bradyarrhythmias	47 (4.9)	34 (4.2)	1.14 (0.72-1.82)	30 (4.1)	31 (3.9)	1.08 (0.64-1.82)
Other supraventricular	63 (6.5)	49 (6.1)	1.21 (0.82-1.78)	49 (6.7)	48 (6.0)	1.20 (0.80-1.80)

cular
arrhythmia
s
Ventricular
arrhythmia
s/cardiac
arrest

106 (11.0) 47 (5.8) 1.68 (1.17-
2.40) 79 (10.8) 45 (5.6) 1.72 (1.18-
2.51)

Adjusted for age at Inflammatory bowel disease diagnosis, sex, calendar year at index date, county of residence, educational attainment, country of birth, number of health care visits, hypertension, diabetes, obesity, dyslipidemia, chronic kidney disease, and COPD. IBD: Inflammatory bowel disease; CI: Confidence interval; HR: Hazard ratio; IR: Incidence rate.

Supplementary Table 16 Baseline characteristics of inflammatory bowel disease patients in the cohort of clinically active and quiescent inflammatory bowel disease in 2006–2020

Item	Patients with IBD	Subtypes of IBD			
		CD	UC	IBD-U	
No. of patients	96,154	31,967	56,704	7483	
Age at IBD diagnosis, years					
Mean ± SD	40.3 ± 18.8	37.9 ± 18.6	41.4 ± 18.5	42.4 ± 21.3	
Median (IQR)	37.3 (25.1-54.5)	34.2 (22.7-51.8)	38.7 (26.6-55.2)	39.2 (24.1-60.2)	
< 18	9921 (10.3)	4290 (13.4)	4662 (8.2)	969 (13.0)	
18-40	42,420 (44.1)	14,659 (45.9)	24,914 (43.9)	2847 (38.1)	
40-60	26,379 (27.4)	8129 (25.4)	16,473 (29.1)	1777 (23.8)	

≥ 60	17,434 (18.1)	4889 (15.3)	10,655 (18.8)	1890 (25.3)
Female	48,040 (50.0)	16,659 (52.1)	27,452 (48.4)	3929 (52.5)
Born in Nordic country	86,826 (90.3)	28,489 (89.1)	51,578 (91.0)	6759 (90.3)
Calendar period at IBD diagnosis				
1969-1989	9245 (9.6)	3933 (12.3)	4511 (8.0)	801 (10.7)
1990-2001	17,316 (18.0)	5821 (18.2)	11,026 (19.4)	469 (6.3)
2002-2009	26,102 (27.2)	8283 (25.9)	16,686 (29.4)	1133 (15.1)
2010-2020	43,491 (45.2)	13,930 (43.6)	24,481 (43.2)	5080 (67.9)
Educational attainment				
0-9 years	19,801 (20.6)	6965 (21.8)	11,236 (19.8)	1600 (21.4)
10-12 years	40,793 (42.4)	13,524 (42.3)	24,315 (42.9)	2954 (39.5)
≥13 years	26,495 (27.6)	8037 (25.1)	16,699 (29.5)	1759 (23.5)
Missing	9065 (9.4)	3441 (10.8)	4454 (7.9)	1170 (15.6)
Montreal Classification CD at IBD diagnosis				
No location information	-	6488 (20.3)	-	-
L1, L3/LX (Ileal, ileocolonic or location not defined)	-	20,819 (65.1)	-	-
L2 (Colonic)	-	4660	-	-

			(14.6)		
Perianal	-		1707 (5.3)	-	-
Montreal Classification UC at IBD diagnosis					
No extent information	-	-	8781 (15.5)	-	-
E1/E2 (Proctitis, left-sided colitis)	-	-	20,030 (35.3)	-	-
E3 (Extensive colitis)	-	-	8913 (15.7)	-	-
EX (Extent not defined)	-	-	18,980 (33.5)	-	-
Extraintestinal manifestations at IBD diagnosis					
Primary sclerosing cholangitis	767 (0.8)	141 (0.4)	570 (1.0)	56 (0.8)	
Other extraintestinal manifestations	5218 (5.4)	2105 (6.6)	2509 (4.4)	604 (8.1)	

CD: Crohn's disease; IBD(-U): Inflammatory bowel disease (unclassified); IQR: Interquartile range; SD: Standard deviation; UC: Ulcerative colitis.

Supplementary Table 17 2-year risk of arrhythmias in clinically active and quiescent inflammatory bowel disease in patients with inflammatory bowel disease

Outcomes	No. of events (IR, IR per 10000 person-years)		IR difference (95%CI), per 10000 person-years	HR (95%CI)			
	Active IBD	Quiescent IBD		Model 1 ¹		Model 2 ²	
Arrhythmias	2248 (108.4)	1724 (67.4)	41.1 (35.6-46.6)	1.79 (1.68-1.90)	1.77 (1.66-1.88)		

Atrial fibrillation/flutter	1717 (82.7)	1242 (48.5)	34.2 (29.5-39.0)	1.91 (1.77-2.05)	1.91 (1.77-2.05)
Bradyarrhythmias	195 (9.3)	224 (8.7)	0.6 (-1.1 to 2.4)	1.17 (0.96-1.42)	1.17 (0.97-1.42)
Other supraventricular arrhythmias	181 (8.7)	149 (5.8)	2.9 (1.3-4.4)	1.58 (1.27-1.96)	1.56 (1.26-1.94)
Ventricular arrhythmias/cardi- ac arrest	294 (14.1)	189 (7.4)	6.7 (4.8-8.6)	2.07 (1.73-2.49)	1.94 (1.61-2.33)

¹Adjusted for age at Inflammatory bowel disease diagnosis, sex, and calendar year at index date.

²Further adjusted for county of residence, educational attainment, country of birth, number of health care visits, hypertension, diabetes, obesity, dyslipidemia, chronic kidney disease, and COPD.

IBD: Inflammatory bowel disease; CI: Confidence interval; HR: Hazard ratio; IR: Incidence rate.

Supplementary Table 18 2-year risk of arrhythmias in clinically active and quiescent Inflammatory bowel disease in patients with Crohn’s disease, ulcerative colitis, and inflammatory bowel disease unclassified

Outcomes	No. of events (IR, IR per 10000 person- years)		IR difference (95%CI), per 10000 person- years		HR (95%CI)			
	Active IBD	Quiesce nt IBD			Model 1 ¹		Model 2 ²	
Patients with CD								
Arrhythmias	783 (94.7)	509 (63.2)	31.5 (22.9-40.1)		1.71 (1.53-1.92)		1.70 (1.52-1.91)	

Atrial fibrillation/flutter	583 (70.4)	373 (46.3)	24.1 (16.7-31.5)	1.76 (1.54-2.00)	1.76 (1.55-2.01)
Bradyarrhythmias	79 (9.5)	68 (8.4)	1.1 (-1.8 to 4.0)	1.28 (0.92-1.77)	1.30 (0.94-1.80)
Other supraventricular arrhythmias	85 (10.2)	49 (6.1)	4.1 (1.4-6.9)	1.78 (1.25-2.53)	1.77 (1.25-2.52)
Ventricular arrhythmias/cardi- ac arrest	90 (10.8)	51 (6.3)	4.5 (1.7-7.3)	1.91 (1.35-2.69)	1.82 (1.28-2.57)
Patients with UC					
Arrhythmias	1290 (115.7)	1093 (68.8)	46.9 (39.4-54.4)	1.80 (1.66-1.95)	1.78 (1.64-1.93)
Atrial fibrillation/flutter	993 (89.0)	783 (49.3)	39.7 (33.2-46.2)	1.94 (1.77-2.13)	1.94 (1.77-2.13)
Bradyarrhythmias	101 (9.0)	139 (8.7)	0.3 (-2.0 to 2.5)	1.08 (0.84-1.40)	1.08 (0.84-1.40)
Other supraventricular arrhythmias	84 (7.5)	92 (5.8)	1.7 (-0.3 to 3.7)	1.36 (1.01-1.83)	1.35 (1.00-1.81)
Ventricular arrhythmias/cardi- ac arrest	182 (16.2)	126 (7.9)	8.3 (5.6-11.0)	2.16 (1.72-2.71)	1.99 (1.58-2.51)
Patients with IBD-U					
Arrhythmias	175 (132.5)	122 (73.4)	59.1 (35.6-82.7)	2.04 (1.62-2.58)	2.04 (1.62-2.58)
Atrial fibrillation/flutter	141 (106.6)	86 (51.7)	54.9 (34.2-75.6)	2.37 (1.81-3.10)	2.41 (1.84-3.15)

Bradyarrhythmias	15 (11.3)	17 (10.2)	1.1 (-6.4 to 8.6)	1.16 (0.58-2.33)	1.08 (0.53-2.19)
Other supraventricular arrhythmias	12 (9.0)	8 (4.8)	4.2 (-1.9 to 10.3)	2.05 (0.83-5.02)	2.11 (0.85-5.20)
Ventricular arrhythmias/cardioidiac arrest	22 (16.5)	12 (7.2)	9.3 (1.3-17.3)	2.58 (1.28-5.22)	2.47 (1.21-5.04)

¹Adjusted for age at Inflammatory bowel disease diagnosis, sex, and calendar year at index date.

²Further adjusted for county of residence, educational attainment, country of birth, number of health care visits, hypertension, diabetes, obesity, dyslipidemia, chronic kidney disease, and COPD.

IBD: Inflammatory bowel disease; CI: Confidence interval; HR: Hazard ratio; IR: Incidence rate; NA: Not available.

Supplementary Table 19 Subgroup analyses for 2-year risk of arrhythmias in clinically active and quiescent inflammatory bowel disease in patients with inflammatory bowel disease

Outcomes	No. of events (IR, per 10000 person-years)		IR difference (95%CI), per 10000 person-years	HR (95%CI)	
	Active IBD	Quiescent IBD		Model 1 ¹	Model 2 ²
Sex					
Male	1273 (124.0)	924 (76.5)	47.5 (39.1-55.9)	1.87 (1.72-2.04)	1.86 (1.70-2.02)
Female	975 (93.1)	800 (59.2)	33.9 (26.8-41.1)	1.68 (1.53-1.85)	1.66 (1.51-1.82)
Age at IBD diagnosis,					

years

< 18	36 (12.5)	19 (7.5)	5.1 (-0.2 to 10.4)	1.94 (1.11- 3.40)	1.89 (1.08- 3.32)
18-40	366 (37.4)	331 (27.9)	9.5 (4.6-14.4)	1.46 (1.26- 1.69)	1.39 (1.19- 1.61)
40-60	713 (131.9)	603 (81.5)	50.5 (38.8- 62.1)	1.62 (1.45- 1.80)	1.61 (1.45- 1.80)
≥ 60	1133 (422.3)	771 (202.9)	219.4 (190.9- 247.8)	2.06 (1.88- 2.25)	2.05 (1.87- 2.25)

Age at index date,

years

< 18	8 (7.4)	≤ 2	NA	5.23 (0.65- 41.94)	5.53 (0.69- 44.56)
18-40	64 (9.0)	62 (7.6)	1.5 (-1.4 to 4.4)	1.20 (0.84- 1.70)	1.16 (0.82- 1.65)
40-60	314 (47.2)	298 (34.5)	12.7 (6.1- 19.2)	1.39 (1.19- 1.63)	1.36 (1.16- 1.59)
≥ 60	1862 (314.9)	1363 (168.9)	146.0 (129.1- 162.9)	1.90 (1.77- 2.03)	1.88 (1.76- 2.02)

Calendar period at
IBD diagnosis

1969-1989	413 (180.6)	342 (113.3)	67.3 (46.1- 88.5)	1.73 (1.50- 1.99)	1.64 (1.42- 1.89)
1990-2001	565 (116.8)	455 (79.6)	37.2 (25.1- 49.3)	1.60 (1.41- 1.81)	1.62 (1.43- 1.84)
2002-2009	695 (98.6)	491 (56.2)	42.4 (33.5- 51.3)	1.91 (1.70- 2.14)	1.92 (1.71- 2.16)
2010-2017	575 (87.6)	436 (53.6)	34.0 (25.2- 42.7)	1.89 (1.67- 2.14)	1.85 (1.63- 2.09)

Calendar period at
index date

2002-2009	439 (98.2)	338 (59.0)	39.2 50.3)	(28.0- 50.3)	1.82 2.09)	(1.58- 2.04)	1.77 2.04)	(1.54- 2.04)
2010-2021	1809 (111.2)	1386 (69.7)	41.5 47.8)	(35.2- 47.8)	1.78 1.91)	(1.66- 1.89)	1.76 1.89)	(1.64- 1.89)
IBD duration, years								
0	308 (109.5)	123 (37.2)	72.3 86.2)	(58.4- 86.2)	3.32 4.10)	(2.69- 3.65)	2.94 3.65)	(2.37- 3.65)
1-5	428 (78.2)	421 (56.2)	22.0 31.2)	(12.9- 31.2)	1.61 1.85)	(1.41- 1.88)	1.64 1.88)	(1.43- 1.88)
> 5	1512 (121.4)	1180 (79.7)	41.7 49.3)	(34.1- 49.3)	1.68 1.82)	(1.56- 1.81)	1.68 1.81)	(1.56- 1.81)
Educational attainment								
0-9 years	759 (184.8)	602 (120.1)	64.6 80.9)	(48.4- 80.9)	1.72 1.92)	(1.55- 1.93)	1.74 1.93)	(1.56- 1.93)
10-12 years	920 (97.5)	705 (59.4)	38.1 45.7)	(30.4- 45.7)	1.80 1.99)	(1.63- 1.99)	1.81 1.99)	(1.64- 1.99)
≥ 13 years	419 (67.6)	372 (46.5)	21.1 29.1)	(13.1- 29.1)	1.58 1.81)	(1.37- 1.81)	1.58 1.81)	(1.37- 1.81)
Missing	150 (152.0)	45 (63.1)	88.9 119.4)	(58.4- 119.4)	2.97 4.15)	(2.12- 3.98)	2.84 3.98)	(2.03- 3.98)
Number of healthcare visits								
0	411 (88.6)	350 (54.1)	34.6 44.8)	(24.3- 44.8)	1.93 2.23)	(1.67- 2.19)	1.89 2.19)	(1.64- 2.19)
1	351 (89.2)	282 (57.2)	32.0 43.5)	(20.5- 43.5)	1.76 2.06)	(1.50- 2.11)	1.80 2.11)	(1.54- 2.11)
2-3	523 (104.3)	411 (67.4)	36.9 47.9)	(25.8- 47.9)	1.72 1.96)	(1.51- 1.96)	1.72 1.96)	(1.51- 1.96)
≥ 4	963 (134.7)	681 (84.1)	50.6 61.2)	(40.0- 61.2)	1.74 1.92)	(1.58- 1.91)	1.73 1.91)	(1.57- 1.91)

Hypertension								
No	1177 (66.0)	914 (42.4)	23.6 (28.3)	(19.0-	1.69 (1.85)	(1.55-	1.66 (1.81)	(1.52-
Yes	1071 (367.9)	810 (200.6)	167.3 (193.3)	(141.3-	1.92 (2.10)	(1.75-	1.88 (2.06)	(1.72-
Dyslipidemia								
No	1982 (99.0)	1492 (60.9)	38.1 (43.4)	(32.7-	1.79 (1.92)	(1.68-	1.77 (1.90)	(1.66-
Yes	266 (371.2)	232 (208.9)	162.4 (214.4)	(110.3-	1.80 (2.15)	(1.51-	1.72 (2.06)	(1.44-
Diabetes								
No	1867 (95.8)	1405 (58.9)	37.0 (42.3)	(31.6-	1.80 (1.93)	(1.68-	1.78 (1.91)	(1.66-
Yes	381 (303.3)	319 (184.2)	119.2 (155.7)	(82.6-	1.74 (2.01)	(1.49-	1.69 (1.96)	(1.45-
Obesity								
No	2129 (106.1)	1618 (65.5)	40.6 (46.1)	(35.1-	1.80 (1.92)	(1.68-	1.77 (1.89)	(1.66-
Yes	119 (177.7)	106 (117.4)	60.3 (99.2)	(21.3-	1.70 (2.21)	(1.31-	1.64 (2.13)	(1.26-
Chronic kidney diseases								
No	2069 (102.2)	1601 (63.8)	38.4 (43.8)	(33.0-	1.78 (1.90)	(1.66-	1.76 (1.88)	(1.65-
Yes	179 (361.2)	123 (248.5)	112.7 (181.4)	(43.9-	1.75 (2.20)	(1.39-	1.72 (2.17)	(1.36-
COPD								
No	1973 (98.6)	1518 (61.4)	37.2 (42.5)	(31.8-	1.79 (1.92)	(1.68-	1.78 (1.91)	(1.67-
Yes	275 (378.3)	206 (231.4)	147.0 (201.7)	(92.2-	1.68 (2.01)	(1.40-	1.66 (1.99)	(1.39-

¹Adjusted for age at Inflammatory bowel disease diagnosis, sex, and calendar year at index date.

²Further adjusted for county of residence, educational attainment, country of birth, number of health care visits, hypertension, diabetes, obesity, dyslipidemia, chronic kidney disease, and COPD.

CI: Confidence interval; HR: Hazard ratio; IR: Incidence rate; NA: Not applicable.

Supplementary Table 20 2-year risk of arrhythmias in clinically active and quiescent inflammatory bowel disease in patients with Inflammatory bowel disease, stratified by the phenotypes of the Montreal Classification

Item	No. of events (IR, per 10000 person-years)		IR difference (95%CI), per 10000 person-years	HR (95%CI)					
	Active IBD	Quiescent IBD		Model 1 ¹	Model 2 ²				
IBD									
Primary sclerosing cholangitis	14 (72.7)	11 (60.1)	12.6 (-39.5 to 64.7)	1.12 (0.50-2.49)	1.13 (0.51-2.52)				
Other extraintestinal manifestations	117 (110.5)	78 (71.6)	38.9 (13.3-64.4)	1.68 (1.26-2.23)	1.67 (1.25-2.23)				
CD									
No location information	302 (152.8)	188 (89.8)	63.0 (41.6-84.5)	1.90 (1.58-2.28)	1.87 (1.55-2.24)				
L1, L3/LX (Ileal, ileocolonic or location not defined)	399 (78.6)	264 (55.1)	23.5 (13.4-33.7)	1.59 (1.36-1.86)	1.59 (1.36-1.86)				
L2 (Colonic)	82 (67.3)	57 (48.9)	18.4 (-1.0 to 37.7)	1.73 (1.23-2.44)	1.73 (1.22-2.44)				
Perianal	26 (56.2)	20 (55.3)	0.9 (-31.5 to 33.3)	1.34 (0.74-2.44)	1.44 (0.79-2.61)				

				33.4)		2.43)		2.63)
Primary sclerosing cholangitis	≤ 2	≤ 2	NA	NA	NA	NA	NA	NA
Other extraintestinal manifestations	40 (81.4)	19 (46.8)	34.6 (1.7- 67.4)	1.95 (1.12- 3.38)	1.94 (1.12- 3.36)			
UC								
No extent information ³	334 (171.2)	326 (112.3)	58.9 (36.8- 80.9)	1.60 (1.37- 1.87)	1.52 (1.30- 1.78)			
E1/E2 (Proctitis, left-sided colitis)	304 (103.0)	291 (54.3)	48.7 (35.5- 61.9)	1.83 (1.56- 2.15)	1.83 (1.55- 2.15)			
E3 (Extensive colitis)	194 (94.7)	135 (57.3)	37.5 (21.0- 53.9)	1.90 (1.52- 2.37)	1.89 (1.52- 2.36)			
EX (Extent not defined)	458 (109.2)	341 (64.8)	44.4 (32.2- 56.5)	1.90 (1.65- 2.19)	1.89 (1.65- 2.18)			
Primary sclerosing cholangitis	13 (87.5)	10 (69.8)	17.7 (-46.6 to 82.0)	1.17 (0.50- 2.69)	1.17 (0.51- 2.71)			
Other extraintestinal manifestations	59 (127.2)	46 (79.7)	47.4 (7.6-87.2)	1.58 (1.07- 2.33)	1.57 (1.06- 2.32)			

¹Adjusted for age at Inflammatory bowel disease diagnosis, sex, and calendar year at index date.

²Further adjusted for county of residence, educational attainment, country of birth, number of health care visits, hypertension, diabetes, obesity, dyslipidemia, chronic kidney disease, and COPD.

³No extent information refers to patients who were diagnosed with UC before the introduction of ICD-10 in 1997.

IBD: Inflammatory bowel disease; CD: Crohn's disease; CI: Confidence interval; E: Extent; HR: Hazard ratio; IR: Incident rate; L: Location; NA: Not available; UC: Ulcerative colitis.

Supplementary Table 21 5-year risk of arrhythmias in clinically active and quiescent inflammatory bowel disease in patients with inflammatory bowel disease

Outcomes	No. of events (IR, IR		HR (95% CIs)					
	per 10000	person- difference						
	years)	years)	(95% CIs),					
	Active	Quiesce	per 10000	Model 1 ¹	Model 2 ²			
	IBD	nt IBD	person- years					
Arrhythmias	2626 (100.3)	2709 (66.2)	34.0 (29.4-38.6)	1.77 (1.68-1.87)	1.73 (1.64-1.83)			
Atrial fibrillation/flutter	1993 (75.9)	2007 (49.0)	27.0 (23.0-30.9)	1.84 (1.73-1.96)	1.82 (1.71-1.94)			
Bradyarrhythmias	240 (9.1)	340 (8.3)	0.8 (-0.6 to 2.3)	1.27 (1.07-1.49)	1.24 (1.05-1.47)			
Other supraventricular arrhythmias	223 (8.4)	225 (5.5)	3.0 (1.6-4.3)	1.68 (1.39-2.02)	1.64 (1.36-1.98)			
Ventricular arrhythmias/cardioid arrest	355 (13.4)	291 (7.1)	6.3 (4.7-8.0)	2.15 (1.84-2.52)	1.94 (1.66-2.27)			

¹Adjusted for age at Inflammatory bowel disease diagnosis, sex, and calendar year at index date.

²Further adjusted for county of residence, educational attainment, country of birth, number of health care visits, hypertension, diabetes, obesity, dyslipidemia, chronic kidney disease, and COPD.

IBD: Inflammatory bowel disease; CI: Confidence interval; HR: Hazard ratio; IR: Incidence rate.

Supplementary Table 22 2-year risk of arrhythmias in clinically active and

quiescent Inflammatory bowel disease in patients with inflammatory bowel disease

Outcomes	No. of events (IR, IR		HR (95%CI)					
	per 10000 person-years)		difference (95%CI),					
	Active IBD	Quiescent IBD	per 10000 person-years		Model 1 ¹		Model 2 ²	
Arrhythmias	2120 (108.8)	1420 (64.4)	44.4 (38.7-50.1)		1.83 (1.71-1.96)		1.81 (1.69-1.94)	
Atrial fibrillation/flutter	1592 (81.6)	1027 (46.6)	35.0 (30.1-39.9)		1.91 (1.76-2.06)		1.90 (1.76-2.06)	
Bradyarrhythmias	201 (10.2)	190 (8.6)	1.6 (-0.2 to 3.5)		1.26 (1.04-1.54)		1.26 (1.04-1.54)	
Other supraventricular arrhythmias	173 (8.8)	122 (5.5)	3.3 (1.6-4.9)		1.66 (1.32-2.10)		1.66 (1.32-2.10)	
Ventricular arrhythmias/cardioidiac arrest	304 (15.5)	150 (6.8)	8.7 (6.6-10.7)		2.42 (1.99-2.94)		2.26 (1.86-2.75)	

¹Adjusted for age at Inflammatory bowel disease diagnosis, sex, and calendar year at index date.

²Further adjusted for county of residence, educational attainment, country of birth, number of health care visits, hypertension, diabetes, obesity, dyslipidemia, chronic kidney disease, and COPD.

A clinical active period was considered present six months and would extend for an additional six months if another proxy occurred within six months of the previous one. IBD: Inflammatory bowel disease; CI: Confidence interval; HR: Hazard ratio; IR: Incidence rate.

Reference

- 1 Ludvigsson JF, Andersson E, Ekbom A, Feychting M, Kim JL, Reuterwall C, Heurgren M, Olausson PO. External review and validation of the Swedish national inpatient register. *BMC Public Health* 2011; **11**: 450 [PMID: 21658213 PMCID: PMC3142234 DOI: 10.1186/1471-2458-11-450]
- 2 Wettermark B, Hammar N, Forel CM, Leimanis A, Otterblad Olausson P, Bergman U, Persson I, Sundstrom A, Westerholm B, Rosen M. The new Swedish Prescribed Drug Register--opportunities for pharmacoepidemiological research and experience from the first six months. *Pharmacoepidemiol Drug Saf* 2007; **16**(7): 726-735 [PMID: 16897791 DOI: 10.1002/pds.1294]
- 3 Ludvigsson JF, Almqvist C, Bonamy AK, Ljung R, Michaelsson K, Neovius M, Stephansson O, Ye W. Registers of the Swedish total population and their use in medical research. *Eur J Epidemiol* 2016; **31**(2): 125-136 [PMID: 26769609 DOI: 10.1007/s10654-016-0117-y]
- 4 Brooke HL, Talback M, Hornblad J, Johansson LA, Ludvigsson JF, Druid H, Feychting M, Ljung R. The Swedish cause of death register. *Eur J Epidemiol* 2017; **32**(9): 765-773 [PMID: 28983736 PMCID: PMC5662659 DOI: 10.1007/s10654-017-0316-1]
- 5 Ludvigsson JF, Svedberg P, Olen O, Bruze G, Neovius M. The longitudinal integrated database for health insurance and labour market studies (LISA) and its use in medical research. *Eur J Epidemiol* 2019; **34**(4): 423-437 [PMID: 30929112 PMCID: PMC6451717 DOI: 10.1007/s10654-019-00511-8]
- 6 Ludvigsson JF, Lashkariani M. Cohort profile: ESPRESSO (Epidemiology Strengthened by histoPathology Reports in Sweden). *Clin Epidemiol* 2019; **11**: 101-114 [PMID: 30679926 PMCID: PMC6336132 DOI: 10.2147/CLEP.S191914]
- 7 Ludvigsson JF, Andersson M, Bengtsson J, Eberhardson M, Fagerberg UL, Grip O, Halfvarson J, Hjortswang H, Jaghult S, Karling P, Nordenvall C, Olen O, Olsson M, Rejler M, Strid H, Myrelid P. Swedish Inflammatory Bowel Disease Register (SWIBREG) - a nationwide quality register. *Scand J Gastroenterol* 2019; **54**(9): 1089-1101 [PMID: 31498717 DOI: 10.1080/00365521.2019.1660799]
- 8 Ludvigsson JF, Svedberg P, Olén O, Bruze G, Neovius M. The longitudinal integrated database for health insurance and labour market studies (LISA) and its use

in medical research. *European Journal of Epidemiology* 2019; **34**(4): 423-437 [DOI: 10.1007/s10654-019-00511-8]