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Factors associated with lower disease-specific and generic health-related quality of life in Rome IV irritable bowel syndrome

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Summary

Background: Little is known about associations with reduced quality of life in irritable bowel syndrome (IBS) or impact of IBS on quality of life compared with other chronic conditions.

Methods: We collected demographic, gastrointestinal and psychological symptoms, healthcare usage, direct healthcare costs, impact on work and activities of daily living data from 752 individuals with Rome IV-defined IBS. We used the irritable bowel syndrome quality of life (IBS-QOL) and the EQ-5D-5L questionnaires to examine characteristics associated with lower quality of life.

Results: The mean IBS-QOL among all 752 individuals with Rome IV IBS was 48.4 (SD 22.3) and the mean EQ-5D score was 0.570 (SD 0.283), the latter being comparable to people with stroke, leg ulcers or chronic obstructive pulmonary disease. Lower levels of both disease-specific and generic quality of life were associated with severe IBS symptom scores, abnormal anxiety or depression scores, and higher somatoform symptom-reporting and gastrointestinal symptom-specific anxiety scores ($p < 0.001$ for all analyses). Those with lower quality of life had significantly higher healthcare usage and direct healthcare costs and more impairment in work and activities of daily living ($p < 0.01$ for all analyses). Avoidance of alcohol, lower educational level, abnormal anxiety, depression or somatoform symptom-reporting scores, and impairment in social leisure activities, home management or maintaining close relationships were all independently associated with lower quality of life.

Conclusion: IBS has a substantial impact on the quality of life of those affected, and worse than observed in some severe chronic organic conditions.

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1 | INTRODUCTION

Irritable bowel syndrome (IBS) is a chronic gastrointestinal condition, affecting between 5% and 10% of the world's population.[1,2] It is a disorder of gut-brain interaction, characterised by recurrent abdominal pain in association with a change in stool form and/or frequency.[3] Understanding of the underlying pathophysiology is limited and, hence, there is no available biomarker to accurately identify patients with IBS.[4] These constraints mean that researchers tend to resort to a purely phenotypic definition of IBS. In the absence of red flags and with the aid of limited investigations,[5,6] a diagnosis of IBS is reached via symptom-based criteria proposed by the Rome Foundation, with the latest iteration being the Rome IV criteria.[7] Without a treatment target, current management strategies focus on alleviating predominant symptom(s), with modest efficacy rates of therapies in meta-analyses of randomised controlled trials (RCTs).[8–12]

For most individuals, IBS runs a chronic relapsing and remitting course.[13] It does not only cause bothersome gastrointestinal symptoms but also impacts on various aspects of daily life, including psychological health,[14–16] work productivity[17,18] and social functioning.[19,20] There is an increased recognition of the importance of patient-centred outcome data in assessing the impact of chronic conditions, such as IBS, to enable clinicians, healthcare systems, funding bodies and regulatory authorities to best serve all patients. With limited resources, funds are usually first allocated to prevalent, life-limiting and yet treatable conditions, with the least funds available to less prevalent conditions that do not cause significant morbidity and are not curable. IBS does not seem to confer an increased mortality risk[21,22] and is not curable.

However, individuals with IBS report significant morbidity and quality of life may be affected to the same degree as organic gastrointestinal disorders, such as Crohn's disease.[23] Hence, it is important to understand what may influence this and to be able to compare the quality of life of individuals with IBS with other chronic conditions. Contemporaneous estimates are particularly important as definitions of IBS evolve. The Rome IV criteria seem to select a more extreme spectrum of IBS than previous iterations, with more severe symptoms and higher rates of psychological comorbidity.[14]

Multiple studies have examined the quality of life of individuals with IBS.[23–34] However, to the best of our knowledge, only one of these recruited individuals with Rome IV-defined IBS.[34] This study used a generic health-related quality of life questionnaire, the EQ-5D and reported the mean EQ-5D among these individuals. However, the study was relatively small, utilised data from patients taking part in two RCTs, and excluded those with anxiety or depression, which may have affected the results. In addition, it made no comparison with EQ-5D scores in other chronic conditions. Finally, none of the previous studies have examined features associated with lower quality of life among individuals with IBS. We, therefore, assessed both disease-specific and generic health-related quality of life of individuals with Rome IV IBS to identify factors associated with lower quality of life, and compared generic quality of life scores observed in IBS with other chronic conditions.

2 | METHODS

2.1 | Participants and setting

We recruited individuals registered with ContactME-IBS, a national UK registry of people with IBS who are interested in research.[35] We have reported data from this cohort previously.[17,36–38] Briefly, the registry is run by County Durham and Darlington National Health Service (NHS) Foundation Trust and recruits individuals in the UK through advertisements in primary care, hospital clinics, pharmacies or on social media. Individuals enrol by completing a short questionnaire about bowel symptoms and providing contact details. Of the 4280 registrants, 2268 (53%) have seen their primary care physician with IBS, and another 1455 (34%) have seen a gastroenterologist. We contacted all individuals registered with ContactME-IBS, via electronic mailshot, in July 2021. There were no exclusion criteria other than the inability to understand written English. All responses were stored in an online database and non-responders received a reminder email in August 2021. Participants had a chance of winning one of three gift cards (worth £200, £100 or £50) in return for completing the questionnaire. The University of Leeds research ethics committee approved the study 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 (tobacco and alcohol consumption), ethnicity, marital status, educational level and annual income. We defined the presence of IBS using the Rome IV or Rome III questionnaires,[39,40] assigning the presence or absence of Rome IV- or Rome III-defined IBS among all individuals according to the proposed scoring algorithms.[7,41] We categorised Rome IV IBS subtype according to the criteria recommended in the questionnaire, using the proportion of time stools were abnormal according to the Bristol stool form scale. We asked all participants to provide time since their diagnosis of IBS, whether IBS was triggered after an acute enteric infection, and whether they used opiates for any reason, as well as their most troublesome symptom from a list of five possibilities, including abdominal pain, constipation, diarrhoea, bloating or urgency. Finally, we collected data on the presence of co-existing functional dyspepsia according to Rome IV criteria,[42] assigning the presence or absence of epigastric pain syndrome (EPS) or postprandial distress syndrome (PDS).

2.2.2 | 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.[43,44] This consists of 34 items ranked on a 5-point

Likert scale ranging from 0 to 4, with a total possible score of 0–136. Lower scores indicate better quality of life. We transformed scores to a 0 to 100-point scale with zero indicating the worst quality of life and 100 indicating the best quality of life.[43] We also administered the EQ-5D,[45] a generic health-related quality of life questionnaire from EuroQOL, used widely in healthcare. We utilised the EQ-5D-5L instrument,[46] one of the three versions of EQ-5D, consisting of five items capturing different aspects of health, including mobility, self-care, ability to carry out usual activities, pain/discomfort and anxiety/depression. Each item has five levels of responses, giving 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,[47] a mapping function recommended by the National Institute for Health and Care Excellence.[48]

2.2.3 | IBS symptom severity, mood, somatic symptoms and gastrointestinal symptom-specific anxiety

We assessed symptom severity using the IBS severity scoring system (IBS-SSS),[49] which carries a maximum score of 500 points, with <75 points indicating remission, 75–174 points mild, 175–299 points moderate and 300–500 points severe symptoms. We used the hospital anxiety and depression scale (HADS) to collect anxiety and depression data,[50] with a total score ranging from 0 to 21 for either anxiety or depression. We categorised the severity for each into normal (total HADS depression or anxiety score 0–7), borderline normal,[8–10] or abnormal (≥11), as recommended.[50] We collected somatic symptom-reporting data using the patient health questionnaire-12 (PHQ-12),[51] derived from the validated PHQ-15.[52] The total PHQ-12 score ranges from 0 to 24. We categorised severity into high (total PHQ-12 ≥13), medium,[8–12] low,[4–7] or minimal (≤3). Finally, we used the visceral sensitivity index (VSI),[53] 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 cut offs to define low, medium or high levels of gastrointestinal symptom-specific anxiety.

2.2.4 | IBS-related resource use

We collected data on healthcare usage related to a person's IBS over the 12 months prior to recruitment. We asked them to report number of appointments (primary care physicians, gastroenterologists, specialist nurses, dietitians or psychologists), number of investigations (blood or stool tests, endoscopies, radiological investigations or breath tests), number of unplanned emergency department attendances or inpatient admissions (including length of stay in days), and over the counter or prescribed drug usage (in months). We applied costs for primary care physician appointments from Unit Costs of Health and Social Care 2020,[54] and other appointments, investigations, or unplanned inpatient days in secondary care using 2019/20 NHS National Cost Collection Data.[55] We assumed all appointments were follow-up appointments, which cost less than a new patient appointment. We applied the lowest price for a 1-month supply of each drug using the British National Formulary online.[56]

2.2.5 | Impact of IBS on work and activities of daily living

We used the work productivity and activity impairment questionnaire for irritable bowel syndrome (WPAI:IBS),[57] which is validated to assess the level of work productivity loss in employed people with IBS, as well as impairment in activities of daily living. There are four domains: absenteeism (percentage of work hours missed because of IBS); presenteeism (percentage of impairment experienced at work because of IBS); overall work impairment (percentage of work productivity loss); or activity impairment (percentage impairment in activities of daily living). We also used the work and social adjustment scale (WSAS),[58] which has been used to measure impact of IBS on an individual's ability to work, manage at home, engage in social or private leisure activities, or maintain close relationships.[17,59–62] The five domains are scored on a 9-point scale from "not at all" (score 0), through "definitely" (score 4), to "very severely" (score 8). We dichotomised presence (≥1%) or absence (0%) of absenteeism, presenteeism, overall work impairment or activity impairment and presence (score ≥4 ("definitely" impacting)) or absence (score <4) of an impact of IBS on home management activities, social or private leisure activities, or maintaining close relationships.

2.3 | Statistical analysis

We calculated the mean IBS-QOL and EQ-5D scores for individuals with Rome IV IBS, those with Rome III IBS, and all individuals with a self-reported diagnosis of IBS. We compared the mean EQ-5D score in our study with those for other chronic illnesses. For only those with Rome IV IBS, we also dichotomised presence or absence of severe impairment in health-related quality of life, with an IBS-QOL ≤ 50.86 corresponding to a severe score on the functional bowel disorder severity index in the original IBS-QOL validation study.[43] Because there are no validated cut-offs to define low, medium or high generic health-related quality of life according to the EQ-5D, we divided these data into tertiles of equal size. We compared the characteristics of individuals with Rome IV IBS in the lowest EQ-5D tertile with the remaining individuals with Rome IV IBS in our cohort. We compared categorical variables using a χ^2 test and continuous data using an independent samples *t*-test, with statistical significance defined as a $p < 0.01$.

We performed logistic regression, controlling for baseline data to examine factors associated with severe IBS-related quality of life or the lowest EQ-5D tertile, and reported results with odds ratios (ORs) with 95% confidence intervals (CIs). The variance in the data explained by the logistical regression model was assessed using the Nagelkerke R^2 statistic. We performed all analyses using SPSS for Windows (version 27.0 SPSS).

3 | RESULTS

In total, 1278 (29.9%) of 4280 registrants (mean age 47.2 years (range 18–89 years), 1086 (85.0%) female) responded and completed the questionnaire. Mean IBS-QOL and EQ-5D scores in all individuals with self-reported IBS were 55.0 (SD 23.3) and 0.633 (SD 0.269), respectively. In total, 995 individuals met Rome III criteria for IBS (mean age 46.5 years (range 18–85 years), 852 (85.6%) female and 961 (96.6%) White), among whom mean IBS-QOL scores were 52.3 (SD 22.6) and mean EQ-5D scores were 0.615 (SD 0.274). There were 752 (58.8%) individuals meeting Rome IV criteria for IBS (mean age 45.3 years (range 18–81 years), 655 (87.1%) female and 729 (96.9%) White). In total, 136 (18.1%) had IBS with constipation (IBS-C), 306 (40.7%) IBS-D and 301 (40.0%) IBS with mixed bowel habits (IBS-M). The mean IBS-QOL was 48.4 (SD 22.3) and the mean EQ-5D score was 0.570 (SD 0.283). The latter is on a par with people living with a stroke, leg ulcers or chronic obstructive pulmonary disease (Table 1).[63–67] Mean IBS-QOL scores were significantly lower among those with IBS-D (IBS-C 52.3 (SD 19.9), IBS-D 45.4 (SD 23.0), IBS-M 49.4 (SD 22.0), $p = 0.005$) but there was no difference in the mean EQ-5D score according to IBS subtype (IBS-C 0.595 (SD 0.268), IBS-D 0.569 (SD 0.280), IBS-M 0.558 (SD 0.294), $p = 0.45$).

TABLE 1 EQ-5D score among individuals with other chronic conditions compared with those with IBS in the present study[63–67]

Chronic condition	Mean EQ-5D score (SD)
Asthma	0.840 (0.200)
Menopause	0.729 (0.262)
Diabetes mellitus	0.673 (0.283)
Rheumatoid arthritis	0.660 (0.270)
Heart failure	0.640 (0.270)
Low back pain	0.636 (0.266)
Self-reported IBS (from the present study)	0.633 (0.269)
Rome III IBS (from the present study)	0.615 (0.274)
Elderly (age >75)	0.614 (0.299)
Stroke	0.612 (0.318)
Rome IV IBS (from the present study)	0.570 (0.283)
Leg ulcers	0.552 (0.307)
Chronic obstructive pulmonary disease	0.540 (0.309)
Osteoarthritis	0.442 (0.336)

3.1 | Characteristics of individuals with, compared with those without, severely impaired IBS-related quality of life

Individuals with, compared with those without, severely impaired IBS-related quality of life were significantly younger (mean age, 44.0 vs. 46.9 years, $p = 0.006$), less likely to use alcohol (49.0% vs. 69.5%, $p < 0.001$), to have a higher level of education (34.1% vs. 50.9%, $p < 0.001$), or to have an income of £30,000 or more (24.0% vs. 34.6%, $p = 0.002$), and more likely to use opiates for any reason (24.3% vs. 14.2%, $p < 0.001$) (Table 2). There was a higher proportion of individuals with co-existing EPS or PDS ($p < 0.001$ for both) among those with severely impaired IBS-related quality of life. A greater proportion of those with severely impaired IBS-related quality of life had severe IBS symptom scores, abnormal HADS-anxiety scores or HADS-depression scores, higher somatic symptom-reporting scores or higher VSI scores ($p < 0.001$ for trend for all analyses). Proportion of individuals having seen a primary care physician or gastroenterologist in the previous 12 months with IBS symptoms was significantly higher ($p < 0.001$ for both) among those with severely impaired IBS-related quality of life. Mean cost of appointments, investigations, unplanned attendances and total direct healthcare costs were all significantly higher with severely impaired IBS-related quality of life ($p < 0.001$ for all analyses). Finally, a higher proportion of those with severely impaired IBS-related quality of life reported any IBS-related absenteeism, presenteeism or overall work or activity impairment, or reported that IBS affected home management, social or private leisure activities, or close relationships ($p < 0.001$ for all analyses).

Following logistic regression controlling for all other data, only those who reported medium (OR = 10.8; 95% CI 5.41–21.5) or high levels of gastrointestinal symptom-specific anxiety (OR = 44.0; 95% CI 19.0–102.1), those with borderline abnormal HADS-depression scores (OR = 2.65; 95% CI 1.34–5.26), those with impairment in their social leisure activities because of IBS (OR = 3.62; 95% CI 2.01–6.53), and those with impairment in their close relationships because of IBS (OR = 5.67; 95% CI 2.60–12.4) were more likely to report severely impaired IBS-related quality of life. The logistic regression model explained 69.3% of the variance of the data.

3.2 | Overlap between visceral sensitivity index and irritable bowel syndrome quality of life

Because of the highly significant association between gastrointestinal symptom-specific anxiety and severely impaired IBS-related quality of life, we examined the VSI and IBS-QOL questionnaires side-by-side (Table S1). Of the 15 items of the VSI questionnaire, eight assessed almost identical issues to items on the IBS-QOL, and a further six shared similar themes. We, therefore, reran the model excluding the VSI. In this analysis, those with a university or postgraduate level of education (OR = 0.43; 95% CI 0.26–0.70) were less likely to report severely impaired IBS-related quality of life whilst

TABLE 2 Characteristics of individuals with, compared with those without, severely impaired IBS-related quality of life among those with Rome IV IBS

	Severely impaired IBS-related QoL		
	Yes ($n = 408$)	No ($n = 344$)	p value*
Mean age (SD)	44.0 (14.4)	46.9 (15.1)	0.006
Female (%)	364 (89.2)	291 (84.6)	0.06
Smoker (%)	48 (11.8)	34 (9.9)	0.41
Alcohol use (%)	200 (49.0)	239 (69.5)	<0.001
White ethnicity (%)	394 (96.6)	335 (97.4)	0.52
Married (%)	249 (61.0)	238 (69.2)	0.02
University or postgraduate level of education (%)	139 (34.1)	175 (50.9)	<0.001
Annual income of £30,000 or more (%)	87 (24.0)	110 (34.6)	0.002
IBS subtype (%)			
IBS-C	70 (17.3)	66 (19.5)	
IBS-D	180 (44.6)	126 (37.2)	
IBS-M	154 (38.1)	147 (43.4)	0.13
Duration of IBS diagnosis, year(s) (%)			
1	14 (3.4)	11 (3.2)	
2	24 (5.9)	17 (4.9)	
3	31 (7.6)	23 (6.7)	
4	13 (3.2)	20 (5.8)	
5	25 (6.1)	13 (3.8)	
>5	301 (73.8)	260 (75.6)	0.35
IBS after acute enteric infection (%)	52 (12.7)	39 (11.3)	0.56
Opiate use (%)	99 (24.3)	49 (14.2)	<0.001
Most troublesome symptom (%)			
Abdominal pain	85 (20.8)	84 (24.4)	
Constipation	27 (6.6)	26 (7.6)	
Diarrhoea	70 (17.2)	47 (13.7)	
Bloating/distension	108 (26.5)	110 (32.0)	
Urgency	118 (28.9)	77 (22.4)	0.10
Co-existent EPS (%)	162 (39.7)	72 (21.0)	<0.001
Co-existent PDS (%)	235 (57.9)	96 (28.2)	<0.001
IBS-SSS severity (%)			
Mild	20 (4.9)	66 (19.6)	
Moderate	124 (30.4)	176 (52.2)	
Severe	264 (64.7)	95 (28.2)	<0.001
HADS-anxiety categories (%)			
Normal	52 (12.7)	148 (43.0)	
Borderline abnormal	88 (21.6)	86 (25.0)	
Abnormal	268 (65.7)	110 (32.0)	<0.001
HADS-depression categories (%)			
Normal	141 (34.6)	263 (76.5)	
Borderline abnormal	118 (28.9)	47 (13.7)	
Abnormal	149 (36.5)	34 (9.9)	<0.001
PHQ-12 severity (%)			
Low	8 (2.0)	28 (8.1)	
Mild	59 (14.5)	117 (34.0)	
Moderate	175 (42.9)	132 (38.4)	
Severe	166 (40.7)	67 (19.5)	<0.001
VSI scores (%)			
Low	35 (8.6)	212 (61.6)	
Medium	144 (35.3)	103 (29.9)	
High	229 (56.1)	29 (8.4)	<0.001
Seen a primary care physician regarding IBS in the last 12 months (%)	189 (46.3)	105 (30.5)	<0.001
Seen a gastroenterologist regarding IBS in the last 12 months (%)	107 (26.2)	40 (11.6)	<0.001
Number of IBS-related drugs in the last 12 months (%)			
0	40 (9.8)	56 (16.3)	
1	98 (24.0)	91 (26.5)	
2	106 (26.0)	90 (26.2)	
3	72 (17.6)	57 (16.6)	
4	46 (11.3)	30 (8.7)	
≥5	46 (11.3)	20 (5.8)	0.014
Mean direct healthcare costs of IBS (SD)			
Appointments	303.28 (644.32)	131.02 (464.73)	<0.001
Investigations	215.30 (410.07)	89.37 (252.26)	<0.001
IBS-related drugs	81.73 (105.78)	61.82 (82.50)	0.011
Unplanned attendances	150.84 (538.18)	43.76 (253.29)	<0.001
Total direct healthcare costs	751.14 (1201.36)	325.96 (696.11)	<0.001
WPAI:IBS (%)			
Any IBS-related absenteeism	95 (38.3)	38 (17.4)	<0.001
Any IBS-related presenteeism	212 (92.6)	161 (77.8)	<0.001
Any IBS-related overall work impairment	218 (87.9)	164 (74.9)	<0.001
Any IBS-related activity impairment	395 (96.8)	289 (84.0)	<0.001

(Continues)

(Continues)

TABLE 2 (Continued)

	Severely impaired IBS-related QoL		
	Yes ($n = 408$)	No ($n = 344$)	p value*
WSAS (%)			
IBS affected home management	183 (44.9)	37 (10.8)	<0.001
IBS affected social leisure activities	328 (80.4)	95 (27.6)	<0.001
IBS affected private leisure activities	172 (42.2)	35 (10.2)	<0.001
IBS affected close relationships	181 (44.4)	22 (6.4)	<0.001

*p value for independent samples t-test for continuous data and Pearson χ^2 for comparison of categorical data.

those with borderline abnormal (OR = 3.19; 95% CI 1.65–6.17) or abnormal (OR = 4.49; 95% CI 2.46–8.19) HADS-anxiety scores, those with borderline abnormal HADS-depression scores (OR = 2.43; 95% CI 1.37–4.33), those with impairment in their social leisure activities because of IBS (OR = 5.54; 95% CI 3.29–9.35), and those with impairment in their close relationships because of IBS (OR = 4.13; 95% CI 2.14–7.96) were more likely to report severely impaired IBS-related quality of life. The logistic regression model explained 57.5% of the variance of the data.

3.3 | Characteristics of individuals in the lowest, compared with the middle and highest, tertiles of generic health-related quality of life

Those in the lowest EQ-5D tertile were significantly more likely to smoke (17.2% vs 7.8%, $p < 0.001$) or use opiates for any reason (37.2% vs 11.1%, $p < 0.001$) and significantly less likely to use alcohol (38.8% vs 68.1%, $p < 0.001$), to be married (55.6% vs 69.3%, $p < 0.001$), to have a university or postgraduate level of education (29.2% vs 48.0%, $p < 0.001$), or to have an income of £30,000 or more (15.9% vs 35.5%, $p < 0.001$) (Table 3). We observed a significantly higher proportion with co-existing EPS or PDS ($p < 0.001$ for both) among those in the lowest EQ-5D tertile. Again, a significantly greater proportion of those in the lowest EQ-5D tertile had severe IBS symptom scores, abnormal HADS-anxiety or HADS-depression scores, higher somatic symptom-reporting scores or higher VSI scores ($p < 0.001$ for trend for all analyses). A significantly greater proportion of those in the lowest tertile had seen a primary care physician or gastroenterologist in the previous 12 months with IBS symptoms, and the number of drugs used for IBS in the last 12 months was significantly higher ($p < 0.001$ for all). All mean costs for IBS were significantly higher in those in the lowest EQ-5D tertile ($p < 0.01$ for all analyses). Finally, a higher proportion of those in the lowest EQ-5D tertile reported any IBS-related absenteeism, presenteeism, or activity impairment or reported that IBS affected home management, social or private leisure activities, or close relationships ($p < 0.01$ for all analyses).

Following logistic regression controlling for all data, those who used alcohol (OR = 0.52; 95% CI 0.32–0.85) were less likely to be in the lowest EQ-5D tertile whilst those with abnormal HADS-depression scores (OR = 5.27; 95% CI 2.73–10.2), those with moderate (OR = 5.04; 95% 2.24–11.3) or higher levels of somatization (OR = 9.11; 95% CI 3.90–21.3), or those with impairment in home management (OR = 2.89; 95% CI 1.49–5.60) were more likely to report lower EQ-5D scores for quality of life. The logistic regression model explained 59.0% of the variance of the data.

4 | DISCUSSION

We recruited 752 individuals with Rome IV-defined IBS, assessing both disease-specific and generic health-related quality of life, using both the IBS-QOL and the EQ-5D, and comparing scores for the latter with other chronic conditions. We also examined IBS-QOL and EQ-5D scores in all individuals with self-reported IBS and those with Rome III IBS, as well as characteristics associated with poorer quality of life in Rome IV IBS. Disease-specific quality of life was significantly lower among those with Rome IV IBS-D, but there were no significant differences in generic quality of life according to Rome IV IBS subtype. Generic health-related quality of life among those with IBS, irrespective of the definition used, was comparable with chronic conditions like stroke, leg ulcers or chronic obstructive pulmonary disease, although it was lowest in Rome IV IBS. Lower levels of both disease-specific and generic quality of life in Rome IV IBS were associated with severe IBS-SSS scores, abnormal HADS-anxiety or HADS-depression scores, and higher somatization and gastrointestinal symptom-specific anxiety scores. Not surprisingly, those with lower quality of life had significantly higher healthcare usage and direct healthcare costs, as well as significantly more impairment in work and activities of daily living. A highly significant association between gastrointestinal symptom-specific anxiety and severely impaired IBS-related quality of life was demonstrated, which is probably related to the substantial overlap between the individual items the instruments (VSI and IBS-QOL) we used to measure these factors. Finally, our results showed that there were several factors independently associated with lower quality of life. These included avoidance of alcohol, lower educational level, abnormal anxiety, depression and somatization scores, and impairment in social leisure activities, home management or maintaining close relationships.

We recruited over 750 individuals who self-identified as having IBS and met the Rome IV criteria. Those included are likely to be broadly representative of people living with IBS because some had never seen a doctor, some had seen only their primary care physician, and some had seen a gastroenterologist. Moreover, the sample consisted of individuals of different ages, levels of education and income brackets, and is, therefore, likely to include a wide spectrum of individuals in the UK. We used validated questionnaires, and administered the IBS-QOL and the EQ-5D simultaneously to

examine both disease-specific and generic health-related quality of life, respectively.[43,45,46] The IBS-QOL has been used widely in patients with IBS, and the EQ-5D allows comparison of quality of life across different chronic conditions and is often used for health economic evaluation.[48] In addition, the latter has been shown to be a valid and responsive measure of the quality of life in patients with IBS.[24,68] We used an online questionnaire, a validated method to administer both the IBS-QOL and EQ-5D questionnaires,[69] and obtained near-complete data for variables of interest because of the use of mandatory fields.

There are several weaknesses that should be taken into consideration when interpreting the results of this study. To include individuals with IBS who had never seen a doctor for a more generalizable sample, we recruited participants from a national UK registry. This meant that we were unable to check participants' medical records to ensure that IBS mimics were ruled out. Despite this, we believe that our participants had IBS for a number of reasons. Participants applied to join a registry for people with IBS and almost 90% of the members of the ContactME-IBS register have seen either a GP or a gastroenterologist for their IBS. Because UK national guidance recommends ruling out conditions like coeliac disease or inflammatory bowel disease prior to diagnosing IBS,[6,70] and IBS is more prevalent than either of these conditions, we can reasonably assume that our participants had IBS. In addition, almost 60% of the entire sample of individuals surveyed met the Rome IV criteria, which are more stringent than the Rome III criteria in terms of the required frequency of abdominal pain. Finally, nearly 80% of our participants had IBS for ≥5 years, which suggests the diagnosis was stable. However, our results may not be applicable to individuals with IBS elsewhere, as all participants were UK residents and 97% were White. We used the Rome IV criteria to define IBS, which are the current gold standard. These criteria select individuals with more severe gastrointestinal symptoms, higher levels of psychological comorbidities, and a poorer prognosis,[14,71–74] so it is not surprising that quality of life was lowest in these individuals compared with all 1278 participants with a self-reported diagnosis of IBS, or those meeting Rome III criteria for IBS. As this was a cross-sectional survey, with associations examined at one point in time, we cannot determine the direction of the effects we observed. Lastly, we did not ask participants to report other chronic medical conditions, which could have affected the results.

Although previous studies have assessed the quality of life in individuals with IBS,[23–34] we are aware of only one study that has examined this issue in Rome IV IBS.[34] As in our study, the authors used the IBS-QOL and the EQ-5D simultaneously, but the main objective of their study was to develop a mapping algorithm for the EQ-5D-5L to enable the IBS-QOL to be transformed for economic evaluations. Associations with lower quality of life were not examined as only data on IBS subtype, IBS severity, anxiety and depression were collected. Another limitation of this study is that patients were those participating in two RCTs of peppermint oil and hypnotherapy. The authors also excluded those with clinically significant anxiety or depression, which together with the strict inclusion criteria of the RCTs, means the participants are unlikely to be generalizable to the wider population with Rome IV IBS. Perhaps because of the exclusion of those with significant anxiety or depression, both of which were independently associated with lower quality of life in our study, the reported mean IBS-QOL and EQ-5D, 71.1 and 0.73, respectively, were higher than we observed. Other studies using prior iterations of the Rome criteria, or even the Manning criteria, have estimated the mean IBS-QOL to be between 61.4 and 83.6,[24,26,28–30,32] and the mean EQ-5D to be between 0.64 and 0.76.[24,26,29,31] We anticipated that the mean IBS-QOL and EQ-5D scores observed would be lower among those meeting Rome IV criteria in our study compared with that reported in these prior studies because these criteria, as previously discussed, select a more severely affected group of individuals with IBS with a worse prognosis.[14,71–74] The results of our study are also consistent with previous studies demonstrating that individuals with IBS experience substantial reduction in their quality of life that is on a par with, or worse than, those with other chronic conditions.[23,25,27,28] Our findings that more severe IBS or higher levels of psychological comorbidities were significantly associated with lower quality of life are similar to one previous study.[33] To our knowledge, no other studies have examined these issues.

This study has demonstrated that individuals with Rome IV IBS have a reduced quality of life using both disease-specific and generic health-related quality of life questionnaires. Mean IBS-QOL scores were significantly lower among those with IBS-D, but generic quality of life did not seem to differ by subtype. It is, perhaps, not surprising that more severe IBS symptoms, psychological symptoms, increased healthcare costs and higher levels of impairment in work and activities of daily living were associated with lower quality of life. Interestingly, after logistic regression IBS severity was not independently associated with lower quality of life. This suggests it may not be the gastrointestinal symptoms per se driving lower quality of life. Our results demonstrated that the quality of life of those with Rome IV IBS was comparable with, or worse than, many chronic organic conditions, even though IBS is not associated with increased mortality. Possible explanations are the higher levels of coexisting psychological comorbidities associated with IBS,[75,76] and the nature of IBS symptoms, such as the embarrassment of having to use the toilet frequently in public or passing flatus, the unpredictability of symptoms or the stigma associated with a "functional" disorder,[77–80] compared with other chronic conditions.

Although alcohol abstinence was associated with better quality of life in one population-based study,[81] our observation that alcohol abstinence was associated with lower quality of life may be because alcohol exacerbates symptoms of IBS. Binge, but not light or moderate, drinking was associated with the next day's gastrointestinal symptoms of abdominal pain, diarrhoea, nausea and indigestion the next day in one study.[82] Alcohol has been associated with self-reported dyspepsia, but not IBS.[83] However, given the overlap between IBS and functional dyspepsia,[84] this may explain the association we observed, as it is likely that patients who suffer from both these conditions will have greater impairment in their quality of life. The strong correlation between VSI and IBS-QOL was also observed in a recent study recruiting individuals with Rome II or

TABLE 3 Characteristics of individuals with Rome IV IBS in the lowest, compared with the middle and highest, tertiles of generic health-related quality of life

	Lowest tertile for EQ-5D		
	Yes ($n = 250$)	No ($n = 502$)	p value*
Mean age (SD)	43.4 (14.1)	46.3 (15.1)	0.013
Female (%)	214 (85.6)	441 (87.8)	0.39
Smoker (%)	43 (17.2)	39 (7.8)	<0.001
Alcohol use (%)	97 (38.8)	342 (68.1)	<0.001
Married (%)	139 (55.6)	348 (69.3)	<0.001
White ethnicity (%)	239 (95.6)	490 (97.6)	0.13
University or postgraduate level of education (%)	73 (29.2)	241 (48.0)	<0.001
Annual income of £30,000 or more (%)	36 (15.9)	161 (35.5)	<0.001
IBS subtype (%)			
IBS-C	36 (14.6)	100 (20.2)	
IBS-D	107 (43.3)	199 (40.1)	
IBS-M	104 (42.1)	197 (39.7)	0.18
Duration of IBS diagnosis, year(s) (%)			
1	8 (3.2)	17 (3.4)	
2	17 (6.8)	24 (4.8)	
3	15 (6.0)	39 (7.8)	
4	11 (4.4)	22 (4.4)	
5	14 (5.6)	24 (4.8)	
>5	185 (74.0)	376 (74.9)	0.82
IBS after acute enteric infection (%)	29 (11.6)	62 (12.4)	0.77
Opiate use (%)	93 (37.2)	55 (11.0)	<0.001
Most troublesome symptom (%)			
Abdominal pain	64 (25.6)	105 (20.9)	
Constipation	15 (6.0)	38 (7.6)	
Diarrhoea	41 (16.4)	76 (15.1)	
Bloating/distension	65 (26.0)	153 (30.5)	
Urgency	65 (26.0)	130 (25.9)	0.47
Co-existent EPS (%)	124 (49.6)	110 (22.0)	<0.001
Co-existent PDS (%)	154 (62.3)	177 (35.4)	<0.001
IBS-SSS severity (%)			
Mild	12 (4.8)	74 (14.9)	
Moderate	63 (25.2)	237 (47.9)	
Severe	175 (70.0)	184 (37.2)	<0.001
HADS anxiety categories (%)			
Normal	31 (12.4)	169 (33.7)	
Borderline abnormal	33 (13.2)	141 (28.1)	
Abnormal	186 (74.4)	192 (38.2)	<0.001
HADS depression categories (%)			
Normal	56 (22.4)	348 (69.3)	
Borderline abnormal	61 (24.4)	104 (20.7)	
Abnormal	133 (53.2)	50 (10.0)	<0.001
PHQ-12 severity (%)			
Low	0 (0.0)	36 (7.2)	
Mild	16 (6.4)	160 (31.9)	
Moderate	91 (36.4)	216 (43.0)	
Severe	143 (57.2)	90 (17.9)	<0.001
VSI scores (%)			
Low	45 (18.0)	202 (40.2)	
Medium	71 (28.4)	176 (35.1)	
High	134 (53.6)	124 (24.7)	<0.001
Seen a primary care physician regarding IBS in the last 12 months (%)	122 (48.8)	172 (34.3)	<0.001
Seen a gastroenterologist regarding IBS in the last 12 months (%)	78 (31.2)	69 (13.7)	<0.001
Number of IBS drugs in the last 12 months (%)			
0	23 (9.2)	73 (14.5)	
1	53 (21.2)	136 (27.1)	
2	61 (24.4)	135 (26.9)	
3	44 (17.6)	85 (16.9)	
4	30 (12.0)	46 (9.2)	
≥5	39 (15.6)	27 (5.4)	<0.001
Mean direct healthcare costs of IBS (SD)			
Appointments	391.23 (693.37)	141.44 (486.25)	<0.001
Investigations	260.33 (475.19)	106.58 (256.86)	<0.001
IBS-related drugs	86.01 (97.25)	65.95 (95.20)	0.007
Unplanned attendances	208.95 (641.29)	48.52 (265.55)	<0.001
Total direct healthcare costs	946.52 (1393.31)	362.48 (702.21)	<0.001
WPAI:IBS (%)			
Any IBS-related absenteeism	44 (38.3)	89 (25.3)	0.007
Any IBS-related presenteeism	98 (93.3)	275 (83.1)	0.009
Any IBS-related overall work impairment	103 (89.6)	279 (79.3)	0.013
Any IBS-related activity impairment	244 (97.6)	440 (87.6)	<0.001
WSAS (%)			
IBS affected home management	148 (59.2)	72 (14.3)	<0.001

TABLE 3 (Continued)

	Lowest tertile for EQ-5D		
	Yes ($n = 250$)	No ($n = 502$)	p value*
IBS affected social leisure activities	203 (81.2)	220 (43.8)	<0.001
IBS affected private leisure activities	141 (56.4)	66 (13.1)	<0.001
IBS affected close relationships	125 (50.0)	78 (15.5)	<0.001

*p value for independent samples t-test for continuous data and Pearson χ^2 for comparison of categorical data.

III IBS, with the VSI being the most important factor in explaining overall IBS-QOL.[85] Our analysis of these two questionnaires side-by-side demonstrated that the most likely reason is because of overlap between items on the IBS-QOL and the VSI, suggesting other investigators should be vigilant when analysing data from these two questionnaires together.

The results from our study have important implications. The substantial impairment of quality of life seen in Rome IV IBS highlights the impact of a prevalent disorder, still viewed as "functional" by many physicians, on individuals. Our results should encourage those with IBS to feel less ashamed or embarrassed of their illness and reduce the stigma associated with a diagnosis. The latter is especially important, given we have demonstrated that impairment in generic health-related quality of life in IBS is comparable with many chronic organic conditions. Our findings that anxiety, depression and somatic symptom-reporting were independently associated with lower quality of life is further evidence that routine psychological assessment is crucial in those with IBS. Effective multidisciplinary management of IBS should be encouraged to improve patients' quality of life.[86,87] Funding bodies should consider commissioning more research to identify the causes of IBS, as well as effective management strategies for it, more seriously given it is so prevalent and affects the quality of life to a degree similar to other chronic conditions.[88] Finally, clinical trials should consider using the EQ-5D as it allows quality-adjusted life year calculations and cost-effectiveness analyses, both of which are important for making decisions about the ability to access novel treatments.[48]

AUTHOR CONTRIBUTIONS

Vivek Goodoory: Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); resources (equal); software (equal); writing – original draft (equal); writing – review and editing (equal). **Elspeth A Guthrie:** Conceptualization (equal); writing – review and editing (equal). **Cho Ee Ng:** Conceptualization (equal); data curation (equal); project administration (equal); writing – review and editing (equal). **Christopher Black:** Conceptualization (equal); formal analysis (equal); investigation (equal); methodology (equal); resources (equal); supervision (equal); writing – review and editing (equal). **Alexander Ford:** Conceptualization (equal); formal analysis (equal); funding acquisition (equal); investigation (equal); methodology (equal); project administration (equal); resources (equal); software (equal); supervision (equal); validation (equal); writing – original draft (equal); writing – review and editing (equal).

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CONFLICT OF INTEREST

Vivek C. Goodoory: none. Elspeth A. Guthrie: none. Cho Ee Ng: none. Christopher J. Black: none. Alexander C. Ford: none.

AUTHORSHIP

Guarantor of the article: ACF is guarantor.

Author contributions: VCG, EAG, CEN, CJB, and ACF conceived and drafted the study. VCG and CEN collected all data. VCG, CJB, and ACF analysed and interpreted the data. VCG and ACF drafted the manuscript. All authors have approved the final draft of the manuscript.

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REFERENCES

1. Oka P, Parr H, Barberio B, Black CJ, Savarino EV, Ford AC. Global prevalence of irritable bowel syndrome according to Rome III or IV criteria: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol. 2020;5(10):908–17.
2. Sperber AD, Bangdiwala SI, Drossman DA, Ghoshal UC, Simren M, Tack J, et al. Worldwide prevalence and burden of functional gastrointestinal disorders, results of Rome foundation global study. Gastroenterology. 2021;160(1):99–114 e3.
3. Ford AC, Sperber AD, Corsetti M, Camilleri M. Irritable bowel syndrome. Lancet. 2020;396(10263):1675–88.
4. Holtmann GJ, Ford AC, Talley NJ. Pathophysiology of irritable bowel syndrome. Lancet Gastroenterol Hepatol. 2016;1(2):133–46.
5. Lacy BE, Pimentel M, Brenner DM, Chey WD, Keefer LA, Long MD, et al. ACG clinical guideline: management of Irritable Bowel Syndrome. Am J Gastroenterol. 2021;116(1):17–44.
6. Vasant DH, Paine PA, Black CJ, Houghton LA, Everitt HA, Corsetti M, et al. British Society of Gastroenterology guidelines on the management of irritable bowel syndrome. Gut. 2021;70(7):1214–40.
7. Mearin F, Lacy BE, Chang L, Chey WD, Lembo AJ, Simren M, et al. Bowel disorders. Gastroenterology. 2016;150(6):1393–407.
8. Black CJ, Burr NE, Camilleri M, Earnest DL, Quigley EM, Moayyedi P, et al. Efficacy of pharmacological therapies in patients with IBS with diarrhoea or mixed stool pattern: systematic review and network meta-analysis. Gut. 2020;69(1):74–82.

9. Black CJ, Burr NE, Quigley EMM, Moayyedi P, Houghton LA, Ford AC. Efficacy of secretagogues in patients with irritable bowel syndrome with constipation: systematic review and network meta-analysis. Gastroenterology. 2018;155(6):1753–63.
10. Black CJ, Staudacher HM, Ford AC. Efficacy of a low FODMAP diet in irritable bowel syndrome: systematic review and network meta-analysis. Gut. 2022;71:1117–26.
11. Black CJ, Thakur ER, Houghton LA, Quigley EMM, Moayyedi P, Ford AC. Efficacy of psychological therapies for irritable bowel syndrome: systematic review and network meta-analysis. Gut. 2020;69(8):1441–51.
12. Black CJ, Yuan Y, Selinger CP, Camilleri M, Quigley EMM, Moayyedi P, et al. Efficacy of soluble fibre, antispasmodic drugs, and gut-brain neuromodulators in irritable bowel syndrome: a systematic review and network meta-analysis. Lancet Gastroenterol Hepatol. 2020;5(2):117–31.
13. Ford AC, Forman D, Bailey AG, Axon AT, Moayyedi P. Irritable bowel syndrome: a 10-yr natural history of symptoms and factors that influence consultation behavior. Am J Gastroenterol. 2008;103(5):1229–39. quiz 40.
14. Black CJ, Yiannakou Y, Houghton LA, Ford AC. Epidemiological, clinical, and psychological characteristics of individuals with self-reported irritable bowel syndrome based on the Rome IV vs Rome III criteria. Clin Gastroenterol Hepatol. 2020;18(2):392–8 e2.
15. Patel P, Bercik P, Morgan DG, Bolino C, Pintos-Sanchez MI, Moayyedi P, et al. Irritable bowel syndrome is significantly associated with somatisation in 840 patients, which may drive bloating. Aliment Pharmacol Ther. 2015;41(5):449–58.
16. Goodoory VC, Mikocka-Walus A, Yiannakou Y, Houghton LA, Black CJ, Ford AC. Impact of psychological comorbidity on the prognosis of irritable bowel syndrome. Am J Gastroenterol. 2021;116(7):1485–94.
17. Goodoory VC, Ng CE, Black CJ, Ford AC. Impact of Rome IV irritable bowel syndrome on work and activities of daily living. Aliment Pharmacol Ther. 2022;56(5):844–56.
18. Frandemark A, Tornblom H, Jakobsson S, Simren M. Work productivity and activity impairment in irritable bowel syndrome (IBS): a multifaceted problem. Am J Gastroenterol. 2018;113(10):1540–9.
19. Corney RH, Stanton R. Physical symptom severity, psychological and social dysfunction in a series of outpatients with irritable bowel syndrome. J Psychosom Res. 1990;34(5):483–91.
20. Ballou S, McMahon C, Lee HN, Katon J, Shin A, Rangan V, et al. Effects of irritable bowel syndrome on daily activities vary among subtypes based on results from the IBS in America survey. Clin Gastroenterol Hepatol. 2019;17(12):2471–8 e3.
21. Chang JY, Locke GR 3rd, McNally MA, Halder SL, Schleck CD, Zinsmeister AR, et al. Impact of functional gastrointestinal disorders on survival in the community. Am J Gastroenterol. 2010;105(4):822–32.
22. Staller K, Olen O, Soderling J, Roelstraete B, Tornblom H, Khalili H, et al. Mortality risk in irritable bowel syndrome: results from a Nationwide prospective cohort study. Am J Gastroenterol. 2020;115(5):746–55.
23. Pace F, Molteni P, Bollani S, Sarzi-Puttini P, Stockbrugger R, Bianchi Porro G, et al. Inflammatory bowel disease versus irritable bowel syndrome: a hospital-based, case-control study of disease impact on quality of life. Scand J Gastroenterol. 2003;38(10):1031–8.
24. Spiegel B, Harris L, Lucak S, Mayer E, Naliboff B, Bolus R, et al. Developing valid and reliable health utilities in irritable bowel syndrome: results from the IBS PROOF cohort. Am J Gastroenterol. 2009;104(8):1984–91.
25. Gralnek IM, Hays RD, Kilbourne A, Naliboff B, Mayer EA. The impact of irritable bowel syndrome on health-related quality of life. Gastroenterology. 2000;119(3):654–60.
26. Akehurst RL, Brazier JE, Mathers N, O'Keefe C, Kaltenthaler E, Morgan A, et al. Health-related quality of life and cost impact of irritable bowel syndrome in a UK primary care setting. Pharmacoeconomics. 2002;20(7):455–62.
27. Frank L, Kleinman L, Rentz A, Ciesla G, Kim JJ, Zacker C. Health-related quality of life associated with irritable bowel syndrome: comparison with other chronic diseases. Clin Ther. 2002;24(4):675–89. discussion 4, 89; discussion 674.
28. ten Berg MJ, Goettsch WG, van den Boom G, Smout AJ, Herings RM. Quality of life of patients with irritable bowel syndrome is low compared to others with chronic diseases. Eur J Gastroenterol Hepatol. 2006;18(5):475–81.
29. Pare P, Gray J, Lam S, Balshaw R, Khorasheh S, Barbeau M, et al. Health-related quality of life, work productivity, and health care resource utilization of subjects with irritable bowel syndrome: baseline results from LOGIC (longitudinal outcomes study of gastrointestinal symptoms in Canada), a naturalistic study. Clin Ther. 2006;28(10):1726–35. discussion 10-1.
30. Seres G, Kovacs Z, Kovacs A, Kerekgyarto O, Sardi K, Demeter P, et al. Different associations of health related quality of life with pain, psychological distress and coping strategies in patients with irritable bowel syndrome and inflammatory bowel disorder. J Clin Psychol Med Settings. 2008;15(4):287–95.
31. Canavan C, West J, Card T. Change in quality of life for patients with irritable bowel syndrome following referral to a gastroenterologist: a cohort study. PLoS One. 2015;10(10):e0139389.
32. Singh P, Staller K, Barshop K, Dai E, Newman J, Yoon S, et al. Patients with irritable bowel syndrome-diarrhea have lower disease-specific quality of life than irritable bowel syndrome-constipation. World J Gastroenterol. 2015;21(26):8103–9.
33. Ballou S, Keefer L. The impact of irritable bowel syndrome on daily functioning: characterizing and understanding daily consequences of IBS. Neurogastroenterol Motil. 2017;29(4) 1–7.
34. Sturkenboom R, Keszthelyi D, Brandts L, Weerts Z, Snijkers JTW, Masclee AAM, et al. The estimation of a preference-based single index for the IBS-QoL by mapping to the EQ-5D-5L in patients with irritable bowel syndrome. Qual Life Res. 2022;31(4):1209–21.
35. County Durham and Darlington NHS Foundation Trust. ContactME-IBS [Internet]. County Durham and Darlington NHS Foundation Trust; 2021 [cited 2022 May 5]. Available from: https://www.contactme-ibs.co.uk.
36. Goodoory VC, Ng CE, Black CJ, Ford AC. Willingness to accept risk with medication in return for cure of symptoms among patients with Rome IV irritable bowel syndrome. Aliment Pharmacol Ther. 2022;55(10):1311–9.
37. Goodoory VC, Ng CE, Black CJ, Ford AC. Direct healthcare costs of Rome IV or Rome III-defined irritable bowel syndrome in the United Kingdom. Aliment Pharmacol Ther. 2022;56(1):110–20.
38. Goodoory VC, Ng CE, Black CJ, Ford AC. Willingness to pay for medications among patients with Rome IV irritable bowel syndrome. Neurogastroenterol Motil. 2022;e14483. https://doi.org/10.1111/nmo.14483
39. Palsson OS, Whitehead WE, van Tilburg MA, Chang L, Chey W, Crowell MD, et al. Rome IV diagnostic questionnaires and tables for investigators and clinicians. Gastroenterology. 2016;150(6):1481–91.
40. Whitehead WE, the Validation Working Team Committee in association with the Rome Questionnaire C. Development and validation of the Rome III diagnostic questionnaire. In: Drossman DA, editor. Rome III: the functional gastrointestinal disorders. Virginia: Degnon Associates Inc; 2006. p. 835–53.
41. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. Gastroenterology. 2006;130(5):1480–91.

42. Stanghellini V, Chan FK, Hasler WL, Malagelada JR, Suzuki H, Tack J, et al. Gastroduodenal disorders. Gastroenterology. 2016;150(6):1380–92.
43. Patrick DL, Drossman DA, Frederick IO, DiCesare J, Puder KL. Quality of life in persons with irritable bowel syndrome: development and validation of a new measure. Dig Dis Sci. 1998;43(2):400–11.
44. Drossman DA, Patrick DL, Whitehead WE, Toner BB, Diamant NE, Hu Y, et al. Further validation of the IBS-QOL: a disease-specific quality-of-life questionnaire. Am J Gastroenterol. 2000;95(4):999–1007.
45. EuroQol Group. EuroQol--a new facility for the measurement of health-related quality of life. Health Policy. 1990;16(3):199–208.
46. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res. 2011;20(10):1727–36.
47. Hernández Alava M, Pudney S, Wailoo A. Estimating the relationship between EQ-5D-5L and EQ-5D-3L: results from an English population study. Sheffield: Policy Research Unit In Economic Evaluation Of Health And Care Interventions. Universities of Sheffield and York; 2020.
48. National Institute for Health and Care Excellence (NICE). NICE Health Technology Evaluations: The Manual [Internet]. London: NICE; 2022 [cited 2022 August 16]. Available from: https://www.nice.org.uk/process/pmg36/chapter/economic-evaluation#measuring-and-valuing-health-effects-in-cost-utility-analyses
49. Francis CY, Morris J, Whorwell PJ. The irritable bowel severity scoring system: a simple method of monitoring irritable bowel syndrome and its progress. Aliment Pharmacol Ther. 1997;11(2):395–402.
50. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67(6):361–70.
51. Spiller RC, Humes DJ, Campbell E, Hastings M, Neal KR, Dukes GE, et al. The patient health questionnaire 12 somatic symptom scale as a predictor of symptom severity and consulting behaviour in patients with irritable bowel syndrome and symptomatic diverticular disease. Aliment Pharmacol Ther. 2010;32(6):811–20.
52. Kroenke K, Spitzer RL, Williams JB. The PHQ-15: validity of a new measure for evaluating the severity of somatic symptoms. Psychosom Med. 2002;64(2):258–66.
53. Labus JS, Bolus R, Chang L, Wiklund I, Naesdal J, Mayer EA, et al. The visceral sensitivity index: development and validation of a gastrointestinal symptom-specific anxiety scale. Aliment Pharmacol Ther. 2004;20(1):89–97.
54. Curtis L, Burns A. Unit costs of health and social care 2020. Canterbury: Personal Social Services Research Unit (PSSRU), University of Kent; 2020 [updated 2021 January 31] [cited 2021 September 14]. Available from: https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2020/
55. National Health Service (NHS). National cost collection for the NHS [Internet]. England: NHS; 2020 [cited 2021 October 15]. 2020;Available from: https://www.england.nhs.uk/national-cost-collection/#ncc1819
56. National Institue for Health and Care Excellance (NICE). British National Formulary (BNF) [internet]. London: NICE; 2021 [cited 2021 October 15]. 2021;Available from: https://bnf.nice.org.uk
57. Reilly MC, Bracco A, Ricci JF, Santoro J, Stevens T. The validity and accuracy of the work productivity and activity impairment questionnaire--irritable bowel syndrome version (WPAI:IBS). Aliment Pharmacol Ther. 2004;20(4):459–67.
58. Mundt JC, Marks IM, Shear MK, Greist JH. The work and social adjustment scale: a simple measure of impairment in functioning. Br J Psychiatry. 2002;180:461–4.
59. Kennedy TM, Chalder T, McCrone P, Darnley S, Knapp M, Jones RH, et al. Cognitive behavioural therapy in addition to antispasmodic therapy for irritable bowel syndrome in primary care: randomised controlled trial. Health Technol Assess. 2006;10(19): iii-iv, ix-x, 1–67.
60. Moss-Morris R, McAlpine L, Didsbury LP, Spence MJ. A randomized controlled trial of a cognitive behavioural therapy-based self-management intervention for irritable bowel syndrome in primary care. Psychol Med. 2010;40(1):85–94.
61. Everitt HA, Landau S, O'Reilly G, Sibelli A, Hughes S, Windgassen S, et al. Assessing telephone-delivered cognitive-behavioural therapy (CBT) and web-delivered CBT versus treatment as usual in irritable bowel syndrome (ACTIB): a multicentre randomised trial. Gut. 2019;68(9):1613–23.
62. Everitt HA, Landau S, O'Reilly G, Sibelli A, Hughes S, Windgassen S, et al. Cognitive behavioural therapy for irritable bowel syndrome: 24-month follow-up of participants in the ACTIB randomised trial. Lancet Gastroenterol Hepatol. 2019;4(11):863–72.
63. Brazier J, Roberts J, Tsuchiya A, Busschbach J. A comparison of the EQ-5D and SF-6D across seven patient groups. Health Econ. 2004;13(9):873–84.
64. Barton GR, Sach TH, Doherty M, Avery AJ, Jenkinson C, Muir KR. An assessment of the discriminative ability of the EQ-5Dindex, SF-6D, and EQ VAS, using sociodemographic factors and clinical conditions. Eur J Health Econ. 2008;9(3):237–49.
65. Szentes BL, Schultz K, Nowak D, Schuler M, Schwarzkopf L. How does the EQ-5D-5L perform in asthma patients compared with an asthma-specific quality of life questionnaire? BMC Pulm Med. 2020;20(1):168.
66. Gallagher AM, Lucas R, Cowie MR. Assessing health-related quality of life in heart failure patients attending an outpatient clinic: a pragmatic approach. ESC Heart Fail. 2019;6(1):3–9.
67. Hernandez Alava M, Wailoo A, Wolfe F, Michaud K. The relationship between EQ-5D, HAQ and pain in patients with rheumatoid arthritis. Rheumatology (Oxford). 2013;52(5):944–50.
68. Bushnell DM, Martin ML, Ricci JF, Bracco A. Performance of the EQ-5D in patients with irritable bowel syndrome. Value Health. 2006;9(2):90–7.
69. Bushnell DM, Reilly MC, Galani C, Martin ML, Ricci JF, Patrick DL, et al. Validation of electronic data capture of the irritable bowel syndrome--quality of life measure, the work productivity and activity impairment questionnaire for irritable bowel syndrome and the EuroQol. Value Health. 2006;9(2):98–105.
70. Hookway C, Buckner S, Crosland P, Longson D. Irritable bowel syndrome in adults in primary care: summary of updated NICE guidance. BMJ. 2015;350:h701.
71. Goodoory VC, Yiannakou Y, Houghton LA, Black CJ, Ford AC. Natural history and disease impact of Rome IV versus Rome III irritable bowel syndrome: a longitudinal follow-up study. Clin Gastroenterol Hepatol. 2022;20(3):569–77.
72. Aziz I, Tornblom H, Palsson OS, Whitehead WE, Simren M. How the change in IBS criteria from Rome III to Rome IV impacts on clinical characteristics and key pathophysiological factors. Am J Gastroenterol. 2018;113(7):1017–25.
73. Bai T, Xia J, Jiang Y, Cao H, Zhao Y, Zhang L, et al. Comparison of the Rome IV and Rome III criteria for IBS diagnosis: a cross-sectional survey. J Gastroenterol Hepatol. 2017;32(5):1018–25.
74. Vork L, Weerts Z, Mujagic Z, Kruimel JW, Hesselink MAM, Muris JWM, et al. Rome III vs Rome IV criteria for irritable bowel syndrome: a comparison of clinical characteristics in a large cohort study. Neurogastroenterol Motil. 2018;30(2):e13189.
75. Zamani M, Alizadeh-Tabari S, Zamani V. Systematic review with meta-analysis: the prevalence of anxiety and depression in patients with irritable bowel syndrome. Aliment Pharmacol Ther. 2019;50(2):132–43.
76. Whitehead WE, Palsson O, Jones KR. Systematic review of the comorbidity of irritable bowel syndrome with other

disorders: what are the causes and implications? Gastroenterology. 2002;122(4):1140–56.
77. Drossman DA, Chang L, Schneck S, Blackman C, Norton WF, Norton NJ. A focus group assessment of patient perspectives on irritable bowel syndrome and illness severity. Dig Dis Sci. 2009;54(7):1532–41.
78. Farndale R, Roberts L. Long-term impact of irritable bowel syndrome: a qualitative study. Prim Health Care Res Dev. 2011;12(1):52–67.
79. Jakobsson Ung E, Ringstrom G, Sjövall H, Simrén M. How patients with long-term experience of living with irritable bowel syndrome manage illness in daily life: a qualitative study. Eur J Gastroenterol Hepatol. 2013;25(12):1478–83.
80. Frandemark A, Tornblom H, Simren M, Jakobsson S. Maintaining work life under threat of symptoms: a grounded theory study of work life experiences in persons with irritable bowel syndrome. BMC Gastroenterol. 2022;22(1):73.
81. Yao XI, Ni MY, Cheung F, Wu JT, Schooling CM, Leung GM, et al. Change in moderate alcohol consumption and quality of life: evidence from 2 population-based cohorts. CMAJ. 2019;191(27):E753–60.
82. Reding KW, Cain KC, Jarrett ME, Eugenio MD, Heitkemper MM. Relationship between patterns of alcohol consumption and gastrointestinal symptoms among patients with irritable bowel syndrome. Am J Gastroenterol. 2013;108(2):270–6.
83. Halder SL, Locke GR 3rd, Schleck CD, Zinsmeister AR, Talley NJ. Influence of alcohol consumption on IBS and dyspepsia. Neurogastroenterol Motil. 2006;18(11):1001–8.
84. Ford AC, Marwaha A, Lim A, Moayyedi P. Systematic review and meta-analysis of the prevalence of irritable bowel syndrome in individuals with dyspepsia. Clin Gastroenterol Hepatol. 2010;8(5):401–9.
85. Melchior C, Colomier E, Trindade IA, Khadija M, Hreinsson JP, Tornblom H, et al. Irritable bowel syndrome: factors of importance for disease-specific quality of life. United European Gastroenterol J. 2022;10(7):754–64.
86. Basnayake C, Kamm MA, Stanley A, Wilson-O'Brien A, Burrell K, Lees-Trinca I, et al. Long-term outcome of multidisciplinary versus standard gastroenterologist care for functional gastrointestinal disorders: a randomized trial. Clin Gastroenterol Hepatol. 2022;20(9):2102–2111.e9.
87. Basnayake C, Kamm MA, Stanley A, Wilson-O'Brien A, Burrell K, Lees-Trinca I, et al. Standard gastroenterologist versus multidisciplinary treatment for functional gastrointestinal disorders (MANTRA): an open-label, single-centre, randomised controlled trial. Lancet Gastroenterol Hepatol. 2020;5(10):890–9.
88. The Lancet Gastroenterology Hepatology. Unmet needs of patients with irritable bowel syndrome. Lancet Gastroenterol Hepatol. 2018;3(9):587.

SUPPORTING INFORMATION

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

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