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# Natural history and impact of irritable bowel syndrome-type symptoms in inflammatory bowel disease during 12 months of longitudinal follow-up

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## Abstract

**Background:** Little is known about the natural history and impact of irritable bowel syndrome (IBS)-type symptoms on psychological health and quality of life in inflammatory bowel disease (IBD). We aimed to address this in a 12-month longitudinal follow-up study of secondary care patients.

**Methods:** We collected demographic, Rome III IBS-type symptom, psychological, and quality of life data, with questionnaires at 3-month intervals, over 12 months of follow-up in patients with IBD in clinical remission at baseline. We assessed the natural history of Rome III IBS-type symptoms over the 12 months of the study and compared psychological and quality of life data between those reporting Rome III IBS-type symptoms at each of the points of follow-up with those not reporting such symptoms.

**Key Results:** Among 206 patients with IBD in clinical remission at baseline (104 [50.5%] women, mean age 56.9 years [range 18–83 years], 79 [38.3%] Crohn's disease), 33 (16.0%) reported Rome III IBS-type symptoms at baseline and 72 (35.0%) reported Rome III IBS-type symptoms at one or more time points. Among the 33 patients with Rome III IBS-type symptoms at baseline, symptoms resolved in 6 (18.2%) patients, were present throughout in 6 (18.2%) patients, and fluctuated in the remaining 21 (63.6%) patients. Among the 39 patients with new onset of Rome III IBS-type symptoms after baseline, 24 (65.1%) had symptoms at one point in time only, 10 (25.6%) at two points, four (10.3%) at three points, and one (2.6%) at four points. At each point in time, reporting IBS-type symptoms was associated with significantly higher anxiety, depression, or somatoform symptom-reporting scores, and/or lower quality of life scores.

**Conclusions & Inferences:** In this 12-month follow-up study, one-third of patients with IBD reported presence of Rome III IBS-type symptoms at any point in time. Reporting such symptoms was associated with significant impacts on psychological health and/or quality of life.

**Abbreviations:** 5-ASA, 5-aminosalicylate; CD, Crohn's disease; HADS, hospital anxiety and depression scale; IBD, inflammatory bowel disease; IBD-U, inflammatory bowel disease unclassified; PHQ, patient health questionnaire; UC, ulcerative colitis.

KEYWORDS
IBS-type symptoms, inflammatory bowel disease, irritable bowel syndrome

## 1 | INTRODUCTION

Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic disorders of the gastrointestinal tract, characterized by periods of remission and flare. Their prevalence is increasing worldwide, and it is estimated that by 2028 1% of the population in some Western countries will have IBD.[1] A combination of genetics, environment, and immunology, alongside microbial alternations are proposed to play a role in the pathogenesis.[2,3] Research suggests that environmental and emotional stimuli may activate the hypothalamic–pituitary–adrenal axis, via gut-brain axis communication, leading to release of cortisol and pro-inflammatory cytokines.[4] Gut-brain communication is bidirectional; afferent signals from the gut are transmitted to the brain, which can send signals via efferent pathways back to the gut.

One of the most common disorders arising from abnormalities in gut-brain interaction is irritable bowel syndrome (IBS), a chronic functional condition characterized by persistent and recurrent abdominal pain and disordered defecation.[5] There is evidence that an inflammatory insult to the bowel, such as diverticulitis or acute gastroenteritis, can cause neuromuscular remodeling, leading to abnormal gut motility and visceral hypersensitivity and, ultimately, the development of IBS.[6,7] In patients with IBD, a disease flare or recurrence may cause similar key physiological changes leading to IBS-type symptoms. Such symptoms are reported by between one-in-three and one-in four patients with IBD.[8] Interestingly, the presence of IBS-type symptoms does not necessarily correlate with inflammation given that, even among patients with IBD in histological remission, up to 25% report symptoms consistent with IBS.[9] In this context, confusion between IBS-type symptoms and a recurrence of IBD activity can lead to difficulties in making clinical and therapeutic decisions.[10]

The natural history of IBS-type symptoms in patients with IBD, and their impact on disease outcomes, psychological health, and quality of life has not been examined extensively, with only a few studies conducting longitudinal follow-up in patients who report these symptoms. A Swedish study, recruiting 94 patients with newly diagnosed UC in endoscopic remission, reported that the presence of these symptoms at baseline was not associated with subsequent disease activity.[11] A previous study from our group demonstrated that presence of IBS-type symptoms was associated with increased healthcare utilization, worse anxiety, depression, somatoform symptom-reporting, and quality of life scores, but not adverse disease activity outcomes.[12] In the first of these two studies patients were followed up on an annual basis for 3 years and in the second at 2 and 6 years, respectively.

**Key Points**

Little is known about the natural history and impact of irritable bowel syndrome (IBS)-type symptoms on psychological health and quality of life in inflammatory bowel disease (IBD). In our 12-month longitudinal study, we found that one-third of patients with IBD in clinical remission reported IBS-type symptoms, according to Rome III criteria, at one or more points of follow-up. Prevalence of IBS-type symptoms remained similar at each 3-month follow-up interval, and presence of these symptoms was associated with higher anxiety, depression, and somatoform symptom-reporting scores and lower quality of life. There is a clear need to screen for IBS-type symptoms in patients with IBD, even if they are in clinical remission, with appropriate intervention to reduce the impact on psychological health and quality of life.

Such intervals do not allow the assessment of rapid fluctuations of symptoms. Therefore, we conducted a 12-month longitudinal study, with regular follow-up at 3-month intervals, to examine the natural history of IBS-type symptoms in patients with IBD in clinical remission at baseline. We aimed to assess the characteristics of patients with different symptom courses, and how such symptom trajectories influence psychological health and quality of life.

## 2 | METHODS

### 2.1 | Participants and setting

We sent postal invitations to all patients aged ≥18 years with an established histological, endoscopic, or radiological diagnosis of CD, UC, or IBD-unclassified (IBD-U) attending outpatient clinics at Leeds Teaching Hospitals NHS Trust between 2017 and 2020. These invitations provided a web-link with a personalized uniform resource locator to an online patient information leaflet, consent form, and online questionnaire. We offered a paper version of these documents, if preferred. We then sent four follow-up questionnaires, at 3-month intervals, over a 12-month period. To limit losses to follow-up, we sent a reminder to all those who initially consented to participate but did not respond to each of the 3-monthly questionnaires. This longitudinal study was approved by the Wales research ethics committee in February 2020 (REC ref: 20/WA/0044).

## 2.2 | Data collection and synthesis

We recorded demographic data, including sex, age, marital status, ethnicity, educational level, and lifestyle factors, including tobacco and alcohol use. We collected the presence of IBS-type symptoms at baseline and each of the 3-monthly points of follow-up using the Rome III questionnaire for IBS, assigning the presence of IBS-type symptoms at baseline and each of the points of follow-up according to the scoring algorithm recommended by the Rome Foundation.[13,14]

We only included patients who were in clinical remission at baseline in this longitudinal follow-up study, in order not to inflate the presence of IBS-type symptoms, which may be reported by patients experiencing flares of IBD activity. Clinical disease activity at baseline was assessed using a modified Harvey-Bradshaw index for CD, excluding examination for abdominal mass,[15,16] and the simple clinical colitis activity index for UC,[17] with a score of <5 used to define clinical remission for both, as recommended.[18,19]

We used the hospital anxiety and depression scale (HADS) to assess for symptoms of anxiety or depression at baseline and each of the four points of follow-up.[20] The total HADS score ranges from 0 to 21. We defined HADS-anxiety or depression scores at baseline as normal (score 0–7), borderline (8–10), or abnormal (≥11), as previously recommended.[20] Similarly, we collected somatoform symptom-reporting data using the patient health questionnaire-12 (PHQ-12),[21] at baseline and 3-monthly intervals. This is derived from the PHQ-15,[22] with scores ranging from 0 to 24. We characterized severity at baseline as high (total score ≥13), medium (8–12), low (4–7), or minimal (≤3). We assessed quality of life at baseline and each of the four points of follow-up using the short IBD questionnaire (SIBDQ) health survey.[23]

One investigator (KMF), blinded to questionnaire responses, reviewed electronic medical records for all participants. We verified IBD type (CD, UC, or IBD-U), extent and location of disease, and prior IBD-related intestinal resection. We documented current IBD-related medication use, including 5-aminosalicylates (5-ASAs), immunosuppressants, biologics, or glucocorticosteroids, as well as current use of antidepressant drugs.

## 2.3 | Statistical analysis

We reported the prevalence of Rome III IBS-type symptoms at baseline, and the natural history of these symptoms during 12-month follow-up. We compared characteristics of those reporting Rome III IBS-type symptoms at baseline with patients who did not. We used a Pearson's $\chi^2$ test for categorical data and an independent samples *t*-test for continuous data. We also reported the proportion of patients reporting new onset of Rome III IBS-type symptoms at each of the subsequent points of follow-up and the natural history of these symptoms during the remaining duration of follow-up in the study. Finally, we reported the proportion of patients reporting Rome III IBS-type symptoms at each individual point of follow-up, including at baseline, and compared anxiety, depression, somatoform symptom-reporting and quality of life scores between those reporting and those not reporting such symptoms at each of these time points using an independent samples *t*-test. Due to multiple comparisons, we considered a 2-tailed *p* value of <0.01 as statistically significant. We performed all analyses using SPSS for Windows version 26.0.

# 3 | RESULTS

We contacted 4823 patients with IBD seen in the outpatient clinic between January 2017 and June 2020 and 1119 (23.2%) responded to the baseline questionnaire. Of these, 320 (169 [52.8%] female, mean age 56.5 years [range 18 to 83 years], 132 [41.3%] CD) provided Rome III IBS-type symptom data at baseline and all four subsequent points of follow-up. Among these 320 individuals, 206 (104 [50.5%] women, mean age 56.9 years [range 18 to 83 years], 79 [38.3%] CD) were in clinical remission at baseline and served as the population of interest for this study. Of these, 72 (35.0%) patients reported Rome III IBS-type symptoms at one or more points of follow-up. Patients with IBD reporting Rome III IBS-type symptoms were younger than those not reporting such symptoms (51.7 vs. 59.7 years, $p=0.001$) and more likely to be female (63.9% vs. 43.3%, $p=0.005$; Table 1). However, there were no other significant differences in demographic or clinical characteristics, including according to type of IBD or disease location or behavior. Significantly more patients with IBD with Rome III IBS-type symptoms had abnormal HADS-anxiety scores or high PHQ-12 scores, and mean SIBDQ scores were lower.

## 3.1 | Characteristics of patients according to Rome III IBS-type symptom trajectories

Among the 72 (35.0%) patients reporting IBS-type symptoms according to Rome III criteria at any point in time, 33 (16.0%) patients had IBS-type symptoms at baseline, 35 (17.0%) at 3 months, 25 (12.1%) at 6 months, 33 (16.0%) at 9 months and 34 (16.5%) at 12 months (Figure 1). Among the 33 patients who had IBS-type symptoms at baseline, in six (18.2%) IBS-type symptoms resolved, six (18.2%) had persistent symptoms, and 21 (63.3%) had fluctuating symptoms (Figure 2).

In total, 134 patients with IBD had no IBS-type symptoms at baseline, according to Rome III criteria. However, 39 (29.1%) experienced new onset IBS-type symptoms. Among this latter group of patients, 24 (61.5%) had IBS-type symptoms at only one of five points in time, 10 (25.6%) at two points, four (10.3%) at three points and one (2.6%) had IBS-type symptoms at four points (Figure 3).

Among the 206 patients, only 15 (7.3%) patients flared, seven (3.4%) required glucocorticosteroids, and 12 (5.8%) escalation of therapy during the 12 months of the study, supporting the likelihood of these observations being due to a flux of functional-type symptoms rather than due to changes in disease activity in the vast majority of patients.

**TABLE 1** Characteristics of patients with IBD reporting Rome III IBS-type symptoms at baseline compared with those not reporting Rome III IBS-type symptoms.

| | Rome III IBS-type symptoms at any point ($n=72$) | No Rome III IBS-type symptoms at any point ($n=134$) | $p$-Value |
|---|---|---|---|
| Female sex (%) | 46 (63.9) | 58 (43.3) | 0.005 |
| Mean age (SD) | 51.7 (15.8) | 59.7 (15.2) | 0.001 |
| Smoker (%) | 5 (7.0) | 7 (5.3) | 0.62 |
| Alcohol use (%) | 56 (80.0) | 91 (68.9) | 0.093 |
| Married (%) | 53 (74.6) | 100 (75.2) | 0.93 |
| University or postgraduate education (%) | 32 (45.1) | 45 (33.8) | 0.12 |
| CD (%) | 32 (44.4) | 47 (35.6) | 0.28 |
| CD location (%) | | | |
| Ileal | 6 (18.8) | 10 (21.3) | 0.21 |
| Colonic | 9 (28.1) | 21 (44.7) | |
| Ileocolonic | 15 (53.1) | 16 (34.0) | |
| Stricturing disease (%) | 9 (28.1) | 11 (23.4) | 0.64 |
| Penetrating disease (%) | 3 (9.4) | 9 (19.1) | 0.24 |
| Perianal disease (%) | 4 (12.5) | 5 (10.6) | 0.80 |
| UC extent (%) | | | |
| Proctitis | 12 (31.6) | 18 (24.3) | 0.70 |
| Left-sided | 16 (42.1) | 33 (44.6) | |
| Extensive | 10 (26.3) | 23 (31.1) | |
| Previous intestinal resection (%) | 11 (15.3) | 18 (13.5) | 0.73 |
| 5-ASAs at baseline (%) | 42 (58.3) | 83 (62.9) | 0.52 |
| Immunosuppressants at baseline (%) | 21 (29.2) | 31 (23.5) | 0.37 |
| Biologics at baseline (%) | 9 (12.5) | 14 (10.6) | 0.68 |
| Glucocorticosteroids at baseline (%) | 2 (2.8) | 2 (1.5) | 0.53 |
| Antidepressants at baseline (%) | 12 (16.9) | 16 (12.0) | 0.34 |
| Diagnosed with IBD within last 12 months (%) | 3 (4.2) | 8 (6.0) | 0.59 |
| HADS-anxiety categories at baseline (%) | | | |
| Normal | 35 (50.7) | 110 (82.1) | <0.001 |
| Borderline abnormal | 22 (31.9) | 11 (8.2) | |
| Abnormal | 12 (17.4) | 13 (9.7) | |
| HADS-depression categories at baseline (%) | | | |
| Normal | 59 (81.9) | 124 (93.2) | 0.039 |
| Borderline abnormal | 10 (13.9) | 10 (13.9) | |
| Abnormal | 3 (4.2) | 3 (2.3) | |
| Level of somatoform symptom-reporting at baseline (%) | | | |
| Minimal | 22 (31.4) | 79 (61.2) | 0.001 |
| Low | 33 (47.1) | 37 (28.7) | |
| Medium | 11 (15.7) | 11 (8.5) | |
| High | 4 (5.7) | 2 (1.6) | |
| Mean SIBDQ score at baseline (SD) | 53.1 (9.2) | 61.2 (7.3) | <0.001 |

## 3.2 | Characteristics of patients according to HADS-anxiety, HADS-depression, PHQ-12, and SIBDQ trajectories

Mean HADS-A scores were statistically significant higher in patients with IBD with IBS-type symptoms compared with those without such symptoms at baseline (7.8 vs. 4.8, $p<0.001$), 3 months (7.7 vs. 4.9, $p<0.001$), 6 months (8.5 vs. 4.8, $p<0.001$), and 9 months (7.1 vs. 4.9, $p<0.01$), but not at 12 months (Table 2). When we evaluated HADS-D scores, mean scores were statistically significant higher in patients with IBD with IBS-type symptoms than those without IBS-type symptoms at baseline (5.0 vs.

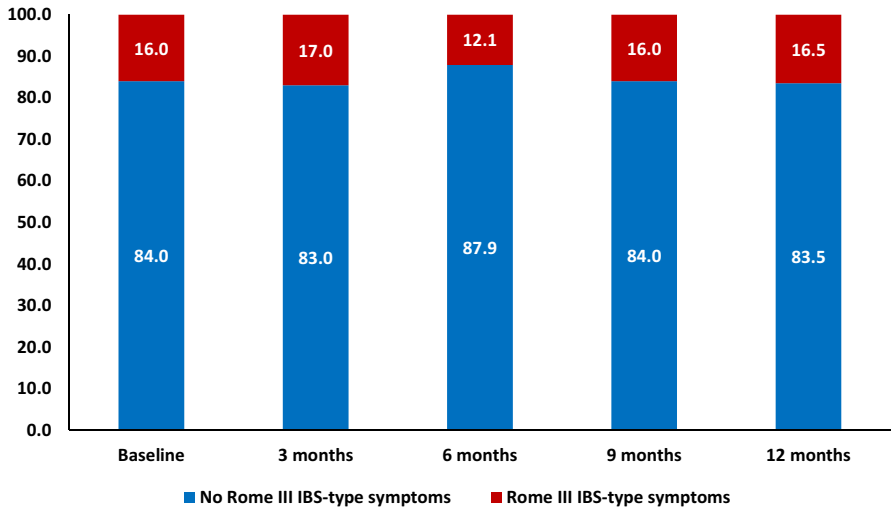


**FIGURE 1** Prevalence of Rome III IBS-type symptoms at each point of follow-up during the study.

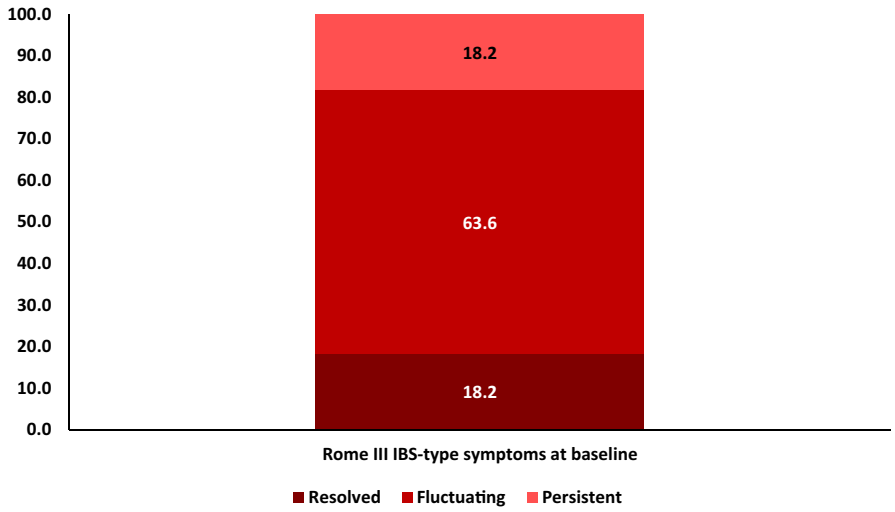


**FIGURE 2** Natural history of Rome III IBS-type symptoms in patients with IBD reporting IBS-type symptoms at baseline.

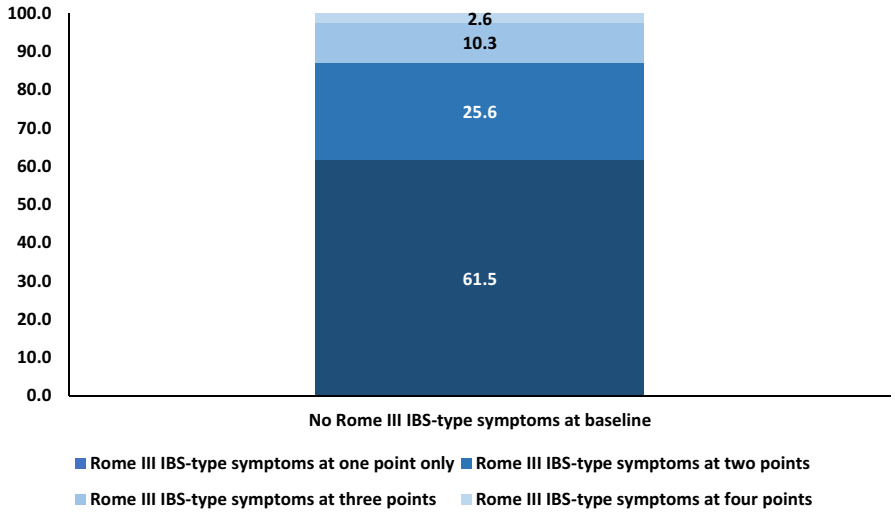


**FIGURE 3** Natural history of IBS-type symptoms in patients with IBD without Rome III IBS-type symptoms at baseline who developed Rome III IBS-type symptoms subsequently.

2.8, $p < 0.001$), 3 months (5.4 vs. 2.9, $p < 0.001$) and 9 months (5.2 vs. 0.3.2, $p < 0.01$) (Table 2). In terms of mean PHQ-12 scores between patients with IBD with and without IBS-type symptoms, these were statistically significant higher at baseline (7.0 vs. 3.8, $p < 0.001$) and 3 months (6.5 vs. 4.2, $p < 0.01$) (Table 2). Finally, patients with IBD with IBS-type symptoms had statistically significant lower SIBDQ score than those without at all time points (49.8 vs. 60.0, $p < 0.001$ at baseline; 50.2 vs. 59.8, $p < 0.001$ at 3 months; 48.8 vs. 59.3, $p < 0.001$ at 6 months; 49.8 vs. 58.4, $p < 0.001$ at 9 months; and 52.0 vs. 58.1, $p < 0.01$; Table 2).

**TABLE 2** Impact of Rome III IBS-type symptoms on HADS-anxiety, HADS-depression, somatoform symptom-reporting, and quality of life scores at each point of follow-up during the study.

| | Baseline | | 3 months | | 6 months | | 9 months | | 12 months | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Rome III IBS-type symptoms | | Rome III IBS-type symptoms | | Rome III IBS-type symptoms | | Rome III IBS-type symptoms | | Rome III IBS-type symptoms | |
| | Yes ($n=33$) | No ($n=173$) | Yes ($n=35$) | No ($n=171$) | Yes ($n=25$) | No ($n=181$) | Yes ($n=33$) | No ($n=173$) | Yes ($n=34$) | No ($n=172$) |
| Mean HADS-A (SD) | 7.8 (4.0)** | 4.8 (3.7) | 7.7 (4.2)** | 4.9 (3.9) | 8.5 (4.7)** | 4.8 (4.0) | 7.1 (3.9)* | 4.9 (4.2) | 6.1 (4.7) | 5.1 (4.2) |
| Mean HADS-D (SD) | 5.0 (3.3)** | 2.8 (2.9) | 5.4 (3.9)** | 2.9 (3.0) | 5.6 (4.2) | 3.4 (3.5) | 5.2 (3.6)* | 3.2 (3.4) | 4.7 (4.1) | 3.3 (3.4) |
| Mean PHQ-12 (SD) | 7.0 (3.6)** | 3.8 (3.1) | 6.5 (3.9)* | 4.2 (3.3) | 5.6 (2.8) | 4.2 (3.6) | 5.9 (3.9) | 4.0 (3.1) | 5.9 (4.1) | 4.1 (3.4) |
| Mean SIBDQ (SD) | 49.8 (8.6)** | 60.0 (7.9) | 50.2 (10.7)** | 59.8 (8.3) | 48.8 (12.9)** | 59.3 (8.8) | 49.8 (10.9)** | 58.4 (9.8) | 52.0 (9.8)* | 58.1 (10.1) |

*$p<0.01$ versus patients with IBD with no IBS-type symptoms. **$p<0.001$ versus patients with IBD with no IBS-type symptoms.

## 4 | DISCUSSION

This 12-month longitudinal study, with regular follow-up at 3-month intervals, has examined the natural history of IBS-type symptoms in patients with IBD in clinical remission at baseline and assessed the characteristics of patients with different symptom courses, and how such symptom trajectories influence psychological health and quality of life. Overall, around one-third of patients with IBD in clinical remission reported IBS-type symptoms, according to Rome III criteria, at one or more points of follow-up. The prevalence of Rome III IBS-type symptoms at each point of follow-up ranged from 12.1% to 17.0%. Patients with IBD with IBS-type symptoms were younger than those not reporting such symptoms and more likely to be female. Two-thirds of patients reporting IBS-type symptoms at baseline had fluctuating symptoms during 12 months of follow-up. In addition, among patients with IBD without Rome III IBS-type symptoms at baseline, almost 30% reported IBS-type symptoms at least one subsequent point of follow-up. Among those reporting IBS-type symptoms at each of the points of follow-up, HADS-A, HADS-D, and PHQ-12 scores were higher, and SIBDQ scores lower than in patients not reporting such symptoms.

We recruited a cohort of patients with IBD in clinical remission, which means that the reported symptoms were more likely to be attributed to overlapping IBS than to their organic condition. Initial enrollment, and subsequent follow-up, was predominantly via personalized links to online questionnaires, minimizing missing data from participants. Although a structured interview may have provided greater sensitivity or specificity than the HADS for the detection of common mental disorders,[24] we also used the PHQ-12 questionnaire, which collects other somatic symptoms of depression, such as poor sleep and fatigue, which are not captured by the HADS. The regular contact with participants, at 3-monthly intervals, allowed us to better study the fluctuation of IBS-type symptoms. We were unable to assess the characteristics of non-responders to our baseline questionnaire and, therefore, cannot exclude a volunteer bias, with those with IBS-type symptoms being more likely to participate, which may have led to an overestimation of the prevalence of IBS-type symptoms in IBD. However, the study was not designed with the assessment of IBS-type symptoms as its main aim and the prevalence we observed is slightly lower than previous studies examining this issue.[8,25] We used the Rome III criteria to define the presence of IBS-type symptoms, rather than the more recent Rome IV criteria. We have shown previously that the Rome IV criteria are more restrictive than Rome III, both in patients with IBS and patients with IBD.[26,27] Applying the Rome IV criteria in this dataset would have meant that only around 10% of patients would have met criteria for reporting IBS-type symptoms at baseline, meaning any examination of the natural history of these symptoms would have been problematic. We relied on patient-reported clinical disease activity scores, rather than an objective measure of inflammation, such as fecal calprotectin, to assess IBD activity at baseline. Given the COVID-19 pandemic, persuading patients with IBD to attend an appointment in-person to provide a stool sample would

have been impractical. However, this means that we cannot exclude the possibility that in some patients ongoing occult disease activity was responsible for the prevalence of IBS-type symptoms we report. Finally, as our recruitment began in 2020, at the height of the COVID-19 pandemic, we also cannot exclude an impact of repeated lockdowns and concerns over shielding, among a group of patients who were potentially vulnerable to COVID-19, which may have affected IBS-type symptoms among those taking part.

A recent meta-analysis reported that one-in-four patients with UC and one-in-three with CD in clinical remission reported IBS-like symptoms.[8] What is more, in accordance with our findings, different studies observed that these symptoms were more frequent in females, especially with possible anxiety or depression. Psychological factors are considered to be involved in the pathogenesis of both disorders, but they may be more crucial in IBS than in IBD.[28] Moreover, recent evidence demonstrates that patients with active IBD are more likely to report symptoms of anxiety or depression.[29] However, in our study, which recruited patients with IBD in clinical remission, patients with IBD with IBS-type symptoms had higher anxiety or depression scores compared to those without IBS-type symptoms at baseline and multiple other time points. A smaller study, enrolling 47 patients with CD and 24 with UC in clinical remission, demonstrated a prevalence of Rome III IBS-like symptoms in 29.8% and 50.0% of patients, respectively.[30] As observed in our cohort, quality of life scores were lower, and anxiety or depression scores higher, in patients with IBS-type symptoms than those without. However, the authors did not evaluate fluctuations in, or stability of, these scores over time. A more recent study demonstrated higher levels of symptoms of anxiety and depression among patients with IBD in biochemical remission with ongoing abdominal pain.[31]

Previous studies from our group, where patients with IBD were followed up at 2 and 6 years,[12,32] demonstrated that the presence of IBS-type symptoms was associated with increased healthcare utilization, worse anxiety, depression, somatoform symptom-reporting, and quality of life scores, but not adverse IBD outcomes. However, although the longer duration of follow-up is useful to assess the impact of IBS-type symptoms on prognosis of IBD, these studies were unable to assess the rapid fluctuations of symptoms due to the longer interval between questionnaires. Although gut-brain behavioral therapies are a recommended part of IBS management,[33] as they have a confirmed benefit for the symptoms of IBS,[34] there have been fewer trials of these interventions in IBD.[35] In trials conducted, to date, there appears to be no effect of gut-brain behavioral therapies on IBD activity, although they may lead to short-term improvements in symptoms of anxiety or depression, and quality of life. It is important to point out that most of these trials have recruited unselected patients with IBD, rather than those with IBS-type symptoms, or abnormal anxiety or depression scores, who may be expected to have a greater benefit. This may have diluted the treatment effect. It could, therefore, be argued that this group of patients should be considered for these kinds of therapies, as they may improve both their IBS-type symptoms and their mental health and quality of life.

In conclusion, we have reported the trajectories of IBS-type symptoms and their associated characteristics and impact on mental health and quality of life in patients with IBD in clinical remission over a 12-month period. One-in-three patients in clinical remission at baseline reported IBS-type symptoms at any point during the study and the number of patients whose symptoms resolved entirely was small. Prevalence of IBS-type symptoms remained similar at each 3-month follow-up interval and presence of these symptoms was associated with higher anxiety, depression, and somatoform symptom-reporting scores and lower quality of life. Based on our findings, there is a clear need to screen for IBS-type symptoms in patients with IBD, even if they are in clinical remission, with appropriate intervention to reduce the impact on psychological health and quality of life. Given the more restrictive nature of the Rome IV criteria,[26] these are likely to underestimate both prevalence and impact of these symptoms on patients.[27] The Rome III criteria would, therefore, be preferable with treatment targeted towards the most troublesome symptom or symptoms, as would be the case in IBS itself. In this regard, there is a growing need for evidence that will assist physicians in the care of such patients.

## AUTHOR CONTRIBUTIONS

Brigida Barberio, Keeley M. Fairbrass, David J. Gracie, and Alexander C. Ford conceived and drafted the study. Keeley M. Fairbrass collected all data. Alexander C. Ford analyzed and interpreted the data. Brigida Barberio and Alexander C. Ford drafted the manuscript. All authors contributed to and approved the final draft of the manuscript.

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## CONFLICT OF INTEREST STATEMENT

No competing interests declared.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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