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Differential relationships of somatization, depression, and anxiety to severity of Crohn's disease

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Abstract

Patients with Crohn's disease, an inflammatory bowel disease, struggle with chronic somatic symptoms that could bring about emotional distress. This study assessed the relative role of somatization, and depressive and anxiety symptoms in disease activity among 619 Crohn's patients (18–79 years; 58.3% women). Structural equation modeling revealed that somatization was the only unique predictor of disease activity beyond depression and anxiety. In addition, the effect of somatization on disease activity was stronger in men compared to women. Findings suggest that somatization represents a distinct domain of psychological distress that may play a role in the health of patients with Crohn's disease.

Introduction

Crohn's disease is a common type of a chronic lifelong inflammatory bowel disease (IBD), characterized by abdominal pain, persistent diarrhea, weight loss, and fatigue (Baumgart and Sandborn, 2012; Torres et al., 2017). Most Crohn's patients have disease onset in young adulthood and suffer from recurrent episodes of active symptomatic disease leading to impairment in daily functioning, followed by remissions of varying degree (Baumgart and Sandborn, 2012; Torres et al., 2017).

Previous studies have shown that patients with IBD (including Crohn's disease and ulcerative colitis—another form of IBD) have high prevalence of mental health symptoms compared to the general population (Häuser et al., 2011; Mikocka-Walus et al., 2016). In a recent review, it was estimated that one in three patients with IBD has symptoms of anxiety and one in five has symptoms of depression (Neuendorf et al., 2016). Similarly, in a community sample of people with IBD, one-fifth reported having a mental health diagnosis, most commonly depression (Sirois and Wood, 2017).

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In addition, poor mental health has been consistently associated with disease severity among patients with IBD (Byrne et al., 2017; Graff et al., 2009; Neuendorf et al., 2016; Rochelle and Fidler, 2013; Trindade et al., 2016). For example, a recent study found that the link between stressful life events and worse Crohn's disease activity was mediated by psychological distress (Sarid et al., 2018). Some studies suggested that psychological distress may represent a consequence of disease activity (Kurina et al., 2001), whereas others argued that psychological distress increases likelihood of disease relapse (Mittermaier et al., 2004). However, these previous studies have mostly focused on depressive and anxiety symptoms (Graff et al., 2009; Mikocka-Walus et al., 2016) and seldom addressed other indices of psychological distress.

One plausible construct of psychological distress that might play a role in symptom severity is somatization, defined as distress due to somatic symptoms. Somatization is a complex concept, which has both physical and psychological components (Sitnikova et al., 2017). In populations of patients with chronic disorders, somatization refers to bothersome physical symptoms that cannot be solely attributed to the underlying disease (e.g. dizziness or muscular aches; Hyphantis et al., 2013; Zijlema et al., 2013). Past research has shown that somatization is associated with increased disease symptom severity in less serious functional gastrointestinal disorders such as irritable bowel syndrome (Van Oudenhove et al., 2016; Van Tilburg et al., 2013; Whitehead, 1994).

Interestingly, gender differences in the prevalence of psychological distress in IBD patients and the associations between psychological distress and disease activity have not yet received much attention. Previous studies found a higher prevalence of depressive symptoms in women with Crohn's disease compared with their male counterparts (Freitas et al., 2015; Panara et al., 2014); however, others have failed to identify any gender differences in rates of depression (Häuser et al., 2011; Nahon et al., 2012). Thus, the role of a patient's gender in psychological distress among Crohn's patients remains an open question (Sarid et al., 2017).

The aim of this study was to investigate the relative impact of somatization compared with anxiety and depression on disease activity in a large cohort of patients with Crohn's disease. Previous work with IBD patients has found that older age and poor socio-economic status are related to anxiety and depressive symptoms (Nahon et al., 2012); thus, age and economic status were considered as control variables in this study. We also consider whether the patient's gender moderates the relationships between severity of Crohn's disease and symptoms of depression, anxiety, and somatization.

Guided by the literature reviewed above, we proposed the following hypotheses:

1. Somatization would have moderate-to-high correlations with depressive and anxiety symptoms.
2. Somatization would be an independent predictor of Crohn's disease severity after accounting for depression and anxiety, and after adjustment for the patient's age and economic status.
3. Women would show higher levels of depression, anxiety, and somatization than men.

Method

Study design and sample

The study used cross-sectional data from a survey of adult patients with IBD carried out from July 2013 through June 2016 (Sarid et al., 2018). The inclusion criteria for this study were being an adult (aged 18 years and over), having a diagnosis of Crohn's disease (confirmed for hospital-recruited patients and self-reported for Internet-recruited patients), and not having a diagnosis of psychiatric disease or taking medication for such disease. The current analysis focused on a sample of 619 patients with Crohn's disease. Participants were recruited primarily ($n = 439$, 69.5%) from five different outpatient gastroenterology clinics at university-affiliated

hospitals across Israel (Rambam Health Campus, Tel-Aviv Medical Center, Soroka Medical Center, Shaare Zedek Medical Center, Chaim Sheba Medical Center). Patients with a confirmed diagnosis of Crohn's disease who consented to participate completed a questionnaire either on paper or online at their discretion. An additional group of 189 participants (30.5% of the sample) with a self-reported diagnosis of Crohn's disease were recruited by advertisements on "The Israel Foundation for Crohn's Disease and Ulcerative Colitis' and the 'Camoni' ("patients as me") social networks" websites and completed the online questionnaire. Medical charts of patients recruited through the hospitals were reviewed for evidence of psychological or psychiatric disorders. Fewer than 5 percent of these patients had a psychological comorbidity and none had a psychiatric disorder. This information, however, could not be determined for the Internet-recruited patients. Approximately 45 percent of IBD patients invited for participation during their hospital visits and 32 percent of those who accessed the link to the online questionnaire completed the survey. Hospital-recruited patients who agreed to participate read and signed a consent form containing information about the nature of the study. Patients recruited via websites were provided with a similar explanation of the study and were deemed to have consented to participate if they chose to respond to the survey. The study was approved by the Ethics Committees of all participating hospitals.

Measures

Demographic and clinical information were collected, including gender, age, years of education, number of Crohn's disease-related operations, and time since diagnosis in years. Economic status was assessed by self-rated statement with 5-point scale from 1 = "poorest" to 5 = "richest."

Depression, anxiety, and somatization symptoms were assessed using the Brief Symptom Inventory (BSI; Derogatis and Melisaratos, 1983). Participants were asked to rate the extent to which they have been distressed by various psychopathological and physical symptoms during the past 7 days on a 5-point scale (0 = "not at all," 1 = "a little bit," 2 = "moderately," 3 = "quite a bit," and 4 = "extremely."). The BSI consists of 53 items measuring nine dimensions of psychological distress symptoms; however, only the depression, anxiety, and somatization subscales were included in the current analysis.

The depression subscale of the BSI consists of six items: "thoughts of ending your life," "feeling lonely," "feeling blue," "feeling no interest in things," "feeling hopeless about the future," and "feelings of worthlessness." The first item about suicidal thoughts was highly skewed due to an excessive number of zero responses (i.e. endorsement of no suicidality) and contributed to a reduced internal consistency of the scale; thus, this item was excluded from the depression scale. The anxiety subscale consists of six items: "nervousness or shakiness inside," "suddenly scared for no reason," "feeling fearful," "feeling tense or keyed up," "having fear or panic attack," and "feeling so restless you couldn't sit still." The original somatization subscale consists of seven items asking the participant to rate how distressed they felt by the following somatic symptoms: "faintness or dizziness," "pains in the heart or chest," "trouble getting your breath," "hot or cold spells," "numbness or tingling in parts of your body," and "feeling weak in parts of your body." The seventh item referring to "nausea or upset stomach" was excluded from the current analyses due to overlap with Crohn's disease symptoms (see next paragraph on measurement of activity of Crohn's disease). All three psychological subscales demonstrated good reliability (Cronbach's α = .89, .86, and .87 for depression, anxiety, and somatization, respectively).

The severity (activity) of Crohn's disease was assessed using the Patient Harvey-Bradshaw Index (P-HBI), a patient-based questionnaire designed to measure overall disease activity in Crohn's disease patients (Evertsz et al., 2013; Sarid et al., 2017). The P-HBI consists of five questions filled in by the patient, covering symptoms of Crohn's disease during preceding

24 hours (general well-being, abdominal pain, diarrheal episodes, and complications). The question about an abdominal mass, which requires a physician to examine the patients, is omitted from the P-HBI. A disease activity score is generated by summing the scores for each item. A total P-HBI score of ⩽4 indicates disease remission, 5–7 mild disease, 8–16 moderate disease, and >16 severe disease.

Statistical analysis

Descriptive analyses were performed using SPSS 22.0 (SPSS Inc., Chicago, IL, USA). A missing item of each of the BSI subscales was substituted by the individual median. Missing values on the socio-demographic variables age and economic status were substituted by the mean of the sample. Less than 2 percent of the data at scale level were missing.

Structural equation modeling (SEM) analyses were performed with AMOS 18.0 software (Amos Development Corporation, Crawfordville, FL, USA). The SEM approach is a way to test simultaneously multiple pathways between factors in order to examine their relative effect toward the outcome variable. In addition, SEM makes it possible to estimate whether a certain variable may act as a moderator of these associations. A two-step procedure of SEM with maximum likelihood estimation was conducted to examine the proposed hypotheses (Kline, 2015). First, we estimated the measurement model by confirmatory factor analysis (CFA) to examine the validity of the three latent variables (i.e. depression, anxiety, and somatization). In the second step of the procedure, we estimated the fit of the structural model to examine the hypothesized associations between the study variables. Based on recommended guidelines, the following criteria were used to determine model fit: relative χ^2 (χ^2/degrees of freedom (df)) ⩽3, root mean square error of approximation (RMSEA) ⩽.06, standardized root-mean square residual (SRMR) ⩽.08, comparative fit index (CFI) ⩾.95 (Hooper et al., 2008; Hu and Bentler, 1999).

To test the potential role of gender as a moderator on the model, we employed multi-group comparison. First, we tested whether the same measurement model is applicable to both men and women by fitting the data of the two groups simultaneously without constraints (configural invariance model) and after constraining the factor loadings to be equal (metric invariance model). The unconstrained and constrained models were compared in χ^2 and CFI values, with insignificant result in χ^2 difference test and a change in CFI value smaller than .01 indicating that the measurement model is invariant across groups (Cheung and Rensvold, 2002). Next, we examined the impact of gender on the path coefficients in the structural model. This analysis was based on the critical ratio difference test which provides a z-score that indicates whether specific pathway coefficients are significantly different between men and women. We controlled for the effects of age and economic status in the multi-group SEM analyses by including paths from these control variables to the dependent variable P-HBI.

Results

Sample characteristics

The cohort had a mean age of 37.7 years (standard deviation (SD) = 13.9; age range = 18–79) and 361 (58.3%) were women. Participants were predominantly Jewish (95.5%) and had a mean of 14.7 (SD = 2.8) years of education. Half of the participants (50.7%) rated their economic status as in the middle, 26.0 percent as good, 14.2 percent as poor, with the rest reporting it to be very poor (5.6%) or very good (3.1%). The majority (79.0%) had not undergone Crohn's disease–related surgery. The mean disease duration was 9.10 (SD = 6.28) years. About a third of patients (31.2%) had been diagnosed with Crohn's disease 1–5 years earlier, 20.8 percent of patients 6–10 years previously, and 47.9 percent of patients had been diagnosed at least 10 years before the survey. Based on P-HBI scores, 3.9 percent of patients reported severe disease activity (score > 16), 19.1 and 19.9 percent had moderate (5–7) or mild (5–7) disease activity, respectively, and 57.2 percent of patients were in remission (⩽4) at the time of the study.

Table 1. Differences on study variables between women (*n* = 361) and men (*n* = 258).

Scale	Women Mean (SD)	Men Mean (SD)	t	df	Effect size
Economic status	3.05 (.8)	3.09 (.9)	−.659	497.1	−.05
Age	39.2 (14.4)	35.7 (12.8)	3.164¥	589.9	.25
Depression	1.10 (1.0)	1.10 (.9)	−.032	617	−.002
Anxiety	1.20 (.9)	1.10 (.9)	1.432	617	.12
Somatization	1.11 (.9)	.88 (.9)	3.162¥	583.8	.25
P-HBI	5.22 (5.1)	4.64 (5.1)	1.402	617	.11

Sex differences within each severity levels are reported in percentage. Hedges' *g* effect sizes are reported; SD: standard deviation; *df*: degrees of freedom; P-HBI: Patient Harvey-Bradshaw Index.
¥*p* = .002.

Preliminary analyses

Age, economic status, P-HBI, and all items on the three BSI subscales had normal distribution (i.e. skewness < 3 and kurtosis > 8; Kline, 2015). Table 1 shows differences in the study variables across gender. Women were somewhat older than men (*p* = .02) and both groups showed similar levels of economic status. There were no significant gender differences in P-HBI, depression subscale, or anxiety subscale scores (*p* > .15). In contrast, men reported lower somatization levels compared to women (*p* = .002).

SEM on the total sample

Across the whole sample, the model with the three constructs of depression, anxiety, and somatization showed an adequate fit: χ^2/df=5.388; RMSEA=.084; SRMR=.0536; and CFI=.918. Inspection of the modification indices (MI) suggested that the fit of the model could be further improved by correlating the measurement errors between three items on the depression subscale: errors of items 2 and 5 (MI=66.182), errors of items 2 and 3 (MI=71.679), and errors of items 3 and 5 (MI=49.725). We reasoned that these specific items had correlated error variances because they all asked about fear ("feeling fearful," "having fear or panic attacks," and "suddenly scared for no reason"), thus suggesting that these three variables shared some variance related to fear that was not included in the latent variable of anxiety. Fit indices for the modified model

were improved: χ^2/df=3.287; RMSEA=.061; SRMR=.0333; and CFI=.959. Moreover, there were significant correlations between errors of items 2 and 5 (*r*=.54, *p*<.001), errors of items 2 and 3 (*r*=.51, *p*<.001), and errors of items 3 and 5 (*r*=.40, *p*<.001).

All item loadings were significant at *p* < .001 and ranged from .63 to .87, thus exceeding the recommended level of .6 (Kline, 2015). Somatization had a correlation of .73 with depression and a correlation of .80 with anxiety suggesting these subscales represent distinct constructs. However, the factor correlation between depression and anxiety of .89 was high enough to raise concerns about discriminant validity between these dimensions (Brown, 2015). Therefore, the latent factors depression and anxiety were combined into a second-order factor named "anxiety-depression" to correct for the possible lack of discriminant validity and overcome potential multi-collinearity (Whitehead, 1994). The loadings of depression and anxiety onto their higher order factor were .90 and .99 (*p*<.001), respectively.

The final structural model is shown in Figure 1. The path from the latent factor "somatization" to P-HBI was significant (.542, *p*<.001), whereas the path from the factor "anxiety-depression" to P-HBI was not (−.068, *p*=.410). Furthermore, the two paths could not be fixed to be equal without a significant worsening of the model fit ($\Delta\chi^2$(1)=16.178, *p*<.001). Together, these findings indicate that somatization has a stronger unique effect on P-HBI than depression-anxiety.
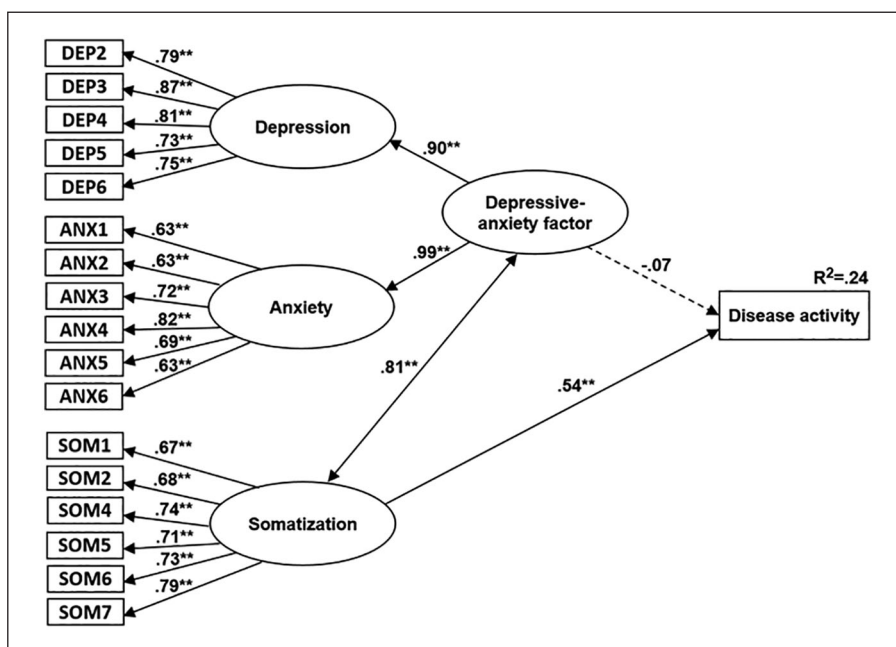
Figure 1. The finalized structural model (*n* = 619) relating depressive-anxiety, somatization, and disease activity.
DEP2–DEP6: five items of depression; ANX1–ANX6: six items of anxiety; SOM1–SOM7 (except SOM3): six items of somatization; factor loadings and parameter estimates are standardized; latent variables are represented by ellipses and manifest variables are represented by rectangles; R2: the proportion of variance in the endogenous variable disease activity that was accounted for by the variables somatization and depressive-anxiety.
**p < .001.

In addition, it shows that distress due to somatic symptoms is uniquely associated with Crohn's disease symptoms. The somatization model explained 35 percent of the variance in P-HBI.

Testing the gender moderation role

Multi-group SEM analyses were conducted to examine whether the path coefficients between the psychological factor and P-HBI differ across men and women. Separate models were conducted for anxiety-depression versus somatization, with economic status and patient's age added as control variables.

Depressive-anxiety model. A multi-group analysis was performed to examine whether the path between the second-order factor depression-anxiety and the manifest variable P-HBI differ

across genders. First, a configural model was tested to verify that the baseline model without constraints has a good fit and the loading pattern is similar in both groups. MI suggested adding a correlation between depression-anxiety latent factor and economic status. This additional correlation showed that lower economic status was associated with higher levels of depressive-anxiety symptoms. This is a theoretically sound relationship and was, therefore, retained. The fit of the modified model was good ($\chi^2/df = 2.394$; RMSEA = .048; SRMR = .0609; CFI = .955), indicating configural invariance by gender (i.e. the structure of the depressive-anxiety model is the same across men and women). Next, metric invariance was tested by constraining the item loadings in the depression-anxiety subscales to be equivalent across the genders and comparing the fit of the metric invariance model to the
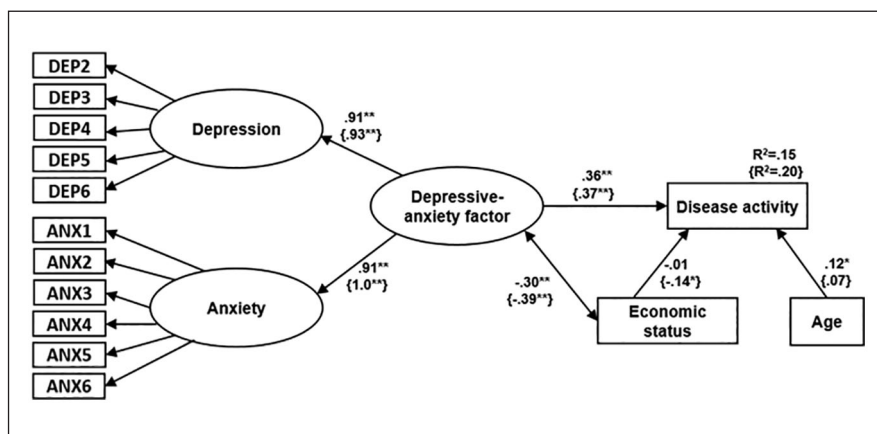
Figure 2. Multi-group model of the relationship between depressive-anxiety symptoms and disease activity across gender, after adjusting for age and economic status.
For ease of presentation, standardized estimates of indicators (which were invariant across genders) and error terms are not shown; data for men are presented in {}; R^2: the proportion of variance in disease activity accounted for by other variables in the model.
$*p < .05$; $**p < .001$.

configural invariance model. The changes in χ^2 and in CFI were small and insignificant ($\Delta\chi^2(9) = 6.984$, $p = 639$; ΔCFI $= .001$), indicating metric invariance by gender (i.e. item loadings are similar across men and women). Using the critical ratio approach to compare the pathway from the second-order factor depression-anxiety to the manifest variable P-HBI across gender, it was found that this path did not significantly differ between groups (see Figure 2 and Table 2). Overall, this model explained 15 and 20 percent of the variance in P-HBI for women and men, respectively.

Somatization model. A second multi-group analysis was performed to examine whether the path between somatization factor and P-HBI differs across the genders. As in the depression-anxiety model, MI suggested an added correlation between economic status and somatic distress would significantly improve model fit. This correlation indicated that poorer economic status was associated with greater somatization. The modified somatization model had satisfactory fit to the data ($\chi^2/df = 2.652$; RMSEA $= .052$; SRMR $= .0464$; CFI $= .952$),

indicating configural invariance by gender. Metric invariance was then tested to validate the item loadings in the somatization subscale, which were equivalent across groups. The fit of the metric invariance model was not substantially worse than the fit of the configural invariance model ($\Delta\chi^2(5) = 3.448$, $p = 631$; ΔCFI $= .001$), indicating the relationship between the items and the underlying latent construct somatization is the same across men and women. Finally, an analysis based on the critical ratios indicated that the pathway coefficients from somatization to P-HBI were significantly different between men and women (see Figure 3 and Table 2). Namely, the positive relationship between somatization and disease activity was stronger for men compared with women. Overall, this model explained 18 and 35 percent of the variance in P-HBI for women and men, respectively.

Discussion

This study assessed the relationships between disease activity, P-HBI, and dimensions of psychological distress symptoms (depression,

Table 2. Summary of critical ratio tests comparing path coefficients across gender.

Path	Men model	Women model	z score
Anxiety-depression → P-HBI	.371	.360	−.363
Somatization → P-HBI	.558	.419	2.524*

P-HBI: Patient Harvey-Bradshaw Index.
*Significant difference (i.e. z score > 1.96).
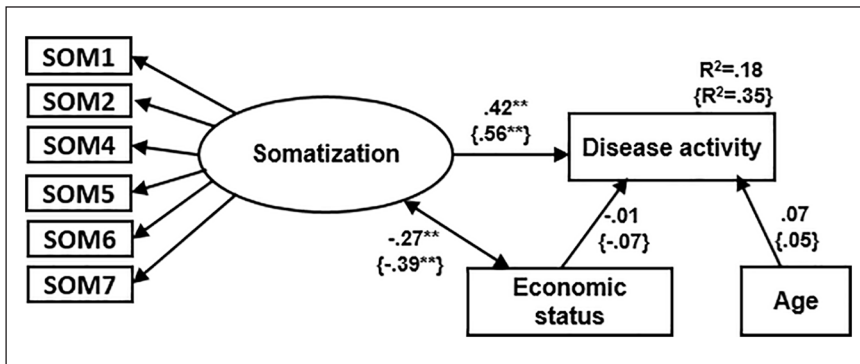
Figure 3. Multi-group model of the relationship between somatization symptoms and disease activity across gender, after adjusting for age and economic status.
For ease of presentation, standardized estimates of indicators (which were invariant across genders) and error terms are not shown; data for men are presented in {}; R^2: the proportion of variance in disease activity accounted for by other variables in the model.
**$p < .001$.

anxiety, and somatization) in a large cohort of Crohn's patients. Consistent with our first hypothesis and previous research, the current findings obtained by SEM show that psychological distress due to somatization was related to but conceptually distinct from depressive and anxiety symptoms. Consistent with our second hypothesis, somatization was uniquely associated with disease activity in Crohn's patients, above and beyond the effects of depression and anxiety as well as patients' age and economic status. Finally, our third hypothesis that women would show higher levels of psychological distress than men was supported for somatization, but not for depression and anxiety. Interestingly, we also found that while patient's gender moderated the effect of somatization on disease activity, it did not influence the relation between depressive and anxiety symptoms and disease activity.

The high correlations of somatization with depressive and anxiety symptoms found in Crohn's cohort are consistent with previous research among healthy individuals and patients with chronic illness (Creed et al., 2012; Hyphantis et al., 2013) and indicate that somatization is likely a concept that primarily reflects a dimension of psychological distress.

Consistent with past research (Neuendorf et al., 2016), depressive and anxiety symptoms were associated with worse disease severity in Pearson correlations. Interestingly, the relationship between depressive-anxiety symptoms and P-HBI was no longer significant after including somatization in the model. In contrast, somatization remained a significant predictor of disease severity even after accounting for the effect of depressive-anxiety symptoms. The current finding of a unique role for somatization in Crohn's disease severity can be explained in relation to

the fluctuating and unpredictable course of exacerbations and remissions that characterized this disease (Baumgart and Sandborn, 2012; Torres et al., 2017). Namely, it is possible that Crohn's patients, particularly hyper-vigilant regarding their physical health, would tend to interpret any physical sensations they might be experiencing as indicative of acute inflammation, leading them to report high levels of bothersome somatic symptoms (Hyphantis et al., 2013; Van Tilburg et al., 2013). These high levels of somatic-related distress may, in turn, result in worsening of disease activity, thus possibly generating a self-fulfilling prophecy (Keough et al., 2011; McKinnon et al., 2015).

This bio-psycho-social interpretation is consistent with findings in patients with IBD associating perceived threat of disease flare-up with reduced physical and psychological functioning (Goldring et al., 2002). It is also in line with previous research (Hyphantis et al., 2013; McKinnon et al., 2015) which showed that a personality trait of neuroticism and dysfunctional cognitions were related to higher severity of somatic symptoms and gastrointestinal symptom–specific anxiety in both healthy and patient populations.

Previous research has shown that women with Crohn's disease tend to report greater depressive symptoms than men (Freitas et al., 2015; Panara et al., 2014). In this study, the levels of depressive or anxiety symptoms did not vary by gender, nor did the negative effect of these symptoms on Crohn's disease severity. In contrast, women did show significantly higher somatization scores than men; yet, the association between somatization and disease activity was actually stronger for men than for women.

To our knowledge, this is the first study to compare the relationship between somatization and disease activity across men and women with IBD. The current finding that the somatization-disease association was stronger in men suggests that, despite having lower levels of somatization, men with Crohn's disease seem to exhibit higher vulnerability to somatic distress than female Crohn's patients. This raises the possibility that some subgroups of Crohn's patients (e.g. men) stand to benefit most from lowering their somatic distress level in terms of improved disease symptomatology. Strengths of this study include the relatively large sample size and the diversity of the sample in terms of P-HBI scores, which allowed us to assess somatization in patients with different levels of disease activity. In addition, by recruiting participants from nationwide outpatient clinics as well as advertisements on social media, we were able to minimize selection bias and increase generalizability to represent the broader population of Crohn's patients. The large sample also allowed the use of complex structural analysis that provides unique statistical contributions. Another strength of this study is the use of a validated instrument to evaluate somatization, which has been used widely in the general population as well as among patients with chronic diseases (Sitnikova et al., 2017; Van Tilburg et al., 2013).

This study also has limitations. First, the current measure of somatization was made up of six items, which may appear insufficient to measure a complex construct like somatic distress. Future research might benefit from the use of a more extended scale for medically unexplained somatic symptoms. Second, the cross-sectional nature of the data precludes us from drawing conclusions about the causality of the relationships between psychological distress and disease activity. The association of P-HBI with somatic, depressive, and anxiety symptoms is likely to be bidirectional: that is, worsening of disease activity may also affect severity of psychological symptoms. Longitudinal studies with repeated measures of disease activity and mental health symptoms are required to establish causal directions. Third, it is possible that our recruitment procedures were subject to self-selection bias, reaching only Crohn's patients who are receptive to participating in questionnaire studies. In addition, the sample of this study was mainly composed of Crohn's patients from the adult Jewish population in Israel. Thus, it would be desirable to

replicate this work in other countries and in other clinical settings (such as pediatric gastroenterology clinics). Finally, self-assessment of active disease symptoms could have been influenced by patients' psychological functioning. Future research should include self-report measures as well as objective indicators of disease activity, such as physician ratings or biological markers of inflammation.

Conclusion

This study is the first to examine the unique role of somatization compared to depression and anxiety in disease severity for patients with Crohn's disease. The current findings provide significant implications and directions for clinicians and researchers. The finding that somatic symptoms are uniquely associated with greater disease activity suggests that monitoring for somatization in Crohn's patients might be an important aspect in patient management. Namely, routine screening for somatization, as well as for depressive and anxiety symptoms may enable clinicians and patients to monitor and receive, respectively, appropriate care and support, which in turn could lead to both improved well-being and reduced disease severity. In a similar vein, the present findings can inform development of interventions directly targeting distress associated with somatic sensations in Crohn's patients. Furthermore, this study found a moderating role for patients' gender in the link between somatization and disease activity. Future studies should estimative other patient characteristic as potential moderators in order to identify subgroups of Crohn's patients that are particularly vulnerable to the effect of somatization on disease course. Finally, future work is warranted to further investigate the importance of somatization in disease severity for other patient populations with chronic somatic illnesses.

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