



Scientific Report

Implementation and effectiveness of a transdiagnostic emotion
focused treatment in clinical context

In society today, mental health problems, specifically stress-, anxiety- and depressive disorders, are a primary cause of long-term sick leave, leading to significant societal costs and suffering [1]. One important issue hindering implementation of successful treatments is that there is a marked co-occurrence *between* these problems and somatic health problems, such as different types of pain. For example, in a Swedish study mapping reasons for primary care visits, 20% of those who sought care for pain stated explicitly that they also sought care for mental health problems [2]. In addition, another 20% reached clinical cut-offs for anxiety and depression while seeking care for pain and not explicitly for mental health problems. As another example, in a Swedish general population study investigating commonalities between stress, pain and sleep, we found that, among those indicating their primary problem as 'stress', 60% also reported problems with pain and sleep [3]. Thus, patients with mental health problems typically also have somatic health problems.

The comorbidity between mental health and somatic problems has serious adverse consequences. Typically, the allocation of patient-to-treatment is based on the identification of a 'primary' problem area, disregarding this significant group of patients with concurrent emotional and somatic problems. In our system of healthcare, patients with mental and somatic health problems do not fit the template of psychiatry or pain rehabilitation, and primary care has difficulty integrating and coordinating the input of various health care providers that may become involved. These systemic issues enhance the development of problems rather than alleviate them.

A key to solving this problem is to develop a more integrated conceptualization of these patients' health problems. One way to understand the co-occurrence between mental and somatic health problems is offered by the 'transdiagnostic' perspective ([4, 5]; see figure 1). This perspective focuses on key emotion regulation processes that contribute to the maintenance and exacerbation of both mental and somatic health problems [6]. With respect to stress, anxiety, depression and pain this means that, instead of the one being a consequence of another, the co-occurrence is explained by the (over) activation of processes such as worry, rumination, emotional suppression and avoidance behaviors. Also, sleep is thought to play an important role, interacting with both mental and somatic health problems [24, 25].

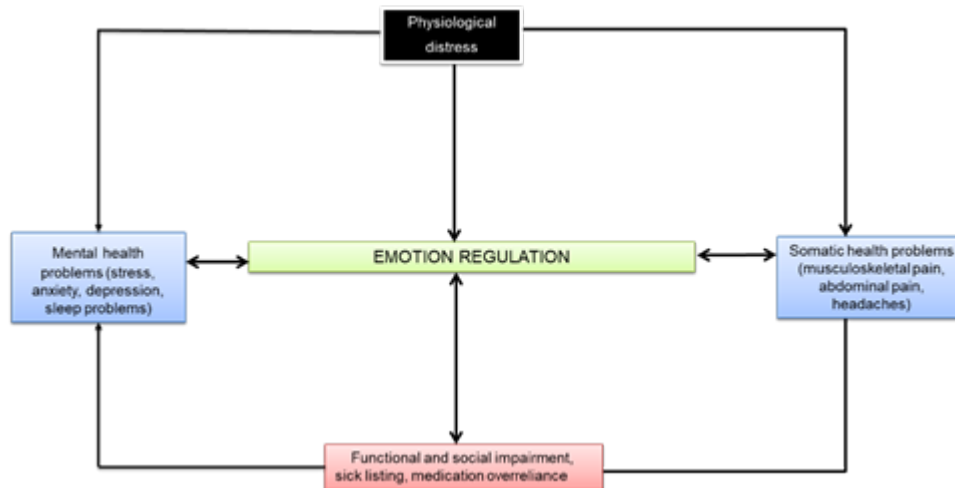


Figure 1. A transdiagnostic view of the relation between mental and somatic health problems. Adapted from [7].

This perspective has gained considerable empirical support in the literature [8, 9]. Based on this, we have systematically developed a new treatment model that targets underlying emotion regulation problems. This hybrid emotion-focused treatment combines exposure methods from cognitive behavior therapy (CBT) with an emotion regulation approach informed by procedures in Dialectical Behavior Therapy (DBT). Exposure is a state-of-the-art CBT method that tackles functional impairment through systematic and gradual approach of feared and avoided activities [eg. 10, 11]. However, exposure may insufficiently address the needs of patients with high levels of emotional distress. Emotional dysregulation needs more specific therapeutic attention for these patients to benefit from exposure practices [12]. DBT is such a

treatment approach, originally developed for chronically suicidal patients [13] but successfully adapted for patient groups with other complex problems characterized by high levels of emotional dysregulation. It centers on teaching patients to accurately identify, understand, soothe and effectively act upon their emotional responses to aversive stimuli by means of a range of techniques [14]. The hybrid emotion-focused treatment thus integrates procedures from exposure and DBT with a uniting conceptualization focused on targeting shared processes that maintain co-occurring mental and somatic health problems.

After initial feasibility studies on the hybrid emotion-focused treatment model, we recently confirmed the efficacy of this treatment in a randomized controlled trial against an active comparison group, consisting of standard CBT methodology [15]. After 10-16 sessions, patients suffering from longstanding debilitating pain *and* high levels of anxiety and depression achieved significantly better results on key outcomes such as function and depression. Furthermore, we found that changes in the ability to regulate pain and emotion mediated the effects of treatment, supporting the transdiagnostic theoretical underpinnings of the treatment model [26]. As a next step, this treatment's effectiveness needs to be tested, broadening the target group to focus on patients with mental health problems comorbid with somatic problems and delivered by clinicians in 'real world' clinical contexts. Methodologically, we propose to use a replicated single-case experimental AB design with randomized baseline lengths. Participants will be followed using repeated and randomized measurement of key variables across both phases. This design allows for solid effectiveness testing using randomization tests, will provide detailed information on individual variation, and also allows the probing of mechanisms of change when aggregated across patients [17, 18]. Included in the design is also standardized pre-post and follow up measurement allowing for further validation and single group analysis of change. In addition, targeting the involved clinicians, we perform a qualitative process evaluation to identify what may influence the conduct and quality of the implementation (using semi-structured interviews).

Aim: The aim of this project is to implement and evaluate the effectiveness of a transdiagnostic emotion-focused treatment protocol (hereafter called 'the hybrid treatment') in clinical context. The treatment addresses comorbid mental (anxiety- and depressive) and somatic health (pain) problems and targets core emotion regulation processes that are hypothesized to maintain and exacerbate these problems.

Specific questions:

1. Can the hybrid treatment be successfully implemented within the health care system?
2. What is the effectiveness of the hybrid treatment when delivered by regular clinical psychologists within first line clinical care and when addressing a variety of problems within the spectrum of stress, anxiety, depression and pain problems?

Study design

This study uses a sequential single-case experimental AB design [27] with randomized baseline lengths (4, 5, or 6 weeks; [28]), repeated weekly outcome measurement for 20 weeks and standardized pre-post and 12-months follow-up measurements. Recruitment was conducted from October 1st 2021 to January 1st 2023. This study was approved by the Swedish Ethical Review Authority (EPN Uppsala D-No 2020-06083; 1-2) and preregistered at ClinicalTrials.gov (ID: NCT05082922).

Sample and recruitment

Inclusion criteria were:

- (1) Emotional problems operationalized as ≥ 11 points on either subscale of the Hospital Anxiety and Depression Scale (HADS) [29, 30, 31].
- (2) Chronic pain, i.e. prevalence of pain problems > 3 months.

(3) Functional impairment operationalized as > 20 points on items 21-24 of the Orebro Musculoskeletal Pain Questionnaire (OMPSQ) [32] OR >3 points on item 2 of the Multidimensional Pain Inventory (MPI) pain interference subscale [33, 34].

Exclusion criteria were:

- (1) Insufficient mastery of Swedish
- (2) Severe psychiatric problems requiring immediate other treatment
- (3) Ongoing psychological treatment or recently started psychopharmacological treatment for anxiety or depression (<3 months prior to planned treatment)

Participants were recruited by psychologists at enrolled primary or specialized pain care units throughout Sweden. Patients eligible for inclusion were identified by referral groups at the units, psychologists, or other unit clinicians, such as nurses, physiotherapists, or doctors. Participants were informed by the psychologist about the study, received written information and filled out a screening form. Mini International Neuropsychiatric Interview 7.0.1 (MINI) was conducted with individuals who fulfilled initial inclusion criteria. After consent, the research coordinator randomized the participants to a 4-, 5-, or 6-week baseline, after which they were contacted to fill out the baseline questionnaire. After completion, the research coordinator coordinated treatment start with the treating psychologist. Figure 2 shows a flowchart of study participation. In total 41 participants were recruited. Among these, 31 participants provided weekly measures with no more than three missing weeks and were included in the presented analyses. In an intention to treat approach, participants were asked to continue their study participation regardless of level of engagement in the treatment.

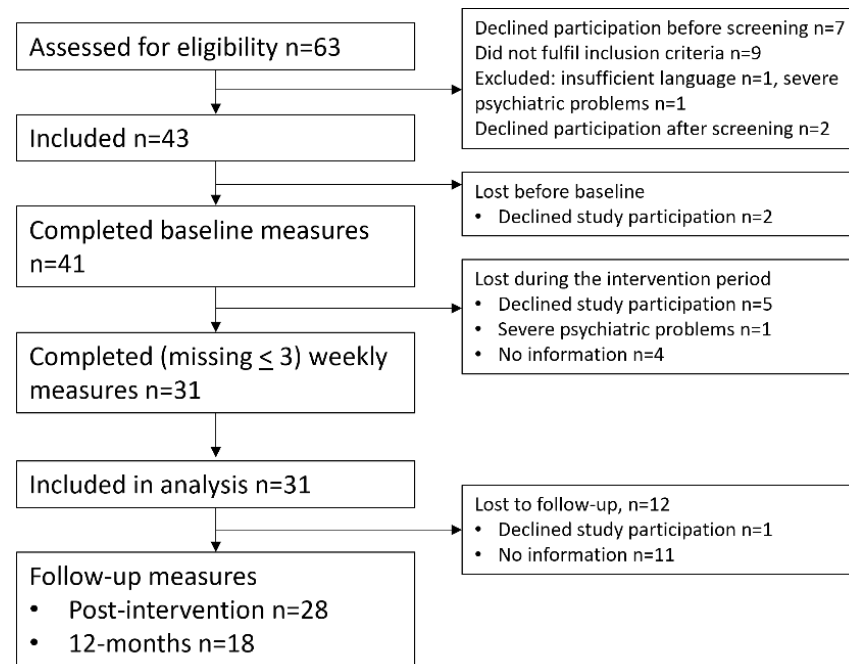


Figure 2. Flowchart of study participation and available data.

Therapists

For therapists not already trained in the method, training was addressed in two ways: a) a designated 5-week university course during the spring term of 2021 (7.5 credits, accredited by the Swedish psychologist association (psykologförbundet)), and b) an online course and workshops during the spring of 2022 (four days of workshops and 10 hours of lectures). A digital learning platform was created for the project, including written materials, video demonstrations and recorded lectures. Therapists were recruited through snowball recruitment and through advertisements in relevant Facebook groups. All therapists were licensed psychologists and were offered supervision in a group every 6th week during the treatment period. Total 43 psychologists were trained, and 16 participated in the study as therapists. The participating therapists were employed at 14 different care sites in ranging from mid-, to south Sweden. The number of participants treated per therapist ranged from 1 to 8 with a median of 2.

Care sites included specialist pain clinics in larger cities (>500 000 inhabitants) as well as primary care clinics in smaller cities (<50 000 inhabitants). In total 58% (n=18) of the participants were treated in specialist care and 42% (n=13) were treated in primary care.

Hybrid treatment

The hybrid treatment, presented in table 1, is principle based. As described in the background, the hybrid treatment aims to address transdiagnostic processes that are hypothesized to maintain emotional problems and somatic problems. Exposure for both pain and emotion-related avoidance behaviors is the central component. The hybrid treatment is structured in 5 stages which provides a systematic approach, while allowing for tailoring of the treatment to the individual. Each stage has clearly outlined aims and suggested methods, all described in a manual. A target of 10-15 weekly sessions was set.

Table 1. A short overview of the hybrid treatment.

Treatment stages
Phase I. Building a working relationship, soothing distress and developing relevant goals
Phase II. Developing skills to prepare for exposure and improve regulation of emotions and somatic symptoms in everyday life
Phase III. Exposure to emotion and somatic symptom provoking situations and activities
Phase IV. Developing communication skills to cope with social situations that provoke emotional distress
Phase V. Maintaining and refining skills into the future

Data collection and measures

Data were collected by self-report questionnaires completed online using RedCap. Demographic data were collected at baseline and included age, sex, education level, occupational status, sick leave during the previous year, health care visits during the previous year, symptom duration, and pain location. The weekly diary covered emotional and pain problems as well as hypothesized mechanisms. The weekly diary was repeated for 20 weeks covering the baseline (A) as well as intervention period (B). In addition, supplementary measurement using standardized questionnaires of emotional and pain problems, as well as work functioning and general health, was administered at baseline, post-intervention, and at 12-month follow-up. Swedish versions of all questionnaires were used. Therapists' treatment fidelity and patient treatment adherence was assessed through therapists' self-report session checklists, which were completed after each session. Therapists also evaluated whether treatment targets were reached at the end of treatment. Targeting the involved clinicians, we performed a qualitative process evaluation to identify what may influence the conduct and quality of the implementation (using semi-structured interviews). Also, patients were interviewed after participation using semi structured interviews. For details on assessment see attachment.

Analyses

For the weekly diary, a criterion was set for missing data to be ≤ 3 , out of the 20 data points, to facilitate visual and statistical analyses. No imputation of data was used. Regardless of level of treatment adherence, those with complete data according to the criterion were included in the subsequent analyses (n=31). For pre-post and 12-months follow-up measures, analyses were based on available data. Session report checklists from therapists were available for all participants that were included in the analyses (n=31). To analyze the treatment effect aggregated across individuals, multilevel model with randomization test was used [37]. This method was considered to suit the study purpose of providing inferential statistics and effect sizes on the study level. As an effect measure for treatment effect on the individual level non-overlap of all pairs (NAP) was used [35]. The NAP is a commonly used method and was considered to suit the purpose of a non-parametric method for the sequential AB-design in this

study [36]. We used $NAP \geq 0.65$ as criterion signifying a moderate effect [35]. NAP calculations and graphing of figures were performed using the sced package in R [38]. Furthermore, we described aspects of treatment acceptability, adherence and fidelity and related them to treatment response. Specifically, between-group statistics were conducted to assess differences between treatment responders and non-responders, regarding fidelity and acceptability. To this mean, we used a cut-off of an average $NAP \geq 0.65$ across all 10 outcome measures. As a measure of validation, we used Wilcoxon signed rank test to assess within-group effects on standardized measures from pre to post and from pre to 12-months follow-up, for the subgroups classified as responders and non-responders. Non-parametric statistics were used due to the small sample size. For continuous variables Mann-Whitney U-test was used and for categorical variables, the Chi-square test of homogeneity or Fishers exact test were used. Clinicians semi-structured interviews were analyzed using the CIFR framework. See Löfstand et al. 2024, attached publication, for details.

Results

Participants

Table 2 provides demographic and clinical characteristics of the sample (n=31). The participants were on average approaching their 40-ies, and a substantial proportion (42%) were not working or studying. Long-term sick leave was common, 48% had sick leave >180 days during the past year. A majority (71%) were women. About four out of five had maximum completed either middle school (grundskolan) or upper secondary school (gymnasium) and about two-thirds had Swedish nationality. On average, participants fulfilled criteria for moderate depression, clinical insomnia of moderate severity and rated their general health as low. As assessed with diagnostic clinical interviews, 82% fulfilled the clinical criteria for an anxiety or depressive disorder, indicating substantial functional interference due to emotional problems for the large majority of the sample. Multiple pain locations were common, especially back and neck pain and headaches, as were visits to health care professionals during the past year.

Table 2. Participants' demographic and clinical characteristics at baseline.

	n=31
Age, mean (SD)	38.9 (13.0)
Gender, women, n (%)	22 (71.0)
Nationality, Swedish, n (%)	20 (64.5)
Education, n (%)	
Middle school	2 (6.5)
Upper secondary/ vocational	23 (74.2)
University	6 (19.4)
Occupational status, n (%)	
Working	14 (45.2)
Unemployed	7 (22.6)
Student	4 (12.9)
Non-working (e.g. retirement pension)	6 (19.4)
Sick leave past year, n (%)	
0-14 days	11 (35.5)
15-180 days	5 (16.1)
181-365 days	15 (48.4)
Pain locations, n (%)	
Back, neck, and/or shoulders	30 (96.8)
Legs and arms (including feet and hands)	25 (80.6)
Stomach	17 (54.8)
Head	28 (90.3)
Symptom duration > 1 year, n (%)	30 (96.8)
Health care visits, median (range) past year	

Physician	5 (0 to >10 visits)
Specialist/hospital	2 (0 to >10 visits)
Psychologist	4 (0 to >10 visits)
Physiotherapist	8 (0 to >10 visits)
Social worker	0 (0 to >10 visits)
Other (e.g., chiropractor, acupuncturist)	0 (0 to >10 visits)
Total number of >2 visits, n (%)	30 (96.8)
Psychiatric comorbidity (MINI-criteria) n (%)	n=22
Not fulfilling disorder criteria	4 (18.2)
Major depressive disorder	13 (59.1)
Anxiety disorder	13 (59.1)
Comorbid depressive and anxiety disorder	8 (36.4)
Depression (MADRS-S)	28.06 (7.42)
Insomnia (ISI)	16.65 (6.71)
General health (VAS, 0-100)	30.45 (16.88)

Note: MINI, Mini International Neuropsychiatric Interview 7.0.1. ISI, Insomnia Severity Index 0-28, MADRS-S, Montgomery Åsberg Depression Rating Scale 0-54

Treatment effects, weekly diaries

Aggregated across participants, the multilevel shift model with randomization test for the weekly outcome measures revealed a significant treatment effect for one of the pain interference items (*In general, how much does your pain problems interfere with your day-to-day activities*; $\delta=.34$, $p=.005$). At the single case level, table 3 provides an overview of treatment effects on the weekly outcome measures for each participant using non-overlap of all pairs (NAP). Of the 31 participants, 27 (87%) responded with at least a moderate treatment response on at least one outcome measure, and over half (55%) responded with at least a moderate treatment response on at least three outcome measures. Four participants (13%) did not respond on any of the outcome measures.

Table 3. Non-overlap of all pairs (NAP) for weekly diary outcome measures, n=31.

Id	Emotional problems				Pain problems			Mechanisms			
	Average	Dep	Anx	Emo_int	P_sev	P_int1	P_int2	Worry	Avoid1	Avoid2	SCS
1	0.81	0.88	0.80	0.79	0.88	0.83	0.71	0.79	0.78	0.80	0.88
2	0.70	0.68	0.85	0.62	0.88	0.75	0.75	0.53	0.52	0.68	0.73
3	0.66	0.77	0.70	0.48	0.65	0.71	0.87	0.70	0.39	0.47	0.86
4	0.65	0.82	0.52	0.65	0.50	0.67	0.65	0.65	0.65	0.66	0.69
5	0.79	0.87	0.60	0.77	0.64	0.81	0.77	0.83	0.78	0.88	0.91
6	0.73	0.90	0.81	0.61	0.69	0.51	0.71	0.64	0.71	0.86	0.89
7	0.76	0.99	0.65	0.60	0.87	0.59	0.63	0.67	0.76	0.87	0.98
8	0.65	0.89	0.43	0.50	0.89	0.94	0.42	0.37	0.60	0.50	0.94
9	0.76	0.89	0.83	0.63	0.84	0.88	0.84	0.44	0.62	0.77	0.85
10	0.65	0.61	0.32	0.48	0.50	0.68	0.95	0.76	0.61	0.75	0.80
11	0.52	0.66	0.20	0.69	0.48	0.68	0.51	0.49	0.44	0.67	0.38
12	0.48	0.82	0.39	0.47	0.30	0.56	0.73	0.29	0.33	0.40	0.48
13	0.49	0.20	0.54	0.50	0.53	0.50	0.44	0.50	0.50	0.38	0.80
14	0.45	0.41	0.41	0.31	0.63	0.69	0.31	0.44	0.37	0.59	0.29
15	0.32	0.22	0.09	0.20	0.50	0.50	0.50	0.25	0.38	0.50	0.06
16	0.40	0.43	0.26	0.37	0.27	0.53	0.40	0.43	0.32	0.71	0.30
17	0.27	0.02	0.04	0.45	0.21	0.29	0.41	0.44	0.46	0.39	0.01
18	0.30	0.26	0.25	0.19	0.21	0.50	0.50	0.24	0.54	0.24	0.04
19	0.46	0.55	0.82	0.50	0.21	0.33	0.58	0.28	0.48	0.66	0.20
20	0.56	0.49	0.55	0.36	0.40	0.88	0.52	0.34	0.74	0.53	0.75
21	0.39	0.61	0.39	0.46	0.20	0.41	0.45	0.54	0.30	0.53	0.01

22	0.48	0.79	0.70	0.56	0.19	0.26	0.23	0.54	0.16	0.50	0.86
23	0.60	0.39	0.72	0.50	0.57	0.67	0.64	0.42	0.70	0.83	0.54
24	0.37	0.02	0.16	0.66	0.36	0.38	0.72	0.31	0.53	0.28	0.23
25	0.55	0.63	0.51	0.44	0.69	0.57	0.76	0.39	0.84	0.52	0.14
26	0.54	0.35	0.56	0.50	0.56	0.70	0.68	0.39	0.62	0.52	0.54
27	0.39	0.54	0.37	0.12	0.43	0.56	0.42	0.28	0.25	0.29	0.67
28	0.56	0.46	0.91	0.59	0.38	0.34	0.20	0.66	0.58	0.78	0.70
29	0.54	0.49	0.46	0.35	0.86	0.77	0.64	0.52	0.35	0.45	0.49
30	0.60	0.88	0.64	0.57	0.91	0.81	0.32	0.34	0.52	0.56	0.45
31	0.60	0.63	0.80	0.58	0.60	0.64	0.77	0.30	0.59	0.44	0.60
Tot	32%	42%	35%	16%	32%	48%	42%	23%	26%	42%	48%

Notes: Average= Average NAP across all outcomes, P_sev = Pain severity, P_int1 = Pain interference1, P_int2 = Pain interference2, Dep = Depressive symptoms, Anx = Anxiety, Emo_int = Emotional interference, Worry = Worry, Avoid1 = Avoidance1, Avoid2 = Avoidance2, SCS = Symptom catastrophizing. All NAP ≥ 0.65 marked in green. Id of non-responders on all outcomes marked in red. Tot=percentage of participants with NAP ≥ 0.65 , for each outcome.

Patient and therapist evaluation of effect

Table 4 provides an overview of patient's own evaluation of global improvement and their therapist evaluation of relevant goal achievement, both assessed post treatment. Half of the participants scored an average of ≥ 2.5 (mid-scale) on global improvement, indicating that half the sample had a positive evaluation of the treatment resulting in improved coping and well-being. Of available data, therapists evaluated their patients goal achievement as either positive or very positive for n=11 (58%) out of n=19 of the participants.

Table 4. Patient and therapist improvement evaluation.

Id	Global improvement	Goal achievement
1	4	-
2	1	-
3	3.5	2
4	4.5	2
5	5	3
6	5	4
7	3.5	-
8	4	4
9	3	-
10	0.5	3
11	-	-
12	4.5	-
13	0	-
14	0	2
15	0.5	2
16	5	4
17	-	3
28	1.5	3
19	2	3
20	3.5	3
21	2	2
22	1	-
23	3.5	3
24	1.5	2
25	1	2
26	2.5	2

27	-	-
28	2	2
29	0	-
30	5	3
31	3	-

Global improvement= Participant judgement of global improvement (0-5, score ≥ 2.5 defined as positive and marked in green). Goal achievement=therapist's evaluation of whether patients personally relevant goals have been achieved Items rated from 1-4 where 1= deterioration, 2=unchanged, 3=positive, and 4=very positive. Scores 3 and 4 marked in green to signify improvement.

Treatment acceptability

Table 5 provides an overview of treatment acceptability. Using an average NAP ≥ 0.65 as a criterion for a broad and robust treatment response, 10 of the 31 participants (see also table 3) were classified as treatment responders and 21 participants as non-responders. As can be seen in table 6, there are clear patterns converging this classification of treatment response with statistically significant responsiveness on most standardized pre, post and follow up measurement.

Table 5. Self-report measures at pre-treatment, post-treatment, and 12-months follow-up organized according to treatment responders (n=10) and non-responders (n=21).

Outcome variable	Treatment responders n=10	Within-group statistics	Non-responders n=21	Within-group statistics
Pain severity (MPI)				
Pre	4.75 (1.01)		4.50 (1.07)	
Post	3.70 (1.36)	z=-1.83, p=0.07	4.67 (1.09)	z=1.36, p=0.17
12-months	3.08 (1.11)	z=-2.21, p=0.03*	4.42 (1.36)	z=0.57, p=0.57
Pain interference (MPI)				
Pre	5.16 (1.15)		4.84 (0.96)	
Post	4.18 (1.47)	z=-2.50, p=0.01*	4.63 (0.95)	z=-1.11, p=0.27
12-months	3.56 (1.16)	z=-2.21, p=0.03*	4.88 (1.41)	z=1.49, p=0.13
Depression (MADRS-S)				
Pre	31.30 (7.54)		26.52 (7.01)	
Post	22.50 (11.23)	z=-2.43, p=0.02*	27.17 (8.85)	z=0.44, p=0.66
12-months	21.67 (12.27)	z=-2.02, p=0.04*	27.50 (9.39)	z=0.71, p=0.48
Avoidance (PIPS)				
Pre	47.10 (7.67)		42.76 (7.34)	
Post	38.00 (12.27)	z=-2.31, p=0.02*	39.39 (10.31)	z=-1.89, p=0.06
12-months	36.67 (11.91)	z=-1.75, p=0.08	40.92 (9.89)	z=-1.23, p=0.22
Fusion (PIPS)				
Pre	23.90 (3.03)		21.81 (3.70)	
Post	19.70 (5.70)	z=-2.03, p=0.04*	20.89 (5.52)	z=-0.54, p=0.59
12-months	17.83 (4.45)	z=-2.02, p=0.04*	21.00 (3.98)	z=-1.61, p=0.11
Emotion regulation (DERS)				
Pre	54.80 (11.13)		41.86 (16.26)	
Post	44.50 (15.43)	z=-2.49, p=0.01*	44.00 (17.75)	z=1.50, p=0.13
12-months	49.50 (13.61)	z=-1.99, p=0.05*	50.08 (18.11)	z=1.53, p=0.13
Work limitations (WLQ-16)				
Pre	73.13 (19.76)		57.01 (14.50)	
Post	57.44 (25.43)	z=-1.60, p=0.11	58.25 (23.16)	z=0.60, p=0.55
12-months	55.04 (27.14)	z=-1.21, p=0.23	70.44 (23.15)	z=1.48, p=0.14
Insomnia (ISI)				
Pre	18.50 (6.52)		15.76 (6.77)	
Post	14.10 (5.80)	z=-2.68, p=0.01*	15.11 (6.42)	z=0.18, p=0.86
12-months	15.80 (5.02)	z=-1.75, p=0.08	16.67 (7.22)	z=1.34, p=0.18
Health (VAS)				
Pre	24.90 (13.89)		31.10 (17.83)	
Post	44.30 (14.68)	z=2.55, p=0.01*	31.94 (21.58)	z=-0.38, p=0.71

12-months	52.40 (22.47)	$z=2.02, p=0.04^*$	30.67 (23.14)	$z=-.18, p=0.86$
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Notes: Within groups statistics is Wilcoxon and Mann-Whitney. MADRS-S, Montgomery Åsberg Depression Rating Scale (0-54). MPI, Multidimensional Pain Inventory (0-6), Psychological Inflexibility in Pain Scale avoidance subscale (10-70) and fusion subscale (6-42). DERS-16, The Difficulties in Emotion Regulation Scale (16-80). WLQ-16, Work Limitations Questionnaire -16 item (0-100). ISI, Insomnia Severity Index (0-28). VAS-health, visual analogue scale (0-100). *p-value significant at <0.05 Missing data: Treatment responders: pre-treatment n=10 , post-treatment n=10 except WLQ n=9, 12-months follow-up n=6 except WLQ, ISI, EQ-VAS n=5 Non-responders: pre-treatment n=21 except WLQ n=20, post-treatment n=19 except MADRSS, PIPS, ISI, EQ-VAS all n=18 and WLQ n=17, 12-months follow-up n=12 except WLQ n=10

Using the responder/non-responder classification, potential associations between treatment acceptability and treatment response could be probed. On average, participants viewed the treatment as credible. There were no differences in credibility dependent on treatment response. However, while both treatment responders and non-responders were on average satisfied with treatment, responders reported higher average satisfaction with less variability between participants.

Table 6. Treatment acceptability

	Total sample, n=31	Responders n=10	Non- responders n=21	Between-group statistics
Pre-treatment	n=31	n=10	n=21	
Credibility (0-6)	3.7 (1.7-6.0)	4.0 (3.3–6.0)	3.8 (1.7–6.0)	U=130.50, $z=1.09, p=0.28$
Post-treatment	n=28	n=10	n=18	
Satisfaction (0-5)	3.5 (0–5.0)	4.5 (3.0–5.0)	3.3 (0–5.0)	U=141.50, $z=2.51, p=0.01^*$

Notes. Numbers are median (range). *p-value significant at <0.05.

Treatment adherence and fidelity

Table 7 provides an overview of participant treatment adherence, and therapist treatment fidelity. On average, participants completed 10 sessions out of the designated 10-15. The most common reasons for missed sessions were cancelations or no-show sessions. Four patients among the non-responders dropped out of treatment after respectively two, three, six, and nine sessions, due to stress and lack of time (n=3) and illness (n=1). While there are no significant treatment length differences between those classified as responders and non-responders, there is a notable difference in variability in session attendance (responders range 8-15; non-responders range 2-15). No adverse events were reported.

Regarding treatment fidelity, there was variability between participants in the degree to which treatment addressed all the treatment phases. Notably, among non-responders, a lower degree of progression through treatment phases can be seen, with a relatively large proportion (35%) not progressing beyond phase II. Only 50% of non-responders received treatments that addressed phases IV and V while this was the case for 90% of responders. In concordance, the proportion of treatment spend on higher order phases ($\geq$ phase III) was significantly lower among non-responders. Irrespective of responder classification, therapists included homework in a large proportion (90%) of the sessions. Yet, in the degree to which homework contained exposure there was a tendency towards a difference between responders and non-responders, with responders receiving at least 1 homework assignment related to exposure to a higher degree than those classified as non-responders.

Table 7. Adherence to treatment and treatment fidelity.

	Total sample, n=31	Treatment responders, n=10	Non- responders, n=21	Between-group statistics
Session attendance				
Attended sessions, median (range)	10 (2–15)	11 (8–15)	10 (2–15)	U=120.50, $z=0.66, p=0.52$

Missed sessions ^a , median (range)	4 (0–13)	3 (0–7)	4 (0–13)	U=88.00, z=-0.73, p=0.47
Session length, mean (SD)	56.2 (10.3)	50.0 (16.2)	60.5 (14.6)	U=74.00, z=-1.31, p=0.20
Phases addressed, n (%)	n=30	n=10	n=20	X ₂ =6.83, p=0.08#
Phase I-II	7 (23)	0 (0)	7 (35)	
Phase I-III	4 (13)	1 (10)	3 (15)	
Phase I-IV	10 (30)	6 (60)	4 (20)	
Phase I-V	9 (30)	3 (30)	6 (30)	
Proportion (%) of sessions addressing phases ≥3, median (range)	26 (0–71)	38 (15–50)	16 (0–71)	U=144.50, z=1.97, p=0.05*
Homework				
Proportion (%) of sessions including homework, median (range)	90 (50–100)	91 (80–100)	89 (50–100)	U=125.50, z=1.15, p=0.27
Participants with >1 occasion of homework with exposure content, n (%)	17 (57)	8 (80)	9 (45)	Fisher's exact test, p=0.07#

Notes. ^a Include cancelled sessions, no-show sessions, drop-out of treatment, and missing session information. *p-value significant at <0.05. # p-value significant at <0.10.

Clinician evaluation of implementation

Semi structured interviews were conducted with 9 participating psychologists to map promoting and hindering factors when implementing the hybrid manual from a clinician perspective. The interview guide and analysis were guided by the Consolidated Framework for Implementation Research (CFIR). Regarding the CFIR domain intervention characteristics, analyses showed that the hybrid treatment format suited some, but not all therapists. Specifically, the flexible and principle base format was problematized by some and considered an obstacle in judging whether the intervention suited the patients or not. This obstacle was matched by the results in the individual characteristics CFIR domain, where some therapists raised uncertainty regarding knowledge or confidence in the treatment as an obstacle. Regarding the CFIR domains inner and outer setting, implementation was influenced by whether the treatment model was compatible with existing triaging routines at the care unit, existing collaboration between disciplines and whether psychological treatment was prioritized for patients with comorbid emotional and pain problems.

Figure 3 Promoting and hindering factors in implementing the hybrid model as viewed by clinicians

CFIR-domain	Theme	Promoting	Hindering
<i>Intervention characteristics</i>	Perception of the adaptability of the intervention	Adapted the manual – found the structure helpful	High 'rule based' compliance – increased problematization about whether the intervention suited the patients
<i>Outer setting</i>	Prioritization of pain patients' needs	Clearly stated prioritization of pain patients	Lack of resources – no prioritization of psychological treatment for pain patients
<i>Inner setting</i>	Leadership commitment and autonomy	Support from key personnel and/or manager	Lack of mandate to influence
<i>Inner setting</i>	Structure for collaboration	Compatible with existing flows	Lack of structure or time for collaboration
<i>Characteristics of individuals</i>	The psychologists' commitment	Drive to spread information/ have a key role internally Incentive to drive	Uncertainty regarding knowledge or confidence in the treatment

Discussion

The aim was to evaluate whether the hybrid treatment could be successfully implemented within the health care system.

We received interest from and trained a substantial number of psychologists who work in a variety of health care settings throughout Sweden. Recruitment and data collection proved to be a challenge that we, by and large, succeeded with. Most patients assessed for eligibility were interested and fulfilled inclusion criteria, and subsequent assessment showed a very good match with the intended population. Patients had high levels of comorbidity across a broad spectrum of mental and somatic health indicators. Patients had a demographic profile of low educational attainment, substantial sick leave, high health care utilization and high proportion immigrant status, which reinforces external validity, as these are the indicators of complex and comorbid problems observed in clinical care.

Logistically we also succeeded, despite the pandemic. Likely due to our early adjustments in research design, where we substituted an RCT plus SCED design with repeated SCEDs only. While demanding because of intense and -timewise- prolonged measurement, this methodology proved to be very fitting for the purpose and feasible to apply. This methodology, we note, is increasingly put forward as a viable and important addition to clinical intervention and effectiveness research (39). On a critical note, while we approached our target N of inclusion, we did incur a higher-than-expected level of internal missingness in our data, which made our analytic N lower than projected. While not a problem for the single case analyses as such, this does provide less confidence in our subgroup analyses, which intended to probe associations between treatment response and aspects of implementation. To more robustly analyze on a subgroup level, it would have been preferable with a larger N.

The number of clinicians providing patient data was lower than the number of clinicians trained but then again, the commitment required from both care units and therapists is quite large. We were able to engage 16 committed therapists geographically spread throughout the more populated parts of Sweden, and working in 14 different settings, at both primary and secondary care level. We consider this an adequate reach that gave sufficient opportunity to probe generalizability. Our data suggest that the method is equally feasible to implement in primary and in secondary care, but also that there are several aspects influencing implementation success. Specifically, the treatment format does not suit all therapists and future training needs support clinicians in how to adapt the intervention to context and patient needs. Also, therapists' self-efficacy to perform exposure is a key component in need of further attention. This is supported by one of the main findings showing an association between performing exposure and treatment success. While a key component of the treatment, non-responders to a higher degree never entered the exposure phases of treatment. Whether this is due to therapist and/or patient factors is a subject in need of further study. That exposure is difficult for therapists to perform and subject to 'drift' is a finding that is well corroborated in the literature (40). Furthermore, there are some important contextual characteristics that influence compatibility. Specifically, the need for therapists to have a clear mandate to treat the target patient group supported by leadership and colleagues. Specifically, this means knowledge within the organization supporting the transdiagnostic model of emotion-pain comorbidity, consensus in the care unit on triaging patients to psychological intervention and collaboration between relevant disciplines.

At large, the treatment resulted in robust and broad clinically relevant effects for about a third of the patients. Corroborated by significant changes on the standardized measures, this appears to be a strict but valid estimate of clinically relevant treatment effect. Applying criteria such as the patient's own judgement of improvement and clinician judgment, treatment resulted in relevant effects for about half of the participants. While there is overlap between effectiveness on outcomes, patient- and therapist judgements, there is also variability, showing that effectiveness varies depending on perspective, also within patients. Across patients, effects on depressive symptoms, pain interference, and catastrophizing were most robust, which is in line with the effects we found in our efficacy trial (15). This is also corroborated by the significant effect on interference aggregated across participants, and in relation to the randomization to different baseline lengths.

In summary, our data support that the hybrid treatment model is feasible to apply in clinical care with some effect for most patients and a robust effect for some.

Attachment, assessment details

Weekly diary

Emotional problems

1. Symptoms of depression were assessed using the Patient Health Questionnaire 9-item depression module (PHQ-9), which has acceptable reliability and validity (39, 40). In the PHQ-9, participants rate the frequency of symptoms during the last two weeks on a 4-point scale. A total score of 0–27 is calculated.
2. Symptoms of anxiety were assessed using the Generalized Anxiety Disorder 7-item scale (GAD-7), which has good reliability and validity (41). Like the PHQ-9, patients rate the frequency of symptoms during the last two weeks on a 4-point scale. A total score of 0–27 is calculated.
3. Emotional interference from depressive symptoms and anxiety on daily life activities was assessed using the following item from PHQ-9 and GAD-7: “If you checked any problems, how difficult have they made it for you to do your work, take care of things at home, or get along with other people?” rated 0 = not difficult at all, 1 = somewhat difficult, 2 = very difficult, 3 = extremely difficult.

Pain problems

1. Pain severity was assessed using the following item from MPI-S (33): “On the average, how severe has your pain been during the last week?” rated from 0 = not at all severe to 6 = extremely severe.
2. Pain interference was assessed using the following two items from MPI-S (33): “In general, how much does your pain problems interfere with your day-to-day activities?” rated from 0 = no interference to 6=extreme interference, and “How much do you limit your activities in order to prevent your pain from getting worse?” rated from 0 = not at all to 6 = to a high degree.

Processes

1. Worry was assessed using a study specific item: “During the last week, how often have you been worried about your future health?” rated 0 = never, 1 = rarely, 2 = from time to time, 3 = often, 4 = all the time.
2. Avoidance was assessed using two items, one study specific item: “Due to your health problems: How often have you refrained activities during the last week?” rated 0 = never, 1 = rarely, 2 = from time to time, 3 = often, 4 = all the time and one item modified from the Psychological Inflexibility in Pain questionnaire (42) : “During the last week, how often have you been ruled by thoughts like “I don’t have the energy”, “I am not well enough”, “I don’t dare”, “I have too much pain”, or “I feel too bad” rated 0 = never, 1 = rarely, 2 = from time to time, 3 = often, 4 = all the time.
3. Catastrophizing was assessed using the Symptom Catastrophizing Scale (SCS) (30). SCS was developed from the Pain Catastrophizing Scale and evaluated for reliability and validity among patients with major depressive disorder, with satisfactory results (43). Seven items covering thoughts and feelings in relation to participants’ health or mental health condition are rated for frequency. Examples of items: “I become afraid that my condition will get worse” and “My symptoms are awful and I feel that they overwhelm me”. In the current study, a five-point scale was used, providing a total score of 0–28.

Treatment acceptability

To assess participants’ expectations before treatment, we used 3 items from the Credibility/Expectancy Questionnaire (44), assessed at baseline: “How logical does the therapy offered to you seem for your problems?”, “How successful do you think this treatment will be?”, and “How confident would you be in recommending this treatment to a friend?”. In this study, items were rated from 0–6 and averaged across the three items to form a total score for **credibility**. Treatment satisfaction was assessed after the treatment with the following items: “How pleased are you with the treatment?”, and “Would you recommend the treatment to someone with similar problems?”. Items were rated 0–5 and averaged to form a total score for

satisfaction. Participants were also asked after treatment to report if any adverse events had occurred, and, if so, describe the event and rate the impact.

Treatment fidelity and adherence

A therapist self-report checklist for each session was used to assess therapist treatment fidelity and patient treatment adherence. Therapists reported a short description of session content as well as session date and length, or reasons for missed sessions and homework completion. Using checkboxes with pre-defined items, therapists were asked to indicate which key components in the hybrid treatment had formed an essential part of the session. Items were: *(Phase I)* Validation; Dialectics; Behavior analysis; Values/Goal setting; *(Phase II)* Skills training in emotion regulation; Psychoeducation before exposure; *(Phase III)* Exposure; *(Phase IV)* Skills training social relationships; *(Phase V)* Maintenance. In a corresponding way, homework content was reported. Based on this data, the following variables were created:

1. A variable denoting the range of phases addressed during treatment. Each session was coded according to which treatment phase it belonged. Mode as well as frequency were analyzed for the variable.
2. A variable denoting the median (range) proportion of sessions addressing higher order phases of treatment for each participant.
3. A variable denoting the median (range) proportion of sessions where therapists included homework. Also, a dichotomized variable of participants with > 1 occasions of homework focused on specifically exposure was created, reported in frequency.

Pre- and post-treatment and 12-month follow-up

Global improvement

Participants' experiences of global improvement were assessed after treatment with the following items: "Have your ability to cope with your symptoms been influenced by the treatment?", and "Has your well-being been influenced by the treatment?". Items were rated 0-5 and averaged to form a total score for **global improvement**. The rating of global improvement was described for each participant separately.

Therapist's evaluation of to what degree treatment targets were achieved was rated by the therapist at the end of treatment using 1 item covering whether patients "Achieved personalized prioritized goals". The item was rated from 1-4 where 1= deterioration, 2=unchanged, 3=positive, and 4=very positive. The rating of goal achievement was described for each participant separately.

Pain severity and pain interference were assessed by the Multidimensional Pain Inventory, Swedish version (33, 34) subscales. MPI-S is a well-used and validated measure (17). An average score is calculated for each subscale (pain severity 2 items, pain interference 11 items), ranging 0-6. Depressive symptoms were assessed by the self-rating version of the Montgomery Åsberg Depression Rating Scale, the MADRS-S which has acceptable reliability and validity (45, 46). The MADRS-S has nine items rated 0-6. The total score ranges 0-54 and is interpreted: 0-12 = no depression, 13-19 = mild depression, 20-34 = moderate depression, ≥ 35 = severe depression. Emotion regulation ability was assessed by the Difficulties in Emotion Regulation Scale, 16 item version, which has shown good reliability and validity (47). DERS-16 assess the following domains: nonacceptance of negative emotions, inability to engage in goal-directed behaviors when distressed, difficulties controlling impulsive behaviors when distressed, limited access to emotion regulation strategies perceived as effective, and lack of emotional clarity. A total score is calculated ranging 16-80 with higher scores reflecting greater difficulties.

Avoidance and cognitive fusion were assessed by the Psychological Inflexibility in Pain questionnaire (42). The PIPS is a 12-item scale designed to measure psychological inflexibility in patients with pain and has shown acceptable internal consistency and validity (42). A total score is calculated for each subscale, ranging 10-70 for avoidance and 6-42 for cognitive fusion, lower scores being beneficial. Disability at work was assessed by the Work Limitations Questionnaire - 16 (WLQ-16), which has shown promising psychometric properties (48). In the WLQ, the impact of health problems on occupational performance is measured. An index scale 0-100 is calculated,

where higher scores indicate more problems. Sleep problems were assessed by the Insomnia Severity Index (ISI), which is valid and reliable measure of clinical insomnia (49). Seven items cover severity of insomnia, dissatisfaction with sleep, interference with daily functioning, noticeability of impairment, and distress related to the sleep problem. The total score ranges 0-28 and is interpreted: <8 = no insomnia, 8-14 = sub-threshold insomnia, 15-21 = clinical insomnia (moderate severity), and 22-28 = severe clinical insomnia. Perceived health was measured using a visual analogue scale (VAS) (50) where participants rated perceived health during the last 30 days. The scale was in digital format, horizontal and anchored with 0=worst imaginable and 100=best imaginable.

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