

Impact of disease activity on the quality of life of Crohn's disease patients

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TM VALLIS, GK TURNBULL. Impact of disease activity on the quality of life of Crohn's disease patients. *Can J Gastroenterol* 1996;10(5):310-315. Crohn's disease (CD) patients often suffer severe symptoms that impair their quality of life. A sample of 39 CD patients who were assessed using well validated measures of disease activity and disease-specific quality of life is reported. Twenty-six of these patients were reassessed an average of four months after the initial assessment to determine the impact of changes in disease activity on quality of life. For the total sample (n=39) disease activity did not predict quality of life for any of the scales of the Inflammatory Bowel Disease Questionnaire (IBDQ) ($r < 0.13$ for each). Thus, examining fluctuations in disease activity between patients did not demonstrate a disease activity-quality of life relationship. In contrast, changes in disease activity within the same individuals over time (the repeat assessment sample, n=26) were correlated with changes in quality of life; increases in disease activity predicted decreases in quality of life on the IBDQ bowel symptoms subscale ($r = -0.463$, $P < 0.01$) and the IBDQ systemic symptoms subscale ($r = 0.44$, $P < 0.05$). The 10 patients with the largest decrease in disease activity over time (mean decrease of 43.54 points using the Dutch Activity Index) had significant improvement in quality of life on the bowel and systemic subscales. In contrast, the nine patients with the largest increase in disease activity over time (mean increase of 20.57 points using the Dutch Activity Index) had significant reduction in quality of life on the bowel and systemic symptoms subscales. These differences between extreme groups were significant for both the bowel symptoms ($P < 0.05$) and systemic symptoms ($P < 0.05$) subscales. The authors conclude that changes in disease activity affect some important aspects of quality of life: aspects related to disease-specific (bowel symptoms) and nondisease-specific (systemic symptoms) physical symptoms. Importantly, disease activity was not able to predict the emotional and social aspects of IBD-related quality of life. This suggests that nondisease factors need to be considered when working with CD patients. Future research should evaluate

the role of psychological intervention in improving quality of life for patients with reduced well-being, particularly in areas of emotional and social functioning.

Key Words: Crohn's disease, Disease activity, Inflammatory Bowel Disease Questionnaire, Quality of life, Well-being

Impact de l'activité de la maladie sur la qualité de vie chez les patients atteints de maladie de Crohn

RÉSUMÉ : Les patients atteints de maladie de Crohn (MC) souffrent souvent de symptômes graves qui nuisent à leur qualité de vie. On présente ici un échantillon de 39 patients atteints de maladie de Crohn qui ont été évalués au moyen d'instruments de mesure validés de l'activité de la maladie et de la qualité de vie spécifique à la maladie. Vingt-six de ces patients ont été évalués de nouveau, en moyenne quatre mois plus tard afin de déterminer l'impact de l'évolution de la maladie sur la qualité de vie pour la totalité de l'échantillon (n = 39) l'activité de la maladie n'a pas permis de prédire la qualité de vie selon l'une ou l'autre des échelles du questionnaire sur les maladies inflammatoires de l'intestin (IBDQ, pour *Inflammatory Bowel Disease Questionnaire*) ($r < 0,13$ pour chacun). Ainsi, l'examen des fluctuations de l'activité de la maladie entre les patients n'a pas permis de démontrer un lien entre activité de la maladie et qualité de vie. Par contre, l'évolution de la maladie chez le même individu dans le temps (échantillon ayant subi une nouvelle évaluation, n = 26) était en bonne corrélation avec les changements de qualité de vie. Les augmentations de l'activité de la maladie permettaient de prédire une diminution de la qualité de vie selon la rubrique symptômes intestinaux du IBDQ ($r = -0,463$, $P < 0,01$) et selon la rubrique symptômes systémiques du IBDQ ($r = 0,44$, $P < 0,05$). Les dix patients chez qui l'activité de la maladie avait le plus ralenti pendant cette période (diminution moyenne de 43,54 points

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selon le *Dutch Activity Index*) ont manifesté une amélioration significative de leur qualité de vie selon les rubriques symptômes intestinaux et symptômes systémiques de l'échelle. Par contre, les neuf patients chez qui la maladie s'est le plus exacerbée pendant cette période (augmentation moyenne de 20,57 points selon le *Dutch Activity Index*) présentaient une réduction significative de leur qualité de vie aux rubriques symptômes intestinaux et systémiques de l'échelle. Ces différences entre les deux extrêmes ont été significatives pour les symptômes intestinaux ($P < 0,05$) et les symptômes systémiques ($P < 0,05$). Les auteurs concluent que les changements de l'activité de la maladie affectent certains aspects importants de la qualité de vie,

soient les aspects liés aux symptômes physiques spécifiques à la maladie (symptômes intestinaux) et non spécifiques à la maladie (symptômes systémiques). Il est important de noter que l'activité de la maladie n'a pas été utile pour prédire les aspects émotionnels et sociaux de la qualité de vie liés aux MII. Cela donne à penser que les facteurs non liés à la maladie sont à envisager lorsque l'on travaille auprès de patients atteints de MC. Les recherches à venir devraient se pencher sur le rôle de l'intervention psychologique dans l'amélioration de la qualité de vie des patients dont le bien-être est compromis, particulièrement dans les domaines du fonctionnement émotionnel et social.

Crohn's disease (CD) remains a serious, chronic illness associated with significant management problems. The symptoms of CD, in combination with the uncertainty of remission or relapse, can have a strong negative effect on patient well-being (1). Because there is no cure for CD, the gastroenterologist is left having to manage symptoms and facilitate patient well-being on an ongoing basis. As such, assessing disease activity is an essential part of CD clinical management. Yet there are problems with accurate and reliable assessment of disease activity (2). There are both methodological and conceptual reasons why the assessment of disease activity is difficult. Methodological issues concern sensitivity and predictive validity, and have been addressed elsewhere (2). It has been argued that even if an ideal measure of disease activity were available, it would not be sufficient to explain a patient's illness experience, health status or health outcomes (2-4). Nonetheless, there are disease activity measures available that provide a reliable estimate of the extent of disease activity (eg, the Dutch Activity Index [DAI] and the Crohn's Disease Activity Index [CDAI]) (5,6). These measures can be used to evaluate systematically the extent to which disease activity per se contributes to patient well-being and health outcomes.

Recent research has also focused on assessing health-related quality of life in inflammatory bowel disease (IBD). The Inflammatory Bowel Disease Questionnaire (IBDQ) assesses disease-specific quality of life by evaluating subjective well-being related to bowel and systemic symptoms, as well as social and emotional functioning (7). IBD-specific measures of disease activity and patient well-being are now available. While these measures are not without methodological problems, and certainly do not provide a 'gold standard', they do provide an opportunity to study relationships between disease-based factors and psychological-based factors with improved scientific rigour.

There is increasing evidence, based on scientific data and clinical experience, to sensitize the clinician to the role of nondisease factors in patient well-being or health-related quality of life in IBD (1-4,8-10). The question still remains, however: to what extent do disease and nondisease factors contribute to well-being? There are very few systematic data that address this issue. The data available are somewhat per-

plexing. Some studies report significant correlations between disease activity and quality of life (11), some fail to find such a correlation (12) and some find a correlation for ulcerative colitis (UC) but not CD (8,13).

Thus, while there are very few data available, existing data are not clear on the extent to which disease activity determines patient well-being in CD, although more clear data to this effect exist for UC. Intuitively, one expects to find at least a small to moderate relationship between disease activity and well-being. Yet, for CD at least, the data imply that fluctuations in disease activity may have little bearing on patient well-being. The present study was designed to examine the relationship between disease activity and quality of life in CD in a more methodologically sound manner than previous studies. We used well-validated measures and examined the possible relationship between disease activity and quality of life in two ways. First, we used the standard method of comparing different patients who vary in both disease activity and quality of life. Second, we reassessed a group of patients a second time, approximately four months later, and examined whether changes in disease activity within patients predicted changes in quality of life. This latter analysis is a more sensitive test of the role of disease activity on quality of life because it reduces variability due to differences in psychosocial factors present in a between-subject design.

SUBJECTS AND METHODS

Subjects: Subjects were CD out-patients being treated through the Gastrointestinal Program at Camp Hill Medical Centre/Dalhousie University, Halifax, Nova Scotia. Over five months (December 1992 to May 1993), consecutive CD out-patients seen in the gastrointestinal clinic were approached regarding participation. Thirty-nine out-patients with CD were recruited into the study (all gave written, informed consent). No patient refused to participate initially, although three patients did not complete the administered questionnaires because they thought they were too time-consuming.

Characteristics of the complete sample ($n=39$) and the repeat assessment sample ($n=26$) are presented in Table 1. The repeat assessment sample did not differ on most measures from the total sample in any substantial way. Perusal of the data in Table 1 indicates that the total sample (mostly fe-

TABLE 1
Characteristics of the sample

	Total sample	Repeat assessment sample	
		Time 1	Time 2
Number	39	26	
Males	15 (38%)	10 (38%)	
Females	24 (62%)	16 (62%)	
Age (years)	35.1 (± 14.3)	34.4 (± 13.7)	
Length of disease (years)	6.2 (± 4.8)	4.2 (± 1.9)	
Disease severity (%)			
Nonactive	9 (23%)	4 (15.5%)	2 (8%)
Slight activity	23 (59%)	17 (65%)	16 (61%)
Moderate activity	5 (13%)	4 (15.5%)	8 (31%)
Severe activity	2 (5%)	1 (4%)	0 (0%)

male) had been chronically ill and displayed slight to moderate disease activity at assessment. Those assessed at a repeat visit tended to have had CD for a shorter period (4.3 versus 6.2 years) and tended to be more ill than the complete sample. The greater proportion of female patients in this sample is consistent with findings in other studies (9,14,15) and reflects epidemiological findings that women are more likely than men to develop CD.

Patients were included in this study if they were 18 years or older and had a diagnosis of CD confirmed by a gastroenterologist. Exclusion criteria included patients unwilling to give signed consent and patients unwilling to complete the questionnaires under controlled conditions.

Measures: Patient well-being was assessed using an IBD-specific quality of life measure and disease activity was assessed using objective, validated measures specific to CD.

Quality of life measure: All patients completed the IBDQ (7,16-18), a disease-specific, self-report measure of quality of life. This scale contains 32 items divided into four subscales assessing bowel symptoms, systemic symptoms, emotional functioning and social functioning. Items are rated on a seven-point scale, with higher scores indicating better quality of life. The bowel symptoms subscale ranges from 10 to 70 (10 items); the systemic symptoms subscale from 5 to 35 (five items); the emotional functioning subscale from 12 to 84 (12 items); and the social functioning subscale from 5 to 35 (five items). The IBDQ was developed specifically for IBD patients and has been shown to respond to clinically meaningful changes in IBD symptoms over time. It can be easily completed within 15 to 20 mins.

Disease activity measures: All patients were evaluated using the DAI developed by Van Hees and colleagues (5). The DAI was selected rather than the more commonly used CDAI (6) because the DAI is derived solely from objective parameters. The CDAI requires patients to complete a diary for one week, thus incorporating subjective factors into the measure. Another advantage is that the DAI has been shown to correlate better than the CDAI with other measures of intestinal inflammation (eg, fecal ¹¹¹In excretion) (19,20). Previous studies have shown only a poor correlation of the CDAI with colonoscopic or histological findings of disease (21,22).

The DAI assesses the extent of CD activity by evaluating nine dimensions: albumin level; erythrocyte sedimentation rate; a weight:height ratio called the quetelet index ($[\text{kg}\times 10]/\text{M}^2$); size of abdominal mass; temperature; stool consistency; presence of extraintestinal lesions; history of bowel resection; and sex. Each criterion is weighted and summed to generate a single score of disease activity. Categorical scores for the DAI in CD patients are: less than 90, no activity; between 90 and 150, slight activity; between 151 and 210, moderate activity; and greater than 210, severe activity.

Procedure: Once informed consent was obtained, patients were assessed for disease activity by their treating gastroenterologist. Patients completed the self-report questionnaire. The total sample (n=39) was used in a between-subject analysis of the relationship between disease activity and quality of life. Within-subject analysis involved reassessing a subsample of patients (n=26) at a follow-up visit an average of four months after the first assessment. The procedure for obtaining data at the repeat assessment was the same as that at the initial assessment.

Data analysis: To assess the relationship between disease activity and quality of life a series of regression analyses was conducted. In the between-subject analysis, correlations were calculated between disease activity and the quality of life measure. For the within-subject analysis, change scores were used. Specifically, residualized gain scores (23), which are statistically corrected change scores to control for regression to the mean effects, were calculated. Regression to the mean is a statistical concept in which there is a tendency for extreme scores to change more than less extreme scores. For instance, very high disease activity scores are likely to show greater changes over time than more moderate disease activity scores. As a result, a simple change score (time 2 minus time 1) is not a robust statistical way to assess change (23). By calculating a regression line with time 1 scores predicting time 2 scores, and then taking the difference between the predicted time 2 score (based on the regression line) and the actual time 2 score, a more valid measure of change is produced. This is the residualized gain (change) score. Residualized gain scores are used to evaluate the overall relationship between change in disease activity and change in quality of life. Raw change scores are presented as well, to facilitate interpretation of the data.

RESULTS

Between-subject analysis: Correlations between disease activity and the total score, as well as all subscales of the IBDQ (bowel symptoms, systemic symptoms, emotional functioning and social functioning) were all nonsignificant ($r < 0.13$ for each). These results clearly fail to show any relationship between disease activity and quality of life when evaluated between subjects (ie, where variations in disease activity occur in different patients).

Within-subject analysis: To conduct a more sensitive analysis of the relationship between disease activity and quality of life changes within the same person, the follow-up sample of 26 patients was examined. Results of these analyses were dif-

ferent from the between-subject analysis. Significant negative correlations were found between changes in disease activity and changes in quality of life for the bowel symptoms ($r=-0.463$, $P<0.01$) and systemic symptoms ($r=-0.44$, $P<0.05$) subscales. Although significance levels were not reached, negative correlations were also found for the total scale score ($r=-0.316$, $P<0.1$) and the social functioning subscale ($r=-0.310$, $P<0.15$). The correlation between changes in quality of life and disease activity for the emotional functioning subscale was negligible ($r=-0.077$).

Initial and repeat disease activity scores, as well as raw change scores for disease activity, IBDQ bowel symptoms and IBDQ systemic symptoms, are presented in Table 2. It can be seen that disease activity changes considerably over time. The range of change in the DAI index is from +63.70 (increase in disease activity) to -75.82 (decrease in disease activity). Ten of the 26 patients (38%) show a decrease in disease activity and 16 (62%) show an increase. Clearly there is a wide range of change in disease activity over time.

To examine these findings further the authors compared the subgroup of patients who demonstrated the greatest increase in disease activity (mean change of +20.57 on the DAI, $n=9$) with the subgroup who demonstrated the greatest decrease in disease activity (mean change of -43.54 on the DAI, $n=10$). To provide a more valid measure of change the residualized gain scores were used to form these subgroups. When first assessed these two groups had equivalent disease activity scores (116.83 for the group that worsened and 129.61 for the group that improved; $t=-0.85$). At the follow-up visit, the disease activity score for the worsened group was 160.37 and for the improved group was 109.04 ($t=6.18$, $P<0.001$). These subgroups represent patients who either significantly worsened ($t=-12.99$, $P<0.0001$) or significantly improved ($t=2.64$, $P=0.027$).

Figures 1 and 2 show the changes in quality of life for the improved and worsened subgroups on the bowel symptoms and the systemic symptoms subscales of the IBDQ. Examining the bowel symptoms subscale (Figure 1) reveals an increase in quality of life for the improved group, but a decrease for the worsened group. This difference was significant ($t=-2.18$, $P<0.05$) when residualized gain scores were analyzed. Similarly, on the systemic symptoms subscale (Figure 2) the improved group demonstrated improvements in quality of life, while the worsened group demonstrated reductions, a difference that also reached significance ($t=-2.21$, $P<0.05$) when residualized gain scores were analyzed.

DISCUSSION

Data collected in this study clarified the relationship between CD activity and quality of life. Past studies that have examined this issue have been characterized by methodological problems and have yielded inconsistent results. Drossman et al (8) examined the impact of illness experience, IBD-related concerns and disease activity on health outcomes. In their study, functional status (as assessed by the Sickness Impact Profile, 24) and subjective concerns were

TABLE 2
Changes in disease activity and quality of life between the initial assessment and reassessment

Patient	Initial DAI	Reassessed DAI	Change in DAI	Change in IBDQ BSS	Change in IBDQ SSS
1	121.69	168.35	+46.66	-7	-6
2	146.22	125.34	-20.88	+8	+5
3	212.62	136.80	-75.82	+14	+14
4	103.63	143.16	+39.53	-18	-15
5	91.00	112.74	+21.74	-1	0
6	116.86	106.97	-9.89	-14	-4
7	90.69	154.39	+63.70	-4	0
8	132.16	148.25	+16.09	+8	-3
9	143.21	101.64	-41.57	+6	+9
10	72.64	121.82	+49.18	+7	+3
11	111.22	158.09	+46.87	+4	-3
12	120.42	165.10	+44.68	+15	+7
13	100.32	144.35	+44.03	+1	-8
14	159.79	195.83	+36.04	+10	+2
15	131.13	133.73	+2.60	+8	+8
16	143.41	112.68	-30.73	+8	+4
17	151.57	126.56	-25.01	+1	-10
18	177.96	152.14	-25.82	-5	+2
19	170.39	157.17	-13.22	+12	+3
20	77.77	108.52	+30.75	0	+7
21	109.05	112.84	+3.79	-6	-6
22	76.99	81.60	+4.61	+35	+12
23	94.53	138.92	+44.39	-1	-7
24	106.38	103.89	-2.49	+4	+6
25	149.18	175.18	-26.00	-14	-10
26	89.82	82.03	-7.79	-7	-33

BSS Bowel symptoms subscale; DAI Dutch Activity Index; IBDQ Inflammatory Bowel Disease Questionnaire; SSS Systemic symptoms subscale

better predictors of health status and health care use than disease activity. However, disease activity was assessed by having the attending physician make a global rating (0 = none, 1 = mild/ minimal, 2 = moderate, 3 = severe). Using this nonobjective measure without demonstrated reliability no relationship was found between disease activity and functional status or concerns for Crohn's patients. For UC patients, however, significant correlations reportedly indicated that greater disease activity was associated with poorer functioning and greater concerns. In two other studies by Drossman et al (9,10) psychosocial factors, relative to disease-based factors, had a greater impact on physician visits, whereas disease-based factors, versus psychosocial factors, had a greater impact on hospitalizations and surgeries. These studies also found that CD, compared with UC, had a greater negative effect on psychological functioning.

Turnbull and Vallis (12), in a pilot study of the relationship between quality of life and biopsychosocial factors in IBD, also reported no significant correlation between disease activity and quality of life using the IBDQ. Their sample was too small to allow CD and UC patients to be examined separately. In a follow-up study, Turnbull et al (13) demonstrated that psychological distress, not disease activity, was the best

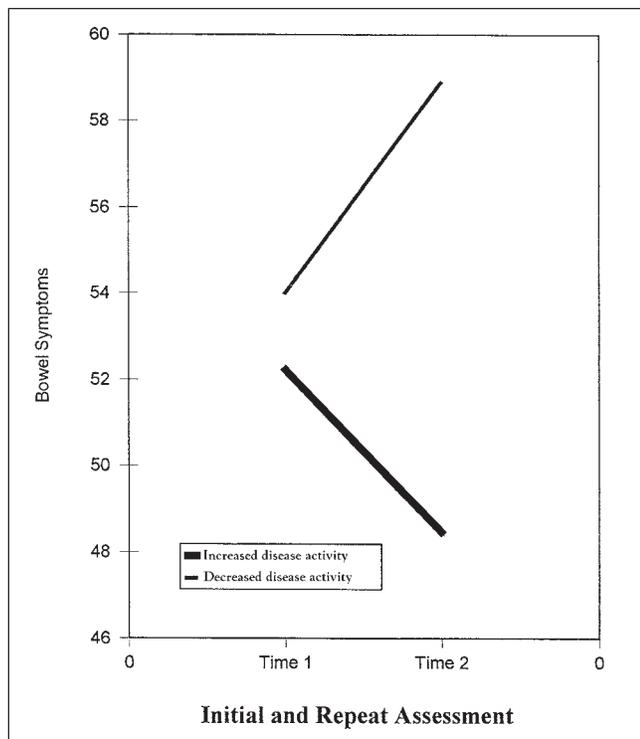


Figure 1) Changes in quality of life (Inflammatory Bowel Disease Questionnaire: bowel symptoms subscale) over time for patients whose disease activity improves and for those whose disease activity worsens

predictor of quality of life for CD patients. In contrast, disease activity was much more important in predicting quality of life for UC patients. Irvine and co-workers (11) reported the results of the multicentre Canadian Crohn's Relapse Prevention Trial, in which the IBDQ and the CDAI were used. These data showed strong negative correlations between disease activity and quality of life. Irvine et al cited a preliminary study, which used the DAI to assess disease activity, in which much lower correlations between disease activity and quality of life were found. Differences in results when different measures of disease activity are used calls into question use of the CDAI because it incorporates subjective ratings of well-being into disease activity scores, unlike the DAI. Combining subjective and objective measures in the CDAI may account for the strong correlations with quality of life judgements (ie, methodological overlap in the measures may inflate the true relationship between disease activity and well-being).

In an attempt to resolve confusion associated with the inconsistent results of previous studies, we chose a more methodologically sound design than previous studies. We used a more objective measure of disease activity, assessed well-being as it specifically relates to IBD and employed both between-subject and within-subject analyses. Methodological factors can account for past inconsistencies in several ways. First, past studies did not always adequately assess disease activity. This is particularly true of the Drossman et al study (8) where overall physician ratings of disease activity were made. As well, Irvine and associates (11) used the

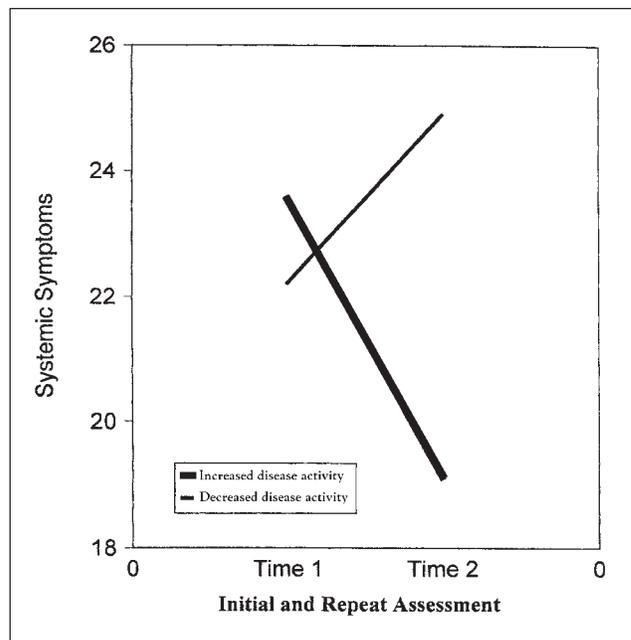


Figure 2) Changes in quality of life (Inflammatory Bowel Disease Questionnaire: systemic symptoms subscale) over time for patients whose disease activity improves and for those whose disease activity worsens

CDAI, which may have produced elevated correlations due to confounding of subjective ratings of disease activity and well-being. Also, the patient sample in the Irvine et al study may have had more active disease, which may also account for differences in findings. Second, past studies used different measures of well-being, some of which may not be adequately sensitive. For instance, the Drossman et al studies (8-10) relied on the Sickness Impact Profile, which is not specific to CD, and on subjective ratings that were not demonstrated to have adequate psychometric properties of reliability or validity. Third, no study except the present study used a within-subject design; for clinical purposes within-patient changes in disease activity (and well-being) are important to the gastroenterologist. Thus, data from within-subject designs are most likely to be helpful to practising clinicians.

Results of the present study indicate that the effect of disease activity on well-being depends on the context in which it is examined. When considered across different patients (eg, those seen in out-patient clinics), whether a patient's CD is highly active appears to be unrelated to well-being. In this context, it is likely that psychosocial factors that differ between patients play a much greater role in determining well-being than disease activity alone. The situation changes, however, when we examine changes over time in a given patient. In this context changes in disease activity over time do predict well-being, particularly for the experience of distressing bowel and systemic symptoms. These data are consistent with clinical experience and should encourage practising gastroenterologists to use objective measures of disease activity and to assess patient well-being systematically. These findings not only clarify those of previous stud-

ies, but also extend our knowledge by indicating that monitoring changes in disease activity is important in identifying determinants of quality of life for CD patients.

Knowing that changes in disease activity significantly affect quality of life is a useful finding. Unfortunately the clinical relevance of these changes is unknown because the IBDQ has yet to be normed. Our group is just completing a study collecting IBDQ data on as wide a range of IBD patients as possible so that clinical norms can be generated. Clinical norms allow us to interpret the significance of an individual's scores and of changes in scores. This then allows a more complete evaluation of the clinical significance of quality of life changes brought about by fluctuating disease activity.

Our results also indicate that, even when examined using a within-patient design, changes in disease activity are not associated with emotional or social functioning. Attending to CD activity alone is not sufficient. Emotional and social functioning must be assessed independently from disease-

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