Journal of Consulting and Clinical Psychology
2017, Vol. 85, No. 9, 918–925

0022-006X/17/$12.00 http://dx.doi.org/10.1037/ccp0000227

BRIEF REPORT

Effectiveness of Cognitive–Behavioral Therapy on Quality of Life, Anxiety, and Depressive Symptoms Among Patients With Inflammatory Bowel Disease: A Multicenter Randomized Controlled Trial

Floor Bennebroek Evertsz' and Mirjam A. G. Sprangers
University of Amsterdam

Kate Sitnikova
VU University Medical Center Amsterdam

Pieter C. F. Stokkers
Sint Lucas Andreas Hospital, Amsterdam, the Netherlands

Cyriel Y. Ponsioen and Joep F. W. M. Bartelsman
University of Amsterdam

Ad A. van Bodegraven
VU University Medical Center Amsterdam and Orbis Medical Center, Sittard-Geleen, the Netherlands

Steven Fischer and Annekatrien C. T. M. Depla
Slotervaart Hospital, Amsterdam, the Netherlands

Rosalie C. Mallant
Flevo Hospital, Almere, the Netherlands

Robbert Sanderman and Huibert Burger
University of Groningen

Claudi L. H. Bockting
University of Utrecht

Objective: Inflammatory bowel disease (IBD) is characterized by a low level of quality of life (QoL) and a high prevalence of anxiety and depression, especially in patients with poor QoL. We examined the effect of IBD-specific cognitive–behavioral therapy (CBT) on QoL, anxiety, and depression in IBD patients with poor mental QoL. ***Method:*** This study is a parallel-group multicenter randomized controlled trial. One hundred eighteen IBD patients with a low level of QoL (score ≤23 on the mental health subscale of the Medical Outcomes Study Short Form 36 Health Survey [SF-36]) were included from 2 academic medical centers (Academic Medical Center Amsterdam, VU University Medical Centre Amsterdam) and 2 peripheral medical centers (Flevo Hospital, Slotervaart Hospital) in the Netherlands. Patients were randomized to an experimental group receiving CBT (n = 59) versus a wait-list control

Floor Bennebroek Evertsz' and Mirjam A. G. Sprangers, Department of Medical Psychology, Academic Medical Center, University of Amsterdam; Kate Sitnikova, Department of General Practice & Elderly Care Medicine, VU University Medical Center Amsterdam; Pieter C. F. Stokkers, Department of Gastroenterology, Sint Lucas Andreas Hospital, Amsterdam, the Netherlands; Cyriel Y. Ponsioen and Joep F. W. M. Bartelsman, Department of Gastroenterology, Academic Medical Center, University of Amsterdam; Ad A. van Bodegraven, Department of Gastroenterology and Hepatology, VU University Medical Center Amsterdam, and Department of Internal Medicine, Geriatrics and Gastroenterology, Orbis Medical Center, Sittard-Geleen, the Netherlands; Steven Fischer, Department of Medical Psychology, Slotervaart Hospital, Amsterdam, the Netherlands; Annekatrien C. T. M. Depla, Department of Gastroenterology and Hepatology, Slotervaart Hospital; Rosalie C. Mallant, Department of Gastroenterology and Hepatology, Flevo Hospital, Almere, the Netherlands; Robbert Sanderman, Department of Health Psychology, University Medical Center Groningen, University of Groningen; Huibert Burger, Department of General Practice, University Medical Center Groningen, University of Groningen; Claudi L. H. Bockting, Department of Clinical and Health Psychology, University of Utrecht.

Floor Bennebroek Evertsz' was the chief investigator and grant holder of the trial. She drafted the final manuscript (which was added to and modified by all other authors), wrote the treatment manual for the cognitive–behavioral therapy (CBT) intervention used (which was added to and modified by Claudi L. H. Bockting), and was responsible for the training and supervision of the psychotherapists. Mirjam A. G. Sprangers was the study's principal investigator. The statistical analysis plan was set up by Floor Bennebroek Evertsz' and Claudi L. H. Bockting. Huibert Burger was responsible for statistical analysis and reporting (adviser statistical analyses). Mirjam A. G. Sprangers, Pieter C. F. Stokkers, Robbert

continued

group ($n = 59$) receiving standard medical care for 3.5 months, followed by CBT. Both groups completed baseline and 3.5 months follow-up assessments. The primary outcome was a self-report questionnaire and disease-specific QoL (Inflammatory Bowel Disease Questionnaire [IBDQ]). Secondary outcomes were depression (Hospital Anxiety and Depression Scale–Depression Subscale [HADS-D], Center for Epidemiologic Studies Depression Scale [CES-D]), anxiety (HADS–Anxiety Subscale [HADS-A]) and generic QoL (SF-36). ***Results:*** Data were analyzed both on intention to treat as well as on per protocol analysis (completed ≥5 sessions). CBT had a positive effect on disease-specific-QoL (Cohen's $d = .64$ for IBDQ total score), depression (Cohen's $d = .48$ for HADS-D and .78 for CES-D), anxiety (Cohen's $d = .58$ for HADS-A), and generic QoL (Cohen's $d = 1.08$ for Mental Component Summary of the SF-36; all $ps < .01$). ***Conclusions:*** IBD-specific CBT is effective in improving QoL and in decreasing anxiety and depression in IBD patients with poor QoL. Clinicians should incorporate screening on poor mental QoL and consider offering CBT.

What is the public health significance of this article?
Given that a substantial proportion of people with chronic somatic disorders have a high prevalence of psychiatric disorders, it is of relevance to examine whether psychological interventions are effective in this comorbid group. In a specific chronic somatic disorder, inflammatory bowel disease (IBD), 'IBD-specific CBT' has a promising effect on QoL, anxiety and depressive symptoms.

Keywords: cognitive–behavioral therapy, inflammatory bowel disease, quality of life, anxiety, depression

Inflammatory bowel disease (IBD) is a debilitating and chronic inflammatory condition of the intestinal tract. In the case of Crohn's disease (CD), it can affect any area between the mouth and the anus, whereas ulcerative colitis (UC) is restricted to the colon. Multiple factors contribute to the etiology of IBD, there is no cure for IBD, and patients usually require lifelong medical treatment and surgery at some point in time (Kilcoyne, Kaplan, & Gee, 2016; Zhang & Li, 2014). Individuals with IBD report poorer quality of life (QoL; Bennebroek Evertsz', Thijssens, et al., 2012) and more anxiety and depressive symptoms (Mittermaier et al., 2004; Walker et al., 2008) than do controls. As in other somatic diseases (Katon, Lin, & Kroenke, 2007), poor QoL and comorbid depression and anxiety have an adverse effect in the form of higher relapse rates and more disease activity (Mittermaier et al., 2004). Between 60% and 80% of IBD patients suffer from anxiety and depressive disorders during exacerbation, and 29%–35% during illness remission (Mikocka-Walus et al., 2007).

Cognitive–behavioral therapy (CBT) is the most studied effective treatment in reducing anxiety and depressive symptoms in patients with chronic illnesses (Van Straten, Geraedts, Verdonck-de Leeuw, Andersson, & Cuijpers, 2010). Nevertheless, reviews have reported mixed results on its effectiveness on anxiety, depression, and QoL in IBD patients (Knowles, Monshat, & Castle, 2013; McCombie, Mulder, & Gearry, 2013; Timmer et al., 2011), and most studies suffered major methodological shortcomings, such as an insufficient sample size (ranging from 21 to 60; e.g., Diaz Sibaja, Comeche Moreno, & Mas Hesse, 2007; Keefer, Doerfler, & Artz, 2012; Langhorst et

Sanderman, and Claudi L. H. Bockting supervised the study and contributed to its design and analytic strategy. Mirjam A. G. Sprangers, Pieter C. F. Stokkers, Robbert Sanderman, Floor Bennebroek Evertsz', and Claudi L. H. Bockting were responsible for the funding. Kate Sitnikova supported in literature searches and reference preparation and reviewed earlier drafts of the article. All authors read and approved the final manuscript. Floor Bennebroek Evertsz' had full access to all data in the study and had final responsibility for the decision to submit for publication.

The protocol is registered in the Dutch Trial Register (Trial registration: NTR [TC = 1869]; http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=1869) and has been published elsewhere (Bennebroek Evertsz', Bockting, et al., 2012).

The research was externally funded by a grant application from the noncommercial Stomach Liver Bowel Foundation (Maag Lever Darm Stichting [MLDS]) of the Netherlands, which carried out the peer review of the proposal (Registration WO 07-45). The sponsor of the study, MLDS, had no role in the study design; gathering, analysis, or interpretation of the data; or writing of the report. Floor Bennebroek Evertsz' received an unrestricted research grant from Scheringh and Plough of 20,000 euros to study psychological factors in inflammatory bowel disease (IBD). The authors declare that they have no competing interests.

First we thank all patients with IBD who took part in this study. We thank all medical specialists (gastroenterologists), support staff, and management of the Academic Medical Center Amsterdam, Flevo Hospital, Slotervaart Hospital, and VU University Medical Centre Amsterdam for enabling the randomized controlled trial. We would also like to thank the Leiden University Medical Centre and the Radboud University medical center for initially participating in this study. Additionally, we thank all cognitive–behavioral clinical psychologists—Truus Wilterdink, Ineke Lauwen, Eva Zuijderland, Annemieke Osendarp, Yvonne Kieviet, Anne Winters, Iris Panders, Katelijne Cornelisse, Dorine van der Schaar, Annemieke Ritzen, Debbie Been, Eric Aalsma, Walter de Vries, Heleen Grandia, Ralph Tinnemans, Aart Beekman, Marjolein Hanson, and Maria Goog—who administered the CBT intervention.

Correspondence concerning this article should be addressed to Floor Bennebroek Evertsz', Department of Medical Psychology, Academic Medical Center, University of Amsterdam, Meibergdreef 15, AZ 1105 Amsterdam, the Netherlands. E-mail: f.bennebroek@amc.uva.nl

al., 2007; Mussell, Bocker, Nagel, Olbrich, & Singer, 2003; Schwarz & Blanchard, 1991).

The current study examines the effectiveness of IBD-specific CBT on QoL, anxiety, and depression in a multicenter randomized controlled trial comparing CBT to a wait-list control group. We specifically focus on IBD patients with poor mental QoL because this is associated with mental health disorders (Walker et al., 2008). We expected an improvement in health-related QoL and a reduction in the depressive and anxiety symptoms of the CBT patients compared to the wait-list control group.

Method

Study Design and Participants

Inclusion criteria were as follows: (a) a diagnosis of Crohn's disease (CD) or ulcerative colitis (UC), (b) age above 18 years, (c) score of ≤23 on the mental health subscale of the Medical Outcomes Study Short Form 36 Health Survey (SF-36; Ware, 1992), (d) physically and mentally able to attend eight weekly sessions, and (e) sufficient command of Dutch. Exclusion criteria were the following: (a) current psychotherapy, (b) severe other psychiatric disorders (e.g., substance abuse, bipolar disorder, or psychosis) as assessed with the Structural Clinical Interview for *DSM–IV* Axis-I Disorders (SCID-I; First, Spitzer, Gibbon, & Williams, 1999). Patients were randomized to receive standard medical care (wait-list control group) or CBT (apart from medical care). Patients were screened for eligibility and enrolled by independent gastroenterologists from four participating medical centers, and IBD was diagnosed using standard clinical criteria (Bennebroek Evertsz', Bockting, et al., 2012). After participants signed informed consent, a trained psychologist carried out a telephone version of the validated SCID-I (First et al., 1999) to determine inclusion–exclusion criteria. The study protocol was approved by the Medical Ethical Committee of the Academic Medical Center.

Randomization and Masking

After the first baseline assessment was completed, an independent collaborator randomly allocated patients using the TENALEA Clinical Trial Data Management System software (http://www.formsvision.com). Randomization was performed on a 1:1 ratio using nondeterministic minimization to enhance balance between the groups on important prognostic factors (gender, disease type [CD and UC]), and type of medical center (peripheral vs. academic; Pocock & Simon, 1975). Our algorithm added a random, nondeterministic component by assigning a probability of .83 of being allocated to the preferred arm. Patients were informed after completing the baseline assessments.

Procedures

The IBD-specific CBT involved eight 1-hr weekly sessions. A treatment manual based on the CBT model (Beck, 2005) was used to enhance treatment integrity (available on request from the first author). Every participant received writing assignments, cognitive interventions focused on specific illness beliefs (e.g., "My illness has major consequences on my life") and dysfunctional attitudes (e.g., "I have to be perfect to be happy") and a relapse-prevention plan (for an extensive description see Bennebroek Evertsz', Bockting, et al., 2012). There were two optional additional modules, depending on the specific psychiatric disorder: (a) behavioral activation and an exposure-based intervention including response prevention (for depressive and anxiety disorders, respectively) and (b) imagination and rescripting (for posttraumatic stress disorder).

Eighteen clinical psychologists specializing in CBT performed the intervention after 16 hr of training and regular group supervision. All CBT sessions were recorded. Independent raters conducted integrity checks on at least two treatments per therapist. Standard medical care involved consultation with medical specialists every 3 months for patients receiving immune suppression and once a year for patients who were not.

Outcomes

The experimental group started CBT immediately and completed follow-up measures 1 month after completion. After the baseline assessment, the wait-list control group waited 3.5 months to start CBT and completed a follow-up assessment 1 month after its completion. All assessments were based on online self-report questionnaires. The primary outcome was the total score on the Inflammatory Bowel Disease Questionnaire (IBDQ), which comprises 32 items assessing these four domains: bowel symptoms, systemic symptoms, and emotional and social functioning (Russel et al., 1997). The secondary outcomes were depression and anxiety, which were assessed using the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983). The Center for Epidemiologic Studies Depression Scale (CES-D) measuring depressive symptomatology in the general population was also used to examine the difference between these two questionnaires (Radloff, 1977). Generic health status was assessed with the SF-36 (Ware, 1992); the 36 items can be aggregated into a Physical Component Summary (PCS) score and a Mental Component Summary (MCS) score. Clinical baseline data were gathered by the gastroenterologist.

Statistical Analysis

With an effect size of .5, an alpha level of .05, and a power of 80%, at least 128 patients were required for the analysis, and assuming a 10% attrition rate, at least 142 patients needed to be included. The primary analysis was the difference of the mean IBDQ total score at the 3.5 months follow-up between the two groups using an intention-to-treat (ITT) approach. We refrained from analyzing the pooled data of the experimental group and the data from the wait-list control group while on CBT. This protocol deviation was agreed upon prior to the analyses because, during the study, 12 of the 59 patients in the wait-list group dropped out. As a result, we felt that the wait-list group, at the end of follow-up, was unlikely to be comparable to the group that started with CBT at randomization. The groups were therefore anticipated to be too heterogeneous to pool reliably, so we limited our analyses to using the data obtained in the parallel groups. Analyses of covariance were used to assess differences between the follow-up scores of all continuous outcomes for the groups while accounting for their baseline values. The effect of CBT on Physician's Global Assessment (PGA) was analyzed as a dichotomous (active vs. inactive) dependent variable using logistic regression, and the result

was presented as an odds ratio. Minimization (Pocock & Simon, 1975) variables were included as covariates in all these analyses. In additional analyses, we included baseline factors that were not balanced between the randomized groups as covariates. Each of the analyses mentioned was carried out on the completers group, defined as those patients with an outcome IBDQ total score at follow-up (49 patients in the CBT group and 47 in the control group). We performed, in addition to the primary ITT analyses, per protocol (PP) analyses on those patients who attended at least five CBT sessions. We performed multiple imputation using chained equations (MICE) as a sensitivity analysis to handle missing values and then reanalyzed the data combining results from 10 imputed data sets into pooled estimates (White, Royston, & Wood, 2011). Around 68% (Nagelkerke R^2) of the outcome variable was missing at random at least to some extent, and consequently multiple imputation may have reduced bias. To compare the relative magnitude of the effects, we standardized mean scores on the continuous outcomes to Cohen's *d* using the pooled standard deviation of the baseline scores for both the completers group and the MICE group. Cohen's *d* of .3, .5, and .8, indicating a small, moderate, and large effect size (ES), respectively, were calculated. Effect size estimates were presented with a 95% confidence interval (CI). The level of significance (alpha) was set at .05.

Results

Between January 2009 and November 2011 we screened 744 patients. Of these, 118 were eligible and randomized (see Figure 1). At follow-up, 96 participants (81%) provided data for analysis for the IBDQ total score (ITT completers). Participants

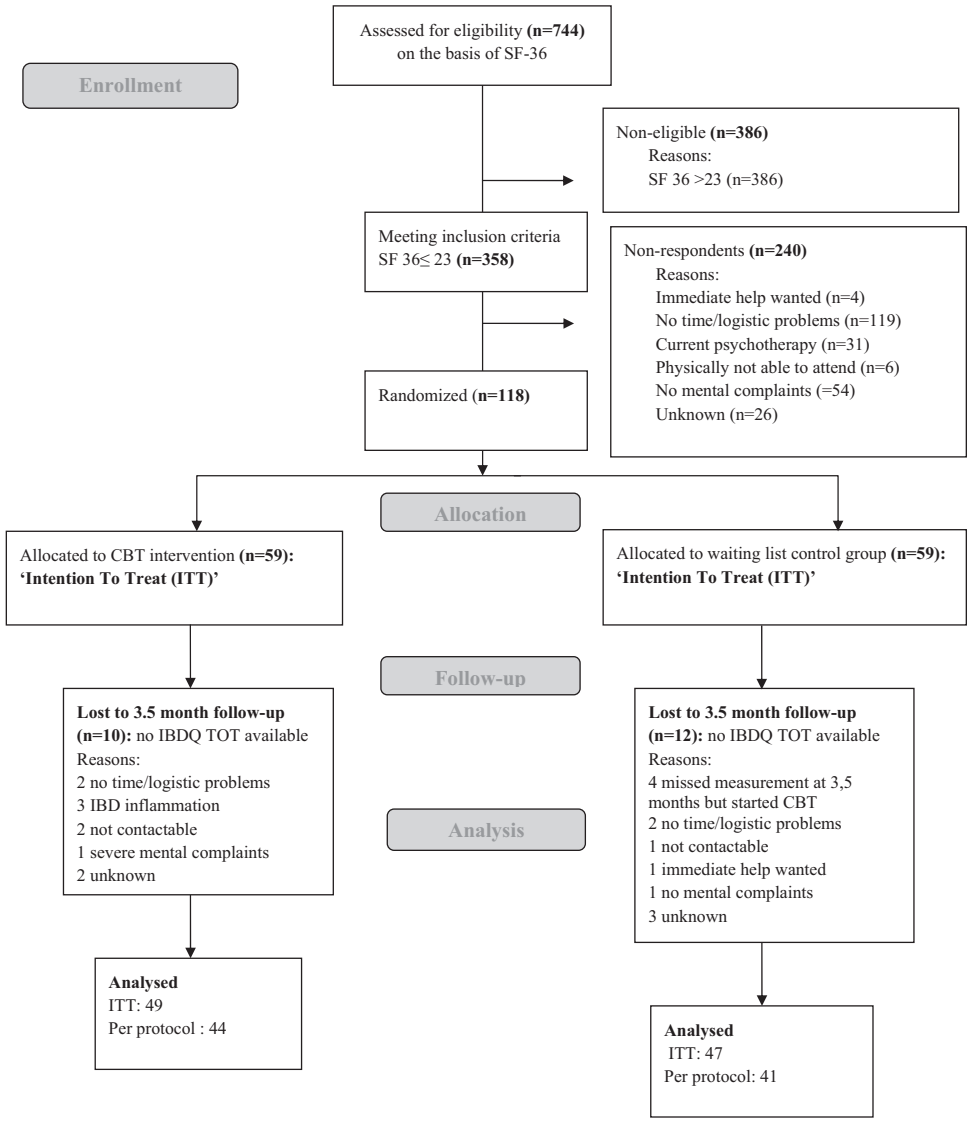

Figure 1. Flow diagram for inflammatory bowel disease patients through the trial, including attrition. SF 36 = Medical Outcomes Study Short Form 36 Health Survey; CBT = cognitive–behavioral therapy; IBDQ TOT = Inflammatory Bowel Disease Questionnaire total score; IBD = inflammatory bowel disease.

who provided follow-up information on the primary outcome (n = 93) did not substantially differ on baseline characteristics from those who did not (n = 25). A mean of six sessions (SD = 3.0) was completed, with 73.7% (n = 87) completing at least five sessions. The demographic and clinical baseline characteristics of the ITT group (n = 118) were similar in both groups (see Table 1). At baseline, the mean clinical outcome scores did not differ significantly between the two groups (see Table 2).

CBT exerted a statistically significant effect on the IBDQ total score with a moderate ES (see Table 3). CBT had a significant effect on the IBDQ subscales Systemic and Emotional, with a moderate and large ES, respectively, whereas for subscales Bowel and Social, the effects were statistically insignificant. CBT also significantly reduced the HADS total score and the anxiety and depression subscales, all with moderate ES. The percentage of the HADS total scores ≥11, indicating a probable psychiatric disorder in the experimental group, decreased from 71.4% at baseline to 43.8% at follow-up compared to a reduction of 6.3% in the wait-list control group. The percentage of anxiety and depression HADS scores ≥11 in the experimental group decreased from 35.7% and 25.0% at baseline to 10.4% and 4.2%, respectively, at follow-up, compared to 2.3% and 3.4%, respectively, in the wait-list control group. Similarly, CBT significantly reduced CES-D scores, with a large ES. It also had a significant effect on the MCS score of the SF-36, with a large ES, but not on its PCS. When we adjusted for unbalanced baseline variables (employment and surgery), the results were similar. The MICE results for the previously mentioned variables were essentially the same (see Table 3). Where we restricted the analyses to patients who attended at least five CBT sessions, the PP sample, results were similar to those obtained in the ITT group (see Table 4). No adverse events related to the CBT were identified. In one case, the therapist was contacted, followed by extra supervision after treatment.

Discussion

CBT was effective in improving the specific IBD-related QoL (primary outcome) and the mental aspects of generic QoL, anxiety, and depressive symptoms (secondary outcomes) compared to the wait-list control group. Our findings partially contrast the reported mixed effects in aforementioned systematic reviews on the effect of psychotherapy on IBD patients (Knowles et al., 2013; McCombie et al., 2013; Timmer et al., 2011).

Table 1
Demographic and Clinical Baseline Characteristics of the ITT Group in the Experimental Versus Waitlist-Control Group

Characteristic	Experimental group (n = 59)		Wait-list control group (n = 59)	
	n (%)	M (range)	n (%)	M (range)
Gender (Female)	39 (66.1)		36 (61.0)	
Age in years		39.4 (19.4–76.5)		38.7 (20.1–61.8)
Marital status (in a relationship)	30 (50.8)		34 (57.6)	
Level of education				
Low (primary or secondary)	33 (55.9)		31 (52.5)	
High (college or university)	26 (44.1)		28 (47.5)	
Employment				
Employed or studying	31 (52.5)		41 (69.5)	
Unemployed	28 (47.5)		18 (30.5)	
Sick leave	12 (20.3)		12 (20.3)	
Hospital type (academic)	40 (67.8)		39 (66.1)	
Diagnosis				
Ulcerative colitis	24 (40.7)		46 (44.1)	
Crohn's disease	35 (59.3)		33 (55.9)	
Disease duration in years		11.9 (.3–46.0)		10.4 (1.0–36.0)
No. of operations				
None	41 (69.5)		32 (54.2)	
≥1	18 (30.5)		27 (45.8)	
Stoma	3 (5.1)		3 (5.1)	
Medication				
Prednisone	14 (23.7)		14 (23.7)	
Antidepressants	4 (6.8)		2 (3.4)	
Family member(s) with IBD	14 (23.7)		16 (27.1)	
Current Axis 1 disorder	40 (67.8)		43 (72.9)	
Mood disorder	11 (18.6)		13 (22.0)	
Anxiety disorder	15 (25.4)		22 (37.3)	
Somatoform disorder	1 (1.7)		0 (.0)	
Eating disorder	4 (6.8)		2 (3.4)	
Adjustment disorder	18 (30.5)		18 (30.5)	
Alcohol related disorder	1 (1.7)		1 (1.7)	
Disorder related to substance abuse	0 (.0)		0 (.0)	
Psychotic disorder	0 (.0)		0 (.0)	

Note. ITT = intention to treat; IBD = inflammatory bowel disease.

Table 2
Baseline Outcome Measures (IBDQ, SF-36, HADS, CES-D) of the ITT Group in the Experimental Versus Waitlist-Control Group

Measure	Experimental group (n = 59)	Wait-list control group (n = 59)
IBDQ		
Total	144.70 (27.91)	152.21 (27.85)
Bowel	49.45 (10.11)	51.93 (10.30)
Systemic	18.02 (5.47)	19.66 (5.64)
Emotional	53.04 (11.80)	54.86 (11.32)
Social	24.20 (6.29)	25.77 (6.05)
SF-36		
Physical	37.24 (7.04)	39.98 (9.39)
Mental	36.27 (10.08)	36.70 (9.92)
HADS		
Anxiety	9.23 (4.25)	8.82 (3.72)
Depression	7.46 (4.28)	7.45 (4.48)
Total	16.70 (7.84)	16.27 (7.38)
CES-D	22.23 (10.46)	20.23 (12.06)

Note. Data are means, with standard deviations in parentheses. ITT = intention to treat; IBDQ = Inflammatory Bowel Disease Questionnaire; SF-36 = Medical Outcomes Study Short Form 36 Health Survey; HADS = Hospital Anxiety and Depression Scale; CES-D = Center for Epidemiologic Studies Depression Scale.

Depression with a comorbid chronic somatic illness increases the likelihood of poorer outcomes and (psychological) treatment response (American Psychiatric Association, 2010; National Collaborating Centre for Mental Health, 2009). Less is known about the impact of anxiety on treatment outcomes in chronic medical illness. In this study 70.3% of the patients had a current Axis-1 disorder. We mainly found patients with depressive disorders (20.3%), anxiety (31.4%), and adjustment (30.5%) disorders. Our study has important strengths. First, patients were screened according to the SCID-I at baseline, to assess not only depressive and anxiety complaints but also mental health disorders. Second, our study focused on IBD patients with poor mental QoL who were expected to have a high-risk prevalence of psychiatric disorders and to be in need of mental care. However, two limitations of this study need to be addressed. First, our study was somewhat underpowered for the primary outcome (n = 96 for the complete case analysis rather than the planned n = 128). Nevertheless, we observed statistically significant results for most outcomes, and our sensitivity analysis using multiple imputations showed effect sizes similar to those in the complete case analysis, indicating little or no bias due to attrition. Second, a wait-list control group is not the optimal control condition (Handley, Schillinger, & Shiboski, 2011). Therefore, future studies should compare the current CBT for IBD with a treatment as usual comparison group or an active control group, such as CBT that has not been adapted specifically for IBD patients.

Conclusions

IBD-specific CBT was effective in improving QoL and in decreasing anxiety and depression. IBD patients require integrated medical and psychological treatment, including standard screening on poor mental QoL by clinicians, and should be considered for

Table 3
ITT Analyses Completers Mean Scores (and Standard Deviations) and Differences Between the Experimental and Wait-List Control Group at 3.5 Months Follow-Up

Assessment	M (SD)		Difference in means			
	Experimental group (n = 49)	Wait-list control group (n = 47)	Completers estimate		MICE estimate	
			Difference [95% CI], p	ES [95% CI]	Difference [95% CI], p	ES [95% CI]
IBDQ						
Total	168.12 (28.60)	152.98 (28.35)	18.16 [8.28, 28.04], <.01	.64 [.29 to .98]	15.80 [7.74, 23.85], <.01	.55 [.27 to .84]
Bowel	53.63 (9.07)	51.45 (9.87)	3.16 [−.46, 6.77], .09	.33 [−.05 to .71]	2.61 [−.3, 5.52], .08	.28 [−.03 to .58]
Systemic	22.20 (6.20)	19.89 (6.69)	3.17 [1.08, 5.25], <.01	.49 [.17 to .81]	2.88 [99, 4.76], <.01	.45 [.15 to .74]
Emotional	64.80 (11.36)	55.13 (10.35)	10.00 [6.10, 13.92], <.01	.92 [.56 to 1.28]	8.48 [5.19, 11.76], <.01	.78 [.47 to 1.08]
Social	27.49 (6.49)	26.51 (6.11)	1.68 [−.47, 3.83], .13	.27 [−.07 to .61]	1.52 [−.29, 3.32], .10	.24 [−.05 to .53]
SF-36						
Physical	40.92 (9.64)[a]	42.57 (10.51)	−.39 [−3.52, 2.74], .80	−.04 [−.35 to .27]	−1.08 [−4.53, 2.36], .53	−.11 [−.45 to .23]
Mental	47.68 (8.15)[a]	38.37 (9.26)	9.38 [6.09, 12.67], <.01	1.08 [.70 to 1.45]	8.90 [5.68, 12.12], p <.01	1.02 [.65 to 1.39]
HADS						
Anxiety	6.06 (4.22)[a]	8.66 (3.75)	−2.33 [−3.71, −.95], <.01	.58 [−.93 to −.24]	−2.26 [−3.50, −.03], <.01	.57 [−.88 to −.01]
Depression	4.33 (3.80)[a]	6.57 (4.02)	−1.89 [−3.18, −.59], <.01	.48 [−.81 to .15]	−1.85 [−3.01, −.68], <.01	.47 [−.77 to −.17]
Total	10.40 (7.32)[a]	15.23 (6.78)	−4.22 [−6.55, −1.89], <.01	.60 [−.93 to −.27]	−4.11 [−6.08, −2.14], <.01	.58 [−.86 to .30]
CES-D	12.40 (8.95)[a]	18.91 (9.32)	−7.12 [−10.06, −4.19], <.01	.78 [−1.10 to −.46]	−5.81 [−8.58, −3.04], <.01	.635 [−.94 to −.33]

Note. Adjusted for baseline value and these stratification variables: gender, disease type, and academic vs peripheral. ITT = intention to treat (where completer is defined as having a follow-up total score on the Inflammatory Bowel Disease Questionnaire); MICE = multiple imputation using chained equations; CI = confidence interval; ES = effect size; IBDQ = Inflammatory Bowel Disease Questionnaire; SF-36 = Medical Outcomes Study Short Form 36 Health Survey; HADS = Hospital Anxiety and Depression Scale; CES-D = Center for Epidemiologic Studies Depression Scale.
[a] Based on n = 48.

Table 4
Per Protocol Analyses Completers Mean Scores and Differences Between the Experimental and Wait-List Control Group at 3.5 Months Follow-Up

Assessment	*n*		*M* (*SD*)		Difference in means			
					ITT estimate		MICE estimate	
	Experimental group	Wait-list control group	Experimental group	Wait-list control group	Difference [95% CI], *p*	ES [95% CI]	Difference [95% CI], *p*	ES [95% CI]
IBDQ								
Total	44	41	168.89 (28.56)	155.59 (26.81)	16.97 [6.37, 27.57], <.01	.61 [.23 to 1.00]	16.15 [6.17, 26.14], <.01	.58 [.22 to .94]
Bowel	44	41	53.61 (9.13)	52.22 (9.87)	2.71 [−1.09, 6.51], .16	.29 [−.11 to .68]	2.39 [−1.18, 5.96], .19	.25 [.12 to .14]
Systemic	44	41	22.64 (6.06)	20.34 (6.81)	3.11 [.85, 5.36], <.01	.48 [.13 to .83]	3.34 [1.17, 5.51], <.01	.52 [.18 to .85]
Emotional	44	41	64.82 (11.59)	56.22 (9.08)	9.42 [5.21, 13.62], <.01	.90 [.50 to 1.31]	8.97 [4.97, 12.97], <.01	.86 [.48 to 1.25]
Social	44	41	27.82 (6.41)	26.80 (5.79)	1.49 [−.83, 3.81], .20	.24 [−.14 to .62]	1.29 [−.94, 3.51], .26	.21 [.15 to .57]
SF-36								
Physical	44	41	41.39 (42.17)	43.01 (10.40)	−.45 [−3.73, 2.83], .79	−.01 [−.12 to .09]	−.27 [−3.48, 2.94], .87	−.01 [−.11 to .10]
Mental	44	41	47.34 (8.32)	38.80 (9.37)	9.40 [5.86, 12.94], <.01	1.06 [.66 to 1.46]	9.24 [5.82, 12.67], <.01	1.04 [.66 to 1.43]
HADS								
Anxiety	44	41	6.36 (4.26)	8.49 (3.72)	−2.15 [−3.65, −.66], <.01	−.54 [−.91 to −.17]	−2.23 [−3.69, −.77], <.01	−.56 [−.92 to −.19]
Depression	44	41	4.41 (3.88)	6.24 (4.05)	−1.66 [−3.07, −.26], .02	−.42 [−.77 to −.07]	−1.75 [−3.09, −.40], .01	−.44 [−.78 to −.10]
Total	44	41	10.77 (7.44)	14.73 (6.70)	−3.82 [−6.37, −1.27], <.01	−.54 [−.90 to −.18]	−3.97 [−6.40, −1.54], <.01	−.56 [−.90 to −.22]
CES-D	44	41	12.84 (9.06)	18.49 (8.90)	−6.98 [−10.16, −3.79], <.01	−.78 [−1.13 to −.42]	−6.99 [−10.07, −3.90], <.01	−.78 [−1.12 to −.43]

Note. Adjusted for baseline value, these stratification variables: gender, disease type, and academic vs peripheral as well as surgery and unemployment. *Per protocol analyses completers* is defined as those who completed five or more sessions of cognitive–behavioral therapy and had a follow-up score on the IBDQ Total. ITT = intention to treat; MICE = multiple imputation using chained equations; CI = confidence interval; ES = effect size; IBDQ = Inflammatory Bowel Disease Questionnaire; SF-36 = Medical Outcomes Study Short Form 36 Health Survey; HADS = Hospital Anxiety and Depression Scale; CES-D = Center for Epidemiologic Studies Depression Scale.

receiving CBT (Fava, Ruini, Tomba, & Wise, 2012; Mikocka-Walus et al., 2015).

References

American Psychiatric Association. (2010). *Practice guideline for the treatment of patients with major depressive disorder* (3rd ed.). Retrieved from http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf

Beck, A. T. (2005). The current state of cognitive therapy: A 40-year retrospective. *Archives of General Psychiatry, 62,* 953–959. http://dx.doi.org/10.1001/archpsyc.62.9.953

Bennebroek Evertsz', F., Bockting, C. L., Stokkers, P. C., Hinnen, C., Sanderman, R., & Sprangers, M. A. G. (2012). The effectiveness of cognitive behavioral therapy on the quality of life of patients with inflammatory bowel disease: Multi-center design and study protocol (KL!C- study). *BMC Psychiatry, 12,* 227. http://dx.doi.org/10.1186/1471-244X-12-227

Bennebroek Evertsz', F., Thijssens, N. A., Stokkers, P. C., Grootenhuis, M. A., Bockting, C. L. H., Nieuwkerk, P. T., & Sprangers, M. A. G. (2012). Do inflammatory bowel disease patients with anxiety and depressive symptoms receive the care they need? *Journal of Crohn's and Colitis, 6,* 68–76. http://dx.doi.org/10.1016/j.crohns.2011.07.006

Diaz Sibaja, M. A., Comeche Moreno, M. I., & Mas Hesse, B. (2007). Protocolized cognitive-behavioural group therapy for inflammatory bowel disease. *Revista Española de Enfermedades Digestivas*. Advance online publication. http://dx.doi.org/10.4321/s1130-01082007001000006

Fava, G. A., Ruini, C., Tomba, E., & Wise, T. N. (2012). The biopsychosocial factor. *Psychotherapy and Psychosomatics, 81,* 1–4. http://dx.doi.org/10.1159/000332085

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. W. (1999). *Structured clinical interview for DSM-IV-TR axis I disorders*. Lisse, Switzerland: Swets & Zeitlinger B. V.

Handley, M. A., Schillinger, D., & Shiboski, S. (2011). Quasi-experimental designs in practice-based research settings: Design and implementation considerations. *Journal of the American Board of Family Medicine, 24,* 589–596. http://dx.doi.org/10.3122/jabfm.2011.05.110067

Katon, W., Lin, E. H. B., & Kroenke, K. (2007). The association of depression and anxiety with medical symptom burden in patients with chronic medical illness. *General Hospital Psychiatry, 29,* 147–155. http://dx.doi.org/10.1016/j.genhosppsych.2006.11.005

Keefer, L., Doerfler, B., & Artz, C. (2012). Optimizing management of Crohn's disease within a project management framework: Results of a pilot study. *Inflammatory Bowel Diseases, 18,* 254–260.

Kilcoyne, A., Kaplan, J. L., & Gee, M. S. (2016). Inflammatory bowel disease imaging: Current practice and future directions. *World Journal of Gastroenterology, 22,* 917–932. http://dx.doi.org/10.3748/wjg.v22.i3.917

Knowles, S. R., Monshat, K., & Castle, D. J. (2013). The efficacy and methodological challenges of psychotherapy for adults with inflammatory bowel disease: A review. *Inflammatory Bowel Diseases, 19,* 2704–2715. http://dx.doi.org/10.1097/MIB.0b013e318296ae5a

Langhorst, J., Mueller, T., Luedtke, R., Franken, U., Paul, A., Michalsen, A., . . . Elsenbruch, S. (2007). Effects of a comprehensive life-style modification program on quality-of-life in patients with ulcerative colitis; a twelve-month follow-up. *Scandinavian Journal of Gastroenterology, 42,* 734–745. http://dx.doi.org/10.1080/00365520601101682

McCombie, A. M., Mulder, R. T., & Gearry, R. B. (2013). Psychotherapy for inflammatory bowel disease: A review and update. *Journal of Crohn's and Colitis, 7,* 935–949. http://dx.doi.org/10.1016/j.crohns.2013.02.004

Mikocka-Walus, A., Bampton, P., Hetzel, D., Hughes, P., Esterman, A., & Andrews, J. M. (2015). Cognitive-behavioural therapy has no effect on disease activity but improves quality of life in subgroups of patients with

inflammatory bowel disease: A pilot randomised controlled trial. *BMC Gastroenterology, 15*. http://dx.doi.org/10.1186/s12876-015-0278-2

Mikocka-Walus, A. A., Turnbull, D. A., Moulding, N. T., Wilson, I. G., Andrews, J. M., & Holtmann, G. J. (2007). Controversies surrounding the comorbidity of depression and anxiety in inflammatory bowel disease patients: A literature review. *Inflammatory Bowel Diseases, 13,* 225–234. http://dx.doi.org/10.1002/ibd.20062

Mittermaier, C., Dejaco, C., Waldhoer, T., Oefferlbauer-Ernst, A., Miehsler, W., Beier, M., . . . Moser, G. (2004). Impact of depressive mood on relapse in patients with inflammatory bowel disease: A prospective 18-month follow-up study. *Psychosomatic Medicine, 66,* 79–84. http://dx.doi.org/10.1097/01.PSY.0000106907.24881.F2

Mussell, M., Bocker, U., Nagel, N., Olbrich, R., & Singer, M. V. (2003). Reducing psychological distress in patients with inflammatory bowel disease by cognitive-behavioural treatment; exploratory study of effectiveness. *Scandinavian Journal of Gastroenterology, 38,* 755–762. http://dx.doi.org/10.1080/00365520310003110

National Collaborating Centre for Mental Health. (2009). *Depression in adults with a chronic physical health problem: Treatment and management* (NICE Clinical Guideline No. 91). London, United Kingdom: Author.

Pocock, S. J., & Simon, R. (1975). Sequential treatment assignment with balancing for prognostic factors in the controlled clinical trial. *Biometrics, 31,* 103–115. http://dx.doi.org/10.2307/2529712

Radloff, L. S. (1977). The CES-D Scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement, 3,* 385–401. http://dx.doi.org/10.1177/014662167700100306

Russel, M. G. V. M., Pastoor, C. J., Brandon, S., Rijken, J., Engels, L. G. J. B., van der Heijde, D. M. F. M., & Stockbrügger, R. W. (1997). Validation of the Dutch translation of the Inflammatory Bowel Disease Questionnaire (IBDQ): A health-related quality of life questionnaire in inflammatory bowel disease. *Digestion, 58,* 282–288. http://dx.doi.org/10.1159/000201455

Schwarz, S. P., & Blanchard, E. B. (1991). Evaluation of a psychological treatment for inflammatory bowel disease. *Behaviour Research and Therapy, 29,* 167–177. http://dx.doi.org/10.1016/0005-7967(91)90045-5

Timmer, A., Preiss, J. C., Motschall, E., Rücker, G., Jantschek, G., & Moser, G. (2011). Psychological interventions for treatment of inflammatory bowel disease. *Cochrane Database of Systematic Reviews, 2011,* CD006913. http://dx.doi.org/10.1002/14651858.CD006913.pub2

van Straten, A., Geraedts, A., Verdonck-de Leeuw, I., Andersson, G., & Cuijpers, P. (2010). Psychological treatment of depressive symptoms in patients with medical disorders: A meta-analysis. *Journal of Psychosomatic Research, 69,* 23–32. http://dx.doi.org/10.1016/j.jpsychores.2010.01.019

Walker, J. R., Ediger, J. P., Graff, L. A., Greenfeld, J. M., Clara, I., Lix, L., . . . Bernstein, C. N. (2008). The Manitoba IBD Cohort Study: A population-based study of the prevalence of lifetime and 12-month anxiety and mood disorders. *American Journal of Gastroenterology, 103,* 1989–1997. http://dx.doi.org/10.1111/j.1572-0241.2008.01980.x

Ware, J. E. (1992). *The MOS 36-item short-form health survey*. Boston, MA: Health Institute.

White, I. R., Royston, P., & Wood, A. M. (2011). Multiple imputation using chained equations: Issues and guidance for practice. *Statistics in Medicine, 30,* 377–399. http://dx.doi.org/10.1002/sim.4067

Zhang, Y. Z., & Li, Y. Y. (2014). Inflammatory bowel disease: Pathogenesis. *World J Gastroenterol, 20,* 91–99.

Zigmond, A. S., & Snaith, R. P. (1983). The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica, 67,* 361–370. http://dx.doi.org/10.1111/j.1600-0447.1983.tb09716.x

Received December 14, 2016
Revision received April 14, 2017
Accepted May 18, 2017 ■