Risk of malignant lymphomas in patients with inflammatory bowel disease: A population-based cohort study

Supplementary Appendix

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Fig. S1. Overview of cohort members included in analysis.

**Norwegian IBD cohort**
- 75,109 patients with at least one diagnostic listing related to IBD
  - Excluded: 2,604 diagnosed with cancer at baseline
  - 3,617 diagnosed with IBD at or after end of follow-up
  - 7 with invalid birth date
- 50,680 patients with two diagnostic listings for IBD during 1987-2015
  - Excluded: 2,604 diagnosed with cancer at baseline
  - 23,906 patients with only one diagnostic listing of IBD
- 44,452 patients with IBD included for analysis

**Swedish IBD cohort**
- 123,829 patients with at least one diagnostic listing related to IBD
  - Excluded: 520 due to irrelevant codes
  - 3 patients due to IBD date before 01 Jan 1987
  - 2 patients due to IBD date before 01 Jan 1987
  - 31,349 patients with only one diagnostic listing of IBD
- 92,480 patients with two diagnostic listings for IBD during 1993-2016
  - Excluded: 12 patients had sex conflict and 17 patients had birth date conflict
  - 1 patient had invalid birth date
  - 5,145 patients had cancer at baseline
- 87,040 patients with IBD included for final analysis
  - Excluded: 262 patients dead before IBD
  - 1 patient emigrated before IBD
Fig. S2. Design diagram of analyses on pharmacotherapy in the Swedish cohort. Diagram inspired by the work of Schneeweiss et al.,¹ made using template available at https://presc.sdu.dk/repeat-diagrams/
Table S1. ICD codes used to define patients with inflammatory bowel disease (IBD) from national patient registry and hospital databases.

<table>
<thead>
<tr>
<th>IBD subtype</th>
<th>ICD-9</th>
<th>ICD-10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcerative colitis (UC)</td>
<td>556</td>
<td>K51</td>
</tr>
<tr>
<td>Crohn’s disease (CD)</td>
<td>555</td>
<td>K50</td>
</tr>
<tr>
<td>Unclassified (IBD-U)</td>
<td>UC+CD</td>
<td>UC+CD or K523</td>
</tr>
</tbody>
</table>

Classification of IBD subtypes is based on the two first diagnostic codes:
Ulcerative colitis, 1st code UC, 2nd code UC;
Crohn’s disease, 1st code CD, 2nd code CD;
Unclassified, 1st code IBD-U, 2nd code IBD-U, or any combination of codes for UC, CD, and IBD-U.
ICD-9 was implemented in Sweden in 1987, and in Norway in 1986. ICD-10 was implemented in Sweden 1997, and in Norway in 1999.
Table S2. Definitions and diagnostic codes used to define ulcerative colitis (UC) and Crohn’s disease (CD) according to the Montreal classification.

<table>
<thead>
<tr>
<th>Ulcerative colitis</th>
<th>Extent</th>
<th>Diagnostic codes</th>
<th>Norway</th>
<th>Sweden</th>
</tr>
</thead>
<tbody>
<tr>
<td>E1</td>
<td>Ulcerative proctitis</td>
<td>ICD-10=K512; ICD-9=5561</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E2</td>
<td>Left-sided UC</td>
<td>ICD-10=K513, K515; ICD-9=5565</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E3</td>
<td>Extensive UC</td>
<td>ICD-10=K510, K511; ICD-9=5562</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ex</td>
<td>Extent not defined</td>
<td>ICD-10=K51, K514, K519; ICD-9=5560, 55606, 5564, 5569</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Crohn’s disease</th>
<th>Location</th>
<th>Diagnostic codes</th>
<th>Norway</th>
<th>Sweden</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1</td>
<td>Small bowel disease or terminal ileitis</td>
<td>ICD-10=K500; ICD-9=5550</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L2</td>
<td>Colon</td>
<td>ICD-10=K501; ICD-9=5551, 55506</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L3</td>
<td>Ileocecal Crohn’s disease</td>
<td>ICD-10=K508; ICD-9=5552</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lx</td>
<td>Location not defined</td>
<td>ICD-10=K509; ICD-9=555, 5559, 55502, 56301</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Crohn’s disease</th>
<th>Behaviour</th>
<th>Diagnostic codes</th>
<th>Norway</th>
<th>Sweden</th>
</tr>
</thead>
<tbody>
<tr>
<td>B1</td>
<td>Non-stricturing, non-penetrating</td>
<td>None of the ICD-codes for B2 or B3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B2</td>
<td>Stricturing</td>
<td>Crohn’s disease AND any of the following codes: ICD-10=K565, K566, K567, K624; ICD-9=5608, 5609</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B3</td>
<td>Penetrating</td>
<td>Crohn’s disease AND any of the following diagnostic codes: ICD-10=K630, K632, K316, N823, N824; ICD-9=5374, 5696, 5961, 6298, OR any of the following surgical procedure codes (JHD20, JHD30, JHD33, JHD50, JHD60, JHD63, JFA76, JFA86, 4603, 4962)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B2B3</td>
<td>Strictureing and penetrating</td>
<td>Both of the ICD codes for B2 and B3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| P                | Perianal disease modifier | Crohn’s disease AND any of the following diagnostic codes: K603, K604, K605, K610, K611, K612, K613, K614, K624; ICD-9=565, 560, 5651, OR any of the following surgical procedure codes (JHD20, JHD30, JHD33, JHD50, JHD60, JHD63, JFA00, JHA20, JHW96) | | |

ICD-9 was implemented in Sweden in 1987, and in Norway in 1986. Swedish ICD-9 codes do not discriminate between different levels of extent of ulcerative colitis. ICD-10 was implemented in Sweden 1997, and in...
Norway in 1999. All codes were captured in the Swedish National Patient Register and Norwegian hospital databases.
Table S3: Definition of IBD-related bowel surgeries in Norway and Sweden.

<table>
<thead>
<tr>
<th></th>
<th>Norway</th>
<th>Sweden</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SIFF codes</td>
<td>NCSP-N codes</td>
</tr>
<tr>
<td>Small bowel resection</td>
<td>4620, 4621, 4722, 4672</td>
<td>JFB00, JFB01, JFC00, JFC01, JFA60</td>
</tr>
<tr>
<td>Colon resection</td>
<td>464, 4723, 4673</td>
<td>JFB4, JFB50, JFB51, JFB6</td>
</tr>
<tr>
<td>Rectum resection</td>
<td>482</td>
<td>JGB</td>
</tr>
<tr>
<td>Other or combinations</td>
<td>4724</td>
<td>JFB20, JFB21, JFB33, JFB34, JFB53, JFB54, JFB96, JFB97</td>
</tr>
<tr>
<td>Total colectomy</td>
<td>465</td>
<td>JFH</td>
</tr>
</tbody>
</table>

Table S4: Definition of biologic drugs and thiopurines according to Anatomical Therapeutic Chemical (ATC) codes in the Swedish Prescribed Drug Register.

<table>
<thead>
<tr>
<th>Medication</th>
<th>ATC code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiopurines (mixed with Allopurinol or not)</td>
<td></td>
</tr>
<tr>
<td>Azathioprine</td>
<td>L04AX01</td>
</tr>
<tr>
<td>Mercaptopurine</td>
<td>L01BB02</td>
</tr>
<tr>
<td>Anti-TNF agents</td>
<td></td>
</tr>
<tr>
<td>Etanercept</td>
<td>L04AB01</td>
</tr>
<tr>
<td>Infliximab</td>
<td>L04AA12, L04AB02</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>L04AB04</td>
</tr>
<tr>
<td>Certolizumab pegol</td>
<td>L04AB05</td>
</tr>
<tr>
<td>Golimumab</td>
<td>L04AB06</td>
</tr>
</tbody>
</table>
### Table S5A: Outcome definitions in Norwegian data, using ICD-10 and ICD-O-3 codes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>ICD-10</th>
<th>ICD-O-3 topography</th>
<th>ICD-O-3 morphology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hodgkin’s lymphoma</td>
<td>C81</td>
<td>C77</td>
<td>965-966</td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B-cell</td>
<td>C82, C83, C85:</td>
<td>C77</td>
<td>967-969, 9728, 973, 9761-9767, 973, 9826, 9833, 9836, 9940</td>
</tr>
<tr>
<td>CLL*</td>
<td>C91.1</td>
<td>C421</td>
<td>9823</td>
</tr>
<tr>
<td>T/NK-cell</td>
<td>C84, C86</td>
<td>C77</td>
<td>970, 971, 9729, 9827, 9831, 9834, 9837, 9948</td>
</tr>
</tbody>
</table>

*CLL, leukemic presentation, morphology code 9823; C42.1. CLL, lymphoma presentation, morphology code 9823.

### Table S5B: ICD-O-2 and SNOMED codes for leukemia and lymphomas in Sweden.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>ICD-O2</th>
<th>SNOMED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hodgkin’s lymphoma (NHL)</td>
<td>C82-C85</td>
<td>Any code starting with 95, 96, 97,98</td>
</tr>
<tr>
<td>Hodgkin’s lymphoma (HL)</td>
<td>C81</td>
<td>Any code starting with 95, 96, 97,98</td>
</tr>
<tr>
<td>Chronic lymphocytic leukemia</td>
<td>C91.1</td>
<td>Any code starting with C98</td>
</tr>
<tr>
<td>------------------------------------</td>
<td>------------------</td>
<td>------------------</td>
</tr>
<tr>
<td></td>
<td>IR (95% CI)</td>
<td>O/E</td>
</tr>
<tr>
<td>Total</td>
<td>20.4 (16.6 to 25.1)</td>
<td>90/69.1</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>16.8 (12.1 to 23.3)</td>
<td>36/27</td>
</tr>
<tr>
<td>Female</td>
<td>23.8 (18.3 to 31.1)</td>
<td>54/42.1</td>
</tr>
<tr>
<td><strong>Age at IBD diagnosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>1.9 (0.3 to 13.6)</td>
<td>1/0.6</td>
</tr>
<tr>
<td>20-39</td>
<td>6.5 (3.7 to 11.1)</td>
<td>13/10.3</td>
</tr>
<tr>
<td>40-59</td>
<td>32.8 (24.4 to 44.1)</td>
<td>44/32.6</td>
</tr>
<tr>
<td>60+</td>
<td>60.8 (43 to 85.9)</td>
<td>32/25.7</td>
</tr>
<tr>
<td><strong>Calendar year of IBD diagnosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1987/93-2002</td>
<td>19.3 (15.1 to 24.7)</td>
<td>63/51.4</td>
</tr>
<tr>
<td>2003-2015/6</td>
<td>23.7 (16.3 to 34.6)</td>
<td>27/17.8</td>
</tr>
<tr>
<td><strong>IBD subtype</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>14.8 (9.6 to 23.0)</td>
<td>20/15.7</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>23 (18 to 29.4)</td>
<td>63/48.6</td>
</tr>
<tr>
<td>IBD-unclassified</td>
<td>22.2 (10.6 to 46.5)</td>
<td>7/4.8</td>
</tr>
<tr>
<td><strong>Extent of ulcerative colitis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E1 (proctitis)</td>
<td>25.6 (16.1 to 40.7)</td>
<td>18/13.3</td>
</tr>
<tr>
<td>E2 (left-sided)</td>
<td>26.8 (11.2 to 64.4)</td>
<td>5/3.7</td>
</tr>
<tr>
<td>E3 (extensive)</td>
<td>21.7 (15.4 to 30.6)</td>
<td>33/24.4</td>
</tr>
<tr>
<td>Ex (not defined)</td>
<td>21 (10.0 to 44.1)</td>
<td>7/7.1</td>
</tr>
<tr>
<td><strong>Location of Crohn’s disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L1 (terminal ileitis)</td>
<td>33.9 (16.9 to 67.8)</td>
<td>8/3.1</td>
</tr>
<tr>
<td>L2 (colonic)</td>
<td>16.4 (6.8 to 39.3)</td>
<td>5/4.2</td>
</tr>
<tr>
<td>L3 (ileocelecal)</td>
<td>9.1 (4.1 to 20.4)</td>
<td>6/6.1</td>
</tr>
<tr>
<td>Lx (not defined)</td>
<td>6.5 (0.9 to 46.5)</td>
<td>1/2.3</td>
</tr>
<tr>
<td><strong>Behavior of Crohn’s disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B1 (non structuring / penetrating)</td>
<td>16.6 (10.2 to 27.1)</td>
<td>16/11.4</td>
</tr>
<tr>
<td>B2 (structuring)</td>
<td>9.3 (2.3 to 37.3)</td>
<td>2/3</td>
</tr>
<tr>
<td>B3 (penetrating)</td>
<td>* 0/0.8</td>
<td>-</td>
</tr>
<tr>
<td>B2B3 (structuring and penetrating)</td>
<td>31.5 (7.9 to 126.1)</td>
<td>2/0.6</td>
</tr>
<tr>
<td><strong>Perianal disease of Crohn’s disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>15.4 (9.6 to 24.8)</td>
<td>17/13.7</td>
</tr>
<tr>
<td>Yes</td>
<td>12.2 (3.9 to 37.8)</td>
<td>3/2</td>
</tr>
<tr>
<td><strong>Years since IBD diagnosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;1 - 2</td>
<td>25.1 (13.5 to 46.6)</td>
<td>10/4.7</td>
</tr>
<tr>
<td>&gt;2 - 5</td>
<td>21.9 (14.5 to 32.9)</td>
<td>23/13.4</td>
</tr>
<tr>
<td>&gt;5 - 10</td>
<td>15 (9.7 to 23.2)</td>
<td>20/19.6</td>
</tr>
<tr>
<td>10+</td>
<td>22.8 (16.5 to 31.5)</td>
<td>37/31.4</td>
</tr>
<tr>
<td><strong>Primary sclerosing cholangitis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>19.7 (15.9 to 24.3)</td>
<td>85/68.1</td>
</tr>
<tr>
<td>Yes</td>
<td>59.5 (24.8 to 143.1)</td>
<td>5/1.1</td>
</tr>
</tbody>
</table>

Bowel surgery during follow-up<sup>d</sup>

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>IR,</td>
<td>21.3 (17 to 26.7)</td>
<td>17.1 (10.3 to 28.3)</td>
</tr>
<tr>
<td>CI</td>
<td>75/56.3</td>
<td>15/12.8</td>
</tr>
<tr>
<td>O</td>
<td>1.3 (1.1 to 1.7)</td>
<td>1.2 (0.7 to 1.9)</td>
</tr>
<tr>
<td>E</td>
<td>34.5 (30.3 to 39.3)</td>
<td>53.3 (40.5 to 70.2)</td>
</tr>
<tr>
<td>SIR</td>
<td>228/184.6</td>
<td>51/24.0</td>
</tr>
<tr>
<td></td>
<td>1.2 (1.1 to 1.4)</td>
<td>2.1 (1.6 to 2.8)</td>
</tr>
</tbody>
</table>

IR, incidence rate, per 100,000 person-years; CI, confidence interval; O, observed number of cases; E, expected number of cases; SIR, standardized incidence ratio.

<sup>a</sup>All patients were at risk from one year after IBD diagnosis;
<sup>b</sup>Patients diagnosed before 2002 could represent a mix of prevalent and incident patients with IBD, as outpatient data were gradually included in hospital databases and the Swedish national patient register;
<sup>c</sup>Definitions and diagnostic codes were used according to the Montreal classifications using ICD9 and ICD10 in Norwegian data and using ICD-10 in Swedish data, representing maximum disease involvement during follow-up, see Table S2 for details;
<sup>d</sup>Patients with primary sclerosing cholangitis contributed person-time to the non-PSC group until the date of PSC diagnosis;
<sup>e</sup>Bowel surgeries included colectomy, small bowel resection, rectal resection, and colon resection during follow-up. See Table S3 for definitions.
Table S7: Number of cases, standardized incidence ratio, and crude incidence rates per 100,000 person-years for Hodgkin lymphoma, Norway and Sweden.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IR (95% CI)</td>
<td>O/E</td>
<td>SIR (95% CI)</td>
<td>IR (95% CI)</td>
</tr>
<tr>
<td>Total Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>3.3 (1.6 to 6.9)</td>
<td>7/4</td>
<td>1.8 (0.8 to 3.7)</td>
<td>2.4 (1.3 to 4.7)</td>
</tr>
<tr>
<td>Male</td>
<td>3.5 (1.8 to 7.1)</td>
<td>8/6.6</td>
<td>1.2 (0.6 to 2.4)</td>
<td>5.2 (3.3 to 8.0)</td>
</tr>
<tr>
<td>Age at IBD diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>3.8 (1 to 15.3)</td>
<td>2/1.7</td>
<td>1.2 (0.3 to 4.8)</td>
<td>2.4 (0.6 to 9.7)</td>
</tr>
<tr>
<td>20-39</td>
<td>3 (1.3 to 6.6)</td>
<td>6/5.1</td>
<td>1.2 (0.5 to 2.6)</td>
<td>3.8 (2.1 to 6.9)</td>
</tr>
<tr>
<td>40-59</td>
<td>3.7 (1.6 to 9)</td>
<td>5/2.6</td>
<td>1.9 (0.8 to 4.6)</td>
<td>2.9 (1.5 to 5.8)</td>
</tr>
<tr>
<td>60+</td>
<td>3.8 (0.9 to 15.2)</td>
<td>2/1.2</td>
<td>1.6 (0.4 to 6.6)</td>
<td>7.1 (3.6 to 14.3)</td>
</tr>
<tr>
<td>Calendar year of IBD diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1987-93/2002</td>
<td>2.4 (1.2 to 4.9)</td>
<td>8/7.7</td>
<td>1.0 (0.5 to 2.1)</td>
<td>4.1 (2.7 to 6.3)</td>
</tr>
<tr>
<td>2003-2015/6</td>
<td>6.1 (2.9 to 12.9)</td>
<td>7/2.9</td>
<td>2.4 (1.1 to 5.1)</td>
<td>3.2 (1.6 to 6.4)</td>
</tr>
<tr>
<td>IBD subtype</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>3.7 (1.5 to 8.9)</td>
<td>5/3.4</td>
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Bowel surgery during follow-up

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IR, incidence rate, per 100 000 person-years; CI, confidence interval; O, observed number of cases; E, expected number of cases; SIR, standardized incidence ratio.

All patients were at risk from one year after IBD diagnosis; patients diagnosed before 2002 could represent a mix of prevalent and incident patients with IBD, as outpatient data were gradually included in hospital databases and the Swedish national patient register; definitions and diagnostic codes were used according to the Montreal classifications using ICD9 and ICD10 in Norwegian data and using ICD-10 in Swedish data, representing maximum disease involvement during follow-up, see Table S2 for details; patients with primary sclerosing cholangitis contributed person-time to the non-PSC group until the date of PSC diagnosis; bowel surgeries included colectomy, small bowel resection, rectal resection, and colon resection during follow-up. See Table S3 for definitions.
Table S8: Number of cases, standardized incidence ratio, and crude incidence rates per 100,000 person-years for non-Hodgkin lymphoma, Norway and Sweden, first year of follow-up included.

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<td>20 to 39</td>
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<td>1987/93-2002</td>
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<td>33.9 (17.6 to 65.2)</td>
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Primary sclerosing cholangitis

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Bowel surgery during follow-up

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<td>Yes</td>
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<td>17/13.2</td>
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IR, incidence rate, per 100 000 person-years; CI, confidence interval; O, observed number of cases; E, expected number of cases; SIR, standardized incidence ratio.

All patients were at risk from one year after IBD diagnosis;

Patients diagnosed before 2002 could represent a mix of prevalent and incident patients with IBD, as outpatient data were gradually included in hospital databases and the Swedish national patient register;

Definitions and diagnostic codes were used according to the Montreal classifications using ICD9 and ICD10 in Norwegian data and using ICD-10 in Swedish data, representing maximum disease involvement during follow-up, see Table S2 for details;

Patients with primary sclerosing cholangitis contributed person-time to the non-PSC group until the date of PSC diagnosis;

Bowel surgeries included colectomy, small bowel resection, rectal resection, and colon resection during follow-up, See Table S3 for definitions.
Table S9: Number of cases, standardized incidence ratio, and crude incidence rates per 100,000 person-years for Hodgkin lymphoma, Norway and Sweden, first year of follow-up included.

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<tr>
<td>L3 (ileocecal)</td>
<td></td>
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<tr>
<td>Behavior of Crohn’s disease</td>
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</tr>
<tr>
<td>B1 (non structuring / penetrating)</td>
<td>3.8 (1.4 to 10)</td>
<td>4/2.6</td>
<td>1.5 (0.6 to 4)</td>
<td>5.4 (3.0-9.8)</td>
<td>11/4.8</td>
<td>2.3 (1.3-4.1)</td>
</tr>
<tr>
<td>B2 (stricturing)</td>
<td>-</td>
<td>0/0.6</td>
<td>-</td>
<td>0/1.4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>B3 (penetrating)</td>
<td>8.6 (1,2 to 60.7)</td>
<td>1/0.3</td>
<td>3.2 (0.4 to 22.6)</td>
<td>8.3 (1.2 to 59.1)</td>
<td>1/0.3</td>
<td>3.4 (0.5 to 24.0)</td>
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<tr>
<td>B2B3 (stricturing and penetrating)</td>
<td>-</td>
<td>0/0.2</td>
<td>-</td>
<td>15.7 (3.9 to 62.8)</td>
<td>2/0.3</td>
<td>7.2 (1.8 to 29.0)</td>
</tr>
<tr>
<td>Perianal disease of Crohn’s disease</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>8.4 (3.8 to 18.8)</td>
<td>6/1.6</td>
<td>3.6 (1.6 to 8.1)</td>
</tr>
<tr>
<td>No</td>
<td>4.1 (1,7 to 9.9)</td>
<td>5/3</td>
<td>1.7 (0.7 to 4)</td>
<td>3.6 (1.8 to 7.3)</td>
<td>8/5.1</td>
<td>1.6 (0.8 to 3.1)</td>
</tr>
<tr>
<td>Yes</td>
<td>-</td>
<td>0/0.7</td>
<td>-</td>
<td>8.4 (3.8 to 18.8)</td>
<td>6/1.6</td>
<td>3.6 (1.6 to 8.1)</td>
</tr>
<tr>
<td>Years since IBD diagnosis</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>0-1</td>
<td>4.7 (1.2 to 18.8)</td>
<td>2/1.1</td>
<td>1.9 (0.5 to 7.5)</td>
<td>6.0 (2.5 to 14.3)</td>
<td>5/2.0</td>
<td>2.5 (1.0 to 6.0)</td>
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<tr>
<td>&gt;1 - 2</td>
<td>7.5 (2.4 to 23.3)</td>
<td>3/1</td>
<td>3 (1 to 9.4)</td>
<td>1.3 (0.2 to 9.0)</td>
<td>1/1.9</td>
<td>0.5 (0.1 to 3.8)</td>
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<tr>
<td>&gt;2 - 5</td>
<td>1.9 (0.5 to 7.6)</td>
<td>2/2.6</td>
<td>0.8 (0.2 to 3.1)</td>
<td>1.4 (0.5 to 4.5)</td>
<td>3/4.9</td>
<td>0.6 (0.2 to 1.9)</td>
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<tr>
<td>&gt;5 - 10</td>
<td>4.5 (2 to 10)</td>
<td>6/3.3</td>
<td>1.8 (0.8 to 4.1)</td>
<td>5.1 (2.9 to 8.7)</td>
<td>13/6.1</td>
<td>2.1 (1.2 to 3.7)</td>
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<tr>
<td>10+</td>
<td>2.5 (0.9 to 6.6)</td>
<td>4/3.7</td>
<td>1.1 (0.4 to 2.9)</td>
<td>5.7 (3.2 to 10.0)</td>
<td>12/5.0</td>
<td>2.4 (1.4 to 4.2)</td>
</tr>
<tr>
<td>Primary sclerosing cholangitis</td>
<td>3.2 (1.9 to 5.2)</td>
<td>15/11.4</td>
<td>1.3 (0.8 to 2.2)</td>
<td>4.0 (2.9 to 5.7)</td>
<td>33/19.2</td>
<td>1.7 (1.2 to 2.4)</td>
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<tr>
<td>Bowel surgery during follow up</td>
<td>Yes</td>
<td>No</td>
<td></td>
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<td>-------------------------------</td>
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<tr>
<td>IR, incidence rate, per 100 000 person-years</td>
<td>22.6 (5.7 to 90.5)</td>
<td>3.6 (2.1 to 6)</td>
<td></td>
<td></td>
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<tr>
<td>CI, confidence interval</td>
<td>2/0.2</td>
<td>14/9.4</td>
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<td></td>
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<tr>
<td>O, observed number of cases</td>
<td>8.7 (2.2 to 34.6)</td>
<td>1.5 (0.9 to 2.5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E, expected number of cases</td>
<td>4.1 (0.6 to 29.0)</td>
<td>3.5 (2.4 to 5.2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIR, standardized incidence ratio</td>
<td>1/0.6</td>
<td>26/17.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#</td>
<td>1.6 (0.2 to 11.5)</td>
<td>1.5 (1.0 to 2.2)</td>
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<td></td>
</tr>
<tr>
<td>c</td>
<td>3.3 (1.1 to 10.2)</td>
<td>3/2.2</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>d</td>
<td>1,3 (0.4 to 4.2)</td>
<td>8.1 (4.1 to 16.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e</td>
<td>8/2.3</td>
<td>3.4 (1.7 to 6.8)</td>
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</tr>
</tbody>
</table>

IR, incidence rate; CI, confidence interval; O, observed number of cases; E, expected number of cases; SIR, standardized incidence ratio.

a All patients were at risk from one year after IBD diagnosis.

b Patients diagnosed before 2002 could represent a mix of prevalent and incident patients with IBD, as outpatient data were gradually included in hospital databases and the Swedish national patient register.

c Definitions and diagnostic codes were used according to the Montreal classifications using ICD9 and ICD10 in Norwegian data and using ICD-10 in Swedish data, representing maximum disease involvement during follow-up, see Table S2 for details.

d Patients with primary sclerosing cholangitis contributed person-time to the non-PSC group until the date of PSC diagnosis.

e Bowel surgeries included colectomy, small bowel resection, rectal resection, and colon resection during follow-up, see Table S3 for definitions.
References


