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Qualitative Assessment of Symptom Experience in Patients with Irritable Bowel Syndrome for the Development of Patient Reported Outcome Instruments

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on Behalf of the Critical Path Institute PRO Consortium's Irritable Bowel Syndrome Working Group

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Introduction

- Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder characterized by abdominal pain or discomfort associated with altered bowel habits.
- IBS is sub-typed based on predominant bowel habits: diarrhea-predominant (IBS-D), constipation-predominant (IBS-C), or mixed (IBS-M).
- There is currently no patient-reported outcome (PRO) measure that is accepted as well-defined and reliable by the FDA for use in determining therapeutic benefit of novel agents in IBS. Therefore, the FDA recommends using interim composite primary endpoints based on abdominal pain ratings and stool consistency (IBS-D) or stool frequency (IBS-C) in clinical treatment trials.[1]

Objective

- To conduct qualitative research with IBS patients to elicit their symptom experience in accordance with the FDA's Guidance for development of a PRO instrument.

Methods

- Prior to conducting interviews, we performed a targeted literature search, developed a preliminary conceptual framework, and conferred with an expert panel.
- Face-to-face interviews were conducted in a representative adult sample in three US geographic locations (Raleigh, NC; San Antonio, TX; and San Diego, CA).
- Patients had a physician confirmed diagnosis of IBS-D (n=17), IBS-C (n=14) or IBS-M (n=18) per Rome III criteria with an average baseline pain level of 3 or greater over the past 7 days at time of screening (0-10 scale). Patients with a history of any condition that could confound attribution of symptoms to IBS were excluded.
- Additional screening criteria ensured interview patients were similar to IBS clinical trial patients.
- Each interview was conducted according to a semi-structured interview guide including spontaneous concept elicitation, probed concept elicitation, and identification of symptoms most bothersome and important to measure.

Examples of open-ended concept elicitation interview questions

- What comes to the top of your mind when you think about your IBS?
- What symptoms do you experience?
- When you say [symptom], what exactly does that mean to you?
- What other terms or words, if any, would you use to describe [symptom]?
- Which of these symptoms is the most bothersome to you? Why?

- Following the spontaneous concept elicitation phase of each interview, patients were probed about other symptoms commonly measured in IBS clinical trials that were not mentioned spontaneously (pre-specified by the IBS WG) in order to fully assess the potential relevance and importance of these symptoms.
  - Symptoms that were probed for all subtypes included: incomplete BMs; abdominal pain; abdominal discomfort; bloating and gas.
  - Each patient was also asked to identify his/her top five most important to treat symptoms and the most bothersome symptom.

- To evaluate concept saturation (i.e., the point at which no new information or themes are observed in the data), each of the three sets of interviews (IBS-D, IBS-C, and IBS-M) were divided into three groups (approximately one-third of the interviews per group), and the amount of new information gleaned from each subsequent group was evaluated.
- Analysis of the qualitative data, using ATLAS.ti software, identified dominant trends within and across interviews to evaluate patient's descriptions of IBS symptoms.
- The preliminary conceptual framework was updated based on the results of IBS patient interviews.

Results

Demographics

- A total of 49 IBS patients participated in the study, with IBS-D (n=17), IBS-C (n=14), IBS-M (n=18). Overall , 83% (n=41) were females, 63% (n=31) were White, 24% (n=12) African American/Black and 83% (n=41) were not Hispanic, and 79% had at least some college education.
- The average age (range) overall was 46.7 yrs (19-75), and 48.6 yrs (25-75) for IBS-D, 45.0 yrs (19-68) for IBS-C, and 46.1 yrs (21-68) for IBS-M.
- The average baseline abdominal pain severity (and range) across the past 7 days was 6.2 (3-10) for the entire sample, and across subtypes: 6.4 (3-10) for IBS-D, 5.8 (3-9) for IBS-C, and 6.2 (3-10) for IBS-M.

Spontaneous symptom reports

- Concept elicitation revealed a range of symptom experiences attributed to IBS, which varied across sub-types
- While almost all IBS patients reported abnormal stool consistency and frequency and abdominal pain, more IBS-D experienced urgency, IBS-C reported more bloating symptoms, and IBS-M shared symptoms with both (Table 1)
- *Concept saturation*: Only undigested food in stool, depression, restless/can't sleep, and salivating were newly identified in the third and final set of interview transcripts. Based on limited number of reports, these concepts do not appear to reflect core symptoms of IBS.

Table 1: Spontaneously Reported IBS Concepts by IBS Subtype with Reported Frequency Greater than 50%

IBS-D (n=17)	IBS-C (n=14)	IBS-M (n=18)
Diarrhea: 17 (100%)	Constipation: 14 (100%)	Constipation: 18 (100%)
Loose or Watery Stools: 16 (94%)	Infrequent BMs: 14 (100%)	Abdominal Pain: 17 (94%)
Urgency: 15 (88%)	Bloating: 13 (93%)	Infrequent BMs: 17 (94%)
Abdominal Pain: 15 (88%)	Can't go: 12 (86%)	Diarrhea: 16 (89%)
Cramping: 12 (71%)	Abdominal Pain: 11 (79%)	Recurrent BMs: 16 (89%)
Recurrent BMs: 12 (71%)	Small Stools: 11 (79%)	Loose or Watery Stools: 15 (83%)
Too Frequent BMs: 12 (71%)	Straining: 10 (71%)	Too Frequent BMs: 14 (78%)
Gas: 10 (59%)	Gas: 9 (64%)	Cramping: 13 (72%)
Abdominal Discomfort: 9 (53%)	Abdominal Discomfort: 9 (64%)	Urgency: 13 (72%)
	Feeling of Fullness: 8 (57%)	Can't go: 12 (67%)
	Hard Stools: 8 (57%)	Long Time in Bathroom: 12 (67%)
		Unsuccessful Attempts: 12 (67%)
		Bloating: 11 (61%)
		Hard Stools: 11 (61%)
BM = bowel movement		Straining: 10 (56%)

Table 2: Summary of Single Most Bothersome Symptoms

Symptom	Number of Patients Reporting Symptom as the Most Bothersome			
	IBS-D (n=17)	IBS-C (n=14)[a]	IBS-M (n=18)[b]	Total (N= 49)
Abdominal Pain	4	2	5	11
Urgency	6	0	4	10
Cramping	1	0	5	6
Bloating	0	4	1	5
Infrequent BMs	0	3	1	4
Abdominal Discomfort	1	1	1	3

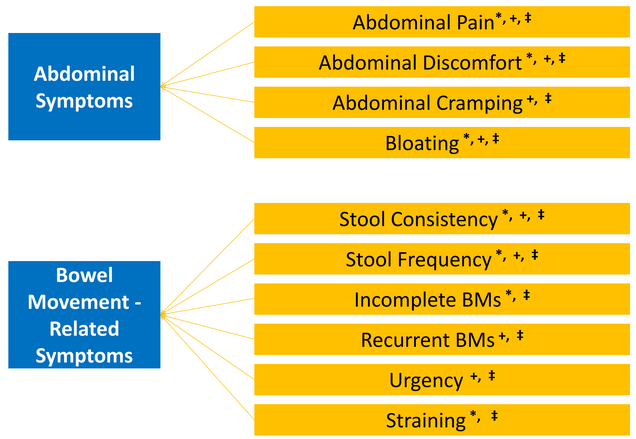
BM = bowel movement; [a]One IBS-C patient did not report a most bothersome symptom; [b]Two IBS-M patients reported two most bothersome symptoms

Table 3: Symptoms Most Important to Treat - Number of Patients Reporting the Symptom Among the Top Five Most Important Symptoms to Treat

IBS-D (n=17)	IBS-C (n=14)	IBS-M (n=18)
Loose/Watery Stools (n=14)	Bloating (n=11)	Abdominal Pain (n=12)
Urgency (n=13)	Infrequent BMs (n=10)	Urgency (n=11)
Abdominal Pain (n=10)	Abdominal Pain (n=10)	Loose/Watery Stools (n=11)
Cramping (n=10)	Incomplete BMs (n=7)	Cramping (n=9)
Too Frequent BMs (n=8)	Gas (n=5)	Bloating (n=8)
Abdominal Discomfort (n=5)	Straining (n=5)	Straining(n=5)
	Abdominal Discomfort (n=5)	Hard Stools (n=5)

BM = bowel movement .
Note: Table includes symptoms reported by at least five patients

Figure 1: Revised Conceptual Framework from the IBS Patient Perspective



Symptoms pertain to the following subtypes: * IBS-C; + IBS-D; ‡ IBS-M

Conclusions

- IBS patients report a range of gastrointestinal symptoms that includes but is not limited to abdominal pain and abnormal stool consistency and frequency
- Findings from this qualitative research suggest that symptoms common across subtypes or specific to each subtype should be considered to comprehensively capture patients' experience on an IBS treatment.
- Further work will include development of an item set, cognitive debriefing, and evaluation of the instrument's psychometric properties.
- This qualitative work stands to support the foundation for future PRO development in IBS.

References

- [1]United States Department of Health and Human Services. Food and Drug Administration Center for Drug Evaluation and Research. May 2012. Guidance for Industry Irritable Bowel Syndrome- Clinical Evaluation of Drugs for Treatment. Available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM205269.pdf. Accessed March 29

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