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Mindfulness therapy for somatization disorder and functional somatic syndromes — Randomized trial with one-year follow-up

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ABSTRACT

Objective: To conduct a feasibility and efficacy trial of mindfulness therapy in somatization disorder and functional somatic syndromes such as fibromyalgia, irritable bowel syndrome, and chronic fatigue syndrome, defined as bodily distress syndrome (BDS).
Methods: We randomized 119 patients to either mindfulness therapy (mindfulness-based stress reduction and some cognitive behavioral therapy elements for BDS) or to enhanced treatment as usual (2-hour specialist medical care and brief cognitive behavioral therapy for BDS). The primary outcome measure was change in physical health (SF-36 Physical Component Summary) from baseline to 15-month follow-up.
Results: The study is negative as we could not demonstrate a different development over time for the two groups ($F(3,2674) = 1.51$, $P = .21$). However, in the mindfulness therapy group, improvement was obtained toward the end of treatment and it remained present at the 15-month follow-up, whereas the enhanced treatment as usual group achieved no significant change until 15-month follow-up. The change scores averaged half a standard deviation which amounts to a clinically significant change, 29% changed more than 1 standard deviation. Significant between-group differences were observed at treatment cessation.
Conclusion: Mindfulness therapy is a feasible and acceptable treatment. The study showed that mindfulness therapy was comparable to enhanced treatment as usual in improving quality of life and symptoms. Nevertheless, considering the more rapid improvement following mindfulness, mindfulness therapy may be a potentially useful intervention in BDS patients. Clinically important changes that seem to be comparable to a CBT treatment approach were obtained. Further research is needed to replicate or even expand these findings.

Introduction

Somatization disorder and functional somatic syndromes such as fibromyalgia, irritable bowel syndrome, and chronic fatigue syndrome are major public health issues for which effective treatment is rarely delivered [1–3]. These disorders are considered by many clinicians to be among the most frustrating disorders to manage, and levels of patient dissatisfaction are reported to be high [4,5]. The management of these disorders may be associated with costly, repetitive diagnostic procedures, and organ-oriented treatments with poor effect [3,6].

Cognitive behavioral therapy (CBT) and graded exercise may improve outcomes [7]. A Cochrane review on fibromyalgia concluded that supervised graded exercise training has effects. However, adherence to many of the interventions was poor [8]. A systematic review concluded that CBT is the best established treatment for a variety of somatoform disorders [4]. White [9] showed that Individual CBT or individual graded exercise therapy alongside specialist medical care were more effective in treating chronic fatigue syndrome than specialist medical care alone. However, randomized controlled trials in this area are few and research is hampered by the heterogeneous nature of these disorders and by the lack of clear definitions [1]. Recently, a new empirically defined definition bodily distress syndrome (BDS) was introduced unifying various functional somatic syndromes and somatization disorder under one diagnostic label [10–12]. Furthermore, a new CBT-based intervention entitled "Specialized Treatment for Severe Bodily Distress Syndrome" (STreSS) has been developed by our group. STreSS was found to be effective in improving self-reported physical health in a previous trial [13].

The potential mechanisms in BDS involve pathophysiological, psychological, and social mechanisms. Functional brain imaging has shown impairments of sensory processing in BDS patients which may indicate a deficiency in the cognitive regulation of symptom perception [14,15]. In contrast, other studies have indicated that mindfulness practice may be associated with changes in specific brain areas, that are essential for cognitive and emotional regulation

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[16–21]. Mindfulness-based stress reduction (MBSR) [22] is a complementary group program that may reduce symptoms of stress, anxiety, fatigue, and depression [23,24]. However, the value of studies on the efficacy of MBSR has so far been limited due to their lack of long-term follow-up and active control groups. The effect of MBSR has been explored on fibromyalgia in three studies, and none of them showed convincing results, but gave some indications as to improvement [25–27]. Mindfulness-based cognitive therapy [28,29] is an adaptation of the MBSR program that may prevent depressive relapse [29–33]. We hypothesized that the strategy of combining MBSR with CBT for a specific disorder would be beneficial in treating BDS. We developed a group program called *mindfulness therapy* which integrates MBSR and some CBT elements from the STreSS-1 manual [13]. We aimed to test the feasibility of this program and to compare the effect of *mindfulness therapy* with that of *enhanced treatment as usual* on change in self-reported physical health from baseline to 15-month follow-up in patients with multi-organ BDS.

Methods

Study design and patients

Between April 2007 and September 2008 primary care physicians and hospital wards referred patients to The Research Clinic for Functional Disorders and Psychosomatics, Aarhus University Hospital, Denmark. The patients were referred from both urban and rural areas covering a population of approximately three million people. The case notes were screened for eligibility, and the patients who were considered likely to meet inclusion criteria were invited to undergo a clinical assessment. The inclusion criteria were: (1) chronic (i.e. at least 2 years) of the multi-organ type BDS, which requires functional somatic symptoms from at least three out of four bodily systems: the cardiopulmonary, gastrointestinal, musculoskeletal, or general symptoms; (2) moderate to severe impairment in daily living [34]; (3) age 20 to 50 years; (4) absence of severe psychiatric morbidity, i.e. psychotic and bipolar disorders. The patients with comorbid depression and anxiety, and with comorbid medical conditions (e.g. asthma, diabetes) were included if symptoms attributed to these conditions could be clearly differentiated from symptoms due to BDS.

Exclusion criteria: (1) Current alcohol or drug abuse; (2) pregnancy; (3) not fluent in the Danish language (operationalized as non-Scandinavian origin); (4) no informed consent.

The trial is reported according to CONSORT criteria.

Assessment

All patients underwent a five-to-seven hour bio–psycho–social assessment, including a laboratory screening battery, schedules for clinical assessment in neuropsychiatry (SCAN)-diagnostic interview, as well as a physical and neurological examination.

Randomization

At the end of the assessment, eligible patients were randomized to either *mindfulness therapy* (n = 60) or *enhanced treatment as usual* (n = 60). To ensure a constant flow and consistent, identical probability for receiving the two treatments, a block randomization was organized in five clusters of 24 patients. The randomization algorithm was prepared by a statistician on the basis of a predefined concealed random number and tied to the consecutive assessments of patients and resulted in opaque envelopes numbered in succession containing the assigned treatment.

Treatment elements within assessment

The assessment was conducted by one out of three psychiatrists specialized in BDS and CBT.

Most of the assessments (95%) were conducted by two investigators, one of whom is an educated mindfulness teacher from the Center for Mindfulness, University of Massachusetts Medical School, USA. The other psychiatrist had participated in two MBSR programs and acceptance and commitment therapy teacher training. The patients received proper diagnoses, psychoeducation, and treatment advice on medicine and graded exercise. Antidepressant medication was only recommended if a patient had a comorbid depression, and the recommendations followed the guidelines of the National Board of Health, Denmark. The same was true for analgesics; patients were generally advised to gradually taper off morphine derivatives and benzodiazepines. All medications were administered by the patient's family physician.

Treatment elements after randomization

Fig. 1 depicts the treatment elements provided to each group [35].

Mindfulness therapy

The manualized *mindfulness therapy* features eight weekly 3 1/2 h sessions and one follow-up session, involving 12 patients per group. We included psychoeducation, symptom registration, and a model for graded exercise from the STreSS-1 manual. We excluded individual treatment goals and the use of individual treatment plans. We closely followed the MBSR manual developed by Jon Kabat-Zinn, Center For Mindfulness [22,36,37], except the all-day retreat which lasted only 3 1/2 h. All five groups were lead by two psychiatrists, one had developed the STreSS-1 manual and had 20 years of psychotherapy experience, the other had 20 years of meditation practice. Mindfulness is based upon concepts of mental training that propose that non-judgemental awareness of moment-to-moment experience (i.e. mindfulness) may positively affect accuracy of perception, acceptance of intractable health-related changes, realistic sense of control, and appreciation of available life experiences [22,38]. The *mindfulness therapy* applied these concepts to a multifactorial illness model. Details about the MBSR and the STreSS treatment modules are given in Table 1 [39]. Two treatment groups were videotaped for therapist supervision, and checks on treatment manual adherence. Two therapists independent of the trial made an overall judgment and found that the treatment was in accordance with the manual.

Enhanced treatment as usual

Within the first month after the assessment, the patients were offered a two-hour individual consultation by the psychiatrist who had performed the assessment. The multifactorial illness model was individualized (as a CBT case formulation), and an individual treatment plan was drawn up, including the definition of individual treatment goals, and identification of perpetuating factors. Advice was given on general lifestyle changes (exercise, nutrition, meditation, network, etc.).

Outcome measures

The patients completed questionnaires at baseline (just prior to the assessment interview), at the end of treatment (3-month follow-up), and again 6 and 12 months after the treatment was completed, i.e. at 9 and 15 months of follow-up (Fig. 1). The primary outcome was decided a priori as the mean change in the SF-36 Physical Component Summary (PCS) from baseline to 15-month follow-up. PCS is a summary measures of physical health constructed from eight subscales. The PSC

Time line	Mindfulness therapy	Enhanced treatment as usual
Clinical assessment	a b	a b
Randomization Baseline (time 0)	Baseline measurement (just before the assessment)	
During treatment period (0-3 months)	c d e f	g h e f
3 months	First outcome measurement (end of treatment)	
During follow-up period (3-9 months)	i	i
9 months	Second outcome measurement	
During follow-up period (9-15 months)	i	i
15 months	Third outcome measurement (Trial Endpoint)	
a	Comprehensive life-time review of case notes and clinical records from primary care physicians, ambulatory, care and hospital wards.	
b	Comprehensive bio-psycho-social assessment, including SCAN-diagnostic interview, physical and neurological examination, and laboratory screening battery. At the end of the assessment, patients received information about the nature, course, and treatment of BDS.	
c	Treatment manual, including schedule, symptom diary, educational material, worksheets, and homework assignment for the nine treatment modules. Non-attending patients received the chapters by mail.	
d	Nine treatment modules, 3.5 hours each, based on a mindfulness-based stress reduction and a cognitive-behavioral approach, delivered in groups of 12 patients by two psychiatrists, at weeks 1,2,3,4,5,6,7,8,12.	
e	Letter to the patients' primary care physician and referring doctor regarding diagnosis and illness history as well as treatment recommendations in case of a comorbid depression or anxiety.	
f	Letters to social authorities, when needed.	
g	Individual treatment plan conducted from a manual. Treatment manual, including a CBT case formulation, definition of individual treatment goals, identification of perpetuating factors, and lifestyle changes.	
h	Individual psychiatric consultation, two hours within the first month after the clinical assessment.	
i	Treatment as usual.	

Fig. 1. Timing and treatment elements.

score ranges from 0 to 100; the highest score is the best function, with a mean of 52.5 in the general Danish population [40]. A change of 0.5 standard deviation (SD) is regarded as a clinically important difference [41–43]. For the subscales improvements exceeding or equal to 5 points indicate clinically and socially relevant changes [44].

The secondary outcome measures were change in other health-related quality of life measures of the SF-36 and symptoms such as: illness worry (Whitely-8-index [45]; range 100–0; lowest score is the best function), physical symptoms (SCL-90-R Somatization Subscale [46]; range 100–0; lowest score is the best function), and severity of depression and anxiety (SCL-8 range 100–0; lowest score is the best function). Furthermore, we split the change in primary outcome from baseline to the different follow-up times into two categories in the following ways: 1) the patients who reported improvement, i.e. change

Table 1
Overview of treatment modules in *mindfulness therapy*

Week	Four ennobling truths	Foundation of mindfulness	MBSR curriculum	Objective STreSS	Homework	Teaching intentions
1	Understanding suffering	Mindfulness of body	There is more right than wrong with you	What is BDS? Registration and differentiation of fluctuating symptoms	Body scan meditation, sitting meditation	Experiencing new possibilities
2			Perception and creative responding or response?	What are symptoms? Diagnostic labels for BDS		Discovering embodiment
3	Letting go of craving	Mindfulness of feelings	Pleasure and the power of presence	Biological, psychological, and social factors contributing to the development and maintenance of BDS	Body scan meditation/yoga, sitting meditation	Cultivating observation
4			Shadow of stress (unpleasant events)	Connecting bodily symptoms, emotions, thoughts, and behaviors. Restoring sleep		
5	Realizing liberation	Mindfulness of mind states	Finding space for responding	Defusion of inflexible symptom attributions, impact of negative illness perceptions	Sitting meditation, yoga/walking meditation	Moving toward acceptance
6			Working with difficult situations	Identifying cognitive distortions		
7	Cultivating the path	Mindfulness of mental states	Cultivating kindness		Choosing your preferred practices	Increasing compassion
8			A new beginning	Recapitulation of theories/exercises		
12			What is mindfulness?	What is BDS?		

greater than half a SD (SD for PCS at baseline); 2) the patients who reported marked improvement, i.e. change greater than 1 SD. Also, the time spent on mindfulness yoga and meditation practice was measured.

Power

The power calculation is based on change in PCS [41]. Uncertainty evaluation for PCS score is estimated from given estimates in a previous randomized controlled trial [47] and quoted in population studies [40]. The power was estimated to 0.84 based on 60 patients in each group, an expected dropout rate of 15% (*mindfulness therapy*), and five-points group difference of PCS change scores between groups ($P = .05$). A three-to-six-points change in PCS is often stated as a clinically and socially important difference [48,49].

Statistical analysis

Descriptive statistics are used to characterize the patients and to provide information of primary and secondary outcomes at baseline and follow-up times. All other analyses are based on intention to treat.

We entered the primary as well as the majority of the secondary outcomes as a dependent variable in one model. The model is a mixed model with a random intercept [50]. The model has two primary explanatory variables; the variable indicates treatment group and time. We did not expect the development over time to be linear, and therefore time enters the model as a categorical variable.

We enabled different developments over time for the two treatment groups by adding an interaction term between treatment groups and time. We further adjusted for a number of variables where the choice of adjustment variables was made prior to the analysis and based on previous research [51]. The variables are gender, age, social status, impairment of symptoms, and life time psychiatric comorbidity. All adjustment variables are entered in a linear fashion with age as a continuous variable and the rest as categorical variables. The results from the model are presented as tests for the same development over time for the two groups, i.e. test of no interaction. Furthermore, we present estimates of difference in scores from baseline to follow-up in each group with 95% confidence intervals (CI). We estimated the effect size of the group differences as Cohen's d. For all analyses, statistical significance was set to $p<0.05$.

To ensure the intention to treat analysis, we used multiple imputations of missing outcomes. The multiple imputations were made by means of a multivariate normal data augmentation method with 50 unique dataset separately applied to each group. All adjustment variables were included as covariates in the imputation method [50]. The probability of patients reporting a marked improvement was calculated from log odds from a simple logistic regression model applied to the imputed data with 95% CI. All analyses were done in Stata version 11 [50].

Results

Fig. 2 illustrates the trial profile. Of 267 consecutively referred patients screened by review of clinical records, 165 were eligible for the trial and 135 (82%) agreed to participate in the assessment. Of these, seven did not meet primary consent criteria, eight were excluded due to other reasons, and 120 were randomized. One later withdrew informed consent, thus 119 (94%) agreed to participate in the trial. The majority of the patients completed treatment: 58 (97%) completed the *enhanced treatment as usual*, whereas 52 (88%) completed the *mindfulness therapy*, defined as attending four or more classes, 49 (83%) attended six or more classes. Seven (12%) attended 0 or one class, the remaining 52 (88%) attended on average eight classes. The patient satisfaction was high; 91% in both treatment arms evaluated the treatment as good or outstanding. The baseline characteristics are presented in Table 2, and the groups did not differ on any variable. The majority of the patients were women out of work; moreover, half had primary school as their highest level of education. The majority also had multiple functional somatic syndromes diagnoses, and all met the criteria for somatization disorder. The transportation was arranged from the hospital for 20% of the patients, because otherwise they would have been unable to attend the hospital. An attrition analysis found no significant differences between completers and non-completers with respect to baseline characteristics. The proportion of patients taking antidepressant medication at some point the year before treatment (40–46%) and the year after treatment (37–40%) was similar in both groups. Table 3 shows the mean (SD) for scores of SF-36 (raw data). At 9- and 15-month follow-up, patients had improved at least five points on seven out of eight subscales.

Main results

The study is negative as we could not demonstrate a different development over time of PCS for *mindfulness therapy* and *enhanced treatment as usual* ($F(3,2674) = 1.51$, $P = .21$). However, the *mindfulness therapy* group significantly changed at the end of treatment, and this change remained at 15-month follow-up, whereas no significant change was seen in the *enhanced treatment as usual* group until at the 15-month follow-up (Table 4).

Secondary results

Significant between-group differences were observed at treatment cessation, 26%; CI, 14–38 of the patients in the *mindfulness therapy* group reported a marked improvement (>1SD) compared with 10%; CI, 2–18 in the *enhanced treatment as usual* group (OR = 3.21; CI, 1.05–9.78, $P = .04$). On the SF-36 subscales and symptom outcomes such as bodily pain, physical symptoms, illness worry, and anxiety and depression, both groups registered statistically and clinically significant improvements across time, but similar to the main results, no significant between-group differences were

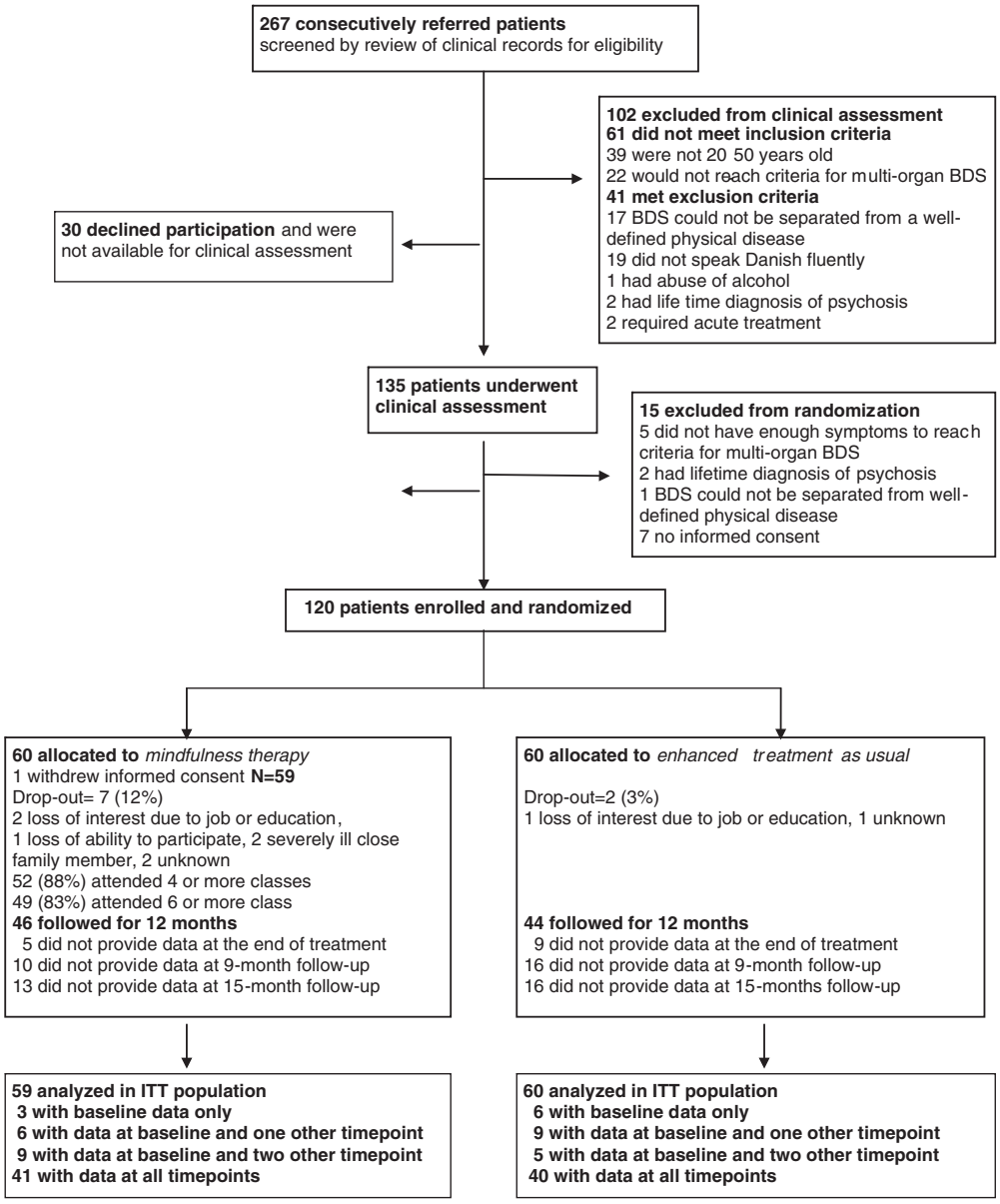

Fig. 2. Trial profile.

observed (Table 4). Among the completers of treatment, 92% reported that they practiced meditation at the end of treatment, which declined to 63% and 52% at 9-month and 15-month follow-up, respectively.

Discussion

This trial may be the first mindfulness study in which patients fulfilling criteria for somatization disorder and for several functional somatic syndrome diagnoses are treated with MBSR and some CBT elements. The trial is one of the few mindfulness studies where referred patients are compared with enhanced treatment as usual over a period of 15 months. 82% agreed to participate in the assessment consultation, 94% agreed to participate in the trial, and 88% completed *mindfulness therapy*. Thus, the trial demonstrated that *mindfulness therapy* is feasible and acceptable to patients with multi-organ BDS. Our findings on the effect of *mindfulness therapy* suggest that the trial is negative, *mindfulness therapy* was superior to *enhanced treatment as usual* at the end of treatment. However, at the 15-month follow-up, the *enhanced treatment as usual* group showed comparable gains.

The fact that the primary result is a negative one can be interpreted in several ways. First, it could be the result of unspecific factors, regression toward the mean, or the natural history of the disorder. Since the positive findings were maintained at 15-month follow-up and the participants had been ill for at least two years prior to the treatment (on average 13.5 years), it is unlikely that the observed effect is attributable to the natural history of the disorder or to regression toward the mean, although the study design cannot completely rule out this possibility. A second interpretation is that both treatment modalities had some therapeutic effect for the patients, the possibility in this case being that both interventions were uniquely responsible for the positive therapeutic changes that were observed. Based on the findings it is not clear, however, whether the apparent changes were the results of some similar features or the results of particular components that were unique to each of the groups. In that sense, our findings join a large body of evidence in psychotherapy research, where, overall, good benefits are reported, but differential effects are difficult to demonstrate, because generic and common factors seem to have the strongest influence [52].

Table 2
Patient characteristics

	Mindfulness therapy N = 59	*Enhanced treatment as usual* N = 60
Age (years) mean (SD), median	38 (9), 40	40 (8), 40
Female gender	47 80%	48 80%
Married/living with a partner	47 80%	41 70%
Children living at home	33 58%	38 59%
Only primary school (DK: 7–10th grade)	31 54%	28 48%
Employed, student, vocational rehabilitation	19 32%	17 28%
Unemployed	6 10%	6 10%
On sick leave	21 36%	23 38%
Disability pension or flexible work	13 22%	14 23%
Somatization disorder (ICD-10 codes)	59 100%	60 100%
Somatization disorder (DSM-IV codes)	56 95%	57 95%
Undifferentiated somatoform disorder (DSM-IV codes)	3 5%	3 5%
Illness duration (years)	12 (10.6)	15 (12.6)
Clinically rated impairment in daily living		
Moderate	15 25%	13 22%
Severe	44 75%	47 78%
Functional somatic syndromes		
Chronic fatigue syndrome	42 71%	46 77%
Fibromyalgia	48 81%	51 85%
Irritable bowel syndrome	26 44%	25 42%
Non-cardiac chest pain	30 51%	41 68%
Hyperventilation syndrome	12 20%	11 18%
Tension headache	45 76%	48 80%
Health anxiety	18 31%	19 32%
Current Major depressive disorder (DSM-IV codes)	13 22%	12 20%
Current Anxiety disorder (DSM-IV codes)	14 24%	14 23%
Previous Major depressive disorder (DSM-IV codes)	19 32%	20 33%
Previous Anxiety disorder (DSM-IV codes)	16 27%	16 27 %
Lifetime psychiatric comorbidity	42 71%	37 62 %

Data are number, mean (SD).

The relationship between clinician and the patient lies at heart of a successful outcome of therapy according to extant literature on bodily distress [6] and a treatment method that in previous research has been found effective for the disorder in question is the most stringent comparison condition to use [53]. It was deemed unethical to compare the *mindfulness therapy* group with a group of patients recruited from a waiting list or usual care since individual CBT and psychiatric consultation have previously been found to have positive outcomes [54]. We therefore decided to do our very best in the control group and established a control group where an individual treatment plan was devised in collaboration between the patient and a MD specialized in BDS, CBT, psychiatry, and mindfulness, within one or two weeks after they had spent a whole day together, going through all the patient's illness and suffering history, an intervention that we believe is far more comprehensive than usual care in most countries. A control condition consisting of one single 2-hour individual consultation may seem very little, but it should be compared with 5 h of individual treatment time in the *mindfulness therapy* condition (9 × 3.5-hour sessions × 2 because the groups were held by two psychiatrists/12 patients in each group).

Table 3
Raw data: SF-36

Outcome	Group	N	Baseline Mean (SD)	N	3 months Mean (SD)	N	9 months Mean (SD)	N	15 months Mean (SD)
PCS*	*Mindfulness*	57	30.3 (9.8)	53	33.8 (10.8)	49	34.3 (11.4)	45	34.0 (10.6)
	Enhanced treatment	60	31.2 (9.4)	51	31.5 (9.6)	43	32.2 (9.8)	45	35.3 (9.5)
MCS*	*Mindfulness*	57	43.2 (12.9)	53	43.6 (11.6)	49	44.9 (11.8)	45	45.6 (13.5)
	Enhanced treatment	60	41.8 (11.6)	51	44.1 (13.1)	43	44.2 (12.9)	45	43.6 (11.4)
Physical functioning	*Mindfulness*	59	60.4 (20.9)	54	64.6 (22.1)	49	65.5 (22.1)	46	63.1 (22.6)
	Enhanced treatment	60	57.1 (22.2)	51	59.2 (22.2)	43	60.5 (23.2)	45	66.8 (19.4)
Role physical	*Mindfulness*	59	16.9 (32.0)	54	23.9 (33.5)	50	28.0 (37.3)	45	33.3 (39.2)
	Enhanced treatment	60	20.8 (28.4)	51	20.1 (31.6)	44	19.9 (31.7)	45	30.0 (34.8)
Bodily pain	*Mindfulness*	59	27.2 (23.1)	55	35.7 (25.7)	50	39.2 (27.5)	46	36.7 (27.9)
	Enhanced treatment	60	29.8 (21.3)	51	32.0 (22.0)	44	33.4 (22.7)	45	39.2 (21.6)
General health	*Mindfulness*	57	32.8 (15.9)	55	41.4 (20.5)	50	42.1 (22.9)	46	42.8 (19.2)
	Enhanced treatment	60	35.0 (15.8)	51	39.2 (18.4)	44	41.2 (21.3)	45	42.9 (19.1)
Vitality	*Mindfulness*	58	29.5 (20.7)	55	32.9 (23.0)	50	37.9 (23.4)	46	36.3 (21.8)
	Enhanced treatment	60	29.2 (18.3)	51	32.7 (22.6)	44	33.6 (25.4)	45	34.6 (22.9)
Social functioning	*Mindfulness*	59	56.6 (23.9)	55	58.6 (26.0)	50	62.0 (28.5)	46	64.1 (26.8)
	Enhanced treatment	60	52.9 (26.3)	51	55.9 (30.7)	44	57.4 (23.9)	45	59.4 (26.1)
Role emotional	*Mindfulness*	59	60.5 (44.8)	54	59.6 (39.6)	50	61.3 (43.8)	45	65.2 (41.1)
	Enhanced treatment	60	57.2 (41.2)	51	59.5 (41.8)	44	61.4 (41.9)	45	63.7 (43.1)
Mental health	*Mindfulness*	58	59.9 (19.5)	55	61.6 (17.5)	50	65.0 (16.3)	46	65.4 (19.0)
	Enhanced treatment	60	56.4 (19.6)	51	62.5 (20.1)	44	62.1 (20.0)	45	61.4 (20.4)

PCS: physical component summary, MCS: mental component summary.

Table 4
Mean of difference from baseline to follow-up

	Estimate	95% CI	t	*P*-value	Effect size
Primary outcome					
SF-36 PCS				Within group	
Mindfulness					
3 months	3.8	1.6; 5.9	3.47	.001	0.45
9 months	3.6	1.4; 5.8	3.23	.001	0.42
15 months	3.8	1.5; 6.1	3.24	.001	0.42
Enhanced treatment					
3 months	0.8	−14; 2.9	0.72	.470	0.09
9 months	1.8	−0.6; 4.1	1.47	.141	0.19
15 months	3.7	1.3; 6.0	3.05	.002	0.39
Secondary outcome					
Probability of change > 1SD (dichotomized outcome PCS)				Between groups	
Mindfulness					
3 months	26%	14; 28		.04*	
9 months	28%	15; 40		.07*	
15 months	29%	16; 42			
Enhanced treatment					
3 months	10%	2; 18			
9 months	12%	2; 22			
15 months	25%	12; 37			
SF-36 bodily pain				Within group	
Mindfulness					
3 months	7.8	2.6; 12.9	2.96	.003	0.39
9 months	10.7	5.5; 16.0	4.02	<.001	0.52
15 months	8.5	3.0; 14.0	3.05	.002	0.40
Enhanced treatment					
3 months	2.7	−2.4; 7.9	1.04	.297	0.13
9 months	4.0	−1.4: 9.5	1.46	.145	0.19
15 months	9.0	3.2; 14.8	3.06	.002	0.39
SF-36 general health					
Mindfulness					
3 months	8.5	4.0; 13.1	3.70	<.001	0.48
9 months	9.3	4.5; 14.1	3.82	<.001	0.50
15 months	9.8	5.0; 14.5	4.05	<.001	0.53
Enhanced treatment					
3 months	5.3	0.6; 10.1	2.19	.029	0.28
9 months	9.0	3.7; 14.3	3.35	.001	0.43
15 months	10.1	5.0; 15.3	3.89	<.001	0.50
Health anxiety (Whitely-8)					
Mindfulness					
3 months	−12.8	−18.0; −7,5	−4.76	<.001	−0.62
9 months	−15.3	−20.5; −10.0	−5.66	<.001	−0.74
15 months	−17.1	−22.5; −11.6	−6.13	<.001	−0.80
Enhanced treatment					
3 months	−15.0	−20.4; −9.5	−5.34	<.001	−0.70
9 months	−17.4	−23.0; −11.9	−6.20	<.001	−0.79
15 months	−14.9	−20.7; −9.2	−5.09	<.001	−0.66
Physical symptoms (SCL-som)					
Mindfulness					
3 months	−4.4	−8.6; −0.3	−2.10	.036	−0.27
9 months	−4.9	−9.0; −0.8	−2.31	.021	−0.30
15 months	−7.8	−12.3; −3.3	−3.40	.001	−0.44
Enhanced treatment					
3 months	−6.7	−10.8; −2.5	−3.14	.002	−0.41
9 months	−9.0	−13.5; −4.5	−3.92	<.001	−0.51
15 months	−8.5	−13.0; −4.0	−3.72	<.001	−0.48
Anxiety and depression (SCL-8)					
Mindfulness					
3 months	−6.7	−12.4; −1.1	−2.35	.019	−0.31
9 months	−7.7	−13.6; −1.9	−2.58	.010	−0.34
15 months	−8.8	−14.6; −3.0	−2.97	.003	−0.39
Enhanced treatment					
3 months	−8.8	−14.4; −3.2	−3.06	.002	−0.40
9 months	−9.7	−15.5; −3.9	−3.26	.001	−0.42
15 months	−9.4	−15.7; −3.1	−2.93	.004	−0.38

The estimates stem from a mixed model with random intercepts adjusted linearly for age, gender, social status, impairment, lifetime psychiatric co-morbidity estimated in 50 multiple imputed datasets.

* The differences between groups were significant at 3 months $P = .04$, but fell short of significant at 9 months $P = .07$.

The power calculation was based on our former STreSS-1 trial, where CBT was compared with enhanced usual care in terms of assessment interview, but without the individual 2-hour consultation. No improvements on the SF-36 scale were observed in the enhanced usual care group in the STreSS-1 trial, which indicates that the changes found in the two treatments *mindfulness therapy* and

enhanced treatment as usual in the present STreSS-2 trial reflect a real change attributable to the interventions, results that speak against regression toward the mean. We were surprised that the *enhanced treatment as usual* offered in the present STreSS-2 trial improved treatment to a point that it seemed to be beneficial to the patients.

A different level of daily performance could be a third interpretation of the results that showed an early improvement in the *mindfulness group,* which the control group caught up with at 15-month follow-up. We speculated if a treatment response could be explained by receiving disability pension. The proportion of patients receiving disability pension was significantly lower in the *mindfulness therapy* group (25%) than in the *enhanced treatment as usual* group (45%) at 15-month follow-up [55]. We analyzed if a clinically significant treatment response (PCS change score > 1/2SD) at 15-month follow-up was associated with receiving disability pension [55]. Receiving disability pension in general cannot explain a clinical treatment response, and a clinical treatment response was not at all associated with disability pension in the *mindfulness therapy* group, although it may be in the *enhanced treatment as usual* group [55]. It should be emphasized that we do not have the authority to grant disability pension; the social authorities have this responsibility. However, the *enhanced treatment as usual* group may have cleared the way for disability pension.

The negative trial may speak against mindfulness therapy, but on the other hand, mindfulness training may improve stress and emotion regulation and among other factors, bodily symptoms may be experienced due to destructive emotions as a result of distress and/or impaired regulation of emotions, symptoms, and pain. Thus, as a theoretical model mindfulness training in the form of mindfulness therapy may gain health.

Comparison with other studies

The SF-36 health survey has been administered longitudinally to measure important health and functioning domains in The Medical Outcome Study (MOS), which is a large-scale multiyear survey of patients with chronic health conditions. The percentage of MOS patients who were eligible for work and could not work was 57.6% for PCS scores below 35. For each one-point decrease in the PCS scale score below 45, a two-point increase was observed in the percentage of patients unable to work, which is similar to the findings in our study where, at baseline, 68% were out of work [41]. Thus, a mean increase in PCS from 30 to 34 may reflect a clinically and socially significant change. Also, on seven out of eight subscales on the SF-36 patients improved by more than five points, which is indicative of clinically and socially relevant changes [44]. The physical functioning subscale of the SF-36, which measures impairments in physical activities such as climbing stairs, changed very little in the *mindfulness therapy* group. To understand this, we tested the baseline physical functioning among the responders (change in PCS > 1/2 SD) and non-responders in the two groups. At baseline, the mean physical functioning subscale was lower both in the *enhanced treatment as usual* group when compared to the *mindfulness therapy* group and among responders compared with the non-responders; the non-responders had physical functioning scores close to or within the normal range. When physical functioning scores fall within the normal range, there may be less room for improvement. A recent study [9] on chronic fatigue syndrome excluded patients with a physical functioning > 60; in our *mindfulness therapy* group the mean physical functioning was 60.4 at baseline. Also, the non-responders on the primary outcome had significantly more health anxiety (Whiteley 8) and more severe anxiety and depression (Scl-8) than the responders, and they improved on these scales. These improvements may have been necessary before they were able to improve in physical function, and these patients may have needed longer treatment time in order to do so.

Another explanation of the low response on the physical functioning scale could be that the strong focus on the observation of the body in the *mindfulness therapy* group made some patients realize that they were actually worse than they thought.

The present study is a continuation of the STreSS-1 trial which did not include yoga, meditation, or mindfulness training. How to engage BDS patients in the work of observing and embracing a painful and/or fatigued body, how to inspire them to use what is now known from modern medicine to be helpful (physical exercises, healthy nutrition, healthy relationships, CBT, etc.) is an ever evolving process, in which *mindfulness therapy* is a contribution.

The StreSS-1 trial reported an effect size of 0.51; 95% CI 0.19–0.83 on the primary outcome, which should be compared with an effect size of 0.42; 0.17–0.68 in the present STreSS-2 trial. But the group size (12 versus 9) and the age (≤50 versus ≤45) were higher, the social marginalization was worse, and the intervention covered a shorter period (3 versus 4 months) in STreSS-2. In the STreSS-1 trial 25%, reported a marked improvement, while 29% reported a marked improvement in the STreSS-2 trial. Both trials reached high effect sizes for illness worry and small effect sizes for anxiety and depression. Therefore it seems that CBT in STreSS-1 and *mindfulness therapy* in STreSS-2 were equally effective.

Strengths and limitations

Our findings are strengthened by a relatively small number of patients needed to be screened and assessed in order to identify the 119 included patients, and we did not exclude the patients who were unable to attend hospital. Also, the drop-out rate was small; the attendance was high; we used manually-defined treatments provided by competent clinicians; and the treatment acceptance and participant satisfaction were high.

The methodological limitations may have influenced our results. We only included patients with severe and chronic illness and they had very low levels of social functioning. In the context of the present study where mindfulness was used as a treatment and not solely as part of a prevention program or a complementary program, the patients might have needed more individual guidance before they entered the *mindfulness therapy* group. A personal admission interview could have defined realistic patient goals and helped them move in the desired direction. We might have been too optimistic about the specific benefit of meditation and the nonspecific group effect. Another weakness of the *mindfulness therapy* group is that we did not include booster classes, as is often done in mindfulness trials. Many patients requested this, and we saw a decline in some outcomes from 9 to 15 months follow-up and a corresponding drop in formal mindfulness practice. Many patients described positive experiences from participating in the mindfulness intervention. The fact that this is not reflected more in the quantitative data may be ascribed to measurement problems, as the SF-36 is known to be not very sensitive to change, and mindfulness studies generally use other scales. Treatment adherence was checked by independent raters, who checked if the treatment followed the agenda presented in the manual and made an overall judgment, but they did not use a checklist which is a limitation.

Recommendations

This group of patients is currently very expensive to the healthcare system, and little or no health gain is achieved in spite of the effort [6]. This testifies to the clear need for specific treatments that can achieve health gains, but also for tools that patients may use and practice by themselves to gain better health or maintain improvements. The findings from the *mindfulness therapy* study suggest that even socially marginalized patients suffering from chronic BDS are willing to participate and engage in a treatment that requires a high level of patient involvement.

In future trials, we recommend that the effect of longer treatment times or the inclusion of booster sessions be explored.

Conclusions

To conclude, a mindfulness approach can safely be integrated into the treatment of BDS, and *mindfulness therapy* is a feasible and acceptable treatment. The study showed that *mindfulness therapy* was comparable to *enhanced treatment as usual* in improving quality of life and symptoms. Nevertheless, considering the more rapid improvement following mindfulness, *mindfulness therapy* may be a potentially useful intervention in BDS patients. Clinically important changes that seem to be comparable to a CBT treatment approach were obtained. Further research is needed to replicate or even expand these findings.

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The sponsors of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data, and all the named authors had final responsibility for the decision to submit the manuscript for publication.

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