Received: 27 October 2023 | Revised: 20 January 2024 | Accepted: 23 January 2024

DOI: 10.1111/nmo.14756

ORIGINAL ARTICLE

Neurogastroenterology & Motility NGM WILEY

Utility of irritable bowel syndrome subtypes and most troublesome symptom in predicting disease impact and burden

Mais Khasawneh[1,2] | Fahad Ali Shaikh[2] | Cho Ee Ng[3] | Christopher J. Black[1,2] | Vivek C. Goodoory[1,2] | Alexander C. Ford[1,2]

[1]Leeds Institute of Medical Research at St. James's, University of Leeds, Leeds, UK

[2]Leeds Gastroenterology Institute, St. James's University Hospital, Leeds, UK

[3]County Durham and Darlington NHS Foundation Trust, Durham, UK

Correspondence
Alexander C. Ford, Leeds Gastroenterology Institute, Room 125, 4th Floor, Bexley Wing, St. James's University Hospital, Beckett Street, Leeds LS9 7TF, UK.
Email: alexford@nhs.net

Funding information
Tillotts Pharma

Abstract

Background: Little is known about the characteristics of individuals with irritable bowel syndrome (IBS) according to stool subtype or the most troublesome symptom reported by the individual, or whether these are useful in predicting the impact of IBS.

Methods: We collected demographic, gastrointestinal, and psychological symptoms, healthcare usage and direct healthcare costs, impact on work and activities of daily living, and quality of life data from individuals with Rome IV-defined IBS.

Key Results: We recruited 752 people with Rome IV IBS. Individuals with IBS-D reported a poorer disease-specific quality of life than those with IBS-C or IBS-M (mean (SD) IBS-QOL 45.3 (23.0) for IBS-D, vs. 52.3 (19.9) for IBS-C, vs. 49.4 (22.0) for IBS-M, $p = 0.005$). Mean (SD) IBS-QOL scores were also lower amongst those who reported diarrhea (44.8 (22.3)) or urgency (44.6 (22.3)) as their most troublesome symptom, compared with those reporting abdominal pain (52.2 (22.9)), constipation (49.5 (21.8)), or abdominal bloating or distension (50.4 (21.3)). However, there were no differences in mean EQ-5D scores, IBS severity, levels of anxiety, depression, somatoform symptom-reporting, or gastrointestinal symptom-specific anxiety. Direct healthcare costs of IBS were similar across all subtypes and all most troublesome symptom groups, although some differences in work productivity and social leisure activities were detected.

Conclusions and Inferences: There appears to be limited variation in the characteristics of individuals with Rome IV IBS based on both stool subtypes and most troublesome symptom reported, suggesting that gastrointestinal symptoms alone have limited ability to predict disease impact and burden.

KEYWORDS
burden, gastrointestinal symptoms, IBS subtypes, impact

Abbreviations: HADS, hospital anxiety and depression scale; IBS, irritable bowel syndrome; IBS-C, irritable bowel syndrome with constipation; IBS-D, irritable bowel syndrome with diarrhea; IBS-M, irritable bowel syndrome with mixed bowel habits; IBS-QOL, irritable bowel syndrome quality of life; IBS-SSS, irritable bowel syndrome severity scoring system; IBS-U, irritable bowel syndrome unclassified; IQR, interquartile range; PHQ-12, patient health questionnaire-12; VSI, visceral sensitivity index; WPAI:IBS, work productivity and activity impairment questionnaire: irritable bowel syndrome.

Vivek C. Goodoory and Alexander C. Ford joint last author.

1 | INTRODUCTION

Irritable bowel syndrome (IBS) is a prevalent disorder of gut–brain interaction that affects 5%–10% of the global population.[1–3] It is characterized by abdominal pain and altered stool form and/or frequency.[4] The Rome criteria for IBS are the gold-standard diagnostic criteria for IBS.[5,6] They are based on patient-reported symptoms and have undergone several revisions to improve their diagnostic performance, with the most recent being the Rome IV criteria.[4] Because the pathophysiology of IBS is poorly understood, the treatment goal is to alleviate symptoms, rather than addressing the cause(s) of IBS. Individuals with IBS are grouped according to different stool subtypes using the Bristol stool form scale.[5] The four subtypes, defined by the Rome IV criteria, are IBS with constipation (IBS-C), diarrhea (IBS-D), mixed bowel habits (IBS-M), and unclassified (IBS-U). Originally, subtyping was developed as a research tool for participant selection and description, but it is also used in clinical practice to guide need for investigation and treatment selection.[7]

Using IBS subtypes to direct therapy or recruit patients in clinical trials is not ideal because predominant stool type fluctuates, as demonstrated in longitudinal studies.[8,9] Nevertheless, understanding the distinction between IBS subtypes is important as it constitutes the prevailing classification system employed routinely in clinical practice, research trials, drug licensing, and guideline development. Several studies have examined the characteristics of individuals with IBS according to stool subtype, but none have used the Rome IV criteria and they have other limitations.[10–15] Given the fluctuation of stool subtype and the fact that IBS is a heterogeneous disorder characterized by a multitude of symptoms, an alternative to subgrouping by stool form or frequency would be to ask patients what their most troublesome symptom is. However, there have been no studies examining the characteristics of individuals with IBS according to the most troublesome symptom reported. It is unclear whether subtyping IBS according to predominant stool form or frequency or most troublesome symptom reported is a useful way of predicting disease impact and burden.

We, therefore, conducted a cross-sectional study to examine the characteristics of individuals with Rome IV-defined IBS according to both IBS stool subtype and most troublesome symptom reported by the individual. We aimed to assess their utility in predicting the impact of IBS on individuals, in terms of quality of life and ability to carry out daily activities and work duties, and the healthcare system, in terms of healthcare usage and direct healthcare costs.

What is known

- IBS is a chronic disorder characterized by a multitude of GI symptoms.
- IBS is classified according to stool form and frequency but subtypes in IBS lack stability over time.
- There is little research examining the characteristics of individuals with IBS based on their reported most troublesome symptom.

What is new here

- Few variations were observed in the characteristics of individuals with respect to both the subtype of IBS and the reported most troublesome symptom.
- Gastrointestinal symptoms alone have limited ability to predict disease impact and burden in IBS.
- Assessing patients with IBS using both gastrointestinal and psychological symptoms may allow clinicians and healthcare systems to better stratify individuals in terms of disease impact and burden.

2 | METHODS

2.1 | Participants and setting

This study recruited individuals registered with ContactME-IBS, a UK national registry run by County Durham and Darlington NHS Foundation Trust, of over 4280 members with IBS who are interested in research.[16] ContactME-IBS recruits individuals in the UK through advertisements in primary care, hospital clinics, pharmacies, or on social media. Those interested enroll by completing a short online questionnaire about their bowel symptoms and providing their contact details. Of the registrants, 2268 (53%) have seen their primary care physician with IBS and another 1455 (34%) have seen a gastroenterologist. We have previously reported data from this cohort.[17–22] All participants were contacted via electronic mailshot in July 2021, with non-responders receiving a reminder email in August 2021. There were no exclusion criteria apart from the inability to understand written English. Participants' responses were stored in an online database. Those who completed the questionnaire were given a chance to win one of three gift cards worth £200, £100, or £50. The study was approved by the University of Leeds research ethics committee in March 2021 (MREC 20–051).

2.2 | Data collection and synthesis

2.2.1 | Demographic and symptom data

We collected demographic data, including age, sex, lifestyle factors such as tobacco and alcohol consumption, ethnicity, marital status, educational level, and annual income. We defined the presence of IBS using the Rome IV questionnaire,[23] assigning presence or absence of Rome IV-defined IBS among all individuals according to the scoring algorithm proposed for its use.[4] We categorized IBS subtype, as recommended, using the proportion of time stools were abnormal according to the Bristol stool form scale. All participants were also asked to identify their most troublesome symptom from a list of five possibilities, including abdominal pain, constipation, diarrhea,

abdominal bloating or distension, or fecal urgency. We asked participants about the duration of their IBS diagnosis and whether their IBS symptoms started after an acute enteric infection.

2.2.2 | IBS symptom severity

We assessed severity of symptoms using the IBS severity scoring system (IBS-SSS),[24] which measures presence, severity, and frequency of abdominal pain, presence and severity of abdominal distension, satisfaction with bowel habit, and degree to which IBS symptoms are affecting, or interfering with, the individual's life. The IBS-SSS carries a maximum score of 500 points, with <75 points indicating remission of symptoms; 75–174 points mild symptoms; 175–299 points moderate symptoms; 300–500 points severe symptoms.

2.2.3 | Mood and somatic symptoms

We used the hospital anxiety and depression scale (HADS) to collect anxiety and depression data. The total HADS score ranges from 0 to 21 for either anxiety or depression. We categorized severity for each into normal (total HADS depression or anxiety score 0–7), borderline normal,[8–10] or abnormal (≥11).[25] We collected somatoform symptom-reporting data using the patient health questionnaire-12 (PHQ-12),[26] derived from the validated PHQ-15.[27] The total PHQ-12 score ranges from 0 to 24. We categorized severity into high (total PHQ-12 ≥ 13), medium (8-12), low (4-7), or minimal (≤3).

2.2.4 | Gastrointestinal symptom-specific anxiety

We used the visceral sensitivity index (VSI),[28] which measures gastrointestinal symptom-specific anxiety. Replies to each of the 15 items are provided on a 6-point scale from "strongly disagree" (score 0) to "strongly agree" (score 5). We divided these data into equally sized tertiles, as there are no validated cutoffs to define low, medium, or high levels of gastrointestinal symptom-specific anxiety.

2.2.5 | IBS-specific and generic health-related quality of life

We used the irritable bowel syndrome quality of life (IBS-QOL), a validated IBS-specific questionnaire, to measure health-related quality of life in individuals with IBS.[29,30] The IBS-QOL consists of 34 items, each ranked on a 5-point Likert scale ranging from 0 to 4, with a total possible score of 0–136 and lower scores indicating better quality of life. The 34 items are based on the following eight variables: dysphoria, interference with activity, body image, health worry, food avoidance, social reactions, sexual activity, and relationships. As in the original validation studies, scores were transformed to a 0 to 100-point scale with zero indicating worst quality of life and 100 indicating best quality of life.[29,30] We divided these data into equally sized tertiles as, again, there are no validated cutoffs to define low, medium, or high levels of quality of life. We also used the EQ-5D-5L instrument,[31] one of the three versions of the EuroQOL,[32] a generic health-related quality of life questionnaire, used widely throughout health care. The EQ-5D-5L consists of five items covering different aspects of health: mobility, self-care, ability to carry out usual activities, pain/discomfort, and anxiety/depression. Each item has five levels of responses, allowing for a total of 3125 possible health states. We mapped each health state to obtain a utility score for a UK population using a crosswalk calculator.[33]

2.2.6 | IBS-related resource use

We collected data on healthcare usage related to a person's IBS over the 12 months prior to recruitment to the study. We asked participants to report any appointments with healthcare professionals (general practitioners (GPs), gastroenterologists, specialist nurses, dietitians, or psychologists), including the number of appointments, number of investigations (blood tests, stool tests, endoscopies, abdominal ultrasounds, computed tomography (CT) scans, magnetic resonance imaging (MRI) scans, hydrogen breath tests, or 23-seleno-25-homo-tauro-cholic acid (SeHCAT) scans), number of unplanned emergency department attendances or inpatient admissions (including length of stay), and over the counter and prescribed medication usage (in months). We applied costs for GP appointments from Unit Costs of Health and Social Care 2020,[34] and appointments, investigations, and unplanned inpatient days in secondary care using the NHS's 2019/20 National Cost Collection Data.[35] We assumed that all the appointments for IBS were follow-up appointments, which cost less than a new patient appointment. We applied the lowest price for a 1-month supply of each IBS-related medication using the online version of the British National Formulary.[36]

2.2.7 | Impact of IBS on productivity and ability to work

We used the work productivity and activity impairment questionnaire for irritable bowel syndrome (WPAI:IBS),[37] which is a validated questionnaire to assess the level of work productivity loss in people with IBS who are employed, as well as activity impairment in their activities of daily living. The WPAI:IBS consists of six questions related to current employment status, hours of work missed due to IBS, hours of work missed due to other reasons, hours actually worked, the degree to which IBS has affected work productivity whilst working, and the degree to which IBS has affected other activities of daily living in the last 7 days. The WPAI:IBS measures four domains: absenteeism, which is the percentage of work hours missed because of IBS; presenteeism, which is the percentage of impairment experienced whilst working because of IBS; overall work impairment, which is the percentage of work productivity loss; and

activity impairment, which is the percentage impairment in activities of daily living. We also used the work and social adjustment scale (WSAS),[38] which has been used by others to measure the effect of IBS on individuals' ability to work, manage at home, engage in social and private leisure activities, and maintain close relationships.[39–42] The five domains are scored on a 9-point scale from "not at all" (score 0) to "very severely" (score 8).

2.3 | Statistical analysis

All participants who met Rome IV criteria for IBS were included in the analysis. We dichotomized the presence (score ≥4 ("definitely" impacting)) or absence (score <4) of an impact of IBS on home management activities, social leisure activities, private leisure activities, or maintaining close relationships. We compared the characteristics of participants according to IBS stool subtypes and most troublesome symptom reported. Categorical variables such as sex, IBS subtype, IBS symptom severity, presence or absence of abnormal anxiety or depression scores, level of somatoform symptom reporting, level of gastrointestinal symptom-specific anxiety, and level of IBS-related quality of life were compared using a χ^2 test. Data such as age, healthcare costs related to IBS, and scores for absenteeism, presenteeism, overall work impairment, or activity impairment were compared between groups using an independent samples *t*-test or Mann–Whitney *U*-test. Because of multiple comparisons, a two-tailed *p*-value of <0.01 was considered statistically significant for all analyses. We performed all analyses using SPSS for Windows (version 27.0 SPSS, Chicago, IL).

3 | RESULTS

In total, 1278 (29.9%) of 4280 registrants (mean age 47.2 years (range 18–89 years), 1086 (85.0%) female) completed the questionnaire. Of these, 752 (58.8%) met Rome IV criteria (mean age 45.3 years (range 18–81 years), 655 (87.1%) female, and 729 (96.9%) White). There were 136 (18.1%) individuals with IBS-C, 306 (40.7%) with IBS-D, 301 (40.0%) with IBS-M, and nine (1.2%) with IBS-U. Given the small size of the latter group, these individuals were excluded from further analysis. When asked about their most troublesome symptom, 169 (22.5%) individuals reported abdominal pain, 53 (7.0%) constipation, 117 (15.6%) diarrhea, 218 (29.0%) abdominal bloating or distension, and 195 (25.9%) urgency.

3.1 | Characteristics of individuals according to IBS subtypes

We examined the characteristics of individuals with Rome IV IBS according to IBS subtypes (Table 1). A significantly higher proportion of those with IBS-C were female (95.6% with IBS-C, vs. 82.0% with IBS-D, vs. 88.7% with IBS-M, $p<0.001$), and a significantly higher proportion of those with IBS-D reported onset of IBS after an acute enteric infection (7.4% with IBS-C, vs. 16.7% with IBS-D, vs. 9.6% with IBS-M, $p=0.005$). There was no significant difference in age, ethnicity, marital status, smoking or alcohol use, level of education, annual income, or the proportion of individuals seeing a GP or gastroenterologist for their IBS in the 12 months prior to study recruitment according to subtype. There were significant differences in the most troublesome symptom reported according to subtype ($p<0.001$ for trend), with the most prevalent troublesome symptom being abdominal bloating or distension for those with IBS-C and IBS-M (36.8% and 36.9%, respectively), and urgency for those with IBS-D (36.9%) (Figure 1).

There was no difference in IBS severity, levels of anxiety, depression, somatoform symptom-reporting, gastrointestinal symptom-specific anxiety, or direct healthcare cost of IBS according to stool subtype. Levels of absenteeism, presenteeism, overall work impairment, or activity impairment were also similar across subtypes. A higher proportion of those with IBS-D (63.1%), compared with those with IBS-C (51.5%) or IBS-M (51.5%), reported that IBS affected their social leisure activities ($p=0.007$) but there was no difference in impairment in home management, private leisure activities, or close relationships. There was a statistically significant difference in mean IBS-QOL scores among individuals with different IBS subtypes (52.3 (standard deviation (SD) 19.9) for IBS-C, vs. 45.3 (SD 23.0) for IBS-D and 49.4 (SD 22.0) for IBS-M, $p=0.005$) and a higher proportion of participants with IBS-D (37.9%), compared with those with IBS-C (20.6%) or IBS-M (30.6%) were in the lowest tertile of IBS-specific quality of life ($p=0.003$). However, there was no significant difference in mean EQ-5D scores according to IBS subtype.

3.2 | Characteristics of individuals according to most troublesome symptom

We then examined the characteristics of individuals with Rome IV IBS according to the most troublesome symptom reported (Table 2). Among the 752 participants, those who reported diarrhea (mean age (SD) 43.4 (16.2)), or abdominal bloating or distention (43.1 (13.6)) were younger compared with those reporting abdominal pain (45.1 (15.6)), constipation (48.4 (13.9)), or urgency (48.3 (14.2)) ($p<0.002$). There were no differences in sex, ethnicity, marital status, smoking, alcohol use, level of education, or annual income according to most troublesome symptom reported. A significantly higher proportion of patients who reported diarrhea as their most troublesome symptom had IBS after an acute enteric infection ($p<0.001$). There were significant differences in the proportion of individuals meeting criteria for the different IBS subtypes according to most troublesome symptom reported ($p<0.001$ for trend). (Figure 2).

Most troublesome symptom reported was not associated with IBS severity, levels of anxiety, depression, somatoform symptom-reporting, gastrointestinal symptom-specific anxiety, or direct healthcare cost of IBS. Levels of presenteeism were significantly higher among those reporting abdominal pain as the most

TABLE 1 Characteristics of individuals with Rome IV IBS according to IBS subtype.

	IBS-C ($n=136$)	IBS-D ($n=306$)	IBS-M ($n=301$)	p Value*
Female (%)	130 (95.6)	251 (82.0)	267 (88.7)	<0.001
Mean age (SD)	44.14 (13.96)	44.86 (14.64)	45.86 (15.13)	0.48
White ethnicity (%)	133 (97.8)	291 (95.1)	296 (98.3)	0.06
Married (%)	87 (64.0)	199 (65.0)	195 (64.8)	0.98
Smoker (%)	9 (6.6)	38 (12.4)	35 (11.6)	0.18
Alcohol user (%)	72 (52.9)	178 (58.2)	183 (60.8)	0.30
University or postgraduate level of education (%)	63 (46.3)	121 (39.5)	127 (42.2)	0.41
Annual income of £30,000 or more (%)	31 (25.6)	86 (31.3)	79 (28.6)	0.51
IBS after acute infection (%)	10 (7.4)	51 (16.7)	29 (9.6)	0.005
Seen a primary care physician regarding IBS in the last 12 months (%)	51(37.5)	111(36.3)	127 (42.2)	0.31
Seen a gastroenterologist regarding IBS in the last 12 months (%)	27 (19.9)	52 (17.0)	66 (21.9)	0.31
Mean IBS-QOL (SD)	52.3 (19.9)	45.3 (23.0)	49.4 (22.0)	0.005
Mean EQ-5D (SD)	0.595 (0.268)	0.569 (0.280)	0.558 (0.293)	0.45
Duration of IBS diagnosis, year(s) (%)				
1	3 (2.2)	7 (2.3)	15 (5.0)	
2	4 (2.9)	20 (6.5)	17 (5.6)	
3	8 (5.9)	18 (5.9)	27 (9.0)	
4	8 (5.9)	16 (5.2)	9 (3.0)	
5	5 (3.7)	21 (6.9)	12 (4.0)	
>5	108 (79.4)	224 (73.2)	221 (73.4)	0.14
Most troublesome symptom (%)				
Abdominal pain	43 (31.6)	47 (15.4)	76 (25.2)	
Constipation	34 (25.0)	1 (0.3)	18 (6.0)	
Diarrhea	0 (0.0)	92 (30.1)	25 (8.3)	
Abdominal bloating or distension	50 (36.8)	53 (17.3)	111 (36.9)	
Urgency	9 (6.6)	113 (36.9)	71 (23.6)	<0.001
IBS-SSS severity (%)				
Mild	14 (10.4)	31 (10.2)	39 (13.0)	
Moderate	65 (48.5)	115 (38.0)	117 (39.1)	
Severe	55 (41.0)	157 (51.8)	143 (47.8)	0.19
HADS anxiety categories (%)				
Normal	39 (28.7)	81 (26.5)	79 (26.2)	
Borderline abnormal	36 (26.5)	68 (22.2)	66 (21.9)	
Abnormal	61 (44.9)	157 (51.3)	156 (51.8)	0.70
HADS depression categories (%)				
Normal	75 (55.1)	156 (51.0)	169 (56.1)	
Borderline abnormal	31 (22.8)	70 (22.9)	62 (20.6)	
Abnormal	30 (22.1)	80 (26.1)	70 (23.3)	0.72
PHQ-12 severity (%)				
Low	9 (6.6)	20 (6.5)	7 (2.3)	
Mild	30 (22.1)	78 (25.5)	66 (21.9)	
Moderate	51 (37.5)	125 (40.8)	125 (41.5)	
Severe	46 (33.8)	83 (27.1)	103 (34.2)	0.10

(Continues)

TABLE 1 (Continued)

	IBS-C ($n=136$)	IBS-D ($n=306$)	IBS-M ($n=301$)	p Value*
VSI scores (%)				
Low	52 (38.2)	84 (27.5)	107 (35.5)	
Medium	43 (31.6)	102 (33.3)	101 (33.6)	
High	41 (30.1)	120 (39.2)	93 (30.9)	0.07
IBS-QOL score (%)				
Low	28 (20.6)	116 (37.9)	92 (30.6)	
Medium	58 (42.6)	97 (31.7)	95 (31.6)	
High	50 (36.8)	93 (30.4)	114 (37.9)	0.003
WPAI:IBS, median (IQR)				
Absenteeism	0.0 (0.0–0.0)	0.0 (0.0–5.2)	0.0 (0.0–2.7)	0.05
Presenteeism	30.0 (10.0–60.0)	40.0 (20.0–70.0)	40.0 (10.0–60.0)	0.10
Overall work impairment	30.0 (10.0–50.0)	30.6 (10.0–65.6)	30.0 (10.0–55.0)	0.15
Activity impairment	40.0 (20.0–60.0)	50.0 (20.0–72.5)	40.0 (20.0–60.0)	0.04
WSAS (%)				
IBS affected home management	33 (24.3)	96 (31.4)	88 (29.2)	0.32
IBS affected social leisure activities	70 (51.5)	193 (63.1)	155 (51.5)	0.007
IBS affected private leisure activities	27 (19.9)	99 (32.4)	79 (26.2)	0.02
IBS affected close relationships	32 (23.5)	93 (30.4)	76 (25.2)	0.21
Mean costs of IBS (SD)				
Appointments	303.02 (845.10)	184.02 (411.51)	230.08 (568.51)	0.13
Investigations	97.75 (220.33)	158.75 (360.88)	176.76 (379.08)	0.09
IBS-related medications	88.13 (132.08)	62.01 (73.77)	76.47 (97.48)	0.57
Unplanned attendances	69.96 (379.65)	117.97 (424.17)	102.92 (473.92)	0.02
Total direct healthcare costs	558.85 (1159.35)	522.75 (941.01)	586.22 (1043.37)	0.75

Note: Independent samples t-test for continuous data, and Mann–Whitney U-test for all four dimensions of work productivity and activity impairment: irritable bowel syndrome.

*p-value for Pearson χ^2 for the comparison of categorical data.

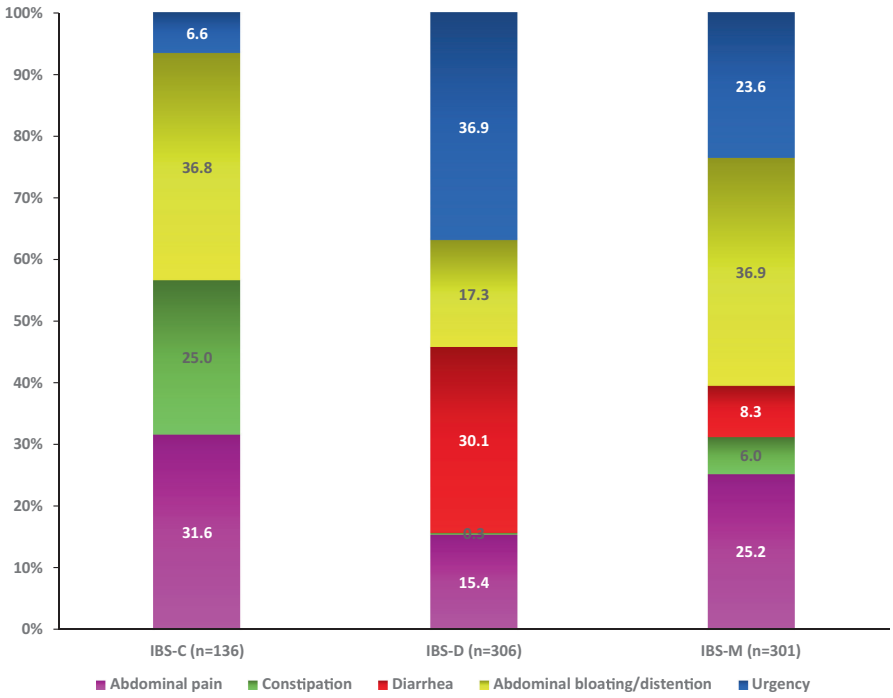

FIGURE 1 Prevalence of most troublesome symptom according to IBS subtype.

TABLE 2 Characteristics of individuals with Rome IV IBS according to most troublesome symptom.

	Abdominal pain ($n=169$)	Constipation ($n=53$)	Diarrhea ($n=117$)	Abdominal bloating/distension ($n=218$)	Urgency ($n=195$)	p-Value*
Female (%)	150 (88.8)	47 (88.7)	98 (83.8)	196 (89.9)	164 (84.1)	0.31
Mean age (SD)	45.1 (15.6)	48.4 (13.9)	43.4 (16.2)	43.1 (13.6)	48.3 (14.2)	0.002
White ethnicity (%)	165 (97.6)	50 (94.3)	111 (94.9)	212 (97.2)	191 (97.9)	0.42
Married (%)	103 (60.9)	37 (69.8)	68 (58.1)	147 (67.4)	132 (67.7)	0.25
Smoker (%)	21 (12.4)	4 (7.5)	14 (12.0)	25 (11.5)	18 (9.2)	0.78
Alcohol user (%)	94 (55.6)	33 (62.3)	68 (58.1)	130 (59.6)	114 (58.5)	0.91
University or postgraduate level of education (%)	69 (40.8)	24 (45.3)	43 (36.8)	110 (50.5)	68 (34.9)	0.016
Annual income of £30,000 or more (%)	45 (29.0)	12 (24.5)	31 (29.2)	59 (30.3)	50 (28.6)	0.96
IBS after acute enteric infection (%)	19 (11.2)	4 (7.5)	27 (23.1)	14 (6.4)	27 (13.8)	<0.001
Seen a primary care physician regarding IBS in the last 12 months (%)	83 (49.1)	21 (39.6)	42 (35.9)	80 (36.7)	68 (34.9)	0.05
Seen a gastroenterologist regarding IBS in the last 12 months (%)	39 (23.1)	13 (24.5)	20 (17.1)	42 (19.3)	33 (16.9)	0.48
Mean IBS-QOL (SD)	52.2 (22.9)	49.5 (21.8)	44.8 (22.3)	50.4 (21.3)	44.6 (22.3)	0.003
Mean EQ-5D (SD)	0.510 (0.330)	0.593 (0.268)	0.577 (0.265)	0.601 (0.258)	0.575 (0.274)	0.03
IBS subtype (%)						
IBS-C	43 (25.9)	34 (64.2)	0 (0.0)	50 (23.4)	9 (4.7)	
IBS-D	47 (28.3)	1 (1.9)	92 (78.6)	53 (24.8)	113 (58.5)	
IBS-M	76 (45.8)	18 (34.0)	25 (21.4)	111 (51.9)	71 (36.8)	<0.001
Duration of IBS diagnosis, year(s) (%)						
1	4 (2.4)	1 (1.9)	4 (3.4)	10 (4.6)	6 (3.1)	
2	12 (7.1)	0 (0.0)	13 (11.1)	9 (4.1)	7 (3.6)	
3	11(6.5)	5 (9.0)	13 (11.1)	19 (8.7)	6 (3.1)	
4	5 (3.0)	2 (3.8)	7 (6.0)	15 (6.9)	4 (2.1)	
5	11 (6.5)	1 (1.9)	6 (5.1)	8 (3.7)	12 (6.2)	
>5	126 (74.6)	44 (83.0)	74 (63.2)	157 (72.0)	160 (82.1)	0.012
IBS-SSS severity (%)						
Mild	18 (10.8)	11 (21.2)	12 (10.4)	23 (10.6)	22 (11.3)	
Moderate	61 (36.5)	24 (46.2)	45 (39.1)	91 (41.9)	79 (40.7)	
Severe	88 (52.7)	17 (32.7)	58 (50.4)	103 (47.5)	93 (47.9)	0.33
HADS anxiety categories (%)						
Normal	53 (31.4)	15 (28.3)	28 (23.9)	50 (22.9)	54 (27.7)	
Borderline abnormal	32 (18.9)	12 (22.6)	34 (29.1)	62 (28.4)	34 (17.4)	
Abnormal	84 (49.7)	26 (49.1)	55 (47.0)	106 (48.6)	107 (54.9)	0.12
HADS depression categories (%)						
Normal	86 (50.9)	31 (58.5)	56 (47.9)	136 (62.4)	95 (48.7)	
Borderline abnormal	40 (23.7)	8 (15.1)	31 (26.5)	41 (18.8)	45 (23.1)	
Abnormal	43 (25.4)	14 (26.4)	30 (25.6)	41 (18.8)	55 (28.2)	0.11
PHQ-12 severity (%)						
Low	9 (5.3)	3 (5.7)	6 (5.1)	11 (5.0)	7 (3.6)	
Mild	39 (23.1)	13 (24.5)	31 (26.5)	46 (21.1)	47 (24.1)	

(Continues)

TABLE 2 (Continued)

	Abdominal pain ($n=169$)	Constipation ($n=53$)	Diarrhea ($n=117$)	Abdominal bloating/distension ($n=218$)	Urgency ($n=195$)	p-Value*
Moderate	59 (34.9)	22 (41.5)	46 (39.3)	94 (43.1)	86 (44.1)	
Severe	62 (36.7)	15 (28.3)	34 (29.1)	67 (30.7)	55 (28.2)	0.88
VSI scores (%)						
Low	65 (38.5)	23 (43.4)	31 (26.5)	73 (33.5)	55 (28.2)	
Medium	51 (30.2)	13 (24.5)	46 (39.3)	70 (32.1)	67 (34.4)	
High	53 (31.4)	17 (32.1)	40 (34.2)	75 (34.4)	73 (37.4)	0.24
IBS-QOL score (%)						
Low	42 (24.9)	16 (30.2)	50 (42.7)	57 (26.1)	74 (37.9)	
Medium	60 (35.5)	14 (26.4)	31 (26.5)	80 (36.7)	67 (34.4)	
High	67 (39.6)	23 (43.4)	36 (30.8)	81 (37.2)	54 (27.7)	0.007
WPAI:IBS, median (IQR)						
Absenteeism	0.0 (0.0–5.1)	0.0 (0.0–4.2)	0.0 (0.0–7.0)	0.0 (0.0–0.0)	0.0 (0.0–5.0)	0.09
Presenteeism	50.0 (20.0–70.0)	20.0 (10.0–50.0)	40.0 (30.0–60.0)	30.0 (10.0–60.0)	35.0 (10.0–70.0)	0.009
Overall work impairment	40.0 (20.0–60.0)	30.0 (10.0–57.7)	40.0 (11.6–66.5)	30.0 (8.7–50.0)	30.0 (10.0–69.2)	0.02
Activity impairment	50.0 (20.0–70.0)	30.0 (20.0–50.0)	50.0 (20.0–80.0)	40.0 (20.0–60.0)	50.0 (20.0–70.0)	0.002
WSAS (%)						
IBS affected home management	66 (39.0)	7 (13.2)	34 (29.1)	56 (25.7)	57 (29.2)	0.003
IBS affected social leisure activities	89 (52.7)	23 (43.4)	67 (57.3)	111 (50.9)	133 (68.2)	0.001
IBS affected private leisure activities	52 (30.8)	6 (11.3)	33 (28.2)	52 (23.9)	64 (32.8)	0.02
IBS affected close relationships	52 (30.8)	11 (20.8)	30 (25.6)	49 (22.5)	61 (31.3)	0.17
Mean costs of IBS (SD)						
Appointments	281.92 (738.94)	239.25 (561.10)	184.42 (411.57)	192.36 (480.39)	230.62 (599.65)	0.56
Investigations	166.17 (334.22)	139.30 (292.60)	174.27 (398.81)	134.08 (325.34)	171.77 (382.38)	0.78
IBS-related medications	74.25 (83.57)	94.00 (155.53)	65.72 (83.76)	82.50 (111.49)	58.49 (69.23)	0.04
Unplanned attendances	163.69 (590.92)	45.92 (223.09)	141.92 (494.59)	48.71 (302.44)	98.85 (399.31)	0.07
Total direct healthcare costs	686.02 (1191.23)	518.47 (810.23)	566.34 (1055.48)	457.65 (885.32)	559.74 (1041.55)	0.31

Note: Independent samples t-test for continuous data, and Mann–Whitney U-test for all four dimensions of work productivity and activity impairment: irritable bowel syndrome.

*p-value for Pearson χ^2 for the comparison of categorical data.

troublesome symptom ($p=0.009$), but there was no difference in the level of absenteeism or overall work impairment. A significantly higher proportion of individuals with abdominal pain as their most troublesome symptom reported that IBS affected their home management ($p=0.003$) and a significantly higher proportion of those with urgency reported IBS affected their social leisure activities ($p=0.001$). There was a statistically significant difference in mean IBS-QOL scores among those reporting different most troublesome symptoms (52.2 (22.9) for abdominal pain, vs. 49.5 (21.8) for constipation, vs. 44.8 (22.3) for diarrhea, vs. 50.4 (21.3) for bloating or distension, vs. 44.6 (22.3) for urgency, $p=0.003$), but no significant difference in mean EQ-5D scores. Finally, a higher proportion of those who reported diarrhea or urgency as their most troublesome symptom were in the lowest tertile of IBS-specific quality of life ($p=0.007$).

4 | DISCUSSION

We recruited over 700 individuals with Rome IV IBS and examined their characteristics according to both IBS subtype and the most troublesome symptom reported. Individuals with IBS-D, compared

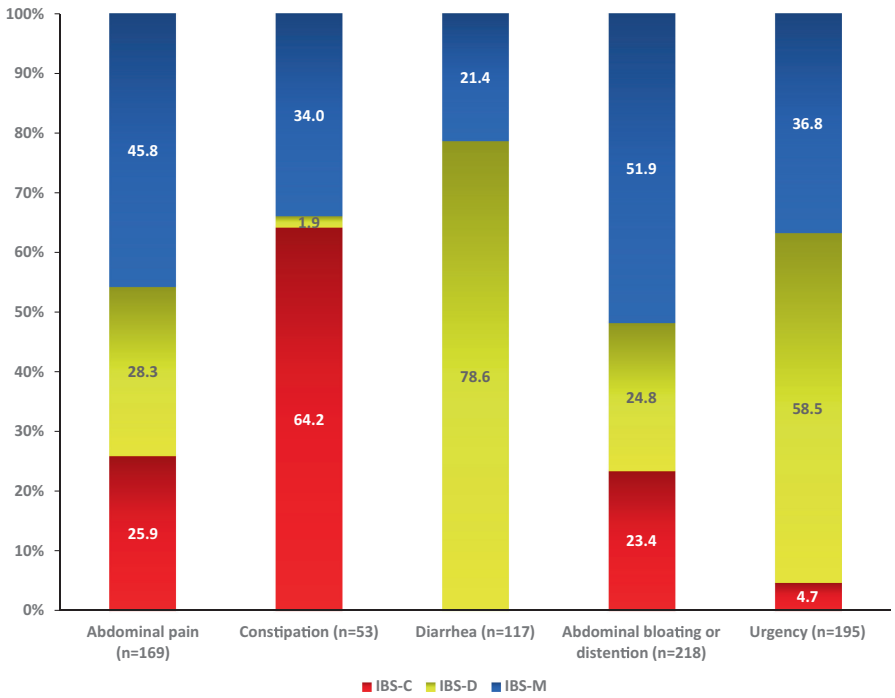

FIGURE 2 Prevalence of IBS subtype according to most troublesome symptom.

with those with IBS-C or IBS-M, and those who reported diarrhea or urgency, as opposed to abdominal pain, constipation, or bloating or distension, as their most troublesome symptom had lower disease-specific quality of life. However, there was no difference in generic health-related quality of life according to different IBS subtypes or most troublesome symptom reported. Interestingly, there were also no significant differences in symptom severity, levels of anxiety, depression, somatoform symptom-reporting, gastrointestinal symptom-specific anxiety, or direct healthcare costs of IBS according to either IBS subtype or most troublesome symptom reported. In addition, there was no difference in work productivity or impairment in most areas of daily living among those with different IBS subtypes. Conversely, those who reported abdominal pain as their most troublesome symptom had higher levels of presenteeism and reported greater impact of their IBS on home management whilst those with diarrhea or urgency reported greater impact on social leisure activities.

Our study recruited individuals with IBS who met Rome IV criteria. It included a large, diverse sample of individuals, who are likely to be representative of people with IBS living in the UK. This is because it consisted of participants who had various healthcare experiences, including those who had never sought medical attention, those who had visited a primary care physician, and those who had consulted a gastroenterologist. It also included individuals from different age groups, educational backgrounds, income levels, and relationship statuses, representing people from all walks of life. We used validated questionnaires and obtained near-complete data for variables of interest because of the use of mandatory fields in our online questionnaire.

We recruited individuals with self-reported IBS from a UK national registry, expanding beyond the traditional recruitment from primary, secondary, or tertiary care settings. These individuals may differ from people in the community. As an example, over 40% of participants had reached university or postgraduate level of education, which is higher than the UK average of 34% in the 2021 census.[43] Other issues include the absence of access to participants' medical records hindered the ability to definitively exclude other conditions, including celiac disease, bile acid diarrhea, or inflammatory bowel disease, which may exhibit similar symptomatology or coexist with IBS.[44–48] However, IBS has a higher prevalence compared with these conditions, and national guidelines in the UK advocate for the consideration or exclusion of these conditions during the diagnostic process for IBS.[49,50] Moreover, nearly 90% of the individuals registered with ContactME-IBS had sought medical attention from their primary care physician or gastroenterologist for their IBS symptoms. Furthermore, nearly 80% of the study participants reported a minimum IBS duration of 5 years, and all participants were enrolled in a specialized IBS research registry. Considering these factors, it is reasonable to assume that most of the study participants genuinely had IBS. The study sample consisted of UK residents, predominantly of white ethnicity, which may limit generalizability to populations outside the UK or individuals from other ethnic backgrounds. The proportion of individuals with constipation may be under-represented in our study, with only 18% meeting criteria for IBS-C, compared with previous reports of a similar prevalence of IBS-C, IBS-D, and IBS-M in the general population,[51,52] which may have affected our results. In addition, only nine of the 752 individuals met criteria for IBS-U, and we excluded this group in our analysis to preserve the ability to find meaningful differences among the other IBS subtypes. This is not unique to our study and in fact, most previous studies have only compared characteristics of individuals with IBS-C and IBS-D.[10,14,15]

To the best of our knowledge, this is the first study to examine the impact of IBS according to both stool subtype and most troublesome symptom reported. We not only assessed gastrointestinal symptoms but also examined psychological symptoms and healthcare usage and costs, as well as impact of IBS on work and activities of daily living. Our results demonstrating a higher proportion of females with IBS-C, compared with IBS-D and IBS-M, is similar to a large meta-analysis reporting the results of population-based studies on prevalence of IBS according to sex.[53] Prior studies examining similar issues have important limitations including the use of referral populations,[10,12] inclusion of only patients with severe refractory IBS,[11] or those with IBS-C and IBS-D only,[10,14] small sample size,[10] or use of historical definitions of IBS.[10–13] Nevertheless, there are some similarities between the results of these studies and our own. Two large cross-sectional studies recruiting individuals with Rome III-defined IBS reported no significant differences in symptom severity among those with IBS-C, IBS-D, or IBS-M.[11,12] In terms of psychological symptoms, previous studies are conflicting in terms of levels of anxiety or depression according to subtype.[10–14,54] However, other than Ray de Castro et al., who reported similar levels of somatoform symptom-reporting among subtypes,[12] albeit using a non-validated questionnaire, to our knowledge no previous studies have examined the spectrum of psychological comorbidities including anxiety, depression, somatoform symptom-reporting, and gastrointestinal symptom-specific anxiety, according to IBS subtype. Although there are conflicting results on impact of different IBS subtypes on activities of daily living,[11,15] results of one prior cross-sectional survey were consistent with our findings, showing no influence of IBS subtypes on work productivity outcomes.[15] Our results do, however, suggest that those who report abdominal pain as their most troublesome symptom experience more impairment at work compared with other symptoms of IBS. This is in line with a recent study demonstrating that painful disorders of gut–brain interaction are associated with higher levels of impairment at work.[55] Finally, our results demonstrating similar generic health-related quality of life among different IBS subtypes are similar to previous studies.[10,12,14] However, to our knowledge, this is the first study to also examine characteristics of individuals with IBS according to the most troublesome symptom reported.

The results from our study are important. Those with IBS-D, compared with IBS-C or IBS-M, and those who rated diarrhea or urgency, compared with abdominal pain, constipation, or bloating or distension, as their most troublesome symptom, had lower IBS-QOL scores. This suggests that, in terms of gastrointestinal symptoms, it is diarrhea or urgency, rather than abdominal pain or abdominal bloating or distension, which impact more on disease-specific quality of life. Urgency also had a particularly notable effect on social engagement and leisure activities. This may be because those with IBS-D or those who report urgency as their most troublesome symptom are more likely to experience fecal incontinence.[20] However, generic health-related quality of life, although reduced in IBS, and to a level comparable with other chronic diseases,[22] was similar across all IBS subtypes and most troublesome symptom reported. The additional finding that IBS subtypes or most troublesome symptom are poor discriminants of the presence or absence of psychological comorbidities, impact of IBS on work and activities of daily living, healthcare usage, and direct healthcare cost of IBS question the ability of differences in gastrointestinal symptoms alone to predict disease impact and burden. This is perhaps not unexpected given that the symptoms of IBS are known to fluctuate over time.

In contrast, we have previously demonstrated that a novel classification system for IBS, derived using latent class analysis, that groups patients according to both gastrointestinal and psychological symptoms,[56,57] can identify those with substantial impairment in ability to work, activities of daily living, generic health-related quality of life, and who are higher utilizers of healthcare. Given the multifaceted symptom profile of people with IBS, the modest efficacy of gut-specific medications,[58,59] the lack of availability of licensed medications for those with IBS-M or IBS-U, and the fact that brain–gut behavioral therapies, such as cognitive behavioral therapy or gut-directed hypnotherapy,[60] assessing patients with IBS using both gastrointestinal and psychological symptoms may allow clinicians and healthcare systems to better stratify individuals in terms of disease impact and burden.

In summary, this study, which enrolled individuals with Rome IV IBS, found few differences in the characteristics of individuals according to IBS subtype or most troublesome symptom. Severity of IBS, levels of anxiety, depression, somatoform symptom-reporting, or gastrointestinal symptom-specific anxiety, and generic health-related quality of life were similar irrespective of IBS subtype or most troublesome symptom reported. Individuals with IBS-D, compared with those with IBS-C or IBS-M, reported greater impairment in their social leisure activities. Participants who reported abdominal pain as their most troublesome symptom had higher levels of presenteeism and reported greater impact of their IBS on their home management, whereas those with diarrhea or urgency reported greater impact on social leisure activities. Clinicians should be sympathetic to the fact that diarrhea, urgency, and abdominal pain are key symptoms that impact on quality of life and social functioning. Although neither IBS subtype nor most troublesome symptom appeared to predict disease impact and burden, these classification systems are still useful for recruiting patients into trials of candidate drugs and to direct therapy in routine practice. Future studies should focus on whether gastrointestinal symptoms alone can predict disease impact and burden in longitudinal studies.

AUTHOR CONTRIBUTIONS

MK, FAS, CEN, CJB, VCG, and ACF conceived and drafted the study. VCG and CEN collected all data. VCG, CJB, and ACF analyzed and interpreted the data. MK and FAS drafted the manuscript. All authors have approved the final draft of the manuscript.

ACKNOWLEDGMENTS

We are grateful to the patients who gave their time freely to answer our questionnaire.

FUNDING INFORMATION

Unrestricted research monies were provided by Tillotts Pharma UK Ltd. The funder had no input into the concept, design, analysis, or reporting of the study.

CONFLICT OF INTEREST STATEMENT

Mais Khasawneh: None. Fahad Ali Shaikh: None. Cho Ee Ng: None. Christopher J. Black: None. Vivek C. Goodoory: None. Alexander C. Ford: None.

DATA AVAILABILITY STATEMENT

Data are available on request from the authors.

GUARANTOR OF THE ARTICLE

VCG is guarantor.

ORCID

Christopher J. Black https://orcid.org/0000-0001-5449-3603

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How to cite this article: Khasawneh M, Shaikh FA, Ng CE, Black CJ, Goodoory VC, Ford AC. Utility of irritable bowel syndrome subtypes and most troublesome symptom in predicting disease impact and burden. *Neurogastroenterology & Motility*. 2024;00:e14756. doi:10.1111/nmo.14756