

CLINICAL—ALIMENTARY TRACT

Incidence and Treatment of Patients Diagnosed With Inflammatory Bowel Diseases at 60 Years or Older in Sweden



Åsa H. Everhov,^{1,2} Jonas Halfvarson,³ Pär Myrelid,⁴ Michael C. Sachs,⁵ Caroline Nordenvall,^{6,7} Jonas Söderling,² Anders Ekbohm,² Martin Neovius,² Jonas F. Ludvigsson,^{8,9,10,11} Johan Askling,² and Ola Olén^{1,2,12}

¹Department of Clinical Science and Education, Södersjukhuset, Karolinska Institutet, Stockholm, Sweden; ²Clinical Epidemiology Unit, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden; ³Department of Gastroenterology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden; ⁴Division of Surgery, Department of Clinical and Experimental Medicine, Faculty of Health Sciences, Linköping University and Department of Surgery, County Council of Östergötland Linköping, Sweden; ⁵Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden; ⁶Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden; ⁷Center for Digestive Disease, Division of Coloproctology, Karolinska University Hospital, Stockholm, Sweden; ⁸Department Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden; ⁹Department of Pediatrics, Örebro University Hospital, Örebro University, Örebro, Sweden; ¹⁰Division of Epidemiology and Public Health, School of Medicine, University of Nottingham, Nottingham, UK; ¹¹Department of Medicine, Columbia University College of Physicians and Surgeons, New York, New York; and ¹²Department of Pediatric Gastroenterology and Nutrition, Sachs' Children and Youth Hospital, Stockholm, Sweden

BACKGROUND & AIMS: Diagnosis of inflammatory bowel diseases (IBD) is increasing among elderly persons (60 years or older). We performed a nationwide population-based study to estimate incidence and treatment of IBD. **METHODS:** We identified all incident IBD cases in Sweden from 2006 through 2013 using national registers and up to 10 matched population comparator subjects. We collected data on the patients' health care contacts and estimated incidence rates, health service burden, pharmacologic treatments, extra-intestinal manifestations, and surgeries in relation to age of IBD onset (pediatric, <18 years; adults, 18–59 years; elderly, ≥60 years). **RESULTS:** Of 27,834 persons diagnosed with incident IBD, 6443 (23%) had a first diagnosis of IBD at 60 years or older, corresponding to an incidence rate of 35/100,000 person-years (10/100,000 person-years for Crohn's disease, 19/100,000 person-years for ulcerative colitis, and 5/100,000 person-years for IBD unclassified). During a median follow-up period of 4.2 years (range, 0–9 years), elderly patients had less IBD-specific outpatient health care but more IBD-related hospitalizations and overall health care use than adult patients with IBD. Compared with patients with pediatric or adult-onset IBD, elderly patients used fewer biologics and immunomodulators but more systemic corticosteroids. Occurrence of extra-intestinal manifestations was similar in elderly and adult patients, but bowel surgery was more common in the elderly (13% after 5 years vs 10% in adults) ($P < .001$). The absolute risk of bowel surgery was higher in the elderly than in the general population, but in relative terms, the risk increase was larger in younger age groups. **CONCLUSIONS:** In a nationwide cohort study in Sweden, we associated diagnosis of IBD at age 60 years or older with a lower use of biologics and immunomodulators but higher absolute risk of bowel surgery, compared with diagnosis at a younger age. The large differences in pharmacologic treatment of adults and elderly patients are not necessarily because of a milder course of disease and warrant further investigation.

Keywords: CD; UC; Age Differences; Bowel Resection; Colectomy.

The incidence of elderly onset inflammatory bowel disease (IBD) (defined as onset at ≥60 years of age¹) is expected to increase, because of an ageing population² and a rising incidence of IBD worldwide.³ Studies on the incidence of IBD have presented large variations in incidence rates (IRs) between age strata in the elderly (Supplementary Table 1)^{4–26} with IRs for Crohn's disease (CD) between 3 and 6, and IRs between 3 and 17 per 100,000 for ulcerative colitis (UC) in aggregated data for individuals above 60 years of age.^{11–13}

The disease characteristics of IBD seem to differ by age at onset.²⁷ Population-based studies have suggested that late-onset IBD has a milder clinical course, based on a proportionally lower frequency of treatments with immunomodulators and biologics,^{11–13} a lower rate of extra-intestinal manifestations,^{12,13} yet similar surgery rates.^{11–13} However, more recent studies have described a more aggressive disease in elderly onset UC,²⁸ and higher rates of IBD-associated surgery compared with younger age groups.²⁹ The use of medical treatment data as a proxy for disease characteristics in patients with elderly onset IBD may be misleading,^{1,30–34} because drug treatment in the

Abbreviations used in this paper: CD, Crohn's disease; CI, confidence interval; HR, hazard ratio; IBD, inflammatory bowel disease; IBD-U, inflammatory bowel disease unclassified; ICD, International Classification of Disease; IR, incidence rate; IRR, incidence rate ratio; UC, ulcerative colitis.

Most current article

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0016-5085/\$36.00

<https://doi.org/10.1053/j.gastro.2017.10.034>

EDITOR'S NOTES**BACKGROUND AND CONTEXT**

Diagnosis of inflammatory bowel diseases (IBD) is increasing among elderly persons (60 years or older).

NEW FINDINGS

Elderly onset IBD was associated with a lower use of biologics and immunomodulators and a higher absolute risk of bowel surgery compared to younger patients.

LIMITATIONS

Swedish healthcare system offers universal access practically free of charge. The results may not be generalizable in countries where the individual bears more of the cost of medical treatment.

IMPACT

The authors found no evidence of milder clinical course in elderly-onset IBD. The large differences in pharmacological treatment of adults and elderly patients warrant further investigation.

elderly is complicated by comorbidity and polypharmacy³⁵ with the potential for adverse effects.^{36,37} The proposed differences between adult and elderly onset IBD could therefore reflect a cautious attitude among clinicians regarding treatment of the elderly, rather than actual differences in clinical course.

So far, studies on elderly onset IBD have been restricted to tertiary care centers,^{11–13} selected multiple tertiary care centers,^{28,38} or regional databases,^{29,39} and national data are lacking. In Sweden, high-quality data from prospectively collected registers with full coverage enables assessment of both health care⁴⁰ and drug use⁴¹ in the whole Swedish population. The aim of this study was to perform a nationwide study investigating the clinical course of IBD in elderly patients by estimating the incidence and describing the treatment of IBD.

Methods

Design

We conducted a cohort study where medical treatment, IBD-related surgeries, extra-intestinal manifestations, and health care use were assessed in relation to age at IBD onset. We also compared health care use and surgery rates in IBD patients and matched reference individuals from the general population.

Register Sources

The unique personal identity number, issued to all Swedish residents,⁴² was used to link records from the following nationwide and population-based registers:

The National Patient Register, which holds dates on hospital admissions since 1964, with national coverage since 1987. From 1997 and onwards surgical day care procedures, and since 2001, non-primary outpatient physician visits have been reported to the register. Visits to general

practitioners (ie, primary care in Sweden) are not included. Main and contributory diagnoses are coded according to the International Classification of Disease (Tenth Revision since 1997, ICD-10) codes and assigned by the treating physician.⁴⁰

The Prescribed Drug Register contains data on all prescribed drugs dispensed from pharmacies in Sweden from 1 July 2005 and onwards. The coverage of the register is complete for prescriptions in ambulatory care (both specialist and primary care), while in-hospital drug treatment is generally not recorded.⁴³ Overall, more than 99% of non-infusion biologics use is captured in the Prescribed Drug Register, but infusion biologics are covered to a lesser extent. About 20% of infliximab use in 2009 was found in the prescribed drug register. However, some counties have complete coverage of infliximab in the Patient Register (eg, Stockholm county since 2007).⁴⁴

The Total Population Register covers the entire Swedish population and includes information on age, sex, and place of residence, as well as dates of birth, death, and emigration status.⁴⁵ This register was used to identify general population comparator subjects.

Setting

In 2014 Sweden had a population of 9.7 million inhabitants.⁴⁵ The Swedish health care system is tax funded and offers universal access. Prescription drugs are provided free of charge above a threshold of 1,800 SEK annually (\$185). Patients with IBD are typically diagnosed and treated by gastroenterologists (or pediatric gastroenterologists) in hospital-based outpatient facilities.

Identification of Patients With IBD

The Swedish National Patient Register was used to identify all patients with a first-ever diagnosis of UC, CD, or IBD unclassified (IBD-U) (the list of ICD codes used is provided in [Supplementary Table 2](#)) from Jan 1st, 2006 to Dec 31st, 2013. We excluded all patients with an IBD diagnosis before 2006 (diagnosis from inpatient care 1987–2005 or outpatient care 2001–2005). Using 2006 as the first year in the study enabled (a) standardized definition of IBD based on registers with complete coverage from inpatient and outpatient care and prescribed drugs, and (b) up to 42 years of washout with respect to IBD diagnoses from inpatient care, and up to 5 years of washout with respect to IBD diagnoses from non-primary outpatient care, thus minimizing the risk of misclassifying prevalent IBD patients as incident IBD patients. Because the National Patient Register at the time of linkage was updated through 2014, 2013 was used as the last entry year in the study to allow the possibility of a second visit for IBD within 1 year of the first visit.

The definition of IBD required a minimum of 2 inpatient or non-primary outpatient care visits listing a diagnosis of IBD. This definition has a positive predictive value of 93% (95% confidence interval [CI], 87–97).⁴⁶ Patients who shifted between UC and CD but only had 1 of the diagnoses during the last 5 years were classified according to their most recent diagnosis. Otherwise, we classified patients with a mix of codes

for UC, CD, or indeterminate colitis during follow-up as inflammatory bowel disease unclassified (IBD-U). However, patients who had a diagnostic or procedure code typical of CD (eg, small bowel resection or CD of the small bowel, [Supplementary Table 3](#)) were classified as CD. Patients' phenotypes were defined by the highest ever available degree of extent, location, or behaviour according to ICD codes as prospectively recorded in routine care during follow-up ([Supplementary Table 4](#)). Patients who were never diagnosed with a code representing a specific phenotype of UC or CD were classified as unclassified extent/unclassified location (EX/LX). Cut-offs for age groups were: pediatric, <18; adult, 18 to 59; and elderly, ≥60 years.

Identification of General Population Comparators

Up to 10 general population comparator subjects were matched to each IBD patient by age, sex, and place of residence at the time of the first IBD diagnosis. These general population reference individuals were excluded in case of IBD diagnosis before their matching date, and were censored if diagnosed with IBD during follow-up.

Medical Treatment

Medical treatment data included dispensed prescriptions of 5-aminosalicylate/sulfasalazine, corticosteroids, immunomodulators, and biologics ([Supplementary Table 5](#)). For identification of infusion biologics administered in the hospital setting, we also used the Patient register (procedure code: DT016, followed by Anatomical Therapeutic Chemical Classification codes.

Extraintestinal Manifestations

We obtained information on extra-intestinal manifestations⁴⁷ through the National Patient Register ([Supplementary Table 6](#)) and investigated the cumulative incidence of inflammatory arthritis (peripheral and axial arthritis), ocular manifestations (episcleritis, uveitis), primary sclerosing cholangitis, and cutaneous manifestations (pyoderma gangraenosum, erythema nodosum, Sweet's syndrome).

Surgical Outcomes

To identify IBD-related treatment, we collected information on surgical procedures from the National Patient Register using surgical procedure codes. We defined bowel surgery as colectomy, resection of intestine, resection of rectum, strictureplasty, and stoma and pouch operations. Perianal surgeries were incisions and fistula operations ([Supplementary Table 7](#)).

Statistics

We computed an overall incidence estimate for the time period 2006–2013 based on date of first IBD diagnosis and on demographic data for the Swedish population during the time period in question, as well as annual IRs from 1987 to 2013. We computed the mean number of outpatient visits and hospitalizations for patients and comparators per year before and after first IBD diagnosis, and estimated 95% CIs by nonparametric bootstrapping to avoid distributional assumptions. For the other outcome variables, patients were

considered at risk from the date of their second IBD diagnosis (or the corresponding date in the non-IBD reference individuals) until death, emigration, or end of follow-up (Dec 31, 2014). Prevalence estimates of drug use (any dispensing) were calculated for each year (year 1 to 5) following second IBD diagnosis, with the number of remaining patients in the beginning of each 1-year period in the denominator. The cumulative incidence (1-Kaplan-Meier) of ever-use of IBD medication, surgery, and extra-intestinal manifestations was estimated for the entire follow-up and compared between age groups by the log-rank test. The hazard ratio (HR) for bowel surgery was also compared between IBD patients and population comparator subjects in the 3 age groups. We used the likelihood ratio test to examine the effect of age of IBD onset on risk of surgery using age category (adult and elderly) as an interaction term. A negative binomial regression model, incorporating time at risk as an offset term to account for unequal follow-up time, was used to estimate incidence rate ratios (IRR) with CIs for hospitalizations and outpatient visits with IBD as a main diagnosis in patients of different age groups (with adult onset as reference category). The negative binomial regression model was also used to estimate IRRs for total number of outpatient visits and hospitalizations (any diagnosis) in IBD patients vs population comparator subjects (with the population as reference category). Patients were considered at risk during the time in the study when they were not hospitalized. All statistical tests were 2-sided and a *P* value <.05 was considered significant. R (version 3.3.2, R Foundation for Statistical Computing, Vienna, Austria), SAS (version 9.4, SAS Institute Inc, Cary, NC), and STATA (StataCorp, release 12.0. College Station, TX) software were used.

Sensitivity Analysis

To investigate if the observed differences between age groups were explained by differences in phenotypes, separate analyses were performed stratified according to the Montreal classification. CD patients were grouped by location (small bowel, colonic, and ileocecal/undefined), and behavior, where non-complicated behavior was defined as non-stricturing, non-penetrating, and with no perianal disease, and complicated behavior was stricturing or penetrating behavior or perianal disease. UC patients with extensive colitis (E3), distal disease (E1 or E2), and unclassified extent were analyzed separately.

Ethical Approval

Ethical approval for this study was granted by the Regional Ethics Committee, Karolinska Institutet, Stockholm, Sweden (2007/785-31/5; 2011/1509-32; 2015/0004-31; 2015/615-32).

Results

Between 2006 and 2013, 27,834 patients were diagnosed with incident IBD, of whom 6443 (23%) were 60 years or older ([Figure 1](#)). Patients were matched to 276,100 population comparators. Elderly patients had a

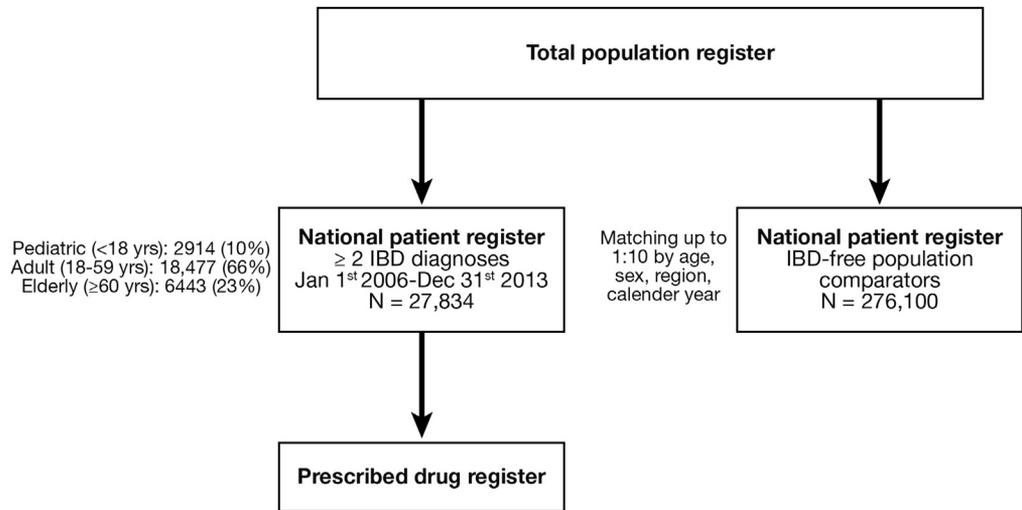


Figure 1. Flow chart of the study population and registers used.

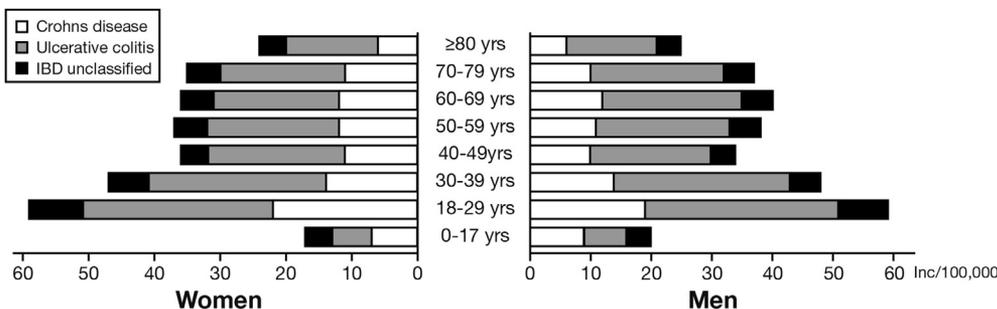
median age of 69 years at IBD diagnosis, adult patients (defined as 18–59 years) had a median age of 35, and pediatric patients (defined as age <18) had a median age of 15 years. Median follow-up from date of second diagnosis was 4.8 years (range, 0–9 years) in IBD patients and 4.9 years (0–9 years) in the general population. Median follow-up among elderly patients was 4.2 years (0–9 years) and 4.4 (0–9 years) in the general population. Out of 6443 elderly patients, the majority (n = 4282) had at least 3 years of follow-up, 2516 patients had at least 5 years of follow-up. Elderly CD patients had similar disease location as the adults. Stricturing behavior was more common (23% in elderly vs 9% in adults) and penetrating disease was less common (5% in elderly vs 11% in adults). For UC, proctitis was less common in the elderly (14%) than adults (23%), fewer elderly patients had extensive colitis (28% in elderly vs 34% in adults), but UC undefined was more common in the elderly (28% vs 15% in adults), [Supplementary Table 8](#).

IR

The mean IR of IBD 2006–2013 in all age groups was 37/100,000 (CD 12; UC 20; IBD-U 5). In elderly patients the IBD IR was 35/100,000 person years (male, 37; female, 33). The IR was 10 for CD, 19 for UC, and 5 for IBD-U. Rates were similar between 60 and 69 years of age (40 for men; 36 for women) and 70–79 years of age (38 and 35, respectively), but decreased in patients above 80 years (25 and 24, respectively) ([Figure 2](#)). The annual IR was consistently the highest for adult patients and lowest for pediatric patients, and the rate for elderly patients fell in between ([Supplementary Figure 1](#)).

Health Service Use

Elderly IBD vs adult and pediatric. The mean number of outpatient visits and hospitalizations (all diagnoses) during follow-up were higher in elderly and pediatric IBD patients than in adults ([Figure 3](#)). When



All IBD	IBD unclassified	Ulcerative colitis	Crohn's disease	Age (years)	Crohn's disease	Ulcerative colitis	IBD unclassified	All IBD
17	4	6	7	0-17	9	7	4	20
59	8	29	22	18-29	19	32	8	59
46	6	27	14	30-39	14	29	5	48
35	4	21	11	40-49	10	20	4	35
37	5	20	12	50-59	11	22	5	37
36	5	19	12	60-69	12	23	5	40
35	5	19	11	70-79	10	22	5	38
24	4	14	6	≥80	6	15	4	25

Figure 2. Incidence rate (IR) of IBD per 100,000 in Sweden 2006–2013, by type of IBD, sex, and age of IBD onset.

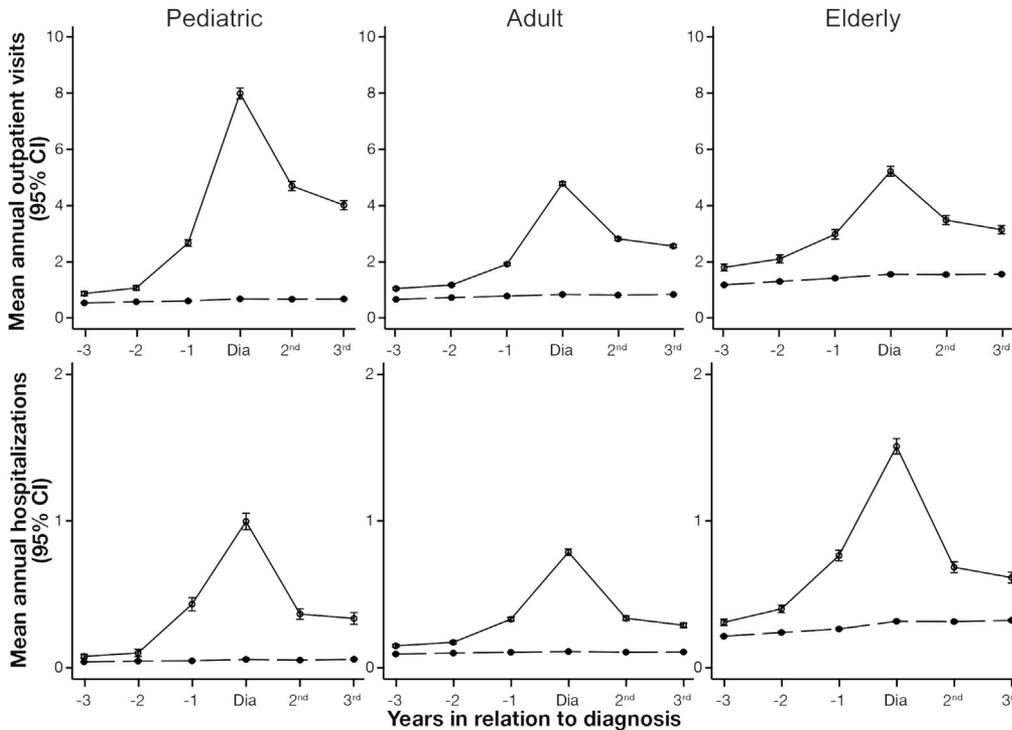


Figure 3. Mean annual number of outpatient visits (*upper panels*) and hospitalizations (*lower panels*) in pediatric, adult, and elderly IBD patients (*solid line*) and population comparators (*long dash*) 3 to 1 years before (-3), 2 to 1 year before (-2), the year before (-1), during the year of first IBD diagnosis, and during the 2nd and 3rd following year.

restricting the analyses of hospitalization to those with IBD as the main diagnosis, the median number of outpatient visits during follow-up was lower in elderly patients, and the IRR was 0.71 for elderly vs adult patients (Table 1). The majority of patients, of all ages, had no hospitalizations with IBD as a main diagnosis during follow-up. The IRR for hospitalization with IBD as a main diagnosis in elderly patients vs adults was slightly increased (1.14), driven by an increased IRR for elderly UC patients vs adult (1.49). Elderly CD patients were less likely to be hospitalized than adults (IRR 0.88). These differences remained when stratifying for phenotype (Supplementary Table 9).

Elderly IBD vs the general population. IBD patients of all age groups had a higher mean number of outpatient visits and hospitalizations than the general population when all diagnoses were considered (Figure 3). The IRR estimates for outpatient visits and hospitalizations (all diagnoses) in patients vs the general population ranged from 2.2 to 7.5 (Supplementary Table 10), and the relative difference between the patients and the population was less pronounced in elderly patients, especially with regards to outpatient visits (IRR for outpatient visits in elderly vs population, 2.5; adults vs population, 3.6; IRR for hospitalization in elderly vs population, 3.4; adults vs population, 3.6).

Pharmacological Treatment

Prevalence of drug use per year after IBD diagnosis. Biologic treatment was low in elderly patients during the first 5 years following diagnosis. Around 1% of elderly UC patients and 3% of elderly CD patients used biologics each year (Supplementary Figure 2). Immunomodulators were dispensed to 9–10% of elderly patients with UC each year. In elderly CD patients, 23% were dispensed

immunomodulators the first year, which declined to 17% during the fifth year. The use of systemic corticosteroids was highest in all age groups during the first year. During later years a larger proportion of elderly patients were dispensed systemic corticosteroids than were adult patients. 5-aminosalicylates/sulfasalazine was dispensed to 72% of elderly UC patients during the first year, which declined to 57% during the fifth year.

Cumulative drug use during follow-up. The cumulative use of biologics during follow-up was lower among elderly patients for both CD and UC patients. After 5 years, 2% of UC patients had used biologics, compared with 7% of adults and 10% of the children. The cumulative use of biologics in elderly CD patients after 5 years was 6% (20% of adults and 23% of children; Figure 4). However, the cumulative use of second-line biologics was similar between age groups (Supplementary Figure 3). The cumulative use of immunomodulators was also lower in elderly patients compared with other age groups (33% elderly CD patients vs 54% adults and 17% elderly UC patients vs 28% adults after 5 years). The use of 5-aminosalicylates/sulfasalazine was lower in elderly compared with adult patients, and for systemic steroids, elderly CD patients had a slightly lower use, and UC patients a slightly higher use than adult patients. The differences between adult and elderly patients regarding use of biologics and immunomodulators remained when stratifying for phenotype (Supplementary Figures 4 and 5).

Extra-intestinal Manifestations

Primary sclerosing cholangitis was more common in pediatric patients (5%) than in adults (2%) and elderly

Table 1. Number (n) and Incidence Rate Ratios (IRR) of Hospital-based Outpatient Visits and Hospitalizations With IBD as Main Diagnosis From Date of Second Diagnosis to End of Follow up. Comparing Pediatric (<18 Years), Adult (18-59 Years) and Elderly (≥60 Years) Onset Patients (Adult Onset is Reference)

	No. of patients	Time at risk, Y, Median (min-max)	Outpatient visits			Hospitalizations		
			Total no. of visits, Median (min-max)	Mean, median No. of visits/years at risk	IRR (95% CI)	Total no. of visits, Median (min-max)	Mean, median No. of visits/years at risk	IRR (95% CI)
IBD								
Pediatric	2914	4.9 (0.1-9.0)	12 (0-153)	3.6, 2.7	2.16 (2.08-2.23)	0 (0-39)	0.2, 0	1.78 (1.63-1.95)
Adult	18477	4.2 (0-9.0)	4 (0-125)	1.8, 1.2	1 (ref)	0 (0-45)	0.2, 0	1 (ref)
Elderly	6443	3.6 (0-8.9)	2 (0-61)	1.3, 0.8	0.71 (0.69-0.73)	0 (0-19)	1.4, 0	1.14 (1.06-1.23)
Crohn's disease								
Pediatric	1239	5.1 (0.3-9.0)	14 (0-153)	3.9, 3.2	2.04 (1.92-2.16)	0 (0-16)	0.3, 0	1.38 (1.23-1.56)
Adult	5847	4.4 (0-9.0)	5 (0-105)	2.1, 1.4	1 (ref)	0 (0-45)	0.2, 0	1 (ref)
Elderly	1937	3.6 (0-8.9)	3 (0-54)	1.4, 1.0	0.71 (0.67-0.75)	0 (0-11)	1.2, 0	0.88 (0.78-0.99)
Ulcerative colitis								
Pediatric	1058	5.2 (0.1-9.0)	11 (0-75)	3.1, 2.3	2.15 (2.04-2.27)	0 (0-24)	0.2, 0	2.13 (1.81-2.51)
Adult	10290	4.2 (0-9.0)	4 (0-125)	1.5, 1.1	1 (ref)	0 (0-19)	0.1, 0	1 (ref)
Elderly	3595	3.6 (0-8.9)	2 (0-50)	1.2, 0.8	0.76 (0.73-0.78)	0 (0-19)	1.2, 0	1.49 (1.33-1.67)

NOTE. Bold values indicate P value <0.

(1%) 5 years after diagnosis (Figure 5). Diagnosis of cutaneous manifestations was uncommon in all age groups (<1%) with no significant differences. Ocular manifestations were more common in the elderly (2%) than other age groups (1%), but arthritis was more common in adults (8%) than in elderly and pediatric patients (6%).

Surgical Treatment

During follow-up bowel surgery rates were higher in elderly IBD patients than adults (Figure 6). After 5 years, 13% (95% CI 12-14%) of the elderly had undergone bowel surgery vs 10% (95% CI 9-10%) in adults and 9% (95% CI 8-10%) in pediatric patients. Among elderly UC patients without history of colectomy (n = 3442), 6% had undergone total colectomy after 5 years, compared with 5% of adults and 6% of children. For CD, 22% of elderly patients had undergone bowel surgery after 5 years, compared with 16% of adults and 13% of the children. Contrarily, only 2% of elderly CD patients underwent perianal surgery during the first 5 years compared with 8% of adults and 10% of children. The cumulative incidence of bowel surgery in elderly CD patients vs adults was increased for complicated as well as uncomplicated disease behavior, and for colonic and ileocolic/undefined location, but was not significantly different for small bowel CD. The cumulative risk of total colectomy in UC was increased for elderly vs adult patients with extensive and distal colitis, but not for undefined extension (Supplementary Figure 6).

Association Between Age at Onset and Occurrence of Surgery in Relation to the General Population

The rates of bowel surgery in IBD patients were compared with those in age-matched population comparator subjects. The absolute risk difference among pediatric and adult patients was equal to the cumulative incidence (ie, 10%) because the population had a risk of surgery close to 0. In the elderly population, the 5-year incidence of bowel surgery was 2%, giving an absolute risk increase of 11%. However, the HR for bowel surgery in the elderly was lower (HR, 9; 95% CI 8-10) than in adult (HR, 43; 95% CI 39-48) IBD patients vs the population. The association between age of IBD onset and surgery risk was significant (P for interaction <.001).

Discussion

In this national cohort study including 27,834 incident IBD cases, we observed a higher incidence of elderly onset IBD (35/100,000) than previously reported. More than 1 out of 5 incident CD (21%) and UC (24%) cases occurred in elderly individuals. In line with previous reports, elderly patients used less immunomodulators and biologics¹¹⁻¹³ than younger individuals, but contrary to previous studies,¹¹⁻¹³ the absolute risk of bowel surgery in elderly patients was increased (13% after 5 years) compared with adults (10% at 5 years).

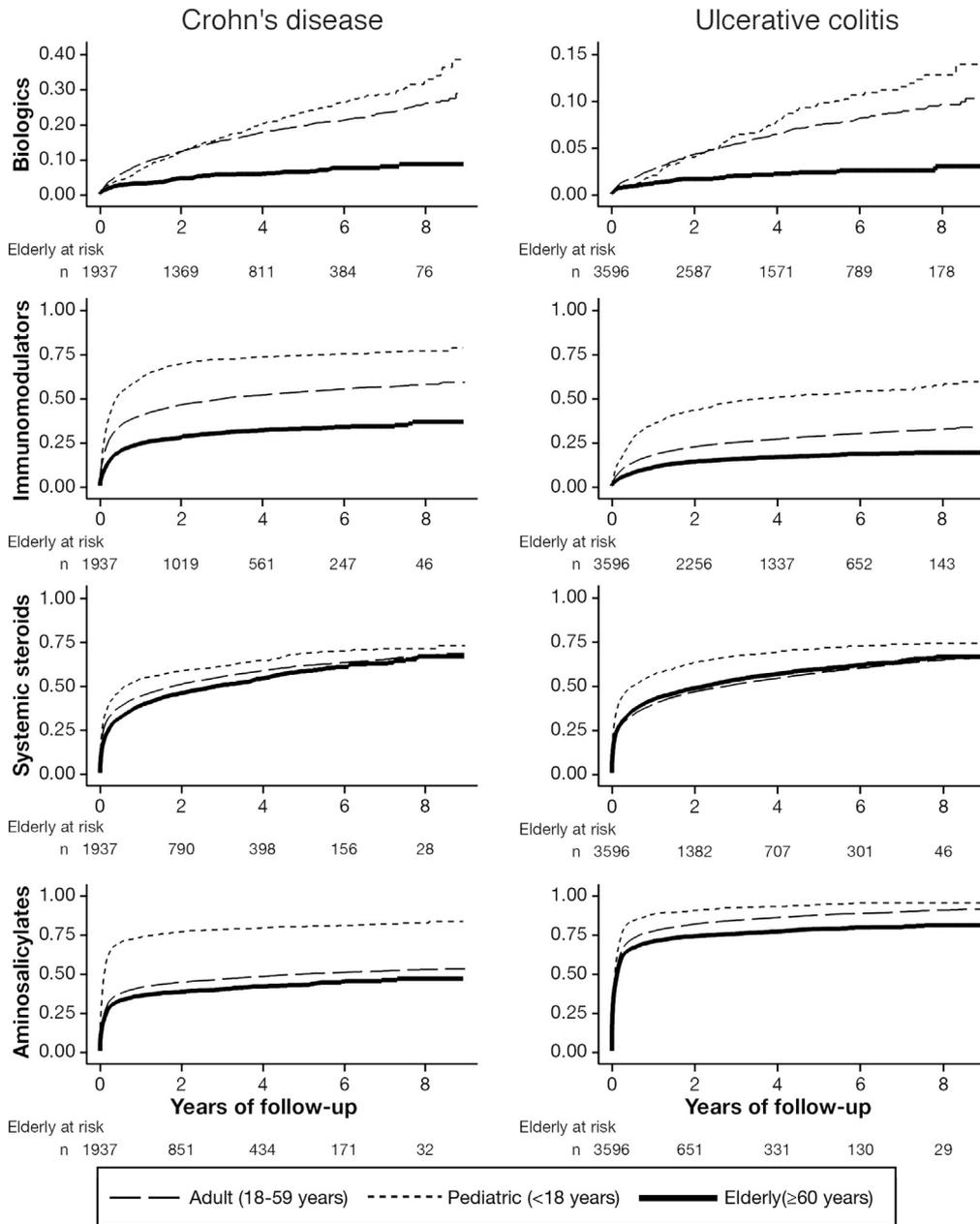


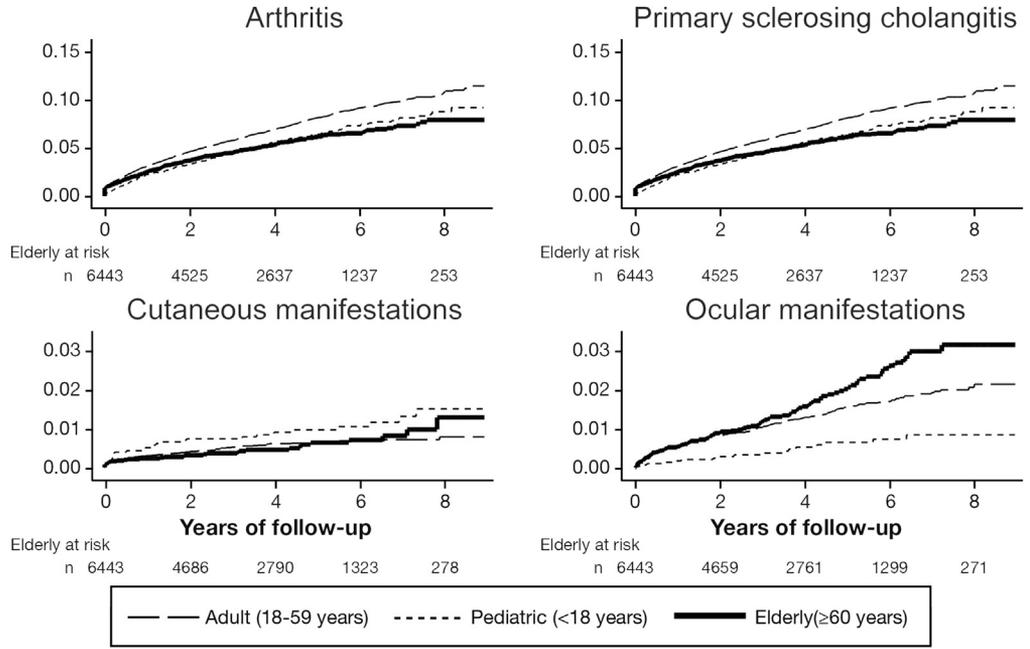
Figure 4. Cumulative use of first-line biologics, immunomodulators, systemic corticosteroids, and aminosallylates from date of second IBD diagnosis in CD and UC patients with pediatric, adult, and elderly onset ($P < .0001$ for all outcomes).

To our knowledge, this is the largest study so far on elderly onset IBD, and the first study to evaluate how age at onset affected the clinical course and consequences of IBD, both in relation to other IBD patients and in relation to an IBD-free population. The milder clinical course in elderly onset IBD described in previous studies¹¹⁻¹³ could not be confirmed in this study. Elderly patients used less IBD-specific medication and had fewer outpatient visits with IBD as a main diagnosis than other patients, both in absolute and relative terms. However, elderly patients were hospitalized more frequently than younger patients. When investigating surgery rates in relation to matched general population comparator subjects, the absolute risk difference was slightly larger in the elderly, while the HR in relation to the general population was lower than in younger patients.

The elderly population is increasing, and the IR of elderly IBD is likely increasing. In contrast to earlier regional studies,^{48,49} our study was based on national data from registers with compulsory data entry, which might explain the higher IRs in our study in ages 60-69 years. Studies from the 2000s have reported varying IRs (Supplementary Table 1)⁴⁻²⁵. Three major studies found IBD IRs of 3, 3, and 6 per 100,000 for CD and 3, 11, and 17, for UC, respectively.¹¹⁻¹³ High rates have been reported from northern countries such as Iceland¹⁸ and Canada.¹⁵ These differences may reflect methodologic or geographical differences.^{50,51}

The register-based IBD definition will influence the estimated incidence, and stricter definitions will result in lower IRs. We used ICD codes from the Swedish Patient

Figure 5. Cumulative incidence of primary sclerosing cholangitis ($P = .01$), arthritis ($P < .0001$), cutaneous manifestations ($P = .9$), and ocular manifestations ($P = .02$) in IBD patients from date of second IBD diagnosis, by age at onset.



Register, which has virtually complete coverage. We required ≥ 2 IBD diagnoses from inpatient or outpatient care. This definition has a positive predictive value of 93% (95% CI, 87–97%) for IBD.⁴⁶ Previous studies of similar design have all used different definitions combining inpatient and outpatient care, and sometimes prescription data.^{14–16,52} Given the high quality of the Swedish patient register and the long washout period, we believe that our IBD classification is reliable.

Not surprisingly, the elderly patients had a higher mean rate of hospitalizations than the younger patients (Figure 3),

as has been reported in a previous study.⁵³ This could be explained by more comorbidity not related to IBD. An American study reported that 54% of geriatric IBD patients had a Charlson comorbidity index ≥ 4 .⁵⁴ When considering IBD only as a main diagnosis, the rate of hospitalizations for elderly onset IBD in comparison to adult IBD patients was larger only for UC patients in the present study. Elderly UC patients have been reported to be hospitalized more frequently for the first flare than younger adult patients.¹¹

The rates of outpatient visits related to IBD were lower in the elderly. This is in accordance with a Canadian study,³⁹

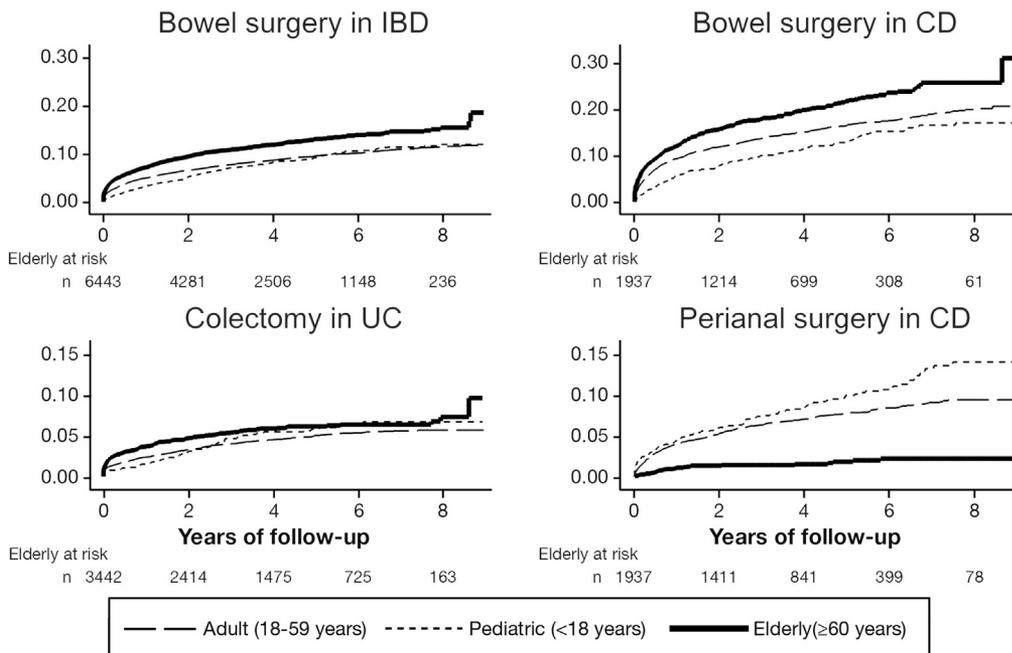


Figure 6. Cumulative incidence of abdominal surgery in IBD patients ($P < .0001$), total colectomy in UC patients ($P = .006$), and bowel and perianal surgery in CD patients ($P < .0001$), from date of second IBD diagnosis, by age at onset.

where IBD-specific health care utilization was lower in elderly patients compared with younger patients. This may reflect a milder clinical course, or simply the fact that biologics use, which generates more intense supervision, was lower in the elderly. There may be an element of health care underutilization in the elderly population; however, this seems unlikely given that the overall health care use was greater in the elderly. Another potential explanation could be that a larger proportion of the elderly were handled by non-gastroenterologists at a visit for primarily another cause or disease.

The principles of medical management of IBD in patients ≥ 60 years are generally the same as in other age groups,⁵⁵ and the benefits of using highly potent agents early in IBD treatment is becoming widely accepted^{56,57} (even though some concerns have been raised about the use of thiopurines in the elderly³¹). In spite of this recommendation, elderly patients were prescribed less immunomodulators and more corticosteroids than adults, especially CD patients (Supplementary Figure 2). Because corticosteroids can be used for other disorders that are more prevalent in the elderly, its use does not with certainty reflect more frequent flares or chronic active disease. Corticosteroid use in elderly onset IBD patients can, however, be compared with the use among age-matched comparators. During the 2nd to 5th year, 23–27% of the elderly IBD patients used systemic corticosteroids (9% in the general population 2nd to 5th year, data on request). This extensive use of oral corticosteroids in combination with the distinctively lower use of immunomodulators and biologics supports previously reported underuse of immunosuppressives in elderly patients.^{11–13,54,58,59} A recent study on Medicaid/Medicare beneficiaries showed reduced mortality in patients treated with biologics as compared with prolonged corticosteroids.⁶⁰ Thus, the risk–benefit ratio of an intensified treatment algorithm in elderly IBD needs to be assessed, based on more robust data.

Several previous studies have reported similar surgery risks in elderly and younger patients,^{11–13,59} although a more recent study presented higher rates of IBD-related surgery in elderly than in adult UC patients.²⁹ In our study, bowel surgery was more common in elderly patients than adult patients overall, and more common in elderly IBD patients than in population reference individuals. Elderly CD patients have been reported to have a higher rate of surgery shortly after diagnosis.¹¹ In both UC and CD patients in our study, most events in the elderly occurred during the first year. This may reflect a higher rate of acute surgery, or a conscious choice from the treating physician. Especially in elderly CD patients, a resection bears a possibility to refrain from future medical therapy. Because of the design of the study, where follow-up started at date of second diagnosis, surgery occurring at first diagnosis was not accounted for. When surgical events were investigated from date of first IBD diagnosis, the differences between adult and elderly patients were even more pronounced because 6% of elderly CD patients had surgery between first and second diagnosis compared with 3% of adult CD patients. Conversely, perianal surgery was much less common in elderly patients, in

contrast to other studies.^{12,13} Either the incidence of perianal disease was indeed lower, or elderly patients had an indolent disease course and therefore less need for surgery.

A major strength of this study was the access to routinely collected nationwide data on inpatient and non-primary outpatient care and dispensed prescription drugs. Complete data on infliximab infusions in-hospital was limited to the Stockholm region; however, this applied to all age groups, and hence differences should still be valid. The population-based design minimizes selection bias and the large sample size enhances precision and allowed us to calculate exact IRs in different age strata. Regarding generalizability, social systems differ, and the Swedish health care system offers universal access practically free of charge. Therefore, our results may not be generalizable in countries where the individual bears more of the cost of medical treatment, or where the reimbursement for the individual clinician is affected by the choice of treatment.

Conclusion

Our study showed that IBD onset was common in elderly patients. Elderly IBD patients used less IBD-specific health care and medication compared with younger, the occurrence of extra-intestinal manifestations was similar, but IBD-associated surgery rates were higher in the elderly than in younger age groups. Our study does not support the notion that elderly onset IBD has a milder clinical course than younger onset, and the reasons for the large differences in pharmacologic treatment between younger and elderly patients need further investigation.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at <https://doi.org/10.1053/j.gastro.2017.10.034>.

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Received April 26, 2017. Accepted October 26, 2017.

Reprint requests

Address requests for reprints to: Åsa Hallqvist Everhov, MD, PhD, Department of Surgery, Stockholm South General Hospital, SE 118 61 Stockholm, Sweden. e-mail: asa.hallqvist-everhov@ki.se.

Acknowledgments

Ethical approval for this study was granted by the Regional Ethics Committee, Karolinska Institutet, Stockholm, Sweden.

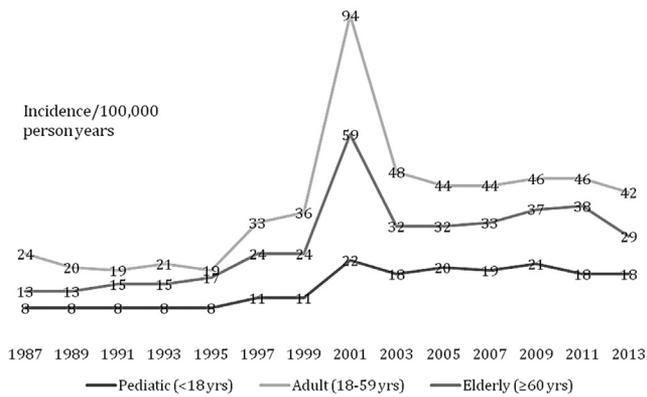
Conflict of interest

The authors disclose no conflict.

Funding

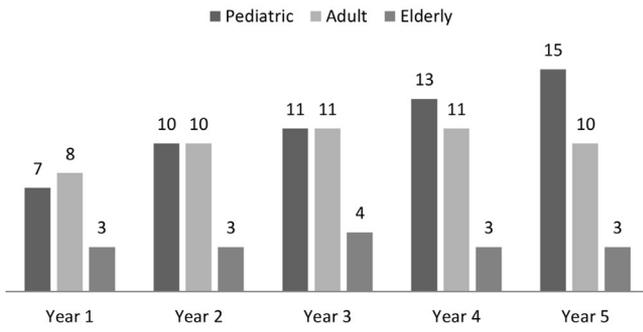
This project was supported by grants from the Swedish Medical Society (Project grants, the fund for research in gastroenterology and the Ibre foundation), Mag-tarmfonden, the Jane and Dan Olsson foundation, the Mjölkdroppen foundation, The Swedish Foundation for Strategic Research, The Swedish Research Council, The Swedish Cancer Society, The Bengt Ihre research fellowship in gastroenterology, and Karolinska Institutet foundations. Financial support was provided through the regional agreement on medical training and clinical research between Stockholm County Council and Karolinska Institutet (ALF). None of the funding organizations above has had any role in the design and conduct of the study; in the collection, management, and analysis of the data; or in the preparation, review, and approval of the manuscript. The study also received an unrestricted grant by Janssen Pharmaceutica NV, who had the right to review the manuscript before submission, but did not have any role in the design and conduct of the study; in the collection, management, and analysis of the data; or in the preparation, and approval of the manuscript.

Annual IBD incidence rate 1987-2013

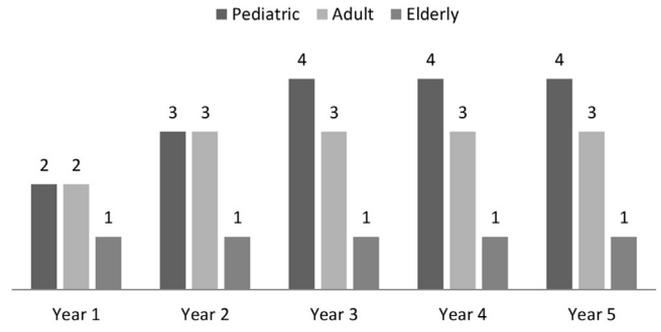


Supplementary Figure 1. Observed number of new cases of IBD/100,000 person-years from 1987 to 2013 in pediatric, adult, and elderly onset IBD patients with at least 1 subsequent registration of IBD. The peak in 2001 represents the addition of specialized outpatient visits to the National Patient Register. IBD patients without previous hospitalizations were recorded in the register at their first outpatient visit after 2001, and are thus perceived as incident cases.

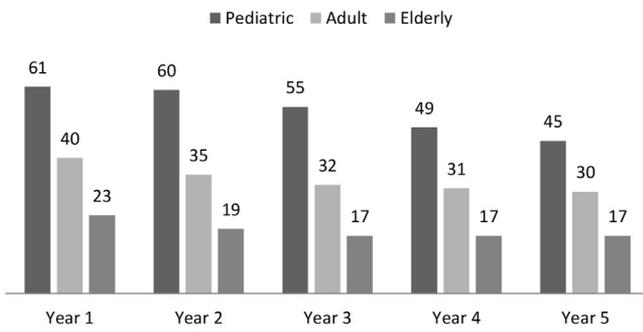
Biologics CD



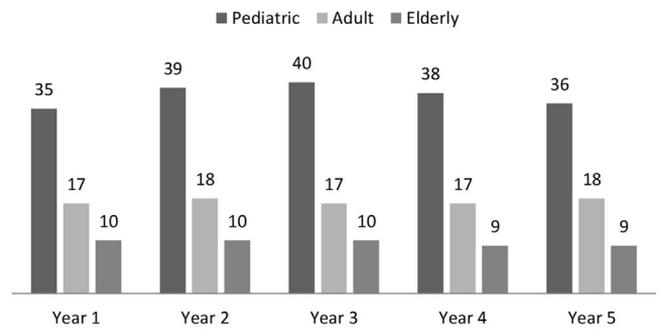
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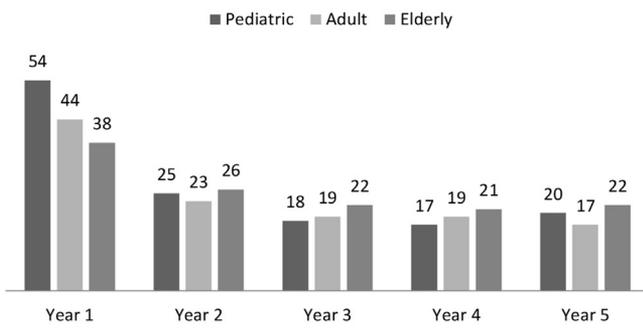
Immunomodulators CD



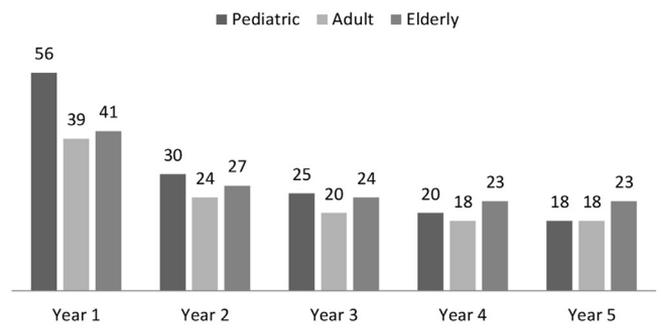
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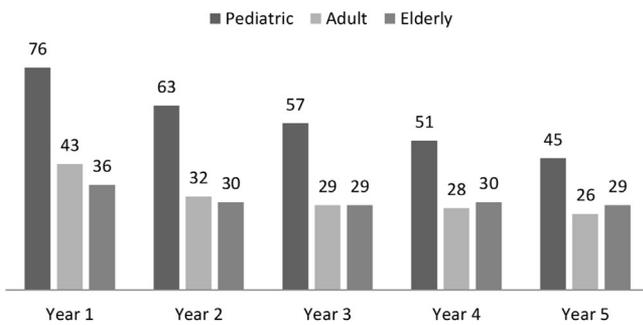
Systemic steroids CD



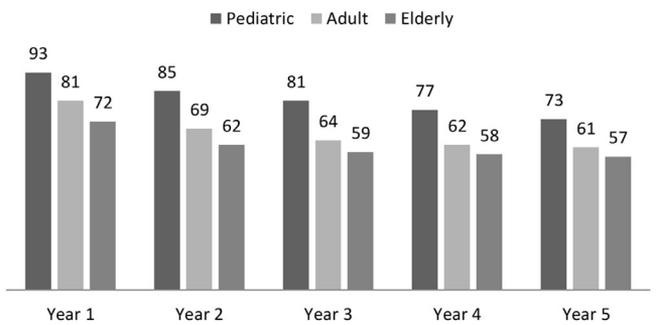
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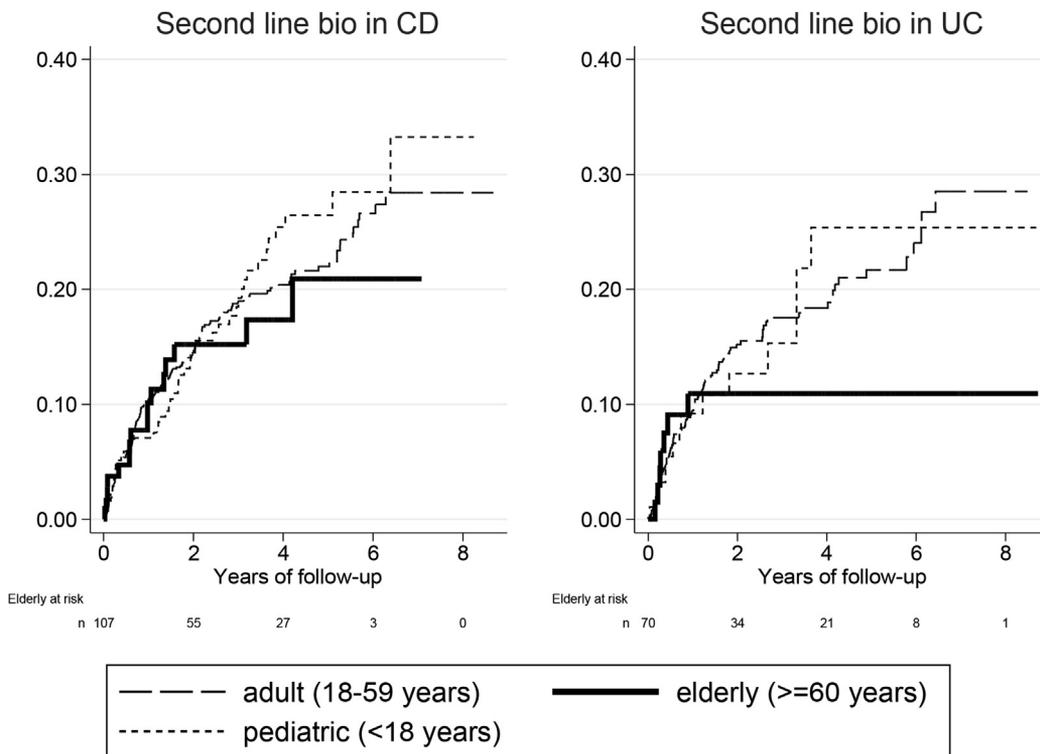


Aminosalicylates CD



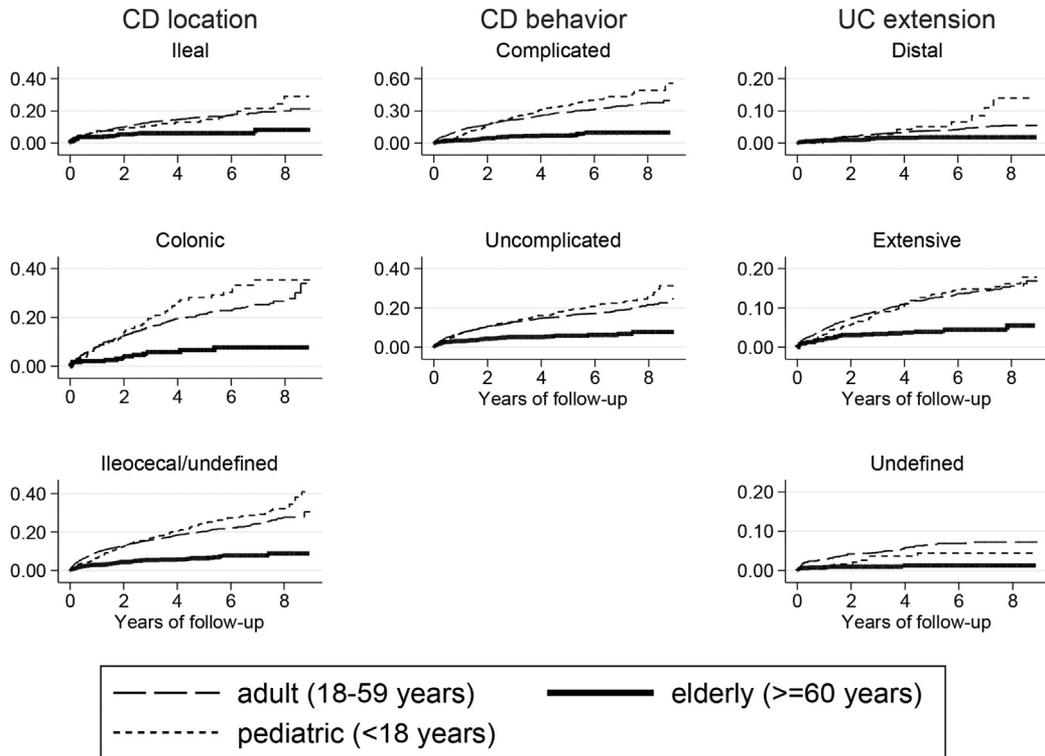
Aminosalicylates UC



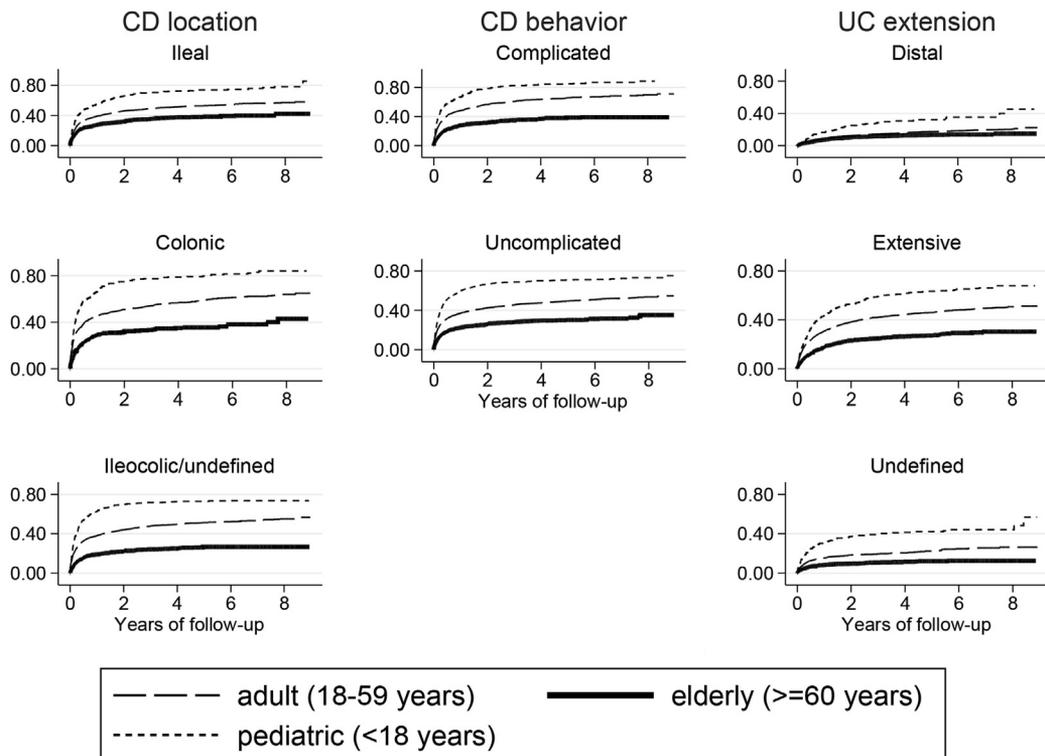


Supplementary Figure 3. Cumulative use of second-line biologics from date of second IBD diagnosis in CD ($P = .8$) and UC ($P = .4$) patients with pediatric, adult, and elderly onset.

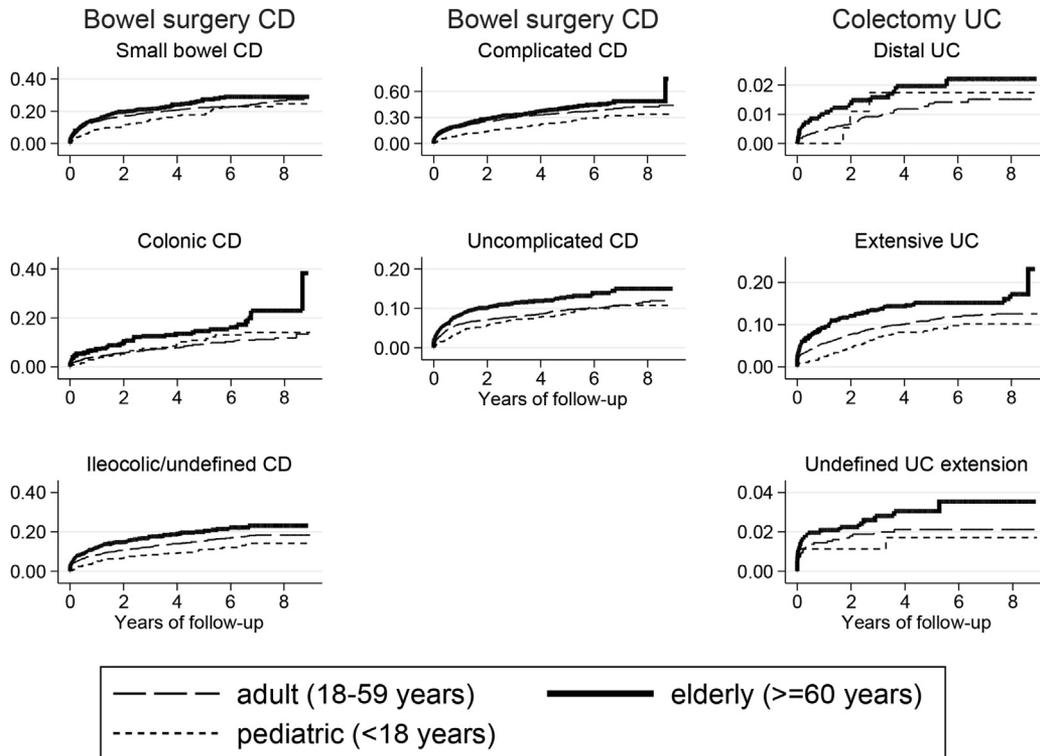
← **Supplementary Figure 2.** Proportion (%) of patients with pediatric, adult, and elderly onset CD and UC treated with biologics, immunomodulators, systemic corticosteroids, and aminosalicylates per year (1 to 5) following second IBD diagnosis. For biologics, all dispensed adalimumab doses and some 20% of infliximab doses were identified through the Prescribed Drug Register. All Infliximab infusions in Stockholm since 2007 were identified through the Patient Register.



Supplementary Figure 4. Cumulative use of biologics from date of second IBD diagnosis in CD and UC patients with pediatric, adult, and elderly onset, stratified for Montreal classification. Log-rank test for differences across different ages: $P \leq .0003$ for all phenotypes.



Supplementary Figure 5. Cumulative use of immunomodulators from date of second IBD diagnosis in CD and UC patients with pediatric, adult, and elderly onset, stratified for Montreal classification. Log-rank test for differences across different ages: $P \leq .0001$ for all phenotypes.



Supplementary Figure 6. Cumulative incidence of bowel surgery in CD patients, and cumulative incidence of colectomy in UC patients, stratified for Montreal classification. Log-rank test for differences between elderly and adult patients: Small bowel CD, $P = .05$; colonic CD, $P = .0001$; ileocolic/undefined CD, $P = .001$; extensive UC, $P < .0001$; distal UC $P = .04$; undefined UC, $P = .15$.

Supplementary Table 1. Studies From the 2000's Reporting Incidence of IBD in Patients ≥ 60 Years of Age

Author	Country	Region and time period	Data source/case acerntainment	Age	IR CD			IR UC		
					Male	Female	All	Male	Female	All
Vind et al. 2006 ⁴	Denmark	Copenhagen 2003-2005	Danish Crohn Colitis Database	66-75	4.5	4.5	4.5	14	13	14
				76-85	9.5	7.5	8	12	18	16
				86-95				10	16.5	15
Sincic et al. 2006 ⁵	Croatia	Primorsko-goranska County 2000-2004	Data form completed by gastroenterologists	≥ 65	5.5	4		7.5	5.5	
Bernstein et al. 2006 ²⁰	Canada	British Columbia, Alberta, Saskatchewan, Manitoba, Nova Scotia 1998-2000	Provincial health databases	60-69	10	14		18	15	
				70-79	9	10		17	15	
				≥ 80	5	8		11	11	
Lapidus et al. 2006 ²⁵	Sweden	Stockholm county 1990-2001	Patient records	60	8.5	8.4				
Nerich et al. 2006 ⁷	France	Metropolitan France 2000-2002	Health insurance data	75	7	6.9				
				60-64	6	5		10.5	5.5	8
				65-69	5.5	4.5		8.5	6	7.5
				70-74	5	5		9	5.5	7
				75-79	5	7		7.5	5.5	6
				80-84	4	6		5	5	5
				85-89	3.5	6.5		6	4.5	4.75
Geary et al. 2006 ¹⁰	New Zealand	Canterbury 2004-2005	Patient records	90-94	3	3		4	3	3
				95-99	0	2.5				
				60-64	22	30	25	32	0	18
				65-69	65	40	45	0	0	9
				70-74	30	30	25	0	15	18
				75-79	40	85	55	0	0	0
				80-84	0	0	0	40	0	25
Abakar-Mahamat et al. 2007 ⁶	France	Corsica 2002-2003	Patient records	≥ 85	0	45	30	0	0	0
				60-74	0	0		22.5	20	
				≥ 75	0	0		12.5	0	
Loftus et al. 2007 ²⁴	USA	Olmsted County 1940-2000	Patient records	60-69	7.1	4.3	5.6	10.0	5.5	7.6
Ott et al. 2008 ⁸	Germany	Oberpfalz 2004-2006	Data form completed by the attending physician	≥ 70	6.1	4.2	4.9	7.0	4.7	5.6
				66-75			1.75			4
				>75			1		2	

Supplementary Table 1. Continued

Author	Country	Region and time period	Data source/case ascertainment	Age	IR CD			IR UC		
					Male	Female	All	Male	Female	All
Herrinton et al. 2008 ²¹	USA	Members of Kaiser Permanente, Northern California 1996–2002	ICD code in health database multiplied by proportion of confirmed cases in randomly sampled patient chart review	60–69	9.5	9.0	9.4	21.1	14.4	17.6
Romberg-Camps et al. 2009 ²²	Netherlands	South Limburg 1991–2002	IBD South Limburg Registry	70–89	6.1	12.2	6.3	16.3	14.9	15.5
				60–69	4.5	4.5	12.5	6		
				70–79	3	2.5	10	4		
				80–89	0	0	5	2		
Wilson et al. 2010 ⁹	Australia	Geelong 2007–2008	Patient records	90–99	0	0	0	0		
				≥65			3		17.5	
Rönnblom et al. 2010 ²³	Sweden	Uppsala 2005–2007	Patient records	60–60					14	
Lakatos et al. 2011 ¹²	Hungary	Veszprem Province 2002–2007	Veszprem Province database	≥70						14
				>60			3.0		10.8	
Sjöberg et al. 2013 ⁴⁸	Sweden	2005–2009	The IBD Cohort of Uppsala Region (ICURE)	60–69	6	9		22	15	
Ng et al. 2013 ¹⁹	Asia-Pacific	21 centers across Asia-Pacific 2011–2012	Asia-Pacific Crohn's and Colitis Epidemiology study (ACCESS)	70–79	13	13		22	12	
				80–89	2	3		18	11	
				90–99	0	2.5				
				≥60	0.25	0.2		0.8	0.7	
Charpentier et al. 2014 ¹³	France	Northern France 1988–2006	Registre des Maladies inflammatoires chroniques de l'Intestin du Nord Ouest de la France (EPIMAD) registry	>60			2.6		3.1	
Norgård et al. 2014 ¹⁴	Denmark	Denmark 1995–2012	ICD codes in health administrative data	60–74	6.1	7.9		23.4	18.0	
				≥75	4.8	5.9		19.1	14.6	
Bitton et al. 2014 ¹⁵	Canada	Quebec 2001–2008	ICD codes in health administrative data	60–69	13.65	17.47		15.01		
				70–79	13.45	18.89		15.87	13.31	
				≥80	12.77	15.51		14.81	12.8	
Benchimol et al. 2014 ¹⁶	Canada	Ontario 1999–2008	ICD codes in health administrative data	≥65			6.6		12.4	
Kim et al. 2015 ¹⁷	Korea	2006–2012	ICD code in health administrative data	60	2	2	2	7	5.5	6.25
				65	2	2	2	7	6	6.5
				70	2	2	2	6.5	5.5	6
				75	2	2	2	5.5	4	4.75
				≥80	1	1.5	1.25	4	3	3.5

Supplementary Table 1. Continued

Author	Country	Region and time period	Data source/case ascertainment	Age	IR CD			IR UC		
					Male	Female	All	Male	Female	All
Björnsson et al. 2015 ¹⁸	Iceland	Iceland 1995–2009	Patient records	60–69	7	15	11	25	10	18
				70–79	3.5	9	6.5	24	19	21
				80–89	2.5	9.5	6.5	18	20	20
				90–99	0	0	0	18	0	6
Jeuring et al. 2016 ¹¹	Holland	South Limburg 2010	IBD South Limburg Registry	≥60			6.23			17.43
Shivashankar et al. 2017 ²⁶	USA	Olmsted county 1970–2010	Rochester Epidemiology Project	60–69	8.2	3.6	5.8	12.4	7.8	9.9
				70–93	5.5	8.7	7.5	15.7	6.8	10.2

Supplementary Table 2. ICD Codes Used to Identify Patients With Inflammatory Bowel Disease (IBD)

	ICD-7 1964–1968	ICD-8 1969–1986	ICD-9 1987–1996	ICD-10 1997–
Ulcerative colitis (UC)	572,20; 572,21; 578,03	563,10; 563,99; 569,02	556	K51
Crohn's disease (CD)	572,00; 572,09	563,00	555	K50
IBD unclassified (IBD-U)	UC+CD	UC+CD	UC+CD	UC+CD, or K52.3

Supplementary Table 3. ICD Codes Associated With Crohn's Disease

Surgical procedure	7th edition (KKÅ97)
Resection of small bowel	
Small bowel resection	JFB00-01
Enteroanastomosis	JFC00-01
Strictureplasty to the small bowel	JFA60
Partial resection of the colon	
Left-sided hemicolectomy	JFB43-44
Right-sided hemicolectomy	JFB30-31
Ileocaecal resection	JFB20-21
Resection of the transverse colon	JFB40-41
Resection of the sigmoideum	JFB46-47,
Ileocolonic re-resection	
Other type of partial colon resection	JFB50-51
Other type of partial colon or small bowel resection	JFB33-34, JFB96-97
Other colon resection with colonostomy and distal closure	JFB63-64, JGB10-11
Resection of the sigmoid colon with sigmoidostomy and closure of the rectum	JFB60-61
Fistula treatment	
Lay open or excision of perianal fistula	JHD20-33, JHD50-63 JHD63, JHA00
Other anal or perianal surgery (e.g. examination under anesthesia)	JHW96,
Closure of fistula of small intestine	JFA76
Closure of fistula of colon	JFA86
Other fistulas	KCH30-33, LEE30
Perianal abscess	
Incision abscess, hematoma	JAJ00
Dilatation	
Dilatation of the duodenum	JDH32
Endoscopic dilatation of the small bowel	JFA38
Endoscopic dilatation of the colon	JFA58
Endoscopic dilatation of the rectum	JGA58
Ultrascan of the anus/rectum	
Transanal endoscopic ultrascan	XJH00
ICD-codes not compatible with ulcerative colitis	
Crohn's disease of the small bowel	
Perianal disease modifier	

Supplementary Table 4. ICD Codes for Montreal Classification

Montreal classification		Diagnostic codes
Crohn's disease	Location	
L1	Small bowel disease or terminal ileitis	K50.0
L2	Colon	K50.1
L3/LX	Ileocecal Crohn's disease or location not defined	K50.8, K50.9
	Behavior	
B1	Non-stricturing, non-penetrating	None of the ICD-codes for B2 or B3
B2	Stricturing	Crohn's disease AND any of the following codes (K56.5; K56.6; K56.7; K62.4)
B3	Penetrating	Crohn's disease AND any of the following diagnostic codes (K63.0, K63.2, K31.6, N82.3, N82.3, N82.4) OR any of the following surgical procedure codes (JFA76, JFA86)
P	Perianal disease modifier	Crohn's disease AND any of the following diagnostic codes: (K60.3, K60.4, K60.5, K61.0, K61.1, K61.2, K61.3, K61.4, K62.4) OR any of the following surgical procedure codes: (JHD20, JHD30, JHD33, JHD50, JHD60, JHD63, JHA00, JHA20, JHW96)
Ulcerative colitis	Extent	
E1	Ulcerative proctitis	K51.2
E2	Left-sided UC	K51.3; K51.5
E3	Extensive UC	K51.0
EX	Extent not defined	K51.4; K51.8; K51.9

NOTE. Patients' phenotypes were defined by the highest available degree ever of anatomic distribution of inflammation. Patients who were never diagnosed with a code representing a specific phenotype of CD or UC, were classified as LX/EX.

Supplementary Table 5. ATC Codes for Medical Treatment of IBD

Drug group	Substance	ATC code
Immune modulators	Azathioprine	L04AX01
	Mercaptopurine	L01BB02
	Methotrexate	L04AX03/L01BA01
Anti-TNF treatment	Infliximab	L04AB02 (L04AA12 before 2008)
	Adalimumab	L04AB04 (L04AA17 before 2008)
	Golimumab	L04AB06
	Vedolizumab	L04AA33
Systemic corticosteroids	Betamethasone	H02AB01
	Dexamethasone	H02AB02
	Methylprednisolone	H02AB04
	Prednisolone	H02AB06
	Prednisone	H02AB07
	Hydrocortisone	H02AB09
	Cortisone	H02AB10
Aminosalicylates (5-ASA)	Sulfasalazine	A07EC01
	Mesalazine	A07EC02
	Olsalazine	A07EC03
	Balsalazide	A07EC04
	Mesalazine	A07EC02

Supplementary Table 6. ICD Codes for Extraintestinal Manifestations

	ICD-10
Complication	1997-
Primary sclerosing cholangitis	K83.0
Extra-intestinal manifestations	
Erythema nodosum	L52
Pyoderma gangraenosum	L88
Sweet syndrome	L98.2
Iridocyclitis	H20
Arthropathy in Crohn's disease	M07.4
Arthropathy in Ulcerative colitis	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	M45
Spondylarthritis, inflammatory NOD	M460, M461, M468, M469
Arthritis NOD	M139, M255

Supplementary Table 7. Surgical Procedure Codes

Surgical procedure	7th revision (KKÅ97)
Colectomy	
Subtotal colectomy with end ileostomy	
Colectomy and ileostomy, with closure of the rectum	JFH10
Laparoscopic colectomy and ileostomy	JFH11
Other colectomy	JFH96
Colectomy with IRA (ileorectal anastomosis)	
Colectomy with ileorectal anastomosis	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 colon	JFG26
Partial colectomies	
Right-sided colectomy	JFB30, JFB31
Resection of colon transversum	JGB40, JFB41
Left-sided colectomy	JFB43, JFB44
Resection of sigmoid colon	JFB46, JFB47
Other colon resection	JFB50, JFB51
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	JGB50
Extirpation of rectum or making of an ileoanal anastomosis after previous colectomy	JGB60
Continent ileostomy at time of colectomy	
Proctocolectomy with continent ileostomy, Kock	JFH40
Converting a conventional ileostomy to a continent ileostomy	JFG60
Proctocolectomy	
Proctocolektomy with ileostomy	JFH20
Other bowel surgery	
Strictureplasty to the small bowel	JFA60
Strictureplasty to the colon	JFA63
Closure of fistula of small intestine	JFA76
Closure of fistula of colon	JFA86
Colonic and/or small bowel resection	JFB
Formation of stoma	JFF
Operations on intestinal stoma or reservoir	JFG
Other operation of small bowel and/or colon	JFW96
Other laparoscopic operation of small bowel and/or colon	JFW97
Rectal resection	JGB
Perianal surgery	
Perianal incision and drainage	JHA00
Dilatation of the anal sphincter	JHD00
Lay open or excision of perianal fistula	JHD20
Partial lay open or excision of perianal fistula (including seton placement)	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 (eg, examination under anesthesia)	JHW96

Supplementary Table 8. Montreal Classification of Pediatric, Adult, and Elderly Patients in Sweden 2006–2013, According to all Available Registry Entries (as Prospectively Recorded in Routine Care) at End of Follow-up

	Pediatric n (%)	Adult n (%)	Elderly n (%)
Crohn's disease	(N = 1239)	(N = 5847)	(N = 1937)
L1	352 (28)	2216 (38)	708 (37)
L2	251 (20)	1356 (23)	378 (20)
L3LX	636 (51)	2275 (39)	851 (44)
B1	1036 (84)	4763 (81)	1433 (74)
B2	58 (5)	542 (9)	436 (23)
B3	158 (13)	646 (11)	105 (5)
P	260 (21)	1008 (17)	150 (8)
Ulcerative colitis	(N = 1058)	(N = 10,290)	(N = 3596)
E1	83 (8)	2385 (23)	509 (14)
E2	127 (12)	2862 (28)	1088 (30)
E3	578 (55)	3541 (34)	989 (28)
EX	270 (26)	1502 (15)	1010 (28)

Supplementary Table 9. Number (n) and Incidence Rate Ratios (IRR) of Outpatient Visits and Hospitalizations With Inflammatory Bowel Disease (IBD) as Main Diagnosis From Date of Second Diagnosis to End of Follow-up. Comparing Adult and Elderly Onset Crohn's Disease (CD) and Ulcerative Colitis (UC) Patients, Stratified for Montreal Classification (Adult Onset is Reference)

	No. of patients	Follow-up time, y median (min-max)	Outpatient visits			Hospitalizations		
			Total no. of visits Median (min-max)	Mean, median no. of visits/years of follow-up	IRR (95% CI)	Total no. of visits Median (min-max)	Mean, median no. of visits/years of follow-up	IRR (95% CI)
CD								
L1								
Adult	2216	4.3 (0-8.9)	5 (0-57)	2.0, 1.4	1 (ref)	0 (0-26)	0.2, 0	1 (ref)
Elderly	708	3.9 (0-8.9)	4 (0-49)	1.6, 1.2	0.8 (0.8-0.9)	0 (0-10)	0.7, 0	0.8 (0.7-1.0)
L2								
Adult	1356	5.0 (0-8.9)	6 (0-103)	2.4, 1.6	1 (ref)	0 (0-45)	0.2, 0	1 (ref)
Elderly	378	4.1 (0-8.9)	4 (0-54)	1.7, 1.1	0.8 (0.7-0.9)	0 (0-11)	0.5, 0	1.1 (0.8-1.4)
L3, LX								
Adult	2275	4.3 (0-9.0)	5 (0-105)	1.9, 1.3	1 (ref)	0 (0-42)	0.2, 0	1 (ref)
Elderly	851	3.1 (0-8.9)	1 (0-47)	1.1, 0.6	0.6 (0.5-0.6)	0 (0-11)	1.8, 0	0.9 (0.7-1.1)
B1								
Adult	4338	4.3 (0-8.9)	5 (0-97)	1.9, 1.3	1 (ref)	0 (0-17)	0.1, 0	1 (ref)
Elderly	1364	3.4 (0-8.9)	2 (0-47)	1.3, 0.8	0.7 (0.7-0.8)	0 (0-9)	0.9, 0	0.9 (0.8-1.1)
B2, B3, P								
Adult	1509	4.8 (0-9.0)	8 (0-105)	2.5, 1.9	1 (ref)	1 (0-45)	0.3, 0.1	1 (ref)
Elderly	573	3.9 (0-8.8)	4 (0-54)	1.6, 1.2	0.7 (0.6-0.7)	0 (0-11)	1.7, 0	0.8 (0.7-0.9)
UC								
E1, E2								
Adult	5247	3.9 (0-9.0)	3 (0-125)	1.4, 1.0	1 (ref)	0 (0-17)	0.1, 0	1 (ref)
Elderly	1597	3.7 (0-8.9)	2 (0-50)	1.2, 0.8	0.8 (0.8-0.9)	0 (0-19)	0.3, 0	1.9 (1.5-2.3)
E3								
Adult	3541	4.9 (0-9.0)	6 (0-84)	1.9, 1.4	1 (ref)	0 (0-19)	0.3, 0	1 (ref)
Elderly	989	4.5 (0-8.9)	4 (0-33)	1.5, 1.1	0.8 (0.8-0.8)	0 (0-10)	1.7, 0	1.4 (1.2-1.6)
EX								
Adult	1502	3.7 (0-8.9)	2 (0-44)	1.1, 0.8	1 (ref)	0 (0-5)	0.1, 0	1 (ref)
Elderly	1010	2.9 (0-8.9)	1 (0-20)	0.8, 0.3	0.7 (0.6-0.7)	0 (0-5)	2.2, 0	2.3 (1.7-3.0)

NOTE. Bold values indicate P value $<.05$.
B, behaviour; E, extent; L, location; P, perianal modifier.

Supplementary Table 10. Number (n) and Incidence Rate Ratio's (IRR) of Outpatient Visits and Hospitalizations (due to any Diagnosis) Following Second IBD Diagnosis. Comparing Pediatric, Adult and Elderly Onset IBD Patients With Matched IBD-free Reference Individuals

	No. of patients	Follow-up time, y Median (min-max)	Outpatient visits		Hospitalizations	
			N visits Median (min-max)	IRR (95% CI)	No. of visits median (min-max)	IRR (95% CI)
Pediatric						
IBD						
Patients	2914	4.9 (0.1–9.0)	18 (0–226)	6.9 (6.5–7.2)	1 (0–75)	6.9 (6.3–7.5)
Comparators	29,103	4.9 (0–9.0)	1 (0–189)	1 (ref)	0 (0–83)	1 (ref)
CD						
Patients	1239	5.1 (0.3–9.0)	20 (0–194)	7.5 (6.9–8.0)	1 (0–41)	7.5 (6.6–8.5)
Comparators	12,364	5.1 (0–9.0)	1 (0–145)	1 (ref)	0 (0–83)	1 (ref)
UC						
Patients	1058	5.2 (0.1–9.0)	16 (0–107)	6.0 (5.5–6.5)	1 (0–61)	5.9 (5.1–6.7)
Comparators	10,571	5.2 (0–9.0)	1 (0–118)	1 (ref)	0 (0–47)	1 (ref)
Adult						
IBD						
Patients	18,477	4.2 (0–9.0)	9 (0–963)	3.6 (3.6–3.7)	0 (0–184)	3.6 (3.5–3.7)
Comparators	183,721	4.2 (0–9.0)	1 (0–953)	1 (ref)	0 (0–131)	1 (ref)
CD						
Patients	5847	4.4 (0–9.0)	12 (0–516)	4.3 (4.2–4.5)	1 (0–184)	4.9 (4.6–5.2)
Comparators	58,187	4.4 (0–9.0)	2 (0–953)	1 (ref)	0 (0–131)	1 (ref)
UC						
Patients	10,290	4.2 (0–9.0)	8 (0–963)	3.1 (3.0–3.2)	0 (0–71)	2.6 (2.5–2.8)
Comparators	102,252	4.2 (0–9.0)	1 (0–787)	1 (ref)	0 (0–98)	1 (ref)
Elderly						
IBD						
Patients	6443	3.5 (0–8.9)	10 (0–954)	2.5 (2.4–2.6)	2 (0–48)	3.4 (3.2–3.6)
Comparators	63,276	3.8 (0–9.0)	3 (0–1186)	1 (ref)	0 (0–75)	1 (ref)
CD						
Patients	1937	3.6 (0–8.9)	12 (0–457)	2.8 (2.6–3.0)	2 (0–48)	4.0 (3.7–4.4)
Comparators	19,042	3.9 (0–9.0)	4 (0–852)	1 (ref)	0 (0–62)	1 (ref)
UC						
Patients	3596	3.6 (0–8.9)	10 (0–954)	2.2 (2.1–2.3)	1 (0–37)	2.9 (2.7–3.1)
Comparators	35,274	3.8 (0–9.0)	3 (0–1186)	1 (ref)	0 (0–75)	1 (ref)

Bold values indicate P value $< .05$.

CD, Crohn's disease; IBD, inflammatory bowel disease; UC, ulcerative colitis.