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Review article

# A systematic review and meta-analysis of randomized controlled trials of cognitive behavior therapy for patients with diabetes and depression

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ABSTRACT

*Objective:* The aim of this meta-analysis was to systematically examine the efficacy of cognitive behavior therapy (CBT) for diabetic patients who have comorbid depression and to identify which aspects can be improved through intervention.
*Methods:* A systematic literature review was performed using multiple databases. The inclusion criteria included randomized controlled trials (RCTs) of CBT that were conducted with diabetes patients with clinically relevant depression. Review Manager version 5.3 was used to obtain pooled results.
*Results:* Ten RCTs, with a total sample size of 998 participants, met the inclusion criteria. Compared with control groups, the CBT groups had statistically significant, long-term improvements in depression (standardized mean differences [SMD] = −0.65, 95% confidence interval [CI] (−0.98 to −0.31), P = 0.0002), quality of life (SMD = 0.29, 95%CI (0.08 to 0.51), P = 0.007), fasting glucose (SMD = 0.21, 95%CI (0.04 to 0.37), P = 0.01) and anxiety (SMD = −0.49, 95%CI (−0.88 to −0.10), P = 0.01). No improvements were found in glycemic control or in diabetes-related distress.
*Conclusions:* The results of this meta-analysis showed that CBT can be effective in reducing depression symptoms and fasting glucose in diabetes patients with comorbid depression as well as in improving quality of life and anxiety in the long-term. The results showed that CBT can serve as a promising treatment alternative for diabetes patients with comorbid depression.



## 1. Introduction

Diabetes mellitus (DM) is one of the largest health emergencies of the 21st century. According to IDF Diabetes Atlas's global estimates, approximately 415 million people worldwide suffer from diabetes, and 46.5% of adults with diabetes are undiagnosed [1]. Depression is a common comorbidity in individuals with diabetes, compared to those without diabetes [2], affecting approximately 20% of all patients [3]. In addition, 25% of patients with type 2 diabetes mellitus (T2DM) in primary care settings experience depression every 2.5 years [4]. In two-thirds of all cases, depressive symptoms are generally recurrent or persistent over time so long as depression is present [5]. Substantial evidence demonstrates that depression in the context of diabetes is associated with a wide range of adverse consequences. Depression is associated with reduced adherence to the prescribed treatment regimen [6], lower quality of life, higher fasting glucose and HbA1c levels [7,8,9], and higher health expenditures [10]. Poor self-care behaviors are also observed in diabetes patients with depression, which may lead to poorer glycemic control [11]. Even worse, diabetes patients with comorbid depression tend to have complications of microvascular or macrovascular diseases [12,13]. The high prevalence of depression in diabetes patients and its potentially-negative outcomes promoted us to identify effective and enduring treatments aimed at improving patients' conditions.

In recent years, more studies have been focused on psychotherapy interventions, such as cognitive behavior therapy (CBT) [14], for diabetes patients with comorbid depression. CBT refers to a series of methods that are based on the fact that mental disorders and psychological distress are manifested by cognitive factors [15]. CBT is an organized and time-limited approach [16] that can get the patient and therapist actively involved [17]. The content of CBT may include psychoeducation, behavioral activation, cognitive restructuring, relapse prevention and homework assignments [18]. It reduces depressive symptoms by conferring the ability to identify and reappraise the negative thoughts that have an impact on feelings and behaviors [19].

Reviews and meta-analysis [15,20,21] have shown the efficacy of CBT for reducing symptoms in the treatment of depression. For diabetes, some meta-analyses [22,23] have demonstrated that compared to standard care, CBT contributes to improving glycemic control and psychological outcomes. Considering the presence of depression and the negative impact of depression on diabetes, it is necessary to explore

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whether CBT is also effective in improving psychological and glycemic outcomes in diabetes patients with comorbid depression.

Taking into account the interaction between depression and chronic disease, CBT is increasingly being adopted as a useful intervention in condition such as insomnia [24] and multiple sclerosis [25]. A systematic review and meta-analysis [26] summarized the effects of carious psychotherapy, including CBT, on diabetes patients with comorbid depression. Therefore, in order to explore whether CBT can eliminate the negative effects of depression on diabetes, this review focuses specifically on studies that performed CBT on comorbid depression in diabetes patients. There are several studies that focus on the effects of CBT on patients with diabetes and depression. However, results have demonstrated promise but have not yet reached a definite conclusion. The aim of the present review was to conduct a meta-analysis of all completed studies. The study design was comprised of randomized controlled trials (RCTs) and aimed to quantify the effect of CBT across a mixed sample of studies of patients with diabetes and depression.

## 2. Methods

### 2.1. Literature search

Review methods and reporting were performed according to the preferred reporting items in systematic review and meta-analyses (PRISMA) guidelines [27]. To identify potentially relevant studies, two reviewers performed a comprehensive literature search in electronic databases, including PubMed, EMBase, the Cochrane central register of randomized controlled trials (CENTRAL), PsycINFO, Web of Science electronic databases, Chinese National Knowledge Infrastructure (CNKI), Weipu (VIP) and Wanfang Data. The studies for which we searched were limited to a range between the database's inception and May 2016.

Search strategies were customized to each database. For PubMed, search strategies utilized a combination of keywords and medical subject headings (MESH) to represent the definitions of diabetes, depression, CBT, and randomized controlled trials (RCTs). Similar strategies were used to search other databases. Missing articles on outcomes of interest were obtained by contacting corresponding authors.

### 2.2. Criteria for inclusion

Studies were included in the meta-analysis if they met the following criteria: (1) study population (individuals diagnosed with diabetes mellitus and depression; for diabetes, patients clinically diagnosed with either Type 1 (T1DM) or Type 2 diabetes of ≥6 months duration; for depression, patients having either a psychiatric diagnosis or having met clinically criteria on various, validated depression scales); (2) intervention method (patients receiving cognitive behavior therapy or a therapy based on cognitive behavior therapy); (3) study design (RCTs); (4) study results (reported details of the effects of intervention, or detailed data that could be obtained by contacting the corresponding author). Exclusion criteria for the meta-analysis were as follows: (1) reviews of the literature; (2) single case reports; (3) studies unrelated to the theme; (4) reports of study protocols; (5) studies in which the intervention method was not CBT; (6) studies that included participants without diabetes or depression.

### 2.3. Study selection

After eliminating duplicate studies, two reviewers independently screened the titles and abstracts of all potentially relevant studies. Any disagreements were resolved through discussion with a third reviewer. Then, they reviewed the full text of studies deemed to be potentially relevant and further assessed them for inclusion.

### 2.4. Data extraction

Two reviewers independently conducted data extraction from each included study, and any inconsistencies were resolved through discussion with a third reviewer. A standardized extraction form was created to record study characteristics. Data were collected from each study, including author, year of publication, participant baseline characteristics (e.g., sample size, diagnosis, screening tool), intervention details (e.g., duration of intervention, form), control details, intervention length, and outcomes. The primary outcome of interest was depression; secondary outcomes were glycemic control, fasting glucose, diabetes-related distress, anxiety and quality of life.

### 2.5. Quality assessment

The Cochrane Collaboration 'risk of bias' tool for systematic reviews of interventions version (v. 5.1.0) was used to assess all included studies. Studies were assessed via six criteria: selection bias, performance bias, detection bias, attrition bias, reporting bias and other bias [28]. All included studies were independently assessed, and scores were achieved via consensus.

### 2.6. Statistical analysis

In original studies, outcomes of interest were assessed on the same scale and with the same units; mean differences (MD) were used for effect size calculation. Otherwise, standardized mean differences (SMD) were used. MDs and SMDs were interpreted per Cohen's definitions: 0.2 to 0.5 is defined as a small effect; 0.5 to 0.8 a moderate effect, and >0.8 a large effect [29]. All statistical calculations were performed using Revman 5.3 (The Nordic Cochrane Center, The Cochrane Collaboration). Tests of heterogeneity were used to decide which method would be used to get the pooled results. Results were considered heterogeneous if $I^2$ statistic is moderate (25–50%) or high (>50%) [30].

Subgroup analysis was undertaken to explore the length of CBT sessions that are most beneficial for patients, and whether patients with different types of diabetes benefit from CBT interventions. The intervention length will be synthesized in the meta-analysis as short-term (up to 6 months) and long-term (not <6 months).

## 3. Results

The selection process was illustrated in Fig. 1. First, 601 articles were retrieved from English databases and 103 from Chinese databases. Excluding 258 duplicate documents, 446 articles were included and screened for further assessment. It can be seen from Fig. 1 that 11 studies were included for meta-analysis. For one trial [31], the original data for meta-analysis could not be obtained. Ten RCTs [17,32–40] that fulfill all eligibility criteria for inclusion and meta-analysis were selected.

### 3.1. Study characteristics

Table 1 provides the characteristics of the included studies. Characteristics include sample characteristics, the number of CBT and control groups, screening tools, outcomes, and the length of the interventions. The data for the included RCTs were from 998 diabetes patients with clinically-relevant depression (496 in CBT groups, 502 in control groups). In ten studies, seven [17,33–37,39,40] reported outcomes for patients with type 2 diabetes mellitus (T2DM) and depression; the rest [32,38] reported outcomes for patients with diabetes mellitus (type 1 and type 2) and depression.

The CBT interventions were presented in a wide variety of formats. Seven studies [17,34–38,39] compared CBT to standard treatment; one [33] assessed motivational enhancement therapy, one [32] assessed diabetes-specific CBT, and one [40] assessed CBT plus citalopram hydrobromide. Because of the limited number of included studies, we