

# Unfavourable outcome for women in a study of health-related quality of life, social factors and work disability in Crohn's disease

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**Objective** The aim was to describe health-related quality of life (HRQL) and social factors, sickness and disability variables in a large population-based cohort of patients with Crohn's disease (CD).

**Methods** HRQL was measured with Short Form-36 in 497 adult patients with CD at three outpatient clinics. Comparisons were made with age–sex-matched background population and with ulcerative colitis (UC). Social factors, employment, sickness compensation and disability pension for CD were compared with national population registers.

**Results** CD had a greater negative effect on HRQL than did UC. This difference was more pronounced for women. Compared with background population, patients with CD had lower educational level, and had a two-fold rise in long-term sickness and disability pension rate. Women with CD had higher rates of sickness and disability than men with CD and were more often living single, though procreation was not affected.

**Conclusion** This study characterized the burden of CD in a large population-based cohort. CD had higher impact on

HRQL, compared with UC. Women with CD had worse outcome in subjective health status, but not in objective assessment of disease activity. Women also had higher rates of sickness, disability pension and single living. The mechanism underlying the sex-related inequalities in outcome for CD warrants further elucidation. *Eur J Gastroenterol Hepatol* 23:671–679 © 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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## Introduction

Crohn's disease (CD) is a lifelong inflammatory bowel disease (IBD) afflicting millions of people worldwide [1]. Typically, the disease makes its debut in the early decades of life with the potential to injuriously impact life prospects [2]. The patient's subjective perception of how the disease affects life is encompassed in the term health-related quality of life (HRQL) [3]. HRQL has become indispensable in the assessment of treatment outcome as well as in the estimations of societal burden, especially as no definitive cure is at hand, and while the most potent treatment options also tend to be the most risky and costly [4]. Another aspect of disease burden is limitations of life achievements and work performance, major determinants of societal cost of illness [5–7]. Disability has recently been deemed as an underestimated problem in the management of IBD [8]. Consequently, an international project in collaboration with the WHO has been launched, in an attempt to develop a comprehensive classification of functioning, disability and health (International Classification of Functioning, Disability and Health core sets), enabling research to improve functioning

and minimize impact on disability in IBD [8]. The disability imposed upon the patient, as well as the subjective health perception, for a given burden of symptoms depends closely on expectations and coping capacity with regard to both the individual and the society [9,10]. These contextual prerequisites may be subject to an appreciable variation between different populations, cultures and countries.

The aim of this study was to characterize the general HRQL, social factors, and disability in a large population-based cohort of Swedish patients with CD, to better understand the impact of the disease on subjective health perception, functioning and well-being.

## Methods

### Patients

Adult patients with CD were recruited at regular visits at three outpatient gastroenterology clinics (Jönköping County Hospital, Örebro University Hospital and Linköping University Hospital) during 1999–2001. All patients with IBD in the catchment area of the hospitals are intended to be monitored at the clinics at least once per year.

Participants were asked to complete the generic HRQL questionnaire Short Form-36 (SF-36) (described below) and a symptom diary 1 week before their scheduled appointment. Demographic data concerning family (marriage/cohabiting/children), educational level (compulsory/secondary school/university), working status (employed/unemployed/studying), sickness compensation (long-term sickness benefit/disability pension) and smoking (no/ex/yes) were collected. Medical history, a 4-point physician's global assessment (PGA) of disease activity (remission, mild, moderate, or severe disease activity) and a 3-point summary of disease course during the preceding year (remission, remission with relapse, chronic active) were provided by the treating physician. In addition, disease activity was measured with CD activity index (CDAI) according to the standard algorithm [11].

### Short Form-36

The SF-36 is a generic HRQL questionnaire subdivided into eight dimensions [12]: physical function (10 items), physical role (four items), bodily pain (two items), general health (five items), vitality (four items), social functioning (two items), emotional role (three items) and mental health (five items). The dimensional scores, ranging from 0 (worst health) to 100 (best health), and the two physical and mental component summary scores, (standardized to a mean of 50 and a standard deviation of 10 in normal population), were calculated according to the standard SF-36 algorithm [13,14]. The Swedish translation of SF-36 has been validated [15].

### Comparative data - Short Form-36

For comparison of SF-36 data versus background population, a match-case analysis was performed. Two gender-matched and exactly age-matched referents per patient were randomly selected from a large SF-36 database ( $n = 8930$ ) obtained from a national health survey [15] to form the control population. To further elucidate any HRQL issues specific for CD, comparisons were made with ulcerative colitis (UC). SF-36 data for UC were available from a HRQL study performed a few years earlier (1996–1997) by our group [16]. The methods of patient recruitment and data collection were identical, except for the exclusion of patients with an ileostomy in the UC study. That study also used PGA of disease activity. In addition, UC disease activity was measured with the Seo Activity Index according to the standard algorithm [17]. Direct comparison between CD and UC was hampered by differing age and sex distributions in the two populations. To overcome this, the UC population was compared with gender-matched and age-matched controls selected from the SF-36 database in a procedure identical to the one for patients with CD.

### Comparative data - social factors

Data concerning educational level, smoking status, marital status and sickness in the normal population

were obtained from the Living Conditions Survey (LCS), provided by the national agency of statistics, Sweden Statistics ([www.scb.se](http://www.scb.se)). Every second year, a large sample ( $n = 15\,000$ ) representative of the Swedish population is randomly selected and interviewed regarding living conditions. The following rates from the 2000–2001 survey were directly compared with study population rates: compulsory school education only, postsecondary school education, current daily smoking and living single. The rates of patients with partially or totally reduced work capacity (long-term sickness compensation and/or disability pension) were compared with the rates of survey controls having 'a long-lasting disease (or injury or other weakness) that reduces work capacity to a high degree'. Background population rates were available for the age groups 16–24, 25–44, 45–64 and 65–84 years, but we used only the 25–44 and 45–64 years age groups for comparison ( $n = 7708$ – $7743$ , depending on variable) as the age range in this study population was 18–82 years. Parenthood rate and number of children per parent for each year of age in the population were obtained from the Swedish Population Registry at Sweden Statistics ( $n = 6\,679\,321$ ). The data were matched for sex and age in groups of 5-year intervals excluding patients with diagnosis after 45 years of age. The disability pension rate in the background population of the three counties Jönköping, Örebro and Linköping by the end of the year 2000 (grouped by sex and age in 5-year groups from 20 to 64 years) was provided by the Swedish Social Insurance Agency ( $n = 580\,574$ ). The unemployment rate, defined as the proportion of the labour force (excluding students, sick leave, parental leave and disability pension) that was unemployed at the end of the year 2000, matched for sex and age in the age groups 20–44, and 45–64 years, was obtained from the Labour Force Survey, Sweden Statistics ( $n = 4\,235\,800$ ).

### Statistical analysis

HRQL constructs cannot be assumed to follow a normal distribution. Nonparametric methods are therefore preferably employed. The  $\chi^2$  test was used for comparison of nominal data, Mann–Whitney *U*-test for continuous data in two-sample cases, and Kruskal–Wallis one-way analysis of variance for continuous data over more than two groups. However, as only means and standard deviations were obtainable from the SF-36 background population database, unpaired two-tailed *t*-test was used for SF-36 group comparison. To further evaluate the importance of any difference detected, effect size (Cohen's *d*) was calculated as difference in means, divided by the pooled standard deviation [18]. In general, an effect size of 0.8 is deemed large, 0.5 medium and 0.2 small.

For social factors, data were compared with background population, adjusting for age and sex using indirect standardisation. For each sex, rates of specific age groups in the background population were applied to the corresponding age groups in the study population in

order to obtain the standardized ratio between expected and observed number of cases. This ratio was further used to calculate the age-adjusted and sex-adjusted rate in the study population. The significance of the differences was appraised with Mantel–Haenszels  $\chi^2$  test [19]. The age-group interval varied for the different social factors, depending on available background population data. To analyse the influence of sex on reduced work capacity (long-term sickness benefit/disability pension) logistic regression analysis was performed, controlling for age, education, current smoking, concomitant disease, disease location, disease behaviour, extraintestinal manifestation, and disease course preceding year. Consideration was given to the risk of mass significance by interpreting *P* values below 0.01 as significant, and *P* values from 0.01 to 0.05 as borderline significant.

### Ethics

The study was approved by the Committee of Research Ethics at the Faculty of Health Sciences, Linköping University. The participants gave informed consent before participation.

### Results

Of 593 invited patients with CD, 505 (85.2%) agreed to participate. No differences regarding age, sex distribution, disease location or duration were found between participants and those who declined. However, previous bowel resection was more common among included patients (63.7 vs. 48.9%, *P* < 0.01). In the UC study, 300 of 380 (78.9%) invited patients participated [16]. The basic characteristics of demography and disease-related factors of these patients are presented in Table 1. Compared with patients with UC, patients with CD comprised a greater proportion of women and current smokers, and the disease duration was longer. No other significant differences in demography or disease-related factors were noted.

### Subjective health perception

Complete SF-36 data were available for 497 patients with CD, and 284 patients with UC. Comparisons of the SF-36 subscales and summary scores with sex–age-matched controls for both IBD types are presented in Table 2. Male patients with CD had significantly reduced scores for five of the subscales (role physical, general health, vitality, social function and mental health) and both summary scores (physical and mental component summary scores). Female patients with CD had significantly reduced scores for all eight subscales and both summary scores. Male patients with UC had significantly reduced score in one subscale (general health), whereas two subscales (physical function and bodily pain) had higher scores. The summary scores were unaffected for male patients with UC. Female patients with UC had significantly reduced scores in two subscales (general health and vitality) and in the mental summary score.

**Table 1 Demography and disease-related characteristics of the study populations**

	Frequency %		<i>P</i>
	CD ( <i>n</i> =497)	UC ( <i>n</i> =284)	
Sex (males/females)	40.8/59.2	55.6/44.4	<0.001
Age (years)	46 (33–56) <sup>a</sup>	46 (36–58) <sup>a</sup>	NS
Living single	31.4	27.7	NS
Parenthood	72.1	71.9	NS
Smoker/exsmoker/nonsmoker	35.5/28.2/36.3	21.9/43.5/34.6	<0.001
Compulsory school/secondary school/university	39.0/38.2/22.8	43.2/32.3/24.5	NS
Disease duration (years)	15 (6–25) <sup>a</sup>	10 (4–17) <sup>a</sup>	<0.001
CDAI	103.4 (50.7–177.2) <sup>a</sup>	–	
Seo AI	–	104.2 (93.2–150.9) <sup>a</sup>	
Active disease (CDAI >150 or Seo AI >150)	31.9	25.9	NS
Active disease (physician's global assessment)	31.0	25.0	NS
Disease classification (montreal)			
A (Age at diagnosis)			
≤ 16 years	13.1	–	–
17–40 years	66.1	–	–
>40 years	20.8	–	–
L (Location)			
Ileal	34.7	–	–
Colonic	28.7	–	–
Ileocolonic	36.4	–	–
Upper	0.2	–	–
gastrointestinal			
B (Behaviour)			
Inflammatory	40.6	–	–
Strictureing	21.5	–	–
Penetrating	37.8	–	–
Extent of UC			
Proctitis	–	19.0	–
Distal colitis	–	39.4	–
Extensive/total colitis	–	41.6	–
Perianal disease	27.2	–	–
Extraintestinal manifestation	17.7	16.1	NS
Previous bowel resection	63.7	–	–
Ostomy bag	11.3	–	–
Corticosteroids	24.7	–	–
Immunomodulators	26.2	–	–
Concomitant disease	35.6	38.2	NS

CD, Crohn's disease; NS, not significant; UC, ulcerative colitis.

<sup>a</sup>Median (25th–75th percentile).

The effect sizes of the deviances from the background population are listed in Table 2 and illustrated in the sex-specific and disease-specific spider web diagrams in Fig. 1. For male patients with CD general health was the only subscale that was reduced with a medium effect size; all other impairments had small effect sizes. For female patients with CD, three subscales (role physical, vitality and general health) were reduced with at least medium effect sizes, of which general health even reached a large effect size. For female patients with UC, only general health was reduced with a medium effect size, whereas the significant discrepancies from background population for male patients with UC only reached small effect sizes.

**Table 2 Mean Short Form-36 subscale and summary scores compared with sex-matched and age-matched controls using unpaired two-tailed *t*-test and effect size (Cohen's *d*)**

SF-36 subscale	CD				UC			
	Sample ( <i>n</i> =203)	Controls ( <i>n</i> =406)	Diff	Effect size ( <i>d</i> )	Sample ( <i>n</i> =158)	Controls ( <i>n</i> =316)	Diff	Effect size ( <i>d</i> )
<b>Men</b>								
Physical function	88.8	88.4	-0.4	-0.02	91.9	87.0	4.9**	0.28
Role physical	73.1	82.1	-9.0***	-0.25	81.3	79.8	1.5	0.04
Bodily pain	71.9	74.2	-2.3	-0.09	80.2	75.4	4.8*	0.20
General health	<b>58.3</b>	<b>74.3</b>	<b>-16.0***</b>	<b>-0.75</b>	67.7	74.7	<b>-7.0***</b>	<b>-0.32</b>
Vitality	62.2	69.2	-7.0***	-0.28	68.6	69.8	-1.2	-0.05
Social function	83.6	90.0	-6.4***	-0.31	87.9	88.5	-0.6	-0.03
Role emotional	82.4	85.6	-3.2	-0.10	85.2	84.5	0.7	0.02
Mental health	79.0	82.9	-3.9**	-0.21	80.6	82.5	-1.9	-0.11
PCS	46.7	49.6	-2.9***	-0.30	50.2	49.5	0.7	0.08
MCS	48.0	50.9	-2.9**	-0.27	49.0	50.6	-1.6	-0.16
	Sample ( <i>n</i> =294)	Controls ( <i>n</i> =588)	Diff	Effect size ( <i>d</i> )	Sample ( <i>n</i> =126)	Controls ( <i>n</i> =252)	Diff	Effect size ( <i>d</i> )
<b>Women</b>								
Physical function	79.9	86.2	-6.3***	-0.31	88.7	86.0	2.7	0.14
Role physical	<b>59.6</b>	<b>82.3</b>	<b>-22.7***</b>	<b>-0.59</b>	76.2	84.2	-8.0*	-0.23
Bodily pain	61.4	73.0	-11.6***	-0.43	71.5	71.2	0.3	0.01
General health	<b>51.5</b>	<b>76.2</b>	<b>-24.7***</b>	<b>-1.14</b>	<b>63.6</b>	<b>76.4</b>	<b>-12.8***</b>	<b>-0.56</b>
Vitality	<b>50.2</b>	<b>68.9</b>	<b>-18.7***</b>	<b>-0.77</b>	59.7	67.5	-7.8**	-0.31
Social function	77.3	87.9	-10.6***	-0.47	82.6	87.8	-5.2*	-0.23
Role emotional	71.3	84.8	-13.5***	-0.39	78.3	84.8	-6.5	-0.20
Mental health	71.7	81.2	-9.5***	-0.49	75.0	80.1	-5.1*	-0.26
PCS	<b>42.6</b>	<b>49.8</b>	<b>-7.2***</b>	<b>-0.68</b>	48.4	49.5	-1.1	-0.11
MCS	<b>44.4</b>	<b>50.3</b>	<b>-5.9***</b>	<b>-0.53</b>	45.8	49.5	-3.7**	-0.32

Medium (0.5–0.8) to large (>0.8) effect sizes are printed in bold.

CD, Crohn's disease; Diff, difference; MCS, mental component summary; PCS, physical component summary; SF-36, Short Form-36; UC, ulcerative colitis.

\**P*<0.05.

\*\**P*<0.01.

\*\*\**P*<0.001.

### Social factors

The study on social factors included patients with CD only. The sex-adjusted and age-adjusted comparisons with LCS concerning educational level and smoking habits are presented in Table 3. A larger proportion of the patients had a low educational level (only compulsory school). For patients diagnosed at the age of 26 years or more (median age at diagnosis), the proportion was even larger (40.7%). The proportion of the patients with secondary school education, who had attained post-secondary school education, was equal to the LCS. However, for patients diagnosed at the age of 26 years or more, the proportion was smaller (31.5%, *P*<0.05). The smoking rate was almost double among patients. The sex-adjusted and age-adjusted rates of single living and parenthood are presented in Table 4. The single living rate was increased for women with CD, but not for men with CD. For women with late diagnosis (≥ 26 years of age), this rate was even higher (29.4%). No difference from the population registry was detected for the parenthood rate of patients diagnosed before the age of 45 years. The mean number of children per parent in this group, 2.16 [95% confidence interval (CI): 2.07–2.25], equalled the mean in the population registry (2.17), also when the mean was compared for each sex and age group separately (18–44 and 45–80 years).

The sex-adjusted and age-adjusted rates of reduced work capacity, disability pension and unemployment compared with background population, respectively, are listed in

Table 5. The rates of reduced work capacity and disability pension were more than doubled in the study population. For patients with later diagnosis (age ≥ 26) these rates were even higher (26.7 and 16.3%, respectively). The reduced work capacity or disability pension was attributed to the bowel disease in 50.0 and 41.4% of the cases, respectively, (no significant sex differences detected). Logistic regression analysis of reduced work capacity (long-term sickness benefit/disability pension) showed a significant association with female sex [odds ratio (OR) 2.34, 95% CI: 1.24–3.66, *P*=0.003], age (OR: 1.07, 95% CI: 1.04–1.11, *P*<0.001), concomitant disease (OR: 2.78, 95% CI: 1.50–4.33, *P*<0.001) and disease course preceding year (OR 2.12, 95% CI: 1.24–3.66, *P*<0.006). Smoking, education, disease location/behaviour or extraintestinal manifestation did not contribute. The results were similar when disability pension was used as dependent variable (disease course preceding year omitted), except for the ORs being borderline significant for female sex (OR: 2.04, 95% CI: 1.03–3.85, *P*=0.04), and concomitant disease (OR: 2.20, 95% CI: 1.09–3.84, *P*=0.017).

The adjusted unemployment rate was raised for women, but with only borderline significance. The unadjusted labour force participation rate (defined as the proportion of the population of age group 20–64 years that was in partial or full-time employment, or unemployed but able to work) was 65.7% compared with 81.3% in background population at the end of 2000.

**Discussion**

The main finding of this study was that patients with CD had a poorer general HRQL compared with background population and patients with UC, and that this impairment was more pronounced for women. Female patients with CD also had worse outcome in terms of sickness and work disability, and were more often living alone.

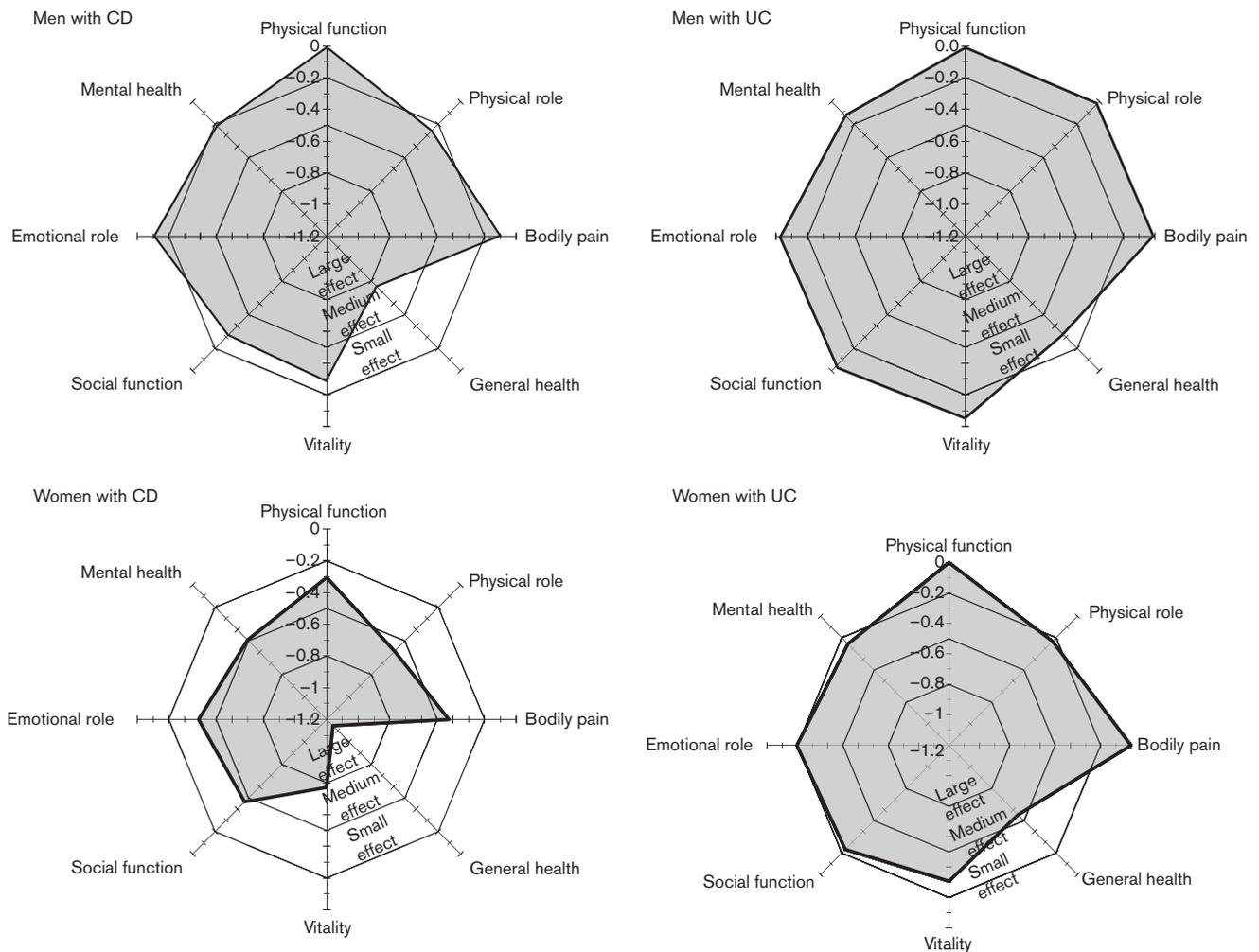
**Subjective health perception**

The general HRQL measured with SF-36 was significantly reduced for patients with CD on most subscales compared with background population, which is in agreement with previous studies [20–25]. There was a tendency towards a greater impact on the physical component (especially general health and physical role), although vitality and mental health were affected too (Table 2). A noticeably larger effect on SF-36 scores was

found for female patients with CD. Worse HRQL for female patients with IBD has been reported in several studies [26]. Two studies reported worse SF-36 scores for female patients with CD comparing the sexes ‘head to head’ [20,23]. In contrast, several studies using multivariate techniques to find predictors of SF-36 scores in CD or IBD populations, could not identify sex as a significant predictor [22,24,27–29]. However, these models all included ‘disease activity’ defined by self-reported symptoms as an independent variable, which might be problematic, as it includes aspects of what SF-36 is intended to measure, that is, subjective health perception. A marked overlap between the independent and dependent variables could encumber the detection of other predictors of importance.

Women generally have worse SF-36 scores, according to the background population survey [15], but the sex-adjusted

**Fig. 1**



Sex-specific and disease-specific spider web diagrams of effect size for SF-36 subscale difference in patients with Crohn's disease ( $n=497$ ) and ulcerative colitis ( $n=284$ ) compared with controls. The eight radiating scales of each diagram represent the effect size of reduced scores for each subscale, with the effect size verging into the centre. CD, Crohn's disease; UC, ulcerative colitis.

**Table 3 Age-adjusted rates for each sex and sex-age adjusted rates for the totals of attained educational level and current smokers in the Crohn's disease population (age 25–64 years)**

	<i>n</i>	Observed number	Expected number	Normal rate (%)	Adjusted rate in CD (%)	<i>P</i>
Compulsory school						
Women	240	87	31.85	13.9	38.0	<0.001
Men	158	57	29.62	16.8	32.3	<0.001
<b>Total</b>	<b>398<sup>b</sup></b>	<b>144</b>	<b>61.47</b>	<b>15.3</b>	<b>35.9</b>	<b>&lt;0.001</b>
Postsecondary school <sup>a</sup>						
Women	153	58	65.28	42.1	37.4	NS
Men	101	36	39.22	38.9	35.7	NS
<b>Total</b>	<b>254</b>	<b>94</b>	<b>104.50</b>	<b>40.6</b>	<b>36.5</b>	<b>NS</b>
Smokers						
Women	240	101	56.19	23.6	42.5	<0.001
Men	157	55	31.25	19.1	33.5	<0.001
<b>Total</b>	<b>397<sup>c</sup></b>	<b>156</b>	<b>87.44</b>	<b>21.4</b>	<b>38.1</b>	<b>&lt;0.001</b>

The adjusted rates are calculated from the ratio between observed and expected number of patients based on the background rate in the living conditions survey for each age group (indirect standardization).

CD, Crohn's disease; NS, not significant.

<sup>a</sup>Proportion of patients with at least secondary school education who also had tertiary education (university or equivalent).

<sup>b</sup>Missing data in 15 cases.

<sup>c</sup>Missing data in 16 cases.

**Table 4 Age-adjusted rates for each sex and sex-age adjusted rate for the totals (in bold) of living single and parenthood in the Crohn's disease population**

	<i>n</i>	Observed number	Expected number	Normal rate (%)	Adjusted rate in CD (%)	<i>P</i>
Living single						
Women	245	68	37.76	15.7	28.2	<0.001
Men	163	34	35.65	23.2	22.1	NS
<b>Total</b>	<b>408<sup>a</sup></b>	<b>102</b>	<b>73.41</b>	<b>19.4</b>	<b>26.9</b>	<b>&lt;0.001</b>
Parenthood						
Women	251	173	181.5	70.4	67.1	NS
Men	164	106	99.5	61.7	65.7	NS
<b>Total</b>	<b>415<sup>b</sup></b>	<b>279</b>	<b>281.0</b>	<b>66.0</b>	<b>65.5</b>	<b>NS</b>

The adjusted rates are calculated from the ratio between observed and expected number of patients based on the background rate in the living conditions survey (living single) and Swedish Population Registry (parenthood) for each age group (indirect standardization).

CD, Crohn's disease; NS, not significant.

<sup>a</sup>Age 25–64 years, missing data in five cases.

<sup>b</sup>Age 18–78 years, diagnosis before 45 years of age, missing data in 12 cases.

**Table 5 Age-adjusted rates for each sex and sex-age adjusted rate for the totals (in bold) of reduced work capacity, disability pension, and unemployment in the Crohn's disease population**

	<i>n</i>	Observed number	Expected number	Normal rate (%)	Adjusted rate in CD (%)	<i>P</i>
Reduced work capacity						
Women	242	72	30.70	13.3	31.1	<0.001
Men	160	36	17.14	9.4	19.7	<0.001
<b>Total</b>	<b>402<sup>a</sup></b>	<b>108</b>	<b>47.84</b>	<b>11.4</b>	<b>25.7</b>	<b>&lt;0.001</b>
Disability pension						
Women	254	44	19.35	8.4	19.2	<0.001
Men	179	25	14.25	6.4	11.3	<0.005
<b>Total</b>	<b>433<sup>b</sup></b>	<b>69</b>	<b>33.60</b>	<b>7.4</b>	<b>15.2</b>	<b>&lt;0.001</b>
Unemployment						
Women	174	11	5.84	3.3	6.3	<0.05
Men	134	2	5.51	4.1	1.5	NS
<b>Total</b>	<b>308<sup>c</sup></b>	<b>13</b>	<b>11.35</b>	<b>3.7</b>	<b>4.3</b>	<b>NS</b>

The adjusted rates are calculated from the ratio between observed and expected number of patients based on the background rate for each age group (indirect standardization) in the Living Conditions Survey (reduced work capacity), Social Insurance Agency statistics (disability pension), and Labour Force Survey (unemployment), respectively.

CD, Crohn's disease; NS, not significant.

<sup>a</sup>Age 25–64 years, missing data in six cases, five patients with early retirement excluded.

<sup>b</sup>Age 20–64 years, missing data in seven cases.

<sup>c</sup>Labour force, age 20–64 years.

design of this study obviously excludes this explanation. Women may have had a more severe disease type. The median CDAI was higher among women (113.5 vs. 92.3,

$P = 0.027$ ) indicating a more active disease. However, as we showed in a previous study based on this study population [30], the greater CDAI score in women was

attributed only to subjective CDAI variables (abdominal pain and general well-being). We found no significant sex differences when comparing rates and medians of more objective markers of disease activity (PGA, C-reactive protein, orosomucoid or anaemia). The disease related and demographic variables listed in Table 1 did not differ significantly, except for current extraintestinal manifestations being more common in women (21.7 vs. 11.8%,  $P = 0.005$ ). This difference was ascribed to arthralgia that dominated the extraintestinal symptoms (91%), and may have contributed to lower HRQL for women, a phenomenon noted in a previous study [31]. Concomitant irritable bowel syndrome could be another explanation, as it is more frequent in women [32], and also prevalent in patients with CD [33]. Further explanations could be sex-related differences in coping strategies, and psychopathology, or sex inequalities in society and family life, leading to greater demands on and expectations of daily function for women [34]. Finally, sex inequality in choice of treatment or quality of care as discussed in other medical fields needs to be investigated [35]. For UC, SF-36 scores were affected to a lesser extent, consistent with previous studies [21,23,27]. The differences in smoking status and disease duration could be confounding factors in this comparison, as could the exclusion of patients with ileostomy in the UC study. However, ileostomy was associated with a worse score in CD only for physical function and physical role (data not shown). The proportions of patients having active disease were similar in CD and UC, regardless of whether they were assessed by the PGA or by the clinical activity indices (CDAI and Seo Activity Index, Table 1). The clinical manifestations of UC and CD differ in many ways. For instance, abdominal pain, perianal problems, concomitant irritable bowel syndrome, systemic symptoms, fatigue and need for surgery are more frequent issues in CD [33,36,37]. A higher degree of anxiety and depression in CD has been reported [21,38,39], although differences in coping strategies and psychological functioning have not been firmly established [25,38,40]. Interestingly, the negative effect of female sex in scores was less pronounced in UC patients.

### Social factors

The lower rate of secondary and higher school education in patients with CD is probably not disease-related, as this finding was even more significant for patients diagnosed later in life. It might instead be explained by social background, as the higher rate of smoking in the CD population is a confounding factor linking the disease to a social context with low educational level [41]. In contrast, patients who completed secondary school, and had an early disease onset, had a lower rate of university degree than background population, implying a possible negative impact of the disease on the prospect of a more advanced education. No significant sex differences were found concerning education. Previous smaller studies

have not shown any difference in educational level for CD compared with background controls [22,42–44]. However, an association between low educational level and the likelihood of CD was found in a recent Swedish hospital discharge register study [45]. The doubled smoking rate was expected from the previously established close connection between smoking and disease development [46]. Still, this reminds us that greater efforts are needed to encourage smoking cessation in CD. Living single was more common among female patients with CD than in background controls. Male patients with CD showed a contrary tendency, though not significant. This finding could be related to the deeper impact of the disease on HRQL for women, but the cross-sectional design of this study does not allow for any firm conclusion on this matter. Lindberg *et al.* [47] noted a similar finding of a higher proportion of singles among female patients with CD compared with background controls (25.6 vs. 12.0%,  $P < 0.05$ ) in a study on smoking habits in CD. One hypothesis that calls for further study is the role of sex inequalities in partner-related and/or social support and demands [48,49]. Bernstein *et al.* [50] studied Canadian patients with IBD and found no difference from the general population regarding the probability of getting married after diagnosis. However, 20% of female and 10% of male patients who were married at diagnosis were single for 5 or more years later. Although not commented on in the study, their data show that the sex difference seemed to be attributed to a higher rate of female patients being widowed rather than divorced. The proportions of divorcees or widows/widowers among the single-living persons in our study did not differ significantly between the sexes. The prospect of becoming a parent and the number of children procreated for each parent seemed to be unaffected by CD, irrespective of sex. This is consistent with larger population-based fertility studies on female patients with CD, although the risk of adverse pregnancy outcome is increased [51]. Limited data exist for male patients with CD, but a lower number of children have been found in smaller studies [52,53]. The rate of long-term sickness and disability pension rate was more than double in the CD population. Again, this effect was more pronounced in women, a finding corroborated by the logistic regression analysis. Other factors associated with work disability were unsurprisingly older age, comorbidity and disease course preceding year. Women had a higher unemployment rate but we desist from drawing any firm conclusion, because of small numbers. The rates of sickness, employment and disability have varied between studies, and are difficult to compare because of different definitions, time periods and social security systems [54]. In a clinical multinational trial on highly selected moderately to severely ill patients with CD, female sex was associated with a greater risk of unemployment, and a tendency to a greater rate of disability pension [55]. Twice as many women as men were reported from a German disability pension

register for CD, but not for UC [56]. Two more recent studies from countries with social structures similar to Sweden are comparable. Bernklev *et al.* [57] reported an almost double unadjusted disability pension rate in Norwegian patients with CD 5 years after diagnosis (14.9 vs. 8.8% in background population), with three-fold to four-fold higher rate in women. A Dutch study found a sex-neutral three-fold rise in age-adjusted disability pension rate in CD, but the rate of employment was reduced only for men [58].

### Strengths and limitations

The study was performed on a large population-based cohort of outpatients from both county and university hospitals. Comparisons with background population and UC were limited by the lack of directly included controls of healthy individuals or patients with UC. However, the access of data from very large national registers, health surveys, and a nearly identical UC study, made meticulously age-matched and sex-matched comparisons possible. Furthermore, by calculating the effect size of any HRQL differences found, clinical relevance (and not merely statistical significance) was brought to the fore.

### Conclusion

CD had a substantial negative effect on several dimensions of general HRQL. The most striking deterioration was seen for female patients with CD. Male patients with CD experienced impairment comparable to female patients with UC, whereas male patients with UC only had a small effect on general HRQL. Patients with CD had a lower educational level compared with general population but this seems not to be caused by the disease. We found no difference in the ability to procreate, but female patients were more often living single. The rate of long-term sickness and disability pension was double for patients with CD, once again with an unfavourable outcome for women. Although a higher rate of arthralgia in women may have contributed to the sex-related disparity, no objective difference in disease activity was found. Further studies on both sex-related and sex-neutral internal and external determinants of the ability to cope and live with CD are warranted in order to target efforts to improve health perception and minimize disability.

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