

Health-related Quality of Life in Patients with Ulcerative Colitis After a 10-year Disease Course: Results from the IBSEN Study

Marte L. Hoivik, MD,* Bjorn Moum, PhD,* Inger C. Solberg, PhD,[†] Milada Cvancarova, MSc,[‡] Ole Hoie, PhD,[§] Morten H. Vatn, PhD,^{||} and Tomm Bernklev, PhD[¶], for the IBSEN Study Group

Background: Ulcerative colitis (UC) negatively affects health-related quality of life (HRQoL), but population-based and long-term data on this topic are scarce. Our aim was to determine the HRQoL in UC patients after a 10-year disease duration.

Methods: UC patients from a population-based inception cohort met at a prescheduled 10-year follow-up visit. In addition to a clinical examination, interview, and blood samples, the patients completed the Short Form 36 (SF-36) and the Norwegian Inflammatory Bowel Disease Questionnaire (N-IBDQ). The SF-36 scores were compared to scores from a general population sample using one-sample *t*-tests. Standardized scores were calculated and interpreted according to Cohen's effect size index. The associations between relevant clinical and demographic factors and HRQoL were examined through linear regression analyses.

Results: A total of 196 patients completed the HRQoL questionnaires (response rate: 80%), of whom 54% were women; the mean age of all patients was 48 years (range: 22–86). The SF-36 scores were comparable to those of the general population except for lower scores in the General Health dimension. The SF-36 scores were significantly lower in the presence of current symptoms, in patients who had used corticosteroids, and in patients who reported not working. Overall N-IBDQ scores were equivalent to scores of patients in remission. Female gender, work status (not working), current symptoms, and smoking were associated with significantly lower N-IBDQ scores.

Conclusions: SF-36 scores were not reduced compared to the general population sample. The presence of current symptoms, the use of corticosteroids, work status (not working), female gender, and smoking had a negative impact on HRQoL.

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Key Words: ulcerative colitis (UC), health-related quality of life (HRQoL), population-based, minimal clinically important difference (MCID), epidemiology

Ulcerative colitis (UC) is a chronic inflammatory bowel disease with a heterogeneous and unpredictable disease course. Previous studies have shown that health-related quality of life (HRQoL) is reduced in UC patients compared to the general population.^{1,2} Several factors contribute to this reduction, the most consistent of which is disease activity.^{3–5} Medical treatment (corticosteroids and

immunosuppressives),⁶ extraintestinal manifestations,^{7,8} and work status^{9,10} also seem to be associated with reduced HRQoL; however, for factors such as gender and smoking, the results are somewhat inconsistent.^{5,11} Both psychiatric¹² and somatic^{11,13} comorbidities can reduce the HRQoL of patients with UC. Psychological factors, such as perceived stress and negative coping mechanisms, have also been suggested as determinants of HRQoL.^{4,14}

Despite an increasing number of studies on HRQoL in patients with UC, there are still important shortages in this field of research. Most studies are based on selected patient populations and vary in design, which makes generalization of the results problematic.¹⁵ The disease duration is short in the majority of the studies, and thus we know little about how UC affects HRQoL over a longer time span. The interpretation of statistical HRQoL results is debated; the use of anchor-based minimal clinically important changes (MCID) has been proposed as a means of assessing the clinical relevance of results.^{16,17}

The IBSEN study (Inflammatory Bowel in South Eastern Norway) is a population-based inception cohort of IBD patients.^{18–20} The study was designed in order to describe the natural course of inflammatory bowel disease (IBD). In addition to comprehensive clinical data, the study

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From the *Department of Gastroenterology, Oslo University Hospital, Norway, and the Institute of Clinical Medicine, University of Oslo, Norway, [†]Department of Gastroenterology, Oslo University Hospital, Norway, [‡]National Resource Center for Late Effects, Department of Oncology, Oslo University Hospital and University of Oslo, Norway, [§]Department of Internal Medicine, Sørlandet Hospital HF, Arendal, Norway, ^{||}EpiGen Institute, Akershus University Hospital and the Department of Gastroenterology, Oslo University Hospital, and the Institute of Clinical Medicine, University of Oslo, Norway, [¶]Research and Development Department, Telemark Hospital HF, Skien, Norway.

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Reprints: Marte L. Hoivik, MD, Department of Gastroenterology, Oslo University Hospital, Aker Hospital, P.O. Box 4959 Nydalen, 0424 Oslo, Norway (e-mail: marte.hoivik@medisin.uio.no).

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has also focused on patient-reported outcomes, including HRQoL. The group has previously published HRQoL data from the 5-year follow-up, where they found that HRQoL was reduced in UC patients compared to the Norwegian background population and that in addition to disease activity, the use of corticosteroids and immunosuppressive drugs, relapse, extraintestinal manifestations, work disability, unemployment, and sick leave were also associated with reduced HRQoL.^{2,6-9}

The primary aim of this study was to determine the HRQoL in UC patients after a 10-year disease course and to compare the results with a general population sample. Secondary aims were to identify demographic and clinical variables with a significant impact on the patients' HRQoL after a 10-year disease duration.

MATERIALS AND METHODS

Study Design and Study Population

From 1 January 1990 to 31 December 1993, all newly diagnosed cases of IBD or possible IBD in four well-defined areas in south-eastern Norway (the counties of Oslo, Østfold, Telemark, and Aust-Agder) were registered prospectively; 843 patients were included in this inception cohort. The cohort has been followed comprehensively for 10 years with scheduled follow-up visits at 1, 5, and 10 years (± 1 year) after diagnosis. The organization of the cohort, the diagnostic criteria, and the clinical follow-up, including HRQoL, are described in detail elsewhere.^{2,6,7,9,19-22} The present HRQoL study was conducted as a part of the 10-year follow-up study, including the subgroup of UC patients recruited between 1 October 1991 and 31 December 1993.

Data Collection

The 10-year follow-up visit consisted of a patient-reported questionnaire including two HRQoL questionnaires (the Norwegian Inflammatory Bowel Disease Questionnaire [N-IBDQ] and the Short Form 36 [SF-36]), a structured interview, a review of hospital records, a clinical examination, laboratory tests, and when indicated, an ileocolonoscopy and small bowel enema. The patient-reported questionnaires were administered during the hospital visits and were completed before the clinical interview and examination. The questionnaires were checked by the investigator or study nurse to ensure that all questions had been answered.

HRQoL Questionnaires

The IBDQ is a disease-specific questionnaire that consists of 32 items scored on a seven-point Likert scale.²³ Scores are given for each dimension or as a total score (32–224 points). Higher scores indicate better HRQoL. The IBDQ has been translated into Norwegian (N-IBDQ) and validated in the IBSEN cohort.²⁴ This validation process yielded a different factor structure than the original, with five dimensions instead

of four: stool consistency and pattern (B1), emotional function (EF1), bowel pain and discomfort (B2), social function (SF), and worries (EF2). The total score is nevertheless the same in different versions of the questionnaire and can therefore be used in comparisons between studies.

The SF-36 is a generic HRQoL questionnaire designed to assess functional status, well-being, and general perception of health. The questionnaire has been shown to have a high validity and reliability²⁵⁻²⁸ and is one of the most frequently used generic HRQoL instruments. The SF-36 consists of 36 items and one multi-item scale for each of eight conceptual domains. Higher scores indicate better HRQoL. The domains are as follows: Physical Functioning (PF, 10 items), Role limitation due to Physical health (RP, 4 items), Bodily Pain (BP, 2 items), General Health (GH, 5 items), Vitality (VT, 4 items), Social Functioning (SF, 2 items), Role limitations due to Emotional problems (RE, 3 items), and Mental Health (MH, 5 items). A physical and a mental component summary score (PCS and MCS) can be computed, but this is conditioned by norm-based, country-specific conversion factors. The SF-36 has been translated and validated in Norwegian. It has previously been demonstrated that the SF-36 has satisfactory psychometric properties in our IBD population.² The Norwegian SF-36 population sample was described by Loge and Kaasa.²⁹ The sample was selected at random and retrieved from the National Population Register. The subjects received questionnaires sent by regular mail. The response rate was 67% (2323 persons). From this population, we used overall scores adjusted for age, gender, and level of education³⁰ and crude, gender-stratified scores.²⁹

Patient-reported Symptoms and Demographic Data

Current IBD symptom severity was patient-reported with a recall period of 2 weeks prior to the follow-up visits and were grouped into four categories: (1) no symptoms, (2) mild symptoms (do not interfere with everyday activities), (3) moderate symptoms (interfere with everyday activities, may result in sick leave), or (4) severe symptoms (unable to perform everyday activities, on sick leave or hospitalized). Other patient-reported information included the following: current smoking status, defined as yes (more than one cigarette daily) or no; marital status (single, married/cohabitant, divorced, widower); educational status (grouped according to the Norwegian educational system as (1) second level, first stage [≤ 9 years], (2) second level, second stage [10–12 years], or (3) third level [>12 years]); and work status (patients were grouped as either working [including students and pupils] or not working [including unemployed, work disability, pensioners, housewives]).

Structured Interview and Patient Records

Information on relapse and medication was collected in the structured interviews as well as through a review of the patients' hospital records. Relapse was defined as "a change

in the clinical condition that required more aggressive medical treatment or surgery” and was further classified based on whether it had occurred during the year preceding the 10-year follow-up (yes/no); the number of relapses that had occurred during the year preceding the 10-year follow-up (none, 1–2 relapses, 3–5 relapses, or more than 5 relapses) was also recorded. The use of systemic corticosteroids was recorded as yes/no during the year preceding the 10-year follow-up, whereas the use of immunomodulators, including azathioprine (AZA) and 5-aminosalicylic acid (5-ASA), was recorded as yes/no during the last 5 years. Information on the use of anti-tumor necrosis factor (TNF) inhibitors was recorded as any use at any time since the diagnosis. During the interview, patients were asked to categorize the clinical course of their disease from the time of diagnosis to the present 10-year follow-up according to predefined curves depicting the following: (1) remission or mild severity of intestinal symptoms after an initial peak of activity; (2) increases in the severity of intestinal symptoms after an initial period of low activity; (3) chronic continuous activity; or (4) chronic intermittent activity.

Assessment of Disease Distribution

An assessment of phenotype/distribution of inflammation was performed using ileocolonoscopy. Proctitis was defined as mucosal changes in the rectum up to 15 cm from the anus, left-sided colitis was defined as mucosal changes up to the splenic flexure, and extensive colitis was defined as inflammation beyond the splenic flexure.

Statistical Analyses

The distributions of all dimensional scores in the SF-36 and the N-IBDQ were checked for normality. Because some of the dimensions had a skewed distribution, univariate analyses were executed with both standard parametric methods (Pearson’s correlation, *t*-test, and one-way analysis of variance [ANOVA]) and nonparametric methods (Spearman, Mann–Whitney *U* and Kruskal–Wallis tests). However, this did not change the results with regard to statistical significance and further analyses were performed with parametric methods.

Mean scores were adjusted for age, gender, and level of education when appropriate using ANCOVA (analysis of covariance); hence, they are presented as estimated marginal means with 95% confidence intervals. The comparison of SF-36 scores to normal population scores was performed by transforming the original data to standard difference scores (*s*-scores = [mean patient score minus mean population score] divided by population standard deviation) and one-sample *t*-tests. *S*-scores were evaluated according to Cohen’s effect size index, where <0.2 indicated no difference, 0.2–0.5 indicated a small difference, 0.5–0.8 indicated a moderate difference, and >0.8 indicated a large difference.³¹

We used multiple linear regression analysis (enter method) to assess the impact of different demographic and clinical variables on HRQoL scores. The choice of variables

to be included in the multiple linear regression model was based on results from the univariate analyses on relevant variables used in articles available in the literature^{2,6,7,9} as well as on variables that were chosen on the basis of the writer’s assessment of clinical importance. Variables that in the univariate analyses yielded a $P < 0.20$ and variables that were deemed clinically important were included in further analyses. We examined possible interactions between the included variables. Because of multiple testing, the significance level was set to 1% in all analyses. All statistical analyses were performed with the Predictive Analytics Software PASW (v. 18.0; IBM, Somers, NY).

Ethical Requirements

The study was approved by the regional Ethics Committee and the Norwegian Data Inspectorate. Confidentiality of patient identity and records was maintained using guidelines from the Norwegian Ministry of Health. The study was conducted in accordance with the Declaration of Helsinki.

RESULTS

At the 10-year follow-up, 305 patients included between 1 October 1991 and 31 December 1993 had a definite UC diagnosis; 33 (10.8%) had died and 18 (5.9%) were lost to follow-up. For 10 patients clinical data were collected with telephone interviews and/or hospital records. The remaining 244 patients met at a prescheduled hospital visit. Of the 244 patients, 196 completed the SF-36 (response rate 80.3%) and 204 completed the N-IBDQ (response rate 81.6%). Demographic and clinical characteristics of the study population and the reference population are shown in Table 1.

The patients who died were older and those who were lost to follow-up were younger than the patients who were included in this study, with mean ages at diagnosis of 73, 26, and 36 years, respectively ($P < 0.001$). Patients who had died or were lost to follow-up did not differ from the rest of the cohort with regard to gender, disease distribution at inclusion, or smoking habits at inclusion (data not shown).

Among those attending the prescheduled hospital visit ($n = 244$), patients who completed the HRQoL questionnaires were younger than those who did not (mean age at 10-year follow-up, 48 vs. 55, $P = 0.02$). Except for this one factor, we found no differences between the groups with regard to gender, disease distribution, disease duration, symptom severity, colectomy, relapse, use of systemic steroids, smoking habits, educational status, marital status, or employment status.

Compared to the reference population, the patients in our cohort were somewhat older (48 vs. 45 years), had a higher level of education, and were more often married (Table 1).

TABLE 1. Demographic and Clinical Characteristics of Study Population and Reference Population

		Study Population (n = 196)	General Population (n = 2323)
Age	Years, mean (SD)	48 (13)	45 (17)
Gender	% women	54%	51%
Educational status (missing, n=25)	≤9 years	12%	27%
	10 to 12 years	46%	45%
	>12 years	42%	28%
Marital status (missing, n=9)	Single	9%	20%
	Married/cohabitant	81%	70%
	Divorced	5%	5%
	Widow(er)	5%	5%
Working status (missing, n=5)	Working/student	72%	
	Unemployed, pensioner, disability or other	28%	
Smoking (missing, n=3)	Yes	21%	
Distribution	Proctitis	20%	
	Left sided	36%	
	Extensive	44%	
Relapse last year	Yes	32%	
Steroids last year	Yes	13%	
5-ASA last 5 years	Yes	53%	
Azathioprine last 5 years	Yes	4%	
Disease course	Decreasing (1)	55%	
	Increasing (2)	0.5%	
	Chronic continuous (3)	8%	
	Chronic intermittent (4)	36%	
Current symptom severity	None	48%	
	Mild	45%	
	Moderate/severe	6%	
Colectomized	Yes	7%	
Disease duration	Months median (range)	122 (107–146)	

Age given as mean with standard deviation, disease duration as median and range, while all other variables are given as percentage of total.

Medication

In all, 13% of the patients included in the study had used corticosteroids at some time in the preceding year, whereas 53% had used 5-ASA during the previous 5 years. Only eight (4%) patients had used AZA during the previous 5 years (Table 1). No patients had received anti-TNF inhibitors.

Relapse and Patient-reported Symptom Burden

In all, 32% of the included patients experienced one or more relapses during the last year of follow-up, with no difference between genders; 45% reported current symptoms that were mild, whereas only 6% reported moderate to severe current symptoms. In the group with one or more relapses during the preceding year, the proportions of males and females reporting current symptoms (mild, moderate, or severe) were very similar: 82% of women and 80% of men reported experiencing current symptoms. In the group with no relapses in the preceding year, 52% of the females and 28% of the males reported current symptoms ($P = 0.005$).

HRQoL Results

N-IBDQ

Fourteen patients who had undergone colectomies were excluded from the analyses because the N-IBDQ includes items that are not relevant for colectomized patients.

Men had significantly higher scores than women in terms of both total N-IBDQ scores and in the emotional dimension (Table 2). In age- and gender-adjusted analyses, we scrutinized the effect of relapse, use of medication (corticosteroids, 5-ASA and AZA), current symptoms, disease course, work status, smoking, disease distribution, education, and marital status. Relapse, use of corticosteroids, current symptoms, chronic intermittent or chronic continuous disease course, smoking, and work status (not working) significantly reduced total N-IBDQ scores ($P < 0.01$) (Fig. 1).

The variables age, gender, relapse, current symptoms (dichotomized as yes = mild, moderate or severe symptoms or no = no symptoms), use of corticosteroids, work status, and smoking fulfilled the set criteria for inclusion in the linear regression model for total N-IBDQ scores. Disease course could not be included due to limited numbers

TABLE 2. IBDQ Dimensional Scores

	All Patients ^a (n = 190)	Women ^b (n = 100)	Men ^b (n = 90)
Total	186 [182 to 191]	180 [173 to 186]	193 [186 to 199]*
B1	44 [43 to 45]	42 [41 to 44]	45 [43 to 46]
E1	59 [57 to 61]	55 [53 to 58]	62 [59 to 64]*
SF	25 [25 to 26]	25 [24 to 26]	26 [25 to 27]
B2	28 [27 to 29]	27 [25 to 28]	29 [27 to 30]
E2	25 [25 to 26]	25 [24 to 26]	26 [25 to 27]

Adjusted means with 95% confidence intervals.

^aAdjusted for age and gender.

^bAdjusted for age.

*Statistically significant difference between male and female, $P < 0.01$.

B1: stool consistency and pattern, E1: emotional function,

SF: social function, B2: bowel pain and discomfort, E2: worries.

of patients in two of the categories. The linear regression analysis was further stratified by gender and relapse because there was a significant interaction between these two variables (Table 3). In women, relapse and current symptoms reduced scores significantly, while work status (not working) and current symptoms reduced N-IBDQ scores in men. In patients with no relapse, smoking, work status (not working), and current symptoms reduced total N-IBDQ scores significantly, while only current symptoms reduced N-IBDQ scores in patients with relapse.

SF-36

Because data on adjusted scores in the reference population was only available for patients who were younger than 75 years of age,³⁰ we excluded the 10

patients who were 75 years of age or older from this analysis. The SF-36 dimensional scores adjusted for age, gender, and education were comparable to the scores of the general population sample (Table 4). The only significant difference was seen in the General Health dimension, where the general population had an absolute score that was 13 points higher than the study population ($P < 0.001$). The only dimension with a significant gender difference was Bodily Pain (absolute difference 15 points, $P < 0.01$).

We did observe differences within gender in the S-scores (Fig. 2); compared to women in the general population, women with UC reported small to moderate negative effects in all but the Physical and Social Functioning dimensions, with the most noticeable difference being in the General Health dimension. The only difference between men in the general population and men with UC was found in the General Health dimension.

Figure 3 depicts SF-36 dimensional scores adjusted for age, gender, and education in relevant variables. Statistically significant differences between categories were found in seven of eight dimensions for the variables of current symptoms and work status. Use of systemic steroids affected Physical Function, Role Physical, and General Health, while patient-reported disease course affected General Health, Social Function, and Role Emotional. Relapse only affected the Role Physical dimension, while neither smoking, disease distribution, marital status, nor educational status affected the scores.

The variables age, gender, current symptoms (dichotomized as yes = mild, moderate or severe symptoms or no = no symptoms), use of cortico steroids, work status,

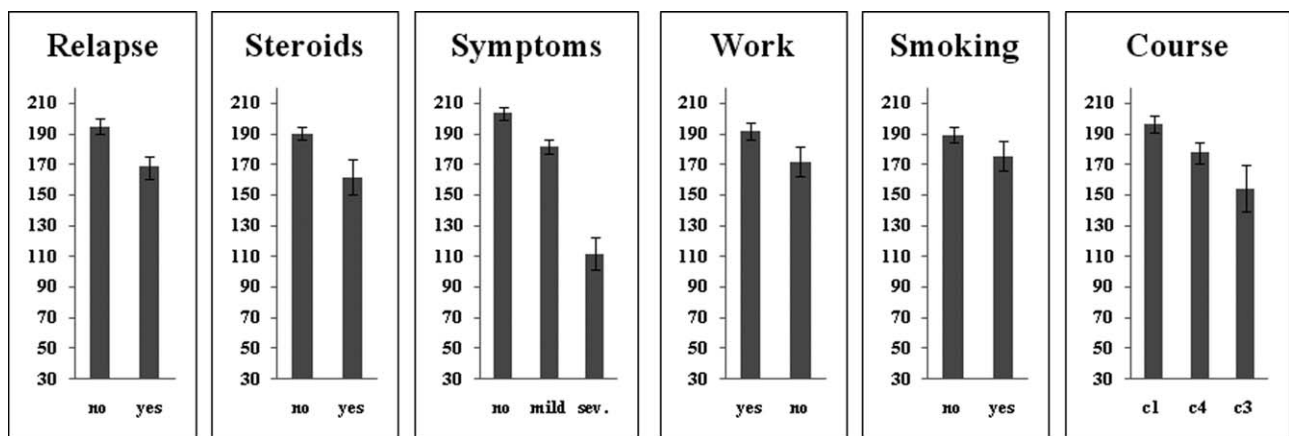


FIGURE 1. IBDQ total scores. Estimated mean age and gender adjusted IBDQ total scores with 95% confidence intervals, $P < 0.01$ for all comparisons. Relapse: Relapse last year, no = no relapse, yes = one or more relapses. Steroids: Use of corticosteroids last year, no = no use of corticosteroids last year, yes = one or more treatments with corticosteroids last year. Symptoms: Patient-reported society symptom last 14 days, no = no symptoms, mild = symptoms do not interfere with everyday activity, sev. = moderate to severe symptoms that interfere with everyday activities, lead to sick leave or hospitalization. Work: Current working status, yes = working or student, no = all others. Smoking: Current smoking status, no = not smoking/ex-smoker, yes = current smoker. Course: Predefined curves for disease course, 1 = remission or mild severity after initial high activity, 4 = chronic intermittent symptoms, 3 = chronic continuous symptoms (c2 = increase in severity of intestinal symptoms after initial low activity - 2 is omitted due to $n = 1$).

TABLE 3. IBDQ Total Score Regression Models

	Stratified by Gender	
	Men (n = 90)	Women (n = 100)
Older age		
Relapse last year		-23 [-36 to -11]
Current symptoms	-23 [-35 to -10]	-28 [-40 to -16]
Not working	-20 [-36 to -5]	
Smoking		
Use of corticosteroids		

	Stratified by Relapse	
	No relapse (n = 127)	Relapse (n = 63)
Older age		
Female gender		
Current symptoms	-22 [-30 to -15]	-31 [-54 to -7]
Not working	-15 [-25 to -5]	
Smoking	-22 [-31 to -14]	
Use of corticosteroids		

Stratified linear regression models. Linear regression models fitted to estimate the effect of selected variables on IBDQ total scores. The presented results are estimated β 's with 95% confidence intervals. Only results where $P < 0.01$ are shown.

and smoking were included in the multiple regression model for the SF-36 dimensional scores (Table 5). We found no significant interactions between the included variables, and thus stratification by those variables was not needed. Current symptoms had a significant effect in six out of eight dimensions, use of corticosteroids and working status each affected three dimensions, while smoking only affected the Bodily Pain dimension.

DISCUSSION

This study examined the HRQoL status in UC patients after a 10-year disease course in a well-characterized, population-based inception cohort. In general, SF-36 scores were comparable to the reference population and N-IBDQ scores were equivalent to scores of patients in remission. Current self-reported symptoms, use of corticosteroids, and work status (not working) had negative impacts on SF-36 scores, whereas female gender, current symptoms, relapse of the disease in the preceding year, work status (not working), and smoking affected N-IBDQ scores negatively. Because all patients in our study had the disease for 10 years during the same time period and were recruited from a well-defined geographic area, they had similar access to healthcare and had been subject to the same treatment traditions (the study was conducted before immunomodulators as maintenance therapy was generally accepted and before anti-TNF inhibitors were part of a standard treatment regimen). We therefore believe that this cohort represents the general variation in HRQoL among UC patients after a 10-year disease course.

The SF-36 scores were consistent with the reference population except for a significant reduction in the General Health dimension. These results were in agreement with previous population-based studies.^{1,2} The questions in the General Health dimension focus on the perception of one's own health in general, health compared to others, as well as expectations for future health. The General Health dimension correlates well with both the physical and the mental component summary scores in the SF-36.²⁶ Our results could therefore reflect the patients' experience of having a chronic disease with an unpredictable course.

The total N-IBDQ mean score for the group as a whole was 186, which corresponds to the scores of patients

TABLE 4. SF-36 Dimensional Scores

	Reference Population ^{a,c} (n = 2214)	All Patients ^a (n = 186)	Women ^b (n = 98)	Men ^b (n = 88)
PF	88	90 [87 to 93]	88 [85 to 92]	91 [86 to 96]
RP	80	73 [65 to 80]	66 [58 to 75]	79 [67 to 91]
BP	76	72 [67 to 78]	65 [59 to 71]	80 [71 to 89]**
GH	77	64 [59 to 69]*	62 [57 to 68]	65 [57 to 73]
VT	60	56 [52 to 61]	52 [47 to 58]	61 [53 to 69]
SF	86	85 [80 to 90]	81 [75 to 87]	89 [81 to 97]
RE	83	81 [74 to 89]	74 [65 to 83]	88 [76 to 100]
MH	79	76 [72 to 80]	73 [69 to 78]	78 [72 to 84]

Adjusted means with 95% confidence intervals. Patients ≤ 74 years.

^aAdjusted for age, gender and level of education

^bAdjusted for age and level of education

^cConfidence intervals or standard deviations are not available in the literature

*Statistically significant difference between reference population and all patients, $P < 0.01$.

**Statistically significant difference between male and female, $P < 0.01$.

PF: Physical Function, RP: Role Physical, BP: Bodily Pain, GH: General Health, VT: Vitality, SF: Social Function, RE: Role Emotional, MH: Mental Health.

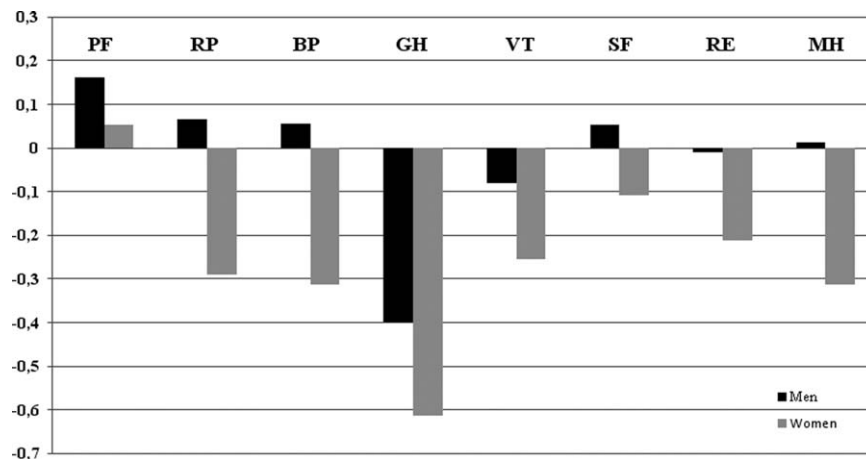


FIGURE 2. SF-36 dimensions. S-scores, stratified by gender. S-scores = (mean patient score minus mean population score) divided by population standard deviation. Cohen's effect size index: <0.2 no difference, 0.2–0.5 small difference, 0.5–0.8 moderate difference, and >0.8 large difference. PF: Physical Function, RP: Role Physical, BP: Bodily Pain, GH: General Health, VT: Vitality, SF: Social Function, RE: Role Emotional, MH: Mental Health.

in clinical remission in other cohorts and in previous cross-sectional studies,³² but is well below 205 points, which was the patient-defined endpoint for remission in an observational study.³³

In HRQoL studies, both in the general population and in IBD cohorts, women often report lower scores than men.^{3,29,34} Therefore, it was somewhat surprising that we found no gender differences in seven out of eight SF-36 dimensions. However, this could be due to a type II error.

We found a more pronounced gender difference in the N-IBDQ scores, where women had significantly lower total scores than men. The difference increased when the analysis was stratified by relapse, which could indicate that women are more affected by relapsing disease than men. Women also reported significantly more current symptoms than men, even when they did not have a relapsing disease (52% vs. 28%, respectively, $P = 0.005$); thus, it seems that women have a different perception of disease and

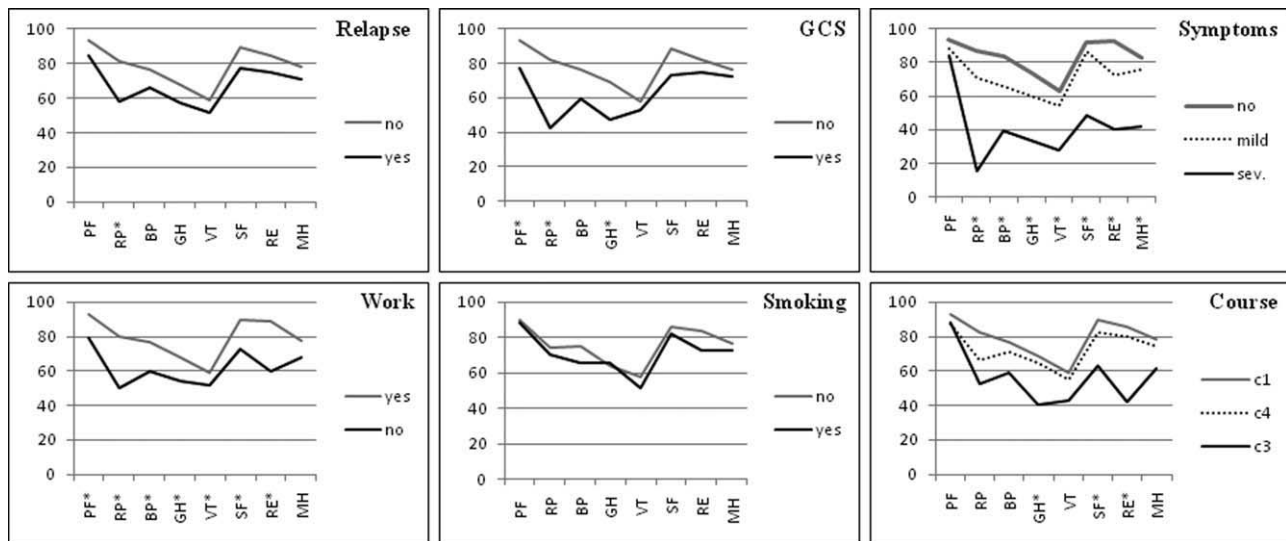


FIGURE 3. SF-36 dimensional scores. Estimated mean age, gender, and education adjusted SF-36 dimensional scores. *Significant comparison, $P < 0.01$. Relapse: Relapse last year, no = no relapse, yes = one or more relapses. Steroids: Use of corticosteroids last year, no = no use of corticosteroids last year, yes = one or more treatments with corticosteroids last year. Symptoms: Patient-reported current symptom severity last 14 days, no = no symptoms, mild = symptoms do not interfere with everyday activity, sev. = moderate to severe symptoms that interfere with everyday activities, lead to sick leave or hospitalization. Work: Current working status, yes = working or student, no = all others. Smoking: Current smoking status, no = not smoking/ex-smoker, yes = current smoker. Course: Predefined curves for disease course, 1 = remission or mild severity after initial high activity, 4 = chronic intermittent symptoms, 3 = chronic continuous symptoms (c2 = increase in severity of intestinal symptoms after initial low activity; 2 is omitted due to $n = 2$).

TABLE 5. SF-36 Dimensional Scores Regression Models

	PF	RP	BP	GH	VT	SF	RE	MH
Older age (pr year)	-0.3 [-1 to 0]							
Female gender								
Current symptoms		-13 [-23 to -4]	-17 [-24 to -10]	-13 [-20 to -7]	-14 [-21 to -8]		-16 [-26 to -5]	-10 [-16 to -5]
Corticosteroids	-11 [-17 to -6]	-31 [-45 to -17]		-15 [4 to -5]		-13 [-22 to -3]		
Not working	-9 [-14 to -4]	-16 [-29 to -3]					-21 [-35 to -7]	
Smoking			-15 [-23 to -6]					

Linear regression model fitted to estimate the effect of selected variables on SF-36 dimensional scores. The presented results are estimated β 's with 95% confidence intervals. Only variables with $P < 0.01$ are shown.
 PF: Physical Function, RP: Role Physical, BP: Bodily Pain, GH: General Health, VT: Vitality, SF: Social Function, RE: Role Emotional, MH: Mental Health.

symptoms than men. Whether this is a result of general sex differences in symptom perception as described in both healthy and diseased populations³⁵ or of gender-related issues caused by the disease itself³⁶ is debatable.

The effect of relapse on HRQoL was limited. We did not record the time of relapse during the last year; thus, patients who experienced one relapse 11 months ago could have been indistinguishable from the group with no relapse during the last year. This highlights the importance of a clear definition of disease activity and recall periods. In the many studies that have shown that disease activity is an important factor for HRQoL,^{1,3,4,5} the definition of disease activity and the length of the recall period were not standardized.¹⁵

Corticosteroids are usually given when moderate to severe relapses are present. We therefore expected a strong correlation between the use of corticosteroids and low HRQoL scores. We did find that corticosteroids were negatively associated with four out of eight SF-36 dimensions (including Physical Function and General Health). In contrast to this finding, the use of corticosteroids did not affect N-IBDQ scores when adjusted for other variables. There were few patients in the corticosteroid group, and thus it is difficult to draw conclusions from these results. However, one could hypothesize that the generic SF-36 questionnaire did capture nonspecific symptoms caused by corticosteroids.

A patient-reported chronic continuous disease course was associated with significantly reduced scores in both the SF-36 and the N-IBDQ compared to patients who reported a mild disease course. This was expected and emphasizes the importance of these predefined curves as an adequate means of describing disease courses. On the other hand, recall bias may have affected the patients' reporting of disease course. Unfortunately, we could not include disease course in the multivariate analyses due to the small number of patients in two of the categories. Important questions related to disease course and confounding factors, therefore, remain unanswered.

The only demographic variables that affected HRQoL scores were smoking and work status. The effect of smoking was very limited. Most studies on IBD patients have failed to show any effect of smoking on HRQoL when the analyses have been adjusted for other factors.^{5,7} Our results indicated that men were more negatively affected by their work status than by relapsing disease. This suggests that the social consequences of the disease might be as important as the disease itself, especially for men.

All the statistically significant differences we found in the SF-36 dimensional scores between different variables were within the ranges of what has been considered minimal clinically important differences (MCID) in a previous study on patients with Crohn's disease.³⁷ To our

knowledge, no MCIDs for SF-36 in UC are available. In the multivariate regression analyses, the significant estimated effects were also comparable to these MCIDs. We did not find any nonsignificant differences with absolute values above the MCIDs. We therefore consider the statistically significant results in our study to be of clinical importance.

With regard to IBDQ, the estimated effects on total N-IBDQ scores in our analyses were in the range of 15–31 points. A cutoff value of 20 points corresponded to patient-reported improvement in an observational study.³³ A medical intervention trial in UC patients found that a change in the total IBDQ score of 20–23 points corresponded to clinical response (defined as a change in the Mayo score of 3),³⁸ whereas a study on CD patients receiving infliximab suggested that a 32-point change corresponded to a change of 100 points on the Crohn's Disease Activity Index (CDAI). This further supports the clinical relevance of our findings.

Our data included patient-reported symptom burden in the last 14 days and patient-reported 10-year disease course, but did not include a clinical disease activity index. The many disease activity measures that are available have major limitations, and there are no accepted gold standards.³⁹ Maunder and Greenberg⁴⁰ stated that patients' self-reported symptom severity is a valid alternative to the St. Marks index (endoscopic and clinician-scored index) in determining disease activity. Furthermore, many authors advocate that the patients' definition of remission and clinical improvement are the most important parameters because the patients' perception of the disease is the primary determinant of their search for and use of health-care.³⁴ This position supports our use of patient-reported symptom burden as a proxy for disease activity.

Both somatic^{13,41} and psychiatric comorbidities^{1,42} can be associated with reductions in HRQoL. We do not have detailed data on comorbidity and cannot exclude that our results were confounded with such factors. If the present results had been influenced by high rates of either somatic or psychiatric comorbidities, a reduction in the physical and mental health domains in the SF-36 scores compared to the reference population would have been expected.¹² Because this was not the case, we find it unlikely that somatic or psychiatric comorbidities influenced our results substantially.

CONCLUSION

In this population-based cross-sectional study of UC patients 10 years after the onset of the disease, generic HRQoL (SF-36) was not generally reduced compared to a general population sample. However, we did find that the patients had a statistically significant and probably a clinically important reduction in the General Health dimension. There were no substantial gender differences in the SF-36

scores; however, women had lower disease-specific scores (N-IBDQ) than men. Relapsing disease reduced HRQoL scores to a greater degree in women than in men, whereas work status influenced HRQoL to a greater extent in men than in women.

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