



REVIEW ARTICLE

# Acceptance, Cognitive-Behavioural and Mindfulness-Based Psychological Interventions for Fibromyalgia: A Systematic Review

Seán Heaney MSc<sup>1</sup>, Nicola Adams PhD\*<sup>2</sup>

<sup>1</sup> Cooldorragha, Portumna, Co. Galway, Ireland H53 FY96

<sup>2</sup> Health and Life Sciences, Northumbria University, Newcastle-upon-Tyne NE7 7XA, UK.

\* [nicola.adams@northumbria.ac.uk](mailto:nicola.adams@northumbria.ac.uk)



OPEN ACCESS

## PUBLISHED

31 July 2024

## CITATION

Heagney, S. and Adams, N., 2024. The Article Acceptance, Cognitive-Behavioural and Mindfulness-Based Psychological Interventions for Fibromyalgia: A Systematic Review, Archives, [online] 12(7). <https://doi.org/10.18103/mra.v12i7.5242>

## COPYRIGHT

© 2024 European Society of Medicine. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

## DOI

<https://doi.org/10.18103/mra.v12i7.5242>

## ISSN

2375-1924

## ABSTRACT

**Objective:** To analyse the effectiveness of cognitive-behaviour therapy (CBT), acceptance and commitment therapy (ACT), and mindfulness-based stress reduction (MBSR), for treating symptoms of fibromyalgia.

**Methods:** PubMed, Cochrane and Science Direct electronic libraries were searched (from January 2015 to October 2023). Randomised controlled trials (RCTs), of CBT, ACT, and MBSR-based interventions for pain intensity, pain catastrophising, depression, anxiety, sleep quality, fatigue and health-related quality of life in people diagnosed with fibromyalgia were considered. Studies were selected and data was extracted by two independent reviewers using the Template for Intervention Description and Replication (TIDieR) checklist, while quality appraisals of the evidence was also conducted using the Physiotherapy Evidence Database and Cochrane Risk of Bias version 2 tools.

**Results:** Seven RCTs (n = 730 participants) were analysed. CBT was associated with improved pain intensity, sleep quality and quality of life, but not fatigue and uncertain for depression. MBSR reduced depression and anxiety and enhanced quality of life scores. Improvements in pain intensity, depression and quality of life were demonstrated with digital ACT, with superior participant adherence versus other face-to-face interventions. Considerable heterogeneity of interventions was apparent. The evidence for all interventions was equivocal with four studies deemed 'high risk' of bias and three with 'some concerns' following quality appraisal.

**Conclusion:** Cognitive-behaviour therapy, acceptance and commitment therapy and mindfulness based stress reduction demonstrate mostly small effects on fibromyalgia symptoms in favour of the intervention. However, when delivered in digital therapy format, these shows promise as a means of enhancing patient adherence to treatment, and potentially accelerating access to care with subsequent reduction of burden on waiting lists for health care providers.

**Keywords:** Cognitive-behaviour therapy, acceptance and commitment therapy, mindfulness-based stress reduction, fibromyalgia, pain, quality of life

## 1. Introduction

Fibromyalgia Syndrome (FMS) is a complex and disabling chronic condition characterised by widespread pain, disrupted sleep, fatigue, depression, anxiety and low exercise tolerance<sup>1,2,3</sup> with an estimated population prevalence of between 0.2% and 6.6%<sup>4,5</sup>. While the precise cause of fibromyalgia remains elusive, current evidence proposes a complex interplay between individuals' biological and psychosocial environment which triggers its development<sup>6</sup>. Such susceptibility factors include gender; with females disproportionately affected compared to males, genetic predisposition, traumatic early life events, physical and sexual abuse, and psychological distress including depression<sup>4</sup>.

Although no curative therapy currently exists for fibromyalgia, a combined non-pharmacological approach of exercise therapy, pain neuroscience education and psychologically-based interventions is the recommended first-line treatment<sup>7</sup>. It is posited that this holistic biopsychosocial approach yields greater outcomes in a person's pain experience, mood and overall quality of life compared to any one in isolation as multiple maladaptive thoughts, beliefs and behaviours can be addressed simultaneously<sup>8</sup>. This pertains to fear avoidance, pain catastrophising, poor exercise tolerance, depression and low self-efficacy, which are strong predictors of chronic pain and pain-related disability<sup>9,10,11</sup>.

However, inconsistencies have been identified between evidence-based guidelines from some professional organisations<sup>12</sup>, notably the European League Against Rheumatism<sup>7</sup> (EULAR), American Pain Society<sup>13</sup> (APS), Canadian Pain Society<sup>14</sup> (CPS) and Association of The Scientific Medical Societies in Germany<sup>15</sup> (AWMF). While EULAR are most recent, questions have been raised about the validity of some of its recommendations<sup>12</sup>, particularly that evidence is "weak for" CBT. This is particularly perplexing as cognitive-behaviour therapy (CBT) was closest of all other interventions to meeting the criteria achieved for exercise for which the evidence was deemed "strong for" by EULAR<sup>7</sup>, and also received a "strong for" recommendation from the other three organisations<sup>13,14,15</sup>. The heterogenous nature of fibromyalgia, different inclusion criteria dictating studies assessed and evidence weighting systems selected may provide context for these recommendations.

Psychologically-based interventions for fibromyalgia include CBT, acceptance and commitment therapy (ACT), mindfulness-based stress reduction therapy (MBSR) and mindfulness-based cognitive therapy (MBCT), with CBT most well-known and widely used<sup>16,17</sup>. However, the extent of their precise health effects are unclear due to equivocal research findings, making clinical reasoning for the most appropriate therapeutic modality a significant challenge for practitioners<sup>9,18,19</sup>. Further, patients' long-term adherence and outcomes are heavily influenced by their shared therapeutic alliance with their practitioner, which may be strongly dictated by the patient's perceived relevance of the therapy<sup>20</sup>.

A 2019 review of nine RCTs measuring the impact of ACT, MBSR or MBCT on pain, fatigue, sleep quality, psychological distress, depression, anxiety, mindfulness,

health-related quality of life (HRQoL) and work ability in 841 people living with fibromyalgia found small to moderate effects in favour of mindfulness and acceptance-based interventions compared with controls on the above symptoms of fibromyalgia and HRQoL. However, results were uncertain due to heterogeneity between trials and other study limitations, resulting in downgrading in the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) to very low, low and moderate certainty of evidence. The authors concluded that the overall health effects were promising but uncertain<sup>18</sup>.

Kundakci and colleagues conducted the largest systematic review of 167 RCTs of non-pharmacological therapies to date involving 29 RCTs specific to an array of psychologically-based interventions on symptoms and disease-specific quality of life<sup>8</sup>. However, whereas greater improvements were reported for CBT for treating pain, mindfulness was superior for fatigue and depression compared to usual care, but not for pain. No improvement in sleep outcomes for psychological interventions were found. Individual study characteristics and results following Cochrane risk of bias (RoB) were not presented for psychologically-based interventions alone. Considerable heterogeneity of interventions was also reported.

The purpose of this review was to update previous reviews by systematic appraisal of the effectiveness of CBT, ACT and MBSR on pain intensity, pain catastrophising, depression, anxiety, sleep quality, fatigue and health-reported quality of life in people living with fibromyalgia, and to provide detail of intervention components.

## 2. Methods

### 2.1 STUDY DESIGN

This systematic review was conducted in accordance with the Cochrane Handbook<sup>21</sup> and reported in accordance with the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) statement<sup>22</sup>.

The methodological quality of included studies was assessed via the Template for Intervention Description and Replication (TIDieR) checklist<sup>23</sup>, Cochrane (RoB) version 2 tool<sup>24</sup> and Physiotherapy evidence database<sup>25</sup> (PEDro).

### 2.2 INCLUSION/EXCLUSION CRITERIA

All studies considered for inclusion were randomised controlled trials (RCTs) assessing the effectiveness of CBT, ACT, or MBSR for people living with fibromyalgia. The study population was limited to adults 18 years or older and diagnosed with fibromyalgia based on the American College of Rheumatology criteria originally defined in 1990 or modified in 2010 and 2016<sup>26,27,28</sup>. Only full-text articles published in peer-reviewed journals between 2015 and 2023 were included. RCTs were considered if they assessed the effects of CBT, ACT or MBSR compared to treatment as usual, wait-list control, or no intervention, and involved a minimum of six sessions over at least 6 weeks in either face-to-face, group or online formats. Finally, studies were included if they assessed outcomes of the main clinical symptoms of fibromyalgia (pain intensity, depression, anxiety, sleep quality, fatigue), and/or pain catastrophising or health-related quality of life.

### 2.3 SEARCH STRATEGY

Cochrane, PubMed and Science Direct databases were searched to identify all potentially relevant RCTs. The search strategy was formulated in line with the PICOS (population, intervention, comparison, outcome, study

design) acronym<sup>29</sup> and executed using Boolean operators to amalgamate keywords (Table 1). Furthermore, the reference lists of included studies were explored for additional relevant studies.

**Table 1 Search terms**

Criteria	Search Terms	Sources Results	Results
<b>Population</b>	Fibromyalgia OR Fibromyalgia syndrome OR FM OR FMS	PubMed	
		Field: Title/Abstract	7
<b>Intervention</b>	Acceptance and commitment therapy OR cognitive behavio* OR mindfulness-based stress reduction OR mindfulness-based cognitive therapy	Cochrane	
		Field: Title/Abstract	150
<b>Comparison</b>	Activity OR exercise OR education OR treatment as usual OR wait-list OR no intervention	Science Direct	
		Field: Title/Abstract	12
<b>Outcome</b>	Pain intensity OR pain catastrophising OR depression OR anxiety OR sleep quality OR fatigue OR health-related quality of life		
<b>Study Design</b>	Randomised controlled trials		
<b>Filters</b>	Full-text access, English language, published from 2015		

\* indicates that all ending variations of this word will be returned.

### 2.4 SELECTION OF STUDIES

All studies were systematically screened using the eligibility criteria to identify RCTs relevant for review. After duplicate papers were removed, remaining studies were screened by titles and abstracts, following which full-text articles were reviewed.

### 2.5 DATA EXTRACTION

All relevant studies were presented in a PRISMA flow chart (Figure 1). Individual study characteristics are summarised in Table 2. Detailed data pertaining to study interventions were extracted using the TIDieR<sup>23</sup> as shown in Table 3.

### 2.6 QUALITY APPRAISAL

The methodological quality of eligible studies was assessed using the 11-item Physiotherapy Evidence Database (PEDro) scale<sup>25</sup>. The Cochrane Risk of Bias (RoB) version 2 tool<sup>24</sup> defined the overall risk of an RCTs bias as either 'low', 'some concerns' or 'high' following individual appraisal for selection bias, performance bias, attrition bias, detection bias and reporting bias.

### 2.7 EFFECT SIZE

Cohen's *d* effect sizes of participants' pain intensity levels, pain catastrophising, depression, anxiety, sleep quality, fatigue and health-related quality of life at post-treatment and follow-up were measured to evaluate the effect of intervention therapy compared to control<sup>30</sup>.

### 2.8 DATA SYNTHESIS

To provide a high-quality synthesis of the available

evidence, the Centre for Reviews and Dissemination framework (CRD)<sup>31</sup> was employed. Specifically, it helped to draw conclusions from the included body of literature with consideration for its strengths, limitations and overall outcomes while also helping to provide recommendations for future practice.

## 3. Results

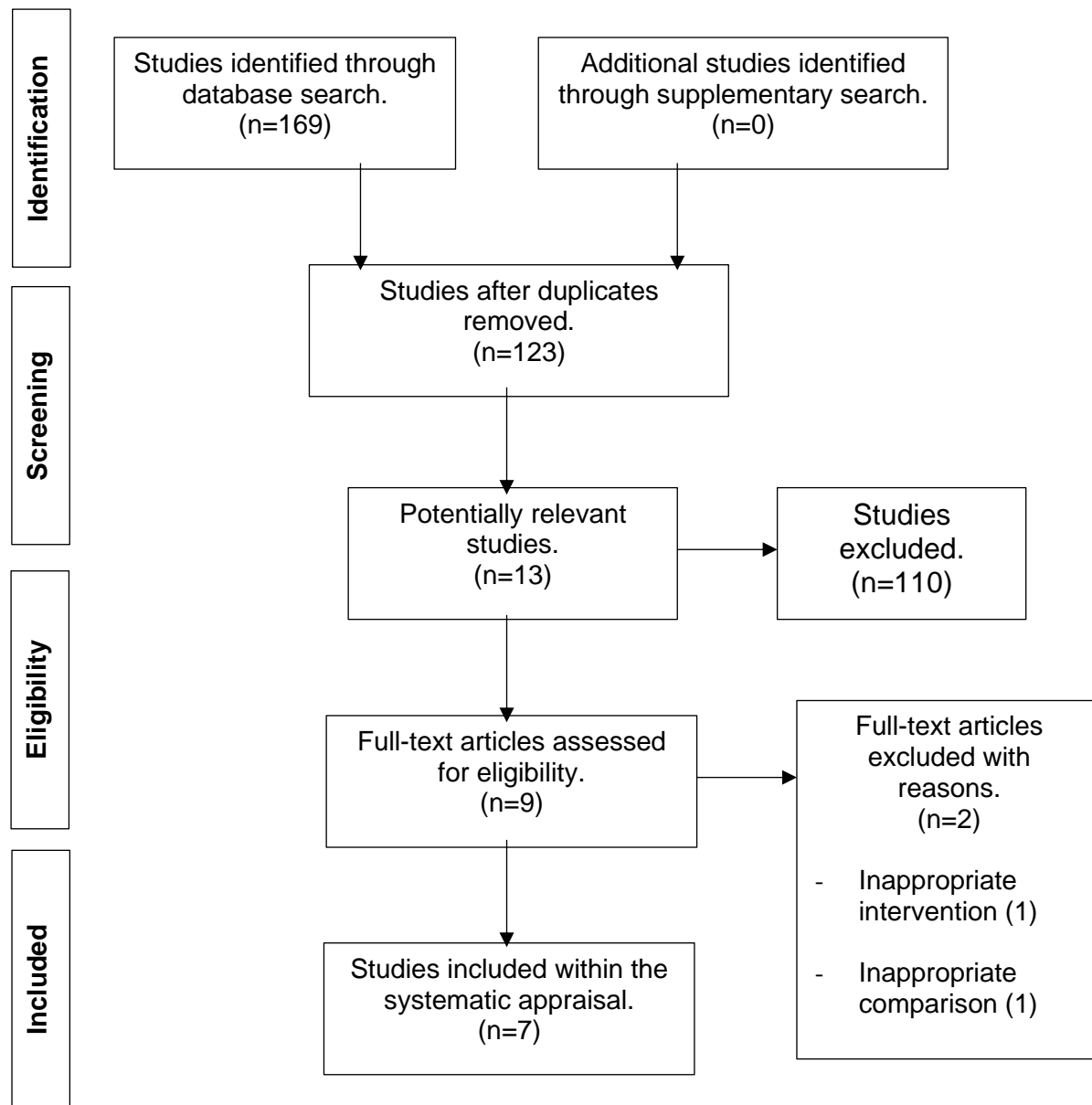
### 3.1 SEARCH RESULTS

Applying the PICOS framework<sup>29</sup>, 169 results were initially identified. Nine full-text articles were assessed and seven RCTs were included in this systematic review following full-text screening<sup>32-38</sup>. The full details of this screening process are displayed in a PRISMA flow diagram (Figure 1).

### 3.2 STUDY AND PARTICIPANT CHARACTERISTICS

Study characteristics are summarised within Table 2. Sample sizes varied greatly between individual studies, ranging from 48 to 225 participants. In total, 730 people living with fibromyalgia were included, 98.4% of whom were female with a mean age of 49 years. Treatment and control groups shared similar baseline characteristics for most pertinent prognostic factors relevant to this review; pain intensity, pain catastrophising, sleep quality, fatigue, depression, anxiety and self-reported quality of life, in all but one study. However, Pérez-Aranda<sup>37</sup> observed significantly less participants currently depressed in the control group compared to the MBSR group.

**FIGURE 1** PRISMA flow diagram of study selection for systematic review.



**Table 2 Study Characteristics**

Author, year, country (Ref)	Participant characteristics	Outcome measures	Measurement time points
Cash et al. (2015), USA	n = 91, 100% women, mean age 48yrs MBSR (n = 51) Wait-list (n = 40)	VAS, BDI, SSQ, FSI, FIQ	Baseline, end of treatment (8 weeks) and follow-up (2 months)
Karlsson et al. (2015), Sweden	n = 41, 100% women, mean age 49yrs CBT (n = 24) Wait-list (n = 24)	MPI, MQ, MADRS-S	Baseline, end of treatment (6 months), follow-up (6 months), wait-list control follow-up (12 months)
Lami et al., (2017), Spain	n = 126, 100% women, mean age 50yrs Usual medical care (n = 42) CBT for insomnia (n = 42) CBT for pain (n = 42)	PSQI, MPQ-SF, MFI, FIQ, SCL-90-R, PCS	Baseline, one week post-treatment (10 weeks), follow-up (3 months)
Simister et al., (2018), Canada	n = 67, 95% women, mean age 40yrs ACT + TAU (n = 33) TAU (n = 34)	FIQ-R, CES-D, MPQ-SF, PSQI	Baseline, end of treatment (8 weeks) and follow-up (5 months)
McCrae et al., (2019), USA	n = 113, 97.3% women, mean age 53yrs CBT for insomnia (n = 39) CBT for pain (n = 37)	SRS, VAS, MPQ, PDI, BDI-II, STAI-YI	Baseline, post-treatment (8 weeks), follow-up (6 months)

Author, year, country (Ref)	Participant characteristics	Outcome measures	Measurement time points
	Wait-list control (n = 37)		
<i>Pérez-Aranda et al., (2019), Spain</i>	n = 113, 98.2% women, mean age 53yrs	FIQ-R, FSDC, HADS, PCS	Baseline, post-treatment (8 weeks), follow-up (12 months)
	MBSR + TAU (n = 75)		
	FibroQol + TAU (n = 75)		
	TAU (n = 75)		
<i>Catella et al., (2023), Spain</i>	n = 67	FIQ-R, NRS, BDI-II	Baseline, post-treatment (12 weeks)
	mean age 53yrs, 98.5% women		
	ACT (n = 39)		
	Symptom-tracking (n = 28)		

VAS, Visual Analogue Scale; SSQ, Stanford Sleep Questionnaire; FSI, Fatigue Symptom Inventory; FIQ, Fibromyalgia Impact Questionnaire; MPI, West Haven-Yale Multidimensional Pain Inventory; MQ, Maastricht Questionnaire; MADRS-S; Montgomery-Åsberg Depression Rating Scale – self-reported; PSQI, Pittsburgh Sleep Quality Index; MPQ-SF, McGill Pain Questionnaire-Short Form; MFI, Multidimensional Fatigue Inventory; PCS, Pain Catastrophizing Scale; TAU, Treatment as Usual; FIQ-R, Fibromyalgia Impact Questionnaire-Revised; CES-D, Center for Epidemiological Studies Depression Scale; SRS, Self-Reported Sleep; Pain Disability Inventory; BDI-II, Beck Depression Inventory-Second Edition; STAI-YI, State-Trait Anxiety Inventory-Form Y1; HADS, Hospital Anxiety and Depression Scale; NRS, Numerical Rating Scale; ST, Symptom Tracking

### 3.3 INTERVENTIONS

The specific interventions employed in each study are detailed in accordance with the TiDiEr checklist (Table 3). Three studies assessed the efficacy of CBT for treating fibromyalgia symptoms<sup>33,34,36</sup>, two assessed MBSR<sup>32,37</sup> and two assessed ACT<sup>35,38</sup> which were delivered remotely via a virtual platform. Considerable heterogeneity was observed between studies with respect to their overall duration, individual session length and site of implementation of interventions.

Studies had a mean duration of 10.4 weeks, ranging from 8 to 20 weeks and an average single session duration of 1 hour 42 minutes, which varied from 20 minutes to 3 hours. Regarding mode of delivery, four studies delivered weekly face-to-face group sessions, while McCrae<sup>36</sup> provided 1-1 in-person sessions. The setting and location of treatment also varied between studies and included the University of Granada, Spain<sup>34</sup>, University of Florida, USA<sup>35</sup> and Sant Boi de Llobregat Teaching, Research and Innovation Unit in Barcelona, Spain<sup>37</sup>. Cash *et al*<sup>32</sup> and Karlsson *et al*<sup>33</sup> didn't specify the exact site of treatment delivery but were conducted in the USA and Sweden respectively, while Simister *et al*<sup>35</sup> and Catella *et al*<sup>38</sup> prescribed remote digital-based ACT. All seven RCTs endeavoured to enhance their fidelity, either through efforts to improve the precision of intervention delivery or via monitoring and promoting participant engagement throughout the course of therapy (Table 3).

Cash *et al*<sup>32</sup> tracked session attendance and made phone calls to remind absent participants of their upcoming sessions. Karlsson *et al*<sup>33</sup> arranged for all sessions to be supervised by one co-author. Additionally, the subjective pain, stress and well-being scores of participants were

recorded after each session to gain insight into the feasibility and acceptability of engaging with the intervention. Lami *et al*<sup>34</sup> equipped participants with a treatment manual outlining the session plans and explaining the intervention rationale in order to optimise the integrity of delivered sessions. The therapists and research group also held regular meetings to review delivery and troubleshoot any problems, while video recordings of all sessions facilitated the assessment of intervention delivery.

Simister *et al*<sup>35</sup> sent weekly emails to participants as a reminder to attend upcoming sessions and reach out to team members if they experienced any difficulties. McCrae *et al*<sup>36</sup> monitored intervention fidelity by randomly assigning 50% of an interventionist's recorded tapes to another interventionist, and a random 25% to be double-scored by a co-author. This cross-examination and scoring was practiced to enhance consistency of intervention delivery across all groups. Patients also received a detailed workbook explaining the treatment rationale as well as practice logs to promote intervention adherence and at-home engagement.

Pérez-Aranda *et al*<sup>37</sup> provided participants with practice logs to record home practice as a means of assessing engagement, while also actively encouraging home practice within each session. Furthermore, all sessions were videotaped so precision of intervention provision could be analysed against the treatment manual, while treatment provider competency was assessed using the validated *Mindfulness-Based Interventions: Teaching Assessment Criteria*. Catella *et al*<sup>38</sup> conducted safety assessments and reviewed protocol adherence within research visits 3-6, while also reviewing intervention efficacy on a weekly basis following randomisation.

Table 3 Extracted Intervention Data using the TIDieR checklist

Study	Brief name + why	What materials, procedures + who provided	How + where	When + how much	Intervention tailoring	If intervention adherence/fidelity assessed, describe the extent
Cash et al. (2015)	Evaluate whether MBSR alleviates Fibromyalgia symptoms in women	Home practice assignments  Experienced MBSR instructor	Group (n = 10-12) face-to-face sessions at university	8 weekly 2.5-hour sessions  Participants encouraged to practice at home 6 times a week for 45 minutes	Not reported	Participant attendance recorded and absent participants received phone calls as a reminder for future sessions.  Attendance dropped from 90% to 57% between 1st and 4th meeting. Maintained between 57% and 65% in the following 4 sessions. 67.5% controls provided full follow-up data
Karlsson et al. (2015)	Assess the effects of CBT on stress, wellbeing and life control in women living with Fibromyalgia	Case illustrations, audio-visuals, readings, hand-outs, exercises and discussions led by CBT-trained psychologists	Group (n = 5-7) face-to-face sessions  Location not reported	20 weekly 3-hour sessions  3 subsequent CBT 'booster's sessions were delivered over the next six months	Not reported	Treatment delivery supervised by co-author  Patient VAS scores for pain, stress and well-being monitored in each session
Lami et al., (2017)	Compare the effects of CBT for pain, and insomnia and pain to usual medical care on Fibromyalgia symptoms	Therapy manual detailing each session  Therapists experienced in domain of chronic pain and sleep disorder	Group (n = 5-7) face-to-face sessions at university  CBT-P based on Fear-Avoidance Model (Leeuw et al. 2007; Vlaeyen and Linton 2012). CBT-IP based on AASM recommendations (Morgenthaler et al. 2006) and insomnia therapeutic guidelines (Moran 1998; Harvey 2005).	9 weekly 90-minute sessions	Not reported	Participants received therapy manual detailing each session to ensure integrity of delivery  Regular meetings between therapists and research group with video-recorded sessions to monitor intervention provision
Simister et al., (2018)	Assess the effectiveness of online ACT for people living with Fibromyalgia	Online platform with self-guided mp3 audio recordings, videos, and experiential homework	Online ACT platform with 7 modules	7 specific modules and optional written assignments for participants to complete within two months	Not reported	Weekly email reminders sent to participants.  First author reviewed written assignments and provided feedback for clarification and positive reinforcement
McCrae et al., (2019), USA	Study CBT effectiveness for people living with Fibromyalgia and comorbid insomnia	Workbook describing treatment instructions and rationale  Predoctoral students in clinical psychology	1-1 in-person sessions	8 weekly 50-minute sessions	Not reported	Expertise psychologists provided training, weekly supervision, and monitoring of interventions via audiotape  50% tapes scored by another interventionist to enhance intervention delivery. Interventionists promoted regular home practice.
Pérez-Aranda et al., (2019)	Compare MBSR to a multicomponent treatment and usual care for Fibromyalgia	MBSR book and audio CD to promote home exercise adherence  Accredited MBSR instructors	Group (n = ~15) face-to-face sessions	8 weekly 2-hour sessions  Optional silent 6-hour retreat offered in week six. Weekly home practice encouraged and recorded in practice log.	Not reported	5 instructors across the 5 groups served to minimise any instructor effect on outcomes  All sessions were videotaped and compared to the treatment manual
Catella et al., (2023)	Assess the efficacy of self-guided digital ACT for Fibromyalgia	Digital app platform where participants submitted self-reported outcomes at baseline and weekly following randomisation	Smartphone-based ACT	41 self-guided digital ACT sessions each 15-20 mins long over 12 weeks  6 individual check-ins (C) for each participant; C1 in-person, C2-5 virtually, C6 virtually or in-person.	Cohort 2 randomised to modified symptom-tracking control or ACT with daily symptom tracking or 4 weeks ACT reinforcement questions	Safety assessments and a review of protocol adherence were performed by trial investigators between check-in 3 and 6  Participant engagement and program completion rate were recorded electronically

### 3.4 QUALITY APPRAISAL

PEDro: see Table 4 for the specific results of each study. Classifying the methodological quality of each study in accordance with the PEDro score<sup>23</sup>, only Catella *et al*<sup>38</sup> was deemed ‘excellent’. Cash *et al*<sup>32</sup>, Karlsson *et al*<sup>33</sup>, Lami *et al*<sup>34</sup>, Simister *et al*<sup>35</sup>, McCrae *et al*<sup>36</sup> and Pérez-Aranda *et al*<sup>3</sup> all scored ‘good’ in terms of their methodological quality.

Cochrane RoB2 tool: see table 5. Cash *et al*<sup>32</sup>, Karlsson *et al*<sup>33</sup> and Catella *et al*<sup>38</sup> were scored as having ‘some concerns’ regarding RoB while Lami *et al*<sup>34</sup>, Simister *et al*

<sup>35</sup>, McCrae *et al*<sup>36</sup> and Pérez-Aranda *et al*<sup>37</sup> were classified as a ‘high’ RoB.

Given the nature of the interventions being assessed, performance bias due to inadequate participant blinding was a highlighted limitation of all RCTs following Cochrane RoB assessment. Similarly, PEDro results indicate that participant and treatment provider blinding was absent in all studies except for Catella *et al*<sup>38</sup> which involved self-directed digital ACT and so therapists were not required to deliver treatment.

**Table 4 PEDro scores**

Criterion	Study						
	Cash <i>et al.</i> , (2015)	Karlsson <i>et al.</i> , (2015)	Lami <i>et al.</i> , (2017)	Simister <i>et al.</i> , (2018)	McCrae <i>et al.</i> , (2019)	Pérez-Aranda <i>et al.</i> , (2019)	Catella <i>et al.</i> , (2023)
Eligibility criteria were specified (external validity)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Subjects were randomly allocated to groups	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Allocation was concealed	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Groups were similar at baseline regarding the most important prognostic indicators	Yes	Yes	Yes	Yes	Yes	No	Yes
There was blinding of all subjects	No	No	No	No	No	No	No
Blinding of all therapists who administered the therapy	No	No	No	No	No	No	Yes
Blinding of all assessors who measured at least one key outcome	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups	Yes	Yes	No	Yes	Yes	Yes	Yes
All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by “intention to treat”	Yes	Yes	No	Yes	Yes	Yes	Yes
Results of between-group statistical comparisons are reported for at least one key outcome	Yes	Yes	Yes	Yes	Yes	Yes	Yes
The study provides both point measures and measures of variability for at least one key outcome	Yes	Yes	Yes	Yes	Yes	Yes	Yes
<b>Total / 10</b>	<b>8/10</b>	<b>8/10</b>	<b>6/10</b>	<b>8/10</b>	<b>8/10</b>	<b>7/10</b>	<b>9/10</b>

**Table 5 Cochrane Risk of Bias Version 2 Tool**

Domain	Study						
	Cash <i>et al.</i> , (2015)	Karlsson <i>et al.</i> , (2015)	Lami <i>et al.</i> , (2017)	Simister <i>et al.</i> , (2018)	McCrae <i>et al.</i> , (2019)	Pérez-Aranda <i>et al.</i> , (2019)	Catella <i>et al.</i> , (2023)
Risk of bias in randomisation (selection bias)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Risk of bias due to blinding of participants/ personnel (Performance bias)	Some concerns	Some concerns	High risk	High risk	High risk	High risk	Some concerns
Incomplete outcome data (Attrition bias)	Some concerns	Low risk	High risk	Low risk	Some concerns	Some concerns	Some concerns
Risk of bias in outcome assessment (Detection bias)	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns
Risk of bias in selectively reporting results (Reporting bias)	Some concerns	Low risk	Low risk	Some concerns	Low risk	Low risk	Low risk
<b>Overall risk</b>	<b>Some concerns</b>	<b>Some concerns</b>	<b>High risk</b>	<b>High risk</b>	<b>High risk</b>	<b>High risk</b>	<b>Some concerns</b>

### 3.5 EFFECT SIZE

See Tables 6-9 for Cohen’s d effect size calculations at post-treatment and follow-up for pain intensity, pain catastrophising, depression, anxiety, sleep quality, fatigue and health-related quality of life.

Only post-treatment effect sizes were calculated for outcome measures assessed by Karlsson *et al*<sup>33</sup> as no

follow-up data was provided, while Catella *et al*<sup>38</sup> only included mean change from baseline values and so were excluded from effect size calculations for the purposes of clarity and making valid comparisons. One study showed only a small effect in favour of MBSR for treating depression, sleep quality, fatigue and health-related quality of life, with no effect on FIQ-related physical functioning at post-treatment or follow-up (d = 0). A

large effect size was demonstrated in favour of online ACT for improving pain intensity ( $d = 0.84$ ) and depression ( $d = 0.87$ ) at post-treatment<sup>35</sup>, while the same study also showed large effects in favour of ACT for improving HRQoL at post-treatment ( $d = 1.26$ ) and 5 month follow-up ( $d = 1.59$ ) which were also statistically

significant ( $p < 0.001$ ). One study assessing the efficacy of CBT for pain (CBT-P) and CBT for Insomnia and Pain (CBT-IP) on fatigue found large effect sizes in favour of waitlist control (WLC) at post-treatment ( $d = 1.3$ ) and 3 month follow-up ( $d = 1.3$ )<sup>34</sup>.

**Table 6 Pain Intensity and Pain Catastrophising Effect sizes**

Pain Intensity				Cohen's $d$ $d = \frac{(M2-M1)}{SD_{pooled}}$	Cohen's $d$ $d = \frac{(M2-M1)}{SD_{pooled}}$					
Study	Measure	Posttreatment Mean (SD)	Control Mean (SD)	$d$ posttreatment	Posttreatment effect size	Follow-up Mean (SD)	Control Mean (SD)	$d$ follow-up	Follow-up effect size	
Cash et al. (2015)	VAS	60.4 (26.4)	68.5 (23.5)	$d = 0.3$	Small	65.2 (25)	65.1 (22.1)	$d = 0.4$	Small	
Lami et al. (2017)	VAS (MPQ-SF)	CBT-P: 7.35 (2.08)	7.4 (1.29)	CBT-P: $d = 0.03$	CBT-P: Very small	CBT-P: 7.21 (1.79)	7.2 (1.58)	CBT-P: $d = 0.006$	CBT-P: Very small	
		CBT-IP: 7.29 (1.46)		CBT-IP: $d = 0.08$	CBT-IP: Very small	CBT-IP: 6.62 (1.47)		CBT-IP: $d = 0.4$	CBT-IP: Small	
Simister et al. (2018)	Likert scale (MPQ-SF)	13.8 (8.81)	21 (8.41)	$d = 0.84$	Large	21.46 (9.1)	22.49 (9.21)	$d = 0.11$	Small	
McCrae et al. (2019)	VAS	CBT-I morning: 47.01 (24.79)	Morning: 52.38 (24.04)	CBT-I morning: $d = 0.22$	CBT-I morning: Small	CBT-I morning: 43.29 (26.4)	Morning: 50.6 (25.66)	CBT-I morning: $d = 0.28$	CBT-I morning: Small	
		CBT-I evening: 45.77 (33.44)	Evening: 51.18 (32.62)	CBT-I evening: $d = 0.16$	CBT-I evening: Very small	CBT-I evening: 41.99 (34.52)	Evening: 49.26 (33.81)	CBT-I evening: $d = 0.21$	CBT-I evening: Small	
		CBT-P morning: 46.72 (23.81)		CBT-P morning: $d = 0.24$	CBT-P morning: Small	CBT-P morning: 47.78 (24.45)		CBT-P morning: $d = 0.11$	CBT-P evening: Very small	
		CBT-P evening: 49.39 (32.61)		CBT-P evening: $d = 0.05$	CBT-P evening: Very small	CBT-P evening: 49.77 (33.35)		CBT-P evening: $d = 0.02$	CBT-I evening: Very small	
Pain Catastrophising										
Study	Measure	Posttreatment Mean (SD)	Control Mean (SD)	$d$ posttreatment	Posttreatment effect size	Follow-up Mean (SD)	Control Mean (SD)	$d$ follow-up	Follow-up effect size	
Lami et al. (2017)	PCS	CBT-P: 20 (10.59)	24.91 (12.41)	CBT-P: $d = 0.4$	CBT-P: Small	CBT-P: 22.84 (14.14)	24.2 (11.78)	CBT-P: $d = 0.1$	CBT-P: Very small	
		CBT-IP: 24.44 (13.01)		CBT-IP: $d = 0.04$	CBT-IP: Very small	CBT-IP: 24.05 (14.14)		CBT-IP: $d = 0.01$	CBT-IP: Very small	
Pérez-Aranda et al. (2019)	PCS	12.93 (10.49)	19.55 (14.39)	$d = 0.53$	Moderate	11.43 (11.08)	18.61 (12.34)	0.61	Moderate	

Abbreviations: d, difference; SD, standard deviation

Note: Effect size: 0.2 = small; 0.5 = medium; 0.8 = large.

**Table 7 Depression and Anxiety Effect Sizes**

Study	Measure	Posttreatment Mean (SD)	Control Mean (SD)	$d$ posttreatment	Posttreatment effect size	Follow-up Mean (SD)	Control Mean (SD)	$d$ follow-up	Follow-up effect size
Karlsson et al., (2015)	MADRS-S	14.75 (7.96)	14.79 (6.37)	$d = 0.06$	Very Small	Not available	N/A	N/A	N/A
Lami et al., (2017)	SCL-90-R Depression	CBT-P: 2.15 (0.78)	1.68 (0.98)	CBT-P: $d = 0.5$	Moderate	CBT-P: 2.11 (0.9)	1.47 (0.78)	CBT-P: $d = 0.76$	CBT-P: Moderate
		CBT-IP: 2.03 (0.96)		CBT-IP: $d = 0.4$	Small	CBT-IP: 2.01 (1.01)		CBT-IP: $d = 0.6$	CBT-IP: Moderate



Acceptance, Cognitive-Behavioural and Mindfulness-Based Psychological Interventions for Fibromyalgia:

Lami et al., (2017)	SCL-90-R Anxiety	CBT-P: 1.71 (0.94) CBT-IP: 1.68 (1.05)	1.37 (0.91)	CBT-P: $d = 0.4$ CBT-IP: $d = 0.3$	Small Small	CBT-P: 1.69 (1.05) CBT-IP: 1.62 (0.98)	1.18 (0.69)	CBT-P: $d = 0.5$ CBT-IP: $d = 0.5$	CBT-P: Moderate CBT-IP: Moderate
Simister et al., (2018)	CES-D	17.76 (10.83)	26.97 (10.46)	$d = 0.87$	Large	25.13 (12.29)	21.46 (9.1)	$d = 0.56$	Moderate
McCrae et al. (2019)	BDI-II	CBT-I: 8.52 (11.12) CBT-P: 15.58 (10.68)	16.94 (10.94)	CBT-I: $d = 0.76$ CBT-P: $d = 0.13$	CBT-I: Moderate CBT-P: Small	CBT-I: 8.22 (11.93) CBT-P: 14.38 (11.22)	15.01 (11.68)	CBT-I: $d = 0.58$ CBT-P: $d = 0.06$	CBT-I: Moderate CBT-P: Very Small
McCrae et al., (2019)	STAI-Y1	CBT-I: 38.95 (12.72) CBT-P: 45.22 (12.12)	47.72 (12.87)	CBT-I: $d = 0.69$ CBT-P: $d = 0.17$	CBT-I: Moderate CBT-P: Small	CBT-I: 38.07 (13.73) CBT-P: 43.86 (12.78)	43.87 (13.7)	CBT-I: $d = 0.42$ CBT-P: $d = 0.0008$	CBT-I: Small CBT-P: Very Small
Pérez-Aranda et al., (2019)	HADS	14.39 (9.09)	20.16 (9.41)	$d = 0.63$	Moderate	15.69 (9.21)	21.12 (10)	$d = 0.56$	Moderate

Abbreviations: d, difference; SD, standard deviation

Note: Effect size: 0.2 = small; 0.5 = medium; 0.8 = large.

**Table 8 Sleep Quality and Fatigue Effect Sizes**

Study	Measure	Posttreatment Mean (SD)	Control Mean (SD)	d posttreatment	Posttreatment effect size	Follow-up Mean (SD)	Control Mean (SD)	d follow-up	Follow-up effect size
Cash et al., (2015)	SSQ	8.5 (3.3)	9.3 (3.1)	$d = 0.25$	Small	8.4 (4)	9.5 (2.7)	$d = 0.32$	Small
Lami et al., (2017)	PSQI	CBT-P: 13.68 (4.61) CBT-IP: 13.19 (4.31)	13.08 (5.33)	CBT-P: $d = 0.1$ CBT-IP: $d = 0.02$	CBT-P: Small CBT-IP: Very Small	CBT-P: 13.79 (4.22) CBT-IP: 13.57 (3.64)	11.88 (4.68)	CBT-P: $d = 0.4$ CBT-IP: $d = 0.4$	CBT-P: Small CBT-IP: Small
Simister et al. (2018)	PSQI	10.24 (3.6)	13 (3.47)	$d = 0.79$	Moderate	10.7 (4.71)	13.21 (4.76)	$d = 0.53$	Moderate
McCrae et al., (2019)	SRS	CBT-I: 3.32 (3.44) CBT-P: 3.1 (3.35)	2.66 (3.35)	CBT-I: $d = 0.19$ CBT-P: $d = 0.13$	CBT-I: Small CBT-P: Small	CBT-I: 3.27 (3.45) CBT-P: 3.14 (3.35)	2.65 (3.66)	CBT-I: $d = 0.17$ CBT-P: $d = 0.14$	CBT-I: Small CBT-P: Small
<b>Fatigue</b>									
Study	Measure	Posttreatment Mean (SD)	Control Mean (SD)	d posttreatment	Posttreatment effect size	Follow-up Mean (SD)	Control Mean (SD)	d follow-up	Follow-up effect size
Cash et al., (2015)	FSI	5.6 (1.8)	6.4 (1.6)	$d = 0.47$	Small/ Moderate	5.5 (1.8)	6 (1.9)	$d = 0.27$	Small
Karlsson et al., (2015)	MQ	22.04 (5.14)	21.71 (6.8)	$d = 0.05$	Very Small	N/A	N/A	N/A	N/A
Lami et al., (2017)	MFI	CBT-P: 4.31 (0.68) CBT-IP: 4.31 (0.66)	3.18 (1.04)	CBT-P: $d = 1.3$ CBT-IP: $d = 1.3$	CBT-P: Very large CBT-IP: Very large	CBT-P: 4.35 (0.72) CBT-IP: 4.05 (0.67)	4.03 (0.77)	CBT-P: $d = 0.4$ CBT-IP: $d = 0.03$	CBT-P: Small CBT-IP: Very small

Abbreviations: d, difference; SD, standard deviation

Note: Effect size: 0.2 = small; 0.5 = medium; 0.8 = large.

**Table 9 Health-Related Quality of Life Effect Sizes**

Study	Measure	Posttreatment Mean (SD)	Control Mean (SD)	<i>d</i> posttreatment	Posttreatment effect size	Follow-up Mean (SD)	Control Mean (SD)	<i>d</i> follow-up	Follow-up effect size
Cash et al., (2015)	FIQ Symptom Severity	58.4 (21)	67.2 (16.7)	<i>d</i> = 0.47	Small/Moderate	62 (18.6)	66.7 (16.8)	<i>d</i> = 0.27	Small
Cash et al., (2015)	FIQ Physical Functioning	1.2 (0.73)	1.2 (0.84)	<i>d</i> = 0	No effect	1.2 (0.74)	1.2 (0.76)	<i>d</i> = 0	No effect
Karlsson et al., (2015)	MPI Interference	4.08 (0.85)	3.43 (0.82)	<i>d</i> = 0.74	Moderate	N/A	N/A	N/A	N/A
Karlsson et al., (2015)	MPI Life control	3.51 (1.03)	2.94 (1.18)	<i>d</i> = 0.51	Moderate	N/A	N/A	N/A	N/A
Lami et al. (2017)	FIQ	CBT-P: 57.93 (14.16) CBT-IP: 55.82 (14.52)	55.45 (16.79)	CBT-P: <i>d</i> = 0.16 CBT-IP: <i>d</i> = 0.02	CBT-P: Small CBT-IP: Very Small	CBT-P: 53.33 (14.85) CBT-IP: 56.53 (13.97)	53.22 (16.59)	CBT-P: <i>d</i> = 0.007 CBT-IP: <i>d</i> = 0.2	CBT-P: Very Small CBT-IP: Small
Simister et al., (2018)	FIQ-R	39.07 (13.07)	55.30 (12.65)	<i>d</i> = 1.26	Large	31.95 (13.80)	53.82 (13.92)	<i>d</i> = 1.59	Large
Pérez-Aranda et al., (2019)	FIQ-R	47.99 (19.5)	60.73 (21.28)	<i>d</i> = 0.62	Moderate	53.98 (22)	63.75 (18.88)	<i>d</i> = 0.48	Small/Moderate

Abbreviations: *d*, difference; SD, standard deviation

Note: Effect size: 0.2 = small; 0.5 = medium; 0.8 = large.

### 3.6 CLINICAL OUTCOMES

#### 3.6.1 Pain intensity

Cash et al.<sup>32</sup>, Lami et al.<sup>34</sup> and McCrae et al.<sup>36</sup> assessed pain intensity using the visual analogue scale, while Simister et al.<sup>35</sup> employed the 4-point likert scale (McGill Pain Questionnaire – Short Form), and Catella et al.<sup>38</sup> utilised the 11-point numerical rating scale. Cash et al.<sup>32</sup> reported that MBSR had no significant effects on pain intensity at post-treatment or follow-up stage. Lami et al.<sup>34</sup> reported a significant reduction in pain intensity within the CBT-IP group only from post-treatment to 3 month follow-up, ( $p < 0.05$ ) but had a small effect size compared to the usual care control ( $d = 0.4$ ). Similarly, Simister et al.<sup>35</sup> noted significant between-group differences at post-treatment, favouring ACT alongside treatment as usual (TAU) compared to TAU alone ( $p = 0.01$ ) with a large effect size ( $d = 0.84$ ). This was not significant at 5 month follow-up.

Interestingly, McCrae et al.<sup>36</sup> reported a significant decrease in morning pain intensity within but not between all 3 CBT-I, CBT-P and WLC groups at post-treatment ( $p = 0.004$ ), which was maintained at 6 month follow-up ( $p = 0.006$ ). However, significantly more participants reported a moderate improvement in morning pain (>30% reduction on VAS) in CBT-I ( $p < 0.01$ ) and CBT-P ( $p < 0.04$ ) groups compared to WLC at post-treatment stage, while only CBT-I demonstrated a significantly higher proportion of participants with moderate improvements in evening pain at 6 month follow-up ( $p = 0.01$ ) compared to WLC ( $p = 0.048$ ). Despite this, effect sizes were small for both CBT groups compared to control. While reductions in pain intensity were observed

by Catella et al.<sup>38</sup> following online ACT, none reached statistical significance.

#### 3.6.2 Pain catastrophising

Only Lami et al.<sup>34</sup> and Pérez-Aranda et al.<sup>37</sup> measured pain catastrophising, both of whom used the 13-item pain catastrophising scale (PCS). Significant improvements in pain catastrophising were found immediately following CBT-P, although by 3 month follow-up this reversed to non-significance<sup>34</sup>. In both cases, reported effect sizes were small ( $d = 0.4$ ,  $d = 0.1$ ). MBSR achieved significant improvements compared to TAU control paired with moderate effect sizes at post-treatment ( $p < 0.001$ ,  $d = 0.53$ ) and follow-up ( $p < 0.001$ ,  $d = 0.61$ )<sup>37</sup>. Interestingly, Pérez-Aranda et al.<sup>37</sup> also reported at-home meditation twice or more per week was associated with lower baseline PCS levels ( $p = 0.01$ ).

#### 3.6.3 Depression & Anxiety

Considerable methodological heterogeneity was evident across the five studies measuring changes in depression scores following intervention. Karlsson et al.<sup>33</sup> used the Montgomery-Asberg Depression Rating Scale (MADRS), Lami et al.<sup>34</sup> employed the Symptoms Check List 90-Revised (SCL-90-R), Simister et al.<sup>35</sup> selected the Center for Epidemiological Studies Depression Scale (CES-D), McCrae et al.<sup>36</sup> employed the BDI-II, and Pérez-Aranda et al.<sup>37</sup> used the Hospital Anxiety and Depression Scale (HADS). Cash et al.<sup>32</sup> measured depression via the Beck Depression Inventory (BDI) to be used as a potential mediator of other health outcomes, however with no results available. Catella et al.<sup>38</sup> used the BDI second edition (BDI-II) as a safety assessment for suicidal

ideation at multiple stages throughout the intervention period.

Karlsson *et al*<sup>33</sup> reported a significant 20% improvement ( $p < 0.01$ ) in participant depression scores at 6 month follow-up analysis following CBT, though follow-up data was not presented. While Lami *et al*<sup>34</sup> reported no significant within-group changes from baseline to 3 month follow-up, significant differences were observed between usual care and CBT-P in favour of usual care at post-treatment ( $p < 0.05$ ) and follow-up ( $p < 0.01$ ). However the significantly lower baseline depression scores ( $p = 0.049$ ) in the usual care group may explain this result<sup>34</sup>. Moderate effect sizes were calculated for these significant differences ( $d$  ranging from 0.53 to 0.76)

Simister *et al*<sup>35</sup> observed significant improvements in ACT + TAU participants versus TAU only participants for depression ( $p = 0.02$ ), with a large post-treatment effect size ( $d = 0.87$ ) which subsequently reduced to a moderate effect by 5 month follow-up ( $d = 0.56$ ). McCrae *et al*<sup>36</sup> reported lower BDI-II scores for all groups from baseline to post-treatment ( $p < 0.00$ ) and 6 month follow-up ( $p < 0.00$ ), implying that changes may not be treatment-specific. The State Trait Anxiety Inventory Form Y1 (STAI-Y1) was also employed to measure participant anxiety levels, for which no significant results were reported. In the Pérez-Aranda *et al* study<sup>37</sup>, participants receiving MBSR reported moderate effect significant improvements in HADS scores immediately following treatment completion ( $p < 0.001$ ,  $d = 0.63$ ) and 12 month follow-up ( $p < 0.01$ ,  $d = 0.56$ ) were reported.

### 3.6.4 Sleep quality & fatigue

Four studies assessed sleep quality while three studies assessed fatigue, with Cash *et al*<sup>32</sup> and Lami *et al*<sup>34</sup> assessing both outcome measures. Cash *et al*<sup>32</sup> reported significant reductions in sleep quality problems among MBSR participants in the primary intention-to-treat analysis ( $p = 0.038$ ) at post-treatment, although this wasn't replicated within secondary analysis only including data from those who attended at least two of eight sessions ( $p = 0.094$ ). As measured by the Fatigue Symptom Index (FSI), there was a significant reduction in fatigue in the MBSR group ( $p < 0.002$ ), although this was not maintained at follow-up. Karlsson *et al*<sup>33</sup> also found small improvements in fatigue for the group CBT and control group before and after treatment, although the differences were not significant. However, a significant 12% reduction in fatigue ( $p < 0.001$ ) was reported from the before and after treatment in which control participants received CBT intervention after completion of the RCT and were assessed alongside the initial CBT group. The authors described this to be a more efficient use of participant data and to cross-check results between both designs.

Two studies<sup>34,35</sup> used the Pittsburgh Sleep Quality Index (PSQI) which has a reported diagnostic sensitivity of nearly 90% for measuring sleep quality<sup>39</sup>. Lami *et al*<sup>34</sup> reported significant improvements in total sleep quality ( $p < 0.01$ ) only for CBT-IP compared to usual care between baseline and post-treatment analysis, but with a small effect size ( $d = 0.02$ ). Significant reductions in fatigue were reported with the usual care group from baseline to post-treatment ( $p < 0.001$ ), which was

superior to both CBT-P and CBT-IP and CBT-IP with large effect sizes demonstrated. This may be explained by the usual care group having lower fatigue scores at baseline compared to the intervention groups.

Simister *et al*<sup>35</sup> observed greater participant improvements in sleep quality among the ACT+TAU group compared to TAU, but none of these findings were significant. McCrae *et al*<sup>36</sup> reported positive significant changes in participant sleep-quality from baseline to post-treatment in both treatment groups, CBT-I ( $p < 0.008$ ) and CBT-P ( $p < 0.008$ ) groups which were maintained at 6 month follow-up ( $p < 0.008$ ) but with small effect sizes compared to the control group ( $d$  ranging from 0.13 to 0.19) in favour of the intervention groups. The use of self-reported sleep quality by participants who are unblinded versus a standardised and validated tool such as the PSQI may also limit the validity of the findings.

### 3.6.5 Health-related quality of life (HRQoL)

The revised Fibromyalgia Impact Questionnaire (FIQ) was the most frequently used assessment tool for measuring HRQoL, being employed by Simister *et al*<sup>35</sup>, Pérez-Aranda *et al*<sup>37</sup> and Catella *et al*<sup>38</sup>. Cash *et al*<sup>32</sup> and Lami *et al*<sup>34</sup> used the original FIQ scale and Karlsson *et al*<sup>33</sup> used the West Haven-Yale Multidimensional Pain Inventory (MPI), while McCrae *et al*<sup>36</sup> did not directly assess HRQoL at all.

Cash *et al*<sup>32</sup> reported significant improvements following MBSR at post-treatment for FIQ-related symptom severity ( $p = 0.012$ ) which was maintained following slope analysis ( $p = 0.003$ ), while FIQ-related symptom severity for the control group increased over the same period. FIQ-related physical functioning did not show any significant improvements in either group and had no effect size ( $d = 0$ ). Pain interference as part of the MPI and observed by Karlsson *et al*<sup>33</sup> increased more in the CBT group compared to usual care from baseline to post-treatment, although overall life control was enhanced in the treatment group compared to control ( $p = 0.01$ ). Moderate effect sizes were calculated for both domains.

Lami *et al*<sup>34</sup> reported significant within-group improvements at post-treatment for CBT-P ( $p < 0.001$ ) and CBT-IP ( $p < 0.05$ ) groups. Small effect sizes were reported at baseline and follow-up for both CBT groups in favour of the usual care group, though this group was significantly less impacted by fibromyalgia at baseline ( $p < 0.01$ ). Simister *et al*<sup>35</sup> observed a statistically significant improvement of 14% or greater in FIQ-R scores among 70% of online ACT+TAU participants compared to only 8% of TAU control participants at post-treatment ( $p < 0.001$ ). This was extended to 77% at 5 month follow-up compared with a drop to 23% for the control group ( $p < 0.001$ ). Large effect sizes favouring ACT + TAU group over control were reported for post-treatment ( $d = 1.26$ ) and follow-up ( $d = 1.59$ ).

Pérez-Aranda *et al*<sup>37</sup> reported a significant reduction in fibromyalgia functional impact for the MBSR group using the FIQ-R at post-treatment ( $p < 0.001$ ), and 12 month follow-up ( $p = 0.001$ ) compared to TAU control. A significant improvement with MBSR was also achieved at post-treatment ( $p < 0.001$ ), compared to multicomponent treatment, although it was not maintained at follow-up.

The moderate effect size determined at post-treatment reversed to a small effect at follow-up. Catella *et al*<sup>38</sup> also assessed fibromyalgia impact on quality of life via the FIQ-R and recorded an improvement from baseline to post-treatment, although these results were not significant with intention-to-treat (ITT) analysis. Statistically significant improvements in total FIQ-R scores were recorded with per-protocol (PP) analysis, however the results need to be taken in the context of the reduced statistical power, loss of randomisation and limited external validity.

#### 4. Discussion

This systematic review offers an account of current evidence from 2015 exploring the effectiveness of ACT, CBT, and MBSR on pain intensity, pain catastrophising, depression, anxiety, sleep quality, fatigue and health-related quality of life in people living with fibromyalgia. In total, 730 participants living with fibromyalgia were included from seven studies<sup>32-38</sup>, having met the American College of Rheumatology criteria<sup>26-28</sup>, with 98% of those being women and predominantly middle-aged.

All but two interventions were delivered face-to-face, both of which assessed the therapeutic effect of ACT for fibromyalgia. Simister *et al*<sup>35</sup> observed large effect significant improvements in pain intensity, depression and quality of life, but not sleep quality following ACT compared to control. Catella *et al*<sup>38</sup> also reported reduced pain intensity and enhanced quality of life following ACT, but which were non-significant using intention-to-treat analysis. Although significant quality of life improvements were found with per-protocol analysis, selection bias due to excluding participants who didn't adhere to treatment limits generalisability of the findings.

Differences in outcomes between these studies may be explained by the extent of therapist support made available to participants. Whereas Catella *et al*<sup>38</sup> conducted a largely self-directed ACT intervention, Simister *et al*<sup>35</sup> ensured therapists were available to resolve participant concerns, remind of upcoming sessions, offer individual participant feedback to written assignments and reinforce positive thoughts and behaviours. This additional support is likely to have positively influenced participants' perceptions of ACT and promoted a positive therapeutic alliance, which is a strong predictor for improved patient outcomes<sup>40-42</sup>. This is a worthy consideration for future studies to enhance patient outcomes which can also be trialled with other psychologically-based interventions via a digital platform.

Both ACT studies achieved high treatment adherence rates of greater than 80%<sup>38</sup> and 93%<sup>35</sup> respectively, which are higher than included face-to-face studies<sup>32,33,34,36,37</sup>. Together, these averaged a 20% treatment non-completion rate, with one study experiencing 44% non-compliance<sup>37</sup>. Thus, online interventions appear to overcome issues of high attrition and dropout rates commonly seen among chronic pain patients<sup>43,44</sup>. Specifically, digital therapy holds promise as a means of enhancing patient accessibility to treatment by affording participants greater flexibility to engage with therapy in a way which complements their everyday

lives. Furthermore, it presents as feasible option model to reducing healthcare waiting lists, accelerating patient access and augmenting reach.

Results of this appraisal are largely consistent with previous publications in terms of improved anxiety and depression<sup>18,45,46</sup>. However, inconsistencies exist with respect to the effect of ACT on pain intensity and quality of life<sup>45</sup> and may be overestimated in this review as only 33<sup>35</sup> and 39<sup>38</sup> participants were randomly allocated to treatment groups of both studies. Hence, caution must be taken when discussing these results as they cannot be considered representative of the broader population. Further research with larger study samples is warranted to better understand their true effect.

Three studies assessed CBT, and two evaluated CBT sub-groups previously designed for pain and insomnia respectively<sup>33,34,36</sup>. McCrae *et al*<sup>36</sup> reported no significant between-group differences regarding pain intensity levels, with each recording significant post-treatment and follow-up improvements, hinting changes may be non-specific to intervention. However, consistent with findings of Lami *et al*<sup>34</sup>, significant long-term improvements were reported in pain intensity following CBT for insomnia<sup>36</sup>. This suggests the merit in addressing symptoms of poor sleep and insomnia when treating pain intensity as recommended in previous fibromyalgia research<sup>47-49</sup>, and poses an effective means for doing so. These findings are consistent with a 2022 systematic review<sup>8</sup> but offers greater insights into the unique effects of CBT sub-types which was not directly discussed. Future research should follow this line of investigation as there appears to be scope to prescribe specific therapies in accordance with patients' primary symptoms and thus potentially enhance their outcomes to interventions.

CBT is also implicated in improved sleep quality, with one study showing short-term improvements with CBT-IP only<sup>34</sup> and the other achieving long-term improvements in both CBT-I and CBT-P<sup>36</sup> as demonstrated in previous publications<sup>19,50</sup>. Only one study assessed pain catastrophising<sup>34</sup> and showed short-term improvements in favour of CBT. The same study showed no significant bearing on fatigue, which was contrasted with superior outcomes following the usual care control compared with CBT-I or CBT-P, although this control group reported considerably lower baseline fatigue scores<sup>34</sup>.

Both studies measuring quality of life changes with CBT achieved short-term improvements<sup>33,34</sup>. Conflicting findings were reported across all studies regarding depression, with one McCrae *et al*<sup>36</sup> observing non-significant improvements, Karlsson<sup>3</sup> declaring significant long-term reductions<sup>3</sup>, and Lami *et al*<sup>34</sup> reporting greater improvements following usual care over CBT-P. However, similar to fatigue in this study, it may be explained by considerably lower baseline depression scores in the usual care group compared to the CBT-P group. Furthermore, this study conducted a pre-planned per-protocol analysis which doesn't consider drop-outs in its calculations. The control group experienced a higher rate of non-compliance compared to treatment groups<sup>34</sup>. Favouring an intention-to-treat analysis in future studies will enhance the quality of results which can be directly compared with the wider evidence base.

While pain intensity wasn't improved with MBSR<sup>32</sup>, short term benefits for pain catastrophising were achieved<sup>37</sup>. Sleep quality and fatigue levels were not enhanced. However, both studies evaluating MBSR highlighted short-term quality of life improvements, and which were maintained at 12 months follow-up in one study<sup>37</sup>. The same study reported significant short and long-term improvements in participant depression and anxiety levels compared to TAU control with similar levels of uncertainty described for MBSR in a 2019 review<sup>18</sup>. The certainty of evidence from this current review regarding the efficacy of CBT in improving fibromyalgia symptoms and overall quality of life is limited considerably by the small study sample size, very high attrition rates, heterogeneity in employed interventions and follow-up times between the three studies<sup>33,34,36</sup>. Thus, employing tighter protocols in future studies would serve to enhance the quality of evidence by comparing similarly robust interventions and allow for more certain conclusions to be drawn with respect to its effects.

The current review suggests promise for MBSR as a potential mediator for better depression, anxiety and quality of life outcomes while CBT appears preferentially favoured for reducing pain intensity and ameliorating health-related quality of life.

All studies within this review demonstrated performance bias as per Cochrane RoB analysis (Table 5). Four studies were deemed high risk<sup>34,35,36,37</sup> while three had 'some concerns'<sup>32,33,38</sup>. PEDro appraisal made it apparent that no study employed participant blinding. All protocols measured self-reported outcomes, and with combined participant non-blinding, risk of bias and uncertainty of results within this review was increased.<sup>55</sup>

While the findings of this review concur with some findings of previous reports, there are also some contradictions and surprising results, possibly explained by high heterogeneity in employed interventions, participant sample sizes and follow-up timescales, as well as the small study sample size reviewed. Additionally, the vast majority (98%) of participants were women, so findings cannot be deemed representative of the male fibromyalgia population.

In terms of its implications for practice, this review offers novel insights with respect to the potential success of

digital formats which may enhance patient adherence and outcomes, as well as relieve pressure on healthcare waiting lists. Additionally, the associations identified between specific CBT sub-types and patient outcomes indicates a potential means of personalising care in accordance with patients' most concerning symptoms to enhance the extent of improved outcomes.

## 5. Conclusion

This review demonstrates that CBT, ACT and MBSR interventions have mostly small, positive effects on pain intensity, pain catastrophising, depression, anxiety, sleep quality, fatigue and health-related quality of life, somewhat consistent with previous literature. However, a more detailed account of the evidence quality relating to the unique effects of CBT sub-types was provided with CBT for insomnia showing greater promise, although further research is warranted. In one study, large effects were shown in favour of ACT for pain intensity, depression and quality of life. Greater patient adherence to therapy following digital ACT compared to face-to-face interventions was found, providing directions for future digital intervention development.

This review sought to update previous reviews with similarity of findings demonstrated. Considerable heterogeneity was also found between trials in terms of intervention type and duration along with small study sample size and mostly small participant sample sizes within RCTs which reduces the certainty of evidence for each of these psychological therapies.

A further limitation is that the vast majority of participants were women, therefore further research focusing on males is necessary to achieve more representative findings for the entire fibromyalgia population.

## Conflict of Interest

The authors declare no conflict of interest

## Data availability statement:

Data from included studies was extracted and included in tables within the text.

## Acknowledgements:

No financial support was received in supporting this review

## References

1. Clauw DJ. Fibromyalgia: a clinical review. *JAMA*. 2014 Apr 16;311(15):1547-55.
2. Arnold LM. Management of fibromyalgia and comorbid psychiatric disorders. *Journal of Clinical Psychiatry*. 2008 Jan 1;69(2):14-9.
3. Maquet D, Croisier JL, Renard C, Crielaard JM. Muscle performance in patients with fibromyalgia. *Joint Bone Spine*. 2002 May 1;69(3):293-9.
4. Marques AP, Santo AD, Berssaneti AA, Matsutani LA, Yuan SL. Prevalence of fibromyalgia: literature review update. *Revista Brasileira de Reumatologia*. 2017 Jul;57:356-63.
5. Guymer EK, Littlejohn GO, Brand CK, Kwiatek RA. Fibromyalgia onset has a high impact on work ability in Australians. *Internal Medicine Journal*. 2016 Sep;46(9):1069-74.
6. Siracusa R, Paola RD, Cuzzocrea S, Impellizzeri D. Fibromyalgia: pathogenesis, mechanisms, diagnosis and treatment options update. *International Journal of Molecular Sciences*. 2021 Apr 9;22(8):3891.
7. Macfarlane GJ, Kronisch C, Dean LE, Atzeni F, Häuser W, Fluß E, Choy E, Kosek E, Amris K, Branco J, Dincer Fİ. EULAR revised recommendations for the management of fibromyalgia. *Annals of the Rheumatic Diseases*. 2017 Feb 1;76(2):318-28.
8. Kundakci B, Kaur J, Goh SL, Hall M, Doherty M, Zhang W, Abhishek A. Efficacy of nonpharmacological interventions for individual features of fibromyalgia: A systematic review and meta-analysis of randomised controlled trials. *Pain*. 2022 Aug 1;163(8):1432-45.
9. Paschali M, Lazaridou A, Paschalis T, Napadow V, Edwards RR. Modifiable psychological factors affecting functioning in fibromyalgia. *Journal of Clinical Medicine*. 2021 Feb 17;10(4):803.
10. Alhowimel AS, Alotaibi MA, Alenazi AM, Alqahtani BA, Alshehri MA, Alamam D, Alodaibi FA. Psychosocial predictors of pain and disability outcomes in people with chronic low back pain treated conservatively by guideline-based intervention: a systematic review. *Journal of Multidisciplinary Healthcare*. 2021 Dec 30:3549-59.
11. Gracely RH, Geisser ME, Giesecke T, Grant MA, Petzke F, Williams DA, Clauw DJ. Pain catastrophizing and neural responses to pain among persons with fibromyalgia. *Brain*. 2004 Apr 1;127(4):835-43.
12. Thieme K, Mathys M, Turk DC. Evidenced-based guidelines on the treatment of fibromyalgia patients: are they consistent and if not, why not? Have effective psychological treatments been overlooked?. *The Journal of Pain*. 2017 Jul 1;18(7):747-56.
13. Buckhardt CS, Goldenberg D, Crofford L, Gerwin R, Gowens S, Jackson K, Kugel P, McCarberg W, Rudin N, Schanberg L, Taylor AG. Guideline for the Management of Fibromyalgia Syndrome Pain in Adults and Children (2005). Glenview (IL): American Pain Society (APS).
14. Fitzcharles MA, Ste-Marie PA, Goldenberg DL, Pereira JX, Abbey S, Choinière M, Ko G, Moulin DE, Panopalis P, Proulx J, Shir Y. 2012 Canadian guidelines for the diagnosis and management of fibromyalgia syndrome: executive summary. *Pain Research and Management*. 2013 May 1;18:119-26.
15. Dreher T, Häuser W, Schiltenwolf M. Fibromyalgia syndrome—updated s3 guidelines. *Zeitschrift für Orthopädie und Unfallchirurgie*. 2013 Dec 17;151(6):603-9.
16. Lami MJ, Martínez MP, Sánchez AI. Systematic review of psychological treatment in fibromyalgia. *Current Pain and Headache Reports*. 2013 Jul;17:1-4.
17. Mascarenhas RO, Souza MB, Oliveira MX, Lacerda AC, Mendonça VA, Henschke N, Oliveira VC. Association of therapies with reduced pain and improved quality of life in patients with fibromyalgia: a systematic review and meta-analysis. *JAMA Internal Medicine*. 2021 Jan 1;181(1):104-12.
18. Haugmark T, Hagen KB, Smedslund G, Zangi HA. Mindfulness-and acceptance-based interventions for patients with fibromyalgia—A systematic review and meta-analyses. *PloS One*. 2019 Sep 3;14(9):e0221897.
19. Glombiewski JA, Sawyer AT, Gutermann J, Koenig K, Rief W, Hofmann SG. Psychological treatments for fibromyalgia: a meta-analysis. *Pain*. 2010 Nov 1;151(2):280-95.
20. Pate JW, Tran E, Radhakrishnan S, Leaver AM. The Importance of Perceived Relevance: A Qualitative Evaluation of Patient's Perceptions of Value and Impact Following a Low-Intensity Group-Based Pain Management Program. *Medicina*. 2021 Jan 7;57(1):46.
21. Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP, Thomas J. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. *The Cochrane Database of Systematic Reviews*. 2019;2019(10).
22. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Annals of Internal Medicine*. 2009 Aug 18;151(4):W-65.
23. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, Altman DG, Barbour V, Macdonald H, Johnston M, Lamb SE. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ*. 2014 Mar 7;348.
24. Sterne JA, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng HY, Corbett MS, Eldridge SM, Emberson JR. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019 Aug 28;366.
25. Moseley AM, Elkins MR, Van der Wees PJ, Pinheiro MB. Using research to guide practice: the physiotherapy evidence database (PEDro). *Brazilian Journal of Physical Therapy*. 2020 Sep 1;24(5):384-91.
26. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, Tugwell P, Campbell SM, Abeles M, Clark P, Fam AG. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology*. 1990 Feb;33(2):160-72.
27. Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Katz RS, Mease P, Russell AS, Russell IJ, Winfield JB, Yunus MB. The American College of Rheumatology

- preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. *Arthritis Care & Research*. 2010 May;62(5):600-10.
28. Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Häuser W, Katz RL, Mease PJ, Russell AS, Russell IJ, Walitt B. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. In: *Seminars in Arthritis and Rheumatism* 2016 Dec 1 (Vol. 46, No. 3, pp. 319-329). WB Saunders.
  29. Richardson WS, Wilson MC, Nishikawa J, Hayward RS. The well-built clinical question: a key to evidence-based decisions. *ACP Journal Club*. 1995 Nov 1;123(3):A12-3.
  30. Cohen J. *Statistical power analysis for the behavioral sciences*. Academic press; 2013 Sep 3.
  31. Centre for Reviews and Dissemination. *CRD's guidance for undertaking reviews in healthcare*. York Publ. Services; 2009.
  32. Cash E, Salmon P, Weissbecker I, Rebholz WN, Bayley-Veloso R, Zimmaro LA, Floyd A, Dedert E, Sephton SE. Mindfulness meditation alleviates fibromyalgia symptoms in women: results of a randomized clinical trial. *Annals of Behavioral Medicine*. 2015 Jun 1;49(3):319-30.
  33. Karlsson B, Burell G, Anderberg UM, Svärdsudd K. Cognitive behaviour therapy in women with fibromyalgia: a randomized clinical trial. *Scandinavian Journal of Pain*. 2015 Oct 1;9(1):11-21.
  34. Lami MJ, Martínez MP, Miro E, Sanchez AI, Prados G, Caliz R, Vlaeyen JW. Efficacy of combined cognitive-behavioral therapy for insomnia and pain in patients with fibromyalgia: a randomized controlled trial. *Cognitive Therapy and Research*. 2018 Feb;42:63-79.
  35. Simister HD, Tkachuk GA, Shay BL, Vincent N, Pear JJ, Skrabek RQ. Randomized controlled trial of online acceptance and commitment therapy for fibromyalgia. *The Journal of Pain*. 2018 Jul 1;19(7):741-53.
  36. McCrae CS, Williams J, Roditi D, Anderson R, Mundt JM, Miller MB, Curtis AF, Waxenberg LB, Staud R, Berry RB, Robinson ME. Cognitive behavioral treatments for insomnia and pain in adults with comorbid chronic insomnia and fibromyalgia: clinical outcomes from the SPIN randomized controlled trial. *Sleep*. 2019 Mar;42(3):zsy234.
  37. Pérez-Aranda A, Feliu-Soler A, Montero-Marín J, García-Campayo J, Andrés-Rodríguez L, Borràs X, Rozadilla-Sacanell A, Peñarrubia-Maria MT, Angarita-Osorio N, McCracken LM, Luciano JV. A randomized controlled efficacy trial of mindfulness-based stress reduction compared with an active control group and usual care for fibromyalgia: The EUDAIMON study. *Pain*. 2019 Nov 1;160(11):2508-23.
  38. Catella S, Gendreau RM, Kraus AC, Vega N, Rosenbluth MJ, Soefje S, Malhotra S, Luciano JV, McCracken LM, Williams DA, Arnold LM. Self-guided digital acceptance and commitment therapy for fibromyalgia management: results of a randomized, active-controlled, phase II pilot clinical trial. *Journal of Behavioral Medicine*. 2023 Jun 29:1-6.
  39. Buysse DJ, Reynolds III CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research*. 1989 May 1;28(2):193-213.
  40. Kinney M, Seider J, Beaty AF, Coughlin K, Dyal M, Clewley D. The impact of therapeutic alliance in physical therapy for chronic musculoskeletal pain: a systematic review of the literature. *Physiotherapy Theory and Practice*. 2020 Aug 2;36(8):886-98.
  41. Lakke SE, Meerman S. Does working alliance have an influence on pain and physical functioning in patients with chronic musculoskeletal pain; a systematic review. *Journal of Compassionate Health Care*. 2016 Dec;3(1):1-0.
  42. Ferreira PH, Ferreira ML, Maher CG, Refshauge KM, Latimer J, Adams RD. The therapeutic alliance between clinicians and patients predicts outcome in chronic low back pain. *Physical Therapy*. 2013 Apr 1;93(4):470-8.
  43. Cardenas-Rojas A, Castelo-Branco L, Pacheco-Barrios K, Shaikh ES, Uygur-Kucukseymen E, Giannoni-Luza S, Felipe LV, Gonzalez-Mego P, Luna-Cuadros MA, Gianlorenco AC, Teixeira PE. Recruitment characteristics and non-adherence associated factors of fibromyalgia patients in a randomized clinical trial: a retrospective survival analysis. *Contemporary Clinical Trials Communications*. 2021 Dec 1;24:100860.
  44. Kim Y. Missing data handling in chronic pain trials. *Journal of Biopharmaceutical Statistics*. 2011 Feb 28;21(2):311-25.
  45. Hughes LS, Clark J, Colclough JA, Dale E, McMillan D. Acceptance and commitment therapy (ACT) for chronic pain. *The Clinical Journal of Pain*. 2017 Jun 1;33(6):552-68.
  46. McCracken LM, Sato A, Taylor GJ. A trial of a brief group-based form of acceptance and commitment therapy (ACT) for chronic pain in general practice: pilot outcome and process results. *The Journal of Pain*. 2013 Nov 1;14(11):1398-406.
  47. Andrade A, Vilarino GT, Siczowska SM, Coimbra DR, Bevilacqua GG, Steffens RD. The relationship between sleep quality and fibromyalgia symptoms. *Journal of Health Psychology*. 2020 Aug;25(9):1176-86.
  48. Keskindag B, Karaaziz M. The association between pain and sleep in fibromyalgia. *Saudi Medical Journal*. 2017 May;38(5):465.
  49. Bigatti, S.M., Hernandez, A.M., Cronan, T.A. and Rand, K.L., 2008. Sleep disturbances in fibromyalgia syndrome: relationship to pain and depression. *Arthritis Care & Research: Official Journal of the American College of Rheumatology*, 59(7), pp.961-967.
  50. Bernardy K, Klose P, Busch AJ, Choy EH, Häuser W. Cognitive behavioural therapies for fibromyalgia. *Cochrane Database of Systematic Reviews*. 2013(9).
  51. Hróbjartsson A, Emanuelsson F, Skou Thomsen AS, Hilden J, Brorson S. Bias due to lack of patient blinding in clinical trials. A systematic review of trials randomizing patients to blind and nonblind sub-studies. *International Journal of Epidemiology*. 2014 Aug 1;43(4):1272-83.