The Manitoba IBD Index:

Evidence for a New and Simple Indicator of IBD Activity

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ABSTRACT

Background: A single-item indicator of disease activity over an extended time, the Manitoba IBD Index (MIBDI) is proposed, and compared against several standard measures for assessing activity in patients with Crohn's disease (CD) and ulcerative colitis (UC). **Methods:** Participants enrolled in the Manitoba IBD Cohort Study, a population based longitudinal cohort (n=353) were assessed semi-annually by survey, clinical interview, and blood sample across a two-year period. The MIBDI is based on patient self-report of symptom persistence for the previous 6 months, using a 6-level response format. **Results:** The MIBDI had good sensitivity compared to the Harvey-Bradshaw (HB; 0.88), Powell-Tuck (PT; 0.84) and Inflammatory Bowel Disease Questionnaire (IBDQ; 0.89), which was maintained at two subsequent annual measurements. Test-retest reliability was also strong (Spearman r = 0.81). Discriminant function analyses identified common discriminating variables of active disease for CD and UC that included HB, PT, IBDQ subscales of bowel and systemic symptoms, prolonged symptom severity (e.g., abdominal and joint pain, tiredness, diarrhea), and recent persistent pain related to IBD. Unique discriminators included weight problems (CD) and blood in stool (UC). **Conclusions:** A single-item patient-defined disease activity measure, the MIBDI, showed a high degree of sensitivity for classifying individuals with regard to disease status over time compared to existing disease activity measures, and strong convergent validity with expected proxy measures of disease. These relationships remained consistent over time. Thus, the MIBDI shows promise as a valid brief tool for measuring disease activity over an extended period.

Introduction

Assessing disease activity in inflammatory bowel disease (IBD) is an important aspect of clinical trials. It would seem to be a straightforward task to determine whether individuals with IBD have active disease **and** disease activity changes over time. However, there is no single indicator of disease activity that is widely adopted as the gold standard. One popular clinical index is the *Crohn's Disease Activity Index* (*CDAI*)[1], which identifies symptoms and is enhanced by a single objective measure of hematocrit. Other indices such as the *Harvey Bradshaw Index* (*HB*)[2] for Crohn's disease and the *Powell Tuck Index* (*PT*)[3] for ulcerative colitis, are based on self-reports of active disease symptoms at the time of assessment with cursory clinical examination. When used in clinical trials they are re-administered at regular intervals to assess changes in disease activity over time.

The importance of including a self-assessment of the patient's health has been shown by Drossman et al[4]. They found that self-assessment scales for IBD correlated well with physician ratings of disease activity, and accounted for a high percentage of the variation in overall health status. Similarly, Higgins and his colleagues demonstrated the value of patient definition of clinically meaningful improvement and remission status in IBD[5].

Serological measures, such as the C-reactive protein (CRP) or serum hemoglobin and albumin, are also used as markers of disease activity. While an elevated CRP reflects current active inflammation, low serum hemoglobin or albumin may reflect IBD activity over time or other health problems. Imaging modalities have also been used to assess disease activity. This approach avoids the subjective element of symptom inquiry, but it correlates poorly with active

symptoms and it is problematic to repeat imaging, endoscopic or radiological methods for sequential assessment of activity[6, 7].

While assessing disease activity in clinical trials is imperfect, there is yet another layer of complexity to assessing activity in natural history or cohort studies. Individuals followed prospectively and at regular intervals have provided key outcome data from regions as disparate as Manitoba, Canada[8], Olmsted County in the U.S.[9], Norway[10] and multiple European centres[11]. However, cohort research typically studies participants over longer intervals (6, 12, or 24 months, for example) to understand natural history and 'real-life' experiences with the disease. Prospective studies would be enhanced by having an index that could better characterize disease activity over these longer time periods. Since the current clinical indices in use have very short time frames (usually one day to a few weeks) and there is no available measure of extended disease activity, we endeavored to develop a brief, informative activity index, using patient assessment of disease activity, in order to address this need.

The purpose of this study is to propose a new self-report measure of disease activity and compare it to existing measures, both cross-sectionally and over time. The index was assessed in relation to a variety of other measures that relate to disease activity either directly or indirectly, including physical symptoms, biological markers, IBD medication use, and daily productivity loss.

Methods

Cohort *Participants*

The Manitoba IBD Cohort Study was initiated in 2002, drawing on participants from the University of Manitoba IBD Research Registry. Most participants were at least 18 years old (with a small number nearing their 18th birthday at the time of entry into the study), and diagnosed within the previous 7 years, the latter to capture relatively recent onset. The population-based Registry was established in 1995. Residents of the province of Manitoba, Canada (population approximately 1 150 000) identified as having IBD through the administrative health database of Manitoba Health (the government agency that provides comprehensive health coverage to all residents) were eligible for inclusion in the Registry. Of those eligible, that is, all those with IBD in the province, just over half participated in the Registry[12].

The Manitoba IBD Cohort Study was approved by the University of Manitoba Health Research Ethics Board and participants provided written informed consent for their involvement in the research. At the time of study recruitment, there were 3192 participants in the Research Registry, of which 606 were eligible for this study, given the age and recent onset criteria. Of those, 418 could be contacted and enrolled over an 18 month period.

Complete data were obtained in the first contact of the longitudinal Manitoba IBD Cohort from 388 of those enrolled, and they have subsequently served as the Cohort. More details on the creation of this sample are provided in an earlier report by our group[13]. Participants were similar in age and sex distribution to those with parallel duration of disease in the University of Manitoba IBD Epidemiology Database, an administrative data set which includes all those in the province with IBD, suggesting excellent representativeness of the cohort. The data for this study

were obtained from 353 participants who provided information at three measurement occasions: 0-month (baseline), 12-month, and 24-month assessments.

Disease Activity Measures

The Manitoba IBD Index (MIBDI) was designed to assess disease activity based on patient report of symptom persistence for the previous six months, using a 6-level response format. It used frequency anchors to provide more consistent reporting. Participants were asked to respond to the following; "In the past six months my disease has been (a) constantly active, giving me symptoms every day (b) often active, giving me symptoms most days (c) sometimes active, giving me symptoms on some days (for instance 1-2 days/week) (d) occasionally active, giving me symptoms 1-2 days/month (e) rarely active, giving me symptoms on a few days in the past six months and (f) I was well in the past 6 months, what I consider a remission or absence of symptoms." A dichotomous disease activity measure was defined as follows: active disease included experiencing symptoms constantly to occasionally (responses a to d), and inactive disease as experiencing infrequent symptoms or feeling well (responses e or f).

Clinical Indices

The HB and PT multi-item measures were administered during each of the annual clinical interviews; each measure describes symptom levels at the time of assessment. The measures are 6 and 8 items in length, respectively, and the items are summed to provide a summary index score. Scores greater than or equal to four on either scale are indicative of active disease[5, 14].

Another measure of disease activity that was compared with the MIBDI was the 32-item Inflammatory Bowel Disease Questionnaire (IBDQ)[15], which summarizes physical, social and emotional health in the preceding two weeks as reported from the patient's perspective[16]. The IBDQ yields a total score, as well as scores for four subdomains: Bowel Symptoms, Systemic Symptoms, Emotional Function and Social Function. Responses are made on a 7-point Likert scale (0 = "All of the time", 7 = "None of the time"). Higher total IBDQ scores (over and including 180) are associated with remission, and lower scores (<180) are associated with moderate to severe IBD symptoms[17].

IBD Symptom Severity

The severity of nine common IBD symptoms over the previous six months were rated using a five-point scale ranging from "Not at all" to "Extremely". They included: abdominal pain, diarrhea, problems sleeping, tiredness, joint pain, urgency to have bowel movements, loss of appetite, weight loss, and the presence of blood in stool. Participants were also asked about the average number of bowel movements per day they had in the past month. A single item from the McGill Pain Questionnaire[18] was also used, asking participants if they had any persistent pain (answered as yes/no) related to IBD over the past two weeks.

Biological markers and medication use

The CRP level is often used in chronic inflammatory diseases as a marker of active inflammation; it is typically understood to be an acute phase reactant[19]. While anemia can be secondary to a number of factors in IBD, its presence can certainly be a marker of ongoing active disease. Further, those with a normal serum hemoglobin are less likely to have severely active

disease. CRP and hemoglobin were obtained through a blood draw at the time of the clinical interview. For CRP, a "normal" level was defined as a value from 0 to 7 mg/L, with CRP values higher than 7 mg/L being classified as "high CRP". For the serum hemoglobin readings, values higher than or equal to 120 g/L were classified as "normal", and values lower than 120 g/L were classified as "low serum hemoglobin".

Use of prednisone and infliximab can also serve as markers of active disease. Because of their side effect profiles, they would only be initiated for treatment if a patient was truly symptomatic with active disease. Prednisone has not typically been useful to maintain disease remission and hence is used primarily to settle active disease, with the exception of a small subset who are prednisone-dependent (i.e., can only sustain inactive disease if prednisone is maintained). Infliximab has been proven to have utility to maintain remission[20] but its persistent use implies that the patient at one time had sufficiently active disease to warrant prescription. Hence recent initiation of infliximab can identify recently active disease even though long term usage does not[20]. Participants were asked whether they had used any of these medications in the previous six months, including number of weeks of use and maximum daily dosage.

Reduction in Activity/Disability

Recent illness-related disability was assessed based on three questions drawn from a national health survey[21]: "In the last 14 days a) did you *stay in bed* for all or most of the day due to illness or injury; b) were there any days that you *cut down* on things you normally do because of illness or injury; c) were there any days when it took *extra effort* to perform up to your usual level at work or at your other daily activities".

Clinic Sample

To further assess the validity of the MIBDI, a secondary investigation was undertaken for an independent sample of 80 consecutive IBD patients attending an outpatient hospital clinic. These patients completed the MIBDI in addition to routine clinical measures, including either the HB or PT depending on their diagnosis. Retrospective chart reviews were done (by CNB) to determine patient patterns of disease over the prior 6 months. Patient disease was categorized as active or inactive during that period, based on indications of disease flare including symptom reporting, change in medication, histology, or interventions required. The reviewer was blind to the MIBDI score.

Statistical Methods

Summary statistics, including means, standard deviations, Spearman correlations, and the percentage of individuals classified as active and inactive, were computed for all of the disease activity measures included in the study. Sensitivity and specificity [22] were estimated for the MIBDI. Specifically, the proportion of respondents with active and inactive disease as classified by the MIBDI was compared to the proportion of respondents with active and inactive disease as classified by the IBDQ total score (IBDQ < 180 = active[23]) and to the proportion determined to be active based on the HB or the PT (HB or PT ≥ 4 = active[24]). Sensitivity is defined as the likelihood the MIBDI positively identified individuals with active disease when disease status was identified as active by one of the other measures, with values closer to 1.0 indicating excellent identification of active disease. Specificity is defined as the likelihood the MIBDI identified individuals with inactive disease when the other measures identified inactive disease,

with values closer to 1.0 indicating excellent identification of inactive disease. Test-retest reliability was assessed using both the Spearman correlation and the kappa statistic.

Discriminant function analyses were conducted to assess validity. Analyses were carried out for each measurement occasion (0, 12, and 24 months) and each subtype of IBD (Crohn's disease, ulcerative colitis). A discriminant function analysis is used to predict the probability of group membership from a set of predictors[25]. In the current study, individuals were classified to active or inactive disease groups using responses from the MIBDI. The predictors were: clinical indices of current disease activity, past 6-month severity ratings of common IBD-related symptoms, average daily bowel movements over the previous month, persistent pain intensity related to IBD in the past two weeks, recent restriction of activities due to illness, high current CRP, low current hemoglobin levels, and reported use of infliximab or prednisone in the prior six months. A predictor was considered to be a *good* discriminatory variable of active and inactive disease as per the MIBDI if it showed a discriminant function coefficient of at least 0.35 in absolute value[26]; it was considered to be a *consistent* discriminatory variable if the coefficient was 0.35 or higher for at least two of the three assessment points. These coefficients reflect correlations between the proposed predictor variables and the discriminant function (the linear combination of predictor variables that classifies cases, in this instance inactive versus active disease status according to the MIBDI)[26].

Results

At study entry (baseline), the mean age of participants was 41 years (SD =14.53, range 17 to 79 years), and 59% were female. The sample was 95% Caucasian, with few having self-described backgrounds as East Indian, Hispanic, or Metis (mixed aboriginal and European background). Two thirds of participants were married (67.5%), 53.6% were employed full time, and 27.5% had a university degree. Chart review confirmed that 184 had Crohn's disease, and 169 had ulcerative colitis; 18 with indeterminate colitis were not included in this analysis. The average duration of disease was 4.3 years (SD = 2.1). Forty-eight percent were taking 5-ASA, 21% were taking immunosuppresants, and 5% were taking prednisone at study entry.

Table 1 presents the proportion of respondents reporting each of the six levels of symptom activity on the MIBDI at each of the 0-, 12-, and 24-month assessment periods. The reporting pattern of disease activity from constantly active disease to remission during the past six months clearly shows a normal distribution, which is not surprising for this population-based cohort. The distribution was consistent across the three assessment periods. Further, there was stability across time regarding the proportion of individuals who were relatively well (i.e., 16-21% no symptoms; 13-20% rare symptoms), had daily symptoms (i.e., 10%), or who had symptoms occasionally to often (50-55%).

Table 2 reports summary statistics (i.e., means and standard deviations) for the four disease activity measures (the MIBDI, HB, PT, and IBDQ total score) for each of the three assessment periods (0-month, 12-month, and 24-month), as well as their intercorrelations and the percentage of individuals classified as "inactive" or "active" for each measure. The correlation between the

MIBDI and the other disease activity measures is in the medium range[27]. Each of the four measures showed a consistent proportion of individuals who were classified as active over time. The MIBDI showed similar rates of classification compared to the HB and PT classifications, but identified a higher proportion of individuals as having active disease compared to the other disease activity measures. This seems reasonable given the considerably longer time period encompassed by the MIBDI.

The sensitivity and specificity results, shown in Table 3, suggested good sensitivity and modest specificity for the Manitoba IBD Index. The MIBDI had good sensitivity in describing active versus inactive disease when compared to the HB, PT, and IBDQ indices, with the majority of values ranging from 0.84 to 0.90 across the 0-, 12-, and 24-month assessment periods. Specificity ranged from 0.51 to 0.68 when compared to the HB, PT, and IBDQ indices. This lower specificity was not unexpected since the MIBDI was assessing activity over 6 months whereas the HB and PT indices were assessing activity at a single time point. Respondents could be identified by the MIBDI as having active disease over the last six months even if the disease was not active in the most recent few days to few weeks.

There was strong test-retest reliability of the MIBDI in the 1-week retest subsample. The Spearman correlation between the MIBDI scores at the two measurement occasions was high ($r = 0.81$, 95% CI: 0.76-0.86), and the kappa value for active versus inactive categorization at these two measurement points was also good (0.76; 95% CI: 0.67-0.85).

Based on the independent sample of 80 clinic patients, 67.50% (n=54) had a positive concordance between their MIBDI and HB or PT disease activity categorization, 26.25% (n=21) had a discordant relationship between these two disease activity measures, and 6.25% (n=5) could not be assessed on the HB or PT due to the presence of stomas. Chart review data were consistent with the disease activity indices for 100% of the 54 patients with concordant HB/PT and MIBDI ratings. Of those with discordant ratings, chart review data from 86% of these patients was consistent with the MIBDI categorization of disease activity over the HB or PT. Further, the remaining five patients with stomas also had concordance between chart indications of active (or inactive) disease in the previous six months and MIBDI categorization of disease activity. Overall, the MIBDI was able to provide accurate disease activity classification for the prior six month period for 96% of this clinic sample, relative to chart information. The sensitivity of the MIBDI in this clinic sample was 0.85 (95% CI: 0.70, 0.94), and the specificity was 0.58 (0.41, 0.73).

The results of the discriminant function analyses are presented in Tables 4 and 5 for those with Crohn's disease and ulcerative colitis, respectively. For both groups of patients, common discriminating variables that categorized respondents as active or inactive as per the MIBDI consistently across time included clinical indices (HB and PT), all four of the IBDQ subscales (bowel, systemic symptoms, social functioning, emotional health), several of the IBD symptom severity ratings (abdominal pain, tiredness, diarrhea, urgency of bowel movements), and recent pain intensity.

For Crohn's disease, unique discriminators were loss of appetite and weight problems. For ulcerative colitis patients, the presence of blood in stool during the past six months emerged as a unique disease activity discriminator. Several other variables showed moderate discriminatory power (e.g., days requiring extra effort), but only showed high discriminative ability for a single assessment point, and so were not considered to be consistent discriminatory variables. Medication use and blood markers were not discriminatory for extended disease activity.

Discussion

Disease activity in IBD, and in particular over an extended period of time, is challenging to assess. A proposed single-item patient-defined disease activity measure, the MIBDI, was compared to existing disease activity measures (i.e., HB, PT, IBDQ) with respect to sensitivity and convergent validity. The MIBDI showed a high degree of sensitivity for classifying individuals with regard to their disease activity over time compared to these existing disease activity measures, and demonstrated excellent test-retest reliability. The correlations between the MIBDI and the HB, PT, and IBDQ indices were, in fact, similar to those reported by Irvine et al[23] for the IBDQ. Strong convergent validity with expected proxy measures of disease activity was found, and these relationships were consistent across a period of two years. Discriminant function analyses supported the MIBDI definition of disease activity in relation to active symptoms. Additional evidence of validity for the MIBDI was established in a clinic setting, where the patient's report of disease in the previous six months using the MIBDI was highly consistent with evidence of disease status based on retrospective review of the clinical record.

There is commonly a distinction between disease activity, often reported by the patient, and disease severity, often assessed by imaging, histologic assessment and the presence of certain disease characteristics (e.g., fistulas). It has been suggested that disease activity reflected the symptomatic status of the patient, in other words their direct experience of the disease, while severity was reflected by the degree and extent of architectural changes[28]. Some patients may have active disease with little abnormality found on imaging studies, whereas others may have clear inflammation as established by endoscopy or histology, but experience minimal symptoms. The GETAID group has repeatedly shown that endoscopic activity of Crohn's disease correlates either poorly or not at all with a clinical disease activity index[6, 7, 29]. Similarly in ulcerative colitis, macroscopic changes at colonoscopy have correlated poorly with the PT clinical index, so an objective measure of inflammation is not necessarily reflective of a patient's symptoms[30]. While some may question the validity of equating symptoms with 'true' disease activity, this latter study shows that using an objective measure such as macroscopic mucosal appearance does not correlate with how the patient is feeling. Other objective measures associated with disease activity for IBD such as fecal calprotectin[31], gut permeability[32] or gut lavage fluid protein have high sensitivity for presence or absence of active disease[33].

One critique of using patient symptom report to identify their disease activity status is the notion that some symptoms may not be generated by active inflammation but rather by functional complaints. One example is the overlap of irritable bowel syndrome (a very common condition in the community) in patients with IBD[34]. However, it has previously been shown that in general, patients with IBD are not any more likely to have IBS than the general population[8]. Preliminary research has also suggested that assumed functional complaints in IBD may in fact

reflect sub threshold IBD inflammatory activity or be the result of IBD complications such as fibrous strictures[35], which further supports the value of patient report regarding their disease activity.

Certainly, patient report of problematic symptoms should and usually does encourage physicians to treat an IBD patient's gastrointestinal symptoms as if they are arising from active IBD. That is, in clinical practice, most physicians tailor therapy to the symptoms described by the patient, particularly when there are regular visits for ongoing consultation or treatment. It is symptoms that motivate patients to seek health services and to use medications in order to improve productivity and quality of life. People do not miss work because of macroscopic colonic disease, but do miss work because of active symptoms. Hence the use of symptom inquiry is an important way to directly assess a patient's health status.

Currently available disease activity measures are in the form of patient self report (e.g., IBDQ), clinician-administered symptom report (e.g., HB and PT), and combinations of self report plus objective data such as hematocrit measurements (e.g., CDAI), endoscopic scores, or serological markers of active inflammation[36]. One of the most widely-used combination measures, the CDAI, has been criticized for its lack of standardization in administration and scoring. Recommendations for change have included simplifying it to include just patient report[37].

Self-report measures have the advantage of being quick and easy to administer, low in cost, nonintrusive, reasonably consistent over time, and relate strongly to important clinical outcomes[13]. These measures differ in the time period assessed, with most IBD self-report

measures considering very recent periods, ranging from same-day assessment to the previous two weeks (for the IBDQ). However, there has been no evaluation of the correspondence between these same-day or recent few-week current disease activity measurements and longer-term existence of problematic symptoms and disease activity (i.e., over several months). While the brief time frame can be useful for some purposes, the experience of persistent active disease may well have a different impact on the individual than a quickly-resolved episode, but the brief disease activity measures do not allow differentiation.

The MIBDI captures the longer-term experience of the individual with their disease, assessing the presence of problematic symptoms. It can also be used in those situations where other self-report measures such as the HB or PT cannot be used (e.g., in the presence of stomas). Further, our evaluation in a clinic sample suggested greater accuracy of the MIBDI in reflecting disease activity over time than the HB or PT. That is, many of the patients who were categorized as inactive based on the HB or PT were classified as active based on the MIBDI, and had clear chart evidence of disease flare occurring in the previous six months, including initiation of new medication. This finding highlights a disadvantage of the current indices in use such as the HB, PT, CDAI or IBDQ; namely that inactive disease recently achieved through prednisone or other treatment is not able to be differentiated from longstanding 'true' remission, even though the experience of these two scenarios may be quite different for the patient.

There was striking stability of IBD symptomatology across time. Given that these data are drawn from a population-based cohort, it provides some indication of the experiences of IBD 'in the community' in the context of usual care. With at least half of those with IBD experiencing

symptoms occasionally to daily in a six month time frame, it raises the question of whether treatment may be suboptimal or whether many accept some level of symptoms as part of their disease experience. This aspect of symptom tolerance versus suboptimal therapy warrants further exploration.

Ultimately, of course, an index cannot be determined to be "valid" in an absolute sense. Rather it can be determined to have utility for particular circumstances[36]. In conducting longitudinal research in patients with IBD, researchers need to choose the disease measures based on what is critical for the research. Consideration of endoscopic inflammation and healing as an important therapeutic target has only recently emerged as a potentially important goal[38]. If this is the goal in a longitudinal study then endoscopy or imaging should be incorporated. In many longitudinal studies, however, repeated imaging or biopsies may be too expensive and intrusive. If symptom status and related disease interference are key outcomes in a study, then patient-report measures of disease activity can be quite appropriate and have strong advantages. The MIBDI has the further advantage that it encompasses a six month period, which may be highly relevant in many longitudinal studies.

A potential limitation of the MIBDI is the lack of detail about specific symptoms. In our study, we also asked about common IBD-related symptoms and severity over the same time frame, which could be used as an adjunct measure when that type of detail is needed. Another limitation is the potential for a recency effect biasing the MIBDI six-month report. That is, recent disease activity could influence recall and characterization of disease in the previous six months and that will need to be addressed empirically in subsequent work with the measure.

In conclusion, there is no one absolute way to capture disease activity. The best measure for a particular situation may depend on the research or clinical goals. The MIBDI meets goals previously identified in the literature for an ideal disease activity measurement tool: (a) that it have well-understood operating characteristics and a dynamic range to accurately reflect gradations of illness and (b) that it be reproducible, valid and responsive[39]. Advantages of the MIBDI described in this study are its brevity, six-month time frame, focus on the person's experience of the frequency of significant symptoms, and the strong agreement with widely used disease activity measures and proxy markers of disease. The MIBDI had high levels of sensitivity across a two year time period, indicating that the MIBDI relates consistently to existing measures of disease activity. There was some indication that the MIBDI could potentially be used for those whose stoma, short bowel syndrome or intestinal stricture may preclude the use of symptom-based activity indices such as the CDAI, HB and PT. Finally, our assessment of the MIBDI in a clinic sample strengthens the evidence for the MIBDI as a versatile measure of disease activity.

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What is Known

There are a number of measures used to assess disease activity but most assess disease activity at the time of undertaking the measurement or for the prior 1-2 weeks. Hence, no measures are currently used which assess disease activity over a prolonged period.

There can be a discrepancy between patient self-report of symptoms with objective measures of disease activity such as with blood tests or imaging studies.

The Manitoba IBD Cohort Study is a prospective longitudinal population-based study wherein among a variety of parameters subject disease activity is measured on a semi-annual basis using several methods

What is new

The Manitoba IBD Index (MIBDI) was developed as a simple measure of disease activity over the prior 6 months using a single question with 6 possible responses

A comparison of the MIBDI with previously validated disease activity indices such as the CDAI, IBDQ, Harvey-Bradshaw and the Powell-Tuck, as well as against the serum CRP and hemoglobin levels

The best activity measure for a particular situation may depend on the research or clinical goals. The MIBDI meets goals previously identified in the literature for an ideal disease activity measurement tool: (a) that it have well-understood operating characteristics and a dynamic range to accurately reflect gradations of illness and (b) that it be reproducible, valid and responsive. Advantages of the MIBDI described in this study are its brevity, six-month time frame, focus on the person's experience of the frequency of significant symptoms, and the strong agreement with widely used disease activity measures and proxy markers of disease.

Table 1

Frequency (%) Distribution of the MIBDI at 0-, 12-, and 24-Month Assessments (overall n = 353).

Index Category	0-Month Assessment n (%)	12-Month Assessment n (%)	24-Month Assessment n (%)
Constantly active, giving me symptoms every day	49 (14.0)	28 (8.5)	29 (9.2)
Often active, giving me symptoms most days	66 (18.9)	47 (14.2)	35 (11.1)
Sometimes active, giving me symptoms on some days	77 (22.1)	81 (24.5)	59 (18.7)
Occasionally active, giving me symptoms 1-2 days / month	52 (14.9)	59 (17.9)	62 (19.6)
Rarely active, giving me symptoms only a few days of the past six months	47 (13.5)	56 (17.0)	64 (20.3)
I was well in the past 6 months, what I consider a remission	58 (16.6)	59 (17.9)	67 (21.2)

Table 2

Summary Statistics for the MIBDI and other Disease Activity Measures at 0-, 12-, and 24-Month Assessments (overall n = 353).

	0-Month Assessment				12-Month Assessment				24-Month Assessment			
	MIBDI	HB	PT	IBDQ	MIBDI	HB	PT	IBDQ	MIBDI	HB	PT	IBDQ
Mean	3.45	6.09	5.48	167.07	3.74	5.36	5.02	171.49	3.94	5.15	5.01	175.40
SD	1.66	4.87	4.32	1.66	1.55	4.29	4.07	32.20	1.59	4.19	3.99	1.59
Correlation												
MIBDI	1.00	-0.49	-0.53	0.60	1.00	-0.57	-0.59	0.61	1.00	-0.60	-0.42	0.61
HB		1.00	--	-0.60		1.00	--	-0.66		1.00	--	-0.77
PT			1.00	-0.79			1.00	-0.78			1.00	-0.71
IBDQ				1.00				1.00				1.00
% Active	69.9	66.5	58.9	59.1	65.2	59.9	59.0	49.1	58.5	57.3	57.5	46.3

Note: All Spearman correlations are significant at $\alpha = 0.05$. MIBD = Manitoba IBD Index; HB = Harvey-Bradshaw Index; PT = Powell-Tuck Index; IBDQ = Inflammatory Bowel Disease Questionnaire; SD = standard deviation. There is no correlation for the HB and PT scores.

Table 3

Sensitivity and Specificity (95% confidence intervals; CIs) of the MIBDI at 0-, 12-, and 24-Month Assessments (overall n = 353).

		0 Month Assessment		12 Month Assessment		24 Month Assessment	
		MIBDI		MIBDI		MIBDI	
		Inactive	Active	Inactive	Active	Inactive	Active
IBDQ	Inactive	82	61	96	71	108	62
	Active	22	183	19	144	23	123
		Sensitivity = 0.89 (0.86, 0.93)	Specificity = 0.57 (0.52, 0.62)	Sensitivity = 0.88 (0.85, 0.91)	Specificity = 0.57 (0.52, 0.62)	Sensitivity = 0.84 (0.80, 0.88)	Specificity = 0.64 (0.59, 0.69)
HB	Inactive	31	30	39	29	45	23
	Active	15	105	15	88	15	79
		Sensitivity = 0.88 (0.85, 0.91)	Specificity = 0.51 (0.46, 0.56)	Sensitivity = 0.85 (0.81, 0.89)	Specificity = 0.57 (0.52, 0.62)	Sensitivity = 0.84 (0.80, 0.88)	Specificity = 0.66 (0.61, 0.71)
PT	Inactive	42	27	43	20	41	26
	Active	15	81	17	76	29	56
		Sensitivity = 0.84 (0.80, 0.88)	Specificity = 0.61 (0.56, 0.66)	Sensitivity = 0.82 (0.78, 0.86)	Specificity = 0.68 (0.63, 0.73)	Sensitivity = 0.66 (0.61, 0.71)	Specificity = 0.61 (0.56, 0.66)

Note: MIBD = Manitoba IBD Index; IBDQ = Inflammatory Bowel Disease Questionnaire; HB = Harvey-Bradshaw Index; PT = Powell-Tuck Index.

Table 4

Crohn's Disease: Discriminant Function Coefficients for the MIBDI Categories of Inactive and Active Disease at 0-, 12-, and 24-Month Assessments (n=184).

Discriminant Variable	0-Month	12-Month	24-Month
Harvey-Bradshaw	**0.52**	**0.53**	**0.73**
IBDQ Bowel Systems	**-0.73**	**-0.74**	**-0.80**
IBDQ Systemic Systems	**-0.52**	**-0.54**	**-0.54**
IBDQ Emotion Health	**-0.51**	**-0.51**	**-0.50**
IBDQ Social Function	**-0.45**	**-0.51**	**-0.59**
Prior 6 months:			
Abdominal Pain	**0.70**	**0.76**	**0.62**
Diarrhea	**0.52**	**0.62**	**0.49**
Tiredness	**0.48**	**0.46**	**0.49**
Difficulty with Sleep	**0.48**	**0.56**	**0.41**
Joint Pain	**0.39**	0.27	0.32
Urgency	**0.39**	**0.56**	**0.54**
Loss of Appetite	0.34	**0.51**	**0.48**
Weight Problems	0.21	**0.35**	**0.35**
Blood in Stool	0.13	0.22	0.18
Past month: Average bowel movements	-0.17	**0.41**	0.26
Prior 2 weeks:			
Persistent Pain due to IBD	**-0.48**	**-0.52**	**-0.62**
Days Stayed in Bed	-0.15	-0.18	-0.33
Days Cut Down on Normal Things	-0.14	-0.28	**0.36**
Days Requiring Extra Effort	-0.25	-0.28	**-0.41**
Biological Markers:			
infliximab	-	-0.28	-0.15
Prednisone	-	-0.21	-0.16
C-reactive protein	-	-	-0.06
Hemoglobin	-	-	-0.05

Note: Values in bold text represent variables that are strong (i.e. greater than 0.35 in absolute value) discriminating variables between inactive and active disease status. MIBDI = Manitoba IBD Index; IBDQ = Inflammatory Bowel Disease Questionnaire.

Table 5

Ulcerative Colitis: Discriminant Function Coefficients for the MIBDI Categories of Inactive Versus Active Disease at 0-, 12-, and 24-Month Assessments (n=169).

Discriminant Variable	0-Month Assessment	12-Month Assessment	24-Month Assessment
Powell-Tuck	**0.53**	**0.58**	**-0.38**
IBDQ Bowel Systems	**-0.58**	**-0.59**	**0.61**
IBDQ Systemic Systems	**-0.51**	-0.33	**0.50**
IBDQ Emotion Health	**-0.55**	**-0.48**	**0.51**
IBDQ Social Function	**-0.45**	-0.34	**0.42**
Prior 6 Months:			
Abdominal Pain	**0.47**	**0.55**	**-0.40**
Diarrhea	**0.57**	**0.55**	**-0.38**
Tiredness	**0.57**	**0.38**	**-0.44**
Difficulty with Sleep	**0.37**	0.32	**-0.55**
Joint Pain	**0.37**	0.34	-0.22
Urgency	**0.78**	**0.62**	**-0.62**
Loss of Appetite	**0.40**	0.24	-0.11
Weight Problems	0.30	0.16	-0.06
Blood in Stool	**0.57**	**0.38**	**-0.41**
Past month: average bowel movements	0.00	0.20	-0.06
Prior 2 Weeks:			
Persistent Pain due to IBD	-0.27	**-0.39**	**0.42**
Days Stayed in Bed	-0.15	-0.05	0.13
Days Cut Down on Normal Things	-0.28	-0.07	-0.15
Days Requiring Extra Effort	-0.26	-0.03	0.17
Biological Markers:			
infliximab	-	-0.11	0.13
Prednisone	-	-0.21	0.23
C-reactive protein	-	-	-0.17
Hemoglobin	-	-	0.10

Note: Values in bold correspond to variables that are strong (i.e. greater than 0.35 in absolute value) discriminators of inactive and active disease. MIBDI = Manitoba IBD Index; IBDQ = Inflammatory Bowel Disease Questionnaire.

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