

University of Groningen

## Assessing activity of pediatric Crohn's disease

Otley, A; Loonen, H; Parekh, N; Corey, M; Sherman, P M; Griffiths, A M

*Published in:*  
Gastroenterology

*DOI:*  
[10.1016/s0016-5085\(99\)70173-3](https://doi.org/10.1016/s0016-5085(99)70173-3)

**IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.**

*Document Version*  
Publisher's PDF, also known as Version of record

*Publication date:*  
1999

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Otley, A., Loonen, H., Parekh, N., Corey, M., Sherman, P. M., & Griffiths, A. M. (1999). Assessing activity of pediatric Crohn's disease: which index to use? *Gastroenterology*, 116(3), 527-31.  
[https://doi.org/10.1016/s0016-5085\(99\)70173-3](https://doi.org/10.1016/s0016-5085(99)70173-3)

### Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

### Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

*Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.*

# Assessing Activity of Pediatric Crohn's Disease: Which Index to Use?

ANTHONY OTLEY,\* HESTER LOONEN,<sup>†</sup> NAMITA PAREKH,\* MARY COREY,\*  
PHILIP M. SHERMAN,\* and ANNE M. GRIFFITHS\*

\*Division of Gastroenterology/Clinical Nutrition, The Hospital for Sick Children, Department of Pediatrics, University of Toronto, Toronto, Canada; and <sup>†</sup>Faculty of Medicine, University of Amsterdam, Amsterdam, The Netherlands

**Background & Aims:** The Pediatric Crohn's Disease Activity Index (PCDAI) is a multi-item measure that, in contrast to the adult-derived CDAI, includes linear growth and places less emphasis on subjectively reported symptoms but more on laboratory parameters of intestinal inflammation. This study compared the feasibility, validity, and responsiveness of PCDAI vs. CDAI in the assessment of Crohn's disease activity among pediatric patients. **Methods:** Eighty-one children and adolescents with Crohn's disease were studied. A gastroenterologist provided a categorical global assessment of disease activity as quiescent, mild, moderate, or severe after interview and physical examination. CDAI and PCDAI scores were calculated by an independent appraiser. **Results:** Mean values within each category for CDAI and PCDAI differed significantly between strata. PCDAI values were quiescent,  $6.8 \pm 6.6$ ; mild,  $18.7 \pm 7.3$ ; moderate,  $38.5 \pm 12.9$ ; and severe,  $54.2 \pm 14.0$ . CDAI values were quiescent,  $23.5 \pm 53.6$ ; mild,  $96.0 \pm 60.7$ ; moderate,  $184.5 \pm 97.0$ ; and severe,  $284.4 \pm 85.8$ . Individual scores showed less overlap between strata for PCDAI than for CDAI. PCDAI showed better correlation with serum orosomucoid and platelet count, laboratory parameters of inflammation not included in either index. **Conclusions:** Both PCDAI and CDAI reflect disease activity in pediatric Crohn's disease. PCDAI is better at discriminating between levels of disease activity.

No single clinical or laboratory parameter always accurately reflects activity of intestinal inflammation in Crohn's disease.<sup>1</sup> Hence, multi-item measures of disease activity have been developed for use in clinical trials.<sup>2-4</sup> The widely used Crohn's Disease Activity Index (CDAI) was developed for use in adult patients.<sup>2</sup> However, the CDAI does not consider aspects of Crohn's disease unique to children, most notably the potential for linear growth impairment as a manifestation of active disease. The Pediatric Crohn's Disease Activity Index (PCDAI) was developed and validated as an evaluative multi-item index for use in multicenter trials among

children and adolescents.<sup>5,6</sup> There is considerable overlap with the domains of the CDAI. The differences can be summarized as follows: the PCDAI discarded use of antidiarrheal agents; decreased the weighting of subjectively reported abdominal pain, general well-being, and diarrhea; increased the number of laboratory parameters; and added linear growth.

Clinical experience has suggested that the CDAI may underrepresent disease activity among pediatric patients<sup>7</sup> because of the heavy weighting on subjective reporting of symptoms and the tendency for many children and teenagers to minimize somatic complaints. Nevertheless, the CDAI is still used as the primary outcome variable in pediatric trials despite its lack of validation in pediatric populations and recognized difficulties in both feasibility and reproducibility even among adult patients with Crohn's disease. We compared the PCDAI with the CDAI in the assessment of intestinal inflammatory activity in children and adolescents with Crohn's disease. The aim was to provide data on feasibility, validity, significance of scores, and responsiveness that will guide investigators in the selection of a multi-item measure for future clinical trials in pediatric Crohn's disease.

## Materials and Methods

Between May 1997 and August 1997, children and adolescents younger than 18 years attending The Hospital for Sick Children for assessment of Crohn's disease were asked to complete a 7-day diary to facilitate computation of the CDAI.<sup>2</sup> The diagnosis of Crohn's disease was established in all patients according to conventional radiological, endoscopic, and histological criteria. The diary and an explanatory letter were mailed to families 1 week before their appointment. If patients did not receive the diary or forgot to complete it, they were asked to fill out the diary retrospectively.

At the hospital visit, each patient was interviewed by the

---

*Abbreviations used in this paper:* CDAI, Crohn's Disease Activity Index; ESR, erythrocyte sedimentation rate; PCDAI, Pediatric Crohn's Disease Activity Index.

© 1999 by the American Gastroenterological Association  
0016-5085/99/\$10.00

attending pediatric gastroenterologist (A.M.G. or P.M.S.) who provided a global assessment of disease activity as quiescent, mild, moderate, or severe on the basis of history and physical examination. Height and weight were measured and plotted on the standard growth charts of Tanner et al.<sup>8</sup>

The research assistant (H.L.) recorded patient demographic data and laboratory parameters. These included those required for calculation of the CDAI (hematocrit) and PCDAI (hematocrit, serum albumin, and erythrocyte sedimentation rate [ESR]), as well as serum orosomucoid and platelet count. Two versions of the CDAI were calculated for all patients: an original version<sup>2</sup> and one previously modified for use in pediatric patients.<sup>7</sup> In the modified CDAI, "use of opiates or Lomotil for diarrhea" is replaced by "number of days unable to go to school or participate in normal activities because of Crohn's disease." The concept of "standard weight" is not applicable to growing children and is therefore replaced by "the ideal weight for height" as determined from the growth curves of Tanner et al.<sup>8</sup> An additional measure of disease activity, the Harvey-Bradshaw index,<sup>4</sup> as modified by Myren et al.,<sup>9</sup> was calculated for all patients.

To assess the ability of the CDAI and PCDAI to detect a change in clinical status, patients attending the inflammatory bowel disease clinic for a second visit during the period of study had all assessments repeated. Disease activity was categorized as the same, somewhat improved, much improved, somewhat worse, or much worse, according to change in physician global assessment.

The study was approved by The Hospital for Sick Children Research Ethics Board.

### Statistical Analysis

All statistical analyses were performed using SAS (SAS Institute, Cary, NC).<sup>10</sup> Results are expressed as means  $\pm$  SD. Mean CDAI (original and modified) and PCDAI for the initial patient visit were calculated for all patients. Box-and-whisker plots were generated to show the distribution of PCDAI and CDAI scores within each category of disease severity, as assigned by physician global assessment. Analysis of variance (ANOVA) was used to compare means for each index across the four levels of global assessment. Pearson coefficients were used to assess correlation between CDAI and PCDAI scores, the Harvey-Bradshaw scores, and individual laboratory parameters of disease activity. Because the physician global assessment is an ordinal variable, these analyses were also performed using Spearman rank coefficients. PCDAI and CDAI were analyzed as the independent variables in a linear regression model to assess how well each was predictive of the physician global assessment. Because of the ordinal nature of the physician global assessment, ordinal logistic regression was applied to assess the predictability of the indices on global assessment. To compare the responsiveness over time of the two measures, we determined the correlation between the change in PCDAI scores against the change in CDAI scores for patients having a second visit during the study period.

### Results

The clinical characteristics of the 81 children and adolescents included in the study are summarized in Table 1. Four patients were evaluated at the time of their initial diagnosis of Crohn's disease. Twenty-seven of 81 patients (35%) forgot to bring the diary card to the hospital visit or had failed to complete it as instructed, necessitating completion by recall or completion prospectively from the time of the clinic visit. Based on physician global assessment, 36 patients had quiescent Crohn's disease at the time of evaluation. Activity of Crohn's disease was judged to be mild in 19 patients, moderate in 20, and severe in 6.

The modified CDAI correlated very closely with the original CDAI ( $r = 0.98$ ), and further comparisons with the PCDAI and with laboratory parameters are therefore reported for the original CDAI alone. As shown in Table 2, correlations between the CDAI, PCDAI, physician global assessment, and Harvey-Bradshaw index were excellent. However, the PCDAI showed a better correlation with laboratory parameters of intestinal inflammation, including serum orosomucoid, which does not factor in the PCDAI scale. Because hematocrit, ESR, and serum albumin are included in the calculation of the PCDAI and hematocrit alone in the CDAI, correlation coefficients with each individual laboratory parameter were recalculated with the specific laboratory parameter contribution removed from the index. The three correlation coefficients of the three revised PCDAI (PCDAI without hematocrit, PCDAI without ESR, and PCDAI without albumin) with hematocrit, ESR, and albumin predictably lessened but still remained significant. The correlation coefficient between the revised CDAI (CDAI without hematocrit) and hematocrit was no longer significant. The results obtained using Spearman rank coefficients yielded similar results and are not reported.

Prediction of physician global assessment was more reliable for the PCDAI ( $R^2 = 0.75$ ) than the original CDAI ( $R^2 = 0.59$ ) by regression analysis. When both indices were analyzed simultaneously, the CDAI did not

**Table 1.** Patient Characteristics at Baseline

Total number of subjects	81
Sex (M/F) <sup>a</sup>	48 (59.3)/33 (40.7)
Age (yr) <sup>b</sup>	14.1 $\pm$ 2.4
Age range (yr)	5.1-18.0
Disease distribution <sup>a</sup>	
Small bowel only	28 (34.6)
Small and large bowel	41 (50.6)
Large bowel only	12 (14.8)
Previous surgery <sup>a</sup>	14 (18.2)

<sup>a</sup>Values are expressed as n with the percentage in parentheses.

<sup>b</sup>Values are expressed as mean  $\pm$  SD.

**Table 2.** Correlations Between Indices and Laboratory Parameters

	PCDAI	Original CDAI	Modified CDAI	Harvey-Bradshaw	ESR	Orosomucoid	Albumin	Platelet count	Hematocrit
Global assessment	0.86	0.77	0.76	0.72	0.50	0.54	-0.60	0.37	-0.37
PCDAI		0.86	0.86	0.84	0.58	0.57	-0.68	0.24	-0.41
Original CDAI			0.98	0.91	0.45	0.34	-0.60	0.15 <sup>a</sup>	-0.40
Modified CDAI				0.93	0.40	0.32	-0.54	0.10 <sup>b</sup>	-0.30
Harvey-Bradshaw					0.41	0.40	-0.46	0.02 <sup>c</sup>	-0.26

<sup>a</sup>*P* = 0.200.

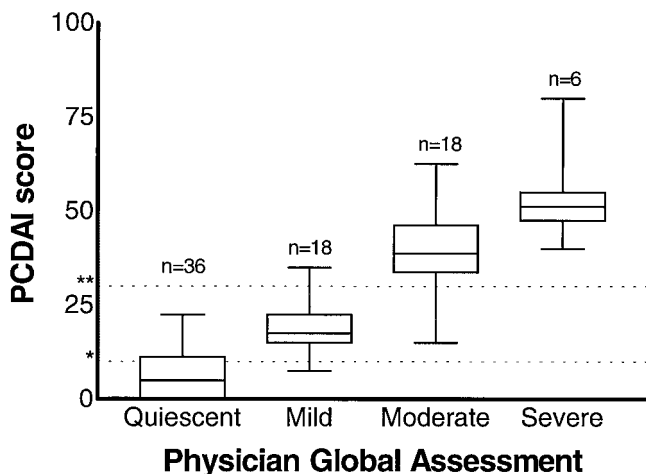
<sup>b</sup>*P* = 0.394.

<sup>c</sup>*P* = 0.849; for all other values, *P* < 0.05.

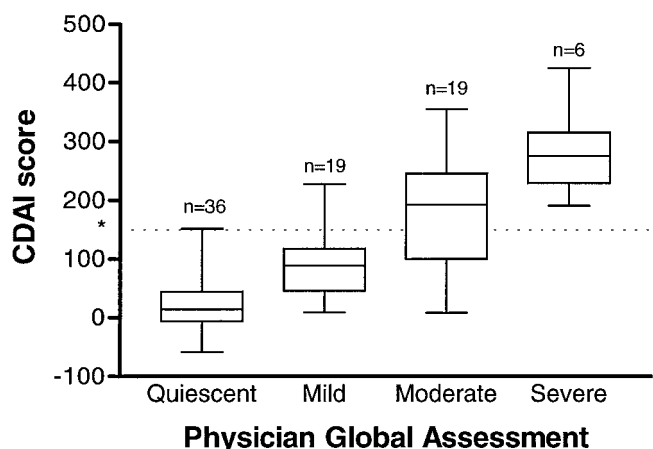
add to the predictiveness of the PCDAI model ( $R^2 = 0.75$ ). CDAI and PCDAI values within each stratum of disease activity (determined by physician global assessment) are shown in box-and-whisker plots in Figures 1 and 2. The mean values for CDAI and PCDAI differed significantly between strata ( $F = 37.4$  and  $P = 0.0001$  for original CDAI;  $F = 76.4$  and  $P = 0.0001$  for PCDAI). However, as shown in Figures 1 and 2, there was less overlap for PCDAI scores between patients in different categories of disease activity. When the previously determined cut scores for the two indices were used, there was a greater number of misclassified subjects with the CDAI than the PCDAI. Roughly 80% of children judged to have mild disease and 35% of those judged to have moderate disease had CDAI values of <150, scores indicative of inactive disease in adults (Figure 2).<sup>2</sup> Children judged by the physician to have mild or moderate disease activity, who were misclassified by the CDAI, had a significantly ( $P < 0.0001$ ) lower mean value for the subjective symptom diary component ( $69.5 \pm 45.1$ ) than those in the same global assessment

category who were correctly classified by the CDAI ( $192.3 \pm 82.9$ ). When the results were compared for patients who completed the CDAI diary prospectively with those who completed it by recall, no significant difference was noted in the percentage of misclassified patients (data not shown).

Using physician global assessment of disease activity as the gold standard, Hyams et al.<sup>5</sup> determined cut scores for the PCDAI, which correctly classified the greatest number of patients:  $\leq 10$  for inactive disease, 11–30 for mild disease, and  $> 30$  for moderate/severe disease. In the present study, again using the physician global assessment as the gold standard, 27 (75%) of 36 patients with quiescent disease, 13 (72%) of 18 patients with mild disease, and 20 (83%) of 24 children with moderate or severe disease were correctly classified by the previously recommended PCDAI cut scores. Focusing on the discrimination between quiescent and mild disease and using the data from our study, a receiver operating characteristic curve was calculated to select a cut score that would provide optimal sensitivity and specificity. The previously recommended cut score of  $\leq 10$  gave a



**Figure 1.** Box-and-whisker plot of PCDAI scores among patients categorized by physician global assessment of disease activity. The box shows the 25th percentile, median, and 75th percentile. The whiskers show the range of the data. The PCDAI score could not be calculated (laboratory value missing) for 3 patients (1 mild, 2 moderate). \*Cut score for inactive disease (<10).<sup>5</sup> \*\*Cut score for moderate/severe disease (>30).<sup>5</sup>



**Figure 2.** Box-and-whisker plot of CDAI scores among patients categorized by physician global assessment of disease activity. The box shows the 25th percentile, median, and 75th percentile. The whiskers show the range of the data. The CDAI score could not be calculated (diary not available) for 1 patient (moderate). \*CDAI cut score for inactive disease (<150).<sup>2</sup>

sensitivity of 75% and a specificity of 90.5%.<sup>5</sup> The best discrimination occurred with a cut score of <15, whereby the sensitivity increased to 83% even though the specificity remained unchanged at 90.5%.

Seventeen patients were reviewed at a second visit. PCDAI and CDAI were similar in reflecting change over the short term. The correlation between the adult CDAI difference scores and PCDAI difference scores was strong ( $r = 0.92$ ;  $P < 0.0001$ ).

## Discussion

The choice of a multi-item measure for use as a primary outcome variable in clinical trials should be based on evidence of its feasibility, reliability, validity, and responsiveness.<sup>11</sup> When the PCDAI was originally validated,<sup>5</sup> PCDAI scores were compared with physician global assessment and with the Harvey-Bradshaw index but not with the CDAI, the instrument most often used to quantitate disease activity. The results of the current study support the preferential use of the PCDAI vs. the CDAI as a multi-item measure of disease activity in all future clinical trials in pediatric Crohn's disease.

The benefits of the PCDAI with respect to feasibility are clear-cut. The PCDAI is easy to complete at the time of a patient's visit. The children and adolescents in our study showed difficulties prospectively completing the 7-day CDAI diary card before a clinic visit. In the context of a randomized controlled trial, parents are often hesitant to delay initiation of treatment so that the CDAI can be calculated before study entry. Obviation of such a record will facilitate patient recruitment into clinical research protocols.

The reliability of an instrument refers to its reproducibility.<sup>12</sup> Measurement variability is present when different results are obtained on repeated measurement of the same entity. An instrument cannot be valid unless it is reproducible. We did not reassess the reliability of the PCDAI because a previous assessment indicates that it is good. In the study by Hyams et al.,<sup>5</sup> 131 patients at 14 different hospitals were evaluated by a pair of pediatric gastroenterologists.<sup>5</sup> Each physician evaluating a patient was blinded to the assessment of the other examining physician. There was excellent correlation between two physicians using the total PCDAI to assess the same patient under the same circumstance (Spearman rank correlation coefficient, 0.86), despite weaker correlation for individual items, notably abdominal examination (Kendall's  $\tau$ , 0.64).<sup>5</sup> A study among adult patients has documented that CDAI scores are not reproducible.<sup>13</sup> Considerable scatter of individual CDAI values was observed by deDombal et al.<sup>13</sup> even among the most

experienced clinicians and after intensive discussion regarding the use of the CDAI.

Comparisons of the PCDAI and the CDAI show why the former tool is more reliable. The PCDAI includes more objective data (laboratory parameters, height, and weight), which are less subject to uninformative variability. Subjective variables contribute only 20% to the maximal possible score of 100 on the PCDAI but roughly 39% to the CDAI. Furthermore, in the CDAI, individual observer ratings of items are multiplied by coefficients, thereby making minor discrepancies much larger for heavily weighted items.<sup>13</sup>

Validity addresses the issue of the degree of confidence that can be placed in inferences drawn from scores on scales.<sup>14</sup> A high PCDAI score should imply a high level of intestinal inflammatory activity and a low-score quiescent disease. Validity assessment begins with careful qualitative appraisal of an instrument to consider whether the included items truly contribute to what is being measured. The domains of the PCDAI chosen to constitute disease activity are abdominal pain, altered stool pattern, general well-being, weight, linear growth, perianal disease, extraintestinal manifestations, abdominal examination, and laboratory parameters of inflammation. There are some inappropriate inclusions. Perianal disease often runs a course separate from the intestinal inflammation and requires its own treatment. A separate index of perianal disease activity has been proposed.<sup>15</sup> Secondly, although linear growth is an important parameter by which to judge activity of disease in children, height changes more slowly than other parameters included in the index. Inclusion in an index to be evaluative over a relatively short interval, as in most trials of drug efficacy, may be problematic.

There is no true gold standard of Crohn's disease activity against which to validate either the PCDAI or CDAI. The present study confirms the observations of Hyams et al.<sup>5</sup> that the PCDAI is strongly correlated with physician global assessment. Although the CDAI also correlates well with physician global assessment, it more often incorrectly classifies disease activity. Patients with disease of mild and even moderate severity may score in the quiescent range if they fail to report symptoms in the heavily weighted diary component of the measure. The correlation of the PCDAI with laboratory parameters was superior to that of CDAI. Given that all laboratory measures of Crohn's disease activity are imperfect, excellent correlations would not be expected.<sup>16,17</sup>

This study provides additional data indicating the significance of numerical values, information that is essential in the selection of inclusion and exclusion criteria and in defining clinical remission in efficacy

trials. The data support the originally specified PCDAI value of  $>30$  for moderate and severe disease. The requirement of a PCDAI of  $\leq 10$  as an indicator of inactive disease appears to be too stringent. A value of  $<15$  could prove to be superior.

One performance characteristic of the PCDAI that has not been examined previously is its responsiveness. Responsiveness, "the ability to detect clinically important change," is extremely important for an evaluative instrument such as the PCDAI and is best studied in the context of a randomized controlled trial.<sup>18</sup> The ability to detect a treatment effect is assessed because change over and above a control group is measured. Our study provides initial evidence, in a subgroup of patients assessed longitudinally, that the PCDAI does change even in a short period of time when the disease activity changes. This is reassuring because of the concerns about inclusion of linear growth in an index that is to be evaluative in drug trials of typically 4–6 weeks' duration. One can accept this item as an inappropriate inclusion if responsiveness of the measure is nevertheless good.

Although the PCDAI was validated previously as an evaluative instrument, pediatric investigators have been slow to adopt it in the assessment of disease activity. Our study indicates that, in comparison to the CDAI, the PCDAI is a more feasible multi-item measure that more validly reflects the severity of intestinal inflammation in pediatric patients. We have provided further information regarding significance of individual scores and evidence in support of the tool's responsiveness. Future trials in children and adolescents with Crohn's disease should use the PCDAI as an outcome variable.

## References

1. Bartholomeusz FDL, Shearman DJC. Measurement of activity in Crohn's disease. *J Gastroenterol Hepatol* 1989;4:81–94.
2. Best WR, Beckett JM, Singleton JW, Kern F. Development of a Crohn's disease activity index. National Cooperative Crohn's Disease Study. *Gastroenterology* 1976;70:439–444.
3. Van Hees PAM, Van Elteren PH, Van Lier HJJ, Van Tongeren JHM. An index of inflammatory activity in patients with Crohn's disease. *Gut* 1980;21:279–286.
4. Harvey RF, Bradshaw JM. A simple index of Crohn's disease activity. *Lancet* 1980;1:514.
5. Hyams JS, Ferry G, Mandel FS, Gryboski JD, Kibort PM, Kirschner BS, Griffiths AM, Katz AJ, Grand RJ, Boyle JT, Michener WM, Levy JS, Lesser ML. Development and validation of a pediatric Crohn's disease activity index. *J Pediatr Gastroenterol Nutr* 1991;12:439–447.
6. Hyams JS, Mandel F, Ferry GD, Gryboski JD, Kibort PM, Kirschner BS, Griffiths AM, Katz AJ, Boyle JT. Relationship of common laboratory parameters to the activity of Crohn's disease in children. *J Pediatr Gastroenterol Nutr* 1992;14:216–222.
7. Seidman EG, Griffiths AM, Jones A, Issenman R, The Canadian Paediatric Crohn's Disease Study Group. Semielemental diet versus prednisone in the treatment of active Crohn's disease in children and adolescents (abstr). *Gastroenterology* 1993;104:A778.
8. Tanner JM, Whitehouse RH, Takaishi M. Standards from birth to maturity for height, weight, height velocity, and weight velocity: British children, 1965. I. *Arch Dis Child* 1966;41:454–471.
9. Myren J, Bouchier IAD, Watkinson G, Softley A, Clamp SE, deDombal FT. The O.M.G.E. multinational inflammatory bowel disease survey 1976–1982. A further report on 2,657 cases. *Scand J Gastroenterol* 1984;95(suppl):1–27.
10. SAS Institute, Inc. SAS/STAT user's guide, release 6.10 edition. Cary, NC: SAS Institute, Inc., 1992.
11. Wright JG, McLeod RS, Lossing A, Walters BC, Hu X. Measurement in surgical clinical research. *Surgery* 1996;119:241–244.
12. Streiner DL, Norman GR. Reliability. In: Health measurement scales: a practical guide to their development and use. New York: Oxford, 1995:104–128.
13. deDombal FT, Softley A. IOIBD report no 1: observer variation in calculating indices of severity and activity in Crohn's disease. *Gut* 1987;28:474–481.
14. Felson DT, Anderson JJ, Boers M, Bombardier C, Chernoff M, Fried B, Furst D, Goldsmith C, Kieszak S, Lightfoot R, Paulus H, Tugwell P, Weinblatt M, Widmark R, Williams HJ, Wolfe F. The American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials. *Arthritis Rheum* 1993;36:729–740.
15. Irvine EJ, Stoskopf B, Donnelly M. A disease activity index for patients with perianal Crohn's disease. *J Clin Gastroenterol* 1995;20:27–32.
16. Andre C, Descos L, Landais, Fermanian J. Assessment of appropriate laboratory measurements to supplement the Crohn's disease activity index. *Gut* 1981;22:571–574.
17. Macfarlane PI, Miller V, Wells F, Richards B. Laboratory assessment of disease activity in childhood Crohn's disease and ulcerative colitis. *J Pediatr Gastroenterol Nutr* 1986;5:93–96.
18. Guyatt GH, Deyo RA, Charlson M, Levine MN, Mitchell A. Responsiveness and validity in health status measurement: a clarification. *J Clin Epidemiol* 1989;42:403–408.

---

Received June 25, 1998. Accepted November 30, 1998.

Address requests for reprints to: Anne M. Griffiths, M.D., Division of Gastroenterology/Nutrition, The Hospital for Sick Children, 555 University Avenue, Toronto, Ontario, Canada M5G 1X8. Fax: (416) 813-6531.

Supported by a Duncan Gordon Research Fellowship and a Janssen Ortho Fellowship (to A.O.).

Presented at both the 1998 annual meeting of the Canadian Association of Gastroenterology in Banff, Alberta, Canada, and the 1998 joint meeting of the ESPGAN-NASPGN in Toulouse, France, and published in abstract form (*Can J Gastroenterol* 1998;12[suppl A]:118A; *J Pediatr Gastroenterol Nutr* 1998;26:555).