



Review Article

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Integrative Review on Cognitive Behavioral Therapy in Chronic Diseases: The Responses Predictors

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Abstract

Background: Cognitive behavioral therapy (CBT) is a self-management strategy used by patients with chronic diseases. Studies consistently report the effectiveness of this therapy in managing symptoms and improving patients' quality of life. However, evidence also shows that not all patients benefit from the therapy.

Methods: This article presents findings from an integrative review of studies published between 2010 and 2014 that investigated outcome predictors of CBT in chronic illness. The use of CBT in psychological disorders was excluded from the review.

Result: Eleven studies were included into this review. Every study supported the effectiveness of CBT for both immediate and long-term outcomes. The intervention components of CBT used in these studies were varied in the number and duration of sessions and the methods of identifying the effectiveness of the CBT. Most studies investigated the significant predictability of the psychological variables. Only one study investigated physiological predictors, and none investigated biological predictors.

Conclusion: This result highlighted the importance of consistency in the CBT components and methods used to identify the effectiveness of therapy. Furthermore, including physical and biological predictors of CBT outcomes is warranted, specifically in patients with a chronic illness.

Keywords: Cognitive behavioral therapy; Outcome predictors; Chronic diseases

Introduction

Chronic illnesses are rapidly becoming a major health concern in the United States. Over half of the adult population is reported to have at least one major chronic condition. Chronic illnesses often cause permanent and irreversible physiological changes that impact the individual's physical, psychological, social, and economic status. Chronic conditions are associated with substantial disability and considerable health care cost [1]. Despite differences in disease etiology, people living with chronic illnesses encounter similar diseases management challenges. These challenges include adjusting their lifestyle, dealing with emotion and psychological responses to chronic illnesses, identifying associated symptoms,

and adhering to a medication regimen [2]. While there are many self-management strategies or ways to improve self-care activities and optimize health while living with a chronic illness, cognitive behavioral therapy (CBT) is one that shows evidence of good outcomes.

Cognitive-behavioral therapy is a biopsychosocial intervention that combines techniques such as cognitive restructuring, relaxation, problem-solving, and stress management [3]. The underlying concept of CBT is an appraisal of individual behavioral responses to ways of thinking, mood expression, physical symptoms, and behavioral responses to an event or events [4]. Therefore, the goals

of CBT focus on challenging cognitive distortions and dysfunctional underlying beliefs and teaching coping and problem-solving skills [5]. To achieve cognitive and behavioral changes, the individual must actively participate in a collaborative problem-solving process and modify maladaptive behavioral patterns. The overall outcomes of CBT include symptom reduction, improvement of function, disease control, and an improved quality of life [6-8].

Since CBT was developed in 1995, it has been extensively used for the treatment of psychological conditions. It has also been found to have potential benefits to persons with chronic physical illnesses who cannot adjust to the disease, or beliefs and behaviors related to it. Cognitive behavioral therapy has been used in studies of people with cancer Thomas & Weiss [9], Parkinson's diseases Dobkin et al. [10], diabetes Welschen et al. [11], human immunodeficiency Inouye, Flannelly, Flannelly, Wagner et al. [12], fibromyalgia and arthritis V. G. Sinclair & Wallston [13], and diabetes K. A. Sinclair et al. [14,15].

Several studies report that CBT:

- Improved mood problems such as anxiety and depression.
- Changed disease-specific beliefs and attitudes.
- Improved psychological and physiological outcomes and.
- Changed health behaviors such as medication adherence and improved quality of life [16-18].

Outcome measurements for these studies included symptom reduction [19-21], enhanced physical function [22], and improved psychological conditions, including depression, anxiety, and fear [23]. The similarity in implementing CBT for a variety of chronic diseases is that it is delivered by clinicians or healthcare professionals with a masters-level education or higher, including nurses and psychologists.

Not all studies report that patients who receive CBT demonstrate improved outcomes. Systematic reviews have reported inconsistent findings on the effectiveness of CBT on physical outcomes, such as pain, fatigue, and sleep [24,25]. A review of randomized control trails on the self- management of chronic illness found that CBT was an effective strategy and increased self- efficacy, improved moods and coping ability, and improved the quality of life in Asians and Pacific Islanders living with chronic illnesses [26]. Based on variable outcomes in studies of CBT, investigators have begun to examine predictors of treatment success.

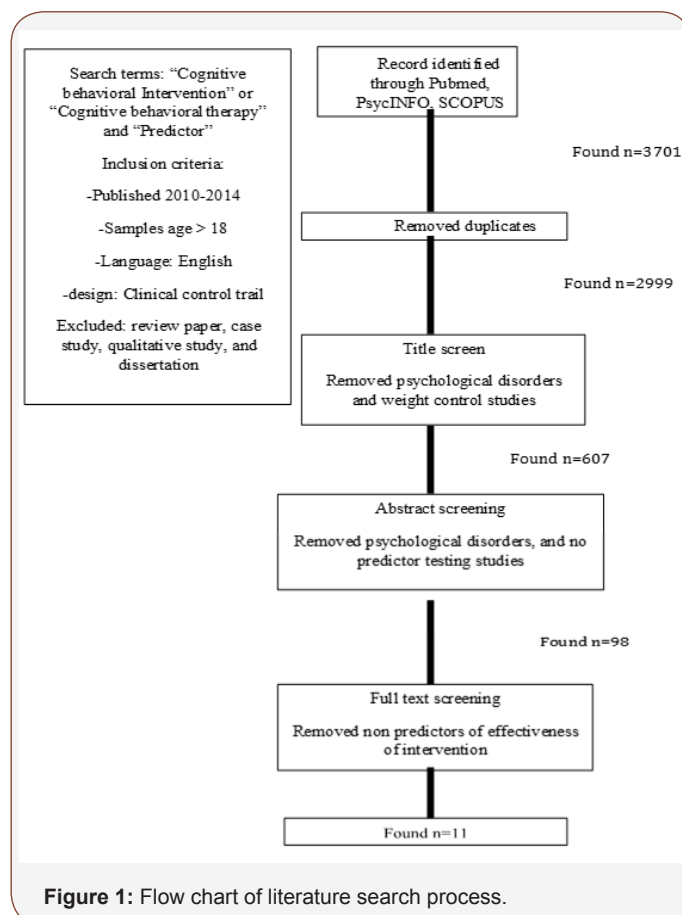
Systematic reviews and meta-analyses have reported the effectiveness of CBT and predictors of treatment outcomes in different psychological disorders, including schizophrenia, bipolar disorder, major depression, anxiety disorder, eating disorders, and obesity [27,28]. Fewer studies have investigated the effectiveness of CBT in physiological illnesses such as cancer, fibromyalgia, arthritis, chronic pain, diabetes, and HIV [29]. One review article included the outcome predictors as part of the review of behavioral and cognitive-behavioral treatment in persons with chronic pain McCracken & Turk [30]. These authors reviewed studies published

between 1989 and 1999 using both behavioral treatment and CBT but limited their search to a population with chronic pain. A more recent systematic review published in 2013 reported the predictors of treatment outcomes for patients with fibromyalgia de Rooij et al. [31]. Although they found that the level of depression, belief, disability, and pain were predictors of treatment outcomes, the treatment used in this review was not specific for CBT. The purpose of this paper is to review the predictors of outcomes of CBT intervention among the people with chronic diseases.

Methods

Study selection

We searched PubMed, PsycINFO, SCOPUS, and EMBASE for articles published between 2010 and 2014 that included clinical trials of adults aged 18 years and older, published in English, and with the following keywords as all fields: "Cognitive Behavioral Therapy" OR "Cognitive Behavioral Intervention" AND "Predictor." The search yielded 3,701 articles, but the removal of duplicates left 2,999. To investigate the use of CBT in chronic physical illnesses, these studies were then screened by title to remove those that focused on psychological disorders and weight control. The refined search yielded 607 articles. Abstracts from these articles were reviewed to determine if they met the final inclusion criterion of including the predictors of the cognitive behavioral intervention. Ninety-eight articles remained after the abstract review. Finally, the full text of the 98 articles was reviewed for inclusion of the predictors of CBT effectiveness. Eleven articles met the criteria and were included in this review (Figure 1).



Quality assessment

Four reviewers independently evaluated the quality of 11 studies using the Jadad Scoring of Quality of Reports of Randomized Clinical Trials instrument Jadad, Carroll, Moore, & McQuay [32]. This is a validated instrument used to evaluate the quality of randomized clinical trials. It emphasizes specific parts of a study, including randomization, blinding, withdrawal, and dropouts. It is an 11-item assessment the reviewer uses to evaluate the quality of a study based on the description of the study and its methodology.

Each item is rated either 0 = does not describe, or 1 = describe. Two extra points can be added if the methods of randomization and a double-blind are described. Therefore, the total Jadad quality score ranges from 0 to 13 with the higher score indicating better quality. Of the 11 articles reviewed, 6 reported the details of their intervention and methodology in the original studies. Therefore, the reviewers evaluated the quality of these six articles based on the descriptions in the original studies [33,34]. The reviewers discussed the item scores among themselves until they came to a consensus (Table 1).

Table 1: Study characteristics.

Authors (year)	Study location	Jadad score	Sample Characteristics			Chronic conditions
			Age (mean ±SD)	Gender, n (%)	Race, n (%)	
Chader, Godfrey, Ridsdale, King and Wessely	Primary care in London and the South East of England	10	39.4±13.6	Male: 43 (27%) Female: 117 (73%) n= 160	NA	Chronic fatigue syndrome
Currie, Wilson and Curran	Outpatients from chronic pain treatment clinics	8	45.0±8.0	Male: 27 (45%) Female: 33 (55%) n=60	NA	Chronic nonmalignant pain with insomnia
Flor and Birbaumer	Outpatients at the psychophysiological pain clinic	7	42.4±9.7	Male: 31 (40%) Female: 47 (60%) n=78	White: 100%	Chronic musculoskeletal pain
Gersh, et al. [38]	Outpatients from pain center at Victoria, Australia	5	49.5±14.1	Male: 97 (37%) Female: 164 (63%) n=261	NA	Chronic nonmalignant pain
Kempke, et al. [35]	Patients from tertiary care centre for CFS in Belgium	3	40.4±9.6	Male: 27 (15%) Female: 151 (85%) n=178	NA	Chronic fatigue syndrome
Litt & Porto [37]	Outpatients from dental clinic in Connecticut, USA	7	39.4±12.1	Male: 16 (16%) Female: 85 (84%) n=101	White: 76% Black: 9% Hispanic origin: 9%	Temporomandibular disorder (TMD) pain patients
Ljotsson, et al. [51]	Outpatients Stockholm, Sweden	7	34.3±9.3	Male: 12 (15%) Female: 67 (85%) n = 79		Irritable bowel syndrome (IBS)
Prins, et al.	Outpatients from department of internal medicine of 2 universities	9	36.7±10.1	Male:58 (21%) Female: 212 (79%) n=270	N/A	Chronic fatigue syndrome

a Information was published in Ridsdale, et al.

b Information was published in Currie, Wilson, Pontefract & deLaplante 2000.

d Information was published in Zonneveld, van Rood, Timman, et al.

Results

Of the 11 articles evaluated, 9 (82%) were in an outpatient setting. Only two studies (18%) were done with inpatients receiving treatment at a tertiary rehabilitation center. The participants' ages ranged from 34 to 65 years. The number of participants in each study varied from 13 to 261 and in 9 studies, the majority was female, ranging from 62 to 88%. Most of the studies in Europe and Australia did not report race or ethnicity, Studies conducted in the United States, however, reported a majority of white/Caucasians (76 to 93%). Clinical populations investigated in the 11 articles had chronic nonmalignant pain, such as temporomandibular disorder, chronic low back pain (n = 4 articles, 36%), chronic fatigue syndrome (n = 2 articles, 18%), irritable bowel syndrome (n = 1 article, 10%), posttraumatic stress disorders in cancer survivor and civilian trauma (n = 2 articles, 18%), Parkinson's disease (n =

1 article, 10%), and unexplained physical symptoms (n = 1 article, 10%). (Table 1) summarizes the characteristics of studies used in this review paper. The quality of the 11 articles based on the Jadad score ranged from 3 to 11.

Intervention implementation

Cognitive behavioral interventions used in the 11 articles (Table 2) varied in terms of the CBT features of treatment modality, delivery methods, and format. Several reviewed articles indicated that detailed information of their CBT intervention was published elsewhere. Therefore, the original articles were reviewed except for one study Kempke et al. [35], which was referenced in a non-published paper. The cognitive restructuring was the key CBT feature used in eight of the studies. Only two studies included relapse prevention (18%) and three included the homework/workbook requirement (27%). Relative to treatment modality,

four studies (36%) evaluated the effectiveness of CBT as a single intervention, while the majority used CBT as an adjunct intervention (n = 7, 64%). CBT was primarily delivered in a face-to-face format (n = 9, 82%) with individual participants (n = 6, 55%). Two studies used either the telephone or internet (Table 3). The length of an

intervention varied from 1 to 5 hours per session and the number of sessions ranged from 6 to 75. The most common length a session was 60 to 90 minutes (n = 4, 36%) with 10 sessions (n = 5, 45%) to complete the study (Table 3).

Table 2: Study characteristics.

Authors	Intervention (s)	Theoretical bases/focus of intervention	CBT components	CBT Delivering methods			Treatment fidelity
				Method	Type	Therapist	
Chalder, Godfrey, Ridsdale, King and Wessely	Comparing between Counseling with psychodynamic approach and Cognitive behavioral therapy (CBT)		providing treatment rationale activity planning home work	Face to face Six of 1-h sessions	N/A	Qualified CBT therapists	The session were rated by 4 independent CBT specialists
Currie, Wilson and Curran	Cognitive behavioral Treatment of insomnia	The development of insomnia secondary to chronic pain	Basic education Behavioral therapy targeted sleep problem Relaxation training Sleep hygiene education	Face to face Seven 2-h session	Group (5-7 participants)	Doctoral students or interns in clinical psychology, who had previous training of CBT	Therapists were required to follow the writing manual and were supervised weekly
Flor and Birbaumer	Cognitive-behavioral therapy (CBT) vs. electromyographic biofeedback (EMG-BFB) vs. conservative medical treatment (MED)	Patients with psychophysiological reactivity would be benefit from EMG- BFB. Patients with negative self-statement would be benefit from the CBT	Progressive muscle relaxation identification of pain and tension-eliciting events relaxation exercise problem solving practice pain coping skill (e.g, positive self statement,distraction)	Face to face Eight 1-h sessions	N/A	Clinical psychologists trained in psychological pain treatment	N/A
Gersh et al. [38]	Multidisciplinary pain management program included Cognitive behavioral therapy (CBT) and functional restoration group (FRG)		Modify the maladaptive beliefs and attitudes about pain New coping strategies Relaxation Stress reduction techniques Goal setting Planned behavioral reactivation Pacing of physical activity Guided gentle exercise with Feldenkrias, tai chi or individualized gym program	Face-to-face 8 full day sessions twice a week (5 hours of interactive participation)	Group	Trained psychologist in pain management	N/A
Kempke et al. [35]	Cognitive-behavioral based Multi-component treatment program Combination of the group CBT, flexible graded exercise therapy (GET) and progressive relaxation therapy (PRT)	Cognitive- behavioral model (Vercoulen et al., 1998)	N/A	Face-to-face	Group	N/A	N/A

Litt & Porto [37]	Combination of Standard conservative care (STD) and Cognitive behavioral therapy (CBT)		Briefs cognitive-behavioral program include Relaxation training Stress management Cognitive restructuring	Face to face 6 sessions over 6-9 week period	N/A	Four master – level therapists with at least 2 year experience in CBT with medical patients.	Treatment sessions were videotaped and reviewed by first author
Ljotsson et al., [53]	Internet-delivered cognitive behavioral treatment based on exposure exercises (ICBT)	The principle of behavioral exposure and mindfulness exercise	Rational and instructions on mindfulness Identify the thoughts and symptoms using mindfulness practice Exposure exercises include 1) Engaging in activities that provoke symptoms 2) Establish behaviors controlling symptoms 3) Exposure to situations where symptoms are unwanted.	Internet Administering online (10 weeks)	Individual	Graduate psychology student trained in CBT respond to online synchronous message system from participants	No therapist adherence to the manual was tested. All participant contact monitored and supervised.
Prins, et al.	Cognitive behavioral therapy and support group	The model of CFS focus on bodily symptoms. The CBT is directed at the low sense of control, low physical activity and functional impairment	Explain the model of CFS and perpetuate factors Cognitive restructuring to improve sense of control over symptoms and facilitate the behavior change Maintain physical activity, gradually increase physical activity relapse prevention	Face to face 16 sessions of 1-hour CBT over 8 months	Individual	CBT trained behavior therapists (include psychologist, psychiatrists and health scientists)	Therapists were supervised once every 2 weeks. Audiotaped CBT sessions were randomly checked to ensure the integrity of the intervention.
Samwel et al., [39]	Multidisciplinary allocation of chronic pain treatment. The modalities include 1) Medical treatment 2) Self adjusted Transcutaneous electrical nerve stimulation (TENS) 3) Cognitive-behavioral group therapy	Multidisciplinary approaches	Cognitive behavioral group therapy was selected if pain was not reduced by both medication and TENS. Treatment components included Goal setting Stress management Problem-solving techniques Cognitive therapy Relaxation exercise	Face-to-face Ten 90-minute sessions Group of 5 to 12 patients CBT	Group	Psychologist	
Schreurs, et al. [41]	Multidisciplinary rehabilitation program: Combination of the Graded exercise therapy (GET) and Cognitive behavioral therapy (CBT)	Evidence based treatments	CBT components include Cognitive restructuring Problem solving Individual goal setting	Face to face 75 therapy sessions within 25 weeks	Group	Psychologists and social workers	

Sharpe, et al.	Combination of medical care and cognitive behavioral therapy	The intervention is based on the hypothesis that factors such as beliefs, coping behavior, mood, social and pathophysiological process are interacted to impact the illness	Identify the illness perception, and consider the psychological and social factors that influences the illness Gradual and consistent increase in activity and evaluation of the strategy excessive perfectionism reduction active problem solving to interpersonal and occupational difficulties	Face to face 16 one-hour sessions over 4 months.	Individual	Three expert therapists	Therapy was codified in a manual and supervised by an expert experienced cognitive therapist.
Siemonsma, et al. [42]	Combination of grade activity, gradual exposure in vivo, and cognitive treatment of illness perceptions (CTIP)	Evidence-based methods of cognitive behavioral treatment (CBT) in rehabilitation	Identify illness perceptions and maladaptive illness perception Create question about maladaptive illness perceptions Formulate and test alternative illness perceptions Apply and practice alternative illness perceptions	Face to face 10-14 of 1-hour individual treatment sessions	Individual	Physical therapists, occupational therapists or psychologists received 21 hours training with 20 hours refresher course.	Therapists required discussing the progress of each patient with psychologist supervisor at least twice.
Zonneveld, et al., [52]	Cognitive behavioral group training	The consequence model (Zonneveld, et al., 2012b)	Psychoeducation Response prevention Pacing activity Graded activity and exercise Problem solving Breath and relaxation exercise Cognitive intervention using the Ellis' ABC worksheet Relapse prevention	Face to face 13 weekly of 2 hours session	Group	Psychologists with master's degree and > 3 years postmaster experience with group therapy and/or group CBT or trained with first author	

a intervention information was published in Ridsdale, et al. 2001.

e intervention information was published in Zonneveld, van Rood, Timman., et al. 2012.

Table 3: Intervention Features, Treatment Modality and Delivery Methods, and Format.

Studies	CBT Features										Treatment Modality		Delivery Method		Delivery Format	
	Education	Goal setting	Identify thoughts	Cognitive re-structure	Behavior activation	Grade exposure	Behavioral experiment	Stress reduction/relaxation	Relapse prevention	Home-work/work-book	Single	Combined/supplement	Telephone/internet	Face to face	Individual	Group
Chalder, Godfrey, Ridsdale, King and Wessely										✓	✓			✓		✓
Currie, Wilson and Curran	✓						✓	✓		✓	✓			✓		✓
Flor and Birbaumer			✓					✓			✓			✓		✓

Gersh, et al. [38]		✓		✓	✓		✓	✓			✓		✓		✓	
Kempke, et al. [35]											✓		✓		✓	
Litt & Porto [37]				✓				✓		✓		✓		✓		
Ljotsson, et al. [51]	✓		✓		✓	✓	✓			✓	✓		✓(1)		✓	
Prins, et al.	✓		✓	✓					✓		✓			✓		
Samwel et al. [39]		✓		✓	✓				✓			✓		✓	✓	
Schreurs, et al. [41]		✓		✓								✓		✓	✓	
Sharpe, et al.			✓		✓	✓	✓	✓				✓		✓	✓	
Siemonsma, et al. [41]			✓	✓	✓		✓					✓		✓	✓	
Zonneveld, et al., [52]	✓	✓	✓	✓	✓		✓	✓	✓		✓			✓		
Total	4/11	4/11	6/11	8/11	6/11	2/11	6/11	6/11	2/11	3/11	4/11	7/11	2/11	9/11	6/11	4/11

Note: I=internet; T = telephone

In all studies, therapists who delivered the CBT intervention were required to have at least a master’s level of education and were either trained or accredited for conducting CBT intervention. The integrity of the interventions was monitored using a variety of

methods, such as supervision by a senior clinician and psychologist, videotaping the session [36,37], and discussion of the patient’s progress with a supervisor.

Methodology and identification of clinically significant outcomes

Table 4: Methodology and Clinically Significant Outcome Identification Methods and Results.

Authors	Design/data Collection	Outcome Measurement	Clinically Significant Outcomes Identification Methods	Predictors	Result
Short term effectiveness (immediately after the treatment)					
Gersh et al. [38]	Pre-post test Data was collected pre and post intervention	Brief pain inventory average pain rating, Short form health survey (SF-36 version2) mental health and physical functioning subscales	1.Using the score of PSOCQ as a continuous variable and investigate the association of score change 2.Allocated the participants into the 4 stages of changes include, precontemplation, contemplation, action and maintenance based on the maximum score. If score was high in more than one scale, participants will be placed in the further progression stage. 3.Classified participants based on the change of PSOCQ score into progressor (move from precontemplation to contemplation, action and maintenance and people who remain in the maintenance stage) and non-progressors (regressed or no change of the stage)	Pain stages of change questionnaire (PSOCQ)	Improvement in mood rating associated with the decreased precontemplation (r=-.24, p<0.05) and increased maintenance rating (r=.29, p<0.05) Decrease disability rating associated with increase rating on action (r=.22, p<0.05) and maintenance (r=.18, p<0.05) scales. High in precontemplation and low in other subscale of PSOCQ are less likely to complete treatment Progressors showed more improved of mood (F (1,117)=9.60, p<0.01) and function (F (1, 117) =4.00, p<0.01) than non-progressors Both progressors and non-progressors showed no significant different of pain change magnitude (F (1.117)= 0.88, p<0.05) Treatment groups were not differ regarding to the stage of change

Kempke, et al. [35]	Pre-post test The predictors were measured at baseline. The outcome variables were measured at completion of the intervention	Post- Fatigue measured by the checklist individual strength (CIS-20)	The association of the predictors at baseline with the level of outcome variables (fatigue) at treatment completion was tested Participants were classified into substantial improved using the 10% reduction of fatigue (CIS-20) based on the effect sized (Cohen's d =0.79)	Pre-Fatigue measured by the checklist individual strength(-CIS-20) Patient's opinions regarding the cause of their fatigue measured by Causal Attribution list (CAL) Self-efficacy scale (SES) General activity level index of the Multi-dimensional Pain Inventory (MPI) Function impairment measured by Functioning Scale (SF-36) Psychiatric and somatic conditions: the somatization subscale of the symptom Checklist-90 (SCL-90) Severity of depression measured by the depression subscale of the Hospital Anxiety and Depression Scale (HADS)	High pre-treatment depression was associated with high post treatment fatigue ($\beta = .239, p < .05$) Higher pre-treatment depression patients were less likely to experience fatigue improved after the treatment (Wald=5.527, p = .05, OR=.862, 95% CI=.762-.976).
Samwel, et al. [39]	Pre-post test design	Pain intensity: 10- centimeter visual analogue scale (VAS) rating for 7 days Functional disability: Dutch version of the pain disability index (PDI), measure role of functioning: family/ home responsibilities, recreation, social activities, occupation, sexual behavior, self-care, life supporting activities Depression: Dutch version of the symptoms checklist-90 Medication Use: calculated from the actual daily used of drugs (UDD)/ amount of drugs needed to obtain the desired effect on pain in the general population (DDD)	The association between the baseline predictor variable scores and the change score of the outcomes from baseline to completion was tested.	Avoidance behavior: passive pain coping scales retreating and resting of the pain coping inventory (PCI) Worrying: worrying scale of the PCI Fear of pain: adjusted version of Tampa scale of Kinesiophobia Helplessness: helplessness scale of the illness cognition questionnaire (ICQ) Acceptance: acceptance items of ICQ	Higher levels of acceptance to significantly predict larger reductions of pain intensity in intervention but not in the control group
Siemonsma, et al. [42]	Pre-post test Data was collected before and at the completion of the intervention	Patient-specific Functioning list (PSFL) change: the change score from baseline to treatment completion	Association of the baseline predictor variable scores and the change of outcome variable: PSFL were tested. Use the criteria of minimum decrease of the PSFL at least 18 mm to identify the clinical significant change	Rational problem-solving: The relational problem-solving (RPS) scale Discussion skills: Aggrievedness Scale of Dutch Personality questionnaire Verbal skills: Multicultural Capacity Test (MCT), Word Relation Scale (MCT-WR and World Analogies Scale (MCT-WA)	Rational problem-solving found to be significant predictor for the change in physical activity. Discussion skills and verbal skills were not significant. Rational problem-solving explained 3.9% of total variance.

Both short time and long-term effectiveness					
Currie, Wilson and Curran	<p>Longitudinal study</p> <p>Outcome variables were measured at baseline, posttreatment, and 3 month follow up assessment</p>	<p>Sleep was measured by the Pittsburgh Sleep Quality (PSQI)</p> <p>Sleep onset latency (SOL)</p> <p>Wake time after sleep onset (WASO)</p>	<p>The effectiveness of the CBT was identified by the clinical improvement of the outcome variables criteria include</p> <p>1) Reliable change index (RCI) of PSQI >1.96</p> <p>2) SOL ≤ 30 min</p> <p>3) WASO ≤ 30 min</p> <p>Predictors were measured at the baseline to predict the outcome improvement</p>	<p>demographic status (age, gender, employment, smoking status)</p> <p>sleep and pain history (duration, age at onset)</p> <p>insomnia severity: Structured Interview for Sleep Disorders (SIS-D)</p> <p>medication usage</p> <p>Pain: baseline pain severity, primary pain site</p> <p>Depression: Beck Depression Inventory</p> <p>sleep self-efficacy</p> <p>number of sessions attended</p> <p>disability: Roland and Morris Disability Questionnaire (RMDQ)</p>	<p>Higher score of sleep self efficacy (SSS) at baseline was a significant predictor of the RCI > 1.96 of PSQI</p> <p>Higher score of BDI at baseline significantly predict the SOL of less than 30 min</p> <p>Greater pain severity at baseline predicted a WASO of less than 30 min</p>
Flor and Birbaumer	<p>A longitudinal study</p> <p>Data was collected at baseline, immediate post treatment, 6 month and 24 months follow up</p>	<p>1) Verbal-subjective level Pain: Multidimensional Pain Inventory (MPI)</p> <p>Depression: Beck Depression Inventory, Pain related self statements</p> <p>Pain related control scale</p> <p>Pain diary: patient rated pain, interference, stress, mood and medication intake (2 week prior to the treatment, throughout the treatment, 1 week, 6 month and 18 month)</p> <p>2) Behavioral level Pain behavior scale (PBS) was used to rate the unaware behavior on the videotape of patients during their functional assessment tasks</p> <p>Use of health care system (number of doctor visits in previous 3 months)</p> <p>3) Psychophysiological assessment</p> <p>Record of surface EMG levels during 2-min resting baseline and 1-min imagery tasks</p>	<p>Combined score of the percentage change in pain severity and interference.</p>	<p>Chronicity of pain problem</p> <p>Cognitive variables</p> <p>Psychophysiological reactivity variables</p>	<p>Chronicity of pain problem negatively associated with the treatment outcomes for both BFB and CBP</p> <p>The psychophysiological reactivity predicted the outcome of BFB treatment. Patients with low physical reactivity and patients who practiced relaxation and distraction received higher benefit from the BFB</p> <p>The cognitive variables predicted the CBT treatment outcomes. Patient with less cognitive distortion will be profit from the CBT.</p>

Litt & Porto [37]	<p>Pre, post test</p> <p>Data was collected at pre-treatment, treatment completion (6 weeks) and at weeks 12, 24, 36 and 52</p>	Pain (multiple pain Inventory: MPI) response at baseline and 1 year post treatment	The responders and non-responders were identified using the statistic methods, Growth Mixture modeling (GMM) to investigate the pattern of MPI pain changes over times.	<p>Demographic information (sex, age, race, education, employment status, marital status, income)</p> <p>Pain and TMJ pathology variables: patient history questionnaire of Research Diagnostic Criteria for temporomandibular disorders (RDC/TMJ): Axis I Physical disorder and Axis II psychosocial axis</p> <p>Psychiatric symptoms:</p> <ol style="list-style-type: none"> 1) Depression (Center of epidemiological studies depression scale (CESD)) 2) Anxiety: state-trait anxiety inventory 3) Somatization: 12-item somatization subscale of the symptoms checklist 90-revised (SCL-9-R) <p>Cognitive constructs:</p> <ol style="list-style-type: none"> 1) Readiness to engage in self-management treatment: the pain stages of change questionnaire 2) Pain management self-efficacy: Chronic pain Self-efficacy scale (CPSS) 	Treatment conditions, and catastrophizing change were significant predictors of the member in the high pain, treatment responder group
Ljotsson et al. [53]	<p>Randomized controlled crossed over design</p> <p>Data was collected at pre and post intervention with follow up assessment at 18 months (intervention) and 15 months (control waiting group)</p>	Gastrointestinal symptom rating scale-IBS version (GSRs-IBS)	The associations of the baseline predictor variables scores and the GSRs-IBS scores at the post treatment, follow up scores were tested	<p>Psychological distress measured by Mini-International Neuropsychiatric Interview (MINI)</p> <p>Depression measured by Montgomery Asberg Depression Rating Scale-Self report (MADRS-S)</p> <p>Severity of somatic symptoms measured by Somatization subscale of Symptoms Checklist-90 (SCL-SOM)</p> <p>Gastrointestinal symptom-specific anxiety (GSA) and related constructs measured by Visceral Sensitivity Index (VSI)</p> <p>Catastrophizing measured by Catastrophizing subscale of Coping Strategies Questionnaire</p> <p>Anxiety measured by Anxiety Sensitivity Index (ASI)</p> <p>Disability</p> <p>Quality of life measured by Irritable Bowel Syndrome Quality of Life (IBS-QOL)</p>	When control for the pre-treatment symptoms, no significant predictors

Schreurs, et al. [41]	Longitudinal study. Outcomes were measured baseline, post treatment, and 6 month follow-up	Fatigue: Checklist Individual Strength-20 (CIS-20) subscale Physical impairment: Sort form-36 health survey (SF- 36)	Using criteria to identify treatment effectiveness Participants identified as clinically significantly improved if 1.had reliable change index >1.96 on the CIS-20 subjective fatigue subscale 2.a CIS-20 subjective fatigue score ≤ 35 and a SF-36 physical score ≥ 65 (Scheeres et al., 2008)	Socio demographic: age, gender, living status, education, disablement insurance benefit Somatic and psychological attribute: causal attribution list (CAL) Sense of control: Self efficacy scale (SES) Depression: depression subscale of symptoms checklist-90 (SCL-90) Somatic focus: Somatization subscale of the SCL-90 Level of physical activity: Actilog-scale V3.0 (actometer attached to ankle and worn for 14 consecutive days)	Post treatment improvement of fatigue predicted by not receiving a disablement insurance benefit, shorter duration of fatigue, higher sense of control over symptoms 6 month follow-up improvement of fatigue was predicted by pretreatment Physical activity.
Sharpe et al.	Longitudinal Data was collected at baseline, 5 month, 8 month and 12 month post treatment	Patient functioning was measured using the Karnofsky scale Symptoms: a)fatigue was measured on the 0-10 Likert scale b)depression and anxiety were measured on the Hospital anxiety and depression scale	The therapy outcome was measured by using 1)Improvement of patient functioning as outcomes (Kanofsky is ≥ 80 or clinical significant change of kanofsky scale (increase ≥ 10)) Overall change was measured on the 7 point self-report scale	Illness beliefs and coping behaviours were measured using the 5 point-Likert scales of the strength of beliefs or coping strategies. The reduction of the strength then analyzed it association with the therapy outcomes.	Beliefs about illness and previous coping behavior associated with the change of the outcomes among patients receiving CBT
Zonneveld, et al. [52]	Longitudinal Data was collected at baseline and immediate, 3 month and one year post treatment.	The summary scales of the 36-item Medical Outcomes Study Short-Form General Health Survey (SF-36) Physical Component Summary' (PCS) Mental Component Summary (MCS).	Association of predictor variables short-term and long-term outcomes were tested	1)Psychological symptoms (global severity score of SCL- 90) 2)Personality-disorder characteristics (sum of DSM-IV axis II criteria confirmed) 3) Psychiatric history (past presence of DSM-IV axis I disorders), 4.) Health-related quality of life in Mental Domain (mental component summary of SF-36).	Predictor set alone significantly associated only with short-term CBT outcome. At this time-point, all predictors were significant. Psychological symptoms had strongest association with short-term outcome. Predictor set did not significantly predict outcomes at any of the three time points; its effects not stable over time.

Only long term effectiveness of CBT (more than one month post treatment)					
Chalder, Godfrey, Ridsdale, King and Wessely	Longitudinal study Outcome variables were measured at baseline and 6 month post treatment	Fatigue is measured by the fatigue questionnaire. Fatigue score range from 0 to 11	Patients scored fatigue of 4 or higher at 6 month post treatment is consider fatigue case	1)Disability is measured by social adjustment scale 2)Anxiety and depression are measured using the Hospital Anxiety and Depression Scale 3) Illness perception was measured on the how individual perceived their illness which scored of symptoms quality on causes, consequences, timeline and controllability 4) Attribution is measured by using 5 response options for the contribution of physical or psychological on their illness	Among fatigue case at 6 month post CBT. no significant association of demographics variables and outcome variable at 6 months Perception of the persistent of illness, belief that state of illness caused by physical, poor social adjustment were associated with fatigue
Prins, et al	Longitudinal study Outcome variables were measured at baseline, immediate follow up (8 month) and 14- month follow up	Fatigue severity: a subscale of checklist individual strength Functional impairment: the sickness impact profile Performance status: the Karnofsky performance status scale Quality of life: the visual analogue scale of the EuroQol Hours working in a job Self-rated improvement Physical activity: actometer (a motion-sensing device attached the ankle and worn for 12 days	Patients will be classified as showing clinically improvement of both of these criteria were met 1.The reliable change index of fatigue score (RCI > 1.64, p <0.05) 2.Patients' fatigue score move from the range of CFS to the range of healthy control (the cut-off score of 36 or lower for healthy control fatigue)	Psychological well-being: the symptom checklist 90 Self efficacy: self-efficacy scale Somatic attributions: The causal attribution list Focusing on bodily symptoms: the subscale somatization of the symptoms checklist 90	In CBT group, patients who have low sense of control and have passive activity pattern experienced less improvement of fatigue severity at immediate after treatment. In CBT group, patients who have high level of focusing on bodily symptoms showed little improve of the treatment outcomes.

(Table 4) describes the study design, outcome variables, clinically significant outcomes identification methods, predictors, and results. Four studies only investigated the immediate effectiveness of CBT by measuring pre- and post-treatment outcomes [38,39]. Seven studies evaluated both short- and long-term outcomes by evaluating participants for up to one year following the intervention [40]. Methods used to identify the success or responsiveness to the intervention were varied. Gersh et al. [41] identified criteria to classify participants into different groups based on the stage of change scores. Five studies classified participants into clinical improvement and nonclinical improvement groups using the cut-off score of outcome variables such as fatigue, function, and depression. One study used a sophisticated statistical method to analyze the pattern of change in outcomes over time and then used it as a criterion to group responders to the intervention Litt & Porto [42]. Ten other studies investigated the predictability of the predictors on either the outcome variables post-treatment.

Psychosocial predictors of CBT success

Most of the predictors in these 11 articles were psychosocial. The predictors included: states of change Gersh et al. [41,42] post-intervention psychiatric and somatic conditions Kempke

et al. Litt & Porto, Ljotsson, Andersson, et al., 2013; Zonneveld et al., self-efficacy Kempke et al., Schreurs et al., behaviors such as avoidance, worrying, fear, helplessness, and acceptance Samwel et al., skills such as problem solving, discussion, and verbal skills Siemonsma et al., therapeutic alliance Applebaum et al., and caregiver participation Dobkin et al. Only one study investigated the functional brain circuit in association with the response to the CBT intervention Falconer et al.

Discussion

All 11 studies determined that patients with physical illnesses benefit from CBT in both the short and long term. However, these results also found that not all participants receive the same level of benefit. Several factors may influence the effectiveness of a CBT intervention. First, although the 11 articles used the term CBT intervention, they differed in their intervention components, treatment modalities, and delivery methods. Although evidence suggests that the phone/internet-based CBT intervention and a face-to-face CBT intervention can have comparable effects, [43-47] the intervention components of CBT used in these studies varied (Table 3). The recommended intervention features for CBT as an adjunctive treatment in chronic physical illnesses include cognitive

intervention (e.g., goal setting, education, cognitive restructuring, identifying thoughts/beliefs) and behavior intervention (e.g., behavioral activation, grade exposure, behavioral experiments and pacing, stress reduction training, and relapse prevention; Halford & Brown, 2009). To ensure that patients use these techniques, homework or workbook assignments are needed. However, the CBT studies described in these articles do not include all of these features (Table 3). Second, social support may have had a major influence on the effectiveness of studies that compared group sessions to individual sessions. Third, the number of sessions and time spent for each session varied widely among the reviewed articles. Finally, 7 of the 11 studies used CBT as an adjunct treatment with other interventions. These differences of treatment modality and methods may have led to differences in outcomes.

Methods used to identify the success of CBT were inconsistent among the articles. These Two main methods were used by the reviewed articles include the use of criteria to classify the participants into treatment responders and non-responders and the use outcome variables at the treatment completion or the level of outcome change at completion from baseline. These inconsistencies can have a major impact on the identification of predictors and make it difficult to determine who will benefit from CBT intervention. The standard criteria or expected outcomes for the CBT intervention should be developed to identify the effectiveness.

Consistent with McCracken & Turk's (2002) review article on the predictors of outcomes of CBT in patients with chronic pain, we found that most of the significant predictors were psychosocial predictors. Unlike McCracken and Turk's review, however, our results showed that the patients' level of readiness to change, acceptance, rational problem-solving, and depression predicted improvement of the outcomes. These outcomes included a short-term effectiveness of the CBT intervention on pain, fatigue, and physical activity. Interestingly, these predictors often overlapped or were associated with each other. For example, the stage of readiness to change "contemplation," requires persons to think rationally about their situation and its solution, which can overlap with rational problem solving. The association among states of readiness to change, acceptance, and rational-problem solving with depression were reported in three of the studies [48-50]. These associations and overlapping outcome predictors could influence the results of a study. Each of these predictors was studied separately and no study investigated all of the predictors in one disease phenomenon.

To investigate the predictors that help identify responders to CBT intervention, seven studies identified predictors of both immediate and long-term effectiveness [51]. However, results among the studies were inconsistent, with different significant predictors for immediate and long-term outcomes. In patients with chronic fatigue syndrome, for example, physical activity and a feeling of control over symptoms predicted an immediate outcome improvement, but disability benefit was a predictor for outcomes at

6 months Schreurs et al. [52]. For patients with unexplained physical symptoms, the mental component was a significant outcome predictor of CBT at 3 months, but not significant for the immediate and long-term (1 year after the intervention) outcomes. Using a sophisticated statistical technique, Growth Mixture Modeling, Litt and Porto demonstrated that the change of catastrophizing, persons' negative evaluation and attention on a specific event, predicted the member of CBT responders' group. Two studies found consistent significant predictors of immediate and long-term outcomes. Dopkin et al. discovered that caregiver participation was the only significant predictor of the CBT responders at the end of the intervention and one month after. Applebaum et al. [53] determined that the therapeutic alliance significantly predicted immediate outcomes and outcomes one year after the intervention. In one study there was no significant outcome predictor for CBT in people with irritable bowel syndrome. A number of studies reported the biological predictors of the CBT outcomes in the psychological disorder [54-56]. Moreover, a recent study reported the expression change of genes associated with mood states in major depression patients Keri, Szabo, & Kelemen [57,58]. This information will not only help identify the biological mechanism associated with the CBT effectiveness but also identify person potentially will benefit from the intervention. Based on the articles reviewed, only one study investigated the association of physiological outcome predictors of CBT outcomes posttraumatic stress disorder in civilian trauma. The study result suggested the neural activation pattern of the left-lateralized front striatal inhibitory control associated with the response to CBT. This finding suggested future research should examine the biological pathways or mechanisms associated with CBT outcomes.

This rigorous, targeted review of 11 randomized control trials adds to the field of knowledge on CBT outcome predictors for physical illnesses. The results can be used as a guide for future researchers in investigating CBT intervention outcomes predictors in people with chronic physical illnesses, especially physiological and biological predictors. Furthermore, psychological predictors such as acceptance, therapeutic alliance, self-efficacy, physical ability, and depression should be tested for their predictability among people with different physical illnesses. Finally, a standardized guideline of CBT intervention with common components applicable to physical illnesses should be developed and tested.

Limitations

The sample size was small because our search was limited to randomized control trials that included an investigation of the outcome predictors. Therefore, several comparable but non-randomized trials were not reviewed. Additionally, the review only included physiological illnesses, so numbers of studies investigating biological predictors associated with CBT outcomes on depression and most other psychological disorders were not included.

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Conflict of interest

No conflict of interest.

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