Research Paper

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Efficacy of a transdiagnostic emotion–focused exposure treatment for chronic pain patients with comorbid anxiety and depression: a randomized controlled trial

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Abstract

The comorbidity between chronic pain and emotional problems has proven difficult to address with current treatment options. This study addresses the efficacy of a transdiagnostic emotion–focused exposure treatment ("hybrid") for chronic pain patients with comorbid emotional problems. Adults (n = 115) with chronic musculoskeletal pain and functional and emotional problems were included in a 2-centre, parallel randomized controlled, open-label trial comparing this treatment to an active control condition receiving a guided Internet-delivered pain management treatment based on CBT principles (iCBT). The hybrid treatment (n = 58, 10-16 sessions) integrates exposure in vivo for chronic pain based on the fear-avoidance model with an emotion-regulation approach informed by procedures in Dialectical Behavior Therapy. The iCBT (n = 57; 8 treatment modules) addresses topics such as pain education, coping strategies, relaxation, problem solving, stress, and sleep management using standard CBT techniques. Patient-reported outcomes were assessed before and after treatment as well as at a 9-month primary end point. Across conditions, 78% participants completed post-treatment and 81% follow-up assessment. Intent-to-treat analyses showed that the hybrid had a significantly better post-treatment outcome on pain catastrophizing (d = 0.39) and pain interference (d = 0.63) and significantly better follow-up outcomes on depression (d = 0.43) and pain interference (d = 0.51). There were no differences on anxiety and pain intensity. Observed proportions of clinically significant improvement favoured the hybrid on all but one comparison, but no statistically significant differences were observed. We conclude that the hybrid emotion–focused treatment may be considered an acceptable, credible, and efficacious treatment option for chronic pain patients with comorbid emotional problems.

Keywords: Chronic pain, Emotional problems, Transdiagnostic, Cognitive-behavioral therapy, Internet, Randomized clinical trial, Exposure

1. Introduction

There is a marked co-occurrence between chronic pain and emotional problems, which has proven difficult to address parsimoniously and effectively with state-of-the-art treatments.[2,4] A recent meta-analysis on prognostic factors for multidisciplinary pain rehabilitation outcome shows that emotional distress and cognitive-behavioral risk factors are among the most clear-cut prognostic indicators for worse long-term physical functioning.[47] Although these factors are potentially modifiable and often actively targeted in treatment, they are insufficiently addressed. For example, in a study investigating the clinical effects of cognitive behaviorally informed treatment (CBT) for chronic pain, 56% of patients with pre-treatment anxiety problems and 77% with high pain catastrophizing did not show reliable or clinical improvement on these variables.[37] In another study investigating the effects of CBT for work rehabilitation, 81% of patients with pre-treatment depressive problems still scored in the depression range after treatment.[44] These residual mood problems were predictive of lower return to work at follow-up, indicating their negative influence on long-term disability outcome. In summary, empirical findings point toward a need to improve methods to influence patients' emotional status in the context of pain management treatments.

Theoretical developments in clinical psychology have contributed to the development of new psychological treatments for pain that specifically focus on addressing emotion. Examples are treatments focusing on emotion awareness and expression,[28] exposure in vivo,[20,32] and emotional exposure.[29] Although these treatments vary in theoretical underpinnings, they all key on changing negative emotion. Building on these efforts, we

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.painjournalonline.com).

PAIN 160 (2019) 1708–1718

http://dx.doi.org/10.1097/j.pain.0000000000001575

developed a hybrid treatment targeting transdiagnostic emotion–regulation mechanisms. The term "transdiagnostic" here denotes the psychological mechanisms that may maintain and exacerbate both pain and emotional problems.[33] The treatment integrates exposure methods based on the fear-avoidance model[50] with a more explicit emotion-regulation approach informed by procedures in Dialectical Behavior Therapy.[26] It aims to teach patients emotion-regulation skills necessary for effective emotion regulation and to approach valued but avoided behaviors and goals. The combination therefore should specifically benefit patients with chronic pain conditions and emotional problems.

We tested the effects of this treatment in a feasibility study with a single-case experimental design with promising results.[34] An important next step is to establish whether effects generalize and the treatment produces significant changes in key emotion and pain-related outcomes for a broader range of patients. To this end, we use a randomized controlled design that allows for comparison of the hybrid treatment against an active control condition. As a comparator, we use an evidence-based CBT pain treatment (iCBT) delivered through the Internet.[10–12] Findings suggest that iCBT treatments are efficacious and changes in pain, function, catastrophizing, and mood are in line with face-to-face trials in clinical settings.[13] This treatment is therefore hypothesized to provide an active and credible control to evaluate the effectiveness of the hybrid treatment. This article investigates whether the hybrid treatment produces superior results on comorbid emotion and pain-related variables and is considered acceptable as compared to the iCBT.

2. Methods

2.1. Overview of the design

This is a multicenter parallel group study in which 115 chronic pain patients with co-occurring emotional problems were randomized (in a 1:1 ratio) to either the hybrid emotion–focused treatment (hybrid; n = 58) or an active control condition receiving a guided Internet-delivered pain management treatment based on CBT principles (iCBT; n = 57). The study was conducted between January 2016 and September 2018 at 2 sites in Sweden (Center for Health and Medical Psychology, Örebro University, and Pain and Rehabilitation Centre, Region Östergötland, Linköping). The Ethics Review Board in Uppsala approved the study (2015/479), and the trial was preregistered at Clinicaltrails.gov (NCT02808286).

2.2. Recruitment and sample

Patients with chronic pain aged 18 to 70 years were recruited through advertisements in local newspapers, social media, and through clinical departments of pain rehabilitation. The inclusion criteria were as follows:

(1) Chronic musculoskeletal pain (>6 months of duration), not emanating from malignancies, systemic diseases (eg, rheumatoid arthritis), or localized single-joint osteoarthritic conditions in the lower extremities (eg, knee-osteoarthritis and hip-osteoarthritis).
(2) Functional problems in daily life due to pain (Örebro Musculoskeletal Pain Screening Questionnaire [ÖMPSQ][30]): The ÖMPSQ was developed to assess risk of long-term pain-related disability and has good psychometric properties.[31] For the purpose of this study, we only used the items that measure functional problems in daily life due to pain (items 21-24, range 0-40). To ensure at least some functional difficulties, we used a cutoff of ≥11. Initial cutoff criteria were set to ≥20 points but were relaxed 6 months after the study was started to increase participation rates. All patients eligible in accordance with the new criteria who applied during the months before were retroactively included.
(3) Emotional problems (anxiety and depression subscales of the Hospital Anxiety and Depression Scale [HADS][52]): The HADS has good measurement properties when applied to samples in general practice.[8] Each subscale consists of 7 statements each (range 0-21), expressing common symptoms of anxiety and depression. To ensure at least a possible case, we used a cutoff of ≥8 points on one of the subscales. Initial cutoff criteria were set to ≥11 but were relaxed 6 months after the study was started to increase participation rates. All patients eligible in accordance with the new criteria who applied during the months before were retroactively included.
(4) Access to a computer or tablet, and sufficient mastery of the Swedish language to enable engagement in treatment.

The exclusion criteria were as follows:

(1) Severe psychiatric disorders that may have required immediate or other treatment (alcohol abuse, psychotic disorders, or at risk of suicide).
(2) Ongoing psychological treatment elsewhere.
(3) Recently started, or changed, psychopharmacological treatment (cutoff criterion: <3 months before planned treatment start).

Figure 1 shows the flow chart of the study procedure. Applicants were mailed a screening questionnaire, written information about the study, and an informed consent form. To reduce risks of performance bias, the study aim was described neutrally as "comparing 2 forms of Cognitive Behavior Therapy for individuals who have long-lasting pain while feeling stressed, depressed, or worried." Upon return of the screening questionnaire, the study coordinator assessed eligibility and, in case of ambiguity, followed up by a telephone interview and consultation with (medical and/or psychological) professionals in the research team. When eligible, applicants received a personal code and link to the electronic pre-treatment assessment battery. On completion of the assessment, participants were randomized. The retention rate to post-treatment assessment was 81% for the hybrid and 75% for the iCBT treatment. The retention rate to follow-up assessment was, respectively, 79% and 84%. Primary outcome analyses were conducted according to intention-to-treat principles, making use of all available data.

Table 1 provides clinical and demographic characteristics of the included participants. As can be seen, this is a middle-aged, predominantly female sample with musculoskeletal pain in more than one bodily location. More than half of the participants were working, but sick leave was common. Over half of the sample reported more than 14 days of complaint-related sick leave during the past year. As an indication of the level of pain-related functional problems in daily life, the problem level was on average around 5 on a 0 (no problem) to 10 (cannot do it due to pain) scale. In addition, over 80% of the sample reported more than 2 health care visits for their complaints during the past year. Although all participants reported anxiety and depressive symptoms, around two-thirds of the sample also fulfilled the clinical criteria for a DSM-V anxiety or depressive disorder. None of the numerical differences between treatment groups were statistically significant.

2.3. Randomization

Participants were randomized using a computer-generated block randomization procedure (www.randomizer.org) with a 1:1 allocation ratio and block sizes varying between 2 and 18. The procedure

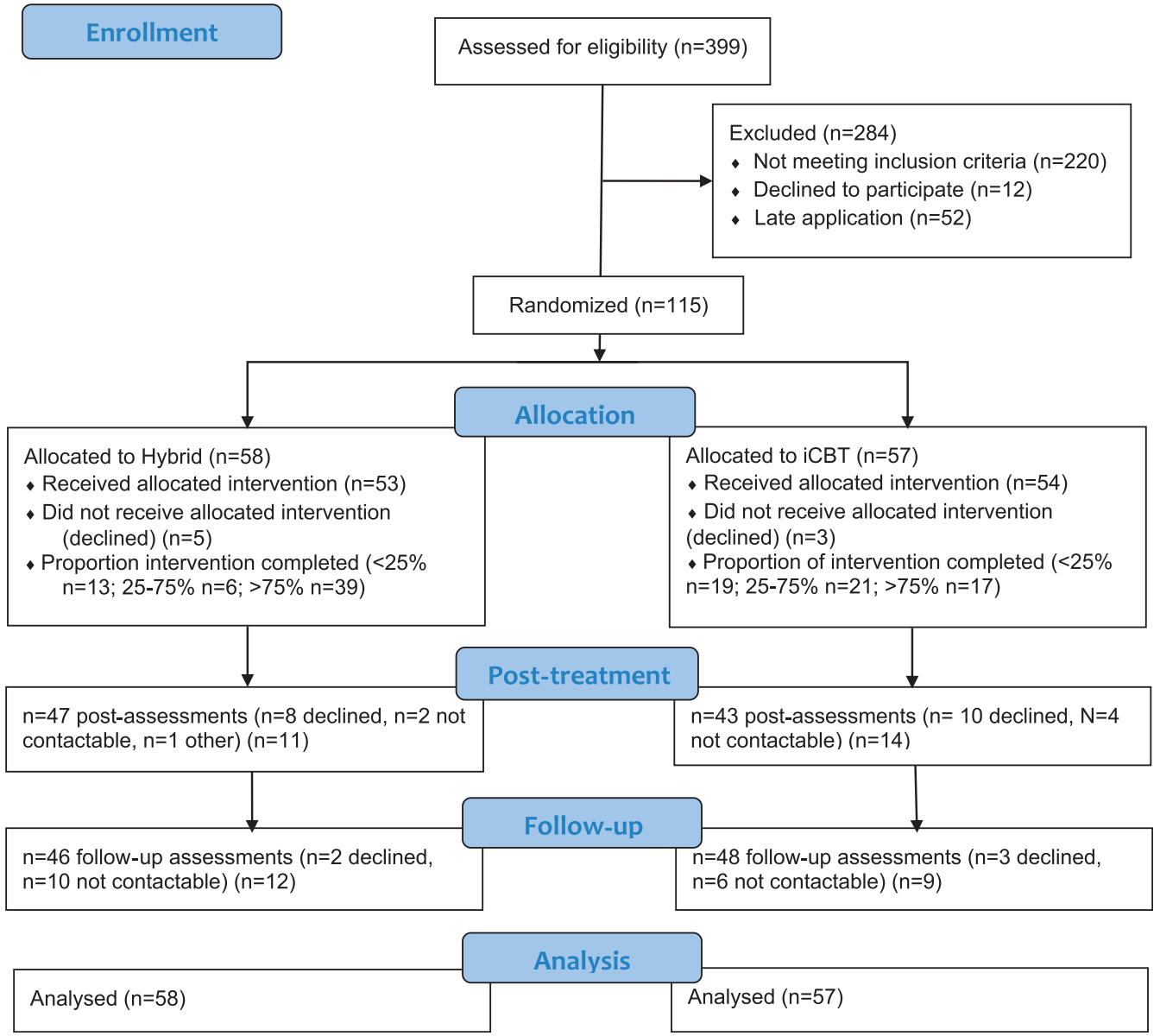

Figure 1. Flow chart: Hybrid, hybrid emotion–focused treatment; iCBT, Internet-delivered cognitive behavioral therapy. All randomized participants were included in ITT analyses. ITT, intention to treat.

was conducted by the study coordinator, and allocation was concealed for therapists and patients.

2.4. Sample size

Pretrial power calculations resulted in a targeted sample size of n = 84 (d = 0.5, P = 0.05, and ß = 0.80; based on an estimated between-group difference on the HADS), using data from Refs. 11, 34 as benchmarks and compensating for an approximate drop-out rate of 20% per condition. De facto sample size (n = 115) exceeds this projected number and therefore ensures sufficient power.

2.5. Patient-reported outcome measures

Participants filled out assessment batteries electronically in their own environment, at baseline before randomization, at mid-treatment, at post-treatment, and at the 9-month follow-up. The focus of this report is on key pain and emotion-related outcome measures (assessed at baseline, post-treatment, and 9-month follow-up). The assessment battery also included measures addressing potential treatment mechanisms (emotion regulation, fear-avoidance beliefs, acceptance, behavioral avoidance, self-compassion, and sleep; assessed at baseline, mid-treatment, and post-treatment) and quality of life (assessed at baseline, mid-treatment, and post-treatment), which will be reported elsewhere in articles focused on mediation/moderation and health-related outcomes, respectively.

2.6. Demographic data

Demographic data regarding age, sex, education level, occupational status, sick leave during the previous year, health care visits during the previous year, pain duration, and pain location were assessed at baseline. Except for age and pain duration, these

Table 1

Baseline description of participants' demographic and clinical characteristics.

	Hybrid (n = 58)	iCBT (n = 57)
Gender N (% women)	52 (89.7%)	44 (77.2%)
Age, mean (SD)	45 (12)	44 (12)
Pain locations		
Back, neck, and/or shoulders	58 (100%)	57 (100%)
Legs and arms	58 (100%)	57 (100%)
Other areas	16 (27.6%)	15 (26.3%)
Pain duration, median years (IQR)	11 (11)	9 (12)
Education N (% university or above)	22 (37.9)	23 (40.4)
Occupational status, N (%)		
Working	33 (56.9%)	34 (59.6%)
Unemployed	3 (5.2%)	4 (7%)
Student	3 (5.2%)	4 (7%)
Pensioner	9 (15.5%)	6 (10.5%)
Other	10 (17.2%)	9 (15.8%)
Sick leave (N, % during the past year)		
0-14 d	25 (43.1%)	25 (43.9%)
15-180 d	8 (13.8%)	11 (19.3%)
181-365 d	25 (43.1%)	21 (36.8%)
Screening measures, mean (SD)		
Function (ÖMPSQ) (0-40)	21 (7.5)	21.7 (7.3)
HADS anxiety (0-21)	12.2 (4.0)	11.2 (4.1)
HADS depression (0-21)	11.4 (3.8)	11.8 (4.3)
Health care visits, median past year (IQR)		
Physician	2 (3)	3 (3)
Physiotherapist	2 (6)	2 (7)
Specialist/hospital	0 (1)	1 (2)
Other (eg, chiropractor and acupuncturist)	0.5 (6)	0 (5)
Total number visits >2	79.3%	84.2%
	Hybrid (n = 52)	**iCBT (n = 55)**
Psychiatric comorbidity (MINI-criteria)*		
Not fulfilling disorder criteria	16 (30.8%)	23 (41.8%)
Major depressive disorder	24 (46%)	21 (38.2%)
Anxiety disorder	29 (55.8%)	24 (43.6%)
Comorbid depressive and anxiety disorder	17 (32.7%)	13 (23.6%)
Neuropsychiatric impairment†	3 (5.8%)	1 (1.8%)

* Only assessed with participants starting treatment.

† Additional question on whether the participant had received a neuropsychiatric diagnosis (Attention Deficit Hyperactivity Disorder, Asperger syndrome, and Tourette syndrome).

HADS, Hospital Anxiety and Depression Scale; Hybrid, hybrid emotion–focused treatment; iCBT, Internet-delivered cognitive behavioral therapy; MINI, The Mini International Neuropsychiatric Interview; ÖMPSQ, Örebro Musculoskeletal Pain Screening Questionnaire, items 21 to 24.

variables were categorical with categories as shown in **Table 1** (condensed for sick leave and education level).

2.7. Primary outcome measures

As the intervention in focus is a transdiagnostic treatment aiming to influence both pain-related and emotional problems, several primary outcomes were selected ensuring coverage of both areas: general anxiety and depressive symptoms, pain-specific distress, pain intensity, and pain interference.

To assess depressive symptoms, we used the Montgomery–Åsberg Depression Rating Scale—Self-report (MADRS-S; 9 items, range 0-60[35]) with acceptable test–retest reliability (r = 0.78[17]) and acceptable internal consistency in this sample at baseline (Cronbach's α = 0.78). To assess general anxiety symptoms, we used the Generalized Anxiety Disorder 7-item Scale (GAD-7; range 0-27; test–retest reliability r = 0.83 and Cronbach's α = 0.87[42]). To assess pain catastrophizing, we used the Pain Catastrophizing Scale (PCS; 13 items, range 0-52; test–retest reliability r = 0.75 and Cronbach's α = 0.91[43]). To assess pain intensity and physical functioning in daily life, we used 2 subscales from the Swedish version of the West Haven-Yale Multidimensional Pain Inventory (MPI-S[25]; MPI-intensity [2 items: pain currently and during the past week], range 0-12; test–retest reliability r = 0.75 and Cronbach's α = 0.87[6]) and MPI-pain interference (11 items, range 0-66; test–retest reliability r = 0.85 and Cronbach's α = 0.87[6]). Missing values regarding the item "interference with work" due to the participant not working were replaced with the mean of the other items on the interference scale. All measures are frequently used and validated in a Swedish context.[6,7,9,24,46]

2.8. Treatment acceptability

To assess treatment credibility, we used 3 questions of the Credibility/Expectancy Questionnaire.[15] At mid-treatment (after session 6 in the hybrid and module 4 in the iCBT), participants were asked to rate: (1) whether they considered their assigned treatment to be logical for them (numerical rating scale 0-10), (2) whether they thought the treatment could be successful in reducing their symptoms (numerical rating scale 0-10), and (3) whether they would recommend the treatment to a friend experiencing similar problems (numerical rating scale 0-6). The last item was converted to a 0 to 10 scale, and all 3 items were summed to form a 0 to 30 scale of treatment credibility. The internal consistency of this scale in the sample was Cronbach's α = 0.94.

Treatment satisfaction, participant ratings of global improvement, and adverse event data were assessed after treatment. To assess treatment satisfaction, participants were asked to rate: (1) how pleased they were with the treatment, and (2) if they would recommend it to someone with similar difficulties, both on numerical rating scales ranging from 0 to 5 (range 0-10; Cronbach's α = 0.82). To assess participants' ratings of global improvement, they were asked, also on 0 to 5 numerical scales, to rate the degree to whether the treatment had influenced: (1) their ability to cope with pain and (2) their well-being (range 0-10; Cronbach's α = 0.85). Participants were also asked after treatment to report if any adverse events had occurred and, if so, provide specifics in free text as well as an estimate on a 0 ("not at all") to 6 ("very adverse") scale how the event affected their well-being in the moment and during the past week.

2.9. Interventions

2.9.1. Hybrid emotion–focused treatment (hybrid)

The hybrid treatment format is principle based and presented in 5 stages with exposure for both pain and emotion-related avoidance behaviors being central. The treatment integrates methodology from Dialectical Behavior Therapy to address emotion-regulation difficulties and skill deficits. Dialectical Behavior Therapy is a treatment approach that aims to teach patients emotion-regulation skills in a context of nonjudgmental acceptance and desired goal pursuit. Thus, before commencing exposure, room is made to soothe emotions and promote emotional experiencing and regulation. Room is also made to train various emotion-regulation strategies to prepare for exposure.[26] Each stage progresses so that the entire therapy can be conducted in a systematic manner. Yet, given the variation in the clinical presentation of patients with comorbid pain and emotional

problems, the stages allow a certain amount of room to tailor the intervention to the patient. Therefore, although a target of 10 to 15 (when possible) weekly sessions was set, no specific formulations of session content, number of sessions per stage, or detailed step-by-step method instructions were provided. Instead, the treatment manual clearly outlined the theme, goals, and function of each stage and provided suggestions and materials for treatment methods and exercises. **Table 2** gives a short description of the theme of each stage and examples of typical methods used. The treatment was conducted by 5 licensed clinical psychologists and 2 clinical psychologists in their postgraduate year of supervised professional training for accreditation. To ensure that the treatment was presented as intended and according to the protocol, all therapists received training and supervision and filled out session checklists recording adherence to the therapeutic methods within each treatment phase. Checklists confirmed that therapists used suggested therapeutic methods in line with the protocol. Counting the last session attended as the "end" of treatment, treatments lasted for a median of 17.5 weeks (IQR 5, interval 16-21), with the therapist spending approximately 74 (IQR 24, interval 62-86) minutes per session and 12.6 (IQR 11.5, interval 7.9-19.4) hours per treatment with each participant. Before exposure and behavioural experiments commenced (stage 3), a licensed physiotherapist performed a physical examination to ensure the absence of red flags and to provide, when needed, reassurance for any misperceptions of perceived harmfulness of physical activity and movement.[49] At the start of the treatment, the therapists also conducted a MINI (Mini International Neuropsychiatric Interview) assessment.[41]

Table 2

A short overview of the hybrid emotion–focused treatment.

Treatment stage	Typical methods
I. Building a working relationship, soothing distress, and developing relevant goals	Validation, self-monitoring and behavioural chain analyses, dialectic stance, metaphors and psychoeducation, goal setting, and valued commitment.
II. Developing skills to prepare for exposure and improve regulation of pain and emotion in everyday life	Psychoeducation, metaphors, dialectics, and skills training (self-validation, acceptance, breathing and relaxation techniques, distraction, refocusing, problem solving, and opposite action).
III. Exposure for emotions and movements	Exposure in vivo, behavioral experiments, generalize to home and work by practice.
IV. Training context sensitivity; applying skills in tune with environmental demands	Chain analyses and identifying relevant cues, rehearse context sensitive responses, implementing validation, communication, and emotion-regulation skills, coping with responses from others.
V. Maintaining and refining	Identifying key elements, strategies, and skills to cope with flare-ups.

2.9.2. Internet-delivered cognitive-behavioral therapy (iCBT)

The iCBT includes 8 treatment modules consisting of educational texts, pictures, case examples, audio files, and 2 to 3 homework assignments per module. **Table 3** provides a short description of the theme and content of each of the modules. Participants were guided by licensed clinical psychologists (n = 2), psychology students in their final stage of clinical training (n = 4), and clinical psychologists in their postacademic year of supervised professional training for accreditation (n = 2). All therapists received training and supervision in the treatment protocol. Before the start of the program, the therapists contacted participants over the phone to conduct a clinical interview (MINI and pain anamnesis) and to provide instruction on the details of the Internet platform and the treatment. All further communication was conducted through the chat function of the Internet platform. Participants could ask questions on a need basis receiving a response within 24 hours during the work week. Contingent upon completing homework assignments, written support and feedback was provided. Treatments lasted a median of 12 weeks (IQR 9, interval 8-17). The therapists corresponded with participants a median of 20 times (IQR 17, interval 11-28) through the chat function and talked over the phone for a median of 2.4 hours (IQR 1.2, interval 1.8-3), including initial screening and assessment.

2.10. Statistical methods

All descriptive statistics (proportion (n[%]), mean [SD], and median [interquartile range]) and analyses of simple associations were conducted using SPSS Version 24. Analysis of variance and *t*-tests were used for continuous distributed variables, and the χ^2 test of independent, logistic regression and Mann–Whitney *U* for unordered and ordered categorical variables, respectively. Within-group effect sizes (Cohen's *d*) were calculated for descriptive purposes using the pooled SD at pre-treatment assessment as the denominator.[5] All primary outcome analyses were conducted using Mplus Version 8.1.[39] Throughout, comparisons were 2-tailed and treated as statistically significant at the level of $P < 0.05$. Confidence intervals are given with 95% margin (95% CI).

To estimate clinical significance at post-treatment and 9-month follow-up, we used the criteria of Jacobson and Truax[21] and Jacobson et al.[22] We calculated the reliable change index using the pooled SD of the observed sample at baseline and test–retest reliability of the measures (see under measures). We defined clinical significant improvement as fulfilling criteria for reliable improvement according to the reliable change index and for "recovery", where "recovery" was operationalized as an individual score shifts from a clinical to a nonclinical distribution. We used recommended cutoff points for highest possible specificity and sensitivity in detecting clinical and nonclinical cases for the MADRS-S (value = 9[53]) and GAD-7 (value = 10[42]). For the PCS, we used the midpoint between distributions of catastrophizers and noncatastrophizers (value = 21[43]), and for the MPI-subscales, we used values lying 2 SDs below the mean in our sample at baseline (pain intensity value = 2.98, pain interference value = 26.63). These data were thereafter treated as categorical outcome variables in the primary outcome analyses.

Regression for continuous and categorical outcome variables, estimated using maximum likelihood with non-normality robust SEs (returned by the MLR option in Mplus), was used as the primary analytic model to test for the difference between the hybrid treatment and iCBT at post-treatment assessment and at 9-month follow-up using the treatment variable (0.5 = hybrid, −0.5 = iCBT) and the pre-treatment values of the outcome variable (grand mean centered) as predictors in the model (similar to analysis of covariance).[38,48] Using model-implied (adjusted) mean and variance, we computed a standardized mean difference between-group effect size measure (Cohen's *d*) for continuous distributed variables with the SD at pre-treatment assessment as the denominator. Effect sizes of 0.2 to 0.5 were considered small, 0.5 to 0.8 moderate, and ≥0.8 large.[14]

Table 3

A short overview of the iCBT (adapted from Ref. 12).

Module, theme	Content
1: Introduction	Information: Chronic pain and goal-setting. Assignments: Set personal goals, identify obstacles, and introduction to applied relaxation (step 1).
2: Coping with pain through graded exercise	Information: Physical exercise and the body's anatomy. Create an exercise plan and applied relaxation (step 2).
3: Coping with pain through behavioral strategies	Information: Behavioral coping (eg, pacing and activity planning). Create an activity plan and applied relaxation (step 3).
4: Coping with pain through cognitive strategies	Information: Coping with negative thoughts about pain using cognitive techniques. Assignments: Identify and challenge negative automatic thoughts, applied relaxation (step 4), and continued activity planning.
5: Mindfulness	Information: Coping with thoughts and pain through mindfulness and acceptance. Assignments: Mindfulness in daily activities and continued activity planning.
6: Stress and pain	Information: Stress responses and stress management. Assignments: Practice stress management techniques and continued activity planning.
7: Sleep and pain	Information: Sleep hygiene and stimulus control in relation to sleep problems. Assignments: Apply module 4 techniques to cope with sleep-related negative thoughts and continued activity planning.
8: Maintenance	Setbacks and maintenance planning, summary of the program. Assignments: Develop a maintenance plan

iCBT, Internet-delivered cognitive behavioral therapy.

For categorical outcomes, the odds ratio was computed as a standardized effect size measure based on model estimates.

Following the principle of intention to treat, all participants who were randomized were included in the primary outcome analyses of both continuous and categorical outcomes. Using full information maximum likelihood (FIML), all primary analytic models used all available data to estimate model parameters and their associated SEs. Full information maximum likelihood is one of 2 recommended methods for analysis with missing data[40] because it returns unbiased estimates and SEs under a lenient missing data assumption (ie, missing at random) in which observed variables in the model are allowed to be associated with missing data. Given that baseline anxiety was associated with missing data, we also reanalyzed the data using multiple imputation as a sensitivity analysis (technical details and results are available in supplement 1, http://links.lww.com/PAIN/A781).

3. Results

3.1. Missing data analysis

Of the 115 included participants, 90 (78%) completed the post-treatment and 94 (82%) the follow-up assessments (**Fig. 1**). In 3 separate models, we examined whether missing data were related to treatment allocation and baseline variables (block 1: sex, age, education, pain location, sick leave, and health care visits; block 2: outcome variables) using logistic regression. Missing data did not differ between the 2 conditions but were related to baseline anxiety for the iCBT group. In this condition, higher anxiety increased the likelihood for nonparticipation at post-treatment (B = 0.24, SE = 0.11, $P = 0.03$) and at follow-up assessment (B = 0.39, SE = 0.16, $P = 0.01$). None of the other variables were related to nonparticipation in the post-treatment or follow-up assessment.

3.2. Primary outcomes (continuous)

Table 4 shows the observed descriptives and within-group effect sizes (based on observed data) for the continuous primary outcomes, and **Table 5** presents the results obtained from the regression models (based on FIML). For the hybrid treatment, the within-group effect sizes ranged from $d = 0.35$ (pain intensity) to $d = 1.01$ (depressive symptoms) at post-treatment and from $d = 0.40$ (pain intensity) to $d = 1.17$ (pain interference) at follow-up. For the iCBT, the within-group effect sizes ranged from $d = 0.31$ (pain intensity) to $d = 0.76$ (depressive symptoms) at post-treatment and $d = 0.60$ (anxiety) to $d = 0.73$ (pain catastrophizing) at follow-up. Covarying pre-treatment scores on the outcome variable, statistically significant differences between conditions were observed on MPI-pain interference and PCS at post-treatment, favoring the hybrid treatment over iCBT. The standardized mean difference effect sizes were in the small to moderate range. In addition, the difference on the MADRS-S approached but did not reach significance at post-assessment ($P = 0.061$), with an associated effect size in the small range. There were no statistically significant differences on MPI-pain intensity and GAD-7.

At 9-month follow-up (**Fig. 2**), statistically significant differences between conditions were observed on MPI-interference ($P = 0.02$) and MADRS-S ($P = 0.043$). Point estimate of effect sizes were in the small to moderate range. None of the other observed differences between conditions were statistically significant at 9-month follow-up.

3.3. Primary outcomes (clinically significant changes)

Table 6 gives an overview of proportions of reliable and clinical significant improvement for the 2 treatment arms (based on observed data), and **Table 5** presents the results obtained from the regression models (based on FIML). Clinically significant improvement is calculated as the proportion of participants in each treatment arm who, besides reliably improving, also exceed the set clinical criterion for each measure. The difference in the proportions of the participants who showed a clinical significant improvement on at least one of the outcome variables at post-assessment approached significance ($P = 0.055$), favouring the hybrid treatment (n = 20, 43%) over iCBT (n = 10, 23%). The difference in proportions of participants who met criteria for clinically significant improvement on the PCS at post-assessment also approached but did not reach significance ($P = 0.077$). Although observed proportions favoured the hybrid treatment over iCBT on all but one comparison at post-assessment and 9-month follow-up, no statistically significant differences were observed between conditions.

Sensitivity analyses were run to test whether the method used to handle missing data (FIML vs multiple imputation) influenced the primary outcome results. Although minor differences were

Table 4

Means and SDs for the continuous primary outcome variables at pre-treatment, post-treatment, and 9-month follow-up, and within-group effect sizes (Cohen's *d*) from pre-treatment to post-treatment, and pre-treatment to follow-up.

Measure (range)	Hybrid treatment, M (SD)	iCBT treatment, M (SD)	Within-group effect sizes		
				Hybrid	iCBT
MADRS-S (0-60)					
Pre-treatment	23.72 (7.62)	23.11 (7.05)			
Post-treatment	16.27 (8.08)	17.54 (7.75)	Pre to post	1.01	0.76
Follow-up	15.40 (9.73)	17.79 (9.28)	Pre to follow-up	1.13	0.72
GAD-7 (0-27)					
Pre-treatment	13.33 (6.07)	12.07 (5.21)			
Post-treatment	9.22 (6.41)	8.96 (4.73)	Pre to post	0.73	0.66
Follow-up	8.58 (6.61)	8.70 (5.78)	Pre to follow-up	0.84	0.60
PCS (0-52)					
Pre-treatment	24.14 (10.21)	26.86 (10.54)			
Post-treatment	16.98 (9.97)	22.91 (11.83)	Pre to post	0.69	0.38
Follow-up	14.11 (10.04)	19.25 (12.68)	Pre to follow-up	0.97	0.73
MPI-pain intensity (0-12)					
Pre-treatment	7.71 (2.51)	7.68 (2.23)			
Post-treatment	6.89 (2.78)	6.95 (2.45)	Pre to post	0.35	0.31
Follow-up	6.76 (2.42)	6.15 (2.46)	Pre to follow-up	0.40	0.65
MPI-pain interference (0-66)					
Pre-treatment	49.63 (10.46)	48.62 (12.09)			
Post-treatment	38.92 (14.07)	44.39 (14.11)	Pre to post	0.95	0.38
Follow-up	36.39 (16.30)	41.32 (16.47)	Pre to follow-up	1.17	0.65

Pre: N for Hybrid = 58, for iCBT, N = 57 (except for GAD-7 where N = 56); post: N for Hybrid = 47 (except for GAD-7 where N = 46), for iCBT, N = 43; follow-up: N for Hybrid = 46 (except for GAD-7 where N = 45), for iCBT, N = 48 (except for GAD-7 where N = 46).

GAD-7, Generalized Anxiety Disorder 7-item Scale; Hybrid, hybrid emotion–focused treatment; iCBT, Internet-delivered cognitive behavioral therapy; MADRS, Montgomery–Åsberg Depression Rating Scale; MPI, West Haven-Yale Multidimensional Pain Inventory; PCS, Pain Catastrophizing Scale.

observed, these analyses revealed a similar pattern of findings in terms of estimates and SEs (see supplement 1, available at http://links.lww.com/PAIN/A781).

3.4. Treatment acceptability

Figure 3 displays the proportion of treatment adherence and **Table 7** acceptability ratings. There was a significant difference in degree of treatment adherence between the 2 conditions where participants in the hybrid treatment completed a larger proportion of the recommended content ($\chi^2 = 18.094$, $df = 2$, $P < 0.001$). Proportion of completed content did not however significantly relate to pre-to-post changes in any of the primary outcomes for participants in the hybrid treatment ($r = 0.01$-0.17, $P > 0.26$) or iCBT ($r = 0.04$-0.23, $P > 0.14$).

On average, participants receiving the hybrid treatment reported higher treatment credibility (U = 1353, z = 3.22, $P = 0.001$, $r = 0.34$), treatment satisfaction (U = 1478.5, z = 4.12,

Table 5

Results from maximum likelihood robust regression analyses of continuous and categorical outcomes (clinical significant improvement) evaluating treatment differences at post-assessment and 9-month follow-up.

Outcome	Post-assessment				9-month follow-up			
	b (SE)	*P*	Effect size	95% CI	b (SE)	*P*	Effect size	95% CI
Continuous outcomes								
MADRS-S	−2.66 (1.42)	0.061	−0.37	−0.75 to 0.02	−3.15 (1.56)	0.043	−0.43	−0.85 to −0.01
GAD-7	−0.31 (0.95)	0.741	−0.06	−0.39 to 0.27	−1.50 (1.05)	0.153	−0.26	−0.63 to 0.10
PCS	−4.07 (1.51)	0.007	−0.39	−0.68 to −0.10	−2.83 (1.74)	0.104	−0.27	−0.60 to 0.06
MPI-pain intensity	−0.24 (0.44)	0.583	−0.10	−0.48 to 0.27	0.60 (0.44)	0.171	0.26	−0.11 to 0.62
MPI-pain interference	−7.00 (1.93)	<0.001	−0.63	−0.96 to −0.29	−5.69 (2.44)	0.02	−0.51	−0.94 to −0.08
Categorical outcomes (clinical significant improvement)								
MADRS-S	0.92 (0.75)	0.22	2.50	0.58 to 10.76	0.57 (0.59)	0.331	1.78	0.56 to 5.64
GAD-7	−0.09 (0.64)	0.887	0.91	0.26 to 3.17	0.25 (0.60)	0.681	1.28	0.40 to 4.14
PCS	2.04 (1.15)	0.077	7.66	0.80 to 73.14	0.84 (0.60)	0.165	2.32	0.71 to 7.56
MPI-pain intensity	0.64 (1.27)	0.615	1.89	0.16 to 22.66	−0.87 (1.21)	0.47	0.42	0.04 to 4.44
MPI-pain interference	0.89 (0.86)	0.3	2.43	0.45 to 12.96	0.99 (0.64)	0.12	2.69	0.77 to 9.42
Any measure	0.89 (0.47)	0.055	2.44	0.98 to 6.10	0.69 (0.42)	0.103	1.99	0.87 to 4.55

Regression models covaried pre-treatment scores on the outcome variables and were based on all individuals who were randomized (N = 115). The unstandardized beta coefficient (b) for continuous outcomes is the adjusted estimated mean difference and can thus be interpreted as an unstandardized effect sizes in original metric of the scale. The effect size for continuous outcomes is the standardized mean difference (*d*) and is negative when it favored Hybrid. The effect size for categorical outcomes is the odds ratio and is above 1 when it favored Hybrid.

GAD-7, Generalized Anxiety Disorder 7-item Scale; MADRS-S, Montgomery–Åsberg Depression Rating Scale; MPI, West Haven-Yale Multidimensional Pain Inventory; PCS, Pain Catastrophizing Scale.

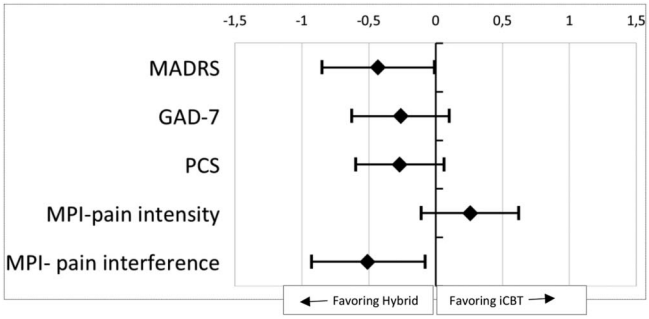

Figure 2. Between-group effect sizes on primary outcomes: GAD-7, Generalized Anxiety Disorder 7-item Scale; Hybrid, hybrid emotion–focused treatment; iCBT, Internet-delivered cognitive behavioral therapy; MADRS, Montgomery–Åsberg Depression Rating Scale; MPI, West Haven-Yale Multidimensional Pain Inventory; PCS, Pain Catastrophizing Scale.

$P < 0.001$, $r = 0.44$), and global impression of improvement ($t = -3.581$, $df = 82.097$, $P = 0.001$, $d = 0.76$) than participants receiving the iCBT. The difference between treatments regarding reports of adverse events was not significant. Six participants (13%) in the hybrid treatment reported adverse events (most commonly increased anxiety or depressive symptoms; n = 3), compared with 11 (26%) participants in the iCBT group (most commonly stress due to assignments; n = 6). In the Hybrid treatment arm, in one case, additional follow-up sessions were warranted, and in 2 cases, additional psychological intervention was recommended.

4. Discussion

This study evaluated the effectiveness of a novel transdiagnostic approach to treating chronic pain patients with high levels of comorbid anxiety and depression as compared to an active control. Our results suggest that this treatment may provide a viable option for improving results for this patient group. We found that the hybrid emotion–focused treatment was well accepted and gave moderately better treatment outcome on several emotion and pain-related outcomes, although notably, not on pain intensity itself. The most robust difference was on pain interference, suggesting that the hybrid treatment was superior in altering the negative influence of pain on participants' daily life in terms of, for example, work, leisure activities, and socializing with family and friends.

Our results may be compared to a recent treatment study evaluating emotional awareness and expression therapy (EAET) for fibromyalgia patients.[28] Although the EAET targets emotional activation and expression in the context of relational encounters, our hybrid treatment targets emotion regulation to cope with exposure. Thus, both treatments actively target emotion-regulation patterns. In a similar fashion to Lumley et al., we found that the emotion-focused treatment improved results as compared to an active control. Therefore, this study adds to the support for an emotion-focused approach. However, we plead for caution in drawing conclusions because there are important differences in the designs of these studies such as patient characteristics (fibromyalgia vs more heterogeneous chronic musculoskeletal pain) and the setting (United States vs Sweden).

One notable difference between our results and Lumley et al.'s results is that the EAET intervention in that study resulted in larger clinically significant improvements on pain intensity. It could thus be that this treatment method produced better pain relief for a subgroup of patients. Indeed, the hybrid protocol may be improved by integrating more direct ways to influence pain intensity itself, such as by using methods from EAET or by more extensively targeting reappraisal of damage interpretations.[27] Another feature in our results on pain intensity worth noting is that, at follow-up, the outcome favoured the iCBT by 0.26 SD. Although not statistically significant, this difference is nevertheless

Table 6

Percentage of reliable and clinical significant improvement at post-treatment and follow-up for all outcome variables.

Measure	Pre-treatment to post-treatment		Pre-treatment to follow-up	
	Reliable improvement	Clinical significant improvement	Reliable improvement	Clinical significant improvement
MADRS-S				
Hybrid	18 (38%)	7 (15%)	19 (41%)	9 (20%)
iCBT	10 (23%)	3 (7%)	13 (27%)	6 (13%)
GAD-7				
Hybrid	12 (26%)	10 (22%)	16 (36%)	11 (24%)
iCBT	8 (19%)	7 (16%)	9 (20%)	7 (16%)
PCS				
Hybrid	11 (23%)	6 (13%)	16 (36%)	10 (22%)
iCBT	2 (5%)	1 (2%)	9 (20%)	7 (15%)
MPI-pain intensity				
Hybrid	9 (19%)	2 (4%)	5 (11%)	1 (2%)
iCBT	3 (7%)	1 (2%)	12 (25%)	2 (4%)
MPI-pain interference				
Hybrid	16 (34%)	5 (11%)	23 (50%)	9 (20%)
iCBT	5 (12%)	2 (5%)	14 (29%)	4 (8%)
On any measure				
Hybrid	34 (72%)	20 (43%)	33 (72%)	24 (52%)
iCBT	16 (37%)	10 (23%)	27 (56%)	17 (35%)

Pre-treatment to post-treatment: N for Hybrid = 47 (except for GAD-7 where N = 46), for iCBT, N = 43; pre-treatment to follow-up: N for Hybrid = 46, for iCBT, N = 48 (except for GAD-7 where N = 45 for both groups). GAD-7, Generalized Anxiety Disorder 7-item Scale; Hybrid, hybrid emotion–focused treatment; iCBT, Internet-delivered cognitive behavioral therapy; MADRS-S, Montgomery–Åsberg Depression Rating Scale; MPI, West Haven-Yale Multidimensional Pain Inventory; PCS, Pain Catastrophizing Scale.

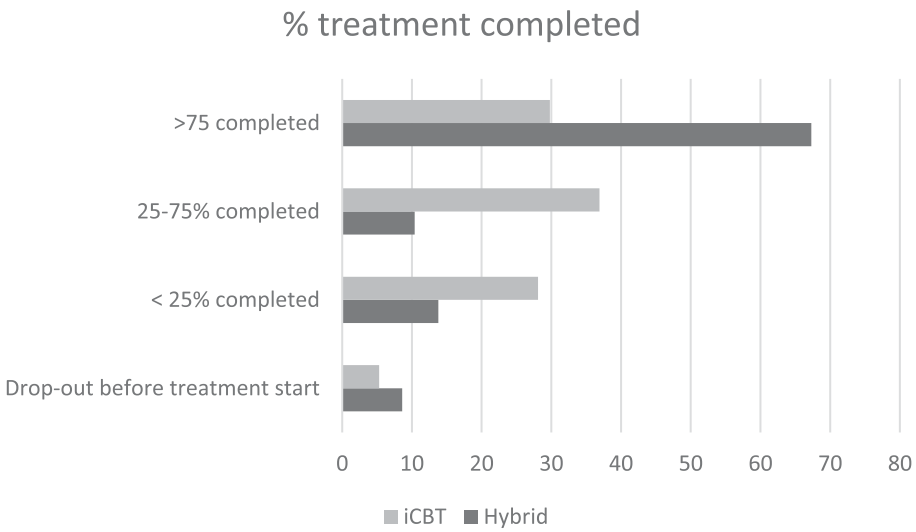

Figure 3. Proportion of completed treatment content: Hybrid, hybrid emotion–focused treatment; iCBT, Internet-delivered cognitive behavioral therapy.

in an unexpected direction because results on the other outcomes were generally in favour of the hybrid.

Although our results support the conclusion that a transdiagnostic emotion–focused treatment approach could provide better results for chronic pain patients with high levels of comorbid anxiety and depression, the proportions of clinically significant improvement clearly show only modest recovery rates and ample room for improvement. To improve the treatment, it is particularly important to study what may moderate treatment results. On the other hand, we used strict criteria as cutoffs for reliable recovery, and the results may therefore be conservative.

Thirteen percent of the participants reported some form of adverse event related to the hybrid treatment. These events consisted mostly of temporary and transient increases in emotional symptoms. However, in 2 cases, psychological symptomatology increased significantly and further referral to psychological treatment was warranted. Although psychological interventions almost always entail that participants are exposed to emotional discomfort, this underscores the importance of preparing patients for possible emotional reactions as well as availability of proper referral routines and procedures when actively treating emotional comorbidity in pain treatment.

This study also sought to investigate the hybrid treatment's acceptability. Average credibility, global improvement, and satisfaction ratings were above each scale's midpoint for both conditions, which suggests that both treatments in general were considered acceptable. However, ratings were lower and more heterogeneous for the iCBT arm, as was treatment adherence.

Table 7

Descriptives for treatment acceptability variables.

	Hybrid treatment	iCBT treatment
Credibility (0-30)‡, median (IQR)	23.3 (5)	21.5 (12)*
Satisfaction (0-20)§, median (IQR)	16 (4)	12 (7)†
Global improvement (0-10)§, mean (SD)	6.6 (2.1)	4.9 (2.4)*
Adverse events reported, N (%)§	6 (13%)	11 (26.2%)

* $P < 0.01$.
† $P < 0.001$.
‡ n = 44 in the Hybrid and iCBT.
§ n = 47 in the Hybrid treatment and n = 42 in the iCBT.
iCBT, Internet-delivered cognitive behavioral therapy.

Treatment adherence was, surprisingly, unrelated to outcome in both conditions. Possibly, the lack of a significant dose–response relation could be due to characteristics of the sample and due to the variety of reasons for nonadherence. For example, for some, higher treatment dosage covaried with higher problem complexity and therefore possibly greater difficulties to achieve change. Likewise, shorter treatment durations sometimes reflected not only drop-out due to treatment dissatisfaction but also early discontinuation due to a satisfying treatment response. Indeed, studies showing a positive relation between adherence and outcomes in CBT for emotional disorders often do not satisfactorily address important preexisting factors such as symptom severities and comorbidities, as well as other important aspects of treatment such as session content.[18]

Although acceptability ratings confirm that the hybrid treatment was well received by most participants, the iCBT treatment appears to have been highly acceptable for some but clearly less acceptable for others. These ratings could reflect reactivity to the format of delivery or to the content of treatment, as well as a mismatch with the needs of some patients. Mismatch between the characteristics of the treatment and the patient has been put forth as a major reason for dissatisfaction with Internet-delivered psychological treatment.[23] Indeed, feedback provided by some of the participants indicated disappointment with having to conduct treatment through the Internet, dissatisfaction with the order of the presentation of content (eg, addressing pain and activity first and emotion-regulation skills thereafter), and interference of distress and pain in their ability to attend to and process the materials. Although a recent review and meta-analysis on the comparative effects of guided iCBT and face-to-face treatment concluded that the 2 treatment formats produce equivalent overall effects,[1] there are important questions that remain on the noninferiority of the iCBT, not in the least concerning for whom this may be a good treatment format.[3]

This study has some limitations. First, patients self-selected into the study, potentially limiting generalizability. As we explicitly advertised the study as "CBT interventions for individuals with long-lasting pain who felt stressed, depressed, or worried," the results may not generalize to individuals who do not identify with these characteristics. Indeed, in a recent study, we observed that pain patients with high levels of emotional distress and high levels of pain-related fear, somewhat counter intuitively, were less likely

to participate in a multimodal pain management program.[45] This could indicate that some pain patients, while highly emotionally distressed, are more somatically focused and opt for other more biomedical directions of care. It is unclear whether this treatment model would be acceptable for these patients.

Second, the iCBT condition differs in a range of ways from the hybrid beyond differences in content, for example, in format and in planned dose of the intervention. As such, the results of this study should not be interpreted as a test of the comparative effects of the hybrid to CBT. Rather, the study was designed as a first comparison of the hybrid treatment to an active control condition where selection of the iCBT treatment package provided an ethical, evidence-based, and therefore potentially credible comparator. Also, given that the design did not include a no treatment or other minimal control condition, we cannot determine what proportion of the effects was due to factors such as regression to the mean, passage of time, or mere demand characteristics. This being said, improvements in the iCBT arm were comparable or possibly somewhat larger than those found in other (Internet and face-to-face) CBT studies for chronic pain.[13,16,36,51] This may add confidence to an interpretation of the between-group differences as indicative of an incremental effect of the hybrid treatment approach above and beyond standard CBT. However, for a more adequate estimation of the hybrid's comparative effects, further research should compare the treatment to comparators matched in format and delivery.

Third, although we conducted a semistructured interview to screen for the presence of clinical emotional disorders, we did not repeat these interviews at follow-up to corroborate changes in emotional status. The diagnostic interviews at baseline validate the sample as having significant emotional problems, but an independent clinician conducted interviews would have strengthened the internal validity of the study by providing independent, non–patient-reported information on emotional outcome. Moreover, our reliance on patient-reported outcome only has some obvious shortcomings of subjectivity and would have been strengthened by objective performance measures or, for example, register data on work absenteeism and medication use.

Fourth, we performed fidelity checks using therapist self-report. Although these provided detailed information on the specific methods used in each session, the method potentially opens up for reporting bias and it would thus have been advantageous to use independent judgement of video or audio recordings. Unfortunately, this was not logistically feasible.

In conclusion, our results suggest that an intervention that integrates targeting problematic emotion regulation and pain coping may increase effects on emotion-related variables and pain disability. Our treatment model is based on a so-called transdiagnostic approach, which is conceptually rooted in the idea that chronic pain and emotional problems share certain cognitive and behavioral processes that maintain and contribute to the exacerbation of the observed comorbidities.[19,33] The results of this study suggest that treatments that focus on addressing these specific processes can be a parsimonious option to treat comorbid problems and facilitate improvements in the subgroup of pain patients with high levels of emotional problems.

Conflict of interest statement

The authors have no conflict of interest to declare.

Acknowledgments

The authors acknowledge all participants in this study as well as invaluable study coordinators Maria Lind, Sara Nygren, and Sara Edlund. They also acknowledge Dr Monica Buhrman for generously sharing the content of the Internet treatment used as a control condition in this study. Funding for this study was provided by AFA insurance (140356), Region Östergötland (LIO-724821), and the Swedish Foundation for Humanities and Social Sciences (P14-0799:1). The content of this study is the sole responsibility of the authors; financial sponsors had no role in study design, data collection, data analysis, data interpretation, writing of the report, or the decision to submit for publication. An abstract and poster of the preliminary results of this study have been presented at the IASP world conference in Boston, USA, September 12 to 16, 2018.

Appendix A. Supplemental digital content

Supplemental digital content associated with this article can be found online at http://links.lww.com/PAIN/A781.

Article history:
Received 21 November 2018
Received in revised form 18 February 2019
Accepted 26 February 2019
Available online 6 April 2019

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