

SUPPLEMENTALS*Table S1. Other gastrointestinal diseases*

| Disease | International classification of disease (ICD10) code |
|--|---|
| Other diseases in the gastrointestinal tract | K90-K93* |
| Other intestinal diseases | K55-K63* |
| Other non-infectious inflammatory conditions of the stomach and intestines | K52* |
| Symptoms and abnormal findings in the digestive system and abdomen | R1* |
| Ulcer on the duodenum | K26* |

*Including all sub-codes

Table S2. The recommended routine diagnostic procedures for the diagnosis of IBD

| Main diagnostic procedures | Complementary procedures |
|---|---|
| <p>A full medical history including questioning about:</p> <ul style="list-style-type: none"> - Symptoms - Stool consistency and frequency - Recent travel and possible risk of infectious illnesses - Medication | <ul style="list-style-type: none"> ▪ Cross-sectional imaging (CT scan, MR scan, small bowel ultrasound) – recommended in CD and as routine in children ▪ Upper gastrointestinal tract endoscopy (only in case of upper gastrointestinal symptoms) – routine in children, but only when suspected CD in adults ▪ Capsule endoscopy and enteroscopy (can be performed where IBD is still suspected despite normal cross-sectional imaging) |
| <p>Stool sample for microbiological analysis</p> <ul style="list-style-type: none"> - including test for <i>Clostridium difficile</i> | |
| <p>Biochemical assessment:</p> <p>Blood:</p> <ul style="list-style-type: none"> - Inflammatory markers (C reactive protein) - Full blood count (examine for thrombocytosis, anaemia, leucocytosis) - Electrolytes - Liver enzymes <p>Stool:</p> <ul style="list-style-type: none"> - Calprotectin | |
| <p>Ileocolonoscopy with multiple biopsy specimens (in case of gastrointestinal symptoms and a raised stool marker of inflammation)</p> | |
| <p>Imaging</p> <p>Routine in children, but not necessary if typical UC is diagnosed using endoscopy and histology</p> | |

The procedures presented are recommended diagnostic procedures according to international guidelines.(1-6)

Table S3. The Nordic Medico-Statistical Committee (NOMESCO) codes for endoscopic and imaging procedures

| Diagnostic procedure | Code |
|--|--|
| <i>Endoscopies (regardless of biopsy taking)</i> | |
| Capsule endoscopy | UJF92 |
| Gastroscopy (upper incl. oesophagus scopy) | UJC , UJD |
| Entero- or colonoscopy (incl. sigmoidoscopy) | UJF - not UJF92 |
| <i>Endoscopy with biopsy</i> | |
| Colonoscopy with biopsy | UJF35 |
| Enteroscopy with biopsy | UJF05, UJF15, UJF25 |
| Flexible sigmoidoscopy with biopsy | UJF45 |
| Gastroscopy with biopsy | UJD05 |
| <i>Imaging</i> | |
| Ultrasound (abdominal and bowel) | UXUD10, UXUD12, UXUD15, UXUD33, UXUD34, UXUD35, UXUD36, UXUD38 |
| CT-scan | UXCD00, UXCD10, UXCD15, UXCD20, UXCD80 |
| MR-scan | UXMD10, UXMD15, UXMD20, UXMD22 UXMD25, UXMD25A, UXMD25B |

Table S4. Danish SNOMED codes for gastrointestinal biopsies

| Code | Code Class | Description of code |
|--------|------------|--|
| M40000 | Morphology | Inflammation |
| M41000 | Morphology | Acute inflammation |
| M42100 | Morphology | Acute and chronic inflammation |
| M43000 | Morphology | Chronic inflammation |
| M43005 | Morphology | Chronic active inflammation |
| P30610 | Procedure | Biopsy |
| P30615 | Procedure | Endoscopic biopsy |
| T62* | Topology | Esophagus |
| T63* | Topology | Ventricle |
| T64* | Topology | Small intestine |
| T65* | Topology | Jejunum, ileum and colon, skin, rectum |
| T66* | Topology | Appendix |
| T67* | Topology | Colon |
| T68* | Topology | Rectum |
| T69000 | Topology | Anus |
| T69010 | Topology | Anal channel |

*Including all sub-codes available at: <https://www.patobank.dk/kodebog/?tag=L>

Table S5. Anatomical Therapeutic Chemical (ATC) Classification codes and Nordic Medico-Statistical Committee (NOMESCO) codes for IBD relevant medical treatment

| Name of treatment | Anatomical Therapeutic Chemical (ATC) classification | NOMESCO code |
|---|--|--------------|
| <i>Systemic corticosteroids</i> | | |
| Prednisolone | A07EA01 | |
| Hydrocortisone | A07EA02 | |
| Prednisone | A07EA03 | |
| Budesonide | A07EA06 | |
| <i>Aminosalicylic acids and analogs</i> | | |
| Sulfasalazine | A07EC01 | |
| Mesalazine | A07EC02 | |
| Olsalazine | A07EC03 | |
| Balsalazide | A07EC04 | |
| <i>Antibodies and immune modulating treatment</i> | | |
| Intestinal anti-inflammatories | | BIHA10 |
| Glucocorticoid-containing enema | | BIHA11 |
| Infliximab | | BOHJ18A1 |
| Adalimumab | | BOHJ18A3 |
| Golimumab | | BOHJ18A4 |
| Ustekinumab | | BOHJ18B3 |
| Vedolizumab | | BOHJ19H4 |
| Ciclosporin | | BOHJ20 |
| <i>Other biologically modulating drugs</i> | | |
| Tofacitinib | L04AA29 | BOHJ28D |
| Azathioprin | L04AX01 | BWHB83 |
| Darvadstrocel | L04AX08 | |
| 6-mercaptopurine | L01BB02 | |
| Methotrexate | L01BA01 | |

Table S6. Clinical information on patients not having undergone a diagnostic procedure compared to patients with at least one diagnostic procedure

| | Total (N=12 871) | Patients with no diagnostic procedures (N=968) | Patients with at least one diagnostic procedure (N=11 903) | P values |
|--|---------------------|--|--|----------|
| Diagnosis of either irritable bowel syndrome or infectious enteritis within 180 after first IBD diagnosis, n (%) | 500 (3.9%) | 23 (2.4%) | 477 (4.0%) | 0.012 |
| Having only one ICD10 diagnosis code of K50 or K51 and a hospital contact lasting at least seven days, n (%) | 4 484 (34.8%) | 606 (62.6%) | 3 878 (32.6%) | <0.001 |
| Bowel surgery ¹ before or at date of first IBD diagnosis, n (%) | 908 (7.1%) | 22 (2.3%) | 886 (7.4%) | <0.001 |
| Diagnosed at relevant hospital department ² , n (%) | 11 805 (91.7%) | 773 (79.9%) | 11 032 (92.7%) | <0.001 |
| IBD-related medical treatment ³ within 365 days after first IBD diagnosis, n (%) | 8 525 (66.2%) | 414 (42.8%) | 8 111 (68.1%) | <0.001 |
| Median days between first and second IBD diagnosis, median (IQR) | 44 (12-202) | 273.5 (70-558) | 41 (11-183) | <0.001 |
| Only one IBD diagnosis and given in 2018 ⁴ , n (%) | 618 (4.8%) | 50 (5.2%) | 568 (4.8%) | 0.58 |

Abbreviations: IQR=interquartile range (25th and 75th percentiles)

¹ Bowel surgery is defined as Nordic Medico-Statistical Committee (NOMESCO) codes: KJF (small intestine and colon), KJG (rectal) and KJH (rectal opening and perianal tissue) including all sub-codes

² Relevant hospital department is defined as internal medicine; medical gastroenterology; surgical gastroenterology; surgery; paediatric

³ IBD related medical treatment is defined as the Anatomical Therapeutic Chemical (ATC) Classification codes and NOMESCO codes described in supplementary table S5

⁴ Register data were only available until Dec 31th 2018. Thus, a second qualifying diagnosis may have been registered after the end of follow-up in this study (31th of December 2018).

Table S7. Diagnostic procedures within a diagnostic period of 365 days before and after date of first IBD hospital admission

| | Total IBD population (N = 12 871) | Crohn's disease cases (N = 4 748) | Ulcerative colitis cases (N = 8 123) | Female (N = 6 691) | Male (N = 6 180) | Child (N = 836) | Adult (N = 12 035) |
|--|---|---|--|-----------------------|---------------------|--------------------|-----------------------|
| At least one diagnostic procedure^{1 2} | 12 183 (94.7%) | 4 539 (95.6%) | 7 644 (94.1%) | 6 285 (93.9%) | 5 898 (95.4%) | 778 (93.1%) | 11 405 (94.8%) |
| <i>Endoscopy</i> | 11 230 (87.3%) | 4 214 (88.8%) | 7 016 (86.4%) | 5 773 (86.3%) | 5 457 (88.3%) | 723 (86.5%) | 10 507 (87.3%) |
| Gastroscopy (upper incl. oesophagus scopy) | 2 373 (18.4%) | 1 405 (29.6%) | 968 (11.9%) | 1 297 (19.4%) | 1 076 (17.4%) | 534 (63.9%) | 1 839 (15.3%) |
| Entero- or colonoscopy (incl. sigmoidoscopy) | 10 984 (85.3%) | 4 057 (85.4%) | 6 927 (85.3%) | 5 646 (84.4%) | 5 338 (86.4%) | 697 (83.4%) | 10 287 (85.5%) |
| Capsule endoscopy | 1 057 (8.2%) | 897 (18.9%) | 160 (2.0%) | 604 (9.0%) | 453 (7.3%) | 73 (8.7%) | 984 (8.2%) |
| <i>Imaging</i> | 6 400 (49.7%) | 3 552 (74.8%) | 2 848 (35.1%) | 3 363 (50.3%) | 3 037 (49.1%) | 566 (67.7%) | 5 834 (48.5%) |
| MR scan | 3 244 (25.2%) | 2 316 (48.8%) | 928 (11.4%) | 1 707 (25.5%) | 1 537 (24.9%) | 447 (53.5%) | 2 797 (23.2%) |
| CT scan | 3 451 (26.8%) | 1 814 (38.2%) | 1 637 (20.2%) | 1 769 (26.4%) | 1 682 (27.2%) | 67 (8.0%) | 3 384 (28.1%) |
| Ultrasound | 2 742 (21.3%) | 1 561 (32.9%) | 1 181 (14.5%) | 1 523 (22.8%) | 1 219 (19.7%) | 306 (36.6%) | 2 436 (20.2%) |
| <i>Gastrointestinal biopsy³</i> | 11 259 (87.5%) | 4 029 (84.9%) | 7 230 (89.0%) | 5 758 (86.1%) | 5 501 (89.0%) | 717 (85.8%) | 10 542 (87.6%) |
| DNPR registration | 9 528 (74.0%) | 3 509 (73.9%) | 6 019 (74.1%) | 4 877 (72.9%) | 4 651 (75.3%) | 640 (76.6%) | 8 888 (73.9%) |
| DPR registration | 10 147 (78.8%) | 3 391 (71.4%) | 6 756 (83.2%) | 5 146 (76.9%) | 5 001 (80.9%) | 680 (81.3%) | 9 467 (78.7%) |

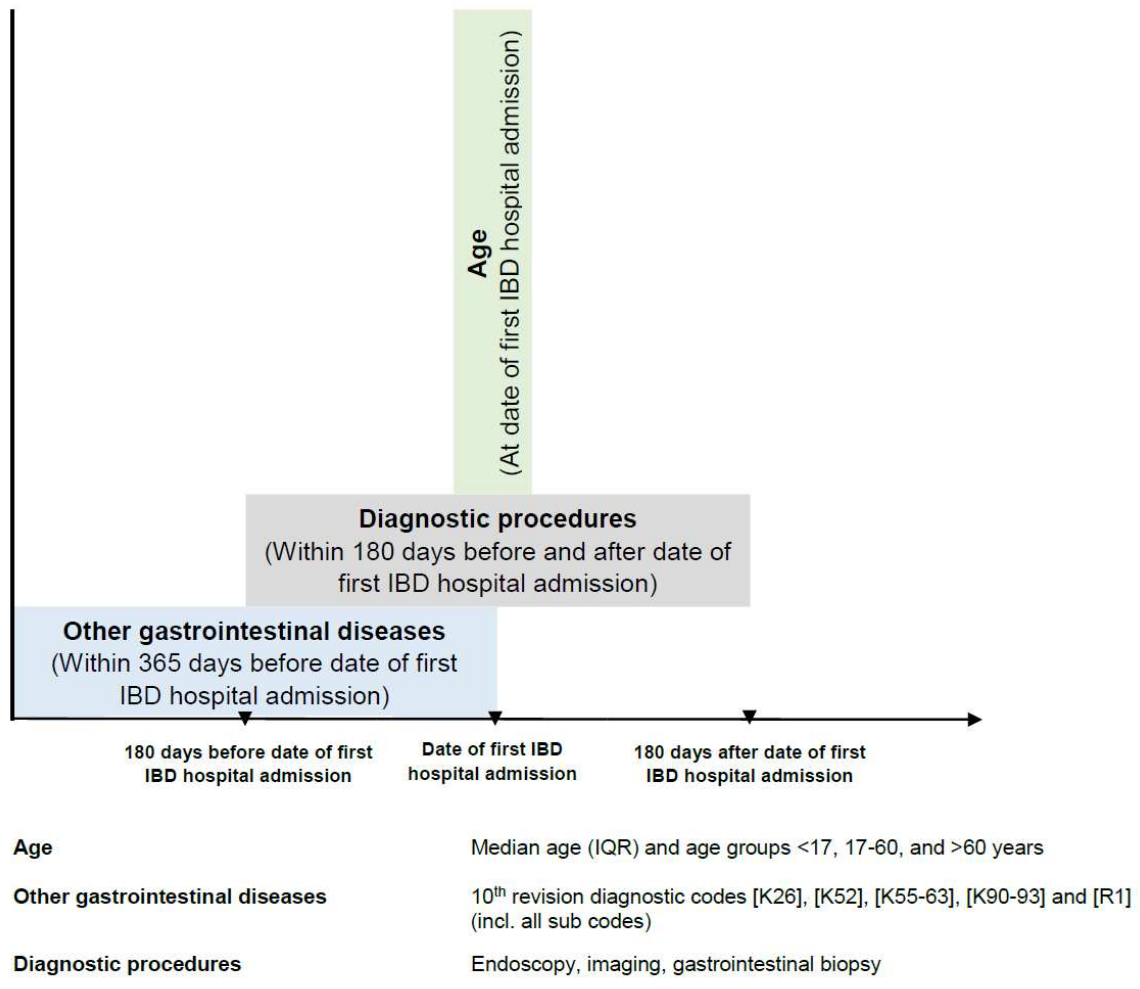
Abbreviations: MR = magnetic resonance, CT = computed tomography, DNPR = Danish National Patient Register, DPR = Danish Pathology Register

¹Within the period: 180 days before or after the admission date of the first IBD hospital contact

²All percentages are out of total number of patients (N (total population)=12 871; N (CD)=4 748; N (UC)=8 123); (N (women) = 6 691; N (men)=6 180); (N (children)=836; N (adults)=12 035). Patients may be represented in more than one sub-group of each procedure type, therefore percentages do not sum to 100%.

³The date of requisition of a biopsy may differ by several days from the date where the endoscopic procedures has been performed. This may explain why the proportion of gastrointestinal biopsies was higher than the proportion of endoscopies.

Figure S1. Inclusion period for study variables



Abbreviations: IBD = Inflammatory bowel disease, IQR = Interquartile range

References

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