

Cognitive-behavioral therapy and acceptance and commitment therapy for anxiety and depression in patients with fibromyalgia: a systematic review and meta-analysis

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Abstract

Introduction. Defined by chronic, musculoskeletal pain, fibromyalgia is often comorbid with depression and anxiety. In these cases, the first line medical treatment can be successfully combined with psychological interventions. Cognitive-behavioral therapy and acceptance and commitment therapy are among the most widely studied approaches in relation to chronic pain, including fibromyalgia. The objective of this review is to analyze the efficiency of these psychological treatments for alleviating emotional distress in fibromyalgia.

Method. The search was conducted on the PubMed, Scopus and Web of Science online databases. Clinical trials that fulfilled eligibility criteria were included in this review. A meta-analysis was performed on depression and anxiety scores at post-test. Heterogeneity was assessed using the Chi2 and I2 indicators. For evaluating publication bias, we resorted to a funnel plot graph.

Results. A total of 17 reports were selected, among which 4 articles studied the efficiency of acceptance and commitment therapy. Main demographic characteristics were homogenous throughout the included samples. The overall effect was -0.31 (95% CI: -0.47 to -0.15) for depression, and -0.15 (95%: -0.29 to -0.02), reaching statistical significance.

Conclusions. Both psychological interventions proved to be efficient for decreasing depression and anxiety in fibromyalgia. For this reason, we believe psychotherapeutic protocols can be reliably implemented within multicomponent treatments, facilitating emotional adjustment in the context of physical disability and pain. Future research directions include the exploration of change processes and multiple moderators, enabling the development of tailored psychological treatments in fibromyalgia.

Keywords: fibromyalgia, depression, anxiety, psychotherapy, cognitive-behavioral therapy, acceptance and commitment therapy

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DOI: 10.15386/mpr-2661

Manuscript received: 04.08.2023 Accepted: 31.10.2023

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Introduction

Fibromvalgia represents а rheumatologic condition characterized by chronic, widespread pain, of varying severity [1]. Other common symptoms include fatigue, weakness, sleep problems, and reduced cognitive functioning [2]. The prevalence of this medical condition in the general population was estimated between 1.7% and 5.4%, presenting an increased frequency among women [3]. Given its multiple implications for the quality of life, besides the numerous physical comorbidities, emotional disorders such as depression and anxiety are frequently co-occurring with fibromyalgia [4]. The first line pharmacological treatment for fibromyalgia involves the administration of antidepressants (e.g., Duloxetine, Milnacipran), anticonvulsants (e.g., Pregabalin), muscle relaxants, analgesics, but also hypnotic (e.g., Zolpidem) or antipsychotic drugs like Quetiapine [5].

Along with the recommended medical treatment, several psychological interventions proved to be successful in the management of fibromyalgia [6]. Particularly, cognitive-behavioral therapy (CBT), which emphasizes the role of thoughts in the occurrence of emotions and behaviors, accumulated a large body of evidence in terms of its efficiency for treating various psychopathologies [7]. Interventions based on CBT were found to be successful in chronic pain conditions, including fibromyalgia and cooccurring anxiety and depression [8,9]. Specifically, CBT strategies in fibromyalgia target pain catastrophizing, defined as a common cognitive error contributing to the onset of emotional disorders, by exacerbating potential consequences of the pain sensation [10,11]. In addition, acceptance and commitment therapy (ACT) is a new generation CBT approach aiming to decrease rigid behavioral patterns, while improving psychological flexibility as a healthier alternative for dealing with prolonged pain and disability [12,13]. In this approach, the tendency to avoid unpleasant internal experiences or various activities due to pain-related fear, called experiential avoidance, is replaced with the development of pain acceptance, together with the promotion of valuesbased action [14]. Moreover, important objectives in ACT interventions focus on mindfulness skills, by improving present moment awareness, as well as cognitive defusion strategies that concentrate on changing one's attitude towards own thoughts and facilitate an observer's perspective towards distressing cognitive content [15]. When applied within the chronic pain population and fibromyalgia, ACT strategies were found to decrease disability and depression scores, while increasing pain acceptance [16].

To date, research demonstrated the efficiency of CBT and ACT intervention either separately, or integrated within combined and multicomponent treatment protocols [17,18]. Importantly, benefits in terms of wellbeing and

treatment adherence were maintained, regardless of the format in which the psychotherapy was delivered [19,20]. Furthermore, there is promising evidence related to the ratio between costs and effectiveness of psychological approaches in fibromyalgia, emphasizing their health economic utility and role within an integrated medical care paradigm [21]. Although both CBT and ACT interventions were reliably applied in patients with fibromyalgia syndrome, their implications for anxiety and depression entail further exploration. In this way, the objective of this review and meta-analysis is to analyze the effectiveness of standard CBT and ACT interventions for patients with fibromyalgia, focusing on correlated anxiety and depressive symptoms.

Method

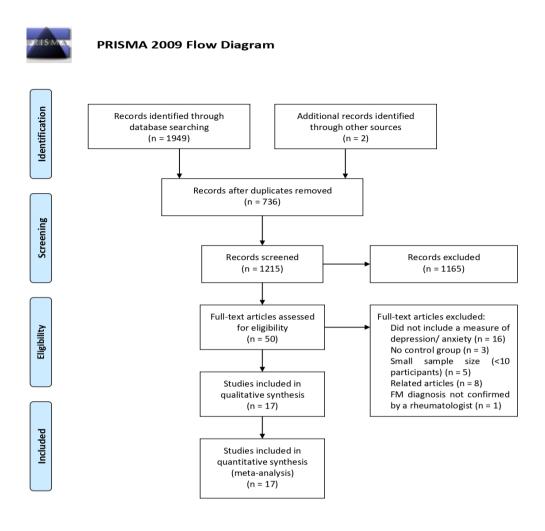
The present research was conducted according to the revised Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2009 checklist, as well as the Cochrane Collaboration guidelines for systematic reviews of interventions [22,23]. The review protocol was registered on the PROSPERO database, with the ID number CRD42022354119.

Eligibility criteria

Inclusion criterion for selected articles were the following: (1) randomized clinical trials written in English language and available in a full text format; (2) sample comprised of adults with a diagnosis of fibromyalgia established by a specialized physician (i.e, rheumatologist), according to the American College of Rheumatology Criteria [24] in use at the time when the research was performed; (3) studies including at least 10 participants; (4) the efficiency of standard CBT and ACT protocols, delivered individually or in a group format, as well as using various modalities (e.g., face-to-face, telephonic, or online delivery) was investigated; (5) a control group was involved; (6) a measure of depression and/or anxiety symptom severity was used. Exclusion criteria were : (1) samples that involved children and adolescents, adults with severe cognitive impairment and/ or severe psychiatric disorders (i.e. psychotic disorders); (2) articles with a single-subject design or case reports; (3) studies that did not include a control group; (4) no measure of anxiety/depression symptom severity; (5) not available full-text in English language; (6) the diagnosis of fibromyalgia was not confirmed by a rheumatologist.

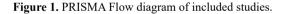
Search strategy, selection process and data extraction

We searched reports on the electronic databases PubMed, Scopus and Web of Science, the last search being conducted in March 2023. The keywords "fibromyalgia" AND "cognitive behavioral therapy", along with "fibromyalgia" AND "acceptance commitment therapy" were used. Articles published from January 2020 to the present were considered.



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting /tems for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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Additionally, our search involved the Association for Contextual Behavioral Science (ACBS) website [25] for identifying articles on ACT interventions for fibromyalgia, using the same keywords.

The selection of studies involved a screening phase, when two of the review authors independently screened the titles and abstracts. If abstracts did not include enough information to document a further decision, the articles were extensively read. Reports considered eligible after screening were subjected to further independent assessment by the same review authors. Any disagreement was resolved through discussion, and the involvement of a third review author, when necessary. Extracted data from each study included the sample characteristics (number of participants, age, gender), intervention type and duration, control group, and specific measures of depression and/ or anxiety.

Risk of bias assessment, summary measures and synthesis of results

The risk of bias was assessed at the study level based on the major domains integrated within the Cochrane Collaboration's tool [26]. According to existing recommendations concerning the specificity of the psychotherapeutic treatment, we did not assess the risk of bias related to "blinding participants and personnel" [27,28]. Specific outcomes analyzed were the effect of CBT and ACT interventions on depression and anxiety scores at post-test. We performed a meta-analysis on these results using the Review Manager (RevMan) software, version 5.4, obtaining an overall effect estimate by calculating standardized mean differences (SMD) based on the means and standard deviations reported in each study. When an article reported multiple measures for the same variable, we selected the measures treated as primary outcomes in the original research. For incomplete results, we used the Intention-to-Treat (ITT) data, if available. Also, when there was an active comparison group involving an alternative intervention in addition to a passive condition, we integrated data based on the active group in our analysis. Heterogeneity was established by using the Chi² and I² indicators. For addressing potential heterogeneity, the random effect model was applied in this meta-analysis. Funnel plots were inspected for evaluating publication bias related to the effect of psychological interventions on depressive symptoms at post-test, with all included studies reporting this outcome.

Results

Main characteristics of included studies

The flow diagram of the screening process is represented in Figure 1. Our search resulted in 1951 articles that were subsequently screened for meeting the eligibility criteria. After the selection process, 17 studies were included in this review and meta-analysis, comprising a total number of 1499 participants diagnosed with fibromyalgia. Among individual articles, sample sizes varied from 31 to 230 participants that shared similar socio-demographic particularities in terms of age, gender, occupational and marital status. Among the included references, 13 applied CBT [29-41], while 4 implemented ACT protocols [42-45]. The mean duration of interventions was 10 sessions / modules, lasting for an average of 95 minutes, depending on the delivery format. Regarding the comparison groups, 11 studies implemented an active group consisting of an alternative psychological intervention, prescribed medical treatment, or educational programs. The main characteristics of included studies are summarized in table I.

Table I. Characteristics of included studies.

Reference	N	Age (M,SD)	Gender (% Women)	Intervention ^a	Duration	Control ^a	Follow-up	Depression ^b	Anxiety ^b
Aguilera et al. (2022)	106	54.5 (9)	100%	Hybrid CBT	18 sessions/ 60 minutes	Active (PCT)	6-month	HADS	HADS
Alda et al. (2011)	169	46.83 (6.49)	94%	Group CBT	10 sessions/ 90 minutes	Active (RPT) + Passive (TAU)	3- and 6-month	HRSD	HARS
Ang et al. (2013)	58	46.59 (10.39)	93%	Telephone- delivered CBT	8 sessions/ 35 minutes	Active (RPT + Education)	9- and 21- week	PHQ-9	-
Falcao et al. (2008)	60	45.67 (11.09)	100%	Group CBT	10 sessions	Passive (UMC)	3-month	BDI-II	STAI
Friesen et al. (2017)	60	48 (11)	95%	Online CBT	5 modules	Passive (WL)	1-month	PHQ-9; HADS	GAD-7; HADS
Govillard et al. (2022)	88	50.16 (9.13)	100%	Group CBT	10 sessions/ 75 minutes	Active (Biofeedback) + Passive (WL)	6-month	SCL-90-R	SCL-90-R
Jensen et al. (2012)	43	45.6 (6.4)	100%	Group ACT	12 sessions/ 90 minutes	Passive (WL)	3-month	BDI-II	STAI
Karlsson et al. (2015)	48	48.55 (9)	100%	Group CBT	20 sessions/ 180 minutes	Passive (WL)	12-month	MADRS	-
Lami et al. (2018)	126	50.19 (8.24)	100%	Group CBT for Insomnia	9 sessions/ 90 minutes	Active (CBT for Pain) + Passive (UMC)	3-month	SCL-90-R	SCL-90-R
Luciano et al. (2014)	156	48.31 (5.84)	96%	Group ACT	8 sessions/ 150 minutes	Active (RFT) + Passive (WL)	6-month	HADS	HADS
Lumley et al. (2017)	230	49.13 (12.22)	94%	Group CBT	8 sessions/ 90 minutes	Active (EAET + Education)	6-month	CES-D	GAD-7
Martínez et al. (2014)	64	47.58 (6.82)	100%	Group CBT for Insomnia	6 sessions/ 90 minutes	Active (SH Education)	3- and 6-month	SCL-90-R	SCL-90-R
McCrae et al. (2019)	113	53 (10.9)	97%	Individual CBT for Insomnia	8 sessions/ 50 minutes	Active (CBT for Pain) + Passive (WL)	6-month	BDI-II	STAI
Miró et al. (2011)	31	46.45 (7.03)	100%	Group CBT for Insomnia	6 sessions/ 90 minutes	Active (SH Education)	-	HADS	HADS
Redondo et al. (2004)	40	Not provided	100%	Group CBT	8 sessions/ 150 minutes	Active (PE)	6- and 12-month	BDI-II	BAI
Simister et al. (2018)	67	39.7 (9.36)	95%	Online ACT	6 modules	Passive (TAU)	3-month	CES-D	-
Wicksell et al. (2013)	40	45.1 (6.6)	100%	Group ACT	12 sessions/ 90 minutes	Passive (WL)	3-month	BDI-II	STAI

^aAbbreviations for interventions and control groups: CBT, Cognitive-Behavioral Therapy; ACT, Acceptance and Commitment Therapy; PCT, Personal Construct Therapy; RPT, Recommended Pharmacological Treatment; TAU, Treatment as Usual; UMC, Usual Medical Care; WL, Waitlist; EAET, Emotional Awareness and Expression Therapy; SH, Sleep Hygene; PE, Physical Exercise.

^bAbbreviations for measures of depression and/ or anxiety symptom severity: HADS, Hospital Anxiety and Depression Scale; HRSD, Hamilton Rating Scale for Depression; HARS, Hamilton Anxiety Rating Scale; PHQ-9, Patient Health Questionnaire-9; BDI-II, Beck Depression Inventory; STAI, State-Trait Anxiety Inventory; GAD-7, Generalized Anxiety Disorder-7; SCL-90-R, Symptom Checklist-90-Revised; MADRS, Montgomery-Asberg Depression Rating Scale; CES-D, Center for Epidemiologic Studies Depression Scale.

Risk of bias in selected studies

Two independent review authors investigated the risk of bias for each report, any serious discrepancy that was not solved through discussion implying the participation of a third review author. The assessment for each domain is depicted in figure 2. The majority of evidence stems from studies with an unclear overall risk of bias. The domain with the lowest risk of bias was "selective reporting", most articles providing data for all included outcomes. Conversely, "incomplete outcome data" was the domain that presented the highest risk of bias in our review, pointing to an increased attrition rate in relation to psychological interventions.

Meta-analysis

The summary effect of CBT/ACT interventions on the intensity of depressive symptoms was -0.31 (95% CI: -0.47 to -0.15), Z = 3.72, p = 0.0002, indicating a statistically significant impact of the psychological treatments. As shown in figure 3, individual effect sizes were significant in 3 studies implementing a passive control condition. As expected, heterogeneity measured by I² was 42%, and Chi² = 27.64 (df = 16), p = 0.03, indicating considerable variability among outcome reports.

Regarding the severity of anxiety symptoms, the overall effect of CBT/ACT interventions was -0.15 (95%: -0.29 to -0.02), Z = 2.18, p = 0.03, also proving a statistically significant, but weaker general efficiency of psychotherapy. The individual improvement was substantial in one study comparing a CBT protocol with an educational program (Figure 4). Our analysis did not indicate a substantial heterogeneity among studies, with $I^2 = 11\%$, and $Chi^2 = 14.62$, df = 13, p = 0.33.

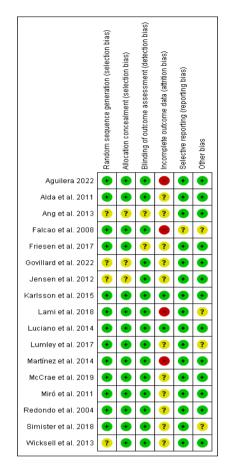


Figure 2. Risk of bias summary.

	C	BT/ACT		0	Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Aguilera et al. 2022	8.54	4.81	55	8.77	4.45	51	8.1%	-0.05 [-0.43, 0.33]	
Alda et al. 2011	7.78	2.46	57	7.98	1.8	56	8.3%	-0.09 [-0.46, 0.28]	
Ang et al. 2013	3.19	1.11	15	2.93	1.07	17	4.0%	0.23 [-0.46, 0.93]	
Falcao et al. 2008	7.56	7.71	25	13.96	11.37	26	5.3%	-0.65 [-1.21, -0.08]	
Friesen et al. 2017	10.13	5.3	25	14	5.44	27	5.3%	-0.71 [-1.27, -0.15]	
Govillard et al. 2022	1.88	0.86	32	1.86	0.92	20	5.4%	0.02 [-0.54, 0.58]	
Jensen et al. 2012	11	5	19	16	10	15	4.0%	-0.64 [-1.34, 0.05]	
Karlsson et al. 2015	14.75	7.96	23	14.79	6.37	24	5.2%	-0.01 [-0.58, 0.57]	
Lami et al. 2018	2.03	0.96	27	1.68	0.98	27	5.6%	0.36 [-0.18, 0.89]	
Luciano et al. 2014	8	2.88	51	9.04	3.68	52	8.0%	-0.31 [-0.70, 0.08]	
Lumley et al. 2017	16.35	11.44	75	19.62	12.1	79	9.4%	-0.28 [-0.59, 0.04]	
Martínez et al. 2014	1.63	0.84	30	2.29	0.77	29	5.7%	-0.81 [-1.34, -0.28]	
McCrae et al. 2019	8.52	11.12	39	15.58	10.68	37	6.7%	-0.64 [-1.10, -0.18]	
Miró et al. 2011	9.65	4.39	20	11.3	4.61	20	4.6%	-0.36 [-0.98, 0.27]	
Redondo et al. 2004	15.4	8.8	21	16.8	10.2	19	4.7%	-0.14 [-0.77, 0.48]	
Simister et al. 2018	17.76	10.83	27	26.97	10.46	31	5.6%	-0.85 [-1.39, -0.31]	
Wicksell et al. 2013	11.7	6	20	14.8	7.8	16	4.2%	-0.44 [-1.11, 0.22]	
Total (95% CI)			561			546	100.0%	-0.31 [-0.47, -0.15]	•
Heterogeneity: Tau ² =	0.05; Ch	i² = 27.6	64.df=	16 (P =	0.03); l ^a	²= 42%	5		
Test for overall effect: J			•						-2 -1 U 1 Favours [CBT/ACT] Favours [control]

Figure 3. Forest plot of Standardized Mean Difference (SMD): CBT/ACT interventions versus Control conditions on the severity of depressive symptoms in fibromyalgia.

CBT/ACT				Control			9	Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Aguilera et al. 2022	10.37	4.72	55	10.41	4.74	51	10.6%	-0.01 [-0.39, 0.37]	_
Alda et al. 2011	7.09	2.96	57	7.11	2.39	56	11.2%	-0.01 [-0.38, 0.36]	_
Falcao et al. 2008	46.6	3.05	25	46.65	3.35	26	5.6%	-0.02 [-0.56, 0.53]	
Friesen et al. 2017	9.22	4.33	25	10.43	4.69	27	5.6%	-0.26 [-0.81, 0.28]	
Govillard et al. 2022	1.56	1.07	32	1.26	0.87	20	5.4%	0.30 [-0.27, 0.86]	_
Jensen et al. 2012	40	12	19	47	13	15	3.6%	-0.55 [-1.24, 0.14]	
Lami et al. 2018	1.68	1.05	27	1.37	0.91	36	6.6%	0.31 [-0.19, 0.82]	
Luciano et al. 2014	8.28	2.38	51	9.07	2.19	52	10.3%	-0.34 [-0.73, 0.05]	
Lumley et al. 2017	6.23	5.19	75	7.18	5.16	79	14.3%	-0.18 [-0.50, 0.13]	
Martínez et al. 2014	1.23	0.79	30	1.62	0.92	29	6.2%	-0.45 [-0.97, 0.07]	
McCrae et al. 2019	38.95	12.72	39	45.22	12.12	37	7.8%	-0.50 [-0.96, -0.04]	
Miró et al. 2011	10.95	4.26	20	11.55	3.84	20	4.5%	-0.15 [-0.77, 0.48]	
Redondo et al. 2004	23.3	11.9	21	22.3	11.3	19	4.5%	0.08 [-0.54, 0.71]	
Wicksell et al. 2013	40.8	12.3	20	47.6	14.4	16	3.9%	-0.50 [-1.17, 0.17]	
Total (95% CI) 496 483 100.0% -0.15 [-0.29, -0.02								-0.15 [-0.29, -0.02]	•
Heterogeneity: Tau ² =	0.01: Ch	i ² = 14.6	62. df=	13 (P =	0.33); P	²= 11%	,		
Test for overall effect: $Z = 2.18$ (P = 0.03)									
			-7						Favours [CBT/ACT] Favours [control]

Figure 4. Forest plot of Standardized Mean Difference (SMD): CBT/ACT interventions versus Control conditions on the severity of anxiety symptoms in fibromyalgia.

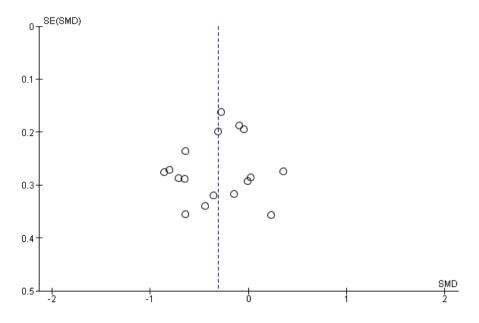


Figure 5. Funnel plot of depression scores at post-treatment. SE, Standard Error; SMD, Standardized Mean Difference.

The funnel plot of depression scores at post-treatment permitted us to evaluate publication bias in this metaanalysis. The horizontal axis depicts the standardized mean difference and the vertical axis indicates the standard error, or precision of the results, while the central line represents the pooled effect size (Figure 5). Given the symmetrical distribution of studies above and below the overall effect size, we assumed a reduced likelihood of publication bias and an accurate estimation of improvements associated with CBT/ACT psychological interventions, according to selected articles.

Discussion

The majority of trials included in this review and meta-analysis involved CBT protocols, applying specific techniques like cognitive restructuring, planning behaviors according to important personal goals, relaxation and coping skills training. At the same time, newer generation ACT interventions facilitate psychological flexibility in fibromyalgia patients, by focusing on pain acceptance, mindfulness, cognitive defusion and action plans based on personal values. The main difference between the CBT and ACT paradigms refers to a transition from cognitive modification to a selection of an appropriate response in a challenging life context, which may address the specific needs of fibromyalgia patients [13,46]. The discrepancy in the quantity of identified research papers could be associated to the temporal emergence of the two interventions, the CBT approach presenting a longer tradition and wellestablished efficiency within the chronic pain population [47]. However, this also highlights the idea that ACT interventions require further exploration in patients with fibromyalgia and comorbid emotional disorders.

Despite this imbalance related to the number of reports on CBT compared to ACT interventions, we demonstrated that both approaches are efficient in the treatment of depressive and anxiety symptoms in fibromyalgia. This is in line with previous research showing that CBT and ACT interventions are associated with moderate improvements for emotional symptoms in fibromyalgia patients [28,48,49]. Also, our findings are concordant with other reviews that outlined the benefits of psychological treatment in various formats, especially online CBT and ACT programs [50,51].

Interestingly, we observed that interventions with a narrower focus, such as reducing sleeping problems, proved to be highly useful for treating anxiety symptoms. In the same light, it has been proven that CBT treatments for insomnia may result in the improvement of general wellbeing and mental health difficulties in fibromyalgia [52]. In this way, we believe that the development of tailored psychotherapeutic programs for fibromyalgia patients with different patterns of depressive and anxiety symptoms would be a promising future direction.

From a clinical perspective, we discuss that the implementation of CBT/ACT interventions could be especially useful for optimizing medication doses according to the severity of symptoms, in terms of adjusting pharmacological treatments for both the physical features of fibromyalgia, and the associated emotional disorders [46,54,55].

Limitations and implications for future research

This research has several methodological limitations. First, we included studies with homogenous sample characteristics, which does not allow the generalizability of our findings to the entire population of fibromyalgia patients experiencing anxiety and depression symptoms. Since there is evidence that some particularities, such as age, may differentiate outcomes following CBT and ACT interventions [53], we suggest that broadening the range of inclusion criteria could advance knowledge in this field. Second, the exploration of change processes, like the reduction of pain catastrophizing in CBT, along with the increase of pain acceptance in ACT, was beyond the scope of our analysis, as only few included studies reported these outcomes. Future investigations could address such aspects in detail, by highlighting the relation between change mediators and modification in emotional distress. Third,

we did not include studies on the effects of multimodal treatments, integrating CBT and ACT strategies within complex interventions that address multiple components, including pharmacological treatment and physical therapy. A direction for further analyses would be to study the impact of such interventions on symptoms of depression and anxiety in fibromyalgia. Finally, different outcomes of psychological treatments in fibromyalgia patients could be targets of future reviews, such as their association with treatment adherence, lifestyle modification, or problematic behaviors related to medication consumption.

Conclusions

This review outlined the efficiency of CBT and ACT interventions for reducing emotional distress associated with fibromyalgia. All included studies reported the effects on the intensity of depressive symptoms, and the majority of articles investigated the change of anxiety symptoms severity following psychotherapy, obtaining a modest to moderate overall effect size. We consider that both CBT and ACT techniques can be reliably applied in integrated care programs for improving the quality of life in fibromyalgia, with the possibility of adjusting psychological interventions according to the particularities of various patient groups. Finally, the implementation of CBT/ACT interventions in clinical practice could be particularly useful for the augmentation of the standard medical treatment in fibromyalgia associated with emotional disorders.

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