

SUPPLEMENTARY MATERIAL

Appendix 1 -Read codes

List of CPRD med-codes used in the definition of gastrointestinal symptoms

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	2056

Left iliac fossa pain 2982	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.ilic	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.ilic	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

Diarrhoea

Description	ICD-10 Code
Functional diarrhoea	K59.1
Protozoal intestinal disease, unspecified	A07.9
Flagellate diarrhoea	
Protozoal:	
colitis	
diarrhoea	
dysentery	
Viral and other specified intestinal infections	A08
Excl.:	
influenza with involvement of gastrointestinal tract (J09, J10.8, J11.8)	
Rotaviral enteritis	A08.0
Acute gastroenteropathy due to Norwalk agent	A08.1
Small round structured virus enteritis	
Adenoviral enteritis	A08.2
Other viral enteritis	A08.3
Viral intestinal infection, unspecified	A08.4
Viral:	
enteritis NOS	
gastroenteritis NOS	
gastroenteropathy NOS	
Other specified intestinal infections	A08.5
Other gastroenteritis and colitis of infectious and unspecified origin	A09
Excl.:	
due to bacterial, protozoal, viral and other specified infectious agents (A00-A08)	
noninfective (see noninfectious) diarrhoea (K52.9)	
noninfective (see noninfectious) diarrhoea	
neonatal (P78.3)	

Other and unspecified gastroenteritis and colitis of infectious origin	A09.0
Catarrh, enteric or intestinal	
Diarrhoea:	
acute bloody	
acute haemorrhagic	
acute watery	
dysenteric	
epidemic	
Infectious or septic	
colitis	
enteritis	
gastroenteritis	
NOS	
haemorrhagic	
Infectious diarrhoea NOS	
Gastroenteritis and colitis of unspecified origin	A09.9
Chronic intestinal amoebiasis	A06.1
Amoebic nondysenteric colitis	A06.2
Amoeboma of intestine	A06.3
Amoeboma NOS	
Noninfective gastroenteritis and colitis, unspecified	K52.9
Diarrhoea	
Enteritis	
Ileitis	
Jejunitis	
Sigmoiditis	
specified as noninfectious	
Excl.:	
colitis, diarrhoea, enteritis, gastroenteritis:	
infectious (A09.0)	
unspecified origin (A09.9)	
functional diarrhoea (K59.1)	
neonatal diarrhoea (noninfective) (P78.3)	
psychogenic diarrhoea (F45.3)	
Vascular disorder of intestine, unspecified	K55.9
Ischaemic:	
colitis	
enteritis	
enterocolitis	
NOS	
Gastroenteritis and colitis due to radiation	K52.0
Toxic gastroenteritis and colitis	K52.1
Use additional external cause code (Chapter XX), if desired, to identify toxic agent.	
Allergic and dietetic gastroenteritis and colitis	K52.2
Food hypersensitivity gastroenteritis or colitis	
Noninfective gastroenteritis and colitis, unspecified	K52.9
Diarrhoea	
Enteritis	

Ileitis	
Jejunitis	
Sigmoiditis	
specified as noninfectious	
Excl.:	
colitis, diarrhoea, enteritis, gastroenteritis:	
infectious (A09.0)	
unspecified origin (A09.9)	
functional diarrhoea (K59.1)	
neonatal diarrhoea (noninfective) (P78.3)	
psychogenic diarrhoea (F45.3)	
psychogenic diarrhoea	F45.3
Irritable bowel syndrome with diarrhoea	K58.0

Abdominal or perianal pain

Description	ICD-10 Code
Acute abdomen	R10.0
Severe abdominal pain (generalized)(localized)(with abdominal rigidity)	
Pain localized to upper abdomen	R10.1
Epigastric pain	
Pelvic and perineal pain	R10.2
Pain localized to other parts of lower abdomen	R10.3
Other and unspecified abdominal pain	R10.4
Abdominal tenderness NOS	
Colic:	
NOS	
Infantile	
Other specified disease of anus and rectum	K62.8
Pain rectum	

Rectal bleeding

Description	ICD-10 Code
Internal haemorrhoids with other complications	I84.1
Internal haemorrhoids:	
bleeding	
prolapsed	
strangulated	
ulcerated	
Internal haemorrhoids without complication	I84.2
Internal haemorrhoids NOS	

External thrombosed haemorrhoids	184.3
Perianal haematoma (nontraumatic)	
Perianal thrombosis	
External haemorrhoids with other complications	184.4
External haemorrhoids:	
bleeding	
prolapsed	
strangulated	
ulcerated	
External haemorrhoids without complication	184.5
External haemorrhoids NOS	
184.6	
Residual haemorrhoidal skin tags	
Skin tags of anus or rectum	
Unspecified thrombosed haemorrhoids	184.7
Thrombosed haemorrhoids, unspecified whether internal or external	
Unspecified haemorrhoids with other complications	184.8
Haemorrhoids, unspecified whether internal or external:	
bleeding	
prolapsed	
strangulated	
ulcerated	
Unspecified haemorrhoids without complication	184.9
Haemorrhoids NOS	
Other faecal abnormalities	R19.5
Abnormal stool colour	
Bulky stools	
Mucus in stools	
Occult blood in stools	
Excl.:	
melaena (K92.1)	
melaena	
Haemorrhage of anus and rectum	K62.5
Gastrointestinal haemorrhage, unspecified	K92.2
Haemorrhage:	
gastric NOS	
intestinal NOS	
Excl.:	
acute haemorrhagic gastritis (K29.0)	
haemorrhage of anus and rectum (K62.5)	
with peptic ulcer (K25-K28)	

List of CPRD prod-codes for corticosteroid prescriptions

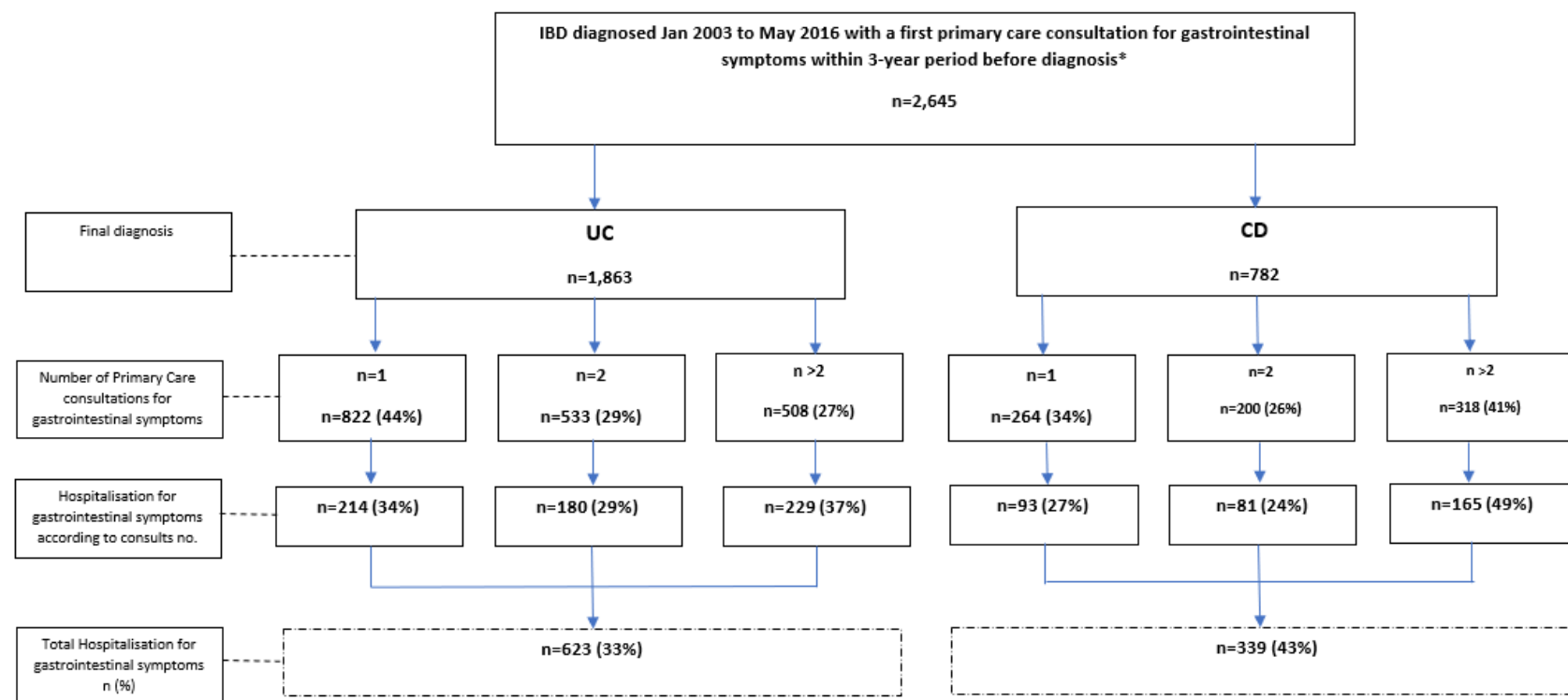
Prodcode	Product Name
5913	Deltacortril 2.5mg gastro-resistant tablets (Alliance Pharmaceuticals Ltd)
5490	Deltacortril 5mg gastro-resistant tablets (Alliance Pharmaceuticals Ltd)
27962	Deltastab 1mg Tablet (Waymade Healthcare Plc)
28859	Deltastab 5mg Tablet (Waymade Healthcare Plc)
59283	Dilacort 2.5mg gastro-resistant tablets (Auden McKenzie (Pharma Division) Ltd)
59229	Dilacort 5mg gastro-resistant tablets (Auden McKenzie (Pharma Division) Ltd)
25272	Precortisyl 1mg Tablet (Hoechst Marion Roussel)
23512	Precortisyl 5mg Tablet (Hoechst Marion Roussel)
20095	Precortisyl forte 25mg Tablet (Aventis Pharma)
10934	Predenema 20mg/100ml long tube (Forest Laboratories UK Ltd)
58234	Prednisolone 10mg/5ml oral solution
34914	Prednisolone 1mg Tablet (Celltech Pharma Europe Ltd)
34631	Prednisolone 1mg Tablet (Co-Pharma Ltd)
578	Prednisolone 1mg tablets
34452	Prednisolone 1mg tablets (A A H Pharmaceuticals Ltd)
34404	Prednisolone 1mg tablets (Actavis UK Ltd)
58384	Prednisolone 1mg tablets (Almus Pharmaceuticals Ltd)
34660	Prednisolone 1mg tablets (Kent Pharmaceuticals Ltd)
34748	Prednisolone 1mg tablets (Teva UK Ltd)
56891	Prednisolone 1mg tablets (Waymade Healthcare Plc)
34978	Prednisolone 1mg tablets (Wockhardt UK Ltd)
59338	Prednisolone 1mg/5ml oral solution
28376	Prednisolone 2.5mg Gastro-resistant tablet (Biorex Laboratories Ltd)
557	Prednisolone 2.5mg gastro-resistant tablets
28375	Prednisolone 2.5mg gastro-resistant tablets (A A H Pharmaceuticals Ltd)
34461	Prednisolone 2.5mg gastro-resistant tablets (Actavis UK Ltd)
2368	Prednisolone 2.5mg tablet
54434	Prednisolone 2.5mg/5ml oral suspension
38407	Prednisolone 20mg tablet
820	Prednisolone 20mg/100ml retention enema
53313	Prednisolone 20mg/5ml oral suspension
2704	Prednisolone 25mg tablets
41745	Prednisolone 25mg tablets (Zentiva)
54118	Prednisolone 25mg/5ml oral suspension
42408	Prednisolone 40mg/100ml enema
34109	Prednisolone 5 mg gastro-resistant tablet
9727	Prednisolone 50mg tablets
33691	Prednisolone 5mg Gastro-resistant tablet (Biorex Laboratories Ltd)
45302	Prednisolone 5mg Tablet (Biorex Laboratories Ltd)
33988	Prednisolone 5mg Tablet (Co-Pharma Ltd)
33990	Prednisolone 5mg Tablet (IVAX Pharmaceuticals UK Ltd)
44	Prednisolone 5mg gastro-resistant tablets
31532	Prednisolone 5mg gastro-resistant tablets (A A H Pharmaceuticals Ltd)
32803	Prednisolone 5mg gastro-resistant tablets (Actavis UK Ltd)
34393	Prednisolone 5mg gastro-resistant tablets (Teva UK Ltd)
59912	Prednisolone 5mg gastro-resistant tablets (Waymade Healthcare Plc)
95	Prednisolone 5mg tablets

21417	Prednisolone 5mg tablets (A A H Pharmaceuticals Ltd)
29333	Prednisolone 5mg tablets (Actavis UK Ltd)
58000	Prednisolone 5mg tablets (Almus Pharmaceuticals Ltd)
34781	Prednisolone 5mg tablets (Kent Pharmaceuticals Ltd)
41515	Prednisolone 5mg tablets (Teva UK Ltd)
61162	Prednisolone 5mg tablets (Waymade Healthcare Plc)
32835	Prednisolone 5mg tablets (Wockhardt UK Ltd)
55024	Prednisolone 5mg/5ml oral solution
34221	Prednisolone suppositories
16525	Budenofalk 3mg gastro-resistant capsules (Dr. Falk Pharma UK Ltd)
56144	Budenofalk 9mg gastro-resistant granules sachets (Dr. Falk Pharma UK Ltd)
6095	Budesonide 3mg gastro-resistant capsules
51997	Budesonide 9mg gastro-resistant granules sachets
1380	Entocort CR 3mg capsules (AstraZeneca UK Ltd)

List of CPRD Read Codes for IBS diagnosis

Read Code	Read Term
Eu453	[X]Psychogenic IBS
J521.	Irritable bowel syndrome
J5210	Irritable bowel syndrome with diarrhoea
J5211	Irritable bowel syndrome characterised by constipation
J5212	Irritable bowel syndrome characterised by alternating bowel habit

Appendix 2-Flow diagram of patients stratified by primary care consultation frequency and hospitalisation prior to IBD diagnosis



* All individuals had at least four years of follow-up from registering with their general practice before IBD diagnosis, and the first of these years free of any record of gastrointestinal symptoms. Abbreviations CD: Crohn's Disease; UC: Ulcerative colitis

Appendix 3: Association of time to diagnosis, consultation frequency and hospitalisation for gastrointestinal symptoms before diagnosis with clinical outcomes following diagnosis of (a) Crohn's disease (b) Ulcerative colitis

(a) Crohn's disease

	CS use		CS dependency		IM use		IBD Hospitalisation		Intestinal surgery		Perianal surgery	
	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Consultation frequency												
1	-	-	-	-	-	-	-	-	-	-	-	-
2	0.90 (0.70-1.18)	0.90 (0.68-1.18)	1.11 (0.75-1.64)	1.11 (0.74-1.65)	1.09 (0.81-1.47)	1.05 (0.78-1.43)	1.78 (1.24-2.54)	1.35 (0.94-1.93)	1.49 (0.94-2.36)	1.58 (0.99-2.51)	1.13 (0.86-1.48)	1.08 (0.81-1.44)
≥ 3	1.18 (0.94-1.49)	1.21 (0.94-1.56)	1.23 (0.87-1.75)	1.23 (0.84-1.80)	1.14 (0.88-1.48)	1.11 (0.84-1.52)	1.76 (1.27-2.44)	1.80 (1.29-2.50)	2.13 (1.44-3.16)	2.22 (1.45-3.39)	1.12 (0.88-1.43)	1.00 (0.79-1.36)
Time to diagnosis	0.92 (0.81-1.03)	0.89 (0.78-1.01)	0.68 (0.79-1.12)	0.89 (0.73-1.07)	0.94 (0.74-1.22)	0.92 (0.80-1.06)	0.98 (0.84-1.15)	1.03 (1.01-1.68)	0.99 (0.82-1.19)	0.87 (0.71-1.06)	1.01 (0.87-1.14)	1.00 (0.88-1.15)
Pre-diagnosis hospital admission	1.03 (0.82-1.30)	0.96 (0.76-1.21)	0.94 (0.50-0.93)	1.05 (0.78-1.42)	0.95 (0.82-1.07)	0.78 (0.60-1.01)	1.42 (1.09-1.84)	1.30 (1.01-1.68)	1.77 (1.18-2.68)	1.71 (1.13-2.58)	1.37 (1.11-1.69)	1.19 (0.96-1.48)
Sex												
Female	-	-	-	-	-	-	-	-	-	-	-	-
Male	1.11 (0.91-1.35)	1.13 (0.55-0.86)	0.76 (0.58-1.04)	0.85 (0.62-1.15)	1.16 (0.93-1.45)	1.04 (0.83-1.32)	1.14 (0.87-1.48)	1.12 (0.87-1.44)	1.11 (0.82-1.53)	1.20 (0.86-1.66)	1.16 (0.94-1.43)	1.05 (0.84-1.30)
Age at IBD diagnosis												
> 40 years	-	-	-	-	-	-	-	-	-	-	-	-
< 17 years	1.50 (1.21-1.86)	1.45 (1.00-2.09)	1.06 (0.63-1.79)	1.20 (0.68-2.12)	3.67 (2.63-5.10)	3.60 (2.47-5.24)	2.78 (1.86-4.15)	2.31 (1.51-3.56)	0.86 (0.47-1.58)	0.71 (0.37-1.36)	1.55 (1.11-1.46)	1.72 (1.18-2.51)
17 - 40 years	1.50 (1.21- 1.87)	1.46 (1.16-1.83)	1.36 (0.98-1.86)	1.26 (0.90-1.76)	1.79 (1.37- 2.33)	1.89 (1.43-2.49)	1.77 (1.34-2.33)	1.52 (1.14- 2.03)	1.41 (1.00-1.98)	1.18 (0.83-1.68)	1.17 (0.93-1.46)	1.27 (0.99-1.62)
Era of IBD diagnosis												
Era 1	-	-	-	-	-	-	-	-	-	-	-	-
Era 2	1.06 (0.81-1.39)	1.07 (0.82-1.42)	0.89 (0.60-1.31)	0.88 (0.59-1.29)	1.47 (1.03-2.07)	1.50 (0.66-1.41)	1.28 (0.88-1.85)	1.18 (0.83-1.69)	1.25 (0.81-1.94)	1.34 (0.86-2.08)	1.35 (0.96-1.88)	1.37 (0.98-1.92)
Era 3	0.94 (0.71-1.26)	0.90 (0.91-0.68)	0.73 (0.48-1.11)	0.72 (0.47-1.11)	1.97 (1.40-2.79)	2.02 (1.41-1.26)	1.19 (0.80-1.75)	1.15 (0.80-1.65)	1.33 (0.84-2.08)	1.29 (0.81-2.06)	2.25 (1.62-3.11)	2.21 (1.58-3.09)
Era 4	1.34 (1.01-1.77)	1.32 (0.99-1.77)	0.77 (0.50-1.17)	0.76 (0.49-1.18)	3.31 (2.34-4.65)	3.32 (2.34-4.74)	1.88 (1.28-2.76)	2.00 (1.35-2.98)	1.29 (0.80-2.07)	1.25 (0.76-2.04)	4.78 (3.48-6.55)	4.54 (3.28-6.28)
Smoking status*												

Never	-	-	-	-	-	-	-	-	-	-	-	-
Ex-smoker	0.95 (0.72-1.25)	0.85 (0.61-1.18)	1.22 (0.83-1.83)	0.90 (0.55-1.48)	0.83 (0.60-1.14)	0.91 (0.65-1.26)	0.90 (0.63-1.31)	0.60 (0.38-0.93)	0.97 (0.64-1.47)	0.96 (0.63-1.46)	0.82 (0.60-1.12)	0.94 (0.67-1.31)
Current	0.78 (0.61-1.01)	0.99 (0.75-1.31)	0.80 (0.50-1.31)	1.22 (0.82-1.83)	0.93 (0.70-1.23)	0.88 (0.65-1.19)	0.91 (0.66-1.24)	1.05 (0.75-1.48)	0.67 (0.45-0.99)	0.76 (0.50-1.16)	0.80 (0.60-1.06)	0.90 (0.67-1.20)
Social deprivation												
IMD 1-3	-	-	-	-	-	-	-	-	-	-	-	-
IMD 4-5	1.20 (0.99-1.48)	1.12 (0.91-1.39)	1.23 (0.91-1.66)	1.14 (0.83-1.56)	1.16 (0.92-1.47)	0.97 (0.76-1.24)	1.16 (0.88-1.52)	1.12 (0.86-1.46)	1.21 (0.87-1.67)	1.11 (0.80-1.55)	1.02 (0.82-1.27)	0.87 (0.69-1.08)

(b) Ulcerative Colitis

	CS use		CS dependency		IM use		IBD-Hospitalisation		Colectomy	
	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Consultation frequency										
1	-	-	-	-	-	-	-	-	-	-
2	1.22 (1.01-1.48)	1.26 (1.04-1.60)	1.27 (0.94-1.73)	1.28 (0.94-1.75)	1.15 (0.86-1.54)	1.12 (0.83-1.51)	1.33 (0.97-1.81)	1.24 (0.93-1.66)	0.86 (0.51-1.44)	0.93 (0.55-1.57)
≥ 3	1.53 (1.27-1.84)	1.60 (1.31-1.96)	1.72 (1.29-2.31)	1.76 (1.28-2.41)	1.71 (1.30-2.24)	1.68 (1.24-2.26)	1.66 (1.23-2.44)	1.43 (1.05-1.95)	1.57 (0.99-2.46)	2.01 (1.22-3.27)
Time to diagnosis	0.96 (0.87-1.05)	0.87 (0.79-0.97)	1.04 (0.90-1.20)	0.95 (0.81-1.11)	0.98 (0.86-1.13)	0.88 (0.76-1.03)	0.91 (0.78-1.06)	0.83 (0.70-0.98)	0.71 (0.54-0.95)	0.59 (0.43-0.80)
Pre-diagnosis hospital admission	1.25 (1.06-1.46)	1.18 (0.99-1.39)	1.10 (0.85-1.42)	1.04 (0.80-1.36)	1.51 (1.19-1.91)	1.42 (1.11-1.81)	1.58 (1.22-2.03)	1.36 (1.06-1.95)	1.41 (0.94-2.11)	1.54 (1.01-2.34)
Sex										
Female	-	-	-	-	-	-	-	-	-	-
Male	1.01 (0.86-1.18)	1.00 (0.85-1.17)	1.31 (1.02-1.69)	1.37 (1.06-1.76)	1.17 (0.92-1.47)	1.16 (0.92-1.48)	0.97 (0.75-1.25)	1.01 (0.79-1.29)	1.45 (0.96-2.19)	1.42 (0.93-2.16)
Age at IBD diagnosis										
>40	-	-	-	-	-	-	-	-	-	-
<17	1.88 (1.302-72)	1.82 (1.24-2.69)	2.41 (1.44-4.04)	2.38 (1.37-4.12)	3.40 (2.17-5.32)	3.35 (2.07-5.43)	3.54 (2.19-5.71)	3.40 (1.47-1.89)	2.77 (1.25-6.11)	2.54 (1.09-5.95)
17 – 39	1.39 (1.18- 1.63)	1.34 (1.14-1.60)	1.55 (1.20-2.00)	1.52 (1.17-1.98)	1.87 (0.46- 2.38)	1.83 (1.42-2.34)	1.56 (1.22-2.00)	1.47 (1.14- 1.89)	1.68 (1.11- 2.55)	1.81 (1.17-2.79)
Era of IBD diagnosis										

Era 1	-	-	-	-	-	-	-	-	-	-
Era 2	1.16 (0.93-1.45)	1.14 (0.92-1.43)	1.04 (0.76-1.43)	1.05 (0.76-1.44)	1.15 (0.81-1.62)	1.11 (0.78-1.57)	0.91 (0.64-1.30)	0.82 (0.58-1.13)	0.73 (0.43-1.22)	0.65 (0.38-1.09)
Era 3	1.42 (1.14-1.78)	1.35 (1.07-1.70)	0.89 (0.63-1.26)	0.83 (0.58-1.20)	1.71 (1.23-2.39)	1.53 (1.08-2.15)	1.05 (0.73-1.50)	0.91 (0.66-1.29)	0.76 (0.43-1.31)	0.62 (0.35-1.11)
Era 4	1.49 (1.17-1.89)	1.44 (1.14-1.83)	0.80 (0.55-1.17)	0.76 (0.52-1.12)	2.06 (1.45-2.93)	1.95 (1.36-2.80)	1.56 (1.09-2.23)	1.15 (0.79-1.58)	0.93 (0.52-1.67)	0.85 (0.46-1.54)
Smoking status*										
Never	-	-	-	-	-	-	-	-	-	-
Ex-smoker	0.89 (0.73-1.10)	0.94 (0.99-1.54)	0.83 (0.60-1.15)	0.88 (0.63-1.23)	0.78 (0.57-1.05)	0.89 (0.64-1.22)	0.59 (0.42- 0.84)	0.79 (0.51-1.03)	1.15 (0.66-1.99)	1.33 (0.75-2.34)
Current	0.93 (0.68-1.29)	0.97 (1.13-1.79)	0.64 (0.37-1.15)	0.59 (0.32-1.05)	0.80 (0.49-1.30)	0.81 (0.49-1.32)	0.70 (0.40-1.22)	0.78 (0.48-1.30)	0.98 (0.39-2.43)	0.89 (0.36-2.20)
Social deprivation										
IMD 1-3	-	-	-	-	-	-	-	-	-	-
IMD 4-5	1.11 (0.94-1.31)	1.06 (0.89-1.26)	0.94 (0.72-1.24)	0.91 (0.69-1.1)	0.89 (0.69-1.16)	0.79 (0.61-1.02)	1.40 (1.08-1.82)	1.26 (0.98-1.62)	0.72 (0.44-1.16)	0.65 (0.40-1.05)

Bold indicates statistical significance in adjusted model. CS, Corticosteroids; IM, Immunomodulator; HR, Hazard Ratio; CI, confidence interval; IMD, index of multiple deprivations

IMD categories 4 and 5 [most deprived] vs IMD categories 1, 2 and 3 [least deprived]

Era 1: 2003 – 2005, Era 2 2006 – 2008, Era 3 2009 – 2011 and Era 4 2012 – 2016

First CS use: Time to first CS prescription following diagnosis

CS dependency: Corticosteroid dependency defined as a repeat steroid prescription within 3 months of the end of a previous steroid prescription or patients with steroid prescriptions for greater than 3 consecutive months

Hospitalisation: IBD-related hospital admission following diagnosis

Time to diagnosis: Time from first primary care consultation for gastrointestinal symptom(s)

Appendix 4: Association of consultation intensity with gastrointestinal symptoms before diagnosis with clinical outcomes following (a) Crohn's disease diagnosis (b) Ulcerative colitis

(a) Crohn's disease

Year before diagnosis	CS use		CS dependency		IM use		IBD Hospitalisation		Intestinal surgery		Perianal surgery	
	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Year 1	1.08 (1.02-1.14)	1.03 (0.98-1.08)	1.06 (0.98-1.15)	1.01 (0.96-1.07)	0.99 (0.94-1.04)	1.00 (0.95-1.06)	1.19 (1.12-1.26)	1.19 (1.12-1.28)	1.11 (1.03-1.20)	1.13 (1.03-1.23)	1.01 (0.95-1.07)	1.05 (0.98-1.13)
Year 2	0.99 (0.89-1.09)	1.00 (0.92-1.09)	1.00 (0.86-1.17)	0.99 (0.90-1.09)	1.02 (0.94-1.12)	1.03 (0.94-1.12)	1.12 (1.00-1.24)	1.13 (1.01-1.25)	0.90 (0.74-1.08)	0.86 (0.71-1.03)	1.01 (0.92-1.12)	1.00 (0.90-1.12)
Year 3	0.93 (0.81-1.07)	0.96 (0.95-1.08)	1.03 (0.87-1.23)	0.99 (0.88-1.11)	0.92 (0.82-1.04)	0.90 (0.80-1.02)	1.09 (0.90-1.31)	1.10 (0.91-1.33)	1.18 (0.99-1.42)	1.25 (0.99-1.48)	1.02 (0.91-1.48)	0.98 (0.87-1.11)

(b) Ulcerative colitis

Year before diagnosis	CS use		CS dependency		IM use		IBD Hospitalisation		Colectomy	
	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Year 1	1.16 (1.10-1.21)	1.08 (1.04-1.13)	1.22 (1.13-1.31)	1.05 (1.00-1.11)	1.01 (0.97-1.06)	1.03 (0.98-1.08)	1.14 (1.05-1.24)	1.12 (1.03-1.21)	1.14 (1.00-1.28)	1.12 (0.99-1.26)
Year 2	1.09 (0.99-1.19)	1.03 (0.96-1.11)	1.23 (1.09-1.39)	1.07 (0.98-1.15)	1.03 (0.94-1.12)	1.03 (0.95-1.13)	1.08 (0.94-1.24)	1.05 (0.92-1.20)	0.92 (0.68-1.23)	0.91 (0.68-1.20)
Year 3	0.98 (0.87-1.12)	1.02 (0.93-1.12)	1.03 (0.85-1.24)	1.05 (0.96-1.16)	1.00 (0.91-1.11)	1.03 (0.93-1.13)	0.96 (0.78-1.18)	1.00 (0.81-1.23)	1.00 (0.73-1.37)	1.00 (0.73-1.28)

Bold indicates statistical significance in adjusted model. CS, Corticosteroids; IM, Immunomodulator; HR, Hazard Ratio; CI, confidence interval; IMD, index of multiple deprivations

IMD categories 4 and 5 [most deprived] vs IMD categories 1, 2 and 3 [least deprived]

Era 1: 2003 – 2005, Era 2 2006 – 2008, Era 3 2009 – 2011 and Era 4 2012 – 2016

First CS use: Time to first CS prescription following diagnosis

CS dependency: Corticosteroid dependency defined as a repeat steroid prescription within 3 months of the end of a previous steroid prescription or patients with steroid prescriptions for greater than 3 consecutive months

Hospitalisation: IBD-related hospital admission following diagnosis

Consultation intensity consultation frequency per person, as a continuous variable, in each individual year over the 3-year period before diagnosis

Appendix 5 Factors associated with time to diagnosis, consultation frequency, consultation intensity and hospitalisation before diagnosis of IBD

	Time to diagnosis		Consultation frequency		Consultation Intensity		Prior GI hospitalisation	
	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted Coefficient (95% CI)	Adjusted Coefficient (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Age								
> 40	-	-	-	-	-	-	-	-
< 17	1.05 (0.90 - 1.06)	0.99 (0.82 - 1.17)	1.71 (1.44 - 2.03)	2.32 (1.40 - 2.01)	0.01 (-0.14 - 0.14)	0.44 (0.20 - 0.67)	1.62 (1.15 - 2.27)	1.74 (1.21 - 2.48)
17-39	0.98 (0.89 - 1.25)	0.99 (0.91 - 1.07)	1.75 (1.23 - 2.47)	1.68 (1.60 - 3.38)	0.07 (0.01 - 0.14)	0.37 (0.25 - 0.48)	0.96 (0.81 - 1.13)	0.95 (0.80 - 1.14)
Sex								
Male	-	-	-	-	-	-	-	-
Female	0.85 (0.78 - 0.91)	0.89 (0.82 - 0.96)	1.23 (1.04 - 1.45)	1.12 (0.94 - 1.33)	0.05 (-0.06 - 0.15)	0.00 (-0.11 - 1.11)	0.95 (0.81 - 1.11)	0.96 (0.81 - 1.13)
Social Deprivation								
IMD 1-3	-	-	-	-	-	-	-	-
IMD 4-5	0.99 (0.91 - 1.08)	1.01 (0.93 - 1.10)	1.18 (0.99 - 1.41)	1.09 (0.91 - 1.30)	0.14 (0.03 - 0.26)	0.10 (-0.02 - 0.22)	1.33 (1.12 - 1.58)	1.29 (1.09 - 1.54)
Smoking status*								
Never	-	-	-	-	-	-	-	-
Ex-smoker	0.95 (0.87 - 1.04)	0.91 (0.82 - 1.01)	0.89 (0.71 - 1.11)	1.06 (0.84 - 1.34)	-0.90 (-0.22 - 0.04)	0.03 (-0.10 - 0.25)	1.16 (0.93 - 1.43)	1.16 (0.93 - 1.46)
Current	0.92 (0.81 - 1.03)	0.93 (0.88 - 1.08)	1.48 (1.12 - 1.95)	1.42 (1.07 - 1.88)	0.34 (0.17 - 0.51)	0.34 (0.16 - 0.51)	1.26 (0.96 - 1.65)	1.23 (0.94 - 1.63)
Premorbid Depression-anxiety	0.84 (0.76 - 0.93)	0.87 (0.78 - 0.96)	1.26 (1.01 - 1.56)	1.28 (1.02 - 1.60)	0.09 (-0.06 - 0.23)	0.12 (-0.22 - 0.27)	1.19 (0.96 - 1.46)	1.17 (0.91 - 1.52)
Premorbid IBS	0.64 (0.56 - 0.72)	0.66 (0.58 - 0.75)	2.05(1.60 - 2.62)	1.87 (1.44 - 2.41)	0.16 (-0.01 - 0.34)	0.08 (-0.10 - 0.25)	1.12 (0.87 - 1.44)	1.18 (0.95 - 1.46)
Era of diagnosis								
Era 1	-	-	-	-	-	-	-	-
Era 2	1.06 (0.95 - 1.18)	1.06 (0.95 - 1.18)	1.08 (0.86 - 1.36)	1.04 (0.82 - 1.32)	-0.06 (-0.21 - 0.08)	-0.74 (-0.22 - 0.07)	1.34 (1.07 - 1.68)	1.31 (1.04 - 1.64)
Era 3	1.03 (0.92 - 1.15)	1.01 (0.91 - 1.13)	1.13 (0.89 - 1.42)	1.05 (0.83 - 1.32)	-0.10 (-0.25 - 0.06)	-1.13 (-0.28 - 0.27)	1.62 (1.29 - 2.05)	1.57 (1.23 - 1.99)
Era 4	1.02 (0.92 - 1.14)	1.00 (0.89 - 1.12)	0.94 (0.74 - 1.20)	0.88 (0.68 - 1.12)	-0.18 (-0.34 - -0.03)	-0.22 (-0.37 - 0.06)	1.69 (1.34 - 2.12)	1.61 (1.26 - 2.03)

Bold indicates statistical significance in adjusted model Note: Multiple regression includes all variables and covariates of simple regression. Abbreviations: CS, Corticosteroids; IM, Immunomodulator; HR, Hazard Ratio; CI, confidence interval; IMD, index of multiple deprivations

IMD categories 4 and 5 [most deprived] vs IMD categories 1, 2 and 3 [least deprived]

Era 1: 2003 – 2005, Era 2 2006 – 2008, Era 3 2009- 2011 and Era 4 2012 – 2016

First CS use: Time to first CS prescription following diagnosis

CS dependency: Corticosteroid dependency defined as a repeat steroid prescription within 3 months of the end of a previous steroid prescription or patients with steroid prescriptions for greater than 3 consecutive months

Hospitalisation: First IBD-related hospital admission following diagnosis

Time to diagnosis: Time from first primary care consultation for gastrointestinal symptom(s)

Consultation intensity: consultation frequency per person in the year prior to IBD diagnosis

Abbreviation gastrointestinal (GI)