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ORIGINAL PAPER

Effectiveness of Cognitive-Behavioral and Mindfulness Intervention in Improving Life Satisfaction of Patients with Crohn's Disease: Evaluating Stress, Interpersonal Sensitivity, and Social Support as Mechanisms of Change

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Abstract

Objectives Cognitive behavioral and mindfulness interventions have been shown to promote well-being in individuals with chronic illness. However, the underlying psychological processes through which these interventions impact well-being are not fully explored. This secondary analysis study aimed to examine the role of perceived social support, interpersonal sensitivity, and perceived stress as mediators of the positive effect of individualized online Cognitive Behavioral and Mindfulness Intervention (COBMINDEX) on life satisfaction among patients with Crohn's disease (CD).

Method Patients with mild or moderately active disease (n=142) were randomly assigned to either COBMINDEX intervention or treatment-as-usual control group. After a period of 3 months, the control group also received the COBMINDEX intervention. Complete data were collected from 120 patients (COBMINDEX=60, TAU=60). Analysis of covariance assessed group differences in post-intervention scores, controlling for baseline scores. Multiple parallel mediation analysis assessed the proposed mechanisms for the entire sample.

Results Individuals in the COBMINDEX condition reported significantly lower levels of perceived stress (F=28.06, p<0.01) and interpersonal sensitivity (F=12.78, p<0.01) than those in the control condition. The COBMINDEX group also had significantly higher levels of life satisfaction (F=9.79, p<0.01) compared to the control group. Perceived social support did not differ across groups (F=2.73, p=0.10). Analysis of indirect effects revealed significant effects of perceived stress (b=0.52, 95% *CI* [0.16, 1.03]) and interpersonal sensitivity (b=0.73, 95% *CI* [0.31, 1.35]); thus, the positive effect of COBMINDEX on life satisfaction was mediated by changes in interpersonal sensitivity and perceived stress.

Conclusions The findings highlight the importance of targeting mental processes such as interpersonal sensitivity to enhance patients' life satisfaction. These findings suggest that practitioners might consider COBMINDEX as an adjunct intervention for patients with CD.

Preregistration

The study was registered with ClinicalTrials.gov (Identifier: NCT05085925) and with the Ministry of Health in Israel (https://my.health.gov.il/CliniTrials/Pages/MOH_2020-02-24_008721.aspx).

Keywords Mindfulness-based cognitive therapy · Patients · Mechanism of change · Interpersonal sensitivity · Stress · Life satisfaction

Crohn's disease (CD) is one common form of chronic inflammatory bowel disease (IBD), and is characterized by recurrent symptoms of abdominal pain, diarrhea, and fatigue (Roda et al., 2020; Torres et al., 2017). Patients with CD are faced with a lifetime of unpredictable periods of active symptoms along with periods of disease remission (Roda et al., 2020; Torres et al., 2017). CD is associated with significant interference with daily activities, relationships, and work that can result in decreased psychological well-being (Devlen et al., 2014; Høivik et al., 2013; Sarid et al., 2018).

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Due to the unpredictable and uncontrollable nature of the disease, individuals living with CD often experience concerns over loss of bowel control during interpersonal interactions (Polak et al., 2020). These worries can result in increased feelings of embarrassment and inadequacy, which can cause people with IBD to limit participation in social activities, negatively affecting their relationships (Polak et al., 2020; Trindade et al., 2020). In line with this, studies have shown that compared with the general population, patients with IBD had higher levels of interpersonal sensitivity (Langhorst et al., 2007; Regev et al., 2022), defined as maladaptive beliefs of personal inferiority and inadequacy in interpersonal interactions (Derogatis & Melisaratos, 1983).

Relatedly, research has shown that patients with IBD also tend to report lower perceived interpersonal support compared with healthy individuals (Jones et al., 2006). This could be cause for concern as previous research indicated perceived availability of support from close others plays a significant role in adjustment to chronic illness (Steptoe, 1991). In the IBD literature, perceived social support has been associated with greater quality of life and improved mental health (Kamp et al., 2019; Katz et al., 2016; Tempchin et al., 2021).

Psychiatric comorbidities, such as anxiety and depression, are prevalent among patients with CD, particularly those with active disease (Neuendorf et al., 2016; Regev et al., 2021). A recent meta-analysis reported that over one in three patients with CD has symptoms of anxiety and one in four has symptoms of depression (Barberio et al., 2021). Thus, it is not surprising that patients with active CD were found to have lower levels of life satisfaction compared to patients in remission (Sarid et al., 2017) and healthy individuals (Janke et al., 2005).

According to recent biopsychosocial models of CD, there is a bi-directional relationship between patients' psychological well-being and the onset and remission of disease symptoms. Specifically, longitudinal research with IBD patients has shown that experiencing disease symptoms resulted in subsequent increase in perceived stress (Sexton et al., 2017) and development of anxiety and depression (Fairbrass et al., 2022; Gracie et al., 2018). Studies also indicated that prolonged psychological distress can trigger and exacerbate disease symptoms in individuals with CD (Black et al., 2022; Sexton et al., 2017). Therefore, given the high prevalence of poor psychological distress in patients with CD and its bi-directional relationship with disease severity, there is a clear need for effective therapy designed to reduce distress in these patients (Gracie et al., 2018).

In recent years, accumulating evidence has demonstrated the beneficial influence of mindfulness-based interventions, including Mindfulness-Based Cognitive Therapy (MBCT), on the psychological health of patients with a chronic health condition (Maddock et al., 2019; Schroevers et al., 2016). Previous studies conducted in patients with IBD have shown that mindfulness-based interventions are efficacious in improving symptoms of anxiety and depression, stress, fatigue, and disease-specific quality of life (Bredero et al., 2023; Ewais et al., 2021; Hood & Jedel, 2017; Neilson et al., 2015). A meta-analysis of randomized controlled trials (RCTs) for IBD indicated long-term efficacy of mindfulness-based interventions in reducing the severity of stress and depression and improving quality of life (Ewais et al., 2019). Similarly, a more recent meta-analysis reported that mindfulness-based interventions are more effective than control conditions in improving stress and disease-related quality of life in patients with IBD (Naude et al., 2023).

While previous research has demonstrated benefits for mindfulness-based interventions on psychological outcomes in patients with IBD, most studies did not differentiate between subtypes (such as CD) and were limited to small cohorts of patients in clinical remission. Specifically, active disease in CD has been linked with lower levels of psychological well-being (Fairbrass et al., 2022; Sarid et al., 2017); yet, the majority of RCTs assessing the effects of psychological interventions in CD have been conducted in patients who were actually in disease remission (Ewais et al., 2019; Gracie et al., 2017; Naude et al., 2023). Consequently, it has been suggested that lack of significant effects in these studies could be due to little variability in clinical outcomes overtime for patients in remission; thus, studies in patients with active CD could have better power to detect changes in response to intervention as well as identify potential mediators (Ewais et al., 2019; Naude et al., 2023).

In the growing literature on cognitive-behavioral and mindfulness interventions in populations with chronic illnesses, most studies have focused on the effectiveness of treatments on psychological outcomes. Less explored, however, are the mechanisms by which improvement in well-being occurs. Understanding these mechanisms will provide insights regarding the therapeutic processes involved in practicing cognitive-behavioral and mindfulness techniques and may represent key therapeutic targets for improving psychological well-being in CD.

Among potential mechanisms of change, stress seems to play a key role. People living with CD were susceptible to experiencing stress (Cooper et al., 2010), with higher levels of stress associated with worse disease symptoms (Black et al., 2022). Mindfulness-based programs are typically focused on facilitating effective stress management skills (Roemer et al., 2015), and have been shown to successfully reduce perceived stress in IBD (Black et al., 2022; Ewais et al., 2021). Perceived stress has been previously identified as a potential mediator of the relationship between mindfulness-based interventions and psychological outcomes (Koch et al., 2020; Lengacher et al., 2021). For example, in a recent yoga intervention for IBD, reductions in perceived stress

mediated improvements in patients' quality of life (Koch et al., 2020).

Interpersonal sensitivity in particular may be another possible mechanism driving the beneficial effect of MBCT on patients with CD. Cognitive-behavioral and mindfulness interventions have been previously associated with reduced maladaptive interpersonal beliefs in the general population (Hiçdurmaz & Öz, 2016; Oró et al., 2021). Moreover, research in non-clinical population suggested that interpersonal sensitivity was highly correlated with diminished life satisfaction (Smorti et al., 2022). As noted above, we have recently found decrease in interpersonal sensitivity following CD-tailored cognitive-behavioral and mindfulness intervention (Goren et al., 2022). However, it is unclear whether changes in interpersonal sensitivity mediate treatment effects on well-being in CD.

Mindfulness has been found to be positively associated with perceived social support among patients with chronic illness (Williams & Cano, 2014; Wilson et al., 2022). While group mindfulness-based interventions are not designed to provide group therapy or serve as a support group (Dobkin et al., 2014), the group format appeared to facilitate not only learning and practicing of intervention techniques, but also emotional closeness and sense of togetherness between participants (Griffith et al., 2019; Portnoy et al., 2023). Studies investigating the effect of group mindfulness-based interventions on social support are scarce; however, the few studies conducted in patients with chronic illnesses tend to report an improvement in perceived social support (Carlson et al., 2016; Molavi et al., 2020). No study has yet investigated whether one-to-one mindfulness-based intervention can change perceptions of social support from close others.

Most studies evaluating the efficacy of psychological interventions for CD have used disease-related quality of life as an indicator of psychological well-being (Irvine et al., 1996). While the value of this measure is wildly accepted in the IBD literature, a critical issue is that it represents the perceived burden of the disease on daily living and therefore may not necessarily reflect general evaluation of one's life (Camfield & Skevington, 2008; Strine et al., 2008). That is, individuals who live with disability due to their chronic illness may report low disease-related quality of life but high life satisfaction because they evaluate their life as a whole positively (Pavot & Diener, 2008). There is no study, to our knowledge, that has assessed the effect of a psychological therapeutic intervention in CD on life satisfaction.

Mindfulness-based interventions, including MBCT, typically involve face-to-face sessions in a group setting. However, it has been questioned whether the group format is an essential part of mindfulness-based interventions in terms of reducing stress and promoting psychological well-being (McCown et al., 2010; van Aalderen et al., 2014). Moreover, one-to-one format might be more feasible for people who have difficulty in regularly attending group sessions due to a disabling disease, such as CD (Bredero et al., 2023). Yet, little is known about the use and effectiveness of individualized mindfulness-based interventions, particularly in patients with chronic diseases (Michalak et al., 2019; Schroevers & Fleer, 2019). Two pilot studies of individualized MBCT have reported improvement of psychological symptoms, and disease-related distress in patients with somatic illnesses (Schroevers et al., 2015, 2016). Another more recent study provided preliminary evidence of the efficacy of individualized MBCT for clinically depressed patients (Paterniti et al., 2022).

This study presented secondary analyses from an RCT evaluating cognitive-behavioral and mindfulness-based stress reduction with daily exercise (COBMINDEX)—an online one-to-one intervention combining cognitive-behavioral and mindfulness techniques tailored for patients with CD (Goren et al., 2022). In prior analyses, we found that COBMINDEX led to significant reductions in disease activity, fatigue, interpersonal sensitivity, and disease-related quality of life in patients with active CD (Goren et al., 2022). We also showed that patients with lower baseline inflammatory biomarkers reported greater reduction in disease symptoms following COBMINDEX (Nemirovsky et al., 2022). Additionally, lower baseline levels of cortisol, a stress hormone, were correlated with larger improvement in mental health symptoms following COBMINDEX (Nemirovsky et al., 2022). Another prior report indicated that COBMINDEX reduced abdominal pain and fatigue, which in turn led to improvement in patients' work productivity and daily activities (Regev et al., 2023).

The present study, using a larger sample than the original report (Goren et al., 2022), examined the effectiveness of COBMINDEX on life satisfaction. Additionally, this paper examined the psychological mechanisms by which COBMINDEX may promote patients' life satisfaction. Specifically, we examined interpersonal sensitivity, social support, and stress as potential mediators of the effect of COBMINDEX on changes in life satisfaction. We hypothesized that participants randomized to the COBMINDEX condition would experience greater improvements in life satisfaction compared with control participants. We also hypothesized that COBMIDEX participants would show greater decrease in perceived stress and interpersonal sensitivity compared with control participants. Additionally, we hypothesized that post-treatment reductions in perceived stress and interpersonal sensitivity would mediate improvement in life satisfaction following COBMINDEX. Despite lack of research on social support in a one-to-one setting of mindfulness-based interventions, but some support for it as an outcome in a group setting, we hypothesize that post-treatment perceptions of social support would be higher for individuals assigned to the COBMINDEX condition relative to the control condition.

Given the well-known beneficial effects of social support on psychological well-being of participants with IBD (Slonim-Nevo et al., 2018; Tempchin et al., 2021), we hypothesized that perceived social support will additionally mediate the association between COBMINDEX and life satisfaction.

Method

Participants

Participants were recruited consecutively at gastroenterology clinics at two university-affiliated hospitals located in the south and center of Israel, and via advertisements in social media. Interested patients were informed that they would be participating in a program of training in cognitive-behavioral skills and mindfulness designed for individuals with CD. Sample size was calculated based on α=0.05, power=0.8, standard deviation=14 in order to achieve a 6-point change in SIBDQ, the primary outcome of the original study (≥86 patients; Goren et al., 2022). To be eligible for the study, patients had to have verified diagnosis of CD for at least 3 months; had to have mild or moderate disease activity (Harvey-Bradshaw Index scores in range 5–16); had to be aged 18 years or over; had the ability to read and write Hebrew; had no psychiatric illness or alcohol/drug dependency; had no planned surgery and no surgery in the past 6 months; and had to be not pregnant. A total of 142 patients met the inclusion criteria and provided baseline data between July 2018 and July 2020. Patients were randomly assigned, stratified by sex, to either COBMINDEX (n=72) or treatment-as-usual control (n=70). Participants in both groups maintained their routine gastroenterology medical care with their respective physicians; individuals assigned to COBMINDEX group received the intervention immediately, whereas participants assigned to the control group received the intervention after the second data collection at 3-month follow-up. Of the 72 participants assigned to COBMINDEX condition, 60 completed pre- and post-intervention assessments; of the 70 participants assigned to control condition, 60 completed pre-, second, and post-intervention assessments. See Fig. 1 for CONSORT diagram of patient flow through the study and reasons for attrition.

Procedure

The COBMINDEX program was administered to individuals in the treatment condition via seven 60-min individualized sessions using videoconferencing over a period of 3 months. The therapists were certified clinical social workers holding a Master's degree in social work with at least 5 years of therapeutic experience. All therapists underwent an intensive 20-hr training in delivering COBMINDEX protocol provided by the developers of this treatment approach (O.S. and V.S.). The therapists were instructed to follow a standardized manual specifying the content of the seven sessions of COBMINDEX. To ensure treatment integrity, therapists provided detailed protocol after each session; these were reviewed by the investigators (G.G, O.S., and V.S) who provided ongoing feedback and consultation throughout the course of the study. Finally, all study investigators and therapists completed Good Clinical Practice training to ensure adherence to field norms of good practice (Crane & Hecht, 2018).

The COBMINDEX intervention comprised seven weekly sessions lasting approximately 1 h each (Goren et al., 2022). COBMINDEX intervention incorporated various mind-body techniques into an integrative therapeutic model adapted to meet the needs of individuals with Crohn's disease. The theme of the first session was "behavioral techniques" and focused on breathing awareness, body scanning, and progressive muscle relaxation (Davis et al., 2008). The theme of the second session was "guided imagery techniques" and focused on developing an image of a safe place and dealing with pain or negative emotions (Boufis, 2009). The theme of the third and fourth sessions was "cognitive techniques" and focused on identifying dysfunctional automatic thoughts and distorted beliefs and creating healthy and adaptive ways of thinking (Beck, 2020; David et al., 2010). The theme of the fifth, sixth, and seventh sessions was "mindfulness techniques" and focused on learning core mindfulness principles and meditations, such as guided breathing meditations, eating, and walking meditations and emotion recognition meditation (Ivtzan, 2019; Kabat-Zinn, 2013).

Participants receiving the intervention were instructed to practice twice daily for least 10 min and were asked to report their daily practice via an app. Podcasts related to COBMINDEX sessions were made available for participants throughout the intervention and post-intervention. After the completion of the second assessment at Month 3, patients in the control group participated in COBMINDEX were given access to the podcasts and completed post-intervention assessment at Month 6.

The study was registered with ClinicalTrials.gov (Identifier: NCT05085925) and with the Ministry of Health in Israel (https://my.health.gov.il/CliniTrials/Pages/MOH_2020-02-24_008721.aspx). All participants were given a detailed written and oral description of the research project and provided their written informed consent. The study was approved by the institutional review boards of the participating hospitals. All procedures contributing to this work complied with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Measures

Life Satisfaction Life satisfaction was measured using the Satisfaction with Life Scale (SWLS). The SWLS is a 5-item

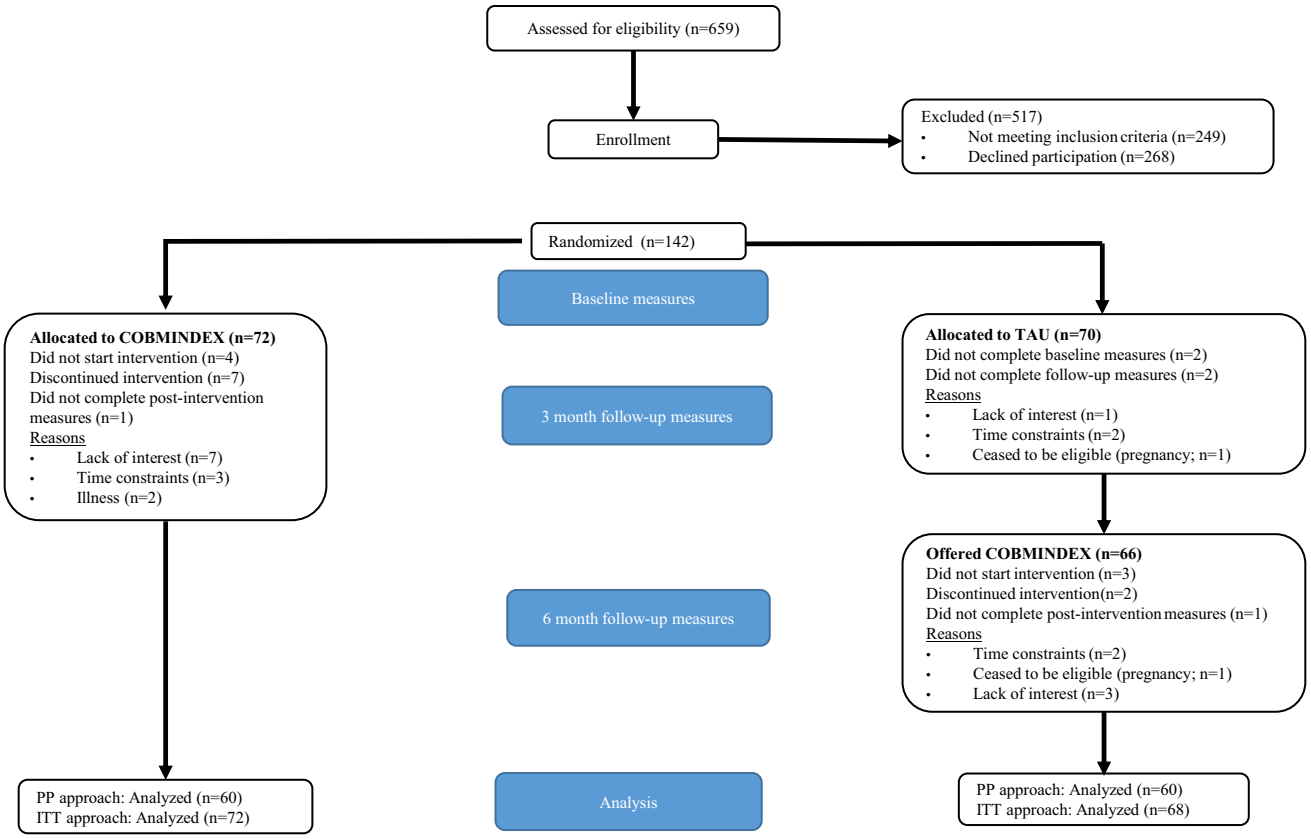

Fig. 1 CONSORT flow diagram

instrument used to assess an individual's global cognitive judgment of their life satisfaction (Diener et al., 1985). Individuals were asked to indicate their level of agreement on a 7-point Likert-type scale. Item scores were added up to generate total scores (range 5–35) where higher scores represented greater life satisfaction. The SWLS included the following items: "In most ways my life is close to my ideal"; "The conditions of my life are excellent"; "I am satisfied with my life"; "So far, I have gotten the important things I want in life"; "If I could live my life over, I would change almost nothing." In the current study, the baseline internal consistency of SWLS was high (Cronbach's α=0.85, McDonald's ω=0.85).

Perceived Stress Perceived stress was measured using the Perceived Stress Scale-4 (PSS-4; Cohen et al., 1983). The PSS-4 is a 4-item measure used to assess the degree to which individuals perceived their lives over the past month as stressful, unpredictable, and uncontrollable. The PSS-4 included the following items: "In the last month how often have you felt you were unable to control the important things in your life"; "In the last month how often have you felt confident about your ability to handle your personal problems?"; "In the last month how often have you felt that things were going your way?"; "In the last month how often have you felt difficulties were piling up so high that you could not overcome them?." Items were rated on a 5-point scale from 0 (*never*) to 4 (*very often*). Item scores were summed to provide a total perceived stress score (range 0–16). Higher scores indicated higher levels of perceived stress. In this sample, the PSS-4 scale had a good baseline internal consistency (α=0.76, ω=0.77).

Perceived Social Support Perceived social support was measured via the 12-item Multidimensional Scale of Perceived Social Support (MSPSS; Zimet et al., 1988). Respondents rated their perceptions of social support from family, friends, and significant other on a 7-point Likert scale ranging from 1 (*very strongly disagree*) to 7 (*very strongly agree*). Item scores were averaged; higher scores indicated better perceived social support. Sample items included "I get the emotional help and support I need from my family" and "I can talk about my problems with my friends." In the present study, the MSPSS had a high baseline internal consistency (α=0.89, ω=0.88).

Interpersonal Sensitivity Interpersonal sensitivity was measured via the Brief Symptom Inventory (BSI; Derogatis & Melisaratos, 1983). The BSI is a 53-item scale used to measure nine dimensions of psychiatric symptomatology that occurred within the past month. In the current study, we focused on the BSI interpersonal sensitivity subscale that consisted of 4 items assessing perceptions of personal inadequacy and inferiority during interpersonal interactions. These items included the following: "feeling that people are unfriendly or dislike you," "feeling inferior to others," "feeling self-conscious with others," and "your feelings being easily hurt." The items were rated on a 5-point Likert scale that ranged from 0 (*not at all*) to 4 (*extremely*). Item scores were averaged and higher scores indicated greater interpersonal sensitivity. In the present study, interpersonal sensitivity subscale had a good baseline internal consistency (α=0.82, ω=0.83).

Disease Activity Disease activity was measured using the Harvey-Bradshaw Index (HBI; Harvey & Bradshaw, 1980). The HBI is a physician-based measurement consisting of five clinical parameters: general well-being (0=*very well*, 1=*slightly below par*, 2=*poor*, 3=*very poor*, and 4=*terrible*), abdominal pain (0=*none*, 1=*mild*, 2=*moderate*, 3=*severe*), abdominal mass (0=*none*, 1=*dubious*, 2=*definite*, 3=*definite and tender*), frequency of diarrheal episodes and complications (e.g., abscess, 1 point per item) that occurred in the past 24 hr. A sum score for disease activity was calculated, with higher scores indicating worse disease activity. A clinical remission was regarded as HBI <5, mild disease 5–7, moderate disease 8–16, and severe disease >16. Measurement of internal consistency was not appropriate for HBI given that this instrument did not assess a latent construct, but rather the presence or severity of discrete symptoms.

In addition, the study gastroenterologists provided clinical details of CD and its treatments from each patient's medical record. Finally, patients provided demographic and socio-economic data that included age, sex, marital status, education level, monthly income, and employment status.

Data Analyses

Treatment completion was defined as completion of all seven sessions. Study retention was defined as completing the post-intervention assessment. Accordingly, per-protocol (PP) sample constituted COBMINDEX participants who completed assessments at baseline (pre-intervention) and 3-month follow-up (post- intervention) and control participants who completed assessment at baseline, 3-month follow-up (pre-intervention), and 6-month follow-up (post-intervention).

An intention-to-treat (ITT) sample was also created using baseline observation carried forward method (Gupta, 2011). This sample comprised of all participants who enrolled in the study and had baseline data, including dropouts. Each participant in the ITT sample was analyzed according to the condition in which they were randomized. The statistical analyses in the paper were based on the PP sample where each participant was analyzed according to the treatment they received. In addition, analyses were also conducted on the ITT sample to examine whether they produced similar results to those in the PP sample.

Data were analyzed using descriptive statistics (means, standard deviations [*SD*], frequencies, and percentages). Differences between the intervention and control groups and between completers and non-completers were investigated using independent-samples *t*-tests and χ^2 tests. Relationships between sociodemographic, clinical, and psychological baseline measures were evaluated using Pearson bivariate correlations.

Two statistical approaches were applied to investigate the main research questions. First, to examine the effect of COBMINDEX on stress, interpersonal sensitivity, social support, and life satisfaction, analysis of covariance (ANCOVA) was used. Four ANCOVAs were conducted with group type (COBMINDEX versus control) as the independent variable, and scores at 3-month follow-up as the dependent variable, with baseline scores as the covariate. Effect sizes for between-group comparisons in ANCOVA were measured using partial eta squared (η^2_p) to indicate the portion of variance in 3-month follow-up scores explained by group type, after adjusting for baseline values.

Next, we employed a within-participant mediation analysis for repeated measures design using the MEMORE macro (version 2.1; Montoya & Hayes, 2017). This procedure was applied to assess the mediating roles of perceived stress, interpersonal sensitivity, and social support in the effect of COBMINDEX on life satisfaction. To this end, we combined the intervention and control patients' pre- and post-intervention assessments. For participants in the control group, data from 3-month follow-up were used as pre-intervention assessment. Using a parallel multiple-mediation model, we estimated the indirect effect of each mediator, controlling for the other mediators in the model. This method also allows comparing between the magnitudes of the indirect effects (see Montoya & Hayes, 2017, for further details on the MEMORE methodology). Standard errors (*SE*) and confidence intervals (*CI*) for the indirect, direct, and total effects were generated from bias-corrected bootstrapping method with 10,000 bootstrap samples. Statistical significance was determined at $p<0.05$ and when the *CI* did not include zero. All analyses were conducted using IBM SPSS version 26 (Armonk, NY: IBM Corp).

Results

Baseline Characteristics

Preliminary analyses compared control versus intervention groups and completers versus non-completers on baseline demographic, clinical, and psychological measures. The attrition rate was not significantly different between COBMINDEX and control groups (17% vs. 13%, p=0.52). Moreover, no significant differences were found between completers and non-completers on demographic and clinical characteristics (sex, age, marital status, income, education years, employment, disease duration, disease activity) and psychological outcome variables (all p>0.05). Table 1 presents comparisons of baseline characteristics of completers in the intervention and control groups. There were no statistically significant differences between COBMINDEX and control participants at baseline on any demographic or clinical variable; thus, the randomization was successful. Moreover, the groups did not differ significantly in the outcome variables at baseline assessment (all p>0.05). Control participants had non-significantly higher perceived stress scores than COBMINDEX participants. Homework compliance was assessed as the percentage of days during the treatment period on which respondents reported through the app that they had practiced mindfulness and/or cognitive behavioral techniques. A third of the sample (33.6%) reported practicing >75% of the days; approximately another third (35.4%) reported practicing on 25–50% of the days; 18.6% of participants practiced on 25–50% of the days and 12.4% of participants practiced on less than 25% of the days.

The PP sample consisted of 120 patients with CD, 75 women (62.5%) and 45 men (37.5%). Participants had a mean age of 34.0 years (SD=10.7, range 18 to 70) and a mean education of 14.9 years (SD=2.4, range 12 to 24). At enrollment, approximately half (48%) reported being in a relationship and the majority of participants (67.5%) were working part- or full-time. In accordance with study criteria, all patients had mild to moderate disease severity at baseline: 58 (48%) had mild CD (HBI 5–7) and 62 (52%) had moderate CD (HBI 8–16). The mean disease duration was 9.2 years (SD=8.4), ranging from less than a year to 37 years.

Table 1 Baseline socio-demographic and clinical characteristics of completers by group

Variable % (n)	COBMINDEX (n=60)	Control (n=60)	p
Gender			
Female	67 (40)	58 (35)	
Male	33 (20)	42 (25)	0.35
Age (mean ±SD; in years)	34.4 ±11.7	33.6 ±9.7	0.68
Marital status			
In a relationship	53 (32)	43 (26)	
Not in a relationship	47 (28)	57 (34)	0.27
Education (mean ±SD; in years)	14.9 ±2.4	14.8 ±2.4	0.91
Education level			
High school	20 (12)	25 (15)	
Vocational	15 (9)	10 (6)	
Academic	65 (39)	65 (39)	0.75
Monthly income			
Below average	54 (32)	69 (41)	
Average	20 (12)	13 (8)	
Above average	26 (15)	18 (11)	0.28
Employment status			
Part-/full-time	73 (44)	73 (44)	
Unemployed	27 (16)	27 (16)	1.00
Disease duration (mean ±SD; in years)	9.4 ±8.9	9.0 ±8.0	0.80
Disease activity[Ψ]			
Mild disease (HBI 5–7)	47 (28)	50 (30)	
Moderate disease (HBI 8–16)	53 (32)	50 (30)	0.71

The p value shows significance levels based on t-tests for continuous variables and χ^2 test for categorical variables.

COBMINDEX Cognitive behavioral and mindfulness-based stress reduction intervention

[Ψ]Based on scores on Harvey-Bradshaw Index

ANCOVAs were conducted to examine differences between COBMINDEX and control participants in the outcome variables at 3-month follow-up (post-intervention for the COBMINDEX group and pre-intervention for the control group), adjusted for baseline values. Based on per-protocol analysis, at 3-month follow-up, individuals in the COBMINDEX condition reported significantly higher post-intervention levels of life satisfaction (F=9.79, p=0.002) than those in the control condition. At 3-month follow-up, the COBMINDEX group also had significantly lower levels of perceived stress (F=28.06, p<0.001) and interpersonal sensitivity (F=12.78, p=0.001) compared with the control group. No significant effect of group was observed for social support at 3-month follow-up (p=0.10); therefore, no further mediation analysis was conducted with this measure. Measures at baseline and at 3-month follow-up and respective ANCOVA results are reported in Table 2. Intention-to-treat analysis showed similar results (Table 3). Although the proportion of women was higher in our sample, there was no significant difference concerning gender between the intervention and control groups and covarying for gender did not change the results.

Based on the combined sample of participants that underwent the COBMINDEX program and completed pre- and post-intervention assessments (n=120), we conducted a within-participant parallel mediation analysis (Montoya & Hayes, 2017). The mediators were change in perceived stress and change in interpersonal sensitivity. The outcome was change in life satisfaction. The results showed that the total effect of COBMINDEX on life satisfaction was significant (b=2.22, SE=0.47, p<0.01, 95% CI [1.29, 3.16]). The total indirect effect through the two mediators was also significant (b=1.26, SE=0.31, 95% CI [0.71, 1.92]). The specific indirect pathways through interpersonal sensitivity (b=0.73, SE=0.26, 95% CI [0.31, 1.35]) and perceived stress (b=0.52, SE=0.22, 95% CI [0.16, 1.03]) were both significant. Thus, reductions in interpersonal sensitivity significantly mediated improvement in life satisfaction beyond the effect of reduced stress symptoms. Similarly, reductions in stress significantly mediated improvement in life satisfaction beyond the effect of reduced interpersonal sensitivity. Pairwise contrasts revealed that the difference between these two specific indirect effects was not statistically significant (contrast=0.21, SE=0.37, 95% CI [−0.51, 0.97]). This suggests that the positive effects of both psychological processes on life satisfaction are independent and are of similar magnitude. Finally, when controlling for the potential mediators, the direct effect was substantially reduced but remained significant (b=0.97, SE=0.48, p=0.04, 95% CI [0.03, 1.91]), indicating that treatment effect on life satisfaction was partially mediated by

Table 2 Per-protocol ANCOVA of COBMINDEX (n=60) versus control (n=60) on study variables

	COBMINDEX		Control		ANCOVA[Ψ]		
	Baseline	3-month	Baseline	3-month	F	p	η^2_p
PSS-4	6.72 ±2.80	4.82 ±2.54	7.70 ±2.98	7.72 ±3.18	28.06	<0.01	0.19
BSI-IS	1.13 ±0.92	0.68 ±0.70	1.24 ±0.83	1.13 ±0.83	12.78	<0.01	0.10
MSPSS	5.75 ±0.91	5.90 ±0.97	5.65 ±0.96	5.62 ±1.09	2.73	0.10	0.02
SWLS	20.78 ±6.68	23.72 ± 5.73	19.13±6.54	20.15 ±6.55	9.79	<0.01	0.08

Values are presented as mean ± standard deviation. *ANCOVA* Analysis of covariance, *COBMINDEX* Cognitive behavioral and mindfulness-based stress reduction intervention, *SWLS* Satisfaction with Life Scale, *MSPSS* Multidimensional Scale of Perceived Social Support, *PSS-4* Perceived Stress Scale-4, *BSI-IS* Brief Symptom Inventory-Interpersonal Sensitivity subscale

[Ψ] The ANCOVA results are for group effect comparing COBMINDEX versus control on 3-month follow-up scores, controlling for baseline scores

Table 3 Intention-to-treat ANCOVA of COBMINDEX (n=72) versus control (n=68) on study variables

	COBMINDEX		Control		ANCOVA[Ψ]		
	Baseline	3-month	Baseline	3-month	F	p	η^2_p
PSS-4	7.01 ±2.88	5.43 ±2.93	7.76 ±3.05	7.57 ±3.14	16.63	<0.01	0.11
BSI-IS	1.20 ±0.92	0.82 ±0.78	1.21 ±0.83	1.08 ±0.81	6.41	0.01	0.04
MSPSS	5.74 ±0.88	5.87 ±0.93	5.70 ±0.97	5.68 ±1.09	2.16	0.14	0.02
SWLS	20.17 ±6.83	22.61 ± 6.41	19.21 ±6.66	20.24 ±6.63	5.53	0.02	0.04

Values are presented as mean ± standard deviation. *ANCOVA* Analysis of covariance, *COBMINDEX* Cognitive behavioral and mindfulness-based stress reduction intervention, *SWLS* Satisfaction with Life Scale, *MSPSS* Multidimensional Scale of Perceived Social Support, *PSS-4* Perceived Stress Scale-4, *BSI-IS* Brief Symptom Inventory-Interpersonal Sensitivity subscale

[Ψ]The ANCOVA results are for group effect comparing COBMINDEX versus control on 3-month follow-up scores, controlling for baseline scores

change in interpersonal sensitivity and stress. See Fig. 2 for the mediation model.

The findings of the ITT analysis were similar to those of the PP analysis. The total effect of the model was significant (b=1.91, SE=0.41, p< 0.01, 95% CI [1.10, 2.72]). The total indirect effect through interpersonal sensitivity and perceived stress was also significant (b=1.10, SE=0.25, 95% CI [0.65, 1.66]). The specific indirect effects of COBMINDEX on life satisfaction through interpersonal sensitivity (b=0.64, SE=0.22, 95% CI [0.28, 1.17]) and perceived stress (b=0.46, SE=0.18, 95% CI [0.15, 0.89]) were both significant. Pairwise contrasts suggested no significant difference in size between the two indirect effects (contrast=0.18, SE=0.32, 95% CI [−0.42, 0.84]). After controlling for the two mediators, the effect of the intervention decreased but remained statistically significant (b=0.81, SE=0.40, p=0.04, 95% CI [0.02, 1.60]).

Discussion

This secondary analysis study examined the effectiveness of cognitive-behavioral and mindfulness intervention on increasing life satisfaction in Crohn's disease. This study also aimed to investigate potential psychological mechanisms underlying the effects of COBMINDEX intervention on life satisfaction. Results revealed that participating in COBMINDEX was associated with improvement in life satisfaction as well as reductions in perceived stress and interpersonal sensitivity. In contrast, there were no changes in perceived social support following COBMINDEX. Furthermore, we found that reductions in interpersonal sensitivity and perceived stress significantly mediated the beneficial effect of COBMINDEX on patient's life satisfaction.

Consistent with our hypothesis, COBMINDEX had a beneficial effect on life satisfaction of patients with CD. Previous meta-analyses have shown that mindfulness-based interventions for IBD are associated with improvement in disease-related quality of life (Ewais et al., 2019; Naude et al., 2023). Our findings are consistent with and extend previous work by demonstrating the effectiveness of MBCT in increasing general well-being in terms of quality of life that is independent of disease status (Pavot & Diener, 2008).

Our finding of reduced perceived stress are in agreement with previous reports in individuals with IBD demonstrating decreased stress-related symptoms following cognitive-behavioral and/or mindfulness interventions (Ewais et al., 2021; Mohamadi et al., 2019). These results support the claim that cognitive reappraisal strategies encourage reframing of events in order to alter their emotional impact (Fresco & Mennin, 2019). Thus, by promoting positive reappraisal, individuals are able to perceive negative inner and outer experiences as tolerable and manageable, thereby leading to reduced stress (Garland et al., 2011; Roemer et al., 2015). In a similar and complementary manner, our results are also consistent with the notion of mindfulness as a process of maintaining attitude of acceptance toward unpleasant sensations and events (Kabat-Zinn, 2013; Roemer et al., 2015).

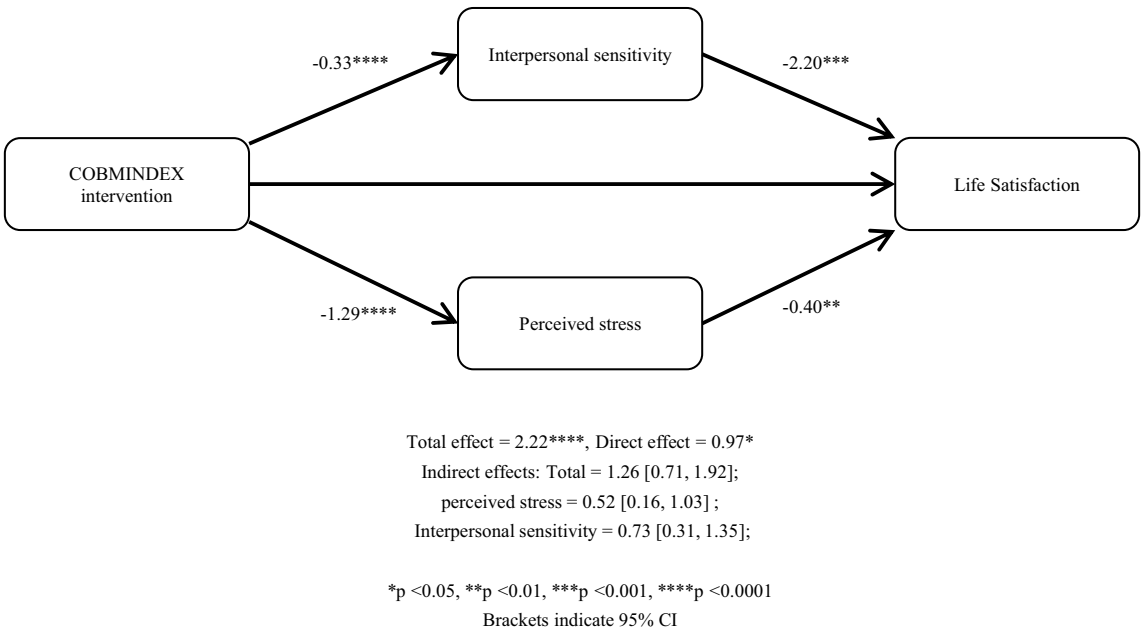

Fig. 2 Parallel multiple-mediator model predicting increase in life satisfaction following COBMINDEX intervention through reductions in perceived stress and interpersonal sensitivity among patients with Crohn's disease (n=120)

To our knowledge, this is the first RCT to examine the efficacy of cognitive-behavioral and mindfulness intervention on interpersonal sensitivity among patients with a chronic physical illness. Our findings indicate that COBMINDEX was able to reduce interpersonal sensitivity, i.e., maladaptive beliefs of self-inadequacy within interpersonal interactions. This effect was evident despite lack of improvement in feelings of social support from close others and therefore cannot be attributed to increased social support. Several possible mechanisms could explain the observed effect of COBMINDEX on interpersonal sensitivity. First, techniques of cognitive restructuring enable individuals to recognize their negative beliefs about themselves in social interactions as dysfunctional and unrealistic and to replace them with more adaptive beliefs (Clark, 2014). Additionally, mindfulness training aims to enhance one's ability to observe the contents of the present experience without judging or interpreting it (Bishop et al., 2004; Kabat-Zinn, 2013). In this process, a person may learn to re-perceive their thoughts and emotions more clearly and objectively as passing mental states rather than accurate reflection of reality (Kabat-Zinn, 2013; Shapiro et al., 2006). It has also been suggested that practice of cognitive-behavioral and/or mindfulness techniques can reduce preoccupation with self-centered thoughts and emotions (Garland & Fredrickson, 2019; Mörtberg et al., 2015). In turn, this shift from egocentric processing might contribute to reductions in concerns about negative social evaluation and rejection (Lavy & Berkovich-Ohana, 2020).

The present study demonstrated that reductions in interpersonal sensitivity and perceived stress following a cognitive-behavioral and mindfulness intervention were associated with improved well-being in patients with CD. While perceived stress has been previously shown to act as a mediator of mindfulness-based interventions (Koch et al., 2020; Lengacher et al., 2021), our results identify interpersonal sensitivity as a novel mechanism of action of MBCT. Overall, these findings suggest that treatment approaches that target dysfunctional interpersonal beliefs may be beneficial for improving well-being in patients with CD. Future studies are needed to investigate the potential role of interpersonal sensitivity as a therapeutic target in chronically ill populations, particularly those presenting unpredictable and uncontrollable symptoms. Additional studies could explore whether aspects of mindfulness specific to interpersonal interactions may act as a specific mechanism of action (Pratscher et al., 2022) or could examine the extent to which reduced interpersonal sensitivity influences actual interpersonal behaviors, such as participation in social activities (Trindade et al., 2020).

Of note, although COBMINDEX intervention reduced perceptions of being viewed negatively by others, it did not influence perceptions of support received from others. These findings resonate with a recent review on resilience in individuals with IBD (Tempchin et al., 2021) suggesting that perceptions of social acceptance and perceptions of social support reflect different constructs of social functioning that are differentially associated with well-being. Furthermore, our results suggest that improved perceived social support previously reported in studies of group mindfulness interventions may be attributed more to non-specific group processes, such as supportive interactions between members and shared experiences (Griffith et al., 2019; Portnoy et al., 2023), than to MBCT specific skills.

Importantly, while mindfulness-based interventions are typically delivered in a group format (Naude et al., 2023), our study indicates that MBCT offered in individual therapy settings is also effective in promoting well-being in patients with a chronic illness. Our results are consistent with previous preliminary studies showing beneficial effects of one-to-one MBCT in reducing depressive symptoms in patients with clinical depression (Paterniti et al., 2022) and in patients with somatic illnesses (Schroevers et al., 2015, 2016). Although the benefits of group mindfulness interventions in terms of shared information and peer support have been recognized (Portnoy et al., 2023; van Aalderen et al., 2014), individualized sessions of MBCT may be more feasible for people who are not able to participate in a group program due to chronic and disabling illness. Moreover, research has suggested that patients with a medical condition perceived individualized MBCT sessions more favorably than group sessions (Schroevers et al., 2016). Future research is needed to examine the effectiveness of one-to-one MBCT in other populations with medical illness and to further identify which psychological constructs are more attributable to the group setting rather than to specific treatment effects. Given the partial mediation results of this study, future work is needed to identify additional mechanisms through which MBCT increases well-being in patients with CD, such as negative illness perceptions (Polak et al., 2020) and self-compassion (Mistretta & Davis, 2022).

The strengths of this study lie in the use of random assignment and recruitment across multiple regions and via various methods (hospital outpatient settings, social media). Additionally, the current program was delivered by qualified therapists who followed a standardized protocol and completed session reports to ensure that the intervention was delivered as intended. This issue of intervention integrity has been a matter of debate as it could be argued that effective teaching of mindfulness practices requires the instructor to convey the program themes via interactive inquiry and personalization to the particular needs of the participant. Nevertheless, the importance of structured and detailed intervention manual along with assessment of adherence has been well-recognized in terms of interpretation and replication of research results (Crane & Hecht, 2018; Dobkin et al., 2014; McCown et al., 2010).

Importantly, the current study demonstrated the potential of video conferencing as a mode for delivering psychological interventions for patients with chronic and disabling diseases. The existing literature indicates that some patients with IBD struggle to attend sessions in face-to-face interventions due to time constrains, reluctance, or inability to travel and burden of illness (Berrill et al., 2014; Hashash et al., 2022). Internet-delivered interventions, such as COBMINDEX, can overcome these patient-specific barriers and improve use of psychological therapies. Our findings extend those of previous studies reporting that group-based mindfulness delivered via video-conferencing can be feasible and beneficial in reducing distress and promoting well-being (Krägeloh et al., 2019; Moulton-Perkins et al., 2022; Portnoy et al., 2023). Future studies should explore differences in feasibility and effectiveness of face-to-face versus video conferencing formats of MBCT, and their corresponding mechanisms of action. For example, future research could compare the nature of non-specific processes, such as therapeutic alliance or social support, between traditional in-person delivery and online delivery of mindfulness-based interventions.

Limitations and Future Research

Several limitations should be noted. First, as with other mindfulness-based intervention studies, self-report questionnaires were used as outcome measures. Second, we focused on individuals with mild-moderate active disease as they have greater variability in psychological functioning compared with individuals in remission, which could improve power to detect change in outcomes; they are also more able to participate in the intervention and practice the learned skills compared with individuals with severe disease activity. However, this may limit generalizability of our findings to CD patients in remission or with severe disease activity. Third, the ability and willingness to participate in an Internet-mediated intervention served as an eligibility criterion; thus, the sampling frame for this study may not include patients with CD without access to a computer and the Internet, or lacking those skills. Additionally, our sample was relatively young, with an average age of 34 years, and so extrapolation of the findings to older patients should be made with caution.

Future research should also include a wider range of ages to determine the efficacy of Internet-based psychological interventions for older individuals, who may be less computer literate. More objective measures of psychological distress and adjustment to disease would also be useful in future MBCT studies of patients with chronic illnesses. Additionally, future studies could also assess the response to MBCT in chronically ill patients with varying degrees of disease severity, especially over the long term.

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Author Contribution SR: methodology, formal analyses, writing—original draft preparation, subsequent drafts, review, and editing. GG: investigation, project administration, writing—review and editing. VSN: conceptualization, methodology, writing—review and editing. DS: conceptualization; writing—review and editing; funding acquisition. MF: conceptualization, writing—review and editing. RS: software, data curation. DG: conceptualization, writing—review and editing. AM: conceptualization, writing—review and editing. AN: writing—review and editing. SO: conceptualization; writing—review and editing; funding acquisition; supervision. OS: conceptualization, methodology, supervision, writing—review and editing.

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Data Availability The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics The institutional review boards of the participating hospitals Soroka Medical Center and Rabin Medical Center, Israel, approved the study in accordance with the Helsinki Declaration of 1975, as revised in 2008. The study was conducted in line with all requirements.

Informed Consent Written informed consent was obtained from all individual participants included in the study.

Conflict of Interest DS has served as a speaker, a consultant, and/or an advisory board member for Takeda Pharmaceutical Co. Ltd., AbbVie Inc., Pfizer Inc., Janssen Pharmaceuticals Inc., Ferring Pharmaceuticals Inc., and Neopharm Labs Inc. GG has served as a speaker for Ferring Pharmaceuticals. All other authors have no conflicts to report.

Use of Artificial Intelligence AI was not used while preparing or editing this manuscript.

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