



Original Article

# Health-Related Utility Weights in a Cohort of Real-World Crohn's Disease Patients

Dan Greenberg,<sup>a</sup> Doron Schwartz,<sup>b</sup> Hillel Vardi,<sup>c</sup> Michael Friger,<sup>c</sup>  
Orly Sarid,<sup>d</sup> Vered Slonim-Nevo,<sup>d</sup> Shmuel Odes<sup>e</sup>; on behalf of the Israeli  
IBD Research Nucleus [IIRN]

<sup>a</sup>Department of Health Systems Management, Faculty of Health Sciences & Guilford Glazer Faculty of Business and Management, Ben-Gurion University of the Negev, Beer-Sheva, Israel <sup>b</sup>Department of Gastroenterology and Hepatology, Soroka Medical Center, Beer-Sheva, Israel <sup>c</sup>Department of Public Health, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel <sup>d</sup>The Spitzer Department of Social Work, Ben-Gurion University of the Negev, Beer-Sheva, Israel <sup>e</sup>Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel

Corresponding author: Dan Greenberg, PhD, Department of Health Systems Management, Faculty of Health Sciences & Guilford Glazer Faculty of Business and Management, Ben-Gurion University of the Negev, P.O. Box 653, Beer-Sheva, 84105, Israel. Tel: 972-8-6477422; fax: 972-8-6477634; Email: [dangr@bgu.ac.il](mailto:dangr@bgu.ac.il)

## Abstract

**Background and Aims:** Estimating health-related utility weights in Crohn's Disease [CD] patients is crucial for assessing the cost-effectiveness of new pharmaceutical interventions. Values used in most analyses are based on secondary data and vary substantially among studies. We estimated utility weights in a consecutive sample of real-world CD patients.

**Methods:** Patients enrolled in an ongoing socioeconomic study of CD in the Israeli adult patient population completed a self-administered Short Form 36 health survey [SF-36] and Short Inflammatory Bowel Disease [SIBDQ] questionnaires and were assessed for their current clinical status, including the Harvey-Bradshaw Index [HBI] of disease severity. For each patient enrolled we calculated a utility weight using the SF-6D scoring system.

**Results:** The cohort comprised 425 patients [40% male] with mean age of 39.1 [ $\pm$  14.0] years. The average HBI was 6.1 [ $\pm$  5.4]; 198 [47%] patients were in remission state [HBI < 5], 99 [23%] had mild disease [HBI 5–7], 102 [25%] moderate [HBI 8–16], and 26 [6%] severe disease [HBI > 16]. Mean utility weights were: 0.667 in all patients, 0.744 in patients with disease remission, 0.638 in mild disease, 0.587 in moderate disease, and 0.505 in severe disease. The significant predictors of utility weights in a multivariable regression analysis were the HBI [ $\beta$  = -0.494;  $p$  < 0.001], economic status [ $\beta$  = 0.198;  $p$  < 0.001], time since diagnosis [ $\beta$  = 0.106;  $p$  < 0.001], male [compared with female] gender [ $\beta$  = 0.099;  $p$  = 0.009], hospital admission in the past year for any cause [ $\beta$  = -0.086;  $p$  = 0.027], and treatment with steroids [ $\beta$  = -0.100;  $p$  = 0.012] where  $\beta$  denotes the standardised regression coefficients; model adjusted  $R^2$  = 0.428.

**Conclusions:** Utility weights for patients in the remission and mild disease states were generally lower as compared with values used in published cost-effectiveness analyses. These values should be considered when assessing the value for money of future interventions for CD.

## 1. Background

Crohn's disease [CD] is a chronic inflammatory condition of the gastrointestinal tract that poses a substantial burden on patients,

their family, and society.<sup>1</sup> As CD is a prevalent and very expensive medical condition, its economic burden on Western countries' healthcare systems and societies is large.<sup>2</sup> This burden is amplified

by the substantial negative impact on patients' health-related quality of life [HRQoL] resulting from a range of physical, psychological, and social stressors.<sup>3</sup> Cost-effectiveness analyses [CEAs] are used in many jurisdictions to inform resource allocation decisions based on 'value for money' which is frequently measured by the cost per quality-adjusted life year [QALY] gained. Recent reviews of CEAs suggest that new biological treatments may be cost-effective in treating CD under certain clinical scenarios, but are usually not cost-saving.<sup>4,5</sup> The ongoing introduction of new biological agents, together with possible changes in their use [e.g., different doses, maintenance vs on-demand treatment], imply that future economic evaluations will be needed to compare their respective benefits and costs.

As CD is associated with very low mortality rates but with a major impact on patients' HRQoL, estimating health-related utility weights in these patients is crucial for assessing the cost-effectiveness of existing and new pharmaceutical and biological interventions. Utility weights are preference-based outcome measures that range between 0 [death] and 1 [perfect health]. Quality-adjusted life-years [QALYs] are calculated by multiplying the utility weight of each health state by the time spent in that state. Many of the economic evaluations in CD patients use utility weights from secondary sources to populate decision-analytical models [eg Markov models]. A review of these studies listed in the Tufts Medical Center Cost-Effectiveness Registry<sup>6</sup> suggests that these values are based on very few primary studies,<sup>7,8,9</sup> or on 'expert opinion'. Studies reporting on utility weights vary substantially in regard to the methods used to elicit these values (eg direct elicitation using the standard gamble or time trade-off techniques, EuroQoL [EQ-5D]), and in the methods used to classify CD patients by disease severity [eg disease remission, mild, moderate, severe, and very severe disease]. Moreover, even if studies use similar instruments, comparing reported results may be challenging as some report median utility-weights values, whereas others report mean values. Finally, assessment of HRQoL in CD patients is frequently based on single center studies recruiting a relatively small number of patients. We therefore sought to evaluate utility weights and estimate their predictors in a large non-selected consecutive cohort of patients enrolled in an ongoing study of CD in Israel.

## 2. Patients and Methods

### 2.1. Study population

Consecutive adult [age 18 years and over] patients with a confirmed CD diagnosis consenting to participate in an ongoing socioeconomic study of CD in the Israeli adult patient population were recruited. The broader socioeconomic study aims to determine the social and psychological stresses and coping strategies of patients with CD, their healthcare resource utilisation and costs, and the associations and correlations between these variables.

Patients were eligible to participate whatever the duration or severity of their illness, and irrespective of the treatment [including any surgery] they received. There were two methods of patient ascertainment; approximately two-thirds of patients were recruited on a consecutive basis when presenting for follow-up or for acute care at the outpatient gastroenterology departments of the five participating university-affiliated tertiary care hospitals across the country. These patients met the standard criteria for diagnosis as CD at their respective hospitals, and were given the option of completing the self-administered questionnaires on paper or online in their own time at home. A total of 60% of the patients approached in this fashion consented to complete the questionnaires. The other one-third of

patients were canvassed on the website of the Israel Foundation for Crohn's Disease and Ulcerative Colitis, and completed the questionnaires online. Of the patients who examined the questionnaire on the website, the majority went on to fill them in.

### 2.2. Patient demographics, disease, and treatment characteristics

Patients completing the study questionnaire were asked to report on a series of background and socio-demographic characteristics [eg gender, year of birth, marital status, self-reported economic status, education, history of smoking], as well as disease and treatment characteristics [eg year of CD diagnosis, history of surgery for CD, type of pharmaceutical treatment prescribed].

### 2.3. Assessment of health-related quality of life

General HRQoL was assessed using the Short-Form 36 health survey [SF-36] questionnaire. The SF-36 is a generic measure of quality of life. The 36 items investigate eight subscales: physical functioning, physical role, bodily pain, general health, vitality, social function, emotional role, and mental health. Two summary scores describe physical health and mental health. Scores for each subscale range from 0 to 100, with higher scores indicating better HRQoL. We used the Hebrew translation of the SF-36, which has been validated in Israel.<sup>10</sup> We also used the short version of the Inflammatory Bowel Disease Questionnaire [SIBDQ] to assess patients' disease-specific quality of life. The SIBDQ consists of 10 questions with a seven-point scale and measures physical, social, and emotional status. Total scores range from 10 [poor] to 70 [optimal] HRQoL.<sup>11</sup>

### 2.4. Assessment of disease activity

We have used the Harvey-Bradshaw Index [HBI] to assess disease activity.<sup>12</sup> The HBI assesses five domains: general well-being, abdominal pain, number of liquid stools per day, abdominal mass, and complications. These data were collected directly from patients and were not based on medical records or physical examination. The HBI is a reliable tool for assessing disease severity and is highly correlated with the Crohn's Disease Activity Index [CDAI].<sup>13</sup> Patients were classified to one of the four disease states: disease remission [HBI < 5]; mild disease [HBI 5–7]; moderate disease [HBI 8–16], and severe disease [HBI > 16].

### 2.5. Evaluation of utility weights

For each patient enrolled we have used the responses to the SF-36 questionnaire to calculate utility weights, using the SF-6D preference-based scoring system developed by Brazier *et al.*<sup>14</sup> and provided by agreement with the University of Sheffield, UK.<sup>15</sup> The resulting SF-6D index, scored from 0.0 [worst health state] to 1.0 [best health state] can be used to calculate QALYs in cost-effectiveness analyses applying decision-analytical modelling [eg Markov models].

### 2.6. Statistical analysis

Patient characteristics are reported as percentages, mean (standard deviation [SD]), median, and ranges. The relationship between patient background characteristics [ie age, sex, years of education, disease duration] and the measures of HRQoL, disease severity, and utility weights were assessed using the Pearson's non-parametric correlation coefficient. As SF-6D values are normally distributed, we have used multiple linear regression analysis to develop a model for predicting utility weights. The model included patients' age, sex, years of education, disease duration, SIBDQ scores, and the

Harvey-Bradshaw Index. Data analyses were performed using IBM SPSS Statistics 22 for Windows [Armonk, NY: IBM Corp];  $p$ -values less than 0.05 were considered statistically significant for all analyses.

## 2.7. Ethical considerations

The study was approved by the institutional review board of each participating hospital. All patients recruited at the hospitals signed an informed consent form, and their data were treated anonymously. Patients completing the questionnaire by internet were deemed to have consented; these patients did not provide any identifying information.

## 3. Results

A total of 598 patients completed the study questionnaires of which 425 [71%] were included in the analysis. Patients were excluded if they had incomplete SF-6D or HBI scores [Figure 1]. Included and excluded patients were similar in terms of present age, years of education, family and economic status, and history of smoking. Included [vs excluded] patients were characterised by a lower proportion of females [60% vs 71%, respectively;  $p = 0.011$ ] and a longer duration of disease [11.2 vs 9.4 years respectively;  $p = 0.039$ ]. The socio-demographic and treatment characteristics and HRQoL of included patients are presented in Table 1. Patient main characteristics are consistent with previous studies, suggesting that CD is more prevalent among women [60% of study population], and in relatively young patients [mean age  $39.1 \pm 14.0$  years].

Patients completing the questionnaire while visiting the out-patient clinic at one of the participating hospitals [ $N = 295$ ] were similar to patients completing the web-based version of the questionnaire [ $N = 130$ ] in the following characteristics: gender, family status, economic status, education, history of smoking, duration of disease, various types of pharmaceutical interventions, previous surgery for CD, and hospital admissions. However, patients completing the questionnaire online were younger [35.9 years old vs 40.5 years;  $p = 0.002$ ]. Patients in both groups did not differ in the average total SF-6D utility weights scores or by disease severity. Patients completing the questionnaire online had somewhat lower SIBDQ scores and lower HBI scores but, except for the disease remission state, these did not differ by disease severity strata [Table 2].

Utility weights scores were correlated with: HBI scores [ $-0.624$ ;  $p < 0.001$ ], SIBDQ scores [ $0.841$ ;  $p < 0.001$ ], disease duration [ $0.120$ ;  $p = 0.013$ ] [Figure 2], and years of education [ $0.180$ ;  $p < 0.001$ ]. HBI scores were also highly correlated with SIBDQ scores [ $-0.688$ ;  $p < 0.001$ ]. Scores were higher in males [ $0.69$  vs  $0.65$ ;  $p = 0.001$ ], in patients not receiving biological drugs [ $0.69$  vs  $0.65$ ;  $p = 0.004$ ], not treated with steroids [ $0.69$  vs  $0.59$ ;  $p < 0.001$ ], or immunomodulators [ $0.68$  vs  $0.65$ ;  $p = 0.035$ ] and increased with improvement in patients' economic status [ $p < 0.001$ ] [Table 1]. The significant predictors of utility weights in a multivariable regression analysis [model adjusted  $R^2 = 0.428$ ] were the HBI [ $\beta = -0.494$ ;  $p < 0.001$ ], economic status [ $\beta = 0.198$ ;  $p < 0.001$ ], time since diagnosis [ $\beta = 0.106$ ;  $p < 0.001$ ], male [compared with female] gender [ $\beta = 0.099$ ;  $p = 0.009$ ], hospital admission in the past year for any cause [ $\beta = -0.086$ ;  $p = 0.027$ ], and treatment with steroids [ $\beta = -0.100$ ;  $p = 0.012$ ] where  $\beta$  denotes the

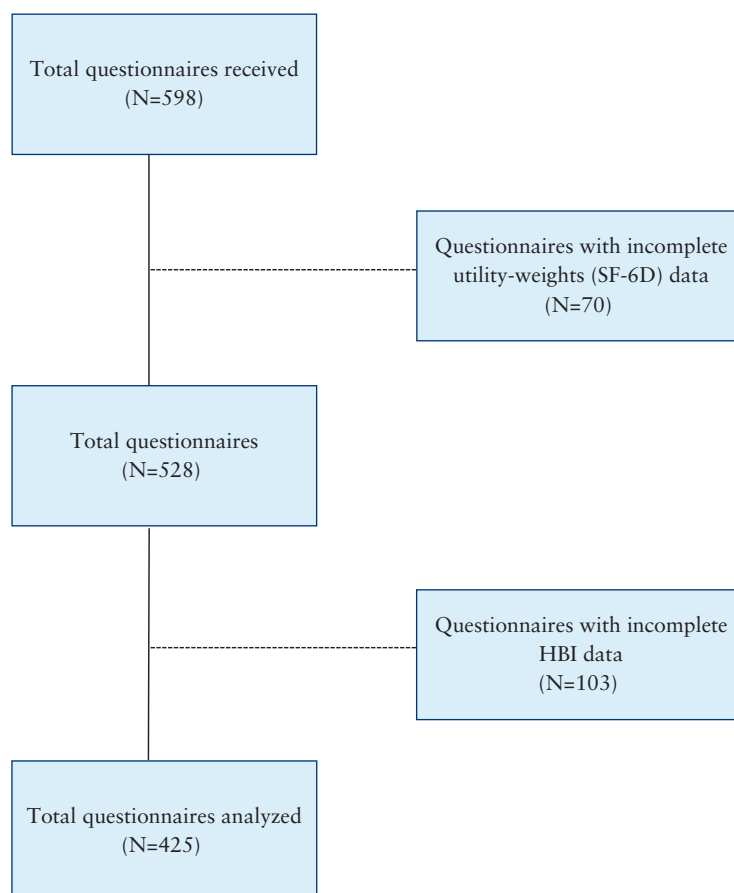


Figure 1. Flowchart of CD patients included in the analysis.

**Table 1.** Patient demographic and disease characteristics and utility-weight scores.

Patient characteristics	Number [%] or Mean [ $\pm$ SD]	SF-6D mean [ $\pm$ SD] score	<i>p</i> -Value
<b>Gender</b>			
Male	170 [40.0]	0.690 [ $\pm$ 0.134]	0.004
Female	255 [60.0]	0.652 [ $\pm$ 0.134]	
<b>Age [years]</b>			
Mean [ $\pm$ SD]	39.1 [ $\pm$ 14.0]		
Median [range]	36.0 [18.0–79.0]		
<b>Family status</b>			
Married/living with a spouse	249 [58.7]	0.675 [ $\pm$ 0.136]	0.374
Widowed	7 [1.7]	0.640 [ $\pm$ 0.146]	
Single/divorced	168 [39.6]	0.657 [ $\pm$ 0.135]	
<b>Economic status</b>			
Very bad/bad	80 [19.1]	0.575 [ $\pm$ 0.114]	<0.001
Moderate	221 [52.7]	0.675 [ $\pm$ 0.127]	
Good/very good	118 [28.2]	0.719 [ $\pm$ 0.135]	
<b>Education [years]</b>			
Mean [ $\pm$ SD]	14.7 [ $\pm$ 3.0]		
Median [range]	15.0 [4–30]		
<b>Smoking [ever smoker]</b>			
Yes	189 [44.8]	0.644 [ $\pm$ 0.135]	0.001
No	233 [55.2]	0.687 [ $\pm$ 0.134]	
<b>Disease duration [years]</b>			
Mean [ $\pm$ SD]	11.2 [ $\pm$ 9.0]		
Median [range]	10.0 [0–48]		
<b>Treated with biological drugs</b>			
Yes	190 [43.5]	0.650 [ $\pm$ 0.135]	0.017
No	235 [56.5]	0.681 [ $\pm$ 0.135]	
<b>Treated with steroids</b>			
Yes	83 [19.5]	0.588 [ $\pm$ 0.130]	<0.001
No	342 [80.5]	0.686 [ $\pm$ 0.128]	
<b>Treated with immunomodulators</b>			
Yes	216 [50.8]	0.654 [ $\pm$ 0.132]	0.035
No	209 [49.2]	0.681 [ $\pm$ 0.138]	
<b>Treated with 5-ASA</b>			
Yes	125 [29.4]	0.665 [ $\pm$ 0.134]	0.693
No	300 [70.6]	0.671 [ $\pm$ 0.140]	
<b>Previous surgery for CD</b>			
Yes	145 [34.3]	0.671 [ $\pm$ 0.136]	0.648
No	280 [65.7]	0.665 [ $\pm$ 0.136]	
<b>Hospitalised in past year for any reason</b>			
Yes	107 [23.1]	0.611 [ $\pm$ 0.133]	<0.001
No	313 [74.9]	0.686 [ $\pm$ 0.132]	
<b>Harvey-Bradshaw Index [HBI]</b>			
Total Score [ $\pm$ SD]	6.1 [ $\pm$ 5.4]	0.667 [ $\pm$ 0.136]; [0.630]*	<0.001**
Disease remission	198 [46.6]	0.744 [ $\pm$ 0.116]; [0.753]*	
Mild disease	99 [23.3]	0.638 [ $\pm$ 0.100]; [0.620]*	
Moderate disease	102 [24.5]	0.587 [ $\pm$ 0.108]; [0.580]*	
Severe disease	26 [6.1]	0.505 [ $\pm$ 0.117]; [0.485]*	
<b>SIBDQ</b>			
Total score [ $\pm$ SD]	46.9 [ $\pm$ 13.9]		<0.001
Disease remission	55.7 [ $\pm$ 10.2]; [58.0]		
Mild disease	44.5 [ $\pm$ 10.7]; [43.0]		
Moderate disease	37.1 [ $\pm$ 10.7]; [36.0]		
Severe disease	28.2 [ $\pm$ 13.0]; [23.5]		

SD, standard deviation; 5-ASA, 5-aminosalicylic acid; CD, Crohn's disease; SIBDQ, Short Inflammatory Bowel Disease Questionnaire; SF-6D, Short Form survey of health 6D.

\*\*Difference between utility values of four severity states of HBI.

standardised regression coefficients. Other variables, including the method of patient recruitment [ie hospital's outpatient clinic or CD foundation], as well as other socio-demographic and disease characteristics were not significant covariates in our analysis.

#### 4. Discussion

The objective of this study was to assess HRQoL and utility weights in a large cohort of CD patients in Israel. HRQoL assessment is particularly important in these patients because of the young age of disease onset,

**Table 2.** Comparison of patient demographics, disease states, and utilityweight scores between patients completing the paper questionnaire and patients completing the online version.

Patient characteristics	Paper questionnaire N = 295 Mean [%] or Mean [ $\pm$ SD]	Online questionnaire N = 130 Mean [%] or Mean [ $\pm$ SD]	p-Value*
<b>Gender</b>			
Male	114 [38.6]	56 [43.1]	0.390
Female	181 [61.4]	74 [56.9]	
<b>Age [years]</b>	40.5 [ $\pm$ 14.6]	35.9 [ $\pm$ 12.1]	0.002
<b>Family status</b>			
Married/living with a spouse	176 [59.7]	73 [56.6]	0.823
Widowed	5 [1.7]	2 [1.6]	
Single/divorced	114 [38.6]	54 [41.9]	
<b>Economic status</b>			
Very bad/bad	56 [19.3]	24 [18.6]	0.266
Moderate	146 [50.3]	75 [58.1]	
Good/very good	88 [30.3]	30 [23.3]	
<b>Education [years]</b>	14.7 [ $\pm$ 3.0]	14.8 [ $\pm$ 2.8]	0.780
<b>Smoking [ever smoker]</b>			
Yes	140 [47.6]	49 [38.3]	0.076
No	154 [52.4]	79 [61.7]	
<b>Disease duration [years]</b>	11.6 [ $\pm$ 9.1]	11.2 [ $\pm$ 9.0]	0.163
<b>Treated with biological drugs</b>			
Yes	130 [44.1]	60 [46.2]	0.690
No	165 [55.9]	70 [53.8]	
<b>Treated with steroids</b>			
Yes	56 [19.0]	27 [20.8]	0.380
No	239 [81.0]	103 [79.2]	
<b>Treated with immunomodulators</b>			
Yes	146 [49.5]	70 [53.8]	0.235
No	149 [50.5]	60 [46.2]	
<b>Treated with 5-ASA</b>			
Yes	88 [29.8]	37 [28.5]	0.435
No	207 [70.2]	93 [71.5]	
<b>Previous surgery for CD</b>			
Yes	102 [34.6]	43 [33.1]	0.764
No	193 [65.4]	87 [66.9]	
<b>Hospitalised in past year for CD</b>			
Yes	72 [24.4]	35 [26.9]	0.582
No	233 [75.6]	95 [73.1]	
<b>Harvey-Bradshaw Index [HBI]</b>			
Total score	5.6 [ $\pm$ 5.0]	7.2 [ $\pm$ 6.2]	0.008
Disease remission	148 [50.2]	50 [38.5]	0.090
Mild disease	68 [23.1]	31 [23.8]	
Moderate disease	64 [21.7]	38 [29.2]	
Severe disease	15 [5.1]	11 [8.5]	
<b>SIBDQ*</b>			
Total score	48.5 [ $\pm$ 13.8]	43.3 [ $\pm$ 13.6]	<0.001
Disease remission	56.5 [ $\pm$ 10.0]	53.2 [ $\pm$ 10.5]	0.049
Mild disease	45.1 [ $\pm$ 10.8]	43.1 [ $\pm$ 10.5]	0.387
Moderate disease	38.0 [ $\pm$ 11.3]	35.5 [ $\pm$ 9.5]	0.255
Severe disease	29.6 [ $\pm$ 13.0]	26.2 [ $\pm$ 12.1]	0.518
<b>SF-6D utility weights*</b>			
Total score	0.67 [ $\pm$ 0.14]	0.65 [ $\pm$ 0.13]	0.121
Disease remission	0.75 [ $\pm$ 0.12]	0.73 [ $\pm$ 0.12]	0.270
Mild disease	0.63 [ $\pm$ 0.10]	0.64 [ $\pm$ 0.10]	0.654
Moderate disease	0.58 [ $\pm$ 0.11]	0.60 [ $\pm$ 0.11]	0.263
Severe disease	0.51 [ $\pm$ 0.12]	0.49 [ $\pm$ 0.12]	0.651

SD, standard deviation; 5-ASA, 5-aminosalicylic acid; CD, Crohn's disease; SIBDQ, Short Inflammatory Bowel Disease Questionnaire; SF-6D, Short Form survey of health 6D.

\*p-Values indicate differences in total SIBDQ or utility weights scores or differences in each stratum of severity of disease.

the severity of symptoms, and the unpredictability of disease flares. As the disease is not curable and is marked by high morbidity but low to no mortality, the main objective of CD treatment is achieving and maintaining disease remission and improving patients' HRQoL.

We found that the significant predictors of utility weights in our analysis were the HBI, economic status, disease duration, and male gender. The negative association between the disease activity [HBI] score and HRQoL has been confirmed in the vast majority of

studies.<sup>16,17</sup> Health-related quality of life was lower in females compared with males. This finding is consistent with previous studies of IBD as well as other chronic diseases.<sup>16,18,19</sup> This discrepancy in HRQoL could be explained by psychological factors, disease-related concerns, and worries that may play a greater role in females than in males. Furthermore, disease duration was positively correlated with improvement in HRQoL in a series of studies.<sup>20</sup> It is possible that CD patients develop coping strategies as the disease progresses, and it becomes less of a burden over time. To the best of our knowledge, only very few analyses reported that IBD patients of lower socioeconomic class have increased morbidity and reduced HRQoL scores.<sup>19</sup> It has been suggested that patients in a lower socioeconomic class may be less likely to seek health care and that their reduced quality of life may be also affected by non-health factors. These differences could not be explained by variations in treatment patterns or access to healthcare in our cohort, as there were no differences in the proportion of patients treated with biological drugs or undergoing surgery by economic status. Thus, the mechanism underlying the income-related inequalities in HRQoL for CD patients warrants further investigation.

Our findings suggest that CD patients have deprived HRQoL even if their disease is not active. The utility-weight value [0.744] for patients with disease remission as well as the mean value [0.667] in patients with mild disease are considerably lower compared with values reported in previous studies [Table 3]. In severe disease, however, the values found in our study [0.505] are similar to those previously reported.<sup>7,8</sup>

The lower utility weights reported in the present study, as compared with previous reports, could be partially explained by the elicitation method. The EQ-5D and SF-6D used in many studies differ in their valuation techniques, items covered, and classification systems. Therefore, they can generate different utility weight scores for the same health states.<sup>23,24</sup> The evidence on differences between EQ-5D and SF-6D scores is mixed, but in many chronic conditions, as well as in population-level studies, the SF-6D classification system tends

to generate lower scores than the EQ-5D.<sup>25,26,27,28,29</sup> Similar findings were reported for IBD patients.<sup>22</sup> Moreover, it is well documented that using direct elicitation approaches as used by Gregor *et al.*<sup>8</sup> generated substantially higher utility scores as compared with indirect methods [eg EQ-5D, SF-6D].<sup>30</sup>

Due to variation in methods and study population used to elicit utility weights, it is essential to accurately measure these values that could be then used to populate cost-effectiveness models, assess 'value for money' of different treatment modalities, and inform resource allocation decisions.<sup>31</sup> Indeed, the difference between utility weights used for disease remission state and active disease may have a substantial impact on the incremental cost-effectiveness ratio [ICER]. To illustrate, Blackhouse *et al.*<sup>32</sup> presented a cost-effectiveness analysis of initiation and maintenance treatment with anti-tumour necrosis factor alpha [TNF- $\alpha$ ] drugs for refractory CD in Canada. They use a utility value of: 0.82 for mild disease [medical or surgical remission]; 0.73 for moderate [drug-responsive] disease; and 0.54 for severe [drug refractory, surgery] disease. A 50% reduction in differences between utility weights for remission compared with the worse health states more than doubled the ICER. Xie *et al.*,<sup>33</sup> who used a utility value of 0.79 for the remission state, varied this value in a one-way sensitivity analysis and suggest that, compared with the base-case analysis, the ICER increase by approximately 50% when a value of 0.72 was used and decreased by approximately 30% when the respective value for the remission state was 0.86. Tang *et al.*<sup>34</sup> in their analysis of the cost-effectiveness of biological treatments for Crohn's disease suggest that utility weights for remission and non-remission states were the most influential variables on study results. Other studies, however, suggest that ranging utility weights values by 10% reported lower impacts on study results.<sup>21,35,36</sup>

Our study has several limitations. First, as our study is based on an observational cohort where two-thirds of the patients were attending at the hospitals, and it may be subject to sampling bias of more severe patients. However, CD patients in Israel are treated by gastroenterologists, usually at hospitals' outpatient clinics and not by their primary

**Table 3.** Summary of utility weights reported by disease severity.

Disease state	Utility weight score	Methods used to elicit utility weights	Number of patients included in the analysis	Reference
Disease remission	0.88	Standard gamble	180	Gregor <i>et al.</i> <sup>7</sup>
Mild disease	0.82			
Moderate disease	0.73			
Severe disease	0.54			
Chronically active therapy-responsive	0.86	Standard gamble	180	Loftus <i>et al.</i> <sup>21a</sup>
Acute disease exacerbation	0.77			
Chronically active therapy-resistant	0.74			
Disease remission	0.859			
Moderate disease	0.795	EQ-5D	628	Casellas <i>et al.</i> <sup>8b</sup>
Severe disease	0.693			
Very severe disease	0.433			
Disease remission	0.80			
Mild disease	0.72	Time trade off	48	Arseneau <i>et al.</i> <sup>9c</sup>
Moderate-severe disease	0.6			
Disease remission	0.79	SF-6D	425	Present study
Severe disease	0.32			
Disease remission	0.744			
Mild disease	0.638			
Moderate disease	0.587			
Severe disease	0.505			

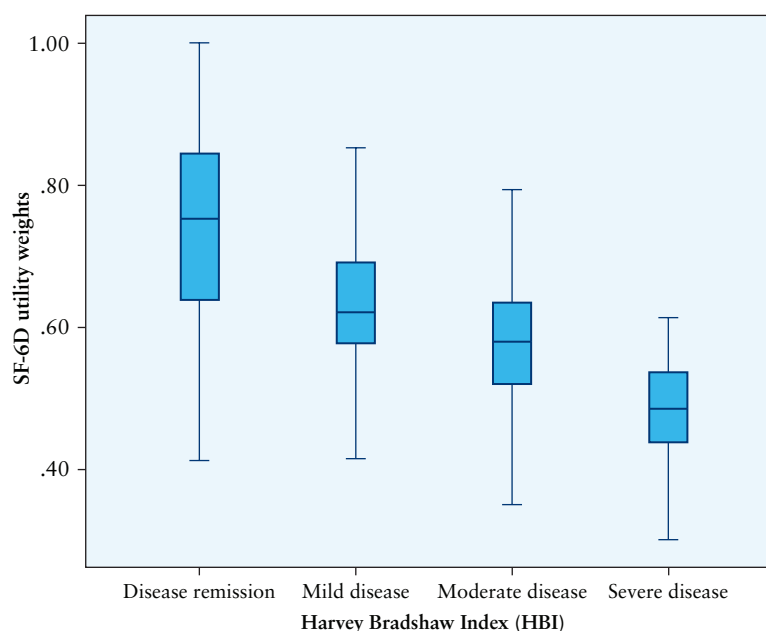
EQ-5D, EuroQoL 5D; SF-6D, Short Form survey of health 6D.

<sup>a</sup>These values are based on a post-hoc analysis performed on data collected by Gregor *et al.*<sup>7</sup>

<sup>b</sup>Values reported by Casellas *et al.*<sup>8</sup> are median values.

<sup>c</sup>Steroid-refractory ulcerative colitis patients.





**Figure 2.** Mean Short Form health survey 6D [SF-6D] utility weight values, 95% confidence intervals and range. The mean values of SF-6D are decreasing with the increase in disease severity by Harvey-Bradshaw Index [HBI].

care physicians. We recruited patients from various medical centres throughout the country and also recruited participants from the Israel Foundation for Crohn's Disease and Ulcerative Colitis. These patients had similar characteristics to patients recruited from hospitals and a slightly more severe disease and impaired disease-specific HRQoL. Approximately one-half of patients in our study were in the remission state and another quarter had mild disease, suggesting that our patient population was not characterised by a more severe disease. Moreover, we report utility weights by disease severity rather than reporting one utility weight value for the entire cohort. Thus, we believe that our study findings are most likely to be generalisable.

Second, many clinical studies use the Crohn's Disease Activity Index [CDAI] to assess disease activity. Our estimates of disease activity were based on the HBI; thus the results may not be applicable to studies reporting utility weights by disease severity based on the CDAI. However, although the HBI is a simpler tool, a recent study suggested that it is highly correlated with CDAI scores and equally effective in assessing disease severity.<sup>13</sup>

Third, since this study was conducted based on questionnaires filled in by patients without the need to obtain information from their physicians or their medical records, we used data reported by patients rather than results of a physical examination to estimate the HBI. Therefore we included in our analysis only patients that completed all HBI questions.

Finally, self-reported HRQoL may differ among countries due to geographical and cultural differences. These potential differences, which may apply to all studies conducted in various settings, could not be explored in the current study. Notwithstanding these possible limitations, our study is based on a large number of patients treated in a real-world setting and may add to the existing knowledge on HRQoL and utility weights in CD patients.

## 5. Conclusions

Crohn's disease patients suffer from a deprived HRQoL even in the remission and mild stages of the disease. Utility weights for

these patients were generally lower as compared with values used in published cost-effectiveness analyses, especially in the disease remission state. These values should be considered when assessing the 'value for money' of current and future interventions for CD, either in the base-case analysis or in the sensitivity analysis exploring the influence of various study parameters on cost-effectiveness results.

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## Conflict of Interest

None of the authors have conflicts of interests in regard to this manuscript

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