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The association between inflammatory bowel disease and mental ill health: A retrospective cohort study using data from UK primary care

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Summary

Background: Patients with active inflammatory bowel disease (IBD) and mental illnesses experience worse IBD outcomes.

Aim: To describe the incidence of mental illnesses, including deliberate self-harm, in IBD patients.

Methods: A population-based retrospective cohort study using IQVIA medical research data of a primary care database covering the whole UK, between January 1995 and January 2021. IBD patients of all ages were matched 4:1 by demographics and primary care practice to unexposed controls. Following exclusion of patients with mental ill health at study entry, adjusted hazard ratios (HR) of developing depression, anxiety, deliberate self-harm, severe mental illness and insomnia were calculated using a Cox proportional hazards model.

Results: We included 48,799 incident IBD patients: 28,352 with ulcerative colitis and 20,447 with Crohn's disease. Incidence rate ratios of mental illness were higher in IBD patients than controls (all $p < 0.001$): deliberate self-harm 1.31 (95% CI 1.16–1.47), anxiety 1.17 (1.11–1.24), depression 1.36 (1.31–1.42) and insomnia 1.62 (1.54–1.69). Patients with Crohn's disease were more likely to develop deliberate self-harm HR 1.51 (95% CI 1.28–1.78), anxiety 1.38 (1.16–1.65), depression 1.36 (1.26–1.47) and insomnia 1.74 (1.62–1.86). Patients with IBD are at increased risk of deliberate self-harm (HR 1.20 [1.07–1.35]). The incidence rate ratios of mental illnesses were particularly high during the first year following IBD diagnosis: anxiety 1.28 (1.13–1.46), depression 1.62 (1.48–1.77) and insomnia 1.99 (1.78–2.21).

Conclusion: Deliberate self-harm, depression, anxiety and insomnia were more frequent among patients with IBD. IBD is independently associated with an increased risk of deliberate self-harm.

1 | INTRODUCTION

The association between inflammatory bowel disease (IBD) and anxiety and depression has been described in a number of studies worldwide.[1] Active symptomatic IBD is associated with increased rates of anxiety and depression.[2,3] Patients with IBD and psychological comorbidity also experience worse IBD outcomes such as increased disease activity requiring escalation of therapy and lower IBD remission rates than those without psychological co-morbidity.[4,5] Patients with both IBD and a mental health disorder, such as depression and anxiety, have higher rates of workplace absenteeism, increased healthcare utilisation and higher rates of psychotropic medication use when compared to patients with a mental health disorder without coexisting IBD.[6] Disordered sleep or insomnia has also been reported to be associated with IBD, and significantly affect the quality of life of patients with IBD.[7,8] Finally, IBD is associated with an increased risk of self-harm, especially among patients diagnosed with IBD in childhood.[9-11] A recent study in Denmark and Finland reported that deliberate self-harm was a leading cause of mortality among IBD patients.[11] However, factors associated with deliberate self-harm in patients with IBD have not been previously described. There have been no previous UK population-based studies to examine the incidence of mental health diagnoses in IBD patients.

Our study aims to investigate the incidence of a wide range of mental health diagnoses in patients with IBD, and factors associated with deliberate self-harm.

2 | MATERIALS AND METHODS

2.1 | Study design, setting and population

A population-based retrospective open cohort study was undertaken using IQVIA medical research data (IMRD), UK, between January 1995 and January 2021. IMRD was previously named 'The Health Improvement Network (THIN)' and is derived from electronic health records from UK primary care providers who use the Vision software system.

The THIN database is representative of the UK population in terms of demographic structure and the prevalence of key comorbidities.[12] IMRD primary care practices record patient-level phenotypical data through Read codes.[13] Read codes are a hierarchical coding system that can be used to record information on symptoms, examination findings and diagnoses.

In this study, records from 831 primary care practices in all regions of the UK were utilised, which in total related to 16,630,426 eligible patients. As entry into the database relies on the use of Vision software, the number of contributing practices can vary over time. For this study, data extraction, transformation and analysis were facilitated using the data extraction for epidemiological research (DExtER) tool.[14] To improve data quality and reduce underrecording, primary care practices were deemed eligible to contribute data at the later of the two following dates: 1 year after the date of the practice electronic record system was installed, and the date the practice attained acceptable mortality recording (AMR).[15] The AMR date is derived from IMRD-UK practices recording of death compared with the predicted mortality rate based on national figures, given a practice's demographic characteristics. Consequently, when the national and practice IMRD-UK mortality figures align, an AMR date is assigned.

2.2 | Exposure and outcome definitions

The purpose of this study was to compare exposed patients (those with a code identifying IBD; either Crohn's disease or ulcerative colitis) to matched unexposed patients (those without such codes) and then calculate their risk of developing mental ill health defined through certain Read codes (deliberate self-harm, depression, anxiety, severe mental illness and insomnia). All ages were included in the study. Read codes relating to IBD exposure and mental ill health were selected with the assistance of gastroenterologists, general practitioners and public health clinicians. The methodology for Read code selection and their validity has been described previously.[16] The clinical codes used in this study can be found in Appendix S2. The code lists used to identify patients with IBD, Crohn's disease and ulcerative colitis have been previously validated by other authors.[17,18] Lewis et al reported that the probability of having Crohn's disease and ulcerative colitis based on GP-reported gastroenterology consultation, surgery, intestinal biopsy, endoscopy or barium radiography were 94% and 97%, respectively, in the general practitioner research database (GPRD). In patients who had codes for both Crohn's disease (CD) and ulcerative colitis (UC), the most recent code was used as the final diagnosis for the patient while the earliest code or diagnosis date was considered as an index date. Patients with undifferentiated IBD diagnoses and those with a pre-existing mental health diagnosis were excluded from the study cohort.

2.3 | Selection of unexposed group

Each exposed patient was matched to up to four unexposed control patients, who had no previously documented Read code relating to the exposure or a previous mental health diagnosis. Controls were taken from the same primary care practice and were matched by age at index date (±1 year), Townsend deprivation score[19] and sex. The Townsend score is a measure of material deprivation within a locality, incorporating information on unemployment, household overcrowding and car/home ownership.[19]

2.4 | Follow-up period

An open cohort study allows patients to enter and exit the study at different time points, with each individual patient only

contributing person years of follow-up from the time of cohort entry (index date) to the time they leave the cohort (exit date). In this study, only those with a new diagnosis of IBD during the study period, who met the eligibility criteria, were included in the exposed group and their index date was assigned as the date of their first inputted code relating to an IBD diagnosis. To mitigate immortality time bias,[20] eligible unexposed patients were assigned the same index date. The follow-up period for each patient was from the index date until the exit date. The exit date was defined as the earliest of the following dates: study end date; last date of data collection from a given primary care practice; date patient transferred from the practice; date of death or date the outcome of interest occurred. This time period was considered to be the time at risk for calculating incidence rates.

2.5 | Covariates

Covariates considered in the model were selected due to their potential independent relationship with the development of mental ill health. These included: age, sex, Townsend deprivation score, ethnicity, smoking status and Charlson comorbidity score.[21] Age, sex and Townsend deprivation score were also used in the modelling despite their inclusion in the matching criteria to account for any residual confounding. Due to small numbers of patients in minority ethnicity groups, these were combined for analysis.

2.6 | Statistical analysis

Categorical baseline data were described using proportions, continuous data were described using means or median with standard deviations or inter-quartile range respectively. Missing data are highlighted in relevant baseline characteristic tables. Where there were missing covariate data, the data are described as a missing category. In order to calculate the incidence rate (IR per 1000 years) for mental ill health, the number of incident outcomes divided by the person years contributed by each group were examined. A Cox proportional hazards regression model was then used to estimate adjusted hazard ratios (adj HRs) for each mental health disorder after adjusting for demographic factors including Charlson co-morbidity score, Townsend deprivation score, age quintile, ethnicity, sex and UC/CD exposed group. Hazard ratios were calculated with 95% confidence intervals (CI) and a statistical significance threshold of $p < 0.05$. A Cox proportional hazards model was used to identify associations with increased deliberate self-harm. Variables included IBD and demographic characteristics including age quintile, sex and a co-existing diagnosis of mental illness, such as depression, anxiety, insomnia and severe mental illness. The proportional hazards assumption was assessed using log–log plots and the Schoenfeld residuals test. p values of <0.05 were considered to be statistically significant. Statistical analysis was undertaken in Stata version 15.[22]

3 | RESULTS

3.1 | Cohort demographics

A total of 48,799 incident patients with IBD, of whom 28,352 (58.1%) had ulcerative colitis and 20,447 (41.9%) had Crohn's disease, and 190,075 controls without IBD were included in the study (Figure 1). The demographic details of the IBD patients and controls are shown in Table 1. The median age of the IBD patients was 41.5 (IQR 29.6–57.5) years, with a similar proportion of males and females with IBD (51.7% vs. 48.3%).

3.2 | Incident rates of and associations with deliberate self-harm

The results of the incidence analysis of deliberate self-harm are in Table 2. The incidence rate of deliberate self-harm was higher in patients with IBD compared to controls (1.18 vs. 0.9 per 1000 person-years). The observed difference persisted when adjusted for demographic factors (adj HR 1.33 [95% CI 1.18–1.49]). In Crohn's disease, higher rates of deliberate self-harm were observed (1.50 vs. controls 1.02 per 1000 years, adj HR 1.51 [1.28–1.78]) but no difference was seen in deliberate self-harm rates in ulcerative colitis (IR 0.93 vs. 0.81/1000 person-years, adj HR 1.16 [0.98–1.38]). No increase in the incidence rate of deliberate self-harm was observed for IBD patients diagnosed in childhood (10–18 years) (IR 3.65 vs. controls 3.01/1000 person-years IRR 1.21 [0.85–1.69], $p = 0.25$) but higher rates of deliberate self-harm were observed in IBD patients diagnosed over the age of 50 (IR 0.58 vs. 0.34/1000 person-years, IRR 1.66 [1.23–2.23] $p < 0.001$). Higher incidence rates of deliberate self-harm were observed in IBD patients who were current smokers than in smokers in the unexposed cohort without IBD (IR 2.4 vs. 1.7 per 1000 person-years, IRR 1.4 [1.13–1.72]). The results are shown in Table S4.

The results of Cox proportional hazards modelling for associations with deliberate self-harm are shown in Table 3. Deliberate self-harm was associated with: IBD (adj HR 1.20 [1.07–1.35]), decreasing age (<27.4 adj HR 4.84 [3.95–5.93]), anxiety (1.57 [1.35–1.82]), insomnia (2.32 [2.02–2.66]), severe mental illness (5.74 [4.56–7.22]) and depression (5.97 [5.33–6.69]).

3.3 | Incident rates of anxiety

The results of the incidence analysis of anxiety are shown in Table 4. The incidence rate of anxiety was higher in patients with IBD (5.48 per 1000 person-years) than controls (4.67 per 1000 person-years, adj HR 1.31 [95% CI 1.16–1.47]). The incidence rate of anxiety was increased in both ulcerative colitis and Crohn's disease: ulcerative colitis 5.03 versus 4.41 per 1000 person-years, adj HR 1.26 (1.07–1.47); Crohn's disease 6.14 versus 5.04 per 1000 person-years, adj HR 1.38 (1.16–1.65). There was no difference
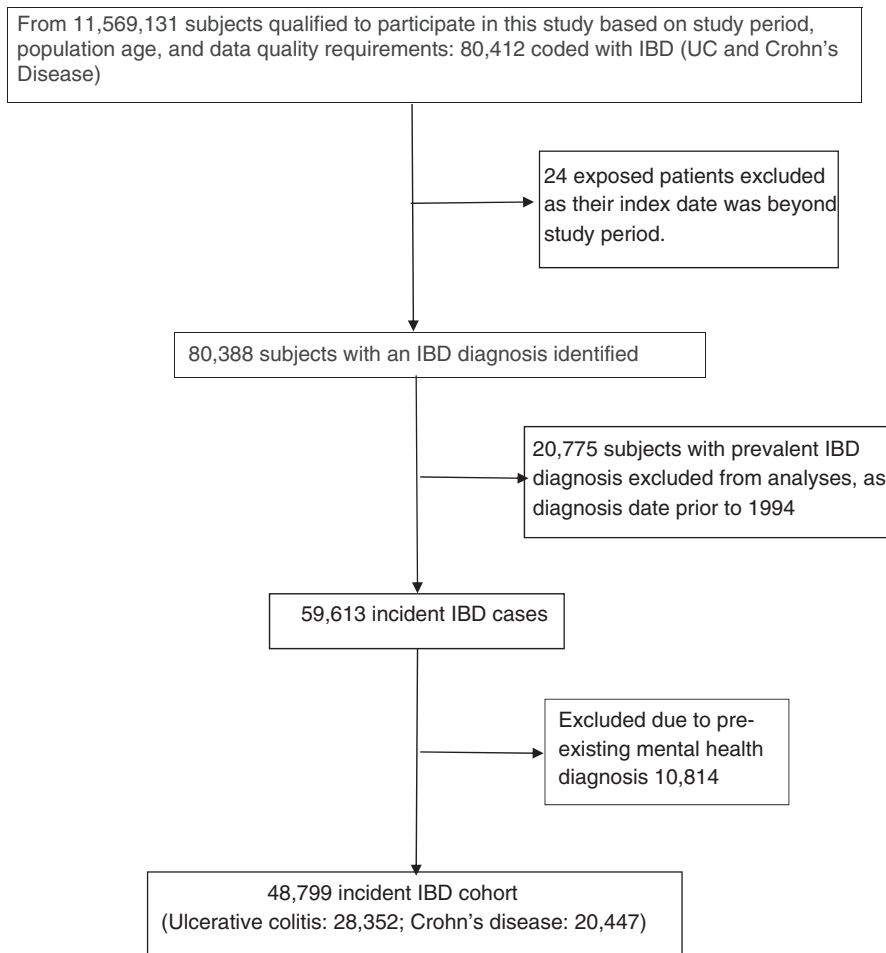
From 11,569,131 subjects qualified to participate in this study based on study period, population age, and data quality requirements: 80,412 coded with IBD (UC and Crohn's Disease)

24 exposed patients excluded as their index date was beyond study period.

80,388 subjects with an IBD diagnosis identified

20,775 subjects with prevalent IBD diagnosis excluded from analyses, as diagnosis date prior to 1994

59,613 incident IBD cases

Excluded due to pre-existing mental health diagnosis 10,814

48,799 incident IBD cohort
(Ulcerative colitis: 28,352; Crohn's disease: 20,447)

in anxiety incidence rates among patients diagnosed with IBD between 10 and 18 years of age (IRR 0.96 [95% CI 0.72–1.25], $p = 0.77$). In contrast, in patients diagnosed in later life over the age of 50, the incidence of anxiety was higher among patients with IBD compared to controls (3.58 vs. 3.01 per 1000 person-years, IRR 1.19 [95% CI 1.06–1.33], $p < 0.003$).

Rates of anxiety varied by ethnicity, with higher incidence rates seen in white IBD patients compared to controls (IR 5.81 vs. 5.06 per 1000 person-years, IRR 1.15 [1.06–1.24], $p < 0.001$), but there was no difference between minority ethnicity patients compared to controls (3.43 vs. 3.37 per 1000 person-years, IRR 1.01 [0.70–1.44], $p = 0.90$). These results are shown in Table S1.

3.4 | Incident rates of depression

The results of the incidence analysis of depression are shown in Table 5. The incidence rate of depression was higher in patients with IBD compared to controls (10.75 vs. 7.9 per 1000 person-years, adj HR 1.30 [95% CI 1.23–1.36]).

Patients with both CD (12.7 vs. 8.6 per 1000 person-years, adj HR 1.36 [1.26–1.47]) and ulcerative colitis (9.4 vs. 7.4 per 1000 person-years, adj HR 1.24 [1.16–1.33]) had higher rates of depression than controls. The incidence rate ratio of depression in patients

with IBD was significantly higher during the first year after IBD diagnosis (1.62 [1.48–1.77]) than overall (1.36 [1.31–1.42]) (Table S3).

3.5 | Incident rates of severe mental illness

No difference was observed in the incidence rates of severe mental illness in patients with IBD compared to controls (0.35 vs. 0.40 per 1000 person-years, IRR 0.87 [95% CI 0.70–1.07], $p = 0.19$).

3.6 | Incident rates of insomnia

The results of incidence analysis of insomnia are shown in Table S2. The incidence rate of insomnia among patients with IBD was higher than in controls (IR 8.53 vs. 5.3 per 1000 person-years, adj HR 1.56 [95% CI 1.49–1.63]). Similar effect sizes were noted in both ulcerative colitis (adj HR 1.44 [1.35–1.53]) and Crohn's disease (adj HR 1.74 [1.62–1.86]). Insomnia was more common among IBD patients diagnosed over the age of 50 (incidence rate 9.42 per 1000, IRR 1.52 [1.42–1.64], $p < 0.001$). However, the group with the largest relative risk compared to controls were IBD patients diagnosed in childhood[10-18] (IRR 2.14 [1.67–2.73], $p < 0.001$). The incidence rate ratio of insomnia in patients with IBD was significantly higher during

TABLE 1 The demographic details of the IBD patients and controls studied

Variable	Controls	%	Number of IBD patients	%	Full cohort	%
Age quintiles (years)	190,075	79.6	48,799	20.4	238,874	
<27.4	42,874	22.5	9903	20.1	52,777	22.1
27.4–36.3	39,396	20.7	10,083	20.1	49,479	20.7
36.4–47.4	37,401	19.7	9507	19.5	46,908	19.6
47.4–61.3	35,603	18.7	9049	18.5	44,652	18.7
>61.3	34,801	18.3	10,257	20.9	45,058	18.9
Sex						
Female	91,808	48.3	23,572	48.3	115,380	48.3
Male	98,267	51.7	25,227	51.7	123,494	51.7
IBD						
UC	109,665	57.7	28,352	58.1	138,017	57.8
CD	80,410	42.3	20,447	41.9	100,857	42.2
Townsend quintile						
1	39,356	20.7	10,092	20.7	49,448	26.0
2	35,784	18.8	9193	18.8	44,977	18.6
3	34,468	18.1	8996	18.4	43,464	18.8
4	27,670	14.6	7292	14.9	34,962	14.6
5	17,921	9.4	4730	9.7	22,651	9.5
Missing	34,876	18.3	8496	17.4	43,372	18.1
Ethnicity						
White	75,409	39.7	23,732	48.6	99,141	41.5
Black	2685	1.4	313	0.6	2998	1.2
South Asian	4309	2.3	1170	2.4	5479	2.3
Mixed Race	890	0.5	202	0.4	1092	0.4
Other ethnicity	3013	1.6	434	0.9	3447	1.4
Missing	103,769	54.6	22,948	47.0	126,717	53.0
Smoking status						
Never	98,375	51.7	24,832	50.1	123,207	51.6
Current	35,987	18.9	7937	16.3	43,924	18.3
Ex-smoker	29,025	16.3	11,518	23.6	40,543	17.0
Missing	26,688	15.6	4512	9.2	31,200	13.1
Charlson comorbidity score category						
0	146,592	77.1	34,293	70.3	180,885	75.7
1	30,912	16.3	9943	20.4	40,855	17.1
2	8194	4.3	2769	5.6	10,963	4.6
>2	4377	2.3	1794	3.7	6171	2.6

Abbreviations: CD, Crohn's disease; IBD, inflammatory bowel disease; UC, ulcerative colitis.

the first year after IBD diagnosis (1.99 [1.78–2.21]) than overall (1.62 [1.54–1.69]) (Table S3).

4 | DISCUSSION

This study has examined in detail the incidence of mental health morbidity in patients with IBD using a large, population-based dataset in the UK. We have shown that patients with IBD, without a diagnosis of mental health disorder at baseline, had a 33% increased risk of deliberate self-harm, 31% increased risk of anxiety, a 30% increased risk of depression and a 56% increased risk of insomnia. The highest relative risks were in patients with Crohn's disease. Higher rates of anxiety and deliberate self-harm were observed in adults diagnosed with IBD over the age of 50. A sixfold increased risk of deliberate self-harm was associated with depression and severe mental illness

TABLE 2 The incidence rates of deliberate self-harm among IBD patients and controls

	IBD patients	Controls	p-value
Full Cohort			
Number	368	1111	
Person years at risk	311,616	1,232,025	
Incidence rate per 1000	1.18	0.9	
Incidence rate ratio	1.31 (95% CI 1.16–1.47)		<0.001
Adjusted hazard ratio	1.33 (95% CI 1.18–1.49)		<0.001
Ulcerative colitis patients			
Number	172	585	
Person years at risk	184,118	718,416	
Incidence rate per 1000	0.93	0.81	
Incidence rate ratio	1.15 (95% CI 0.96–1.36)		0.11
Adjusted hazard ratio	1.16 (95% CI 0.98–1.38)		0.08
Crohn's disease patients			
Number	196	526	
Person years at risk	127,498	513,609	
Incidence rate per 1000	1.5	1.02	
Incidence rate ratio	1.50 (95% CI 1.27–1.77)		<0.001
Adjusted hazard ratio	1.51 (95% CI 1.28–1.78)		<0.001
Childhood IBD diagnosis (aged 10–18)			
Number	45	166	
Person years at risk	12,332	55,058	
Incidence rate per 1000	3.65	3.01	
Incidence rate ratio	1.21 (95% CI 0.85–1.69)		0.25
Diagnosed with IBD over the age of 50			
Number	68	153	
Person years at risk	117,878	442,662	
Incidence rate per 1000	0.58	0.34	
Incidence rate ratio	1.66 (95% CI 1.23–2.23)		<0.001

Abbreviations: CI confidence interval; IBD Inflammatory bowel disease.

TABLE 3 Cox proportional hazards modelling of associations with deliberate self-harm in the IBD patients and controls

	Adj HR	95% CI	p-value
IBD	1.20	1.07–1.35	<0.002
Sex			
Female	1.06	0.95–1.17	0.300
Age			
<27.4	4.84	3.95–5.93	<0.001
27.4–36.3	2.47	1.99–3.07	<0.001
36.4–47.4	1.87	1.50–2.33	<0.001
47.4–61.3	1.23	0.96–1.56	0.099
>61.3	Reference category		
Co-existent mental health diagnoses			
Depression	5.97	5.33–6.69	<0.001
Anxiety	1.57	1.35–1.82	<0.001
Insomnia	2.32	2.02–2.66	<0.001
Severe mental illness	5.74	4.56–7.22	<0.001

Abbreviations: adj HR, Adjusted Hazard Ratio; CI, confidence interval; IBD, Inflammatory bowel disease.

in IBD patients compared to the general population.[10,11] Patient surveys conducted in Canada and Korea have reported more than 30% increased risk of suicide in IBD patients, similar to the findings of the present study.[27-29] The higher incidence rates of depression and deliberate self-harm observed in the present study in patients with IBD diagnosed over the age of 50 are consistent with a recent study from Sweden, which highlighted higher rates of suicide in individuals with late-onset IBD and Crohn's disease.[30] Doctors caring for patients with IBD should be conscious of the increased burden of psychiatric morbidity, with early mental health diagnosis providing the potential opportunity to improve patient outcomes and reduce the risk of deliberate self-harm.[23]

A number of studies have highlighted the increased incidence and prevalence of anxiety and depression in patients with IBD.[1,3,31-40] The adjusted risks of anxiety and depression in the present study (adjusted hazard ratios 1.31 and 1.30) were lower than a recent population-based Korean study, which reported adjusted hazard ratios of 1.6 and 2.0 respectively.[39] Female sex, smoking, surgery and extraintestinal manifestations of IBD all increase the risk of anxiety and depression in patients with IBD, resulting in more hospital admissions and imaging.[40] There have been several mechanisms proposed for the increased risk of anxiety and depression in patients with IBD. The gut–brain dysregulation hypothesis highlighted in recent animal model-based studies proposes mechanisms such as an increase in peripheral cytokines or damaged nerve terminals in the gut resulting in neuroinflammation and activation of the hypothalamic pituitary axis, which may then cause anxiety and depression in patients with IBD.[41,42] Anxiety and depression in patients with IBD are associated with increased healthcare utilisation and taking time

in IBD patients than controls. Higher incidence rates of mental illness were observed in current smokers compared to non-smokers for both IBD patients and controls.

The present study highlights the association of deliberate self-harm with IBD. IBD patients have been noted to be at increased risk of suicide compared with the general population in previous studies.[23-26] A recent Swedish study highlighted the increased risk of self-harm in childhood-onset IBD patients suggesting an adjusted HR of 1.4 compared with 1.33 in the present study.[9] The potential confounding factors considered in the Swedish analyses were age, year of birth, education and family history in contrast to the present study, which was adjusted for age, sex, ethnicity, Townsend deprivation index and Charlson comorbidity index. A study of Danish and Finnish paediatric IBD patients examined cancer and mortality risks and incidentally found a fourfold increased death rate due to suicide

TABLE 4 The incidence rates of anxiety among IBD patients and controls

	IBD patients	Controls	p-value
Full cohort			
Number	1669	5643	
Person years at risk	304296.4	1,206,866	
Incidence rate per 1000	5.48	4.67	
Incidence rate ratio	1.17 (95% CI 1.11–1.24)		<0.001
Adjusted hazard ratio	1.31 (95% CI 1.16–1.47)		<0.001
Ulcerative colitis patients			
Number	905	3111	
Person years at risk	179,787	704,444	
Incidence rate per 1000	5.03	4.41	
Incidence rate ratio	1.14 (95% CI 1.06–1.23)		<0.001
Adjusted hazard ratio	1.26 (95% CI 1.07–1.47)		<0.005
Crohn's disease patients			
Number	764	2532	
Person years at risk	124,509	502,422	
Incidence rate per 1000	6.14	5.04	
Incidence rate ratio	1.22 (95% CI 1.12–1.32)		<0.001
Adjusted Hazard Ratio	1.38 (95% CI 1.16–1.65)		<0.001
Childhood IBD DIAGNOSIS (aged 10–18)			
Number	67	310	
Person years at risk	12,259	54,422	
Incidence Rate per 1000	5.46	5.69	
Incidence Rate Ratio	0.96 (95% CI 0.72–1.25)		0.077
Diagnosed with IBD over the age of 50			
Number	415	1315	
Person years at risk	115,762	435,588	
Incidence Rate per 1000	3.58	3.01	
Incidence Rate Ratio	1.19 (95% CI 1.06–1.33)		<0.003

Abbreviations: CI, confidence interval; IBD, Inflammatory bowel disease.

TABLE 5 The incidence rates of depression among IBD patients and controls

	IBD patients	Controls	p-value
Full cohort			
Number	3167	9317	
Person years at risk	294,659	1,182,021	
Incidence rate per 1000	10.75	7.9	
Incidence rate ratio	1.36 (95% CI 1.31–1.42)		<0.001
Adjusted hazard ratio	1.30 (95% CI 1.23–1.36)		<0.001
Ulcerative colitis patients			
Number	1652	5088	
Person years at risk	175,204	690,654	
Incidence rate per 1000	9.43	7.4	
Incidence rate ratio	1.28 (95% CI 1.21–1.35)		<0.001
Adjusted hazard ratio	1.24 (95% CI 1.16–1.33)		<0.001
Crohn's disease patients			
Number	1515	4229	
Person years at risk	119,456	491367.5	
Incidence rate per 1000	12.7	8.6	
Incidence rate ratio	1.47 (95% CI 1.39–1.56)		<0.001
Adjusted hazard ratio	1.36 (95% CI 1.26–1.47)		<0.001
Childhood IBD diagnosis (aged 10–18)			
Number	130	381	
Person years at risk	12,010	53,976	
Incidence rate per 1000	10.82	7.05	
Incidence rate ratio	1.53 (95% CI 1.25–1.87)		<0.001
Diagnosed with IBD over the age of 50			
Number	891	2365	
Person years at risk	112,892	429,655	
Incidence rate per 1000	7.9	5.5	
Incidence rate ratio	1.43 (95% CI 1.33–1.55)		<0.001

Abbreviations: CI, confidence interval; IBD Inflammatory bowel disease.

off work.[6] Previous UK studies have focused on the prevalence of these mental health disorders in IBD patients but an increased incidence of anxiety and depression particularly in the first year following an IBD diagnosis has been reported which was also observed in the present study for depression and insomnia.[43] However, there are a number of limitations to the study of Kurina et al, as only secondary care data were analysed and incidence rates were not reported.[43] The present study is the first study in UK which reports the incidence rates of anxiety and depression in IBD patients, without a prior mental health diagnosis.

The association of insomnia with IBD has been examined through the global measure of sleep quality but only a few single-centre studies have highlighted the relationship between insomnia and IBD previously.[8,43,44] The present study has highlighted the markedly increased incidence of insomnia in patients with IBD. Although both physical IBD symptoms and mental health disorders may contribute to such symptoms, potential impact of both requires clinical assessment in IBD patients presenting with insomnia.

5 | STRENGTHS AND LIMITATIONS

The key strength of this study is the large study population from a UK primary care database. The data are collected at the time of consultation, reducing recall bias. Potential confounding factors are mitigated through the use of multivariable Cox proportional hazards models for analysis. There are some potential limitations given the

data source for this study. General practitioners may improve their coding of prevalent diseases over time. However, one would then expect all conditions in such databases to increase in prevalence over time, which is not the case.[45] As highlighted in other studies using primary care research databases, there is a recognised margin for error in the diagnosis of IBD based on Read codes[17] and the IBD diagnoses of individual patients could not be externally validated in the present study. It is important to recognise that both 'anxiety' and 'depression' may represent symptoms of these disorders, rather than a formal diagnosis given the broad Read code inclusion criteria in the present study. READ codes may have limited sensitivity for mild mental illness but it was beyond the scope of this study to also study prescriptions for mental illness.

There is also a possibility of underreporting those with a 'mixed anxiety-depressive disorder' in this study. This study has considered all Crohn's disease and all ulcerative colitis as single disease but due to paucity of data in the THIN database regarding inflammatory bowel disease phenotypic subtypes, the impact of subtypes on the risk of mental illness could not be analysed. The analysis of the impact of ethnicity on mental health disorders was limited due to missing data on ethnicity in 47% of the IBD cohort. The impact of substance and alcohol abuse could also not be examined in the present study. The impact of clinical factors such as the severity of IBD and related symptoms, which might have increased the risk of mental illness after IBD diagnosis, also could not be examined in this study.

6 | CONCLUSIONS

The incidence of deliberate self-harm, anxiety, depression and insomnia is increased in patients diagnosed with IBD. More research is required to determine the causes of these associations and optimise the treatment of mental health disorders in patients with IBD. Clinicians caring for patients with IBD should be aware of these associations and diagnose and treat them when present for the benefit of both the patient's mental health and IBD.

AUTHOR CONTRIBUTIONS

Nosheen Umar: Formal analysis (equal); writing – original draft (equal); writing – review and editing (equal). **Dominic Stephen King:** Conceptualization (equal); formal analysis (supporting). **Joht Singh Chandan:** Formal analysis (supporting); methodology (equal); writing – review and editing (equal). **Neeraj Bhala:** Project administration (equal); supervision (supporting). **Krishnarajah Nirantharakumar:** Supervision (supporting). **Nicola J Adderley:** Formal analysis (supporting); supervision (supporting). **Dawit Zemedikun:** Formal analysis (supporting); writing – review and editing (supporting). **Philip R Harvey:** Conceptualization (equal); data curation (equal); formal analysis (equal); methodology (equal); writing – original draft (equal). **Nigel John Trudgill:** Conceptualization (equal); formal analysis (equal); project administration (lead); supervision (lead); writing – review and editing (equal).

CONFLICT OF INTEREST

No conflicts of interest to declare.

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SUPPORTING INFORMATION

Additional supporting information will be found online in the Supporting Information section.