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Quality of life in irritable bowel syndrome: Exploring mediating factors through structural equation modelling

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ABSTRACT

Background: Irritable Bowel Syndrome (IBS) negatively influences mental and physical quality of life (QoL), but factors that explain this impact are still unclear. Increasing evidence has associated IBS severity, psychological distress, somatic symptoms, and gastrointestinal (GI)-specific anxiety with QoL in IBS. The aim of this study is to further explore these associations and to analyze potential mediating factors.

Method: A total of 1017 IBS patients (69.3% female, mean age 40.6 years) who completed a QoL measure (SF-36) were included in this study. A proportion of these participants (N = 183; 72.7% female, mean age 41.7), who additionally completed psychological distress, somatic symptoms, and GI-specific anxiety measures, was included in the mediation analysis. This analysis was conducted via structural equation modelling to identify factors of importance for generic QoL, using a cross-sectional design.

Results: IBS patients reported lower QoL than what is observed in the general population, in particular regarding role limitations caused by health and emotional functioning, vitality, and social functioning. Female patients scored lower than male patients on most QoL dimensions. The effects of IBS severity on mental and physical QoL were mediated by GI-specific anxiety. In addition to GI-specific anxiety, depressive symptoms were also of importance for mental QoL, and somatic symptom severity for physical QoL.

Conclusion: QoL is reduced in patients with IBS and GI-specific anxiety, depressive symptoms, and somatic complaints are particularly important for this outcome. Future trials should test the efficacy of psychological interventions specifically targeting these factors in improving QoL in IBS.

1. Introduction

Irritable Bowel Syndrome (IBS) is a highly prevalent Disorder of Gut-Brain Interaction (DGBI), characterized by recurrent abdominal pain associated with abnormal bowel habits [1,2]. About 4% of the world population is estimated to fulfill the criteria for an IBS diagnosis according to the most recent classification of DGBIs (Rome IV; [1]). In addition to abdominal pain and disordered bowel habits, other GI symptoms such as abdominal discomfort and abdominal bloating/distension are also commonly present [3]. IBS is associated with high health care costs [4,5], high comorbidity with psychological disorders [6], and significant disease burden with decrements in work productivity and activity [7–9].

Several previous publications have pointed out the negative influence of IBS on patients' quality of life (QoL) [10–15], which has been confirmed by meta-analytical evidence [16,17]. QoL in IBS patients has been consistently found to be markedly poor, even in comparison with organic diseases, such as ischaemic heart disease, heart failure, diabetes mellitus, end-stage renal disease, and gastroesophageal reflux disease [11,13]. In a study using the 36-item Short Form Health Survey (SF-36), a widely used generic QoL instrument, and comparing QoL in IBS with other medical conditions, the reductions in QoL in IBS were particularly pronounced regarding vitality, role limitations caused by physical health problems, bodily pain, and general health perceptions [11].

The identification of the variables that explain QoL decrements in IBS is needed to determine factors to address and treat to successfully

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improve IBS patients' QoL. Nevertheless, the relative importance of various identified explanatory factors still needs to be better characterized. Identified predictors of low generic QoL, considering both its mental and physical dimensions, can be grouped into: a) gastrointestinal (GI) symptoms; b) psychological variables such as anxiety, depression, stress, and GI-specific anxiety; and c) non-GI somatic symptoms [10,13,18,19]. Demographic characteristics have also been implicated as important determinants of QoL in IBS, with women demonstrating lower QoL overall [19,20], and older patients reporting better social functioning [21].

Although GI symptom severity is of importance for QoL in IBS patients, it appears to have a relatively modest role, while other factors take a more prominent role as explanatory factors for QoL [22]. Spiegel and colleagues [23] found that both mental and physical QoL in IBS seem to be primarily related to extra-intestinal rather than to GI symptoms. Extra-intestinal symptoms, often referred to as non-GI somatic symptoms in the DGBI literature, are frequent among IBS patients [14], and commonly associated with psychological distress [24], and include different manifestations such as fatigue, musculoskeletal pain, or difficulty sleeping. In line with this, Tang and colleagues [19] found somatic symptoms, anxiety, and depression to independently contribute to QoL, while abdominal pain did not contribute significantly. Furthermore, Lackner and colleagues [25] found anxiety, depression, stress, social functioning, extra-intestinal symptoms, and mental comorbidities to be associated with self-ratings of health, while IBS symptoms were of minor importance in how IBS patients evaluate their general health. Considering that anxiety and depression can lead to somatic complaints [26,27], it is likely that somatic symptoms may at least partially explain the known association between psychological distress and QoL in IBS.

GI-specific anxiety, defined as anxiety/worry about experiencing certain GI sensations/symptoms, is another factor that has been found to negatively influence QoL in IBS patients [18]. In fact, GI-specific anxiety has been found to be the most important determining factor of QoL in this population, even when taking other known clinical and psychological predictors into consideration [28]. GI-specific anxiety appears indeed to have a central role for mental QoL and has been revealed as the strongest predictor of physical QoL in IBS [10]. Due to the strong predictive power, and seemingly determinant role, of this variable for QoL, it may be possible that GI-specific anxiety is a driver of the effect of other known factors on the mental and physical QoL of IBS patients. This hypothesis has never been tested regarding QoL, but the mediating role of GI-specific anxiety has been demonstrated for the association between psychological variables (e.g., coping, psychological distress) and IBS severity [18,29,30]. Furthermore, reductions in GI-specific anxiety have been found to mediate treatment improvements after psychological interventions for IBS patients [31], which further highlights the role of this variable as a mediator of well-being in this population.

Taken together, these findings are suggestive of a potential mediation role of GI-specific anxiety and somatic symptoms in the association between IBS symptom severity and lower mental and physical QoL. We hypothesize that IBS symptoms may lead to increased GI-specific anxiety, which then predicts reduced QoL. We also hypothesize that anxiety and depression, inserted in the model as controlling variables, may predict non-GI somatic symptom severity, which will then explain lower levels of QoL. Therefore, the main aim of the current study was to test these hypotheses through a path analysis mediation model, also controlling for the effects of age and sex, and analyzing mental and physical QoL separately. This analysis will provide a better understanding of the drivers for diminished QoL in IBS, and a more comprehensive view on how predictors of QoL interact, which is lacking in the IBS literature. We will also compare QoL scores with normative data, taking age group, sex, and the different QoL dimensions into consideration.

2. Materials and methods

2.1. Procedure

We included IBS patients at the Salgrenska University Hospital in Gothenburg, Sweden, with the primary aim to study the link between pathophysiology and IBS symptoms. This study uses a cross-sectional design and self-report measures to assess the variables of interest. All participants included in this study (N = 1017) completed the SF-36 questionnaire [32]. A proportion of participants from the total sample (N = 183) also completed all the other measures needed to conduct the mediation analyses (see below).

Patients were recruited between 2003 and 2007 from primary care, self-referral, or advertisement in newspapers or social media. Inclusion criteria were age between 18 and 75, and an IBS diagnosis, established by a gastroenterologist specialized in DGBIs using the Rome criteria in use at the time of recruitment (Rome II or III). The subtyping was conducted in accordance to Rome II [33]. Exclusion criteria comprised celiac disease, food allergies, conditions or surgery that affects GI function, or any other GI diseases explaining the GI symptoms, as well as severe psychiatric disorders (e.g., major depressive episode, schizophrenia, obsessive-compulsive disorder) or other severe physical diseases (e.g., heart, kidney, liver, rheumatological, or neurological diseases). All the studies were approved by the Regional Ethical Review Board in Gothenburg and were in accordance with the declaration of Helsinki. Verbal and written informed consent were obtained from all participants before data was collected.

2.2. Self-report questionnaires

2.2.1. Quality of life

The SF-36 [32] was used to assess generic mental and physical QoL. This 36-item instrument is a measure of health status and comprises eight dimensions: physical functioning, role limitations due to physical functioning (role functioning—physical), bodily pain, general health perception, vitality, social functioning, role limitations due to emotional functioning (role functioning—emotional), and general mental health. Physical functioning refers to limitations caused by health problems in typical daily activities. The role physical/emotional limitations dimensions assess the extent to which physical health and emotional problems affect daily activities. The impact of physical health or emotional problems on social activities such as visiting friends and relatives is measured by the social functioning scale. Bodily pain refers to frequency of pain and interference of pain with work activities and household responsibilities. The general health perception dimension assesses global evaluations of health level, and the vitality dimension measures energy and tiredness levels. General mood, depressive symptoms, and anxiety are assessed by the general mental health domain. In samples from our center, the Cronbach's alphas of the dimensions of the SF-36 ranged from 0.82 to 0.90.

The eight SF-36's domains can be used to calculate two component scores: a mental QoL score and a physical QoL score. Each dimension of the SF-36 is scored from 0 to 100, with higher scores indicating better QoL and less disability.

2.2.2. IBS severity

IBS symptom severity was assessed using two instruments, the Gastrointestinal Symptom Rating Scale – IBS version (GSRIS-IBS [34]) and the IBS Severity Scoring System (IBS-SSS [35]). The GSRIS-IBS is a 13-item questionnaire that assesses abdominal pain, bloating, constipation, diarrhea, and satiety. The items of the GSRIS-IBS are rated using a response scale ranging from 1 to 7. The IBS-SSS includes 5 items covering abdominal pain frequency and intensity, bloating/distension severity, bowel habit dissatisfaction, and interference with daily life on a 100-point scale. The total scores range from 0 to 500. For both questionnaires, higher scores indicate more severe IBS symptoms. In samples

from our center, the Cronbach's alphas of the IBS-SSS and the GSRS-IBS were 0.79 and 0.92, respectively.

2.2.3. GI-specific anxiety

This variable was assessed by the Visceral Sensitivity Index (VSI [30]), a unidimensional 15-item measure of GI symptoms-related anxiety, i.e., anxiety related to gastrointestinal sensations/symptoms, and the contexts in which these occur. The items are rated from 1 to 6, with the total score ranging from 0 to 75, where higher scores indicate higher severity of GI-specific anxiety. We used the VSI as a unidimensional scale, as this is the structure supported by both the original [30] and the Swedish [36] VSI studies. In this study, the Cronbach's alpha of the VSI was 0.92.

2.2.4. Somatic symptoms

This variable was assessed using two measures, the Patient Health Questionnaire (PHQ-15 [37]) and the Symptom Checklist-90-Revised (SCL-90 [38]). The PHQ-15 is a measure of somatic symptom severity that includes GI (e.g., stomach pain, nausea, gas, or indigestion) and non-GI symptoms (e.g., headaches, dizziness, shortness of breath). Item responses range from 0 ("not bothered at all") to 2 ("bothered a lot"). The SCL-90 is a questionnaire with 90 items rated on a 5-point scale (0–4) that assesses a range of symptoms of psychopathology in nine symptomatic dimensions. In this study, only the somatization dimension was considered. Higher scores indicate more severe somatic symptoms in both measures. For the purpose of this study, only the non-GI items of the scales were considered (i.e., three items from the PHQ-15 and one item from the somatization dimension of the SCL90 referring to GI symptoms were removed from the analyses) In samples from our center, the PHQ-12 and the somatic dimension of the SCL-90 showed Cronbach's alphas of 0.83 and 0.93, respectively.

2.2.5. Psychological distress (anxiety and depression)

The Hospital Anxiety and Depression Scale (HADS [39]) was used to assess symptoms of psychological distress. This is a 21-item instrument that uses a 4-point scale (0–3) and is composed of two subscales (anxiety and depression), each comprising 7 items, providing total scores for general anxiety and depression between 0 and 21. Both subscales have presented adequate internal consistencies ($\alpha_{\text{anx}} = 0.84$; $\alpha_{\text{dep}} = 0.81$) in samples from our center.

2.3. Data analysis and statistics

To analyze levels of generic QoL in our sample, descriptive analyses and tests of differences (one-way analyses of variance - ANOVAs) between age groups, sexes, and IBS subtypes were conducted using the total sample of the study for each of eight dimensions of SF-36 (N = 1017). Data from our sample was then contrasted with Swedish normative data [40], to generally compare scores on SF-36 between the two samples, across age and sex groups.

Using a subsample of the patients where information from all the questionnaires were available (N = 183), bivariate Pearson correlation analyses were then conducted to examine the bivariate associations between the studied variables. Z-scores were calculated to allow the use of a single variable for IBS severity (GRSR and IBS-SSS) and non-GI somatic symptoms (PHQ-12, and SCL-90 without the nausea item). The Manifest Fornell-Larcker Criterion [41] between the pairs of variables with the highest correlation scores was calculated to analyze whether the variables were independent in addition to being associated. All the pairs of variables demonstrated distinctiveness.

Considering the results from the correlation analyses and previous findings presented in the introduction, a path model was performed to test whether GI-specific anxiety and non-GI somatic symptom severity (mediators) explain the effect of IBS severity (independent variable) on mental and physical QoL (dependent variables). The effects of general anxiety, depressive symptoms, age, and sex as independent, controlling

variables in the model were also examined. Path analysis is a form of Structural Equation Modelling (SEM) used to assess the effects of a set of variables acting on specific outcomes through multiple causal pathways [42]. The relationships between variables are specified in a single step, which results in a model showing the mechanisms through which independent variables produce both direct and indirect effects on dependent variables. Indirect effects are found when an independent variable affects a dependent variable at least partially through the mechanisms of a mediator. The bootstrap procedure (with 5000 samples) was used in this analysis. The adjustment of the tested path model to empirical data was examined recurring to well-known goodness of fit indicators: the relative chi-square (χ^2/df , acceptable when <5 [43]), the Comparative Fit Index (CFI; > 0.90 [44]), the Root Mean Squared Error of Approximation (RMSEA; <0.10 [45]), and the Standardized Root Mean Residual (SRMR; < 0.10 [45]). Significant mediation results were identified at a 95% confidence interval range that does not contain zero.

Descriptive analyses, ANOVAs, and Pearson correlations were conducted using the IBM SPSS Statistics software (v. 28). The path analysis was conducted with the IBM SPSS Amos software (v. 27).

3. Results

3.1. Participants

A total of 1017 IBS patients (69.3% female, mean age 40.6 ± 13.4 years) were included in this study. These participants completed the SF-36. According to the Rome II criteria [33], 33.40% percent of participants had IBS-A (IBS with alternating constipation and diarrhea), 17.90% IBS-C (constipation-predominant IBS), and 31.90% IBS-D (diarrhea-predominant IBS). A smaller percentage (16.80%) were missing information about IBS subtype.

A proportion of the total sample, comprising 183 participants (72.7% female; mean age 41.7 ± 13.7 years; 20.20% IBS-A, 11.50% IBS-C, 24.60% IBS-D, 43.70% missing information on IBS subtype) completed the SF-36 and the remaining study questionnaires. These participants were included in the mediation path analysis.

3.2. QoL scores in IBS patients

Table 1 presents the SF-36 subscale scores per age group, sex, and IBS subtype in our sample (N = 1017). There were significant differences between age groups for physical functioning, general health, vitality, social functioning, emotional role, and mental health. Physical functioning overall decreased with increasing age, while vitality, emotional role, and mental health overall increased with age. General health and social functioning appeared to peak in the 35–44 years age group.

Furthermore, female IBS patients presented significantly lower quality of life on the physical functioning, physical role, bodily pain, vitality, social functioning, and mental health domains than male patients. Differences between IBS subtypes were only found for physical role and emotional role, in which IBS-A patients presented lower scores than patients with IBS-C and IBS-D.

Table 2 shows SF-36 subscale scores by sex and age groups across our IBS sample and a normative Swedish sample [40] (N = 7676). In this analysis, we did not include the older age group (65–74) present in the normative sample, due to lack of IBS patients in our sample in this age group. The IBS patients presented lower scores overall than the normative sample. Differences in physical functioning were minor, whereas larger differences were noted for the other domains. The most pronounced differences were seen for physical role, vitality, social functioning, and emotional role, especially in the younger group.

3.3. Associations and predictors of QoL

3.3.1. Bivariate associations

Correlation analyses (Table 3), conducted within the participants

Table 1
Results for SF-36 scores per age group, sex, and IBS subtype (N = 1017).

	n (%)	PF	RP	BP	GH	VT	SF	RE	MH
Age group									
18–24	143 (14.06)	91.81 ± 13.84	64.51 ± 38.27	55.51 ± 27.34	64.28 ± 24.78	50.98 ± 24.88	70.37 ± 24.63	55.71 ± 43.66	65.93 ± 20.71
25–34	244 (23.99)	90.07 ± 14.67	57.17 ± 38.08	55.73 ± 25.90	60.55 ± 24.82	46.31 ± 24.25	68.19 ± 27.36	60.52 ± 43.55	68.31 ± 19.04
35–44	241 (23.70)	91.06 ± 16.06	65.87 ± 39.79	56.54 ± 26.32	68.87 ± 22.04	53.09 ± 23.68	79.56 ± 21.86	69.29 ± 38.58	72.19 ± 19.14
45–54	191 (18.78)	88.10 ± 15.02	59.38 ± 41.54	58.08 ± 24.79	65.65 ± 23.86	48.95 ± 24.28	71.40 ± 26.86	67.36 ± 40.17	67.46 ± 20.68
55–64	160 (15.73)	82.92 ± 16.69	64.53 ± 40.54	54.78 ± 24.35	62.68 ± 22.46	54.59 ± 23.94	76.17 ± 22.11	67.08 ± 39.91	71.83 ± 18.29
65+	38 (3.74)	85.01 ± 15.86	55.26 ± 40.09	54.79 ± 17.42	63.21 ± 15.96	60.26 ± 17.74	80.59 ± 18.31	71.05 ± 38.88	74.95 ± 16.73
F [†]		7.73, p < 0.001	1.80, p = 0.110	0.38, p = 0.865	3.40, p = 0.005	4.37, p < 0.001	6.98, p < 0.001	2.93, p = 0.012	3.55, p = 0.003
Sex									
Male	312 (30.68)	90.34 ± 14.32	65.79 ± 39.40	61.48 ± 24.71	66.42 ± 23.77	55.42 ± 22.87	75.92 ± 24.18	66.35 ± 41.28	71.98 ± 18.58
Female	705 (69.32)	88.19 ± 16.08	59.99 ± 39.85	53.79 ± 25.45	63.56 ± 23.32	48.89 ± 24.45	72.45 ± 25.19	63.88 ± 41.25	68.45 ± 19.55
F [†]		4.30, p = 0.038	4.61, p = 0.032	20.09, p < 0.001	3.23, p = 0.070	16.01, p < 0.001	4.22, p = 0.040	0.78, p = 0.379	7.08, p = 0.008
IBS subtype (Rome II)^{††}									
IBS-A	340 (40.19)	86.19 ± 15.61	49.61 ± 38.03	48.90 ± 21.08	58.97 ± 22.09	45.51 ± 22.30	67.98 ± 24.96	55.69 ± 41.72	66.01 ± 19.17
IBS-C	182 (21.51)	87.28 ± 17.37	62.77 ± 41.28	50.13 ± 22.65	59.92 ± 22.84	45.77 ± 24.64	71.70 ± 26.89	60.26 ± 41.92	67.37 ± 20.28
IBS-D	324 (38.30)	89.24 ± 14.03	58.02 ± 39.65	52.47 ± 22.55	62.47 ± 23.42	46.24 ± 22.75	71.76 ± 23.44	63.89 ± 42.00	68.38 ± 19.53
F [†]		1.71, p = 0.182	7.57, p < 0.001	2.23, p = 0.108	2.03, p = 0.132	0.533, p = 0.587	2.33, p = 0.098	3.20, p = 0.041	1.23, p = 0.292

Data are presented as mean ± standard deviation.

Abbreviations: PF = Physical Functioning; RP = Role-Physical (role limitations due to physical functioning); BP = Bodily Pain; GH = General Health; VT = Vitality; SF = Social Functioning; RE = Role-Emotional (role limitations due to emotional functioning); MH = Mental Health. (IBS-C: constipation-predominant IBS; IBS-D: diarrhea-predominant IBS; IBS-A: IBS with alternating constipation and diarrhea).

[†] ANOVA.

^{††} Missing data from 171 patients.

with data on all questionnaires (N = 183) demonstrated that both mental and physical QoL were negatively associated with IBS severity, depressive symptoms, GI-specific anxiety, and non-GI somatic symptom severity. Mental QoL was additionally associated with general anxiety. Lower age was correlated with less general and GI-specific anxiety, and female sex was linked to higher IBS severity, general and GI-specific anxiety, and non-GI somatic symptoms. IBS severity, depressive symptoms, GI-specific anxiety, and somatic symptom severity were all positively associated with each other.

3.3.2. Predictors of QoL: mediation analyses

The association between IBS severity on QoL through the mediating effects of GI-specific anxiety and non-GI somatic symptoms was analysed through a path analysis model (N = 183). This model also examined the effects of general anxiety, depressive symptoms, age, and sex. The model was first analysed as a fully saturated model in which non-significant paths were progressively removed (Supplementary Table 1).

After the removal of these paths, the model fit was excellent ($\chi^2/df = 1.07$; CFI = 1.00; RMSEA = 0.02, p = 0.792; SRMR = 0.04), indicating that the model presents a good adjustment to data.

The final path model (Fig. 1) showed that IBS severity was associated with GI-specific anxiety, and that GI-specific anxiety, in turn, was linked to mental and physical QoL. IBS severity was associated with mental and physical QoL via GI-specific anxiety. This suggests that the effect of IBS severity on mental and physical QoL may not be direct but rather mediated by GI-specific anxiety. General anxiety was linked to GI-specific anxiety and non-GI somatic symptom severity, and was also associated with mental and physical QoL although only through the mediating effects of other variables. The associations of general anxiety

with mental and physical QoL were fully mediated by GI-specific anxiety, and GI-specific anxiety and non-GI somatic symptom severity, respectively. Non-GI somatic symptom severity was linked to physical QoL. Depressive symptoms presented a non-mediated, direct association with mental QoL, whereas no significant association with GI-specific anxiety or physical QoL could be identified. Regarding the demographic variables included in the model, age was linked to mental and physical QoL through a mediation by GI-specific anxiety, suggesting that older patients may present better QoL due to less severe GI-specific anxiety. Sex presented no significant associations except for female sex being linked to higher non-GI somatic symptom severity. Hence, GI-specific anxiety and depressive symptoms appear to be particularly important variables for the prediction of mental QoL, whereas GI-specific anxiety and non-GI somatic symptom severity appear to be central factors for physical QoL.

4. Discussion

In this study we have demonstrated that IBS patients report lower QoL than individuals from the general population, in particular regarding role limitations caused by health and emotional functioning, vitality, and social functioning. In our sample of IBS patients, physical functioning decreased with age, whereas vitality, role limitations due to emotional functioning, and mental health were generally higher in older participants. Female patients scored lower than male patients on most QoL dimensions, and presented higher non-GI somatic symptom severity. We further showed that the impact of IBS severity per se on both mental and physical QoL is limited and mostly explained by GI-specific anxiety. In addition to GI-specific anxiety, depressive

Table 2
Results for SF-36 scores by sex and age across IBS patients and a normative sample.

Age group	PF		RP		BP		GH		VT		SF		RE		MH			
	IBS patients, n (%)	Normative sample, n (%)*	IBS patients	Normative sample *	IBS patients	Normative sample *	IBS patients	Normative sample *	IBS patients	Normative sample *	IBS patients	Normative sample *	IBS patients	Normative sample *	IBS patients	Normative sample *		
15 [†] -44																		
Males	160 (15.73)	2461 (27.56)	93.18 ± 11.62	94.5 ± 0.3	68.59 ± 37.22	90.7 ± 0.5	67.29 ± 24.89	80.7 ± 0.5	68.93 ± 23.88	80.4 ± 0.4	56.88 ± 22.80	72.0 ± 0.4	75.94 ± 25.06	90.7 ± 0.4	64.79 ± 42.83	89.9 ± 0.5	73.39 ± 18.47	82.3 ± 0.4
Females	468 (46.02)	2679 (30)	90.05 ± 15.96	92.3 ± 0.3	59.99 ± 39.30	87.0 ± 0.5	52.12 ± 25.75	76.2 ± 0.5	63.11 ± 23.92	79.1 ± 0.4	47.62 ± 24.41	66.8 ± 0.4	72.06 ± 25.27	88.5 ± 0.4	62.11 ± 41.77	86.0 ± 0.5	67.85 ± 19.79	80.0 ± 0.4
45-64 ^{††}																		
Males	135 (13.27)	1239 (13.87)	87.73 ± 5.38	87.0 ± 0.6	64.81 ± 40.78	81.3 ± 1.0	55.90 ± 23.92	73.2 ± 0.8	64.47 ± 24.17	73.0 ± 0.7	53.93 ± 23.95	70.0 ± 0.7	76.02 ± 24.05	89.0 ± 0.6	67.41 ± 40.00	86.8 ± 0.8	70.84 ± 18.89	82.0 ± 0.5
Females	216 (21.24)	1297 (14.52)	84.49 ± 16.27	82.5 ± 0.6	59.80 ± 40.96	79.9 ± 1.0	57.00 ± 25.08	68.5 ± 0.8	64.19 ± 22.70	71.9 ± 0.7	50.02 ± 24.38	67.5 ± 0.7	72.05 ± 25.22	87.5 ± 0.6	67.13 ± 0.09	84.7 ± 0.9	68.57 ± 20.21	79.7 ± 0.6

Data are presented as mean ± standard deviation (our sample) or standard error (normative sample).

Abbreviations: PF = Physical Functioning; RP = Role-Physical (role limitations due to physical functioning); BP = Bodily Pain; GH = General Health; VT = Vitality; SF = Social Functioning; RE = Role-Emotional (role limitations due to emotional functioning); MH = Mental Health.

*Sullivan et al. (1998).

†The IBS sample had a minimum age of 18.

††Thirty-eight (3.74%) participants from the IBS sample with ages >64 were not included in this analysis.

Table 3
Correlations between variables (N = 183).

	M ± SD	1	2	3	4	5	6	7	8
1. Age	41.74 ± 13.74	–							
2. Sex (0: male; 1: female)	–	–0.16*	–						
3. IBS severity (z-score)	–0.01 ± 0.97	–0.10	0.21**	–					
4. General anxiety	6.54 ± 4.31	–0.20**	0.16*	0.32***	–				
5. Depressive symptoms	4.47 ± 3.70	0.03	0	0.18*	0.58***	–			
6. GI-specific anxiety	37.52 ± 16.62	–0.22**	0.23**	0.36***	0.39***	0.26***	–		
7. Non-GI somatic symptoms (z-score)	–0.01 ± 0.98	–0.09	0.29***	0.24***	0.50***	0.40***	0.35***	–	
8. Mental QoL	42.55 ± 13.09	0.1	–0.14	–0.20**	–0.30***	–0.44***	–0.30***	–0.30***	–
9. Physical QoL	46.18 ± 7.87	–0.04	–0.06	–0.19**	–0.14	–0.19*	–0.29***	–0.24**	0.08

*p < .05; **p < .01; ***p < .001.

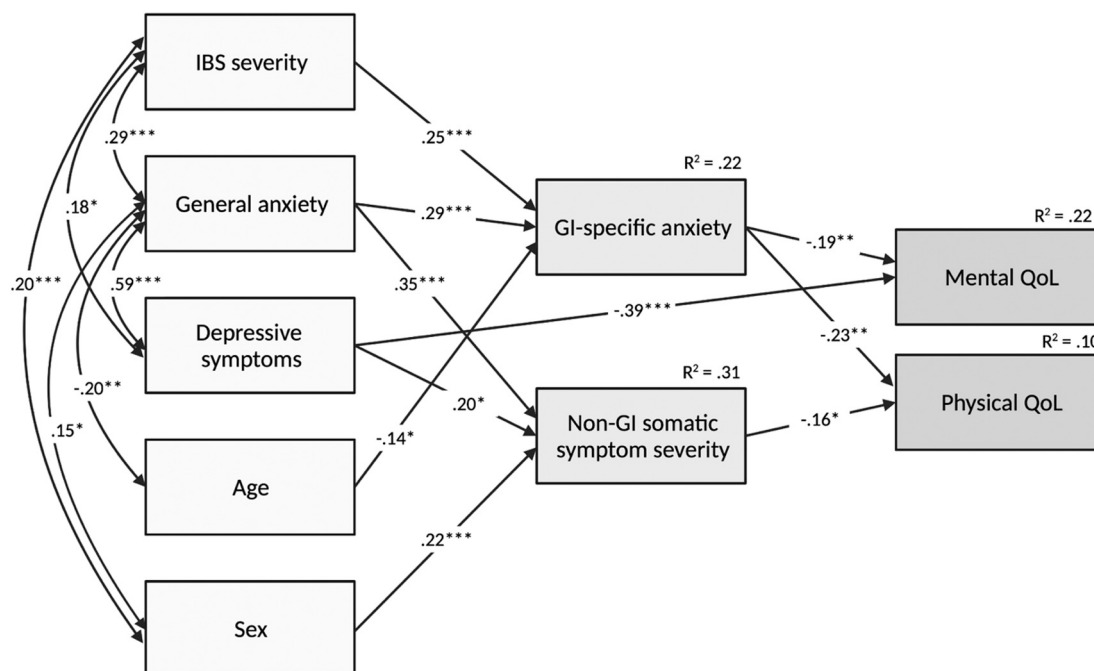


Fig. 1. Final Path Model. Standardized regression coefficients (β) are presented for each path, representing the magnitude of the effect of an independent variable on a dependent variable. Only the significant effects achieved by the model are presented. R² (squared multiple correlation) refers to proportion of total variance explained by the model.

*p < 0.05; **p < 0.01; ***p < 0.001.

symptoms were also of importance for the prediction of mental QoL, and somatic symptom severity was a relevant factor for physical QoL.

This study confirmed previous evidence on the detrimental effects of IBS on QoL [9–15] in comparison with a normative Swedish sample. It is however interesting to note that differences in physical functioning did not differ substantially between our IBS sample and a normative sample from the Swedish population [40]. Within our sample, it was found, unsurprisingly, that physical functioning significantly decreased with age, which is in line with previous evidence [40]. Vitality, role limitations due to emotional functioning, and mental health generally increased with age in our sample, which is in contrast with the Swedish normative data [40], in which all QoL dimensions were negatively affected by age. Furthermore, general health and social functioning appeared to peak in the 35–44 years age group in our IBS sample. QoL in IBS may present distinct temporal trajectories from what is found in the general population possibly due to most IBS patients appearing to have symptom trajectories with symptom reduction over time [46,47]. Patients may also progressively adjust better to the illness with the passing of time. It has in fact been found that longer disease duration is associated with better QoL in chronic conditions such as inflammatory bowel disease [48]. Younger patients may be less well adapted to the illness' challenges and may still be developing healthy psychological strategies

to cope with IBS, whereas older individuals may have accepted such limitations in their life. In the tested path model, the finding that older patients may have better QoL due to the less GI-specific anxiety is highly supportive of this. It is also likely that older patients have been diagnosed and treated for IBS for a longer time, while younger patients may have had dealt with the severe symptomatology, uncertainty, and anxiety characteristic of the pre-diagnosis period in a recent past. It is nevertheless important to note that previous studies have failed to show a correlation between disease duration and QoL in patients attending a gastroenterology outpatient clinic [19,49]. It can be the case that the link between longer disease duration and better QoL may only be found in primary care settings, such as the one concerned by this study. It may be possible that patients in higher levels of care do not become as adapted to the illness over time as patients from primary care might do. This may, at least in part, explain why IBS patients in higher levels of care appear to present poorer QoL than patients in primary care (although this seems to be the case only for female patients [20]). The consideration of the psychological aspects found to be pertinent for QoL in the current study may thus be important for preventable approaches that would minimize the transition to higher levels of care.

Our results on sex differences were consistent with the previous literature. Female IBS patients had significantly lower scores on most of

QoL dimensions, corroborating findings from the general population [40] and IBS samples [19,20]. In our path model, female sex was also associated with higher non-GI somatic symptom severity, which was also expected based on existing studies [50]. Patients with different IBS subtypes showed similar scores on most QoL dimensions, with the exception of IBS patients with alternating diarrhea and constipation (IBS-A) presenting worse scores than patients with IBS with diarrhea- or constipation-predominant symptoms on role limitations caused by physical and emotional functioning. There is not a consensus in the literature on this topic: some research indicates that there are no QoL differences among IBS subtypes [20,51], while others suggest that patients with IBS-D and IBS-M/A have the lowest QoL [52]. These inconsistencies may also be due to the instability of IBS subtypes over time presented by most patients [53].

The main findings from this study concern the tested mediation model. Our results corroborated previous findings that IBS severity may have some, but limited, impact on QoL [10,19,22–24,28,46]. IBS severity may have limited prediction power on QoL because its effect may be explained by other mechanisms. In the model tested in this study, GI-specific anxiety was the only identified mediator of this association, for both mental and physical QoL. This finding suggests that interventional approaches aiming at QoL improvement in IBS should focus on psychological factors [54–57], in particular GI-specific anxiety. This had already been highlighted in a previous IBS study showing that GI-specific anxiety can predict increases in GI symptom severity and decreases in QoL in the subsequent year [46].

Similar results were found for the association between general anxiety and QoL. GI-specific anxiety fully explained the relationship between general anxiety and mental QoL, which suggests that general anxiety is of minor importance for QoL in IBS patients, having an impact on mental QoL driven by worry and hypervigilance about GI-related sensations and contexts. Both GI-specific anxiety and non-GI somatic symptom severity explained the association between anxiety and physical QoL. Somatic symptom severity had already been linked to anxiety [29] and QoL [19,23–25] in IBS, but not as a mediator of the association between anxiety and QoL. Depressive symptoms were also associated with somatic symptom severity, which is consistent with previous IBS studies [29]. Nevertheless, surprisingly, depression did not present any link to physical QoL, which may have been due to the presence of more important variables for the determination of this outcome variable in the tested model. Depression, nonetheless, even in the presence of other relevant variables for mental health in IBS presented a direct association with mental QoL and was the strongest of all independent variables. As the level of depressive symptoms is itself an indicator of mental health, this result was also partly expected.

Although several studies have demonstrated the importance of GI-specific anxiety for QoL [10,18,28] and the direct mechanisms through which its impact on QoL occurs are straightforward (see, for example, review on the effects of worry on subjective and physiological indicators of emotional state [58]), there may be indirect mechanisms of clinical interest that are not yet clearly studied in IBS. One of these mechanisms may be behavioural avoidance. GI-specific anxiety is possibly associated with avoidance of activities important to patients' life satisfaction and well-being (e.g., having a healthy diet, eating in restaurants, going out with friends). Avoidance is well established as a process that maintains and augments anxiety and drives psychological distress [59], being associated with worry, fear of somatic symptoms, fear of traumatic events, and contextual stressors [60]. One study in IBS has demonstrated that acceptance, the process that opposes avoidance, is linked to better generic and disease-specific QoL and lower IBS severity, anxiety, and depression [55]. There is also evidence that the effects of GI-specific anxiety and behavioural response in the association between IBS severity and QoL may be conditional on levels of IBS acceptance (the less IBS acceptance, the stronger the mediation) [61]. This goes in line with the findings from a study with adolescents with IBS where reduction in avoidance behavior explained a large proportion of

the total treatment effect of exposure-based internet cognitive and behavioural therapy on GI symptoms [62]. Avoidance may also at least partially explain the effects of somatic symptoms on QoL, as there is strong evidence supporting that the debilitating impact of chronic pain is substantially driven by avoidance behavior [63,64].

The relatively small variance in GI-specific anxiety that the tested model explained should also be noted. This is indicative that other factors, not included in the model, are important to the presentation of GI-specific anxiety in IBS. Factors including trauma, modelling, and the experience of acute illness have been pointed out as potentially relevant for the development of symptom-specific anxiety [65,66]. Models such as the one presented in this study would thus benefit from the inclusion of such variables. The amount of the variance in QoL, especially in the physical domain, explained by the tested model was also small. Other factors such as socioeconomic status, employment, education, and safety, that are considered of pertinence for generic QoL [67], should additionally be explored further. The duration of illness would be of interest to analyze as well [48]. As stress [10], coping [29], and pain catastrophizing [68] have previously been found to be important factors for the determination of QoL in IBS, future studies should also consider these variables and explore how they interact with GI-specific anxiety and somatic symptom severity for the determination of QoL. As implied above, avoidance coping or avoidant emotion regulation strategies could also be of particular interest.

There are of course limitations to this study that should be noted. The cross-sectional nature of the study, which does not allow the inference of causal relationships, is the most pertinent limitation. The identified direction of the associations between variables, although probable and theoretically consistent, should be interpreted with caution. It is known that cross-sectional mediation analyses may produce biased estimates of longitudinal parameters and that this happens even for total mediations [69]. The present study should be considered a preliminary examination of the identified mediation model. Future longitudinal studies are required to confirm our findings. Furthermore, as in practicality the tested model might be, in some points, circular, with variables being likely to influence each other in bidirectional relationships, it is important to note that the studied model does not intend to suggest that the tested associations solely occur through the tested directions. For example, although it is likely that GI-specific anxiety might lead to depressive symptomatology, the latter was tested as a controlling variable to achieve a parsimonious model clearly exploring the potential mediator effects of GI-specific anxiety and non-GI somatic symptoms in the association between IBS severity and QoL. The sample size used for the mediation model can also be pointed out as a possible limitation. Although the sample size was adequate and the model was well fitted to data, results would be more robust with a larger sample. It would thus be interesting if future studies would attempt at replicating our results using larger samples of IBS patients and by using longitudinal study designs. The limited sample size could also have led to the surprisingly non-significant correlation found between physical and mental QoL. Nevertheless, this result appears to be in line with previous studies using the SF-36 in Swedish samples. Taft et al. (2004) found weak correlations between the mental QoL composite and the Physical Functioning ($r = 0.15$) and Bodily Pain ($r = 0.27$) subscales, and between the physical QoL composite and the mental health subscale ($r = 0.12$). Moreover, Sullivan et al. (1998) found weak associations between the physical QoL composite and psychological symptoms such as nervousness ($r = -0.16$), difficulty in relaxing ($r = -0.15$), irritability ($r = -0.02$), and impaired concentration ($r = -0.10$) (correlation coefficients were negative due to reversed scoring). Another important limitation relates to the recruitment of patients solely from primary care settings, self-referral, or advertisements. This limits the generalization of results to secondary and tertiary care settings. Future studies should attempt at replicating the results of this study in IBS patients receiving higher levels of care. The use of Rome II and Rome III criteria to diagnose and subtype participants, current at the time of recruitment but not presently

(current criteria refers to Rome IV), poses another limitation to this study.

In conclusion, this study provides a closer, although preliminary, examination of the factors that may drive the negative influence of IBS on QoL. It highlights that IBS severity per se only modestly influence QoL, and demonstrates that GI-specific anxiety and depressive symptoms may be of particular relevance for decreased mental QoL in IBS patients, and GI-specific anxiety and non-GI somatic complaints for physical QoL. It is likely that reductions in worry and hypervigilance about GI-related sensations and situations, somatic symptom severity, and/or depressive symptoms, would result in increased well-being in IBS patients with low QoL. Hence, after the corroboration of the current findings using longitudinal methods, future trials should test the efficacy of psychological interventions specifically targeting GI-specific anxiety and addressing depressive and somatic symptoms in improving mental and physical QoL in patients with IBS. Considering previous evidence on the mechanisms of IBS acceptance on the relationship between GI-specific anxiety and QoL, it could be of interest to test the efficacy of third wave cognitive and behavioural therapies such as Acceptance and Commitment Therapy in improving acceptance of GI anxiety and reducing its impact on QoL. To our knowledge, only one pilot study has explored this, with positive results, and more research on the topic is certainly needed [70].

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Data availability statement

Data will be shared upon reasonable request.

Declaration of Competing Interest

Outside of the current work, I.T. has served as a consultant for Pfizer Inc. C.M. has served as a consultant/advisory board member for Kyowa Kirin, Norgine, Biocodex, Mayoly Spindler, Tillots, and Ipsen. M.S. has received unrestricted research grants from Danone Nutricia Research, and Glycom; served as a consultant/advisory board member for Danone Nutricia Research, Ironwood, Menarini, Biocodex, GeneticAnalysis AS, Glycom, Arena, and Adnovate and been on the Speakers' bureau for Tillots, Menarini, Kyowa Kirin, Takeda, Shire, Biocodex, Alimentary Health, Alfasigma, and Falk Foundation.

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