Health-related Quality of Life in Patients with Inflammatory Bowel Disease 20 Years After Diagnosis: Results from the IBSEN Study

Gert Huppertz-Hauss, MD, Marte Lie Høivik, MD, PhD,† Lars-Petter Jelsness-Jørgensen, PhD,‡ Magne Henriksen, MD, PhD,§ Ole Høie, MD, PhD,‖ Jørgen Jahnsen, MD, PhD,¶ Geir Hoff, MD, PhD,** Bjørn Moum, MD, PhD,†† and Tomm Bernklev, PhD***

Background: Data on the long-term observation of health-related quality of life (HRQoL) in the inflammatory bowel diseases (IBD), Crohn's disease (CD), and ulcerative colitis are scarce. Our aim was to determine HRQoL in a population-based cohort of patients with IBD 20 years after diagnosis and its association with demographic and clinical factors and to compare HRQoL of the cohort with that of the background population.

Methods: Patients with IBD from a large population-based inception cohort (the IBSEN cohort) were invited to a prescheduled 20-year follow-up visit with a structured interview, a clinical examination, and laboratory tests. They completed the Short-Form 36 and the Norwegian Inflammatory Bowel Disease Questionnaire. The association between demographic and clinical factors and HRQoL was assessed with a linear regression analysis. Standardized scores were used to compare HRQoL in patients with that of the background population.

Results: Of the still-living patients with IBD, 438 (73.1%) completed the HRQoL questionnaires. There were no differences in HRQoL scores between the patients with ulcerative colitis and those with CD. Women with CD obtained scores lower than those of men and women with CD in the background population. Current symptoms, increased disease activity, and not working were identified as factors associated with reduced HRQoL.

Conclusions: In this population-based IBD cohort, the overall HRQoL scores obtained 20 years after diagnosis were relatively unaffected compared with the background population. However, women with CD had lower HRQoL scores than men with CD and women in the background population. Active disease and not working were the main factors associated with impaired HRQoL scores.

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Key Words: health-related quality of life, quality of life in IBD, Crohn's disease, ulcerative colitis

Inflammatory bowel diseases (IBD), which consist of ulcerative colitis (UC) and Crohn's disease (CD), are chronic relapsing disorders of the gastrointestinal tract. The disease course of IBD may be unpredictable, but life expectancy seems unaffected.[1–4] Previous population-based studies have found that health-related quality of life (HRQoL) is impaired in patients with IBD and that this impairment is associated with disease activity, CD, female gender, older age, and IBD-related surgery. However, the disease duration in these population-based studies has been relatively short, leaving us with limited knowledge of the long-term effects of IBD on HRQoL. Additionally, there are few studies that compare the HRQoL in patients with IBD with that of the background population.

The IBSEN study (Inflammatory Bowel disease in South-East Norway), a population-based inception cohort of patients with IBD,[5–9] was designed to describe the natural course of IBD. The IBSEN study has focused on measuring patient-reported outcomes, which were previously reported at 5 and 10 years after the diagnosis of IBD.[10–12] The results at these time points showed that impaired HRQoL was linked to disease-specific factors, such as disease activity and the CD diagnosis, as well as demographic factors, such as female gender and not working. A 20-year follow-up of the remaining patients in the IBSEN study has recently been completed, providing us an observation period longer than that of previous prospective population-based studies.[13–15]

The primary aim of this study was to determine the patient-reported HRQoL 20 years after diagnosis in a population-based cohort of patients with IBD and to investigate the relationship between demographic and disease-related factors and HRQoL. The secondary aim was to compare the results with those of the Norwegian background population.

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From the *Department of Gastroenterology, Telemark Hospital, Skien, Norway; †Department of Gastroenterology, Oslo University Hospital Ullevål, Oslo, Norway; ‡Østfold University College, Østfold Hospital Trust, Fredrikstad, Norway; §Østfold Hospital Trust, Fredrikstad, Norway; ‖Department of Internal Medicine, Sørlandet Hospital, Arendal, Norway; ¶Department of Gastroenterology, Akershus University Hospital, Lørenskog, Norway; **Department of Research and Development, Telemark Hospital, Skien, Norway; and ††Department of Gastroenterology, Oslo University Hospital Ullevål, Oslo, Norway.

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Reprints: Gert Huppertz-Hauss, MD, Department of Gastroenterology, Telemark Hospital, 3710 Skien, Norway (e-mail: hhge@sthf.no).

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MATERIALS AND METHODS

Study Population

From January 1990 to December 1993, all newly diagnosed patients with IBD from a well-defined area in South-East Norway (843 patients in total) were included in a population-based inception cohort (Inflammatory Bowel disease in South-East Norway—IBSEN). Patients were invited to prescheduled follow-up visits at 1, 5, 10, and 20 years after diagnosis. During the follow-up, 87 patients were identified as not having IBD, leaving 756 patients in the cohort. The diagnostic criteria, organization of the cohort, and follow-ups have been described in detail elsewhere.[5–7] The 20-year follow-up was conducted between February 2011 and October 2014. All living patients with a confirmed IBD diagnosis were invited to participate.

Data Collection

The 20-year follow-up visit consisted of a structured interview, a review of the hospital records, and a clinical examination. Blood and stool samples were drawn for analyses. In addition, all patients were asked to complete 2 HRQoL questionnaires: the Short-Form 36 (SF-36)[16] and the Norwegian version of the Inflammatory Bowel Disease Questionnaire (N-IBDQ).[17] The questionnaires were answered during the follow-up visit, and completeness was checked by the investigator or a study nurse.

Structured Interview, Patient Records, and Clinical Examination

Hospital records were used to obtain information on last-year relapses and medications used during the 10 years before the follow-up visit. The patients provided complementary information when considered necessary. Relapse was defined as "a change in the clinical condition that entailed surgery or changes in medical treatment."

IBD surgery (bowel resections, revision of fistulae, or abscesses) and extraintestinal manifestations were also recorded. Disease activity was assessed using the Harvey-Bradshaw Index (HBI) in CD, with a score ≤ 4 defined as remission,[18] and the Simple Clinical Colitis Activity Index (SCCAI) in UC.[19] For the SCCAI, a cutoff of 2.5 was chosen to discriminate patients in remission from those with active disease, as defined by Higgins et al.[20]

Patient-reported Symptoms and Demographic Data

Disease-specific symptoms were self-reported by patients at the follow-up visit, with a recall period of 2 weeks. The symptoms were categorized into 4 groups: (1) no symptoms, (2) mild symptoms, (3) moderate symptoms, and (4) severe symptoms. The symptoms were later dichotomized into symptoms or no symptoms in the data analysis. Working status was dichotomized into working (including studying) or not working (including unemployed, retired, disabled, and housewives). Categorization of education was based on the Norwegian educational system and dichotomized into the following 2 categories: (1) education equivalent to 12 years or less or (2) education exceeding 12 years (higher education). Additional information about smoking status and marital status (living together with a partner versus living alone) was obtained.

Laboratory Tests

C-reactive protein in blood samples was used as an objective marker of inflammation, and values above 4 mg/L were considered elevated. Fecal calprotectin values were determined using an enzyme-linked immunosorbent assay (Bühlmann fCAL, Bühlmann Laboratories AG, Schönenbuch, Switzerland). Values above 50 mg/kg were considered elevated indicating inflammatory activity of the IBD.[21]

HRQoL

Short-form 36

The SF-36 is a generic HRQoL questionnaire with 36 items divided into 8 dimensions: physical functioning (PF, 10 items), role limitations due to physical problems (RP, role physical, 4 items), social functioning (SF, 2 items), bodily pain (BP, 2 items), mental health (MH, 5 items), role limitations due to emotional problems (role emotional, RE, 3 items), vitality (VT, 4 items), general health perceptions (GH, 5 items), and 1 item about general health (transitional health) not included in any of the 8 domains.[16,22] Dimension scores between 0 and 100 are calculated, with higher scores representing a better HRQoL. The SF-36 has been translated into Norwegian and has been validated in the Norwegian population.[23]

Validation studies have reported a possible ceiling effect for some of the dimensions in the SF-36,[16] i.e., a tendency of high scores to cluster and a poor discriminative ability for small differences in patients with relatively unaffected HRQoL. An SF-36 assessment of the Norwegian reference population was performed in a sample randomly retrieved from the National Population Register with a response rate of 67% (2323 subjects). From this reference group, we used crude, sex-stratified scores.[23,24]

Inflammatory Bowel Disease Questionnaire

The IBDQ is a disease-specific 32-item HRQoL questionnaire that confers the ability to calculate 4 dimensional scores and a total score (32-224). Higher scores indicate better HRQoL.[17] The Norwegian version has been translated previously and has been validated in the IBSEN cohort.[25] The 32 items of the N-IBDQ were restructured into 5 dimensions: stool consistency and pattern (B1), emotional function (EF1), bowel pain and discomfort (B2), social function (SF), and worries (EF2). The total score remained unchanged.[25]

Statistics

Comparisons of clinical characteristics between UC and CD were assessed with Student's *t* test for continuous data and Pearson's chi-square test for categorical data. The HRQoL data are presented as dimensional scores for SF-36 and a total score for N-IBDQ. Most of the SF-36 dimensional scores and the N-IBDQ

total score were not normally distributed. Therefore, comparisons of scores between groups of patients were performed with the Mann–Whitney test. However, calculations with Student's *t* test provided the same level of significance. Half of the SD was used as a threshold for a clinically meaningful difference according to Norman et al.[26] Comparison of the mean SF-36 dimensional scores between the study population and the Norwegian reference population[23,24] was performed with Student's *t* test and with Z scores (Z score = the mean patient score minus the mean population score divided by the SD of the population scores). Scores larger than zero indicated higher dimensional scores, and those lower than zero indicated lower dimensional scores in the study population than in the background population. Z scores were evaluated with the Cohen's effect size index (<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).[27] A moderate to large difference was interpreted as clinically relevant.[28]

We performed a multiple linear regression analysis to identify demographic and clinical variables that were significantly associated with impaired SF-36 dimensional scores and the N-IBDQ total score. To identify factors to be included in the multiple regression analysis, we performed a univariate analysis of variables known from the literature to influence HRQoL, as well as those assessed as clinically important by the authors. Variables that revealed $P < 0.2$ for the N-IBDQ total score or at least 3 SF-36 dimensional scores were included in the multiple regression analysis. Because of multiple comparisons, we chose a significance level of 1% when appropriate. All statistical analyses were performed using SPSS version 21 (IBM SPSS Statistics, Chicago, IL) for Windows.

Ethical Considerations

The regional ethics committee and the Norwegian Data Inspectorate approved the study. Confidentiality of patient identity and records was maintained using guidelines from the Norwegian Ministry of Health. All patients included gave their informed consent. The study was conducted in accordance with the Declaration of Helsinki.

RESULTS

At the 20-year follow-up, 599 of the initial 756 patients with confirmed IBD diagnosis were still alive (Fig. 1). Of these, 78.5% (N = 470, UC 314, CD 156) participated in the 20-year follow-up study, and 73.1% (N = 438, UC 294, CD 144) completed the HRQoL questionnaires.

Among the patients still living at the 20-year follow-up, there were no differences with regard to sex, age, or disease distribution at the time of diagnosis when those who participated in the follow-up were compared with those who did not ($P = 0.6$–0.8). Moreover, there were no differences regarding sex, marital status, education, smoking habits, disease distribution, relapse, current symptoms, or previous surgery between those patients who completed the HRQoL questionnaires and those who did not ($P = 0.16$–0.9, data not shown). However, the persons who answered the questionnaires were statistically significantly older (53.9 yr) at the time of follow-up than those who did not (48.5 yr, $P = 0.006$).

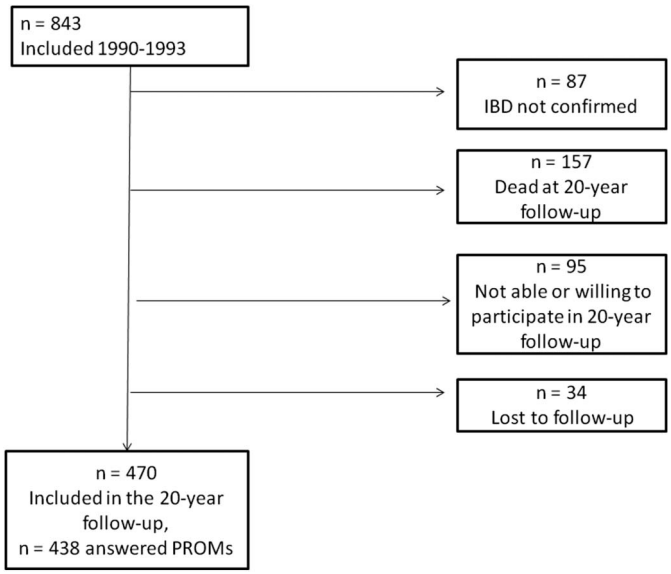

FIGURE 1. Flowchart of the IBSEN cohort.

Demographic and Clinical Characteristics of the Study Population

The mean age was higher in the study population than in the Norwegian reference population[23] (Table 1). In our cohort, a higher proportion of women than men were single. Furthermore, the proportion of patients with higher education (>12 yr) was also higher in the study population than in the Norwegian reference population, with the exception of women with CD. We registered a higher proportion of working men with CD than women with CD (Table 2). Patients with CD used more immune-modulating and biological treatments than did patients with UC.

HRQoL

In general, there was no difference in the HRQoL scores between the patients with CD and those with UC (Table 3). However, there was a trend toward statistically significant differences between women with CD and women with UC in the SF-36 dimensions vitality, general health, and mental health and in the N-IBDQ total scores. Women reported significantly lower SF-36 scores than men in both UC and CD (in 5 of 8 and 6 of 8 dimensions, respectively) and also significantly lower N-IBDQ total scores (see further details in Table 3). No differences in SF-36 and N-IBDQ scores were registered between men with CD and men with UC.

Multiple Linear Regression Analysis

We performed univariate analyses separately for UC and CD with the variables listed in Tables 1 and 2. However, given

TABLE 1. Demographic Characteristics of the Study Population and the General Population

	Patients (N = 438)				General Population (n = 2323)
	UC (N = 294)		CD (N = 144)		
	Men	Women	Men	Women	
Age, yr (1,2)					
Mean (range)	55 (29–86)	55 (34–85)	50 (27–87)	52 (32–94)	45 (19–80)
Sex (1,2)					
Women, N (%)		154 (52.4)		72 (50)	1185 (51)
Education (1,2)					
N (%) over 12 yr	57 (40.7)	65 (42.2)	34 (47.2)	20 (27.8)[a]	28
Marital status (1,2)					
N (%) married/living together	108 (77.1)	95 (61.7)[b]	56 (77.8)	39 (54.2)[c]	70

(1,2): implemented in the multiple regression analysis, 1: UC, 2: CD.
[a]Significance level of the difference between men and women calculated with the chi-square test: $P < 0.05$.
[b]Significance level of the difference between men and women calculated with the chi-square test: $P < 0.001$.
[c]Significance level of the difference between men and women calculated with the chi-square test: $P < 0.01$.

that few of the patients with UC used biological treatments, this variable was included in only the analysis of patients with CD. The variables that fulfilled the criteria for inclusion in the multiple regression analysis are also marked in Tables 1 and 2.

In the CD group, the variable "not working" was associated with a significant reduction in the N-IBDQ total score in all but one of the SF-36 dimension scores. Additionally, current symptoms were associated with a reduction in the N-IBDQ total score and the SF-36 dimension scores for role physical, bodily pain, general health, and vitality. A C-reactive protein value >4 and not living together were associated with a significant reduction of 1 and 2 of 8 SF-36 dimensional scores, respectively (Table 4). An HBI score >4 was associated with a reduction of the N-IBDQ total score.

In the UC group, an SCCAI >2.5 was the most important variable associated with a reduction of almost all SF-36 dimension scores. Additionally, current symptoms were associated with reduced N-IBDQ total scores and bodily pain scores. Daily joint pain, not working, female gender, and not living together were associated with a reduction in 1 or 2 SF-36 dimensions (Table 4).

Comparison with the Background Population

Compared with the background population, the patients with CD and those with UC had statistically significantly lower SF-36 scores in 6 of 8 dimensions and in 3 of 8 dimensions, respectively (Table 3). When calculating the standardized scores for patients with CD, we found a moderate reduction of HRQoL ($z = -0.65$) in general health compared with the background population. For the other dimensions, the Z scores did not exceed −0.5 in either patients with CD or those with UC, indicating no reductions or only small reductions in the HRQoL scores (data not shown).

When comparing SF-36 scores in patients with IBD and the Norwegian reference population stratified by sex, we found a significant reduction in 4 and 5 of 8 dimensions in women with UC and women with CD, respectively. In men, only the general health dimension score was significantly reduced regardless of the diagnosis. The calculation of Z scores revealed either no reductions or only small reductions in SF-36 scores in both men with UC and men with CD (Fig. 2). In contrast, female patients with CD reported Z scores beyond −0.5 in the dimensions of role physical and vitality and beyond −0.8 in the general health dimension, indicating a moderate to large reduction in HRQoL compared with the reference population. Women with UC reported a moderately reduced Z score in the general health dimension.

DISCUSSION

This 20-year follow-up study of patients with IBD in the IBSEN cohort did not detect any significant differences in HRQoL between patients with UC and those with CD. However, female patients with CD reported lower HRQoL scores than did male patients with CD. "Not working" (CD) and clinical signs of active disease (CD and UC) were the most important factors associated with reduced HRQoL. Furthermore, we found that, overall, HRQoL levels in the IBSEN cohort were comparable to the background population except for women with CD.

Several studies, including the 5-year follow-up study in the IBSEN cohort, have reported lower HRQoL scores in patients with CD than in those with UC.[10,13,14] In this study, no statistically significant reduction in HRQoL was found to depend on the CD diagnosis alone, which is in concordance with the study from Graff et al.[15] However, there was a trend toward a statistically significant difference in some SF-36 dimensional scores and in the N-IBDQ total score between women with CD and women with UC. Because of a known ceiling effect in some SF-36

TABLE 2. Clinical Characteristics of the Study Population, N (%)

	UC (N = 294)			CD (N = 144)		
Sex (1,2)	All	Men, N (%), 140 (47.6)	Women, N (%), 154 (52.4)	All	Men, N (%), 72 (50)	Women, N (%), 72 (50)
Relapse previous year (1)	78 (26.5)	29 (20.7)	49 (31.8)[a]	30 (20.8)	12 (16.7)	18 (25)
Current symptoms (1,2)	135 (45.9)	63 (45)	72 (46.7)	73 (50.7)	31 (43.1)	42 (58.3)
Fecal calprotectin, mg/kg						
Mean ± SD	219 ± 801	294 ± 1090	145 ± 318	249 ± 543	352 ± 736	149 ± 204
>50	101 (34.4)	51 (36.4)	50 (32.5)	66 (45.8)	33 (45.8)	33 (45.8)
Missing	67 (22.8)	28 (20)	39 (25.3)	30 (20.8)	16 (20.2)	17 (23.6)
CRP, mg/L (1,2)						
Mean	4.4	4	4.7	5.1	4.9	5.3
>5	46 (15.5)	20 (14.3)	26 (16.9)	33 (22.9)	16 (22.2)	17 (23.6)
Missing	28 (9.5)	11 (7.9)	17 (11)	9 (6.3)	2 (2.8)	7 (9.7)
Working (1,2)	176 (59.9)	93 (66.4)	83 (53.9)	87 (60.4)	53 (73.6)[b]	34 (47.2)
Daily joint pain (1,2)	121 (41.2)	49 (35)	72 (46.8)	56 (38.9)	20 (27.8)	36 (50)
IBD-related surgery the previous 20 yr (1,2)	41 (13.9)	21 (15)	20 (13)	70 (48.6)[c]	37 (51.4)	33 (45.8)
Medication						
5-ASA (current use)	119 (40.5)	66 (47.1)	53 (34.4)[a]	29 (20.1)[c]	16 (22.2)	13 (18.1)
Azathioprine (previous 10 yr) (1,2)	27 (9.2)	13 (9.3)	14 (9.1)	53 (36.8)[c]	22 (30.6)	31 (43.1)
Steroids (previous year) (1,2)	22 (7.5)	12 (8.6)	10 (6.5)	14 (9.7)[d]	6 (8.3)	8 (11.1)
Ever used biologics (2)	10 (3.4)	5 (3.6)	5 (3.2)	33 (23.1)[c]	14 (19.4)	19 (26.4)
Active smoker	41 (14.1)	18 (12.9)	23 (14.9)	42 (29.6)[c]	16 (22.2)	26 (36.1)
Activity Index						
HBI > 4 (2)				37 (25.7)	13 (18.1)	24 (33.3)
SCCAI > 2 (1)	69 (23.5)	26 (18.6)	43 (27.9)			

(1,2): implemented in the multiple regression analysis, 1: UC, 2: CD.
[a]Difference between men and women: chi-square test: $P < 0.05$ (trend).
[b]Difference between men and women: chi-square test: $P < 0.01$.
[c]Difference between CD and UC: chi-square test: $P < 0.001$.
[d]Difference between CD and UC: chi-square test: $P < 0.05$ (trend).
5-ASA, 5 amino salicylic acid; CRP, C-reactive protein; HBI, Harvey Bradshaw Index.

dimensions,[16] small differences between patients with relatively high HRQoL scores might be difficult to detect. Therefore, it cannot be ruled out that small HRQoL differences between patients with UC and those with CD in this study are difficult to discover.

It has been suggested that a higher symptom burden in CD can explain why patients with CD have a more pronounced reduction in HRQoL than those with UC.[10,13] In our cohort, no differences were observed between the diagnostic groups related to relapses in the previous year or to current symptoms after 20 years, which might be part of the reason for the lack of a difference in the HRQoL scores between patients with CD and UC. However, it remains unclear whether self-reported IBD symptoms or HRQoL are suitable to compare the intensity of symptoms between the 2 different diseases, UC and CD.

In our study, women had significantly lower HRQoL scores than did men, but significance does not necessarily imply clinical relevance. According to Norman's criterion,[26] we found that the statistically significant differences between SF-36 dimensional scores were also clinically relevant in CD, but not in UC. The N-IBDQ score differences between sexes were not clinically relevant in either of the diagnoses. These results replicate previous reports showing that HRQoL is more impaired in women than in men, especially in patients with CD.[10,14,29] However, the multiple regression analysis showed that female sex only was independently associated with reduced scores in the physical health dimension in UC. Therefore, there were probably other factors besides sex that contribute to impaired HRQoL in women with IBD, such as disease activity or lack of participation in working life.[10–14,29–31] Disease activity, which has previously been

TABLE 3. Mean SF-36 Dimensional Scores and N-IBDQ Total Score (SD)

	General Population			UC			CD		
	Men	Women	All	Men	Women	All	Men	Women	All
PF	90 (16)	85 (21)	88 (17)	90[a] (16)	82 (22)	86 (20)	92[a] (13)	77 (24)	85 (21)
RP	81 (34)	75 (38)	80 (34)	80[a] (32)	64[b] (40)	72[c] (37)	74[a] (34)	54[d] (41)	65[c] (39)
BP	77 (25)	73 (27)	76 (26)	74[a] (23)	64[d] (26)	69[c] (25)	76[a] (24)	63[b] (23)	70[c] (24)
GH	77 (21)	76 (23)	77 (22)	70[b] (21)	65[d] (24)	67[c] (23)	69[a,b] (22)	58[d,e] (21)	63[c] (22)
VT	63 (20)	57 (21)	60 (21)	62[a] (20)	52[b] (21)	57 (21)	57[a] (23)	46[d,e] (20)	52[c] (22)
SF	88 (21)	84 (23)	86 (22)	87 (19)	80 (25)	83 (22)	84 (22)	74[b] (26)	79[c] (25)
RE	85 (30)	79 (35)	83 (32)	87[a] (27)	73 (35)	80 (32)	78 (36)	67 (41)	73[c] (39)
MH	80 (16)	78 (17)	79 (16)	81 (14)	77 (16)	79 (15)	81[a] (16)	71[e] (19)	76[c] (18)
N-IBDQ total score				187[a] (23)	179 (28)	183 (26)	184[a] (26)	172[e] (26)	178 (26)

[a]Statistically significant difference between sex: $P < 0.01$ in each disease group (Mann–Whitney test).
[b]Statistical significant difference between men/women in the cohort and men/women in the background population: $P < 0.01$.
[c]Statistical significant difference between patients overall and the background population: $P < 0.01$ (Student's t test).
[d]Statistical significant difference between men/women in the cohort and men/women in the background population: $P < 0.001$ (Student's t test).
[e]Trend to statistically significant difference between patients with UC and those with CD of the same sex: $P < 0.05$ (Mann–Whitney test).
BP, bodily pain; GH, general health; MH, mental health; PF, physical function; RE, role emotional; RP, role physical; SF, social functioning; VT, vitality.

associated with reduced HRQoL in IBD,[10–14,29,30] was not different between sexes.

An association between reduced participation in working life and reduced HRQoL has been shown, especially in patients with CD.[11,12,29,31] Our results confirm this association. Significantly more female patients than male patients with CD were not working at the time of the 20-year follow-up. Hence, there might be an association between not participating in working life and the observed reduction in HRQoL in female patients with CD. However, data from the 10-year follow-up in patients with UC of the IBSEN cohort[12] showed that the factor "not working" was associated with reduced HRQoL in men, but not in women. This contradiction must be elucidated in future studies. A higher proportion of women than men were living single. Living single was associated with a reduction in the mental health dimension in patients with CD, which is in line with results of a study of a European cohort.[29] Living single may therefore contribute to a reduction of HRQoL in women with CD.

In the 20-year follow-up, the HRQoL scores were statistically and clinically significantly lower in women with CD than in women in the background population. The Z scores, as measures of clinical relevance, revealed a large reduction in the general health dimension. This is in line with the results of the 10-year follow-up.[11,12] The general health dimension focuses not only on the current self-perceived health status but also on concerns regarding future health. A higher tendency toward disease-related worries and concerns in women with IBD than in men has been proposed as an explanation for the observed reduction in HRQoL.[32] However, although Canavan et al.[32] showed that women tend to have more concerns than do men, the difference did not reach statistical significance and thus could not support this explanation.

Another finding in our study was the moderate reduction in Z scores in the dimensions representing the physical capacity and energy for professional and recreational activities, as reported in the study by Stjernman et al.[33] It remains unclear why these issues have a stronger impact on the HRQoL in women than in men.

Current symptoms and disease severity have previously been identified as independent risk factors for decreased HRQoL scores in IBD.[11,12,14,15,32,34] In our cohort, SCCAI scores above the cutoff value (2.5) and current symptoms in UC were significantly associated with a reduction in most of the SF-36 dimension scores and in the N-IBDQ total score. In CD, an HBI >4 and current symptoms were associated with significantly reduced disease-specific HRQoL. Thus, our study confirms the earlier findings that self-reported disease activity is associated with a significant reduction of HRQoL in IBD. C-reactive protein, as an objective parameter for disease activity, was associated with a reduction of the dimension scores role physical and bodily pain in patients with CD, but not in patients with UC. This association has not been reported previously. We could not detect an association between elevated fecal calprotectin values and HRQoL scores.

In this study, "daily joint pain" was associated with reduced HRQoL in UC, but not in CD, although patients with CD complained as frequently as patients with UC of these symptoms. Joint pain was also identified as an independent factor for reduced HRQoL in patients with UC and those with CD at the 5-year follow-up.[35] Although the 5-year follow-up revealed an association between corticosteroid use and reduced HRQoL in UC, we could not detect this association in the 20-year follow-up. The use of corticosteroids might be a surrogate marker for disease activity and is therefore not independently associated with reduced HRQoL.

TABLE 4. Factors Independently Associated with Reduced HRQoL, Linear Regression Model for SF-36 Dimensional Scores and N-IBDQ Total Score

	PF	RP	BP	GH	VT	SF	RE	MH	IBDQ Total Score
UC									
SCCAI > 2.5		−27 (−38 to −16)[a]	−14 (−22 to −7)[a]	−19 (−26 to −12)[a]	12 (−19 to −5)[b]	−13 (−20 to −5)[b]		−8 (−13 to −3)[b]	−19 (−25 to −12)[a]
Current symptoms			−10 (−17 to −4)[b]						−16 (−22 to −10)[a]
Not active working	−10 to 7 (−12 to −2)[b]	−14 (−25 to −4)[b]							
Daily joint pain	−3 (−6 to −1)[b]		−7 (−10 to −4)[a]						
Female sex	−7 (−11 to −2)[b]								
Not living together	−7 (−12 to −2)[b]								
CD									
Not active working	−19 (−27 to −11)[a]	−31 (−47 to −16)[a]	−23 (−31 to −14)[a]	22 (−30 to −13)[a]	−19 (−28 to −9)[a]		−32 (−51 to −13)[b]	−14 (−23 to −5)[b]	−18 (−28 to −8)[b]
Current symptoms		−27 (−41 to −12)[a]	−17 (−25 to −8)[a]	−14 (−22 to −6)[b]	−15 (−24 to −7)[b]				−23 (−33 to −13)[a]
CRP > 4		−20 (−44 to −14)[a]	−14 (−23 to −5)[b]						
HBI > 4									−15 (−25 to −4)[b]
Not living together								−12 (−21 to −4)[b]	

Linear regression model fitted to estimate the effect of selected variables on SF-36 dimensional scores and the N-IBDQ total score. The presented results are estimated β's with 95% confidence intervals.
[a]$P < 0.001$.
[b]$P < 0.01$.
BP, bodily pain; CRP, C-reactive protein; GH, general health; HBI, Harvey Bradshaw Index; MH, mental health; PF, physical function; RE, role emotional; RP, role physical; SF, social functioning; VT, vitality.

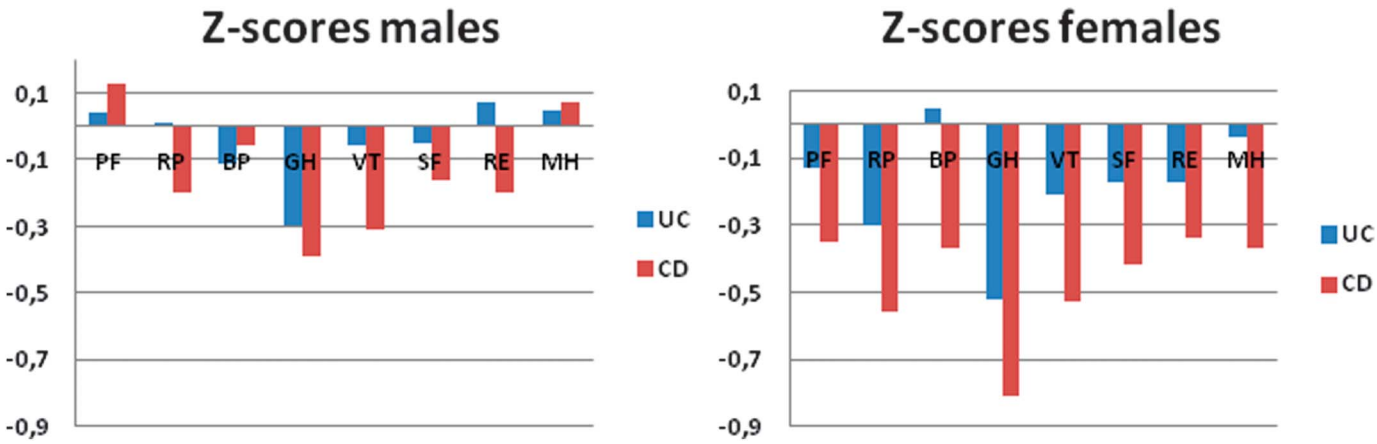

FIGURE 2. SF-36 dimensions stratified by diagnosis and sex. Z scores = mean patient score minus the mean population score divided by the SD of the population scores. Cohen's effect size index: <0.2 no difference, 0.2 to 0.5 small difference, 0.5 to 0.8 moderate difference, >0.8 large difference. BP, bodily pain; GH, general health; MH, mental health; PF, physical function; RE, role emotional; RP, role physical; SF, social function; VT, vitality.

Compared with the background population, a statistically significant reduction in 6 and 3 of 8 SF-36 dimensions scores was registered in patients with CD and those with UC, respectively. This contrasts our findings in the 10-year follow-up study, in which significant differences were seen in only 1 dimension in UC and in 2 dimensions in CD.[11,12] A possible explanation might be a type II error due to smaller samples (N = 196 in UC and 98 in CD) in the 10-year follow-up. However, although the difference between HRQoL scores in our cohort and the background population was statistically significant, it might not be of clinical importance. Therefore, we estimated Z scores according to Cohen's effect size to determine the clinical relevance of the differences in HRQoL between patients with IBD and the background population.[27,28] Despite a moderate difference in the general health dimension in CD, we detected mainly small or no differences between the SF-36 scores of patients and those of the background population. Thus, the 20-year follow-up aligns with previous population-based studies, revealing no clinically important differences in HRQoL between patients with IBD and the background population.[11–13]

The IBDQ cutoff values for patients with CD and those with UC in remission have been reported to be 168 and 186, respectively.[36,37] Hence, the mean N-IBDQ total scores in our study emphasize that our patients, on average, had relatively good HRQoL, although some of the patients had impaired HRQoL. In contrast, a recently published large survey of patients with IBD found a substantial impact of the disease on daily life, even in patients in remission.[38] However, HRQoL was not assessed by validated instruments, and the patients were recruited from members of 25 national IBD organizations, indicating a possibility of selection bias toward patients with symptomatic active disease.

As estimated from the Z scores, we observed that women with CD showed a large reduction in HRQoL in the general health dimension and a moderate reduction in role physical and vitality compared with women in the background population. This confirms previous results from the IBSEN cohort[10–12] and the results from other studies.[15,33] Whether social and psychological factors may attribute to this reduction, as suggested by some of the authors, remains unknown and must be investigated in future studies.[13,15,32,33]

The major strength of this study is the well-characterized, population-based cohort with a longitudinal 20-year follow-up period. Many of the patients have been to regular or unscheduled visits in addition to the 1-, 5-, 10-, and 20-year visits in the study, which has resulted in outstanding data completeness in a majority of the patients. We therefore believe that the findings in this study are representative of patients with IBD in not only South-East Norway but Norway at large.

We were not able to detect statistically significant HRQoL differences between patients with CD and those with UC, although there was a trend toward statistical significance between women with UC and women with CD. The reason for this finding might be a type II error due to the smaller sample size of the CD population.

Unfortunately, the mean age in the reference population is lower than that in our cohort. However, the multiple regression analysis could not identify age as to be independently associated with reduced HRQoL.

In conclusion, this study showed that 20 years after diagnosis, patients with IBD have relatively unaffected HRQoL that is comparable to the background population. We could not detect any significant differences in HRQoL between patients with UC and those with CD overall, but women with CD reported impaired HRQoL compared with men with CD. A significant reduction in HRQoL was also seen in women, but not in men, compared with the Norwegian background population. Active disease and not working were the 2 main factors associated with reduced HRQoL.

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