

## Review Article

# Management of depression in diabetes: A review of psycho-social interventions

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### ABSTRACT

Diabetes and depression are major public health problems associated with significant burden. They share many commonalities. Both the diseases have a very high prevalence, mortality, and disability. The current article reviews the available evidence on psycho-social interventions in management of depression in diabetes. A literature search was performed using MEDLINE, PubMed, PsycINFO, Embase, and Cochrane Review for English language articles published during 1960-2012. There is limited published literature on role of psycho-social interventions in management of depression among diabetics. The available evidence suggests that psycho-social interventions, particularly CBT, are effective in improving depression in patients with diabetes. However, these interventions are not consistently associated with improvement in markers of glycemia control (HbA1c levels).

**Key words:** Cognitive behavioral therapy, collaborative care, depression, diabetes, psycho-social interventions

## INTRODUCTION

Diabetes and depression are major public health problems associated with significant burden. They share many commonalities. Both diabetes and depression are considered as civilization disease, i.e., diseases, which increases with the development of the society, due to change in the environmental and social factors. Diabetes and depression also share a bi-directional causal association.<sup>[1]</sup>

Both the diseases have a very high prevalence, mortality, and disability. When present together, these conditions impact individuals' quality of life significantly. The prevalence of depression in diabetes ranges between 15-40% in multi-national studies.<sup>[2]</sup> Anderson *et al.*<sup>[3]</sup> in a meta-analysis of 42 studies found that the prevalence of major depression

in people with diabetes was 11% and the prevalence of clinically relevant depression was 31%. A study conducted by World Health Organization across 60 countries found health decrement to be greater with co-morbid depression and diabetes in comparison to either of them present alone.<sup>[4]</sup> Individuals with diabetes and depression had a 2-fold increase in health care costs compared with those who did not have depression.<sup>[5]</sup> Diabetics with co-morbid depression had a 36-38% increased risk for mortality over a 2-year period.<sup>[6]</sup>

Most cases of depression among diabetics get undetected due to commonality of the symptoms of the two conditions (fatigue, weight gain or weight loss, appetite changes, and sleep disturbances), associated stigma and negative perception of depression. The current article reviews the available evidence on psycho-social interventions in management of depression in diabetes.

## METHODOLOGY

A literature search was performed using MEDLINE, PubMed, PsycINFO, Embase, and Cochrane Review for English language articles published during 1960-2012. Key search terms were "diabetes," "depression," "cognitive

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behavioral therapy,” “treatment or management or intervention or trial,” “collaborative care,” “primary care,” “psycho-social,” and “psychotherapy.” Only publications focused on managing depression in diabetic individuals were included.

Psycho-social interventions were those in which the participants received some type of talk therapy designed to improve depressive symptoms without prescribing any medications. Only these interventions have been reviewed in this article.

Four published and completed randomized controlled trial (RCT) of psycho-social therapies for depression in diabetes,<sup>[7-10]</sup> two uncontrolled pilot studies of group cognitive behavioral therapy (CBT),<sup>[11,12]</sup> and two RCTs of CBT intervention designs but unpublished results were retrieved.<sup>[13,14]</sup> Additionally, there were five systemic reviews/meta analyses for assessing effectiveness of psycho-social treatment of depression in diabetics.<sup>[15-19]</sup> The findings from these studies have been presented in the subsequent sections.

## RCTs

There were two RCTs on CBT, one using a web-based model.<sup>[7,10]</sup> Among the other 2 RCTs, minimal psychological intervention (MPI) was used in one study while other used supportive therapy (SP).<sup>[8,9]</sup>

Lustman *et al.*<sup>[7]</sup> conducted the first RCT of psycho-social intervention for treating depression in patients with diabetes enrolling 51 participants of age 21-70 years. All the participants had type 2 diabetes. Depressive disorder was diagnosed by diagnostic interview schedule, and severity was assessed by beck depression inventory (BDI). The participants were randomized to either intervention group receiving individual CBT for 10 weeks ( $n = 20$ ) or control group receiving no specific anti-depressant treatment ( $n = 22$ ). All participants received a one-hour diabetes education program with a trained diabetes educator every other week. Glycemic control was assessed using glycosylated hemoglobin levels. Assessments were made immediately after treatment and 6 months later. An intent-to-treat (ITT) analysis revealed that a greater percentage of patients achieved remission of depression (BDI score  $\leq 9$ ) and clinically significant improvement (CSI) (defined as  $\geq 50\%$  reduction in BDI score) in the experimental group than in the control group. At post-treatment, 85% of patients in the CBT group achieved remission compared with 27.3% of controls [difference: 57.7 percentage points, 95%

CI: 33-82 percentage points,  $P < 0.001$ ], and 66.6% of patients in the CBT group achieved CSI compared with 29.6% of controls. At 6-month follow-up, 70% of patients in the CBT group remained in remission compared with 33.3% of controls [Difference: 36.7 percentage points, 95% CI: 9-65 percentage points,  $P = 0.03$ ] while 58.3% of the CBT group reported CSI compared to only 29.6% of the controls ( $P = 0.01$ ). HbA1c levels were similar between the two groups at pre-and post-treatment assessments, but at 6-month follow-up, 9.5% patients in the CBT group had significantly lower levels compared to 10.9% patients of control group ( $P = 0.03$ ). No statistically significant difference was observed among the groups for self-monitoring of blood glucose levels.

The second published RCT of psycho-social intervention for treating depression in diabetes was a pilot study and the only study including SP as intervention.<sup>[8]</sup> It enrolled 30 in-patients with diabetic foot syndrome, of which 80% had type 1 diabetes. The subjects had a mean age of  $60.5 \pm 10.9$  years. Depression was rated using hospital anxiety and depression scale (HADS). Outcome measure for diabetic status was problem areas in diabetes scale (PAID). Participants were randomized to either an intervention group ( $n = 15$ ) with weekly (average five sessions) supportive psychotherapy treatment or a control group ( $n = 15$ ) receiving only treatment as usual (TAU). There was significant improvement in depressive scale of HADS in intervention group as compared to the control group [-1.6 versus 0.3,  $P = 0.02$ ] along with 75% improvement in the diabetic foot syndrome. The study lacked follow-up, and the assessments did not include treatment conditions or HbA1c levels.

The depression in elderly with long-term afflictions (DELTA) study was a RCT that aimed to assess the effectiveness of a nurse-led MPI in elderly individuals with diabetes and depression. The DELTA study has several publications on multiple stages.<sup>[9,20,21]</sup> This RCT included 361 primary care elderly patients with type 2 diabetes or chronic obstructive pulmonary disease. Depression was assessed by the mini international neuropsychiatric interview (MINI). Patients were randomized to either MPI intervention receiving group or control group receiving TAU. The home visit MPI was provided by 4 nurses consisting of 1-hour session over 3-month period (average 4 sessions). Depression score as assessed on beck depression inventory (BDI) was the main outcome measure with follow-up at 9 months. Diabetes-related assessments were made using diabetes symptom checklist-revised (DSC-R) and PAID scales. The study concluded that MPI significantly reduced depressive symptoms with a 50% or more reduction in BDI relative to baseline values.

Overall, there was a statistically significant improvement only in higher educated individuals for both emotional distress and symptom distress at 9 months (DSC-R total score at 9 months  $P = 0.001$ ; PAID, 9 months  $P = 0.03$ ) in intervention group as compared to controls. Moreover, shorter diabetes duration and male gender were significantly associated with emotional distress ( $P = 0.04$ ) and symptom distress ( $P = 0.01$ ), respectively. Also, there was a significant reduction in HbA1c levels in the intervention group ( $P = 0.02$ ).

Another study in Netherlands comprised of a RCT assessing effectiveness of a web-based CBT.<sup>[10]</sup> The study included type 1 ( $n = 114$ ) or 2 diabetic ( $n = 141$ ) subjects of age group 18 and over. Depression was assessed by center for epidemiological studies depression scale (CES-D) and confirmed by the composite international diagnostic interview. Participants were allocated to either a self-help intervention group receiving an 8-week web-based CBT ( $n = 125$ ) or a waitlist control group ( $n = 130$ ). The depression outcome was assessed using CES-D, and the diabetic status was assessed using HbA1c levels and diabetes-specific emotional distress using PAID scale. The assessments were made at baseline, after treatment, and at 1-month follow-up. ITT and per-protocol analysis comparing experimental group and controls revealed that Web-based CBT was effective in reducing CES-D scores [ $d = 0.29$ ,  $P = 0.04$  and  $d = 0.70$ ,  $P < 0.001$ , respectively] over follow-up period. There was a significant improvement on PAID ( $P < 0.001$ ), but no significant treatment effect was found for HbA1c levels ( $P > 0.05$ ) on comparing the two groups.

## OPEN LABEL STUDIES

There were two uncontrolled studies, one each in children/adolescents<sup>[11]</sup> and adults.<sup>[12]</sup>

The study by Rossello *et al.*<sup>[11]</sup> was an open-label pilot study. It enrolled 19 adolescents (age 12-16 years) having type 1 diabetes and depressive symptoms as assessed by the children's depression inventory (CDI). Participants were given 12 week group CBT consisting of 2-hour sessions including psycho-education about depression and diabetes, cognitive restructuring, activity scheduling, and communication skills training by trained psychologists. Out of 19, eleven completed the study (male-2, females-9). Assessments were made using CDI, diabetic management information sheet, glycemic control measure, beck anxiety inventory, hopelessness scale for children, Piers-Harris children's self concept scale, summary of self-care activities,

and self-efficacy for diabetes scale. There was significant improvement in depressive symptoms (Pre-CDI = 19.4 and post-CDI = 9.9,  $P < 0.05$ ). Additionally, improvement was observed for self-concept, diabetes self-efficacy, anxiety, and hopelessness. However, glycemic control remained unchanged.

The other open-label study of 12-month duration enrolled 90 (65 completed the study) adults (age 18 and above) with type 1 and 2 diabetes and depressive symptoms (assessed by a BDI score of 10 or greater).<sup>[12]</sup> Group CBT was provided for 12-weeks (16 90-minute sessions), which included cognitive restructuring, problem-solving, communication, and goal-setting skills, applied especially to diabetes-related thoughts and activities. BDI, HAM-D, HbA1c, and fasting glucose levels were assessed at baseline. Subsequently, BDI/HAM-D was administered bi-weekly, and other assessments were made at 3, 6, 9, and 12 months. Analysis was done using linear mixed-model analysis. A significant reduction in depressive symptoms from baseline was observed at 3 months on HAM-D ( $P < 0.001$ ) and on BDI from baseline over the 12-month period ( $P < 0.001$ ). No significant changes were seen in HbA1c levels.

## PUBLISHED BUT INCOMPLETE STUDIES

There were 2 RCTs of ongoing studies assessing the change in outcome measure by treating depression in diabetics.<sup>[13,14]</sup> The studies have published the methodology but were incomplete in reference to results and conclusion.

Minor depression and diabetes (MIND-DIA) trial (a multicenter, open, observer-blinded, parallel group (3 groups) RCT) was designed to assess effectiveness of CBT for treating minor or mild-major depression in elderly patients (aged 65-85 years) with type 2 diabetes in comparison to TAU and a guided self-help group intervention with a follow-up of 15 months.<sup>[13]</sup> Outcome variables for this study included improvement of health-related quality of life, reduction in depressive symptoms, improvement of glycemic control and mortality. Cost-effective analysis was planned for health sector costs, patient costs and societal productivity/time costs, person-years free of moderate/severe major depression, and cumulative costs of each intervention.

Another reported protocol of RCT on adult (aged 18-65 yrs) type 2 diabetic populations with depressive symptoms (assessed through mail survey) aimed at evaluating the effects of psycho-education and physical exercise for sub-syndromal depression associated with diabetes.<sup>[14]</sup> Participants were randomized to any of

the three arms receiving psycho-education, physical exercise or TAU comprising of 59 patients in each group. Depressive symptoms, diabetes distress, health-related quality of life, and diabetes self-care activities were planned to be assessed at baseline, at 6 weeks, 6 months, and 12 months.

## META-ANALYSIS AND SYSTEMATIC REVIEWS

There have been 5 systemic reviews for assessing effectiveness of psycho-social treatment of depression in diabetics.<sup>[15-19]</sup>

The first systemic review searched studies published on non-pharmacological treatments for treating depression in individuals with diabetes mellitus in English language in Cochrane library, Pubmed, MEDLINE, EBM review, ProQuest Medical Bundle, and SCOPUS databases.<sup>[15]</sup> It included 3 RCTs (involving 788 subjects) published from 1996-2007. One of these studies assessed combined CBT and self-management education,<sup>[7]</sup> and the other two assessed collaborative care models (involving a combination of psychological and pharmacological interventions).<sup>[22,23]</sup> The study concluded that although non-pharmacological treatments reduce depressive symptoms in diabetic patients, CBT on itself had no influence on glycemic control.

Petrak and Herpertz<sup>[16]</sup> in another systemic review searched for all published RCTs on the treatment of depression in patients with diabetes including languages other than English and ongoing research. The analysis included 3 studies<sup>[7,8,24]</sup> with stand alone psychotherapeutic interventions and 4 with a combination of psychological and medical treatments.<sup>[22,23,25,26]</sup> They reported the pooled estimate of effect of psychotherapeutic trials to be -0.645 (95% CI -0.874; -0.415) for depression outcomes and -0.477 (95% CI -0.715; -0.239) for glycemic control. The review concluded that although the generalizability was restricted by methodological limitations, the best results were with non-pharmacological interventions for medical and psychological outcomes with evidence for successful treatment of depression but not of glycemic control.

A meta-analysis by van der Feltz-Cornelis<sup>[17]</sup> synthesized data of all published RCTs in English language on care of depression in persons with type 1 and type 2 diabetes mellitus using psychotherapy, pharmacotherapy, or collaborative care. The search engines used included PubMed, Psycinfo, Embase, and Cochrane library. It included a total of 14 RCTs involving 1724 patients. It included 5 trials<sup>[7,8,27-29]</sup> with only psycho-social interventions and 3 trials of combined intervention.<sup>[22,23,30]</sup> Overall, various depression treatments were effective in terms of

reduction of depressive symptoms [Cohen d -0.512; 95% CI -0.633 to -0.390]. Highest effect sizes were observed for psychological treatments (Cohen d = -0.58, 95% CI, -0.77 to -0.39).

A recent study reviewed 41 pharmacological and non-pharmacological interventions for depression in people with diabetes. The literature search was performed using Ovid, MEDLINE, PubMed, PsycINFO, Embase, and the Allied and Complimentary Health Database for English language articles published during 1960-2008.<sup>[19]</sup> The authors identified 7 RCTs ( $n = 710$ ), 5 open-label trials ( $n = 84$ ), 4 case studies and 2 case series ( $n = 28$ ) of pharmacological treatment (different classes of anti-depressants). Among non-pharmacological treatments, only 2 studies on the use of CBT were included.<sup>[7,12]</sup> The non-pharmacological treatments, especially collaborative-care models, were reported to be effective in the management of depression in diabetic persons.

A recent systematic review by Markowitz *et al.*<sup>[18]</sup> searched the literature in Cochrane Review, PsychINFO, and Pubmed from 1995-2008. It identified 17 studies that investigated intervention intended to treat depressive individuals of both gender and all ages with type 1 or type 2 diabetes. Only English-language journals were included in search. The search generated 1 published and completed RCT of CBT,<sup>[7]</sup> 1 RCT of SP,<sup>[20]</sup> 2 RCTs of CBT interventions with methods but unpublished results,<sup>[8,10]</sup> and 2 uncontrolled pilot studies of CBT.<sup>[11,12]</sup> Three published collaborative care intervention studies were also included. Overall, the authors concluded that psycho-social interventions, particularly CBT, pharmacological management, and collaborative care were effective in the treatment of depression in patients with diabetes while the evidence for the efficacy of these interventions in improving glycemia control was mixed.

## CONCLUSIONS

There is limited published literature on role of psycho-social interventions in management of depression among diabetics. There are some RCTs that have attempted to systematically assess the efficacy of these interventions. The interventions that have been studied in at least one RCT include CBT, web-based CBT, group CBT, SP, minimal psychological intervention (MPI), combined CBT, and self-management education. Additionally, psycho-social interventions have also been studied as a part of collaborative care model in combination with pharmacotherapy. Most of the studies have focused on adult populations. The evidence is limited for children/adolescents and elderly age groups. The available studies have used various measures

to identify and measure depression. The available evidence suggests that psycho-social interventions, particularly CBT, are effective in improving depression in patients with diabetes. Additionally, these have been found to be effective even when used in combination with pharmacotherapy. However, these interventions are not consistently associated with improvement in markers of glycemia control (HbA1c levels).

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How to cite this article: ???.

Source of Support: Nil. Conflict of Interest: None declared.