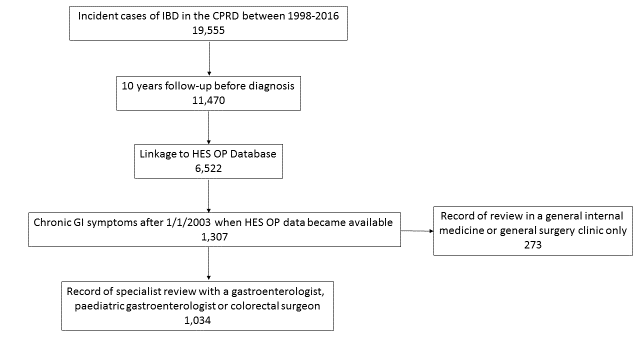
## **Supplementary Appendix 1: Cohort construction of individuals presenting with chronic gastrointestinal symptoms**



IBD - Inflammatory Bowel Disease

CPRD - Clinical Practice Research Datalink

HES OP- Hospital Episodes Statistics Outpatient data

Chronic GI Symptoms – An individual who presented to their primary care physician with gastrointestinal symptoms twice or more within a 6 month period, where the first and last presentations in that period were at least 6 weeks apart.

## **Supplementary Appendix 2: List of CPRD medcodes used in the definition of gastrointestinal symptoms.**

We identified a cohort of 19,555 incident cases of IBD and then identified any medcodes that were used more than 20 times in the entire cohort. This generated a list of 8,948 medcodes which were reviewed by four clinicians with an interest in IBD (JB, SS, CA and RP). Each clinician separately identified any codes indicative of diarrhoea, abdominal or perianal pain, rectal bleeding or miscellaneous gastrointestinal symptoms. We included medcodes in the code list for gastrointestinal symptoms where the majority considered that medcode to be indicative of a gastrointestinal symptom. In the event of a tie the first author (JB) decided whether the medcode should be included in the list.

Codes were excluded if they described a definite diagnosis (eg. Campylobacter Enteritis).

As rectal bleeding from UC is often initially misdiagnosed as haemorrhoids we included codes for haemorrhoids (eg. Bleeding haemorrhoids NOS) in our list for rectal bleeding. However more specific codes such as Prolapsed Haemorrhoids were not included, as a primary care physician would be unlikely to use this code without definite evidence that haemorrhoids were present.

We defined GI symptoms to include all the codes for diarrhoea, abdominal or perianal pain and rectal bleeding as well as miscellaneous codes for GI symptoms (eg. Gastrointestinal symptoms) which did not fit into a specific category.

**Diarrhoea**

|  |  |
| --- | --- |
| **Description** | **Medcode** |
| Diarrhoea symptoms | 5134 |
| Diarrhoea | 192 |
| Diarrhoea | 4343 |
| Loose stools | 1695 |
| Chronic diarrhoea | 6685 |
| Diarrhoea of presumed infectious origin | 5090 |
| Diarrhoea symptom NOS | 14695 |
| Noninfective diarrhoea | 6016 |
| Functional diarrhoea | 5036 |
| Increased frequency of defaecation | 18682 |
| [D] Stools loose | 14881 |
| Irritable bowel syndrome with diarrhoea | 29835 |
| Infectious diarrhoea | 4542 |
| Gastroenteritis | 139 |
| Diarrhoea & vomiting, symptom | 2182 |
| Diarrhoea and vomiting | 7644 |
| Viral gastroenteritis | 3107 |
| Diarrhoea & vomiting -? Infect | 14665 |
| [D]Change in bowel habit | 16665 |
| Travellers' diarrhoea | 11155 |
| Viral diarrhoea | 15289 |
| Infectious gastroenteritis | 10294 |

**Abdominal or perianal pain**

|  |  |
| --- | --- |
| **Description** | **Medcode** |
| Abdominal pain | 177 |
| [D]Abdominal pain | 1763 |
| Abdominal pain type | 1976 |
| Abdominal discomfort | 2383 |
| Anal pain | 3049 |
| Right iliac fossa pain | 1181 |
| [D]Abdominal colic | 2056 |
| Left iliac fossa pain | 2982 |
| Colicky abdominal pain | 7812 |
| Rectal pain | 2767 |
| [D]Abdominal cramps | 716 |
| O/E - abdomen tender | 5782 |
| [D]Abdominal pain NOS | 3338 |
| Site of abdominal pain | 5960 |
| Lower abdominal pain | 22608 |
| Central abdominal pain | 4617 |
| Flank pain | 7490 |
| [D]Nonspecific abdominal pain | 19283 |
| [D]Functional abdominal pain syndrome | 103540 |
| Iliac fossa pain | 421 |
| [D]Acute abdomen | 948 |
| O/E - abdo. pain on palpation | 15180 |
| Anorectal pain | 2866 |
| Generalised abdominal pain | 24661 |
| O/E -abd.pain on palpation NOS | 14916 |
| O/E - abd. pain - L.iliac | 21583 |
| Non-colicky abdominal pain | 5691 |
| Abdominal pain in pregnancy | 3191 |
| [D]Pain in left iliac fossa | 16868 |
| [D]Pain in right iliac fossa | 16806 |
| O/E - abd. pain - R.iliac | 11647 |
| C/O pelvic pain | 2781 |
| Suprapubic pain | 7300 |
| Perianal irritation | 9837 |
| [D]Colic NOS | 1239 |
| Perianal itch | 5830 |
| [D]Epigastric pain | 542 |
| Perineal irritation | 7090 |
| [D] Perineal pain | 7248 |
| [D]Pelvic and perineal pain | 9920 |
| [D]Recurrent acute abdominal pain | 2234 |
| Upper abdominal pain | 3978 |
| Right upper quadrant pain | 9695 |
| [D]Right upper quadrant pain | 7726 |
| O/E - abd. pain – epigastrium | 19223 |
| [D]Upper abdominal pain | 8436 |
| Left flank pain | 701 |
| Epigastric pain | 290 |
| [D]Flatulence, eructation and gas pain | 14807 |
| Type of GIT pain | 14989 |
| Type of GIT pain – symptom | 6395 |
| [D]Umbilical pain | 4771 |

**Rectal Bleeding**

|  |  |
| --- | --- |
| **Description** | **Medcode** |
| Rectal bleeding | 621 |
| Bleeding PR | 3872 |
| Painless rectal bleeding | 11698 |
| Painful rectal bleeding | 11718 |
| Blood in stool | 2873 |
| Blood in faeces | 5462 |
| Blood in faeces symptom | 6151 |
| Gastrointestinal haemorrhage | 3097 |
| GIB - Gastrointestinal bleeding | 1642 |
| Haemorrhoids | 195 |
| Piles – haemorrhoids | 3833 |
| Haemorrhoids NOS | 2096 |
| Bleeding haemorrhoids NOS | 2832 |
| PRB - Rectal bleeding | 6554 |
|  |  |

**Miscellaneous Gastrointestinal Symptoms**

|  |  |
| --- | --- |
| **Description** | **Medcode** |
| Gastrointestinal symptoms | 13015 |
| GIT symptoms | 10896 |

## Supplementary Appendix 3: Prevalence of gastrointestinal symptoms before Crohn’s disease diagnosis

|  |  |  |  |
| --- | --- | --- | --- |
|  | |  | |
|  | **Prevalence of GI symptoms (%)** | | | | **Risk Difference (%)** | **95% Confidence Interval** |
|  | **Crohn’s Disease** | | **Controls** | |  |  |
| **n=** | **5,874** | | **23,436** | |  |  |
| Years before IBD diagnosis |  | |  | |  |  |
|  |  | |  | |  |  |
| 1 | 29.1 | | 6.5 | | 22.6 | 21.3-23.9 |
| 2 | 16.8 | | 6.2 | | 10.7 | 9.5-11.8 |
| 3 | 13.6 | | 5.7 | | 7.9 | 6.8-8.9 |
| 4 | 11.8 | | 6.0 | | 5.9 | 4.8-6.9 |
| 5 | 10.4 | | 6.2 | | 4.2 | 3.2-5.2 |
| 6 | 9.1 | | 6.7 | | 3.5 | 2.5-4.4 |
| 7 | 8.1 | | 5.3 | | 2.7 | 1.8-3.7 |
| 8 | 7.6 | | 5.1 | | 2.5 | 1.5-3.4 |
| 9 | 7.4 | | 4.8 | | 2.6 | 1.6-3.5 |
| 10 | 6.0 | | 4.7 | | 1.3 | 0.4-2.2 |
|  |  | |  | |  |  |

**Prevalence of GI symptoms –** The percentage of individuals who presented to a primary care physician for gastrointestinal symptoms in that 12 month period.

## Supplementary Appendix 4: Prevalence of gastrointestinal symptoms before ulcerative colitis diagnosis

|  |  |  |  |
| --- | --- | --- | --- |
|  | |  | |
|  | **Prevalence of GI symptoms (%)** | | | | **Risk Difference (%)** | **95% Confidence Interval** |
|  | **Ulcerative colitis** | | **Controls** | |  |  |
| **n=** | **13,681** | | **54,616** | |  |  |
| Years before IBD diagnosis |  | |  | |  |  |
|  |  | |  | |  |  |
| 1 | 23.9 | | 6.7 | | 17.2 | 16.4-18.0 |
| 2 | 15.4 | | 6.4 | | 9.0 | 8.3-9.7 |
| 3 | 12.8 | | 5.8 | | 7.0 | 6.3-7.6 |
| 4 | 11.3 | | 5.9 | | 5.4 | 4.8-6.1 |
| 5 | 9.6 | | 5.6 | | 4.0 | 3.4-4.6 |
| 6 | 9.6 | | 5.4 | | 4.2 | 3.6-4.9 |
| 7 | 8.4 | | 5.4 | | 3.0 | 2.3-3.6 |
| 8 | 7.7 | | 5.2 | | 2.5 | 1.9-3.1 |
| 9 | 8.0 | | 4.9 | | 3.1 | 2.5-3.8 |
| 10 | 6.8 | | 4.3 | | 2.5 | 1.9-3.1 |

**Prevalence of GI symptoms –** The percentage of individuals who presented to a primary care physician for gastrointestinal symptoms in that 12 month period.

## Supplementary Appendix 5: Sensitivity Analysis - Probability of specialist review, including general internal medicine and surgery appointments, after presentation with chronic GI symptoms according to era of presentation

## 

Chronic GI symptoms – Individuals presented to their GP with gastrointestinal symptoms twice within a 6 month period, where the presentations were at least 6 weeks apart.

Specialist review – Outpatient appointment with a gastroenterologist, paediatric gastroenterologist or colorectal surgeon *or any appointment coded only as general internal medicine or general surgery*