

Impact of irritable bowel syndrome on patients' lives: development and psychometric documentation of a disease-specific measure for use in clinical trials

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Objective To develop a disease-specific questionnaire to capture the impact of irritable bowel syndrome (IBS) and its treatment on patients' lives, the Irritable Bowel Syndrome Impact Scale (IBS-IS).

Patients and methods One hundred and fifty-five IBS patients participated (126 (81%) female; age (mean \pm SD) 45.5 \pm 12.4 years). We developed the initial 39 items from the literature, available IBS-specific instruments and input from physicians, nurses and patients. We deleted IBS-IS items with a high ceiling effect, items that measured a different construct and items showing a high correlation ($r > 0.90$) with another item and with Rasch analysis, leaving 26 items. We then applied exploratory factor analysis to examine domain groupings. Subjects completed the IBS-IS instrument, the Gastrointestinal Symptom Rating Scale for IBS (GSRS-IBS), Short Form-36 (SF-36), Visceral Sensitivity Index (VSI), and Hospital Anxiety and Depression (HAD) scale. Internal consistency, construct validity and discriminate validity were assessed.

Results The 26 items represented five domains: fatigue, impact on daily activities, sleep disturbance, emotional distress and eating habits. The internal consistency reliability for the domains was 0.87 to 0.96. Most

associations between similar constructs in the IBS-IS, GSRS-IBS, SF-36, VSI, and HAD were > 0.40 . Each IBS-IS domain score decreased with increasing IBS symptom severity ($P < 0.05$), and the patients scored > 5 score units lower than a US general population scored on all eight SF-36 dimensions.

Conclusion The IBS-IS is a short, user-friendly instrument with excellent psychometric properties that has potential usefulness for clinical trials. *Eur J Gastroenterol Hepatol* 17:411–420 © 2005 Lippincott Williams & Wilkins

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Introduction

Irritable bowel syndrome (IBS) is one of the most common disorders diagnosed by gastroenterologists and a common cause of general practice visits [1]. The disorder affects approximately 10% of the population in industrialized countries [1,2]. IBS is a major economic burden to society, primarily due to physician visits, diagnostic test and drug costs, and work absenteeism [3–6].

A diagnosis of IBS can usually be made from the Rome II symptom criteria in conjunction with negative results of a physical examination and limited diagnostic tests [7]. The symptoms comprise chronic or recurrent abdominal discomfort or pain, abnormal bowel habit and abdominal bloating. A majority of patients are women, and their age tends to be lower than that of patients with upper gastrointestinal symptoms [8,9]. Etiological structural

pathology is absent, and there are no laboratory markers of disease activity. Health-related quality of life (HRQL) assessment expands patient data beyond symptoms alone, as it measures the impact of disease from a patient's viewpoint. Assessment of HRQL is potentially useful as an outcome measurement in treatment trials [5,10–14]. In fact, the U.S. Food and Drug Administration advises the use of HRQL measurement in trials of IBS treatment [15]. Similarly, the role of HRQL outcome measures in clinical trials is also endorsed by regulators in Europe because IBS clearly has a negative impact on patients' well-being and daily life [16].

Much effort has been directed towards developing validated IBS outcome measures [17]. This review concluded that among available IBS-specific HRQL instruments [18–21] only one [18] measured the impact

of the wide spectrum of IBS symptoms on patients' lives in a reliable, valid and responsive fashion. Other key criteria for a patient-based outcome measure for use in clinical trials are that it be short, easy to administer and interpret, and accurately reflect the aspects of life that are most relevant to patients. The goal of this study was to develop a new disease-specific questionnaire, the Irritable Bowel Syndrome Impact Scale (IBS-IS) instrument, specifically for use in clinical trials, and to evaluate its psychometric properties.

Methods

Initial questionnaire development

We developed the initial items for the questionnaire from a literature review and scrutiny of available IBS-specific instruments [18–23] and discussions with experienced physicians and nurses. The potential items were discussed with IBS patients at group focus meetings, and their concerns were emphasized. Open-ended questions allowed each patient to react to the items, and we prompted patients to disclose additional issues related to IBS symptoms. Items relating to anxiety and psychological stress were included because their importance in IBS is well-documented [24–26]. Sleep disturbance was included, as it is disrupted in IBS patients [27,28]. Highly symptomatic conditions tend to deplete vitality; hence, we included fatigue items. Items depicting the impact of IBS on daily life and daily activities were included, having been described as prominent consequences of IBS [29,30]. Finally, IBS induces dietary restriction and problems eating preferred food [31], so we included eating habit items. We excluded items relating to sexual relations, even though they are important to some patients, because we had previously found a non-completion rate of 20–25% on them [32,33]. Items relating to financial problems were also discarded because they were not relevant to potential treatment outcome research. We also deleted items that were of a mediating nature rather than an outcome measure, such as coping ability. Symptom items are often captured in a separate symptom scale, so we also excluded them.

In the development process, the relevance and wording of the specific items, including the response scale, were tested on patient and expert clinician groups. This process generated 39 preliminary items of well-documented importance: emotional distress, 10; eating problems, seven; impact on activities, seven; fatigue, five; sleep disturbance, four; and other items, six.

Overall study design

We recruited patients from the gastroenterology clinics at the UCLA Neuroenteric Disease Program and the Kaiser Permanente Medical Center in San Diego in order to enroll a diverse patient group, as in our previous experience [34]. The institutional review boards ap-

proved the study. Patients gave written consent to participate and were free to discontinue their participation at any time without prejudice to further treatment. The gastroenterologists obtained a history, performed a physical examination and recorded demographic and clinical data on each patient using a paper case report form.

Patients

Enrollment criteria were: the Rome II symptom criteria [7]; age, 18–65 years; ≥ 2 days of IBS symptoms during the past 7 days; and ability to complete the questionnaires in English.

Measurements

Demographic and clinical data

The gastroenterologists recorded age, gender, employment status, tobacco smoking, duration of IBS symptoms, family history of IBS, use of alternative therapy, symptom severity (mild: can be ignored but does not affect life style; moderate: cannot be ignored but does not affect life style; severe: affects life style; very severe: markedly affects life style), and number of days with at least moderate symptoms during the past 7 days. IBS symptoms other than pain and bowel habit dysfunction, the most bothersome IBS symptom, the predominant bowel habit, fibromyalgia, and urogenital problems were also recorded.

All patients completed our IBS-IS instrument, the Gastrointestinal Symptom Rating scale IBS version (GSRS-IBS), the Visceral Sensitivity Index (VSI), the Hospital Anxiety and Depression (HAD) scale and the Short Form-36 (SF-36).

Irritable Bowel Syndrome Impact Scale

The pilot version of the new instrument had 39 items. A 7-point Likert response scale was used to assess how often ('none of the time' to 'all of the time') each item was present during the past 7 days. A mean item score was used to provide a score from 1 to 7 for each dimension. Responses on a 7-point Likert scale facilitate determining the significance of any differences observed, such as the minimal clinically important difference [35,36].

Gastrointestinal Symptom Rating Scale

The GSRS-IBS is a reliable, valid, disease-specific symptom scale [37]. It includes 13 items in five symptom clusters: abdominal pain, bloating, diarrhoea, constipation and satiety. It measures symptoms during the past 7 days with a 7-point Likert scale ('no discomfort' to 'very severe discomfort'). A mean item score was used to provide a score from 1 to 7 for each dimension.

Visceral Sensitivity Index

The VSI is a recently developed instrument that assesses the sensitivity and anxiety related to IBS-specific

symptoms and situations, represented by 15 items. Responses are scored on a 0 to 5 scale ('strongly disagree' to 'strongly agree'), and an overall dimension (total score) is calculated from 0 to 75 [38]. The responses to negatively worded items are reversed in polarity, such that the higher the level of agreement with the statement, the higher the total VSI.

Hospital Anxiety and Depression Scale

The HAD is a reliable, valid instrument consisting of 14 items, seven each for anxiety and depression, on which the patient rates each item on a 4-point Likert scale [39,40]. Increasing severity of each disorder is indicated by an increasing total score: 7, absent; 8–10, probable cases; and ≥ 11 , definite cases.

Short Form-36

The SF-36 is a reliable [41,42], valid [12], self-administered, generic HRQOL questionnaire containing 36 items. It measures health on eight multi-item dimensions, covering functional status, well-being and overall evaluation of health.

Psychometric evaluation

Standard psychometric principles were applied to test the IBS-IS [43,44]. In item reduction, we considered removing items with the following characteristics: (1) items with a high ceiling effect, which could show little or no improvement; i.e., to which $> 50\%$ patients responded 'not at all'; (2) items measuring a different construct; i.e., those with a low squared multiple correlation ($r < 0.5$) with the other items; and (3) items that showed redundancy of measurement by a high correlation ($r > 0.90$) with another item. Rasch analysis was applied to evaluate person-item threshold distribution, unidimensionality, item separation and linearity. Before items were removed, their clinical importance was considered as judged by the investigating gastroenterologists' opinions on their content validity.

After the initial item reduction, we used factor analysis to explore whether the selected questions grouped into relevant domains or concepts. Hence, an exploratory factor analysis using principal components factor analysis with Varimax orthogonal rotation was performed to identify the underlying domains.

The internal consistency reliability was assessed by Cronbach's alpha. A high alpha coefficient suggests that the items within a domain measure the same construct, which also supports the construct validity [4]. A minimum correlation of 0.70 was necessary, although alpha values above 0.90 are optimal for individual comparisons.

Construct validity was assessed by determining whether similar domains in the various measures (GSRS-IBS, VSI,

HAD and SF-36) had higher correlations with each other than with domains that were not expected to be closely related. The same approach (i.e., correlating the new measure with the SF-36 and other measures) has been used previously in validating IBS-specific questionnaires [18,21,22]. This relationship was tested using correlation coefficients (Pearson's product moment correlation). Strong correlations were considered to be > 0.40 , and all correlations above this limit were statistically significant ($P < 0.0004$) after adjustment for multiple testing (Bonferroni) [45].

We postulated that the IBS-IS scores would worsen as symptom severity increased and we tested its discriminate validity as its ability to discriminate the severity of symptoms using Pearson product moment correlations and comparisons of means with standard deviations. The Jonckheere–Terpstra test was used to detect whether the IBS-IS dimension scores decreased in a symptom-related manner.

Statistical analysis

Continuous data were summarized as mean \pm SD, and statistics were calculated by SAS version 8.02 [46]. P values were adjusted for multiplicity (Bonferroni) [47]. Rasch analysis was performed using RUMM2010 software [48]. In the case of missing data, the mean of the completed items in one dimension was imputed to substitute the missing item, provided $> 50\%$ of the items in one dimension were completed [49].

Results

One hundred fifty-five patients were enrolled: 80 patients were from UCLA Neuroenteric Disease Program and 75 from Kaiser Permanente Medical Center, a managed care setting. Constipation (47%) was the most predominant bowel habit, followed by alternating, 31% and diarrhea 23%. Table 1 shows the demographic and other clinical characteristics.

Item reduction, Rasch analysis and factor analysis

We deleted 13 items from the initial 39-item questionnaire: one sexual activity item; three items with a high correlation with another item (> 0.90) and three with a low squared multiple correlation (< 0.22). Four more items were removed because the factor analysis showed they did not fit with any distinct factors representing the different concepts. Rasch analysis led to deleting two items.

Exploratory factor analysis yielded 5 distinct factors denoting fatigue, impairment of daily activities, sleep disturbance, emotional distress and eating habits. Table 2 shows the factors and their factor loadings. Only items with factor loadings > 0.60 were retained, with the exception of two items (feeling depressed and food appearing unappealing).

Table 1 Demographic and clinical characteristics (n=155)

Age, in years; mean (SD)	45.5 (12.4)
Female, %	81.3
Employment	
Paid employment, %	70.3
Sick pension, %	10.3
Retired, %	10.3
Smoker, %	14.8
Years since first IBS symptom, mean (SD)	15.1 (13.1)
Family history of IBS, %	23.9
Alternative therapy for IBS, %	36.1
Severity of symptoms	
Mild, %	3.9
Moderate, %	33.6
Severe, %	47.1
Very severe, %	15.5
Days of at least moderate symptoms during the past 7 days, mean (SD)	4.3 (2.0)
Non-pain, non-bowel habit symptoms	
Abdominal fullness/bloating, %	88.4
Abdominal distension, %	76.8
Rectal fullness, %	75.5
Fecal urgency, %	77.4
Nausea, %	47.4
Most bothersome IBS symptom	
Abdominal pain, %	26.8
Fecal urgency, %	24.8
Fullness/bloating, %	20.2
Irregular bowel habits, %	15.7
Abdominal distension, %	5.2
Rectal fullness, %	4.6
Nausea	0.6
Predominant bowel habit	
Diarrhea, %	22.6
Constipation, %	47.1
Alternating, %	31.3
Other diagnoses	
Fibromyalgia, %	13.6
Urogenital problems, %	14.8

The final 26-item version required about 10 min to complete.

IBS-IS: intercorrelations of dimensions

The intercorrelation between the IBS-IS domains ranged from 0.50 to 0.78, indicating that the dimensions were associated but still could be regarded as separate constructs (Table 3).

IBS-IS scale by gender

There were no statistically different differences in any of the IBS-IS dimension related to gender. However, the number of male patients was low. There was no relationship to age.

Internal consistency reliability

Each of the 5 IBS-IS dimensions showed high internal consistency (Table 4).

GSRs-IBS and IBS-IS item scores

As shown in Table 5, bloating and pain affected the patients most. In terms of HRQL, the impact of IBS on eating habits, daily activities and emotional distress was most pronounced. Sleep was the least affected area.

Construct validity

The associations between the IBS-IS dimensions and the scores of the GSRs-IBS, SF-36, HAD and VSI, were all in the expected direction and high (Table 6).

Table 2 Irritable Bowel Syndrome Impact Scale (IBS-IS)*

Symptom	Fatigue	Daily activities	Sleep	Emotional	Eating habits
Felt tired	0.78	0.24	0.30	0.22	0.20
Felt worn out	0.78	0.24	0.28	0.27	0.19
Physically worn out	0.76	0.27	0.30	0.28	0.12
Impact energy level	0.76	0.25	0.25	0.30	0.21
Felt generally ill	0.67	0.23	0.29	0.34	0.19
Emotionally worn out	0.63	0.37	0.23	0.41	0.20
Social functioning	0.17	0.77	0.05	0.29	0.14
Avoid social regarding bathroom	0.12	0.73	0.08	0.17	0.23
Concern regarding the unexpected	0.18	0.70	0.05	0.26	0.25
Impact on work	0.38	0.66	0.37	0.05	0.23
Leisure activities	0.35	0.65	0.28	0.24	0.23
Bothered by toilet time	0.15	0.63	0.34	0.18	0.03
Suffering at work	0.41	0.62	0.36	0.07	0.23
Falling back to sleep	0.34	0.20	0.79	0.17	0.12
Awaken from sleep	0.28	0.18	0.79	0.12	0.19
Falling asleep	0.28	0.21	0.76	0.26	0.14
Awaken early	0.21	0.17	0.73	0.34	0.15
Felt angry	0.22	0.19	0.28	0.72	0.20
Frustrated by symptoms	0.35	0.25	0.18	0.71	0.15
Worried about symptoms	0.32	0.35	0.20	0.67	0.31
Symptoms not better	0.36	0.26	0.24	0.66	0.26
Felt depressed	0.42	0.38	0.24	0.58	0.06
Avoided foods	0.12	0.19	0.12	0.13	0.87
Careful eating	0.18	0.21	0.20	0.14	0.83
Worried food is trigger	0.15	0.37	0.04	0.30	0.73
Food unappealing	0.37	0.05	0.38	0.13	0.57
Explained variance	19%	17%	14%	13%	12%

*Factor loadings (correlations between individual items and symptom clusters). Correlations in the range 0.50–0.90 are in bold type.

Table 3 Intercorrelations of Irritable Bowel Syndrome Impact Scale (IBS-IS) subscales

Dimension	Fatigue	Daily activities	Sleep	Emotional	Eating habits
QOLIBS					
Fatigue	–				
Daily activities	0.68				
Sleep	0.72	0.58			
Emotional	0.78	0.70	0.65		
Eating habits	0.58	0.59	0.50	0.60	–

Table 4 Irritable Bowel Syndrome Impact Scale (IBS-IS) subscale internal consistency analysis

Dimension	Cronbach's α coefficient
Fatigue	0.96
Daily activities	0.91
Sleep	0.91
Emotional	0.91
Eating habits	0.87

Table 5 Gastrointestinal Symptom Rating Scale–Irritable Bowel Syndrome (GSRs-IBS) and Irritable Bowel Syndrome Impact Scale (IBS-IS) in IBS patients by dimension ($n=155$)

GSRs-IBS dimensions	Mean (SD)	IBS-IS dimensions	Mean (SD)
Pain	3.9 (2.2)	Fatigue	4.0 (1.5)
Bloating	5.0 (2.4)	Daily activities	3.8 (1.4)
Constipation	3.5 (1.4)	Sleep	4.9 (1.5)
Diarrhea	2.8 (0.9)	Emotional	3.9 (1.5)
Satiety	2.1 (0.7)	Eating habits	3.4 (1.5)

The pain domain of the GSRs-IBS yielded the strongest correlations with all IBS-IS domains. Diarrhea also had a strong impact on most dimensions. The correlations between constipation and the IBS-IS domains were low.

The relationship between the SF-36 and the IBS-IS scores indicated that fatigue was related to all types of dysfunction. The correlations for daily activities, sleep and emotional distress were also high, suggesting that role and mental functioning are closely related to IBS distress and dysfunction. The strongest correlation was found between the SF-36 bodily pain dimension and IBS-IS dimension impact on daily activities. Eating habits had a low association with the SF-36 dimensions except for social functioning.

The HAD classified 33% and 13% as definite anxiety and depression cases, respectively, and 42% and 67% as 'non-cases' of anxiety and depression, respectively. Both the HAD anxiety and depression scores were strongly related with the IBS-IS scores depicting fatigue, sleep and emotion dimensions, as expected.

The VSI mean (SD) score of 18 (43) was highly correlated with all IBS-IS dimensions.

Table 6 Intercorrelation (r values) of Irritable Bowel Syndrome Impact Scale (IBS-IS) subscales with Gastrointestinal Symptom Rating Scale–Irritable Bowel Syndrome (GSRs-IBS), Short Form-36 (SF-36), Hospital Anxiety and Depression Scale (HAD), and Visceral Sensitivity Index (VSI)

Dimension	Fatigue	Daily activities	Sleep	Emotional	Eating habits
GSRs-IBS					
Pain	–0.48	–0.55	–0.36	–0.43	–0.30
Bloating	–0.41	–0.32	–0.19	–0.35	–0.16
Constipation	–0.21	–0.24	–0.16	–0.21	0.01
Diarrhea	–0.43	–0.55	–0.39	–0.38	–0.26
Satiety	–0.46	–0.39	–0.37	–0.41	–0.29
SF-36					
General health	0.51	0.39	0.42	0.42	0.20
Physical functioning	0.50	0.47	0.41	0.40	0.21
Role functioning	0.61	0.49	0.49	0.47	0.38
Role emotional	0.43	0.31	0.41	0.35	0.27
Social functioning	0.58	0.56	0.50	0.48	0.34
Mental functioning	0.47	0.30	0.35	0.41	0.15
Bodily pain	0.57	0.60	0.45	0.48	0.30
Vitality	0.58	0.45	0.39	0.41	0.21
HAD					
Anxiety	–0.51	–0.39	–0.40	–0.54	–0.31
Depression	–0.51	–0.43	–0.36	–0.48	–0.27
VSI					
Total score	–0.55	–0.53	–0.45	–0.67	–0.51

Discriminant validity

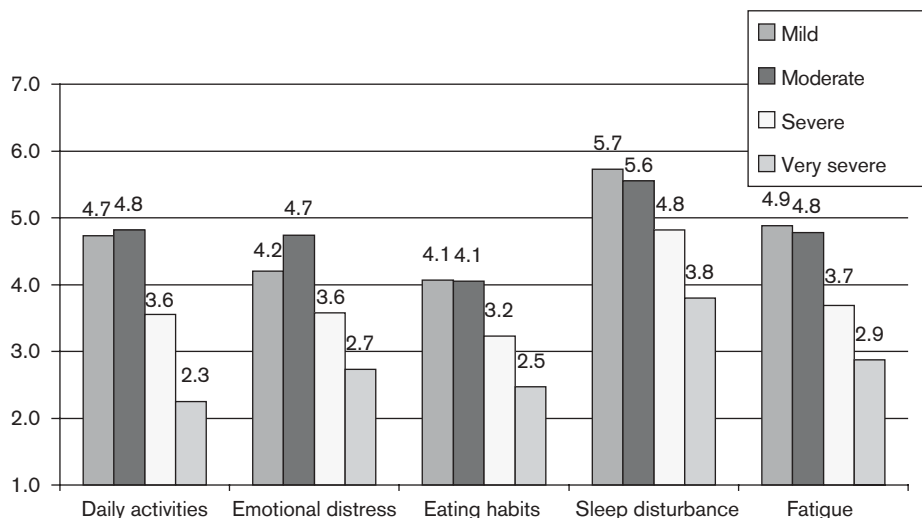
The Jonckheere–Terpstra test revealed that the IBS-IS dimension scores decreased with increasing IBS symptom severity (Fig. 1). The asymptotic P values for each of the IBS-IS dimensions were <0.05 . The corresponding correlation coefficients were 0.36–0.61. The IBS patients scored >5 score units lower on all dimensions of the SF-36 than did a US general population [50,51] (Fig. 2).

Discussion

Interest in HRQL measurement in gastroenterology patients has recently accelerated [52]. Since no morphological or physiological marker for IBS is known, simple and valid measures are needed to characterize the impact of symptoms and measure treatment effects on various aspects of HRQL. Several studies have shown that the HRQL of IBS patients is severely impaired, often greater than in patients with other chronic conditions [11].

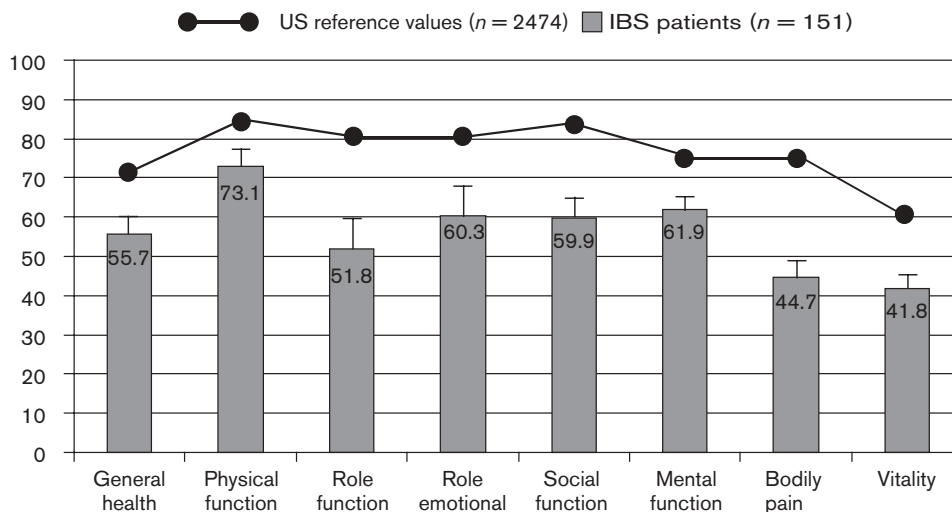
There are many similarities in content among available measures. The impact on well-being and vitality, as well as daily life and physical functioning, are addressed. However, existing IBS-specific HRQL measures are more lengthy and may not be practical to use [18,19], contain a wide range of dimensions that in a clinical trials setting may lead to multiplicity problems [18,19,21], include dimensions addressing mediating factors such as coping rather than outcome measures related to the impact of IBS [53] or are primarily derived from generic concepts [21]. Interpretability and sensitivity in detecting treatment induced changes over time are critical instrument features in a clinical trial context. One of the instruments uses multiple response option and requires

Fig. 1



Irritable Bowel Syndrome Impact Scale (IBS-IS) dimensions and symptom severity.

Fig. 2



Short Form-36 (SF-36) scores in IBS patients compared to US reference values by dimension.

scale transformation which makes it difficult to interpret [21]. Responsiveness is closely related to the number of response options and it has recently been suggested that a 7 grade scale is optimal [54,55]. Two of the instruments use a 5 graded scale [18,19]. Finally, one of the scales integrates the symptom assessment which may not be optimal if the purpose is to address the impact of symptoms on patients' lives with the measurement of the same symptoms. Hence, we recognized the need for another short, simple, reliable and valid measure with a

responsive scale, focusing on the most pronounced impact of IBS, easy to score and using a mean item score which facilitates interpretability, for use in clinical trials.

Validated HRQL instruments can be discriminative; i.e., differentiate levels of HRQL among IBS patients or between IBS patients and another group. Validation of the latter ability would require comparison of scores with those of patients with another disorder, such as inflammatory bowel disease, or with a control group. We aimed

to develop an instrument to measure change in HRQL in response to treatment [56], which could discriminate IBS symptom severity. The IBS-IS is a disease-specific instrument, which demonstrates validity and reliability and has potential for this use.

We used sound psychometric practices to identify the retained items in the final instrument. Rasch analysis, a procedure that has recently been recommended [57,58], was used to facilitate item deletion. Since a 7-point scale is optimal to capture small changes over time, we used this response format [35]. Additionally, an exploratory factor analysis was used to indicate which items combined into relevant aspects of HRQL. We identified five subscales, which capture the connotation of suffering from IBS. The internal consistency of the instrument clearly exceeded the recommended cut-off level [59].

To assess its ability to measure the most relevant problems induced by IBS, we utilized a construct validity process: (1) the domain of measured symptoms was evidence-based (i.e., review of the IBS literature and content analysis of available IBS instruments); and (2) we performed a comparison between validated generic measures such as the 'gold standard' SF-36 as well as another disease-specific measure, the VSI, and the IBS-IS [56]. The IBS-IS related to other measures in an expected way with high correlations between similar constructs. Specifically, the IBS-IS dimension scores were strongly correlated with the HAD and the disease-specific VSI. Similarly, the relevant domains of the GRSR-IBS and, specifically, the pain dimension related to all domains of the IBS-IS dimensions, indicating that pain causes considerable impairment. These associations attest to the convergent validity of the IBS-IS. The discriminant validity, its ability to discriminate by severity of IBS symptoms, supports the clinical relevance of the new questionnaire. The comparison with the reference values in the SF-36 similarly suggests that IBS-IS discriminates in the expected fashion between a random population sample and patients with IBS. The magnitude of differences resemble those of other studies comparing the SF-36 in IBS patients and patients with other disorders [11,14,18,22,60,61], with the most impact on vitality, pain and physical functioning dimensions. Abdominal pain and severity of symptoms have previously been identified as especially important [14,62].

The strong relationship between IBS-IS scores and HAD anxiety and depression scores suggests that the contribution of psychosocial factors is significant and agrees with previous findings [24,25,63]. Furthermore, this relationship supports the notion that there is a small subgroup of patients in whom psychiatric distress represents the primary dysfunction [25]. In clinical trials, it is important that these potentially confounding variables are taken into account.

Previous studies, which have focused on selective IBS symptom clusters such as diarrhea [64] or constipation [65], have provided only equivocal evidence for an effective IBS treatment [66,67]. By providing HRQL data on 5 domains, the IBS-IS has the potential to more comprehensively characterize patients studied in clinical trials using a 7 grade scale. The fact that a validation study was conducted in both primary and secondary care patients represents an advantage since these patients populations have previously been shown to differ [34] and they may also respond differently to therapy. Furthermore, if the IBS-IS is shown to respond to change in a currently ongoing study, this instrument could help establish the most effective therapies for IBS. In summary, the IBS-IS is a short, user-friendly instrument with excellent psychometric properties. Its responsiveness to change in clinical trials needs to be proven, however.

Conflict of interest

None declared.

Authors' contributions

Ingela Wiklund and Jörgen Naesdal originated the study and wrote the first draft of the manuscript. George Longstreth, Emeran Mayer, Lin Chang and Bruce Naliboff obtained demographic, clinical and questionnaire data. George Longstreth edited the manuscript. Jonas Carlsson performed statistical analysis. Roger Bolus served as primary statistician and Károly Kulich provided administrative support.

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Appendix 1

IRRITABLE BOWEL SYNDROME IMPACT SCALE (IBS-IS)

PLEASE READ THIS CAREFULLY BEFORE ANSWERING THE QUESTIONS

On the following pages you will find some questions asking about how you have felt **DURING THE PAST 7 DAYS** due to your IRRITABLE BOWEL SYMPTOMS. These symptoms may include pain, discomfort, diarrhea, constipation, bloating or sense of urgency that you have felt in your LOWER abdomen (below the navel). Please answer all of these questions as honestly as you can. For each question, mark with an X the alternative that best describes how you have been feeling.

How much of the time during the past 7 days...

1. Have your irritable bowel symptoms LIMITED YOUR ABILITY TO SUCCEED AT WORK or YOUR MAIN ACTIVITY?

Response options: a 7-graded scale

All of the time
 Most of the time
 Quite a lot of the time
 Some of the time
 A little of the time
 Hardly any of the time
 None of the time

(Same response options for all the questions)

2. Have you been DEPRESSED about your irritable bowel symptoms?
3. Have you been CAREFUL ABOUT WHAT YOU WERE EATING because of your irritable bowel symptoms?
4. Have your irritable bowel symptoms made you FEEL UNCOMFORTABLE DURING SOCIAL SITUATIONS?
5. Have you been concerned that you COULD NOT FORESEE WHEN TO EXPECT THE NEXT EPISODE of irritable bowel symptoms?
6. Has your WORK or MAIN ACTIVITY SUFFERED because of your irritable bowel symptoms?
7. HAVE YOU BEEN BOTHERED BY THE TIME YOU SPENT ON THE TOILET because of your irritable bowel symptoms?
8. Have you had difficulty in FALLING BACK TO SLEEP because of your irritable bowel symptoms?
9. Have you AVOIDED CERTAIN FOODS because of your irritable bowel symptoms?
10. Have you been WORRIED that your irritable bowel symptoms HAVE NOT GOT BETTER?
11. Have you had DIFFICULTY CARRYING OUT YOUR LEISURE ACTIVITIES because of your irritable bowel symptoms?
12. Have you had TROUBLE IN FALLING ASLEEP because of your irritable bowel symptoms?
13. Have you AVOIDED SOCIAL ACTIVITIES because of the LACK OF BATHROOM FACILITIES?

14. Have your irritable bowel symptoms made you feel **PHYSICALLY WORN OUT**?
15. Have you been **WORRIED ABOUT** your irritable bowel **SYMPTOMS**?
16. Have you **WOKEN UP EARLIER THAN USUAL** due to your irritable bowel symptoms?
17. Have your irritable bowel symptoms made you feel **EMOTIONALLY WORN OUT**?
18. Have you been worried that **WHAT YOU WERE EATING WOULD TRIGGER** your irritable bowel symptoms?
19. **HAVE YOU BEEN ANGRY** about your irritable bowel symptoms?
20. Have your irritable bowel symptoms **AFFECTED YOUR ENERGY**?
21. **HAVE YOU FELT GENERALLY ILL** because of your irritable bowel symptoms?
22. Has **FOOD SEEMED UNAPPEALING** because of your irritable bowel symptoms?
23. Have you been **TIRED** because of your irritable bowel symptoms?
24. Have you been **WORN OUT** because of your irritable bowel symptoms?
25. Have you been **FRUSTRATED** by your irritable bowel symptoms?
26. Have your irritable bowel symptoms **WOKEN YOU FROM SLEEP**?