Inflammatory bowel disease and pancreatic cancer: a Scandinavian register-based cohort study 1969-2017

Åsa H. Everhov1 | Rune Erichsen2,3 | Michael C. Sachs1 | Lars Pedersen2 | Jonas Halfvarson4 | Johan Askling1 | Anders Ekbom1 | Jonas F. Ludvigsson1,4,5,6 | Henrik Toft Sørensen2 | Ola Olén1

Summary

Background: Patients with inflammatory bowel disease (IBD) have an increased risk of cancer.

Aim: To assess the risk of pancreatic cancer in IBD compared to the general population.

Methods: Patients with incident IBD 1969-2017 were identified in Danish and Swedish National Patient Registers and through biopsy data, and were matched to IBD-free reference individuals by sex, age, place of residence and year of IBD diagnosis. We linked data to Cancer and Causes of Death Registers and examined the absolute and relative risks of pancreatic cancer and pancreatic cancer death.

Results: Among 161 926 patients followed for 2 000 951 person years, 442 (0.27%) were diagnosed with pancreatic cancer compared to 3386 (0.21%) of the 1 599 024 reference individuals. The 20-year cumulative incidence was 0.34% (95% confidence interval 0.30-0.38) vs 0.29% (0.28-0.30). The incidence rate was 22.1 (20.1-24.2)/100 000 person years in the patients (excluding the first year of follow-up: 20.8 [18.8-23.0]), and 16.6 (16.0-17.2) in the reference individuals. The hazard ratio (HR) for pancreatic cancer was increased overall: 1.43 (1.30-1.58), in subtypes (Crohn’s disease: 1.44 [1.18-1.74]; ulcerative colitis: 1.35 [1.19-1.53]; IBD unclassified: 1.99 [1.50-2.64]) and especially in IBD patients with primary sclerosing cholangitis: 7.55 (4.94-11.5). Patients and reference individuals with pancreatic cancer did not differ in cancer stage (P = 0.17) or pancreatic cancer mortality (HR 1.07 [0.95-1.21]).

Conclusions: Patients with IBD had an excess risk of pancreatic cancer, in particular patients with primary sclerosing cholangitis. However, the cumulative incidence difference after 20 years was small: 0.05%, that is, one extra pancreatic cancer per 2000 IBD patients.

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1 | INTRODUCTION

Pancreatic cancer is the seventh leading cause of cancer death worldwide, and both its incidence and mortality are expected to increase. In 2018, the age-standardised incidence rate was 4.8 per 100,000 person years and the mortality rate 4.4. Pancreatic cancer occurs more frequently in men than in women and is more common in industrialised parts of the world, possibly due to lifestyle factors, differences in diagnostic intensity and an older population. Established risk factors for pancreatic cancer include smoking, obesity, chronic pancreatitis, diabetes mellitus, non-0 blood type, cystic fibrosis, neoplastic pancreatic cyst, helicobacter pylori infection, and hereditary factors.

Patients with inflammatory bowel disease (IBD) have an increased risk of intestinal and extra-intestinal cancer overall, as well as an increased risk of other pancreatic diseases, such as pancreatitis. An increased risk of pancreatic cancer was reported in patients with primary sclerosing cholangitis (PSC) compared to the general population in a study where 79% of the patients with PSC had IBD, and one study found an increased risk of pancreatic cancer in IBD patients with PSC compared to IBD patients without PSC. However, no significant excess risk has been observed in previous population-based studies of pancreatic cancer in patients with IBD compared to the population, except among female patients with Crohn’s disease in Korea. However, previous studies on overall cancer risk may have been too underpowered to analyse specific cancers (26 cases of pancreatic cancer found in six studies combined), and no study has specifically investigated the risk of pancreatic cancer in patients with IBD.

To test the hypothesis that IBD patients have an increased risk of pancreatic cancer, we performed a binational register-based cohort study, based on data prospectively recorded in routine clinical practice, with the aim to assess the absolute and relative risks of pancreatic cancer and pancreatic cancer death in patients with IBD compared to the general population.

2 | METHODS

2.1 | Study design

We performed a cohort study where patients with IBD were compared to a matched reference population with respect to pancreatic cancer.

2.2 | Setting and data sources

Denmark and Sweden are high-income countries with populations of 5.7 and 10.1 million in 2017 respectively. In both countries, healthcare is tax-funded with universal access to care. The personal identity number assigned to all residents in each country allows for linkage of registers containing national data on demographics, morbidity, mortality and histopathology with virtually no loss to follow-up (Table S2). Patients with IBD are typically handled by gastroenterologists in hospital-based outpatient clinics.

2.3 | Participants

2.3.1 | Patients with IBD

We used the International Classification of Disease (ICD) codes (Table S3) in the National Patient Registers (Table S2) to identify incident cases with IBD (in Denmark between January 1979 and December 2011 and in Sweden between January 1969 and December 2017). We requested either ≥2 records of IBD in the National Patient Registers or ≥1 record of IBD in the National Patient Registers plus a colorectal biopsy record suggestive of IBD from the Swedish ESPRESSO Biopsy Register or the Danish Pathology Register. The IBD subtype definition was based on the first two diagnostic listings, and patients with listings of both Crohn’s disease and ulcerative colitis, or a listing of IBD unclassified (IBD-U) were defined as IBD-U, and included in the IBD group.

We defined PSC according to ICD-codes in the National Patient Registers (≥1 listing) (Table S3).

2.3.2 | Matched reference individuals

For each IBD patient, we identified up to 10 reference individuals in the National Population Registers and matched them by sex, age, calendar year and place of residence. The matched reference individuals had to be alive and free of IBD at the start of follow-up of the index patient, and stopped contributing person-time as reference individuals if and when they were diagnosed with IBD.

2.4 | Pancreatic cancer

Data on diagnosis of exocrine pancreatic cancer and cancer stage were retrieved from the Cancer Registers (Table S4), and pancreatic cancer death from the Causes of Death Registers. The proportion of patients and reference individuals undergoing pancreatic resections (indicating potentially curable disease) was estimated using procedure codes for pancreatic surgery (Table S5).

2.5 | Statistical methods

2.5.1 | Time at risk

To avoid immortal time bias, follow-up started on the date of the second diagnostic record of IBD in a patient register or the date when a patient had first accumulated one diagnostic record of IBD and one record of a colorectal biopsy suggestive of IBD. Stratification for age
and year of IBD onset was based on the date of the first diagnostic record. Follow-up ended with death, emigration or end of follow-up (31 December 2011 in Denmark and 31 December 2017 in Sweden), whichever came first.

2.5.2 Incidence rates and hazard ratios

We report crude incidence rates (number of pancreatic cancer diagnoses by person-time at risk) but also country-specific incidence rates standardised to the Nordic population in the year 2000. We calculated hazard ratios (HRs) with 95% confidence intervals (CIs) to quantify the association between IBD case status and pancreatic cancer diagnosis using Cox regression adjusted for age at IBD diagnosis, sex, year of IBD diagnosis and place of residence. We additionally calculated incidence rates and HRs stratified by country, sex, year of IBD diagnosis and age at IBD diagnosis in categories. In the stratum-specific estimates of incidence rates and HRs for patients with PSC, follow-up started when the patient fulfilled criteria for both IBD and PSC.

2.5.3 Multi-state model

To investigate the associations between IBD and the occurrence of different competing events during follow-up, we specified a multi-state model with the following states: initial (start of follow-up), pancreatic cancer, pancreatic cancer death and death from other causes. Individuals started in the initial state, and were considered censored at the date of emigration, or at the end of the study period. We estimated the cause-specific cumulative incidence rates for the transitions: initial to pancreatic cancer, initial to pancreatic cancer death, initial to other death, pancreatic cancer to pancreatic cancer death, pancreatic cancer to other death, using the Aalen-Johansen estimator. We computed adjusted transition HRs for each of those transitions using a series of Cox regression models, adjusted for the same covariates as above and additionally adjusting for tumour stage for the transitions from pancreatic cancer. Finally, we assessed the time-varying association between IBD and each of the transition hazards using the semi-parametric additive hazards model as implemented in the timereg R package. These models allowed for a time-varying effect of IBD on each transition hazard and were adjusted for time-invariant effects of sex, age at diagnosis, year of IBD diagnosis and country.

2.5.4 Quantitative bias analysis

We conducted a sensitivity analysis for the HRs of IBD for pancreatic cancer to unmeasured confounding due to smoking using

FIGURE 1 Flow chart of inclusion and exclusion criteria
the quantitative bias analysis. The figures display the estimated HRs that would have been observed (y-axis), if smoking were measured and had a particular association with the exposure and the outcome.

R statistical software (version 3.6.1, R Foundation for Statistical Computing, Vienna, Austria) and the survival package (version 2.38, Therneau, T (2015), https://CRAN.R-project.org/package=survival) were used for the analyses.

3 | RESULTS

3.1 | Characteristics of the study population

We identified 161 926 patients with incident IBD and no previous diagnosis of pancreatic cancer from Denmark and Sweden, who were matched to 1 599 024 IBD-free reference individuals from the general population (Figure 1). The majority (70%) of patients were from
Sweden. Ulcerative colitis was more common (60%) than Crohn's disease (29%) and IBD-U (11%) (Table 1). Median age at IBD diagnosis was 38 years, 51% were followed for 10 years or more and 2.1% were diagnosed with PSC at or during follow-up (Table S6). Descriptive statistics by country are found in Table S6.

### 3.2 | Pancreatic cancer

During a follow-up of 2,000,951 person-years, 442 patients with IBD (0.27%) were diagnosed with pancreatic cancer compared to 3386 (0.21%) individuals from the reference population during 20,402,533 person years (Table 2). The 10-year cumulative incidence was 0.18% (95% CI: 0.16-0.20) in patients and 0.14% (0.13-0.15) in the reference population (difference 0.04% [0.02-0.06]), and the 20-year cumulative incidence was 0.34% (0.30-0.38) vs 0.29% (0.28-0.30) (difference 0.05% [0.01-0.09]). The incidence rate was 22.1 (20.1-24.2) events/100,000 person-years in the patients and 16.6 (16.0-17.2) in the reference population. The standardised incidence rate was 9.04 (8.15-9.93) in patients vs 7.02 (6.77-7.26) in the matched reference individuals and more common for both patients with IBD and matched reference population in Denmark than in Sweden (Table S7).

The adjusted HR for pancreatic cancer in patients with IBD compared to the reference population was 1.43 (1.30-1.58) and decreased to 1.34 (1.20-1.48) excluding the first year of follow-up (Table 3). The HR was 1.44 (1.18-1.74) in patients with Crohn's disease, 1.35 (1.19-1.53) for ulcerative colitis and 1.99 (1.50-2.64) for IBD-U. The HR was 1.56 (1.37-1.79) in men and 1.30 (1.12-1.50) in women. The HR point estimates were highest in patients diagnosed with IBD as children: 2.78 (1.13-6.86) and lowest in those diagnosed as elderly (≥60 years): 1.33 (1.14-1.56), but with overlapping 95% CIs. IBD patients with PSC were at increased risk of pancreatic cancer with 34/442 (8%) of pancreatic cancer cases in IBD occurring in IBD patients with a PSC diagnosis. The overall HR in IBD patients with PSC was 7.55 (4.94-11.5) and the risk decreased with the duration of concurrent PSC (HR duration <5 years: 12.0 [6.42-22.3], duration 5-10 years: 10.1 [4.06-25.3], duration ≥10 years: 2.83 [1.09-7.32]). Stratified risk estimates by IBD subtype are presented in Table S8.

### 3.3 | Pancreatic cancer stage, surgery and death

Cancer stage was not different between patients with IBD and the reference population (P = 0.17), and less than 10% of both IBD patients and reference individuals underwent resectional surgery of the pancreas (Table S9). In the multi-state model, patients with IBD were at increased risk of pancreatic cancer, pancreatic cancer death and death from other causes. However, IBD patients with a diagnosis of pancreatic cancer were not at increased risk of dying from pancreatic cancer compared to reference individuals also diagnosed with pancreatic cancer (Figure 2, Figure 3, Table S10). The results were similar when stratifying for IBD subtype (Crohn's disease: Figure S1 and Table S11; ulcerative colitis: Figure S2 and Table S12). The cumulative additive effect of IBD on the hazard for pancreatic cancer diagnosis in patients with IBD vs reference individuals increased with time from diagnosis, as did the risk of dying from other causes (Figure 4). The relative pancreatic cancer-free survival
rate decreased with time from diagnosis, but we did not observe any
dramatic changes across calendar periods (Figure 5). The HR for pancre-
atic cancer diagnosis restricted to all study participants at risk during the
last 10 years of follow-up was 1.34 (1.01-1.77) for Crohn’s disease, 1.30
(1.09-1.55) for ulcerative colitis and 1.64 (1.04-2.59) for IBD-U.

3.4 | Quantitative bias analysis

Smoking has been positively associated with pancreatic cancer
with an HR of 1.74 (95% CI 1.61-1.87) for current smokers and 1.20
(95% CI 1.11-1.29) for former smokers. The prevalence of daily
smoking in Sweden was 14% in 2006 and 7% in 2018 and daily
smoking in Danish adults (>15 years old) was 16% in 2015. An
unmeasured binary confounding variable (eg smoking status) with
an HR for pancreatic cancer diagnosis of two (ie even higher than
described) would need to have at least a 60% difference in preva-
lence between patients with IBD and the reference population,
that is, 80% among IBD and 20% in the reference population, to
lower the estimated HR for IBD to 1.00 (Figure S2). It is, therefore,
extremely implausible that smoking explains our main findings
more than marginally.

### TABLE 3

| Incidence rates (per 100 000 person years) and hazard ratios for pancreatic cancer in patients with inflammatory bowel disease and matched reference population |
|---------------------------------------------------------------|
| **Incidence rate in cases** | **Incidence rate in reference** | **Hazard ratio** |
| **N events, IR (95% CI)** | **N events, IR (95% CI)** | **(95% CI)** |
| Total | 442, 22.1 (20.1-24.2) | 3386, 16.6 (16.0-17.2) | 1.43 (1.30-1.58) |
| Denmark | 177, 36.3 (31.3-42.1) | 1276, 25.6 (24.3-27.1) | 1.53 (1.30-1.79) |
| Sweden | 265, 17.5 (15.5-19.8) | 2110, 13.7 (13.1-14.3) | 1.38 (1.21-1.56) |
| Crohn’s disease | 116, 18.3 (15.3-22.0) | 907, 14.0 (13.1-14.9) | 1.44 (1.18-1.74) |
| Ulcerative colitis | 270, 23.0 (20.4-25.9) | 2146, 18.0 (17.3-18.8) | 1.35 (1.19-1.53) |
| IBD unclassified | 56, 29.0 (22.3-37.7) | 333, 16.6 (14.9-18.5) | 1.99 (1.50-2.64) |

#### Sex

| Incidence rate in cases | Incidence rate in reference | Hazard ratio |
|-------------------------|----------------------------|--------------|
| **N events, IR (95% CI)** | **N events, IR (95% CI)** | **(95% CI)** |
| Female | 198, 19.4 (16.9-22.3) | 1696, 16.3 (15.5-17.0) | 1.30 (1.12-1.50) |
| Male | 244, 24.9 (22.0-28.2) | 1690, 17.0 (16.2-17.8) | 1.56 (1.37-1.79) |

#### Age at first IBD diagnosis (years)

| Incidence rate in cases | Incidence rate in reference | Hazard ratio |
|-------------------------|----------------------------|--------------|
| **N events, IR (95% CI)** | **N events, IR (95% CI)** | **(95% CI)** |
| <18 | 6, 2.69 (1.21-5.99) | 22, 0.99 (0.65-1.50) | 2.78 (1.13-6.86) |
| 18 to <40 | 94, 9.18 (7.50-11.2) | 576, 5.64 (5.20-6.12) | 1.68 (1.35-2.09) |
| 40 to <60 | 168, 32.3 (27.8-37.6) | 1310, 24.6 (23.3-26.0) | 1.34 (1.14-1.57) |
| ≥60 | 174, 74.1 (63.9-86.0) | 1478, 55.9 (53.1-58.8) | 1.33 (1.14-1.56) |

#### Year of first diagnosis

| Incidence rate in cases | Incidence rate in reference | Hazard ratio |
|-------------------------|----------------------------|--------------|
| **N events, IR (95% CI)** | **N events, IR (95% CI)** | **(95% CI)** |
| 2003-2017 | 89, 20.6 (16.8-25.4) | 636, 14.6 (13.5-15.8) | 1.51 (1.21-1.89) |
| 1990-2002 | 164, 21.0 (18.0-24.4) | 1350, 17.0 (16.1-17.9) | 1.33 (1.13-1.57) |
| 1977-1989 | 146, 24.1 (20.5-28.4) | 1049, 16.9 (15.9-18.0) | 1.54 (1.29-1.83) |
| 1969-1976 | 43, 23.6 (17.5-31.9) | 351, 18.4 (16.6-20.4) | 1.37 (1.00-1.88) |

#### Years of follow-up

| Incidence rate in cases | Incidence rate in reference | Hazard ratio |
|-------------------------|----------------------------|--------------|
| **N events, IR (95% CI)** | **N events, IR (95% CI)** | **(95% CI)** |
| 0 to <1 | 58, 37.2 (28.8-48.1) | 216, 13.9 (12.1-15.9) | 2.73 (2.05-3.65) |
| 1 to <5 | 94, 13.6 (11.1-16.7) | 760, 11.0 (10.2-11.8) | 1.31 (1.06-1.62) |
| 5 to <10 | 90, 8.22 (6.69-10.1) | 779, 7.03 (6.55-7.54) | 1.26 (1.01-1.57) |
| 10 to <20 | 108, 7.88 (6.52-9.51) | 993, 7.10 (6.67-7.56) | 1.22 (1.00-1.48) |
| ≥20 | 92, 10.8 (8.80-13.2) | 638, 7.15 (6.62-7.73) | 1.66 (1.33-2.07) |

#### Excluding the first year after diagnosis

| Incidence rate in cases | Incidence rate in reference | Hazard ratio |
|-------------------------|----------------------------|--------------|
| **N events, IR (95% CI)** | **N events, IR (95% CI)** | **(95% CI)** |
| 384, 20.8 (18.8-23.0) | 3170, 16.8 (16.2-17.4) | 1.34 (1.20-1.48) |

#### Primary sclerosing cholangitis

| Incidence rate in cases | Incidence rate in reference | Hazard ratio |
|-------------------------|----------------------------|--------------|
| **N events, IR (95% CI)** | **N events, IR (95% CI)** | **(95% CI)** |
| At or during follow-up | 34, 92.1 (65.8-129) | 61, 14.3 (11.1-18.4) | 7.55 (4.94-11.5) |
| Duration < 5 years | 21, 128 (83.3-196) | 19, 11.0 (7.01-17.2) | 12.0 (6.42-22.3) |
| Duration ≥5 to <10 years | 8, 77.5 (38.7-155) | 11, 9.40 (5.21-17.0) | 10.1 (4.06-25.3) |
| Duration ≥ 10 years | 5, 49.2 (20.5-118) | 31, 22.7 (16.0-32.3) | 2.83 (1.09-7.32) |
**FIGURE 2** Multi-state model showing the states under consideration and the possible transitions between them. The thickness of the transition lines is proportional to the log of the number of transitions.

**FIGURE 3** Cause-specific cumulative incidence curves for each of the transitions in the multi-state model.
We found patients with IBD to be at increased risk of pancreatic cancer and pancreatic cancer death compared to matched reference individuals. The incidence rate for pancreatic cancer was 22.1 in the patients vs 16.6 in the population, and the HR was 1.43, with the highest excess risk (HR 7.55) in IBD patients with PSC. Once diagnosed with pancreatic cancer, IBD patients were not at increased risk of dying earlier than reference individuals also diagnosed with pancreatic cancer.

A previous meta-analysis found a non-significantly decreased risk of pancreatic cancer with a pooled standardised incidence ratio of 0.51 (0.06-4.57) for Crohn’s disease and 0.75 (0.30-1.87) for ulcerative colitis. The six previous population-based cohort studies identified a total of 26 pancreatic cancers in 29,215 patients between 1958 and 2014 (Table S1), whereas our investigation was based on 442 pancreatic cancers in 161,926 patients between 1964 and 2017.

A Korean study compared cancer cases in patients with IBD diagnosed 2011-2014 with the incidence rate of cancer in the general population in 2013. The pancreatic cancer risk was found to be increased only in women with Crohn’s disease (standardised incidence ratio 8.58 [1.04-31.00]), but this analysis was based on only two cases. When stratifying for sex and IBD subtype in our data, there was a statistically significant risk increase for both men and women in Crohn’s disease and IBD-U, but in ulcerative colitis only for men.

Patients with PSC have been found to be at increased risk of pancreatic cancer. In a Swedish study where 79% of the cohort had IBD, patients with PSC had 14 times higher risk of pancreatic cancer than the general population. A study based on the Electronic Medical Record IBD cohort in Boston reported an odds ratio for pancreatic cancer of 11.22 (4.11-30.62) in IBD patients with PSC compared to IBD patients without PSC. In our Scandinavian cohort, the HR for pancreatic cancer in patients with IBD vs the IBD-free population was higher in patients with PSC (7.55) than the overall HR of patients with IBD (1.43) but the highest HR was found in patients recently diagnosed with PSC (duration < 5 years 12.0) and the lowest HR was in patients with duration ≥ 10 years (2.83). It should be noted, though, that >90% of all pancreatic cancer events occurred in IBD patients without a PSC diagnosis. That the risk of pancreatic cancer would
decrease with increasing time from PSC diagnosis is biologically implausible and the fact that PSC-associated pancreatic cancer to such a high degree was diagnosed around the time of IBD diagnosis suggests that this finding to some extent is an effect of detection bias.

Another potential source of bias is the fact that patients with PSC have an excess risk of developing intraductal cholangiocarcinoma. Because of their anatomical and histopathological similarity, the distinction between cancer in the head of the pancreas and distal cholangiocarcinoma (accounting for 40% of cholangiocarcinoma cases) is sometimes difficult. A misclassification of cholangiocarcinoma as pancreatic cancer could increase the relative risk of pancreatic cancer in patients with IBD and PSC (and consequently lower the relative risk of cholangiocarcinoma).

Although investigation of the reasons for the increased risk of pancreatic cancer in patients with IBD is beyond the scope of this article, some possible mechanisms deserve mentioning. Pancreatitis is common among patients with IBD and chronic pancreatitis is associated with pancreatic cancer. Medication commonly used in IBD, such as thiopurines and tumour necrosis factor inhibitors, are associated with an increased risk of cancer due to immunosuppression. Chronic, dysregulated and persistent inflammation is associated with increased risks of certain malignancies.

Increased medical surveillance in patients with IBD may lead to earlier detection of cancers, as well as the reverse situation, where cancer symptoms may lead to a diagnosis of IBD. In order to reduce detection bias we also analysed data excluding the first year of follow-up, and found that the incidence rate of pancreatic cancer only decreased marginally, from 22.1 to 20.8 in the patients with IBD and increased slightly from 16.6 to 16.8 in the general population. However, our results otherwise indicate that pancreatic cancer was not detected earlier in patients with IBD than in the population. First, we did not observe a difference in cancer stage between patients and reference population \( (P = 0.174, \text{Table S9}) \). Second, the proportion undergoing resectional surgery (indicating potentially curable disease) was slightly lower in IBD patients (8.14% vs 9.60% in the reference population). Third, the relative risk of pancreatic cancer death when comparing IBD patients with pancreatic cancer and reference population with pancreatic cancer was not decreased (1.07 [0.95 to 1.21]).

The main strength of this study is its large binational study population based on prospectively recorded data with long follow-up from registers with virtually complete coverage. Due to population-based setting, our results should be highly generalisable to similar populations. Access to histopathology data helped define IBD onset better than in previous reports. Unlike some earlier studies using standardised incidence ratios (which might underestimate the relative risk since reference individuals could be diagnosed with cancer before study entry whereas IBD cases could not), our

**FIGURE 5** Time-trends of hazards for pancreatic cancer comparing patients with incident inflammatory bowel disease with matched general population reference individuals by follow-up time and calendar year at diagnosis.
comparisons of cancer incidence were based on a matched reference cohort drawn from the general population.

Study limitations include lack of data on smoking, which is the main risk factor for pancreatic cancer. We therefore used a quantitative bias analysis to assess how sensitive our main results were to unmeasured confounding and found that an unmeasured confounder such as smoking would have to be highly imbalanced between IBD patients and reference individuals to fully attenuate the relationship between IBD and pancreatic cancer risk (Figure S2). The fact that the incidence of pancreatic cancer was similar between Crohn’s disease and ulcerative colitis, although the prevalence of past and current smoking differs between IBD subtypes, further corroborates that confounding from smoking unlikely explains our finding of increased risk of pancreatic cancer in patients with IBD. This quantitative bias analysis can be used to assess the importance of any unmeasured confounder (eg family history, alcohol abuse).

Our cohort ranged over a large time span during which access to register data has increased to include also outpatient specialist care. Although the patient cohort was based only on inpatient data during the first period of follow-up (until 1995 in Denmark and until 2001 in Sweden), the variations in incidence were small, in accordance with the fact that pancreatic cancer incidence in the population has been quite constant.42

5 | CONCLUSIONS

Patients with IBD had an excess risk of pancreatic cancer, especially in those with PSC. However, the cumulative incidence difference after 20 years of follow-up was small (0.05%), that is, one extra case of pancreatic cancer per 2000 IBD patients, which should be reassuring for patients and clinicians alike.

ACKNOWLEDGEMENTS

Declaration of personal interests: ÅH Everhov has worked on projects at Karolinska Institutet and SWIBREG partly financed by grants from Ferring and Janssen. JF Ludvigsson coordinates a study on behalf of the Swedish IBD quality register (SWIBREG), which has received funding from Janssen corporation. O Olén has been PI on projects at Karolinska Institutet, partly financed by investigator-initiated grants from Janssen and Ferring, and Karolinska Institutet has received fees for lectures and participation on advisory boards from Janssen, Ferring, Takeda and Pfizer. O Olén also reports a grant from Pfizer in the context of a national safety monitoring program. J Askling acts or has acted PI in agreements between Karolinska Institutet and the following entities, mainly regarding safety monitoring of Rheumatology immunomodulators: Abbvie, AstraZeneca, BMS, Eli Lilly, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi and UCB. J Halfvarson served as speaker and/or advisory board member for AbbVie, Celgene, Celltrion, Dr Falk Pharma and the Falk Foundation, Ferring, Hospira, Janssen, MEDA, Medivir, MSD, Novartis, Olink Proteomics, Pfizer, Prometheus Laboratories, Sandoz, Shire, Takeda, Thermo Fisher Scientific, Tillotts Pharma, Vifor Pharma, UCB and received grant support from Janssen, MSD and Takeda. H T Sørensen, R Erichsen and L Pedersen report that the Department of Clinical Epidemiology, Aarhus University Hospital, receives funding for other studies from companies in the form of research grants to (and administered by) Aarhus University. None of these studies have any relation to the present study.

AUTHORSHIP

Guarantor of the article: Ola Olén.

Author contributions: Conception and design: Åsa H Everhov, Ola Olén; Acquisition of data: Ola Olén, Jonas F Ludvigsson, Henrik Toft Sørensen; Statistical analysis: Michael C Sachs; Interpretation of data: All authors. Drafting the manuscript: Åsa H Everhov; Critical revision for intellectual content. All authors. Final approval: All authors. Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: All authors.

ETHICAL APPROVAL

The study was approved by the regional ethics committee in Stockholm (Dnr 2007/785-31/5, 2011/1509-32, 2014/1287-31/4, 2015/0004-31, 2016/192-31/2) and Danish Data Protection Agency. Since this was a strictly register-based study, individual informed consent was not required.

ORCID

Åsa H. Everhov https://orcid.org/0000-0002-0311-8894
Rune Erichsen https://orcid.org/0000-0001-9398-9185
Jonas F. Ludvigsson https://orcid.org/0000-0003-1024-5602

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SUPPORTING INFORMATION

Additional supporting information will be found online in the Supporting Information section.

How to cite this article: Everhov ÅH, Erichsen R, Sachs MC, et al. Inflammatory bowel disease and pancreatic cancer: a Scandinavian register-based cohort study 1969-2017. *Aliment Pharmacol Ther.* 2020;52:143–154. [https://doi.org/10.1111/apt.15785](https://doi.org/10.1111/apt.15785)

APPENDIX

Authors’ complete affiliations

Åsa H. Everhov: Department of Clinical Science and Education Södersjukhuset, Karolinska Institutet, Stockholm, Sweden and Clinical Epidemiology Division, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden. Rune Erichsen: Aarhus University Hospital, Aarhus, Denmark and Randers Regional Hospital, Randers, Denmark. Michael C. Sachs, Johan Askling and Anders Ekblom: Clinical Epidemiology Division, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden. Lars Pedersen and Henrik Toft Sørensen: Aarhus University Hospital, Aarhus, Denmark. Jonas Halfvarson: Örebro University, Örebro, Sweden. Jonas F. Ludvigsson: Karolinska Institutet, Stockholm, Sweden; Örebro University Hospital, Örebro, Sweden; School of Medicine, University of Nottingham, UK; Columbia University College of Physicians and Surgeons, New York, New York, USA. Ola Olén: Department of Clinical Science and Education Södersjukhuset, Karolinska Institutet, Stockholm, Sweden, Clinical Epidemiology Division, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden and Stockholm South General Hospital, Stockholm, Sweden.