Patient-Reported Outcomes Measurement Information System in Children with Crohn's Disease

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Objectives To assess the criterion validity and responsiveness of Patient-Reported Outcomes Measurement Information System (PROMIS) in a web-based cohort of children with Crohn's disease.

Study design We recruited children with Crohn's disease (ages 9-17 years) and their parents from the web-based Crohn's and Colitis Foundation of America Kids and Teens Study cohort. Upon entry into the cohort and 6 months later, children self-reported Crohn's disease activity, health-related quality of life, and PROMIS domains of pain interference, anxiety, depression, fatigue, and peer relationships.

Results Mean PROMIS scores for the 276 participating patients were worse among those with worse self-reported Crohn's disease activity (per Short Crohn's Disease Activity Index, $P < .005$ for all), Crohn's disease activity in the prior 6 months (per Manitoba Index, $P < .01$ for all), and health-related quality of life (per IMPACT-35, $P < .001$ for all). One hundred forty-three patients and their parents completed follow-up questionnaires, 75% of whom reported stable disease activity. Those with improved Crohn's disease activity reported improved PROMIS scores, and those with worsened Crohn's disease activity reported worse PROMIS scores for all domains except anxiety. All participants reported improved anxiety from baseline, but those with stable or worsened Crohn's disease activity reported less improvement ($P = .07$).

Conclusions PROMIS scores were significantly associated with Crohn's disease activity in a linear and clinically meaningful manner, and responded to change in Crohn's disease activity over a 6-month period. This supports the criterion validity and responsiveness of pediatric PROMIS. *(J Pediatr 2016;174:153-9)*.

Patient-reported outcomes (PROs) are measures of how patients feel and function, obtained directly from patients without interpretation, capturing outcomes of importance to patients. PROs both complement standard primary outcomes, such as survival or physiologic measures, and provide primary outcomes that are necessarily patient-focused, such as patient function or quality of life (QoL).[1]

The National Institutes of Health's Patient-Reported Outcomes Measurement Information System (PROMIS) is a set of nondisease specific instruments (one for adults and one for pediatric patients) assessing domains of physical, psychological, and social health, and QoL.[2] PROMIS instruments are unique in that they have been developed using modern measurement theory, including rigorous qualitative and quantitative methods.[3] They are not disease-specific and are standardized to a reference population, allowing for comparison between different domains of health and across a wide range of chronic diseases.[2,4] Pending additional clinical validation in children with chronic disease, PROMIS pediatric measures may serve as endpoints in clinical, observational, comparative effectiveness, and health services research.[5,6] Researchers and clinicians will then be able to use these endpoints to identify previously unrecognized psychological, social, or functional health disorders, reveal correlations between these disorders and underlying chronic disease activity, and prompt appropriate interventions.[7-10]

When the onset of chronic disease is in childhood or adolescence, it can affect physical, psychological, and social development, as well as school performance, resulting in impaired or delayed achievement as an adult in interpersonal relationships, education, and employment.[11,12] PROMIS pediatric instruments, which have been developed to assess these domains of health in children, have been studied in several disease states, including cancer, obesity, asthma, and nephrotic syndrome, and discriminate well among known groups of disease activity and severity.[10,13,14] However, establishing the validity of PROMIS in children requires research in additional chronic diseases.

CCFA	Crohn's and Colitis Foundation of America
IBD	Inflammatory bowel disease
MID	Minimally important difference
NPTOT	Nonparametric tests of trend
PRO	Patient-reported outcome
PROMIS	Patient-Reported Outcomes Measurement Information System
QoL	Quality of life
SCDAI	Short Crohn's Disease Activity Index

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Children with inflammatory bowel disease (IBD) have been found to have lower QoL and social function than their healthy peers, and experience higher rates of depression than children with other chronic diseases.[15-19] Crohn's disease has no definitive cure and commonly relapses, leading to intermittent disruptions to life and well-being, affecting a child's function, development, and QoL; thus, it is an important model of a relapsing pediatric chronic disease in which to further evaluate PROMIS.

In this study, we first aimed to evaluate the concurrent criterion validity of PROMIS (how PROMIS instrument scores relate to established measures of Crohn's disease activity and health-related QoL) by studying a national, prospective cohort of children with Crohn's disease. Second, we sought to explore the responsiveness of PROMIS instruments to change over time among cohort members who participated in a 6-month follow-up.

Methods

We performed cross-sectional analyses to evaluate associations between PROMIS measures, disease activity indices, disease-specific health-related QoL measures, therapy types, and remission status. We also performed exploratory longitudinal analyses to evaluate the associations between change in disease activity indices and the same QoL measures. The study protocol was reviewed and approved by the Institutional Review Board of the University of North Carolina at Chapel Hill.

The Crohn's and Colitis Foundation of America (CCFA) is a nonprofit, volunteer organization that funds, publishes, and advocates for IBD research, and provides support for patients with IBD of all ages. In 2011, the CCFA sponsored the development and maintenance of CCFA Partners, a web-based cohort of over 13 000 adults with self-identified IBD (ie, Crohn's disease and ulcerative or indeterminate colitis).[20,21] Through a web-based portal, adults in the cohort complete research surveys every 6 months, receive research updates, and access CCFA educational resources.

In 2013, we launched a parallel, web-based cohort of pediatric patients with IBD and their parents, the CCFA Partners Kids and Teens Study. The purpose of this cohort is to create a long-term community of children with IBD engaged in research focused on the relationships between patient-reported exposures, health behaviors, and outcomes.[22] We recruited patients with self-reported IBD and their parents via the CCFA by use of their website, e-mail rosters, various social media outlets, promotional efforts, and word-of-mouth at CCFA educational and fundraising events. Patients with at least one participating parent were eligible to enter the study. Patients and parents could access the cohort entry portal through the study website (www.ccfapartners.org) or through a promotional e-mail link. Enrollment began in August 2013 and remains ongoing. Parents completed the section of survey questions regarding the child's diagnosis of Crohn's disease, demographic information, and family history. Children 9-17 years of age completed all symptom-related questions themselves, including PROMIS instruments specifically designed for child respondents. Six months after entering the cohort, participating patients and parents received e-mail reminders to complete follow-up questionnaires of the same disease-related questions and PROMIS instruments. For the present analyses, we included all patients aged 9 years or older with self-reported Crohn's disease who completed all initial surveys, including child-reported PROMIS instruments and parent-reported demographic information, by November 2013.

PROMIS

Participating patients completed 4 items (questions), from each of 5 selected PROMIS pediatric instruments: anxiety, depression, fatigue, pain interference (a measure of the consequences of pain on various aspects of life, including social, cognitive, emotional, physical, recreational activities, sleep, and enjoyment of life), and peer relationships (a measure of the quality of relationships with friends and other acquaintances).[2] We selected these instruments in collaboration with pediatric IBD specialists and experts in PROMIS methodology[3] because they measure domains of health and health-related QoL affected by Crohn's disease in children. In an effort to minimize respondent burden and enhance long-term cohort retention, we chose to use 4-item short forms rather than longer forms or computer adaptive testing. Although 4-item short forms are less precise at the individual level, they can be effectively used in studies of moderate to large populations such as ours. PROMIS instruments are calibrated using a T-score metric with the mean of the original calibration population equal to 50, and the SD in the calibration population equal to 10.[2] Minimally important differences (MIDs) are the smallest differences in PRO scores able to detect a clinically meaningful change in the outcome that the PRO is designed to measure. Any difference in PRO scores smaller than the MID is likely due to measurement error instead of a true change in the outcome. Studies in adults suggest MIDs for many PROMIS items to be in the range of 2-6.[23] Though MIDs are not yet well established in PROMIS pediatric measures, new research using adolescent patients, parents, and physicians as judges of clinically important differences in scores, suggests MIDs of 2-3 for multiple pediatric PROMIS instruments.[24] Higher scores in any PROMIS domain indicate more of the domain being measured, therefore, higher scores for anxiety, depression, fatigue, and pain interference indicate poorer well-being, whereas higher scores for peer relationships indicate better relationships with peers and, therefore, better well-being.

Other Variables

We administered the IMPACT-35 questionnaire to assess health-related QOL, and we measured disease activity using

the Short Crohn's Disease Activity Index (SCDAI). Both of these indices have been validated and are in wide use in both research and clinical care. A SCDAI <150 indicates clinical remission, and values above this threshold indicate active disease.[25] We did not use the Pediatric Crohn's Disease Activity Index,[25,26] which requires physical examination and laboratory assessments, and therefore, is not feasible for survey research. We also assessed IBD activity within the past 6 months via the validated Manitoba IBD Index, which is a single-item, patient-reported indicator of IBD activity within the last 6 months, with scores ranging from 1 (constantly active) to 6 (inactive).[27] In addition, we collected information regarding patient demographics, past IBD-related surgery, and both past and current IBD medication use: oral 5-aminosalicylates, oral corticosteroids, immunomodulators (methotrexate, azathioprine, and 6-mercaptopurine), and biologic therapies (infliximab, adalimumab, certolizumab pegol, and natalizumab). In an effort to minimize survey length and respondent burden, we did not question patients about conditions or treatments other than IBD, such as depression, anxiety, or other mental health diagnoses.

Statistical Analyses

We first performed cross-sectional analyses using descriptive statistics and bivariate comparisons to assess the relationships between PROMIS T-scores and patient demographics, indices of disease activity (SCDAI), symptom activity within the last 6 months (Manitoba IBD Index) and QoL (IMPACT-35), current medication use, and other disease characteristics, including remission status, sex, age, age at diagnosis, time since diagnosis, and current steroid use. As disease activity indices and QoL scores were not normally distributed, we categorized these values into quartiles. We compared mean PROMIS scores between patients in remission and active disease by Pearson χ^2 test. We then compared mean PROMIS scores across quartiles of disease activity and QoL scores using 1-way ANOVA and nonparametric tests of trend (NPTOT) for the ranks across ordered groups. We investigated possible interactions between potential confounders (sex, age, age at diagnosis, time since diagnosis, and current steroid use) and PROMIS scores using a likelihood-ratio method. We then used multinomial logistic regression to evaluate associations between PROMIS measures and disease activity. After fitting models that included all potential confounders, we used a change-in-effect method to remove any variable that did not confound the relationship between PROMIS scores and disease activity or health-related QoL.[28]

We next performed exploratory longitudinal analyses by grouping patients into categories of stable disease, worsening disease, or improving disease, based on a threshold change of 70 points between baseline and follow-up SCDAI scores.[29] We then compared change in mean PROMIS scores across these groups using ANOVA and a NPTOT for the ranks across ordered groups. All data were prepared using SAS v 9.3 (SAS Institute, Cary, North Carolina) and analyzed using Stata v 13.1 (StataCorp, College Station, Texas).

Results

A total of 276 patients with self-reported Crohn's disease in children 9 years of age or older joined the CCFA Partners Kids and Teens cohort through November 2013. The mean age of participating patients was 13 years, and the mean age at diagnosis was 10 years (Table I); 44% were female, and 83% were in remission as determined by SCDAI score (102 ± 71). The mean Manitoba IBD Index score was 4, corresponding to occasional disease activity in the 6 months prior to the survey. Accordingly, only 10% were being treated with oral corticosteroids at the time of the survey, 54% were being treated with a biologic, and 47% with immunomodulators (methotrexate, azathioprine, or 6-mercaptopurine). When asked about prior medication use, the majority of patients (87%) reported being treated with oral corticosteroids at some point since their diagnosis.

Table I. Characteristics of the study population

	n = 276
Demographics	
Age, mean (SD), y	13.2 (2.4)
Sex, % female	43.8
Race	
White	90.6
African American	4.1
Hispanic	6.9
Asian	0.3
Multiracial	5.0
Highest parental education	
12th grade	2.8
Some college	13.2
College	37.6
Graduate school	46.4
Disease characteristics	
% In remission	82.9
Age at diagnosis, mean (SD), y	9.8 (3.0)
Therapy	
Historical therapy, %	
5-Aminosalicylates	63.4
Immunomodulators	74.6
Biologics	61.2
Corticosteroids	86.6
Surgery	16.7
Current therapy, %	
5-Aminosalicylates	27.9
Immunomodulators	47.1
Biologics	54.0
Corticosteroids	9.8
Disease-specific measures	
Disease-specific activity scores, mean (SD) SCDAI*	102 (71)
Health-related QoL scores, mean (SD) IMPACT-35†	131 (22)
Disease activity within the last 6 mo, mean (SD) Manitoba‡	4 (2)
PROMIS measures	
PROMIS T-scores, mean (SD)	
Anxiety	47 (11)
Depression	43 (8)
Fatigue	48 (12)
Pain interference	48 (11)
Peer relationships	49 (9)

*A 3-item questionnaire of Crohn's disease activity, score <150 indicates remission.
†A 35-item, self-administered questionnaire of health-related QoL in children with IBD, scores range 35 (poor) to 175 (best).
‡A 1-item questionnaire of IBD activity within the prior 6 months. A score of 4 indicates "occasional" activity.

PROMIS Results

Mean baseline PROMIS scores for this cohort are displayed in Table I. Compared with boys, girls reported clinically or statistically worse mean PROMIS scores in all domains but peer relationships. Older children (age 14-17 years), compared with younger children (age 9-13 years), reported clinically or statistically worse PROMIS scores in all domains except depression and pain interference (Table II). Those on current corticosteroid treatment reported clinically or statistically worse fatigue, pain interference, and peer relationships, but not anxiety or depression (Table II).

Associations with Disease Severity

Mean PROMIS scores for all domains were worse, indicating worse health or more dysfunction among patients with worse reported Crohn's disease activity, as measured by the SCDAI (Table III). Notable, those who reported the best Crohn's disease activity also reported mean PROMIS scores in all domains that were equivalent to or better than that of the reference population (Table III). For all PROMIS domains, there was both an overall statistically significant difference in mean PROMIS scores among the quartiles of disease activity ($F < 0.001$ for all ANOVA), as well as a significant trend of higher PROMIS scores across rank-ordered SCDAI quartiles ($z < 0.001$ for all NPTOT). Therefore, patients who reported worse Crohn's disease activity correspondingly reported worse anxiety, depression, fatigue, pain interference, and peer relationships. For all domains except peer relationships, the differences in PROMIS scores between any 2 disease activity quartiles represented clinically meaningful differences based on the proposed pediatric MID range of 2-3. These same statistically significant and clinically meaningful differences in scores for all PROMIS domains were maintained when patients were grouped by remission status, as determined by reported SCDAI score (Table IV; available at www.jpeds.com).

Analogous to the findings across SCDAI quartiles, PROMIS scores for all domains of health were worse among patients who reported more active disease in the prior 6 months, as measured by the Manitoba IBD Index (Table V; available at www.jpeds.com). For all domains, there was both an overall statistically significant difference in mean PROMIS scores among the 6 categories ($F \leq 0.01$ for all ANOVA), as well as a trend of higher PROMIS scores across rank-ordered Manitoba IBD Index categories ($z \leq 0.001$ for all NPTOT). The differences in PROMIS scores between any 2 Manitoba IBD Index categories, for all domains except peer relationships, represented clinically meaningful differences (Table V).

Despite potential differences in disease activity based on sex, age, age at diagnosis, time since diagnosis, and current steroid therapy (Table II), we did not find any independent effect of these patient characteristics on the relationship between PROMIS scores and disease activity using multinomial logistic regression and change-in-effect methods (data not shown).

Associations with Health-Related QoL

Mean PROMIS scores for all domains were worse among patients reporting worse pediatric health related QoL, as measured by the IMPACT-35 (Table VI; available at www.jpeds.com). For all domains, there was both an overall statistically significant difference in mean PROMIS scores

Table II. Relationship between patient characteristics and PROMIS T-scores

Patient characteristics	PROMIS scores				
	Anxiety (n = 276), mean (SD)	Depression (n = 276), mean (SD)	Fatigue (n = 276), mean (SD)	Pain interference (n = 276), mean (SD)	Peer relationships (n = 276), mean (SD)
Demographics					
Age					
9-13 y	46 (11)	43 (9)	47 (12)*	48 (12)	50 (9)*
14-17 y	48 (11)	44 (9)	50 (12)*	48 (11)	48 (8)*
Sex					
Male	45 (10)†	42 (8)	47 (11)	47 (11)*	49 (9)
Female	49 (12)†	45 (9)	49 (13)	50 (11)*	49 (9)
Highest parental education					
12th grade	45 (10)	44 (10)	53 (11)	54 (9)	51 (9)
Some college	48 (11)	46 (10)	53 (13)	52 (12)	48 (9)
College	47 (11)	43 (8)	48 (11)	50 (10)	49 (9)
Graduate school	48 (12)	44 (9)	48 (12)	48 (11)	50 (9)
Disease characteristics					
Crohn's disease status					
Remission	45 (11)†	42 (8)†	45 (11)†	45 (10)†	50 (9)*
Active	55 (11)†	50 (10)†	60 (11)†	59 (8)†	46 (9)*
Current therapy					
5-Aminosalicylates	46 (12)	42 (8)	45 (11)*	47 (12)	50 (9)
Immunomodulators	48 (12)	43 (9)	49 (12)	48 (11)	49 (8)
Biologics	46 (11)	43 (8)	48 (12)	48 (11)	49 (9)
Corticosteroids	48 (9)	43 (7)	51 (14)	53 (12)*	47 (10)

*Statistically significant difference between group means as determined by 1-way ANOVA, *P* value ≤.05.
†Statistically significant difference between group means as determined by 1-way ANOVA, *P* value ≤.001.

Table III. Relationship between Crohn's disease activity and PROMIS T-scores

	Quartile SCDAI*				ANOVA	Trend†
PROMIS	1	2	3	4	Prob >F	Prob >|z|
Anxiety	42	45	49	54	<0.001	<0.001
Depression	39	41	44	49	<0.001	<0.001
Fatigue	42	45	49	58	<0.001	<0.001
Pain interference	39	46	50	58	<0.001	<0.001
Peer relationships‡	51	49	49	46	0.005	<0.001

*Highest quartile indicates higher degree of disease activity.
†Nonparametric test of trend.
‡Higher score indicates better peer relationships.

between the quartiles ($F < 0.001$ for all ANOVA), as well as a trend of higher PROMIS scores across rank-ordered quartiles of QoL ($z < 0.001$ for NPTOT). As with the differences in PROMIS scores across SCDAI and Manitoba IBD Index groups, the differences in PROMIS scores between any 2 IMPACT-35 quartiles were not only statistically significant, but also represented clinically meaningful differences for all domains except peer relationships.

Longitudinal Evaluation of PROMIS Measures

Of the 143 patients who completed 6-month follow-up questionnaires, 11% reported worsened, 76% stable, and 13% improved Crohn's disease activity from baseline based on change in SCDAI score. The patients who reported improved Crohn's disease activity from baseline also reported meaningfully improved anxiety, depression, fatigue, pain interference, and peer relationships, with improvement in mean PROMIS scores ranging from 4-11 (**Figure** and **Table VII**; available at www.jpeds.com). Similarly, patients who reported worsened Crohn's disease activity from baseline also reported meaningfully worse PROMIS scores in all domains (**Figure** and **Table VII**). Patients with stable Crohn's disease activity reported little to no change in PROMIS scores as demonstrated by a change in PROMIS scores of 0-1 compared with baseline (**Figure** and **Table VII**). For all domains, the changes in PROMIS scores across groups of patients by change in disease activity were also statistically significant and linear (**Table VII**).

Discussion

In this study, we described a cross-sectional and longitudinal evaluation of PROMIS in a pediatric population with Crohn's disease. We found that mean PROMIS scores were significantly associated with Crohn's disease activity and health-related QoL, in a predictable, linear and clinically meaningful manner, thus, supporting the concurrent criterion validity of PROMIS in our study population. We also observed that patients with well-controlled Crohn's disease reported better PROMIS scores in the domains of psychological and physical functioning than the reference population, suggesting that with adequate disease control, children with Crohn's disease lead normal, healthy lives. In our exploratory longitudinal analyses, we found that changes in mean PROMIS scores were also significantly associated with change reported Crohn's disease activity over a 6-month period, in a predictable, linear and clinically meaningful manner, demonstrating the responsiveness of PROMIS in this cohort.

Although baseline scores for all PROMIS domains of health varied significantly and linearly across rank-ordered groups of Crohn's disease severity and health-related QoL, associations with peer relationships were less dramatic than for other domains. This pattern is consistent with our clinical experience, as well as PROMIS pediatric studies in other chronic disease settings where peer relationships are less affected by disease severity than other domains.[7,14,30] Although incremental changes in Crohn's disease activity and health-related QoL are associated with differences in patient-reported anxiety, depression, fatigue, and pain interference, peer relationships tend to remain intact except in those whose Crohn's disease is very active or QoL very impaired.

Measuring QoL, physical function, psychological, and social health in a valid, reliable, and patient-centered way is centrally important to understanding chronic disease in children and improving their care. When adolescents with IBD and their physicians have been surveyed about what factors most affect their QoL, there was almost no correlation between adolescent and physician reports.[31] Given these disparate viewpoints, it is unlikely that physicians and researchers can capture what is important to patients regarding QoL and disease control without high-quality PROs. If appropriately captured, PROs of depression and other health domains have been shown to independently predict chronic disease activity, including in IBD.[32] In addition, PROs can also help identify barriers to remission and treatment adherence. In IBD, for example, the subset of patients who continue to have impaired health-related QoL despite documented mucosal healing are those with significantly more fatigue, anxiety, and depression.[33] In addition, those patients with IBD with elevated anxiety and depressive symptoms have significantly lower treatment adherence.[34] Interventions for anxiety or depressive symptoms are known to be as effective in patients with chronic disease, including IBD, as in the general population, yet remain underused.[35-37]

We sought to validate PROMIS instruments in a pediatric population with Crohn's disease by surveying patients in our CCFA Kids and Teens cohort, a large, geographically diverse study population, which allowed for longitudinal assessments of PROMIS instruments. The fact that our cohort is a volunteer, internet-based cohort, potentially limits its generalizability. In another internet-based cohort of patients with psoriasis, participants reported that their disease was less of a burden, despite being more extensive, and were significantly better informed regarding psoriasis therapies compared with nonparticipants.[38] Therefore, we may suspect that our population is better informed and less likely to consider their disease a burden than the general population with Crohn's disease. Another potential limitation of our study is that a patient's Crohn's disease status was identified by self-report, rather than review of medical records.

However, in our validation study of the adult CCFA Partners cohort, self-reported IBD status was confirmed by medical records in 96% of participants, suggesting that patients who are involved in the CCFA are reliable reporters of their diagnoses. In order to minimize respondent burden and improve retention in the Kids and Teens Study cohort, we did not assess comorbid diagnoses of anxiety, depression, or other mental health disorders and did not collect data on non-IBD medication use. However, such data are not needed to assess criterion validity and explore longitudinal responsiveness of PROMIS. Another potential limitation of our study is a feature of PROMIS pediatric instruments themselves. Unlike PROMIS adult instruments, which are standardized to a general population, PROMIS pediatric T-scores are currently standardized to a population that includes a higher proportion of children with chronic disease.[39] Although this did not affect our conclusions, it did not allow us to compare our study cohort with the general population.

This study supports the criterion validity and responsiveness of child-reported PROMIS instruments in Crohn's disease, adding to our understanding of how PROMIS functions in a pediatric population with a relapsing chronic disease. With this basis, important patient-centered research can proceed, including studies of how incorporating PROMIS in the clinical care of children with chronic diseases effects the recognition and treatment of psychological, social, and functional burdens of chronic disease, and ultimately, patient well-being. ■

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50 Years Ago in *The Journal of Pediatrics*

Ipecac Syrup: Its Use as an Emetic in Poison Control

Shirkey HC. J Pediatr 1966;69:139-41

Ipecac is derived from *Carapichea ipecacuanha* and comprises 2 active ingredients: emetine and cephaeline. These 2 alkaloids induce vomiting via peripheral and central stimuli. In 1965, the Food and Drug Administration approved ipecac syrup for over-the-counter sale as an emesis inducer drug in poisoning cases.

Fifty years ago, Shirkey described ipecac syrup as the emetic of choice because it was readily available at home and easily administered by parents, with emesis produced in a prompt way after its ingestion. It was established as an effective intervention in 97% of the cases, with recovery of 84%-100% of gastric material.

The recommended initial dose was 15 mL. If no emesis was present after 20 minutes, a second and last equal dose was given. Warnings about its use were stated in the labeling from the first time it was released, including the following: no use in patients who were unconscious or had ingested either corrosives or petroleum distillates.

The author concluded that the proper use of ipecac syrup could produce fewer tragedies from poisonings. During that year, several community programs, physicians, and the media encouraged home availability of the drug.

In 1985, the use of ipecac peaked, and the Academy recommended that its use should be discussed with parents and provided at the 6-month visit. However, several later studies demonstrated no benefit from the administration of the syrup compared with other interventions. They found ipecac could delay the administration or reduce the effectiveness of activated charcoal, oral antidotes, and whole bowel irrigation, which are considered better approaches to poisoning cases. Also, experimental studies showed that with ipecac, the amount of gastric content removed and the amount of poison absorbed by the patient were highly variable.

From 1986 to 1996, 3 million patients received the drug, with potential complications documented but rare serious sequelae reported; thus, it was considered to be a medicine with a high margin of safety but low effectiveness. Hence, in 1997, the American Academy of Clinical Toxicology and the European Association of Poisons Centers and Clinical Toxicologists counseled against routine use of ipecac syrup in the management of patients who were poisoned. By 2001, the drug was used in 0.7% of exposures, compared with 15% in 1985. Today, it is no longer produced or even recommended in the management of poisonings.

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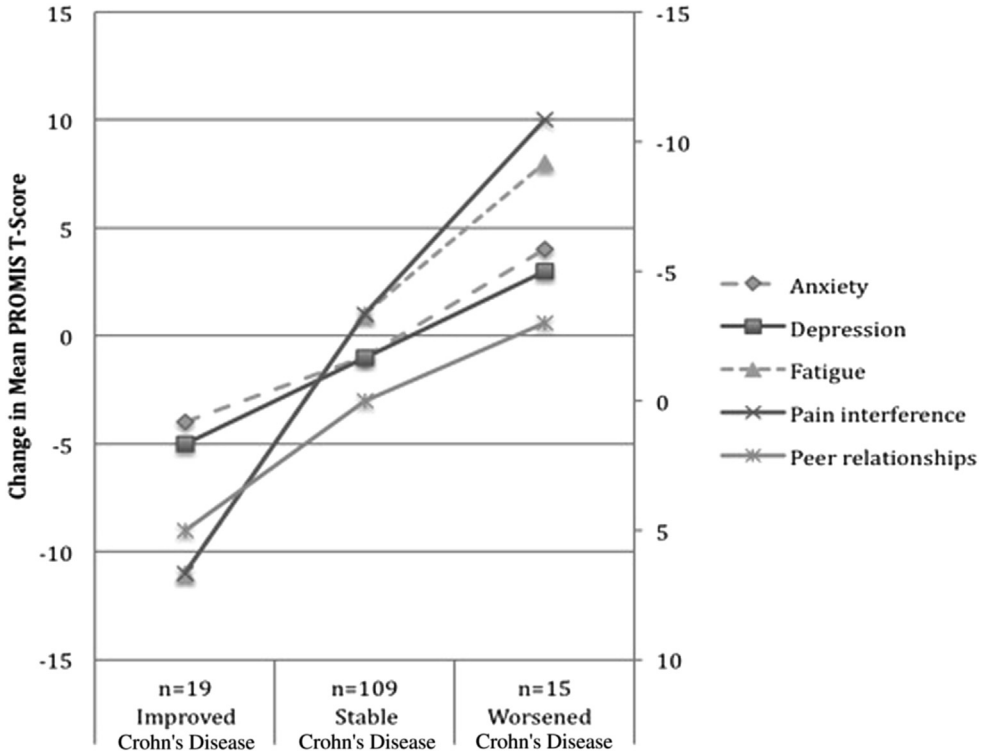

Figure. "Improved" patients reported a 70-point improvement in SCDAI score from baseline to time of 6-month follow-up. "Worsened" patients reported a 70-point worsening in SCDAI score from baseline. Higher T-score indicates worse anxiety, depression, fatigue, pain interference, and better peer relationships. Secondary/right-sided axis for peer relationships scores only.

Table IV. Relationship between remission status and PROMIS T-scores

	Remission status*		
PROMIS	Remission (n = 218)	Active (n = 45)	*P* value
Anxiety	45 (11)	55 (11)	<.001
Depression	42 (8)	50 (10)	<.001
Fatigue	45 (10)	60 (11)	<.001
Pain interference	45 (8)	59 (8)	<.001
Peer relationships†	50 (8)	46 (9)	.02

*Remission status determined by SCDAI score <150.
†Higher score indicates better peer relationships.

Table V. Relationship between Crohn's disease activity within the last 6 months and PROMIS T-scores

	Manitoba IBD index score*						ANOVA	Trend†
PROMIS	1	2	3	4	5	6	Prob >F	Prob >|z|
Anxiety	54	53	49	47	44	41	<0.001	<0.001
Depression	49	47	46	42	41	39	0.01	<0.001
Fatigue	57	55	51	46	45	41	<0.001	<0.001
Pain interference	59	55	51	49	42	40	<0.001	<0.001
Peer relationships‡	46	47	48	48	49	53	0.001	<0.001

*Patient-reported disease activity within the last 6 mo:
1 = constantly.
2 = often.
3 = sometimes.
4 = occasional.
5 = rarely.
6 = inactive.
†Nonparametric test of trend.
‡Higher score indicates better peer relationships.

Table VI. Relationship between health-related QoL and PROMIS T-scores

	Quartile IMPACT-35*				ANOVA	Trend†
PROMIS	1	2	3	4	Prob >F	Prob >|z|
Anxiety	58	49	42	39	<0.001	<0.001
Depression	52	44	39	37	<0.001	<0.001
Fatigue	60	51	45	38	<0.001	<0.001
Pain interference	59	51	43	40	<0.001	<0.001
Peer relationships‡	46	46	50	54	<0.001	<0.001

*Increasing quartile indicates better health-related QoL.
†Nonparametric test of trend.
‡Higher score indicates better peer relationships.

Table VII. Relationship between change in Crohn's disease activity and PROMIS T-scores

	Change in mean PROMIS score at 6-mo follow-up (SD)			ANOVA	Trend†
Change in Crohn's disease activity*	Improved, n = 19	Stable, n = 109	Worsened, n = 15	Prob >F	Prob >|z|
Anxiety	−4 (8)	−1 (9)	4 (10)	0.04	0.04
Depression	−5 (8)	−1 (7)	3 (10)	0.01	0.01
Fatigue	−11 (14)	1 (8)	8 (13)	<0.001	<0.001
Pain interference	−11 (13)	1 (9)	10 (12)	<0.001	<0.001
Peer relationships‡	5 (9)	0 (8)	−3 (7)	0.01	0.001

*A 70-point change in SCDAI score from baseline to time of 6-mo follow-up.
†Nonparametric test of trend.
‡Higher score indicates better peer relationships.