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Acceptance-based interventions for the treatment of chronic pain: A systematic review and meta-analysis

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ABSTRACT

Acceptance-based interventions such as mindfulness-based stress reduction program and acceptance and commitment therapy are alternative therapies for cognitive behavioral therapy for treating chronic pain patients. To assess the effects of acceptance-based interventions on patients with chronic pain, we conducted a systematic review and meta-analysis of controlled and noncontrolled studies reporting effects on mental and physical health of pain patients. All studies were rated for quality. Primary outcome measures were pain intensity and depression. Secondary outcomes were anxiety, physical wellbeing, and quality of life. Twenty-two studies (9 randomized controlled studies, 5 clinical controlled studies [without randomization] and 8 noncontrolled studies) were included, totaling 1235 patients with chronic pain. An effect size on pain of 0.37 was found for the controlled studies. The effect on depression was 0.32. The quality of the studies was not found to moderate the effects of acceptance-based interventions. The results suggest that at present mindfulness-based stress reduction program and acceptance and commitment therapy are not superior to cognitive behavioral therapy but can be good alternatives. More high-quality studies are needed. It is recommended to focus on therapies that integrate mindfulness and behavioral therapy.

1. Introduction

Chronic pain is a major health problem and has high comorbidity, with depression (35%) and other psychological problems [45]. The cognitive-behavioral perspective introduced in 1983 [68] emphasized the role of attributions, efficacy expectations, personal control, and problem solving. Cognitive behavioral therapy (CBT) became the standard treatment for chronic pain patients who have to deal with psychological distress and disabilities. CBT incorporates both cognitive (eg, cognitive restructuring) and behavioral techniques (operant or respondent learning) to alter behavior. Although there is sound evidence that CBT-based treatments are effective with many disorders, only moderate effect sizes were reported for patients with chronic pain [20,47]. Moreover, a proportion of patients appears not to benefit from CBT [66,69]. Therefore, clinicians and researchers have been looking at alternatives.

In recent years there has been growing interest in acceptance-based therapies in which the focus is not so much on controlling or fighting pain, but on acceptance of pain. One of these programs is the mindfulness-based stress reduction program (MBSR) [33]. Kabat-Zinn [33] defined mindfulness as intentional and nonjudgmental present moment awareness. Exercises in MBSR include different types of formal meditation practice, yoga, and exercising mindfulness in everyday life. Mindfulness may result in a state of consciousness that has been described as reperceiving [61] or decentering [56]. It is characterized by the ability to "disidentify from the contents of consciousness (ie, one's thoughts) and view his or her moment-by-moment experience with greater clarity and objectivity" [61]. Mindfulness has also been integrated with cognitive therapy, called mindfulness-based cognitive therapy (MBCT) [59], and was primarily designed to prevent depressive relapse.

Another acceptance-based intervention is acceptance and commitment therapy (ACT) [26]. ACT targets ineffective control strategies and experiential avoidance. People learn to stay in contact with unpleasant emotions, sensations, and thoughts. Negative thoughts associated with pain are used as targets for exposure rather than attempting to change their irrational content [15]. Developing mindfulness is one of the strategies in ACT, but it is claimed that meditation is not needed to become mindful. ACT further focuses on value clarification and the client's ability to commit to these values in daily life.

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The aim of the current study was to conduct a meta-analysis of the effects of acceptance-based interventions on patients with chronic pain and to assess possible moderating factors. To our knowledge, no such specific meta-analysis has been conducted. Teixeira [64] reviewed the effects of meditation on pain and found that meditation programs may help ease the burden of chronic pain in the short and long term. However, she did not conduct a meta-analysis nor assess the quality of the included studies. Baer [3] conducted a meta-analysis on the effects of MBSR and found significant improvements on pain (0.31) and depression (0.86). However, only 4 of her studies examined chronic pain, and she did not include either ACT or an assessment of the quality of the studies. Given the limited number of randomized controlled trials (RCTs) in this field and the explorative character of our meta-analysis, both controlled and noncontrolled studies were included.

2. Methods

2.1. Search strategy

A systematic search was performed in 4 electronic databases: PubMed (1966 to January 2009), Embase (to January 2009), PsycInfo (1960 to January 2009), and the Cochrane Central Register of Controlled Trials (1800 to January 2009). The databases were searched for English language studies using the following terms: "mindfulness" or "vipassana" or "meditation" or "mindfulness-based stress reduction" or "MBSR" or "mindfulness-based cognitive therapy" or "MBCT" or "acceptance-based" or "acceptance based" or "acceptance and commitment", in combination with "chronic pain" or specific chronic pain conditions including "fibromyalgia" or "chronic fatigue syndrome" or "chronic low back pain" or "whiplash associated disorder" or "WAD" or "repetitive strain injury" or "RSI" or "dystrophy". Furthermore, the reference lists of included studies were examined for additional potentially eligible studies.

2.2. Selection of studies

Two reviewers (M.O. and M.V.) independently selected potentially eligible studies on the basis of title and abstract. The interrater reliability was satisfactory (Kappa = 0.80) [9], and most of the inconsistencies in the assessments were due to conservative scoring. Disagreements were resolved by consensus. Studies were included if they reported on the effectiveness of a standardized acceptance (ACT) or mindfulness (MBSR/MBCT)-based treatment program in patients with chronic pain or chronic pain-related conditions. Both controlled and noncontrolled studies were included to estimate within-groups changes, as well as published and unpublished (eg, dissertations) studies. Studies were excluded if (1) the intervention consisted of a single treatment session, (2) no abstract was available, or (3) insufficient data were reported to calculate standardized mean differences. We requested the full-text articles. The definite selection was then made by 2 reviewers (M.O. and M.V.). The interrater reliability was very good, with a Kappa value of 0.93 [9].

2.3. Data extraction

Data extraction and study quality assessment were performed by 1 reviewer (M.O.) and checked by a second reviewer (M.V.) using a standardized data abstraction form created for the study. Disagreements were resolved, if possible, by consensus and otherwise by consultations with a third reviewer (E.B.). Data were extracted on design (randomized controlled trial; controlled clinical trial [CCT], without randomization; other design [OD], noncontrolled study); country; characteristics of participants; intervention type; control group; and attrition rate. In agreement with the Clinical Importance of Treatment Outcomes in Chronic Pain Clinical Trials (IMMPACT) recommendations [19,67], primary outcomes of our review were pain intensity and depressive symptomatology. We also recorded outcome data on anxiety, quality of life, and physical wellbeing.

2.4. Quality assessment

Methodological quality of included studies was assessed using an 8-point scale, based on criteria by the Cochrane Collaboration [28] and the validated Jadad scale [31] tailored for the included studies (Table 1). The quality of a study was assessed as high when 7 or more criteria were met, medium when 4, 5, or 6 criteria were met, and low when 3 or fewer criteria were met.

2.5. Data analysis

For this meta-analysis, Hedges' g effect sizes were calculated using Microsoft Excel with the following formula: $g = M_1 - M_2/S_{pooled}$, where $S = \sqrt{[\sum(X - M)^2/N - 1]}$, and $S_{pooled} = \sqrt{}$Mswithin. We compared posttest scores from the control group and experimental group to calculate this effect size. If no means and standard deviations were reported, other test statistics (*P*, *t*, confidence intervals) were converted into Hedges' g [27]. We also included noncontrolled studies, thus calculating Hedges' g based on pretest and posttest scores from the intervention group for all studies. As recommended by Dunlap et al. [18], noncontrolled studies were excluded if they did not report the means and standard deviations or the correlations between pretest and posttest scores. Using other test statistics to calculate effect sizes in studies comparing pretest and posttest scores would give biased or overestimated effect sizes given the correlation between the 2 scores [18]. Please note that we calculated 2 estimates for controlled studies: 1 compared posttest scores between control and experimental groups, the other compared pretest and posttest results from the experimental group. Cohen [10] has described effect sizes of 0.2, 0.5, and 0.8 as small, medium, and large, respectively.

We used RevMan software version 5.0.18 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2008) for calculating pooled standardized mean differences (SMDs), to test heterogeneity, and to perform subgroup analyses. Precalculated effect sizes were manually entered using the generic inverse variance outcome type. Pooled SMDs for the controlled studies (RCTs and CCTs) were calculated using the fixed-effects model because we observed minimal clinical and methodological diversity between the controlled studies. By using the fixed-effects model, it is assumed that the observed differences among study results are solely due to the play of chance [16]. Pooled SMDs for the noncontrolled studies (OD) were calculated using the random-effects model, also known as the DerSimonian and Laird model [17]. Because there is a major methodological diversity between controlled and noncontrolled studies (eg, risk of bias and study design), we considered studies to be heterogeneous. When using the random-effects model, an average intervention effect is calculated instead of an estimate of the intervention effect.

The χ^2 test was used to measure significant statistical heterogeneity. Statistical heterogeneity is an indicator of clinical and methodological heterogeneity. The I^2 statistic was calculated for indication of the heterogeneity in percentages [29,16]. A value of 0% indicates no observed heterogeneity, and larger shows increasing heterogeneity: 0 to 40% is considered as low heterogeneity, 30% to 60% may represent moderate heterogeneity, 50% to 90% may

Table 1
Criteria methodological quality.

	Criteria	Scoring
1.	Allocation to conditions was based on randomization according to the text	1/0
2.	The randomization scheme was described and appropriate, eg, using a computer, random number table	1/0
3.	A dropout analysis was conducted, or there were no dropouts	1
	Reasons of attrition were reported, but no analysis was conducted	0
4.	Intention to treat analysis was performed, or there were no dropouts	1/0
5.	At least 1 of the trainers was experienced or trained in teaching mindfulness or ACT	1
	Specific experience or training was not reported	0
6.	Patient's pain was diagnosed by a physician or rheumatologist, or patients were referred from a pain clinic where diagnosis is prior to admission	1
	Recruitment through media, or diagnosis based on a scale and self-report, or diagnosis not mentioned	0
7.	The study had a minimal level of statistical power to find significant effects of the treatment, and included 50 or more persons in the comparison between treatment and control group (this allows the study to find standardized effect sizes of 0.80 and larger, assuming a statistical power of 0.80 and alpha of 0.05)	1
	Sample smaller than 50, or the total the sample was bigger than 50, but the results were only reported divided by different studies	0
8.	Treatment integrity was checked during the study by supervision of the therapists during treatment, or by recording the treatment sessions, or by systematic screening of protocol adherence by a standardized measurement instrument	1
	Treatment integrity was not checked, or integrity was supervised by one of the therapists, or they tried to keep the intervention sound by intensive consultation	0

ACT, acceptance and commitment therapy.

represent substantial heterogeneity, and 75% to 100% is considerable heterogeneity. When using the random-effects model, the τ^2 statistic was calculated, which is an estimate of the between-study variance.

Subgroup analyses were performed by testing pooled SMDs for significant differences in pain and depression between subgroups. Analyses were only performed for the controlled studies, and by the following subdivision. (1) Quality score divided by low, medium, and high quality as mentioned earlier. (2) Subgroups for control group; included studies used waitlist controls, education/support groups, or treatment as usual. One study [24] included waitlist and no interest controls, but data were not presented separately. These data were scored as waitlist controls. One study [73] placed participants on a waiting list, but offered them treatment as usual as well, and were scored in this study as waitlist controls. (3) Intervention type; ACT based or MBSR based. (4) Type of pain in 4 subgroups: mixed chronic pain populations, fibromyalgia combined with chronic fatigue syndrome, rheumatoid arthritis, and specific-site pain populations (eg, chronic low back pain, chronic headache). (5) Attrition rate higher or lower than 25%.

To assess for publication bias, we performed a funnel plot for pain and depression [16] for the controlled studies by plotting the pooled SMD against study size. When publication bias is absent, the studies can be expected to be distributed symmetrically around the pooled effect size. Bias can be expected when the plot shows a higher concentration of studies on one side of the pooled SMD than on the other.

3. Results

Initially, 1121 titles were retrieved from the databases (PubMed 894, PsycInfo 89, Cochrane 32, Embase 106). After review of title and abstract and removal of duplicates, 40 studies were identified as being potentially eligible for inclusion in the study. Full-text versions of these articles were obtained and independently assessed by 2 reviewers (M.O. and M.V.). Twenty-one of the 40 articles were excluded for the following reasons: no acceptance-based intervention [8,12,21,38,40,44,65], insufficient data [32,34–36,46,51,53,54,72], sample contained other than pain patients [1,7,11], same sample used in 2 publications [58], and inconsistencies in the intervention protocol [74]. Therefore, 19 studies were included in this systematic review, 14 controlled [2,6,15,22,24,25,48,49,52,57,60,62,73,75], and 5 noncontrolled [41,43,50,70,71]. Nine of the controlled studies were RCTs [2,6,15,48,49,52,60,73,75], the others were CCTs. One controlled study also included 2 noncontrolled substudies, which we also included [62]. One noncontrolled study reported on 2 substudies, which we included [70].

3.1. Characteristics of included studies

Characteristics of the selected studies are presented in Table 2. The 22 (sub-)studies included in the analysis evaluated 1235 subjects. In general, the participants were adults with a mean age between 40 and 60 years. In all studies, except 1 [70], the majority of the participants was female. In 6 studies the attrition rate was higher than 25% (range 25.3% to 49.0%). Fifteen studies measured pain, 17 depression, 13 anxiety, 13 physical wellbeing, and 5 quality of life. All instruments had good psychometric properties. Study size ranged from a small pilot study of 6 subjects [70] to a large-scale study involving 171 subjects [71]. Median study size was 46 subjects (interquartile range 16.8 to 90.3). Fifteen studies used a MBSR(-based) program, and 7 studies an ACT(-based) program. Most MBSR-based studies held 8 weekly sessions in a range from 1.5 hours to 2.5 hours (median 2 hours). Half of the ACT-based studies treated their patients full time for 3 or 4 weeks. The other studies held 4 to 10 weekly sessions in a range from 1 hours to 1.5 hours. In general, group sizes ranged from 6 persons to 25. Some studies used smaller groups [50,71], or even individual sessions [15,73]. Nine studies included patients with some sort of chronic pain, 4 with fibromyalgia, 2 with rheumatoid arthritis, 4 with chronic fatigue syndrome, and 3 studies included patients with specific site pain (eg, chronic low back pain). With respect to the controlled studies, 7 used a waitlist control, 3 used treatment as usual, and 4 used an education/support group as comparison group. Two studies scored high on the quality criteria, 8 scored medium, and 12 scored low. None of the studies met all quality criteria.

3.2. Publication bias

Some indication for publication bias was found for the outcome measure depression. The funnel plot for depression is presented in Fig. 1, and shows asymmetrically distributed studies in the bottom of the figure. In the presence of bias, it can be expected that the bottom of the plot, which displays smaller studies, shows a higher concentration of studies on one side of the pooled SMD than on the other. This is due to the fact that smaller studies are more likely to be published if they have larger-than-average effects [5]. The funnel plot for pain was symmetrically distributed around the pooled SMD, which is an indication for the absence of publication bias.

Table 2
Characteristics of included studies.

Author	Study design	Quality score	Pain	Mean age (SD or range)	Male, %	Intervention	Group size	Sessions (number), duration	Control group	n	Attrition rate, %	Outcome measures
McCracken (2007)	OD	3	Highly disabled chronic pain patients	47.6 (11.6)	35.8	ACT		3 weeks full time, 80 h	–	53	0	Pain: NRS Depression: BDI Anxiety: PASS Physical: SIP
McCracken (2005)	OD	2	Complex chronic pain	44.4 (10.7)	35.8	ACT		3 or 4 weeks full time	–	108	23.9	Pain: NRS Depression: BDI Anxiety: PASS Physical: SIP
Pauzano-Slamm (2005)	OD	3	Chronic fatigue syndrome	52.4 (14.2)	23.6	MBSR	4–5	8, 1.5 h	–	16	17.7	Depression: BDI Anxiety: BSI-18
Surawy (2005) Study 2	OD	2	Chronic fatigue syndrome	(18–65)	25	MBSR	12	8	–	10	18.2	Depression: HADS Anxiety: HADS Physical: SF-36
Surawy (2005) Study 3	OD	2	Chronic fatigue syndrome	(18–65)	36	MBSR	11	8	–	9	18.2	Depression: HADS Anxiety: HADS Physical: SF-36
Vowles (2009) Study 1	OD	1	Chronic pain	49.5 (6.9)	36.4	ACT	6	8, 1.5 h	–	11	31.3	Pain: MPQ Depression CES-D Anxiety: PASS Physical: PDI
Vowles (2009) Study 2	OD	1	Chronic pain	50.4 (17.8)	82	ACT	2–3	4, 1.5 h	–	I: 6		Pain: MPQ Depression: CES-D Anxiety: PASS Physical: PDI
Vowles (2008)	OD	3	Chronic pain	47.3 (11.4)	35.8	ACT		3 or 4 weeks full time	–	171	8.6	Pain: NRS Depression: BCMDI Anxiety: PASS Physical: SIP
Gardner-Nix (2008)	CCT	1	Chronic pain	I: 51 C: 52	I: 20 C: 25	MBSR	10–20	10, 2 h	Waitlist	I: 99 C: 57	I: 49 C: 10	Pain: NRS Physical: SF-36
Goldenberg (1994)	CCT	3	Fibromyalgia	I: 46 (9.9) C: 47.2 (11.8)	I: 10 C: 3	MBSR	7–12	10, 2 h	Waitlist (n = 18) No interest (n = 24)	I: 79 C: 42	I: 9.2	Pain: VAS QoL: FIQ
Grossman (2007)	CCT	3	Fibromyalgia	T: 52 (8) I: 54.4 (8.3) C: 48.8 (9.1)	0	MBSR	10–15	8, 2.5 h	Education/ support	I: 39 C: 13	T: 10.3 I: 9.3 C: 13.3	Pain: VAS Depression: HADS Anxiety: HADS QoL: QoL
Sagula (2004)	CCT		Chronic pain		23.9	MBSR	7–10	8, 1.5 h	TAU	I: 39 C: 18	T: 19.7 I: 20.4 C:18.2	Depression: BDI Anxiety: STAI
Surawy (2005) Study 1	CCT	2	Chronic fatigue syndrome	(18–65)	44.4	MBSR	9	8	Waitlist	I: 9 C: 8	T: 6	Depression: HADS Anxiety: HADS Physical: SF-36

Astin (2003)	RCT	5	Fibromyalgia	T: 47.7 (10.6)	T: 0.8 I: 1.6 C: 0	MBSR + Qigong	10–20	8, 2.5 h	Education/support	I: 32 C: 33	T: 39	Pain: SF-36 Depression: BDI QoL: FIQ
Bruckstein (1999)	RCT	7	Chronic pain	T: 56.4 (13.7)	T: 26.6 I: 22.7 C: 38.9	MBSR		8, 1.5 h	Education/support	I: 15 C: 7	T: 30.4 I: 29.2 C: 31.8	Pain: VAS Depression: BDI Anxiety: SCL-90 Physical: SIP
Dahl (2004)	RCT	4	Chronic pain	T: 40 (13.2) I: 36.7 (12.5) C: 44.4 (13.6)	10.5	ACT	Individual	4, 1 h	TAU	I: 11 C: 8	0	Pain: NRS QoL: LSQ
Morone (2008)	RCT	5	Chronic low back pain	T: 74.9 (65–84)	43	MBSR		8, 1.5 h	Waitlist	I: 19 C: 18	T: 19 I: 32 C: 6	Pain: MPQ-SF Physical: SF-36 QoL: SF-36
Nash-Mc Feron (2006)	RCT	5	Chronic headache	I: 50 (14.6) C: 51 (12.2)	I: 0 C: 35	MBSR	20	8, 1.5 h	TAU	I: 20 C: 20	I: 5 C:10	Pain: SF-36 Physical: SF-36
Pradhan (2007)	RCT	6	Rheumatoid arthritis	I: 56 (9) C: 53 (11)	I: 16 C: 9	MBSR	Cohort I: 18 Cohort II: 13	8, 2.5 h	Waitlist	I: 32 C: 32		Depression: SCL-90
Sephton (2007)	RCT	6	Fibromyalgia	T: 48.2 (10.6) I: 48.4 (8.9) C: 47.6 (11.5)	0	MBSR	25	8, 2.5 h	Waitlist	I: 51 C: 39	25.3	Depression: BDI
Wicksell (2008)	RCT	5	Whiplash-associated disorders	I: 48.2 (7.8) C: 55.1 (11.2)	38.5	ACT	Individual	10, 1 h	Waitlist + TAU	I: 11 C: 9	T: 4.8 I: 0 C: 10	Pain: VAS Depression: HADS Anxiety: HADS Physical: PDI QoL: SWLS
Zautra (2008)	RCT	7	Rheumatoid arthritis	I: 57.3 (15.3) C: 52.4 (13.0)	31.9	MBSR	6–10	8	Education/support	I: 47 C: 44	T: 3.5–4.3	Pain: NRS Depression: own scale

ACT, acceptance and commitment therapy; CBT, cognitive behavioural therapy; MBSR, mindfulness-based stress reduction; C, control group; I, intervention group; T, total group; CCT, controlled clinical trial; RCT, randomized controlled trial; OD, other design; SD, standard deviation; BCMDI, British Columbia Major Depression Inventory; BDI, Beck Depression Inventory; BSI-18, Brief Symptom Inventory 18; CES-D, Center for Epidemiologic Studies Depression Scale; FIQ, Fibromyalgia Impact Questionnaire; HADS, Hospital Anxiety and Depression Scale; LSQ, Life Satisfaction Questionnaire; MPQ, McGill Pain Questionnaire; NRS, numerical rating scale; PASS, Pain Anxiety Symptoms Scale; PDI, Pain Disability Index; POMS, Profile of Mood States; QoL (outcome measure), Quality of Life Profile for the Chronically Ill; SCL-90, 90-item symptom checklist; SF-36, 36-Item Short-Form Health Survey; SIP, Sickness Impact Profile; STAI, State-Trait Anxiety Inventory; SWLS, Satisfaction With Life Scale; VAS, Visual Analogue Scale.

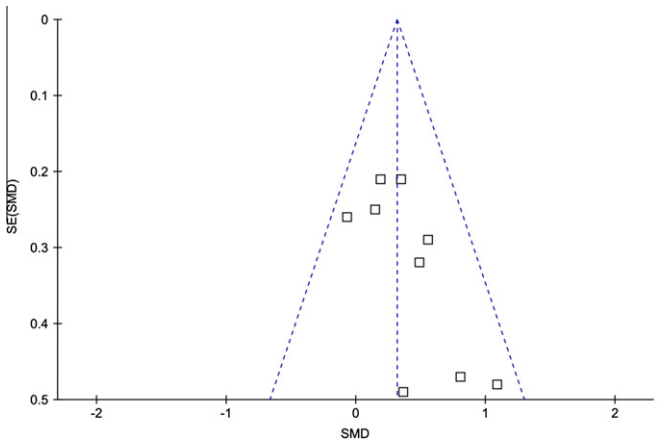

Fig. 1. Funnel plot for depression.

3.3. Effects based on pretest and posttest scores, including controlled and noncontrolled studies

Pooled SMDs and the results of the tests for heterogeneity and overall effect are presented in Table 3. Moderate effect sizes were found for pain (SMD = 0.47; 95% CI: 0.28 to 0.66) and depression (SMD = 0.64; 95% CI: 0.43 to 0.85) when pretest and posttest scores of all studies were analyzed. These effects were significant ($P < .01$). Moderate and significant effects were also found for anxiety, physical wellbeing, and quality of life, with pooled SMDs ranging from 0.48 to 0.69.

3.4. Effects for the controlled studies

When the CCTs were analyzed, moderate and significant effects were found for pain (SMD = 0.48; 95% CI: 0.25 to 0.71) and depression (SMD = 0.50; 95% CI: 0.12 to 0.89). Analyses of the RCTs showed small effects on pain and depression with pooled SMDs of respectively 0.25 (95% CI: 0.01 to 0.49) and 0.26 (95% CI: 0.05 to 0.47). Effects were still significant. Both the CCTs and the RCTs showed small to moderate effects on anxiety, physical wellbeing, and quality of life. Only the effects for quality of life (CCTs; SMD = 0.57) and physical wellbeing (RCTs; SMD = 0.43) were significant. Please note that the number of studies was small when the CCTs and the RCTs were analyzed separately.

Pooling the results of all controlled studies (CCTs and RCTs) gave small but significant effects, with a pooled SMD of 0.37 (95% CI: 0.20 to 0.53) for pain, 0.32 (95% CI: 0.13 to 0.50) for depression, 0.40 for anxiety (95% CI: 0.07 to 0.73), 0.35 for physical wellbeing (95% CI: 0.10 to 0.59), and 0.41 for quality of life (95% CI: 0.16 to 0.65). When studies scored as low quality were excluded, the SMD for pain dropped to 0.25 (95% CI: 0.01 to 0.49) and for depression dropped to 0.30 (95% CI: 0.10 to 0.49).

3.5. Subgroup analyses

Subgroup analyses are presented in Table 4. There were no significant differences between subgroups in the effects on pain or depression ($P > .05$) between the different subgroups, except for publication status. Unpublished studies reported higher effects (SMD = 0.90) on pain than published studies (SMD = 0.32), but note that only 2 unpublished studies were included in this subgroup analysis.

4. Discussion

4.1. Main findings

This was an explorative meta-analysis of studies on the effects of acceptance-based therapies on mental and physical health in patients with chronic pain. When all studies focusing on change score before and after treatment were included in the meta-analysis, we found medium effect sizes for pain intensity, depression, anxiety, physical wellbeing, and quality of life. This finding shows that in general, patients with chronic pain respond reasonably well to acceptance-based therapies.

Table 3
Effects.

Outcome measures	*n*	Studies	Pooled SMD [95% CI]	Heterogeneity	Test for overall effect
Effects for pre- and posttest scores (all studies included)					
Pain	14	[2,6,15,22,25,41,43,49,48,70,71,73,75]	0.43 [0.22–0.64]	$\tau^2 = 0.08$; $\chi^2 = 34.72$, df = 13 ($P < .01$); $I^2 = 63\%$	$Z = 4.06$ ($P < .01$)
Depression	17	[2,6,25,41,43,50,52,57,62,60,70,71,73,75]	0.69 [0.47–0.92]	$\tau^2 = 0.12$; $\chi^2 = 49.04$, df = 16 ($P < .01$); $I^2 = 67\%$	$Z = 6.18$ ($P < .01$)
Anxiety	13	[6,25,41,43,50,57,62,70,71,73]	0.69 [0.51–0.88]	$\tau^2 = 0.03$; $\chi^2 = 18.24$, df = 12 ($P = .11$); $I^2 = 34\%$	$Z = 7.39$ ($P < .01$)
Physical wellbeing	13	[6,22,41,43,48,62,70,71,73]	0.48 [0.27–0.68]	$\tau^2 = 0.06$; $\chi^2 = 24.66$, df = 12 ($P = .02$); $I^2 = 51\%$	$Z = 4.48$ ($P < .01$)
Quality of life	5	[2,15,25,48,73]	0.63 [0.28–0.98]	$\tau^2 = 0.05$; $\chi^2 = 5.78$, df = 4 ($P = .22$); $I^2 = 31\%$	$Z = 3.58$ ($P < .01$)
Effects for CCTs					
Pain	3	[22,24,25]	0.48 [0.25–0.71]	$\chi^2 = 0.12$, df = 2 ($P = .94$); $I^2 = 0\%$	$Z = 4.07$ ($P < .01$)
Depression	3	[25,57,62]	0.50 [0.12–0.89]	$\chi^2 = 0.11$, df = 2 ($P = .94$); $I^2 = 0\%$	$Z = 2.56$ ($P = .01$)
Anxiety	3	[25,57,62]	0.34 [−0.04–0.73]	$\chi^2 = 0.88$, df = 2 ($P = .64$); $I^2 = 0\%$	$Z = 1.75$ ($P = .08$)
Physical wellbeing	2	[22,62]	0.29 [−0.02–0.61]	$\chi^2 = 0.10$, df = 1 ($P = .76$); $I^2 = 0\%$	$Z = 1.82$ ($P = .07$)
Quality of life	2	[24,25]	0.57 [0.22–0.91]	$\chi^2 = 0.05$, df = 1 ($P = .82$); $I^2 = 0\%$	$Z = 3.19$ ($P < .01$)
Effects for RCTs					
Pain	7	[2,6,15,48,49,73,75]	0.25 [0.01–0.49]	$\chi^2 = 8.46$, df = 6 ($P = .21$); $I^2 = 29\%$	$Z = 2.06$ ($P = .04$)
Depression	6	[2,6,52,60,73,75]	0.26 [0.05–0.47]	$\chi^2 = 6.46$, df = 5 ($P = .26$); $I^2 = 23\%$	$Z = 2.39$ ($P = .02$)
Anxiety	2	[6,73]	0.55 [−0.09–1.18]	$\chi^2 = 0.05$, df = 1 ($P = .82$); $I^2 = 0\%$	$Z = 1.68$ ($P = .09$)
Physical wellbeing	4	[6,48,49,73]	0.43 [0.04–0.82]	$\chi^2 = 2.06$, df = 3 ($P = .56$); $I^2 = 0\%$	$Z = 2.16$ ($P = .03$)
Quality of life	4	[2,15,48,73]	0.25 [−0.10–0.59]	$\chi^2 = 3.02$, df = 3 ($P = .39$); $I^2 = 1\%$	$Z = 1.41$ ($P = .16$)
Effects for all controlled studies (CCTs and RCTs)					
Pain	10	[2,6,15,22,24,25,48,49,73,75]	0.37 [0.20–0.53]	$\chi^2 = 10.41$, df = 9 ($P = .32$); $I^2 = 14\%$	$Z = 4.36$ ($P < .01$)
Depression	9	[2,6,25,52,57,60,62,73,75]	0.32 [0.13–0.50]	$\chi^2 = 7.75$, df = 8 ($P = .46$); $I^2 = 0\%$	$Z = 3.32$ ($P = .01$)
Anxiety	5	[6,25,57,62,73]	0.40 [0.07–0.73]	$\chi^2 = 1.21$, df = 4 ($P = .88$); $I^2 = 0\%$	$Z = 2.36$ ($P = .02$)
Physical wellbeing	6	[6,22,48,49,62,73]	0.35 [0.10–0.59]	$\chi^2 = 2.44$, df = 5 ($P = .79$); $I^2 = 0\%$	$Z = 2.78$ ($P < .01$)
Quality of life	6	[2,15,24,25,48,73]	0.41 [0.16–0.65]	$\chi^2 = 4.68$, df = 5 ($P = .46$); $I^2 = 0\%$	$Z = 3.25$ ($P < .01$)

RCT, randomized controlled trial; CCT, controlled clinical trial; SMD, standardized mean difference; 95% CI, 95% confidence interval; df, degrees of freedom.

Table 4
Subgroup analyses of all controlled studies on pain and depression.

Outcome measure	Criteria	Subgroup	*n*	SMD [95% CI]	Test for subgroup differences
Pain	Quality	Low quality [22,24,25]	3	0.48 [0.25–0.71]	χ^2 = 1.85, df = 2 (*P* = .40)
		Medium quality [2,15,48,49,73]	5	0.24 [−0.07–0.54]	
		High quality [6,75]	2	0.27 [−0.11–0.65]	
	Intervention	ACT [15,73]	2	0.29 [−0.35–0.94]	χ^2 = 0.06, df = 1 (*P* = .81)
		MBSR [2,6,24,25,22,48,49,75]	8	0.37 [0.20–0.54]	
	Control group	Education/support [2,6,25,75]	4	0.20 [−0.07–0.47]	χ^2 = 2.32, df = 2 (*P* = .31)
		TAU [15,49]	2	0.51 [−0.03–1.05]	
		Waitlist [22,24,48,73]	4	0.46 [0.23–0.69]	
	Pain type	Chronic pain [6,15,22]	3	0.49 [0.19–0.79]	χ^2 = 2.76, df = 3 (*P* = .43)
		Fibromyalgia [2,24,25]	3	0.34 [0.07–0.61]	
		Special site pain [49,48,73]	3	0.49 [0.06–0.92]	
		Rheumatoid arthritis [75]	1	0.09 [−0.32–0.50]	
	Attrition rate	<25% [15,24,25,49,73,75]	6	0.38 [0.16–0.61]	χ^2 = 0.04, df = 1 (*P* = .83)
		>25% [2,6,22,48]	4	0.35 [0.10–0.60]	
	Publish status	Unpublished [6,49]	2	0.90 [0.35–1.45]	χ^2 = 3.89, df = 1 (*P* = .05)
		Published [2,15,22,24,25,48,73,75]	8	0.32 [0.14–0.49]	
Depression	Quality	Low quality [62,25]	2	0.45 [−0.07–0.98]	χ^2 = 0.31, df = 2 (*P* = .86)
		Medium quality [2,52,57,60,73]	5	0.30 [0.06–0.53]	
		High quality [6,75]	2	0.29 [−0.08–0.67]	
	Intervention	MBSR [2,6,25,52,57,60,62,75]	8	0.28 [0.09–0.47]	χ^2 = 2.71, df = 1 (*P* = .10)
		ACT [73]	1	1.09 [0.15–2.03]	
	Control group	Education/support [62,52,60,73]	4	0.29 [0.02–0.56]	χ^2 = 0.79, df = 2 (*P* = .67)
		Waitlist [6,2,25,75]	4	0.29 [−0.00–0.58]	
		TAU [57]	1	0.56 [−0.01–1.13]	
	Pain type	Chronic pain [6,57]	2	0.63 [0.15–1.11]	χ^2 = 6.17, df = 3 (*P* = .10)
		Fibromyalgia + CFS [2,25,62,60]	4	0.32 [0.05–0.59]	
		Rheumatoid arthritis [52,75]	2	0.09 [−0.23–0.41]	
		Special site pain [73]	1	1.09 [0.15–2.03]	
	Attrition rate	<25% [25,52,57,62,73,75]	6	0.31 [0.07–0.55]	χ^2 = 0.01, df = 1 (*P* = .94)
		>25% [2,6,60]	3	0.32 [0.03–0.62]	
	Publish status	Unpublished [6]	1	0.81 [−0.11–1.73]	χ^2 = 1.15, df = 1 (*P* = .28)
		Published [2,25,52,57,60,62,73,75]	8	0.29 [0.10–0.48]	

SMD, standardized mean difference; 95% CI, 95% confidence interval; ACT, acceptance and commitment therapy; MBSR, mindfulness-based stress reduction program; TAU, treatment as usual; CFS, chronic fatigue syndrome; df, degrees of freedom.

On the basis of 10 controlled studies, it was found that MBSR and ACT have a small effect (SMD = 0.37) on pain intensity. Importantly, within this sample of controlled studies no heterogeneity was found. This is an indication of the robustness of the finding. In other meta-analyses, comparable effects were found for CBT [30,20,47]. Moreover, Baer [3] found a similar effect size for mindfulness interventions in an earlier meta-analysis. Based on the principle of best evidence, it makes sense to include only RCTs or to exclude the studies with low quality. In both cases, a smaller effect size (SMD = 0.25, 0.22) was found. Differences, however, were not significant. Although pain intensity was the most used outcome measure in the included studies, which is in accordance with the IMMPACT recommendations, it is important to note that reduction of pain intensity is not a primary focus of acceptance-based therapies. Participants learn to let go of pain control strategies in favor of acceptance of pain as a part of their daily lives. The pain per definition being chronic, larger effect sizes may not be expected. So, it is questionable whether pain intensity is the most appropriate outcome measure for acceptance-based interventions in chronic pain patients. For future studies, it is recommended not to solely rely on pain intensity as an outcome measure but also to include other pain measures such as interference of pain with daily life. The number of studies that assessed other pain measures was too small to include these outcomes in this meta-analysis.

In a similar way, it was found that acceptance-based therapies have a small effect (SMD = 0.32) on depression. No indication for heterogeneity was found in this cluster of studies either. This effect is comparable with the effect sizes found for CBT, whereas we hypothesized that precisely acceptance would lead to a larger reduction of depressive symptomatology. What could explain this result? One possible factor could be a floor effect, as mentioned by Pradhan et al. [52]. When patients with lower levels of depression are included in studies, there is less room for improvement. Unfortunately we could not study this explanation empirically because different instruments were used and many instruments do not have clear cutoff scores. Another explanation could be that ACT has more similarities than differences with CBT. However, this could only be part of the explanation because just 1 small ACT study was included in this meta-analysis. The others were MBSR based. A final explanation could be that the effectiveness of MBSR specifically on depression is limited [4]. MBSR was developed as a general stress reduction program, mainly combining meditation with psychoeducation. In recent years, new programs have been developed that integrate MBSR with behavioral therapy [55,63]. There is more focus on behavioral change. Mindfulness may very well facilitate effective mechanisms of behavioral therapy [61]. Preliminary studies show promising results [55,63]. In contrast to MBSR, ACT is an intervention with more focus on behavioral change. The one ACT study that was included in this meta-analysis showed a large effect on depression.

Fewer studies reported the effects of ACT and MBSR on anxiety, physical functioning, and quality of life. On the basis of the included controlled studies, it can be concluded that acceptance-based interventions have small effects on these measures.

With respect to the quality of the studies, it was found that quality did not significantly moderate the effects of acceptance-based interventions. This result is somewhat surprising. In several recent, large meta-analyses on the effects of psychotherapy and pharmacotherapy, it has been found that lower effects were found in higher-quality studies [13,14,23,37]. However, only 2 high-quality studies were included in this study, so these findings have to be interpreted with caution. Other factors (type of intervention,

control group and pain, attrition rate) also did not significantly moderate the effects of acceptance-based therapy with chronic pain patients. One exception was publication status, with unpublished studies reporting higher effects on pain intensity.

For the studies on pain intensity and depression, funnel plots were conducted to check the possibility of publication bias. A symmetrical funnel plot was found for pain intensity, suggesting the absence of publication bias. For depression, in the lower left side of the funnel plot, studies were lacking. This may be an indication of publication bias, as studies with small samples that found no or small effects may be underrepresented in the published articles [5]. The only 2 unpublished studies that could be included in the meta-analysis, however, reported a significantly higher effect size than the published studies. But it could be that more unpublished studies exist than were represented in the databases we used in this review.

It is important to note that at present, acceptance-based interventions and CBT produce small but equivalent effects. Given the relatively large number of high-quality studies in CBT, CBT currently remains the standard treatment. Treatment outcomes, however, could be improved if treatments are matched to patient characteristics [66,69]. Recurrent depression might be one important factor for referring patients to either an acceptance-based intervention or CBT. Recently, Zautra et al. [75] have shown that rheumatoid arthritis patients with recurrent depression benefited more from an acceptance-based intervention than from CBT, compared to patients with no recurrent depression. Experiential avoidance and low levels of meaning in life might be other factors. Given their primary focus on decreasing experiential avoidance (or improving acceptance) in combination with exploring values and value-based living, acceptance-based interventions might be more suitable for patients with high levels of experiential avoidance and lower levels of meaning in life than CBT. More research is needed to confirm these findings and to find other characteristics that seem important in referring patients to either CBT or MBSR or ACT, as has been recommended by several scientists [66,69].

5. Study limitations

This study has several limitations. First, we found only 2 high-quality studies and no study that met all criteria. This could be an underestimation, because quality criteria were scored conservatively. When a criterion was not reported in the article, we coded this criterion as negative. It is quite plausible that authors chose to omit certain study characteristics owing to lack of space in the journal. Clearly more high-quality studies are needed to confirm the reported results with regard to effectiveness and quality as a moderating factor. A second limitation is that insufficient data were reported to conduct a meta-analysis of the long-term effects of acceptance-based interventions. Third, PsycInfo solely retrieves unpublished dissertations from North America. Excluding non-American dissertations could lead to bias. Fourth, the subgroup analyses were based on all controlled studies. Given the small number of RCTs, it was not possible to separate the results of the RCTs from the CCTs, which probably would have led to lower effect sizes. Fifth, the representativeness of the participants in some studies was limited. Some patients (eg, rheumatoid arthritis patients) were not representative of those referred to pain clinics. Furthermore, some studies reported a high attrition rate. Both may limit the generalizability of the findings. Sixth, the studies we found were not included in a previous meta-analysis [20] on the effects of psychological therapies in chronic pain. This could be explained by the different criteria we used. We considered MBSR as a psychological intervention. Furthermore, we included small studies, such as 1 ACT study [15]. Moreover, 1 of our ACT studies [73] was just published after the search of the previous meta-analysis was finished. A final limitation of this study is the small number of studies in some subgroups. For example, only 2 small studies on the effects of ACT on pain intensity were found, and 1 study on the effects on depression. More (randomized) controlled studies are thus needed to allow more solid conclusions about most moderating factors.

6. Conclusions and implications

Despite the limitations, this meta-analysis shows that acceptance-based therapies have small to medium effects on physical and mental health in chronic pain patients that are comparable to CBT. However, given the important role acceptance and mindfulness play in adaptation to chronic pain [39,41,42], the development of more effective therapies is warranted. A promising new direction is therapies that integrate MBSR with behavioral therapy [70]. However, few studies have been conducted with chronic pain patients to date. ACT seems promising as well, but more studies are needed to study its effectiveness with chronic pain patients.

All in all, more high-quality studies are needed, and future studies should bear in mind some quality criteria. We would like to conclude with stressing the importance of reporting these quality criteria. Without reporting relevant quality criteria, quality assessments lead to unjust lower-quality scoring in reviews.

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