View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by Carolina Digital Repository

HHS Public Access

Author manuscript

Am J Gastroenterol. Author manuscript; available in PMC 2020 April 01.

Published in final edited form as:

Am J Gastroenterol. 2019 April ; 114(4): 640–647. doi:10.14309/ajg.0000000000000177.

A Novel Patient-Reported Outcome Based Evaluation (PROBE) of Quality of Life in Patients with Inflammatory Bowel Disease

Edward L. Barnes, MD, MPH[1,2], **Michael D. Kappelman, MD, MPH**[2,3,4], **Millie D. Long, MD, MPH**[1,2,3], **Donna M. Evon, PhD**[1,3], **Christopher F. Martin, MSPH**[1,3], and **Robert S. Sandler, MD, MPH**[1,3]

[1]Division of Gastroenterology and Hepatology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

[2]Multidisciplinary Center for Inflammatory Bowel Diseases, University of North Carolina at Chapel Hill, Chapel Hill, NC

[3]Center for Gastrointestinal Biology and Disease, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

[4]Division of Pediatric Gastroenterology and Hepatology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

Abstract

Objectives: There is increased interest in measuring patient reported outcomes (PROs) such as quality of life (QoL) among patients with inflammatory bowel disease (IBD). We aimed to create and validate a new measure of QoL to assess the psychosocial burden of IBD, using publicly available assessment tools.

Methods: Using the Crohn's & Colitis Foundation's IBD Partners cohort, we performed several cross-sectional and longitudinal analyses to create a new PRO-based evaluation (PROBE) of QoL among patients with Crohn's disease (CD) and ulcerative colitis (UC). We used factor analysis and Pearson correlation testing to identify candidate questions for inclusion, Wilcoxon rank sum testing to examine responsiveness of the PROBE to changes in disease activity, and test-retest reliability assessments in patients with stable disease activity. We also compared the PROBE to the Short Inflammatory Bowel Disease Questionnaire to assess construct validity.

Results: A total of 4,854 patients (64% CD, 36% UC) completed surveys with 6 items included in the final PROBE. Compared to baseline, there was a significant decrease in PROBE scores at follow-up among patients who experienced a flare for UC (25.0 vs. 22.2, p=0.001) and CD (23.1

Corresponding Author: Edward L. Barnes, MD, MPH, Division of Gastroenterology and Hepatology, University of North Carolina at Chapel Hill, 130 Mason Farm Road, Bioinformatics Building, CB #7080, Chapel Hill, NC 27599-7080, Phone: 919-962-3112, Fax: 919-966-1036, edward_barnes@med.unc.edu.

Specific Author Contributions: ELB was involved in involved in the study concept and design, acquisition of the data, analysis and interpretation of the data, and drafting and critical revision of the manuscript. MDK, MDL, DME, CFM, and RSS were involved in study concept and design, acquisition of the data, analysis and interpretation of the data, and critical revision of the manuscript. All authors reviewed and approved the final draft of the manuscript submitted.

Potential Competing Interests:

ELB, DME, MDK, MDL, CFM, RSS: Each of these authors report no disclosures or conflicts of interest relevant to this study.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

vs. 21.0, p<0.001). Among patients with stable disease activity, Cronbach's alpha was 0.87 in CD and 0.82 in UC. The PROBE correlated well with the SIBDQ in CD (r=0.88) and UC (r=0.86).

Conclusions: We created a novel assessment of QoL in IBD using publicly available survey items. This new PROBE can be utilized to facilitate clinical care, clinical and epidemiological research, and quality improvement.

Keywords

IBD Partners; Crohn's disease; ulcerative colitis; PROBE

INTRODUCTION

In the past, research studies in inflammatory bowel disease (IBD) focused on clinical outcomes such as surgery, hospitalizations, death, and other objective adverse events. More recently, however, patient-reported outcomes (PROs) such as quality of life (QoL) have gained attention. Unfortunately, validated QoL measures for use in patients with IBD are limited.

Since its development and publication in 1996, the Short Inflammatory Bowel Disease Questionnaire (SIBDQ)[1] has been one of the most widely utilized measures to assess QoL among patients with IBD. Although the SIBDQ is a validated measure for assessing QoL among patients with IBD, it is a proprietary measure, with associated license fees of up to $2,000 required for research and clinical assessment (licensed from McMaster University, Hamilton, Ontario). In recent years, a number of non-disease specific PRO assessment tools, such as the National Institutes of Health Patient-Reported Outcomes Measurement Information System (PROMIS)[2–4] have been developed to assess physical and psychosocial functioning in the general population, and growing literature suggests their relevance to patients with IBD.[5,6] While each of these domains has the potential to significantly impact individual factors associated with QoL in IBD, a combined assessment has the advantage of evaluating overall QoL, including psychological and physiological factors, which has been identified as a critical goal for the assessment of QoL in patients with IBD.[7] Additionally, a combined endpoint offers the opportunity for longitudinal assessment and the potential to monitor for changes in QoL over time.

Understanding the association between QoL and clinical outcomes among patients with IBD is critical. Overall QoL has been reported to be generally poorer among patients with IBD compared to the general population.[7,8] As new medical therapies are developed for IBD, or as existing therapies are compared, it will be critical to use reliable and validated QoL measures that are responsive to change and differences in disease activity.

In this study, we aimed to create and validate a free, minimally burdensome measure of QoL in patients with IBD. We used survey data from the Crohn's and Colitis Foundation's IBD Partners internet cohort to create a new instrument, the PRO-based evaluation ("PROBE") using publicly available PRO measures. We also evaluated the content and construct validity of this new instrument, as well as test-retest reliability and responsiveness to changes in disease activity over time among cohort participants.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

METHODS

Overall Study Design

Within a large internet-based cohort of patients with IBD, we performed several cross-sectional and longitudinal analyses to evaluate potential candidate variables for inclusion in the PROBE. Candidate items were selected from PROMIS items and other PROs utilized in the IBD Partners cohort. Following the identification of candidate items, disease specific activity indices were utilized to evaluate the responsiveness of the PROBE to changes in disease activity over time.

Study Population

IBD Partners is a longitudinal internet-based cohort of patients with self-reported UC or CD. The study cohort has previously been described in detail.[9–11] Briefly, patients age 18 and older, with self-reported IBD were recruited to the IBD Partners cohort registry via social media and email invitations, as well as direct recruitment through Crohn's and Colitis Foundation educational and fundraising events. Participants complete baseline and follow-up surveys (offered at 6 month intervals), including core questions with information on disease phenotype, activity, medication use, and PROs.

Potential Variables for Patient-Reported Outcome Based Evaluation (PROBE)

Participants completed four items from five of the PROMIS item banks assessing individual domains of QoL (anxiety, depression, fatigue, satisfaction with the social role, and pain interference) that reflect three domains of the SIBDQ (emotional, social, and systemic). The full item banks are available in Supplementary Table 1. The construct validity of each of these measures has previously been validated within the IBD Partners population.[12] Each of the questions eligible for inclusion in the PROBE had response options based on a five-point Likert scale (ranges: Never to Always, Not at all to Very much). Rather than including all items from each individual PROMIS domain, we selected single questions to minimize respondent burden. In addition, to capture the fourth domain of the SIBDQ (bowel symptoms) we included a patient-reported measure of disease activity over the past week.

Other Variables

The licensed SIBDQ was also administered to all participants as a disease-specific legacy measure of health-related QoL. We used validated measures of self-reported disease activity, with clinical remission defined as a short Crohn's Disease Activity Index (sCDAI)[13] ≤ 150 for subjects with CD or Simple Clinical Colitis Activity Index (SCCAI)[14] ≤ 2 for subjects with UC. Patient demographics, medication use, phenotype as defined by Montreal Classification, and surgical history were also assessed by patient self-report. Patients with a history of an ostomy or ileal pouch-anal anastomosis were excluded from this analysis given that activity indices based on the number or frequency of bowel movements are not applicable in these subgroups.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Statistical Analysis

Baseline Characteristics, Factor Analysis, and Pearson Correlation Testing:

Descriptive statistics were utilized to assess the baseline demographics and disease characteristics of the study population. We then performed factor analysis to evaluate the relationship between each item within the five potential PROMIS item banks and a respective QoL domain. Given the existing relationship between individual PROMIS domains and QoL in the IBD Partners cohort,[12] confirmatory factor analysis was utilized to test our hypothesis that each question in a particular PROMIS item bank would demonstrate a high loading. Under this hypothesis, if all questions in a PROMIS item bank demonstrated high loading, and subsequently demonstrated high correlation coefficients, the highest loading question could be selected for inclusion in the PROBE. Confirmatory factor analysis was performed among all participants to ensure maximal sample size, allowing for the greatest assessment of both model fit and identification of appropriate domains for inclusion in the PROBE.

Model fit was evaluated using the PROC CALIS procedure, utilizing covariance structure analysis and the maximum-likelihood estimation method. We used five indices to determine model fit: the chi-square statistic, the Root Mean Square Error of Approximation (RMSEA), the Comparative Fit Index (CFI), the Bentler and Bonnett's non-normed index (NNI), and normed fit index (NFI). In these analyses, a non-significant chi-square close to zero indicates that there is little difference between the observed and expected covariances matrices.[15] However, the chi-square value can be affected by sample size, and thus a large chi-square and a significant p-value does not necessarily suggest poor fit.[16] RMSEA and CFI values range from 0 to 1, with a RMSEA value of 0.06 or less indicating acceptable model fit.[15] In contrast, a NNI, NFI, or CFI value of 0.90 or greater indicates acceptable model fit.[15]

Following the factor analysis, we performed Pearson correlation testing to demonstrate that each of the questions within a PROMIS domain was inter-correlated with the other three questions in a domain. These correlations were performed to ensure that no outliers were present among the individual questions, and ultimately to allow for the selection of a single question per domain for the PROBE.

Assessment of the PROBE:

After selection of the six items for the PROBE, Wilcoxon rank sum testing was used to compare scores on the PROBE at the initial assessment and then on an assessment six months later among patients with CD and UC to examine test-retest reliability (among patients with stable disease activity) and responsiveness to changes in disease activity over time (among patients with changes in disease activity). Analyses were grouped by disease subtype and by disease activity: patients with the same disease activity at both assessments, patients in remission at baseline who experienced a flare, and patients who were in a flare at baseline who went into remission prior to the follow-up assessment. For comparison, the SIBDQ was assessed in the same manner. Using Pearson correlation, the PROBE was also compared to the SIBDQ among all patients with IBD, and separately among patients with CD or UC. Among patients with stable disease activity (the same disease state at both assessments), the test-retest reliability of the PROBE measure was assessed using the test-retest reliability coefficient and Cronbach's alpha coefficient.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

In a series of analyses, the PROBE was compared to individual disease activity indices including the sCDAI and the SCCAI using Pearson correlation testing. Patients were then stratified by the severity of flare of disease, using previously published thresholds for the sCDAI[17] and the SCCAI,[18] with PROBE scores compared by category of disease activity. Additionally, we performed a secondary analysis of PROBE scores stratifying by steroid use at baseline and in follow-up. All statistical analyses were performed using SAS (version 8.4, SAS Institute, Cary, NC, USA). The study protocol was approved by the Institutional Review Board at the University of North Carolina at Chapel Hill.

RESULTS

Between February 1, 2012 and June 31, 2016, 4,854 patients with IBD (64% CD, 36% UC) completed initial and follow-up surveys that included candidate items to include in the new PROBE. The mean age of participants at the time of initial survey completion was 44.2 years [standard deviation (SD), 15.2 years, range 18–91], with a mean time since IBD diagnosis of 13.6 years (SD 12.4 years). The majority of participants were female, with 73% of participants with CD and 70% of UC participants reporting female sex (Table 1). At the time of initial evaluation, 66% of participants with CD and 47% of participants with UC were in clinical remission. The median time between completed surveys was 183 days [interquartile range (IQR) 170–201].

When factor analysis was performed analyzing questions in the five PROMIS domains, high loadings were demonstrated in each of the five factors (Table 2). The model demonstrated an acceptable fit to the data, with four of the five pre-stated indices of model fit being fulfilled: chi-square 14,296.5, $p<0.001$; RMSEA: 0.053; CFI: 0.981, NFI: 0.981, NNI: 0.977. Pearson correlations were then performed to analyze the relationship between individual items within each PRO domain. In each of the domains, items were highly correlated, as demonstrated by the following Pearson's coefficients: anxiety (0.636 – 0.718), depression (0.740 – 0.829), fatigue (0.813 – 0 .934), satisfaction with social role (0.756 – 0.860), pain interference (0.884 – 0.932). Given these correlations, the item with the highest loadings from each domain was selected for inclusion in the final PROBE along with the pre-specified patient-reported activity assessment, yielding a six-item measure (Table 3).

Among patients with CD, the PROBE demonstrated a correlation coefficient of 0.88 with the SIBDQ (Figure 1). Among patients with UC, the PROBE demonstrated a Pearson's coefficient of 0.86 with the SIBDQ. When patients were subdivided by disease activity at baseline, these correlations remained high: CD patients in remission (r=0.80), CD patients in a flare (r=0.80), UC patients in remission (r=0.77), and UC patients in a flare (r=0.80).

For all patients assessed, the range of the PROBE values was 6–30, with high scores reflecting higher QoL. The median PROBE value was 24 (IQR 19–27) among patients with CD at the first assessment and 25 (IQR 21–27) among patients with UC at the first assessment (Table 4). When evaluating for ceiling effects, 4% of all respondents scored at the upper extreme, suggesting that the PROBE performed well capturing high QoL. Similarly, only 0.2% of respondents scored at the lowest extreme, indicating negligible floor effects.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

When assessed by Pearson correlation, The PROBE demonstrated a negative correlation with both the sCDAI (−0.77) and the SCCAI (−0.68) indicating a decrease in QoL as the individual disease activity index score increased (Supplementary Figures 1a and 1b). Additionally, when the sCDAI was stratified by severity of flare, significant differences were noted in the median PROBE scores when comparing participants in remission (median 26, IQR 23–28), mild (median 20, IQR 18–23), moderate (median 16, IQR 14–19), and severe flares (median 12, IQR 10–16, $p<0.001$, Supplementary Figure 2a). Similarly, when the SCCAI was stratified by severity of flare, significant differences were noted in the median PROBE scores when comparing participants in remission (median 27, IQR 25–29), mild (median 23, IQR 19–25), moderate (median 18.5, IQR 16–22), and severe flares (median 12, IQR 8–13, $p<0.001$, Supplementary Figure 2b).

Among patients with CD in remission at the first assessment who went on to experience a flare at the time of the second assessment, the mean PROBE value decreased by 2.1 points, (23.1 vs. 21.0, $p<0.001$, Figure 2a). Similarly among patients with UC in remission at baseline who went on to experience a flare, the mean PROBE value decreased by 2.8 points (25.0 vs. 22.2, $p=0.001$, Figure 2b). In patients with CD demonstrating the same disease activity at both assessments, 51% of patients in remission and 56% of patients in a flare at both assessments demonstrated PROBE values that changed by no more than 2 points between baseline and follow-up assessments. Among patients with UC, 51% of patients in remission at both assessments and 53% of patients in a flare demonstrated PROBE values that changed by no more than 2 points between assessments.

In assessing the test-retest reliability of the PROBE among patients with CD with stable disease activity, the test-retest reliability coefficient was 0.78 and the Cronbach's alpha was 0.87. Among patients with UC, the test-retest reliability coefficient was 0.69 and the Cronbach's alpha was 0.82.

In a secondary analysis, PROBE scores were analyzed by steroid use at baseline and follow-up (Supplementary Table 2). The highest PROBE scores were noted among patients that never used steroids [baseline mean 23.4 in CD, standard deviation (SD) 4.8 and baseline mean 24.1 in UC (SD 4.4)]. Patients with CD that were on steroids at baseline and then discontinued steroids prior to follow-up demonstrated an increase in the mean PROBE score of 2.5 points (20.1 vs. 21.6, $p<0.001$) while patients that were initiated on steroids between the baseline survey and follow-up demonstrated a decrease in the mean PROBE value (20.9 vs. 19.9, $p<0.001$). Similar trends were noted among patients with UC, although the decrease in PROBE score among 72 patients with UC who initiated steroids after the baseline evaluation was not statistically significant (23.2 vs. 20.7, $p=0.255$).

DISCUSSION

We developed and evaluated the psychometric properties of a novel, brief, license-free, and potentially clinically useful instrument to measure QoL in patients with IBD. The PROBE was constructed using publicly available items from existing PRO item banks and was evaluated in a national cohort of over 4,000 patients with IBD in multiple disease activity states. This new QOL measure for patients with IBD demonstrated responsiveness to change

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

in disease status among patients with CD and UC, and demonstrated high test-retest reliability in those with stable disease states. When compared to the widely used legacy IBD QoL measure, the SIBDQ, the PROBE demonstrated excellent construct validity in both CD and UC patients. These findings suggest that the PROBE performs well as a new measure of QoL among patients with IBD, and offers several advantages including minimal patient burden and non-proprietary, no-cost access, for use in clinical care and IBD research.

QoL in IBD can differ significantly among patients who are experiencing a flare of disease compared to periods of remission. In a recent systematic review and meta-analysis, Knowles et al. demonstrated that patients with active IBD were more likely to have poor QoL as compared to patients with inactive IBD.[7] In our analyses, the PROBE demonstrated strong responsiveness to changes in disease activity among patients with CD and UC, in addition to strong test-retest reliability among patients with stable disease states. In designing the PROBE, our purpose was to develop a QoL instrument that could be used in patients with CD and UC. While the instrument might have utility in patients with other inflammatory disorders, it was only tested in patients with IBD.

Among patients that demonstrated the same disease state at both assessments, over 50% of patients were found to have a stable PROBE score, with a change of no more than 2 between assessments. While the decreases in the PROBE of 2.1 in patients with CD who experienced a flare and 2.8 in patients with UC likely represent tentative cutoffs for determining clinically meaningful changes, these will need to be further evaluated. The establishment of minimally important differences and threshold values for the PROBE in the assessment of optimal QoL in patients with IBD remain important future directions for the evaluation of this measure.

In recent years there has been an increased recognition of the importance of PROs in the assessment of patients with GI disorders, particularly IBD.[5,6,12,19–21] PROs have been identified as critical measures in the evaluation of patients with IBD given that they can assess specific concerns and patient preferences at the individual level, as well as trends in comparative health and disease at the population level.[20] The National Institutes of Health developed the PROMIS initiative to provide PRO measurement tools as a dynamic resource for both clinical and research application.[22] Although we did not use full PROMIS measures in the creation of the PROBE, the inclusion of previously validated PRO item banks provided several advantages for assessing QoL in a large group of patients with IBD. For example, grouping by multiple factors affecting QoL among patients with IBD, the PROBE could be compared to the full SIBDQ. Moreover, collecting items that had been specifically designed to convey significant information about QoL with minimal patient burden offered another unique advantage.

In addition to creating a measure based on publicly available questions that could be used by other researchers and practitioners, we utilized the minimal number of potential questions to decrease the burden of survey completion by patients. The use of confirmatory factor analysis and Pearson correlation in the evaluation of candidate variables allowed for the selection of those variables with the highest apparent connection to QoL domains in our population. However, a significant limitation of our study is that we did not use focus groups

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

or direct patient interviews to identify the domains or factors of QoL that were most important to patients with IBD. While we created a disease-specific measure of QoL and attempted to use domains that were similar to those that have been validated with the SIBDQ, we did not have the opportunity to directly assess which QoL factors patients with IBD weigh most heavily prior the creation of the PROBE.

The domains examined in the PROBE are focused on factors known to significantly impact QoL among patients with IBD. In addition to a patient-reported evaluation of disease activity over the past week, the five other domains in this novel measure directly assess psychosocial factors that have previously been linked to QoL and outcomes among patients with CD and UC. Among patients with IBD, anxiety and depression have previously been demonstrated as important determinants of health-related QoL.[23,24] Multiple PROMIS domains have been evaluated within the IBD Partners population[12] and externally in ambulatory clinic settings.[5] In these evaluations, patients with both CD and UC demonstrate significant impairments in multiple domains, including anxiety, depression, satisfaction with social role, and pain interference.[5,12] In a large study of patients associated with the French national IBD charity, approximately one half of patients reported poor QoL along with severe fatigue and/or depression.[21]

The PROBE was developed within IBD Partners using existing patient-reported domains and further assessment of the validity of the PROBE in external populations would be helpful to establish the PROBE as a QoL assessment. In future studies, we plan to validate the PROBE within a multidisciplinary IBD clinic where more granular clinical data is available, and perform subanalyses of the PROBE in multiple phenotypes. Perhaps most important will be incorporating patient feedback on the most critical components of QoL as assessed by the PROBE to further tailor the thresholds suggested in the initial creation. Other specialties have incorporated QoL assessments including the PROMIS measures via the electronic medical record.[25,26] Given the increased recognition of psychological factors on the disease course of patients with IBD, integrating QoL measures such as the PROBE into the workflow of a multidisciplinary IBD center may allow for standardized longitudinal assessments of QoL and the recognition of patients who are at risk for worse outcomes.

QoL is a self-reported measure that is influenced by disease activity, and while these are two separate constructs, these represent parallel targets for the multidisciplinary care of patients with IBD. We expect that during a flare of disease, patients would report worse QoL. Indeed, a lack of correlation between QoL and patient-reported disease activity would cast doubt on the face validity of the PROBE. In order to assess this validity, we simply dichotomized patient-reported episodes of flare using pre-determined thresholds, however our exploratory analyses correlating the PROBE with the sCDAI and SCCAI respectively also demonstrated negative correlations. Additionally, disease activity can be influenced by other patient-related factors including depression, anxiety, and social support.[27,28]

Our study has multiple strengths, including the large sample size available for analysis through the IBD Partners cohort and the ability to assess disease activity at multiple time points. However, our study has limitations as well. Although the IBD Partners cohort represents a large population of patients with CD or UC, disease diagnoses were self-

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

reported. Prior studies within IBD Partners have validated multiple factors, including subtype of IBD, disease status, and history of IBD-related surgery,[10] however this remains an internet-based cohort with no validation using medical record data. Although we do not have access to endoscopic or laboratory data in the IBD Partners population, QoL in IBD may not be universally related directly to endoscopic activity or other clinical markers.[29] Additionally, the demographics of the study population are not representative of all patients with IBD. A longer follow-up may be necessary to track QoL changes over longer disease durations and changes in therapy, postoperative changes, and disease progression. Our findings with regards to steroid use and QoL require further study, as steroid use may independently affect QoL in patients with IBD, or may serve as a proxy for increased disease activity.

In conclusion, we have created a novel patient-reported measure for the assessment of QoL among patients with IBD, using survey items that are publicly available to all researchers and clinicians. The PROBE was designed to have minimal patient burden, and can likely be completed by most patients without clinician assistance. This QoL measure demonstrates responsiveness to changes in disease state and high test-retest reliability. In contrast to legacy assessments of QoL in IBD such as the SIBDQ, the PROBE has no associated cost burden to limit implementation in clinical practice or research. The new PROBE instrument can be utilized to assess QoL and important symptoms among patients with UC and CD, thereby facilitating clinical care, quality improvement, and clinical and outcomes research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Grant Support: This work was supported by a grant from the National Institutes of Health (P30DK034987). This work was also supported by the Patient Centered Outcomes Research Institute and the Crohn’s & Colitis Foundation (MDK, RSS).

REFERENCES

1. Irvine EJ, Zhou Q, Thompson AK. The Short Inflammatory Bowel Disease Questionnaire: a quality of life instrument for community physicians managing inflammatory bowel disease. CCRPT Investigators. Canadian Crohn’s Relapse Prevention Trial. Am J Gastroenterol 1996;91:1571–1578. [PubMed: 8759664]
2. Cella D, Yount S, Rothrock N, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH Roadmap cooperative group during its first two years. Med Care 2007;45:S3–S11.
3. Cella D, Riley W, Stone A, et al. The patient-reported outcomes measurement information system (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005–2008. J Clin Epidemiol 2010;63:1179–1194. [PubMed: 20685078]
4. Cook KF, Jensen SE, Schalet BD, et al. PROMIS measures of pain, fatigue, negative affect, physical function, and social function demonstrated clinical validity across a range of chronic conditions. J Clin Epidemiol 2016;73:89–102. [PubMed: 26952842]
5. Ishak WW, Pan D, Steiner AJ, et al. Patient-Reported Outcomes of Quality of Life, Functioning, and GI/Psychiatric Symptom Severity in Patients with Inflammatory Bowel Disease (IBD). Inflamm Bowel Dis 2017;23:798–803. [PubMed: 28301432]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

6. Kochar B, Martin CF, Kappelman MD, et al. Evaluation of Gastrointestinal Patient Reported Outcomes Measurement Information System (GI-PROMIS) Symptom Scales in Subjects With Inflammatory Bowel Diseases. Am J Gastroenterol 2018;113:72–79. [PubMed: 28853727]
7. Knowles SR, Graff LA, Wilding H, et al. Quality of Life in Inflammatory Bowel Disease: A Systematic Review and Meta-analyses—Part II. Inflamm Bowel Dis 2018;24:966–976. [PubMed: 29688466]
8. Knowles SR, Graff LA, Wilding H, et al. Quality of Life in Inflammatory Bowel Disease: A Systematic Review and Meta-analyses—Part I. Inflamm Bowel Dis 2018;24:742–751. [PubMed: 29562277]
9. Long MD, Kappelman MD, Martin CF, et al. Development of an internet-based cohort of patients with inflammatory bowel diseases (CCFA Partners): Methodology and initial results. Inflamm Bowel Dis 2012;18:2099–2106. [PubMed: 22287300]
10. Randell RL, Long MD, Cook SF, et al. Validation of an internet-based cohort of inflammatory bowel disease (CCFA partners). Inflamm Bowel Dis 2014;20:541–544. [PubMed: 24451221]
11. Brotherton CS, Martin CA, Long MD, et al. Avoidance of Fiber is Associated with Greater Risk of Crohn's Disease Flare in a 6 Month Period. Clin Gastroenterol Hepatol 2015;14:1–7.
12. Kappelman MD, Long MD, Martin C, et al. Evaluation of the Patient-Reported Outcomes Measurement Information System in a Large Cohort of Patients With Inflammatory Bowel Diseases. Clin Gastroenterol Hepatol 2014;12:1315–1323.e2. [PubMed: 24183956]
13. Thia K, Faubion W a., Loftus EV, et al. Short CDAI: Development and validation of a shortened and simplified Crohn's disease activity index. Inflamm Bowel Dis 2011;17:105–111. [PubMed: 20629100]
14. Walmsley RS, Ayres RC, Pounder RE, et al. A simple clinical colitis activity index. Gut 1998;43:29–32. [PubMed: 9771402]
15. Hu L, Bentler P. Cutoff criteria for fit indexes in covariance structure analysis: conventional criteria versus new alternatives. Struct Equ Model 1999;6:1–55.
16. Bentler P, Bonnett D. Significance tests and goodness-of-fit in the analysis of covariance structures. Psychol Bull 1980;88:588–606.
17. Peyrin-biroulet L, Panés J, Sandborn WJ, et al. Defining Disease Severity in Inflammatory Bowel Diseases: Current and Future Directions. Clin Gastroenterol Hepatol 2016;14:348–354.e17. [PubMed: 26071941]
18. Walsh AJ, Ghosh A, Brain AO, et al. Comparing disease activity indices in ulcerative colitis. J Crohn's Colitis 2014;8:318–325. [PubMed: 24120021]
19. Williet N, Sandborn WJ, Peyrin-Biroulet L. Patient-reported Outcomes as Primary Endpoints in Clinical Trials of Inflammatory Bowel Disease. Clin Gastroenterol Hepatol 2014;12:1246–1256.e6. [PubMed: 24534550]
20. Cohen ER, Melmed GY. Making a Case for Patient-Reported Outcomes in Clinical Inflammatory Bowel Disease Practice. Clin Gastroenterol Hepatol 2018;16:603–607. [PubMed: 29678238]
21. Williet N, Sarter H, Gower-Rousseau C, et al. Patient-reported Outcomes in a French Nationwide Survey of Inflammatory Bowel Disease Patients. J Crohns Colitis 2017;11:165–174. [PubMed: 27516406]
22. Ader DN. Developing the Patient-Reported Outcomes Measurement Information System (PROMIS). Med Care 2007;45:S1–S2. [PubMed: 18027399]
23. Iglesias-Rey M, Barreiro-de Acosta M, Caamaño-Isorna F, et al. Psychological factors are associated with changes in the health-related quality of life in inflammatory bowel disease. Inflamm Bowel Dis 2014;20:92–102. [PubMed: 24193152]
24. Zhang CK, Hewett J, Hemming J, et al. The influence of depression on quality of life in patients with inflammatory bowel disease. Inflamm Bowel Dis 2013;19:1732–1739. [PubMed: 23669400]
25. Li J, Yazdany J, Trupin L, et al. Capturing a patient-reported measure of physical function through an online electronic health record patient portal in an ambulatory clinic: Implementation study. J Med Internet Res Med Informatics 2018;6:e31.
26. Wagner LI, Schink J, Bass M, et al. Bringing PROMIS to practice: Brief and precise symptom screening in ambulatory cancer care. Cancer 2015;121:927–934. [PubMed: 25376427]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

27. Mikocka-Walus A, Pittet V, Rossel J, et al. Symptoms of Depression and Anxiety Are Independently Associated With Clinical Recurrence of Inflammatory Bowel Disease. Clin Gastroenterol Hepatol 2016;1:1542–3565.

28. Slonim-Nevo V, Sarid O, Friger M, et al. Effect of social support on psychological distress and disease activity in inflammatory bowel disease patients. Inflamm Bowel Dis 2018;24:1389–1400. [PubMed: 29893949]

29. Taleban S, Stewart KO, Li DK, et al. Clinical Activity and Quality of Life Indices Are Valid Across Ulcerative Colitis But Not Crohn's Disease Phenotypes. Dig Dis Sci 2016;61:2627–2635. [PubMed: 27142671]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

WHAT IS CURRENT KNOWLEDGE

- The importance of assessing quality of life in patients with inflammatory bowel disease through validated measures has been recognized in recent years
- Overall quality of life in patients with inflammatory bowel disease is poorer than in the general population
- Using an inflammatory bowel-disease specific combined assessment of psychological and physical factors of quality of life has been identified as critical goal

WHAT IS NEW HERE

- We developed a novel measure (the PROBE) to assess quality of life in patients with inflammatory bowel disease
- The PROBE was developed from known domains affecting quality of life in patients with Crohn's disease and ulcerative colitis
- The PROBE demonstrates responsiveness to change in disease states high test-retest reliability in patients with stable disease patterns

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

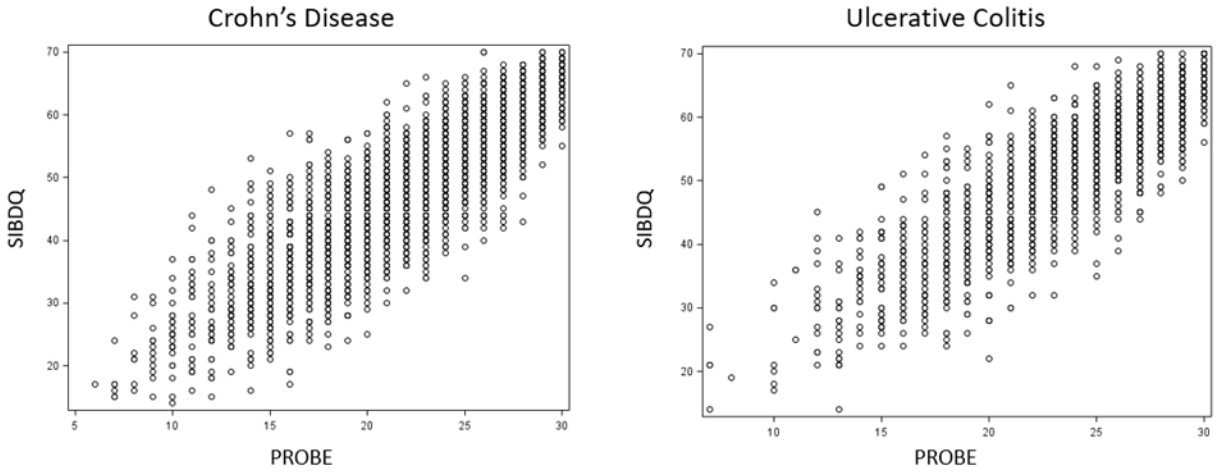

Figure 1.

Scatter plot demonstrating correlation between the Patient Reported Outcome Based Evaluation and the Short Inflammatory Bowel Disease Questionnaire among patients with Crohn's disease and ulcerative colitis

among patients with Crohn's disease, r=0.88; among patients with ulcerative colitis, r=0.86

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

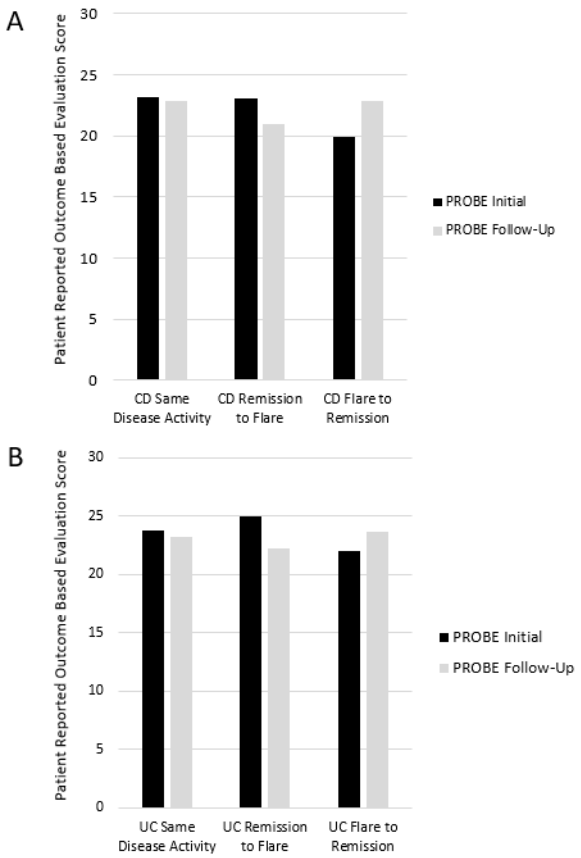

Figure 2.

Disease activity over time, compared to the Patient Reported Outcome Based Evaluation among patients with Crohn's disease and ulcerative colitis

(A) patients with Crohn's disease; (B) patients with ulcerative colitis

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 1.

Demographics and clinical characteristics among participants in IBD Partners at the time of completion of the initial patient reported outcomes based evaluation

	Ulcerative colitis (n=1735)		Crohn's disease (n=3119)	
	n	**%**	**n**	**%**
Age (mean, SD)	45.2	15.1	43.6	15.3
Female Sex	1220	70	2271	73
Disease Activity[a]				
Clinical remission	913	47	2044	66
Flare	822	53	1075	34
Years since IBD diagnosis (mean, SD)	11.7	11.3	14.7	12.8
Smoking status				
Former smoker	553	32	894	29
Current smoker	68	4	224	7
History of IBD-related surgery	N/A		1474	47
Corticosteroids, current user	189	11	446	14
Aminosalicyates, current user	1296	75	1145	37
Immunomodulator, current user	1285	25	1006	33
Biologic therapy, current user	361	21	1395	45

[a]Disease activity defined as clinical remission or flare, where clinical remission was defined as a score of ≤2 on the Simple Clinical Colitis Activity Index for ulcerative colitis or a score of <150 on the Short CDAI

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 2.

Patient Reported Outcome measure factor loadings, grouped by five existing PROMIS measure domains

In the past 7 days…	Anxiety	Depression	Fatigue	Social Satisfaction	Pain
I felt fearful	0.763				
I found it hard to focus on anything other than my anxiety	0.883				
My worries overwhelmed me	0.879				
I felt uneasy	0.830				
I felt worthless		0.857			
I felt helpless		0.902			
I felt depressed		0.847			
I felt hopeless		0.915			
I feel fatigued			0.923		
I have trouble starting things because I am tired			0.871		
How run-down did you feel on average			0.958		
How fatigued were you on average			0.972		
I am satisfied with my ability to meet the needs of my friends				0.941	
I am satisfied with my ability to do things for fun with others				0.909	
I am satisfied with my ability to do things for my family				0.937	
I am satisfied with my ability to do work really important to me				0.851	
How much did pain interfere with your day-to-day activities?					0.947
How much did pain interfere with work around the home?					0.977
How much did pain interfere with ability to participate in social activities?					0.917
How much did pain interfere with your household chores?					0.950

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 3.

Final questions included in the PROBE, a 6 question measure of quality of life among patients with inflammatory bowel disease

In the past 7 days…
I found it hard to focus on anything other than my anxiety
(5) Never
(4) Rarely
(3) Sometimes
(2) Often
(1) Always
I felt hopeless
(5) Never
(4) Rarely
(3) Sometimes
(2) Often
(1) Always
How fatigued were you on average
(5) Not at all
(4) A little bit
(3) Somewhat
(2) Quite a bit
(1) Very much
I am satisfied with my ability to meet the needs of my friends
(1) Not at all
(2) A little bit
(3) Somewhat
(4) Quite a bit
(5) Very much
How much did pain interfere with work around the home?
(5) Not at all
(4) A little bit
(3) Somewhat
(2) Quite a bit
(1) Very much
How would you rate your IBD activity?
(5) Remission
(4) Minimal symptoms
(3) Mildly active
(2) Moderately active
(1) Severely active

Note: Scores for each response to an individual question are listed in parentheses

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 4.

A comparison of the Patient Reported Outcome Based Evaluation and the Short Inflammatory Bowel Disease Questionnaire at baseline survey and follow-up (5-18 months) survey, with analysis by sub-type of inflammatory bowel disease and disease activity[a]

	PROBE Initial	PROBE Follow up	p-value[b]	SIBDQ Initial	SIBDQ Follow up	p-value[b]
Crohn's disease (n=3119)	**22.8**	**22.7**	**<0.001**	**49.7**	**50.1**	**<0.001**
Patients with the same disease activity at both assessments (n=2386)	23.2	22.9	<0.001	50.5	51.1	<0.001
Patients in remission at baseline who experienced a flare at follow up (n=359)	23.1	21.0	<0.001	50.9	44.2	<0.001
Patients in a flare at baseline who went into remission at follow up (n=374)	19.9	22.9	<0.001	42.9	49.7	<0.001
Ulcerative colitis (n=1735)	**23.7**	**23.1**	**<0.001**	**51.7**	**52.6**	**<0.001**
Patients with the same disease activity at both assessments (n=1307)	23.8	23.2	<0.001	52.0	52.8	<0.001
Patients in remission at baseline who experienced a flare at follow up (n=201)	25.0	22.2	0.001	54.9	48.9	<0.001
Patients in a flare at baseline who went into remission at follow up (n=227)	22.0	23.7	<0.001	47.8	55.3	<0.001

[a]Disease activity defined as clinical remission or flare, where clinical remission was defined as a score of ≤2 on the Simple Clinical Colitis Activity Index for ulcerative colitis or a score of <150 on the Short Crohn's Disease Activity Index for Crohn's disease

[b]p-value obtained by Wilcoxon Rank Sum testing