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Review

Measurement of Pain and Related Symptoms in Irritable Bowel Syndrome: The Use of Validated Pain Measurement Tools

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Abstract: This paper reviews the tools available to assess outcomes of treatment in irritable bowel syndrome, especially the effect on abdominal pain. Tools were identified through a wide-ranging scrutiny of PubMed and Google Scholar, together with a review of further references quoted in those publications. It critically considers their development, relevance and reliability. The Irritable Bowel Severity Scoring System (IBS-SSS) was the first simple method of monitoring the progress of the disease and its treatment. It led on to other instruments, such as The Irritable Bowel Syndrome Quality of Life (IBS-QOL). It is easier to read and faster to complete than the IBS-SSS., However, these and other tools were developed for English speaking populations. This review considers the impact of ethnicity and gender, together with the lack of information on the effect of age on the potential validity of these tools in other populations. Issues with the adequacy and appropriateness of translations of such tools are discussed. The overall conclusion is that there are few tools which meet the criteria necessary to place confidence in their validity as appropriate measures of patient outcomes.

Keywords: pain measurement; irritable bowel syndrome; patient outcomes; questionnaires; gender; ethnicity

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1. Introduction

Irritable bowel syndrome (IBS) affects a significant number of people. It is characterized by abdominal pain, bloating and an irregular bowel habit, varying from constipation to diarrhea. It can affect up to 8.8% of people worldwide and, in all countries, it affects women more often than men with a ratio of 1.4:1 [1]. Pain and issues with constipation or diarrhea can affect patients two thirds of the time, with pain being commoner and present half of the time [2]. Indeed, antispasmodics for pain relief are the commonest drug prescribed for people with IBS [3]. However, the therapeutic approach adopted for the management of IBS needs to include effective regularization of bowel habit and control of the elusive symptom of bloatedness. Bloating is a cause of distress to many patients, but its definition is problematic and its role as a symptom varies across cultures and ethnic groups.

The diagnosis of IBS has always been problematic, and this is reflected in the range of names under which it has been described, including spastic colon and mucous colitis. However, it was not until the 1970s that there were attempts to establish clear diagnostic criteria for IBS by means of a questionnaire [4]. Chronic abdominal pain was identified as a major diagnostic feature of IBS following on from this study. Relief of pain with a bowel movement, and more frequent and looser stools at the onset of pain were also identified as significant features. Subsequent to this work, an international movement towards developing a standardized definition of IBS emerged [5]. The Rome Foundation, based in Raleigh, USA, supports work on disorders in which there is a Gut Brain interaction. Between 1989 and 2016 it has published four updates on diagnostic criteria for such functional gastrointestinal disorders. The current criteria embodied in Rome IV are stricter than earlier versions and for IBS require:

"Recurrent abdominal pain, on average, at least 1 day/week in the last 3 months, associated with two or more of the following criteria:

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

These symptoms need to be present for at least three months with an initial onset at least six months earlier [5]. In essence, they are now little different to the original criteria proposed by Manning et al. [4] with pain as the dominant feature. A central problem has now become how best to measure such pain in a reliable, reproducible and robust format.

This is therefore a critical aspect in designing and evaluating trials of treatment in irritable bowel syndrome (IBS), where the desired outcome is a reduction in patients' experience of pain. When choosing a tool to measure changes in pain, it needs to include within it an assessment of pain severity, frequency and duration. In order to assess the efficacy of any treatment, it is critical that there are before and after measures. In some conditions, this is relatively easy with clear changes in biomarkers, which reflect disease activity. In the case of IBS, such biomarkers are extremely limited. Both elevated bile acid in the stool and altered colonic transit have been suggested as possible such markers but they are yet to be generally accepted [6]. Although laboratory-based assessments of visceral sensitivity have been developed, they too are not generally available. Techniques which have been used include colonic and rectal balloon distention by barostat [7]. Therefore, in the case of IBS, in practice, assessments of the severity of disease are usually reported by patients. Alternatives, such as reports and observations from other family members, nurses, doctors or other researchers are problematic. For example, clinicians can under-estimate pain and its consequences. Such discrepancies between general practitioners and patients with IBS were reported by Chassany et al. [8]. Indeed, it is the lived experience of patients with IBS that is central to any assessment of the efficacy of any new treatment. Of course, in the case of IBS, pain is not the only symptom and abdominal pain, straining, disease-related concerns and to a lesser extent myalgias, urgency and bloating have been considered as predictive factors of disease severity, as perceived by patients [9]. Consequently, reliable and robust tools should include within them all of these aspects and, ideally, should be developed with real patient input.

2. Development of Patient-Friendly Tools

Assessment tools can be completed by professionals or by patients. The limitations of professional completion include: an under-assessment of the severity of disease symptoms, as well as potential bias and misinterpretation of patients' comments. Tools to be completed by patients need to be:

- Short;
- Relevant;
- Easy to read and easily understood.

They should share many of the characteristics necessary for questionnaires to achieve high response rates [10]. Perhaps the most important of these criteria is the need for such tools to be easy to read [11–13]. Over the years a number of tools have been developed to assess ease of reading, of which the best known include the Flesch–Kincaid Readability Tests, the Gunning Fog Index and the Simple Measure of Gobbledygook (SMOG) Test of Readability (Table 1). These tests can now be accessed on-line and can help ensure that any tool will be understood by someone with a standard reading age. Once in a readable format such tools need to be assessed for validity, internal consistency and reproducibility. Having been developed through such an intense program of assessment, the tool is only valid for use in the community in which it was developed. For example, a tool developed in the USA may not be valid in the UK, where symptoms and the words used to describe them may have different meanings. Prior to use in a different community the tool will need to be validated in that setting. This is even more true for translations into other languages.

The issue of readability is a universal problem and all tools completed by patients need to be in an understandable form. The general reading level of most communities is relatively low, which originally led to the development of readability calculators. However, they are dominated by English language systems, although the Rix Index and Coleman–Liau Formula can be used for most Latin scripts. As yet there are no validated readability tools for other scripts.

Table 1. Commonly used Readability Formulae to assess ease of reading of texts, such as questionnaire tools.

Formula	Language	Country of Origin
Flesch Reading Ease [14]	English	USA
Gunning Fog Index [15]	English	USA
SMOG (Simple Measure of Gobbledygook) [16]	English	UK/USA/Canada
Rix Formula [17]	English	Australia
Coleman-Liau Index [18]	Western European Languages	USA
Flesch–Vacca formula [19]	Italian	Italy
GulpEase index [20]	Italian	Italy
SATO-CALIBRAGE [21]	French	Canada
Fernandez-Huerta Formula [22]	Spanish	Spain
Läsbarhetsindex [23]	Swedish	Sweden

3. Measurement of Pain in IBS

Despite the importance of pain to patients with IBS, clear questions have not been developed for use in IBS trials. Terms such as "relief of your IBS symptoms" have been used to measure efficacy, but they are not an objective end-point [24]. Regulatory agencies have been generally dissatisfied with such soft end-points which generate a simple "Yes" or "No" [25]. Such requirements have acted as stimuli to the development of reliable and reproducible tools with more nuanced outcome measures. Lackner et al. [26] have shown that, although recall of specific symptoms, such as worst pain or stool frequency, is reasonably accurate, this is not the case for typical pain, which is vulnerable to distortion. Consequently, tools need to be used contemporaneously throughout the period of treatment. As a result of such requirements, the number of validated IBS specific tools is limited. Those that exist tend not to be pain specific but evaluate a range of other symptoms.

In 1997, Francis et al. [27] developed the Irritable Bowel Severity Scoring System (IBS-SSS). It was the first simple method of monitoring the progress of the disease and its treatment. The questionnaire evolved and was simplified over a number of years, rather than being developed from formal patient involvement. It has nine stem questions of which three concern abdominal pain or discomfort. Five questions have scores of between 0 and 100 each, based on visual analogue scales. A score below 75 is seen in healthy people or those in remission, whilst 75–175 indicates mild disease, 175–300 moderate disease and over 300 severe disease.

IBS-SSS is frequently used in clinical trials to monitor the progress of the disease and treatment effect. However, there are several concerns regarding its use. It is an unwieldy 4-page document and when its readability is scored with on-line software, such as that provided by https://readabilityformulas.com/ (accessed on 26 July 2021), the Flesch Reading Ease Score is 64.5, which is generally considered suitable for a person with an average reading age, ref. [28] whilst the Gunning Fog Index is 11.1 indicating that it would be considered a "Hard Read" [29]. Both indices are of American origin and consider sentence length and word complexity, but have been generally accepted as useful tools in assessing healthcare literature [30]. (Table 1) Such scores mean that a significant number of people in the UK will have difficulties understanding the text [31]. It is possibly for these

reasons that in clinical practice, and in many research protocols, only the first part of the document, which consists of five simple and quick questions is used.

The Irritable Bowel Syndrome Quality of Life (IBS-QOL) instrument measures quality of life [32]. The development of this questionnaire and its translation was driven by Novartis Pharmaceuticals Corporation and its agents [33]. It is easier to read and faster to complete than the IBS-SSS, with a Flesch Reading Ease Score of 76.6 ("Fairly easy to read") and a Gunning Fog Index of 5.1 ("Easy to read"). It measures psychological well-being, rather than function, and has been translated into several languages. It has 34 items with a 5-point response scale. Although many of the 34 items could be affected by pain, it is not specifically mentioned and so is of limited value in the specific assessment of this symptom.

International concerns about the need to have adequate tools to measure outcomes led to the Food & Drug Administration issuing Patient Reported Outcomes. (PROs) in 2009 [25]. They consider that good PROs and their appropriateness require no intervention or interpretation by clinicians or anyone else (Table 2). In clinical trials good PROs can be used to measure the effects of an intervention on a single symptom or group of symptoms, or on daily functioning or the severity of a disease. They thus meet the basic requirements for the lived experience of patients. Therefore, in IBS, it will be necessary to define whether pain relief is the main desired outcome or a global improvement in pain, bloating, defecation habit and ability to live a normal life are the desired endpoints.

Table 2. Characteristics of some commonly used tools.

Tool	Abbreviation	Number of Questions	Score
Irritable Bowel Scoring Severity System	IBS-SSS	21	<50 normal; >300 severe disease
Irritable Bowel Syndrome-Quality of Life	IBS-QOL	34	Measures outcome in 4 domains
Numeric Rating Scale	NRS	10	A change of more than 2 in the score indicates a significant improvement
Visceral Sensitivity Index	VSI	15	Score of 0–75 with a high score indicating low visceral sensitivity
Visual Analogue Scale	VAS-IBS	9	Score 0–100, with 100 indicating no discomfort

An important aspect in the development of a PRO, which was flagged up in the FDA advice, was the way in which it originated. Patients are crucial. Through mechanisms, such as interviews and focus groups, PROs can be designed to capture what matters to patients and so are valid. For such reasons, the FDA recommended that when individual scores are added together to give a single overall score it is important that the score represents a recognizable domain rather than being an artificial entity [25]. Kitzinger [34] confirmed the need to ensure focus groups represented a cross section of society, either through use of multiple groups or, less favorably, one group with a widespread membership. However, the Gastrointestinal Pain Pointer, which is an electronic tool developed with the help of patient and control groups representative of Caucasians, African Americans and Asians is the only instrument where this has been attempted [35]. However, although it is now 4 years since this paper was published, there have been no studies where it has been used in clinical trials of treatment. A further issue has been that in a number of studies, there has been a failure to recognise that an instrument cannot be simply translated and used in a new culture. Failure to validate the translation means that the result of such a study cannot be relied on.

4. Perceptions of Pain in IBS

The issue of how patients of different ethnicities view pain and bloating is an important aspect of their assessment, which has received little attention in the field of gastroenterology. Others, who have considered the issue, have often stereotyped communities. For example, as recently as 1985 Wolff [36] wrote: "Scandinavians are tough and stoic with a high tolerance to pain; the British are more sensitive but, in view of their ingrained "stiff upper lip", do not complain when in pain; Italians and other Mediterranean people are emotional and overreact to pain and Jews both overreact to pain and are preoccupied with pain and

suffering as well as physical health". However, extensive clinical and laboratory pain research has confirmed that ethnic groups differ considerably in their response to and expression of pain [37].

Wise et al. [38] have shown that women report lower thresholds and tolerance compared to men and endure pain for less time and are more willing to report pain. Pain also appears to have different meanings for men and women [39]. In a survey, conducted by the United States National Center for Health Statistics, men and women reported differing symptomatology, different pain levels and different analgesic usage associated with the same disease process [40,41]. In a study of startle reactions male patients had reduced sensorimotor gating, suggesting a decreased ability to filter information; in contrast, female IBS patients had enhanced prepulse inhibition, possibly related to increased vigilance and greater attention to threat [42]. However, this difference was abolished by the oral contraceptive pill or the menopause. In a related study Chang et al. [43] was able to demonstrate that premenopausal women with IBS had a lower threshold of response to noxious rectal stimuli than men.

5. Impact of Pain Perception on Clinical Studies

Such findings have direct relevance to any study of treatment in irritable bowel syndrome and the intervention and control groups ideally should have appropriate stratification of ethnicity and gender. There is also concern about the potential impact of age on the measurement of symptoms in IBS. The difficulties of pain measurement in children are well recognized, as is the need for validated clinical outcome measures [44]. Even with attention to such issues difficulties in use of the term "bloating" will remain. For example, there is no equivalent term in Spanish or Italian. This difficulty was recognized by the Rome Foundation Working Team [45]. Although it recommended appropriate techniques for translating and validating tools for use in functional gastrointestinal disorders, it provided very limited guidance on how to tackle specific issues such as translating "Bloatedness" or discovery of appropriate equivalent alternatives.

Based on such advice, Fehnel et al. [46] identified incomplete bowel movements, abnormal stool frequency and consistency, and abdominal pain, discomfort, and bloating as common symptoms, but the one feature that concerned patients was abdominal pain. In an attempt to develop reliable PROs, Ballou & Keefer [47] asked patients with IBS to complete an on-line survey. Three factors emerged as important: pain catastrophizing, visceral hypervigilance and extraintestinal hypervigilance. Their tool is patient-completed and has 15 items to cover these areas, but again has yet to be used in any clinical trials.

In 2015 Mujajic et al. [48] reviewed 110 papers, which had assessed the numerous tools used to assess pain in IBS. They concluded that the most useful questionnaires were:

1. Spiegel et al.'s 10-point Numeric Rating Scale [9], as it was the best validated tool to measure responses to treatment
2. The IBS—Symptom Severity Scale (IBS-SSS) is the best suited to measure abdominal pain because it has been correlated with physical measures, such as the pain induced by rectal distension, is reproducible and is psychometrically robust [27].
3. Visceral Sensitivity Index (VSI) for measurement of emotional response to abdominal pain, but not to its intensity [49].

Mujajic et al. [48] had identified 7 clinical trials which used Visual Analogue Scales to assess chronic abdominal pain in IBS. However, the authors point out that it has not been psychometrically tested for use in IBS and only measures one dimension of pain intensity. This problem has been overcome by Bengtsson et al. [50], who developed a specific and validated Visual Analogue Scale for IBS. The questionnaire has five domains with 15 items and was psychometrically sound.

A Numeric Rating Scale had been used in 4 clinical trials and a 10-point scale used by Spiegel et al. [9] was found to have high validity and sensitive clinical responsiveness. It correlated well with IBS-SSS and generic quality of life measures and resource utilization by patients.

Mujajic et al. [48] identified 15 different multi-item questionnaires used in IBS for the assessment of one or more dimensions of abdominal pain. Of these, the VSI is useful for assessing gastrointestinal-specific anxiety, the cognitive, affective, and behavioral response to fear of gastrointestinal sensations, symptoms, and the context in which these visceral sensations and symptoms occur [49,50]. Its questions reflect the anxieties experienced by many patients with IBS and show that chronic and recurrent abdominal pain can have a devastating effect on patients with IBS sufferers.

6. Conclusions

There are many and varied tools for measuring pain and other aspects of IBS. However, presently available tools have issues:

- Ethnicity;
- Gender;
- Age;
- Validated in the language of the tool if a translation;
- Ability to be read;
- Doctor/Nurse or Patient completed;
- Reproducibility;
- Validity for use in IBS.

In practice PROs are likely to best reflect the benefits of any intervention designed to improve patients' experience of pain and its impact on aspects of day-to-day life. There are clear criteria which should be adopted by those setting up clinical trials as to which tests are most reliable, reproducible and valid. The issue of whether these tools are culturally appropriate needs careful consideration. Translation, retranslation and testing of validity are prolonged and expensive exercises. However, they are critical to ensuring that the results are valid and robust. Studies which use translated tools without revalidation are, in truth, meaningless. Although tools, such as IBS-SSS, exist in a number of translations it does not mean that they have been through a rigorous assessment of their validity in that language or in that culture. Equally studies which fail to take account of the differences in gender experience of pain cannot form the basis for increasing our understanding of effective interventions to control the symptoms of IBS.

How then can one choose a valid tool for clinical or research assessments? Ideally future research will involve patients from the ethnic community in which the tool will be used. It should have validity for use in day-to-day practice as well as clinical research. It will need to be at least gender sensitive, if not gender specific. However, until such tools are available in practice: Spiegel et al.'s 10-point Numeric Rating Scale [9], is the best validated tool to measure responses to treatment and is relatively easy to use. The IBS-SSS is widely used and best suited to measure abdominal pain because it has been correlated with physical measures and is reproducible. The use of specific tools which have been developed around the symptoms that characterize IBS likely has some advantage over more generic tools such as the Brief Pain Inventory, and this was confirmed in a study by Puhan et al. [51].

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