

**Supplementary material for:**

**The risk of common infections in people with Inflammatory Bowel Disease in primary care: a population-based cohort study**

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**Supplementary Table 1: Risk of each sub-infection outcome in CD and UC.****A) Crohn's Disease**

	No.	Patient years at risk	Events	Hazard ratio (95% CI)	
				Unadjusted	Adjusted**
<b>URTI</b>					
Controls (Unexposed)	29876	90493	5002 (16.7%)	1.00 (ref)	1.00 (ref)
Crohn's (Exposed)	7469	20519	1475 (19.7%)	1.29 (1.22-1.37)	1.12 (1.04-1.21)
<b>Pneumonia</b>					
Controls (Unexposed)	29876	88874	136 (0.5%)	1.00 (ref)	1.00 (ref)
Crohn's (Exposed)	7469	19954	59 (0.8%)	1.97 (1.45-2.67)	1.77 (1.20-2.61)
<b>Acute Bronchitis</b>					
Controls (Unexposed)	29876	90367	3211 (10.7%)	1.00 (ref)	1.00 (ref)
Crohn's (Exposed)	7469	20531	1059 (14.2%)	1.45 (1.35-1.56)	1.11 (1.01-1.22)
<b>Influenza</b>					
Controls (Unexposed)	29876	89094	621 (2.1%)	1.00 (ref)	1.00 (ref)
Crohn's (Exposed)	7469	20000	158 (2.1%)	1.14 (0.96-1.36)	1.01 (0.79-1.28)
<b>Skin infection</b>					
Controls (Unexposed)	29876	90122	3294 (11.0%)	1.00 (ref)	1.00 (ref)
Crohn's (Exposed)	7469	20481	1201 (16.1%)	1.61 (1.51-1.72)	1.42 (1.30-1.55)
<b>Genital infection</b>					
Controls (Unexposed)	29876	89130	665 (2.2%)	1.00 (ref)	1.00 (ref)
Crohn's (Exposed)	7469	20077	219 (2.9%)	1.46 (1.25-1.70)	0.97 (0.78-1.21)
<b>UTI</b>					
Controls (Unexposed)	29876	89695	1568 (5.2%)	1.00 (ref)	1.00 (ref)
Crohn's (Exposed)	7469	20221	473 (6.3%)	1.34 (1.21-1.49)	1.09 (0.95-1.26)
<b>GI infection subset*</b>					
Controls (Unexposed)	29876	88854	130 (0.4%)	1.00 (ref)	1.00 (ref)
Crohn's (Exposed)	7469	19941	76 (1.0%)	2.65 (2.00-3.51)	1.45 (0.97-2.18)
<b>Herpes Simplex infection</b>					
Controls (Unexposed)	29876	88928	253 (0.8%)	1.00 (ref)	1.00 (ref)
Crohn's (Exposed)	7469	19970	109 (1.5%)	1.91 (1.53-2.39)	1.37 (1.00-1.87)
<b>Herpes Zoster infection</b>					
Controls (Unexposed)	29876	89058	491 (1.6%)	1.00 (ref)	1.00 (ref)
Crohn's (Exposed)	7469	20048	237 (3.2%)	2.17 (1.86-2.54)	1.68 (1.36-2.08)

\*Composite of stool culture confirmed *Clostridium difficile*, *Salmonella*, *Shigella*, and *Campylobacter* infections.

\*\*Models adjusted for age, sex, IMD quintile, white ethnicity, BMI category, smoking status, alcohol category, hypertension, hyperlipidaemia, type 2 diabetes, peripheral arterial disease, atrial fibrillation, angina, myocardial infarction, stroke, heart failure, chronic kidney disease stage 3-5, chronic obstructive pulmonary disorder, chronic liver disease, malignancy, dementia, rheumatoid arthritis, fracture history, depression and concomitant medication use (from Rectal 5-ASA, Rectal glucocorticoids, Oral 5-ASA, Oral glucocorticoids, Immunotherapies and biologic therapies).

**B) Ulcerative Colitis**

	No.	Patient years at risk	Events	Hazard ratio (95% CI)	
				Unadjusted	Adjusted**
<b>URTI</b>					
Controls (Unexposed)	45440	136128	7143 (15.7%)	1.00 (ref)	1.00 (ref)
UC (Exposed)	11360	31931	2118 (18.6%)	1.26 (1.20-1.32)	1.12 (1.04-1.21)
<b>Pneumonia</b>					
Controls (Unexposed)	45440	133959	288 (0.6%)	1.00 (ref)	1.00 (ref)
UC (Exposed)	11360	31156	100 (0.9%)	1.51 (1.20-1.89)	1.19 (0.85-1.67)
<b>Acute Bronchitis</b>					
Controls (Unexposed)	45440	136263	5554 (12.2%)	1.00 (ref)	1.00 (ref)
UC (Exposed)	11360	31949	1754 (15.4%)	1.35 (1.28-1.42)	1.18 (1.09-1.28)
<b>Influenza</b>					
Controls (Unexposed)	45440	134303	856 (1.9%)	1.00 (ref)	1.00 (ref)
UC (Exposed)	11360	31273	234 (2.1%)	1.18 (1.03-1.37)	1.14 (0.92-1.41)
<b>Skin infection</b>					
Controls (Unexposed)	45440	136062	5268 (11.6%)	1.00 (ref)	1.00 (ref)
UC (Exposed)	11360	31955	1654 (14.6%)	1.34 (1.27-1.42)	1.19 (1.09-1.29)
<b>Genital infection</b>					
Controls (Unexposed)	45440	134285	874 (1.9%)	1.00 (ref)	1.00 (ref)
UC (Exposed)	11360	31267	246 (2.2%)	1.21 (1.05-1.39)	1.13 (0.92-1.40)
<b>UTI</b>					
Controls (Unexposed)	45440	135158	2631 (5.8%)	1.00 (ref)	1.00 (ref)
UC (Exposed)	11360	31503	733 (6.5%)	1.20 (1.10-1.30)	1.14 (1.01-1.28)
<b>GI infection subset*</b>					
Controls (Unexposed)	45440	133849	198 (0.4%)	1.00 (ref)	1.00 (ref)
UC (Exposed)	11360	31151	121 (1.1%)	2.64 (2.11-3.31)	1.82 (1.30-2.56)
<b>Herpes Simplex infection</b>					
Controls (Unexposed)	45440	133916	352 (0.8%)	1.00 (ref)	1.00 (ref)
UC (Exposed)	11360	31138	106 (0.9%)	1.29 (1.04-1.61)	0.85 (0.60-1.22)
<b>Herpes Zoster infection</b>					
Controls (Unexposed)	45440	134225	839 (1.8%)	1.00 (ref)	1.00 (ref)
UC (Exposed)	11360	31255	309 (2.7%)	1.59 (1.40-1.82)	1.37 (1.13-1.65)

\*Composite of stool culture confirmed *Clostridium difficile*, *Salmonella*, *Shigella*, and *Campylobacter* infections.

\*\*Models adjusted for age, sex, IMD quintile, white ethnicity, BMI category, smoking status, alcohol category, hypertension, hyperlipidaemia, type 2 diabetes, peripheral arterial disease, atrial fibrillation, angina, myocardial infarction, stroke, heart failure, chronic kidney disease stage 3-5, chronic obstructive pulmonary disorder, chronic liver disease, malignancy, dementia, rheumatoid arthritis, fracture history, depression and concomitant medication use (from Rectal 5-ASA, Rectal glucocorticoids, Oral 5-ASA, Oral glucocorticoids, Immunotherapies and biologic therapies).

**Supplementary Table 2: Association of baseline measures with time to first infection among individuals with UC and CD.** All values are multivariable adjusted hazard ratios (95% Confidence intervals). For categorical measures we define a reference group (ref) for each measures and hazard ratios with the group are relative to the reference group.

	<b>Ulcerative Colitis N=11,360</b>	<b>Crohn's Disease N=7,469</b>
<b>Demographic characteristics</b>		
Age at study entry (per year increase)	1.001 (0.999, 1.003)	0.997 (0.994, 1.000)
Male vs. Female	0.66 (0.62, 0.70)	0.65 (0.60, 0.70)
Duration of IBD (per year increase)	1.001 (0.999, 1.004)	1.003 (1.000, 1.006)
<i>Ethnicity</i>		
White	1.00 (ref)	1.00 (ref)
Asian	1.27 (1.12, 1.45)	1.20 (1.00, 1.46)
Black	0.95 (0.68, 1.33)	0.83 (0.56, 1.21)
Mixed	1.09 (0.75, 1.57)	0.91 (0.57, 1.44)
Other	1.14 (0.79, 1.64)	2.05 (1.37, 3.05)
Missing	0.95 (0.89, 1.02)	1.00 (0.92, 1.08)
Index of Multiple Deprivation quintile		
1 (most deprived)	1.00 (ref)	1.00 (ref)
2	0.88 (0.79, 0.98)	0.94 (0.83, 1.06)
3	0.85 (0.77, 0.94)	0.92 (0.82, 1.04)
4	0.87 (0.79, 0.95)	0.94 (0.84, 1.05)
5 (least deprived)	0.89 (0.81, 0.98)	0.93 (0.83, 1.05)
IMD not recorded	0.54 (0.41, 0.70)	0.62 (0.47, 0.82)
<b>Lifestyle factors</b>		
<i>BMI (kg/m<sup>2</sup>)</i>		
Underweight ( $\leq 18.5$ )	1.15 (0.95, 1.38)	0.95 (0.81, 1.13)
Normal weight (18.5-25)	1.00 (ref)	1.00 (ref)
Overweight (25-30)	1.07 (1.00, 1.14)	1.13 (1.04, 1.23)
Obese ( $\geq 30$ )	1.26 (1.17, 1.36)	1.30 (1.18, 1.43)
BMI not recorded	0.91 (0.80, 1.03)	0.94 (0.81, 1.09)
<i>Smoking Status</i>		
Non-smoker	1.00 (ref)	1.00 (ref)
Current smoker	1.14 (1.04, 1.25)	1.34 (1.22, 1.47)
Ex-smoker	1.12 (1.05, 1.19)	1.22 (1.12, 1.33)
Smoking status not recorded	0.60 (0.34, 1.07)	0.64 (0.36, 1.15)

<i>Alcohol intake (n (%))</i>		
Non-drinker	1.12 (1.04, 1.22)	1.01 (0.92, 1.12)
Within limits	1.00 (ref)	1.00 (ref)
Over recommended limits	1.08 (0.99, 1.17)	0.99 (0.89, 1.10)
Alcoholism	1.10 (0.88, 1.37)	1.18 (0.91, 1.52)
Alcohol intake not recorded	1.08 (0.98, 1.20)	1.16 (1.03, 1.30)
<b>Co-morbidities</b>		
Hypertension	1.00 (0.93, 1.08)	1.09 (0.98, 1.20)
Hyperlipidaemia	1.00 (0.93, 1.07)	0.95 (0.86, 1.05)
Type 2 diabetes	1.18 (1.07, 1.30)	1.15 (0.99, 1.32)
Peripheral vascular disease	1.10 (0.87, 1.40)	1.30 (0.98, 1.72)
Atrial Fibrillation	1.32 (1.14, 1.52)	1.17 (0.94, 1.46)
Myocardial Infarction	1.17 (1.01, 1.35)	1.26 (1.02, 1.57)
Angina	1.19 (1.00, 1.40)	1.08 (0.84, 1.38)
Stroke	1.24 (1.04, 1.49)	1.23 (0.96, 1.59)
Heart Failure	1.13 (0.92, 1.39)	1.01 (0.74, 1.37)
Chronic Kidney Disease Stages 3 to 5	1.16 (1.04, 1.29)	1.10 (0.95, 1.27)
Chronic Liver Disease	1.10 (0.90, 1.33)	1.15 (0.87, 1.50)
COPD	1.20 (1.06, 1.37)	1.29 (1.12, 1.49)
Malignancy	1.21 (1.08, 1.35)	1.19 (1.01, 1.39)
Dementia	1.27 (1.08, 1.49)	1.38 (1.10, 1.73)
Rheumatoid Arthritis	1.08 (0.87, 1.34)	1.01 (0.75, 1.35)
History of fracture	1.08 (0.98, 1.18)	1.09 (0.97, 1.23)
Depression	1.20 (1.05, 1.37)	1.23 (1.07, 1.41)
<b>Medication use</b>		
Rectal 5-ASA	0.95 (0.88, 1.02)	0.88 (0.73, 1.05)
Rectal glucocorticoids	1.17 (1.08, 1.26)	1.01 (0.85, 1.19)
Oral 5-ASA	0.99 (0.93, 1.05)	0.93 (0.86, 1.00)
Oral glucocorticoids	1.36 (1.28, 1.45)	1.40 (1.30, 1.51)
Immunotherapies	1.15 (1.06, 1.25)	1.13 (1.05, 1.22)
Biologic therapies	1.55 (1.06, 2.27)	1.48 (1.20, 1.83)

**Supplementary Table 3: Adjusted hazard ratios for onset of a common infection by time-varying haematological abnormality status across study follow-up.** Hazard ratios represent the increase in the risk of infections associated with the presence of each haematological abnormality at any time during study follow-up, compared to the absence of the haematological abnormality, in individuals with at least one measure during study follow-up. N's represent the number of individuals with at least one count and were included in the analysis.

Models adjusted for age, sex, IMD quintile, white ethnicity, BMI category, smoking status, alcohol category, hypertension, hyperlipidaemia, type 2 diabetes, peripheral arterial disease, atrial fibrillation, angina, myocardial infarction, stroke, heart failure, chronic kidney disease stage 3-5, chronic obstructive pulmonary disorder, chronic liver disease, malignancy, dementia, rheumatoid arthritis, fracture history, depression and concomitant medication use (from Rectal 5-ASA, Rectal glucocorticoids, Oral 5-ASA, Oral glucocorticoids, Immunotherapies and biologic therapies).

#### A) IBD (both UC and CD)

i) Lymphopenia (lymphocyte count  $<1.0 \times 10^9$  cells/L)

	IBD N=15290*	Controls N=44324*
Number of individuals with at least one episode across follow-up	2806 (18.4%)	2900 (6.5%)
Unadjusted hazard ratio (95% CI)	1.07 (0.99, 1.15), p=0.11	1.41 (1.31-1.52), p<0.001
Adjusted hazard ratio (95% CI)	1.05 (0.97, 1.14), p=0.21	1.26 (1.17-1.36), p<0.001

ii) Neutropenia (neutrophil count  $<1.5 \times 10^9$  cells/L)

	IBD N=15290*	Controls N=44324*
Number of individuals with at least one episode across follow-up	285 (1.9%)	659 (1.5%)
Unadjusted hazard ratio (95%CI)	1.10 (0.79, 1.52), p=0.58	0.98 (0.81-1.18), p=0.80
Adjusted hazard ratio (95% CI)	1.12 (0.80, 1.55), p=0.51	1.05 (0.87-1.27), p=0.60

\*subset of individuals with at least one lymphocyte count and neutrophil count during the study period

**B) Ulcerative Colitis**i) Lymphopenia (lymphocyte count  $<1.0 \times 10^9$  cells/L)

	<b>UC</b> <b>N=9216</b>	<b>Controls</b> <b>N=27296</b>
Number of individuals with at least one episode across follow-up	1411 (15.3%)	1890 (6.9%)
Unadjusted hazard ratio (95% CI)	1.17 (1.05, 1.31), p=0.006	1.41 (1.29-1.55), p<0.001
Adjusted hazard ratio (95% CI)	1.11 (0.99, 1.25), p=0.07	1.24 (1.13-1.37), p<0.001

ii) Neutropenia (neutrophil count  $<1.5 \times 10^9$  cells/L)

	<b>UC</b> <b>N= 9221</b>	<b>Controls</b> <b>N=27307</b>
Number of individuals with at least one episode across follow-up	179 (1.9%)	388 (1.4%)
Unadjusted hazard ratio (95%CI)	1.17 (0.78, 1.77), p=0.44	0.92 (0.71-1.18), p=0.49
Adjusted hazard ratio (95% CI)	1.17 (0.78, 1.77), p=0.45	1.02 (0.79-1.31), p=0.89

**C) Crohn's Disease**i) Lymphopenia (lymphocyte count  $<1.0 \times 10^9$  cells/L)

	<b>CD</b> <b>N=6074</b>	<b>Controls</b> <b>N=17131</b>
Number of individuals with at least one episode across follow-up	1395 (23.0%)	1016 (6.0%)
Unadjusted hazard ratio (95% CI)	0.96 (0.86, 1.07), p=0.44	1.38 (1.21-1.58), p<0.001
Adjusted hazard ratio (95% CI)	1.01 (0.89, 1.13), p=0.88	1.29 (1.12-1.47), p<0.001

ii) Neutropenia (neutrophil count  $<1.5 \times 10^9$  cells/L)

	<b>CD</b> <b>N=6081</b>	<b>Controls</b> <b>N=17133</b>
Number of individuals with at least one episode across follow-up	106 (1.7%)	271 (1.6%)
Unadjusted hazard ratio (95%CI)	0.98 (0.57, 1.69), p=0.95	1.05 (0.79-1.41), p=0.72
Adjusted hazard ratio (95% CI)	1.06 (0.61, 1.83), p=0.84	1.08 (0.81-1.45), p=0.60

**Supplementary Table 4A: Absolute number of individuals within each lymphocyte count category (number of individuals with at least one count recorded within a category over the study period, meaning individuals can be included in more than one category), and number of count values and infections within each category across study follow-up.**

Lymphocyte count category (X 10 <sup>9</sup> cells/L)	IBD N=15290*			Controls N=44324*		
	Number of people with a count in category	Number of counts in category over follow-up	Number of infections in category over follow-up (% = as a percentage of total number of counts in category over follow-up)	Number with a count in category	Number of counts in category over follow-up	Number of infections in category over follow-up (% = as a percentage of total number of counts in category over follow-up)
<b>Severe (&lt;0.5)</b>	420 (2.7%)	1229	66 (5.4%)	289 (0.7%)	644	54 (8.4%)
<b>Moderate (0.5-0.8)</b>	1410 (9.2%)	4726	238 (5.0%)	1105 (2.5%)	2555	230 (9.0%)
<b>Mild (0.8-1.0)</b>	2148 (14.0%)	6008	389 (6.5%)	2160 (4.9%)	4286	421 (9.8%)
<b>Normal (1.0-4.0)</b>	14419 (94.3%)	66918	5886 (8.8%)	43019 (97.0%)	131463	15331 (11.6%)
<b>Lymphocytosis (&gt;4.0)</b>	451 (2.9%)	888	113 (12.7%)	1152 (2.6%)	2578	296 (11.4%)

\*subset of individuals with at least one lymphocyte count and neutrophil count during the study period



**Supplementary Table 4B: Absolute number of individuals within each neutrophil count category (number of individuals with at least one count recorded within a category over the study period, meaning individuals can be included in more than one category), and number of count values and infections within each category across study follow-up.**

Neutrophil count category (X 10 <sup>9</sup> cells/L)	IBD N=15290*			Controls N=44324*		
	Number of individuals with a count in category over follow-up	Number of counts in category over follow-up	Number of infections in category over follow-up (% = as a percentage of total number of counts in category over follow-up)	Number with a count in category	Number of counts in category over follow-up	Number of infections in category over follow-up (% = as a percentage of total number of counts in category over follow-up)
<b>Severe (&lt;0.5)</b>	11 (0.1%)	12	1 (8.3%)	28 (0.1%)	71	8 (11.3%)
<b>Moderate (0.5-1.0)</b>	47 (0.3%)	86	8 (9.3%)	102 (0.2%)	174	16 (9.2%)
<b>Mild (1.0-1.5)</b>	257 (1.7%)	456	27 (5.9%)	587 (1.3%)	1000	83 (8.3%)
<b>Normal (1.5-7.5)</b>	14675 (96.0%)	73152	6088 (8.3%)	42950 (96.9%)	132521	15245 (11.5%)
<b>Neutrophilia (&gt;7.5)</b>	2811 (18.4%)	6197	575 (9.3%)	4249 (9.6%)	7982	989 (12.4%)

\*subset of individuals with at least one lymphocyte count and neutrophil count during the study period

**Supplementary Table 5: Adjusted hazard ratios (aHR) for additional sensitivity analysis for the primary outcomes of common infection, gastrointestinal (GI) infection, and viral infection in cases versus matched controls.** Data in brackets are 95% confidence intervals.

Models adjusted for age, sex, IMD quintile, white ethnicity, BMI category, smoking status, alcohol category, hypertension, hyperlipidaemia, type 2 diabetes, peripheral arterial disease, atrial fibrillation, angina, myocardial infarction, stroke, heart failure, chronic kidney disease stage 3-5, chronic obstructive pulmonary disorder, chronic liver disease, malignancy, dementia, rheumatoid arthritis, fracture history, depression and (except sensitivity analysis iii) concomitant medication use (from Rectal 5-ASA, Rectal glucocorticoids, Oral 5-ASA, Oral glucocorticoids, Immunotherapies and biologic therapies).

**A) Ulcerative colitis**

Sensitivity analysis	Common infection	GI infection	Viral infection
i) excluding controls without a consultation in the year prior to study start date [n=11,360 cases, n=34,173 controls]	1.06 (1.01;1.11)	1.34 (1.15;1.56)	1.05 (0.98;1.13)
ii) excluding IBD cases (and their matched controls) with less than 1 year between practice registration date and study start date [n=9,607 cases, n=38,428 controls]	1.12 (1.07, 1.18)	1.52 (1.30, 1.77)	1.14 (1.06, 1.22)
iii) Multivariable model without adjusting for medications [n=11,360 cases, n=45,4450 controls]	1.24 (1.20, 1.28)	1.58 (1.42, 1.75)	1.27 (1.21, 1.33)
iv) Replacing each comorbidity adjusted for separately in the model with a categorical comorbidity count score [n=11,360 cases, n=45,4450 controls]	1.13 (1.08, 1.19)	1.49 (1.29, 1.73)	1.13 (1.06, 1.21)
v) Excluding IBD cases (and their matched controls) with missing data (ethnicity, BMI, smoking, alcohol, deprivation) [n=7,785 cases, n=23,204 controls]	1.13 (1.07, 1.20)	1.51 (1.27, 1.81)	1.17 (1.08, 1.27)

**B) Crohn's disease**

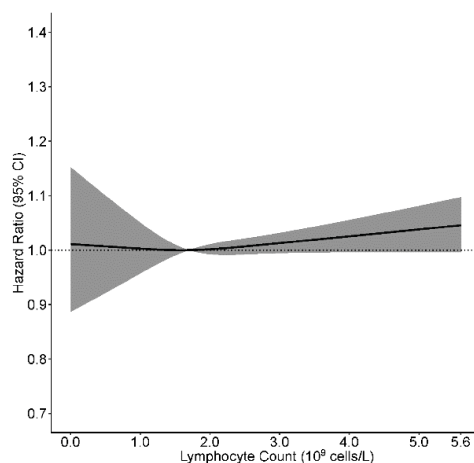
Sensitivity analysis	Common infection	GI infection	Viral infection
i) excluding patients without a consultation in the year prior to study start date [n=7,469 cases, n=22,064 controls]	1.12 (1.06, 1.18)	1.65 (1.41, 1.95)	1.06 (0.99, 1.14)
ii) excluding IBD cases (and their matched controls) with less than 1 year between practice registration date and study start date [n=6,181 cases, n=24,724 controls]	1.20 (1.14, 1.27)	1.96 (1.66, 2.31)	1.15 (1.07, 1.24)
iii) Multivariable model without adjusting for medications [n=7,469 cases, n=29,876 controls]	1.33 (1.28, 1.38)	2.03 (1.79, 2.29)	1.30 (1.23, 1.37)
iv) Replacing each comorbidity adjusted for separately in the model with a categorical comorbidity count score [n=7,469 cases, n=29,876 controls]	1.19 (1.13, 1.25)	1.85 (1.58, 2.17)	1.15 (1.07, 1.23)
v) Excluding IBD cases (and their matched controls) with missing data (ethnicity, BMI, smoking, alcohol, deprivation) [n=4,922 cases, n=14,325 controls]	1.16 (1.10, 1.24)	1.82 (1.50, 2.12)	1.14 (1.04, 1.24)

**Supplementary Figure 1: Association of continuous time-varying lymphocyte and neutrophil count with risk of presentation of common infection in individuals with and without inflammatory bowel disease, with counts in the 2 months prior to an infection excluded as a sensitivity analysis.** Lymphocyte and neutrophil counts each modelled a restricted cubic spline with 3 knots in a multivariable model\*. Associations are shown relative to the mean count in individuals with IBD (lymphocyte count  $1.7 \times 10^9$  cells/L; neutrophil count  $4.4 \times 10^9$  cells/L), up to the 99.5<sup>th</sup> centile of each count variable. Grey shading represents 95% confidence intervals. Models adjusted for age, sex, IMD quintile, white ethnicity, BMI category, smoking status, alcohol category, hypertension, hyperlipidaemia, type 2 diabetes, peripheral arterial disease, atrial fibrillation, angina, myocardial infarction, stroke, heart failure, chronic kidney disease stage 3-5, chronic obstructive pulmonary disorder, chronic liver disease, malignancy, dementia, rheumatoid arthritis, fracture history, depression and medication use (Rectal 5-ASA, Rectal glucocorticoids, Oral 5-ASA, Oral glucocorticoids, Immunotherapies and biologic therapies).

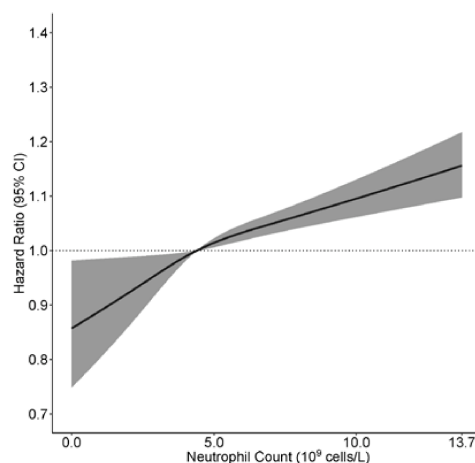
This analysis was undertaken to explore potential effects of reverse causality (i.e. infections causing haematological abnormalities) and potential infection surveillance bias prompted by these abnormalities in the non-IBD patients which is not reproduced in people with IBD.

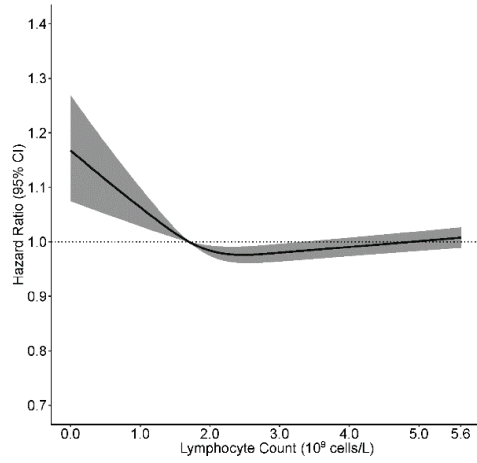
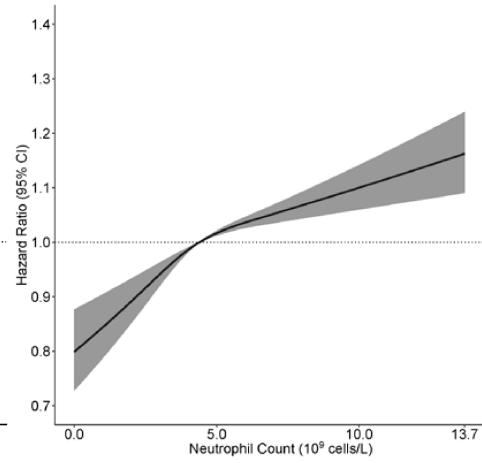
**A) With IBD (n=15,290, infection events=6,692)**

**Lymphocyte count**



**Neutrophil count**



**B) Controls (n=44,324, infection events=16,332)****Lymphocyte count****Neutrophil count**

**Appendix 1:** Read codes used to identify inflammatory bowel disease.

<b>Ulcerative colitis</b>		
<b>Read V2 Code</b>	<b>Term ID</b>	<b>Description</b>
J41..	All	Ulcerative colitis and/or proctitis
J410.	All	Ulcerative proctocolitis
J4100	All	Ulcerative ileocolitis
J4101	All	Ulcerative colitis
J4102	All	Ulcerative rectosigmoiditis
J4103	All	Ulcerative proctitis
J4104	All	Exacerbation of ulcerative colitis
J410z	All	Ulcerative proctocolitis NOS
J411.	All	Ulcerative (chronic) enterocolitis
J412.	All	Ulcerative (chronic) ileocolitis
J413.	All	Ulcerative pancolitis
N0454	All	Juvenile arthritis in ulcerative colitis
N0310	All	Arthropathy in ulcerative colitis
<b>Read CTV3 Code</b>	<b>Term ID</b>	<b>Description</b>
XE0ag	All	Ulcerative colitis
XaZ2j	All	Left sided ulcerative colitis
XaYzX	All	Ulcerative pancolitis
XaK6E	All	Exacerbation of ulcerative colitis
J410.	All	Ulcerative proctocolitis
J4100	All	Ulcerative ileocolitis
J410z	All	Ulcerative proctocolitis NOS
Jyu41	All	[X]Other ulcerative colitis
<b>Crohn's disease</b>		
<b>Read V2 Code</b>	<b>Term ID</b>	<b>Description</b>
J40..	All	Regional enteritis- Crohn's disease
J400.	All	Regional enteritis of the small bowel
J4002	All	Crohn's disease of the terminal ileum
J4003	All	Crohn's disease of the ileum unspecified
J4004	All	Crohn's disease of the ileum NOS
J4005	All	Exacerbation of Crohn's disease of small intestine
J400z	All	Crohn's disease of the small bowel NOS
J40..	All	Crohn's disease
J4012	All	Exacerbation of Crohn's disease of large intestine
J401z	All	Crohn's disease of the large bowel NOS
J402.	All	Regional ileocolitis
J40z.	All	Crohn's disease NOS
<b>Read CTV3 Code</b>	<b>Term ID</b>	<b>Description</b>
XE2QL	All	Crohn's disease
Xa0lh	All	Regional enteritis
X302r	All	Crohn's jejunitis
X302t	All	Crohn's ileitis

J4003	All	Crohn's disease of the ileum unspecified
J4004	All	Crohn's disease of the ileum NOS
J4002	All	Crohn's disease of terminal ileum
J400.	All	Regional enteritis of small bowel
XaK6C	All	Exacerbation of Crohn's disease of small intestine
J400z	All	Crohn's disease of the small bowel NOS
J401.	All	Regional enteritis of the large bowel
XE0af	All	Crohn's disease of the large bowel NOS
XaK6D	All	Exacerbation of Crohn's disease of large intestine
J40z.	All	Regional enteritis NOS
J4010	All	Crohn's colitis
J4011	All	Crohn's proctitis
X3050	All	Perianal Crohn's disease
Jyu40	All	[X]Other Crohn's disease

**Appendix 2:** Read codes used to identify stool culture-confirmed GI infections (a composite of Clostridium difficile, Salmonella, Shigella, and Campylobacter infections).

<b>Salmonella</b>	
<b>Read V2 Code</b>	<b>Description</b>
A020.	Salmonella gastroenteritis
4J230	Sample: salmonella cultured
<b>Read CTV3 Code</b>	<b>Description</b>
Xa8IA	Salmonella infection
XE0Qe	Salmonella gastroenteritis
Xa8I7	Salmonella food poisoning
4J230	Sample: salmonella cultured
A020.	Salmonella gastroenteritis
<b>Shigella</b>	
<b>Read V2 Code</b>	<b>Description</b>
A03..	Shigellosis
A030.	Shigella dysenteriae (group A)
A031.	Shigella flexneri (group B)
A032.	Shigella boydii (group C)
A033.	Shigella sonnei (group D)
A03y.	Other specified shigella infection
A03z.	Shigellosis NOS
Ayu04	[X]Other shigellosis
Ayu05	[X]Shigellosis, unspecified
<b>Read CTV3 Code</b>	<b>Description</b>
A03..	Shigellosis
A030.	(Shigella dysenteriae - group A) or (bacillary dysentery)
A031.	Shigella flexneri (group B)

A032.	Shigella boydii (group C)
A033.	Shigella sonnei: [group D] or [bacillary dysentery]
A03y.	Other specified shigella infection
A03z.	Shigellosis NOS
XE0Qf	Shigella dysenteriae (group A)
XE0Qg	Shigella sonnei (group D)
Ayu04	[X]Other shigellosis
Ayu05	[X]Shigellosis, unspecified
<b>Campylobacter</b>	
<b>Read V2 Code</b>	<b>Description</b>
A0743	Campylobacter gastrointestinal tract infection
<b>Read CTV3 Code</b>	<b>Description</b>
XE0Ql	Campylobacter gastrointestinal tract infection
<b>Clostridium Difficile</b>	
<b>Read V2 Code</b>	<b>Description</b>
A3Ay2	Clostridium difficile infection
J434.	Pseudomembranous colitis
4JD20	Clostridium difficile toxin A detected
<b>Read CTV3 Code</b>	<b>Description</b>
A3Ay2	Clostridium difficile infection
X303u	Pseudomembranous colitis
J434.	Pseudomembranous colitis
XaCJk	Clostridium difficile toxin A detected
4JD20	Clostridium difficile toxin A detected

**Appendix 3:** Included IBD medications

<b>Medication class</b>	<b>Medications</b>
Topical 5-ASA	Mesalazine, Sulfasalazine
Topical glucocorticoids	Budesonide, Hydrocortisone, Prednisolone
Oral 5-ASA	Balsalazide, Mesalazine, Olsalazine, Sulfasalazine
Oral glucocorticoids	Prednisolone, Cortisone, Dexamethasone, Methylprednisolone, Beclomethasone, Betamethasone, Budesonide, Deflazacort
Immunosuppressants	Azathioprine, Mercaptopurine, Methotrexate, Cyclosporine, Tacrolimus
Biologic therapies	Adalimumab, Golimumab, Infliximab, Vedolizumab, Ustekinumab

5-ASA = 5-aminosalicylic acid.