Project No. 848228

DISCOvERIE

Development, dIagnostic and prevention of gender-related Somatic and mental COmorbitiEs in iRritable bowel syndrome In Europe

Work package 2
Deliverable D2.2

Report on IBS pattern comorbidities in prospectively deeply phenotyped cohort

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Table of contents

List of Abbreviations

GI	Gastrointestinal
IBS	Irritable Bowel Syndrome
CRF	Case Report Form
CFS	Chronic Fatigue Syndrome
GAD7	Generalised Anxiety Disorder 7-item scale
PHQ	Patient Health Questionnaire
IBS-SSS	IBS- Symptom Severity Scale
FIQ	Fibromyalgia Impact Questionnaire
BTQ	Brief Trauma Questionnaire
MFI	Multidimensional Fatigue Inventory
MINI	Mini International Neuropsychiatric Interview
WP	Work Package
SD	Standard deviation

Executive summary

Background

Irritable bowel syndrome (IBS) is one of the most common gastrointestinal diseases. In addition to the already debilitating chronic or recurrent gastrointestinal (GI) symptoms, a significant proportion of IBS patients, up to 60-70%, also report mental (such as anxiety, depression) and somatic (such as fibromyalgia, chronic fatigue syndrome) comorbidities, which seem to influence overall disease severity and outcomes. in addition to GI symptoms. While much has been gained recently in the understanding of the origin of IBS-alone, current knowledge on the aetiology and pathophysiology of comorbid IBS is poor and overtly unproven, rendering strategies for prevention, positive diagnosis, and prognosis unsatisfactory and inefficient due to the lack of sensitive and specific biomarkers.

Aim

In the DISCOvERIE project the overall aim is to understand similarities and differences among patients with IBS with and without comorbidities, and to demonstrate mechanisms underlying these differences and similarities. Specifically in this deliverable report, the aim is to describe the clinical and demographic patterns at baseline of the deeply phenotyped participants that will be extensively studied in this project regarding factors of importance in the gut and the brain for disease severity and outcomes.

Methods

IBS patients fulfilling the latest diagnostic criteria, the Rome IV criteria, and disease controls (i.e. patients with the comorbid conditions, but no IBS), and healthy controls were prospectively recruited at nine European centers. Upon inclusion, the subjects were thoroughly characterized through a clinical interview regarding demographic and disease-related information, health history, medications, hereditary factors, infections, and lifestyle following clinical routines and by using and completing a standardized Case Report Form. Besides, to extensively assess the severity of these comorbidities, the subjects completed a set of validated questionnaires.
For the analyses, participants were divided into groups:

- IBS patients without comorbidities (IBS alone);
- IBS patients with only mental or somatic comorbidities (comorbid IBS);
- IBS patients with both somatic and mental comorbidities (multi-comorbid IBS);
- Disease controls without IBS (with depression and/or anxiety, with chronic fatigue and/or fibromyalgia, and with both mental and somatic disorders);
- Healthy controls.

In this report demographic and clinical aspects, as well as results from questionnaires used to assess severity of GI and overall non-GI somatic symptoms, fibromyalgia, fatigue, anxiety, and depression, as well as significant traumatic events were compared between these groups. In addition, associations between severity of GI and non-GI somatic symptoms, mental symptoms and traumatic events were determined.

Results

In this report, data from 867 subjects were analysed. An overall female predominance (as expected) was seen in the IBS groups, and this was even more clear in the IBS groups with comorbid conditions. A lower level of education and a more absence from work were observed in the groups with comorbid conditions. The use of restrictive diets was commonly seen in IBS, especially among those with comorbid conditions. A tendency towards more reports of allergy as well as a history of COVID-19 were seen in the IBS groups with comorbidities, but also in the disease controls. Medication use was relatively common among subjects, and this was especially seen in the IBS groups with comorbidities and the disease controls for antidepressants, benzodiazepines, anti-epileptics and opioids. IBS symptom severity gradually increased with increasing number of comorbidities. In general, congruent findings in the different groups regarding severity of fatigue, fibromyalgia symptoms, overall somatic symptoms, anxiety and depression were demonstrated, with the highest severity in the groups with the respective comorbidity / morbidity (fatigue, fibromyalgia, anxiety and depression), and the most severe symptoms in the multicomorbid groups. Significant traumatic events were commonly reported, in particular in the multicomorbid groups, but the association with severity of somatic and mental symptoms were modest. The severity of GI, other somatic and mental symptoms were moderately to strongly intercorrelated, with the strongest associations between non-GI somatic and mental symptoms. The same pattern was seen in the total sample and in the individual groups separately (IBS, disease controls and healthy controls)

Conclusion

In conclusion, these results strengthen the importance of mental and somatic comorbid conditions and symptoms in IBS, and their influence on outcomes and disease burden. The large and extremely well characterized group of IBS patients and control groups recruited in this project can now be used to further study the importance of different factors in the gut and the brain for IBS, its comorbidities and disease outcomes, and the relative importance of peripheral vs central factors for symptoms in IBS.

Short Introduction

Irritable bowel syndrome (IBS) is a common chronic functional gastrointestinal (GI) disorder, characterized by abdominal pain, excess gas and diarrhoea or constipation, predominantly seen in young and mid-age females. IBS constitutes 20-50% of the outpatient gastroenterology workload and is regularly encountered in general practice. However, there are a significant number of IBS patients, up to 60-70%, whose clinical severity is greatly magnified by the presence of mental (such as anxiety, depression) and somatic (such as fibromyalgia, chronic fatigue syndrome) comorbidities in addition to the already debilitating GI symptoms. While much has been gained recently in the understanding of the origin of IBS-alone, current knowledge on the aetiology and pathophysiology of comorbid IBS is poor and overtly unproven, rendering strategies for prevention, positive diagnosis, and prognosis unsatisfactory and inefficient due to the lack of sensitive and specific biomarkers.

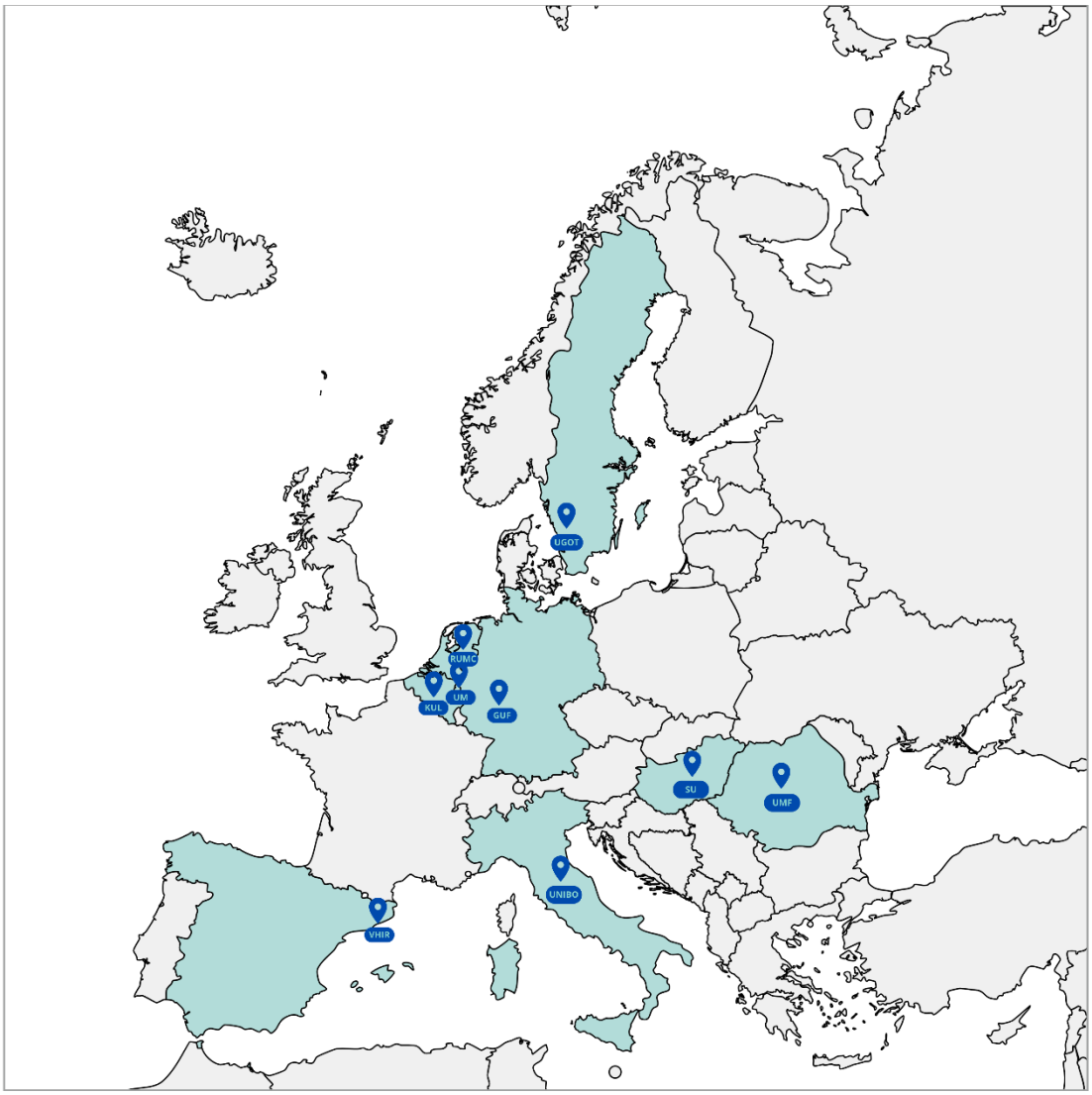
Therefore, in this project the aim is to understand similarities and differences among patients with IBS with and without comorbidities, and to demonstrate mechanisms underlying these differences and similarities. To achieve this, patients with IBS with and without these comorbidities, as well as a small group of healthy control subjects without these conditions, and a group of patients with the comorbid conditions but without IBS, will be included in this pan-European project, with the aim to compare the different aspects within and between the groups. In this deliverable report, the pattern of comorbidities in the recruited participants will be described with focus on clinical and demographic factors determined at baseline in this prospective research program.

Main part

Methods

In order to achieve this, IBS patients fulfilling the latest diagnostic criteria, the Rome IV criteria, and disease controls (i.e. patients with the **comorbid** conditions, but no IBS), and healthy controls were prospectively recruited at nine European centers (UGOT, KUL, VHIR, UNIBO, UM, UMF, RUMS, GUF, SU) (Figure 1).

Figure 1 Geographical distribution of WP2 recruiting centers



The participating centers identified and recruited IBS patients without comorbidities (IBS alone), IBS patients with only mental *or* somatic comorbidities (comorbid IBS), and IBS patients with *both* somatic and mental comorbidities (multi-comorbid IBS). Moreover, disease controls without IBS (with depression and/or anxiety, with chronic fatigue and/or fibromyalgia, and with both mental and somatic disorders) and a small group of healthy controls were also recruited.
Upon inclusion, the subjects were thoroughly characterized through a clinical interview following clinical routines and by using and completing a standardized Case Report Form (CRF; appendix 1) during the interview. In the CRF, information regarding demographic and disease-related information, health history, medications, hereditary factors, infections and lifestyle was collected, together with diagnostic criteria for IBS, i.e. the Rome IV criteria, and psychosocial assessment with validated diagnostic criteria for depression, anxiety (MINI interview), and somatic comorbidities (fibromyalgia and chronic fatigue syndrome). Besides, to extensively assess the severity of these comorbidities, the subjects completed a set of validated questionnaires (see below and appendix 2). The clinical data, as well as the CRF and questionnaires were collected using a multilingual digital platform created for this project (Electronic data capture, CASTOR).

Questionnaires and interview:
The study subjects completed the following self-administered questionnaires and interview-based assessment at baseline. These will be repeated during follow-up (see appendices 1 (CRF) & 2 (questionnaires)):
Case Report Reform based on clinical interview with the information included: patient / subject identification and demographic data, clinical history (IBS- and GI-related; anxiety, depression, fibromyalgia, chronic fatigue syndrome), dietary history, personal and family medical history (general), substance use, medications, clinical Investigations. The diagnoses of IBS, somatic comorbidity, i.e. fibromyalgia or chronic fatigue syndrome (CFS), were determined during the clinical interview, using accepted diagnostic criteria, and presence of the mental comorbid conditions were determined using a structured diagnostic interview (MINI), see below.
***Rome IV Questionnaire, bowel and gastroduodenal modules*:** defines presence of symptoms compatible with functional bowel and gastroduodenal disorders according to the Rome IV criteria.
***IBS Severity Scoring System (IBS-SSS)*:** a five-item questionnaire (visual analogue scales) measuring the severity of IBS symptoms, with cut-off levels to define mild, moderate and severe IBS.
***Patient Health Questionnaire-15 (PHQ-15)*:** assessment of presence and severity of 15 somatic symptoms, used to identify subjects with a risk of and severity of somatoform disorder / somatization, with cut points to define mild, moderate and severe somatic symptom severity.
Generalized Anxiety Disorder 7-Item Scale (GAD-7): anxiety measure including seven anxiety symptoms, with cut-off levels for mild, moderate, and severe anxiety.
Patient Health Questionnaire-9 (PHQ-9): a depression module, which scores each of the nine DSM-IV criteria for depression and can be used to monitor the severity of depression and to make a tentative diagnosis of depression. The questionnaire has cut points for mild, moderate, moderately severe, and severe depression.
***Multidimensional Fatigue Inventory (MFI)*:** a 20-item scale designed to evaluate the severity of fatigue, assessing five dimensions of fatigue: general fatigue, physical fatigue, reduced motivation, reduced activity, and mental fatigue.

***Fibromyalgia Impact Questionnaire (FIQ)*:** measures the severity of fibromyalgia across three domains, i.e. function, overall impact and symptoms.
***The Brief Trauma Questionnaire (BTQ)*:** The BTQ is a brief self- report questionnaire that is derived from the Brief Trauma Interview (Schnurr et al., 1995). The BTQ was originally designed to assess traumatic exposure according to DSM-IV but specifically asked only about Criterion A.1 (life threat/serious injury).
***The Mini International Neuropsychiatric Interview (MINI)*:** a brief structured diagnostic interview for the major psychiatric disorders; it assesses the 17 most common disorders in mental health. For the purpose of this report, the focus was on diagnosing anxiety and depression, to define mental comorbidity as defined previously.

Statistical analysis

All statistics were performed in SPSS version 28. Descriptive statistics were used to analyse the demographic, dietary, and clinical characteristics of the total sample and study groups, and data were presented as mean and standard deviation (SD), or number (n) and proportion (%), as appropriate. Comparison of mean scores of the questionnaires between the participant groups were performed with ANOVA with subsequent postdoc groupwise comparisons with Bonferroni corrections. The A Chi-square test was conducted to analyse differences between groups regarding BTQ (presence vs absence of significant traumatic event). Pearson correlation analyses were performed to analyse associations between the study questionnaires in the total sample, and separately in the IBS patients, the disease controls and the healthy controls, respectively. A Point-Biserial Correlation, a special case of the Pearson correlation, was used to analyse the correlations between BTQ and the remaining questionnaires. In general $p<0.05$ was considered statistically significant.

Results

Subjects

We included 811 participants with complete data at baseline, of which 568 will be followed up longitudinally with re-assessments 1 and 2 years after inclusion (table 1, appendix 3). Relative to the study proposal, a slight over recruitment in the group who will be followed up longitudinally can be noted, and this was due to expected dropouts during follow-up to reach the target of 500 longitudinally followed participants. Recruitment of patients with both mental and somatic comorbidities (IBS Multicomorbid) who were willing to participate in the study was found to be more difficult than expected, so the recruitment in this group was lower than expected / planned, and partly compensated by higher recruitment for some of the other groups. Summarizing graphs of the total recruitment divided into the participants planned for only cross-sectional assessment (i.e. only baseline, no follow-up) and longitudinal assessment (1- and 2-year follow-ups planned) are displayed in appendix 3, figures 2 and 3. For the analyses in this report, we use data from n=867 participants, as we also include participants with valid but incomplete data at baseline, to make this report as comprehensive as possible.

Demographic and clinical factors

The tables for this and the next paragraph are displayed in appendix 4 (tables 2-14). Regarding demographic data, it can be noted that the mean age was similar across the IBS groups, but slightly lower in the healthy controls and higher in the disease controls without IBS (with depression and/or anxiety, with chronic fatigue and/or fibromyalgia, and with both mental and somatic disorders). As expected, there was a female predominance in the IBS groups, and this was even more pronounced in the comorbid and multicomorbid groups. The level of education tended to be lower in the groups (both IBS and disease controls) with somatic comorbidities and in the multicomorbid groups, and in these groups a lower proportion worked full time and a higher proportion were unable to work (table 2). Regarding clinical history of IBS symptoms among the IBS subjects, the duration, or the onset of symptoms (initiating events such as GI infection and surgery) were similar among groups, but there was a tendency towards a larger proportion of IBS patients with comorbid conditions that had visited a physician in secondary / tertiary care for their problems compared to participants with IBS without comorbidities (table 3). Following different restrictive diets were more commonly reported by the IBS patients, and in particular among those with comorbid conditions. In line with this a larger proportion of IBS patients with comorbidities reported that they avoided certain food products due to IBS symptoms and also that they found it to be helpful. Probiotic use was more common among IBS patients overall than among healthy controls or disease controls, and this was most clearly noted in the group with somatic comorbidities and in the multicomorbid group (table 4). In our sample, previous surgical procedures (appendectomy, cholecystectomy and hysterectomy) were not more commonly reported by IBS patients than what was seen in the control groups. Expected differences across groups were noted for previous history of anxiety, depression, fibromyalgia and chronic fatigue. Slight tendencies towards higher proportion of subjects reporting allergy and history of COVID-19 were seen in the comorbid groups (table 5). Among subjects with IBS, a family history of IBS and chronic abdominal symptoms was commonly reported, and this tended to be more common among IBS patients with comorbidities, and the same patterns were seen for family history of anxiety and depression, as well as for fibromyalgia and chronic fatigue (table 6). Alcohol use and smoking was not clearly different among groups (table 7). A variety of different medications were used by the participants, and there was a clear trend toward higher use

of medications in the comorbid groups, which was especially true for antidepressants, benzodiazepines, anti-epileptics and opioids, but there was no clear difference among IBS groups regarding the use of peripherally acting GI pharmacological agents (table 8).

Severity of symptoms related to the comorbid conditions, assessed with questionnaires.

Mean scores of the different questionnaires can be seen in table 9, with posthoc groupwise comparisons (with Bonferroni corrections) in table 10. For all questionnaires, differences across groups were demonstrated.

The IBS symptom severity, measured with IBS-SSS, was higher in the IBS groups compared with the healthy controls and the disease controls groups (i.e. mental and or somatic disorders without IBS), which of course was expected. Among the IBS groups, the most severe IBS symptoms were seen in the group with multiple comorbidities, with significant differences vs the IBS alone and IBS comorbid mental group. The disease control groups had more severe IBS symptoms than the healthy controls.

Regarding fatigue, measured with MFI, and fibromyalgia severity, measured with FIQ, a general pattern with the most severe symptoms in the groups (both the IBS groups and the disease control groups) where somatic morbidity / comorbidity was present (i.e IBS comorbid somatic, IBS multicomorbid, control somatic and control somatic + mental). IBS patients with only mental comorbidity reported more severe fatigue and fibromyalgia symptoms than IBS alone. Healthy controls reported the lowest level of fatigue and fibromyalgia symptoms, significantly lower than all other groups. For overall somatic symptoms, measured with PHQ-15, the same pattern as for fatigue and fibromyalgia symptoms were seen, except for higher overall somatic symptom severity in the IBS multcomorbid than in the disease somatic + mental control group (without IBS), which most likely can be explained of the inclusion of three GI symptoms in PHQ-15.

Severity of anxiety, measured with GAD-7, and depression, measured with PHQ-9, were highest in the groups (both the IBS groups and the disease control groups) where mental morbidity / comorbidity was present (i.e IBS comorbid mental, IBS multicomorbid, control mental and control somatic + mental), with the multicomorbid groups demonstrating the most severe anxiety and depression symptoms. This pattern was more distinct in the IBS group and tended to be more evident for depression than for anxiety. IBS patients with only somatic comorbidity reported similar severity of anxiety as the group with IBS alone, whereas the levels of depression tended to be higher. Healthy controls reported the lowest levels of anxiety and depression, significantly lower than all other groups.

In the BTQ, the participants report absence (score 0) or presence (score 1) of significant traumatic events. Differences in the proportion of subjects reporting significant traumatic events were noted across groups, being most common in groups with mental comorbidity / morbidity and in the multicomorbid groups (table 11).

In the total sample, significant correlations were seen between all questionnaires, except for BTQ and IBS-SSS. Small to medium correlations were observed between IBS symptom severity and the other questionnaires, except for a strong correlation with overall somatic symptom severity. Small correlations were noted between BTQ and the other questionnaires. Between all the other questionnaires (severity of anxiety, depression, fatigue, fibromyalgia and overall somatic symptoms) strong correlations were seen (table 12). Similar patterns were seen when performing the correlation analyses separately in the IBS patients (table 13), the disease controls (table 14) and the healthy controls (table 15).

Summary and Conclusion

- An overall female predominance (as expected) in the IBS groups, and this was even more seen in the IBS groups with comorbid conditions.
- Lower level of education and a more absence from work in the groups with comorbid conditions
- The use of restrictive diets was commonly seen in IBS, especially among those with comorbid conditions.
- A tendency towards more reports of allergy as well as a history of COVID-19 were seen in groups with comorbidities.
- Medication use was relatively common among subjects, and this was especially seen in the groups with comorbidities for antidepressants, benzodiazepines, anti-epileptics and opioids.
- IBS symptom severity demonstrated a gradual increase with increasing number of comorbidities.
- In general, congruent findings in the different groups regarding severity of fatigue, fibromyalgia symptoms, overall somatic symptoms, anxiety and depression were demonstrated, with the highest severity in the groups with the respective comorbidity / morbidity (fatigue, fibromyalgia, anxiety and depression), and the most severe symptoms in the multicomorbid groups.
- Significant traumatic events were commonly reported, in particular in the multicomorbid groups. The association with severity of somatic and mental symptoms were modest.
- The severity of GI, other somatic and mental symptoms were moderately to strongly intercorrelated, with the strongest associations between non-GI somatic and mental symptoms.

In conclusion, these results strengthen the importance of comorbid mental and somatic conditions and symptoms in IBS, and their influence on outcomes and disease burden. The large and extremely well-characterized group of IBS patients and control groups recruited in this project can now be used to further study the importance of different factors in the gut and the brain for IBS, its comorbidities and disease outcomes, and the relative importance of peripheral vs central factors for symptoms in IBS. We believe that this will be of great importance when actively treating these patients, trying to improve their quality of life.

Author contribution

The work of this report is a joint effort by the DISCOvERIE Consortium. The leader of WP2, Prof Magnus Simrén has together with his collaborators, in particular Dr Ines Trindade and Medical student Mahrukh Kahdija, and with close support from Consuelo Cammarota (Project Manager) and Dr Amanda Rodriguez-Urrutia (WP2 Co-Leader), prepared the database, analysed the information from the contributing centres, and prepared the report. Access to data in the cohorts have been granted from nine different centres, UGOT, KUL, VHIR, UNIBO, UM, UMF, RUMS, GUF, SU.

CRF Patient version

1. Patient identification and demographic data

Initials : ……..
Date completed : …….
Date of birth (D/M/Y) : ……/……/…….
Hospital patient number: ……
Gender : M / F/ Other

Ethnic Origin
Country of origin of maternal grandparents:
Grandmother _____ Grandfather_____

Country of origin of paternal grandparents:
Grandmother _____ Grandfather_____

Drop down:

- Albania	- Liechtenstein
- Andorra	- Lituania
- Armenia	- Luxemburg
- Austria	- Macedonia
- Azerbaidzhan	- Malta
- Belarus	- Moldova
- Belgium	- Monaco
- Bosnia and Herzegovina	- Montenegro
- Bulgaria	- Netherlands
- Croatia	- Norway
- Cyprus	- Ukraine
- Czech Republic	- Poland
- Denmark	- Portugal
- Estonia	- Romania
- Finland	- Russia
- France	- San Marino
- Germany	- Serbia
- Georgia	- Slovenia
- Greece	- Slowakia
- Greenland	- Spain
- Hungary	- Sweden
- Ireland	- Switzerland
- Iceland	- Turkey
- Italy	- United Kingdom
- Kazakhstan	- Vatican City
- Latvia	- Unknown - Not European

Were you born by caesarian section? □ no □ yes
Were you breastfed in the first 6 months of life? □ no □ yes

Education:
- □ No University degree
- □ University degree
- □ Doctoral studies (PhD)

Present work status:
- □ Full-time
- □ Part-time
- □ Student
- □ Full time home maker (taking care of family at home)
- □ Unable to work since at least 1 month, but less than 1 year
- □ Unable to work since more than 1 year (disability)
- □ Unemployed (not due to health problem)
- □ Work shifts (day/night □; morning/afternoon □)
- □ Retired

Recruited from:
- □ Primary care
- □ Secondary care
- □ Tertiary care
- □ Public advertisement

2. Clinical history

What is the frequency of your symptoms? :

- O never
- O at least 3 times/month
- O less than 1 day/week
- O 1-2 days/week
- O ≥3 days/week
- O every day
- O unknown

During the first period of your IBS complaints, did symptoms start:

- O acute
- O gradually
- O unknown

Onset of your symptoms:

- ☐ gastrointestinal infection
- ☐ Other infection ……
- ☐ Stressful life event / psychological trauma
- ☐ antibiotics
- ☐ abdominal surgery
- ☐ not clear
- ☐ Change of diet ; If yes, when?
- ☐ Other, specify .....____

What is the duration of your IBS symptoms (time since onset of first symptoms)? :
……(months)

Have you previously attended a physician for your problem (more than 1 option possible)? If so:

- ☐ Primary
- ☐ Secondary
- ☐ Tertiary

ROME IV IBS criteria bowel module:

Did the patient have **recurrent abdominal pain** on average at least 1 day/week in the last 3 months with symptom onset at least 6 months prior to diagnosis, **associated with *two or more* of the following**? (Please indicate which criteria are fulfilled, more options are possible):

- ☐ Related to defecation
- ☐ Associated with a change in frequency of stool
- ☐ Associated with a change in form (appearance) of stool

If the Rome IV criteria for IBS are not fulfilled, exclude patient from study.

Other symptoms:

- ☐ Abnormal stool passage (straining, urgency, or feeling of incomplete evacuation)
- ☐ Passage of mucus
- ☐ Bloating or feeling of abdominal distension
- ☐ Flatulence

Evoking factors: Food intake ☐ no ☐ yes
Stress ☐ no ☐ yes
Other ……..

Alarm symptoms/red flags:

Anemia	☐ no	☐ yes
Age at onset above 45	☐ no	☐ yes
Unintentional weight loss (4.5kg past 3 months)	☐ no	☐ yes
Nocturnal symptoms	☐ no	☐ yes
Rectal blood	☐ no	☐ yes
Family history of colorectal cancer	☐ no	☐ yes
Fever	☐ no	☐ yes

→**If red flag: colonoscopy is required. Patient can only be included if colonoscopy is normal.**

3. Dietary history

Do you follow any special diet (select one or more)? If yes, since when?

- ☐ gluten-free
- ☐ vegetarian
- ☐ vegan
- ☐ lactose free
- ☐ low carbohydrate – high fat
- ☐ high fiber
- ☐ FODMAP ("Fermentable, Oligo-, Di-, Mono-saccharides and Polyols")
- ☐ Other: _____

Do you follow dietary restrictions because of your IBS symptoms? ☐ no ☐ yes

Do you avoid certain food products? ☐ no ☐ yes
If yes, which food products:…….
If yes, does it help your IBS symptoms? ☐ no ☐ yes

Do you use pre-/probiotics on a regular basis? ☐ no ☐ yes

4. Personal history

Appendectomy	:	☐ no	☐ yes
Cholecystectomy	:	☐ no	☐ yes
Hysterectomy	:	☐ no	☐ yes ☐ NA
Other abdominal surgery:		☐ no	☐ yes
Mental disorders	:	☐ no	☐ yes
Anxiety		☐ no	☐ yes

Depression ☐ no ☐ yes
Other ☐ no ☐ yes

Other relevant disease : ☐ no ☐ yes
Fibromyalgia : ☐ no ☐ yes
Chronic fatigue (> 6 months): ☐ no ☐ yes

Does the patient suffer from an allergy :
- skin ☐ no ☐ yes
- food ☐ no ☐ yes
- ENT ☐ no ☐ yes

5. Family history

IBS ☐ no ☐ yes
if yes, specify: ☐ first degree relative
☐ second degree relative
Chronic abdominal symptoms (Pain, diarrhea, constipation)
if yes, specify: ☐ first degree relative
☐ second degree relative

Crohn's disease: ☐ no ☐ yes
if yes, specify: ☐ first degree relative
☐ second degree relative

Ulcerative colitis: ☐ no ☐ yes
if yes, specify: ☐ first degree relative
☐ second degree relative
MENTAL DISORDERS
Depression
if yes, specify: ☐ first degree relative
☐ second degree relative
Anxiety ☐ no ☐ yes
if yes, specify: ☐ first degree relative
☐ second degree relative
Other ☐ no ☐ yes
if yes, specify: ☐ first degree relative
☐ second degree relative
SOMATIC DISORDERS
Fibromyalgia: ☐ no ☐ yes
if yes, specify: ☐ first degree relative
☐ second degree relative
Chronic fatigue (> 6 months): ☐ no ☐ yes
if yes, specify: ☐ first degree relative
☐ second degree relative

Do you have a twin sibling? ☐ no ☐ yes
If yes, do you have an identical twin sibling? ☐ no ☐ yes
If yes, does he/she have abdominal symptoms? ☐ no ☐ yes
Does a first degree relative have abdominal symptoms? ☐ no ☐ yes

6. Substance use

Alcohol ☐ no ☐ yes …… units /week
Smoking ☐ no ☐ yes …… cigarettes/day, ……..pack years
Drugs ☐ no ☐ yes, specify: main classes: Drop down:
- Speed
- LSD
- Cannabis
- Marihuana

- Opiates (Morfin, Heroïn,…)
- Cocaine
- Extasis
- Ketamin
- Methadone
- Other

2010 American College of Rheumatology Diagnostic Criteria Modified for **Fibromyalgia**

A patient meets the modified ACR 2010 criteria for Fibromyalgia if he meets the following conditions:

1. Generalized Pain Index (GDI) ≥7 and Symptom Severity Scale (EGS) ≥5 or GDI of 4-6 and EGS≥9 ☐

2. Symptoms must be present for at least 3 months ☐

3. The patient has no other disorder that can explain the pain ☐

Generalized Pain Index (GDI) (1 point for each area; score: 0-19)

Put a cross over each area in which you have felt pain during the past week, keeping in mind that you should not include pain caused by other diseases that you suffer (osteoarthritis, tendinitis, etc.)

		Left	Right
Scapular Waist		☐	☐
Upper Half Arm		☐	☐
Lower Half Arm		☐	☐
Hip		☐	☐
Upper Half Leg		☐	☐
Lower Half Leg		☐	☐
Mandible		☐	☐
Chest (Thorax)	☐		
Abdomen	☐		
Upper Half Back	☐		
Lower Half Back	☐		
Neck	☐		

Symptom severity scale (EGS) (Score: 0-12 points)

2. Indicate with a cross the severity of these symptoms during the past week, using the following scales, which are scored from 0 (mild) to 3 (severe):

- It has not been a problem
- Mild, occasional problem
- Moderate problem, almost always present
- Serious, ongoing, persistent problem

	NO	MILD	MODERATE	SEVERE
POINTS	**0**	**1**	**2**	**3**
A. FATIGUE	☐	☐	☐	☐
B. NON-RESTORATIVE SLEEP	☐	☐	☐	☐
C. COGNITIVE DISORDERS	☐	☐	☐	☐

Check the appropriate box if you have suffered one of the symptoms during the last **6 months**:

	NO	YES
POINTS	**0**	**1**
A. HEADACHE	☐	☐
B. PAIN OR WIRES IN THE LOWER PART OF THE ABDOMEN	☐	☐
C. DEPRESSION	☐	☐

CHRONIC FATIGUE SYMPTOMS

Diagnosis requires that the patient have the following three symptoms:

1. A substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social, or personal activities, that persists for more than 6 months and is accompanied by fatigue, which is often profound, is of new or definite onset (not lifelong), is not result of ongoing excessive exertion, and is not substantially alleviated by rest, and ☐
2. Post-exertional malaise*, and ☐
3. Unrefreshing sleep* ☐

At least one of the two following manifestations is also required:

1. Cognitive impairment* or ☐
2. Orthostatic intolerance ☐

---

* Frequency and severity of symptoms should be assessed. The diagnosis of ME/CFS should be questioned if patients do not have these symptoms at least half of the time with moderate, substantial, or severe intensity.

7. Medical history

Recent medication (last 3 months)

	Name	dose	indication	Start date?	Stop date?
Antidepressant ISRS TCAs ISRSN Heterocyclics Other					
NSAIDs (incl aspirin)					
Antibiotics					
Probiotics (capsulated or shots)					
Laxatives					
Acid suppressants					
Antispasmodic					
Antidiarrheal drugs					
Fytotherapy					
Prokinetic					
Linaclotide					
Lubiprostone					
Benzodiazepines					
Antipsychotics					
Antiepileptics					
Other					

8. Investigations:

Blood analysis:

Hb? ☐ no ☐ yes
date: ...../...../.....

CRP? ☐ no ☐ yes
date: ...../...../.....

TSH? ☐ no ☐ yes
date: ...../...../.....

transglutaminase antibodies/IgA values ☐ no ☐ yes
date: ...../...../.....

IF NO: EXCLUDE patient

Coproculture: date: ...../...../.....

Giardiasis (D-IBS): ☐ no ☐ yes ☐ not performed

IF YES: EXCLUDE patient

Lactose maldigestion:

Symptoms improved following lactose free diet (6 weeks): ☐ no ☐ yes

IF YES: EXCLUDE patient

Endoscopy

☐ upper endoscopy: date: ...../...../..... ☐ no ☐ yes ☐ not performed
If yes, significant macroscopic abnormalities: ☐ no ☐ yes
If yes, significant microscopic abnormalities: ☐ no ☐ yes

☐ colonoscopy: date: ...../...../..... ☐ no ☐ yes ☐ not performed
If yes, significant macroscopic abnormalities: ☐ no ☐ yes
If yes, significant microscopic abnormalities: ☐ no ☐ yes

☐ sigmoidoscopy: date: ...../...../..... ☐ no ☐ yes ☐ not performed
If yes, significant macroscopic abnormalities: ☐ no ☐ yes
If yes, significant microscopic abnormalities: ☐ no ☐ yes

IF YES: consider EXCLUSION of patient

FECAL SAMPLES: Calprotectin ☐ no ☐ yes ☐ not performed
If yes, significant abnormality: ☐ no ☐ yes

IF YES: consider EXCLUSION of patient

Elastase ☐ no ☐ yes ☐ not performed
If yes, significant abnormality: ☐ no ☐ yes

IF YES: consider EXCLUSION of patient

9. Clinical examination

Weight : _____(kg)
Height : _____(m)
BMI (Body Mass Index) : _____
Blood pressure : Systolic _____ (mmHg)
: Diastolic _____ (mmHg

IBS QUESTIONNAIRE

INSTRUCTIONS

This form is designed to enable us to record and monitor the severity of your IBS. It is to be expected that your symptoms might vary over time, so please try to answer the questions based on how you currently feel (i.e. over the last 10 days or so). All information will be kept in **strict** confidence.

1. For questions where a number of different responses are a possibility please circle the response appropriate to you.

2. Some questions will require you to write in an appropriate response.

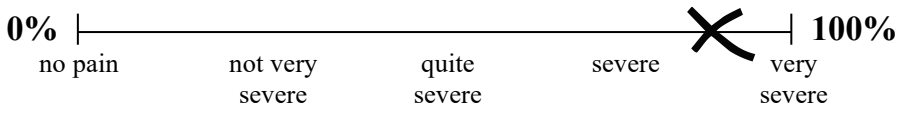
3. Some questions require you to put an x on a line which enables us to judge the severity of a particular problem.

For example:

How severe was your pain?

Please place your x (X) anywhere on the line between 0-100%
in order to indicate as accurately as possible the severity of your symptom.

This example shows a severity of approximately 90%.



PART 1: SEVERITY SCORE

For office use only

SCORE

1. a) Do you currently suffer from abdominal (tummy) pain? **YES** **NO**

Circle appropriate box

b) If yes, how severe is your abdominal (tummy) pain?

0% ├──────────────────────────────────────┤ **100%**

no pain | not very severe | quite severe | severe | very severe

c) Please enter the number of days that you get the pain in every 10 days.

For example if you enter 4 it means that you get pain 4 out of 10 days. If you get pain every day enter 10.

Number of days with pain _____ x10

2. a) Do you currently suffer from abdominal distension* (bloating, swollen or tight tummy) **YES** **NO**

Circle appropriate box

*(*women, please ignore distension related to your periods)*

b) If yes, how severe is your abdominal distension/tightness?

0% ├──────────────────────────────────────┤ **100%**

no distension | not very severe | quite severe | severe | very severe

3. How satisfied are you with your bowel habit?

0% ├──────────────────────────────────────┤ **100%**

very happy | quite happy | unhappy | very unhappy

4. Please indicate with an x on the line below how much your Irritable Bowel Syndrome is affecting or interfering with your life in general

0% ├──────────────────────────────────────┤ **100%**

not at all | not much | quite a lot | completely

National Center for PTSD
POSTTRAUMATIC STRESS DISORDER

Brief Trauma Questionnaire (BTQ)

Version date: 1999

Reference: Schnurr, P., Vielhauer, M., Weathers, F., & Findler, M. (1999). *The Brief Trauma Questionnaire (BTQ)* [Measurement instrument]. Available from http://www.ptsd.va.gov

URL: http://www.ptsd.va.gov/professional/assessment/te-measures/brief_trauma_questionnaire_btq.asp

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Brief Trauma Questionnaire

The BTQ is a brief self- report questionnaire that is derived from the Brief Trauma Interview (Schnurr et al., 1995). (Information about the reliability and validity of the BTI is provided in Schnurr et al., 2002). The BTQ was originally designed to assess traumatic exposure according to *DSM-IV* but specifically asked only about Criterion A.1 (life threat/serious injury) because of the difficulty of accurately assessing A.2 (subjective response) in a brief self- report format. Criterion A.2 has been eliminated from the PTSD diagnostic criteria in DSM- 5, so the BTQ provides a complete assessment of Criterion A.

The questionnaire may be used to determine whether an individual has had an event that meets the A Criterion, or to determine the different types of Criterion A events an individual has experienced. In either case, exposure to an event should be scored as positive if a respondent says yes to either:

- life threat or serious injury for events 1- 3 and 5- 7;
- life threat for event 4;
- serious injury for event 8, or;
- "Has this ever happened to you?" for events 9 and 10.

Information about the BTQ appears in the following articles:

Koenen, K.C., De Vivo, I., Rich- Edwards, J., Smoller, J.W., Wright, R.J., & Purcell, S.M. (2009). Protocol for investigating genetic determinants of posttraumatic stress disorder in women from the Nurses' Health Study II. *BMC Psychiatry, 9* (article 29).

Kubzansky, L. D., Bordelois, P., Jun, H. J., Roberts, A. L., Cerda, M., Bluestong, N., & Koenen, K. C. (2014). The weight of traumatic stress: A prospective study of posttraumatic stress disorder symptoms and weight status in women. *JAMA Psychiatry, 71*, 44-51.

Lancaster, S.L., Melka, S.E., & Rodriguez, B.F. (2009). A factor analytic comparison of five models of PTSD symptoms. *Journal of Anxiety Disorders, 23*, 269- 274.

Morgan, C.A., III, Doran, A.P., Steffians, G., Hazlett, G.,& Southwick, S. (2006). Stress- induced deficits in working memory and visuo- constructive abilites in special operations soldiers. *Biological Psychiatry, 60*, 722- 729.

Morgan, C.A., III, Hazlett, G., Wang, S., Richardson, E.G., Jr., Schnurr, P.P., & Southwick, S.M. (2001). Symptoms of dissociation in humans experiencing acute, uncontrollable stress: A prospective investigation. *American Journal of Psychiatry, 158*, 1239- 1247.

Morgan, C.A., III, Rasmusson, A.M., Winters, B., Hauger, R.L., Morgan, J., Hazlett, G., & Southwick, S.M. (2006). Trauma exposure rather than posttraumatic stress disorder is associated with reduced baseline plasma neuropeptide- Y levels. *Biological Psychiatry, 54*, 1087- 1091.

Schnurr, P.P., Spiro, A. III, Vielhauer, M.J., Findler, M.N., & Hamblen, J.L. (2002). Trauma in the lives of older men: Findings from the Normative Aging Study. *Journal of Clinical Geropsychology, 8*, 175- 187.

Whealin, J.M., Batzer, W.B., Morgan, C.A. III, Schnurr, P.P., & Friedman, M.J. (2007). Cohesion, burnout, and past trauma in Tri- Service medical and support personnel. *Military Medicine, 172*, 266- 272.

Brief Trauma Questionnaire

The following questions ask about events that may be extraordinarily stressful or disturbing for almost everyone. Please circle "Yes" or "No" to report what has happened to you.

If you answer "Yes" for an event, please answer any additional questions that are listed on the right side of the page to report: (1) whether you thought your life was in danger or you might be seriously injured; and (2) whether you were seriously injured.

If you answer "No" for an event, go on to the next event.

Event	Has this ever happened to you?	If the event happened, did you think your life was in danger or you might be seriously injured?	If the event happened, were you seriously injured?
1. Have you ever served in a war zone, or have you ever served in a noncombat job that exposed you to war-related casualties (for example, as a medic or on graves registration duty?)	No Yes	No Yes	No Yes
2. Have you ever been in a serious car accident, or a serious accident at work or somewhere else?	No Yes	No Yes	No Yes
3. Have you ever been in a major natural or technological disaster, such as a fire, tornado, hurricane, flood, earthquake, or chemical spill?	No Yes	No Yes	No Yes
4. Have you ever had a life-threatening illness such as cancer, a heart attack, leukemia, AIDS, multiple sclerosis, etc.?	No Yes	No Yes	*N/A*
5. Before age 18, were you ever physically punished or beaten by a parent, caretaker, or teacher so that: you were very frightened; or you thought you would be injured; or you received bruises, cuts, welts, lumps or other injuries?	No Yes	No Yes	No Yes
6. Not including any punishments or beatings you already reported in Question 5, have you ever been attacked, beaten, or mugged by anyone, including friends, family members or strangers?	No Yes	No Yes	No Yes
7. Has anyone ever made or pressured you into having some type of unwanted sexual contact? Note: By sexual contact we mean any contact between someone else and your private parts or between you and some else's private parts	No Yes	No Yes	No Yes
8. Have you ever been in any other situation in which you were seriously injured, or have you ever been in any other situation in which you feared you might be seriously injured or killed?	No Yes	*N/A*	No Yes
9. Has a close family member or friend died violently, for example, in a serious car crash, mugging, or attack?	No Yes	*N/A*	No Yes
10. Have you ever witnessed a situation in which someone was seriously injured or killed, or have you ever witnessed a situation in which you feared someone would be seriously injured or killed? Note: Do not answer "yes" for any event you already reported in Questions 1-9	No Yes	*N/A*	*N/A*

GAD-7

Over the last 2 weeks, how often have you been bothered by the following problems? *(Use "✔" to indicate your answer)*	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Having trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid, as if something awful might happen	0	1	2	3

(*For office coding: Total Score T____* = ____ + ____ + ____)

MFI® MULTIDIMENSIONAL FATIGUE INVENTORY

Instructions:

By means of the following statements we would like to get an idea of how you have been feeling **lately**. There is, for example, the statement:

"I FEEL RELAXED"

If you think that this is **entirely true**, that indeed you have been feeling relaxed lately, please, place an **X** in the extreme left box; like this:

yes, that is true ☒1 ❑2 ❑3 ❑4 ❑5 **no, that is not true**

The more you **disagree** with the statement, the more you can place an **X** in the direction of "no, that is not true". Please do not miss out a statement and place only one **X** in a box for each statement.

1	I feel fit.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
2	Physically, I feel only able to do a little.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
3	I feel very active.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
4	I feel like doing all sorts of nice things.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
5	I feel tired.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
6	I think I do a lot in a day.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
7	When I am doing something, I can keep my thoughts on it.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
8	Physically I can take on a lot.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
9	I dread having to do things.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
10	I think I do very little in a day.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
11	I can concentrate well.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
12	I am rested.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
13	It takes a lot of effort to concentrate on things.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
14	Physically I feel I am in a bad condition.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
15	I have a lot of plans.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
16	I tire easily.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
17	I get little done.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
18	I don't feel like doing anything.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
19	My thoughts easily wander.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true
20	Physically I feel I am in an excellent condition.	yes, that is true	❑1	❑2	❑3	❑4	❑5	no, that is not true

Thank you very much for your cooperation

PHYSICAL SYMPTOMS (PHQ-15)

During the past 4 weeks, how much have you been bothered by any of the following problems?

	Not bothered at all (0)	Bothered a little (1)	Bothered a lot (2)
a. Stomach pain	☐	☐	☐
b. Back pain	☐	☐	☐
c. Pain in your arms, legs, or joints (knees, hips, etc.)	☐	☐	☐
d. Menstrual cramps or other problems with your periods ***WOMEN ONLY***	☐	☐	☐
e. Headaches	☐	☐	☐
f. Chest pain	☐	☐	☐
g. Dizziness	☐	☐	☐
h. Fainting spells	☐	☐	☐
i. Feeling your heart pound or race	☐	☐	☐
j. Shortness of breath	☐	☐	☐
k. Pain or problems during sexual intercourse	☐	☐	☐
l. Constipation, loose bowels, or diarrhea	☐	☐	☐
m. Nausea, gas, or indigestion	☐	☐	☐
n. Feeling tired or having low energy	☐	☐	☐
o. Trouble sleeping	☐	☐	☐

(*For office coding: Total Score T*_____ = _____ + _____)

PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems? *(Use "✔" to indicate your answer)*	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

FOR OFFICE CODING *0* **+** _____ **+** _____ **+** _____

=Total Score: _____

If you ticked any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	**Somewhat difficult**	**Very difficult**	**Extremely difficult**
☐	☐	☐	☐

The Revised Fibromyalgia Impact Questionnaire

Domain 1 directions: For each of the following nine questions, check the one box that best indicates how much your fibromyalgia made it difficult to do each of the following activities over the past 7 days:

Brush or comb your hair	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult
Walk continuously for 20 minutes	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult
Prepare a homemade meal	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult
Vacuum, scrub, or sweep floors	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult
Lift and carry a bag full of groceries	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult
Climb one flight of stairs	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult
Change bed sheets	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult
Sit in a chair for 45 minutes	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult
Go shopping for groceries	No difficulty ☐☐☐☐☐☐☐☐☐☐☐ Very difficult

Domain 2 directions: For each of the following two questions, check the one box that best describes the overall impact of your fibromyalgia over the past 7 days:

Fibromyalgia prevented me from accomplishing goals for the week	Never ☐☐☐☐☐☐☐☐☐☐☐ Always
I was completely overwhelmed by my fibromyalgia symptoms	Never ☐☐☐☐☐☐☐☐☐☐☐ Always

Domain 3 directions: For each of the following 10 questions, check the one box that best indicates the intensity of your fibromyalgia symptoms over the past 7 days:

Please rate your level of pain	No pain ☐☐☐☐☐☐☐☐☐☐☐ Unbearable pain
Please rate your level of energy	Lots of energy ☐☐☐☐☐☐☐☐☐☐☐ No energy
Please rate your level of stiffness	No stiffness ☐☐☐☐☐☐☐☐☐☐☐ Severe stiffness
Please rate the quality of your sleep	Awoke rested ☐☐☐☐☐☐☐☐☐☐☐ Awoke very tired
Please rate your level of depression	No depression ☐☐☐☐☐☐☐☐☐☐☐ Very depressed
Please rate your level of memory problems	Good memory ☐☐☐☐☐☐☐☐☐☐☐ Very poor memory
Please rate your level of anxiety	Not anxious ☐☐☐☐☐☐☐☐☐☐☐ Very anxious
Please rate your level of tenderness to touch	No tenderness ☐☐☐☐☐☐☐☐☐☐☐ Very tender
Please rate your level of balance problems	No imbalance ☐☐☐☐☐☐☐☐☐☐☐ Severe imbalance
Please rate your level of sensitivity to loud noises, bright lights, odors, and cold	No sensitivity ☐☐☐☐☐☐☐☐☐☐☐ Extreme sensitivity

Scoring: Step 1. Sum the scores for each of the three domains (function, overall, and symptoms). Step 2. Divide domain 1 score by three, divide domain 2 score by one (that is, it is unchanged), and divide domain score 3 by two. Step 3. Add the three resulting domain scores to obtain the total Revised Fibromyalgia Impact Questionnaire score.

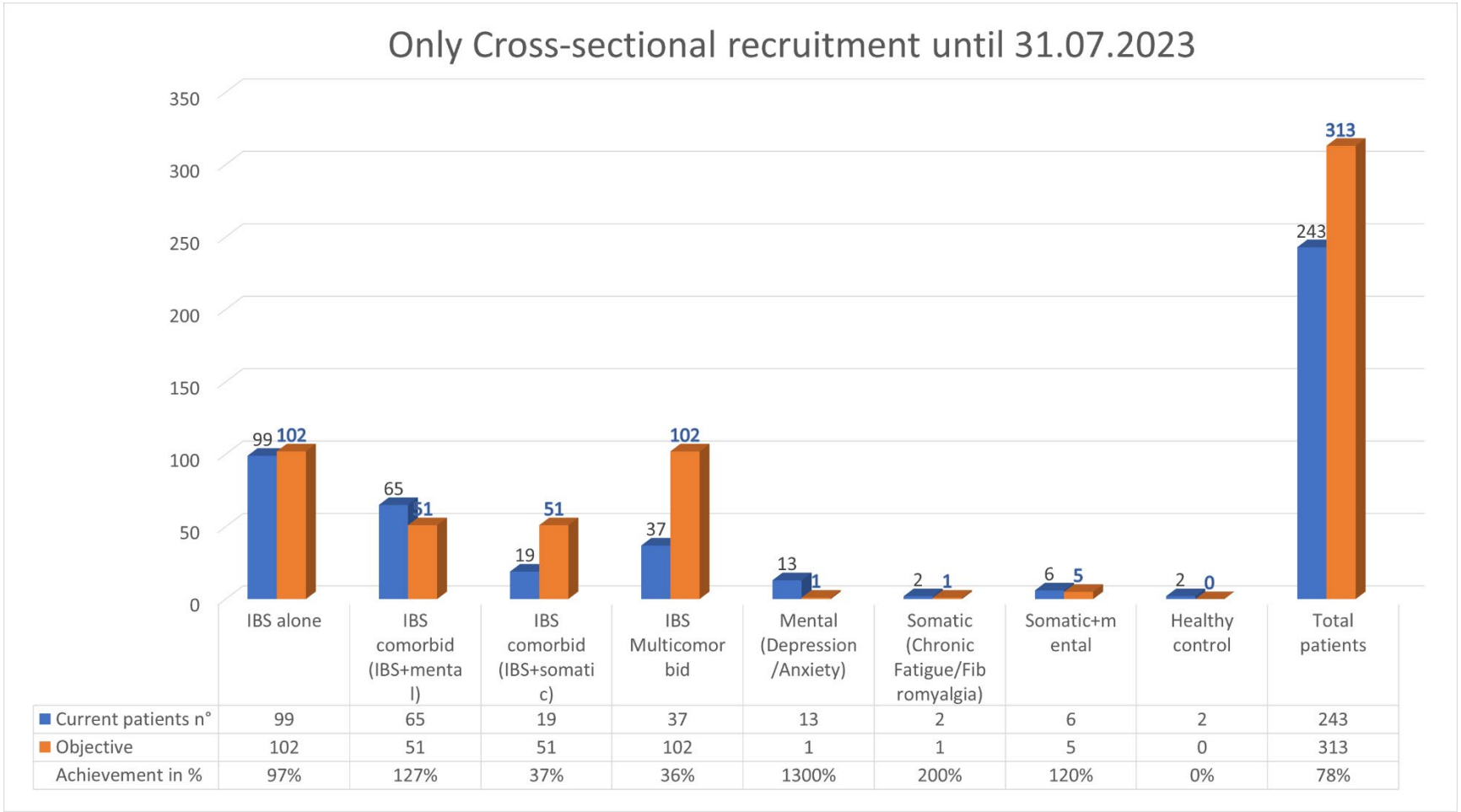
Table 1. Baseline Recruitment

Full Cross Sectional Study	VHIR	KUL	UGOT	UNIBO	UM	UMF	GUF	RUMS	SU	Total target	Target reached as of 31.01.2023	Percentage
IBS alone	34	34	34	34	34	34				204	263	129%
IBS comorbid	34	34	34	34	34	34				204	211	103%
IBS Multicomorbid	34	34	34	34	34	34				204	114	56%
Mental	13						13	13	13	52	54	104%
Somatic	13						13	13	13	52	48	92%
Somatic+mental	13						13	13	13	52	52	100%
Healthy control	17	17	17							51	69	135%
Total	*158*	*119*	*119*	*102*	*102*	*102*	*39*	*39*	*39*	*800*	*811*	*101%*

Longitudinal Study	VHIR	KUL	UGOT	UNIBO	UM	UMF	GUF	RUMS	SU	Total target	Target reached as of 30.12.2022	Percentage
IBS alone	17	17	17	17	17	17				102	164	161%
IBS comorbid (IBS +MENTAL)	9	9	9	8	8	8				51	104	204%
IBS comorbid (IBS +SOMATIC)	8	8	8	9	9	9				51	23	45%
IBS Multicomorbid	17	17	17	17	17	17				102	77	75%
Mental	13						13	13	13	52	41	79%
Somatic	13						13	13	13	52	46	88%
Somatic+mental	13						13	13	13	52	46	88%
Healthy control	17	17	17							51	67	131%
Total	*107*	*68*	*68*	*51*	*51*	*51*	*39*	*39*	*39*	*500*	*568*	*114%*

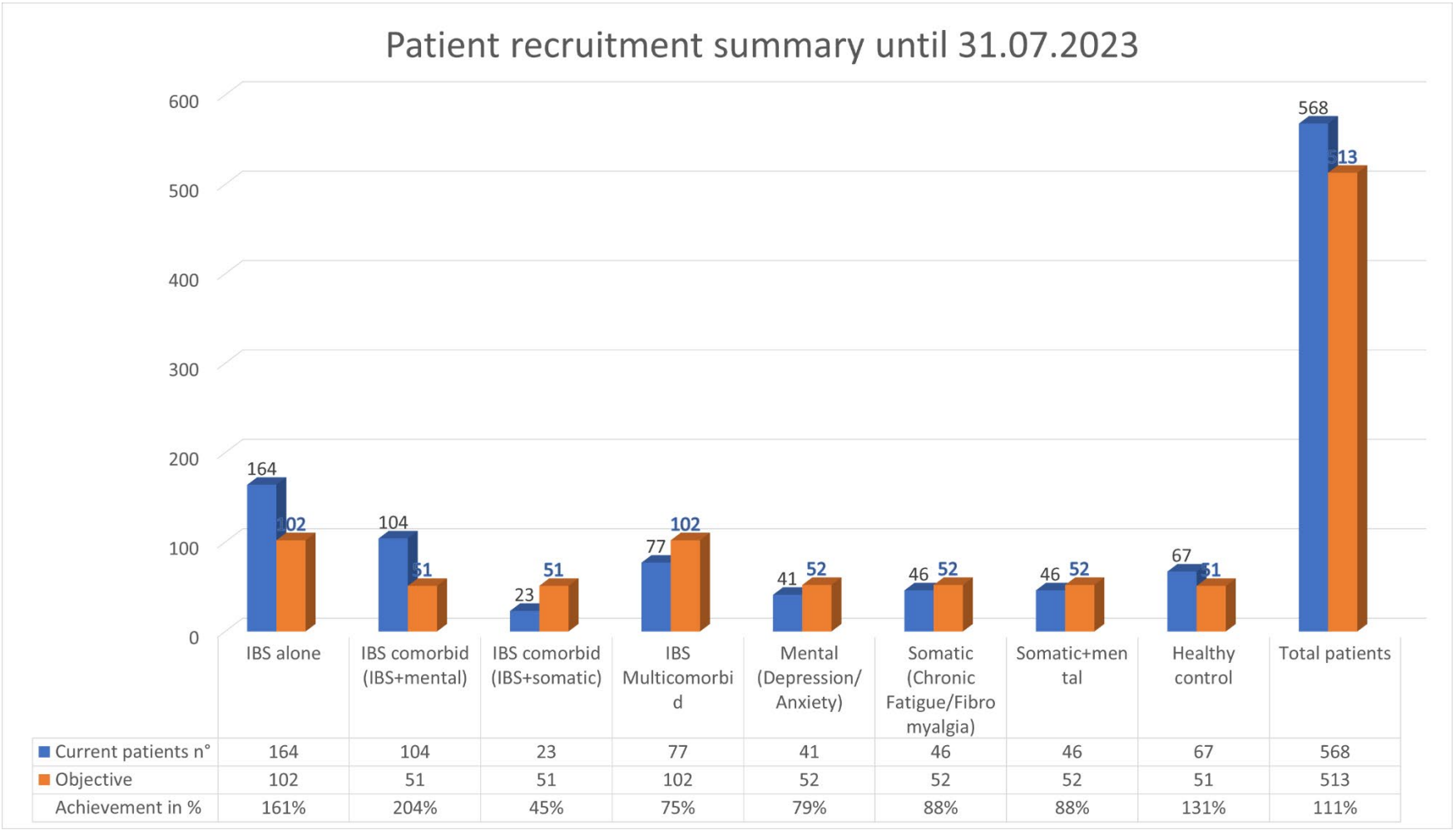
Only Cross-sectional Study	VHIR	KUL	UGOT	UNIBO	UM	UMF	GUF	RUMS	SU	Total target	Target reached as of 30.12.2022	Percentage
IBS alone	17	17	17	17	17	17				102	99	97%
IBS comorbid (IBS +MENTAL)	9	9	9	8	8	8				51	65	127%
IBS comorbid (IBS +SOMATIC)	8	8	8	9	9	9				51	19	37%
IBS Multicomorbid	17	17	17	17	17	17				102	37	36%
Mental										0	13	
Somatic										0	2	
Somatic+mental										0	6	
Healthy control										0	2	

Figure 2. Recruitment – cross-sectional assessment only.



	IBS alone	IBS comorbid (IBS+mental)	IBS comorbid (IBS+somatic)	IBS Multicomorbid	Mental (Depression /Anxiety)	Somatic (Chronic Fatigue/Fibromyalgia)	Somatic+mental	Healthy control	Total patients
Current patients n°	99	65	19	37	13	2	6	2	243
Objective	102	51	51	102	1	1	5	0	313
Achievement in %	97%	127%	37%	36%	1300%	200%	120%	0%	78%

Figure 3. Recruitment planned longitudinal follow-up.



	IBS alone	IBS comorbid (IBS+mental)	IBS comorbid (IBS+somatic)	IBS Multicomorbid	Mental (Depression/ Anxiety)	Somatic (Chronic Fatigue/Fibromyalgia)	Somatic+mental	Healthy control	Total patients
Current patients n°	164	104	23	77	41	46	46	67	568
Objective	102	51	51	102	52	52	52	51	513
Achievement in %	161%	204%	45%	75%	79%	88%	88%	131%	111%

Table 2. DEMOGRAPHIC DATA																			
		Total sample (N = 867)*		IBS alone (n = 272)		IBS comorbid-mental (n = 168)		IBS comorbid-somatic (n = 48)		IBS multi-comorbid (n = 123)		Healthy controls (n = 78)		Control – mental (n = 60)		Control – somatic (n = 51)		Control mental +somatic (n = 53)	
		M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
Age		44.22	15.09	45.13	16.14	41.29	14.64	48.13	14.02	45.20	11.82	35.51	12.97	51.61	13.33	51.61	13.33	49.74	14.34
BMI		19.2	14.3	21.5	17.5	20.1	10.5	20.7	11.6	19.5	12.4	11.5	12.1	16.6	13.7	15.2	15.4	21.1	13
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Gender	Woman	657	75.8	202	74.3	140	83.3	41	85.4	107	87.0	45	57.7	38	63.3	40	78.4	36	67.9
	Man	207	23.9	70	25.7	28	16.7	7	14.6	16	13.0	33	42.3	22	36.7	11	21.6	17	32.1
	Missing	3	.3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Born by cesarian	No	668	77	203	74.6	116	69.0	42	87.5	103	83.7	63	80.8	48	80.0	44	86.3	44	83.0
	Yes	109	12.9	32	11.8	30	17.9	4	8.3	11	8.9	9	11.5	10	16.7	6	11.8	7	13.2
	Not known	20	2.3	6	2.2	4	2.4	1	2.1	3	2.4	72	92.3	2	3.3	1	2.0	2	3.8
	Missing	70	8.1	31	11.4	18	10.7	1	2.1	6	4.9	6	7.7	0	0	0	0	0	0
Breastfed	No	215	24.8	66	24.3	43	25.6	19	39.6	32	26.0	23	29.5	10	16.7	13	25.5	9	17.0
	Yes	466	53.7	132	48.5	78	46.4	23	47.9	69	56.1	45	57.7	47	78.3	32	62.7	36	67.9
	Not known	116	13.4	43	15.8	29	17.3	5	10.4	16	13.0	4	5.1	3	5.0	6	11.8	8	15.1
	Missing	70	8.1	31	11.4	18	10.7	1	2.1	6	4.9	6	7.7	0	0	0	0	0	0
Education	No University degree	469	54.1	132	48.5	89	53.0	36	75.0	87	70.7	29	37.2	28	46.7	32	62.7	32	60.4
	University degree	313	36.1	101	37.1	59	35.1	9	18.8	30	24.4	42	53.8	31	51.7	18	35.3	21	39.6
	Doctoral studies (PhD)	15	1.7	8	2.9	2	1.2	2	4.2	0	0	2	2.6	0	0	1	2.0	0	0
	Missing	70	8.1	31	11.4	18	10.7	1	2.1	6	4.9	5	6.4	1	1.7	0	0	0	0
Work	Full time	373	43.0	136	50.0	87	51.8	9	18.8	40	32.5	38	48.7	28	46.7	17	33.3	14	26.4
	Part-time	96	11.1	27	9.9	16	9.5	11	22.9	17	13.8	8	10.3	5	8.3	9	17.6	3	5.7
	Retired	68	7.8	29	10.7	6	3.6	3	6.3	4	3.3	0	0	9	15.0	7	13.7	9	17.0
	Student	95	11.0	30	11.0	22	13.1	3	6.3	10	8.1	18	23.1	6	10.0	2	3.9	4	7.5

	Unable to work (> 1 month, < 1 year)	39	4.5	4	1.5	5	3.0	8	16.7	14	11.4	0	0	2	3.3	4	7.8	2	3.8
	Unable to work (> 1 year)	89	10.3	7	2.6	9	5.4	12	25.0	29	23.6	0	0	3	5.0	11	21.6	17	32.1
	Unemployed (not due to health problem)	31	3.6	7	2.6	3	1.8	0	0	2	1.6	8	10.3	6	10.0	1	2.0	4	7.5
	Full time home maker	5	.6	1	.4	2	1.2	1	2.1	1	.8	0	0	0	0	0	0	0	0
	Missing	71	8.2	31	11.4	18	10.7	1	2.1	6	4.9	6	7.7	1	1.7	0	0	0	0
Recruitment from	Primary care	24	2.8	7	2.6	0	0	0	0	0	0	0	0	7	11.7	4	7.8	6	11.3
	Secondary care	368	42.4	88	32.4	71	42.3	21	43.8	62	50.4	12	15.4	34	56.7	34	66.7	12	22.6
	Tertiary care	111	12.8	99	36.4	15	8.9	13	27.1	19	15.4	1	1.3	10	16.7	0	0	32	60.4
	Public advertisement	298	34.4	48	17.6	64	38.1	13	27.1	36	29.3	61	78.2	9	15.0	13	25.5	3	5.7
	Missing	66	7.6	30	11.0	18	10.7	1	2.1	6	4.9	4	5.1	0	0	0	0	0	0

*Missing study group allocation: n = 14

Table 3. CLINICAL HISTORY											
		All IBS groups (n = 611)		IBS alone (n = 272)		IBS comorbid-mental (n = 168)		IBS comorbid-somatic (n = 48)		IBS multi-comorbid (n = 123)	
		M	SD	M	SD	M	SD	M	SD	M	SD
Time since onset of IBS symptoms (months)		186.48	163.65	183.47	165.24	187.7	157.19	183.46	179.32	194.82	164.93
		n	%	n	%	n	%	n	%	n	%
Frequency of symptoms	Never	4	0.5	3	1.1	1	0.6	0	0	0	0
	Less than 1 day/week	25	2.9	16	5.9	7	4.2	1	2.1	1	0.8
	1-2 days/week	126	14.5	67	24.6	33	19.6	7	14.6	18	14.6
	At least 3 times/week	70	8.1	26	9.6	15	8.9	11	22.9	17	13.8
	≥ 3 days/week	107	12.3	52	19.1	29	17.3	5	10.4	20	16.3
	Everyday	187	21.6	67	24.6	50	29.8	21	43.8	49	39.8
	Unknown	8	0.9	2	0.7	3	1.8	1	2.1	2	1.6
	Missing	340	39.2	39	14.3	30	17.9	2	4.2	16	13.0
Symptoms started	Acutely	128	14.8	50	18.4	43	25.6	10	20.8	24	19.5
	Gradually	357	41.2	167	61.4	84	50.0	34	70.8	70	56.9
	Unknown	43	5.0	16	5.9	12	7.1	2	4.2	13	10.6
	Missing	339	39.1	39	14.3	29	17.3	2	4.2	16	13.0
Onset of symptoms	Abdominal surgery	11	1.3	7	2.6	1	0.6	1	2.1	2	1.6
	Antibiotics	15	1.7	9	3.3	1	0.6	2	4.2	3	2.4
	Change of diet	12	1.4	7	2.6	4	2.4	0	0	1	0.8
	Gastrointestinal infection	49	5.7	23	8.5	14	8.3	6	12.5	6	4.9
	Not clear	285	32.9	130	47.8	71	42.3	23	47.9	58	47.2
	Other	55	6.3	24	8.8	10	6.0	9	18.8	12	9.8
	Other infection	8	0.9	4	1.5	1	0.6	1	2.1	2	1.6
	Stressful life event/ psychological trauma	93	10.7	29	10.7	37	22.0	4	8.3	23	18.7
	Missing	339	39.1	39	14.3	29	17.3	2	4.2	16	13.0

Previously visited primary care physician for their problem	No	448	51.7	87	32.0	55	32.7	17	35.4	40	32.5
	Yes	411	47.4	182	66.9	113	67.3	31	64.6	83	67.5
	Missing	8	0.9	3	1.1	0	0	0	0	0	0
Previously visited secondary care physician for their problem	No	473	54.6	111	40.8	65	38.7	18	37.5	30	24.4
	Yes	386	44.5	158	58.1	103	61.3	30	62.5	93	75.6
	Missing	8	0.9	3	1.1	0	0	0	0	0	0
Previously visited tertiary care physician for their problem	No	796	91.8	244	89.7	151	89.9	42	87.5	109	88.6
	Yes	63	7.3	25	9.2	17	10.1	6	12.5	14	11.4
	Missing	8	0.9	3	1.1	0	0	0	0	0	0

*Missing study group allocation: n = 14

Table 4. DIETARY HISTORY																			
		Total sample (N = 867)*		IBS alone (n = 272)		IBS comorbid-mental (n = 168)		IBS comorbid-somatic (n = 48)		IBS multi-comorbid (n = 123)		Healthy controls (n = 78)		Control – mental (n = 60)		Control – somatic (n = 51)		Control mental +somatic (n = 53)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Gluten-free diet	No	773	89.2	245	90.1	151	89.9	39	81.3	106	86.2	67	85.9	56	93.3	49	96.1	49	92.5
	Yes	85	9.8	27	9.9	17	10.1	9	18.8	17	13.8	5	6.4	4	6.7	2	3.9	4	7.5
	Missing	9	1.0	0	0	0	0	0	0	0	0	6	7.7	0	0	0	0	0	0
Vegetarian diet	No	817	94.2	264	97.1	153	91.1	46	95.8	120	97.6	67	85.9	55	91.7	51	100	51	96.2
	Yes	41	4.7	8	2.9	15	8.9	2	4.2	3	2.4	5	6.4	5	8.3	0	0	2	3.8
	Missing	9	1.0	0	0	0	0	0	0	0	0	6	7.7	0	0	0	0	0	0
Vegan diet	No	842	97.1	268	98.5	163	97.0	47	97.9	122	99.2	70	89.7	59	98.3	51	100	51	96.2
	Yes	16	1.8	4	1.5	5	3.0	1	2.1	1	0.8	2	2.6	1	1.7	0	0	2	3.8
	Missing	9	1.0	0	0	0	0	0	0	0	0	6	7.7	0	0	0	0	0	0
Lactose-free diet	No	694	80.0	219	80.5	131	78.0	34	70.8	85	69.1	69	88.5	50	83.3	45	88.2	50	94.3
	Yes	164	18.9	53	19.5	37	22.0	14	29.2	38	30.9	3	3.8	10	16.7	6	11.8	3	5.7
	Missing	9	1.0	0	0	0	0	0	0	0	0	6	7.7	0	0	0	0	0	0
Low carbohydrate / high fat diet	No	845	97.5	268	98.5	166	98.8	47	97.9	123	100.0	72	92.3	58	96.7	48	94.1	52	98.1
	Yes	13	1.5	4	1.5	2	1.2	1	2.1	0	0	0	0	2	3.3	3	5.9	1	1.9
	Missing	9	1.0	0	0	0	0	0	0	0	0	6	7.7	0	0	0	0	0	0
High/rich fiber diet	No	834	96.2	268	98.5	166	98.8	46	95.8	123	100.0	71	91.0	54	90.0	47	92.2	48	90.6
	Yes	24	2.8	4	1.5	2	1.2	2	4.2	0	0	1	1.3	6	10.0	4	7.8	5	9.4
	Missing	9	1.0	0	0	0	0	0	0	0	0	6	7.7	0	0	0	0	0	0
FODMAP diet	No	792	91.3	243	89.3	156	92.9	41	85.4	108	87.8	72	92.3	59	98.3	49	96.1	53	100
	Yes	66	7.6	29	10.7	12	7.1	7	14.6	15	12.2	0	0	1	1.7	2	3.9	0	0
	Missing	9	1.0	0	0	0	0	0	0	0	0	6	7.7	0	0	0	0	0	0
Any other special diet	No	792	91.3	257	94.5	155	92.3	40	83.3	117	95.1	68	87.2	53	88.3	45	88.2	46	86.8
	Yes	66	7.6	15	5.5	13	7.7	8	16.7	6	4.9	4	5.1	7	11.7	6	11.8	7	13.2
	Missing	9	1.0	0	0	0	0	0	0	0	0	6	7.7	0	0	0	0	0	0
	No	373	43.0	125	46.0	91	54.2	24	50.0	55	44.7	16	20.5	24	40	13	25.5	19	35.8

No special diet	Yes	485	55.9	147	54.0	77	45.8	24	50.0	68	55.3	56	71.8	36	60.0	38	74.5	34	64.2
	Missing	9	1.0	0	0	0	0	0	0	0	0	6	7.7	0	0	0	0	0	0
Restrictions due to IBS symptoms	No	241	27.8	115	42.3	68	40.5	18	37.5	37	30.1	-	-	-	-	-	-	-	-
	Yes	292	33.7	113	41.5	73	43.5	28	58.3	76	61.8	-	-	-	-	-	-	-	-
	Missing	334	38.5	44	16.2	27	16.1	2	4.2	10	8.1	-	-	-	-	-	-	-	-
Avoidance of certain food products	No	290	33.4	79	29.0	43	25.6	10	20.8	11	8.9	48	61.5	36	60.0	27	52.9	32	60.4
	Yes	499	57.6	158	58.1	105	62.5	37	77.1	105	85.4	23	29.5	24	40.0	24	47.1	21	39.6
	Missing	78	9.0	35	12.9	20	11.9	1	2.1	7	5.7	7	9.0	0	0	0	0	0	0
Avoidance of certain food products is helpful	No	44	5.1	16	5.9	12	7.1	4	8.3	12	9.8	-	-	-	-	-	-	-	-
	Yes	349	40.3	136	50.0	89	53.0	32	66.7	90	73.2	-	-	-	-	-	-	-	-
	Missing	474	54.7	120	44.1	67	39.9	12	25.0	21	17.1	-	-	-	-	-	-	-	-
Use of pre/probiotics in last 3 months	No	636	73.4	188	69.1	115	68.5	33	68.8	82	66.7	67	85.9	57	95.0	45	88.2	44	83.0
	Yes	151	17.4	48	17.6	32	19.0	14	29.2	34	27.6	5	6.4	3	5.0	6	11.8	9	17.0
	Missing	80	9.2	36	13.2	21	12.5	1	2.1	7	5.7	6	7.7	0	0	0	0	0	0
		M	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**
Total duration of probiotics use (days)		163.6	435.9	260.9	603	37.1	34.5	61**	-	58.3	45.1	41**	-	1518 **	-	16**	-	27.67	18.9

*Missing study group allocation: n = 14
** only 1 case

Table 5. PERSONAL HISTORY																			
		Total sample (N = 867)*		IBS alone (n = 272)		IBS comorbid-mental (n = 168)		IBS comorbid-somatic (n = 48)		IBS multi-comorbid (n = 123)		Healthy controls (n = 78)		Control – mental (n = 60)		Control – somatic (n = 51)		Control mental +somatic (n = 53)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Appendectomy	No	692	79.8	211	77.6	133	79.2	41	85.4	101	82.1	64	82.1	53	88.3	40	78.4	45	84.9
	Yes	99	11.4	26	9.6	15	8.9	6	12.5	15	12.2	8	10.3	7	11.7	11	21.6	8	15.1
	Missing	76	8.8	35	12.9	20	11.9	1	2.1	7	5.7	6	7.7	0	0	0	0	0	0
Cholecystectomy	No	763	88.0	229	84.2	145	86.3	45	93.8	107	87.0	71	91.0	60	100.0	48	94.1	51	96.2
	Yes	29	3.3	9	3.3	3	1.8	2	4.2	9	7.3	1	1.3	0	0	3	5.9	2	3.8
	Missing	75	8.7	34	12.5	20	11.9	1	2.1	7	5.7	6	7.7	0	0	0	0	0	0
Hysterectomy	No	640	73.8	188	69.1	132	78.6	41	85.4	103	83.7	49	62.8	44	73.3	37	72.5	40	75.5
	Yes	34	3.9	10	3.7	4	2.4	2	4.2	5	4.1	1	1.3	2	3.3	7	13.7	3	5.7
	N/A	118	13.6	40	14.7	12	7.1	4	8.3	8	6.5	22	28.2	14	23.3	7	13.7	10	18.9
	Missing	75	8.7	34	12.5	20	11.9	1	2.1	7	5.7	6	7.7	0	0	0	0	0	0
Other abdominal surgery	No	659	76.0	198	72.8	125	74.4	38	79.2	87	70.7	69	88.5	47	78.3	45	88.2	45	84.9
	Yes	134	15.5	40	14.7	23	13.7	9	18.8	29	23.6	4	5.1	13	21.7	6	11.8	8	15.1
	Missing	74	8.5	34	12.5	20	11.9	1	2.1	7	5.7	5	6.4	0	0	0	0	0	0
Anxiety	No	488	56.3	224	82.4	48	28.6	46	95.8	26	21.1	73	93.6	16	26.7	45	88.2	8	15.1
	Yes	305	35.2	14	5.1	102	60.7	1	2.1	89	72.4	0	0	44	73.3	6	11.8	45	84.9
	Missing	74	8.5	34	12.5	18	10.7	1	2.1	8	6.5	5	6.4	0	0	0	0	0	0
Depression	No	477	55.0	223	82.0	55	32.7	41	85.4	23	18.7	74	94.9	8	13.3	41	80.4	8	15.1
	Yes	317	36.6	15	5.5	95	56.5	6	12.5	92	74.8	0	0	52	86.7	10	19.6	45	84.9
	Missing	73	8.4	34	12.5	18	10.7	1	2.1	8	6.5	0	0	0	0	0	0	0	0
Other mental disorder	No	709	81.8	223	82.0	127	75.6	44	91.7	90	73.2	74	94.9	50	83.3	48	94.1	47	88.7
	Yes	85	9.8	16	5.9	22	13.1	3	6.3	25	20.3	0	0	10	16.7	3	5.9	6	11.3
	Missing	73	8.4	33	12.1	19	11.3	1	2.1	8	6.5	0	0	0	0	0	0	0	0
Other relevant disease	No	567	65.4	160	58.8	100	59.5	33	68.8	74	60.2	72	92.3	50	83.3	36	70.6	37	69.8
	Yes	229	26.4	79	29.0	50	29.8	14	29.2	41	33.3	2	2.6	10	16.7	15	29.4	16	30.2
	Missing	71	8.2	33	12.1	18	10.7	1	2.1	8	6.5	4	5.1	0	0	0	0	0	0

History of fibromylagia	No	615	70.9	235	86.4	145	86.3	19	39.6	51	41.5	73	93.6	60	100	13	25.5	13	24.5
	Yes	178	20.5	3	1.1	4	2.4	28	58.3	64	52.0	1	1.3	0	0	38	74.5	40	75.5
	Missing	74	8.5	34	12.5	19	11.3	1	2.1	8	6.5	4	5.1	0	0	0	0	0	0
History of chronic fatigue	No	612	70.6	237	87.1	147	87.5	14	29.2	30	24.4	73	93.6	56	93.3	27	52.9	22	41.5
	Yes	180	20.8	1	0.4	2	1.2	33	68.8	84	68.3	1	1.3	4	6.7	24	47.1	31	58.5
	Missing	75	8.7	34	12.5	19	11.3	1	2.1	9	7.3	4	5.1	0	0	0	0	0	0
Skin allergy	No	602	69.4	237	87.1	112	66.7	38	79.2	67	54.5	63	80.8	51	85	41	80.4	37	69.8
	Yes	183	21.1	1	0.4	33	19.6	9	18.8	47	38.2	9	11.5	9	15	10	19.6	16	30.2
	Missing	82	9.5	34	12.5	23	13.7	1	2.1	9	7.3	6	7.7	0	0	0	0	0	0
Food allergy	No	644	74.3	203	74.6	120	71.4	34	70.8	83	67.5	68	87.2	48	80.0	40	78.4	41	77.4
	Yes	141	16.3	32	11.8	26	15.5	13	27.1	31	25.2	4	5.1	12	20.0	11	21.6	12	22.6
	Missing	82	9.5	37	13.6	22	13.1	1	2.1	9	7.3	6	7.7	0	0	0	0	0	0
Eyes/nose/throat allergy	No	507	58.5	159	58.5	94	56	27	56.3	54	43.9	54	69.2	45	75	33	64.7	35	66
	Yes	276	31.8	76	27.9	51	30.4	20	41.7	59	48	18	23.1	15	25	18	35.3	18	34
	Missing	84	9.7	37	13.6	23	13.7	1	2.1	10	8.1	6	7.7	0	0	0	0	0	0
History of COVID	No	439	50.6	141	51.8	74	44.0	27	56.3	66	53.7	31	39.7	39	65	29	56.9	28	52.8
	Yes	296	34.1	86	31.6	63	37.5	19	39.6	42	34.1	38	48.7	13	21.7	14	27.5	19	35.8
	Not known	53	6.1	11	4	11	6.5	1	2.1	6	4.9	3	3.8	7	11.7	8	15.7	6	11.3
	Missing	79	9.1	34	12.5	20	11.9	1	2.1	9	7.3	6	7.7	1	1.7	0	0	0	0

*Missing study group allocation: n = 14

Table 6. FAMILY HISTORY																			
		Total sample (N = 867)*		IBS alone (n = 272)		IBS comorbid-mental (n = 168)		IBS comorbid-somatic (n = 48)		IBS multi-comorbid (n = 123)		Healthy controls (n = 78)		Control – mental (n = 60)		Control – somatic (n = 51)		Control mental +somatic (n = 53)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Family history of IBS	No	313	36.1	141	51.8	77	45.8	29	60.4	62	50.4	0	0	-	-	-	-	-	-
	Yes	158	18.2	57	21.0	46	27.4	14	29.2	40	32.5	1	1.3	-	-	-	-	-	-
	Not known	59	6.8	29	10.7	17	10.1	3	6.3	10	8.1	0	0	-	-	-	-	-	-
	Missing	337	38.9	45	16.5	28	16.7	2	4.2	11	8.9	77	98.7	-	-	-	-	-	-
First degree relative	No	724	83.5	220	80.9	129	76.8	36	75.0	88	71.5	74	94.9	-	-	-	-	-	-
	Yes	139	16.0	52	19.1	39	23.2	12	25.0	35	28.5	1	1.3	-	-	-	-	-	-
	Missing	4	0.5	0	0	0	0	0	0	0	0	3	3.8	-	-	-	-	-	-
Second degree relative	No	823	94.9	258	94.9	155	92.3	45	93.8	113	91.9	75	96.2	-	-	-	-	-	-
	Yes	40	4.6	14	5.1	13	7.7	3	6.3	10	8.1	0	0	-	-	-	-	-	-
	Missing	4	0.5	0	0	0	0	0	0	0	0	3	3.8	-	-	-	-	-	-
Family history of chronic abdominal symptoms	No	222	25.6	102	37.5	55	32.7	21	43.8	40	32.5	1	1.3	-	-	-	-	-	-
	Yes	285	32.9	115	42.3	77	45.8	24	50.0	68	55.3	0	0	-	-	-	-	-	-
	Not known	22	2.5	10	3.7	8	4.8	1	2.1	3	2.4	0	0	-	-	-	-	-	-
	Missing	338	39.0	45	16.5	28	16.7	2	4.2	12	9.8	77	98.7	-	-	-	-	-	-
First degree relative	No	610	70.4	170	62.5	96	57.1	29	60.4	64	52.0	75	96.2	-	-	-	-	-	-
	Yes	253	29.2	102	37.5	72	42.9	19	39.6	59	48.0	0	0	-	-	-	-	-	-
	Missing	4	0.5	0	0	0	0	0	0	0	0	3	3.8	-	-	-	-	-	-
Second degree relative	No	780	90.0	247	90.8	147	87.5	36	75.0	98	79.7	75	96.2	-	-	-	-	-	-
	Yes	83	9.6	25	9.2	21	12.5	12	25.0	25	20.3	0	0	-	-	-	-	-	-
	Missing	4	0.5	0	0	0	0	0	0	0	0	3	3.8	-	-	-	-	-	-
Family history of Crohn's Disease	No	702	81.0	214	78.7	127	75.6	44	91.7	95	77.2	71	91.0	55	91.7	49	96.1	43	81.1
	Yes	49	5.7	12	4.4	14	8.3	2	4.2	13	10.6	1	1.3	1	1.7	1	2.0	4	7.5
	Not known	35	4.0	11	4.0	6	3.6	1	2.1	7	5.7	0	0	3	5.0	1	2.0	6	11.3
	Missing	81	9.3	35	12.9	21	12.5	1	2.1	8	6.5	6	7.7	1	1.7	0	0	0	0
	No	838	96.7	268	98.5	160	95.2	46	95.8	119	96.7	74	94.9	59	98.3	51	100	50	94.3

First degree relative	Yes	24	2.8	4	1.5	8	4.8	2	4.2	4	3.3	1	1.3	1	1.7	0	0	3	5.7
	Missing	5	0.6	0	0	0	0	0	0	0	0	3	3.8	0	0	0	0	0	0
Second degree relative	No	836	96.4	264	97.1	161	95.8	48	100.0	114	92.7	75	96.2	60	100	50	98.0	52	98.1
	Yes	26	3.0	8	2.9	7	4.2	0	0	9	7.3	0	0	0	0	1	2.0	1	1.9
	Missing	5	0.6	0	0	0	0		00	0	0	3	3.8	0	0	0	0	0	0
Family history of Ulcerative Colitis	No	716	82.6	220	80.9	134	79.8	46	95.8	99	80.5	66	84.6	53	88.3	49	96.1	44	83.0
	Yes	23	2.7	6	2.2	6	3.6	0	0	7	5.7	3	3.8	0	0	0	0	1	1.9
	Not known	47	5.4	11	4.0	7	4.2	1	2.1	9	7.3	3	3.8	6	10.0	2	3.9	8	15.1
	Missing	81	9.3	35	12.9	21	12.5	1	2.1	8	6.5	6	7.7	1	1.7	0	0	0	0
First degree relative	No	844	97.3	268	98.5	162	96.4	48	100.0	119	96.7	72	92.3	60	100	51	100	52	98.1
	Yes	18	2.1	4	1.5	6	3.6	0	0	4	3.3	3	3.8	0	0	0	0	1	1.9
	Missing	5	0.6	0	0	0	0	0	0	0	0	3	3.8	0	0	0	0	0	0
Second degree relative	No	855	98.6	270	99.3	166	98.8	48	100.0	120	97.6	75	96.2	60	100	51	100	0	0
	Yes	7	0.8	2	0.7	2	1.2	0	0	3	2.4	0	0	0	0	0	0	0	0
	Missing	5	0.6	0	0	0	0	0	0	0	0	3	3.8	0	0	0	0	53	100
Family history of depression	No	280	32.3	152	55.9	61	36.3	26	54.2	36	29.3	1	1.3	-	-	-	-	-	-
	Yes	213	24.6	63	23.2	64	38.1	17	35.4	69	56.1	0	0	-	-	-	-	-	-
	Not known	35	4.0	12	4.4	14	8.3	3	6.3	6	4.9	0	0	-	-	-	-	-	-
	Missing	339	39.1	45	16.5	29	17.3	2	4.2	12	9.8	77	98.7	-	-	-	-	-	-
First degree relative	No	689	79.5	222	81.6	119	70.8	35	72.9	61	49.6	75	96.2	-	-	-	-	-	-
	Yes	174	20.1	50	18.4	49	29.2	13	27.1	62	50.4	0	0	-	-	-	-	-	-
	Missing	4	0.5	0	0	0	0	0	0	0	0	3	3.8	-	-	-	-	-	-
Second degree relative	No	787	90.8	251	92.3	141	83.9	40	83.3	103	83.7	75	96.2	-	-	-	-	-	-
	Yes	76	8.8	21	7.7	27	16.1	8	16.7	20	16.3	0	0	-	-	-	-	-	-
	Missing	4	0.5	0	0	0	0	0	0	0	0	3	3.8	-	-	-	-	-	-
Family history of anxiety	No	323	37.3	166	61.0	65	38.7	33	68.8	54	43.9	1	1.3	-	-	-	-	-	-
	Yes	165	19.0	50	18.4	55	32.7	9	18.8	51	41.5	0	0	-	-	-	-	-	-
	Not known	40	4.6	11	4.0	19	11.3	4	8.3	6	4.9	0	0	-	-	-	-	-	-
	Missing	339	39.1	45	16.5	29	17.3	2	4.2	12	9.8	77	98.7	-	-	-	-	-	-
	No	715	82.5	229	84.2	119	70.8	40	83.3	75	61.0	75	96.2	-	-	-	-	-	-

First degree relative	Yes	148	17.1	43	15.8	49	29.2	8	16.7	48	39.0	0	0	-	-	-	-	-	-
	Missing	4	0.5	0	0	0	0	0	0	0	0	3	3.8	-	-	-	-	-	-
Second degree relative	No	827	95.4	264	97.1	152	90.5	47	97.9	112	91.1	75	96.2	-	-	-	-	-	-
	Yes	36	4.2	8	2.9	16	9.5	1	2.1	11	8.9	0	0	-	-	-	-	-	-
	Missing	4	0.5	0	0	0	0	0	0	0	0	3	3.8	-	-	-	-	-	-
Family history of other mental disorder	No	412	47.5	191	70.2	101	60.1	37	77.1	79	64.2	0	0	-	-	-	-	-	-
	Yes	80	9.2	24	8.8	22	13.1	7	14.6	26	21.1	1	1.3	-	-	-	-	-	-
	Not known	36	4.2	12	4.4	16	9.5	2	4.2	6	4.9	0	0	-	-	-	-	-	-
	Missing	339	39.1	45	16.5	29	17.3	2	4.2	12	9.8	77	98.7	-	-	-	-	-	-
First degree relative	No	810	93.4	260	95.6	152	90.5	42	87.5	105	85.4	74	94.9	-	-	-	-	-	-
	Yes	53	6.1	12	4.4	16	9.5	6	12.5	18	14.6	1	1.3	-	-	-	-	-	-
	Missing	4	0.5	0	0	0	0	0	0	0	0	3	3.8	-	-	-	-	-	-
Second degree relative	No	830	95.7	260	95.6	159	94.6	45	93.8	114	92.7	75	96.2	-	-	-	-	-	-
	Yes	33	3.8	12	4.4	9	5.4	3	6.3	9	7.3	0	0	-	-	-	-	-	-
	Missing	4	0.5	0	0	0	0	0	0	0	0	3	3.8	-	-	-	-	-	-
Family history of fibromyalgia	No	414	47.8	194	71.3	113	67.3	35	72.9	68	55.3	0	0	-	-	-	-	-	-
	Yes	78	9.0	21	7.7	12	7.1	8	16.7	36	29.3	1	1.3	-	-	-	-	-	-
	Not known	36	4.2	12	4.4	14	8.3	3	6.3	7	5.7	0	0	-	-	-	-	-	-
	Missing	339	39.1	45	16.5	29	17.3	2	4.2	12	9.8	77	98.7	-	-	-	-	-	-
First degree relative	No	807	93.1	257	94.5	160	95.2	42	87.5	97	78.9	74	94.9	-	-	-	-	-	-
	Yes	56	6.5	15	5.5	8	4.8	6	12.5	26	21.1	1	1.3	-	-	-	-	-	-
	Missing	4	0.5	0	0	0	0	0	0	0	0	3	3.8	-	-	-	-	-	-
Second degree relative	No	840	96.9	265	97.4	164	97.6	45	93.8	114	92.7	75	96.2	-	-	-	-	-	-
	Yes	23	2.7	7	2.6	4	2.4	3	6.3	9	7.3	0	0	-	-	-	-	-	-
	Missing	4	0.5	0	0	0	0	0	0	0	0	3	3.8	-	-	-	-	-	-
Family history of chronic fatigue	No	458	52.8	209	76.8	117	69.6	43	89.6	84	68.3	1	1.3	-	-	-	-	-	-
	Yes	28	3.2	7	2.6	6	3.6	0	0	15	12.2	0	0	-	-	-	-	-	-
	Not known	42	4.8	11	4.0	16	9.5	3	6.3	12	9.8	0	0	-	-	-	-	-	-
	Missing	339	39.1	45	16.5	29	17.3	2	4.2	12	9.8	77	98.7	-	-	-	-	-	-
First degree relative	No	843	97.2	269	98.9	163	97.0	48	100.0	111	90.2	75	96.2	-	-	-	-	-	-
	Yes	20	2.3	3	1.1	5	3.0	0	0	12	9.8	0	0	-	-	-	-	-	-

	Missing	4	0.5	0	0	0	0	0	0	0	0	3	3.8	-	-	-	-	-	-
Second degree relative	No	853	98.4	268	98.5	166	98.8	48	100	119	96.7	75	96.2	-	-	-	-	-	-
	Yes	10	1.2	4	1.5	2	1.2	0	0	4	3.3	0	0	-	-	-	-	-	-
	Missing	4	0.5	0	0	0	0	0	0	0	0	3	3.8	-	-	-	-	-	-
Has twin sibling	No	768	88.6	230	84.6	144	85.7	47	97.9	113	91.9	70	89.7	59	98.3	50	98.0	51	96.2
	Yes	11	1.3	6	2.2	2	1.2	0	0	0	0	0	0	-	-	1	2.0	1	1.9
	Not known	7	0.8	1	0.4	1	0.6	0	0	2	1.6	2	2.6	-	-	0	0	1	1.9
	Missing	81	9.3	35	12.9	21	12.5	1	2.1	8	6.5	6	7.7	1	1.7	0	0	0	0
Has identical twin sibling	No	7	0.8	4	1.5	1	0.6	0	0	0	0	-	-	0	0	0	0	1	1.9
	Yes	4	0.5	2	0.7	1	0.6	0	0	0	0	-	-	0	0	1	2.0	0	0
	Missing	856	98.7	266	97.8	166	98.8	48	100	123	100	-	-	60	100	50	98.0	0	0
Identical twin has abdominal symptoms	No	9	1.0	5	1.8	2	1.2	0	0	0	0	-	-	0	0	1	2.0		
	Yes	2	0.2	1	0.4	0	0	0	0	0	0	-	-	0	0	-	-		
	Missing	856	98.7	266	97.8	166	98.8	48	100	123	100	-	-	60	100	50	98.0	52	98.1
First degree relative has abdominal symptoms	No	378	43.6	112	41.2	55	32.7	21	43.8	39	31.7	50	64.1	40	66.7	31	60.8	1	1.9
	Yes	387	44.6	121	44.5	87	51.8	26	54.2	74	60.2	21	26.9	14	23.3	19	37.3	0	0
	Not known	21	2.4	4	1.5	5	3.0	0	0	2	1.6	1	1.3	5	8.3	1	2.0	0	0
	Missing	81	9.3	35	12.9	21	12.5	1	2.1	8	6.5	6	7.7	1	1.7	0	0	52	98.1

*Missing study group allocation: n = 14

Table 7. SUBSTANCE USE

		Total sample (N = 867)*		IBS alone (n = 272)		IBS comorbid-mental (n = 168)		IBS comorbid-somatic (n = 48)		IBS multi-comorbid (n = 123)		Healthy controls (n = 78)		Control – mental (n = 60)		Control – somatic (n = 51)		Control mental +somatic (n = 53)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Alcohol use	No	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Yes	368	42.4	117	43	67	39.9	11	22.9	43	35	54	69.2	23	38.3	22	43.1	28	52.8
	Missing	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cigarette smoking	No	638	73.6	203	74.6	123	73.2	40	83.3	92	74.8	55	70.5	41	68.3	38	74.5	42	79.2
	Yes	148	17.1	34	12.5	24	14.3	7	14.6	23	18.7	17	21.8	18	30.0	13	25.5	11	20.8
	Missing	81	9.3	35	12.9	21	12.5	1	2.1	8	6.5	6	7.7	1	1.7	0	0	0	0
Other smoking modalities	No	750	86.5	230	84.6	141	83.9	44	91.7	107	87.0	69	88.5	57	95.0	50	98.0	48	90.6
	Yes	36	4.2	7	2.6	6	3.6	3	6.3	8	6.5	3	3.8	2	3.3	1	2.0	5	9.4
	Missing	81	9.3	35	12.9	21	12.5	1	2.1	8	6.5	6	7.7	1	1.7	0	0	0	0
Chewing tobacco		11	1.3	2	0.7	1	0.6	1	2.1	2	1.6	2	2.6	1	1.7	0	0	2	3.8
Cigars		1	0.1	0	0	0	0	0	0	0	0	0	0	0	0	1	2.0	0	0
E-cigarettes		22	2.5	5	1.8	5	3.0	2	4.2	6	4.9	1	1.3	1	1.7	0	0	2	3.8
Pipe		1	0.1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1.9
		M	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**	**M**	**SD**
Units of alcohol / week		4.2	4.6	4	4.2	3.8	3.5	6.5	8.1	3.5	5	4.7	4.5	5.5	6.4	3	2.9	4.1	3
Number of cigarettes smoked / day		9.4	6.5	7.7	5.8	11.3	8.1	9.7	4.5	11.9	6.7	8.7	6.4	10.2	6.7	7.9	6.01	7	4.7
Number of cigarette packs smoked / year		113.9	139.2	68	88.5	91.4	156.6	130.1	123.1	135.7	127.6	157.4	140.1	198.5	289.7	147.6	119.2	94.7	95.5

*Missing study group allocation: n = 14

Table 8. RECENT MEDICATION (last 3 months)																		
	Total sample (N = 867)*		IBS alone (n = 272)		IBS comorbid-mental (n = 168)		IBS comorbid-somatic (n = 48)		IBS multi-comorbid (n = 123)		Healthy controls (n = 78)		Control – mental (n = 60)		Control – somatic (n = 51)		Control mental +somatic (n = 53)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Antidepressant	233	26.9	18	6.6	57	33.9	13	27.1	58	47.2	2	2.6	37	61.7	19	37.3	28	52.8
NAIDs (incl aspirin)	131	15.1	27	9.9	17	10.1	6	12.5	31	25.2	5	6.4	8	13.3	18	35.3	18	34.0
Antibiotics	10	1.2	4	1.5	3	1.8	0	0	2	1.6	1	1.3	0	0	0	0	0	0
Probiotics (capsulated or shots)	41	4.7	12	4.4	7	4.2	9	18.8	5	4.1	0	0	2	3.3	1	2.0	5	9.4
Laxatives	71	8.2	28	10.3	20	11.9	7	14.6	11	8.9	0	0	1	1.7	0	0	2	3.8
Acid suppressants	128	14.8	40	14.7	21	12.5	9	18.8	33	26.8	1	1.3	6	10.0	7	13.7	10	18.9
Antipasmodics	59	6.8	20	7.4	15	8.9	7	14.6	9	7.3	0	0	1	1.7	1	2.0	6	11.3
Antidiarrheal drugs	21	2.4	7	2.6	7	4.2	2	4.2	0	0	0	0	2	3.3	0	0	3	5.7
Phytotherapy	13	1.5	4	1.5	0	0	1	2.1	1	0.8	0	0	2	3.3	2	3.9	3	5.7
Prokinetic	7	0.8	0	0	3	1.8	1	2.1	2	1.6	0	0	0	0	1	2.0	0	0
Linaclotide	9	1.0	2	0.7	2	1.2	0	0	5	4.1	0	0	0	0	0	0	0	0
Lubiprostone	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Benzodiazepines	94	10.8	8	2.9	20	11.9	5	10.4	28	22.8	2	2.6	8	13.3	7	13.7	15	28.3
Antipsychotics	25	2.9	2	0.7	5	3.0	1	2.1	8	6.5	0	0	6	10.0	0	0	3	5.7
Antiepileptics	43	5.0	1	0.4	4	2.4	7	14.6	23	18.7	0	0	1	1.7	3	5.9	4	7.5
Opioids	29	3.3	1	0.4	3	1.8	5	10.4	12	9.8	0	0	0	0	5	9.8	3	5.7
Other	480	55.4	152	55.9	85	50.6	34	70.8	79	64.2	24	30.8	27	45.0	36	70.6	38	71.7

*Missing study group allocation: n = 14

Table 9. Questionnaire descriptives and group comparisons (ANOVAs)

	Total sample		IBS alone		IBS comorbid-mental		IBS comorbid-somatic		IBS multi-comorbid		Healthy controls		Control – mental		Control – somatic		Control mental + somatic		F †
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD	
IBS-SSS	202.2	122.6	226.6	101.6	244	97.8	274.1	100.1	294	99.3	26	44.5	112.7	81.7	140.6	102.5	142.7	86.5	74.20***
FIQ	31.3	23.9	17.4	14.6	28.2	17.5	45.2	21.5	54.3	22.8	7.2	10.6	29.9	18.3	52.7	17.2	52	20	89.06***
MFI – general fatigue	14	4.6	12.2	4.2	14.5	3.7	16.6	3.3	17.6	2.5	8.2	3.1	14.2	3.9	16.6	3.6	16.7	3.7	59.89***
MFI – physical fatigue	12.8	4.8	10.7	4.2	13.3	4.3	15.5	4.5	16.4	3.2	8	3.6	11.8	4.1	15.5	3.5	15.4	3.9	46.37***
MFI – reduced activity	11.6	4.7	9.2	4.1	11.9	3.9	13.1	4.8	15.3	4	7	2.8	12.9	4.1	13.3	3.7	14.4	3.9	45.37***
MFI – reduced motivation	10.3	4.2	8.7	3.5	11.2	4	10.4	4.	13.1	3.9	6.4	2.5	11	3.6	10.7	3.8	12.5	4.2	31.26***
MFI – mental fatigue	11.8	4.7	9.7	4.3	12.4	4.1	12.9	4.9	15	4.3	8.1	3.5	13	4.5	12.9	4	14.6	4.1	27.99***
GAD7	6.8	5.4	4.4	4.1	8.2	5.3	5.3	4.5	11.1	5.7	1.9	2.6	8.9	4	6.9	4.9	10.5	4.5	42.01***
PHQ9	8.46	6.33	5.15	4.29	9.6	5.94	8.09	4.12	13.73	6.12	2.08	2.48	11.9	6.7	9.22	5.17	12.76	5.5	53.90***
PHQ15	12.5	6.9	10.7	4.8	13.3	5.2	16.1	5.1	18.9	8.1	3.4	2.8	10.1	4.6	15.3	7	15.3	5.7	59.00***

† Comparisons between groups performed through ANOVAS with the Bonferroni correction.

IBS-SSS = Irritable Bowel Syndrome Severity Scoring System; FIQ = Fibromyalgia Impact Questionnaire; MFI = Multidimensional Fatigue Index; GAD-7 = Generalized Anxiety Disorder questionnaire (anxiety symptoms); PHQ-9 = Patient Health Questionnaire-9 (depressive symptoms); PHQ-15 = Patient Health Questionnaire-15 (somatic symptoms).

***p < .001.

Table 10. ANOVA Multiple Comparisons

Bonferroni

Dependent Variable	Study Group		Mean Difference	Std. Error	p	95% Confidence Interval	
						Lower Bound	Upper Bound
IBS-SSS	1 IBS alone	2 IBS comorbid mental	-17.335	10.254	1.000	-49.49	14.82
		3 IBS comorbid somatic	-47.493	15.539	.065	-96.21	1.23
		4 IBS multicomorbid	**-67.357***	11.119	<.001	-102.22	-32.49
		5 Healthy control	**200.616***	12.726	<.001	160.71	240.52
		6 Control mental	**113.952***	14.193	<.001	69.45	158.45
		7 Control somatic	**85.990***	14.867	<.001	39.38	132.61
		8 Control multicomorbid	**83.932***	14.515	<.001	38.42	129.44
	2 IBS comorbid mental	1 IBS alone	17.335	10.254	1.000	-14.82	49.49
		3 IBS comorbid somatic	-30.158	16.246	1.000	-81.10	20.78
		4 IBS multicomorbid	**-50.022***	12.087	.001	-87.92	-12.12
		5 Healthy control	**217.951***	13.580	<.001	175.37	260.53
		6 Control mental	**131.287***	14.963	<.001	84.37	178.20
		7 Control somatic	**103.325***	15.605	<.001	54.40	152.25
		8 Control multicomorbid	**101.267***	15.269	<.001	53.39	149.14
	3 IBS comorbid somatic	1 IBS alone	47.493	15.539	.065	-1.23	96.21
		2 IBS comorbid mental	30.158	16.246	1.000	-20.78	81.10
		4 IBS multicomorbid	-19.864	16.805	1.000	-72.55	32.83
		5 Healthy control	**248.109***	17.909	<.001	191.96	304.26
		6 Control mental	**161.445***	18.979	<.001	101.94	220.95
		7 Control somatic	**133.483***	19.489	<.001	72.38	194.59
		8 Control multicomorbid	**131.425***	19.221	<.001	71.16	191.69

	4 IBS multicomorbid	1 IBS alone	**67.357***	11.119	<.001	32.49	102.22
		2 IBS comorbid mental	**50.022***	12.087	.001	12.12	87.92
		3 IBS comorbid somatic	19.864	16.805	1.000	-32.83	72.55
		5 Healthy control	**267.973***	14.245	<.001	223.31	312.64
		6 Control mental	**181.309***	15.569	<.001	132.49	230.12
		7 Control somatic	**153.347***	16.186	<.001	102.60	204.10
		8 Control multicomorbid	**151.288***	15.863	<.001	101.55	201.02
	5 Healthy control	1 IBS alone	**-200.616***	12.726	<.001	-240.52	-160.71
		2 IBS comorbid mental	**-217.951***	13.580	<.001	-260.53	-175.37
		3 IBS comorbid somatic	**-248.109***	17.909	<.001	-304.26	-191.96
		4 IBS multicomorbid	**-267.973***	14.245	<.001	-312.64	-223.31
		6 Control mental	**-86.664***	16.755	<.001	-139.20	-34.13
		7 Control somatic	**-114.626***	17.330	<.001	-168.96	-60.29
		8 Control multicomorbid	**-116.684***	17.028	<.001	-170.07	-63.29
	6 Control mental	1 IBS alone	**-113.952***	14.193	<.001	-158.45	-69.45
		2 IBS comorbid mental	**-131.287***	14.963	<.001	-178.20	-84.37
		3 IBS comorbid somatic	**-161.445***	18.979	<.001	-220.95	-101.94
		4 IBS multicomorbid	**-181.309***	15.569	<.001	-230.12	-132.49
		5 Healthy control	**86.664***	16.755	<.001	34.13	139.20
		7 Control somatic	-27.962	18.434	1.000	-85.76	29.83
		8 Control multicomorbid	-30.021	18.150	1.000	-86.93	26.89
	7 Control somatic	1 IBS alone	**-85.990***	14.867	<.001	-132.61	-39.38
		2 IBS comorbid mental	**-103.325***	15.605	<.001	-152.25	-54.40
		3 IBS comorbid somatic	**-133.483***	19.489	<.001	-194.59	-72.38
		4 IBS multicomorbid	**-153.347***	16.186	<.001	-204.10	-102.60
		5 Healthy control	**114.626***	17.330	<.001	60.29	168.96

		6 Control mental	27.962	18.434	1.000	-29.83	85.76
		8 Control multicomorbid	-2.058	18.682	1.000	-60.64	56.52
	8 Control multicomorbid	1 IBS alone	**-83.932***	14.515	<.001	-129.44	-38.42
		2 IBS comorbid mental	**-101.267***	15.269	<.001	-149.14	-53.39
		3 IBS comorbid somatic	**-131.425***	19.221	<.001	-191.69	-71.16
		4 IBS multicomorbid	**-151.288***	15.863	<.001	-201.02	-101.55
		5 Healthy control	**116.684***	17.028	<.001	63.29	170.07
		6 Control mental	30.021	18.150	1.000	-26.89	86.93
		7 Control somatic	2.058	18.682	1.000	-56.52	60.64
FIQ	1 IBS alone	2 IBS comorbid mental	**-10.87780***	1.92615	<.001	-16.9173	-4.8383
		3 IBS comorbid somatic	**-27.86774***	2.91582	<.001	-37.0103	-18.7252
		4 IBS multicomorbid	**-36.91980***	2.08804	<.001	-43.4669	-30.3727
		5 Healthy control	**10.18239***	2.41386	<.001	2.6137	17.7511
		6 Control mental	**-12.49816***	2.70321	<.001	-20.9741	-4.0222
		7 Control somatic	**-35.34146***	2.81349	<.001	-44.1632	-26.5197
		8 Control multicomorbid	**-34.61823***	2.72391	<.001	-43.1591	-26.0774
	2 IBS comorbid mental	1 IBS alone	**10.87780***	1.92615	<.001	4.8383	16.9173
		3 IBS comorbid somatic	**-16.98994***	3.04598	<.001	-26.5406	-7.4392
		4 IBS multicomorbid	**-26.04200***	2.26626	<.001	-33.1479	-18.9361
		5 Healthy control	**21.06019***	2.56958	<.001	13.0033	29.1171
		6 Control mental	-1.62036	2.84313	1.000	-10.5350	7.2943
		7 Control somatic	**-24.46366***	2.94818	<.001	-33.7077	-15.2196
		8 Control multicomorbid	**-23.74043***	2.86281	<.001	-32.7168	-14.7640
	3 IBS comorbid somatic	1 IBS alone	**27.86774***	2.91582	<.001	18.7252	37.0103
		2 IBS comorbid mental	**16.98994***	3.04598	<.001	7.4392	26.5406
		4 IBS multicomorbid	-9.05206	3.15085	.117	-18.9316	.8275

		5 Healthy control	**38.05013***	3.37560	<.001	27.4659	48.6344
		6 Control mental	**15.36958***	3.58822	<.001	4.1187	26.6205
		7 Control somatic	-7.47372	3.67202	1.000	-18.9874	4.0399
		8 Control multicomorbid	-6.75049	3.60384	1.000	-18.0504	4.5494
	4 IBS multicomorbid	1 IBS alone	**36.91980***	2.08804	<.001	30.3727	43.4669
		2 IBS comorbid mental	**26.04200***	2.26626	<.001	18.9361	33.1479
		3 IBS comorbid somatic	9.05206	3.15085	.117	-.8275	18.9316
		5 Healthy control	**47.10219***	2.69306	<.001	38.6581	55.5463
		6 Control mental	**24.42164***	2.95521	<.001	15.1556	33.6877
		7 Control somatic	1.57834	3.05641	1.000	-8.0051	11.1617
		8 Control multicomorbid	2.30157	2.97415	1.000	-7.0239	11.6270
	5 Healthy control	1 IBS alone	**-10.18239***	2.41386	<.001	-17.7511	-2.6137
		2 IBS comorbid mental	**-21.06019***	2.56958	<.001	-29.1171	-13.0033
		3 IBS comorbid somatic	**-38.05013***	3.37560	<.001	-48.6344	-27.4659
		4 IBS multicomorbid	**-47.10219***	2.69306	<.001	-55.5463	-38.6581
		6 Control mental	**-22.68055***	3.19375	<.001	-32.6946	-12.6665
		7 Control somatic	**-45.52385***	3.28762	<.001	-55.8322	-35.2155
		8 Control multicomorbid	**-44.80062***	3.21129	<.001	-54.8696	-34.7316
	6 Control mental	1 IBS alone	**12.49816***	2.70321	<.001	4.0222	20.9741
		2 IBS comorbid mental	1.62036	2.84313	1.000	-7.2943	10.5350
		3 IBS comorbid somatic	**-15.36958***	3.58822	<.001	-26.6205	-4.1187
		4 IBS multicomorbid	**-24.42164***	2.95521	<.001	-33.6877	-15.1556
		5 Healthy control	**22.68055***	3.19375	<.001	12.6665	32.6946
		7 Control somatic	**-22.84330***	3.50558	<.001	-33.8351	-11.8515
		8 Control multicomorbid	**-22.12007***	3.43410	<.001	-32.8877	-11.3524
	7 Control somatic	1 IBS alone	**35.34146***	2.81349	<.001	26.5197	44.1632

		2 IBS comorbid mental	**24.46366***	2.94818	<.001	15.2196	33.7077
		3 IBS comorbid somatic	7.47372	3.67202	1.000	-4.0399	18.9874
		4 IBS multicomorbid	-1.57834	3.05641	1.000	-11.1617	8.0051
		5 Healthy control	**45.52385***	3.28762	<.001	35.2155	55.8322
		6 Control mental	**22.84330***	3.50558	<.001	11.8515	33.8351
		8 Control multicomorbid	.72323	3.52156	1.000	-10.3187	11.7651
	8 Control multicomorbid	1 IBS alone	**34.61823***	2.72391	<.001	26.0774	43.1591
		2 IBS comorbid mental	**23.74043***	2.86281	<.001	14.7640	32.7168
		3 IBS comorbid somatic	6.75049	3.60384	1.000	-4.5494	18.0504
		4 IBS multicomorbid	-2.30157	2.97415	1.000	-11.6270	7.0239
		5 Healthy control	**44.80062***	3.21129	<.001	34.7316	54.8696
		6 Control mental	**22.12007***	3.43410	<.001	11.3524	32.8877
		7 Control somatic	-.72323	3.52156	1.000	-11.7651	10.3187
MFI General fatigue	1 IBS alone	2 IBS comorbid mental	**-2.353***	.398	<.001	-3.60	-1.10
		3 IBS comorbid somatic	**-4.407***	.603	<.001	-6.30	-2.52
		4 IBS multicomorbid	**-5.418***	.432	<.001	-6.77	-4.06
		5 Healthy control	**3.983***	.494	<.001	2.43	5.53
		6 Control mental	**-2.055***	.568	.009	-3.83	-.27
		7 Control somatic	**-4.286***	.587	<.001	-6.13	-2.45
		8 Control multicomorbid	**-4.550***	.563	<.001	-6.32	-2.78
	2 IBS comorbid mental	1 IBS alone	**2.353***	.398	<.001	1.10	3.60
		3 IBS comorbid somatic	**-2.054***	.630	.033	-4.03	-.08
		4 IBS multicomorbid	**-3.065***	.469	<.001	-4.53	-1.60
		5 Healthy control	**6.336***	.527	<.001	4.69	7.99
		6 Control mental	.299	.596	1.000	-1.57	2.17
		7 Control somatic	**-1.932***	.615	.049	-3.86	-.01

	8 Control multicomorbid	**-2.197***	.592	.006	-4.05	-.34
3 IBS comorbid somatic	1 IBS alone	**4.407***	.603	<.001	2.52	6.30
	2 IBS comorbid mental	**2.054***	.630	.033	.08	4.03
	4 IBS multicomorbid	-1.011	.652	1.000	-3.05	1.03
	5 Healthy control	**8.390***	.694	<.001	6.21	10.57
	6 Control mental	**2.352***	.749	.049	.00	4.70
	7 Control somatic	.121	.763	1.000	-2.27	2.51
	8 Control multicomorbid	-.143	.745	1.000	-2.48	2.19
4 IBS multicomorbid	1 IBS alone	**5.418***	.432	<.001	4.06	6.77
	2 IBS comorbid mental	**3.065***	.469	<.001	1.60	4.53
	3 IBS comorbid somatic	1.011	.652	1.000	-1.03	3.05
	5 Healthy control	**9.401***	.552	<.001	7.67	11.13
	6 Control mental	**3.364***	.619	<.001	1.42	5.31
	7 Control somatic	1.133	.637	1.000	-.86	3.13
	8 Control multicomorbid	.868	.615	1.000	-1.06	2.80
5 Healthy control	1 IBS alone	**-3.983***	.494	<.001	-5.53	-2.43
	2 IBS comorbid mental	**-6.336***	.527	<.001	-7.99	-4.69
	3 IBS comorbid somatic	**-8.390***	.694	<.001	-10.57	-6.21
	4 IBS multicomorbid	**-9.401***	.552	<.001	-11.13	-7.67
	6 Control mental	**-6.038***	.664	<.001	-8.12	-3.96
	7 Control somatic	**-8.269***	.681	<.001	-10.40	-6.13
	8 Control multicomorbid	**-8.533***	.660	<.001	-10.60	-6.46
6 Control mental	1 IBS alone	**2.055***	.568	.009	.27	3.83
	2 IBS comorbid mental	-.299	.596	1.000	-2.17	1.57
	3 IBS comorbid somatic	**-2.352***	.749	.049	-4.70	.00
	4 IBS multicomorbid	**-3.364***	.619	<.001	-5.31	-1.42

		5 Healthy control	**6.038***	.664	<.001	3.96	8.12
		7 Control somatic	-2.231	.736	.070	-4.54	.08
		8 Control multicomorbid	**-2.496***	.717	.015	-4.74	-.25
	7 Control somatic	1 IBS alone	**4.286***	.587	<.001	2.45	6.13
		2 IBS comorbid mental	**1.932***	.615	.049	.01	3.86
		3 IBS comorbid somatic	-.121	.763	1.000	-2.51	2.27
		4 IBS multicomorbid	-1.133	.637	1.000	-3.13	.86
		5 Healthy control	**8.269***	.681	<.001	6.13	10.40
		6 Control mental	2.231	.736	.070	-.08	4.54
		8 Control multicomorbid	-.265	.732	1.000	-2.56	2.03
	8 Control multicomorbid	1 IBS alone	**4.550***	.563	<.001	2.78	6.32
		2 IBS comorbid mental	**2.197***	.592	.006	.34	4.05
		3 IBS comorbid somatic	.143	.745	1.000	-2.19	2.48
		4 IBS multicomorbid	-.868	.615	1.000	-2.80	1.06
		5 Healthy control	**8.533***	.660	<.001	6.46	10.60
		6 Control mental	**2.496***	.717	.015	.25	4.74
		7 Control somatic	.265	.732	1.000	-2.03	2.56
MFI Physical fatigue	1 IBS alone	2 IBS comorbid mental	**-2.510***	.434	<.001	-3.87	-1.15
		3 IBS comorbid somatic	**-4.791***	.663	<.001	-6.87	-2.71
		4 IBS multicomorbid	**-5.658***	.470	<.001	-7.13	-4.18
		5 Healthy control	**2.785***	.538	<.001	1.10	4.47
		6 Control mental	-1.079	.618	1.000	-3.02	.86
		7 Control somatic	**-4.798***	.633	<.001	-6.78	-2.81
		8 Control multicomorbid	**-4.648***	.618	<.001	-6.59	-2.71
	2 IBS comorbid mental	1 IBS alone	**2.510***	.434	<.001	1.15	3.87
		3 IBS comorbid somatic	**-2.281***	.692	.029	-4.45	-.11

		4 IBS multicomorbid	**-3.148***	.510	<.001	-4.75	-1.55
		5 Healthy control	**5.295***	.573	<.001	3.50	7.09
		6 Control mental	1.430	.649	.781	-.61	3.47
		7 Control somatic	**-2.288***	.664	.017	-4.37	-.21
		8 Control multicomorbid	**-2.139***	.649	.029	-4.17	-.10
	3 IBS comorbid somatic	1 IBS alone	**4.791***	.663	<.001	2.71	6.87
		2 IBS comorbid mental	**2.281***	.692	.029	.11	4.45
		4 IBS multicomorbid	-.867	.715	1.000	-3.11	1.38
		5 Healthy control	**7.576***	.761	<.001	5.19	9.96
		6 Control mental	**3.711***	.820	<.001	1.14	6.28
		7 Control somatic	-.007	.832	1.000	-2.61	2.60
		8 Control multicomorbid	.143	.820	1.000	-2.43	2.71
	4 IBS multicomorbid	1 IBS alone	**5.658***	.470	<.001	4.18	7.13
		2 IBS comorbid mental	**3.148***	.510	<.001	1.55	4.75
		3 IBS comorbid somatic	.867	.715	1.000	-1.38	3.11
		5 Healthy control	**8.443***	.601	<.001	6.56	10.33
		6 Control mental	**4.578***	.674	<.001	2.46	6.69
		7 Control somatic	.860	.688	1.000	-1.30	3.02
		8 Control multicomorbid	1.010	.674	1.000	-1.10	3.12
	5 Healthy control	1 IBS alone	**-2.785***	.538	<.001	-4.47	-1.10
		2 IBS comorbid mental	**-5.295***	.573	<.001	-7.09	-3.50
		3 IBS comorbid somatic	**-7.576***	.761	<.001	-9.96	-5.19
		4 IBS multicomorbid	**-8.443***	.601	<.001	-10.33	-6.56
		6 Control mental	**-3.865***	.723	<.001	-6.13	-1.60
		7 Control somatic	**-7.583***	.736	<.001	-9.89	-5.27
		8 Control multicomorbid	**-7.433***	.723	<.001	-9.70	-5.17

	6 Control mental	1 IBS alone	1.079	.618	1.000	-.86	3.02
		2 IBS comorbid mental	-1.430	.649	.781	-3.47	.61
		3 IBS comorbid somatic	**-3.711***	.820	<.001	-6.28	-1.14
		4 IBS multicomorbid	**-4.578***	.674	<.001	-6.69	-2.46
		5 Healthy control	**3.865***	.723	<.001	1.60	6.13
		7 Control somatic	**-3.718***	.797	<.001	-6.22	-1.22
		8 Control multicomorbid	**-3.569***	.784	<.001	-6.03	-1.11
	7 Control somatic	1 IBS alone	**4.798***	.633	<.001	2.81	6.78
		2 IBS comorbid mental	**2.288***	.664	.017	.21	4.37
		3 IBS comorbid somatic	.007	.832	1.000	-2.60	2.61
		4 IBS multicomorbid	-.860	.688	1.000	-3.02	1.30
		5 Healthy control	**7.583***	.736	<.001	5.27	9.89
		6 Control mental	**3.718***	.797	<.001	1.22	6.22
		8 Control multicomorbid	.150	.797	1.000	-2.35	2.65
	8 Control multicomorbid	1 IBS alone	**4.648***	.618	<.001	2.71	6.59
		2 IBS comorbid mental	**2.139***	.649	.029	.10	4.17
		3 IBS comorbid somatic	-.143	.820	1.000	-2.71	2.43
		4 IBS multicomorbid	-1.010	.674	1.000	-3.12	1.10
		5 Healthy control	**7.433***	.723	<.001	5.17	9.70
		6 Control mental	**3.569***	.784	<.001	1.11	6.03
		7 Control somatic	-.150	.797	1.000	-2.65	2.35
MFI Reduced Activity	1 IBS alone	2 IBS comorbid mental	**-2.695***	.429	<.001	-4.04	-1.35
		3 IBS comorbid somatic	**-3.813***	.649	<.001	-5.85	-1.78
		4 IBS multicomorbid	**-6.039***	.465	<.001	-7.50	-4.58
		5 Healthy control	**2.205***	.532	.001	.54	3.87
		6 Control mental	**-3.691***	.607	<.001	-5.59	-1.79

	7 Control somatic	**-4.066***	.632	<.001	-6.05	-2.08
	8 Control multicomorbid	**-5.114***	.607	<.001	-7.02	-3.21
2 IBS comorbid mental	1 IBS alone	**2.695***	.429	<.001	1.35	4.04
	3 IBS comorbid somatic	-1.118	.678	1.000	-3.24	1.01
	4 IBS multicomorbid	**-3.343***	.505	<.001	-4.93	-1.76
	5 Healthy control	**4.900***	.567	<.001	3.12	6.68
	6 Control mental	-.996	.637	1.000	-2.99	1.00
	7 Control somatic	-1.370	.662	1.000	-3.44	.70
	8 Control multicomorbid	**-2.419***	.637	.005	-4.42	-.42
3 IBS comorbid somatic	1 IBS alone	**3.813***	.649	<.001	1.78	5.85
	2 IBS comorbid mental	1.118	.678	1.000	-1.01	3.24
	4 IBS multicomorbid	**-2.226***	.702	.044	-4.43	-.03
	5 Healthy control	**6.018***	.748	<.001	3.67	8.36
	6 Control mental	.122	.802	1.000	-2.39	2.64
	7 Control somatic	-.252	.822	1.000	-2.83	2.32
	8 Control multicomorbid	-1.301	.802	1.000	-3.82	1.22
4 IBS multicomorbid	1 IBS alone	**6.039***	.465	<.001	4.58	7.50
	2 IBS comorbid mental	**3.343***	.505	<.001	1.76	4.93
	3 IBS comorbid somatic	**2.226***	.702	.044	.03	4.43
	5 Healthy control	**8.244***	.595	<.001	6.38	10.11
	6 Control mental	**2.348***	.662	.012	.27	4.42
	7 Control somatic	1.973	.686	.115	-.18	4.12
	8 Control multicomorbid	.925	.662	1.000	-1.15	3.00
5 Healthy control	1 IBS alone	**-2.205***	.532	.001	-3.87	-.54
	2 IBS comorbid mental	**-4.900***	.567	<.001	-6.68	-3.12
	3 IBS comorbid somatic	**-6.018***	.748	<.001	-8.36	-3.67

		4 IBS multicomorbid	**-8.244***	.595	<.001	-10.11	-6.38
		6 Control mental	**-5.896***	.711	<.001	-8.12	-3.67
		7 Control somatic	**-6.270***	.733	<.001	-8.57	-3.97
		8 Control multicomorbid	**-7.319***	.711	<.001	-9.55	-5.09
	6 Control mental	1 IBS alone	**3.691***	.607	<.001	1.79	5.59
		2 IBS comorbid mental	.996	.637	1.000	-1.00	2.99
		3 IBS comorbid somatic	-.122	.802	1.000	-2.64	2.39
		4 IBS multicomorbid	**-2.348***	.662	.012	-4.42	-.27
		5 Healthy control	**5.896***	.711	<.001	3.67	8.12
		7 Control somatic	-.375	.788	1.000	-2.85	2.10
		8 Control multicomorbid	-1.423	.768	1.000	-3.83	.99
	7 Control somatic	1 IBS alone	**4.066***	.632	<.001	2.08	6.05
		2 IBS comorbid mental	1.370	.662	1.000	-.70	3.44
		3 IBS comorbid somatic	.252	.822	1.000	-2.32	2.83
		4 IBS multicomorbid	-1.973	.686	.115	-4.12	.18
		5 Healthy control	**6.270***	.733	<.001	3.97	8.57
		6 Control mental	.375	.788	1.000	-2.10	2.85
		8 Control multicomorbid	-1.048	.788	1.000	-3.52	1.42
	8 Control multicomorbid	1 IBS alone	**5.114***	.607	<.001	3.21	7.02
		2 IBS comorbid mental	**2.419***	.637	.005	.42	4.42
		3 IBS comorbid somatic	1.301	.802	1.000	-1.22	3.82
		4 IBS multicomorbid	-.925	.662	1.000	-3.00	1.15
		5 Healthy control	**7.319***	.711	<.001	5.09	9.55
		6 Control mental	1.423	.768	1.000	-.99	3.83
		7 Control somatic	1.048	.788	1.000	-1.42	3.52
MFI	1 IBS alone	2 IBS comorbid mental	**-2.522***	.401	<.001	-3.78	-1.26

Reduced Motivation		3 IBS comorbid somatic	-1.713	.613	.150	-3.64	.21
		4 IBS multicomorbid	**-4.463***	.435	<.001	-5.83	-3.10
		5 Healthy control	**2.303***	.498	<.001	.74	3.86
		6 Control mental	**-2.302***	.572	.002	-4.10	-.51
		7 Control somatic	**-2.080***	.596	.014	-3.95	-.21
		8 Control multicomorbid	**-3.851***	.572	<.001	-5.64	-2.06
	2 IBS comorbid mental	1 IBS alone	**2.522***	.401	<.001	1.26	3.78
		3 IBS comorbid somatic	.809	.640	1.000	-1.20	2.82
		4 IBS multicomorbid	**-1.940***	.472	.001	-3.42	-.46
		5 Healthy control	**4.825***	.531	<.001	3.16	6.49
		6 Control mental	.220	.601	1.000	-1.66	2.10
		7 Control somatic	.442	.624	1.000	-1.51	2.40
		8 Control multicomorbid	-1.329	.601	.764	-3.21	.55
	3 IBS comorbid somatic	1 IBS alone	1.713	.613	.150	-.21	3.64
		2 IBS comorbid mental	-.809	.640	1.000	-2.82	1.20
		4 IBS multicomorbid	**-2.749***	.662	.001	-4.82	-.67
		5 Healthy control	**4.016***	.705	<.001	1.81	6.23
		6 Control mental	-.589	.759	1.000	-2.97	1.79
		7 Control somatic	-.367	.778	1.000	-2.81	2.07
		8 Control multicomorbid	-2.138	.759	.140	-4.52	.24
	4 IBS multicomorbid	1 IBS alone	**4.463***	.435	<.001	3.10	5.83
		2 IBS comorbid mental	**1.940***	.472	.001	.46	3.42
		3 IBS comorbid somatic	**2.749***	.662	.001	.67	4.82
		5 Healthy control	**6.765***	.556	<.001	5.02	8.51
		6 Control mental	**2.161***	.624	.016	.20	4.12
		7 Control somatic	**2.382***	.646	.007	.36	4.41

	8 Control multicomorbid	.612	.624	1.000	-1.34	2.57
5 Healthy control	1 IBS alone	**-2.303***	.498	<.001	-3.86	-.74
	2 IBS comorbid mental	**-4.825***	.531	<.001	-6.49	-3.16
	3 IBS comorbid somatic	**-4.016***	.705	<.001	-6.23	-1.81
	4 IBS multicomorbid	**-6.765***	.556	<.001	-8.51	-5.02
	6 Control mental	**-4.605***	.669	<.001	-6.70	-2.51
	7 Control somatic	**-4.383***	.690	<.001	-6.55	-2.22
	8 Control multicomorbid	**-6.154***	.669	<.001	-8.25	-4.06
6 Control mental	1 IBS alone	**2.302***	.572	.002	.51	4.10
	2 IBS comorbid mental	-.220	.601	1.000	-2.10	1.66
	3 IBS comorbid somatic	.589	.759	1.000	-1.79	2.97
	4 IBS multicomorbid	**-2.161***	.624	.016	-4.12	-.20
	5 Healthy control	**4.605***	.669	<.001	2.51	6.70
	7 Control somatic	.222	.745	1.000	-2.12	2.56
	8 Control multicomorbid	-1.549	.726	.929	-3.83	.73
7 Control somatic	1 IBS alone	**2.080***	.596	.014	.21	3.95
	2 IBS comorbid mental	-.442	.624	1.000	-2.40	1.51
	3 IBS comorbid somatic	.367	.778	1.000	-2.07	2.81
	4 IBS multicomorbid	**-2.382***	.646	.007	-4.41	-.36
	5 Healthy control	**4.383***	.690	<.001	2.22	6.55
	6 Control mental	-.222	.745	1.000	-2.56	2.12
	8 Control multicomorbid	-1.771	.745	.498	-4.11	.57
8 Control multicomorbid	1 IBS alone	**3.851***	.572	<.001	2.06	5.64
	2 IBS comorbid mental	1.329	.601	.764	-.55	3.21
	3 IBS comorbid somatic	2.138	.759	.140	-.24	4.52
	4 IBS multicomorbid	-.612	.624	1.000	-2.57	1.34

		5 Healthy control	**6.154***	.669	<.001	4.06	8.25
		6 Control mental	1.549	.726	.929	-.73	3.83
		7 Control somatic	1.771	.745	.498	-.57	4.11
MFI Mental Fatigue	1 IBS alone	2 IBS comorbid mental	**-2.579***	.462	<.001	-4.03	-1.13
		3 IBS comorbid somatic	**-3.024***	.700	<.001	-5.22	-.83
		4 IBS multicomorbid	**-5.109***	.501	<.001	-6.68	-3.54
		5 Healthy control	**1.808***	.573	.047	.01	3.60
		6 Control mental	**-2.706***	.659	.001	-4.77	-.64
		7 Control somatic	**-3.007***	.687	<.001	-5.16	-.85
		8 Control multicomorbid	**-4.765***	.659	<.001	-6.83	-2.70
	2 IBS comorbid mental	1 IBS alone	**2.579***	.462	<.001	1.13	4.03
		3 IBS comorbid somatic	-.444	.731	1.000	-2.74	1.85
		4 IBS multicomorbid	**-2.530***	.544	<.001	-4.23	-.83
		5 Healthy control	**4.387***	.611	<.001	2.47	6.30
		6 Control mental	-.127	.692	1.000	-2.30	2.04
		7 Control somatic	-.428	.719	1.000	-2.68	1.83
		8 Control multicomorbid	**-2.185***	.692	.046	-4.35	-.02
	3 IBS comorbid somatic	1 IBS alone	**3.024***	.700	<.001	.83	5.22
		2 IBS comorbid mental	.444	.731	1.000	-1.85	2.74
		4 IBS multicomorbid	-2.086	.756	.166	-4.46	.28
		5 Healthy control	**4.832***	.806	<.001	2.31	7.36
		6 Control mental	.318	.868	1.000	-2.41	3.04
		7 Control somatic	.017	.890	1.000	-2.77	2.81
		8 Control multicomorbid	-1.741	.868	1.000	-4.46	.98
	4 IBS multicomorbid	1 IBS alone	**5.109***	.501	<.001	3.54	6.68
		2 IBS comorbid mental	**2.530***	.544	<.001	.83	4.23

		3 IBS comorbid somatic	2.086	.756	.166	-.28	4.46
		5 Healthy control	**6.917***	.641	<.001	4.91	8.93
		6 Control mental	**2.403***	.718	.024	.15	4.66
		7 Control somatic	2.102	.744	.136	-.23	4.44
		8 Control multicomorbid	.345	.718	1.000	-1.91	2.60
	5 Healthy control	1 IBS alone	**-1.808***	.573	.047	-3.60	-.01
		2 IBS comorbid mental	**-4.387***	.611	<.001	-6.30	-2.47
		3 IBS comorbid somatic	**-4.832***	.806	<.001	-7.36	-2.31
		4 IBS multicomorbid	**-6.917***	.641	<.001	-8.93	-4.91
		6 Control mental	**-4.514***	.770	<.001	-6.93	-2.10
		7 Control somatic	**-4.815***	.795	<.001	-7.31	-2.32
		8 Control multicomorbid	**-6.573***	.770	<.001	-8.99	-4.16
	6 Control mental	1 IBS alone	**2.706***	.659	.001	.64	4.77
		2 IBS comorbid mental	.127	.692	1.000	-2.04	2.30
		3 IBS comorbid somatic	-.318	.868	1.000	-3.04	2.41
		4 IBS multicomorbid	**-2.403***	.718	.024	-4.66	-.15
		5 Healthy control	**4.514***	.770	<.001	2.10	6.93
		7 Control somatic	-.301	.858	1.000	-2.99	2.39
		8 Control multicomorbid	-2.059	.836	.392	-4.68	.56
	7 Control somatic	1 IBS alone	**3.007***	.687	<.001	.85	5.16
		2 IBS comorbid mental	.428	.719	1.000	-1.83	2.68
		3 IBS comorbid somatic	-.017	.890	1.000	-2.81	2.77
		4 IBS multicomorbid	-2.102	.744	.136	-4.44	.23
		5 Healthy control	**4.815***	.795	<.001	2.32	7.31
		6 Control mental	.301	.858	1.000	-2.39	2.99
		8 Control multicomorbid	-1.758	.858	1.000	-4.45	.93

	8 Control multicomorbid	1 IBS alone	**4.765***	.659	<.001	2.70	6.83
		2 IBS comorbid mental	**2.185***	.692	.046	.02	4.35
		3 IBS comorbid somatic	1.741	.868	1.000	-.98	4.46
		4 IBS multicomorbid	-.345	.718	1.000	-2.60	1.91
		5 Healthy control	**6.573***	.770	<.001	4.16	8.99
		6 Control mental	2.059	.836	.392	-.56	4.68
		7 Control somatic	1.758	.858	1.000	-.93	4.45
GAD-7	1 IBS alone	2 IBS comorbid mental	**-3.871***	.505	<.001	-5.46	-2.29
		3 IBS comorbid somatic	-.919	.766	1.000	-3.32	1.48
		4 IBS multicomorbid	**-6.693***	.548	<.001	-8.41	-4.97
		5 Healthy control	**2.450***	.627	.003	.48	4.42
		6 Control mental	**-4.517***	.704	<.001	-6.73	-2.31
		7 Control somatic	**-2.503***	.733	.019	-4.80	-.21
		8 Control multicomorbid	**-6.165***	.715	<.001	-8.41	-3.92
	2 IBS comorbid mental	1 IBS alone	**3.871***	.505	<.001	2.29	5.46
		3 IBS comorbid somatic	**2.952***	.800	.007	.44	5.46
		4 IBS multicomorbid	**-2.822***	.595	<.001	-4.69	-.96
		5 Healthy control	**6.321***	.669	<.001	4.22	8.42
		6 Control mental	-.646	.742	1.000	-2.97	1.68
		7 Control somatic	1.367	.769	1.000	-1.04	3.78
		8 Control multicomorbid	-2.295	.752	.066	-4.65	.06
	3 IBS comorbid somatic	1 IBS alone	.919	.766	1.000	-1.48	3.32
		2 IBS comorbid mental	**-2.952***	.800	.007	-5.46	-.44
		4 IBS multicomorbid	**-5.774***	.828	<.001	-8.37	-3.18
		5 Healthy control	**3.369***	.882	.004	.60	6.13
		6 Control mental	**-3.598***	.939	.004	-6.54	-.65

		7 Control somatic	-1.584	.960	1.000	-4.59	1.43
		8 Control multicomorbid	**-5.247***	.947	<.001	-8.21	-2.28
	4 IBS multicomorbid	1 IBS alone	**6.693***	.548	<.001	4.97	8.41
		2 IBS comorbid mental	**2.822***	.595	<.001	.96	4.69
		3 IBS comorbid somatic	**5.774***	.828	<.001	3.18	8.37
		5 Healthy control	**9.143***	.702	<.001	6.94	11.34
		6 Control mental	2.176	.771	.138	-.24	4.60
		7 Control somatic	**4.190***	.797	<.001	1.69	6.69
		8 Control multicomorbid	.527	.781	1.000	-1.92	2.98
	5 Healthy control	1 IBS alone	**-2.450***	.627	.003	-4.42	-.48
		2 IBS comorbid mental	**-6.321***	.669	<.001	-8.42	-4.22
		3 IBS comorbid somatic	**-3.369***	.882	.004	-6.13	-.60
		4 IBS multicomorbid	**-9.143***	.702	<.001	-11.34	-6.94
		6 Control mental	**-6.966***	.830	<.001	-9.57	-4.37
		7 Control somatic	**-4.953***	.854	<.001	-7.63	-2.28
		8 Control multicomorbid	**-8.615***	.839	<.001	-11.24	-5.99
	6 Control mental	1 IBS alone	**4.517***	.704	<.001	2.31	6.73
		2 IBS comorbid mental	.646	.742	1.000	-1.68	2.97
		3 IBS comorbid somatic	**3.598***	.939	.004	.65	6.54
		4 IBS multicomorbid	-2.176	.771	.138	-4.60	.24
		5 Healthy control	**6.966***	.830	<.001	4.37	9.57
		7 Control somatic	2.013	.912	.772	-.85	4.87
		8 Control multicomorbid	-1.649	.898	1.000	-4.46	1.17
	7 Control somatic	1 IBS alone	**2.503***	.733	.019	.21	4.80
		2 IBS comorbid mental	-1.367	.769	1.000	-3.78	1.04
		3 IBS comorbid somatic	1.584	.960	1.000	-1.43	4.59

		4 IBS multicomorbid	**-4.190***	.797	<.001	-6.69	-1.69
		5 Healthy control	**4.953***	.854	<.001	2.28	7.63
		6 Control mental	-2.013	.912	.772	-4.87	.85
		8 Control multicomorbid	**-3.662***	.920	.002	-6.55	-.78
	8 Control multicomorbid	1 IBS alone	**6.165***	.715	<.001	3.92	8.41
		2 IBS comorbid mental	2.295	.752	.066	-.06	4.65
		3 IBS comorbid somatic	**5.247***	.947	<.001	2.28	8.21
		4 IBS multicomorbid	-.527	.781	1.000	-2.98	1.92
		5 Healthy control	**8.615***	.839	<.001	5.99	11.24
		6 Control mental	1.649	.898	1.000	-1.17	4.46
		7 Control somatic	**3.662***	.920	.002	.78	6.55
PHQ-9	1 IBS alone	2 IBS comorbid mental	**-4.455***	.563	<.001	-6.22	-2.69
		3 IBS comorbid somatic	**-2.946***	.861	.018	-5.64	-.25
		4 IBS multicomorbid	**-8.582***	.610	<.001	-10.50	-6.67
		5 Healthy control	**3.064***	.702	<.001	.86	5.26
		6 Control mental	**-6.702***	.790	<.001	-9.18	-4.22
		7 Control somatic	**-4.078***	.816	<.001	-6.64	-1.52
		8 Control multicomorbid	**-7.618***	.803	<.001	-10.13	-5.10
	2 IBS comorbid mental	1 IBS alone	**4.455***	.563	<.001	2.69	6.22
		3 IBS comorbid somatic	1.508	.898	1.000	-1.31	4.33
		4 IBS multicomorbid	**-4.128***	.663	<.001	-6.20	-2.05
		5 Healthy control	**7.518***	.748	<.001	5.17	9.86
		6 Control mental	-2.248	.831	.196	-4.85	.36
		7 Control somatic	.377	.855	1.000	-2.30	3.06
		8 Control multicomorbid	**-3.163***	.843	.005	-5.81	-.52
	3 IBS comorbid somatic	1 IBS alone	**2.946***	.861	.018	.25	5.64

	2 IBS comorbid mental	-1.508	.898	1.000	-4.33	1.31
	4 IBS multicomorbid	**-5.636***	.929	<.001	-8.55	-2.72
	5 Healthy control	**6.010***	.991	<.001	2.90	9.12
	6 Control mental	**-3.756***	1.056	.011	-7.07	-.45
	7 Control somatic	-1.131	1.075	1.000	-4.50	2.24
	8 Control multicomorbid	**-4.672***	1.065	<.001	-8.01	-1.33
4 IBS multicomorbid	1 IBS alone	**8.582***	.610	<.001	6.67	10.50
	2 IBS comorbid mental	**4.128***	.663	<.001	2.05	6.20
	3 IBS comorbid somatic	**5.636***	.929	<.001	2.72	8.55
	5 Healthy control	**11.646***	.784	<.001	9.19	14.10
	6 Control mental	1.880	.864	.837	-.83	4.59
	7 Control somatic	**4.504***	.887	<.001	1.72	7.29
	8 Control multicomorbid	.964	.875	1.000	-1.78	3.71
5 Healthy control	1 IBS alone	**-3.064***	.702	<.001	-5.26	-.86
	2 IBS comorbid mental	**-7.518***	.748	<.001	-9.86	-5.17
	3 IBS comorbid somatic	**-6.010***	.991	<.001	-9.12	-2.90
	4 IBS multicomorbid	**-11.646***	.784	<.001	-14.10	-9.19
	6 Control mental	**-9.766***	.931	<.001	-12.68	-6.85
	7 Control somatic	**-7.141***	.953	<.001	-10.13	-4.15
	8 Control multicomorbid	**-10.681***	.941	<.001	-13.63	-7.73
6 Control mental	1 IBS alone	**6.702***	.790	<.001	4.22	9.18
	2 IBS comorbid mental	2.248	.831	.196	-.36	4.85
	3 IBS comorbid somatic	**3.756***	1.056	.011	.45	7.07
	4 IBS multicomorbid	-1.880	.864	.837	-4.59	.83
	5 Healthy control	**9.766***	.931	<.001	6.85	12.68
	7 Control somatic	2.625	1.019	.286	-.57	5.82

		8 Control multicomorbid	-.916	1.009	1.000	-4.08	2.25
	7 Control somatic	1 IBS alone	**4.078***	.816	<.001	1.52	6.64
		2 IBS comorbid mental	-.377	.855	1.000	-3.06	2.30
		3 IBS comorbid somatic	1.131	1.075	1.000	-2.24	4.50
		4 IBS multicomorbid	**-4.504***	.887	<.001	-7.29	-1.72
		5 Healthy control	**7.141***	.953	<.001	4.15	10.13
		6 Control mental	-2.625	1.019	.286	-5.82	.57
		8 Control multicomorbid	**-3.540***	1.029	.017	-6.77	-.31
	8 Control multicomorbid	1 IBS alone	**7.618***	.803	<.001	5.10	10.13
		2 IBS comorbid mental	**3.163***	.843	.005	.52	5.81
		3 IBS comorbid somatic	**4.672***	1.065	<.001	1.33	8.01
		4 IBS multicomorbid	-.964	.875	1.000	-3.71	1.78
		5 Healthy control	**10.681***	.941	<.001	7.73	13.63
		6 Control mental	.916	1.009	1.000	-2.25	4.08
		7 Control somatic	3.540*	1.029	.017	.31	6.77
PHQ-15	1 IBS alone	2 IBS comorbid mental	**-2.603***	.607	<.001	-4.51	-.70
		3 IBS comorbid somatic	**-5.336***	.926	<.001	-8.24	-2.43
		4 IBS multicomorbid	**-8.211***	.665	<.001	-10.30	-6.12
		5 Healthy control	**7.327***	.752	<.001	4.97	9.68
		6 Control mental	.598	.851	1.000	-2.07	3.27
		7 Control somatic	**-4.585***	.918	<.001	-7.46	-1.71
		8 Control multicomorbid	**-4.589***	.871	<.001	-7.32	-1.86
	2 IBS comorbid mental	1 IBS alone	**2.603***	.607	<.001	.70	4.51
		3 IBS comorbid somatic	-2.733	.968	.137	-5.77	.30
		4 IBS multicomorbid	**-5.608***	.722	<.001	-7.87	-3.34
		5 Healthy control	**9.930***	.802	<.001	7.41	12.45

		6 Control mental	**3.201***	.896	.011	.39	6.01
		7 Control somatic	-1.982	.959	1.000	-4.99	1.03
		8 Control multicomorbid	-1.986	.915	.847	-4.85	.88
	3 IBS comorbid somatic	1 IBS alone	**5.336***	.926	<.001	2.43	8.24
		2 IBS comorbid mental	2.733	.968	.137	-.30	5.77
		4 IBS multicomorbid	-2.876	1.005	.122	-6.03	.28
		5 Healthy control	**12.663***	1.064	<.001	9.33	16.00
		6 Control mental	**5.933***	1.136	<.001	2.37	9.50
		7 Control somatic	.751	1.187	1.000	-2.97	4.47
		8 Control multicomorbid	.747	1.151	1.000	-2.86	4.36
	4 IBS multicomorbid	1 IBS alone	**8.211***	.665	<.001	6.12	10.30
		2 IBS comorbid mental	**5.608***	.722	<.001	3.34	7.87
		3 IBS comorbid somatic	2.876	1.005	.122	-.28	6.03
		5 Healthy control	**15.539***	.847	<.001	12.88	18.19
		6 Control mental	**8.809***	.936	<.001	5.87	11.74
		7 Control somatic	**3.627***	.997	.008	.50	6.75
		8 Control multicomorbid	**3.622***	.954	.004	.63	6.61
	5 Healthy control	1 IBS alone	**-7.327***	.752	<.001	-9.68	-4.97
		2 IBS comorbid mental	**-9.930***	.802	<.001	-12.45	-7.41
		3 IBS comorbid somatic	**-12.663***	1.064	<.001	-16.00	-9.33
		4 IBS multicomorbid	**-15.539***	.847	<.001	-18.19	-12.88
		6 Control mental	**-6.730***	.999	<.001	-9.86	-3.60
		7 Control somatic	**-11.912***	1.057	<.001	-15.23	-8.60
		8 Control multicomorbid	**-11.916***	1.016	<.001	-15.10	-8.73
	6 Control mental	1 IBS alone	-.598	.851	1.000	-3.27	2.07
		2 IBS comorbid mental	**-3.201***	.896	.011	-6.01	-.39

		3 IBS comorbid somatic	**-5.933***	1.136	<.001	-9.50	-2.37
		4 IBS multicomorbid	**-8.809***	.936	<.001	-11.74	-5.87
		5 Healthy control	**6.730***	.999	<.001	3.60	9.86
		7 Control somatic	**-5.182***	1.129	<.001	-8.72	-1.64
		8 Control multicomorbid	**-5.187***	1.092	<.001	-8.61	-1.76
	7 Control somatic	1 IBS alone	**4.585***	.918	<.001	1.71	7.46
		2 IBS comorbid mental	1.982	.959	1.000	-1.03	4.99
		3 IBS comorbid somatic	-.751	1.187	1.000	-4.47	2.97
		4 IBS multicomorbid	**-3.627***	.997	.008	-6.75	-.50
		5 Healthy control	**11.912***	1.057	<.001	8.60	15.23
		6 Control mental	**5.182***	1.129	<.001	1.64	8.72
		8 Control multicomorbid	-.005	1.144	1.000	-3.59	3.58
	8 Control multicomorbid	1 IBS alone	**4.589***	.871	<.001	1.86	7.32
		2 IBS comorbid mental	1.986	.915	.847	-.88	4.85
		3 IBS comorbid somatic	-.747	1.151	1.000	-4.36	2.86
		4 IBS multicomorbid	**-3.622***	.954	.004	-6.61	-.63
		5 Healthy control	**11.916***	1.016	<.001	8.73	15.10
		6 Control mental	**5.187***	1.092	<.001	1.76	8.61
		7 Control somatic	.005	1.144	1.000	-3.58	3.59

* The mean difference is significant at the 0.05 level.

Table 11. Group comparisons, BTQ (Chi-square)

	Total sample (n = 676)		IBS alone (n = 190)		IBS comorbid-mental (n = 113)		IBS comorbid-somatic (n = 43)		IBS multi-comorbid (n = 98)		Healthy controls (n = 64)		Control – mental (n = 54)		Control – somatic (n = 49)		Control mental + somatic (n = 52)		χ2 †
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	
BTQ, n (%)	268	408	58 (30.5)	132 (69.5)	48 (42.5)	65 (57.5)	13 (30.2)	30 (69.8)	55 (56.1)	43 (43.9)	18 (28.1)	46 (71.9)	31 (57.4)	23 (42.6)	14 (28.6)	35 (71.4)	29 (55.8)	23 (44.2)	38.31 ***

† Comparisons between groups performed through Chi-square analysis.

BTQ = Brief Trauma Questionnaire (report of at least one traumatic event).

***p < .001.

Table 12. Pearson correlations between study questionnaires

Total sample

	IBS-SSS	BTQ	FIQ	MFI – general fatigue	MFI – physical fatigue	MFI – reduced activity	MFI – reduced motivation	MFI – mental fatigue	GAD7	PHQ9
IBS-SSS	1									
BTQ	.014	1								
FIQ	.338***	.173***	1							
MFI – general fatigue	.358***	.152***	.678***	1						
MFI – physical fatigue	.318***	.120**	.674***	.801***	1					
MFI – reduced activity	.250***	.212***	.642***	.687***	.734***	1				
MFI – reduced motivation	.266***	.168***	.591***	.639***	.629***	.698**	1			
MFI – mental fatigue	.245***	.139***	.560***	.612***	.561***	.615**	.565***	1		
GAD7	.272***	.238***	.618***	.526***	.453***	.509**	.553***	.551***	1	
PHQ9	.290***	.226***	.712***	.665***	.590***	.657**	.679***	.656***	.776***	1
PHQ15	.517***	.161***	.731***	.606***	.580***	.532**	.527***	.503***	.610***	.679***

IBS-SSS = Irritable Bowel Syndrome Severity Scoring System; BTQ = Brief Trauma Questionnaire (report of at least one traumatic event); FIQ = Fibromyalgia Impact Questionnaire; MFI = Multidimensional Fatigue Index; GAD-7 = Generalized Anxiety Disorder questionnaire (anxiety symptoms); PHQ-9 = Patient Health Questionnaire-9 (depressive symptoms); PHQ-15 = Patient Health Questionnaire-15 (somatic symptoms).

**p < .01.

***p < .001.

Table 13. Pearson correlations between study questionnaires

IBS group

(IBS alone + IBS comorbid mental + IBS comorbid somatic + IBS multicomorbid)

	IBS-SSS	BTQ	FIQ	MFI – general fatigue	MFI – physical fatigue	MFI – reduced activity	MFI – reduced motivation	MFI – mental fatigue	GAD7	PHQ9
IBS-SSS	1									
BTQ	-.022	1								
FIQ	.387***	.185***	1							
MFI – general fatigue	.301***	.152***	.651***	1						
MFI – physical fatigue	.277***	.140***	.652***	.779***	1					
MFI – reduced activity	.238***	.226***	.637***	.662***	.726***	1				
MFI – reduced motivation	.211***	.160***	.569***	.625***	.625***	.693***	1			
MFI – mental fatigue	.201***	.144**	.539***	.590***	.533***	.592***	.528***	1		
GAD7	.258***	.222***	.587***	.485***	.417***	.473***	.505***	.514***	1	
PHQ9	.287***	.207***	.713***	.649***	.582***	.639***	.663***	.629***	.747***	1
PHQ15	.403***	.146**	.721***	.543***	.517***	.511***	.479***	.477***	.586***	.689***

IBS-SSS = Irritable Bowel Syndrome Severity Scoring System; BTQ = Brief Trauma Questionnaire (report of at least one traumatic event); FIQ = Fibromyalgia Impact Questionnaire; MFI = Multidimensional Fatigue Index; GAD-7 = Generalized Anxiety Disorder questionnaire (anxiety symptoms); PHQ-9 = Patient Health Questionnaire-9 (depressive symptoms); PHQ-15 = Patient Health Questionnaire-15 (somatic symptoms).

**p < .01.

***p < .001.

Table 14. Pearson correlations between study questionnaires

Disease control group

(Control mental + control somatic + control mental+somatic)

	IBS-SSS	BTQ	FIQ	MFI – general fatigue	MFI – physical fatigue	MFI – reduced activity	MFI – reduced motivation	MFI – mental fatigue	GAD7	PHQ9
IBS-SSS	1									
BTQ	.083	1								
FIQ	.349***	-.008	1							
MFI – general fatigue	.236**	-.028	.546***	1						
MFI – physical fatigue	.224**	-.113	.648***	.747***	1					
MFI – reduced activity	.141	.092	.431***	.520***	.588***	1				
MFI – reduced motivation	.154	.120	.460***	.411***	.430***	.516***	1			
MFI – mental fatigue	.302***	-.004	.473***	.473***	.451***	.514***	.521***	1		
GAD7	.183*	.228**	.486***	.314***	.247***	.344***	.511***	.494***	1	
PHQ9	.239**	.208*	.515***	.467***	.364***	.486***	.569***	.596***	.755***	1
PHQ15	.502***	.160	.698***	.425***	.528***	.316***	.384***	.382***	.458***	.478***

IBS-SSS = Irritable Bowel Syndrome Severity Scoring System; BTQ = Brief Trauma Questionnaire (report of at least one traumatic event); FIQ = Fibromyalgia Impact Questionnaire; MFI = Multidimensional Fatigue Index; GAD-7 = Generalized Anxiety Disorder questionnaire (anxiety symptoms); PHQ-9 = Patient Health Questionnaire-9 (depressive symptoms); PHQ-15 = Patient Health Questionnaire-15 (somatic symptoms).

*p < .05

**p < .01

***p < .001.

Table 15. Pearson correlations between study questionnaires

Healthy controls

	IBS-SSS	BTQ	FIQ	MFI – general fatigue	MFI – physical fatigue	MFI – reduced activity	MFI – reduced motivation	MFI – mental fatigue	GAD7	PHQ9
IBS-SSS	1									
BTQ	.123	1								
FIQ	.097	.260*	1							
MFI – general fatigue	.234*	.268*	.404***	1						
MFI – physical fatigue	.123	.257*	.226	.709***	1					
MFI – reduced activity	.205	.116	.186	.632***	.661***	1				
MFI – reduced motivation	.311**	.107	.353**	.648***	.492***	.703***	1			
MFI – mental fatigue	.198	.195	.128	.524***	.438***	.461***	.411***	1		
GAD7	.097	.204	.541***	.463***	.370***	.227	.344**	.391***	1	
PHQ9	.137	.193	.343**	.556***	.469***	.448**	.441***	.566***	.728***	1
PHQ15	.246*	.099	.605***	.663***	.430***	.307**	.419***	.318**	.708***	.604***

IBS-SSS = Irritable Bowel Syndrome Severity Scoring System; BTQ = Brief Trauma Questionnaire (report of at least one traumatic event); FIQ = Fibromyalgia Impact Questionnaire; MFI = Multidimensional Fatigue Index; GAD-7 = Generalized Anxiety Disorder questionnaire (anxiety symptoms); PHQ-9 = Patient Health Questionnaire-9 (depressive symptoms); PHQ-15 = Patient Health Questionnaire-15 (somatic symptoms).

*p < .05

**p < .01

***p < .001.