The effectiveness of cognitive behavioral based online interventions for chronic pain: a systematic review and meta-analysis

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Abstract

Chronic pain is a condition with high prevalence (12%-30%) that has a big impact on the daily functioning of those affected. Chronic pain patients have problem with sleeping, walking and other daily activities and often suffer from comorbid depression. Furthermore, it has a big impact on the economy. Cognitive behavioral therapy is an effective treatment, but patients have to wait long times before they can start therapy, and it is time and cost intensive. These problems could be solved by cognitive behavioral online interventions. Therefore, the objective of this review was to examine the effectivity of online-based cognitive-behavioral treatments for chronic pain.

Systematic searches of the databases Scopus, PsychINFO, Pubmed and the Cochrane Database for Clinical trials were conducted. Eligibility criteria were that the studies had to be randomized controlled trials, online-cognitive-behavioral interventions, a sample size of N≥ 20 per study arm, published between 2005 and 2018 and that the patients in the studies were suffering from pain longer than 3 months. The decision was made to examine the effectiveness of cognitive behavioral online interventions on pain intensity, disability, depression, pain catastrophizing and quality of life.

Finally, 18 studies were included with a total of 2711 participants (76% female). The mean age differed across the studies from 14.3 to 63.37 years of age. The results of the meta-analysis revealed small but significant between-group effects on pain intensity (-. 28(-0.37, -0.19)), pain related disability (-.29(-0.38, -0.21)), depression (-.33(-0.41, -0,24)) and pain catastrophizing (-.44(-0.55, - 0.32)) in favor of the online CBT-treatments compared with the control conditions. For quality of life, the between-group effect was moderate (.65(0.45, 0.85)). Subgroup analysis showed that the between-group effect was the highest when comparing online CBT-treatment to a waiting-list control group (moderate). Only for pain catastrophizing, the between-group effect was the highest compared to other active treatment control groups.

The results of this review provide evidence, that online-CBT can be implemented to treat chronic pain and related symptoms effectively, with treatment effects comparable to the effectivity found in review about face-to-face CBT. Online CBT-interventions can develop the greatest benefit when it is implemented across patients on waiting lists. Thus, online-CBT should be included in primary mental health care for chronic pain.

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Introduction

The ICD-11 defines chronic pain as “persistent or recurrent pain lasting longer than 3 months”. Chronic pain can be divided into seven subgroups which describes the affected body region, symptoms, and causes of the chronic pain. The seven groups are chronic primary pain, chronic cancer pain, chronic posttraumatic and postsurgical pain, chronic neuropathic pain, chronic headache and orofacial pain, chronic visceral pain, and chronic musculoskeletal pain (Treede et al., 2015).

According to a Study conducted by Breivik, Collet, Ventafridda, Cohen and Gallacher (2006) across 15 European countries, the prevalence of chronic pain in the Netherlands is at 18%. The prevalence varied from 12% in Spain to 30% in Norway. This indicated that, compared to other European countries, the prevalence of chronic pain in the Netherlands is close to the mean, but is higher than in the direct neighboring countries France and Germany (Breivik et al., 2006). Thus, it seems that chronic pain is a bigger problem in the Netherlands than in other countries in the geographic region.

The impact of chronic pain

A qualitative study (Breivik et al., 2006) showed the serious impact of chronic pain on those effected: 61% of the patient were less able or unable to work outside their home, 19% of them had lost their jobs. Furthermore, in the Netherlands chronic pain was responsible for 13 lost workdays per patient/year and 27% of the participants reported that they have relationship problems. Those relationship problems did not just include sexual relationship related problems, but also negatively influenced relationships to family and friends (Breivik et al., 2006). A majority of 60% had sleeping problems and 30% had difficulties to maintain an independent lifestyle. Even basic body movement becomes painful and difficult for patients with chronic pain. 47% reported that they had difficulties with or were unable to walk, and 72% said that they had problems with lifting things.

Chronic pain also has an impact on the psychological wellbeing of the patients. The results show a high comorbidity of chronic pain with depression. Out of the Dutch respondents, 19% were also suffering from this mental condition (Breivik et al., 2006). However, chronic pain has not only influence on the people who are suffering from this condition, but also on the relatives of those people. According to a study that was conducted in Spain in 2014, 63,2 % of the relatives of participants with chronic pain have perceived sadness and 47,5% reported changes in their leisure activities (Ojeda, Salazar, Duenas, Torres, Mico & Falida, 2014). Moreover, the costs for the treatment of chronic pain are

billions per year. A study from 1995 states that the costs of back pain are 686 million US-dollar per year (van Tulder, Koes & Bouter, 1995). Another study that was conducted in Ireland in 2012 reported that chronic non-cancer pain costs 5665 Euro per patient per year (Raftery, Ryan, Normand, Murphy, de la Harpe & McGuire, 2012). If you assume that the cost of treatment is comparable, and that two million people in the Netherlands are suffering from chronic pain (Regieraad Kwaliteit van Zorg, 2011), then the costs of chronic pain in the Netherlands lies around 11,33 billion Euro per year. This is another strong implication that it is important to find a treatment, which is cost-effective and efficient. This estimation does not yet take the costs for chronic cancer pain into consideration.

These facts underline the importance of taking a closer look into this problem and to develop a treatment as effective as possible. This is necessary, not only because the prevalence of this medical condition is high, but because it also has a significant impact on the lives of the people that are suffering from chronic pain.

The need for cognitive behavioral based online interventions

In the Netherlands, 56% of the patients suffering from chronic pain reported having an insufficient pain management and 70% said that they would prefer a non-drug treatment for their condition (Breivik et al., 2006). A treatment that matches those conditions is cognitive behavioral therapy (CBT) for chronic pain. In the past, several reviews were conducted to examine the effectivity of CBT for the treatment of chronic pain. For example a, review published by Williams, Eccleston and Morley (2012) found that CBT had small positive effects on disability and pain catastrophizing when compared with an active control group and small to moderate effects on pain, disability, mood and pain catastrophizing when compared with treatment as usual or a waiting list (Williams, Eccleston & Morley, 2012). Pain catastrophizing is a concept of interest in the research of chronic pain, because it is known to be associated with higher patient ratings of pain intensity, disability and depression (Sullivan et al., 2001). A review about this concept defines pain catastrophizing as ‘characterized by the tendency to magnify the threat value of pain stimuli and to feel helpless in the context of pain, and by a relative inability to inhibit pain-related thoughts in anticipation of, during or following a painful encounter’ (Quartana, Campbell & Edwards, 2010). In another recent review, the authors included seven studies using online-based CBT (Knoerl, Smith & Weisberg, 2016). The results showed that the pain intensity was significantly reduced in 43% of the trials. But for some reasons, only 2% of those who are suffering from chronic pain were making use of psychotherapy (Breivik et al, 2006). In conclusion, it can be said that cognitive

behavioral therapy is an effective treatment for chronic pain patients, but it is not widely used to treat this condition.

A way to improve the accessibility of CBT-treatment for chronic pain, cognitive behavioral based online interventions can be used. The possible reach of those treatments is huge, because nowadays, nearly the whole population in The Netherlands has access to the Internet (96,5% of the population 12 years or older, Centraal Bureau voor de Statistiek, 2018). Due to this, internet-based CBT interventions have the advantage of being accessible for nearly the entire population. This is also the case in regions with only very few psychotherapists available, resulting in patients which would have to travel long ways to meet a therapist, or chronic pain patients having problems with walking or living independently. For those patients, the access to classic in-person CBT can be difficult. Especially for those patients, online CBT-interventions have the potential to enhance the accessibility to CBT-treatment (Munoz, 2010). In addition to the advanced accessibility of therapy, eHealth therapy has the advantage that it reduces the negative stigma often felt by the patients seeking help for mental health issues. This makes it easier for the patients to ask for mental health help (Munoz et al., 2015). Aside from the benefits for the patients, using widespread online-delivered CBT also has financial benefits. A randomized controlled trial conducted in 2018 in the United States has found that using internet-delivered cognitive behavioral therapy leads to a reduction of health care costs of 4567 US-Dollar per person compared with standard care (Law, Groenewald, Zhou & Palermo, 2018). All in all, cognitive behavioral based online interventions have big potential due to high reach and accessibility. Because of this, the health systems could benefit from including them in the daily care.

During the last years, a growing number of studies have examined the effectiveness of cognitive behavioral based online interventions for the treatment of chronic pain, but as far as the researcher know, there are no reviews focusing on this theme. There is only a review conducted by Knoerl, Smith and Weisberg (2016) that included a few studies that have investigated the effects of online-based CBT. But because of the potential of cognitive behavioral online interventions, it is necessary to review the existing literature about this treatment in order to examine if cognitive behavioral based online interventions can be implemented effectively.

For these reasons, the objective of this systematic review is to examine the effectiveness of cognitive behavioral based online interventions for chronic pain. In order to do this, three sub goals are formulated. First, data about the characteristics of the included studies will be extracted. Second, the quality of the studies must be examined. Through this, it

will be possible to draw conclusions about the validity of the results of the studies and of this review. Third, the effect of the interventions on the outcome variables will be assessed.

Method

Study inclusion and exclusion criteria

A summary of the inclusion criteria can be found in Table 1. The inclusion criteria were based on earlier reviews on the field of cognitive behavioral therapy for chronic pain (Knoerl, Lavoie Smith & Weisberg, 2016; Williams, Eccleston & Morley, 2012; Macea, Gajos, Calil & Fragni, 2010; Eccleston et al., 2014). To be included, the intervention had to only be pure CBT with e-health intervention, not combined with medication or other treatment like physiotherapy. Those mixed studies do not allow drawing conclusions about the effectiveness of CBT interventions, but only that those interventions contribute to the effect of care as usual or medication. Online-CBT combined with treatment-as-usual was only allowed when the control group received the same kind of non-CBT treatment during the study. In this review, the decision was made to include only classic CBT interventions, not so-called third wave cognitive-behavioral therapy like ACT or mindfulness-based interventions. No age restrictions were made. Another criterion was that the studies had to be published between 2005 and 2018. This period was applied because the latest review of the effectiveness of Cognitive-Behavioral Therapy, including a few online interventions, was published in 2016 includes literature published from 2005 until 2015 (Knoerl, Lavoie Smith & Weisberg, 2016). Because in this review other inclusion criteria were handled, it was necessary to examine if the review by Knoerl et al. had exclude articles that are eligible for this review. After studying earlier reviews, it was decided to choose a minimum $N \geq 20$ per condition like having been used in the review from Williams, Eccleston and Morley (2012).

Table 1. *Criteria the studies needed to fulfil to be included in this review*

Inclusion criteria	
Online-CBT	No 3rd wave CBT-interventions
RCT	The studies had to be randomized controlled trials
Kind of control group	Waiting-list, treatment-as-usual, other treatment active control
Publication date	2005-2018
Sample size	N≥ 20
Chronic pain	Pain longer than 3 months

Electronic search strategy

The SCOPUS, PsychINFO, PubMed and Cochrane database for trials was searched for articles published between 2005 and 2018 implementing cognitive behavioral based online interventions for patients with chronic pain. The search terms can be found in table 2.

Table 2. *Search terms for the electronic search*

	Used search terms
Online interventions	internet- based therapy OR internet delivered therapy OR online based therapy OR online delivered therapy OR web-based OR mobile OR App
Chronic pain	chronic pain OR chronic primary pain OR chronic cancer pain OR chronic neuropathic pain OR chronic post traumatic pain OR chronic post-surgical pain OR chronic headache OR chronic orofacial pain OR chronic visceral pain OR chronic musculoskeletal pain OR chronic low back pain OR fibromyalgia
Cognitive-behavioral therapy	Cognitive behavioral therapy OR cognitive behavioral based interventions OR cognitive therapy OR behavioral therapy OR Exposure therapy OR cognitive behavioral treatment

In SCOPUS, the filters PUBYEAR 2005- 2018, LIMIT-TO English and LIMIT-TO Keyword randomized controlled trial and randomized controlled trial(topic) were used. For PsychINFO, the filters publication year 2005 – 2018 and English language were used. In Pubmed, the used filters used were publication year 2005-2018, English language and randomized controlled trial. The publication year filter was also used in the Cochrane database for clinical trials. The last search was conducted on 26.12.2018. For the first screening, the titles were checked, followed by the abstracts. If there were any doubts whether the article would fulfil the selection criteria, it was carefully read and assessed individually. An example for a search string can be found in the Appendix.

Outcome measures

Based on the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) (Dworkin et al., 2005) and after screening other reviews about the treatment of chronic pain with cognitive behavioral therapy (Knoerl et al., 2016; Williams, Eccleston & Morley, 2012; Eccleston, Morley & Williams, 2009), the decision was made to include outcome measures about pain intensity, physical-(e.g. disability or interference) and

emotional functioning (e.g. depression) quality of life and pain catastrophizing. Depression is one of the most frequent comorbid disorders in chronic pain patients. Thus, an effective treatment for chronic pain should also target this mental disorder. As mentioned earlier, pain catastrophizing is associated with perceived higher pain intensity, disability and depression. Because of this, effective treatments for chronic pain need to be also effective in reducing pain catastrophizing, and trough this the related symptoms. Quality of life is a valid measure for the overall wellbeing of the patients and an indicator of how much the condition effects their lives. Because of this, it is important to examine if the online interventions are able to increase it. If the included studies included measures about these outcomes in their primary outcomes, these scales were taken. When they provided multiple scales for one measure in the secondary outcomes, a decision was made based on the psychometric properties of the used scales. Based on the result of the assessment, the most appropriate ones were chosen, and the other outcome measures were extracted.

Assessment of study quality

The risk of bias of the included studies was assessed using the Cochrane guidance (Higgins, 2011). All five suggested "Risk of bias" categories were included in the analysis (selection bias, performance bias, detection bias, attrition bias and reporting bias). The assessment was made independently by two researchers. If there were any disagreements concerning the risk of bias, the researchers discussed together until a consensus was found.

Assessment of heterogeneity

The clinical heterogeneity, or sometimes called clinical diversity, was assessed based on the sample characteristics, the characteristics of the intervention programs (e.g. mode of delivery, duration, etc.), follow-up periods and the used outcome measures. In order to assess the statistical heterogeneity, the I^2-statistic was calculated for each outcome variable. Based on the Cochrane Handbook for Systematic Reviews of Interventions (2011), a value of I^2= 0-40% was seen as not important, I^2= 30-60% as moderate heterogeneity, I^2= 50-90% as substantial, and I^2= 75-100% as considerable heterogeneity. The calculation of I^2 was done with RevMan 5.3.

Statistical analysis

Meta-analysis was conducted with RevMan 5.3. When the included studies used different outcome measures for the same outcome, the standardized mean differences were

computed. Subgroup-analysis were conducted of the studies using the same kind of control-group. The three subgroups were waiting list control, treatment-as-usual and other treatment control group. For the assessment of the intervention effect, the standardized mean difference (SMD) was calculated in the meta-analysis as recommended by the Cochrane Handbook for Systematic Reviews of Interventions (2011) This was done in order to deal with the use of different outcome scales across the studies. For all measures of the effect size (cohen's d for the separate studies and SMD for the meta-analysis) the recommendations of Cohen (1988) were followed. Values around .30 indicated low effect, .50 moderate and .80 and higher a high effect size.

Results

Results of electronic search

The initial results were 356 hits in SCOPUS, 52 in PsychINFO, 73 in PubMed, and 123 in the Cochrane database. In total 604 studies were found. After the removement of the duplicates, 471 studies were remaining for screening of the title and the abstract. Out of these 471 studies, 38 were excluded because they did not focus on chronic pain. 142 further articles were excluded because they did not include a cognitive-behavioral-based intervention as defined in the method section. Next, 96 studies were excluded because the CBT-intervention was not online-based, and another 20 because the design was not a randomized controlled trial. Due to 80 of the screened studies were study protocols, they were excluded as well, and 44 because they were reviews. In the case of 5 articles, the researcher was not able to gain access to them. Lastly, 15 studies were excluded because they were cost-effectiveness or feasibility trials, failed to fulfil the $N \geq 20$ criteria or were moderating or secondary data analyses. Out of the 31 articles that were accessed for eligibility, three were excluded because they were moderating analyses, another three because the intervention was not CBT-based and six because the included intervention was not online-based. One last study was excluded because it failed to provide between-group comparison data, due to a high drop-out rate. So, the overall number of the studies that were included in this review was 18. Detailed information about the process of exclusion can be found in figure 2.

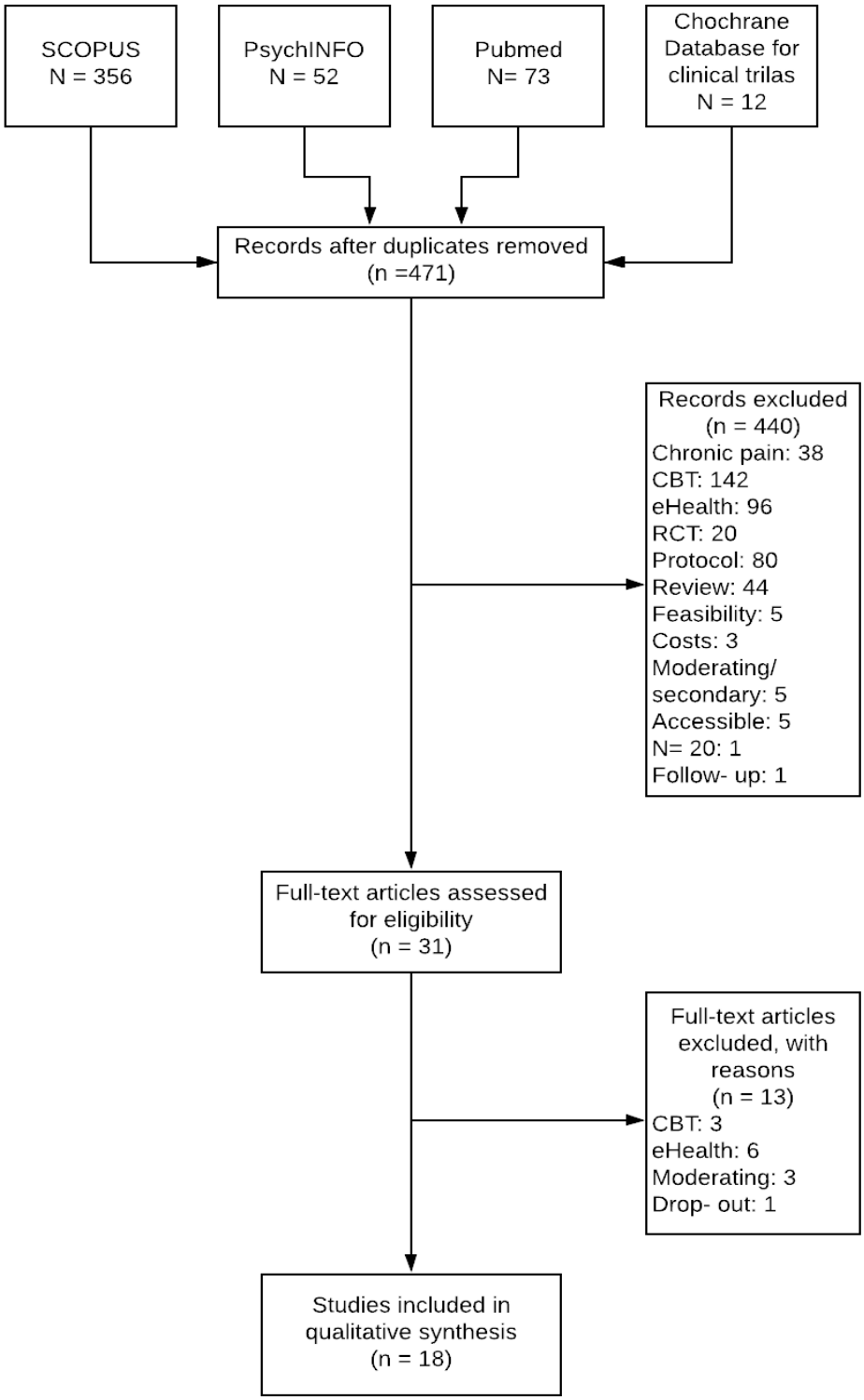

Figure 1. Flow diagram of the literature exclusion process. The flow diagram provides a detailed overview about how many studies were excluded for which reason.

Characteristics of included studies

Patients characteristics. Four of the included studies were carried out in Sweden, six in the USA and three in Australia. Respectively, one study was conducted in Spain, Canada, Canada and the USA combined, the Netherlands, and the Netherlands and Belgium combined. A total of 2711 participants was included in this review. Out of these, 2059 (76%) of them were female, and 652 (24%) were male. The mean age of the participants differed from 14.3 to 63.37 years. In the seven studies that provided information about the ethnic origin of the participants, the majority of the participants was white or Caucasian (82%), followed by African American (5,02%), Hispanic/Latino (3,1%), Asian American (1,83%), American Indian (0,82%), other/ mixed (3,8%) and Pacific Islander (0,1%). Three of the included studies were only for patients with Fibromyalgia, two for participants with chronic back pain, and one for chronic headache, chronic lower back pain, non-specific chronic pain and chronic neuropathy, respectively. Ten of the studies were for chronic pain in general (See "Inclusion criteria"-column in table 3).

Control conditions. Out of the 18 included studies, six had a waiting-list control and another six a treatment-as-usual control group. In two studies, the control group was a moderated online discussion forum or psychoeducation, respectively. Finally, one study had a group CBT intervention, symptom monitoring control group, or a group receiving the same intervention as the treatment group, but in a workbook format, respectively (See 'control group'-column in table 3).

Interventions. In 15 of the included studies, the internet-CBT intervention included some levels of therapist support. In four studies, the intervention condition did not include any kind of support through a therapist. One study included different levels of clinician support until no support at all (See the 'Treatment group'-column in table 3). Most of the interventions in the included studies had a duration of eight weeks. The longest intervention had a duration of eleven weeks and the shortest interventions four weeks (See the 'Treatment group'-column in table 1). All studies had a follow-up, expect one. The follow-up periods differed widely from a minimum of four weeks to a maximum of one year ('Follow-up'-column in table 3). Two studies (Palermo et al. 2009 and Palermo et at. 2015) included the parents of the children and adolescents that participated in the studies.

Outcome measures. Out of the 18 included studies, 17 used outcome measures to access the pain intensity, 15 provided data about the severity of depressive and another 17 also assessed the amount of disease related disability. Of the included studies, 12 made use of an outcome measure for pain catastrophizing and six measured quality of life. The used questionnaires to measure the five different outcomes differed widely between the studies. For pain intensity, eight different scales were used and another eight for outcome depression. In order to access the disability, nine different instruments were used and for the measurement of pain catastrophizing five instruments were used. For quality of life, four scales were used. The mostly used scales for pain, disability, depression, pain catastrophizing and quality of life were a 0-10 Numerical Rating Scale (NRS), the Roland Morris Disability Questionnaire (RMDQ), the Patient Health Questionnaire 9 (PHQ-9), the Pain Catastrophizing Scale (PCS) and the Quality of life Inventory (QOLI), respectively. (See ‘outcome measures’-column in table 3).

Table 3. *Characteristics of the included studies*

Authors, (year), Country	**No. of participants**	**Mean age**	**Ethnical origin of the sample**	**Inclusion criteria**	**Treatment group: Intervention Program length, frequency, duration**	**Control group: Intervention Program length, frequency, duration**	**Longest follow- up**	**Outcome measures**	**Results** **a) post treatment** **b) follow-up**
Buhrman et al. (2011), Sweden	T: N= 26 C: N= 28	T: 43.5(9.8) C: 42.9(9.2)	No information	1.age between 18 and 65 years; 2. access to the Internet 3. having been in contact with a physician 4. back pain of chronic nature (i.e. pain longer than 3 months); 5. in current employment or on short-term sick leave (not longer than 6 months) 6. not a wheelchair user 7. no planned surgical treatment 8. no history of cardiovascular disease	Guided internet- based cognitive behavioral therapy to learn and practice of coping strategies for pain; reminder and therapist contact; 11 weeks, one module per week	Wait- list control group	No follow-up	1. Catastrophizing: CSQ	1a T > C p < 0.001
								2. Pain severity, psychosocial and behavioral consequences of pain, interference: MPI	No significant effects
								3. Thoughts, attitudes and opinions about pain: PAIRS	3a effect of time for both groups p= 0.05
								4. Depression and anxiety: HADS Anxiety	 4a effect of time for both groups p= 0.05
								5. Quality of life: QOLI	5a T > C p < 0.001
Buhrman et al. (2013), Sweden	T: N= 36 C: N= 38	T: 39.9(9.13) C: 40.2(8.8)	No information	1.participants had to have been medically investigated (within 1 year) 2.have completed the multidisciplinary pain rehabilitation program 3.have residual symptoms after the rehabilitation treatment 4. have access to the Internet.	Guided internet- based cognitive behavioral therapy to learn and practice of coping strategies for pain; reminder and therapist contact; 8	Moderated online discussion group	6 months, Treatment group only	1. Catastrophizing: CSQ Catastrophizing Diverting attention	 1a T > C p = 0.03 1a T > C p = 0.047
								2. Pain severity, psychosocial and behavioral consequences of pain, interference: MPI Life- control Affective distress Punishing response	 2a T > C p = 0.018 2b T > C p = 0.048 2a T > C P < 0.001 2a T > C p = 0.048
								3. Quality of life: QOLI	No significant effects

					weeks, one module per week			4. PAIRS	4a T > C p = 0.005
								5. Depression and Anxiety: HADS	
								Anxiety	5a T > C p = 0.01
								Depression	5a T > C p = 0.04
								6. Pain acceptance: CPAQ	No significant effects
									1b, 3b, 4b no change from post- to follow up
Buhrman et al. (2015) Sweden	T: N= 28 C: N= 24	T: 54.1(11.76) C: 46.8(12.9)	No information	1) participants had undergone previous medical investigation(s) (within 1 y) 2) had chronic pain (ie, pain for >3 mo), 3) had regular access to the internet, 4) had problem with depression and anxiety defined in the present study a total score of >10 points on the MADRS-S 5) present psychological distress (assessed with PRIME- MD)	Guided internet-delivered CBT intervention with therapist support, 8 weeks, one module per week	Moderated online discussion forum	12 months	1. Depression: MADR- S	1a T > C p= 0.005
								2. Anxiety: BAI	2a T > C p= 0.032
								3. Interference/ disability: PDI	3a T > C p= 0.031
								4. Fear for symptoms of anxiety: ASI	No significant effects
								5. Catastrophizing: PCS	5a T > C p= 0.004
								6. Activity engagement and pain willingness: CPAQ	
								Activity engagement	6aT > C p= 0.039
								7. Coping: CSQ	
								Catastrophizing	7aT > C p= 0.002
								8. Pain severity, psychosocial and behavioral consequences of pain, interference: MPI	
								Pain severity	T > C p= 0.016
								9. Quality of life: QOLI	No significant effects
									1b- 3b, 5b- 8b no change from post- to follow up
Carpenter et al. (2012), USA	T: N= 70 C: N= 71	42.5(10.3)	6% Hispanic; 7% Black/African American;	1) Age 21 or older 2) self-identified as having had non-cancer related lower back pain for at	Interactive online self-help CBT intervention	Waiting-list	6 weeks	1. SOPA	
								Control	1a T > C p< 0.001
								Disability	1a T > C p< 0.001
								Harm exercise	1a T > C p< 0.001

			7% Asian/ Asian American; 2% American Indian; 1% Pacific Islander	least 6 months 3) average pain rating of 4 or above for the past week 4) had access to a computer 5) English written and spoken 6) had not participated in a multidisciplinary program or CBT for chronic pain within the past three years.	(wellness workbook); 6 chapters, each takes 1 to 1.5 hours			Emotion Medication Solicitude Medical cure	1a T > C p< 0.001 1a T > C p< 0.001 1a T > C p= 0.026 1a Not significant (p= 0.167)
								2. Disability: RMDQ	2a T > C p= 0.011
								3. Self- efficacy: PSES	3a T > C p< 0.001
								4. Beliefs of the effect of physical activity and work on pain: FABQ Physical activity Work	 4a T > C p< 0.001 4a Not significant (p= 0.075)
								5. Catastrophizing: PCS Rumination Magnification Helplessness	 5a T > C p< 0.001 5a T > C p< 0.001 5a T > C p< 0.001
								6. Negative mood regulation	6a T > C p< 0.001
								7. Pain intensity: 0- 10 NRS	Not significant
									1a- 6a no change from post- to follow up
Chiauzzi et al. (2012), USA	T: N= 104 C: N= 105	T: 47.34(12.23) C: 45.05(11.72)	86,4% white, 5,5% African American, 5,5% Hispanic/ Latino, 2% Asian American	1) back pain for at least 10 days each month for at least three consecutive months immediately prior to participation in the study 2) spinal origin of pain 3) English language fluency	Self-management website ("painAction – Back Pain") based on CBT, 8 lesions, 2 per week, 20 min at least per lesion, 4 weeks	back pain guide (National Institute of Neurological Disorders and Stroke)	6 months	1. Pain intensity: BPI	Not significant
								2. Disability: ODQ	Not significant
								3. Depression, Stress and anxiety: DASS Stress	 3a T > C p< 0.01 3b T > C p< 0.05

								4. Global improvement: PGIC	4a T > C p< 0.01 4b T > C p< 0.05
								5. Coping strategies: CPCI- 42	
								Coping	5a T > C p< 0.05 5b T > C p< 0.05
								Social support	5a T > C p< 0.05 5b T > C p< 0.05
								6. Catastrophizing: PCS	Not significant
								7. Belief they can cope with pain: PSEQ	Not significant
								8. Beliefs of the effect of physical activity and work on pain: FABQ	Not significant
DeBoer et al. (2014), The Netherlands	T: N= 38 C: N= 34	T: 50.6(10.7) C: 53.2(11.7)	No information	(1) having non-specific chronic pain for which no somatic treatment could be offered; (2) a minimum age of 18 years; and (3) having access to the internet	Internet- based CBT-intervention, therapist support, 7 modules, one per week, with an 8th booster session after 2 months	Group intervention with the same content and frequency	2 months	1. Catastrophizing: PCS	1a Not significant 1b T > C p= 0.023
								2. Pain intensity, interference and fatigue: VAS	
								Pain	2a Not significant 2b Not significant
								Interference	Not significant
								Fatigue	Not significant
								3. Pain coping, locus of control, pain cognition and catastrophizing: PCCL	
								Pain coping	3a Not significant
								Catastrophizing,	3b T > C p= 0.024
								internal and external pain management	Not significant
								4. Quality of life: RAND- 36	
								Mental health	4a T > C p= 0.038 4b Not significant
								Vitality	4a Not significant 4b T > C p= 0.014
								Pain	4a Not significant 4b T > C p= 0.015
								Perceived health change	4a Not significant

									4b T > C p= 0.0
								Social and physical functioning, role impairment, general health appraisal	Not significant
Dear et al. (2013), Australia	T: N= 31 C: N= 31	T: 47(13) C: 51(12)	No information	1) pain for more than 3 months, 2) pain assessed by GP or a specialist, 3) resident of Australia, 4) at least 18 years of age, 5) had access to a computer and the Internet, 6) not currently participating in CBT, 7) on a stable dose of medication (>1 month) prescribed for anxiety or depression, 8) not currently experiencing a psychotic illness or severe symptoms of depression	internet-delivered CBT program (the Pain Course) Therapist support 5 lessons, 8 weeks	Waiting list	3 months	1. Disability: RMDQ	1a T > C p< 0.001
								2. Depression: PHQ- 9	2a T > C p< 0.001
								3. Anxiety: GAD-7	3a T > C p< 0.001
								4. Pain intensity: WBPQ	4a T > C p= 0.001
								5. Belief they can cope with pain: PSEQ	5a T > C p< 0.001
								6. Fear of movement and re- injury: TSK	6a T > C p< 0.001
								7. Coping and catastrophizing: PRSS Catastrophizing Coping	 7a T > C p= 0.005 Not significant
									1b- 7b not significant
Dear et al. (2015), Australia	T1: N= 143 T3: N= 141 T3: N= 131 C: N= 75	T1: 50(13) T2: 49(12) T3: 50(14) C: 52(13)	No information	1) pain for more than 6 months, 2) pain assessed by GP or a specialist, 3) resident of Australia, 4) at least 18 years of age, 5) access to a computer and the Internet, 6) not currently participating in CBT, 7) on a stable dose of medication (>1 month) prescribed for anxiety or	T1: internet-delivered CBT program (the Pain Course), therapist support; 5 online lessons, 8 weeks, 1 lesson every 7 to 10 days	Treatment- as-usual waiting-list	3 months	1. Disability: RMDQ	1a T1, T2, T3 > C p< 0.001 1b T1, T2, T3 p<= 0.003
								2. Depression: PHQ-9	2a T1, T2, T3 > C p< 0.001 2b not significant
								3. Anxiety: GAD-7	3a T1, T2, T3 > C p< 0.001 3b T2 p= 0.032
								4. Pain intensity: WBPQ	4a T1, T2, T3 > C p<= 0.003

				depression, 8) not currently experiencing a psychotic illness or severe symptoms of depression	T2: internet-delivered CBT program (the Pain Course), optional therapist support; 5 online lessons, 8 weeks, 1 lesson every 7 to 10 days T3: internet-delivered CBT program (the Pain Course), 5 online lessons, 8 weeks, 1 lesson every 7 to 10 days			4b Not significant 5. Belief they can cope with pain: PSEQ 5a T1, T2, T3 > C p<= 0.046 5b Not significant 6. Fear of movement and re- injury: TSK 6a T1, T2, T3 > C p<= 0.046 6b Not significant 7. Pain acceptance: CPAQ 7a T1 > C p= 0.003 7b T1 p = 0.031	1a- 6a and 1b, 2b, 4b, 5b, 6b no significant differences between the 3 treatment groups
Dear et al. (2017), Australia	T: N= 84 C: N= 94	T: 47.43(12.19) C: 48.19(14.98)	No information	(1) pain more than 6 months, (2) pain assessed by GP or a specialist within the last 3 months, (3) at least 18 years of age, (4) resident of Australia, (5) access to a computer and the internet, (6) not currently experiencing very severe symptoms of depression	internet-delivered CBT program (the Pain Course) Therapist support 5 lessons, 8 weeks	workbook-delivered pain management with the same content	12 months	1. Disability: PDI 2. Disability: RMDQ 3. Depression: PHQ-9 4. Anxiety: GAD-7 5. Pain intensity: WBPQ 6. Belief they can cope with pain: PSEQ 7. Fear of movement and re- injury: TSK 8.Pain acceptance: CPAQ 9. Catastrophizing: PCS	No significant group effects were found on all outcome measures
Devineni et al. (2005), USA	T: N= 39 C: N= 47	T: N= 43.6(12) C: N= 41(11.8)	No information	1) Chronic tension and/ or migraine headache for at least one year 2) formal diagnosis for their headache given by a physician	2 CBT- based online interventions (tension type headache and one for migraine and	Symptom monitoring control group	2 months	1. Disability: HDI 2. Pain intensity: HSQ 3. Anxiety: STAI 4. Depression: CES- D	1a T > C p< 0.05 1b Not significant 1a T > C p< 0.01 1b not significant Not significant Not significant

					mixed headache), therapist support, 4 weeks				
Friesen et al. (2017), Canada	T: N= 30 C: N= 30	T: 49(10) C: 46(13)	95% White/ Caucasian, 2% Spanish /Hispanic/ Latino, 3% mixed ethnicity	(1) residents of Canada, (2) 18 years of age or older, (3) diagnosis of FM by a physician, (4) pain for more than three months, (5) pain assessed by GR or a specialist, (6) clinically significant symptoms of FM (7) at least mild symptoms of depression	internet-delivered cognitive behavioral pain management course (the Pain Course); therapist support, 5 lessons, 8 weeks	Treatment- as-usual waiting-list control	4 weeks	1. FM- severity and symptomology: FIQR	1a T > C p= 0.019
								2. Anxiety: GAD-7	2a T > C p= 0.030
								3. Depression: PHQ-9	3a T > C p= 0.037
								4. Depression and Anxiety: HADS Depression Anxiety	 4a T > C p= 0.007 4b T > C p= 0.032 4a T > C p= 0.001
								5. Fear of movement: TSK	5a T > C p= 0.048
								Pain severity (BPI), Belief they can cope with pain (PSEQ), catastrophizing (PRESS), fatigue (FSI), Quality of life (SF- 12)	No significant group effects were found
									1b- 3b and 5b no significant effects
Hedman-Lagerlöf et al. et al. (2017), Sweden	T: N= 70 C: N= 70	T: 51.8(10.7) C: 49.3(10)	No information	1) adults (>=18 y) 2) citizen of Sweden, 3) FM diagnosis 4) Internet access 5) agree to refrain from any other psychological treatment for the duration of the study	Internet-delivered exposure therapy, therapist support, 8 modules, 10 weeks	Waiting- list	12 months	1. FM severity and symptomology: FIQ 32	1a T > C p< 0.001
								2. Pain intensity: FIQ pain	2a T > C p< 0.001
								3. Fatigue: FSS	3a T > C p< 0.001
								4. Disability: WHO-DAS2	4a T > C p< 0.001
								5. Quality of life: BBQ	5a T > C p< 0.001
								6. Depression: PHQ-9	6a T > C p< 0.001
								7. Anxiety: GAD-7	7a T > C p< 0.001
								8. Insomnia: ISI	8a T > C p< 0.001

								9. Pain- related distress: PRS	9a T > C p< 0.001
								10. Non- reactivity to inner experience: FFMQ-NR	10a T > C p< 0.001
								11. PIPS	11a T > C p< 0.001
								12. Global improvement: PGIC	12a T > C p< 0.001
									1b- 12b not significant
Knoerl et al. (2018), USA	T: N= 30 C: N= 30	T: 58.93(9.33) C: 63.37(8.36)	91,7% white, 5% African American, 1,7% Hispanic	1) older than 25 years of age, 2) self-reported ≥4 of 10 worst CIPN pain that persisted 3 months or longer after the neurotoxic che-motherapy, 3) had at least Adverse Events grade 1 sensory CIPN 4)stable analgesic medication regimen, 5) were able to access/use a computer	Self- guided online CBT intervention (PROSPECT), 10 modules, 8 weeks	Treatment- as-usual	8 months	1. Pain intensity (0- 10 NRS) Worst pain Average pain	 1a T > C p= 0.046 Not significant
								Interference (PROMIS pain interference 4a), Global change (PGIC) and symptom severity (QLQ-CIPN20)	No significant group effects were found
Palermo et al. (2009), USA	T: N= 26 C: N= 22	T: 14.3(2.1) C: 15.3(1.8)	89,6% White/ Caucasian, 6,2% Hispanic, 4,2% other	1) ages 11 to 17 years, 2) chronic idiopathic pain the previous 3 months, 3) pain occurs at least once per week, 4) pain interferes with at least one area of daily functioning, and 5) the child was a new patient being evaluated in the specialty clinic	Internet-delivered family CBT intervention (Web- MAP), 30 min per week, 8 weeks	Treatment- as-usual	3 months	1. Pain intensity (0- 10 NRS)	1a T > C p= 0.03 1b Not significant
								2. Activity limitations/ Interference: CALI	2a T > C p= 0.004 2b T > C p< 0.001
								3. Depression: RCADS-MDD	3a Not significant 3b T > C p= 0.05
								4. Parent response to pain: ARCS	Not significant
Palermo et al. (2015), USA and Canada	T: N= 138 C: N= 135	T: 14.63(1.62) C: 14.70(1.72)	85% Anglo-American, 4,8% African American,	(1) age 11 to 17 years, (2) chronic idiopathic pain the previous 3 months, (3) pain at least once per	Internet-delivered family CBT intervention	Internet-delivered pain education	6 months	1. Pain intensity (0- 10 NRS)	No significant group effects were found

			3,7% Hispanic/ Latino, 5%, other, 1,5% missing	week, (4) parent report of pain interfering with at least 1 area of daily functioning, and (5) the adolescent received a new patient evaluation in one of the participating pain clinics.	(Web- MAP), 8 modules, 30 min per week, 8 weeks			2. Activity limitations/ Interference: CALI	2a Not significant 2b T > C p= 0.03
								3. Depression and anxiety: BAPQ Depression Pain specific anxiety	 3a T > C p= 0.04 3b Not significant 3a T > C p= 0.04 3b Not significant
								4. Sleep quality: ASWS	4a Not significant 4b T > C p= 0.04
								5. Parent response to pain: ARCS	5a T> C p< 0.001 5b T> C p= 0.001
								6. Miscarried help: HHI	Not significant
Peters et al. (2017), The Netherlands and Belgium	T1: N= 116 T2: N= 117 C: N= 51	T1: 48.7(11.5) T2: 47.5(13.2) C: 50.6(10.1)	No information	1) Above 18 years, 2) musculoskeletal pain longer than 3 months, either generalized pain (ie, fibromyalgia) or localized in back, neck or shoulders, 3) good command of Dutch, 4) access to the internet.	T1: internet-based CBT intervention, therapist support 8 modules, 8 weeks T2: Internet positive psychology intervention, 8 modules, 8 weeks,	waiting-list	6 months	1. Depression and anxiety: HADS Depression Anxiety	 1a T1 and T2 > C p< 0.001 1a T1 > C p< 0.001 T2 > C p= 0.004
								2. Physical impairement: FIQ	2a Not significant
								3. Self- compassion: SCS- SF	3a T1 and T2 > C p< 0.001
								4. Positive and negative mood: BMIS Positive affect Negative affect	 4a T1 and T2 > C p< 0.001 4a T1 and T2 > C p< 0.001

								5. Optimism: LOT- R	5a T1 and T2 > C p< 0.001
								6. Flexibility in goals: FGA	6a T1 > C p= 0.002 T2 > C p< 0.001
								7. Catastrophizing: PCS	7a T1 > C p= 0.002 T2 > C p< 0.001
								8. Repetitive thinking: PTQ	8a Not significant
								9. ICQ Helplessness Acceptance Desease benefit	9a T1 and T2 both > C p< 0.001 9a T1 > C p= 0.001 T2 > C p= 0.008 9a T1 > C p< 0.001 T2 > C P=0.02
								10. Happines	10a T2 > T1 > C p= 0.05
									1a- 9a no significant difference between T1 and T2; 1b- 10b no significant group effects between T1 and T2
Ruehlman et al. (2012), USA	T: N= 165 C: N= 165	Tot: 44. 93	82% white, 6% African American, 2% American Indian, 2% Asian, 8% more than one race or "other"	1) 18 years or older, 2) chronic pain problem for 6 or more months, 3) access to a computer with high- speed Internet capabilities, 4) the ability to read and write English.	Internet-delivered, CBT-based self-management program, 7 weeks	Treatment- as-usual	14 weeks	1. PCP- S Pain severity Interference Emotional burden	 1a T > C p= 0.01 1a T > C p< 0.001 1a T > C p= 0.03
								2. PCP- EA Disability Control Belief in medical cure Catastrophizing	 2a T > C p= 0.02 2a Not significant 2a Not significant 2a T > C p= 0.01
								3. Depression: CES- D	3a T > C p= 0.03
								4. Depression, stress and anxiety: DASS	

								Depression	4a T > C p= 0.04
								Stress	4a T > C p< 0.001
								Anxiety	4a T > C p= 0.05
								5. Sleep interference	4a T > C p= 0.01
									1b- 5b not significant
Vallejo et al. (2015), Spain	T1: N= 20 T2: N= 20 C: N= 20	T1: 49.82(11.01) T2: 53.50(8.56) C: 51.33(10.03)	No information	1) meet the (ACR) research classification criteria for FM, 2) minimum 18 years of age, 3) adequate reading comprehension, and 4) access to and ability to use a computer	T1: internet-delivered CBT intervention (same treatment components than T2), therapist support, 10 weekly session T2: group CBT intervention, 10 weekly session of 120 min	Treatment- as-usual	12 months	1. Global impact of FM: FIQ	1a T2 > C p< 0.001 1b T1 p> 0.001
								2. General psychological distress: HADS	2a T1 > C p< 0.001 T2 > C p< 0.005
								3. Depression: BDI	3a T1 > C p< 0.001 T2 > C p< 0.001
								4. PCS	
								Catastrophizing	4a T1 > C p< 0.03 T2 > C p< 0.001 4b T1 p> 0.005
								Rumination	4a T1 > C p< 0.001 T2 > C p< 0.001
								Helplessness	4a T2 > C p< 0.001 T1 not significant 4b T1 p< 0.05
								Magnification	4a T2 > C p< 0.02 T1 not significant
								5. Self- efficacy: CPSS	
								Pain self- efficacy	5a T1 > C p< 0.001 T2 not significant
								Coping with symptoms	5a T1 > C p< 0.03 T2 not significant
								Physical function self Efficacy	5a not significant
								Global self- efficacy	5a T1 > C p< 0.05
								6.Coping styles: CPCI	
								Guarding	6a Not significant
								Resting	6a T2 > C p< 0.01 T1 not significant
								Relaxation	6a T2 > C p< 0.001 T1 > C p< 0.02
								Asking for assistance,	Not significant

		seeking social support	
			2b, 5b, 6b not significant compared with post treatment

Risk of bias in included studies

Of the included studies, 15 reported sufficient techniques of randomized sequence allocation, so the risk of bias was judged as low. The risk of bias in 4 categories were rated as unclear, because they did not provide enough information over the randomization method. 10 studies were judged to have an adequate allocation concealment and nine were judged to have an unclear risk of bias. Only one study was judged to have a sufficient blinding of participants. This risk of bias was judged unclear for eight and high for ten studies, mainly because of the strong differences between the control and the treatment group or because the participants were told to which conditions they were randomized. The risk of bias through insufficient blinding of personal was judged to be low in two studies, unclear in eight and high in ten studies. In the studies with a high risk of bias, the interventions were mainly guided, and the personnel knew about the different conditions.

All of the included studies were judged to have a low risk of detection bias, mainly because all measures were taken online and so, no personnel was involved. One study was judged to have an unclear risk of detection bias. In total, 16 studies were judged to have low risk of attrition bias because they reported a convincing method to deal with missing data and an intention-to-treat analysis. One study was considered to have an unclear risk of attrition bias, and two to have a high risk, mainly because they failed to make an intention-to-treat analysis.

Finally, ten studies were considered to have a low risk of reporting bias, because all measures that were predefined in the study protocol were reported, and nine studies were judged to have an unclear risk of reporting bias because no research protocol was given. Detailed information about the risk of bias of the single studies can be found in Figure 1.

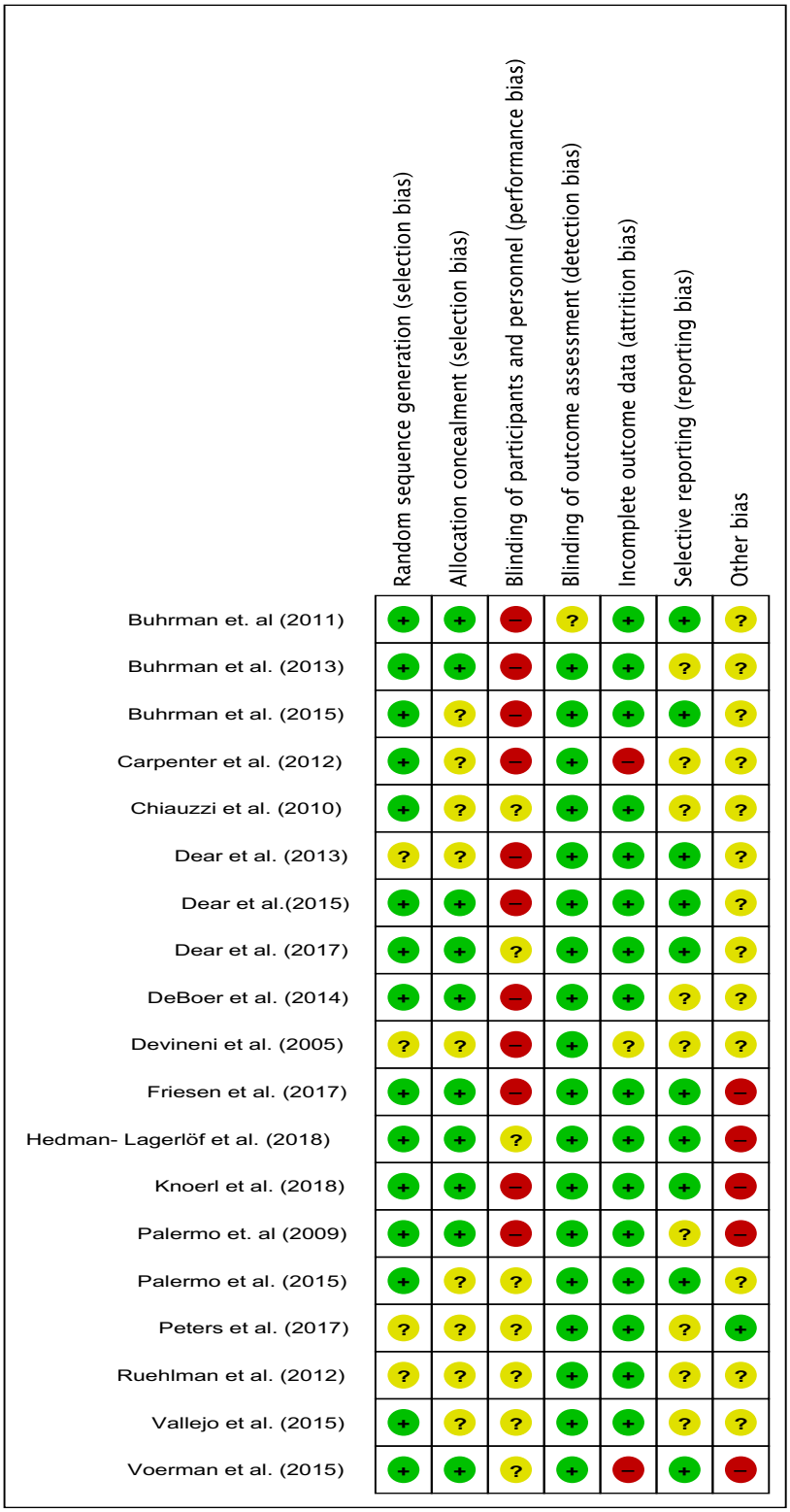

Figure 2. Risk of bias summary of the included studies

Heterogeneity

Based on the characteristics of the interventions, the decision was made to rate the clinical heterogeneity as low enough to conduct a meta-analysis and to calculate I^2. But the meta-analysis was only done for post-treatment scores, because the follow-up periods differed to strongly to make a valid comparison (min. 4 weeks, max. 1 year, see table 1 in the Appendix). The I^2-statistic for the outcome measures pain intensity, disability, depression, pain catastrophizing and quality of life were 84%, 82%, 81%, 96% and 87%, respectively, indicating high statistical heterogeneity.

Effects of interventions

Because the scales that were used to measure the same outcomes differed widely between the studies, the standardized mean differences were computed for the meta-analysis.

Effects on pain intensity. Out of the 17 studies that provided data about the pain intensity, eight reported significant time-by-group interaction in favor for the treatment condition post-treatment compared to pre-treatment, with a range in p- values from p< .001 to p= .04 (see Table 4). The with-in effect sizes in the treatment groups ranged from a minimum of d= .20 to a maximum of d= .82 (Table 4). The with-in effect sizes of the other four studies were moderate (Table 4).

Table 4. *Between- group p-values between treatment and control condition and with- in group- effect sizes in the treatment group comparing pre- and posttreatment for pain intensity*

Author (Year)	Between groups p- values	With- in pre- to posttreatment effect size (d)	Post- treatment to follow- up With- in group effect sizes
Buhrman et al. (2015)	.016	.56**	
Dear et al. (2013)	.001	.65**	
Dear et al. (2015)	< .03		
Devineni et al. (2005)	< .001	.59**	1.04***(< .01)
Hedman- Lagerlöf et al. (2018)	< .001	.63**	
Knoerl et al. (2018)	.04	.20*	
Palermo et al. (2009)	.03	.82***	.33*(.001)
Ruehlman et al. (2012)	.01	.47*	

Notes: * means small, ** means moderate and *** high effect size.

With-in analyses comparing post-treatment with follow-up showed significant reduction in pain severity in the studies conducted by Devineni et al. (2005) and Palermo et al. (2009) (Table 4). In the other five studies, no significant changes in pain intensity between posttreatment and follow-up were found, indicating that the treatment effects were maintained.

The meta-analysis of the post-treatment-effect of CBT-based online interventions revealed an overall effect of $z= 6.38$, $p< .00001$ and a significant mean difference between the treatment and the control condition of – 0.28 (95% CI: - 0.37, - 0.19) in favor of the treatment conditions. Thus, the treatment group had significantly lower ratings on pain intensity at post-treatment compared to the control condition, even if the effect was small. Subgroup-analysis of the control-conditions showed only a minor reduction in heterogeneity in the treatment-as-usual group ($I^2= 69\%$) and a strong reduction in the wait-list control group ($I^2= 59\%$), but the heterogeneity was still high. Additionally, it showed an increased between-group effect on pain intensity in the favor of the treatment group compared to a wait-list control group (-0.43(95% CI: -0.61, -0.26)), meaning that at post-treatment, the treatment groups had significantly lower mean scores for pain intensity compared to the control group. Compared to the treatment-as-usual and other treatment-control groups, the between-group effects were the highest in the wait-list control group. Detailed information can be found in Figure 2.

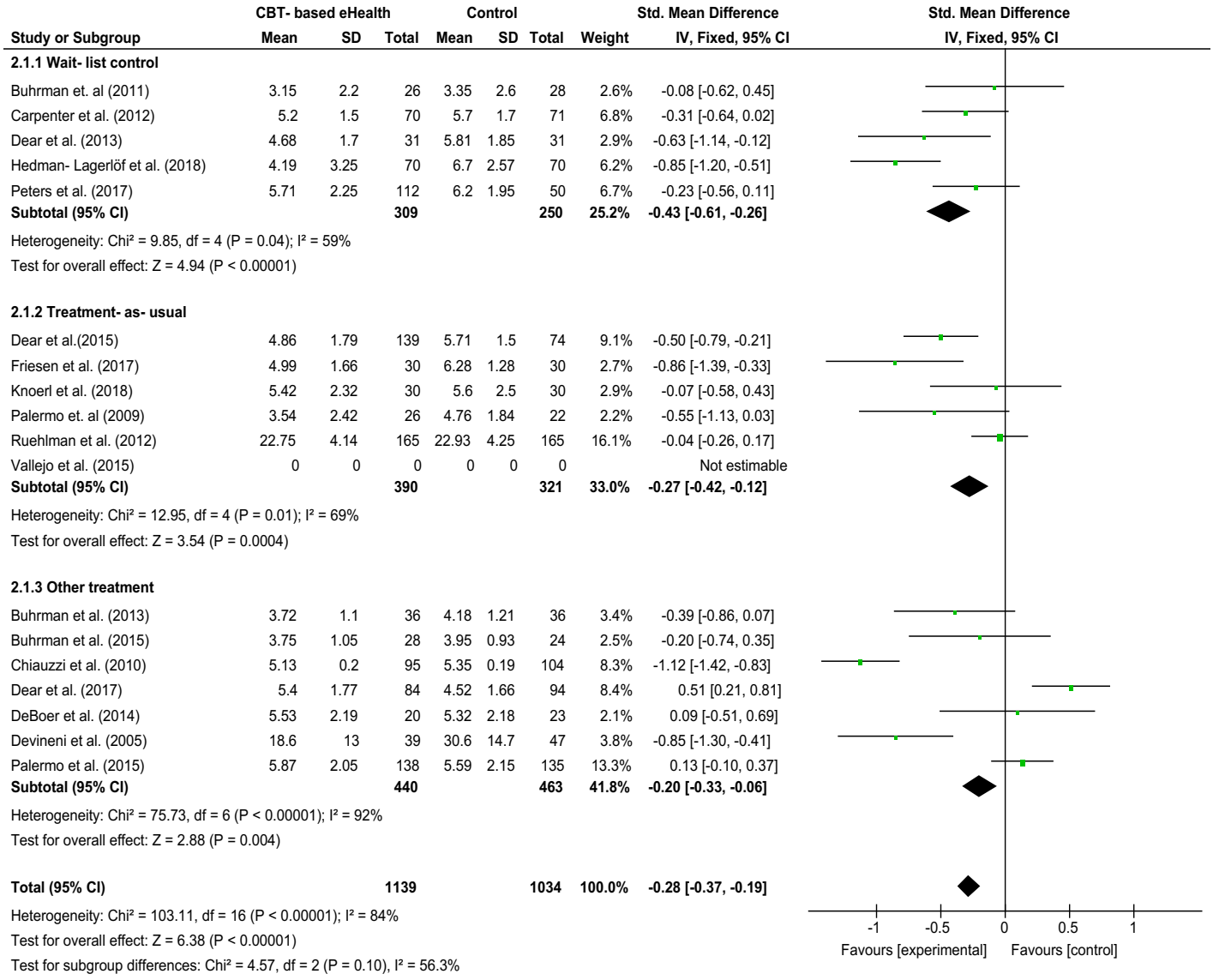

Figure 2. Means and sample size of the treatment and control group, study weight, standardized mean difference and Heterogeneity and overall effects with 95% confidence interval for pain intensity.

Effects on pain related disability. Eight of the 17 studies that measured the pain related disability found significant between group effects in favor of the treatment group at post-treatment compared to pre-treatment (Table 5). The p-values in these studies ranged from p< .001 to p< .05. The analysis of the with-in effects showed effect sizes between d= .27 and d= .78 (Table 5). The effect sizes of the other six studies were small to moderate (Table 5).

Table 5. *Between- group p-values between treatment and control condition and with- in group- effect sizes in the treatment group comparing pre- and posttreatment for pain- related disability*

Author (Year)	Between groups p- values	With- in pre- to posttreatment	Post- treatment to follow- up with- in group effect sizes

		effect size (d)	(p- values)
Buhrman et al. (2015)	.03	.47*	
Carpenter et al. (2012)	.01	.44*	
Dear et al. (2013)	< .001	.63**	
Dear et al. (2015)	< .001	.45*	.17*(<. 003)
Devineni et al. (2005)	< .05	.78	
Hedman- Lagerlöf et al. (2018)	< .001	.46*	
Palermo et al. (2009)	.004	.57**	.34*(<.003)
Ruehlman et al. (2012)	.02	.27*	

Notes: * mean small effect sizes; ** means moderate effect size.

In two of these studies, the researchers found significant with-in group changes between post-treatment and follow up, but the effect sizes were small (Table 5). In the other six studies, no significant changes in pain related disability were found, what means that the intervention effects were maintained.

The meta-analysis of the posttreatment-effect of CBT-based online interventions revealed an overall effect of $z= 6.78$, $p< .00001$ and a significant mean difference between the treatment and the control condition of – 0.28 (95% CI: - 0.378, - 0.21) in favor of the treatment conditions. The treatment group had significant lower ratings on pain-related disability at post-treatment compared to the control condition, but the effect was small. Subgroup analysis of the different control conditions only revealed a reduction in heterogeneity for the wait-list control group ($I^2= 39\%$) and also a higher between group effect for this subgroup (-0.61(95%CI: -0.70, -0.44)). This result indicates the differences in disability are the highest when comparing the treatment group with a waiting-list control group. Detailed information can be found in figure 3.

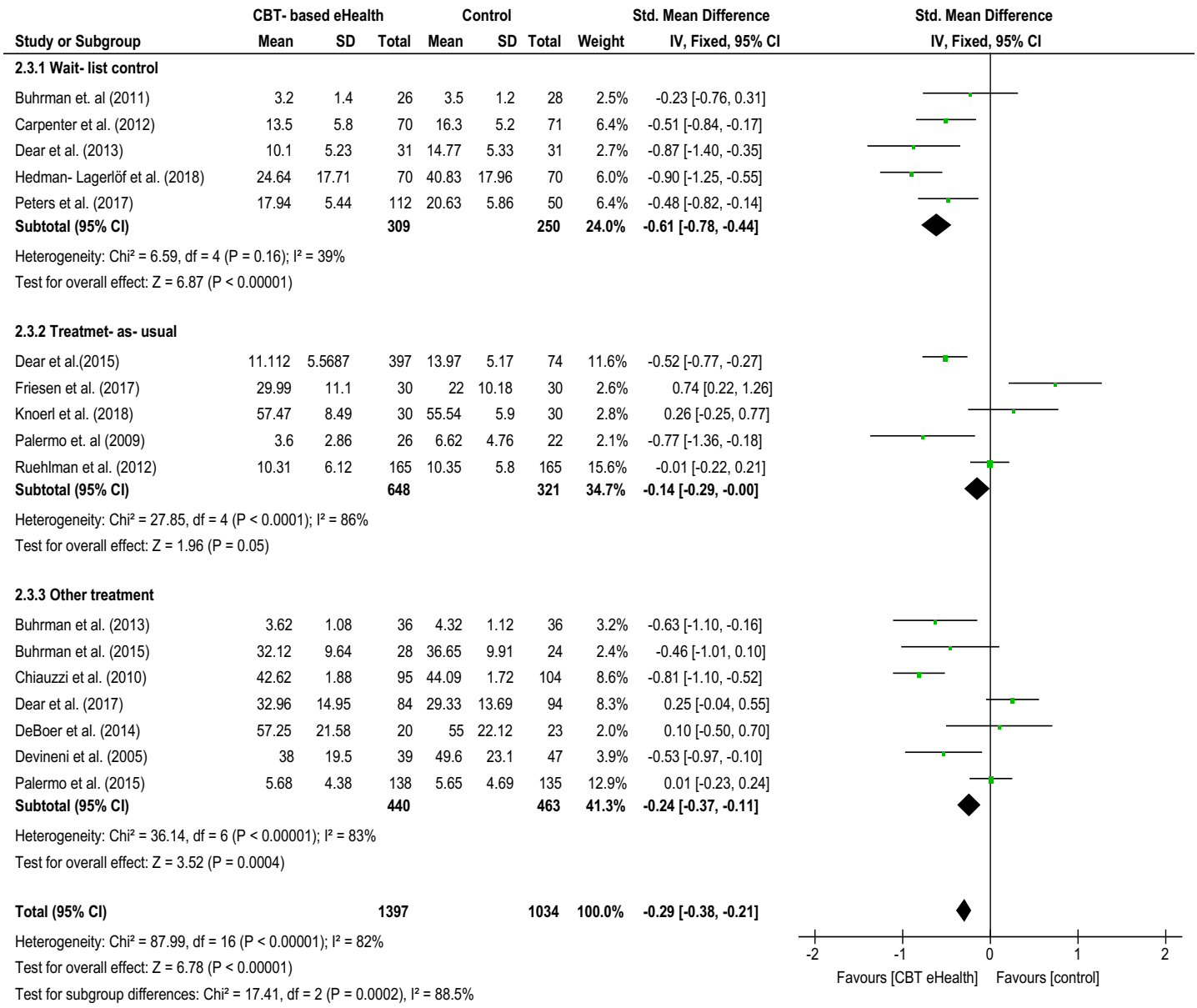

Figure 3. Means and sample size of the treatment and control group, study weight, standardized mean difference and Heterogeneity and overall effects with 95% confidence interval for pain- related disability.

Effects on depression. From the 15 studies that measured the effect of the intervention on depressive symptoms, ten found significant differences between-group effects comparing pre- to post-treatment in favor of the treatment condition (Table 6). The p-values were spread from a minimum of <. 001 to a maximum of =. 04 (Table 6). The effect sizes ranged from d= .24 to d= 1.60 (Table 6). The effect sizes of the other studies differed from low to high. The p-values and the with-in group effect sizes can be found in Table 6.

Table 6. *Between- group p-values between treatment and control condition and with- in group- effect sizes in the treatment group comparing pre- and posttreatment for depression*

Author (Year)	**Between groups p- value**	**With- in pre- to posttreatment effect size (d)**
Buhrman et al. (2013)	.04	.24*
Buhrman et al. (2015)	.005	.99***
Dear et al. (2013)	< .001	.80***
Dear et al. (2015)		
Regular contact	< .001	1.0***
Optional contact		.64**
No contact		.93***
Friesen et al. (2017)	.037	.79***
Hedman- Lagerlöf et al. (2018)	< .001	.60**
Palermo et al. (2015)	.03	.32*
Peters et al. (2017)	< .001	.74**
Ruehlman et al. (2012)	.04	.33*
Vallejo et al. (2015)	< .001	1.6***

Notes: * means small, ** means moderate and *** high effect size.

None of the eight studies found significant changes in depressive symptoms when comparing post-treatment to follow-up outcomes. This means that the treatment effects were stable over the follow-up periods.

The meta-analysis of the post-treatment-effect of CBT-based online interventions revealed an overall effect z= 7.15, p< .00001 and a significant small mean difference between the treatment and the control condition of – 0.33 (95% CI: - 0.41, - 0.24) in favor of the treatment conditions. The results of the subgroup-analysis showed a significant reduction of heterogeneity in the wait-list control group (I^2= 16%) and in the other treatment control group (I^2= 39%) compared to the overall heterogeneity (I^2= 81%). The between-group effects comparing the treatment group with the control groups also changed for the wait-list control group (- 0.43(95%CI: -0.61, -0.26)) and the other treatment control group (- 0.07(95%CI: - 0.20, 0.07)). This indicates that the effect of CBT-online interventions on depression is nearly the same as compared to other psychological treatments (Figure 4).

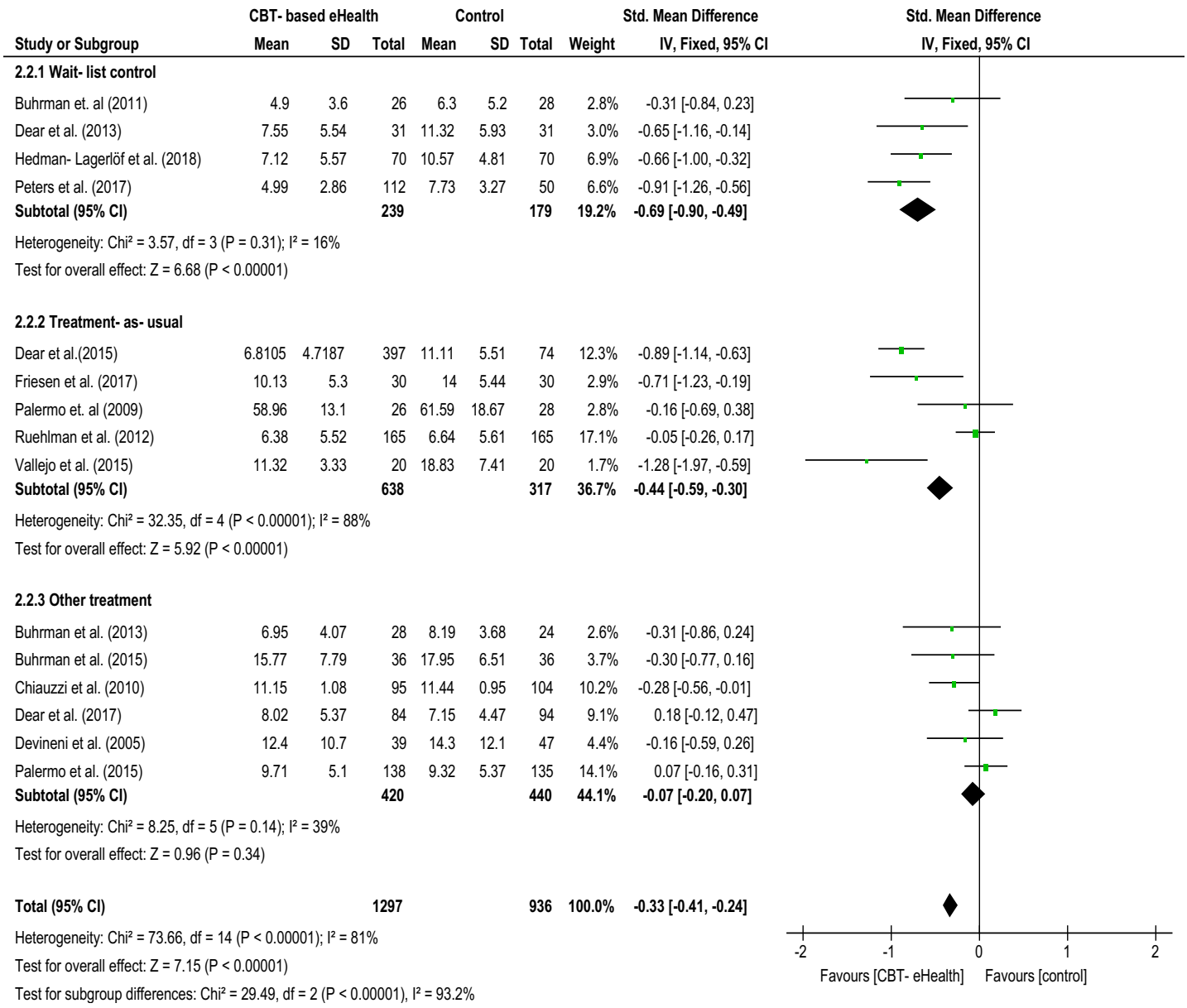

Figure 4. Means and sample size of the treatment and control group, study weight, standardized mean difference and Heterogeneity and overall effects with 95% confidence interval for depression.

Effects on pain catastrophizing. Seven studies out of the 12 that measured the impact of the intervention on pain catastrophizing found significant group effects in favor for the intervention group when comparing pre-treatment to post-treatment outcomes. The between-group effect p-values ranged from p< .001 to p< .03. The effect sizes in the intervention groups had a minimum of d= .16 and a maximum of .83. The effect sizes in the other studies were, with one exception, high to moderate (Table 7).

Table 7. *Between- group p-values between treatment and control condition and with- in group- effect sizes in the treatment group comparing pre- and posttreatment for pain catastrophizing*

Author (Year)	Between groups	With- in pre- to posttreatment
	p- value	effect size (d)
Buhrman et al. (2011)	< .001	.83***
Buhrman et al. (2013)	.03	.16*

Buhrman et al. (2015)	.002	.91***
Carpenter et al. (2015)	.011	
Rumination		.50**
Magnification		.53**
Helplessness		.70**
Dear et al. (2013)	.005	.78**
Peters et al. (2017)	.002	.66**
Ruehlman et al. (2012)	.01	.25*
Vallejo et al. (2015)	< .03	.69**

Notes: * means small, ** means moderate and *** high effect size.

When comparing the post-treatment outcomes to the scores at follow-up, none of the seven studies found a significant change in pain catastrophizing.

The meta-analysis of the post-treatment-effect of CBT-based online interventions revealed an overall effect z= 7.55, p< .00001 and a significant mean difference between the treatment and the control condition of – 0.44 (95% CI: - 0.55, - 0.32) in favor of the treatment conditions. The treatment group had significantly lower ratings on pain-related disability at post-treatment compared to the control condition, but the effect was small. For the effect on pain catastrophizing, subgroup analysis of the different control conditions showed reductions in the heterogeneity of all three subgroups (wait-list: I^2= 32,4%, treatment-as-usual: I^2= 35,6% and other treatment: I^2= 32.1%). It also revealed lower between group effects in the wait-list and treatment-as-usual control groups (-0.31 (95%CI: -0.51, -0.11) and -0.21 (95%CI: -0.40, -0.02) respectively). In the other treatment control group, the between-group effect increased strongly with high effect size of -0.82(95%CI: -1.02, -0.62) in favor of the CBT-based online intervention. Thus, it seems that CBT-based online interventions are highly superior to other treatments in reducing pain catastrophizing (Figure 5).

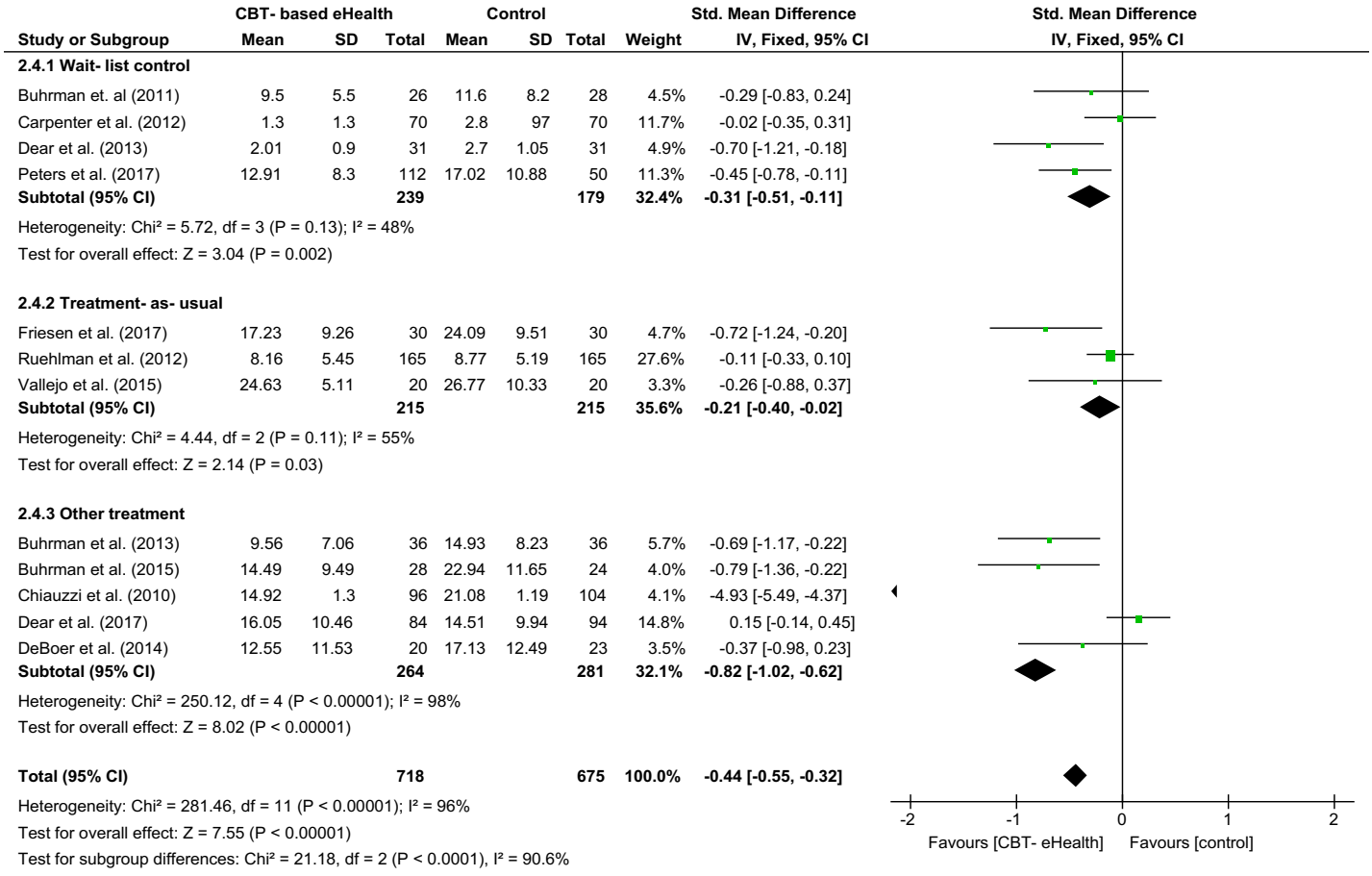

Figure 5. Means and sample size of the treatment and control group, study weight, standardized mean difference and Heterogeneity and overall effects with 95% confidence interval for pain catastrophizing.

Effects on quality of life. Six studies even examined the effects on quality of life, only two studies found a significant between group effect from pre-to post-treatment. The p-value in both studies was < .001. The with-in pre- to post-treatment effect sizes in the studies of Buhrman et al. (2011) and Hedman-Lagerlöf et al. (2018) were d= .36 and d= .49, respectively. Both studies did not find any significant with-in group changes when comparing post-treatment to follow-up.

The meta-analysis of the post-treatment-effect of CBT-based online interventions revealed an overall effect z= 6.36, p< .00001 and a mean difference between the treatment and the control condition of 0.65 (95% CI: 0.45, 0.85) in favor of the treatment conditions. The subgroup analysis of the three different forms of the control-conditions showed strongly reduced heterogeneity for the other treatment control group (I^2= 0%) and a strong decrease of the between group effect (0.24(95%CI: -0.06, 0.55)) compared to the overall effect. The waiting list-control condition was the most responsible for the between-group effect size. The group had a high effect size (d= 1.25) while the effect sizes in the other two groups was low (Figure 6).

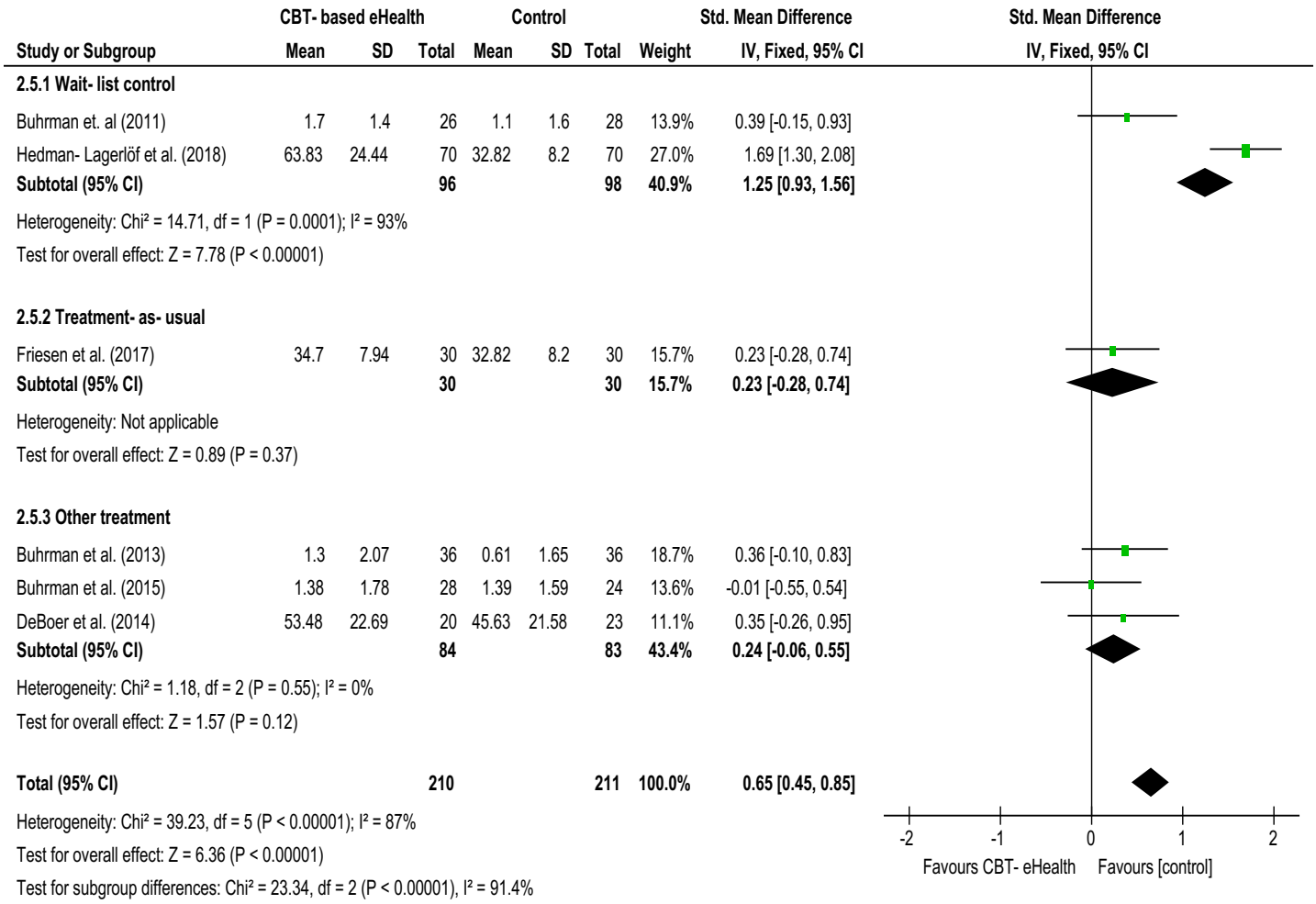

Figure 6. Means and sample size of the treatment and control group, study weight, standardized mean difference and Heterogeneity and overall effects with 95% confidence interval for quality of life.

Discussion

The aim of this review was to examine the effectiveness of cognitive behavioral online interventions for the treatment of chronic pain.

Overall, results of the meta-analysis showed that there was a small but significant effect of treatment of online interventions on pain intensity, depression, disability and pain catastrophizing compared to the control conditions. On quality of life, the treatment effect was moderate. These findings support that cognitive behavioral online interventions are effective for the treatment of chronic pain.

Pain intensity

For pain intensity, the treatment effect comparing pretreatment to posttreatment scores was the highest when comparing the online interventions with a waiting list control group. For this subgroup, the effect was still small, but nearly moderate and significantly higher compared with a treatment-as-usual or other active treatment control group. While the effect size of the subgroup comparing treatment-as-usual with the online intervention was higher than in the other treatment control group, they did not differ much. Only two studies found a significant improvement in pain intensity comparing posttreatment to follow-up measures (Devineni et al, 2005; Palermo et al., 2009), while the treatment effect in the other studies was stable over time. Based on these results, the conclusion can be drawn that online CBT-treatment is effective in reducing pain intensity compared to a passive waiting-list control group but is also more effective than treatment-as-usual or other active treatments in this review. These findings are consistent with the result of the review by Eccleston et al. (2014). In their review, the authors included 14 online CBT-intervention studies. Comparable with this review, they found a small but significant effect on pain intensity. In their analysis, they did not conduct subgroup analysis to differentiate between the different control conditions, so on this level, no comparison can be made. There is another review, targeting internet-based CBT-interventions for chronic pain (Macea, Gajos, Calil & Fragni, 2010). They found a small effect on pain intensity in favor of the treatment group, which strengthens our results. However, it must be considered that they only included studies that had a wait-list control group. For this subgroup, the effect on pain intensity was higher in this review.

Disability

Comparable to pain intensity, the treatment effect on disability between pre and posttreatment was the highest in the wait-list control group (moderate), while the treatment

effects in the treatment-as-usual and the other treatment control subgroup were small. Unlike on pain intensity, for disability, the treatment effect was higher when compared to another treatment control group than when compared with a treatment-as-usual control group. Comparing posttreatment scores with follow-up, the treatment effects were stable over the follow-up period. Thus, online CBT-treatment is superior to a waiting-list control group, but also to the other two examined control groups in reducing disability.

These results differ from the findings of Eccleston et al. (2014). In their review, they found a moderate effect size on the outcome disability. However, the number of included studies differed strongly between the review of Eccleston et al. (2014) and this review. They included only five studies in the meta-analysis on disability, while in this review, seventeen studies were included. Moreover, three of the studies from the Eccleston et al. review were also included in this review. Because of this, it is hard to make a valid comparison between the two reviews.

Depression

Also, for depression, the treatment effect between pre and posttreatment was the highest comparing online CBT-interventions with a waiting list control group. Like for disability, the effect was moderate. When compared with a treatment-as-usual control group, the effect was small, but nearly moderate, while in the other treatment control subgroup, the effect was not significant. Comparable with the outcomes on disability, the treatment effects were stable over the follow-up period. In conclusion, it can be said that online-based CBT-interventions are effective in reducing depression in chronic pain patients when compared to a group doing nothing, but it is also superior to treatment-as-usual and even effective than other active psychological treatments tested in the included studies. The effect sizes found in this review are consistent with the results found in the review by Eccleston et al. (2014). They also found a small effect size of online CBT-interventions on depression.

Pain catastrophizing

The results on pain catastrophizing differed strongly from those on pain intensity, disability and depression. Unlike the results for these outcomes, the treatment effect comparing pre-and posttreatment was the highest when comparing the online interventions with the other active treatment control group. For this subgroup, the treatment effect was high. The effect on the other two subgroups were small, but with a higher effect size in the

subgroup comparing the online treatment with a waiting list control group. Like for the other three outcomes, treatment effects were stable in time over the follow-up period.

It is striking that only for pain catastrophizing, the effect size is the highest compared to the other treatment control group. One would have expected that the online intervention group would do its best when compared with a group doing nothing at all, and not with participants receiving other active treatment. When looking at the results in details, the main reason for the high pre to posttreatment between-group effect size is the extremely high effect size found in the study by Chiauzzi et al. (2010). The meta-analysis revealed an effect size of d= -4.93. After removing this study from the meta-analysis, the effect size in the other treatment control group was only small (d= .22). Through this, the waiting list control group becomes the strongest group in reducing pain catastrophizing and the effect sizes of the other two subgroups are comparable with each other. Based on this, the conclusion can be drawn that online CBT-interventions are most beneficial for patients on a waiting list when it comes to the reduction on pain catastrophizing, but it also performed better than treatment-as-usual and other active treatments.

Remarkable, the study of Chiauzzi et a. (2010) highly effective in reducing pain catastrophizing. A possible explanation could be that the intervention used in this study had the shortest duration of all intervention of the included studies. Moreover, is had the highest frequency of lessons per week. There is evidence that frequent therapy lessons lead to a greater improvement in symptoms (Freedman, Hoffenberg, Vorus & Frosch, 1999; Heinicke & Ramsey-Klee, 1985; Erekson, Lambert & Eggert, 2015). Furthermore, there is evidence that shorter therapy duration leads to faster recovery (Stulz, Lutz, Kopta, Minami & Saunders, 2013). This implies that online interventions should be implemented with a high session frequency in order to maximize the treatment effect.

Quality of life

The pre-to-posttreatment findings in quality of life are more consistent with the findings on pain intensity, disability and depression. For quality of life, the treatment effect was high in the subgroup comparing the online CBT-intervention with a waiting list control group, while the effect size in the other two subgroups was small. The two subgroups did not differ significantly in effect sizes. During the follow-up period, the treatment effects were maintained. It is striking that even though none of the interventions were focused on improving quality of life, the effect size for this outcome was the highest. The main focus of

the online CBT-interventions was pain management, reduction in depression and the change of the underlying mindset that support the maintenance of chronic pain related symptoms. When looking to the results in details, the moderate effect size that was found in the meta-analysis in this review is mainly a result of the high effect size for quality of life in the study of Hedman-Lagerlöf et al. (2018), that was d= 1.69. If this study is excluded in the analysis, the effect on quality of life would have been not significant

It is known that quality of life is negatively related with depression and disability in chronic pain patients (Lee et al., 2017) and that good pain management is related to improved quality of life (Katz, 2002). Furthermore, there is evidence that higher pain catastrophizing is related to a reduction in quality of life (McPeak, Allaire, Williams, Albert, Lisonkova & Yong, 2018). By creating a change on these outcomes, included studies improved the quality of life of their participants. However, as mentioned above, the significant effect based only on one study. This study was the only one in the review comparing internet-delivered cognitive behavioral based exposure therapy with a waiting list control group. The results of the study by Hedman-Lagerlöf et al. (2018) revealed also the highest effect sizes in reducing pain intensity and disability across all included studies and the third highest in reducing depression. It is possible that the unique high effect size on the other outcomes was the reason why only the study by Hedman-Lagerlöf et al. (2018) was effective in improving quality of life according to the meta-analysis.

As far as the researcher knows, there are no studies comparing the effectiveness of exposure therapy and classic cognitive behavioral therapy on quality of life. One study was found that examined the effectiveness of face-to-face exposure therapy (den Hollander et al., 2016). In this study, the effect on quality of life was comparable with the effect found in the study by Hedman-Lagerlöf et al. (2018). Thus, the evidence points towards internet-delivered exposure therapy being more effective than classic internet-delivered cognitive behavioral interventions when it comes to the improvement of quality of life. A possible explanation for the high effect of exposure therapy on quality of life could be that it shares some common effects with other therapies known to be effective in improving quality of life. One of the main goals of ACT for chronic pain patients is to set the patients in state to be active again (Wetherell et al., 2011). This is also the case for exposure therapy for chronic pain (Schemer et al., 2018). It is possible the quality of life improves if the chronic pain patients become more active again and can participate active in the social life.

The results of this review are contradictory to the results of the review by Eccleston et al. (2014) when it comes to the improvement of quality of life, because they didn’t find any

significant changes in quality of life in the online intervention group. This discrepancy could be explained by the fact that the significant improvement of quality of life in this review is mainly caused by one study in this review (Hedman-Lagerlöf et al., 2018), as mentioned earlier. Without this study, the results in the two reviews are comparable.

Practical implications and further research

In light of the results of this review, some practical implications can be drawn. This review has shown that cognitive-behavioral online-interventions are an effective treatment for chronic pain and related symptoms of depression, pain catastrophizing, disability and improvig quality of life. This was especially the case when comparing cognitive behavioral online interventions with a waiting list control group. The ‘Nederlandse Zorgautoriteit' (2018) found that patients with somatoform disorders have to wait seven weeks before they can start the therapy. The average duration of the interventions in this review with a waiting list control group was 8,6 weeks. Thus, cognitive-behavioral online interventions are a great opportunity to treat chronic pain patients waiting for therapy. As a consequence, CBT-based online-interventions should be used as a standard care option and should be implemented widely.

Furthermore, the effectivity of this treatment is not the only argument for the implementation of CBT-based online-interventions for chronic-pain patients in daily health care. Online interventions have the potential to be accessible for more people than face-to-face therapy due to a large number of people having access to the internet, and the significantly lower number of psychologists that are needed to treat the same number of patients. Based on the results of this review, the author recommends providing online cognitive behavioral treatment to patients waiting for therapy. The therapy should have a high frequency, because this is expected to lead to faster recovery. A frequency of two sessions per week is recommended.

Strength and limitations

When interpreting the results of this review, some limitations must be taken into account. More than half of the studies (9 out of 17) failed to find a significant reduction in pain intensity when comparing the treatment with the control group. For three other outcomes, the proportions are comparable. For pain catastrophizing, five out of twelve did not find any significant between-group effects. Based on these results, it seems that not every online CBT-intervention is useful when it comes to the reduction of pain catastrophizing. Because of the important role pain catastrophizing plays in pain experience and for quality of

life, practitioners should examine if the intervention they are going to use has proven to be effective in reducing pain catastrophizing. Comparable to pain intensity, nine studies out of seventeen failed to find a significant reduction in disability. Only for depression, two-thirds found a significant between-group effect in favor of the treatment group, even though only one intervention was specifically developed to reduce depressive symptoms in chronic pain patients (Buhrman et al., 2015). Even though only this study was focused on reducing depression, in most of the interventions reducing depressive symptoms was a sub goal. It is striking that in most of the studies that failed to find significant between-group effects on one outcome, it was also the case on other outcomes. When looking into the characteristics of the studies that failed to find significant between-group effects on two or more variables, it is striking that all but one had an active control group. For those studies with an active control group that did find significant group effects, these effects were only small. Thus, the active control group could be an explanation for the lack of significant between-group effects. The results indicate that online CBT-interventions are even effective than other active treatments like psychoeducation or workbooks for chronic pain patients. When looking into the other characteristics of these studies, they were too heterogeneous to find trends or patterns why these studies failed to produce change in the participants. Further research is needed in order to examine why some interventions are highly effective, while other interventions fail. An example for such a study could be a full factorial design with all known and considered active ingredients of online interventions.

The overall heterogeneity was high across the studies, resulting in an I^2-statistic between 84% and 96% for the different outcome variables. Even when controlling for the different kinds of control groups, in most of the cases the heterogeneity was still substantial. A reason for this could be that many studies targeted different types of chronic pain, and it is possible that some chronic pain conditions can be treated more effectively with cognitive behavioral online interventions than others. Some results are pointing in this direction because the three studies targeting Fibromyalgia were very effective in treating the symptoms with effect sizes higher than the average. Furthermore, they differed in the level of therapist support, while it is known that this can be an active ingredient. Further research should examine the differences in effectiveness for treating different chronic pain conditions to find out which chronic pain patients could benefit the most from this kind of treatment, and why.

The quality of the included studies was mostly rated as poor, thus the studies were highly biased. This was the case for all concerning blinding of the participants, which can be very challenging in studies examining the effect of cognitive behavioral therapy, especially

when using a waiting list control group, or treatment-as-usual. In light of this, it is maybe necessary to make a new evaluation of the risk of bias of the included studies. Because the blinding of personnel and participants is nearly impossible in such kind of studies, maybe the risk of performance bias should not be included in the overall judgment of the study quality. This would lead to a strong improvement in study quality in nearly all included studies. In the review of Williams, Eccleston and Moreley (2012) that examined the effectiveness of CBT interventions for chronic pain, they followed this argumentation and excluded the performance bias from the overall judgment of study quality.

A strength of this review is that all studies included were RCTs. This decision was made because RCTs are the golden standard in intervention research, and only those studies allow to draw valid conclusions about the effectiveness of an intervention.

Another limitations is, that in all of the included studies, the majority of the samples were female, which was also a problem that other authors reported who reviewed studies about online-interventions for chronic pain (Gard, Garg, Turin and Chowdhury, 2016; Buhrman, Gordh and Anderson, 2016; Martorella et al., 2017). This can pose a serious threat to the generalizability of the results of the studies, and therefore of the results of this review. However, the risk of this is decreased by the results of the study of Breivik et al. (2011). In this study, 56% of chronic pain patients were female, while the population estimate of women was 52%, indicating that this condition is more prevalent in women than in men. Those findings were also confirmed in other population studies about chronic pain (Langley et al., 2011). However, in some of the studies, the proportion of female participants was higher than 90%, so the threat to generalizability still exists.

Even though the inclusion criteria $N \geq 20$ per study arm was implemented, this sample size is still small, so the power was low. In order to get more reliable results, the N-criteria should be increased in the next reviews about this topic. However, with a higher N-criteria (like $N < 30$, for example), the number of included studies would have been too low for this review. This could be another point of interest for further research.

However, there are also some issues that must be taken into account when it comes to online interventions in mental health care in general. A review about this theme identified a number of limitations of online therapy (Andersson & Titov, 2014). In online interventions, no valid diagnosis can be made. The diagnosis can only be based on self-rating questionnaires. Furthermore, when the internet is involved, confidentiality is a problem. The data of the patients are saved on the websites, and the email contact between the patients and the therapists is vulnerable. Another important problem that was identified in this review is

that most of the online interventions only focus on one mental disorder, without taking comorbidity into account. This can form a thread to the treatment effectiveness (Andersson & Titov, 2014). Furthermore, a survey conducted in Germany with mental health care specialists found that even though the attitude towards the use of online therapy is positive, and they believe in the benefit of using those treatments, they weren´t using it. The main reasons were that they either thought of themselves as too badly informed about existing effective online interventions or that they think that they lack the knowledge to perform these treatments (Surmann, 2017). This shows the need for government engagement in order to inform and educate the health care providers about online therapy.

A problem that is well known in the field of online interventions is a shortcoming of the usability of the interventions (van Gemert-Pijnen, Peters and Ossebaard, 2013). Many interventions are developed without the use of focus groups of all relevant stakeholders, even though it is known that this is an effective way for improving the usability (van Gemert-Pijnen, Peters and Ossebaard, 2013). More studies about the usability of existing, effective treatments in order to increase its effects and use are needed. Furthermore, guidelines to develop usable online treatments, like the CeHRes Roadmap (van Gemert-Pijnen et al., 2011), need to be used widely.

Conclusion

All in all, this review showed that cognitive-behavioral-based online interventions for chronic pain can have small to moderate effects on pain-intensity, disability, depression, pain catastrophizing and quality of life. When taking the different subgroups into account, treatment effect for pain intensity, depression, disability and quality of life was the highest when comparing online CBT-interventions with a passive waiting-list control group. For pain catastrophizing, the treatment effect was the highest when compared to other active treatments. In light of the high effectivity of cognitive behavioral online interventions for this group and the long time patients have to wait for therapy, the most important implication of this review is that this kind of therapy should be provided for chronic pain patients waiting for the start of their therapy.

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Appendix

Electronic search string Scopus

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