



# Differing Relationship of Psycho-Social Variables with Active Ulcerative Colitis or Crohn's Disease

Orly Sarid<sup>1</sup> · Vered Slonim-Nevo<sup>1</sup> · Doron Schwartz<sup>2</sup> · Michael Friger<sup>3</sup> · Ruslan Sergienko<sup>3</sup> · Avihu Pereg<sup>4</sup> · Hillel Vardi<sup>3</sup> · Elena Chernin<sup>3</sup> · Terri Singer<sup>4</sup> · Dan Greenberg<sup>5</sup> · Shmuel Odes<sup>4</sup> · on behalf of the Israel IBD Research Nucleus (IIRN)

Published online: 9 March 2018  
© International Society of Behavioral Medicine 2018

## Abstract

**Purpose** How psycho-social variables affect the degree of disease activity in patients with ulcerative colitis (UC) or Crohn's disease (CD) is incompletely understood. Therefore, we measured and compared the impact of psycho-social variables on the active disease state in UC and CD.

**Method** One hundred and twenty-two UC and 305 CD patients with active disease completed questionnaires detailing their psychological symptoms, threatening experiences, disease-coping strategies, satisfaction with life, quality of life, and demographics.

**Results** UC and CD patients were aged (mean, SD)  $38.6 \pm 14.0$  and  $45.2 \pm 15.1$  years, respectively. The psychological symptom index (median, IQR) was greater in UC 1.24 (0.8) than CD 0.9 (0.8),  $p < 0.001$ . UC used more emotion-focused strategies, 24.5 (5.7) than CD, 23.0 (5.7),  $p < 0.03$ ; problem-focused strategies, 16.4 (4.5) vs. 15.4 (4.2),  $p < 0.04$ ; and dysfunctional strategies, 23.7 (5.7) vs. 22.0 (5.0),  $p < 0.01$ . UC activity correlated with gender, age, economic status, psychological symptoms, threatening experiences, all coping strategies, satisfaction with life, and quality of life ( $p < 0.02$ – $0.001$ ). CD activity correlated with economic status, psychological symptoms, threatening experiences, dysfunctional strategies, satisfaction with life, and quality of life ( $p < 0.05$ – $0.001$ ). UC activity was predicted by psychological symptoms (9.1% variance), economic status (6.9%), problem-focused strategies (4.2%), and threatening experiences (1.3%); CD activity by threatening experiences (5% variance) and psychological symptoms (4%). In path analysis, psychological symptoms and problem-focused strategies mediated the effects of economic status, age, and threatening experiences on UC activity. In CD, the dominant pathway was threatening experiences impacting on psychological symptoms.

**Conclusion** The impact of psycho-social variables on the active disease state differs between UC and CD, thus indicating a need for specifically tailored psychotherapies.

**Keywords** Ulcerative colitis · Crohn's disease · Psychological distress · Disease-coping strategies · Structural equation modeling

✉ Shmuel Odes  
odes@bgu.ac.il

<sup>1</sup> Spitzer Department of Social Work, Ben-Gurion University of the Negev, POB 653, 84105 Beer Sheva, Israel

<sup>2</sup> Department of Gastroenterology and Hepatology, Soroka Medical Center, Rager Blvd, 84101 Beer Sheva, Israel

<sup>3</sup> Department of Public Health, Faculty of Health Sciences, Ben-Gurion University of the Negev, POB 653, 84105 Beer Sheva, Israel

<sup>4</sup> Faculty of Health Sciences, Ben-Gurion University of the Negev, POB 653, 84105 Beer Sheva, Israel

<sup>5</sup> Department of Health Systems Management, Faculty of Health Sciences, Ben-Gurion University of the Negev, POB 653, 84105 Beer-Sheva, Israel

## Abbreviations

UC	ulcerative colitis
CD	Crohn's disease
ES	economic status
GSI	global severity index
LTE	List of Threatening Experiences
SWLS	Satisfaction with Life Scale
SF-36	MOS 36-Item Health Survey Instrument
P -	Patient Simple Clinical Colitis Activity Index
SCCAI	
P-HBI	Patient Harvey-Bradshaw Index
COPE	Brief Cope Inventory (Brief Coping Operations Preference Enquiry)

## Introduction

Ulcerative colitis (UC) and Crohn's disease (CD) are the common types of chronic Inflammatory Bowel Disease, with onset in young adults and a fluctuating course of exacerbations and remissions [1, 2]. Symptoms include abdominal pain, diarrhea, weight loss, malaise, and extra-intestinal features, like arthralgia. There is reduced quality of life and satisfaction with life. There is absence from work with consequent loss of income, and considerable financial outlay [3, 4].

Exacerbation of UC and CD is related to the fluctuating course of the diseases with their immunological instability, as well as superimposed bacterial and viral infections, smoking habit, non-steroidal anti-inflammatory drugs, non-adherence to therapeutic regimes, nutritional issues, and seasonality [2]. Psycho-social factors also impact considerably on the course of UC and CD [5]. Stressful life events have significant effects involving the neuronal, immune, and endocrine systems [6]. Stress includes threatening experiences, like death, severe illness and injury, and financial strain. Studies controlling for mental illness showed that stressful life events had a negative impact on physical illness [7, 8]. Life events were associated with exacerbation of these diseases [9]. Specifically, our recent study in CD demonstrated that threatening experiences including economic difficulty predicted disease activity [10]. In UC, heightened active disease was predicted by threatening experiences [11].

Coping with disease is a cognizant, mental adjustment with problem-focused, emotion-focused, and dysfunctional coping strategies [12, 13]. Problem-focused coping defines a problem and generates solutions. Emotion-focused coping reduces emotional distress. Dysfunctional, maladaptive coping includes denial and use of alcohol and drugs. Use of emotion-focused coping was associated with worse psychological outcomes [14] whereas a less consistent effect of improved psychological outcomes was observed with problem-focused coping [15]. These two review articles did not distinguish between remittent and flaring diseases, with the exception that one quoted report found that active UC was significantly associated with depression. UC and CD patients in Canada used dysfunctional problem-focused coping more often than healthy individuals; patients with active disease were more distressed, used more avoidant coping strategies, and had lower perceived health [16]. Swedish patients demonstrated no differences in coping use between UC and CD; however, patients with active disease reported more emotional distress and reduced quality of life [17]. Apart from these articles, most studies in the literature have focused on cohorts containing a mix of patients at all stages of disease. This approach fails to delineate specifically those individuals with disease exacerbation or to determine the specific factors that contribute to heightened disease activity. Inflammatory processes are known to be related to unique psychological responses [18].

In this study, we focused on UC and CD patients with active disease. We examined the postulated impact of demographic and psycho-social characteristics on disease activity in these patients. We created models using regression analysis to determine the amount of variance described by a series of psycho-social variables. We used structural equation modeling to identify whether the activity of UC and CD is impacted differently by psycho-social variables.

## Methods

### Study Design

In this cross-sectional study, we collected data of UC and CD patients from July 2013 to June 2016. Patients were recruited from two sources. (1) Patients were ascertained consecutively at the out-patient Gastroenterology Departments of five participating university-affiliated hospitals. These patients met the ECCO diagnostic criteria [19, 20] and completed questionnaires in paper form. (2) Patients were solicited via an advertisement of the study on the websites of "The Israel Foundation for Crohn's Disease and Ulcerative Colitis" and the "CAMONI social network." Those patients who chose to participate then completed the questionnaires on-line. It was assumed that these internet patients would have been correctly diagnosed as UC or CD. All questionnaires were in validated Hebrew translation. By these two methods, we have created a database of 808 patients; those with active UC or CD as defined by specific disease indices were incorporated into the cohort for this study. Examination of electronic records of patients recruited at the hospitals showed that < 5% had mild psychological co-morbidities and none had psychiatric disease, and their inclusion in the cohort did not alter the outcome of the study. Such information was not obtainable from internet-recruited patients.

Patients filled in socio-demography, smoking habits, disease duration, medications, surgery, and hospitalizations. Patients were asked to rate their economic status subjectively on a Likert scale from 1 (poor) to 5 (rich). UC patients completed the Patient Simple Clinical Colitis Activity Index [21, 22] and CD patients the Patient Harvey-Bradshaw Index [23]. All patients completed five socio-psychological questionnaires: Brief Symptom Inventory (BSI) [24]; Brief COPE Inventory (COPE) [12]; Satisfaction with Life Scale (SWLS) [25]; Short-Form Health Survey (SF-36) [26]; and List of Threatening Experiences Questionnaire [27].

### Measures

*Patient Simple Clinical Colitis Activity Index (P-SCCAI)* assesses current activity of UC [21, 22]. Its six questions about bowel frequency, urgency of defecation, blood in the feces,

well-being, and extra-intestinal manifestations in the past week yield a disease activity score in the range 0–20, with 2 being the cut-off between inactive and active disease. Patients with P-SCCAI  $\geq 3$  were entered in the study.

*Patient Harvey-Bradshaw Index (P-HBI)* contains four items reflecting the previous day's symptoms and signs of CD [23]. The question about an abdominal mass is removed in the P-HBI. Scores are as follows:  $< 5$  disease remission, 5–7 mild disease, 8–16 moderate disease, and  $> 16$  severe disease. Patients with P-HBI  $\geq 5$  were entered in the study.

*Brief Symptom Inventory (BSI)* measures psychological stress in the past month, with 53 questions covering depression, somatization, obsession–compulsion, interpersonal sensitivity, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism [24]. It yields a global summary score, the Global Severity Index (GSI), with range 0–4; a higher score reveals more psychological distress. In normal persons, the GSI was  $0.30 \pm 0.31$ .

*List of Threatening Experiences Questionnaire (LTE)* measures the amount of 12 negative life events in the last six months [27]. The score of LTE ranges from 0 to 12, a higher value indicating more negative life events.

*Brief Coping Inventory (Brief Coping Operations Preference Enquiry or Brief COPE)* comprises 28 coping items rated on a 1–4 scale [12]. Items are summed to yield 14 coping subscales that are further grouped into three coping strategies: emotion-focused (comprising emotional support use, positive reframing, humor, acceptance, religion), problem-focused (active coping, instrumental support use, planning), and dysfunctional coping (self-distraction, denial, substance use, behavioral disengagement, venting, self-blame). A greater score indicates more use of that strategy.

*MOS 36-Item Health Survey Instrument (SF-36)*. This generic health-related quality of life measure of the past four weeks comprises 36 items in eight domains [26]; it yields the Physical Health Summary Score (physical functioning, role-physical, bodily pain, general health) and Mental Health Summary Score (vitality, role-emotional, social functioning, mental health), each with range 0–100. A higher score represents a better quality of life.

*Satisfaction with Life Scale (SWLS)* measures one's level of satisfaction with life at the present moment. Its five questions have seven possible responses. The summary score has the range 5–35; a higher value indicating more satisfaction with life [25].

## Analysis

All data were pooled for analysis using the IBM SPSS Statistics 22 for Windows, with the AMOS Module (IBM Corp.: Armonk, NY) for path analysis.  $p$  values  $< 0.05$  determined statistical significance.

In the descriptive statistics, continuous variables are expressed as means and standard deviations for normally distributed variables or medians and interquartile ranges when data distribution was skewed; categorical variables are expressed as frequencies and percentages. The socio-demographic variables were compared between UC and CD using Student's  $t$  test and chi-square tests. Psychological variables were compared using the *Mann-Whitney* test. A correlation analysis was performed separately for UC and CD with the following variables: gender, age, family status, economic status, working, smoking, LTE, SWLS, SF-36, GSI, and COPE. Multiple regression analysis examined the impact of demographic and socio-psychological variables that were significant in univariate analyses on P-HBI and P-SCCAI separately. P-HBI and P-SCCAI had a non-normal distribution and were normalized for the regression using log transformations.

To understand further the relationships and interactions between the independent and dependent variables and identify the mediators, we used the Structural Equation Modeling (SEM) [7, 28, 29]. Variables correlating significantly with the disease activity indices (P-SCCAI for UC, P-HBI for CD) were included in the SEM analysis. We first created a model with both diseases together to define the mediators. In a second model, the diseases were separated. A general model was drawn by placing demographic variables as predictors. Modifications were derived by adding pathways based on AMOS modification indices. In an iterative process, we added pathways that improved the model fit and removed variables that did not add significantly to the model fit. All models were estimated using the maximum likelihood estimation method. Since the quality of fit of SEM models is affected by sample size, multiple model fit indicators were assessed, including  $\chi^2$ , the ratio of the  $\chi^2$  to degrees of freedom ( $\chi^2/\text{df}$ ), the comparative fit index (CFI),  $p$  value, a root mean square error of approximation (RMSEA), and the standardized root mean square residual (SRMR). Since the critical value of each  $\chi^2$  degree of freedom is 3.8, all values that showed less than this value for each degree of freedom were considered non-significant and therefore did not deviate from the saturated model. Values close to 0.95 for the CFI, close to 0.06 for the RMSEA, and close to 0.08 for the SRMR indicate a good fit of the data to the model. In the final model, economic status, LTE, and age were the independent variables, while GSI and problem-focused coping strategy were the mediators. A single-disease activity index, derived by standardizing P-SCCAI and P-HBI, was the dependent variable. Combining these two disease activity indices into a single dependent variable was based on their similar distribution characteristics as kurtosis (P-HBI 1.89, P-SCCAI 1.83) and skewness (P-HBI 1.48, P-SCCAI 1.29). Since SEM analysis is based on correlation matrices, standardization does not affect the relations between variables.

## Results

### Demographic, Medical, and Psycho-Social Characteristics

The cohort (Table 1) comprised 122 UC (50% recruited from hospitals) and 305 CD patients (52.5% from the hospitals) with mean ages  $38.6 \pm 14.0$  and  $45.2 \pm 15.1$  years, respectively ( $p < 0.001$ ). Gender and education were similar in UC and CD, but there were relatively more Israel-born participants in CD ( $p < 0.04$ ) and relatively fewer current smokers ( $p < 0.001$ ). The majority of patients was working and of average self-declared economic status. Most patients were Jewish and secular or traditional in religious practice.

The medical and psycho-social data are shown in Table 2. Mean disease activity scores were 5 points higher than the defined upper score of remission in each disease. Disease duration was similar in both diseases. As expected, CD patients used more immunomodulatory, corticosteroid, and biologic therapies than UC patients and had undergone more surgical procedures. The arithmetically higher GSI median score in UC ( $1.24 \pm 0.78$ ) was suggestive of a greater degree of psychological distress than in CD ( $0.94 \pm 0.78$ ). UC patients reported more threatening experiences (median 2.0) than CD patients (median 1.5). UC patients made  $> 6\%$  more use of all three coping strategies compared with CD patients ( $p < 0.05$ ). The scores of satisfaction with life and SF-36 physical and mental quality of life were similar in both diseases. Only 4% of the hospital-recruited patients had

**Table 1** Comparison of the characteristics of the patients with active ulcerative colitis and Crohn's disease

Variables	Ulcerative colitis ( $n = 122$ )	Crohn's disease ( $n = 305$ )	$p$
Site of recruitment			
Hospitals	61 (50%)	160 (52.5%)	0.646
Internet	61 (50%)	145 (47.5%)	
Age, years	$38.60 \pm 13.95$	$45.19 \pm 15.07$	0.000
Gender			0.490
Female	64 (64.00%)	167 (60.07%)	
Male	36 (36.00%)	111 (39.93%)	
Family status			0.009
Couple	83 (69.75%)	163 (55.82%)	
Single	36 (30.25%)	129 (44.18%)	
Education, years	14.0 (5.0; 30.0) (12.0; 16.0)	14.0 (0.0; 23.0) (12.0; 17.0)	0.482
Number of children	2.0 (0.0; 9.0) (0.0; 3.0)	2.0 (0.0; 7.0) (1.0; 3.0)	0.010
Religion			0.389
Christian	0 (0.00%)	2 (0.66%)	
Jewish	115 (95.04%)	291 (96.04%)	
Muslim	6 (4.96%)	8 (2.64%)	
Other	0 (0.00%)	2 (0.66%)	
Religiosity			0.633
Religious	14 (11.57%)	31 (10.23%)	
Secular	70 (57.85%)	172 (56.77%)	
Traditional	31 (25.62%)	74 (24.42%)	
Ultra-Orthodox	6 (4.96%)	26 (8.58%)	
Birth-place			0.032
Americas	2 (1.64%)	7 (2.30%)	
Asia	4 (3.28%)	2 (0.66%)	
Africa	8 (6.56%)	15 (4.92%)	
Europe	15 (12.30%)	18 (5.90%)	
Israel	90 (73.77%)	260 (85.25%)	
Smoking habit			0.001
Non-smoker	66 (54.10%)	224 (73.44%)	
Smoker	45 (36.88%)	69 (23.55%)	
Economic status	3.0 (1.0; 5.0) (2.0; 3.0)	3.0 (1.0; 5.0) (3.0; 3.0)	0.133
Work status			0.696
Not working	38 (37.25%)	114 (39.45%)	
Working	64 (62.75%)	175 (60.55%)	

Mean  $\pm$  SD, or median (range) (IQR), or value (%)

**Table 2** Medical and psycho-social parameters of the cohort

Variables	Ulcerative colitis	Crohn's disease	<i>p</i> <sup>a</sup>
P-SCCAI			
Hospitals	6.41 ± 3.49		0.202
Internet	7.13 ± 3.69		
P-HBI			
Hospitals		9.34 ± 4.70	0.814
Internet		9.60 ± 5.18	
Disease duration (years)	8.0 (0.0; 24.0) (3.0; 14.0)	9.0 (0.0; 24.0) (4.0; 16.0)	0.291
Surgery for UC or CD	9 (7.38%)	106 (34.75%)	< 0.001
Hospitalization, past year	37 (33.64%)	100 (32.79%)	0.871
5-Aminosalicylic acid	86 (70.49%)	94 (30.82%)	< 0.001
Immunomodulators	18 (14.75%)	143 (46.89%)	< 0.001
Corticosteroids	25 (20.49%)	153 (50.16%)	< 0.001
Biologic agents	22 (18.03%)	85 (27.87%)	0.034
List of threatening experiences	2.0 (0.0; 12.0) (1.0; 4.0)	1.5 (0.0; 8.0) (0.0; 3.0)	0.212
SWLS: Satisfaction With Life Scale	20.12 ± 7.98	21.00 ± 7.86	0.320
SF-36 physical health	37.8 (10.3; 57.8) (29.2; 44.6)	38.5 (20.6; 64.4) (32.4; 46.1)	0.140
SF-36 mental health	37.8 (9.7; 64.2) (30.0; 45.6)	33.0 (14.3; 67.9) (26.6; 44.9)	0.132
COPE: emotion-focused strategies	24.49 ± 5.68	23.04 ± 5.74	0.021
COPE: problem-focused strategies	16.40 ± 4.45	15.42 ± 4.16	0.033
COPE: dysfunctional strategies	23.65 ± 5.68	21.97 ± 5.04	0.010
GSI: Global Severity Index	1.24 ± 0.78	0.94 ± 0.78	0.000

Mean ± SD, or median (range) (IQR), or value (%)

<sup>a</sup> Mann-Whitney test

minor psychiatric co-morbidities and treatments, but no such data were obtainable from the internet patients.

### Sub-Group Analysis: Differences by Site of Patient Recruitment

The demographic, medical, and psycho-social parameters of the cohort (as detailed in Tables 1 and 2) were analyzed separately for hospital-recruited and internet-recruited patients. In UC, patients recruited from the hospitals were found to differ from those recruited by the internet in terms of the following: mean age, 48.6 ± 15.2 versus 41.7 ± 14.2 years, respectively ( $p < 0.02$ ); education, 13.1 ± 3.7 versus 15.3 ± 2.7 years, respectively ( $p < 0.001$ ); and rate of current smoking, 58.9% versus 21.8% ( $p < 0.001$ ). Furthermore, the surgical rate was 14.8% in hospital UC patients versus 0 in internet patients ( $p = 0.002$ ). With regard to CD, hospital-recruited patients used less problem-focused coping strategies than internet recruits, 15.67 ± 4.52 versus 17.21 ± 4.23, respectively ( $p < 0.001$ ). All other demographic, medical, and psycho-social parameters were similar in hospital and internet patients for each disease, including the disease activity mean scores of each disease. Therefore, the remainder of the analysis was performed for UC and CD without regard to source of recruitment.

### Correlation and Regression Analysis

The P-SCCAI score was correlated significantly with gender, age, economic status, threatening experiences, satisfaction with life, quality of life, the three coping strategies, and the GSI distress score (Table 3). Active UC was thus associated with female gender, younger age, poorer economic status, more threatening experiences, less satisfaction with life and less quality of life, more psychological distress, and greater use of all three coping strategies. In Table 4, it is shown that active CD, as depicted by the P-HBI values, was correlated with increasing age, non-working, smoking, and a higher rate of negative life events, lower economic status, lower SWLS, lower physical and mental quality of life, and higher use of dysfunctional coping strategy.

The multiple linear regression model for log transformed P-SCCAI and P-HBI is shown in Table 5. The P-SCCAI score in UC was predicted by economic status, GSI stress measure, and problem-focused coping strategy. This model explained 30.2% of the variance in the dependent variable P-SCCAI. In CD, the P-HBI was predicted by older age and GSI stress; this model explained 17.4% of the variance in the dependent variable P-HBI. Of note, economic status and coping strategies were not significant predictors in the P-HBI model.

**Table 3** Correlations between P-SCCAI and (a) categorical or (b) continuous variables in active ulcerative colitis

<b>a.</b>			
Variables		Median (min; max) (IQR)	<i>p</i> <sup>a</sup>
Gender	Female	4.5 (0.0; 14.0) (2.0; 6.0)	0.028
	Male	3.0 (0.0; 18.0) (1.0; 6.0)	
Marriage status	Couple	0.0 (0.0; 5.0) (0.0; 3.3) 4.0	0.827
	Single	3.0 (0.0; 18.0) (1.0; 6.0)	
Working	No	4.0 (0.0; 13.0) (0.0; 8.0) 5.0	0.639
	Yes	3.0 (0.0; 13.0) (1.0; 6.0)	
Smoking	No	1.0 (0.0; 10.0) (0.0; 6.0)	0.072
	Yes	3.0 (0.0; 18.0) (1.0; 6.0)	
Mann-Whitney test <sup>a</sup>			
<b>b.</b>			
Variables		Correlation coefficient <sup>a</sup>	<i>p</i>
Age		− 0.161	0.014
Economic status		− 0.289	0.000
List of threatening experiences		0.271	0.000
SWLS: satisfaction with life		− 0.335	0.000
SF-36 physical health		− 0.534	0.000
SF-36 mental health		− 0.552	0.000
GSI: Global Severity Index		0.409	0.000
COPE: emotion-focused strategies		0.187	0.005
COPE: problem-focused strategies		0.267	0.000
COPE: dysfunctional strategies		0.393	0.000

<sup>a</sup> Spearman's rank correlation**Table 4** Results of correlations between P-HBI and (a) categorical or (b) continuous variables in active Crohn's disease

<b>a.</b>			
Variables		Median (min; max) (IQR)	<i>p</i> <sup>a</sup>
Gender	Female	2.0 (0.0; 19.0) (0.0; 6.0)	0.062
	Male	4.0 (0.0; 28.0) (1.0; 7.0)	
Marriage status	Couple	1.0 (0.0; 12.0) (0.0; 4.3)	0.300
	Single	4.0 (0.0; 31.0) (1.0; 7.0)	
Working	No	0.0 (0.0; 25.0) (0.0; 6.0)	0.012
	Yes	5.0 (0.0; 35.0) (1.0; 8.0)	
Smoking	No	1.0 (0.0; 15.0) (0.0; 4.0)	0.044
	Yes	4.0 (0.0; 35.0) (1.0; 7.0)	
Mann-Whitney test <sup>a</sup>			
<b>b.</b>			
Variables		Correlation coefficient <sup>a</sup>	<i>p</i>
Age		0.099	0.009
Economic status		− 0.206	0.000
List of threatening experiences		0.159	0.000
SWLS: satisfaction with life		− 0.224	0.000
SF-36 physical health		− 0.483	0.000
SF-36 mental health		− 0.349	0.000
GSI: Global Severity Index		0.345	0.000
COPE: emotion-focused strategies		0.054	0.151
COPE: problem-focused strategies		0.044	0.244
COPE: dysfunctional strategies		0.221	0.000

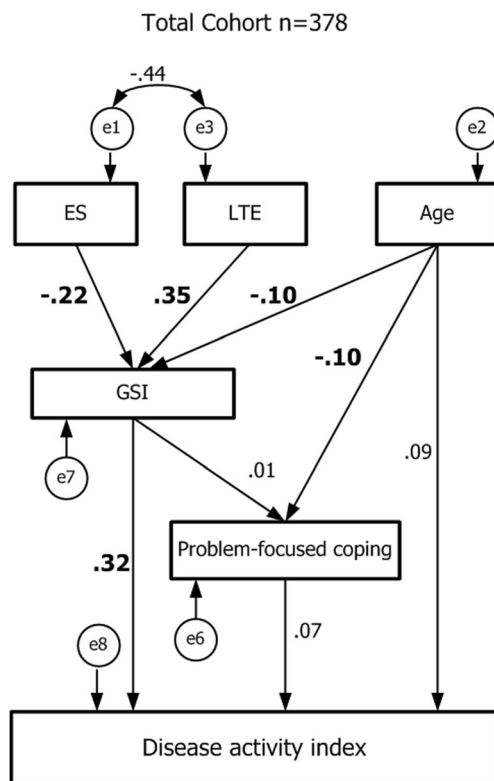
<sup>a</sup> Spearman's rank correlation

**Table 5** Results of multiple linear regression analysis for log-transformed P-SCCAI in patients with active ulcerative colitis and log-transformed P-HBI in patients with active Crohn's disease

Variables	Ulcerative colitis		Crohn's disease	
	P-SCCAI		P-HBI	
	Standardized regression coefficient	<i>p</i>	Standardized regression coefficient	<i>p</i>
Age	−0.094	0.137	0.131	0.001
Economic status	−0.151	0.033	−0.046	0.262
List of threatening experiences	0.007	0.916	0.041	0.341
GSI: Global Severity Index	0.361	0.000	0.352	0.000
COPE: emotion-focused Strategies	−0.084	0.351	0.043	0.360
COPE: problem-focused Strategies	0.214	0.024	−0.017	0.717
COPE: dysfunctional strategies	0.106	0.155	0.049	0.316
Adjusted <i>R</i> <sup>2</sup> ; model significance	0.302; < 0.001		0.174; < 0.001	

## Path Analysis

A general model incorporating 378 patients with UC and CD was drawn (Fig. 1). This model incorporated the variables LTE, GSI, coping strategies, and the respective disease



**Fig. 1** General path analysis model for predicting disease activity index in the whole cohort of ulcerative colitis and Crohn's disease patients. Significant paths are shown in **bold type**. ES, economic status; GSI, global severity index; LTE, list of threatening experiences

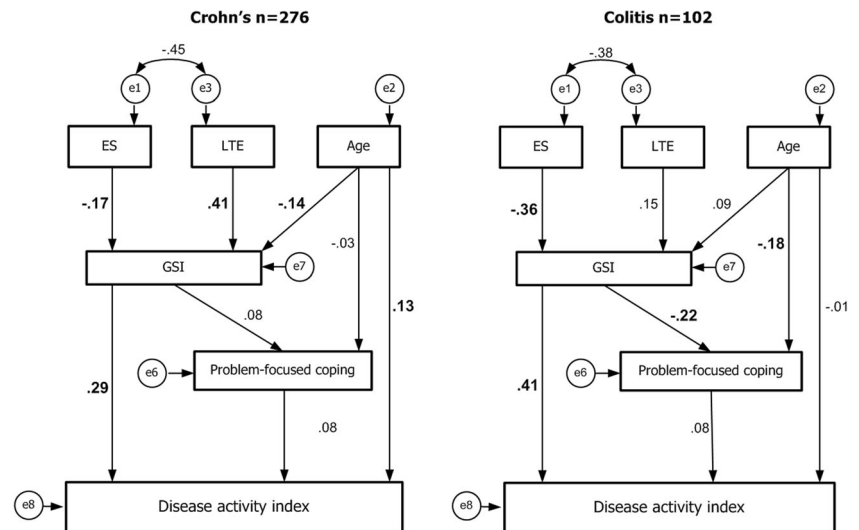
activity indices (P-SCCAI for UC and P-HBI for CD, combined into a single dependent variable) gave a good fit ( $\chi^2 = 12.42$ ,  $DF = 6$ ,  $p = 0.053$ ,  $\chi^2/df = 2.07$ ,  $CFI = 0.973$ ,  $NFI = 0.951$ ,  $RMSEA = 0.053$ ,  $SRMR = 0.0332$ ). Beta coefficient values in bold are significant at  $p < 0.05$ . In the general model, GSI mediated the impact of economic status, age, and threatening experiences on disease activity. GSI had a strong direct link to the disease activity index. Problem-focused coping was impacted by age.

A split model for UC and CD yielded a better fit. Similar beta coefficient values in the split model were then constrained, further increasing the model fit ( $\chi^2 = 22.336$ ,  $DF = 13$ ,  $p = 0.05$ ,  $\chi^2/df = 1.718$ ,  $CFI = 0.961$ ,  $NFI = 0.918$ ,  $RMSEA = 0.044$ ,  $SRMR = 0.0339$ ). By constraining any of the five paths marked in bold type (Fig. 2), a reduced model fit was achieved. So, the five direct paths, economic status to GSI, threatening experiences to GSI, age to GSI and to disease index, and finally GSI to the disease activity index were left unconstrained, indicating significantly different beta values in UC and CD patients. Thus, we could show that the paths in UC and CD were different, with the impact of economic status on GSI, GSI on problem-focused coping, and GSI on the disease activity index being more prominent in UC than CD. In CD, the dominant pathway was threatening experiences on GSI, with age impacting directly on disease activity as well.

## Discussion

We have shown that active UC and CD were associated with more threatening experiences, less satisfaction with life, reduced physical and mental quality of life, and greater psychological distress, as well as poorer economic status. UC patients

**Fig. 2** Split model path analysis for predicting the disease activity index in ulcerative colitis and Crohn's disease patients. Paths shown in **bold type** indicate significant differences between the two diseases. ES, economic status; GSI, global severity index; LTE, list of threatening experiences



reported a worse status for some psycho-social measures, and this likely reflects the observation that UC patients with serious flares are often acutely sicker than CD patients with exacerbation.

Our findings corroborate previous results showing that UC and CD are impacted by deteriorating mental health and reduced psychological resources [6, 7, 10, 11]. Recent findings showed that UC patients in the active disease state had higher levels of interleukin [IL]-1 $\beta$ , IL-6, IL-13, IL-10, and IL-8 and higher levels of anxiety, depression, and perceived distress than patients who were in remission [30].

Regarding coping, UC patients made greater use of all three coping strategies than CD patients, explained perhaps by their higher number of threatening experiences. Others have demonstrated that threatening experiences are related to a deterioration of mental health in chronic illnesses [6, 31]. We noted a greater use of emotion-focused and dysfunctional coping in UC. Emotion-focused and dysfunctional coping are maladaptive unhealthy behaviors that impact negatively on patients' psychological well-being [14, 15]. In UC and CD, the positive mental resource of problem-focused coping was used less than the other forms of coping. A recent review failed to show a consistently improved impact of problem-focused coping on the mental health of UC and CD patients [15]. It was suggested that the use of flexible coping strategies might be the best adaptive coping as a way to improve the individual's psychological health [32]. The role of coping in UC and CD requires further elucidation.

In the whole-cohort SEM analysis, we demonstrated the complex relationships between economic status, threatening experiences, distress, and problem-focused coping on disease activity. Economic status, threatening experiences, and age have a large impact on psychological distress (GSI measure), which has no impact on problem-focused coping. The split

SEM model informed the significant differences between UC and CD in the active disease state. The effect of economic status on psychological distress was greater in active UC than CD. The effect of life events was significant in CD but not UC. Psychological distress impacted the disease activity in both diseases, but the effect was greater in UC. Following Taylor's conceptualization [6], our path analysis showed that psychological distress mediated the links between economic status, threatening experiences, and age to problem-focused coping strategy. Yet, our findings did not show a significant mediating effect of problem-focused coping on the link between psychological distress and disease severity for UC or CD. A possible explanation for this is that current coping scales have inherent defects [15]. These scales do not monitor the attitudes and beliefs of patients and have no temporal framework. Future studies need to implement a more detailed form of coping conceptualization, relying possibly on health belief models to predict patients' coping behavior. Despite the foregoing, it is appreciated that in a cross-sectional study based on correlation data, it cannot be said with certainty that psychological distress leads to greater disease morbidity, since it could equally be true that the greater burden of active disease would impact the patient's psychological condition, and the entire scenario could in fact be bidirectional.

## Strengths and Limitations

The current study has strengths related to the use of a community-based, countrywide cohort with equal numbers of patients recruited in out-patient hospital departments and via the internet. The cohort was representative of typical patients with flares who can be managed at community medical facilities or out-patient clinics. By incorporating about an equal number of

patients responding to the internet call, we were able to double the size of the cohort. While internet responders are often found to be sicker than hospital-based recruits, this was actually not the case in our cohort, as indicated by similar disease activity scores (P-SCCAI or P-HBI) in both recruitment fractions. Thus, we were able to study a very wide spectrum of patients without introducing bias arising from site of recruitment. The use of advanced statistical methods of handling skewed data is a further strength of the study, as is the separate analysis performed for each disease. We are aware of course of the limitations of the study. We could not confirm the diagnosis in internet-recruited patients, nor exclude psychiatric comorbidities in this group. Furthermore, specific information about the extent of disease, as in the Montreal classification of UC and CD which uses the results of radiology and colonoscopy to define disease location, was not available to us. However, this study focused on activity of disease, as given by the self-reported P-SCCAI and P-HBI scores, which has become an acceptable surrogate for physician-classified disease activity. Disease activity is not necessarily related to anatomical extent of disease. Future studies should address these limitations and incorporate a longitudinal design. Our assessment of economic status was based on a self-report measure. This method has been used by others [33] and can be regarded as reliable as those methods based on declaration of actual income, since the latter too are subjective responses. We realize that the transferability of our results to other populations and countries may be limited, given differences between ethnic groups and medical facilities; nonetheless, our findings do provide a model for similar research in diverse patient cohorts.

## Implications for Practice

In conclusion, we have uncovered important psychological contrasts between patients with active UC or CD. Thus, in UC patients, the economic status is linked with disease activity, whereas in CD, age plays an important role. The effect of psychological distress is more prominent in UC where it impacts problem-focused disease coping. Psychotherapy thus needs to take into account the differences between UC and CD shown here and offer appropriate social and psychological counseling to patients.

**Acknowledgements** This work was supported by The Leona M. and Harry B. Helmsley Charitable Trust, grant number 2012PG-IBD006, to Shmuel Odes. This work represents independent research, and the sponsor had no role in the design and performance of the study, analysis and interpretation of the data, writing of the manuscript, and the decision to submit the manuscript for publication. The following physician members of the Israel IBD Research Nucleus (IIRN) at the participating hospitals have collaborated in this research: Iris Dotan, MD, Yehuda Chowers, MD, Dan Turner, MD, Abraham Eliakim, MD, and Shomron Ben-Horin, MD. The following physicians at the Soroka Medical Center have collaborated in this research: Daniella Munteanu, MD, Nava Gaspar, MD,

Leslie Eidelman, MD, Arik Segal, MD, Alexander Mushkalo, MD, Vitaly Dizengof, MD, Gil Ben-Yakov, MD, Naim Abu-Freha, MD, Alexander Rosenthal, MD, and Alexander Fich, MD.

## Compliance with Ethical Standards

**Conflict of Interest** All authors and physician collaborators declare that they have no competing interests to report.

**Ethical Approval** All procedures involving human subjects were in accordance with the standards and approval of the institutional ethics committees of all the participating hospitals. All patients were provided with a detailed explanation of the study protocol.

**Informed Consent** All patients recruited at the hospitals signed an informed consent form approved by the ethics committees. Patients completing the questionnaires via internet were deemed to have consented to participate in the study, did not supply identifying details, and were not obligated to sign a consent form. Data were treated anonymously. The privacy rights of all participants were observed.

## References

1. Mowat C, Cole A, Windsor A, Ahmad T, Arnott I, Driscoll R, et al. Guidelines for the management of inflammatory bowel disease in adults. *Gut*. 2011;60:571–607. <https://doi.org/10.1136/gut2010.224154>.
2. Rahier JF, Magro F, Abreu C, Armuzzi A, Ben-Horin S, Chowers Y, et al. Second European evidence-based consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease. *J Crohns Colitis*. 2014;8:443–68. <https://doi.org/10.1016/j.crohns.2013.12.013>.
3. De Boer AG, Bennebroek Evertsz F, Stokkers PC, Bockting CL, Sanderma R, Hommes DW, et al. Employment status, difficulties at work and quality of life in inflammatory bowel disease patients. *Eur J Gastroenterol Hepatol*. 2016;28:1130–6. <https://doi.org/10.1097/MEG.0000000000000685>.
4. Odes S, Greenberg D. A medicoeconomic review of early intervention with biologic agents in the treatment of inflammatory bowel diseases. *Clinicoecon Outcomes Res*. 2014;8:431–43. <https://doi.org/10.2147/CEOR.S39212>.
5. Naliboff BD, Kim SE, Bolus R, Bernstein CN, Mayer EA, Chang L. Gastrointestinal and psychological mediators of health-related quality of life in IBS and IBD: a structural equation modeling analysis. *Am J Gastroenterol*. 2012;107:451–9. <https://doi.org/10.1038/ajg.2011.377>.
6. Taylor SE. Mechanisms linking early life stress to adult health outcomes. *Proc Natl Acad Sci U S A*. 2010;107:8507–12.
7. Bernstein CN, Singh S, Graff LA, Walker JR, Miller N, Cheang M. A prospective population-based study of triggers of symptomatic flares in IBD. *Am J Gastroenterol*. 2010;105:1994–2002. <https://doi.org/10.1038/ajg.2010.140>.
8. Gómez-Gil E, Vidal A, Panés J, Jaén J, Peri JM, Fernández-Egea E, et al. Relationship between patient's subjective stress perception and the course of inflammatory bowel disease. *Gastroenterol Hepatol*. 2003;26:411–6. Spanish.
9. Mayer EA. The neurobiology of stress and gastrointestinal disease. *Gut*. 2000;47:861–9.
10. Slonim-Nevo V, Sarid O, Friger M, Schwartz D, Chemin E, Shahar I, et al. Effect of psychosocial stressors on patients with Crohn's disease: threatening life experiences and family relations. *Eur J*

- Gastroenterol Hepatol. 2016;28:1073–81. <https://doi.org/10.1097/MEG.0000000000000666>.
11. Slonim-Nevo V, Sarid O, Friger M, Schwartz D, Sergienko R, Pereg A, et al. Effect of threatening life experiences and adverse family relations in ulcerative colitis: analysis using structural equation modeling and comparison with Crohn's disease. *Eur J Gastroenterol Hepatol*. 2017;29:577–86. <https://doi.org/10.1097/MEG.0000000000000826>.
  12. Carver CS. You want to measure coping but your protocol's too long: consider the brief COPE. *Int J Behav Med*. 1997;4:92–100.
  13. Cooper C, Katona C, Livingston G. Validity and reliability of the brief COPE in carers of people with dementia: the LASER-AD Study. *J Nerv Ment Dis*. 2008;196:838–43. <https://doi.org/10.1097/NMD.0b013e3181b504c>.
  14. Jordan C, Sin J, Fear NT, Chalder T. A systematic review of the psychological correlates of adjustment outcomes in adults with inflammatory bowel disease. *Clin Psychol Rev*. 2016;47:28–40. <https://doi.org/10.1016/j.cpr.2016.06.001>.
  15. McCombie AM, Mulder RT, Gearry RB. How IBD patients cope with IBD: a systematic review. *J Crohns Colitis*. 2013;7:89–106. <https://doi.org/10.1016/j.crohns.2012.05.021>.
  16. Graff LA, Walker JR, Clara, Lix L, Miller N, Rogala L, et al. Stress coping, distress, and health perceptions in inflammatory bowel disease and community controls. *Am J Gastroenterol*. 2009;104:2959–69. <https://doi.org/10.1038/ajg.2009.529>.
  17. Larsson K, Löf L, Rönnblom A, Nordin K. Quality of life for patients with exacerbation in inflammatory bowel disease and how they cope with disease activity. *J Psychosom Res*. 2008;64:139–48.
  18. Baumgart DC, Carding SR. Inflammatory bowel disease: cause and immunobiology. *Lancet*. 2007;369:1627–40.
  19. Dignass A, Eliakim R, Magro F, Maaser C, Chowers Y, Geboes K, et al. Second European evidence-based consensus on the diagnosis and management of ulcerative colitis part 1: definitions and diagnosis. *J Crohns Colitis*. 2012;6:965–90. <https://doi.org/10.1016/j.crohns.2012.09.003>.
  20. Lichtenstein GR, Hanauer SB, Sandborn WJ, Practice Parameters Committee of American College of Gastroenterology. Management of Crohn's disease in adults. *Am J Gastroenterol*. 2009;104:465–83. <https://doi.org/10.1038/ajg.2008.168>.
  21. Marín-Jiménez I, Nos P, Domènech E, Riestra S, Gisbert JP, Calvet X, et al. Diagnostic performance of the simple clinical colitis activity index self-administered online at home by patients with ulcerative colitis: CRONICA-UC study. *Am J Gastroenterol*. 2016;111:261–8. <https://doi.org/10.1038/ajg.2015.403>.
  22. Bennebroek Evertsz' F, Nieuwkerk PT, Stokkers PC, Ponsioen CY, Bockting CL, Sanderman R, et al. The patient simple clinical colitis activity index (P-SCCAI) can detect ulcerative colitis (UC) disease activity in remission: a comparison of the P-SCCAI with clinician-based SCCAI and biological markers. *J Crohns Colitis*. 2013;7:890–900. <https://doi.org/10.1016/j.crohns.2012.11.007>.
  23. Bennebroek Evertsz' F, Hoeks CC, Nieuwkerk PT, Stokkers PC, Ponsioen CY, Bockting CL, et al. Development of the patient Harvey Bradshaw index and a comparison with a clinician-based Harvey Bradshaw index assessment of Crohn's disease activity. *J Clin Gastroenterol*. 2013;47:850–6. <https://doi.org/10.1097/MCG.0b013e31828b2196>.
  24. Derogatis LR, Melisaratos N. The Brief Symptom Inventory: an introductory report. *Psychol Med*. 1983;13:595–605.
  25. Anaby D, Jarus T, Zumbo B. Psychometric evaluation of the Hebrew language version of the satisfaction with life scale. *Soc Indic Res*. 2010;96:267–74.
  26. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*. 1992;30:473–83.
  27. Brugha TS, Cragg D. The list of threatening experiences: the reliability and validity of a brief life events questionnaire. *Acta Psychiatr Scand*. 1990;82:77–81.
  28. Knowles SR, Gass C, Macrae F. Illness perceptions in IBD influence psychological status, sexual health and satisfaction, body image and relational functioning: a preliminary exploration using structural equation modeling. *J Crohns Colitis*. 2013;7:e344–50. <https://doi.org/10.1016/j.crohns.2013.01.018>.
  29. Blunch NJ. Introduction to structural equation modelling using SPSS and AMOS. London: SAGE; 2008. p. 186–217.
  30. Jonefjäll B, Öhman L, Simrén M, Strid H. IBS-like symptoms in patients with ulcerative colitis in deep remission are associated with increased levels of serum cytokines and poor psychological well-being. *Inflamm Bowel Dis*. 2016;22:2630–40. <https://doi.org/10.1097/MIB.0000000000000921>.
  31. Allen J, Balfour R, Bell R, Marmot M. Social determinants of mental health. *Int Rev Psychiatry*. 2014;26:392–407. <https://doi.org/10.3109/09540261.2014.928270>.
  32. Kato T. Development of the coping flexibility scale: evidence for the coping flexibility hypothesis. *J Couns Psychol*. 2012;59:262–73. <https://doi.org/10.1037/a0027770>.
  33. Prag P, Mills MC, Wittek R. Subjective socioeconomic status and health in cross-national comparison. *Soc Sci Med*. 2016;149:84–92. <https://doi.org/10.1016/socscimed.2015.11.044>.