



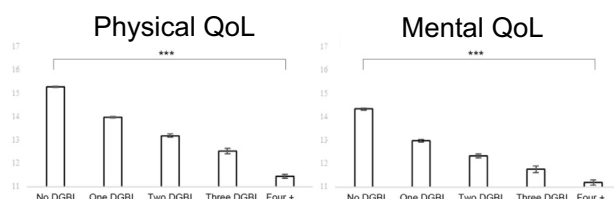
Negative Impact of Disorders of Gut-Brain Interaction on Health-Related Quality of Life: Results From the Rome Foundation Global Epidemiology Survey

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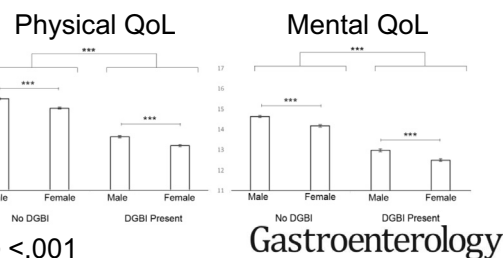
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The Negative Impact of Disorders of Gut-Brain Interaction (DGBI) on Health-related Quality of Life (QoL): Results from the Rome Foundation Global Epidemiology

Individuals with two or more DGBI have significantly poorer QoL than those with only one DGBI or those without any DGBI



Females with DGBI reported poorer QoL than males



*** $p < .001$

Gastroenterology

BACKGROUND & AIMS: This study used the database from the Rome Foundation Global Epidemiology Survey to assess the differences in quality of life overall, and by age and sex, across individual disorders of gut-brain interaction (DGBI), gastrointestinal anatomical region(s), and number of overlapping DGBI. **METHODS:** Data were collected via the Internet in 26 countries, using the Rome IV diagnostic questionnaire and a supplemental questionnaire including the Patient-Reported Outcomes Measurement Information Systems Global-10 quality of life measure. Factorial analyses of variance were used to explore physical and mental quality of life, adjusting for multiple comparisons. **RESULTS:** Among the 54,127 respondents, quality of life deteriorated significantly with increasing number of overlapping DGBI, with respondents reporting ≥ 2 DGBI having significantly poorer quality of life than those with only 1 DGBI or those without any DGBI. Men with DGBI reported better quality of life than women, and those aged ≥ 65 years reported better quality of life than those < 65 years. Age, sex, number of overlapping DGBI, somatization, anxiety, depression, and functional experiences (concern, embarrassment, or stress associated with bowel functioning) relating to DGBI, were

significant predictors of poorer physical and mental quality of life. **CONCLUSIONS:** This study is the most comprehensive assessment of quality of life to date in adults living with a DGBI. It provides a representative picture of DGBI impact on adults in the global adult population and highlights the significant detrimental impact of living with a DGBI on quality of life.

Keywords: Disorders of Gut-Brain Interaction; Sex; Age; Mental Health; Quality of Life.

Abbreviations used in this paper: DGBI, disorders of gut-brain interaction; IBS, Irritable bowel syndrome; PHQ, Patient Health Questionnaire-4; PROMIS, Patient-Reported Outcomes Measurement Information Systems; QoL, quality of life; RFGES, Rome Foundation Global Epidemiology Survey; SMD, standardized mean difference.

Most current article

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Disorders of gut-brain interaction (DGBI), formerly known as functional gastrointestinal disorders, are highly prevalent, affecting >40% of individuals globally.¹ DGBI are associated with substantial health care costs and have an adverse impact on both social and work functioning.²⁻⁶ An important, and frequently assessed, patient-reported outcome related to social and work functioning in DGBI is quality of life (QoL).^{2,7} QoL or its health-specific form, health-related QoL, can be defined generally as well-being and functioning across physical, mental, and social life domains.⁸ Individuals with DGBI have been shown to have poorer QoL compared with other chronic illnesses, including asthma, diabetes mellitus, and end-stage kidney disease.^{2,9-11} Irritable bowel syndrome (IBS) has been the most extensively researched³ in this regard, but other DGBI, including functional dyspepsia,¹²⁻¹⁴ functional constipation,^{15,16} and cyclic vomiting syndrome,¹⁷ are also associated with poor QoL.

QoL has been found consistently to be poorer in individuals with DGBI vs those without DGBI or compared with individuals in the general population.^{9,10,14,18-26} Based on a large random sample of Australian adults, Koloski et al¹⁸ demonstrated that individuals meeting criteria for at least 1 DGBI reported poorer mental and physical QoL compared with those without a DGBI. In another large study, mental and physical QoL was lower in those with a DGBI compared with those without and compared with a normative reference group.²⁴ Further, most individuals with a DGBI had at least 1 significantly poorer mental or physical QoL domain compared with those without.²⁴ However, despite the wealth of previous research exploring QoL in people with DGBI and its use as an outcome measure in clinical trials,^{2,7} only a small number of studies have examined QoL in multiple DGBIs,^{20,21,24,26} with only 1 study having explored potential differences.²⁶

Although numerous studies have reported an adverse impact of DGBI on QoL, these have generally had small sample sizes or been limited to only 1 DGBI. The present study used the database of the Rome Foundation Global Epidemiology Survey (RFGES).¹ In a recent article based on this global study, Sperber et al¹ reported that participants with a greater number of overlapping DGBIs, in different anatomical regions, had poorer QoL life.²⁷ The current study seeks to extend this work and provide a comprehensive assessment of the impact of DGBI on QoL in adults in a large representative sample. Specifically, the study compared perceived mental and physical QoL across different DGBIs, and between those with and without a DGBI, and explored associations between mental and physical QoL and individual characteristics among people with a DGBI. A secondary aim was to explore the influence of demographics (ie, age, sex), number of overlapping DGBIs (0, 1, 2, 3, or 4), mental health (anxiety, depression, and somatization status), and negative functional experiences (concern, embarrassment, or stress associated with bowel functioning) relating to DGBI on mental and physical QoL.

WHAT YOU NEED TO KNOW

BACKGROUND AND CONTEXT

Disorders of gut-brain interaction are highly prevalent and place a significant burden on individuals and health care systems worldwide. Despite their known impact, little is known about their impact on quality of life.

NEW FINDINGS

Results from the largest multinational disorders of gut-brain interaction study to date show that compared with individuals without disorders of gut-brain interaction, quality of life is significantly poorer when individuals with disorders of gut-brain interaction are women, aged older than 65 years, have overlapping disorders of gut-brain interaction, experience mental health symptoms, and report greater negative functional experiences (concern, embarrassment, or stress associated with bowel functioning) relating to disorders of gut-brain interaction.

LIMITATIONS

This was a cross-sectional Internet survey, with self-reported disorders of gut-brain interaction diagnoses based on responses to a validated questionnaire.

CLINICAL RESEARCH RELEVANCE

This is the most comprehensive study of disorders of gut-brain interaction comparing quality of life among individuals with and without a disorders of gut-brain interaction diagnosis, and across different disorders of gut-brain interaction in a large representative sample of adults.

Methods

The methodology of the RFGES has been reported elsewhere.¹ Briefly, the study recruited a minimum of 2000 participants from each of 33 countries (N = 73,076) based on predefined demographics to ensure appropriate representation (ie, 50% women), and all aged >18 years, with 40% aged 18 to 39 years, 40% aged 40 to 64 years, and 20% aged ≥65 years. Data collection was conducted over a period of 1 year in 2017 by Internet survey in 26 countries or by personal household interview in 7 countries where Internet surveys were not feasible. In 2 countries, China and Turkey, both methods were used for comparison purposes. In the current study, the 54,127 participants from the 26 countries who took part in the Internet survey were included, because the data collection method was more uniform among the countries with this method.

Some of the data in this study have already been reported in previous RFGES publications (eg, Sperber et al¹ and Sperber et al²⁸). This is inevitable because the original study included a broad range of descriptive statistics for all countries (33) and all disorders (22).¹ Other studies, including the present one, which use the same database, are reporting in-depth analyses for countries, disorders, and methods, and these include a brief overview of some specific data previously reported.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the

institutional or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Ethical review was completed for all countries. The Internet survey study was exempted from ethics board oversight because the participants were anonymous to the investigators. All survey participants completed an electronic written consent form.

Measures

QoL was assessed using the Patient-Reported Outcomes Measurement Information Systems (PROMIS) Global-10 questionnaire,⁸ with physical and mental QoL subscales (scored 4–20) (see the [Supplementary Table 1](#) for T scores), with higher scores indicating higher perceived QoL. Anxiety and depression were assessed using the Patient Health Questionnaire-4 (PHQ-4),²⁷ whereas somatic symptom severity was assessed using 11 items (scored 0–22) after questions relating to menstruation and 3 gastrointestinal-specific symptoms were omitted from the scoring of the Patient Health Questionnaire (PHQ-15).²⁹ Three questions on the impact of DGBI on respondents, using a 3-point response format (eg, 1 = not at all, 2 = somewhat, 3 = very much), quantified concern, embarrassment, and stress associated with bowel functioning.

DGBI cases were identified using the validated 86-item Adult Rome IV Diagnostic Questionnaire.³⁰ It is reasonable to assume that some individuals would meet the diagnostic criteria for DGBI in this survey even though they had an organic gastrointestinal disease, such as Crohn's disease, leading to a potential overestimation of the prevalence of DGBI. To avoid this, we included questions about whether the participant had ever been diagnosed by a doctor with any of a list of organic gastrointestinal diseases or gastrointestinal operations. Those responding in the affirmative were excluded from the DGBI group but were included in the non-DGBI group. These exclusions included celiac disease, gastrointestinal cancer, or inflammatory bowel disease for any DGBI diagnosis, as well as intestinal resection or diverticulitis for lower gastrointestinal DGBI and peptic ulcer for upper gastrointestinal DGBI.

Statistical Considerations

The primary outcome was QoL and psychological well-being across categories. To evaluate the first study aim, factorial analyses of variance were used to assess group differences in continuous outcomes (ie, physical and mental QoL) across DGBI, sex, and age-groups. Post hoc comparisons were undertaken for interanatomical regional analysis, condition analysis, and IBS and functional dyspepsia subtype, and adjusted for multiple comparisons by setting the α level to .001. Comparisons between DGBI in different gastrointestinal anatomical regions were limited to participants with only 1 DGBI to maintain independence of groups.

Given the large sample size, parametric assumptions were assessed by comparison of the sample means and medians and the ratio of standard errors between sample means. The analysis of variance approach retains robustness even with non-normal distributions in large samples where the ratio of the standard errors approaches 1 and homogeneity of error variances is observed.³¹ Between-group effect sizes were calculated as standardized mean differences (SMDs), where ± 0.41 represents the recommended minimum practical effect size, 1.15

represents a moderate effect, and 2.7 represents a large effect.³² Finally, specific DGBI with <20 diagnosed cases (eg, central nervous system disorders of gastrointestinal pain and functional biliary pain) were excluded from the comparative analyses. Sequential multiple regressions were used to test the second study aim.

Results

Of the 54,127 participants, 50.9% were men, 50.1% were married, and the mean age was 44.3 years ([Table 1](#); see [Supplementary Table 2](#) for frequencies [%] of DGBI by sex and age category). Overall, 59.8% ($n = 32,386$) did not meet diagnostic criteria for any DGBI, and 40.2% reported symptoms compatible with at least 1 DGBI. By excluding participants who reported a doctor's diagnosis of an organic gastrointestinal disease or who had some types of gastrointestinal operation, 7.6% of the participants were disqualified from a DGBI diagnosis.

Quality of Life Differences Across Disorders of Gut-Brain Interaction, Between Those With and Without Disorders of Gut-Brain Interaction, and Between People With Different Numbers of Disorders of Gut-Brain Interactions

Comparisons across only those with one DGBI indicated that excessive belching and mixed IBS had the highest and lowest perceived physical and mental QoL, respectively ([Figure 1](#)). A detailed breakdown of comparisons across the DGBI is provided in the [Supplementary Tables 3 and 4](#). Participants with any DGBI reported significantly worse physical and mental QoL compared with those without DGBI. This was observed across all DGBIs, except for biliary pain and cannabinoid hyperemesis syndrome, where comparison was not undertaken due to low case numbers ($n < 12$) ([Table 2](#) and [Figure 2A and B](#)). In relation to the number of overlapping DGBI, participants reported poorer mental and physical QoL as the number of DGBI increased (physical: $F_{4,54035} = 2591.4$, $P < .001$, $\eta^2 = .16$; mental: $F_{4,54122} = 1292.3$, $P < .001$, $\eta^2 = .08$).

Quality of Life Differences Across Disorders of Gut-Brain Interaction Region, Functional Dyspepsia, and Inflammatory Bowel Syndrome Subtypes

Participants without a DGBI reported significantly better physical and mental QoL compared with individuals with any DGBI, but no interanatomical gastrointestinal region differences were observed after adjustment for multiple comparisons ([Table 3](#) and [Figure 2C and D](#)). In relation to differences across IBS subtypes, only IBS mixed type had significantly lower physical QoL compared with IBS unsubtyped, with all other differences nonsignificant after adjustment for multiple comparisons. Differences for functional dyspepsia subtypes were also nonsignificant after adjustment for multiple comparisons. For summary results relating to QoL and IBS and functional dyspepsia subtypes, see [Supplementary Tables 5 and 6](#).

Table 1. Demographic Characteristics of Involved Individuals, and Disorders of Gut-Brain Interaction Status

Variable	Combined		No DGBI			DGBI			Physical QoL		Mental QoL	
	No.	Column, %	No.	Row, %	Column, %	No.	Row, %	Column, %	Mean	SD	Mean	SD
Total sample	54,127		30,834	56.9		23,293	46.1		14.5	2.7	13.5	3.3
Sex												
Male	27,549	50.9	17,408	63.2	56.5	10,141	36.8	43.5	14.8	2.6	13.9	3.3
Female	26,578	49.1	13,426	50.5	43.5	13,152	49.5	56.5	14.1	2.7	13.2	3.3
Age-groups												
18-39 years	23,003	42.5	12,347	53.7	40.0	10,656	46.3	45.7	14.6	2.6	13.4	3.4
40-64 years	22,281	41.2	12,845	57.7	41.7	9436	42.3	40.5	14.3	2.8	13.4	3.3
≥65 years	8843	16.3	5642	63.8	18.3	3201	36.2	13.7	14.6	2.7	14.3	3.0
Marital status												
Single	15,493	28.6	8832	57.0	28.6	6661	43.0	28.6	14.5	2.7	13.1	3.5
Married/cohabiting	33,398	61.7	19,027	56.9	61.7	14,371	43.1	61.7	14.5	2.7	13.8	3.2
Divorced	3759	6.9	2063	54.9	6.7	1696	45.1	7.3	14.1	2.9	13.2	3.4
Widow/widower	1477	2.7	912	61.7	3.0	565	38.3	2.4	14.2	3.0	13.9	3.2
Anatomical region												
Esophageal	3227	6.0							12.4	2.6	11.8	3.3
Gastroduodenal	5751	10.6							12.6	2.7	12.0	3.5
Bowel	20,065	37.1							13.4	2.6	12.5	3.3
Anorectal	4183	7.7							12.7	2.7	12.0	3.3
Age, mean (SD), y	44.3 (16.2)		44.7 (16.3)			42.5 (15.4)						
Education, mean (SD), y	14.9 (7.1)		14.9 (7.1)			14.9 (7.1)						

No., number; SD, standard deviation.

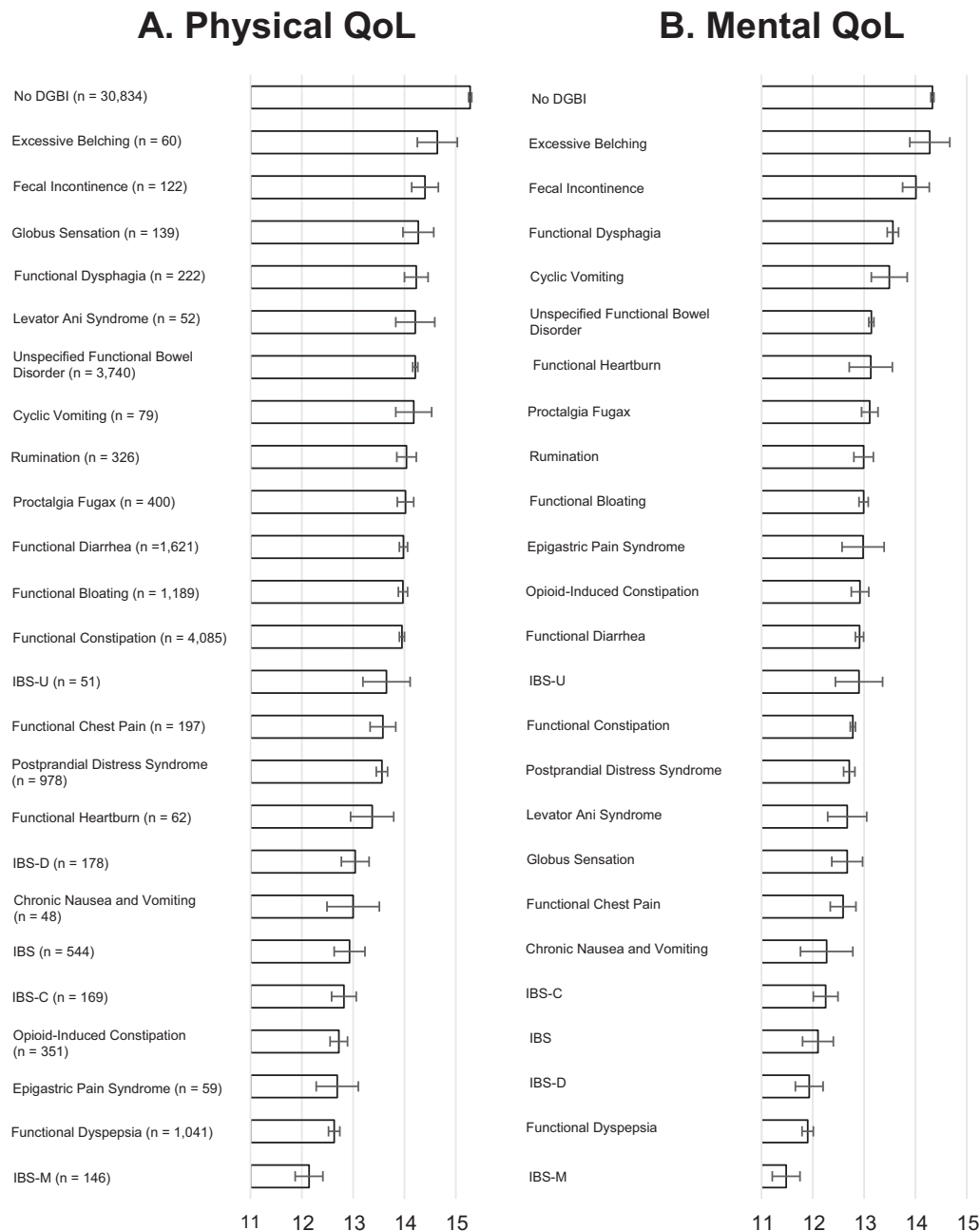


Figure 1. (A) Physical and (B) mental QoL differences across DGBI. Reflux hypersensitivity, biliary pain, and cannabinoid hyperemesis syndrome were excluded due to low case numbers ($n = <12$). IBS-C, irritable bowel syndrome–constipation; IBS-D, irritable bowel syndrome–diarrhea; IBS-M, irritable bowel syndrome–mixed type; IBS-U, irritable bowel syndrome–unsubtyped.

Quality of Life Differences Between Individuals With a Disorders of Gut-Brain Interaction According to Sex

Men reported better physical QoL compared with women across most individual DGBI and gastrointestinal anatomical regions (Table 4 and Figure 2E and F). Sex differences for physical QoL were nonsignificant for participants with globus, IBS-constipation, IBS-diarrhea, functional abdominal bloating or distension, and levator ani syndrome. Men also reported better mental QoL compared with women across

most individual DGBI and anatomical regions, except for functional heartburn, chronic nausea and vomiting, IBS-diarrhea, and levator ani syndrome. On average, men reported significantly better QoL compared with women for all DGBI, although the absolute differences were small (physical: SMD, 0.1661 [95% confidence interval, 0.14–0.18], $P < .001$; mental: SMD, 0.141 [95% confidence interval, 0.12–0.16], $P < .001$). No significant interactions for physical and mental QoL for number of overlapping DGBI and sex were found ($F_{2,54034} = 0.927$, $P = .39$; $F_{2,54121} = 0.585$, $P = .57$).

Table 2. Physical and Mental Quality of Life in Individuals According to Individual Disorders of Gut-Brain Interaction, Anatomical Region of Disorders of Gut-Brain Interaction, and Number of Overlapping Disorders of Gut-Brain Interaction Status

DGBI	Respondents	Physical QoL			Mental QoL		
	(n)	Mean	SD	SMD (95% CI)	Mean	SD	SMD (95% CI)
Esophageal disorders	3227	12.45	2.78	1.06 (1.03–1.08)	11.81	3.53	0.75 (0.71–0.78)
Functional heartburn	614	11.92	2.71	1.27 (1.25–1.3)	11.78	3.49	0.76 (0.73–0.8)
Functional chest pain	741	12.54	2.68	1.03 (1–1.06)	11.38	3.58	0.89 (0.85–0.92)
Reflux hypersensitivity	456	11.23	2.68	1.55 (1.52–1.58)	11.05	3.69	0.99 (0.95–1.02)
Globus sensation	409	13.26	2.69	0.75 (0.72–0.77)	11.93	3.49	0.71 (0.68–0.75)
Functional dysphagia	1714	12.26	2.78	1.14 (1.11–1.16)	11.94	3.49	0.71 (0.67–0.74)
Gastroduodenal disorders	5751	12.65	2.73	0.97 (0.95–1)	12.01	3.46	0.68 (0.65–0.72)
Functional dyspepsia	3914	12.38	2.77	1.08 (1.06–1.11)	11.84	3.48	0.74 (0.7–0.77)
Postprandial distress syndrome	3317	12.44	2.79	1.06 (1.03–1.08)	11.87	3.51	0.73 (0.69–0.76)
Epigastric pain syndrome	1307	11.55	2.62	1.42 (1.39–1.45)	11.44	3.38	0.86 (0.83–0.9)
Excessive belching	527	12.25	2.79	1.14 (1.12–1.17)	12.05	3.51	0.68 (0.64–0.71)
Rumination	1509	12.97	2.61	0.86 (0.83–0.89)	12.09	3.39	0.66 (0.63–0.7)
Chronic nausea and vomiting	503	11.88	2.82	1.29 (1.26–1.32)	11.42	3.65	0.87 (0.84–0.91)
Cyclic vomiting syndrome	625	12.30	2.65	1.13 (1.1–1.15)	11.99	3.28	0.7 (0.66–0.73)
Cannabinoid hyperemesis syndrome	28	13.00	2.02	0.85 (0.82–0.88)	13.64	3.30	0.18 (0.15–0.22)
Bowel disorders	18,004	13.45	2.63	0.66 (0.64–0.69)	12.50	3.30	0.53 (0.51–0.56)
IBS	2195	11.83	2.68	1.31 (1.28–1.33)	11.22	3.38	0.93 (0.9–0.97)
IBS-constipation	712	11.82	2.65	1.31 (1.29–1.34)	11.46	3.32	0.86 (0.83–0.9)
IBS-diarrhea	629	12.00	2.67	1.24 (1.22–1.27)	11.21	3.45	0.94 (0.9–0.97)
IBS-mixed type	712	11.56	2.73	1.42 (1.39–1.44)	10.89	3.35	1.04 (1–1.07)
IBS-unsubtyped	142	12.54	2.47	1.03 (1–1.06)	11.68	3.39	0.79 (0.76–0.83)
Functional constipation	6333	13.62	2.52	0.6 (0.58–0.63)	12.52	3.24	0.53 (0.5–0.56)
Opioid-induced constipation	846	12.11	2.80	1.2 (1.17–1.22)	12.40	3.33	0.57 (0.53–0.6)
Functional diarrhea	2547	13.50	2.68	0.65 (0.62–0.67)	12.55	3.34	0.52 (0.49–0.55)
Functional abdominal bloating or distention	1785	13.69	2.44	0.58 (0.55–0.61)	12.71	3.10	0.48 (0.44–0.51)
Unspecified functional bowel disorder	4762	13.99	2.45	0.46 (0.44–0.49)	12.93	3.26	0.41 (0.37–0.44)
Central nervous system disorders of gastrointestinal pain	44	11.66	2.74	1.38 (1.35–1.41)	11.34	3.44	0.9 (0.86–0.93)
Biliary disorders, functional biliary pain ^a	11	11.27	2.61	...	10.09	2.07	...
Anorectal disorders	4183	12.74	2.75	0.94 (0.92–0.97)	11.97	3.32	0.7 (0.67–0.74)
Fecal incontinence	851	12.39	2.97	1.08 (1.06–1.11)	12.01	3.42	0.69 (0.65–0.72)
Levator ani syndrome	622	11.88	2.94	1.29 (1.26–1.32)	10.99	3.33	1.01 (0.97–1.04)
Proctalgia fugax	3013	12.90	2.63	0.89 (0.86–0.91)	12.08	3.25	0.67 (0.63–0.7)
DGBI frequency							
0	32,386	15.15	2.53	...	14.24	3.13	...
1	13,261	13.96	2.49	0.47 (0.45–0.5)	12.93	3.22	0.4 (0.37–0.43)
2	4590	13.16	2.64	0.78 (0.76–0.81)	12.26	3.36	0.61 (0.58–0.64)
3	1822	12.56	2.61	1.02 (0.99–1.05)	11.74	3.34	0.77 (0.74–0.81)
≥4	2068	11.62	2.61	1.39 (1.37–1.42)	11.28	3.42	0.91 (0.88–0.95)

NOTE. SMD effect sizes are differences between no DGBI and each comparator.
SD, standard deviation.

^aNo comparisons were performed due to low case numbers (n = <20).

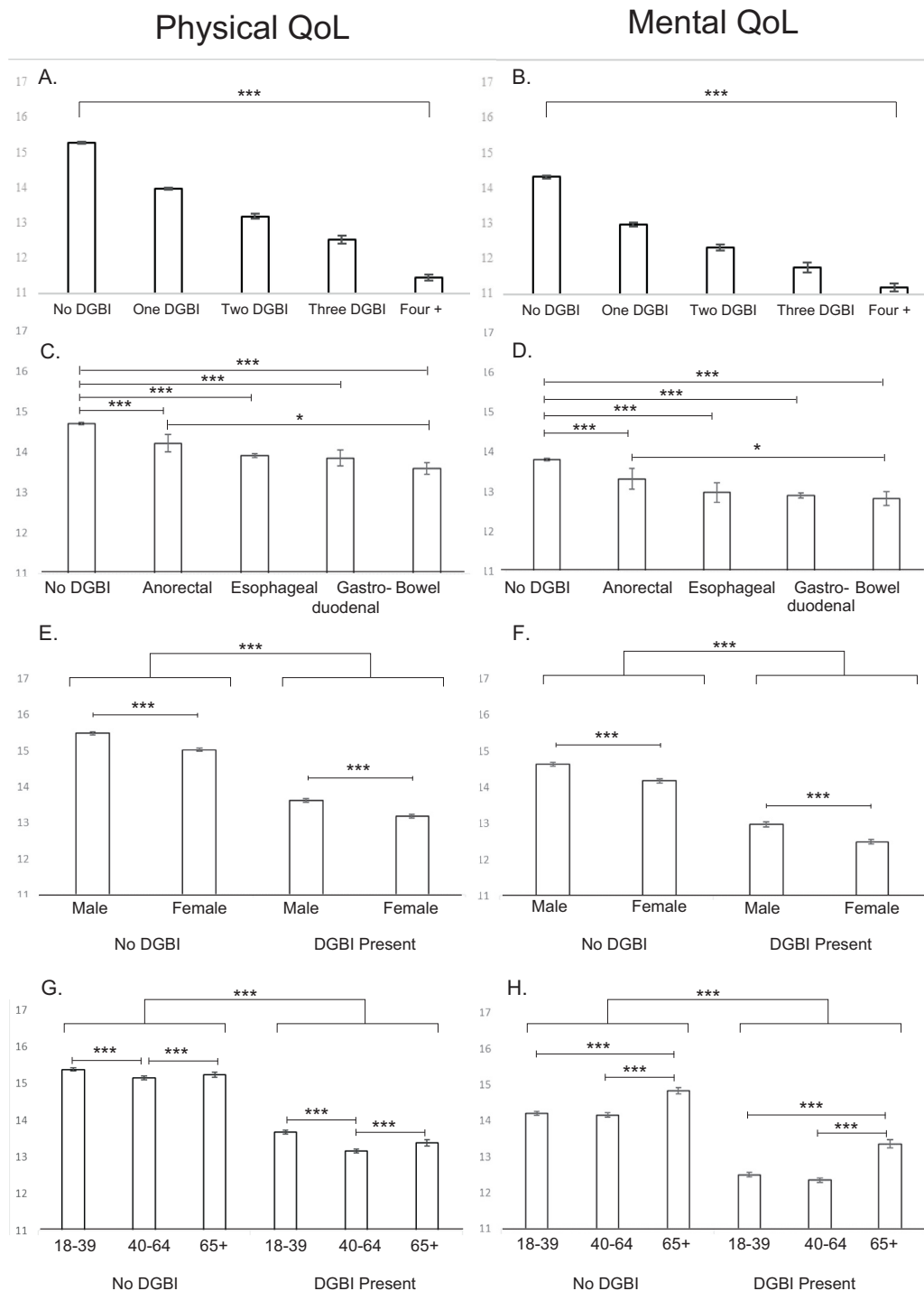


Figure 2. (A) Physical and (B) mental QoL by degree of DGBI overlap. (C) Physical and (D) mental QoL by anatomical region. (E) Physical and (F) mental QoL by sex. (G) Physical and mental (H) QoL by age-group. The horizontal bars represent significant between-groups differences, and the brackets represent all groups that are significantly different from all groups in the adjacent bracket. * $P < .05$; *** $P < .001$.

Quality of Life Differences Between Individuals With a Disorders of Gut-Brain Interaction According to Age-Group

Compared with individuals in the same age-group without DGBI, physical and mental QoL were lower in those with a DGBI (Table 5 and Figure 2G and H). The

difference was significant for those aged 40 to 64 years compared with those <40 years and those ≥ 65 years for physical QoL. However, all participants between 18 and 64 years reported worse mental QoL compared with ≥ 65 years, regardless of DGBI status. For gastroduodenal and bowel DGBI, physical QoL decreased with greater age.

Table 3. Physical and Mental Quality of Life in Individuals According To Anatomical Region of Disorders of Gut-Brain Interaction

Variable		No DGBI	Esophageal	Gastrointestinal	Bowel	Anorectal
No DGBI	Mean difference		−1.25	−1.16	−1.20	−0.94
	<i>t</i> value		−12.43	−10.41	−44.03	−8.75
	<i>P</i> value		<.001	<.001	<.001	<.001
Esophageal	Mean difference	1.26		−0.09	−0.05	−0.31
	<i>t</i> value	9.96		−0.61	−0.47	−2.13
	<i>P</i> value	<.001		.54	.64	.03
Gastrointestinal	Mean difference	1.13	0.13		0.04	−0.22
	<i>t</i> value	8.07	0.71		0.38	−1.43
	<i>P</i> value	<.001	.48		.70	.15
Bowel	Mean difference	1.33	0.08	0.21		−0.26
	<i>t</i> value	38.88	0.59	1.47		−2.41
	<i>P</i> value	<.001	.55	.14		.02
Anorectal	Mean difference	0.91	−0.34	−0.21	0.26	
	<i>t</i> value	6.77	−1.88	−1.11	2.41	
	<i>P</i> value	<.001	.06	.27	.02	

NOTE. Comparisons are made as column minus row; positive mean differences indicate greater QoL in column condition. Physical QoL above diagonal, mental QoL below. Biliary and central nervous system disorders of gastrointestinal pain were excluded due to low case numbers ($n < 20$). Shaded areas represent nonsignificant results.

Participants aged ≥ 65 years reported the highest mental QoL for those who had a DGBI. The impact of having ≥ 2 DGBI on physical and mental QoL was greatest for participants aged 40 to 64 compared with the other age-groups ($F_{4,54031} = 18.82$, $P < .001$; $F_{4,54118} = 6.64$, $P < .001$).

Predictors of Quality of Life

To perform the second study aim of exploring predictors of physical and mental QoL, a series of sequential regression models were tested, including age and sex (model 1), number of overlapping DGBI (model 2), anxiety, depression, and somatic symptom severity (model 3), and concerns, embarrassment, and stress relating to bowel function (model 4). The regressions identified that all 4 models were significant predictors of physical and mental QoL, with each of the individual predictors being statistically significant (see [Supplementary Table 7](#) for regression output). Somatic symptom severity scores were the strongest predictor of decreased physical QoL, followed by anxiety. Depression was the strongest predictor of decreased mental QoL, followed by anxiety. The addition of the number of overlapping DGBI significantly improved both physical and mental QoL models above age and sex alone ($\Delta R^2 = 0.15$ and $\Delta R^2 = 0.07$, respectively). The further addition of depression, anxiety, and somatic symptom severity scores also substantially improved the models ($\Delta R^2 = 0.23$ and $\Delta R^2 = 0.32$, respectively). In total, 41.2% and 42.5% of the physical and mental QoL variance, respectively, were accounted for in the final models.

Discussion

To our knowledge, this study provides the first comprehensive assessment of the impact of DGBI on QoL in a large multinational representative sample. The analysis, mining the database of the RFGES, is the largest study of DGBI to date comparing perceived mental and physical QoL in individuals across different DGBI, as well as those without a DGBI. In practical terms, the data reported in here can be used as a reliable reference to compare against those with no DGBI, individuals with any DGBI, or overlapping DGBI in future studies.

The study showed that participants who met diagnostic criteria for DGBI had poorer physical and mental QoL than those who did not. Across individual DGBI, excessive belching and mixed IBS subtype had the highest and lowest perceived physical and mental QoL, respectively. However, the difference in QoL among gastrointestinal anatomical regions was not substantial. Specifically, the only statistically significant difference was between anorectal and bowel disorders, and this difference was no longer significant after adjusting for multiple comparisons. Although the magnitude of differences in QoL levels among specific DGBI may be small, given the differences in the size of subsamples in the present survey, these data provide strong evidence that people living with DGBI experience poor health-related QoL. For demographics, men with DGBI reported significantly better QoL than women, and those aged ≥ 65 years reported significantly better QoL than younger individuals. In line with previous studies,^{18,23} QoL deteriorated significantly with increasing numbers of overlapping DGBI, with

Table 4. Physical and Mental Quality of Life in Individuals With a Disorder of Gut-Brain Interaction According to Sex

Variable	Male		Female		Comparison	
	Physical QoL	Mental QoL	Physical QoL	Mental QoL	Physical QoL	Mental QoL
	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)		
Total sample	14.8 (14.77–14.83)	13.92 (13.88–13.96)	14.12 (14.09–14.15)	13.18 (13.14–13.22)	$F_{1,54038} = 863.51, P < .001$	$F_{1,54038} = 685.23, P < .001$
Esophageal disorders	12.81 (12.67–12.95)	12.21 (12.03–12.39)	12.14 (12.01–12.27)	11.47 (11.3–11.63)	$F_{1,3221} = 47.3, P < .001$	$F_{1,3225} = 35.29, P < .001$
Functional heartburn	12.26 (11.96–12.56)	12.00 (11.59–12.4)	11.64 (11.33–11.94)	11.60 (11.22–11.98)	$F_{1,612} = 8.24, P = .004$	$F_{1,612} = 1.97, P = .161$
Functional chest pain	12.84 (12.56–13.13)	11.95 (11.57–12.33)	12.27 (12.01–12.53)	10.85 (10.5–11.2)	$F_{1,738} = 8.55, P = .003$	$F_{1,739} = 17.85, P < .001$
Reflux hypersensitivity	11.67 (11.31–12.02)	11.40 (10.9–11.9)	10.81 (10.47–11.14)	10.71 (10.25–11.17)	$F_{1,453} = 11.99, P < .001$	$F_{1,454} = 4.07, P = .045$
Globus sensation	13.48 (13.09–13.88)	12.32 (11.79–12.84)	13.08 (12.73–13.43)	11.62 (11.18–12.07)	$F_{1,405} = 2.2, P = .13$	$F_{1,407} = 4.02, P = .045$
Functional dysphagia	12.70 (12.51–12.89)	12.40 (12.16–12.64)	11.88 (11.7–12.06)	11.55 (11.33–11.78)	$F_{1,1711} = 37.92, P < .001$	$F_{1,1712} = 25.73, P < .001$
Gastroduodenal disorders	13.05 (12.94–13.15)	12.42 (12.28–12.56)	12.36 (12.26–12.45)	11.70 (11.58–11.81)	$F_{1,5742} = 91.42, P < .001$	$F_{1,5749} = 62.34, P < .001$
Functional dyspepsia	12.75 (12.62–12.89)	12.32 (12.15–12.49)	12.12 (12.01–12.24)	11.51 (11.37–11.65)	$F_{1,3908} = 49.68, P < .001$	$F_{1,3912} = 51.89, P < .001$
Postprandial distress syndrome	12.84 (12.7–12.99)	12.36 (12.17–12.55)	12.18 (12.06–12.31)	11.54 (11.39–11.7)	$F_{1,3311} = 45.02, P < .001$	$F_{1,3315} = 43.74, P < .001$
Epigastric pain syndrome	11.91 (11.7–12.12)	11.96 (11.67–12.24)	11.29 (11.1–11.48)	11.06 (10.83–11.3)	$F_{1,1304} = 18.29, P < .001$	$F_{1,1305} = 22.8, P < .001$
Excessive belching	12.70 (12.35–13.05)	12.78 (12.33–13.22)	11.88 (11.56–12.2)	11.45 (11.05–11.84)	$F_{1,524} = 11.59, P < .001$	$F_{1,525} = 19.33, P < .001$
Rumination	13.39 (13.19–13.59)	12.37 (12.11–12.63)	12.63 (12.45–12.8)	11.87 (11.65–12.09)	$F_{1,1505} = 32.25, P < .001$	$F_{1,1507} = 8.16, P = .004$
Chronic nausea and vomiting	12.40 (12.01–12.79)	11.80 (11.28–12.31)	11.56 (11.24–11.88)	11.18 (10.78–11.59)	$F_{1,501} = 10.61, P = .001$	$F_{1,501} = 3.37, P = .067$
Cyclic vomiting syndrome	12.68 (12.4–12.96)	12.34 (11.98–12.69)	11.92 (11.62–12.23)	11.65 (11.28–12.02)	$F_{1,623} = 13.04, P < .001$	$F_{1,623} = 6.87, P = .009$
Bowel disorders	13.66 (13.6–13.71)	12.77 (12.7–12.85)	13.30 (13.25–13.35)	12.30 (12.24–12.36)	$F_{1,17973} = 81.65, P < .001$	$F_{1,18002} = 89.73, P < .001$
IBS	12.08 (11.9–12.26)	11.55 (11.31–11.78)	11.69 (11.55–11.83)	11.02 (10.85–11.2)	$F_{1,2193} = 10.77, P = .001$	$F_{1,2193} = 12.28, P < .001$
IBS-constipation	11.96 (11.62–12.3)	12.02 (11.61–12.44)	11.76 (11.52–12)	11.20 (10.9–11.5)	$F_{1,710} = 0.9, P = .344$	$F_{1,710} = 9.5, P = .002$
IBS-diarrhea	12.16 (11.85–12.47)	11.21 (10.79–11.62)	11.87 (11.59–12.16)	11.20 (10.84–11.56)	$F_{1,627} = 1.83, P = .177$	$F_{1,627} = 0, P = .993$
IBS-mixed type	11.93 (11.57–12.28)	11.30 (10.87–11.73)	11.36 (11.12–11.6)	10.67 (10.37–10.97)	$F_{1,710} = 6.95, P = .008$	$F_{1,710} = 5.69, P = .017$
IBS-unsubtyped	12.78 (12.13–13.43)	12.36 (11.43–13.28)	12.37 (11.84–12.91)	11.19 (10.5–11.89)	$F_{1,54038} = 863.51, P < .001$	$F_{1,54125} = 685.23, P < .001$
Functional constipation	13.76 (13.65–13.86)	12.74 (12.61–12.88)	13.54 (13.47–13.62)	12.40 (12.3–12.5)	$F_{1,6315} = 10.34, P = .001$	$F_{1,6331} = 16.5, P < .001$
Opioid-induced constipation	12.33 (12.05–12.61)	12.66 (12.33–12.99)	11.94 (11.68–12.19)	12.20 (11.89–12.5)	$F_{1,844} = 4.12, P = .042$	$F_{1,844} = 3.98, P = .046$
Functional diarrhea	13.68 (13.55–13.82)	12.76 (12.59–12.93)	13.26 (13.1–13.42)	12.27 (12.08–12.47)	$F_{1,2543} = 15.72, P < .001$	$F_{1,2545} = 13.28, P < .001$
Functional abdominal bloating or distention	13.79 (13.6–13.98)	12.92 (12.68–13.17)	13.64 (13.5–13.78)	12.59 (12.42–12.77)	$F_{1,1781} = 1.53, P = .216$	$F_{1,1783} = 4.62, P = .0312$
Unspecified functional bowel disorder	14.18 (14.08–14.29)	13.17 (13.03–13.3)	13.81 (13.72–13.91)	12.71 (12.59–12.84)	$F_{1,4751} = 27.26, P < .001$	$F_{1,4760} = 23.5, P < .001$
Anorectal disorders	12.94 (12.81–13.06)	12.24 (12.09–12.39)	12.59 (12.48–12.7)	11.75 (11.62–11.89)	$F_{1,4170} = 16.82, P < .001$	$F_{1,4181} = 22, P < .001$
Fecal incontinence	12.69 (12.42–12.96)	12.36 (12.04–12.67)	12.07 (11.77–12.36)	11.62 (11.29–11.96)	$F_{1,847} = 9.38, P = .002$	$F_{1,849} = 9.92, P = .001$
Levator ani syndrome	12.03 (11.66–12.4)	11.14 (10.72–11.55)	11.77 (11.47–12.07)	10.89 (10.55–11.23)	$F_{1,619} = 1.18, P = .276$	$F_{1,620} = 0.84, P = .359$
Proctalgia fugax	13.04 (12.89–13.18)	12.32 (12.15–12.5)	12.80 (12.67–12.92)	11.90 (11.75–12.05)	$F_{1,3003} = 6.07, P = .014$	$F_{1,3011} = 12.55, P < .001$

NOTE. Shaded areas represent nonsignificant results.

Table 5. Physical and Mental Quality of Life in Individuals With a Disorders of Gut-Brain Interaction According to Age Category

Variable	Age categories						Comparison	
	18–39 years		40–64 years		≥65 years			
	Physical QoL	Mental QoL	Physical QoL	Mental QoL	Physical QoL	Mental QoL		
	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Physical QoL	Mental QoL
Total sample	14.57 (14.54–14.6)	13.4 (13.36–13.45)	14.31 (14.27–14.34)	13.4 (13.36–13.44)	14.61 (14.55–14.66)	14.33 (14.26–14.39)	$F_{2,54037} = 66.82$, $P < .001$	$F_{2,54124} = 289.91$, $P < .001$
Esophageal disorders	12.78 (12.64–12.92)	11.64 (11.46–11.83)	12.16 (12–12.31)	11.65 (11.46–11.83)	12.31 (12.06–12.57)	12.94 (12.63–13.24)	$F_{2,3220} = 18.38$, $P < .001$	$F_{2,3224} = 24.24$, $P < .001$
Functional heartburn	12.31 (12.02–12.61)	12.07 (11.68–12.46)	11.61 (11.26–11.96)	11.31 (10.87–11.75)	11.31 (10.66–11.96)	12.38 (11.56–13.2)	$F_{2,611} = 6.35$, $P = .001$	$F_{2,611} = 4.23$, $P = .014$
Functional chest pain	12.92 (12.64–13.2)	10.96 (10.59–11.34)	12.26 (11.95–12.57)	11.49 (11.08–11.9)	12.23 (11.75–12.7)	12.41 (11.77–13.05)	$F_{2,737} = 5.74$, $P = .003$	$F_{2,738} = 6.26$, $P = .002$
Reflux hypersensitivity	11.39 (11.02–11.75)	10.86 (10.34–11.38)	10.91 (10.53–11.29)	10.85 (10.36–11.35)	12.02 (11.36–12.69)	12.84 (11.92–13.76)	$F_{2,452} = 3.81$, $P = .022$	$F_{2,453} = 5.86$, $P = .003$
Globus sensation	13.39 (12.99–13.78)	11.45 (10.91–11.98)	13.05 (12.65–13.45)	11.91 (11.42–12.4)	13.65 (12.93–14.38)	13.87 (13.02–14.72)	$F_{2,404} = 1.25$, $P = .288$	$F_{2,406} = 9.12$, $P < .001$
Functional dysphagia	12.61 (12.43–12.8)	11.93 (11.68–12.18)	11.94 (11.72–12.15)	11.62 (11.37–11.88)	12.08 (11.74–12.42)	12.95 (12.56–13.35)	$F_{2,1710} = 11.7$, $P < .001$	$F_{2,1711} = 13.18$, $P < .001$
Gastroduodenal disorders	13.00 (12.91–13.09)	12.02 (11.9–12.15)	12.20 (12.08–12.31)	11.73 (11.58–11.87)	12.59 (12.35–12.82)	12.94 (12.68–13.2)	$F_{2,5741} = 55.57$, $P < .001$	$F_{2,5748} = 28.84$, $P < .001$
Functional dyspepsia	12.82 (12.71–12.93)	11.94 (11.79–12.09)	11.81 (11.67–11.96)	11.52 (11.34–11.7)	12.08 (11.78–12.38)	12.60 (12.25–12.95)	$F_{2,3907} = 60.96$, $P < .001$	$F_{2,3911} = 15.13$, $P < .001$
Postprandial distress syndrome	12.89 (12.76–13.01)	11.98 (11.81–12.14)	11.88 (11.72–12.04)	11.56 (11.36–11.75)	12.08 (11.75–12.41)	12.53 (12.14–12.91)	$F_{2,3310} = 51.61$, $P < .001$	$F_{2,3314} = 10.84$, $P < .001$
Epigastric pain syndrome	11.89 (11.69–12.08)	11.54 (11.28–11.8)	11.11 (10.89–11.32)	11.09 (10.81–11.37)	11.66 (11.12–12.19)	12.69 (12.08–13.29)	$F_{2,1303} = 13.58$, $P < .001$	$F_{2,1304} = 10.25$, $P < .001$
Excessive belching	12.46 (12.12–12.8)	11.85 (11.4–12.3)	11.84 (11.46–12.21)	11.82 (11.38–12.27)	12.82 (12.05–13.59)	13.64 (12.83–14.45)	$F_{2,523} = 4.39$, $P = .012$	$F_{2,524} = 7.29$, $P < .001$
Rumination	13.12 (12.92–13.32)	11.82 (11.55–12.09)	12.76 (12.56–12.96)	11.96 (11.71–12.22)	13.20 (12.84–13.57)	13.32 (12.9–13.73)	$F_{2,1504} = 4.1$, $P = .016$	$F_{2,1506} = 16.63$, $P < .001$
Chronic nausea and vomiting	12.39 (12.09–12.69)	11.67 (11.27–12.07)	11.04 (10.58–11.49)	10.64 (10.07–11.21)	11.35 (10.36–12.34)	12.91 (11.69–14.13)	$F_{2,500} = 13.52$, $P < .001$	$F_{2,500} = 7.47$, $P < .001$
Cyclic vomiting syndrome	12.62 (12.35–12.89)	12.25 (11.9–12.6)	11.81 (11.45–12.17)	11.48 (11.05–11.92)	11.95 (11.26–12.63)	12.13 (11.41–12.84)	$F_{2,622} = 6.71$, $P = .001$	$F_{2,622} = 3.61$, $P = .027$

Table 5. Continued

Variable	Age categories						Comparison	
	18–39 years		40–64 years		≥65 years			
	Physical QoL	Mental QoL	Physical QoL	Mental QoL	Physical QoL	Mental QoL	Physical QoL	Mental QoL
	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)		
Bowel disorders	13.64 (13.59–13.69)	12.43 (12.35–12.5)	13.22 (13.16–13.28)	12.32 (12.25–12.4)	13.48 (13.37–13.58)	13.34 (13.22–13.46)	$F_{2,17972} = 50.6$, $P < .001$	$F_{2,18001} = 86.44$, $P < .001$
IBS	12.27 (12.12–12.41)	11.32 (11.13–11.52)	11.16 (10.98–11.34)	10.79 (10.57–11.01)	12.03 (11.55–12.5)	12.73 (12.24–13.23)	$F_{2,2192} = 44.04$, $P < .001$	$F_{2,2192} = 22.46$, $P < .001$
IBS–constipation	12.14 (11.89–12.39)	11.47 (11.15–11.8)	11.20 (10.87–11.54)	11.15 (10.73–11.57)	12.19 (11.49–12.88)	12.76 (11.99–13.53)	$F_{2,709} = 10.32$, $P < .001$	$F_{2,709} = 5.24$, $P = .005$
IBS–diarrhea	12.52 (12.25–12.79)	11.50 (11.12–11.87)	11.35 (11.01–11.69)	10.61 (10.18–11.04)	11.37 (10.52–12.21)	12.15 (11.24–13.05)	$F_{2,626} = 15.44$, $P < .001$	$F_{2,626} = 6.37$, $P = .001$
IBS–mixed type	12.06 (11.8–12.32)	11.02 (10.68–11.36)	10.82 (10.52–11.13)	10.44 (10.07–10.81)	12.07 (11.04–13.11)	12.83 (11.76–13.91)	$F_{2,709} = 18.59$, $P < .001$	$F_{2,709} = 10.27$, $P < .001$
IBC–unsubtyped	12.89 (12.35–13.43)	11.22 (10.4–12.04)	11.92 (11.29–12.54)	11.75 (10.93–12.56)	13.70 (11.31–16.09)	14.60 (12.6–16.6)	$F_{2,54037} = 66.82$, $P < .001$	$F_{2,54124} = 289.91$, $P < .001$
Functional constipation	13.74 (13.66–13.83)	12.45 (12.33–12.57)	13.45 (13.34–13.55)	12.36 (12.23–12.48)	13.67 (13.5–13.85)	13.28 (13.08–13.49)	$F_{2,6314} = 9.48$, $P < .001$	$F_{2,6330} = 27.29$, $P < .001$
Opioid-induced constipation	12.88 (12.57–13.19)	12.77 (12.39–13.16)	11.63 (11.36–11.9)	12.03 (11.7–12.36)	11.46 (11.04–11.88)	12.48 (12.03–12.93)	$F_{2,843} = 23.31$, $P < .001$	$F_{2,843} = 4.51$, $P = .011$
Functional diarrhea	13.77 (13.61–13.92)	12.54 (12.33–12.74)	13.31 (13.15–13.48)	12.32 (12.13–12.52)	13.33 (13.06–13.61)	13.32 (12.99–13.65)	$F_{2,2542} = 8.79$, $P < .001$	$F_{2,2544} = 12.44$, $P < .001$
Functional abdominal bloating or distention	13.89 (13.72–14.06)	12.58 (12.35–12.8)	13.48 (13.31–13.65)	12.62 (12.41–12.83)	13.79 (13.44–14.13)	13.59 (13.21–13.97)	$F_{2,1780} = 5.76$, $P = .003$	$F_{2,1782} = 9.14$, $P < .001$
Unspecified functional bowel disorder	14.18 (14.08–14.28)	12.86 (12.72–13)	13.81 (13.7–13.92)	12.78 (12.64–12.92)	13.87 (13.68–14.07)	13.62 (13.39–13.84)	$F_{2,4750} = 12.51$, $P < .001$	$F_{2,4759} = 16.86$, $P < .001$
Anorectal disorders	12.95 (12.83–13.07)	11.90 (11.75–12.06)	12.46 (12.33–12.59)	11.68 (11.53–11.83)	12.95 (12.72–13.18)	13.07 (12.83–13.3)	$F_{2,4169} = 16.56$, $P < .001$	$F_{2,4180} = 39.05$, $P < .001$
Fecal incontinence	12.23 (11.88–12.58)	11.89 (11.45–12.33)	12.02 (11.72–12.32)	11.27 (10.94–11.6)	13.30 (12.9–13.7)	13.56 (13.15–13.96)	$F_{2,846} = 13.31$, $P < .001$	$F_{2,848} = 32.56$, $P < .001$
Levator ani syndrome	12.11 (11.77–12.44)	11.00 (10.62–11.38)	11.54 (11.18–11.89)	10.72 (10.32–11.11)	12.33 (11.5–13.16)	12.35 (11.51–13.18)	$F_{2,618} = 3.37$, $P = .035$	$F_{2,619} = 5.3$, $P = .005$
Proctalgia fugax	13.17 (13.04–13.3)	12.11 (11.93–12.29)	12.65 (12.5–12.81)	11.85 (11.68–12.03)	12.71 (12.43–12.98)	12.81 (12.52–13.09)	$F_{2,3002} = 14.23$, $P < .001$	$F_{2,3010} = 11.91$, $P < .001$

NOTE. The shaded area represents a nonsignificant result.

poorer QoL among those having ≥ 2 DGBI compared with 1 DGBI and those without any DGBI.

Exploration of the predictors of physical and mental QoL indicated that after accounting for age, sex, and number of overlapping DGBI, poorer QoL was predicted by depression, anxiety, and somatic symptom severity scores, and the more negative functional experiences relating to DGBI (concern, embarrassment, or stress associated with bowel functioning). This is in agreement with previous research that documented a close association between poor QoL in people with DGBI and worse mental health,^{14,33,34} somatization,²⁰ poor illness perceptions and coping styles,³⁵ visceral sensitivity or pain catastrophizing,^{2,33,36} and intolerance of uncertainty relating to gastrointestinal symptoms.¹⁷

QoL levels reflect general health in the biopsychosocial sense and are considered an important outcome measure in DGBI research trials⁷ because they correlate with a variety of other key outcome measures such as poor symptom management.^{33,34} Measurement of QoL, in addition to psychological parameters, such as anxiety or depression, should therefore be part of the routine assessment of patients with DGBI,³ as recommended by authoritative gastroenterology organizations.^{37,38} Further, QoL should be included as an outcome measure in clinical trials of all therapeutic interventions in this area.³⁹ At a clinical level, failing to recognize the adverse impact of DGBI on QoL could have a detrimental effect on the physician-patient relationship.³ Thus, models of care that reflect the importance of poor QoL as part of person-focused care need to be promoted.⁴⁰

Although the RFGES recruited a large and diverse sample of people with DGBI from around the world, certain measures commonly used in DGBI research were missing from the survey, including disorder-specific severity measures (other than IBS). Other limitations were that the participant had to have Internet access and be willing to complete the questionnaire, meaning that we cannot exclude some form of volunteer or responder bias, which may have affected our results to some degree. However, most of the general adult population in all of the 26 countries were internet users at the time the survey was conducted.

The diagnosis of a DGBI was not confirmed in each participant by review of medical records, with the exclusion of potential organic explanations for symptoms, which would not have been feasible in a study of this size. Instead, the survey assumed that those reporting symptoms compatible with a DGBI at the required frequency had that condition. Importantly, some organic conditions can present with symptoms similar to a DGBI, but this was at least partly accounted for, as described earlier.

The finding that the prevalence of a DGBI decreased with age may suggest selection bias, with selective survey participation of healthier older adults, which could help explain why individuals aged >65 reported better QoL compared with the younger participant groups.

The Internet survey contacted panels of registered survey takers in each country via email until all quota categories were filled; thus, we have no way of knowing the

overall response rate for the RFGES. Because the study was cross-sectional, conclusions relating to causal processes or directionality cannot be proven.

Another limitation is that the 3 questions exploring the impact of DGBI (concern, embarrassment, and stress associated with bowel functioning) may have been less relevant to those with upper gastrointestinal DGBI.

Finally, the use of a community sample means that the data cannot be extrapolated directly to a patient population with DGBI, whose symptoms and their impact on QoL, are likely to be more severe. It is, therefore, probable that this study underestimates the impact of DGBI on QoL to some extent.

Conclusion

This is the largest study of DGBI to our knowledge to date, comparing perceived mental and physical QoL across different DGBI as well as those without a DGBI in a large representative sample of adults. QoL was found to deteriorate significantly with increasing number of DGBI, with those having ≥ 2 DGBI reporting significantly poorer physical and mental QoL than those with only 1 DGBI and those without a DGBI. Men with DGBI reported better QoL than women, and those aged ≥ 65 years reported better QoL than younger respondents, but although statistically significant, these differences were small. After accounting for age, sex, and number of overlapping DGBI, poorer QoL was predicted by depression, anxiety, and somatic symptom severity scores, and the more negative functional experiences (concern, embarrassment, or stress associated with bowel functioning) relating to DGBI. QoL should play an important role in clinical practice and be a key outcome measure in clinical trials.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at <https://doi.org/10.1053/j.gastro.2022.12.009>

References

1. Sperber AD, Bangdiwala SI, Drossman, et al. Worldwide prevalence and burden of functional gastrointestinal disorders, results of Rome Foundation Global Study. *Gastroenterology* 2021;160:99–114.e113.
2. Chang L. Review article: epidemiology and quality of life in functional gastrointestinal disorders. *Aliment Pharmacol Ther* 2004;20(Suppl 7):31–39.
3. Agarwal N, Spiegel BM. The effect of irritable bowel syndrome on health-related quality of life and health care expenditures. *Gastroenterol Clin North Am* 2011;40:11–19.
4. Frandemark A, Tornblom H, Jakobsson S, et al. Work productivity and activity impairment in irritable bowel syndrome (IBS): a multifaceted problem. *Am J Gastroenterol* 2018;113:1540–1549.

5. Creed F, Ratcliffe J, Fernandez L, et al. Health-related quality of life and health care costs in severe, refractory irritable bowel syndrome. *Ann Intern Med* 2001; 134:860–868.
6. Dean BB, Aguilar D, Barghout V, et al. Impairment in work productivity and health-related quality of life in patients with IBS. *Am J Manag Care* 2005; 11(Suppl):S17–S26.
7. Irvine EJ, Tack J, Crowell MD, et al. Design of treatment trials for functional gastrointestinal disorders. *Gastroenterology* 2016;150:1469–1480.e1461.
8. Hays RD, Bjorner JB, Revicki DA, et al. Development of physical and mental health summary scores from the patient-reported outcomes measurement information system (PROMIS) global items. *Qual Life Res* 2009; 18:873–880.
9. Gralnek IM, Hays RD, Kilbourne A, et al. The impact of irritable bowel syndrome on health-related quality of life. *Gastroenterology* 2000;119:654–660.
10. El-Serag HB, Olden K, Bjorkman D. Health-related quality of life among persons with irritable bowel syndrome: a systematic review. *Aliment Pharmacol Ther* 2002;16:1171–1185.
11. Choi MG, Jung HK. Health related quality of life in functional gastrointestinal disorders in Asia. *J Neurogastroenterol Motil* 2011;17:245–251.
12. Aro P, Talley NJ, Agreus L, et al. Functional dyspepsia impairs quality of life in the adult population. *Aliment Pharmacol Ther* 2011;33:1215–1224.
13. Talley NJ, Locke GR 3rd, Lahr BD, et al. Functional dyspepsia, delayed gastric emptying, and impaired quality of life. *Gut* 2006;55:933–939.
14. Haag S, Senf W, Hauser W, et al. Impairment of health-related quality of life in functional dyspepsia and chronic liver disease: the influence of depression and anxiety. *Aliment Pharmacol Ther* 2008; 27:561–571.
15. Koloski NA, Jones M, Wai R, et al. Impact of persistent constipation on health-related quality of life and mortality in older community-dwelling women. *Am J Gastroenterol* 2013;108:1152–1158.
16. Gila A, Lindberg G. Quality of life in patients with different types of functional constipation. *Scand J Gastroenterol* 1997;32:1083–1089.
17. Levinthal DJ, Romutis S, Rajalaban A, et al. Greater intolerance to uncertainty predicts poorer quality of life in adults with cyclic vomiting syndrome. *Neurogastroenterol Motil* 2021;33:e14159.
18. Koloski NA, Talley NJ, Boyce PM. The impact of functional gastrointestinal disorders on quality of life. *Am J Gastroenterol* 2000;95:67–71.
19. Chen HH, Hung CH, Kao AW, et al. Exploring quality of life, stress, and risk factors associated with irritable bowel syndrome for female university students in Taiwan. *Int J Environ Res Public Health* 2021; 18:3888.
20. Halder SL, Locke GR 3rd, Talley NJ, et al. Impact of functional gastrointestinal disorders on health-related quality of life: a population-based case-control study. *Aliment Pharmacol Ther* 2004;19:233–242.
21. Jeong JJ, Choi MG, Cho YS, et al. Chronic gastrointestinal symptoms and quality of life in the Korean population. *World J Gastroenterol* 2008;14:6388–6394.
22. Cassar GE, Youssef GJ, Knowles S, et al. Health-related quality of life in irritable bowel syndrome: a systematic review and meta-analysis. *Gastroenterol Nurs* 2020; 43:E102–E122.
23. El-Serag HB, Talley NJ. Health-related quality of life in functional dyspepsia. *Aliment Pharmacol Ther* 2003; 18:387–393.
24. Irvine EJ, Ferrazzi S, Pare P, Thompson WG, Rance L. Health-related quality of life in functional GI disorders: focus on constipation and resource utilization. *Am J Gastroenterol* 2002;97:1986–1993.
25. Tang B, Cai HD, Xie HL, et al. Epidemiology of globus symptoms and associated psychological factors in China. *J Dig Dis* 2016;17:319–324.
26. Aziz I, Palsson OS, Whitehead WE, et al. Epidemiology, clinical characteristics, and associations for Rome IV functional nausea and vomiting disorders in adults. *Clin Gastroenterol Hepatol* 2019;17:878–886.
27. Kroenke K, Spitzer RL, Williams JB, et al. An ultra-brief screening scale for anxiety and depression: the PHQ-4. *Psychosomatics* 2009;50:613–621.
28. Sperber AD, Freud T, Aziz I, et al. Greater overlap of Rome IV disorders of gut-brain interactions leads to increased disease severity and poorer quality of life. *Clin Gastroenterol Hepatol* 2022;20:e945–e956.
29. Kroenke K, Spitzer RL, Williams JB. The PHQ-15: validity of a new measure for evaluating the severity of somatic symptoms. *Psychosom Med* 2002;64:258–266.
30. Palsson OS, Whitehead WE, van Tilburg MA, et al. Development and validation of the Rome IV Diagnostic Questionnaire for Adults. *Gastroenterology* 2016; 150:1481–1491.
31. Bradley JV. Nonrobustness in Z, t, and F tests at large sample sizes. *Bull Psychonomic Soc* 1980; 16:333–336.
32. Ferguson CJ. An effect size primer: a guide for clinicians and researchers. *Prof Psychol Res Pr* 2009; 40:532–538.
33. Lackner JM, Gudleski GD, Ma CX, et al. Representing the IOSRG: fear of GI symptoms has an important impact on quality of life in patients with moderate-to-severe IBS. *Am J Gastroenterol* 2014;109:1815–1823.
34. Spiegel BM, Gralnek IM, Bolus R, et al. Clinical determinants of health-related quality of life in patients with irritable bowel syndrome. *Arch Intern Med* 2004; 164:1773–1780.
35. Knowles SR, Austin DW, Sivanesan S, et al. Relations between symptom severity, illness perceptions, visceral sensitivity, coping strategies and well-being in irritable bowel syndrome guided by the common sense model of illness. *Psychol Health Med* 2017;22:524–534.
36. Cassar GE, Knowles S, Youssef GJ, et al. Examining the mediational role of psychological flexibility, pain catastrophizing, and visceral sensitivity in the relationship between psychological distress, irritable bowel symptom frequency, and quality of life. *Psychol Health Med* 2018; 23:1168–1181.

37. American College of Gastroenterology Functional Gastrointestinal Disorders Task Force. Evidence-based position statement on the management of irritable bowel syndrome in North America. *Am J Gastroenterol* 2002; 97(Suppl):S1–S5.
38. Vasant DH, Paine PA, Black CJ, et al. British Society of Gastroenterology guidelines on the management of irritable bowel syndrome. *Gut* 2021;70:1214–1240.
39. Staudacher HM, Mikocka-Walus A, Ford AC. Common mental disorders in irritable bowel syndrome: pathophysiology, management, and considerations for future randomised controlled trials. *Lancet Gastroenterol Hepatol* 2021;6:401–410.
40. Basnayake C, Kamm MA, Stanley A, et al. Long-term outcome of multidisciplinary versus standard gastroenterologist care for functional gastrointestinal disorders: a randomized trial. *Clin Gastroenterol Hepatol* 2022; 20:2102–2111.e9.

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Conflicts of interest

The authors disclose no conflicts.

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Data Availability

The data that support the findings of this study are available from Rome Foundation Global Epidemiology Study, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are, however, available from the authors upon reasonable request and with permission of the Rome Foundation Global Epidemiology Study.

Supplementary Table 1. Patient-Reported Outcomes Measurement Information Systems T Scores and Standard Deviations by Overall, Sex, and Age Category

Variable	Overall		Sex				Age category					
	Physical QoL	Mental QoL	Male		Female		18-39 years		40-64 years		≥65 years	
			Physical QoL	Mental QoL	Physical QoL	Mental QoL	Physical QoL	Mental QoL	Physical QoL	Mental QoL	Physical QoL	Mental QoL
Total sample	50.00 (10.00)	50.00 (10.0)	51.25 (9.70)	51.14 (9.76)	48.70 (10.14)	48.82 (10.10)	53.39 (9.64)	49.60 (10.41)	49.47 (10.28)	49.55 (9.85)	50.32 (10.13)	52.18 (8.92)
Esophageal disorders	42.55 (10.19)	44.54 (10.59)	43.85 (9.98)	45.81 (10.57)	41.44 (10.24)	43.47 (10.48)	43.82 (9.57)	44.14 (10.67)	41.49 (10.83)	43.99 (10.71)	41.77 (9.55)	47.85 (9.21)
Functional heartburn	40.59 (9.82)	44.05 (10.33)	41.79 (9.43)	44.73 (10.18)	39.58 (10.04)	43.48 (10.43)	41.99 (9.25)	44.93 (10.12)	39.62 (10.41)	42.75 (10.68)	37.72 (8.98)	45.34 (9.29)
Functional chest pain	42.9 (9.82)	43.2 (10.94)	44.04 (9.75)	45.16 (11)	41.87 (9.78)	41.43 (10.59)	44.43 (9.4)	42.1 (10.58)	41.74 (10.43)	43.36 (11.58)	41.66 (8.29)	46.51 (9.15)
Reflux hypersensitivity	37.98 (9.8)	42 (10.88)	39.5 (9.69)	43.13 (10.99)	36.53 (9.71)	40.91 (10.68)	38.68 (9.4)	41.56 (10.8)	36.79 (10.34)	41.32 (11)	40.46 (8.23)	47.22 (9.38)
Globus sensation	45.61 (9.88)	45.45 (10.5)	46.31 (9.82)	46.56 (11.02)	45.04 (9.91)	44.55 (9.99)	46.28 (9.34)	44.15 (11.09)	44.7 (10.5)	45.35 (10.09)	46.86 (8.99)	50.75 (8.21)
Functional dysphagia	41.8 (10.21)	44.89 (10.43)	43.37 (10.06)	46.29 (10.22)	40.45 (10.16)	43.69 (10.48)	43.14 (9.51)	44.9 (10.49)	40.7 (10.91)	43.87 (10.56)	40.79 (9.75)	47.89 (9.27)
Gastroduodenal disorders	43.32 (10.14)	45.13 (10.53)	44.79 (9.9)	46.49 (10.47)	42.23 (10.18)	44.12 (10.47)	44.59 (9.69)	45.26 (10.66)	41.73 (10.35)	44.23 (10.44)	42.76 (10.74)	47.88 (9.74)
Functional dyspepsia	39.22 (9.69)	43.08 (10.27)	40.41 (9.47)	44.66 (10.27)	38.35 (9.75)	41.92 (10.13)	40.41 (9.58)	43.43 (10.42)	37.75 (9.55)	42.01 (10.04)	39.05 (10.14)	46.42 (9.76)
Postprandial distress syndrome	42.3 (10.26)	44.58 (10.59)	43.66 (9.96)	46.11 (10.44)	41.38 (10.36)	43.54 (10.57)	43.92 (9.82)	44.97 (10.64)	40.31 (10.42)	43.52 (10.56)	40.86 (10.53)	46.73 (9.89)
Epigastric pain syndrome	42.53 (10.35)	44.7 (10.68)	43.99 (9.96)	46.28 (10.43)	41.56 (10.5)	43.65 (10.72)	44.19 (9.82)	45.13 (10.66)	40.49 (10.62)	43.62 (10.75)	40.88 (10.68)	46.57 (10.1)
Excessive belching	41.84 (10.5)	45.25 (10.7)	43.54 (10.38)	47.52 (10.59)	40.45 (10.42)	43.4 (10.45)	42.76 (10.14)	44.92 (11.18)	40.23 (10.56)	44.21 (10.09)	43.62 (11.17)	50.28 (9.45)
Rumination	44.61 (9.65)	45.56 (10.24)	46.14 (9.58)	46.54 (10.51)	43.36 (9.53)	44.75 (9.95)	45.2 (9.29)	44.83 (10.34)	43.89 (9.78)	45.09 (10.21)	45.18 (10.14)	49.19 (9.27)
Chronic nausea and vomiting	40.41 (10.35)	43.16 (11.11)	42.2 (9.99)	44.34 (11.17)	39.3 (10.43)	42.43 (11.02)	42.26 (9.72)	43.98 (10.95)	37.35 (10.82)	40.66 (11.04)	38.5 (10.03)	47.77 (10.58)
Cyclic vomiting syndrome	41.76 (10.07)	45.03 (10.06)	43.17 (9.5)	46.09 (9.67)	40.39 (10.44)	43.99 (10.35)	43 (9.95)	45.77 (10.5)	40.22 (9.94)	43.56 (9.51)	39.15 (10.29)	45.43 (8.54)
Bowel disorders	46.27 (9.77)	46.78 (9.97)	47.1 (9.62)	47.68 (9.93)	45.66 (9.83)	46.12 (9.95)	46.98 (9.3)	46.59 (10.24)	45.5 (10.19)	46.26 (9.85)	46.14 (9.88)	49.14 (8.99)
IBS	40.35 (9.92)	42.74 (10.22)	41.28 (9.87)	43.89 (10.21)	39.81 (9.92)	42.07 (10.16)	41.97 (9.57)	43.14 (10.3)	37.93 (9.78)	41.39 (9.96)	40.62 (10.87)	47.02 (9.51)
IBS-constipation	40.27 (9.77)	43.38 (10.02)	40.73 (9.63)	45.21 (9.4)	40.06 (9.84)	42.54 (10.19)	41.33 (9.65)	43.26 (9.96)	38.24 (9.77)	42.79 (10.26)	41.31 (9.44)	46.99 (8.71)
IBS-diarrhea	40.89 (9.98)	42.83 (10.48)	41.52 (9.75)	42.89 (10.51)	40.4 (10.15)	42.78 (10.47)	42.85 (9.63)	43.91 (10.63)	38.51 (9.83)	40.74 (10.19)	37.92 (10.39)	45.64 (8.88)
IBS-mixed type	39.42 (10.12)	41.78 (10.08)	40.92 (10.39)	43.33 (10.17)	38.63 (9.9)	40.97 (9.96)	41.33 (9.53)	42.26 (10.24)	36.72 (9.94)	40.4 (9.46)	40.84 (12.42)	47.05 (10.95)
IBS-unsubtyped	43.06 (8.76)	43.88 (10.39)	43.8 (8.87)	45.91 (11.35)	42.53 (8.69)	42.44 (9.45)	44.78 (8.27)	43.31 (10.81)	40.26 (8.21)	43.09 (9.49)	47.03 (11.23)	52.7 (8.99)
Functional constipation	46.91 (9.4)	46.94 (9.81)	47.47 (9.31)	47.61 (9.74)	46.6 (9.44)	46.55 (9.83)	47.38 (9)	46.7 (10.08)	46.35 (9.8)	46.46 (9.67)	46.86 (9.56)	49.2 (8.94)
Opioid-induced constipation	41.36 (10.32)	46.3 (10.07)	42.17 (10.36)	47.2 (9.74)	40.71 (10.25)	45.57 (10.28)	44.31 (10.63)	47.62 (10.95)	39.72 (9.67)	45.09 (9.59)	38.31 (9.37)	46.17 (8.52)
Functional diarrhea	46.52 (9.85)	47.16 (9.95)	47.27 (9.62)	47.9 (9.97)	45.51 (10.07)	46.15 (9.84)	47.52 (9.29)	47.22 (10)	45.86 (10.27)	46.53 (9.94)	45.66 (9.88)	48.91 (9.62)

Supplementary Table 1. Continued

Variable	Overall		Sex				Age category					
	Physical QoL	Mental QoL	Male		Female		18-39 years		40-64 years		≥65 years	
			Physical QoL	Mental QoL	Physical QoL	Mental QoL	Physical QoL	Mental QoL	Physical QoL	Mental QoL	Physical QoL	Mental QoL
Functional abdominal bloating	47.09 (9.15)	47 (9.51)	47.61 (9.13)	47.83 (9.61)	46.82 (9.16)	46.56 (9.43)	47.77 (8.73)	46.7 (9.87)	46.37 (9.47)	46.66 (9.36)	47.49 (9.21)	49.56 (8.26)
Unspecified functional bowel disorder	48.25 (9.08)	48.08 (9.79)	49.05 (8.95)	48.84 (9.8)	47.53 (9.15)	47.4 (9.75)	48.89 (8.62)	47.87 (10.18)	47.72 (9.46)	47.68 (9.63)	47.63 (9.35)	49.99 (8.67)
Biliary disorders functional biliary pain	39.5 (10.13)	42.74 (10.21)	39.4 (8.37)	42.59 (15.33)	39.52 (10.53)	42.77 (9.24)	39.43 (9.89)	43.37 (10.08)	39.87 (11)	40.7 (11.47)	38.29 (15.39)	45.55 (3.78)
Central nervous system disorders of gastrointestinal pain	38.06 (9.95)	39.04 (6.82)			38.06 (9.95)	39.04 (6.82)	42.56 (9.41)	38.68 (5.5)	31.47 (9.13)	41.42 (8.9)		
Anorectal disorders	43.63 (10.14)	44.83 (10.05)	44.41 (9.99)	45.77 (9.86)	43.02 (10.23)	44.1 (10.15)	44.46 (9.68)	44.72 (10.33)	42.67 (10.52)	43.95 (9.99)	43.97 (10.16)	47.97 (8.67)
Fecal incontinence	42.42 (10.68)	45.06 (10.12)	43.58 (10.49)	46.29 (9.91)	41.11 (10.76)	43.67 (10.18)	41.99 (10.06)	44.8 (10.57)	41.15 (10.95)	42.91 (9.74)	45.33 (10.42)	49.4 (8.82)
Levator ani syndrome	40.53 (10.84)	42.02 (10.14)	41.23 (11.07)	42.66 (10.03)	40.04 (10.66)	41.57 (10.2)	41.5 (10.72)	42.16 (10.16)	39.21 (10.8)	41.12 (10.11)	41.79 (11.22)	45.85 (9.41)
Proctalgia fugax	44.18 (9.76)	45.12 (9.89)	44.67 (9.55)	45.91 (9.67)	43.79 (9.9)	44.53 (10.02)	45.19 (9.2)	45.25 (10.23)	43.38 (10.27)	44.44 (9.86)	42.99 (9.63)	47.13 (8.26)
DGBI frequency												
0	52.51 (9.3)	52.1 (9.39)	53.35 (9.04)	52.84 (9.21)	51.42 (9.52)	51.16 (9.54)	53.04 (9.07)	51.92 (9.92)	52.08 (9.39)	51.63 (9.19)	52.32 (9.55)	53.56 (8.5)
1	48.14 (9.25)	48.17 (9.68)	48.97 (9.09)	49.09 (9.57)	47.48 (9.32)	47.44 (9.7)	48.7 (8.76)	47.87 (9.92)	47.61 (9.66)	47.8 (9.58)	47.85 (9.48)	50.22 (8.89)
2	45.21 (9.75)	45.94 (10.14)	46.02 (9.62)	46.73 (10.19)	44.62 (9.8)	45.37 (10.07)	46.46 (9.3)	45.94 (10.5)	44.13 (10.03)	45.36 (9.92)	43.93 (9.95)	47.73 (9.23)
3	43.01 (9.65)	44.34 (10.16)	43.98 (9.63)	45.21 (10.22)	42.34 (9.61)	43.74 (10.07)	44.5 (8.99)	44.32 (10.33)	41.43 (10.1)	43.57 (10.14)	41.5 (9.98)	47.37 (8.74)
4+	39.48 (9.7)	42.78 (10.37)	40.67 (9.36)	44.29 (10.33)	38.63 (9.85)	41.7 (10.26)	40.84 (9.49)	43.23 (10.58)	38.11 (9.81)	41.68 (10.2)	38.45 (9.31)	45.57 (9.28)

NOTE. Standard deviations are identified in parenthesis.

Supplementary Table 2. Frequency and Percentage of Disorders of Gut-Brain Interaction by Sex and Age Category

Variable	Total	Sex		Age categories			Age categories by sex					
		Male	Female	18-39	40-64	≥65	18-39 years		40-64 years		≥65 years	
							Male	Female	Male	Female	Male	Female
Total sample	54,127	27,549 (50.9)	26,578 (49.1)	23,003 (42.5)	22,281 (44.27)	8843 (16.34)	10,883 (47.31)	12,120 (52.69)	11,458 (51.42)	10,823 (48.58)	5208 (58.89)	3635 (41.11)
Esophageal disorders	3715	1731 (46.59)	1984 (53.41)	1612 (43.39)	1617 (45.14)	486 (13.08)	777 (48.2)	835 (51.8)	712 (44.03)	905 (55.97)	242 (49.79)	244 (50.21)
Functional heartburn	768	352 (45.83)	416 (54.17)	368 (47.92)	323 (46.92)	77 (10.03)	181 (49.18)	187 (50.82)	142 (43.96)	181 (56.04)	29 (37.66)	48 (62.34)
Functional chest pain	811	382 (47.1)	429 (52.9)	346 (42.66)	359 (41.55)	106 (13.07)	148 (42.77)	198 (57.23)	169 (47.08)	190 (52.92)	65 (61.32)	41 (38.68)
Reflux hypersensitivity	576	292 (50.69)	284 (49.31)	252 (43.75)	260 (37.53)	64 (11.11)	135 (53.57)	117 (46.43)	129 (49.62)	131 (50.38)	28 (43.75)	36 (56.25)
Globus sensation	439	198 (45.1)	241 (54.9)	181 (41.23)	206 (37.51)	52 (11.85)	81 (44.75)	100 (55.25)	87 (42.23)	119 (57.77)	30 (57.69)	22 (42.31)
Functional dysphagia	2041	967 (47.38)	1074 (52.62)	905 (44.34)	848 (41.32)	288 (14.11)	468 (51.71)	437 (48.29)	360 (42.45)	488 (57.55)	139 (48.26)	149 (51.74)
Gastroduodenal disorders	5457	2330 (42.7)	3127 (57.3)	2880 (52.78)	2048 (38.1)	529 (9.69)	1211 (42.05)	1669 (57.95)	870 (42.48)	1178 (57.52)	249 (47.07)	280 (52.93)
Functional dyspepsia	4575	1922 (42.01)	2653 (57.99)	2401 (52.48)	1743 (34.63)	431 (9.42)	991 (41.27)	1410 (58.73)	733 (42.05)	1010 (57.95)	198 (45.94)	233 (54.06)
Postprandial distress syndrome	3834	1581 (41.24)	2253 (58.76)	2031 (52.97)	1438 (41.5)	365 (9.52)	831 (40.92)	1200 (59.08)	585 (40.68)	853 (59.32)	165 (45.21)	200 (54.79)
Epigastric pain syndrome	1682	738 (43.88)	944 (56.12)	846 (50.3)	695 (44.79)	141 (8.38)	360 (42.55)	486 (57.45)	316 (45.47)	379 (54.53)	62 (43.97)	79 (56.03)
Excessive belching	653	307 (47.01)	346 (52.99)	303 (46.4)	271 (32.82)	79 (12.1)	155 (51.16)	148 (48.84)	112 (41.33)	159 (58.67)	40 (50.63)	39 (49.37)
Rumination	1681	765 (45.51)	916 (54.49)	679 (40.39)	753 (6.45)	249 (14.81)	305 (44.92)	374 (55.08)	327 (43.43)	426 (56.57)	133 (53.41)	116 (46.59)
Chronic nausea and vomiting	618	239 (38.67)	379 (61.33)	357 (57.77)	214 (40.93)	47 (7.61)	139 (38.94)	218 (61.06)	76 (35.51)	138 (64.49)	24 (51.06)	23 (48.94)
Cyclic vomiting syndrome	780	399 (51.15)	381 (48.85)	446 (57.18)	256 (38.8)	78 (10)	228 (51.12)	218 (48.88)	136 (53.13)	120 (46.88)	35 (44.87)	43 (55.13)
Cannabinoid hyperemesis syndrome	31	24 (77.42)	7 (22.58)	28 (90.32)	2 (35.58)	1 (3.23)	22 (78.57)	6 (21.43)	2 (100)			1 (100)
Bowel disorders	20,065	8560 (42.66)	11,505 (57.34)	9070 (45.2)	8212 (39.73)	2783 (13.87)	3590 (39.58)	5480 (60.42)	3533 (43.02)	4679 (56.98)	1437 (51.63)	1346 (48.37)
IBS	2616	986 (37.69)	1630 (62.31)	1384 (52.91)	1015 (40.3)	217 (8.3)	493 (35.62)	891 (64.38)	394 (38.82)	621 (61.18)	99 (45.62)	118 (54.38)
IBS-constipation	832	274 (32.93)	558 (67.07)	459 (55.17)	296 (43.04)	77 (9.25)	143 (31.15)	316 (68.85)	98 (33.11)	198 (66.89)	33 (42.86)	44 (57.14)
IBS-diarrhea	750	327 (43.6)	423 (56.4)	393 (52.4)	298 (38.96)	59 (7.87)	164 (41.73)	229 (58.27)	138 (46.31)	160 (53.69)	25 (42.37)	34 (57.63)
IBS-mixed type	876	321 (36.64)	555 (63.36)	455 (51.94)	353 (43.68)	68 (7.76)	161 (35.38)	294 (64.62)	129 (36.54)	224 (63.46)	31 (45.59)	37 (54.41)
IBS-unsubtyped	158	64 (40.51)	94 (59.49)	77 (48.73)	68 (44.94)	13 (8.23)	25 (32.47)	52 (67.53)	29 (42.65)	39 (57.35)	10 (76.92)	3 (23.08)
Functional constipation	6705	2430 (36.24)	4275 (63.76)	3142 (46.86)	2612 (46.36)	951 (14.18)	1050 (33.42)	2092 (66.58)	920 (35.22)	1692 (64.78)	460 (48.37)	491 (51.63)

Supplementary Table 2. Continued

Variable	Total No.	Sex		Age categories			Age categories by sex					
		Male	Female	18-39	40-64	≥65	18-39 years		40-64 years		≥65 years	
							Male	Female	Male	Female	Male	Female
Opioid-induced constipation	989	436 (44.08)	553 (55.92)	389 (39.33)	432 (40.7)	168 (16.99)	185 (47.56)	204 (52.44)	168 (38.89)	264 (61.11)	83 (49.4)	85 (50.6)
Functional diarrhea	2755	1579 (57.31)	1176 (42.69)	1091 (39.6)	1238 (28.57)	426 (15.46)	597 (54.72)	494 (45.28)	737 (59.53)	501 (40.47)	245 (57.51)	181 (42.49)
Functional abdominal bloating or distention	1894	659 (34.79)	1235 (65.21)	783 (41.34)	878 (41.67)	233 (12.3)	248 (31.67)	535 (68.33)	299 (34.05)	579 (65.95)	112 (48.07)	121 (51.93)
Unspecified functional bowel disorder	5086	2413 (47.44)	2673 (52.56)	2277 (44.77)	2070 (43.07)	739 (14.53)	991 (43.52)	1286 (56.48)	1021 (49.32)	1049 (50.68)	401 (54.26)	338 (45.74)
Central nervous system disorders of gastrointestinal pain	12		12 (100)	6 (50)	5 (43.98)	1 (8.33)		6 (100)		5 (100)		1 (100)
Biliary disorders functional biliary pain	49	8 (16.33)	41 (83.67)	33 (67.35)	14 (44.7)	2 (4.08)	7 (21.21)	26 (78.79)	1 (7.14)	13 (92.86)		2 (100)
Anorectal disorders	4788	2126 (44.4)	2662 (55.6)	2014 (42.06)	2062 (42.44)	712 (14.87)	889 (44.14)	1125 (55.86)	882 (42.77)	1180 (57.23)	355 (49.86)	357 (50.14)
Fecal incontinence	1076	564 (52.42)	512 (47.58)	331 (30.76)	481 (0)	264 (24.54)	201 (60.73)	130 (39.27)	226 (46.99)	255 (53.01)	137 (51.89)	127 (48.11)
Levator ani syndrome	739	313 (42.35)	426 (57.65)	354 (47.9)	325 (41.66)	60 (8.12)	147 (41.53)	207 (58.47)	139 (42.77)	186 (57.23)	27 (45)	33 (55)
Proctalgia fugax	3388	1481 (43.71)	1907 (56.29)	1503 (44.36)	1438 (40.49)	447 (13.19)	655 (43.58)	848 (56.42)	605 (42.07)	833 (57.93)	221 (49.44)	226 (50.56)
DGBI frequency												
0	30,834	17,408 (56.46)	13,426 (43.54)	12,347 (40.04)	12,845 (39.66)	5642 (18.3)	6541 (52.98)	5806 (47.02)	7316 (56.96)	5529 (43.04)	3551 (62.94)	2091 (37.06)
1	13,723	6082 (44.32)	7641 (55.68)	6148 (44.8)	5556 (42.46)	2019 (14.71)	2475 (40.26)	3673 (59.74)	2511 (45.19)	3045 (54.81)	1096 (54.28)	923 (45.72)
2	4871	2076 (42.62)	2795 (57.38)	2250 (46.19)	1942 (39.87)	679 (13.94)	923 (41.02)	1327 (58.98)	832 (42.84)	1110 (57.16)	321 (47.28)	358 (52.72)
3	2045	847 (41.42)	1198 (58.58)	1005 (49.14)	811 (39.66)	229 (11.2)	398 (39.6)	607 (60.4)	334 (41.18)	477 (58.82)	115 (50.22)	114 (49.78)
≥4	2654	1136 (42.8)	1518 (57.2)	1253 (47.21)	1127 (42.46)	274 (10.32)	546 (43.58)	707 (56.42)	465 (41.26)	662 (58.74)	125 (45.62)	149 (54.38)

NOTE. Data are presented as number (No.) (%).

Supplementary Table 3. Physical Health Quality of Life Comparison Among Disorders of Gut-Brain Interaction

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	No.	Mean	SD
1. Functional heartburn																							62	13.37	3.16
2. Functional chest pain	0.568																						197	13.58	2.66
3. Globus sensation	0.019	0.013																					139	14.27	2.28
4. Functional dysphagia	0.016	0.007	0.895																				222	14.23	2.67
5. Excessive belching	0.024	0.000	0.000	0.000																			1041	12.63	2.64
6. Functional dyspepsia	0.568	0.913	0.002	0.000	0.000																		978	13.56	2.72
7. Postprandial distress syndrome	0.136	0.017	0.000	0.000	0.857	0.010																	59	12.69	2.81
8. Epigastric pain syndrome	0.005	0.004	0.336	0.262	0.000	0.001	0.000																60	14.64	2.50
9. Rumination	0.052	0.039	0.372	0.380	0.000	0.002	0.000	0.089															326	14.04	2.41
10. Chronic nausea and vomiting	0.439	0.150	0.002	0.002	0.321	0.131	0.529	0.001	0.007														48	13.00	2.62
11. Cyclic vomiting syndrome	0.057	0.072	0.792	0.862	0.000	0.034	0.001	0.277	0.669	0.010													79	14.18	2.60
12. IBC-constipation	0.135	0.004	0.000	0.000	0.379	0.000	0.747	0.000	0.000	0.653	0.000												169	12.82	2.51
13. IBS-diarrhea	0.376	0.039	0.000	0.000	0.043	0.012	0.350	0.000	0.000	0.912	0.001	0.394											178	13.04	2.40
14. IBS-mixed type	0.001	0.000	0.000	0.000	0.026	0.000	0.152	0.000	0.000	0.039	0.000	0.017	0.001										146	12.14	2.93
15. IBS-unsubtyped	0.558	0.862	0.128	0.130	0.005	0.802	0.046	0.037	0.292	0.197	0.237	0.037	0.129	0.000									51	13.65	2.28
16. Functional constipation	0.068	0.040	0.143	0.102	0.000	0.000	0.000	0.035	0.531	0.009	0.429	0.000	0.000	0.000	0.384								4085	13.95	2.46
17. Opioid-induced constipation	0.056	0.000	0.000	0.000	0.601	0.000	0.954	0.000	0.000	0.458	0.000	0.664	0.151	0.020	0.000	0.000							351	12.72	2.72
18. Functional diarrhea	0.059	0.032	0.194	0.157	0.000	0.000	0.000	0.045	0.684	0.007	0.496	0.000	0.000	0.000	0.697	0.000	0.000						1621	13.98	2.54
19. Functional bloating/distention	0.067	0.043	0.177	0.142	0.000	0.000	0.000	0.042	0.623	0.009	0.467	0.000	0.000	0.000	0.870	0.000	0.874	0.874					1189	13.97	2.40
20. Unspecified functional bowel disorder	0.009	0.001	0.782	0.888	0.000	0.000	0.000	0.185	0.248	0.001	0.908	0.000	0.000	0.000	0.000	0.000	0.002	0.003	0.003				3740	14.21	2.37
21. Fecal incontinence	0.009	0.005	0.684	0.565	0.000	0.000	0.000	0.532	0.184	0.001	0.543	0.000	0.000	0.000	0.054	0.000	0.077	0.071	0.418	0.418			122	14.40	2.68
22. Levator ani syndrome	0.073	0.104	0.885	0.953	0.000	0.066	0.001	0.362	0.652	0.015	0.939	0.000	0.003	0.000	0.458	0.000	0.513	0.488	0.997	0.655	0.655		52	14.21	2.53
23. Proctalgia fugax	0.059	0.045	0.302	0.294	0.000	0.002	0.000	0.071	0.880	0.008	0.598	0.000	0.000	0.000	0.635	0.000	0.810	0.736	0.137	0.140	0.593	0.593	400	14.02	2.48

NOTE. Reflux hypersensitivity, functional biliary pain, and cannabinoid hyperemesis syndrome were excluded due to low case numbers (n = <20). Shaded areas represent nonsignificant results.
No., number; SD, standard deviation.

Supplementary Table 4. Mental Health Quality of Life Comparison Among Disorders of Gut-Brain Interaction

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	No.	Mean	SD
1. Functional heartburn																							62	13.13	3.29
2. Functional chest pain	0.257																						197	12.59	3.45
3. Globus sensation	0.353	0.834																					139	12.67	3.55
4. Functional dysphagia	0.352	0.002	0.011																				222	13.56	3.39
5. Excessive belching	0.004	0.006	0.009	0.000																			1041	11.90	3.43
6. Functional dyspepsia	0.321	0.654	0.896	0.000	0.000																		978	12.71	3.50
7. Postprandial distress syndrome	0.805	0.419	0.533	0.222	0.013	0.527																	59	12.98	3.12
8. Epigastric pain syndrome	0.050	0.000	0.001	0.127	0.000	0.000	0.029																60	14.28	3.03
9. Rumination	0.758	0.175	0.328	0.043	0.000	0.172	0.987	0.005															326	12.99	3.35
10. Chronic nausea and vomiting	0.169	0.536	0.464	0.012	0.438	0.363	0.259	0.001	0.151														48	12.27	3.53
11. Cyclic vomiting syndrome	0.508	0.037	0.071	0.870	0.000	0.038	0.360	0.155	0.217	0.039													79	13.49	3.15
12. IBS-constipation	0.068	0.310	0.258	0.000	0.194	0.089	0.134	0.000	0.016	0.966	0.005												169	12.25	3.16
13. IBS-diarrhea	0.012	0.049	0.045	0.000	0.899	0.003	0.031	0.000	0.000	0.522	0.000	0.365											178	11.93	3.61
14. IBS-mixed type	0.001	0.002	0.002	0.000	0.143	0.000	0.003	0.000	0.000	0.143	0.000	0.036	0.211										146	11.48	3.32
15. IBS-unsubtyped	0.711	0.546	0.661	0.190	0.031	0.677	0.896	0.025	0.856	0.333	0.310	0.208	0.060	0.007									51	12.90	3.26
16. Functional constipation	0.401	0.431	0.691	0.000	0.000	0.530	0.634	0.000	0.259	0.280	0.053	0.037	0.001	0.000	0.790								4085	12.78	3.24
17. Opioid-induced constipation	0.636	0.263	0.445	0.020	0.000	0.299	0.886	0.003	0.769	0.195	0.154	0.028	0.001	0.000	0.975	0.447							351	12.92	3.23

Supplementary Table 4. Continued

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	No.	Mean	SD
18. Functional diarrhea	0.604	0.195	0.399	0.005	0.000	0.121	0.867	0.001	0.686	0.178	0.119	0.012	0.000	0.000	0.984	0.169	0.974						1621	12.91	3.24
19. Functional bloating/ distention	0.748	0.110	0.265	0.016	0.000	0.041	0.981	0.003	0.990	0.130	0.184	0.005	0.000	0.000	0.844	0.046	0.700	0.508					1189	12.99	3.02
20. Unspecified functional bowel disorder	0.984	0.022	0.095	0.058	0.000	0.000	0.717	0.007	0.434	0.066	0.334	0.000	0.000	0.000	0.607	0.000	0.224	0.019	0.182				3740	13.14	3.17
21. Fecal incontinence	0.082	0.000	0.001	0.224	0.000	0.000	0.046	0.591	0.003	0.002	0.272	0.000	0.000	0.000	0.041	0.000	0.001	0.000	0.001	0.004			122	14.01	2.86
22. Levator ani syndrome	0.455	0.876	0.994	0.075	0.093	0.940	0.616	0.009	0.512	0.536	0.157	0.409	0.148	0.023	0.720	0.813	0.612	0.603	0.486	0.305	0.013		52	12.67	2.77
23. Proctalgia fugax	0.957	0.070	0.172	0.092	0.000	0.039	0.788	0.009	0.637	0.092	0.331	0.004	0.000	0.000	0.674	0.056	0.429	0.285	0.551	0.849	0.007	0.367	400	13.11	3.12

NOTE. Reflux hypersensitivity, functional biliary pain, and cannabinoid hyperemesis syndrome were excluded due to low case numbers ($n = <20$). Shaded areas represent nonsignificant results.
No., number; SD, standard deviation.

Supplementary Table 5. Quality of Life Comparisons by Irritable Bowel Syndrome Subtype

Variable		IBS-C	IBS-D	IBS-M	IBS-U
IBS-C	Mean difference		−0.228	−0.673	0.830
	<i>t</i> value		−0.826	−2.312	2.019
	<i>P</i> value		.409	.021	.044
IBS-D	Mean difference	0.316		−0.901	0.602
	<i>t</i> value	0.875		−3.134	1.472
	<i>P</i> value	.382		.002	.142
IBS-M	Mean difference	0.769	0.453		1.503
	<i>t</i> value	2.025	1.207		3.588
	<i>P</i> value	.043	.228		.001
IBS-U	Mean difference	−0.653	−0.969	−1.423	
	<i>t</i> value	−1.217	−1.815	−2.601	
	<i>P</i> value	.224	.070	.010	

NOTE. Comparisons are made as column minus row, positive mean differences indicate greater QoL in column condition. Physical QoL above diagonal, mental QoL below. Shaded areas represent nonsignificant results. C, constipation; D, diarrhea; M, mixed type; U, unsubtyped.

Supplementary Table 6. Quality of Life Comparisons by Functional Dyspepsia Subtype

Variable		Functional dyspepsia	
		PDS	EPS
Functional dyspepsia PDS	Mean difference		-0.862
	<i>t</i> value		-2.368
	<i>P</i> value		.018
EPS	Mean difference	-0.275	
	<i>t</i> value	-0.590	
	<i>P</i> value	.555	

NOTE. Comparisons are made as column minus row, positive mean differences indicate greater QoL in column condition. Physical QoL above diagonal, mental QoL below. Shaded areas represent nonsignificant results. EPS, epigastric pain syndrome; PDS, postprandial distress syndrome.

Supplementary Table 7. Predictors of Quality of Life

Variable	Physical QoL						Mental QoL					
	UB	SE	β	95% CI		P value	UB	SE	β	95% CI		P value
Model 1												
Intercept	15.727	0.05				<.001	13.981	0.062				<.001
Age	−0.005	0.001	−0.03	−0.039	−0.022	<.001	0.014	0.001	0.068	0.06	0.077	<.001
Sex	−0.694	0.023	−0.128	−0.136	−0.12	<.001	−0.703	0.028	−0.106	−0.114	−0.098	<.001
$R^2 = 0.017$						$R^2 = 0.017$						
Model 2												
Intercept	16.298	0.047				<.001	14.472	0.06				<.001
Age	−0.009	0.001	−0.009	−0.053	−0.061	<.001	0.011	0.001	0.052	0.044	0.06	<.001
Sex	−0.478	0.021	−0.478	−0.088	−0.096	<.001	−0.517	0.027	−0.078	−0.086	−0.07	<.001
DGBI comorbidity	−0.973	0.01	−0.973	−0.391	−0.399	<.001	−0.838	0.013	−0.275	−0.283	−0.267	<.001
$R^2 = 0.167$						$R^2 = 0.091$						
Model 3												
Intercept	18.049	0.042				<.001	16.702	0.05				<.001
Age	−0.024	0.001	−0.146	−0.153	−0.139	<.001	−0.015	0.001	−0.072	−0.078	−0.065	<.001
Sex	−0.104	0.018	−0.019	−0.026	−0.012	<.001	−0.107	0.022	−0.016	−0.023	−0.01	<.001
DGBI comorbidity	−0.35	0.009	−0.141	−0.148	−0.133	<.001	−0.093	0.011	−0.031	−0.038	−0.023	<.001
Anxiety	−0.334	0.01	−0.189	−0.2	−0.178	<.001	−0.622	0.013	−0.287	−0.298	−0.276	<.001
Depression	−0.243	0.01	−0.14	−0.152	−0.129	<.001	−0.706	0.012	−0.333	−0.344	−0.322	<.001
Somatization	−0.251	0.003	−0.338	−0.346	−0.33	<.001	−0.088	0.004	−0.097	−0.105	−0.089	<.001
$R^2 = 0.40$						$R^2 = 0.418$						
Model 4												
Intercept	18.93	0.05				<.001	17.56	0.061				<.001
Age	−0.025	0.001	−0.152	−0.158	−0.145	<.001	−0.016	0.001	−0.079	−0.086	−0.073	<.001
Sex	−0.088	0.018	−0.016	−0.023	−0.01	<.001	−0.068	0.022	−0.01	−0.017	−0.004	<.001
DGBI comorbidity	−0.256	0.01	−0.103	−0.11	−0.095	<.001	−0.018	0.012	−0.006	−0.013	0.002	<.001
Anxiety	−0.304	0.01	−0.172	−0.184	−0.161	<.001	−0.585	0.013	−0.27	−0.282	−0.259	<.001
Depression	−0.23	0.01	−0.133	−0.144	−0.121	<.001	−0.688	0.012	−0.324	−0.335	−0.313	<.001
Somatization	−0.235	0.003	−0.317	−0.325	−0.309	<.001	−0.075	0.004	−0.082	−0.09	−0.074	<.001
Are you concerned about bowel function?	−0.409	0.017	−0.094	−0.101	−0.086	<.001	−0.138	0.02	−0.026	−0.033	−0.018	<.001
Are you embarrassed to discuss your bowel functioning with others (family, friends)?	−0.109	0.015	−0.025	−0.032	−0.018	<.001	−0.202	0.018	−0.038	−0.045	−0.031	<.001
Does stress, pressure, or tension affect your bowel functioning?	−0.171	0.015	−0.044	−0.052	−0.037	<.001	−0.318	0.018	−0.068	−0.075	−0.06	<.001
$R^2 = 0.412$						$R^2 = 0.425$						

SE, standardized error; UB, unstandardized β .