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Efficacy of Videoconference Group Acceptance and Commitment Therapy (ACT) and Behavioral Activation Therapy for Depression (BATD) for Chronic Low Back Pain (CLBP) Plus Comorbid Depressive Symptoms: A Randomized Controlled Trial (IMPACT Study)

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Abstract: This study examined the efficacy of adding a remote, synchronous, group, videoconference-based form of acceptance and commitment therapy (ACT) or behavioral activation therapy for depression (BATD) to treatment-as-usual (TAU) in 234 patients with chronic low back pain (CLBP) plus comorbid depressive symptoms. Participants were randomly assigned to ACT, BATD, or TAU. Compared to TAU, ACT produced a significant reduction in pain interference at posttreatment (*d* = .64) and at follow-up (*d* = .73). BATD was only superior to TAU at follow-up (*d* = .66). A significant reduction in pain catastrophizing was reported by patients assigned to ACT and BATD at posttreatment (*d* = .45 and *d* = .59, respectively) and at follow-up (*d* = .59, in both) compared to TAU. Stress was significantly reduced at posttreatment by ACT in comparison to TAU (*d* = .69). No significant between-group differences were found in depressive or anxiety symptoms. Clinically relevant number needed to treat (NNT) values for reduction in pain interference were obtained at posttreatment (ACT vs TAU = 4) and at follow-up (ACT vs TAU = 3; BATD vs TAU = 5). In both active therapies, improvements in pain interference at follow-up were significantly related to improvements at posttreatment in psychological flexibility. These findings suggest that new forms of cognitive-behavioral therapy are clinically useful in improving pain interference and pain catastrophizing. Further research on evidence-based change processes is required to understand the therapeutic needs of patients with chronic pain and comorbid conditions.

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Perspective: **Group videoconference-based ACT and BATD showed greater efficacy than TAU for reducing pain interference and pain catastrophizing in patients with CLBP plus clinically relevant depression. Psychological flexibility appeared to be the main contributor to treatment effects for both ACT and BATD.**

Key words: *Chronic low back pain, depression, acceptance and commitment therapy, behavioral activation, eHealth*

Chronic low back pain (CLBP) is one of the most prevalent chronic pain conditions, and it is associated with substantial healthcare and social impact.[1] It is also connected with effects on mental health, including major depression.[2] Overall, the prevalence of depression in the context of chronic pain exceeds 60%, generating a significant healthcare and societal burden.[3,4] Chronic pain usually exacerbates depression and depression, in turn, exacerbates chronic pain, resulting in a greater overall burden of disability and suffering.[5,6] Due to its high prevalence, treatment resistance,[7-9] and particularly significant burden during recent time,[10] comorbid chronic pain and depression represents an important treatment priority.[11-14] This complex problem is a significant challenge for clinicians and may require greater treatment intensity, duration, complexity, or new approaches.[1,2,8]

The coronavirus disease (COVID-19) pandemic and related lockdowns significantly impacted public healthcare systems around the world, including usual patient care in pain management centers.[15] The physical and mental health conditions of chronic pain patients worsened during the pandemic,[10,16-18] and therapists were forced to adapt the format of interventions based on available resources, including available technology solutions.[19-21] Consequently, eHealth increased in clinical practice from 7 to 85% during this period.[22] The exponential growth of remote-delivered psychotherapies, designed to provide a similar outcome to face-to-face therapies, highlights the relevance of technology as a resource for treating chronic pain patients.[23,24]

Internet- or remote-delivered forms of psychotherapy seem to be effective for both chronic pain and depression management.[25-28] Ease of access, relative ease of delivery, and decrease in social costs position them as alternative or complementary resources to face-to-face therapies.[21,22] Cognitive-behavioral therapy (CBT) is an umbrella term that includes a wide variety of psychotherapies.[13,29] Several forms of CBT such as acceptance and commitment therapy (ACT)[30,31] and behavioral activation therapy for depression (BATD)[32,33] have been developed and appear beneficial. Results from systematic reviews and meta-analysis support the efficacy of Internet-based ACT for chronic pain patients in improving emotional distress and pain-related outcomes.[1,28] The effectiveness of BATD for patients with depression is well-established,[34,35] but as far it is known there is a lack of studies testing its effects in individuals with chronic pain and comorbid depression. Therefore, this is the first randomized controlled trial (RCT) to provide evidence for its efficacy in a remote-delivered form.

Currently, there are no RCTs analyzing the efficacy of adding remote-delivered form of ACT or BATD to treatment-as-usual (TAU) in patients with CLBP plus depression.[36] In Spain, TAU for chronic pain is managed by general practitioners in periodic consultations and includes prescription of medication and recommendations for aerobic exercise.[37] Therefore, the objectives here were 1) to conduct an RCT to examine the efficacy of adding a remote, synchronous, group videoconference-based form of ACT or BATD to TAU in patients with CLBP plus clinically relevant depression for improving pain interference (primary outcome), pain intensity, depression, anxiety, and stress symptoms, and pain catastrophizing (secondary outcomes); and 2) to analyze the effect of pain acceptance, behavioral activation, and psychological flexibility (process outcomes) on clinical changes at long term. Larger improvements in outcomes were expected for ACT[1,28] and BATD[28] when compared to TAU (hypothesis 1). Moreover, improvements in pain interference were expected to be related to increases in psychological flexibility and pain acceptance in ACT[38-40] and by behavioral activation in BATD[38] (hypothesis 2).

Methods

Design

A 12-month, multicenter, single-blinded RCT was conducted with random allocation of patients to 3 arms: 1) ACT + TAU (hereafter, ACT), 2) BATD + TAU (hereafter, BATD), and 3) TAU alone. This RCT was registered on ClinicalTrials.gov (NCT04140838) and followed the guidelines issued by the "Standard Protocol Items: Recommendations for Interventional Trials" (SPIRIT) and the "Consolidated Standards of Reporting Trials" (CONSORT). A detailed description of the study protocol can be found elsewhere.[41]

This RCT, initially designed to deliver the therapies in a face-to-face format,[41] was adapted to be delivered via

a remote, synchronous, videoconferencing platform (ie, Zoom). Data collection was conducted at baseline, at posttreatment (2 months after baseline), and at follow-up (12 months after baseline). This research was carried out in accordance with the 1964 Declaration of Helsinki and subsequent revisions and was approved by the Ethics Committee of the Fundació Sant Joan de Déu (PIC-178-19) and the Hospital del Mar (2019/8866/I). Informed consent was obtained from all participants involved in the study. None of the patients received any financial incentive for participating in this study.

Sample Size

The sample size was estimated through R with RStudio. To detect a medium effect size on the primary outcome (Brief Pain Inventory-Interference Scale, BPI-IS)[42] for either ACT or BATD versus TAU, a total of 63 participants were required for α = .05 (2-tailed) and 1 – β = .80. Considering a possible attrition rate of 20%,[14,43] the stipulated minimum sample size was approximately 78 patients per group.

Participants

Patients with a diagnosis of CLBP who sought services at the Pain Unit of the Parc Sanitari Sant Joan de Déu (Sant Boi de Llobregat, Spain) or Hospital del Mar (Barcelona, Spain) in the last 3 years were invited to participate in this RCT. A total of 234 patients with CLBP who met the selection criteria, including the presence of moderate-to-severe depressive symptoms, were recruited between September 2020 and May 2021. As shown in Fig 1, these patients were randomly allocated into the 3 study arms: ACT (n = 78), BATD (n = 78), and TAU alone (n = 78).

Inclusion criteria were 1) aged between 18 and 70 years old; 2) diagnosis of CLBP (ie, presence of tension, soreness, or stiffness in the lower back pain)[1] ≥3 months according to medical history; 3) pain intensity > 4 points out of 10 points on a Numeric Rating Scale (NRS) in the last week; 4) moderate-to-severe depressive symptoms (≥10 points out of 27 points) in the last 2 weeks according to Patient Health Questionnaire (PHQ-9); and 5) able to understand Spanish language. Exclusion criteria were 1) presence of cognitive impairment according to medical history; 2) previous (last year) or current participation in psychological therapy; 3) diagnosis of severe psychiatric disorder or substance dependence/abuse; 4) radiculopathy; 5) involvement in litigation with the healthcare system; and 6) patients with scheduled surgical intervention and inability to attend group sessions.

Procedure

Patients who met the eligibility criteria attended a baseline face-to-face interview at the hospitals with trained clinical psychologists. Before providing informed consent and administering the battery of self-report measures (see below), patients were informed of the study purpose and confidentiality agreements. They were also notified that they were free to withdraw from the study at any time with the assurance that they could continue to receive their usual treatment. Randomization of patients to treatment arms was performed after the completion of baseline clinical assessments as recommended by the CONSORT guidelines.[44] Following Ost's recommendations,[45] patients were randomly assigned to ACT and BATD therapists to control possible therapist effects on the outcome. This allocation process was performed by a statistician who was not involved in any other research or treatment delivery procedures. Patients were assigned a list of alphanumeric codes and then randomly assigned to groups using SPSS (v26). In this process, stratified randomization was performed

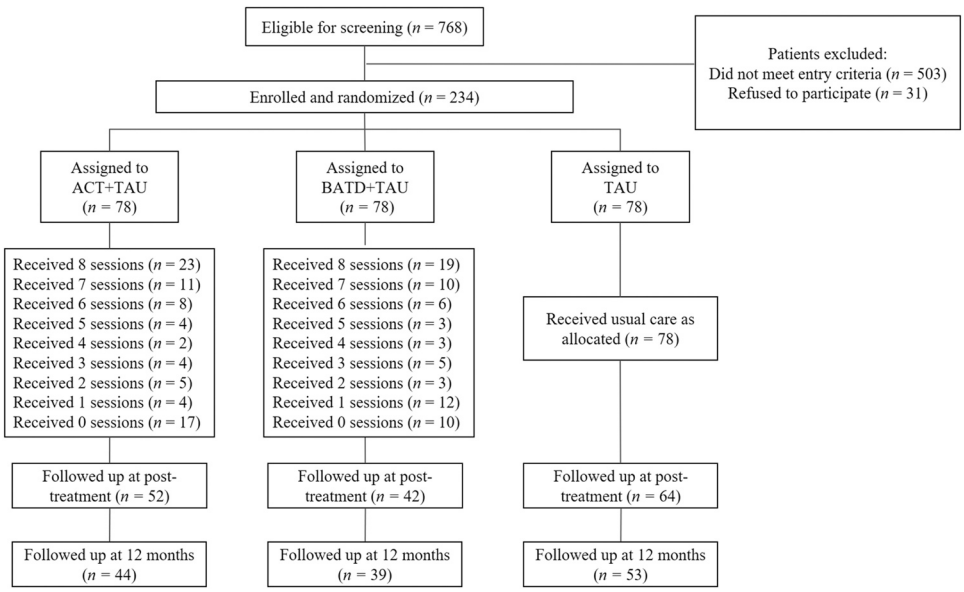

Figure 1. Flowchart of participants in the RCT.

considering baseline pain (NRS; ≥7 points out of 10 points) and depressive symptom (PHQ-9; ≥15 points out of 27 points) scores to ensure comparable clinical severity ratings between groups.

Interventions

Prior to the start of the RCT, all therapists received a 3-hour training to ensure fidelity to the protocol and homogeneity in their intervention. This training was led by 2 therapists with experience in ACT and BATD. Three different therapists guided the groups in each therapy (1 therapist per group with a total of 6). The therapists were technically supported by a research assistant during the 8 sessions. The research assistant was responsible for noting patients' attendance and recording relevant aspects identified during the interventions. A qualitative study nested within this RCT reported the experiences of a group of patients who received the online group form of ACT or BATD.[46]

Study participants were not asked to stop their usual medication regimen during the study period (12 months). After the first session, participants received a homework document to reinforce the main concepts of the therapies. They received weekly reminders with the link to access the therapy session. Both therapies were administered in group format (range: 7–13 participants) and consisted of 8 weekly 1.5-hour sessions via remote synchronous videoconference. ACT and BATD programs were conducted in 3 waves: October to December 2020 (first wave), February to April 2021 (second wave), and May to July 2021 (third wave). This study was conducted during a partial relaxation of the COVID-19 lockdown measures adopted by the Spanish authorities. During this period, people residing in Spain were able to move around, access health services, and go to work, although with some mobility restrictions that were especially stricter during the first and second waves.

Acceptance and Commitment Therapy

ACT promotes acceptance of unwanted experiences and engagement in goal-directed and value-based action. The aim of ACT is not to change internal experiences, but to promote acceptance skills to enable values-based behaviors in the presence of unpleasant experiences.[47] This psychotherapy, developed by Hayes et al,[38] focuses particularly on promoting psychological flexibility and is increasingly used as a treatment for chronic pain.[40] Psychological flexibility is defined as "the ability to contact the present moment more fully as a conscious human being and to change or persist in behavior when doing so serves valued ends" (p. 140).[30] According to Hayes et al (2022),[31] ACT interventions target 3 core pillars[30,47] to build psychological flexibility: 1) openness, 2) awareness, and 3) active engagement. ACT is supported in evidence as treatment for chronic pain.[1,40,48,49] ACT was based on the Vowles et al protocol.[50] An outline of the ACT sessions is detailed in Table 1.

Behavioral Activation Therapy for Depression

BATD applies learning principles to the pattern of withdrawal or reduction of behavioral activity related to depression. The aim of BATD is to reduce depressive symptoms and consequently to enable patients to achieve a satisfying life. This therapy primarily seeks to activate patients diagnosed with depression by scheduling and performing behaviors that are likely to increase experiences of direct positive qualities in their current context. BATD focuses on aspects of activation such as daily monitoring, identification of core life values, selection and planning of valued activities, and social support.[51] Behavioral activation is defined as "structured attempts to increase overt behaviors likely to bring patients into contact with reinforcing environmental contingencies and corresponding improvements in thoughts, mood, and quality of life" (p. 700).[52] It is an effective treatment in patients with depression[34] and other mental health problems. This can lead to increased physical activity, improved sleep, and decreased stress, which can all have positive effects on pain outcomes. This therapy was based on the Lejuez et al protocol.[32] An outline of BATD sessions is detailed in Table 1.

Although there is no prior evidence of the efficacy of BATD in patients with CLBP and comorbid depression, there are several reasons why BATD might be beneficial in improving pain interference in these individuals. First, BATD may indirectly improve pain-related outcomes by reducing the negative impact of depression on pain. Second, this therapy helps to identify and address factors that may contribute to the maintenance of depression, such as negative thinking and avoidance behaviors (variables that also contribute to the maintenance of pain-related disability). Third, it can improve the overall quality of life and functioning, which may indirectly improve pain outcomes by enhancing an individual's ability to cope with pain and engage in meaningful activities.[9,24,32]

Treatment-as-usual

All study patients received TAU. Patients randomized exclusively to TAU did not receive any additional active treatment during the study period. In Spain, chronic pain is managed by general practitioners in regular consultations of approximately 10 minutes to monitor the patient's health.[37] Standard treatment of chronic pain includes medication prescription (analgesics, anxiolytics, antidepressants, anti-inflammatories, and/or opioids) and recommendations for aerobic exercise. For this study, usual care was the same as in routine clinical practice, without any modification. Upon completion of the study's follow-up assessments, patients in the TAU group were given the opportunity to receive the therapy that had demonstrated the highest efficacy.

Study Measures

Patients were assessed with a computer-administered battery of measures, using Research Electronic Data

Table 1. Outline of the Interventions ACT and BATD

SESSION	ACT	BATD
1	*Participants' and clinician's presentation*. Psychoeducation and introduction to ACT (ACT basics; scientific advances in chronic pain and depression management; psychological theories of pain, suffering and stress; stressors, fears, and indicators; identification of values; breathing exercises).	*Participants' and clinician's presentation.* Collection of information related with areas of activity and interaction contexts. Delivery of activity log to obtain an accurate assessment of the patient's daily activities, which is useful for providing a baseline measure and comparing their progress when their activity level increases later in the treatment.
2	*Value analysis I.* Problems of experiential avoidance. Creative hopelessness through metaphors: control is the problem and not the solution. Anxiety, fight and flight, and its effects. Accepting the risk of the life's journey: experiences, feelings, and emotions.	*Problematic behaviors, patients' aims, and personal values.* Identification of information related to depressive behaviors. Exploration of problematic behaviors, identification of patients' objectives regarding treatment, and recognition of personal values.
3	*Value analysis II.* Objectives. Laws of thought and consequences of language. Mind and deactivation of thought (cognitive defusion): creating distance with thoughts. Learning meditation techniques and effects. Practicing meditation exercises.	*Establishing personal goals.* Obtaining complementary information regarding the characteristics of the history of patient interactions and any contexts and interactions that reinforce depressive behaviors. Establishment of short-term, medium-term, and long-term goals.
4	*Value analysis III.* Psychological barriers and obstacles. Emotional distress and its consequences. Emotional phenomena, personality variables and health states. Discovering commitments with committed actions.	*Therapeutic change of problematic behavior*. Explanation of the hypotheses of factors associated with the origins, maintenance, and therapeutic change of problematic behavior. In this session, 10 personalized activities are selected according to each person's own needs and desires, without any order. With the selected activities, a ranking is then generated that goes from the least difficult to the most difficult activity.
5	*Values and feelings.* Taking the initiative with a "Plan of action and willingness." Psychological flexibility, resilience, and self-motivation. Expansion and body scan exercises. Learning to relax.	*Target activities.* Once the 10 target activities have been identified, a record is made to track their progress weekly, including the number of times they would like to complete the activity in a period of 1 week (the ideal frequency). The number of activities varies each week, but they always range between 3 and 5 activities.
6	*Taking a direction.* The self as context, process, and content. Awareness of the present: "here and now." The brain and emotions: managing situations and overwhelming emotional responses.	*Satisfaction with activities.* Discussion of what was obtained from the records in general. Exploration of the satisfaction with the activities.
7	*Dare and change:* willingness and determination. Self-awareness, assertiveness, and self-esteem. Experiential expansion exercises: felt sensations. Happiness according to positive psychology. Benefits of physical exercise: movement.	*Coping abilities*. How to approach emotions and reactions to events and responses associated with depression. Relationship between avoidance behaviors and maintenance of difficulties.
8	*Moving forward.* Prepared to act with ACT: mind, body, thoughts, and feelings. Summarizing the concepts, conclusion, and evaluation.	*New behaviors.* Examination of new behaviors to be incorporated. Discussion about the goals achieved and the barriers to maintain the weekly activity plan. Farewell.

Capture (REDCap) software.[53] Table 2 shows the measures administered at each time point.

Sociodemographic and Clinical Characteristics

A sociodemographic and clinical questionnaire was used to obtain the patient's general information (gender, age, marital status, living arrangement, educational level, and employment status) and clinical characteristics (years of diagnosis and daily medication). Furthermore, the *Composite International Diagnostic Interview* (CIDI v3)[54] was used to evaluate the presence of a current depressive episode.

Primary Outcome Measure

The *BPI-IS* was used to measure pain interference during the last week.[55,56] The BPI-IS is composed of 7 items (general activity, mood, walking ability, normal work/housework, relations with other people, sleep, and enjoyment of life), which are answered on a 0 ("*does not interfere*") to 10 ("*completely interferes*") scale. The total score (0–10) is calculated as the arithmetic mean of all items, with higher scores indicating greater pain interference. Internal consistency in this study was good (Cronbach's alpha [α] = .86).

Secondary Outcome Measures

The *NRS* was used to measure pain intensity during the last week. The NRS is a unidimensional measure composed of only one item that is answered on a 0 ("*no pain*") to 10 ("*worst pain imaginable*") scale.

The *Depression Anxiety Stress Scales-21* (DASS-21) was used to measure depressive, anxiety, and stress symptoms during the last week.[57,58] The DASS-21 is composed of 21 items, which are answered on a 0 ("*did not apply to me at all*") to 3 ("*applied to me very much or most of the time*") scale. One example of DASS-21 items

Table 2. Study Periods at Which Measures and Data Are Collected

MEASURES	PRE	POST	FOLLOW-UP
Screening			
PHQ-9 (depression symptoms)	X		
NRS (pain intensity)	X		
General information			
Sociodemographic data (gender, age, marital status, etc.)	X		
Clinical data (years of diagnosis and daily medication)	X		
CIDI (current episode of depression)	X		
Primary outcome			
BPI-IS (pain interference)	X	X	X
Secondary outcomes			
NRS (pain intensity)	X	X	X
DASS-21 (anxiety, depression, and stress symptoms)	X	X	X
PCS (pain catastrophizing)	X	X	X
Process measures			
CPAQ-8 (pain acceptance)	X	X	X
BADS-SF (behavioural activation for depression)	X	X	X
PIPS (psychological inflexibility)	X	X	X
Other measures			
CEQ (credibility and expectations regarding treatments/technology)	X	X	
AET (negative effects of psychological treatments)		X	
PGIC and PSIC (impression of change)		X	

Abbreviations: AET, Adverse Effects of Treatments checklist; BADS-SF, Behavioural Activation for Depression Scale (short form); BPI-IS, Brief Pain Inventory-Interference Scale; CEQ, Credibility/Expectancy Questionnaire; CIDI, Composite International Diagnostic Interview; CPAQ-8, Chronic Pain Acceptance Questionnaire (8-item version); DASS-21, Depression Anxiety Stress Scales-21; NRS, Numerical Pain Rating Scale; PGIC and PSIC, Patient Global Impression of Change and Pain Specific Impression of Change; PCS, Pain Catastrophizing Scale; PHQ-9, Patient Health Questionnaire.

for depression is *"I found it difficult to work up the initiative to do things,"* for anxiety is *"I felt scared without any good reason,"* and for stress is *"I found it difficult to relax."* Scores range from 0 to 21 for each scale, with higher scores indicating greater depressive, anxiety, or stress symptoms. Internal consistency in the present study for depressive ($\alpha = .89$), anxiety ($\alpha = .75$), and stress ($\alpha = .92$) symptoms was acceptable to excellent.

The *Pain Catastrophizing Scale* (PCS) was used to measure pain catastrophizing.[59,60] The PCS is composed of 13 items, which are answered on a 0 ("*never*") to 5 ("*almost always*") scale. Two examples of PCS items are *"It's awful and I feel that it overwhelms me"* and *"I become afraid that the pain will get worse."* Scores range from 0 to 52, with higher scores indicating more pain catastrophizing. Internal consistency in this study was excellent ($\alpha = .92$).

Process Variables

The *Chronic Pain Acceptance Questionnaire* (CPAQ-8) was used to measure pain acceptance.[61,62] The CPAQ-8 is composed of 8 items, which are answered on a 0 ("*never true*") to 6 ("*always true*") scale. Two examples of CPAQ-8 items are *"Keeping my pain level under control takes first priority whenever I am doing something"* and *"I lead a full life even though I have chronic pain."* Scores range from 0 to 48, with higher scores indicating more pain acceptance. Internal consistency in this study was acceptable (Cronbach's $\alpha = .68$).

The *Behavioral Activation for Depression Scale-Short Form* (BADS-SF) was used to measure behavioral activation.[63,64] The BADS-SF is composed of 9 items, which are answered on a 0 ("*not at all*") to 6 ("*completely*") scale. Two examples of BADS-SF items are "*I am content with the amount and types of things I did*" and "*I spent a long time thinking over and over about my problems.*" Scores range from 0 to 54, with higher scores indicating greater behavioral activation. Internal consistency in this study was acceptable ($\alpha = .73$).

The *Psychological Inflexibility in Pain Scale* (PIPS) was used to measure psychological inflexibility towards pain.[65,66] The PIPS is composed of 12 items, which are answered on a 1 ("*never true*") to 7 ("*always true*") scale. Two examples of PIPS items are *"I cancel planned activities when I am in pain"* and *"I avoid doing things when there is a risk it will hurt or make things worse."* Scores range from 12 to 84, with higher scores indicating greater psychological inflexibility in pain. Internal consistency in this study was excellent ($\alpha = .90$).

Other Measures

The adapted version of the *Credibility/Expectancy Questionnaire* (CEQ) was used to measure credibility and expectancy regarding treatments and technology use.[67] Originally, the CEQ contained 3 items to assess therapy credibility and 3 items for expectancies. In addition, 7 items were included in this study to assess technology use. In this version, credibility and expectancy about therapies (eg, *"To what extent does this therapy seem logical to you?"* and *"To what extent do you think this therapy could be useful in treating other problems or diseases?"*) and technology use (eg, *"To what extent do you feel motivated to do this therapy non-face-to-face?"* and *"To what extent do you think that doing this therapy in a non-face-to-face setting will be useful to you?"*) were assessed at the end of the first and last ACT and BATD sessions. All items were measured on a scale of 0 ("*not at all*") to 10 ("*completely*").

The *Patient Global Impression of Change* (PGIC) and the *Pain Specific Impression of Change* (PSIC) were used to measure the impression of change.[68] The PGIC is composed of 1 item (eg, perception of global improvement) and the PSIC is composed of 5 items (eg, physical functioning, social functioning, work-related activities, mood, and pain), which are answered on a 1 ("*much better*") to 7 ("*much worse*") scale. These scales were only completed by patients who were assigned to the ACT or BATD intervention arms.

The *Adverse Effects of Treatments*[69] was used to measure the potential presence of negative effects of ACT and BATD. This ad hoc instrument is composed of 1 item ("*Have you experienced, during the psychological*

treatment, any unwanted symptom that you think might be directly or indirectly associated with the psychological intervention?"), with a "yes" or "no" answer option. Previous RCTs have used this question to explore adverse events (eg, headaches, dizziness, sleep problems, etc.) across the interventions.[69]

An ad hoc questionnaire was used to identify the characteristics of the therapists who conducted the sessions. Specifically, the therapists' training and experience in the therapies (theoretical concepts, knowledge of the protocol, years of experience as a therapist, years of experience in group therapies, years of experience in individual therapies, and years of experience in non-face-to-face therapies) were described.

Statistical Analyses

Descriptive analyses were calculated for all study measures and presented as means (M) and standard deviations (SD) for continuous variables and as frequencies (n) and percentages (%) for categorical variables. Baseline between-group differences (ACT, BATD, and TAU) in sociodemographic and clinical characteristics were examined by applying the analysis of variance (ANOVA) for continuous variables and the χ^2 test for categorical variables. Following CONSORT recommendations, potential baseline differences in sociodemographic characteristics are considered irrelevant and therefore were not included as covariates in the analyses of study outcomes.[70] Moreover, Student's t-test was used to examine differences in credibility and expectancy (CEQ) regarding therapy and technology use between the ACT and BATD groups at the end of the first session. As this RCT was conducted in 3 waves (in different circumstances of restricted movement and pandemic risk situation), it was also assessed whether there were differences between waves in terms of attrition.

The between-group analysis to assess the therapy effect on primary and secondary outcomes and process variables was carried out on an intention-to-treat (ITT). Generalized linear mixed models (GLM) were used in which restricted maximum likelihood regression was computed. Treatment effects on outcomes and process variables were estimated using these models, accounting for within-patient correlations between repeated measurements. Twisk et al[71] provided evidence that multiple imputation for missing data is not necessary before computing longitudinal mixed models. The set of linear mixed models included random intercept adjusted with the baseline score, as well as time and the interaction between *"group × time."* When the number of observations within each group is relatively small, it is advisable to include a random intercept in the model. This allows for the within-group variability and reference level of the response variable between groups to be accounted for, leading to more accurate parameter estimates and better model predictions.[71] Regression coefficients (β) and 95% confidence intervals (95% CI) were calculated for the *"group × time"* interaction between groups at posttreatment and at 12-month follow-up. The effect sizes were calculated according to Cohen's *d* for each comparison, using the pooled baseline SD to weight the differences in the pre-post or pre-follow-up mean values and to correct the population estimate.[72] The rule of thumb criterion was as follows[73]: very small (.10), small (.20), medium (.50), large (.80), very large (1.20), and huge (2.00).

The Benjamini-Hochberg procedure[74] is designed to control the false discovery rate, which is the expected proportion of false discoveries among all the discoveries conducted. The false discovery rate is calculated as the ratio of false positives to the total number of discoveries, and it provides a more flexible approach to controlling the error rate than the family-wise error rate, which controls the probability of at least one false positive among all the comparisons.[74] The Benjamini-Hochberg procedure works as follows: 1) rank the *P*-values from smallest to largest; 2) define a significance threshold or alpha level, which represents the desired false discovery rate; 3) reject all null hypotheses for which the corresponding *P*-value is less than or equal to the Benjamini-Hochberg critical value.[74] In this study, the threshold for statistical significance was set at $P < .05$. Adjusting the rate helps to prevent apparent significance from emerging by chance, avoiding Type I errors (false positives).[74] This procedure corrected for multiple comparisons by adjusting the significance threshold for each comparison based on the number of comparisons and the rank of the *P*-value.

To assess the clinical significance of improvements in the primary outcome (BPI-IS), patients were classified into 2 categories: responders and nonresponders to treatment.[75,76] Following the IMMPACT recommendations to establish a clinically significant improvement, a 1-point reduction in the pre-post and the pre-follow-up BPI-IS total score at posttreatment and at follow-up as the response criterion was used as a response criterion.[77] This categorization was also used to estimate the number needed to treat (NNT) in ACT and BATD compared to the other arms. A 95% CI for each NNT was calculated at posttreatment and at follow-up. In addition, baseline, post, and follow-up between-group differences in sociodemographic, clinical characteristics, and outcomes were explored for responders versus nonresponders, and for completers (defined here as patients who attended a minimum of 6 therapy sessions out of 8) versus noncompleters. Differences between groups were evaluated using the χ^2 and Student's t-test for categorical and continuous variables, respectively. The differences between active groups regarding patient global and pain-specific impressions of change (PGIC and PSIC) were evaluated using the χ^2 test with continuity correction.

Finally, it was examined whether the effects of ACT and BATD in addition to TAU on primary and secondary outcomes at 12-month follow-up were related to pre-post changes in process variables. Specifically, pre-post change in CPAQ-8, BADS-SF, and PIPS total scores, and pre-follow-up change scores in primary (BPI-IS) and secondary outcomes (NRS, DASS-21, and PCS) were calculated. To detect possible significant relationships, bivariate Pearson correlations were explored between pre-post change in process variables and pre-follow-up

change in primary and secondary outcomes. Direct and indirect associations between treatment conditions (ACT vs TAU and BATD vs TAU, as independent variables), significant process measures according to correlations, and primary and secondary outcomes were explored through path analysis. Regression coefficients (β) reflecting bias-corrected bootstrapped indirect effects based on 10,000 bootstrap samples were calculated, as well as their SEs and 95% CIs. Parameters of indirect effects were considered statistically significant when the 95% CI did not include 0.

SPSS (v26) and MPlus (v7) were used to compute the analysis. A 5% significance level was used in all 2-tailed tests.

Results

Patients Flow and Compliance

Of the 768 potential patients who were eligible, 503 were excluded at the screening phone interview because they did not meet the selection criteria and 31 refused to participate for personal reasons. In total, 234 patients comprised the sample of this RCT, with 78 patients randomly assigned per arm. The mean number of sessions attended in the ACT group was 4.65 (SD = 3.23) and in the BATD group was 4.42 (SD = 3.16). This difference was not statistically significant. As shown in Fig 1, 17 (21.8%) patients assigned to ACT and 10 (12.8%) to BATD did not attend any sessions. The rate of retention for ACT was 66.6 and 56.4% at posttreatment and at 12-month follow-up, respectively. In BATD, the rate of retention was 53.8 and 50% at posttreatment and at 12 months follow-up, respectively. Finally, TAU had an 82% rate of retention at posttreatment and 67.9% at 12 months follow-up.

The dropouts were significantly higher at posttreatment ($P = .001$) in BATD compared to TAU and ACT, but not at 12-month follow-up. Overall, there was a significant difference ($P = .011$) in the dropouts at the end of the study in the third wave (55.3%) compared to the first (38.8%) and second waves (32.1%). Schedule incompatibility for medical procedures (34.2%), loss of interest (28.9%), and perception that the therapy would not be useful (18.4%) were the main reasons for dropping out at posttreatment. In contrast, the main causes for dropping out at 12-month follow-up were inability to contact patients (45.5%), loss of interest (31.8%), and schedule incompatibly for medical procedures (22.7%). No significant differences in reasons for dropout were identified at posttreatment and at 12-month follow-up.

Furthermore, baseline differences (see Supplementary Table 1) were identified in marital status between ACT completers versus noncompleters (7.1% of completers vs 30.6% of noncompleters were separated/divorced; $P = .035$) and in age between BATD completers (M = 59.13, SD = 7.63) and noncompleters (M = 51.25, SD = 10.77, $P < .001$). No significant differences were observed at posttreatment and at 12-month follow-up.

Baseline Sociodemographic and Clinical Characteristics

Most patients were middle-aged women who had completed at least primary education. They mostly lived with their partner and were in paid employment at the start of this study. Most of them had a current episode of depression (70–81%), based on the CIDI, and were prescribed analgesics and antidepressants as part of their daily medication. The mean time with diagnosed chronic pain was >10 years. As shown in Table 3, no significant differences in sociodemographic and baseline clinical characteristics were found between the 3 study arms.

Description of the Therapists' Characteristics

All 6 therapists had postgraduate degrees. All had specialized health training as psychologists in Spain and 3 were studying or had a PhD. As shown in Supplementary Table 2, the mean years of experience in group therapy, individual therapy, and specific therapy of the RCT were higher for ACT therapists than for BATD therapists. In contrast, mean years of non-face-to-face therapy experience were higher in BATD than in ACT. Based on a scale of 0 to 10, ACT therapists reported higher scores than BATD therapists in knowing the core theoretical concepts of their respective therapy and in knowing how to apply the therapeutic protocol. However, none of the differences mentioned were statistically significant.

Expectancies and Technology Use at the End of the First Session

Focusing on the therapies, ACT patients reported higher scores on expecting the therapy to be satisfactory, recommendable, useful for treating other problems, and personally useful. In contrast, BATD patients scored higher on expecting therapy to be logical and not aversive. No significant differences in these scores were identified between the 2 therapies (see Supplementary Table 3).

In terms of technology use, ACT patients scored higher on knowing how to use the electronic device (phone, tablet, or computer) they would use during therapy, having little technical support during therapy, and considering that their electronic device was adequate to follow the therapy, while BATD patients scored higher on having little need for technical support during therapy and on believing that following the therapy non-face-to-face would make it difficult for them to attend or participate. However, these differences were not significant. Compared to BATD patients, ACT patients indicated a significantly greater perceived ability to follow

Table 3. Baseline Characteristics of Patients by Therapy Group

VARIABLES	ACT (N = 78)	BATD (N = 78)	TAU (N = 78)	P
Gender (women), n (%)	54 (69.2)	53 (67.9)	51 (65.4)	.87
Age, mean (SD)	54.9 (8.3)	54.9 (10.2)	53.8 (10.0)	.73
Marital status, n (%)				.54
Single	9 (11.5)	12 (15.4)	6 (7.7)	
Married/living with partner	49 (62.8)	50 (64.1)	53 (67.9)	
Separated/divorced	14 (17.9)	12 (15.4)	17 (21.8)	
Widowed	6 (7.7)	4 (5.1)	2 (2.6)	
Living arrangement, n (%)				.60
Living alone	11 (14.1)	7 (9.0)	9 (11.5)	
Living with partner	67 (85.9)	71 (91.0)	69 (88.5)	
Education level, n (%)				.81
Illiterate	2 (2.6)	0 (.0)	1 (1.3)	
Did not graduate from primary school	2 (2.6)	3 (3.8)	3 (3.8)	
Primary studies	18 (23.1)	20 (25.6)	16 (20.5)	
Secondary studies	42 (53.8)	46 (59.0)	43 (55.1)	
University	14 (17.9)	9 (11.5)	15 (19.2)	
Employment status, n (%)				.33
Homemaker	3 (3.8)	4 (5.1)	2 (2.6)	
Paid employment	20 (25.6)	24 (30.8)	32 (41.0)	
Paid employment but in sick leave	5 (6.4)	4 (5.1)	4 (5.1)	
Unemployed with subsidy	14 (17.9)	10 (12.8)	4 (5.1)	
Unemployed without subsidy	5 (6.4)	4 (5.1)	4 (5.1)	
Retired/pensioner	9 (11.5)	12 (15.4)	14 (17.9)	
Temporal disability	4 (5.1)	8 (10.3)	9 (11.5)	
Others	18 (23.1)	12 (15.4)	9 (11.5)	
Clinical variables				
Years of diagnosis, M (SD)	10.9 (7.9)	11.1 (8.7)	11.2 (8.0)	.98
Current episode of depression, n (%)*	60 (76.9)	63 (80.8)	55 (70.5)	.32
Daily medication, n (%)				
Analgesics	35 (50.7)	33 (50.0)	35 (50.7)	.99
Anti-inflammatory	16 (23.2)	19 (29.2)	16 (23.2)	.58
Opioids	15 (23.1)	18 (27.7)	12 (17.4)	.36
Antiepileptic	11 (16.9)	15 (23.1)	13 (18.8)	.66
Muscle relaxant	6 (9.4)	11 (16.9)	11 (15.9)	.41
Antidepressants	19 (29.7)	24 (36.9)	29 (42.0)	.33
Anxiolytics	12 (18.8)	11 (16.9)	13 (18.8)	.95

Abbreviations: ACT, acceptance and commitment therapy; BATD, behavioral activation therapy for depression; TAU, treatment-as-usual.
*CIDI, Composite International Diagnostic Interview.

the therapy in online format ($P = .026$, $d = .41$) and in believing that doing this therapy non-face-to-face would be useful to them ($P = .041$, $d = .37$; see Supplementary Table 3).

Effects on Pain Interference (Primary Outcome)

Table 4 shows descriptive statistics and between-group analyses for pain interference (BPI-IS) according to the ITT approach. After applying the Benjamini-Hochberg correction for multiple comparisons, ACT achieved a significantly greater reduction in pain interference compared to TAU at posttreatment ($\beta = -1.22$, $P = .001$) and at 12 months follow-up ($\beta = -1.41$, $P < .001$). Likewise, BATD showed greater reduction in pain interference compared to TAU at 12 months follow-up ($\beta = -1.29$, $P = .001$). No significant differences in pain interference reduction were identified in the comparison between ACT and BATD at any assessment point.

Effects on Pain Intensity, Depressive, Anxiety, Stress Symptoms, and Pain Catastrophizing (Secondary Outcomes)

Descriptive statistics and between-group analyses for pain severity (NRS), depression-anxiety-stress (DASS-21), and pain catastrophizing (PCS) are shown in Table 4 according to the ITT approach. After applying the Benjamini-Hochberg correction, no significant differences in pain intensity, depressive and anxiety reductions were found at posttreatment and at 12-month follow-up for any pairwise comparison. Significantly greater reductions were detected in stress symptoms for ACT compared to TAU at posttreatment ($\beta = -2.74$, $P = .001$). Finally, significantly greater reductions were identified in pain catastrophizing for ACT compared to

Table 4. Descriptive Statistics and Between-Group Analyses for Primary and Secondary Outcomes and Process Variables (ITT Approach)

	ACTM (SD)	*BATDM (SD)*	*TAUM (SD)*	*ACT VS TAU*			*BATD VS TAU*			*ACT VS BATD*		
				D	*T (P)*	*B (95% CI)*	*D*	*T (P)*	*B (95% CI)*	*D*	*T (P)*	*B (95% CI)*
Primary outcome												
BPI-IS (0–10)*												
Baseline	6.71 (1.72)	6.46 (2.07)	6.49 (1.91)									
Posttreatment	4.89 (2.26)	5.03 (2.44)	5.84 (2.43)	.64	**−3.41 (.001)**	−1.22 (−1.93 to −.52)	.39	**−2.17 (.030)**†	−.81 (1.54 to −.08)	.20	1.08 (.281)	.41 (−.34 to 1.17)
Follow-up	5.30 (2.42)	5.07 (2.36)	6.42 (2.16)	.73	**−3.88 (< .001)**	−1.41 (−2.12 to −.69)	.66	**−3.48 (.001)**	−1.29 (−2.02 to −.56)	.01	.30 (.764)	.11 (−.64 to .86)
Secondary outcome												
NRS (0–10)*												
Baseline	6.88 (1.74)	6.54 (1.68)	6.95 (1.69)									
Posttreatment	5.96 (1.93)	5.54 (1.98)	6.03 (2.00)	.01	−.15 (.880)	−.05 (−.77 to .66)	.05	.07 (.943)	.03 (−.72 to −1.22)	.05	.21 (.833)	.08 (−.68 to .84)
Follow-up	6.16 (2.41)	6.91 (1.65)	6.74 (1.88)	.30	−1.95 (.052)	−.71 (−1.43 to .01)	.34	−1.32 (.189)	−.49 (−1.22 to .24)	.63	.57 (.568)	.22 (−.53 to .97)
DASS-21-A (0–21)*												
Baseline	5.85 (4.05)	5.87 (4.37)	5.81 (4.65)									
Posttreatment	3.92 (3.63)	3.90 (3.15)	5.61 (5.02)	.39	**−2.00 (.046)**†	−1.32 (−2.62 to −.02)	.39	−1.50 (.135)	−1.03 (−2.37 to .32)	.01	.42 (.677)	.29 (−1.09 to 1.68)
Follow-up	4.93 (4.58)	4.51 (4.11)	6.87 (5.52)	.45	−1.90 (.058)	−1.25 (−2.55 to .04)	.53	−1.80 (.072)	−1.22 (−2.54 to .11)	.10	.05 (.959)	.03 (−1.33 to 1.40)
DASS-21-D (0–21)*												
Baseline	7.29 (5.47)	6.77 (5.26)	7.62 (6.07)									
Posttreatment	5.27 (5.75)	4.67 (4.63)	7.28 (6.30)	.29	−1.80 (.073)	−1.53 (−3.20 to .14)	.31	−1.72 (.086)	−1.51 (−3.25 to .22)	.01	.01 (.988)	.01 (−1.77 to 1.79)
Follow-up	6.68 (5.94)	5.44 (5.08)	9.06 (6.51)	.35	−1.52 (.128)	−1.31 (−3.01 to .38)	.48	**−2.08 (.038)**†	−1.83 (−3.57 to −.10)	.13	−.57 (.565)	−.52 (−2.30 to 1.26)
DASS-21-S (0–21)*												
Baseline	9.31 (4.72)	8.92 (5.24)	8.82 (5.00)									
Posttreatment	6.04 (4.15)	7.74 (4.75)	8.91 (5.59)	.69	**−3.42 (.001)**	−2.74 (−4.32 to −1.17)	.25	−1.27 (.203)	−1.06 (−2.69 to .57)	.42	**1.97 (.049)**†	1.68 (.01–3.36)
Follow-up	8.00 (5.08)	7.92 (5.34)	9.60 (5.30)	.43	−1.50 (.133)	−1.22 (−2.82 to .37)	.35	−1.74 (.083)	−1.45 (−3.08 to .19)	.06	−.26 (.796)	−.22 (−1.90 to 1.46)
PCS (0–52)*												
Baseline	24.88 (11.74)	24.22 (11.75)	24.14 (12.82)									
Posttreatment	17.29 (13.17)	14.83 (10.06)	22.09 (13.38)	.45	**−2.47 (.014)**	−4.25 (−7.63 to −.87)	.59	**−3.35 (.001)**	−5.99 (−9.50 to −2.48)	.15	−.95 (.344)	−1.74 (−5.35 to 1.87)
Follow-up	17.41 (12.03)	16.74 (11.69)	23.98 (13.95)	.59	**−2.83 (.005)**	−4.81 (−8.16 to −1.47)	.59	**−3.09 (.002)**	−5.39 (−8.81 to −1.96)	.01	−.32 (.749)	−.57 (−4.10 to 2.95)
Process variables												
CPAQ-8 (0–48)*												
Baseline	18.08 (7.25)	19.14 (6.98)	18.53 (6.41)									
Posttreatment	20.27 (8.08)	19.67 (5.95)	18.36 (6.42)	.34	**3.03 (.003)**	2.91 (1.03–4.80)	.10	.73 (.464)	.73 (−1.23 to 2.69)	.23	**−2.13 (.034)**†	−2.18 (−4.20 to −.17)
Follow-up	19.41 (6.94)	18.90 (7.62)	16.94 (6.98)	.42	**3.06 (.002)**	2.90 (1.03–4.76)	.20	.55 (.580)	.54 (−1.37 to 2.45)	.22	**−2.36 (.019)**†	−2.36 (−4.33 to −.39)
BADS-SF (0–54)*												
Baseline	29.05 (10.44)	27.94 (8.81)	27.46 (9.59)									
Posttreatment	32.84 (11.10)	32.95 (10.19)	28.22 (10.85)	.30	**2.26 (.024)**	3.79 (.49–7.09)	.46	**2.31 (.021)**	4.01 (.60–7.42)	.13	.12 (.903)	.22 (−3.30 to 3.73)
Follow-up	31.89 (11.79)	32.41 (10.98)	27.36 (12.38)	.29	1.69 (.091)	2.91 (−.47 to 6.28)	.49	1.95 (.051)	3.43 (−.02 to 6.88)	.17	.29 (.771)	.52 (−3.02 to 4.07)

Table 4 (*Continued*)

	ACTM (SD)	BATDM (SD)	TAUM (SD)	ACT VS TAU			BATD VS TAU			ACT VS BATD		
				D	*T* (*P*)	*B* (95% CI)	*D*	*T* (*P*)	*B* (95% CI)	*D*	*T* (*P*)	*B* (95% CI)
PIPS (12–84)*												
Baseline	57.53 (16.92)	56.05 (15.14)	56.47 (16.64)									
Posttreatment	48.38 (15.27)	49.26 (13.98)	56.02 (15.25)	.52	**−4.55 (<.001)**	−9.63 (−13.79 to −5.47)	.40	**−2.48 (.013)**	−5.46 (−9.78 to −1.14)	.15	1.85 (.065)	4.17 (−.26 to 8.61)
Follow-up	51.50 (15.52)	50.23 (15.17)	56.70 (16.56)	.37	**−2.63 (.009)**	−5.59 (−9.77 to −1.41)	.38	−1.85 (.065)	−4.02 (−8.30 to .25)	.01	.70 (.485)	1.57 (−2.83 to 5.97)

Abbreviations: *B*, regression coefficients; CI, confidence interval; *d*, Cohen's *d* as an effect size measure; ITT, intention-to-treat; ACT, acceptance and commitment therapy; BATD, behavioral activation therapy for depression; TAU, treatment-as-usual; BADS- SF, Behavioural Activation for Depression Scale (short form); BPI-IS, Brief Pain Inventory-Interference Scale; CPAQ-8, Chronic Pain Acceptance Questionnaire; DASS-21, Depression Anxiety Stress Scales; PCS, Pain Catastrophizing Scale; NRS, Numeric Rating Scale; PIPS, Psychological Inflexibility in Pain Scale.
NOTE. The baseline level of the variable was controlled. M and SD are not adjusted.
*The baseline level of the variable is a significant covariate in the model.
†When the Benjamini-Hochberg correction was applied to correct for multiple comparisons, the following effects were no longer significant: ACT versus TAU in DASS-21-A (post $P = .069$); BATD versus TAU in BPI-IS (post $P = .090$) and in DASS-21-D (follow-up $P = .076$); ACT versus BATD in DASS-21-S (post $P = .294$) and in CPAQ-8 (post $P = .102$; follow-up $P = .056$). The number of participants varied across assessment periods due to dropouts (see flowchart). Significant values ($P < .05$) are shown in bold.

TAU at posttreatment ($\beta = -4.25$, $P = .014$) and at 12-month follow-up ($\beta = -4.81$, $P = .005$); and for BATD compared to TAU at posttreatment ($\beta = -5.99$, $P = .001$) and at 12-month follow-up ($\beta = -5.39$, $P = .006$). No significant differences in pain catastrophizing were found when comparing ACT and BATD.

Effects on Pain Acceptance, Behavioral Activation, and Psychological Inflexibility (Process Variables)

Table 4 shows descriptive statistics and between-group analyses for pain acceptance (CPAQ-8), behavioral activation (BADS-SF), and psychological inflexibility (PIPS) according to the ITT approach. After applying the Benjamini-Hochberg, significant differences were detected in pain acceptance in ACT compared to TAU at posttreatment ($\beta = 2.91$, $P = .003$) and at 12-month follow-up ($\beta = 2.90$, $P = .002$). No significant differences in pain acceptance were found when comparing BATD and TAU and ACT and BATD. Compared to TAU, ACT ($\beta = 3.79$, $P = .024$) and BATD ($\beta = 4.01$, $P = .021$) showed significant increases in behavioral activation at posttreatment. No significant differences in behavioral activation were found when comparing ACT and BATD. Finally, significantly greater reductions in psychological inflexibility were detected for ACT compared to TAU at posttreatment ($\beta = -9.63$, $P < .001$) and at 12-month follow-up ($\beta = -5.59$, $P = .009$). In addition, there were significantly greater reductions in psychological inflexibility for BATD compared to TAU at posttreatment ($\beta = -5.46$, $P = .013$). No significantly different reductions in psychological inflexibility were found in the comparison between ACT and BATD.

Number Needed to Treat

At posttreatment, a total of 35 patients (67.3%) in ACT, 19 patients (45.2%) in BATD, and 23 patients (35.9%) in TAU reached the criterion 1-point reduction in pain interference (ie, "responders"), with this difference being significant ($P = .003$). Baseline differences between responders and nonresponders were analyzed for all variables (see Supplementary Table 4). In both ACT and BATD, there were no significant differences between responders and nonresponders on sociodemographic or clinical variables. Regarding outcomes, nonresponders in the ACT group scored significantly lower than responders on baseline pain acceptance ($P = .041$, $d = .64$). No significant differences between responders and nonresponders were observed at posttreatment or at 12-month follow-up for any of the variables.

At posttreatment, the absolute risk reduction (ARR) in ACT versus TAU was 31.4% (95% CI 14–48.7%) with NNT = 4 (95% CI 2.1–7.1), meaning that 4 patients would need to be treated with ACT for one of them to become a responder, who would not have done so in the TAU group (see Supplementary Table 5). The ARR obtained with BATD versus TAU was 9.3% (95% CI −9.8 to 28.4%) with NNT = 11; in this case, because the 95% CI for the

ARR extends from a negative number (BATD may harm) to a positive number (BATD may benefit), the NNT result is unreliable. This means that it is not possible to say with 95% certainty whether BATD has no effect or is useful compared to TAU. Comparisons between ACT and BATD also indicated an unreliable NNT result.

At the 12-month follow-up, a total of 26 patients (59.1%) in ACT, 19 patients (48.7%) in BATD, and 13 patients (24.5%) in TAU reached the criterion 1-point reduction in pain interference ($P = .002$). A significant ARR was found for ACT versus TAU (AAR = 34.6%, 95% CI = 15.9–53.1%) with NNT = 3 (95% CI 1.9–6.3) and BATD versus TAU (AAR = 24.2%, 95% CI = 4.7–43.7%) with NNT = 5 (95% CI 2.3–21.3). Finally, comparisons between ACT and BATD showed an unreliable NNT result (see Supplementary Table 5).

Indirect Effects: the Role of Pain Acceptance, Behavioral Activation, and Psychological Inflexibility

Bivariate correlational analyses were calculated between baseline-follow-up differences in primary and secondary outcomes and pre-post-treatment differences in process variables within the ACT group (see Supplementary Table 6) and the BATD group (Supplementary Table 7). Only those variables showing significant correlations were considered in the subsequent path analyses. The results of the path analyses are detailed in Table 5 and Table 6 and illustrated in Fig 2 by a generic example.

Regarding ACT, 1 out of the 3 models with significant effects yielded indirect paths between the study arm and clinical outcome. Specifically, in the model for pain interference, ACT produced a change in psychological inflexibility ($P = .043$), which in turn was associated with a change in pain interference scores at follow-up ($P = .001$). As shown in Table 5, no indirect effects were identified for pain intensity and pain catastrophizing changes in their respective models.

Focusing on BATD, 1 out of the 2 tested models yielded significant indirect paths between the study arm clinical outcome. As shown in Table 6, in the model for pain interference, BATD produced reductions in psychological inflexibility at posttreatment ($P = .001$), which in turn predicted improvements in pain interference scores at follow-up ($P = .001$). In contrast, no indirect effects were found for pain catastrophizing in the model.

Table 5. Direct and Bootstrap Indirect Effects in the Mediational of ACT Versus TAU [Effects of Pre-to-post-changes in Process Variables on Pre-to-follow-up Changes in Primary and Secondary Outcomes]

	DIRECT EFFECTS				INDIRECT EFFECTS			
OUTCOME AND PROCESS VARIABLE (R^2)	PATH	COEFF.	SE	P	PATH	BOOT.	SE	95% CI
BPI-IS (.20)	a	−7.705	2.319	**.001**				
PIPS (.10)	b	.460	.096	**.001**	a × b	−3.542	1.310	−6.700 to −1.432
	c	−1.655	2.382	.487				
NRS (.07)	a	−7.705	2.313	**.001**				
PIPS (.10)	b	−.032	.018	.065	a × b	.250	.152	.040 to .682
	c	−1.011	.467	**.031**				
PCS (.06)	a	2.412	1.071	**.024**				
CPAQ-8 (.05)	b	−.325	.205	.113	a × b	−.785	.675	−2.654 to .062
	c	−3.384	1.946	.082				

Abbreviations: CI, confidence interval; BPI-IS, Brief Pain Inventory-Interference Scale; CPAQ-8, Chronic Pain Acceptance Questionnaire; PCS, Pain Catastrophizing Scale; NRS, Numeric Rating Scale; PIPS, Psychological Inflexibility in Pain Scale.
NOTE. A generic example of a multiple model (with 1 process variable) is displayed in Fig. 2. Significant values (*P < .05) are shown in bold.*

Table 6. Direct and Bootstrap Indirect Effects in the Models of BATD Versus TAU [Effects of Pre-to-post-changes in Process Variables on Pre-to-follow-up Changes in Primary and Secondary Outcomes]

	DIRECT EFFECTS				INDIRECT EFFECTS			
OUTCOME AND PROCESS VARIABLE (R^2)	PATH	COEFF.	SE	P	PATH	BOOT.	SE	95% CI
BPI-IS (.18)	a	−4.707	2.321	**.043**				
PIPS (.04)	b	.477	.102	**.001**	**a × b**	−2.247	1.348	−5.453 to −.150
	c	−1.355	2.488	.586				
PCS (.06)	a	−4.707	2.344	**.045**				
PIPS (.04)	b	.090	.131	.490	**a × b**	−.425	.712	−2.252 to .648
	c	−4.729	2.362	**.045**				

Abbreviations: CI, confidence interval; BPI-IS, Brief Pain Inventory-Interference Scale; PCS, Pain Catastrophizing Scale; PIPS, Psychological Inflexibility in Pain Scale.
NOTE. A generic example of a multiple model (with 1 process variable) is displayed in Fig. 2. Significant values ($P < .05$) are shown in bold.

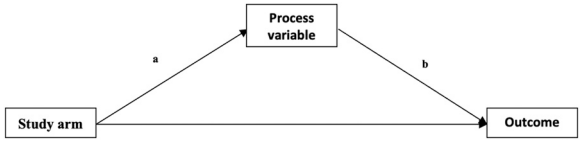

Figure 2. Generic example of a multiple direct and indirect effects model.

Other Clinical Results

Impression of Change

Regarding ACT, 3 patients (5.9%) felt "very much improved," 13 patients (25.5%) felt "much improved," 17 patients (33.3%) reported that they had "minimally improved," and 18 patients (35.3%) reported "no changes." No patient reported feeling worse. Focusing on BATD, only 1 patient (2.4%) felt "very much improved," 11 patients (26.8%) experienced "much improved," 17 patients indicated (41.5%) "minimal improvement," 11 patients (26.8%) reported feeling "no changes," and 1 patient felt "much worse" (2.4%). No significant between-group differences were identified in this analysis.

Most patients attending BATD groups felt improvement to some degree (minimal, much, or very much) in physical activities (43.9%), social activities (43.9%), and work-related activities (31.7%). Except in mood (68.6% vs 63.4% in BATD) and pain (25.4% vs 19.5% in BATD), ACT achieved lower percentages in the remaining areas: physical activities (41.2%), social activities (43.1%), and work-related activities (27.4%). These results are presented in Supplementary Table 8.

Credibility About the Interventions

Patients in the ACT and BATD arms, respectively, considered the therapy as highly recommendable ($M = 8.44$, $SD = 1.47$ vs $M = 8.17$, $SD = 1.62$). Moreover, after completing the sessions, ACT and BATD patients, respectively, showed high scores in knowing how to use the electronic device (phone, tablet, or computer) to receive non-face-to-face therapies ($M = 8.24$, $SD = 2.10$ vs $M = 8.60$, $SD = 1.52$) and the ability to follow this therapy via videoconference ($M = 8.78$, $SD = 1.49$ vs $M = 8.86$, $SD = 1.52$). The differences in scores for the 2 therapies were not significant.

Adverse Effects

In total, 6 patients in the ACT group and 2 in the BATD group reported unpleasant events at posttreatment. In the ACT group, 5 patients described increased emotional distress (depressive, anxiety, or stress symptoms) during body awareness exercises and 1 patient reported increased pain at the end of one therapeutic exercise. In the case of the BATD group, 2 patients mentioned an increase in depressive and anxiety symptoms after the end of the therapy sessions.

Discussion

This RCT examined the efficacy of adding a remote, synchronous, group, videoconference-based form of ACT or BATD to TAU for the psychological management of patients with CLBP plus comorbid depressive symptoms. In addition, the role of theoretically relevant process variables as facilitators of long-term clinical changes was analyzed. Compared to TAU, ACT yielded significantly greater improvements in pain interference (primary outcome) at posttreatment and at follow-up, and BATD yielded greater improvements than TAU at follow-up.

Significantly greater improvements were identified in pain catastrophizing (secondary outcome) in ACT and BATD, compared to TAU, at posttreatment and at follow-up. In addition, ACT showed significantly greater reductions in stress symptoms at posttreatment compared to TAU. Contrary to hypothesis 1, no significant differences in pain intensity, depressive, or anxiety symptoms were found in ACT and BATD compared to TAU at any of the time points. Previous systematic reviews provide evidence for the efficacy of Internet-based ACT in chronic pain patients in reducing pain intensity and emotional distress,[28,78] but with small effects. Treatment resistance associated with the combination of chronic pain and depression could be one of the explanations for the more moderate results obtained by this work compared to previous studies.[7,8]

According to Walsh et al,[9] BATD is a potentially useful treatment for patients with pain because it can help to reduce pain interference and other pain-related variables by its positive effects, namely by increasing self-efficacy (a sense of mastery), and experiencing rewards derived from carrying out actions and achieving goals. Although in this trial, BATD was effective for the improvement of pain interference, pain catastrophizing, behavioral activation, and psychological flexibility (variables relevant to the maintenance of pain-related disability), it did not have the expected effects in this population for decreasing depressive, anxiety, and stress symptoms.[9,24,32] Therefore, the results of the current study would suggest that the improvement in pain-related outcomes would not be as closely linked to the relief of negative symptoms (sadness, anxiety) as to the promotion of positive affectivity through cognitive and motivational mechanisms. Moreover, it is possible that the exceptional conditions under which the trial was developed (which forced a change in the format of delivery of interventions) had a greater impact on the success of BATD compared to ACT.

In addition, some differences observed in therapists' mastery, technological capabilities, and expectations about therapy in patients in favor of ACT could explain why the therapeutic results of BATD were more modest than those obtained with ACT. As far as it is known, the efficacy of BATD in a face-to-face and remote-delivered form had not been explored in patients with chronic pain and comorbid depression, so its effects should be further investigated in the future in other RCTs. Further evidence on the role of comorbidity between depression and chronic pain is needed to know more precisely the therapeutic potential of BATD. In any case, this future

research should clarify whether, as the results of this study suggest, improvements in pain-related outcomes are associated more with the positive than the negative effects of BATD on depression.

Overall, these findings are relevant because they indicate that pain interference and pain catastrophizing are moderately improved in both ACT and BATD compared to TAU, with small differences between the 2 active therapies. Notwithstanding this, some superiority of ACT over BATD and TAU was observed in the proportion of responders (67% vs 45% vs 35%, respectively) and clinically relevant NNT values at posttreatment compared to TAU (NTT = 4). In the same way, differences in the proportion of responders (59% vs 49% vs 24%) were in favor of ACT compared to BATD and TAU at 12 months follow-up. Furthermore, clinically relevant NNT values at 12 months follow-up were observed in ACT (NTT = 3) and BATD (NTT = 5) compared to TAU. It is important to highlight that nonresponders in the ACT group scored significantly lower than responders at baseline in pain acceptance. There were no significant differences between responders and nonresponders in BATD regarding sociodemographic, clinical or outcomes variables.

Retention in trial at posttreatment and at 12-month follow-up was lower than expected in ACT (about 67 and 56%, respectively) and BATD (about 54 and 50%, respectively) and higher than expected in TAU (about 82 and 68%, respectively). Moreover, the dropouts were significantly higher in BATD compared to ACT at posttreatment, although no differences were identified in the clinical improvement perceived by patients in both groups. The dropouts were significantly higher in the third (May to July 2021) than in the first and second waves of the RCT, when mobility restrictions due to the COVID-19 pandemic were relaxed and the preholiday period began in Spain. The adherence problems identified are consistent with those reported in Internet or remote-delivered therapies in patients with chronic pain and psychological distress.[79-81] Furthermore, as indicated in a qualitative study nested within this RCT,[46] barriers identified by these patients such as losing face-to-face contact, missing out on different physical intervention spaces, leaving home, and moments of informal socialization, may have affected their engagement, attendance, and adherence to therapies. Although the benefits of this format are identified (eg, ease of access, flexibility, avoidance of the need to travel, and resources savings), there is a need to improve the technical and social aspects of implementing videoconferencing-based therapies, as well as to strengthen guidelines for adequate support for patients and therapists.[46]

Consistent with hypothesis 2, significant differences were found in decreased psychological inflexibility and increased pain acceptance in ACT[38-40] both at posttreatment and at 12 months follow-up; and in improved behavioral activation in BATD[38] at posttreatment. However, unexpected significant differences were identified in increased behavioral activation in ACT and improved psychological inflexibility in BATD at posttreatment. Changes in pain interference at follow-up were associated with changes in psychological inflexibility in ACT.[39,40,82] Even though BATD is not based on the psychological flexibility model, in this sample changes in pain interference were also related to increases in psychological inflexibility.

Regarding this finding, psychological inflexibility has been found as a nonspecific contributor of the effects of new forms of CBT.[83-86] Thus, this indirect effect may be because "third-wave" psychotherapies commonly address some facets that overlap with the primary components (eg, mindfulness, acceptance, values, goals, and defusion) of psychological flexibility, as reported in a recent systematic review.[40] Committed action and values are at least implicit aspects in more recent forms of CBTs, including but not limited to ACT, Mindfulness-Based Cognitive Therapy, Behavioral Activation, Motivational Interviewing, and Solution-Focused Brief Therapy. All these therapies have in common a focus on helping individuals identify and align their actions and values with their goals and desires and develop strategies for making meaningful changes in their lives.

There are some potential reasons for the loss of efficacy of ACT and BATD in the long term, such as the fact that patients were no longer attending weekly group treatment, reduction of programmed home exercises in both therapies, and possible interferences generated by the COVID-19 pandemic. Specifically, 41% of patients in ACT and 38% in BATD received 4 or fewer sessions (out of 8), making it difficult to perform an accurate analysis of the short- and long-term effects of both therapies under optimal adherence conditions. As reported in a meta-analysis,[87] it is possible that the outcomes of home-practice therapies, such as ACT, BATD, and other forms of CBT, decrease according to patients' frequency of practice. It would be interesting for future research to explore how improving the frequency and assessment of practice in both therapies, which in this RCT was not systematically monitored, could be beneficial for better outcomes. Smartphones are increasingly being included as clinical resources to help address this issue.[85,88] Also, the practice of skills outside the group has been highlighted as a relevant element to improve outcomes in this type of therapy.[87]

The direct and indirect health problems generated by the COVID-19 pandemic are relevant to consider.[10,19,23] This context, combined with the technical and social difficulties related to the implementation of Internet-based therapies,[79] may also have contributed to the decrease in attendance and adherence and, in turn, to the relative loss of overall effects. Even though patients received continuous and personalized technical support, new models of using remote telehealth technologies are needed to help improve the coordination of pain management services and facilitate meaningful patient engagement.[15] In this sense, the implementation of remote synchronous video group form therapies in public healthcare requires improving access to the necessary resources (a private place, an adequate Internet connection, and a suitable device) and facilitating greater technical support for patients and therapists, especially those without prior technical experience.[20,29]

Although the therapists delivering the ACT and BATD modules (3 different therapists per active group) were

trained prior to the start of the RCT, in this study it was not possible to conduct an external assessment of the therapist fidelity and competence due to budget limitations. Therapists in this RCT were selected for their expertise, both in group and individual formats, and received technical support from the research team to adapt their interventions to a videoconferencing format. Furthermore, aspects related to implementation in routine clinical practice were considered in this selection, so that therapists with different years of experience in the therapy and age profiles were included. In terms of expectancy and credibility about therapy, no differences were identified between therapists or groups. In line with some research, future studies should continue to explore the potential role of the therapist profile in improving outcomes.[89,90]

Side effects are often not assessed in RCTs of psychological therapies, but some exercises such as focus on the present moment sometimes can have adverse effects.[91] Some common side effects of ACT include an increased awareness of one's thoughts and emotions, which can initially lead to increased discomfort or distress. However, this is typically short-lived, and over time, individuals typically report decreased distress. In this RCT, 6 participants in the ACT and 2 in the BATD groups reported emotional discomfort related to the therapeutic exercises. Adverse effects related to body awareness or behavioral activation exercises in this population should be further investigated. Specifically, more information is required on the potential impact these effects might exert on adherence and dropouts from both therapies. Finally, it may be necessary to take an individualized approach to adverse effects detected in the therapies administered in group format, including during the intervention sessions, to prevent possible dropouts and improve group adherence.

These findings should be interpreted with the following limitations in mind. First, as mentioned, there was no external assessment of treatment fidelity and therapist competence. Second, treatment adherence in home exercises was not specifically monitored. Third, the inclusion of a random intercept in the GLM was necessary in this study to consider within-group variability; however, estimating this intercept in patients with only one data point could partially lead to overfitting the model. Fourth, the dropout rate was higher than expected, which could have an impact on an accurate analysis of the short- and long-term effects of both therapies under optimal adherence conditions. Specifically, due to the low retention rate at follow-up, path analyses based on change scores were probably underpowered to detect some small indirect effects.

Conclusions

This 12-month, multicenter, single-blind RCT has demonstrated the clinical utility of including remote synchronous video group-based ACT or BATD as adjuncts to usual care for the improvement of pain interference (primary outcome) and pain catastrophizing (secondary outcome) at posttreatment and at 12-month follow-up in patients with CLBP plus comorbid depressive symptoms. Unexpectedly, no significant differences in depressive or anxiety symptoms were found in ACT and BATD compared to TAU at any of the time points. The superiority of ACT versus BATD and TAU was only detected by the significant difference in the proportion of responders at posttreatment and at follow-up. However, no significant differences in any outcome were identified between the 2 active arms. Finally, the reported attrition rates emphasize the importance of finding strategies to increase retention and adherence in therapies delivered via videoconferencing in this type of population. Even though this study was initially designed to deliver the therapies in a face-to-face format, the benefits identified in distance delivery suggest that it is an effective solution that transcends a temporary need generated by the COVID-19 pandemic.

Author Contributions

JPS-M: Data curation, software, formal analysis, methodology, visualization, and writing the original draft. **SE** and **AS:** Methodology, supervision, and writing – review & editing. **AC-C**, **JRC-A**, **LMM**, **JM-M**, **AP-A**, **XB**, and **AF-S:** Writing – review & editing. **JVL**: Conceptualization, funding acquisition, investigation, project administration, methodology, formal analysis, supervision, writing – review & editing.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jpain.2023.04.008.

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