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TITLE PAGE

Title: Irritable Bowel Syndrome is Significantly Associated with Somatisation: A Cross-sectional Survey.

Short running head: Somatisation in Irritable Bowel Syndrome.

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Abbreviations:	BMI	body mass index
	CBT	cognitive behavioural therapy
	CI	confidence interval
	GI	gastrointestinal
	IBS	irritable bowel syndrome
	IBS-C	constipation-predominant irritable bowel syndrome
	IBS-D	diarrhoea-predominant irritable bowel syndrome
	IBS-M	mixed stool pattern irritable bowel syndrome
	OR	odds ratio

PHQ Patient Health Questionnaire

SD standard deviation

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SUMMARY

Background: Psychological factors may influence persistence and perceived severity of symptoms in irritable bowel syndrome (IBS). Literature suggests that somatisation is associated with IBS. However, the relationship between IBS subtype, symptoms of IBS, and somatisation is unclear.

Aims: We examined this issue in a large cohort of secondary care patients.

Methods: Demographic and gastrointestinal (GI) symptom data were collected from 4224 adult patients via the Rome III questionnaire. Somatisation data were collected using the patient health questionnaire-12. Mean somatisation score and number of somatic symptoms were compared between IBS patients and controls with minimal GI symptoms, and between IBS subtypes using analysis of variance. Effect of level of somatisation on symptom frequency was compared according to IBS subtype using a χ^2 test.

Results: 840 patients met Rome III criteria for IBS, controls were 2137 patients with GI symptoms without IBS. Mean somatisation scores and number of somatic symptoms were higher in IBS versus controls ($P < 0.001$), and in mixed stool pattern IBS (IBS-M), versus IBS with constipation (IBS-C) or diarrhoea (IBS-D) ($P < 0.001$). High levels of somatisation were more prevalent in IBS-M (31.7%) versus IBS-C (22.5%) or IBS-D (20.8%) ($P = 0.003$). For all IBS subtypes, high levels of somatisation were associated with a greater frequency of bloating or abdominal distension prior to logistic regression.

Conclusions: IBS is strongly associated with higher levels of somatisation, particularly IBS-M. Bloating may be associated with higher levels of somatisation, perhaps explaining why it can be difficult to treat.

INTRODUCTION

Irritable bowel syndrome (IBS) is a functional lower gastrointestinal (GI) tract disorder, with an estimated prevalence of between 10% and 20%.¹ The condition is characterised by the presence of abdominal pain or discomfort accompanied by a change in frequency and/or form of stool, in the absence of an organic cause.² The symptoms experienced by IBS sufferers are not specific to the condition. Therefore, in order to distinguish IBS from transient bowel symptoms or organic GI disorders, symptom-based diagnostic criteria are used.³

In addition to symptoms referable to the GI tract, psychological symptoms such as anxiety, stress, or depression are also highly prevalent in patients with IBS.^{4,5} These psychological factors may influence the persistence and perceived severity of symptoms.⁶ This, coupled with evidence that treatments such as cognitive behavioural therapy (CBT) and hypnotherapy are effective for the treatment of IBS,⁷⁻⁹ further underlines the influence that psychological factors may have in IBS.

Somatisation, defined as the reporting of physical bodily complaints in the absence of a known medical cause, is another psychological condition that may co-exist with IBS.¹⁰ Although previous studies have alluded to an association between somatisation and IBS, there has been little research conducted to explore this relationship. In particular, there have been few studies conducted since the revision of the Rome diagnostic criteria in 2006.² Furthermore, no study has examined whether the severity of somatisation varies between IBS subtypes, or whether there is an association between reported frequency of GI symptoms and severity of somatisation.

This highlights the need for a contemporaneous study examining the relationship between IBS and somatisation. We have therefore examined this issue in a large cohort of patients with Rome III-defined IBS, and a control group of patients with minimal GI

symptoms. We postulated that the severity of somatisation would be greater in those with IBS compared with controls, may vary between IBS subtypes, and that high levels of somatisation would be associated with more frequent GI symptoms.

MATERIALS AND METHODS

Participants and Setting

All individuals who participated in the study were newly referred from primary care to secondary care for consideration of investigation of GI symptoms. Unselected consecutive patients aged 16 years or over were recruited at two GI outpatient clinics at either McMaster University Medical Center or St. Joseph's Healthcare, two hospitals in Hamilton, Ontario, Canada. These hospitals serve a local population of 520,000 people. The inability to understand written English was the only exclusion criteria. At the first clinic visit, prior to the consultation with a gastroenterologist, individuals were presented with a study information sheet explaining the nature of the study. Patients who agreed to take part were asked to provide written informed consent at this visit. This study was approved by both the Hamilton Health Sciences and McMaster University research ethics boards in January 2008, and data collection ceased in December 2012. We have previously used this dataset to validate the Rome III criteria for functional dyspepsia and IBS, as well as to examine the characteristics of patients meeting criteria for one of the functional bowel disorders.¹¹⁻¹³

Data Collection and Synthesis

Symptom and Demographic Data

Symptom and demographic data were collected at the first clinic appointment via a questionnaire. Demographic data collected included gender, age, ethnicity, marital status, educational level, tobacco and alcohol use, weight (in kilograms) and height (in meters), which were used to calculate body mass index (BMI). Symptom data were collected using the validated Rome III diagnostic questionnaire for adult functional GI disorders.¹⁴ This

questionnaire was used to record the frequency of individual lower GI symptoms, including lower abdominal pain or discomfort, stool frequency, stool consistency, bloating or abdominal distension, tenesmus, and urgency using a Likert scale. We used the validated hospital anxiety and depression scale to collect information about mood.¹⁵ This is a 14-item instrument with seven questions concerning anxiety, and another seven that screen for the presence of depression. Each of these individual questions is scored on a scale from 0 to 3, giving a total possible score of 21 for anxiety or depression separately. We used a score of ≥ 11 on each of these, as suggested by the authors, to classify individuals as exhibiting possible anxiety or depression.

Definition of IBS and Controls

The presence of IBS was defined using the Rome III criteria, with patients subdivided by predominant stool pattern.² Constipation-predominant IBS (IBS-C) was defined when a patient reported lumpy or hard stools $\geq 25\%$ of the time, and watery or loose stools $< 25\%$ of the time. Diarrhoea-predominant IBS (IBS-D) was defined as hard or lumpy stools $< 25\%$ of the time, and watery or loose stools $\geq 25\%$ of the time. Mixed stool pattern IBS (IBS-M) was defined when stools were loose or watery $\geq 25\%$ of the time, and also hard or lumpy $\geq 25\%$ of the time. Controls were all other patients referred with GI symptoms who did not meet the Rome III criteria for IBS.

Definition of Somatisation Severity Using the Patient Health Questionnaire (PHQ)

Somatisation data were collected using the PHQ-15, which is derived from the validated full PHQ.^{16, 17} The PHQ-15 enquires about the presence of 15 somatic symptoms (or symptom clusters) over the last 4 weeks, which are estimated to contribute to more than 90% of physical complaints reported in the outpatient environment.¹⁸ However, three

questions within the original PHQ-15 relate to the GI tract, and were therefore excluded to avoid any overestimation of the severity of somatisation among a group of patients who were already reporting GI symptoms, to form the PHQ-12 (Appendix 1). This approach has been used by other investigators when examining somatisation among patients with GI symptoms.¹⁹ Each individual was asked to rate the severity of each symptom as “not bothered at all” (scored as 0), “bothered a little” (scored as 1), or “bothered a lot” (scored as 2). Therefore the total PHQ-12 score ranges from a minimum of 0 to a maximum of 24. Somatisation severity was categorised, according to total PHQ-12 score, into high (total PHQ-12 ≥ 13), medium (8-12), low (4-7) and minimal (≤ 3) levels of somatisation severity.

Statistical Analysis

The mean PHQ-12 score and the total number of individual somatic symptom items reported were compared between patients with IBS and controls, as well as between IBS subtypes (IBS-D, IBS-C and IBS-M) using one way analysis of variance. The number of patients reporting each of the 12 individual somatic symptom items was compared between those with IBS and controls. The number with a high level of somatisation severity was compared between patients with IBS and controls, and according to presence of possible anxiety or depression, and between IBS subtypes (IBS-D, IBS-C and IBS-M). Adjusted odds ratios (ORs) with 99% confidence intervals (CIs) were calculated, in order to assess whether the prevalence of higher levels of somatisation severity in IBS patients was greater compared with controls, after controlling for differences in lifestyle and demographic variables, as well as mood scores. These analyses were also performed according to IBS subtype. In addition, the effect of level of somatisation on the frequency of individual IBS symptoms, including lower abdominal pain or discomfort, stool frequency, stool consistency, bloating or abdominal distension, tenesmus, and urgency were compared according to IBS subtype. All

of these comparisons were conducted using a χ^2 test. Independent risk factors associated with the frequency of these individual symptom items were determined by performing multivariate logistic regression analysis to control for all lifestyle and demographic factors, as well as mood scores. Due to multiple testing, a two tailed P value of < 0.01 was considered statistically significant. All statistical analyses were performed using SPSS for Windows version 20.0 (SPSS Inc, Chicago, IL, USA).

RESULTS

A total of 4224 (70.7%) of 5978 patients attending the outpatient clinic gave informed consent and were recruited into the study. Of these, 2977 provided complete somatisation data, of whom 840 (28.2%) met the Rome III criteria for IBS (mean age 38.3 years (range 16-89 years), 702 (83.6%) female). The control group consisted of 2137 patients without IBS (mean age 48.3 years (range 16-91 years), 1397 (65.4%) female). Controls were significantly older, less likely to be female, less likely to have never married, more likely to have only been educated to high school level, and less likely to be smokers than those with IBS, and had lower anxiety and depression scores (Table 1). Organic GI disease prevalence among controls is provided in Supplementary Table 1 online. Of those who met Rome III criteria for IBS, 289 (34.4%) had IBS-D, 138 (16.4%) IBS-C, and 413 (49.2%) IBS-M.

Prevalence of Individual PHQ-12 Somatic Symptom Items Among IBS Patients and Controls

Nine of the 12 somatic symptom items listed on the PHQ-12 at a level of “bothered a lot” were reported at a significantly greater frequency by IBS patients compared with controls (Table 2). The commonest somatic symptom item reported among patients with IBS was feeling tired or low in energy (582 (69.3%) individuals), followed by trouble sleeping (399 (47.5%) subjects), and back pain (313 (37.3%) patients). The only somatic symptom items that were not significantly more common in IBS patients were chest pain, fainting spells, and shortness of breath.

PHQ-12 Scores and Somatisation Severity Among IBS Patients and Controls

Distribution of PHQ-12 scores in patients with IBS and controls without is shown in Figure 1. Mean PHQ-12 scores were significantly higher in IBS patients (9.7) compared with

controls (6.8) ($P < 0.001$) (Table 3). In addition, the total number of somatic symptom items reported was significantly higher among IBS patients ($n = 6.8$) compared with patients in the control group ($n = 5.0$) ($P < 0.001$) (Table 3). When levels of somatisation were compared, there were 222 (26.4%) IBS patients with a high level, compared with only 239 (11.2%) controls (χ^2 for trend, $P < 0.001$) (Table 3).

As the majority of patients with IBS were female, we examined somatisation levels according to gender. There were 200 (28.5%) of 702 female patients with IBS with high levels of somatisation, compared with 190 (13.6%) of 1397 ($P < 0.001$). Among 138 male patients with IBS, 22 (15.9%) demonstrated high levels of somatisation, compared with 49 (6.6%) of 740 male controls ($P < 0.001$). After multivariate logistic regression controlling for lifestyle and demographic variables, as well as mood scores, the prevalence of a medium or high level of somatisation remained significantly higher among IBS patients (OR = 1.73; 99% CI 1.22 to 2.43). Among those with IBS, 818 provided complete anxiety data, 277 (33.9%) of whom exhibited possible anxiety. Of those with possible anxiety, 124 (44.8%) had a high level of somatisation, compared with 91 (16.8%) of 541 without ($P < 0.001$). There were 813 IBS patients providing complete depression data. Of the 107 with possible depression, 61 (57.0%) had a high level of somatisation, compared with 152 (21.5%) of 706 without ($P < 0.001$).

PHQ-12 Scores and Somatisation Severity Among IBS Patients According to Subtype

When the effect of IBS subtype on somatisation was studied, mean PHQ-12 scores were significantly higher in patients with IBS-M (10.4) compared with IBS-C (8.9), or IBS-D (9.2) respectively ($P < 0.001$) (Table 4). The total number of somatic symptom items reported was also significantly higher in patients with IBS-M ($n = 7.2$), compared with IBS-C ($n = 6.2$), or IBS-D ($n = 6.4$) ($P < 0.001$) (Table 4). Finally, when somatisation level was assessed

according to IBS subtype, the prevalence of a high level of somatisation was significantly greater in patients with IBS-M (131 patients (31.7%)) compared with IBS-C (31 patients (22.5%)), or IBS-D (60 patients (20.8%)) ($P = 0.003$) (Table 4). After multivariate logistic regression controlling for lifestyle and demographic variables, as well as mood scores, the prevalence of a high level of somatisation remained significantly lower in those with IBS-D, compared with IBS-M (OR = 0.49; 99% CI 0.28 to 0.88), but not IBS-C (OR = 0.65; 99% CI 0.30 to 1.38).

Relationship Between Symptom Frequency and High Levels of Somatisation

For all IBS subtypes, high levels of somatisation were associated with a significantly greater frequency of bloating or abdominal distension ($P < 0.001$ for IBS-M and IBS-D, and $P = 0.004$ for IBS-C respectively) (Table 5). In terms of frequency of bloating across all three subtypes, among those who provided complete data for this analysis there were 332 (81.8%) of 406 IBS-M patients with bloating or distension often, most of the time, or always compared with 207 (72.9%) of 284 patients with IBS-D, and 111 (81.0%) of 137 with IBS-C. For patients with IBS-M, high levels of somatisation were also associated with a significantly greater likelihood of reporting <3 stools per week ($P = 0.001$). No other significant associations between high levels of somatisation and frequency of individual GI symptoms were observed (Table 5), although the absolute numbers of individuals reporting many of the symptoms at a greater frequency were generally higher among those who met criteria for a high level of somatisation. However, after multivariate logistic regression, controlling for all lifestyle and demographic factors, as well as mood scores, the observed association between high levels of somatisation severity and frequency of bloating or reporting <3 stools per week was no longer statistically significant.

DISCUSSION

This study has demonstrated that patients with Rome III IBS had a higher prevalence of somatisation, reported a greater number of somatic symptom items, and experienced a greater severity of somatisation compared with controls without IBS. IBS patients also had a significantly greater prevalence of almost all of the individual somatic symptom items. The commonest somatic symptom item reported among patients with IBS was feeling tired or low in energy. Mean somatisation scores, number of somatic symptom items, and prevalence of a high level of somatisation severity were all significantly greater in IBS-M patients, compared with IBS-C and IBS-D patients. When assessing whether individual GI symptoms worsened with higher levels of somatisation, we found that there was a significantly greater frequency of bloating or abdominal distension across all three subtypes of IBS in the presence of a higher level of somatisation, but this was no longer the case after multivariate logistic regression, although part of the explanation for this could be that due to incomplete data the number of individuals in these analyses fell.

Strengths of this study include the large sample size, with almost 3000 participants. Recruited patients were both consecutive and unselected, meaning that these results are likely to be generalisable to usual clinical practice. We also used validated questionnaires to collect data, including the Rome III diagnostic questionnaire for the adult functional GI disorders and, to our knowledge, this is the first study of its kind to study the association between somatisation and IBS using these criteria, which are the current gold-standard for diagnosing IBS. Although the original PHQ-15 has been validated,²⁰ the derived PHQ-12 utilised in this study has not been fully validated as screening tool for somatisation. However, Spiller *et al.* used the PHQ-12 for assessing somatisation in IBS and diverticular disease patients,¹⁹ and found the PHQ-12 to be a useful clinical tool to assess patient behaviour. In addition, when we repeated our analyses using the full PHQ-15, those with IBS demonstrated significantly

higher PHQ-15 scores and a significantly greater prevalence of high levels of somatisation severity, compared with controls, and those with IBS-M had significantly higher PHQ-15 scores and a significantly greater prevalence of high somatisation severity, compared with those with IBS-D or IBS-C (see Supplementary Table 2 and 3 online). We also performed multivariate logistic regression controlling for lifestyle and demographic variables, as well as mood scores, and our observation that a higher level of somatisation occurred more frequently in IBS patients compared with controls, and in IBS-M patients compared with IBS-D, remained statistically significant.

There were weaknesses in this study. As this was a cross-sectional study, causality cannot be implied by our results. Lower GI investigations were not mandated in order to exclude the presence of an organic disease. This could mean that a proportion of both IBS and control patients may have had an underlying pathology accounting for the symptoms they were presenting with, resulting in some of the differences observed in demographic characteristics and symptoms. As the PHQ-12 is a self-administered questionnaire this means that, without clinical judgment, a distinction cannot be made between medically explained and unexplained symptoms expressed within the questionnaire. Some somatic symptoms may differ during different times, i.e. they may be present at a baseline level during the initial primary care visit, but then disappear before the secondary care assessment. As 70.7% of those approached agreed to take part in the study, there is also the possibility of selection bias, although as studying the relationship between somatisation and IBS was not the primary aim of this study we do not feel this is likely to have had any major impact on the results we observed. Finally, as this study was conducted among a referral population, the results may not be generalisable to subjects in the community.

The significantly higher somatisation scores and total number of somatic items, and significantly greater prevalence of individual PHQ-12 somatic symptom items and high

somatisation severity in IBS patients, compared with controls, observed in this study are in line with other previous studies which have also shown an association between somatisation and IBS.^{10, 21-28} However, some of these studies only used somatisation as a controlling personality variable when assessing its association with IBS,^{27, 28} resulting in no data comparing quantifiable levels of somatisation in IBS patients versus controls, an issue our study was able to address. In addition, other studies could potentially have overestimated the levels of somatisation in IBS,^{24, 25} because they used the screening for somatoform symptoms-7 questionnaire, in which 10 out of the 53 items are GI in nature,²⁹ and these were not excluded in studies by the investigators. We excluded the three GI items in the original PHQ-15 in order to avoid this overestimation. Therefore our study may have provided a more realistic measure of the degree of association between IBS and somatisation.

There have been few studies comparing somatisation between IBS subtypes. Talley *et al.* compared somatisation between IBS-C and IBS-D patients,¹⁰ and found that there was no difference between the two subtypes, utilising the Rome II criteria for IBS, which defines those IBS patients with an alternating stool pattern as IBS-A, but chose to exclude these from their analysis. Our study included data from all three subtypes of IBS allowing us to compare somatisation levels between IBS-C, IBS-D and IBS-M. Other studies have also utilised the now outdated Rome I or Rome II criteria,^{21, 23} with some studies even using a combination of Rome criteria to define IBS.²⁸ It should also be noted that there are varying prevalence rates of IBS associated with the different revisions to the Rome diagnostic criteria.^{30, 31} Our study is also one of the few to examine the association between levels of somatisation and frequency of individual reported IBS symptoms.

Our findings indicate that IBS-M patients experience a greater prevalence and severity of somatisation. Reasons for this are unclear, but given that those with IBS-M have to endorse more GI symptoms to meet criteria for this subtype, compared with their

counterparts with either IBS-D or IBS-C, perhaps this is not unexpected. With no other studies available to compare our findings with, more research needs to be done assessing and quantifying the varying levels of somatisation between the three IBS subtypes we have observed, and examining how this impacts on the natural history of the condition. The increased frequency of bloating associated with higher levels of somatisation suggests that there may be psychological factors that drive this commonly reported symptom, although this is potentially at odds with the results from other investigators who have demonstrated physiological abnormalities that may explain bloating in patients with IBS, including abdomino-phrenic displacement, ventro-caudal redistribution of intestinal contents, and impaired gas propulsion.^{32, 33} Whatever the mechanism, most pharmacological agents have provided disappointing results in the treatment of bloating,³⁴ although newer drugs such as linaclotide appear promising.^{35, 36} Treatments such as hypnotherapy or CBT appearing to have a greater impact on these symptoms,^{37, 38} further highlighting the potential role that psychological stressors may play in the generation of the symptom of bloating. However, an alternative explanation could be that people who meet criteria for a high level of somatisation are more likely to endorse more frequent symptoms across a range of systems, including those that constitute IBS. To further our understanding of the role psychological factors may play in IBS longitudinal studies examining these issues are required.

In summary, patients with IBS had higher levels of somatisation than patients without. This may be partly explained by increased levels of anxiety and depression, which could lower the threshold for somatisation behaviour, leading to increased awareness of any physical symptoms. IBS-M patients report a greater level and severity of somatisation in comparison to IBS-C and IBS-D patients. Furthermore, patients in all three subtypes of IBS who had higher levels of somatisation reported a greater frequency of bloating, although after controlling for all demographic data this was no longer significant. However, this could still

be an indication of the role that psychological factors play in this commonly reported symptom, and may partly explain why it can be difficult to treat.

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STATEMENTS OF INTEREST

Guarantor of the article: ACF is guarantor.

Specific author contributions: PP, PB, DGM, CB, MIP-S, PM, and ACF conceived and drafted the study. ACF, CB, and MIP-S collected all data. PP and ACF analysed and interpreted the data. PM provided statistical advice and support. ACF drafted the manuscript. All authors have approved the final draft of the manuscript.

Authors' declaration of personal interests:

PP: none to declare. PB: none to declare. DGM: none to declare. CB: none to declare. MIP-S: none to declare. PM: none to declare. ACF: none to declare.

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Canadian Association of Gastroenterology (the study sponsor had no role in the study design, collection, analysis, or interpretation of data).

Writing assistance:

None.

REFERENCES

1. Lovell RM, Ford AC. Global prevalence of, and risk factors for, irritable bowel syndrome: A meta-analysis. *Clin Gastroenterol Hepatol* 2012;**10**:712-721.
2. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. *Gastroenterology* 2006;**130**:1480-1491.
3. Quigley EM, Abdel-Hamid H, Barbara G, et al. A global perspective on irritable bowel syndrome: A consensus statement of the World Gastroenterology Organisation Summit Task Force on irritable bowel syndrome. *J Clin Gastroenterol* 2012;**46**:356-366.
4. Chang L. The role of stress on physiologic responses and clinical symptoms in irritable bowel syndrome. *Gastroenterology* 2011;**140**:761-5.
5. Cho HS, Park JM, Lim CH, et al. Anxiety, depression and quality of life in patients with irritable bowel syndrome. *Gut Liver* 2011;**5**:29-36.
6. Chilcot J, Moss-Morris R. Changes in illness-related cognitions rather than distress mediate improvements in irritable bowel syndrome (IBS) symptoms and disability following a brief cognitive behavioural therapy intervention. *Behav Res Ther* 2013;**51**:690-5.
7. Moss-Morris R, McAlpine L, Didsbury LP, Spence MJ. A randomized controlled trial of a cognitive behavioural therapy-based self-management intervention for irritable bowel syndrome in primary care. *Psychol Med* 2010;**40**:85-94.

8. Ford AC, Talley NJ, Schoenfeld PS, Quigley EMM, Moayyedi P. Efficacy of antidepressants and psychological therapies in irritable bowel syndrome: Systematic review and meta-analysis. *Gut* 2009;**58**:367-378.
9. Ford AC, Quigley EM, Lacy BE, et al. Effect of antidepressants and psychological therapies, including hypnotherapy, in irritable bowel syndrome: Systematic review and meta-analysis. *Am J Gastroenterol* 2014;doi: **10.1038/ajg.2014.148**. [Epub ahead of print].
10. Talley NJ, Dennis EH, Schettler-Duncan VA, Lacy BE, Olden KW, Crowell MD. Overlapping upper and lower gastrointestinal symptoms in irritable bowel syndrome patients with constipation or diarrhea. *Am J Gastroenterol* 2003;**98**:2454-2459.
11. Ford AC, Bercik P, Morgan DG, Bolino C, Pintos-Sanchez MI, Moayyedi P. Validation of the Rome III criteria for the diagnosis of irritable bowel syndrome in secondary care. *Gastroenterology* 2013;**145**:1262-1270.
12. Ford AC, Bercik P, Morgan DG, Bolino C, Pintos-Sanchez MI, Moayyedi P. The Rome III criteria for the diagnosis of functional dyspepsia in secondary care are not superior to previous definitions. *Gastroenterology* 2014;**146**:932-40.
13. Ford AC, Bercik P, Morgan DG, Bolino C, Pintos-Sanchez MI, Moayyedi P. Characteristics of functional bowel disorder patients: A cross-sectional survey using the Rome III criteria. *Aliment Pharmacol Ther* 2014;**39**:312-21.
14. Whitehead WE, and the Validation Working Team Committee in association with the Rome Questionnaire C. Development and validation of the Rome III diagnostic

questionnaire. In: *Drossman DA, editor. Rome III: The functional gastrointestinal disorders, 3rd edition. Virginia: Degnon Associates Inc 2006:835-853.*

15. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;**67**:361-370.
16. Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire. *JAMA* 1999;**282**:1737-44.
17. Spitzer RL, Williams JB, Kroenke K, Hornyak R, McMurray J. Validity and utility of the PRIME-MD patient health questionnaire in assessment of 3000 obstetric-gynecologic patients: the PRIME-MD Patient Health Questionnaire Obstetrics-Gynecology Study. *Am J Obstet Gynecol* 2000;**183**:759-69.
18. Kroenke K, Arrington ME, Mangelsdorff AD. The prevalence of symptoms in medical outpatients and the adequacy of therapy. *Arch Intern Med* 1990;**150**:1685-9.
19. Spiller RC, Humes DJ, Campbell E, et al. The Patient Health Questionnaire 12 Somatic Symptom scale as a predictor of symptom severity and consulting behaviour in patients with irritable bowel syndrome and symptomatic diverticular disease. *Aliment Pharmacol Ther* 2010;**32**:811-20.
20. Kroenke K, Spitzer RL, Williams JBW. The PHQ-15: Validity of a new measure for evaluating the severity of somatic symptoms. *Psychosom Med* 2002;**64**:258-266.

21. Choung RS, Locke GR, 3rd, Zinsmeister AR, Schleck CD, Talley NJ. Psychosocial distress and somatic symptoms in community subjects with irritable bowel syndrome: a psychological component is the rule. *Am J Gastroenterol* 2009;**104**:1772-9.
22. Creed F, Tomenson B, Guthrie E, et al. The relationship between somatisation and outcome in patients with severe irritable bowel syndrome. *J Psychosom Res* 2008;**64**:613-20.
23. Lackner J, Jaccard J, Baum C, et al. Patient-reported outcomes for irritable bowel syndrome are associated with patients' severity ratings of gastrointestinal symptoms and psychological factors. *Clin Gastroenterol Hepatol* 2011;**9**:957-964.
24. Lackner JM, Gudleski GD, Firth R, et al. Negative aspects of close relationships are more strongly associated than supportive personal relationships with illness burden of irritable bowel syndrome. *J Psychosom Res* 2013;**74**:493-500.
25. Lackner JM, Gudleski GD, Thakur ER, Stewart TJ, Iacobucci GJ, Spiegel BM. The impact of physical complaints, social environment, and psychological functioning on IBS patients' health perceptions: looking beyond GI symptom severity. *Am J Gastroenterol* 2014;**109**:224-33.
26. Lackner JM, Gudleski GD, Zack MM, et al. Measuring health-related quality of life in patients with irritable bowel syndrome: can less be more? *Psychosom Med* 2006;**68**:312-20.
27. Spiegel BM, Kanwal F, Naliboff B, Mayer E. The impact of somatization on the use of gastrointestinal health-care resources in patients with irritable bowel syndrome. *Am J Gastroenterol* 2005;**100**:2262-73.

28. van Tilburg MA, Palsson OS, Whitehead WE. Which psychological factors exacerbate irritable bowel syndrome? Development of a comprehensive model. *J Psychosom Res* 2013;**74**:486-92.
29. Rief W, Hiller W. A new approach to the assessment of the treatment effects of somatoform disorders. *Psychosomatics* 2003;**44**:492-8.
30. Banerjee R, Choung OW, Gupta R, et al. Rome I criteria are more sensitive than Rome II for diagnosis of irritable bowel syndrome in Indian patients. *Indian J Gastroenterol* 2005;**24**:164-166.
31. Chey WD, Olden K, Carter E, Boyle J, Drossman D, Chang L. Utility of the Rome I and Rome II criteria for irritable bowel syndrome in U.S. women. *Am J Gastroenterol* 2002;**97**:2803-11.
32. Accarino A, Perez F, Azpiroz F, Quiroga S, Malagelada JR. Abdominal distention results from caudo-ventral redistribution of contents. *Gastroenterology* 2009;**136**(5):1544-51.
33. Serra J, Villoria A, Azpiroz F, et al. Impaired intestinal gas propulsion in manometrically proven dysmotility and in irritable bowel syndrome. *Neurogastroenterol Motil* 2010;**22**(4):401-6.
34. Lea R, Whorwell PJ. Expert commentary--bloating, distension, and the irritable bowel syndrome. *MedGenMed* 2005;**7**:18.

35. Chey WD, Lembo AJ, Lavins BJ, et al. Linaclotide for irritable bowel syndrome with constipation: A 26-week, randomized, double-blind, placebo-controlled trial to evaluate efficacy and safety. *Am J Gastroenterol* 2012;**107**:1702-1712.
36. Rao S, Lembo AJ, Shiff SJ, et al. 12-week, randomized, controlled trial with a 4-week randomized withdrawal period to evaluate the efficacy and safety of linaclotide in irritable bowel syndrome with constipation. *Am J Gastroenterol* 2012;**107**:1714-1724.
37. Gonsalkorale WM, Houghton LA, Whorwell PJ. Hypnotherapy in irritable bowel syndrome: a large-scale audit of a clinical service with examination of factors influencing responsiveness. *Am J Gastroenterol* 2002;**97**:954-61.
38. Whorwell PJ, Prior A, Faragher EB. Controlled trial of hypnotherapy in the treatment of severe refractory irritable-bowel syndrome. *Lancet* 1984;**2**(8414):1232-4.

Table 1. Characteristics of 840 Patients Reporting Symptoms Compatible with IBS, Compared with 2137 Controls.

	IBS (n = 840)	Control (n = 2137)	P Value *
Mean age	38.3	48.3	<0.001
Number of females (%)	702 (83.6)	1397 (65.4)	<0.001
White Caucasian ethnicity (%)	762 (90.7)	1906 (89.2)	0.63
Marital status (%)			
Married or co-habiting	451 (53.7)	1300 (60.8)	<0.001
Divorced	94 (11.2)	236 (11.0)	
Never married	272 (32.4)	475 (22.2)	
Widowed	15 (1.8)	106 (5.0)	
Educational level (%)			
Elementary	10 (1.2)	92 (4.3)	<0.001
High school	214 (25.5)	613 (28.7)	
College or technical school	277 (33.0)	611 (28.6)	
University	242 (28.8)	546 (25.5)	
Postgraduate	83 (9.9)	224 (10.5)	
Alcohol user (%)	497 (59.2)	1234 (57.7)	0.46
Tobacco user (%)	214 (25.5)	376 (17.6)	<0.001
Mean BMI	26.2	27.1	0.002
Mean HAD anxiety score	8.7	6.6	<0.001
Mean HAD depression score	5.6	4.0	<0.001

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

Table 2. Prevalence of Individual PHQ-12 Somatic Symptom Items in 840 IBS Patients Compared with 2137 Controls.

PHQ-12 somatic symptom item (“reported as bothered a lot”)	IBS (n = 840)	Controls (n = 2137)	P value*
Back pain (%)	313 (37.3)	468 (21.9)	<0.001
Arm, leg, or joint pain (%)	292 (34.8)	534 (25.0)	<0.001
Period pain or period problems (%)†	166/702 (23.6)	169/1397 (12.1)	<0.001
Headaches (%)	247 (29.4)	297 (13.9)	<0.001
Chest pain (%)	76 (9.0)	137 (6.4)	0.02
Dizziness (%)	127 (15.1)	161 (7.5)	<0.001
Fainting spells (%)	15 (1.8)	32 (1.5)	0.69
Heart pounding or racing (%)	103 (12.3)	130 (6.1)	<0.001
Shortness of breath (%)	93 (11.1)	184 (8.6)	0.04
Pain or problems during intercourse (%)	96 (11.4)	99 (4.6)	<0.001
Tired or low in energy (%)	582 (69.3)	883 (41.3)	<0.001
Trouble sleeping (%)	399 (47.5)	659 (30.8)	<0.001

*P value for Pearson χ^2 .

†Female patients only

Table 3. Somatisation Levels and Severity in 840 IBS Patients Compared with 2137 Controls.

	IBS (n = 840)	Controls (n = 2137)	P value*
Mean PHQ-12 score (SD)	9.7 (4.6)	6.8 (2.6)	<0.001
Mean number of somatic symptom items reported (SD)	6.8 (2.6)	5.0 (2.7)	<0.001
Level of somatisation severity†			
Minimal	59 (7.0)	552 (25.8)	
Low	228 (27.1)	748 (35.0)	
Medium	331 (39.4)	598 (28.0)	
High	222 (26.4)	239 (11.2)	<0.001

*P value for one way analysis of variance, or Pearson χ^2 test for trend.

†The total PHQ-12 score ranges from a minimum of 0 to a maximum of 24.

Somatisation severity was categorised, according to total PHQ-12 score, into high (total PHQ-12 ≥ 13), medium (8-12), low (4-7) and minimal (≤ 3) levels of somatisation severity

Table 4. Somatisation Levels and Severity in 840 IBS Patients According to IBS**Subtype**

	IBS-M (n = 413)	IBS-C (n = 138)	IBS-D (n = 289)	P value*
Mean PHQ-12 score (SD)	10.4 (4.5)	8.9 (4.8)	9.2 (4.4)	<0.001
Mean number of somatic symptom items reported (SD)	7.2 (2.5)	6.2 (2.8)	6.4 (2.6)	<0.001
Level of somatisation severity†				
Minimal	18 (4.4)	14 (10.1)	27 (9.3)	
Low	104 (25.2)	45 (32.6)	79 (27.3)	
Medium	160 (38.7)	48 (34.8)	123 (42.5)	
High	131 (31.7)	31 (22.5)	60 (20.8)	0.003

*P value for one way analysis of variance, or Pearson χ^2 test for trend.

†The total PHQ-12 score ranges from a minimum of 0 to a maximum of 24.

Somatisation severity was categorised, according to total PHQ-12 score, into high (total PHQ-12 ≥ 13), medium (8-12), low (4-7) and minimal (≤ 3) levels of somatisation severity

Table 5. Prevalence of Individual IBS Symptom Items in the Presence of High Somatisation Severity for 840 Patients Reporting Symptoms Compatible with IBS, According to IBS Subtype.

	IBS Subtype	Somatisation Severity†		P Value
		High Somatisation Severity Absent	High Somatisation Severity Present	
Bloating or distension often, most of the time, or always (%)	IBS-C (n=137)	82/106 (77.4)	29/31 (93.5)	0.004
	IBS-M (n=406)	214/276 (77.5)	118/130 (90.8)	<0.001
	IBS-D (n=284)	152/224 (67.9)	55/60 (91.7)	<0.001
Tenesmus often, most of the time, or always (%)	IBS-C (n=138)	73/107 (68.2)	28/31 (90.3)	0.067
	IBS-M (n=413)	161/282 (57.1)	86/131 (65.6)	0.018
	IBS-D (n=288)	103/228 (45.2)	37/60 (61.7)	0.024
Urgency often, most of the time, or always (%)	IBS-C (n=135)	10/106 (9.4)	4/29 (13.8)	0.048
	IBS-M (n=412)	129/281 (45.9)	79/131 (60.3)	0.482
	IBS-D (n=287)	149/227 (65.6)	50/60 (83.3)	0.038
Harder stools when pain starts often, most of the time, or always (%)	IBS-C (n=137)	52/107 (48.6)	17/30 (56.7)	0.939
	IBS-M (n=409)	44/280 (15.7)	29/129 (22.5)	0.075
	IBS-D (n = 287)	N/A*	N/A*	N/A*
<3 stools per week ≥50% of the time (%)	IBS-C (n=138)	52/107 (48.6)	24/31 (77.4)	0.054
	IBS-M (n=413)	55/282 (19.5)	43/131 (32.8)	0.001
	IBS-D (n = 287)	N/A*	N/A*	N/A*
Looser stools when pain	IBS-C (n = 138)	N/A*	N/A*	N/A*

starts often, most of the time, or always	IBS-M (n=410)	143/280 (51.1)	63/130 (48.5)	0.332
	IBS-D (n=287)	184/227 (81.1)	45/60 (75.0)	0.575
>4 stools per day $\geq$50% of the time	IBS-C (n = 138)	N/A*	N/A*	N/A*
	IBS-M (n=410)	89/279 (31.9)	39/131 (29.8)	0.796
	IBS-D (n=287)	126/227 (55.5)	37/60 (61.7)	0.235

* N/A = not applicable. Could not endorse this symptom in order to meet criteria for this IBS subtype.

† The total PHQ-12 score ranges from a minimum of 0 to a maximum of 24.

Somatisation severity was categorised, according to total PHQ-12 score, into high (total PHQ-12 $\geq$ 13), medium (8-12), low (4-7) and minimal ($\leq$ 3) levels of somatisation severity

Figure 1. Distribution of PHQ-12 Scores Among 840 IBS Patients Compared with 2137 Controls.