GASTROENTEROLOGY 1991;100:350–358

The Epidemiology of Inflammatory Bowel Disease: A Large, Population-Based Study in Sweden

ANDERS EKBOM, CHARLES HELMICK, MATTHEW ZACK, and HANS–OLOV ADAMI

Department of Surgery, University Hospital, Uppsala, Sweden; and Aging and Statistics Branch, Division of Chronic Disease Control and Community Intervention, Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control, Atlanta, Georgia

Previous population-based incidence studies of inflammatory bowel disease are limited by small numbers, short duration, or inadequate case-finding. To address these problems, we identified all persons with confirmed ulcerative colitis (n = 2509) or Crohn's disease (n = 1469) in the Uppsala Health Care Region from 1965 to 1983. Age-specific incidence rates by sex were slightly greater for males with ulcerative colitis and females with Crohn's disease. Incidence rates for ulcerative colitis and Crohn's disease were higher in urban than rural areas. The annual incidence rate of ulcerative colitis increased from less than 7 per 100,000 to more than 12 per 100,000 during the study period, while the rate for Crohn's disease remained between 5 and 7 per 100,000. The increase in the incidence of ulcerative colitis was the result of a marked increase in the number of patients with ulcerative proctitis. Analyses by 5-year birth cohorts suggest that those born from 1945 through 1954 were at higher risk for ulcerative colitis and Crohn's disease, and that this effect was accounted for by those born in the first half of the year. The seasonality in the cohort effect, combined with the urban preponderance of disease, suggests that environmental causes may be involved in ulcerative colitis and Crohn's disease.

Inflammatory bowel diseases, consisting of ulcerative colitis and Crohn's disease, are among the most serious and perplexing of digestive diseases. Published studies (1–30) over the past 20 years have described some epidemiological characteristics of inflammatory bowel disease, but many of these deal only with hospitalized patients, small populations, or short time periods and may be unrepresentative of inflammatory bowel disease in the larger population over time. Furthermore, these studies usually examined either ulcerative colitis or Crohn's disease, which makes it difficult to compare the epidemiologic patterns of the two diseases. To overcome those limitations, we describe the crude and age-standardized incidence rates for patients diagnosed with ulcerative colitis or with Crohn's disease in the Uppsala Health Care Region in Sweden from 1965 through 1983 over time and by age, sex, urban/rural residence, extent of disease at diagnosis, and birth cohort.

Materials and Methods

Case Finding

Possible cases were found by searching the Inpatient Registry and pathology department records. The Inpatient Registry is a computerized listing of nonpsychiatric inpatient care anywhere in Sweden for residents of the Uppsala Health Care Region (situated in central Sweden with a population of about 1.3 million) during the period 1965 through 1983 (31). Men doing their compulsory military service lasting just under 1 year are excluded. However, because more than half of Uppsala region conscripts are stationed within the region during their service, it is possible to trace their illness through local pathology departments. Moreover, because a diagnosed inflammatory bowel disease is reason enough for discharge, we have probably failed to detect only a handful of cases—those stationed outside the Uppsala region with just one episode of disease until 1983.

From the Inpatient Registry, we selected all discharges for conditions that might include cases of either ulcerative colitis or Crohn's disease using the Swedish adaptation of ICD-7 codes (572.00, 572.09, 572.20, and 572.21) for the

Abbreviations used in this paper: **CI, confidence interval; OR, odds ratio.**

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period from 1965 to 1968 and of ICD-8 codes (561.04, 563.00, 563.10, 563.99, 564.10, and 569.02) later on. Moreover, patients under the age of 40 with a discharge code of diverticulitis coli (572.11 or 562.10) were also scrutinized. We also used ICD-7 codes after 1968 to find 12 patients who had been miscoded after the formal switch to ICD-8.

To identify individuals who had an outpatient diagnosis of ulcerative colitis or Crohn's disease confirmed by histopathological examination, we reviewed the records of the six departments of clinical pathology in the region for any bowel histopathology. These departments performed all inpatient and outpatient pathology for all but one hospital in the region; this hospital, a forerunner in the use of colonoscopy in Sweden, had a policy of admitting all those with suspected inflammatory bowel disease, thus eliminating the need for histopathologic records to identify cases. We were thus able to identify virtually all outpatients with histopathologically confirmed or suspected inflammatory bowel disease.

Cases among outpatients treated without a biopsy would not be identified by our review methods; however, the number of such cases is probably negligible because of clinical practices in the region during the study period. Until the end of the 1960s, because of a surplus of hospital beds and the prevailing clinical practice of using a barium enema to determine the extent of disease, almost all patients suspected to have ulcerative colitis were admitted. As the surplus of beds decreased and patients suspected to have ulcerative colitis were evaluated as outpatients, evaluation without a rectal biopsy was regarded as incomplete. Therefore, histopathology was routinely studied. The only exception occurred among pediatric patients suspected to have ulcerative colitis, but this group had almost always been evaluated as inpatients. Patients who may have Crohn's disease, especially those with the disease confined to the small bowel or the proximal colon, have nearly always been evaluated and treated as inpatients during the study period (1). Furthermore, evaluations of patients with Crohn's disease would have been considered incomplete without a rectal biopsy or a biopsy derived from colonoscopy.

To assess the extent to which patients diagnosed during the study period were missed because they underwent biopsy for the first time after 1983, we scrutinized reports through 1987 in three pathology departments and through 1984 in one. In those departments, which diagnose more than 80% of inflammatory bowel disease histopathology, only eight new patients diagnosed during the study period were identified and added to the study.

To test the completeness of our case finding, we compared cases from our study cohort with those in a population-based inflammatory bowel disease registry (about 300 patients) at the hospital in Östersund and in previously studied case series in the Uppsala Health Care Region (1,20,24; and Loof, unpublished data). No additional incident cases were found.

Case Definition

The medical histories of possible cases were reviewed from the pathology reports. If the results of the histopathological examination was inconclusive, if information regarding extent and year at diagnosis was missing, or if no histopathological report existed among those identified through the Inpatient Registry, the patient's chart was retrieved from the hospital or physician's office. If the information given in these charts was not sufficient to diagnose ulcerative colitis or Crohn's disease unequivocally on the basis of the following case definition, it was supplemented by information from charts retrieved from other physicians or hospitals.

A case was defined as an instance of ulcerative colitis or Crohn's disease from 1965 through 1983 among residents of the Uppsala Health Care Region that fulfilled the criteria described by Garland (32) for definite and probable cases with some additional requirements.

1. For ulcerative colitis and Crohn's disease: previous radiation treatment of the abdominal tract, antibiotic therapy, or positive stool cultures associated with the patient's symptoms excluded a case from this study.
2. For ulcerative colitis: besides endoscopy, there had to be a history of bleeding or diarrhea.
3. For Crohn's disease: a laparotomy report without positive histology had to be confirmed later by radiologic examination.

Typically, some patients have radiologic, endoscopic, or pathologic evidence of definite or probable inflammatory bowel disease, but the distinction between ulcerative colitis and Crohn's disease is not always clear. In this event, we chose to use the treating physician's latest assessment. When there was no assessment, we assigned the most likely diagnosis on the basis of our review. When reviewing the pathology reports and patient charts in 1988, we used all information available at that date. Because the interval between the original diagnosis and the time the patient's chart was assessed for this study spanned from 5 to 23 years, the disease symptoms and signs had evolved long enough after the original diagnosis that almost all of the patients were probably assigned to the correct group (33).

Data Elements

Information was gathered on each patient's year and month of birth, sex, diagnosis, year of diagnosis, county of residence at diagnosis, extent of disease at diagnosis, positive histopathology, and whether the patient had been in any previous studies. The anatomic extent of ulcerative colitis, which had been assessed by barium enema, endoscopy, or both at the time of diagnosis for most patients, was categorized as follows (Table 1):

1. Proctitis: no involvement proximal to the rectum.
2. Extensive colitis: involvement proximal to the rectum.
    a. Uncertain extent: involvement proximal to the rectum but the extent beyond that was unknown, either because no further evaluation was performed or barium enema revealed no disease despite a sigmoidoscopy showing involvement proximal to the rectum.

Table 1. Number, Percentage, and Mean Age by Anatomic Extent of Disease at Diagnosis for Ulcerative Colitis and Crohn's Disease, Uppsala Health Care Region, 1965–1983

Disease and anatomic extent	Number	%	Mean age (*yr*)
All ulcerative colitis	2509	100.0	37.8
Ulcerative proctitis	1065	42.4	38.7
Extensive colitis[a]	1444	57.6	37.1
Uncertain extent	236	9.4	40.8
Substantial extent	465	18.5	38.1
Pancolitis	743	29.6	35.3
All Crohn's disease	1469	100.0	32.4
Terminal ileum only	543	37.0	33.0
Terminal ileum plus colon	376	25.6	29.4
Colon only	366	24.9	33.0
Terminal ileum plus other small bowel	30	2.0	40.2
Small bowel proximal to terminal ileum	28	1.9	45.6
Small bowl proximal to terminal ileum plus colon	5	0.3	33.8
Terminal ileum, colon, plus other small bowel	18	1.2	30.6
Rectum only	41	2.8	38.1
Appendix only	16	1.1	26.4
Unknown	46	3.1	28.4

[a]See Materials and Methods section for definitions of subtypes.

b. Substantial extent: involvement only up to the hepatic flexure.
c. Pancolitis: involvement of the entire colon.

For 97% of patients, the extent of Crohn's disease had been assessed at the time of diagnosis by radiological contrast studies, endoscopy, and operative specimens; we grouped the extent of disease for these into 10 different categories (Table 1).

Statistics

Population data by age and sex for the region were obtained for each year from the Swedish Population Statistics Registry (34). Incidence rates were directly standardized to the 1970 Swedeish population by 5-year age groups. We fit least-squares estimates to polynomial regression models by using linear or quadratic terms (35). The terms were weighted inversely by the variance of age-specific rates for testing trends in annual age-specific incidence rates and inversely by the variance of the directly standardized rates for testing trends in annual age-standardized incidence rates and mean age at diagnosis (36). For selected comparisons of group means we used Student's *t* test. We calculated odds ratios and test-based 95% confidence intervals (CI) for birth cohort comparisons (37) by using as the expected value the ratio of the actual number of births in the first and second half-years for each specific year in Sweden. Three-year moving averages were used in figures that report annual rates to smoothe the variability in rates and to provide an easier visual image to interpret; actual rates were used for statistical testing.

Results

A total of 6440 persons with a possible diagnosis of ulcerative colitis or Crohn's disease from 1965 through 1983 was found in the Uppsala Health Care Region. Of these, 1434 did not have definite or probable inflammatory bowel disease (most had possible inflammatory bowel disease, but some had ischemic colitis, diverticulitis, and irritable bowel syndrome), 166 were not residents of the region, and 62 had an erroneous national registration number, making diagnostic confirmation impossible. Of the remaining 4778 definite or probable cases, 800 were prevalent cases diagnosed before 1965 and 3978 were incident cases having onset during the study period. The 2509 incident cases of ulcerative colitis yielded a crude average annual incidence rate of 10.4/100,000 persons, and the 1469 incident cases of Crohn's disease yielded a crude average annual incidence rate of 6.1/100,000 persons. Ulcerative colitis and Crohn's disease cases were similar in the proportion that were histopathologically confirmed and that had urban/rural residence at diagnosis; however, patients with ulcerative colitis were older and more often male than patients with Crohn's disease (Table 2).

Annual Age-Adjusted Incidence Rates

The annual age-adjusted incidence rates for ulcerative colitis showed a marked increase from 1965 to 1980, followed by a modest decrease after 1980 (Figure 1). This increase was due almost entirely

Table 2. Characteristics at Diagnosis of Patients With Ulcerative Colitis and Crohn's Disease, Uppsala Health Care Region, 1965–1983

Characteristic	Ulcerative colitis Number	%	Crohn's disease Number	%
Number	2509		1469	
Histopathologically confirmed	2103	84	1303	89
Age group (*yr*)				
0–19	388	15	318	22
20–29	712	28	526	36
30–39	462	18	245	17
40+	947	38	380	26
Mean age (*yr*)	37.8[a]		32.4[a]	
Median age (*yr*)	33		27	
Sex				
Male	1429	57	696	47
Female	1080	43	773	53
Urban/rural residence at diagnosis[b]				
Three urban counties	1575	63	913	62
Three rural counties	934	37	556	38

[a]Difference in mean ages, $P < 0.0001$ by *t* test.
[b]Urban counties are defined as those with ⅔ of residents living in towns of 20,000 or more.

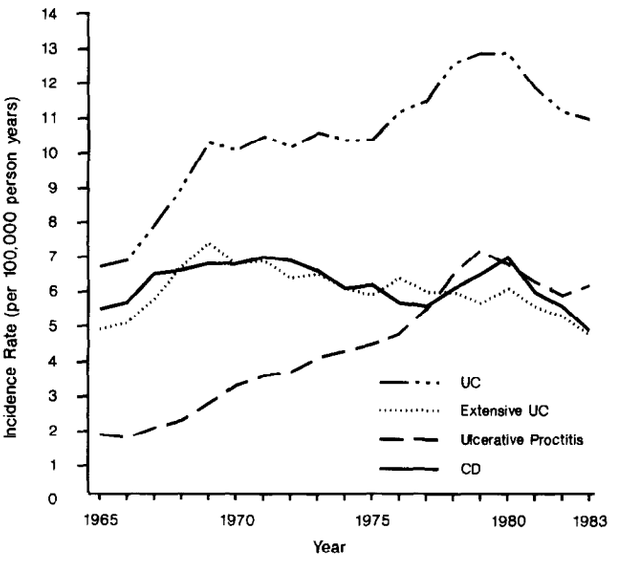

Figure 1. Age-adjusted annual incidence rates for ulcerative colitis (UC), extensive UC, ulcerative proctitis, and Crohn's disease (CD), Uppsala, Sweden, 1965–1983 (moving 3-year average; adjusted to the 1970 Swedish population).

to those with ulcerative proctitis ($P < 0.0001$ for linear term). The rates for extensive colitis varied within a narrow range: the annual incidence rate increased until 1971 and then gradually declined until 1983 ($P = 0.02$ for quadratic term). The rates for Crohn's disease parallelled those for extensive colitis ($P = 0.07$ for quadratic term).

Age-Specific Incidence Rates

Mean age at diagnosis increased over time for ulcerative colitis and its subtypes and for Crohn's disease (Table 3). Age at diagnosis was grouped into four categories: 0–19, 20–29, 30–39, and 40+ years. The annual age-specific incidence rates for extensive colitis, ulcerative proctitis, and Crohn's disease were compared and plotted (Figure 2). Rates for extensive colitis gradually declined for those aged 0–19, ($P = 0.009$ for linear term); markedly increased for those aged 20–29 until the early 1970s, at which time a modest decline began ($P = 0.01$ for quadratic term); and were stable for the older age groups. Rates for ulcerative proctitis increased for all age groups ($P < 0.01$ for linear terms), especially for the three oldest groups ($P = 0.0001$ for linear terms). The annual age-specific incidence rates for Crohn's disease were stable for the youngest and oldest groups, had a bimodal pattern for those aged 20–29 ($P = 0.003$ for quadratic term), and suggest a similar bimodal pattern for those aged 30–39 ($P = 0.06$ for quadratic term).

Age-specific incidence rates for ulcerative colitis and Crohn's disease during the study period suggest a bimodal pattern for the later (1975–1983) years of the study period (Figure 3).

Sex

Ulcerative colitis was 31% more common among males. The male predominance in ulcerative colitis was more striking for those with ulcerative proctitis (male-female ratio, 1.39:1) and those in the 40+ age group (male-female ratio, 1.95:1). Crohn's disease was 12% more common among females (male-female ratio, 1:1.12), but this predominance did not vary by age or extent of disease at diagnosis. Interestingly, when incidence rates for ulcerative colitis and Crohn's disease in each sex were combined, the rates for all inflammatory bowel disease were nearly identical (Figure 4).

Urban/Rural

The annual age-adjusted incidence rates for both diseases in the three most urban counties are consistently higher than those in the three most rural counties (Figure 5). The age-adjusted incidence rates for the entire study period are generally higher in urban than in rural counties for ulcerative proctitis and extensive colitis as well (Table 4).

Extent of Disease

More than 40% of ulcerative colitis patients had ulcerative proctitis, and 30% had pancolitis; more than 65% of Crohn's disease patients had in-

Table 3. Mean Age at Diagnosis, by Type of Disease and Grouped Years at Diagnosis, Uppsala Health Care Region, 1965–1983

Type of disease	1965–1969	1970–1974	1975–1979	1980–1983	*P* value[a] for annual trend
Ulcerative colitis	34.2	37.2	39.2	39.8	<0.0001
Extensive colitis	34.4	37.0	39.3	37.8	0.003
Ulcerative proctitis	33.6	37.6	39.0	41.2	<0.0001
Crohn's disease	30.9	31.0	33.4	34.7	0.06

[a]Probability of *t* test in linear regression model examining trend in mean age over time.

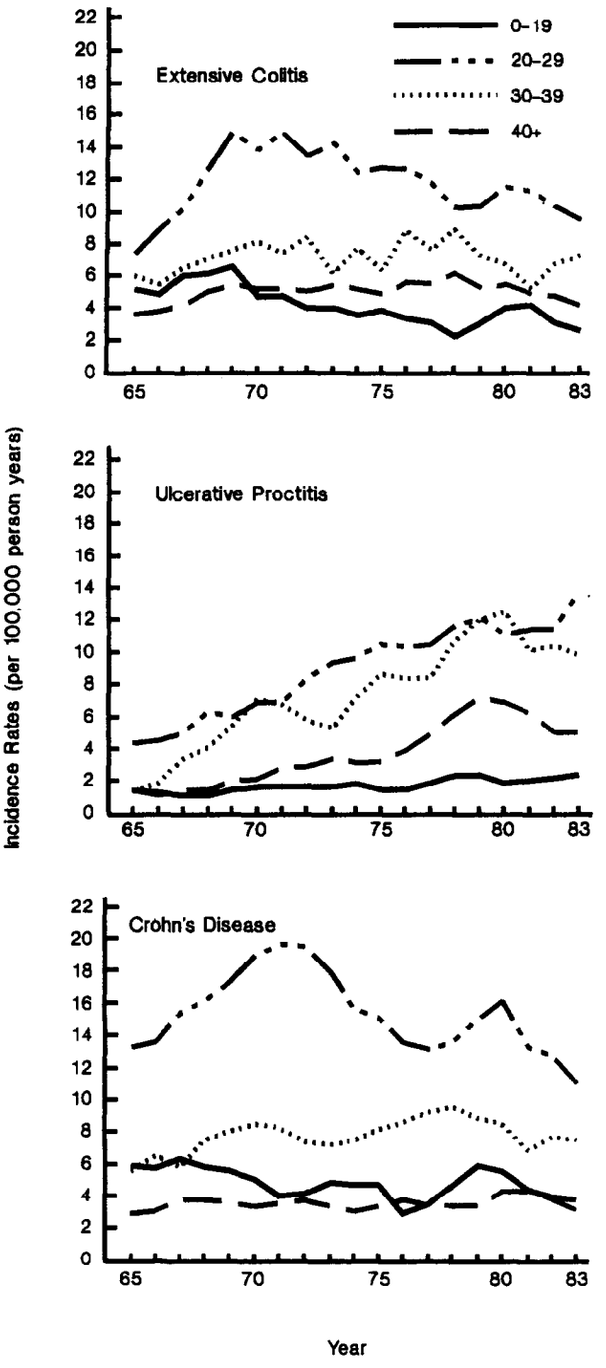

Figure 2. Age-specific annual incidence rates for extensive colitis, ulcerative proctitis, and Crohn's disease, Uppsala, Sweden, 1965–1983 (moving 3-year average).

volvement of terminal ileum at diagnosis (Table 1). Patients with ulcerative colitis were older at diagnosis than those with Crohn's disease (Table 1).

For ulcerative colitis, the mean age at diagnosis was lower for pancolitis than for less extensive disease (Table 1; $P < 0.01$ by t test). The mean age at diagnosis varied depending on the extent of disease. For the three largest categories, there was no difference in the mean age for "terminal ileum only" and "colon only," but a lower mean age at diagnosis for "terminal ileum plus colon" (Table 1; $P < 0.003$ by t test). "Colon only" showed stable incidence rates during the study period, whereas "terminal ileum only" and "terminal ileum plus colon" accounted for the variations in the annual age-standardized incidence rates (Figure 1).

Birth Cohort Effects

We plotted age-specific incidence rates for both ulcerative colitis and Crohn's disease for different 5-year birth cohorts (Figure 6). For comparable age groups, the incidence rates for those born from 1945

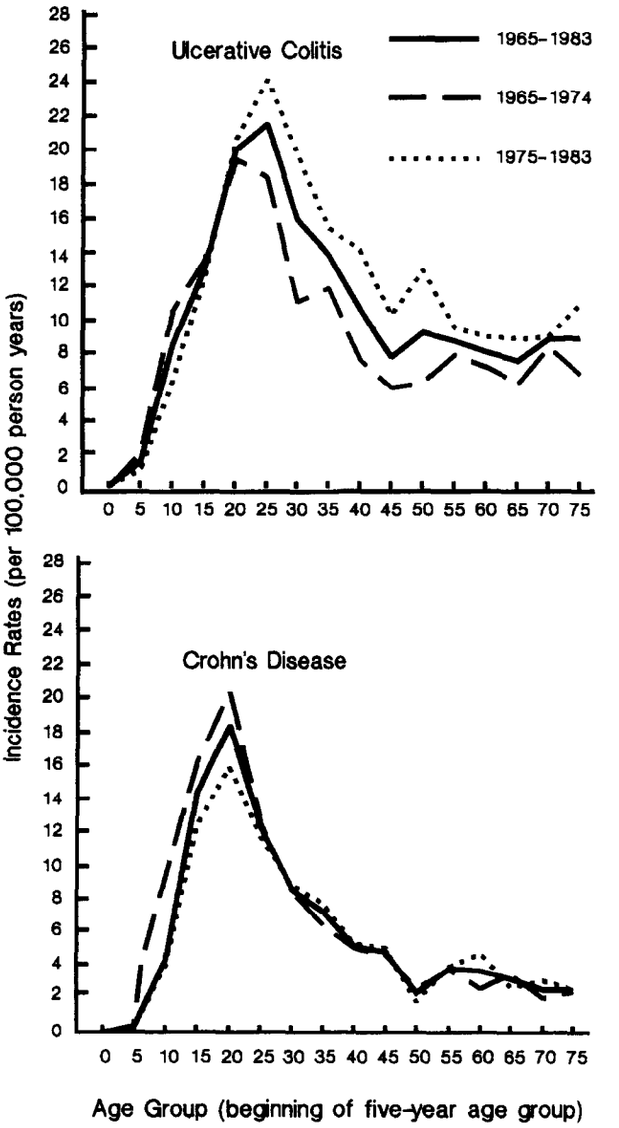

Figure 3. Age-specific incidence rates for ulcerative colitis and Crohn's disease, by overall (1965–1983) and specific (1965–1974, 1975–1983) time periods, Uppsala, Sweden, 1965–1983.

Figure 4. Age-specific incidence rates for ulcerative colitis and Crohn's disease combined, by sex, Uppsala, Sweden, 1965–1983.

through 1954 are higher than for those born before or after this span. In the birth cohort for 1945 through 1949 the age-specific incidence rates are significantly higher ($P < 0.05$) than the others in all age groups with the exception of the age group 35–39 years. However, in the birth cohort 1950 through 1954, only the age group 10–14 years differed significantly from other age groups. This difference is most prominent compared with those born before 1945 but also exists for those born after 1954. Because our preliminary analyses showed an uneven distribution when we were studying time of birth among those born from 1945 through 1954, we calculated age-specific incidence rates for those born the first and second half-

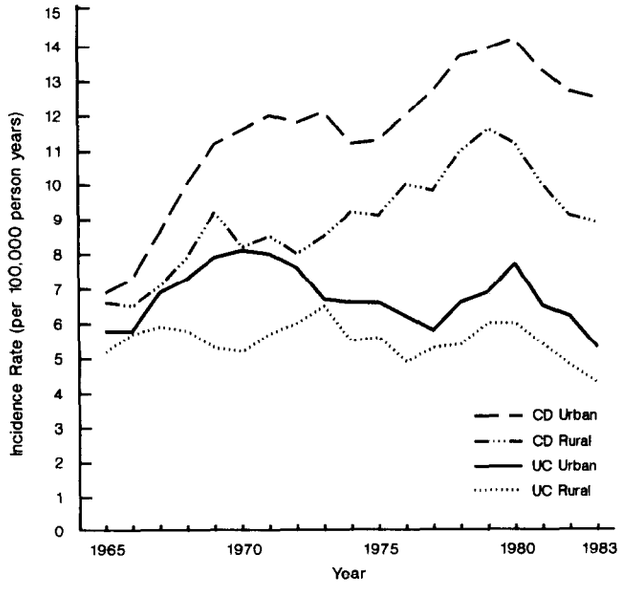

Figure 5. Age-adjusted annual incidence rates for ulcerative colitis (UC) and Crohn's disease (CD), by urban or rural residence, Uppsala, Sweden, 1965–1983 (moving 3-year average; adjusted to the 1970 Swedish population).

years. The age-specific incidence rates for those born in the first half of the year are larger for those born from 1945 through 1954 than for those born outside this period (Figure 7); those born in the second half of the year do not show differences in age-specific rates by birth cohort.

When examined within birth cohorts, incidence rates in the first half-years of 1945 through 1949 and 1950 through 1954 were higher than those in the second half-years [1945–1949: odds ratio (OR) = 1.18, 95% CI, 1.02–1.37; 1950–1954: OR = 1.19, 95% CI, 1.00–1.39]. For all other 5-year birth cohorts, the odds ratios comparing birth during the first and second half-year are very close to 1.0.

Discussion

The increase in the annual age-standardized incidence rates of ulcerative colitis from 1965 through 1983 can be attributed entirely to an increased incidence rate of ulcerative proctitis. The patterns for annual age-standardized incidence rates of extensive ulcerative colitis and Crohn's disease are remarkably similar: both peak in the beginning of the 1970s and gradually decline thereafter. Mean age at diagnosis increased throughout the study period for both ulcerative colitis and Crohn's disease, also evident as a decreasing age-specific rate in the age group from 20 to 29 years and an increasing rate in the age group from 30 to 39 years. This pattern seems to be the result of a cohort phenomenon affecting those born from 1945 through 1954, especially among those born during the first half of the year. For ulcerative colitis, male rates exceed female rates, particularly among older persons and among persons with lesser extent of disease. For Crohn's disease, however, female rates exceed male rates for persons in all age groups and for different extents of disease at diagnosis. Rates for both inflammatory bowel diseases combined were nearly identical for both sexes. For the years studied, urban counties had higher annual incidence rates for both diseases, separately and combined, than rural counties.

References 1–30 consist of all the major population-based studies of inflammatory bowel disease published so far. Compared with the crude rates in the two other population-based Swedish studies, the crude rates in the present study are consistent with trends in rates extrapolated to this study period for ulcerative colitis (24) and nearly identical for Crohn's disease (4). In the case of Crohn's disease, however, the present study shows consistently higher annual incidence rates than three other, largely hospital-based Swedish studies (1,12,20). These values are probably different because the previous studies mainly used inpatient registers supplemented by records

Table 4. Population Characteristics and Age-Standardized Incidence Rates for Inflammatory Bowel Disease by Urban/Rural Counties, Uppsala Health Care Region, 1965–1983

Urban/rural total[a]	1972 Population ($\times 10^6$)	% in towns with 1972 population >20,000	Incidence rate (/100,000) UC	UP	EC	CD
Three urban counties	0.73	70	11.5	4.9	6.7	6.6
Three rural counties	0.54	50	9.2	3.7	5.5	5.4

NOTE. Ages standardized to the 1970 Swedish population.
UC, ulcerative colitis; UP, ulcerative proctitis; EC, extensive colitis; CD, Crohn's disease.
[a]Urban counties defined as those with ⅔ of residents living in towns of 20,000 or more.

from different radiology departments, a procedure that probably missed many outpatient cases, especially those with the disease confined to the colon. Radiology records added only "a few patients" to Bergman's study (1) but none to Hellers's (12); Norlen's study provides no information on this point.

The crude average annual incidence rate for ulcerative colitis in the Uppsala Health Care Region (10.4/100,000) is in the middle of the range of estimates from other countries. The crude average annual incidence rate for Crohn's disease in the region (6.1/100,000) is generally higher than that in other countries except Wales and the United States. Crude incidence rates for ulcerative colitis vary more than the incidence rates for Crohn's disease; this variation is probably due to different diagnostic criteria and case-finding methods in the studies of ulcerative colitis, and to the time trends in diagnosed cases of proctitis.

Findings from all but two international studies (19,30) show the same increasing trend in the annual age-standardized incidence rates observed for ulcerative colitis. Only four other studies (2,3,5,30) have examined the pattern of the incidence of extensive colitis over time. With one exception (2), those studies show, like this one, a slight decrease of annual incidence rate of extensive colitis after the beginning of the 1970s. For proctitis, only two other studies (2,30) have data that address the incidence rate of proctitis over time: both indicate an increasing rate. The decrease in the mean age at diagnosis for patients with more extensive disease has been observed in other studies, but the reason for this decrease is unclear.

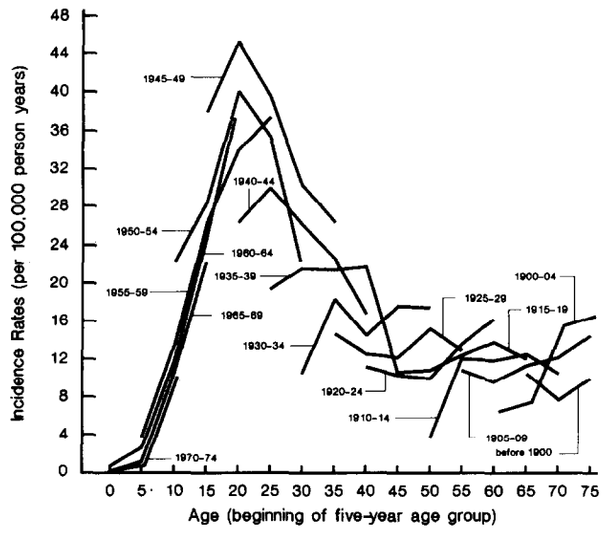

Figure 6. Age-specific incidence rates for ulcerative colitis and Crohn's disease combined, by 5-year birth cohort, Uppsala, Sweden, 1965–1983.

Six other international studies found the trend for Crohn's disease decreased for the annual age-standardized incidence rates after it peaked in the early 1970s, as was found in this study (3–5,10,14,15,18); two other studies, however, do not show this pattern because the incidence rates for the older age groups increased (16,22). For Crohn's disease, only two studies examined extent of disease (14,22): both showed a decreasing proportion confined to the small bowel and an increasing proportion confined to the colon. The female predominance decreased over time. Our findings differ somewhat: although we have a decreasing rate of Crohn's disease confined to the small bowel, the rate for disease confined to the colon remained stable throughout the period studied. The lower mean age at diagnosis for more extensive Crohn's disease, similar to the findings with ulcerative colitis, has not yet been seen in other studies.

The suggestion of bimodality—the second peak in the older age groups—in age-specific incidence rates for both diseases for the period 1975 through 1983 and a hint of bimodality for the period 1965 through 1974 were found in all but two other studies of ulcerative colitis (9,24) and all other studies of Crohn's disease. The amplitude and the age groups involved in the second peak differed substantially, however, among the different studies; but in all studies showing such bimodality, the more recently the study had been undertaken, the more prominent the second peak was—as in the present study (6,15,16,22).

No consensus exists about sex predominance among patients with ulcerative colitis, but most American

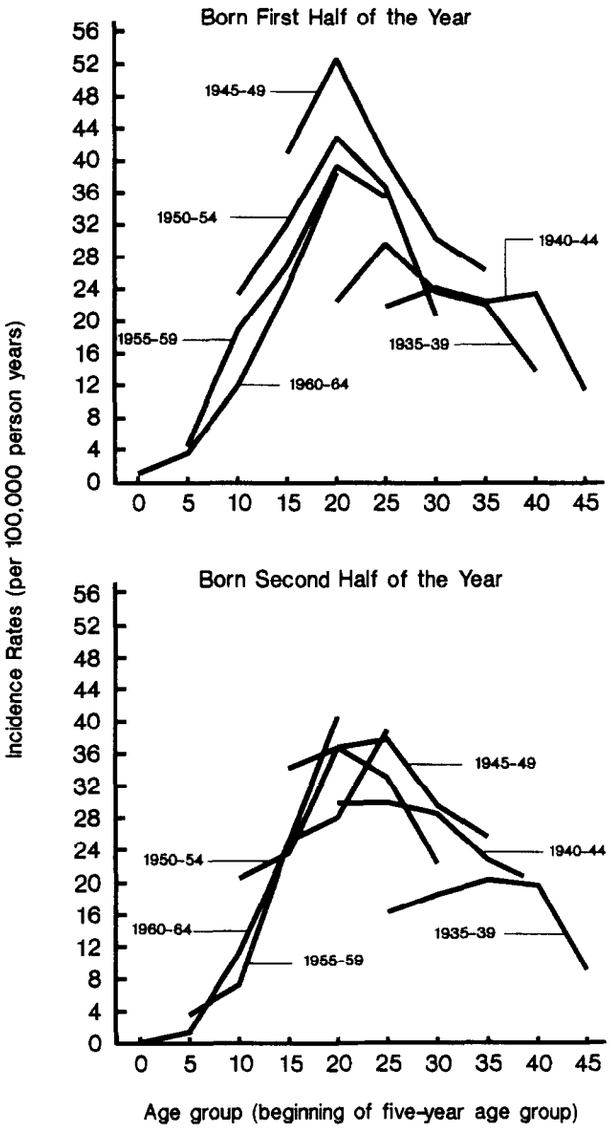

Figure 7. Age-specific incidence rates for ulcerative colitis and Crohn's disease combined, by 5-year birth cohort for those born in the first half year and second half year, Uppsala, Sweden, 1965–1983.

and European studies in the 1970s from areas with high incidence rates show a male predominance (2,5,11,29,30), which our study confirms. The female predominance among Crohn's disease patients in our study is evident in the other studies with only two exceptions (2,23), both of which have few cases.

The three urban counties in our study had consistently higher incidence rates for ulcerative colitis and Crohn's disease than the three rural counties, and this effect might be underestimated as a result of nondifferential misclassification, because the individual information of urban or rural residence at diagnosis was assessed on the basis of the county of residence. This misclassification is likely to be nondifferential and biased towards the null hypothesis, so that the true excess urban risk is underestimated. Among population-based studies examining urban/rural risk, five found a higher incidence rate in urban areas for ulcerative colitis (24,29) or Crohn's disease (10,14,27), and one found no difference for ulcerative colitis (7). In similar studies using the same medical system, urban Copenhagen had a higher incidence rate of extensive ulcerative colitis and Crohn's disease than the rural Faroe Islands (2,3). Better access to health care could explain why the incidence of ulcerative colitis and Crohn's disease is higher in urban areas than that found in rural areas, but such ascertainment bias is unlikely here because the Swedish medical system provides all citizens equal access to medical care of high standard free of change.

The age-specific incidence rates for persons with inflammatory bowel disease who were born from 1945 through 1954 are higher than those for persons who were born in other years (Figure 6); this finding confirms Hellers's observation from Sweden (12) and suggests a birth cohort effect. This effect is most prominent at younger ages but is consistent over all age groups examined and does not represent a shift in age at diagnosis. Other investigators have looked for but not found birth cohort effects for Crohn's disease (3,22), possibly because the number of cases was too small or the period of observation too short or both. No studies, to our knowledge, have tried to find cohort effects for ulcerative colitis.

In our study, much of the birth cohort effect for both diseases occurred in persons born during the first half of the year. The only other study examining possible seasonality in birth dates (38) provided rather vague information and found neither a clear-cut pattern nor significant effects. One conceivable explanation for the birth cohort effect is that throughout the period from 1945 through 1954, with the exception of the years 1945 and 1948, there was evidence of small, annual influenza epidemics in the region, lasting one or more of the months from December to May (39). Although these epidemics were identified on the basis of clinical diagnoses without serological confirmation, it is likely that viruses giving influenzalike symptoms were present in excess during the first half year in 8 of 10 years during the period from 1945 through 1954 compared with 12 of 24 years from 1924 through 1944 and 1955 through 1957.

The presence of a birth cohort effect for both ulcerative colitis and Crohn's disease seems to indicate that events early in life, possibly before birth, play an important role in the etiology of inflammatory bowel disease. An analogous model has been proposed for juvenile diabetes in which most genetically predisposed children infected by rubella in utero will later develop juvenile diabetes (40). Further work,

however, is needed to confirm the birth cohort effect observed and to determine its possible cause.

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Received February 6, 1990. Accepted July 23, 1990.

Address requests for reprints to: Anders Ekbom, M.D., Department of Surgery, University Hospital, S-751 85, Uppsala, Sweden.

Supported by grants from the National Foundation for Ileitis and Colitis, Stiftelsen Nanna och Albert Skantzes minne, Nanna Svartz Grant, and the Swedish Medical Research Council.

The authors thank Dr. Richard Rothenberg and all departments of clinical pathology, internal medicine, pediatrics, and surgery within the Uppsala Health Care Region for valuable support.