

**Title:** Evaluation of Gastrointestinal Patient Reported Outcomes Measurement Information System (GI-PROMIS) Symptom Scales in Patients with Crohn's Disease in CCFA Partners

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**Background/Aims:** Patient reported outcomes (PROs) are increasingly recognized as important treatment endpoints in Crohn's disease (CD). The PRO Measurement Information System (PROMIS) contains reliable and precise measures of patient-reported health status for physical, mental and social well-being; it was recently expanded to include gastrointestinal (GI) symptoms. However, these have not been evaluated in large numbers of CD patients. We aimed to evaluate GI PROMIS measures in CD patients and correlate them with psychosocial PROMIS domains, validated disease-specific instruments for quality of life (QoL) and disease activity.

**Methods:** Crohn's and Colitis Foundation of America (CCFA)'s Partners is an internet based cohort of patients with inflammatory bowel disease (IBD). We assessed GI and psychosocial PROMIS measures, the short CD activity index (sCDAI) and the short IBD questionnaire (SIBDQ) in a cross sectional sample of this cohort. We used descriptive statistics and bivariate analyses to evaluate GI PROMIS measures relative to these validated instruments. All PROMIS measures are calibrated such that the mean in the general population is 50 and standard deviation is 10. Based on prior data, the minimally important difference (MID) for GI PROMIS measures is 3.5. For most other domains, the MID is 2-3.

**Results:** 1839 CD patients completed GI PROMIS questionnaires. Responders were 75% women and 95% Caucasian. Average age was 41 years and average disease duration was 11 years. 45% of responders had previously been hospitalized; 49% were treated with a biological agent; 14% had prior surgery for CD and 60% were in remission. On psychosocial measures, CD patients had more fatigue, anxiety and pain interference compared to the general population based on MIDs. Our CD sample had less reflux, disrupted swallowing and constipation than the general population. Other GI symptoms were in the same range as the general population (table 1). Compared to patients in remission, patients with active CD had significantly poorer GI PROs for all symptoms except disrupted swallowing and constipation ( $p < 0.001$ ). When stratified by quartiles of the Short IBD Questionnaire (SIBDQ), patients in the lower quartiles (worse quality of life) reported poorer GI PROs ( $p < 0.001$ ). Those with more severe nausea, diarrhea, gas/bloat and abdominal pain had significantly poorer psychosocial PROs ( $p < 0.001$ ) (table 2).

**Conclusions:** To date, this is the largest description of general GI symptoms and psychosocial PRO measures in patients with CD. Overall, CD patients did not report worse GI symptoms as compared to the general population. Within the population, there were strong associations between worse GI PROMIS measures and worse quality of life, disease activity and psychosocial symptoms. GI PROMIS measures hold potential as important PRO outcome measures in CD patients.

Table 1: Patient Reported Outcomes in Crohn's disease patients in CCFA Partners (n=1839)

Patient Reported Outcome	T score
Reflux	41.1
Disrupted swallowing	42.9
Diarrhea	52.6
Nausea and vomiting	48.0
Belly pain	51.9
Gas / Bloat / Flatulence	52.8
Bowel incontinence	49.0
Constipation	40.6
Anxiety	52.8
Depressive symptoms	51.3
Fatigue	56.0
Pain interference	52.5
Social satisfaction	48.7
Sleep disturbance	51.9

Table 2: Association between GI PROMIS symptom scales and other measures in patients with Crohn's disease\*

Patient Reported Outcome	Lowest SIBDQ** Quartile (1.2-4) (n=454)	Highest SIBDQ Quartile (6 - 7) (n=462)	p value^
Reflux	47.4	36.4	<0.001
Disrupted swallowing	45.5	41.3	<0.001
Diarrhea	59.1	46.3	<0.001
Nausea and vomiting	56.7	42.2	<0.001
Belly Pain	60.0	43.9	<0.001
Gas / Bloat / Flatulence	59.8	44.8	<0.001
Bowel Incontinence / Soilage	54.2	45.5	<0.001
Constipation	43.3	38.3	<0.001
	Remission# (n=988)	Active disease (n=672)	
Reflux	38.8	44.7	<0.001
Disrupted swallowing	41.7	44.7	<0.001
Diarrhea	49.2	58.3	<0.001
Nausea and vomiting	44.0	53.3	<0.001
Belly pain	47.6	58.4	<0.001
Gas / Bloat / Flatulence	50.4	57.0	<0.001
Bowel incontinence / soilage	46.7	52.5	<0.001
Constipation	40.3	41.8	0.005
	Low diarrhea (n=921)	High diarrhea (n=873)	
Anxiety	49.9	55.8	<0.001
Depressive symptoms	48.3	54.3	<0.001
Fatigue	52.0	60.2	<0.001
Pain interference	48.4	56.7	<0.001
Social satisfaction	52.3	45.0	<0.001
Sleep disturbance	49.2	54.7	<0.001

\*Minimally important difference defined as difference of  $\geq 2$  \*\*Short inflammatory bowel disease questionnaire (SIBDQ): higher scores denote higher quality of life ^p value by t-test

# Remission defined as short Crohn's disease activity index (SCDAI) score <150