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Inaccuracy of patient-reported descriptions of and satisfaction with bowel actions in irritable bowel syndrome

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Short running page heading: Symptom assessment in IBS

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ABSTRACT

Background: Perception of diarrhea and constipation differ greatly. This study aimed to correlate subjective and objective assessment of fecal characteristics in IBS patients.

Methods: Data from two interventional dietary trials with varying FODMAP or gluten content were interrogated. Subjects rated their dissatisfaction with stool consistency daily using a visual analogue scale during the interventions. Subjects collected stools at the end of each intervention. Each stool was scored according to the King's Stool Chart (KSC). Fecal water content (FWC) was measured on pooled feces by freeze-drying with diarrhea defined as $\geq 78\%$.

Results: 70 IBS (Rome III) and 8 healthy subjects were studied. Each subject's self-rating of stool consistency during the most symptomatic diet was approximately double that of their least. Degree of dissatisfaction with stool consistency correlated poorly with changes in FWC and KSC. IBS-subtype related poorly to objective measures of stool consistency. 60% of IBS-D subjects had diarrhea on objective measures. 85% with IBS-C had hard and formed stools but 3 patients met the criteria for diarrhea. One healthy subject had diarrhea on FWC and KSC, and 6 had hard, formed stools. No differences in fecal water content was observed when subjects consumed differing amounts of FODMAPs or gluten (all $P > 0.200$).

Conclusions: There are major disparities between patients' stool descriptions and objective features of constipation and diarrhea. Patient-reported bowel habits require more interrogation for accurate IBS subtyping. Varying FODMAP or gluten content of the diet is not associated with consistent change in fecal water content.

Keywords: diarrhea, constipation, stool chart, fecal water content

KEY POINTS

- Perceptions of diarrhea and constipation differ greatly amongst patients with irritable bowel syndrome (IBS), and few studies have evaluated subjective and objective assessment of fecal characteristics
- During a period of self-reported worsening of stool consistency, dissatisfaction with stool consistency in IBS subjects correlated poorly with objective measures of stool consistency, such as fecal water content and rating by independent observer and altering FODMAP or gluten intake have little discernible effect on faecal water content
- These findings indicate considerable inaccuracy in the assessment of IBS symptoms in both research and clinical settings, and objective measures are needed to overcome limitations in self-reported IBS symptoms

INTRODUCTION

The diagnosis of irritable bowel syndrome (IBS) and other functional gastrointestinal disorders (FGID) is predominantly based upon patients description of symptoms. The nature of the bowel actions - diarrhea and constipation, alone or in combination – are critical to the classification of functional bowel disorders such as functional diarrhea or functional constipation, and form the basis of sub-grouping other entities such as IBS. Nevertheless, such patient-reported symptoms are, by definition, subjective and rely heavily on the patient understanding of the standard terminology utilized by classification systems such as those of the Rome Foundation. Furthermore, perception scales including the nature, severity and definitions of such terms differ greatly between physicians and patients¹. Bowel actions can be objectively assessed in terms of frequency, consistency and water content. However, there are few studies that have correlated the patient-reported assessment of stools with objective and independently-observed assessment.

Altering the intake of FODMAPs or gluten within the bounds of normal dietary intake are perceived to change the consistency of the fecal output. Altering FODMAP intake has been evaluated in patients with IBS-D only in some studies on the hypothesis that low FODMAP intake will lead to relative dessication of stools with resultant improvement in diarrhea but worsening of constipation^{2, 3}, despite efficacy being reported for all subtypes of IBS⁴⁻⁷. The only controlled study to evaluate the effect of a gluten-free diet on fecal characteristics in patients with IBS-D reported reduced stool frequency, interpreted by the investigators as an effect of gluten on stool consistency⁸. However, there is limited description of the true effects of FODMAPs and gluten on objective assessment of feces.

The roles of FODMAPs and gluten in symptom genesis in patients with IBS by providing all food have been examined in a recent series of randomized controlled trials. Independent and objective assessments of feces were conducted prior to, and during dietary interventions. Concomitantly, the patients reported their stool form and habit both retrospectively (prior to starting the studies), and prospectively during the trials. This setting provided the opportunity to compare patient-reported assessment of stool form and bowel habit with that of objective measures under differing and controlled dietary conditions.

METHODS

Study participants participated in one of two trials to investigate dietary therapies for the management of IBS. All IBS participants considered themselves to have IBS, met the Rome III criteria for IBS as defined by a Rome III criteria questionnaire conducted by a gastroenterologist. This was based on the participants' self-assessed recent retrospective symptoms of abdominal pain or discomfort and altered defecation. Participants were further categorised into subtypes of IBS according to predominant bowel pattern. This retrospective classification was compared to prospectively assessed stools collected during the study periods as described below. Healthy participants were also recruited. Study subjects were not permitted to take any pharmacological agents during the studies that may alter their stools (such as laxatives or antidiarrheal agents).

Participants undertook one of two dietary studies, designated 'FODMAP study' and 'Gluten study'. Table 1 shows the features of each study.

FODMAP study

Thirty IBS and eight healthy participants received low FODMAP (Fermentable Oligosaccharides, Disaccharides, Monosaccharides And Polyols) and 'typical FODMAP' diets in a single-blinded, randomized, cross-over design for three weeks each. Detailed description of the study protocol has been previously published⁴.

Participants were asked to rate their symptoms, including dissatisfaction of stool consistency, daily on a 100 mm visual analogue scale (VAS) (0 mm indicating no symptoms at all). As hypothesized, symptoms were greater on the typical FODMAP compared to the low FODMAP diet⁴. Only one participant indicated improved symptoms on the typical FODMAP diet. For this reason, symptom data during the fecal collection on the typical FODMAP diet were used to assess the symptoms experienced. Symptoms remained low and unaltered in the healthy participants and for uniformity, the symptom data for the typical FODMAP diet were also used in the healthy participants and presented in this series. The differences between reported bowel symptoms were also documented and compared with changes in objective measures.

Gluten study

Forty IBS participants first underwent a two-week run-in period, in which they were educated on and asked to follow a low FODMAP and gluten free diet. All participants then received, gluten free diets fortified with high gluten (16 g/d), low gluten (2.0 g/d) and placebo in a double-blinded, randomized,

cross-over design for one week each. Participants rated their symptoms using a 100 mm VAS scale as with the FODMAP study including a daily rating of dissatisfaction with stool consistency. Detailed description of the study protocol has been previously published⁹.

All subjects felt the best during the two-week run-in period, however, there was large variation of symptoms on each of the provided dietary arms. Therefore, fecal analysis during the dietary arm in which the individual rated their dissatisfaction with stool consistency as the worst (highest VAS score) was assessed to compare with objective measures. A comparison of the paired patient-reported results of fecal assessments and symptoms during 'the worst' dietary arm and the run-in period were calculated and comparison made between changes in patient-reported indices with those of objective measures.

Analysis of fecal samples

In the FODMAP study, participants were asked to collect all feces passed over the last five days of both the low and typical FODMAP diets and during the run-in period. In the gluten study, participants collected all feces passed over the last three days of each provided diet, but not during the run-in period. Each bowel motion was collected in a supplied plastic container. Only one investigator for each study (EPH for FODMAP study and JRB for gluten study) conducted the fecal analysis, for uniformity of data collection within each study.

Objective measures of diarrhea and constipation

On delivery to the laboratory, stools were assessed for frequency, weight, consistency and fecal water content (FWC). Stool consistency was determined by comparison of each stool to the King's Stool Chart¹⁰, which uses four visual and written descriptors to estimate consistency. Diarrhea according to fecal consistency estimated using the King's Stool Chart were stools described as 'loose and unformed' or 'liquid'. The number of 'loose and unformed' and 'liquid' stools passed during the collection period was noted for each participant. Constipation determined by consistency via the King's Stool Chart was described as 'hard and formed' stool. 'Soft and formed' descriptor was not considered a marker of diarrhea or constipation.

After analysis for frequency, weight and consistency, the fecal sample of each participant was pooled, mixed and a small specimen jar sample was extracted for assessment of FWC. To assess FWC, the pooled samples were weighed, freeze-dried (Operon, Thermo Fisher Scientific Australia; Scoresby, Victoria, Australia), then reweighed and dry weight obtained. Water-content was

calculated by subtracting dry from wet weight and FWC was expressed as percentage. Past literature have defined diarrhea according to FWC between 78-89% water^{11, 12}. For the current study, the lower definition of 78% FWC was considered diarrhea.

Statistical analyses

Power calculations were conducted and adequate sample size achieved for both the FODMAP and gluten studies to meet their original primary endpoints^{4, 9}. Dissatisfaction of stool consistency and FWC data were parametric and presented as mean [95%CI]. Comparisons between diets and IBS subtypes were made using paired t-tests and ANOVA with post-hoc Tukey's multiple comparison analysis. All other data were non-parametric and presented as median (interquartile range). Categorical data were analysed with chi-squared or Cohen's kappa analysis. Comparisons of fecal measures between IBS and healthy subgroups and different fecal measures were completed using Kruskal-Wallis with post-hoc Dunn's multiple comparison and Mann-Whitney analyses. Correlations between dissatisfaction of stool consistency and FWC were presented as Pearson r [95%CI]. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

Participants

On enrolment of the 70 IBS participants, 27 (39%) were classified as IBS-D, 28 (40%) IBS-C, 13 IBS-M and the remaining two IBS-U. The eight healthy participants did not have IBS on enrolment, all of whom believed their stools were normal. Two of the IBS-D and one IBS-C participants did not collect feces during the collection period, so data from 67 IBS participants are presented. Of these 67 subjects, 16 of them only collected a proportion of their stools passed for the collection period and between 1-4 stools were missing from the collection (five IBS subjects from FODMAP study and 11 from gluten study) and three subjects from the FODMAP study (two IBS and one healthy) only collected a four-day sample. Patient demographics of IBS subjects are described in Table 2.

Self-rated dissatisfaction with stool consistency

During the stool collection period, the dissatisfaction with stool consistency of the 28 IBS subjects in the FODMAP study was mean [95%CI] 42.0 [32.1-52.0] mm on the typical FODMAP diet compared to 23.9 [15.4-32.3] mm on the low FODMAP diet ($P = 0.002$; paired t-test). Similar results were seen across all four subtypes of IBS. Symptoms remained low for the healthy subjects throughout the study, including during fecal collection on the typical FODMAP diet⁴. During the stool collection period in 39 IBS subjects undertaking the gluten study, the dissatisfaction of stool consistency during each subjects' worst diet was 28.0 [20.9-35.0] mm compared to 9.85 [5.81-13.9] mm during the gluten free run-in period ($P < 0.001$; paired t-test).

Objective fecal measures

Of the 25 subjects with IBS-D, 15 (60%) had presence of 'loose and unformed' or 'liquid' stool consistency for $\geq 25\%$ of collected bowel motion (Table 3). Additionally, three subjects with IBS-C, one subject with IBS-U and one healthy subject also had 'loose and unformed' or 'liquid' stools for $\geq 25\%$ of collected bowel motion. Six IBS-M had 'loose and unformed' or 'liquid' stools for $\geq 25\%$ of collected bowel motion. For markers of constipation, 23/27 patients (85%) with IBS-C and 5/13 (38%) with IBS-M had 'hard and formed' stools for $\geq 25\%$ of stools. Additionally, seven subjects with IBS-D, one subject with IBS-U and six healthy subjects also had 'hard and formed' consistency for $\geq 25\%$ stools. There was also no significant difference found between patients with IBS-D and IBS-C in regards to fecal frequency, with 80% and 88% ($p = 0.17$; chi-squared test) of patients, respectively, opening their bowels 1 – 2 times a day.

FWC was $\geq 78\%$ in 15 IBS-D, three IBS-C, four IBS-M and one healthy subject (Table 3). There was a significant difference between the FWC of IBS-D subjects (78.1 [75.8-80.3]%) compared to the IBS-C subjects (71.4 [69.2-73.5]%) and healthy subjects (67.8 [61.9-73.6]%; $P < 0.001$ ANOVA with post-hoc Tukey's multiple comparison) (Table 4). Interestingly, the mean FWC was higher in subjects with IBS-C than that seen in healthy subjects. There was no difference in fecal frequency among the IBS subtypes and healthy subjects, but fecal weight was increased in the IBS-D subjects compared to the IBS-C subjects (Table 4).

Comparison between different IBS subtype on enrolment and objective fecal measures

Using Cohen's kappa analyses, there was a fair strength of agreement between IBS-D and independent observer classifications of diarrhea (Cohen's kappa[95%CI] 0.29[0.05-0.52]), and a moderate strength of agreement between IBS-C and independent observer classifications of constipation (0.50[0.30-0.70]). There was also a moderate strength of agreement between IBS-D and FWC (0.48[0.26-0.70]).

Relationship of patient-reported dissatisfaction in stool consistency to fecal water content

Despite a significantly increased dissatisfaction of stool consistency on the 'worst diet' compared to that seen at other time points during each study, dissatisfaction did not correlate with FWC of the collected samples in IBS-D or IBS-C subjects (r [95%CI] IBS-D -0.23 [-0.57-0.18]; $P = 0.26$; IBS-C -0.14 [-0.50-0.25]; $P = 0.47$; Pearson correlation) (Figure 1).

Change in dissatisfaction in stool consistency compared to change in fecal water content

In the 34 subjects undertaking the FODMAP study who collected stools on both the low FODMAP and typical FODMAP arms, there were positive correlations in changes in dissatisfaction with stool consistency with changes in FWC in IBS-C subjects (0.66 [0.13-0.89]; $P = 0.021$), as shown in Figure 2b. No correlation was seen in the IBS-D subjects (0.36 [-0.46-0.85]; $P = 0.377$) (Figure 2a). Because subjects undertaking the gluten study did not collect stool during their run-in gluten free period, differences in change of FWC during the lowest and highest scores of dissatisfaction with stool consistency could not be determined.

Fecal water content across different diets

As shown in Figure 3, there were no differences in FWC between low and typical FODMAP diets, and between gluten and placebo diets despite significant symptom changes.

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DISCUSSION

Diagnosis of IBS is based upon self-assessed symptoms, which differ greatly in severity and frequency. The lack of objective markers in IBS creates inconsistencies in the interpretation of diagnosis and response of treatment in patients with IBS. Even the gold standard diagnostic tool, the Rome criteria, relies on the descriptive terminology interpreted by the person with the affliction. This study attempted to assess the strength of the association of self-reported symptoms in an IBS population with objective measures.

Data showed that, when asked, 25 subjects described themselves as having IBS-D defined by Rome III criteria, yet only 60% of these subjects had diarrhea according to FWC. Further, only 60% met the diarrhea criteria on third-person observation scoring of loose stools for $\geq 25\%$ of the time, during a period of self-reported symptom induction (Table 3). It seems that as a group, there is heterogeneity in assessment of stool form and/or their satisfaction of it amongst the IBS-D population. Indeed, there was no correlation between FWC and dissatisfaction of stool consistency; in fact, there appeared to be a trend in IBS-D subjects for being more satisfied with higher FWC (Figure 1a), although this observation was not seen when controlled for a more satisfactory rating during the low FODMAP diet (Figure 2a). Conversely, many more subjects than expected had hard, formed stool consistency, indicating that perhaps the definition for IBS-C is more easily reached. Unfortunately, this study only assessed one of the six criteria stipulated for IBS-C so clear assessment of constipation cannot be achieved within the parameters of this study.

FWC is a more objective marker of stool consistency than visual assessments. However, the limitation of using a pooled sample is that variation over that time period cannot be determined. This may be particularly relevant in an IBS population, where symptoms may vary significantly over days, or in IBS-M subjects who may experience both loose and hard stools within a short time frame. Urine contamination of stool samples may also have increased mean FWC, although subjects were asked to avoid urine contamination and measures such as pH and short-chain fatty acid content did not suggest contamination occurred¹³. It should also be noted that approximately one quarter of subjects did not collect all stools passed over the 3- or 5-day collection period, which may have affected results.

The major impact of IBS is on quality of life, with several studies showing this to be comparable to patients with migraines and asthma¹⁴⁻¹⁶. Many patients experience a fear of symptoms¹⁷ and even social phobia, in which an excessive fear of symptoms leads to avoidance of social situations¹⁸. For

this reason, it may be that self-assessment of symptoms may be the most appropriate for clinical management as treatments are aimed to improve symptoms to the patients' level of satisfaction. While patients' interpretation of symptoms is thus clearly important, discrepancies between diarrhea definitions are an important confounder in research, where homogeneity is essential for accurate endpoints and outcomes. Furthermore, in clinical practice, the accuracy of symptoms is also critical to appropriately guide treatment. For example, treatment of self-reported diarrhea with stool-binding agents may not be indicated if stools are not loose. Use of stool charts as a visual and descriptive aid may prompt more accurate description of symptoms. To date, the King's Stool Chart has been validated in patients receiving enteral nutrition¹⁰ rather than in patients with IBS. It has been designed to examine stools in bed-pans and is, therefore, more appropriate to assess stools collected in plastic containers, as was done in this study, rather than in a toilet bowl. As a result it may not be extrapolated to real life. The Bristol Stool Form Chart which is now the most common method of measuring fecal consistency, with numerous clinical studies using this tool¹⁹⁻²¹, may instead be helpful in the clinical setting to increase objectiveness. The Bristol Stool Form Chart is recommended by the Rome Foundation to assess stool form²² and has now been validated in both adults and children for IBS-D^{23, 24}.

This study highlighted the difficulties in evaluating stool form as reported by patients. Furthermore, defining normality is still unclear with, for example, at least one healthy subject having unequivocal diarrhea on objective measures. The results also raise questions about what dissatisfaction with stool consistency and its changes over time actually mean. They might reflect more about dissatisfaction of many other features of altered bowel habit, such as stool volume, frequency, odour, degree of difficulty passing stool or the sensation of evacuation than the stool itself. Overall symptoms and wellbeing of the patient may also influence this ranking as overall and specific gastrointestinal symptoms were rated similarly by individual patients^{4, 9}. Undoubtedly however, inter-individual scoring of stool form leads to inconsistencies in FGID classification and sub-grouping.

There is current belief that a low FODMAP diet is only applicable for diarrhea-predominant symptoms because of the osmotic nature of dietary FODMAPs². This stems from the knowledge that FODMAPs increase small intestinal water content and, therefore, delivery to the colon, and that a big dose of a FODMAP, such as lactose in a hypolactasic person, is associated with diarrhea. However, the dose of FODMAPs in the diet will not usually be sufficient to induce such diarrhea, as shown in this current study. Likewise, the value of a low FODMAP diet in patients with IBS-C has been questioned, as it is believed that the loss of FODMAPs will reduce the 'natural' laxatives from

the diet and exacerbate constipation. It seems the minimal effect of FODMAP content on FWC in the IBS-C subjects participating in the FODMAP study, where all food was provided and adherence was excellent, should permit such beliefs to be removed from current dogma. Perhaps the mechanism of action of a low FODMAP diet in reducing gastrointestinal symptoms is weighed more to its ability to reduce luminal distension, and subsequently to reduced pain and overall symptoms in the majority of patients.

Likewise, the only randomized controlled trial of a gluten free diet in patients with IBS-D found that a gluten-containing diet was associated with increased frequency of bowel actions in patients with IBS-D⁸. The gluten in the diet was blamed for this change. Alternatively, the release of exorphins during gluten ingestion is suggested to induce constipation²⁵. The results from this re-analysis of data from a blinded rechallenge study in which all food was provided oppose these notions, indicating that gluten has no consistent effect on FWC.

In conclusion, the results of these analyses indicate the inaccuracy of historically-obtained descriptions of bowel habits and the lack of value of the concept of dissatisfaction with bowel habit as an index to assess improved bowel actions in a broad cross-section of patients with IBS. Furthermore, they show that both the FODMAP content of the diet and dietary gluten have little impact on the FWC in those who do not have coeliac disease. Detailed guidance of use of the Rome criteria in addition to further exploration in a clinical setting are needed to overcome the limitation of IBS assessment and monitoring without the use of analytical laboratory techniques.

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DISCLOSURES: Peter Gibson has published a book on food intolerances. The Department of Gastroenterology has published an App on the Monash University Low FODMAP Diet, the proceeds of which partly go to the Department, but not to the individuals. There were no conflicts of interest to declare for other authors.

AUTHOR CONTRIBUTIONS:

- EPH, JRB & JGM performed the research
- EPH, JRB, EDN, JGM & PRG designed the research study
- EPH, JRB, EDN, JGM & PRG analysed the data
- All authors wrote, revised and approved the final version of the article

References:

1. Lembo A, Ameen VZ, Drossman DA. Irritable bowel syndrome: toward an understanding of severity. *Clin Gastroenterol Hepatol*. 2005;3(8):717-25.
2. Eswaran SL, Chey WD, Han-Markey T, et al. A randomized controlled trial comparing the low FODMAP diet vs. modified NICE guidelines in US adults with IBS-D. *Am J Gastroenterol*. 2016;111(12):1824-932.
3. Hustoft TN, Hausken T, Ystad SO, et al. Effects of varying dietary content of fermentable short-chain carbohydrates on symptoms, fecal microenvironment, and cytokine profiles in patients with irritable bowel syndrome. *Neurogastroenterol Motil*. 2017;29(4).
4. Halmos EP, Power VA, Shepherd SJ, et al. A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. *Gastroenterol*. 2014;146(1):67-75.
5. McIntosh K, Reed DE, Schneider T, et al. FODMAPs alter symptoms and the metabolome of patients with IBS: a randomised controlled trial. *Gut*. 2017;66(7):1241-51.
6. Peters SL, Yao CK, Philpott H, et al. Randomised clinical trial: the efficacy of gut-directed hypnotherapy is similar to that of the low FODMAP diet for the treatment of irritable bowel syndrome. *Aliment Pharmacol Ther*. 2016;44(5):447-59.
7. Staudacher HM, Whelan K, Irving PM, Lomer MCE. Comparison of symptom response following advice for a diet low in fermentable carbohydrates (FODMAPs) versus standard dietary advice in patients with irritable bowel syndrome. *J Hum Nutr Diet*. 2011;24(5):487-95.
8. Vazquez-Roque MI, Camilleri M, Smyrk T, et al. A controlled trial of gluten-free diet in patients with irritable bowel syndrome-diarrhea: effects on bowel frequency and intestinal function. *Gastroenterol*. 2013;144(5):903-11.
9. Biesiekierski JR, Peters SL, Newnham ED, et al. No effects of gluten in patients with self-reported non-celiac gluten sensitivity after dietary reduction of fermentable, poorly absorbed, short-chain carbohydrates. *Gastroenterol*. 2013;145(2):320-8.
10. Whelan K, Judd PA, Preedy VR, Taylor MA. Covert assessment of concurrent and construct validity of a chart to characterize fecal output and diarrhea in patients receiving enteral nutrition. *JPEN, Journal of parenteral and enteral nutrition*. 2008;32(2):160-8.
11. Goy JA, Eastwood MA, Mitchell WD, et al. Fecal characteristics contrasted in the irritable bowel syndrome and diverticular disease. *Am J Clin Nutr*. 1976;29(12):1480-4.
12. Wenzl HH, Fine KD, Schiller LR, Fordtran JS. Determinants of decreased fecal consistency in patients with diarrhea. *Gastroenterol*. 1995;108(6):1729-38.
13. Halmos EP, Christophersen CT, Bird AR, et al. Diets that differ in their FODMAP content alter the colonic luminal microenvironment. *Gut*. 2015;64:93-100.

14. Frank L, Kleinman L, Rentz A, et al. Health-related quality of life associated with irritable bowel syndrome: comparison with other chronic diseases. *Clin Ther*. 2002;24(4):675-89.
15. Gralnek IM, Hays RD, Kilbourne A, et al. The Impact of Irritable Bowel Syndrome on Health-Related Quality of Life. *Gastroenterol*. 2000;119(3):654-60.
16. Knowles SR, Austin DW, Sivanesan S, et al. Relations between symptom severity, illness perceptions, visceral sensitivity, coping strategies and well-being in irritable bowel syndrome guided by the common sense model of illness. *Psychol Health Med*. 2017;22(5):524-34.
17. Lackner JM, Gudleski GD, Ma CX, et al. Fear of GI Symptoms has an Important Impact on Quality of Life in Patients with Moderate-Severe IBS. *Am J Gastroenterol*. 2014;109(11):1815-23.
18. Grzesiak M, Beszlej JA, Mulak A, et al. The lifetime prevalence of anxiety disorders among patients with irritable bowel syndrome. *Adv Clin Exp Med*. 2014;23(6):987-92.
19. Austin GL, Dalton CB, Hu Y, et al. A Very Low-Carbohydrate Diet Improves Symptoms and Quality of Life in Diarrhea-Predominant Irritable Bowel Syndrome. *Clin Gastroenterol Hepatol*. 2009;7(6):706-8.e1.
20. Heaton KW, Radvan J, Cripps H, et al. Defecation frequency and timing, and stool form in the general population: a prospective study. *Gut*. 1992;33(6):818-24.
21. Tinmouth J, Tomlinson G, Kandel G, et al. Evaluation of stool frequency and stool form as measures of HIV-related diarrhea. *HIV Clin Trials*. 2007;8(6):421-8.
22. Drossman DA, Corazziari E, Delvaux M, et al., editors. The functional gastrointestinal disorders (3rd ed). 2006.
23. Blake MR, Raker JM, Whelan K. Validity and reliability of the Bristol Stool Form Scale in healthy adults and patients with diarrhoea-predominant irritable bowel syndrome. *Aliment Pharmacol Ther*. 2016;44(7):693-703.
24. Lane MM, Czyzewski DI, Chumpitazi BP, Shulman RJ. Reliability and Validity of a Modified Bristol Stool Form Scale for Children. *The Journal of Pediatrics*. 2011;159(3):437-41.e1.
25. Gibson PR, Muir JG, Newnham ED. Other dietary confounders. FODMAPs et al. *Dig Dis*. 2015;33(2):269-76.

Table 1. Features of two dietary studies investigating management of IBS

	FODMAP study	Gluten study
Enrolment of IBS patients by Rome III criteria	n = 30	n = 40
Inclusion of healthy participants	n = 8	No

Study design	Single-blinded, randomized, cross-over	Double-blinded, randomized cross-over
Dietary interventions	Low FODMAP and typical FODMAP diets	High gluten, low gluten fortification and placebo
Food supplied	Yes	Yes
Duration on each diet	Three weeks each	One week each
Washout period between cross-over diets	≥ three weeks	≥ two weeks
Symptom measure	100 mm VAS	100 mm VAS
Fecal collection sample	Five-day	Three-day
Storage of fecal samples	Immediately frozen in -4° C portable freezer	Immediately frozen in -4° C portable freezer
Fecal frequency and weight collected	Each sample stored separately	Each sample stored separately
Fecal consistency independently assessed	King's College Stool Chart	King's College Stool Chart
Fecal water content measured	Yes	Yes

Table 2. Demographics of IBS subjects undergoing one of two studies investigating dietary treatments for IBS

Patient characteristic	FODMAP study	Gluten study
Number of patients	30	40
Sex	9 male	7 male
Median age (range) y	41 (29-53)	46 (29-55)
Median BMI (range) kg/m ²	23.8 (23.0-26.2)	23.7 (21.6-26.3)
IBS subgroup based on Rome III criteria	10 IBS-D 13 IBS-C 5 IBS-M 2 IBS-U	17 IBS-D 15 IBS-C 8 IBS-M

Table 3. Independently assessed stools of irritable bowel syndrome (IBS) subjects categorized into subtypes on enrolment via King's Stool Chart (KSC) and fecal water content (FWC). Data are presented as n (%) and differences between the groups are determined by Cohen's kappa analysis (kappa[95%CI]). There is a fair strength of agreement between IBS-D and KSC classification 0.29[0.05-0.52], moderate strength of agreement between IBS-D and FWC 0.48[0.26-0.70], and a moderate strength of agreement between IBS-C and KSC classification 0.50[0.30-0.70], based upon a kappa index of 0.21-0.40 indicating fair and 0.41-0.60 indicating moderate strength of agreement.

Rome III IBS subtype on enrolment	KSC 'loose & unformed' or 'liquid' $\geq 25\%$ stools	FWC $\geq 78\%$	KSC 'hard & formed' $\geq 25\%$ stools
IBS-D (n = 25)	15 (60)	15 (60)	7 (28)
IBS-M (n = 13)	6 (46)	4 (31)	5 (38)
IBS-C (n = 27)	3 (11)	3 (11)	23 (85)
IBS-U (n = 2)	1 (50)	-	1 (50)
Total n = 67			

IBS-D Diarrhea-predominant irritable bowel syndrome

IBS-M Mixed irritable bowel syndrome

IBS-C Constipation-predominant irritable bowel syndrome

IBS-U Unsubtyped irritable bowel syndrome

Table 4. Comparison of fecal frequency, weight and water content and dissatisfaction with stool consistency between IBS subtypes and healthy subjects during their worst rated dietary period. Fecal frequency is compared by Chi Squared analysis and other measures are compared by Kruskal-Wallis with a post-hoc Dunn's multiple comparison analysis.

IBS subtype on enrolment	Fecal frequency (mean number of stool/day)				Fecal weight (Median (IQR) g/day)		Fecal water content (Median (IQR) %)		Dissatisfaction with stool consistency (Median (IQR) mm)	
	0	1-2	3							
IBS-D (n = 25)	2	20	3	P = 0.349	179 [131-289] [*]	P = 0.001 [*]	78.8 (74.6-82.3) ^{†±}	P < 0.001 ^{†±}	24.3 (13.7-50.0)	P = 0.083
IBS-M (n = 13)	-	11	2		121 [74-174]		75.6 (71.3-78.3)		26.0 (14.2-50.9)	
IBS-C (n = 27)	3	24	-		117 [63-145] [*]		72.7 (68.4-75.3) [†]		41.2 (29.7-59.3)	
IBS-U (n = 2)	-	2	-		106 [90-122]		74.4 (74.0-74.8)		37.3 (15.0-59.6)	
Healthy (n = 8)	2	6	-		126 [117-154]		67.7 (61.5-74.0) [±]		16.8 (12.5-28.7)	

* IBS-D statistically different compared to IBS-C via Dunn's multiple comparison test

† IBS-D statistically different compared to IBS-C via Dunn's multiple comparison test

± IBS-D statistically different compared to healthy via Dunn's multiple comparison test

Figure legend

Figure 1. Correlation of mean self-assessed dissatisfaction of stool consistency to fecal water content (FWC) during 3- or 5-day fecal collection in a) IBS-D subjects, and b) IBS-C subjects while following a typical FODMAP diet or 'worst' diet.

Figure 2. Correlation of the change in mean self-assessed dissatisfaction of stool consistency to change fecal water content (FWC) during a) the 5-day typical FODMAP and low FODMAP fecal collection in IBS-D subjects, and b) IBS-C subjects. A higher score indicates self-assessed worsening of stool consistency. There was a positive correlation between dissatisfaction with stool consistency and FWC in IBS-C subjects undertaking the FODMAP study.

Figure 3. Fecal water content (FWC) of a pooled 5- or 3-day samples from subjects undertaking one of two cross-over dietary trials investigating treatments of irritable bowel syndrome (IBS). Paired data are presented as ratio of FWC during low to typical FODMAP diets and placebo to gluten fortified diets. Diarrhea-predominant IBS subjects are represented with a star.









