Neuropsychiatric Disease and Treatment

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ORIGINAL RESEARCH

Psychosocial intervention for patients with type 2 diabetes mellitus and comorbid depression: a meta-analysis of randomized controlled trials

This article was published in the following Dove Press journal:
Neuropsychiatric Disease and Treatment
24 October 2017
Number of times this article has been viewed

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Background: The efficacy of psychosocial intervention has been proven in treatment of diabetic patients with depression in some studies. This meta-analysis was conducted to explore the efficacy as well as additional effects of this method during diabetic management in patients with type 2 diabetes mellitus (T2DM) and comorbid depression.

Methods: Electronic databases were searched from March 2000 to March 2017 for randomized controlled trials (RCTs) studying the effects of psychosocial intervention on T2DM patients with depression. There was no language limitation. Outcome measurements were symptoms of depression and anxiety, as well as glycemic control. A random effects model was conducted.

Results: In total, 31 RCTs composed of 2,616 patients were eligible for this analysis. The psychosocial intervention was effective for depression symptoms with pooled standardized mean difference (SMD) of −1.50 (95% CI =−1.83, −1.18) and anxiety symptoms with SMD of −1.18 (95% CI =−1.50, −0.85). Meanwhile, the additional effects indicated a better improvement of glycemic control, including the fasting blood-glucose with SMD of −0.93 (95% CI =−1.15, −0.71), 2-hour postprandial plasma glucose with SMD of −0.84 (95% CI =−1.13, −0.56), and hemoglobin A1c with SMD of −0.81 (95% CI =−1.10, −0.53).

Conclusion: These results demonstrate that the psychosocial intervention is very effective in treating T2DM patients with depression.

Keywords: psychosocial intervention, type 2 diabetes mellitus, depression, meta-analysis

Introduction

In 2015 alone, diabetes mellitus has claimed over 1.5 million lives worldwide. As a highly prevalent metabolic disease, diabetes mellitus has been the sixth leading cause of death in the world, especially in developing countries.[1] Among these diabetic patients, approximately 90% have type 2 diabetes mellitus (T2DM).[2] Treating a patient with T2DM entails a complicated and comprehensive strategy. This includes strict diet control, moderate physical exercise, hypoglycemic drug intake, blood glucose monitoring, and treatment education.[3] Managing both diabetes and the economic burden that follows could lead patients to anxiety, helplessness, and depression.[4] Therefore, managing diabetes also involves patients' emotional health.[5]

Depression is a common comorbidity of both type 1 diabetes and T2DM. In the United States, 28% of women and 18% of men with diabetes suffered from symptoms of depression.[6] Compared with non-DM patients, the incidence of depression is two times higher in patients with T2DM.[7] Poor mental health and harmful medical outcomes are prevalent in patients with diabetes and comorbid depression. Previous studies reported that diabetes patients with depression had lower quality of life, worse glycemic

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Dovepress
http://dx.doi.org/10.2147/NDT.S116465

control, poor adherence to self-care practices, and disease-related complications.[8–11] Moreover, depression due to diabetes is often associated with mortality.[12] Therefore, it is important to treat depression during the diabetes management.

Currently, it is still very difficult to treat and/or prevent T2DM, even though we and other researchers have conducted much research.[13–19] Pharmacotherapy is still the first-line treatment for depression, but a significant percentage of patients have little to no response to these treatments. Moreover, the side effects of antidepressants are likely to cause poor adherence for T2DM patients with depression.[20] Researchers found that patients had a preference toward psychosocial interventions.[21] A previous systematic review revealed that psychosocial intervention might be effective for diabetes patients with depression.[22] However, consistent evidence is still lacking on the effect of psychosocial intervention in treating depression in T2DM patients. Additionally, considering the poor diabetes outcomes caused by comorbid depression, it is also ideal to explore the efficacy of this method with regard to glycemic control. Therefore, this meta-analysis was conducted to investigate the effect of psychosocial intervention on patients with T2DM and comorbid depression.

Methods

Literature research

Firstly, potential studies were searched for in the international databases (PubMed, CCTR, Cochrane Library, Web of Science, MEDLINE, PsycINFO, and Embase), two Chinese databases (CNKI and CBM-disc), and relevant websites from March 2000 to March 2017. The used search terms included "diabetes", "mental intervention", "mellitus", "depress*", "psychological", "mental health", "psychosocial state", "psychosocial intervention", "interpersonal therapy", "problem solving therapy", "behavioral therapy", and "cognitive behavioral therapy". To mitigate language bias, no language restriction was used. Conference summaries and the reference documents of the included studies were also researched.

Inclusion/exclusion criteria

The studies which met the following inclusion criteria were selected for the subsequent analysis: i) patients over 18 years with T2DM and comorbid depression; ii) randomized controlled trials (RCTs) with patients randomly assigned to the control and intervention groups; iii) all patients received conventional treatment for T2DM, but patients in the intervention group also received psychosocial intervention; iv) the depressive symptoms were assessed using the Montgomery–Åsberg Depression Rating Scale (MADRS), Self-Rating Depression Scale (SDS), or Hamilton Depression Rating Scale (HDRS); v) acute treatment phase (≤16 weeks). Meanwhile, studies that met any of the following criteria were excluded: i) case reports, retrospective studies, duplicate studies, and reviews; ii) patients with psychiatric diseases, other mental illnesses, other forms of diabetes besides type 2, malignant tumors, and severe physical illness; iii) patients with "narrow" or secondary depression diagnoses, such as post-partum depression, subthreshold depression, and vascular depression. All patients provided written informed consent, and all clinical trials were reviewed and approved by the Ethical Committee.

Outcome indexes

The changes in depressive symptoms were assessed and quantified by the established depression questionnaires (HDRS or SDS) and were used as the primary outcome. The anxiety symptoms were assessed by self-rating anxiety scale (SAS) or Hamilton Anxiety Scale (HAMA) and were used as the secondary outcome. The data about glycemic control, such as fasting plasma-glucose (FPG), 2-hour postprandial plasma glucose (2hPPG), and hemoglobin A1c (HbA1c), were also measured at baseline and post-intervention. These data were also used as the secondary outcome. The time-point that was given in the original study was preferred as the study endpoint.

Data extraction

Two reviewers independently reviewed the potential studies according to the aforementioned inclusion/exclusion criteria, and identified the included studies. Relevant data from these included studies were extracted and saved in the Cochrane data extraction template. The data extraction procedure was also independently completed by two reviewers. Any disagreement during the reviewing and extracting process was resolved by group discussion. The following data were retrieved from the included studies: i) demographic data, including age, sex ratio, disease duration, education level; ii) data about depressive and anxiety symptoms, including HDRS, SDS, HAMA, and SAS score at baseline and post-intervention; iii) data about glycemic control at baseline and post-intervention; iv) method of psychosocial intervention and conventional treatment.

Quality assessment

Two reviewers independently assessed the bias risk in the individual studies according to the Cochrane Handbook

for Systematic Reviews of Intervention. The bias risk was assessed using the following six items: i) randomization used; ii) allocation concealment; iii) outcome blinding assessment; iv) incomplete outcome data addressed; v) free of selective reporting; vi) baseline matched.

Statistical analysis

RevMan 5.0 software was used to carry out the meta-analysis. The standardized mean difference (SMD) was calculated for the randomized studies. For SMD, an effect size of 0.2–0.5 was considered small, 0.5–0.8 was considered moderate, and above 0.8 was considered large.[2] The effect size and the corresponding 95% CIs were calculated for the primary and secondary outcomes. Mantel-Haenszel random-effects model was selected, as it was assumed that the included RCTs probably had the diverse true treatment effects.[23] Moreover, this model was more appropriate when heterogeneity existed. The heterogeneity was assessed by the I^2 (>50%) and Q test ($p<0.10$).[24] Subgroup analysis or sensitivity analysis were performed when appropriate. This meta-analysis was conducted according to the predetermined protocol and the recommendations of Sacks et al.[25]

Results

Search results

The search was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. First, 338 potentially relevant studies were obtained. Then, 307 studies were excluded due to the following reasons: i) duplicates (n=42); ii) not relevant to T2DM and comorbid depression (n=191); iii) not about psychosocial intervention (n=64); and iv) compared the psychosocial intervention with other antidepressants (n=10). Finally, 31 RCTs were included to perform meta-analysis (Figure 1).[26–56]

Study characteristics

There were 2,616 patients with T2DM and comorbid depression in these included studies. The average age of patients in the intervention group was approximately 43 years. Five of these studies were written in English, and 26 studies were written in Chinese. The treatment time ranged from 2 to 16 weeks. The average age of patients in most studies was between 50 and 70 years old. There were 28 studies that assessed the depressive symptoms of patients at the end of trial. The detailed information was described in Tables 1 and 2.

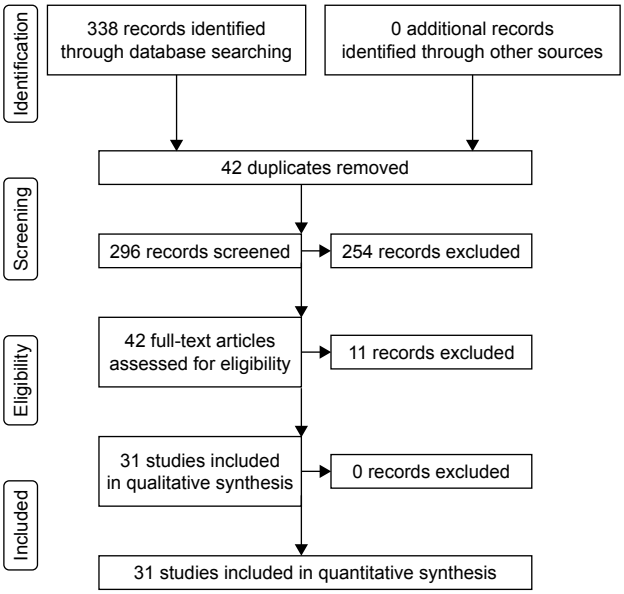

Figure 1 Workflow of literature search.

Study quality

Although all of the included studies had conducted randomization, the allocation concealment was only mentioned in 32.2% (10/31) of studies. Because the blinding of psychological intervention is almost impossible in a clinical trial, all of the included clinical studies were open-label. Studies from which patients withdrew reported the incomplete data, and performed intention-to-treat analysis. Similar baseline characteristics were reported in all studies. The act of randomization could lower the selection bias.[2] Thus, these included studies might be free of selection bias.

Depressive symptoms

In total, 28 studies assessed the depressive symptoms of 2,476 T2DM patients. The SMD was calculated for these studies: one study had no effect of –0.02, four studies had a small effect of –0.31, –0.41, –0.45, and –0.49, three studies had a moderate effect of –0.61, –0.70, and –0.78, and 20 studies had a large effect of above –0.80. Finally, the pooled SMD was –1.50 (95% CI =–1.83, –1.18) for the random-effects model (Figure 2), which indicated a large effect of psychosocial intervention on the depressive symptoms of T2DM patients. Meanwhile, the results of meta-regression analysis showed that the efficacy had a negligible relationship with the baseline depression scores. Among these studies, 13 studies used the HDRS to assess the depressive symptoms of 1,226 T2DM patients, and 13 studies used the SDS to assess the depressive symptoms of 1,189 T2DM patients. Therefore, subgroup analysis was conducted according to the different

Table 1 Clinical characteristics of the included randomized controlled trials

Study	Control			Intervention			Criteria	Time	Conventional treatment	Psychological intervention
	Age (y)	M/F	Duration (y)	Age (y)	M/F	Duration (y)				
Du et al,[26] 2005	53.5 (10.2)	15/15	5.5 (3.2)	52.5 (11.2)	14/16	5.2 (3.8)	SAS ≥50, SDS ≥50	4 w	Diet, exercise, drugs	Group psychotherapy and individual psychotherapy
Qiu et al,[27] 2005	71.6 (3.9)	12/16	NA	71.2 (4.3)	10/18	NA	SDS ≥50	8 w	Diet, exercise, insulin therapy	NA
Ma et al,[28] 2006	44.7 (11.4)	18/15	4.5 (3.6)	44.1 (10.9)	20/14	4.7 (3.3)	SAS ≥50, SDS ≥50	6 w	Gliclazide, 80 mg, three times/day	Group psychotherapy and individual psychotherapy
Sun et al,[29] 2006	52.7 (8.5)	8/12	7.4 (5.5)	54.1 (9.5)	11/10	6.7 (5.0)	HDRS-17>17	8 w	Diet, drugs	Cognitive therapy and supportive diabetes education
Lei et al,[30] 2008	57.3 (10.6)	28/32	NA	57.3 (10.6)	28/32	NA	SDS ≥50	8 w	Diet, exercise, insulin therapy	Health education and psychological counseling
Wu et al,[31] 2008	52.4 (11.2)	104/96	6.3 (4.2)	52.4 (11.2)	104/96	6.3 (4.2)	SDS ≥50	4 w	Drugs	Humanistic therapy, cognitive and behavior intervention
Jiang,[33] 2011	50.7 (11.4)	26/28	4.5 (3.6)	51.1 (10.9)	25/29	4.7 (3.3)	HDRS-24>17	6 w	NA	Relaxation therapy, cognitive and behavior intervention
Lu et al,[34] 2011	56 (5)	36/24	NA	56 (5)	36/24	NA	HDRS-24>17	8 w	Hypoglycemic agent	Health education and psychological counseling
Wang et al,[35] 2011	56.8 (3.5)	21/15	5.2 (1.4)	56.5 (4.0)	20/16	5.0 (1.5)	SAS ≥50, SDS ≥50	8 w	NA	Health education and psychological counseling
Xu et al,[36] 2011	64.0 (7.8)	58/78	NA	64.0 (7.8)	58/78	NA	SAS ≥50, SDS ≥50	5 w	Insulin therapy	Group psychotherapy
Chen et al,[38] 2012	57.1 (5.9)	30/37	9.8 (3.2)	58.1 (6.2)	21/31	9.3 (2.9)	HDRS-24>20	4 w	NA	Cognitive restructuring and psychological counseling
Qin et al,[40] 2012	NA	19/11	NA	NA	35/25	NA	SDS >40, HDRS >17	12 w	Metformin, insulin therapy	Health education and psychological counseling
Gao et al,[41] 2013	46.1 (18.2)	NA	9.3 (4.2)	46.1 (18.2)	NA	9.3 (4.2)	SAS ≥40, SDS ≥50	2 w	Hypoglycemic agent	Group psychotherapy
Gao et al,[42] 2013	64.9 (6.8)	19/16	8.4 (2.1)	65.4 (7.1)	20/17	8.7 (2.3)	HDRS ≥18, HAMA ≥14	8 w	Hypoglycemic agent or insulin	Cognitive and behavior intervention
Lan et al,[44] 2013	60–83	23/19	NA	60–86	24/18	NA	SAS ≥50, SDS ≥50	12 w	NA	Group psychotherapy and individual psychotherapy
Li,[45] 2013	60–83	23/12	NA	60–82	24/11	NA	SAS ≥50, SDS ≥50	8 w	NA	Cognitive and behavior intervention
Li et al,[46] 2013	35.4 (4.5)	24/17	NA	35.2 (4.8)	22/19	NA	HDRS ≥20	6 w	Hypoglycemic agent	Group psychotherapy, cognitive and behavior intervention
Sang,[47] 2013	62.9 (8.1)	8/12	NA	61.3 (7.1)	10/10	NA	SDS ≥50	4 w	Hypoglycemic agent	Health education and group psychotherapy
Wang,[49] 2013	65.8 (8.3)	17/13	10.2 (3.5)	66.2 (7.5)	16/14	9.8 (4.3)	HDRS >8	6 w	Drugs	Psychological counseling and behavior intervention
Zhang et al,[32] 2013	51.3 (4.9)	17/19	NA	51.3 (4.9)	17/19	NA	SAS ≥40, SDS ≥40	12 w	Diet, exercise, hypoglycemic agent	NA
Li and Hu,[53] 2014	61.2 (12.1)	75/45	5.5 (3.9)	62.2 (11.3)	80/40	5.6 (4.5)	HDRS ≥18	8 w	NA	Psychological support, cognitive and behavior intervention
Li et al,[54] 2014	31–88	NA	6.8 (3.9)	31–88	NA	6.8 (3.9)	SAS ≥50, SDS ≥50	6 w	NA	Group psychotherapy and individual psychotherapy
Wang et al,[48] 2009	52.6 (6.9)	32/28	NA	53.5 (6.5)	31/29	NA	HDRS ≥20, HAMA ≥14	2 w	Insulin therapy	Health education and psychological counseling
Zhang et al,[50] 2013	51.8 (3.7)	19/12	3.2 (0.7)	52.4 (3.2)	16/15	3.3 (0.6)	HDRS ≥18	12 w	NA	Group psychotherapy and individual psychotherapy
Du,[39] 2012	59.8 (6.6)	30/32	NA	59.8 (6.6)	30/32	NA	HDRS ≥18	9 w	Drugs	Group psychotherapy
Hu,[43] 2013	60.9 (7.9)	30/30	8.9 (1.8)	62.7 (8.7)	33/27	9.4 (2.1)	HDRS ≥18	8 w	Drugs	Group psychotherapy
Penckofer et al,[37] 2012	54.0 (8.4)	0/36	10.0 (6.5)	54.8 (8.8)	0/38	10.5 (8.2)	CES-D ≥16	12 w	NA	SWEEP Program
Sharif et al,[52] 2014	50–60	3/26	NA	50–60	8/21	NA	DSM-IV criteria	8 w	Anti-diabetic drugs	Group psychotherapy
Zheng et al,[55] 2015	61 (7)	27/30	8.1 (4.5)	62 (6)	27/28	8.2 (3.8)	DSM-IV criteria	12 w	Diet, exercise, drugs	24 Move Shadow Boxing and psychosomatic relaxation
Huang et al,[56] 2016	57.8 (10.4)	13/17	3.8 (1.5)	55.1 (10.4)	16/15	3.7 (1.8)	CES-D ≥16	12 w	Diet, exercise, drugs	MET and cognitive behavioral therapy
Safren et al,[51] 2014	58.3 (7.4)	22/20	NA	55.4 (8.7)	22/23	NA	DSM-IV criteria	16 w	Hypoglycemic agent, insulin	Cognitive behavioral therapy

Abbreviations: M, male; F, female; NA, not available; y, year; SDS, Self-Rating Depression Scale; SAS, Self-Rating Anxiety Scale; HDRS, Hamilton Depression Rating Scale; HAMA, Hamilton Anxiety Scale; CES-D, epidemiologic studies depression scale; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; w, week; SWEEP, Study of Women's Emotions and Evaluation of a Psychoeducational; MET, motivation enhancement therapy.

Table 2 Depressive symptoms and blood glucose of the patients at baseline

Study	Control				Intervention			
	Depression, scores (SD)	FPG, mmol/L (SD)	2hPPG, mmol/L (SD)	HbA1c (%)	Depression, scores (SD)	FPG, mmol/L (SD)	2hPPG, mmol/L (SD)	HbA1c (%)
Du et al,[26] 2005	55.9 (10.2) SDS	11.3 (3.6)	17.9 (5.1)	9.2 (1.8)	55.7 (9.9) SDS	11.1 (3.4)	18.3 (4.1)	9.3 (1.7)
Qiu et al,[27] 2005	NA	8.7 (1.3)	12.6 (0.9)	8.5 (2.4)	NA	8.7 (1.4)	12.7 (0.9)	8.5 (2.3)
Ma et al,[28] 2006	53.7 (11.0) SDS	11.3 (3.3)	17.8 (5.2)	9.2 (1.7)	53.7 (10.0) SDS	11.2 (3.2)	18.5 (4.1)	9.1 (1.6)
Sun et al,[29] 2006	25.2 (5.9) HDRS	NA	NA	8.5 (1.3)	25.1 (6.2) HDRS	NA	NA	8.4 (1.3)
Lei et al,[30] 2008	56.7 (10.9) SDS	8.7 (2.6)	13.7 (4.4)	9.6 (1.8)	56.9 (9.9) SDS	8.6 (2.2)	13.6 (4.5)	9.7 (1.6)
Wu et al,[31] 2008	57.2 (10.3) SDS	12.1 (2.3)	17.2 (6.5)	NA	56.6 (10.3) SDS	11.4 (4.3)	18.7 (4.5)	NA
Jiang,[33] 2011	33.5 (4.7) HDRS	12.1 (3.5)	17.9 (6.2)	9.2 (1.7)	31.2 (7.8) HDRS	11.2 (3.7)	18.3 (5.7)	9.1 (1.6)
Lu et al,[34] 2011	21.8 (3.0) HDRS	9.0 (2.7)	NA	7.9 (3.8)	22.4 (2.8) HDRS	10.0 (2.2)	NA	8.5 (3.2)
Wang et al,[35] 2011	62.8 (4.2) SDS	NA	NA	NA	62.5 (3.9) SDS	NA	NA	NA
Xu et al,[36] 2011	56.0 (10.4) SDS	11.6 (1.7)	15.9 (2.7)	9.2 (1.6)	56.1 (10.2) SDS	11.3 (1.8)	15.5 (2.5)	8.9 (1.7)
Chen et al,[38] 2012	32.9 (9.1) HDRS	7.9 (2.4)	NA	NA	34.2 (8.4) HDRS	8.2 (3.7)	NA	NA
Qin et al,[40] 2012	49 (8) SDS 21 (7) HDRS	NA	NA	NA	48 (7) SDS 30 (7) HDRS	NA	NA	NA
Gao et al,[41] 2013	57.3 (9.2) SDS	13.1 (2.5)	18.3 (5.2)	NA	57.6 (9.1) SDS	11.6 (3.2)	18.2 (4.6)	NA
Gao et al,[42] 2013	23.2 (4.3) HDRS	NA	NA	NA	22.9 (3.6) HDRS	NA	NA	NA
Lan et al,[44] 2013	NA	NA	NA	8.2 (1.1)	NA	NA	NA	8.2 (1.2)
Li,[45] 2013	NA	NA	NA	8.2 (1.2)	NA	NA	NA	8.2 (1.2)
Li et al,[46] 2013	31.4 (5.7) HDRS	10.4 (3.3)	17.3 (2.9)	8.9 (2.3)	31.8 (5.4) HDRS	10.4 (2.8)	16.8 (3.3)	9.5 (2.1)
Sang et al,[47] 2013	58.8 (7.1) SDS	9.8 (2.5)	14.3 (2.7)	NA	56.2 (7.4) SDS	10.2 (2.2)	13.9 (2.7)	NA
Wang,[49] 2013	16.5 (4.1) HDRS	7.2 (0.8)	11.3 (1.1)	NA	16.6 (4.3) HDRS	7.1 (0.8)	11.2 (1.0)	NA
Zhang et al,[32] 2013	51.9 (6.6) SDS	10.2 (1.4)	16.3 (2.5)	8.3 (1.5)	50.6 (6.3) SDS	10.0 (1.6)	16.2 (2.4)	8.6 (2.0)
Li and Hu,[53] 2014	32.2 (3.5) HDRS	13.1 (2.9)	16.7 (5.9)	8.7 (1.2)	30.2 (7.1) HDRS	10.5 (3.5)	17.2 (5.1)	9.0 (1.5)
Li et al,[54] 2014	50.4 (4.3) SDS	10.4 (2.0)	15.6 (3.2)	9.3 (1.5)	51.2 (3.3) SDS	10.9 (2.3)	15.7 (2.1)	9.9 (1.8)
Wang et al,[48] 2009	55.7 (7.8) SDS 25.2 (3.3) HDRS	12.4 (1.4)	NA	NA	55.2 (8.2) SDS 25.1 (3.1) HDRS	13.1 (1.7)	NA	NA
Zhang et al,[50] 2013	23.4 (1.9) HDRS	8.9 (0.5)	11.5 (0.9)	7.9 (0.5)	23.6 (1.8) HDRS	9 (0.5)	11.6 (0.8)	8.2 (0.6)
Du,[39] 2012	21.6 (3.4) HDRS	8.9 (1.3)	12.9 (0.9)	8.5 (2.3)	21.3 (3.2) HDRS	8.9 (1.4)	12.7 (0.9)	8.5 (2.4)
Hu,[43] 2013	23.9 (4.6) HDRS	9.3 (3.6)	13.7 (3.8)	8.5 (1.6)	24.5 (4.2) HDRS	9.2 (3.2)	13.4 (3.1)	8.6 (1.7)
Penckofer et al,[37] 2012	28.9 (9.5) CES-D	9.4 (4.2)	7.9 (2.0)	NA	27.7 (9.3) CES-D	9.2 (3.9)	7.8 (1.8)	NA
Sharif et al,[52] 2014	16.9 (5.4) BDI	NA	NA	8.9 (1.3)	18.2 (5.9) BDI	NA	NA	9.3 (1.3)
Zheng et al,[55] 2015	54.3 (9.2) SDS	NA	NA	7.4 (1.6)	53.2 (8.5) SDS	NA	NA	7.5 (1.5)
Huang et al,[56] 2016	22.0 (3.4) CES-D	8.7 (3.0)	NA	7.8 (1.9)	21.8 (5.7) CES-D	9.4 (3.2)	NA	7.7 (1.4)
Safren et al,[51] 2014	23.3 (7.2) MADRS	NA	NA	8.7 (1.4)	25.6 (8.9) MADRS	NA	NA	8.8 (1.8)

Abbreviations: FPG, fasting plasma-glucose; 2hPPG, 2-hour postprandial plasma glucose; HbA1c, hemoglobin A1c; SD, standardized difference; SDS, Self-Rating Depression Scale; HDRS, Hamilton Depression Rating Scale; NA, not available; CES-D, epidemiologic studies depression scale; BDI, Beck's depression inventory; MADRS, Montgomery–Åsberg Depression Rating Scale.

depression rating scale. The pooled SMD of studies using SDS was −1.37 (95% CI =−1.76, −0.97), and the pooled SMD of studies using HDRS was −1.46 (95% CI =−1.92, −1.00).

Anxiety symptoms

In total, eight studies used the SAS and two studies used HAMA to assess the anxiety symptoms of 871 T2DM patients. The SMD calculated for these studies was: three studies had a moderate effect of −0.51, −0.52, and −0.78, and seven studies had a large effect of above −0.80. Finally, the pooled SMD was −1.18 (95% CI =−1.50, −0.85) for the random-effects model (Figure 3), which indicated a large effect of psychosocial intervention on the anxiety symptoms of T2DM patients. Sensitivity analysis was performed by excluding the two studies using HAMA. The new SMD of −1.21 (95% CI =−1.54, −0.87) had no significant change compared to the original effect-size estimate. Meanwhile, the results of meta-regression analysis showed that efficacy had a negligible relationship with the baseline anxiety scores.

Glycemic control

The values of FPG at the end of trial were available for 22 studies. Among the 2,000 T2DM patients, there were 997 T2DM patients receiving psychosocial intervention. The SMD was calculated for these studies: four studies had a small effect, four studies had a moderate effect, and 12 studies had a large effect. Finally, the pooled SMD was −0.93 (95% CI =−1.15, −0.71) for the random-effects model (Figure 4), which indicated a large effect of psychosocial intervention on the FPG of T2DM patients.

The values of 2hPPG at the end of trial were available for 17 studies. Among the 1,585 T2DM patients, there were 795 T2DM patients receiving psychosocial intervention. The SMD was calculated for these studies: three studies

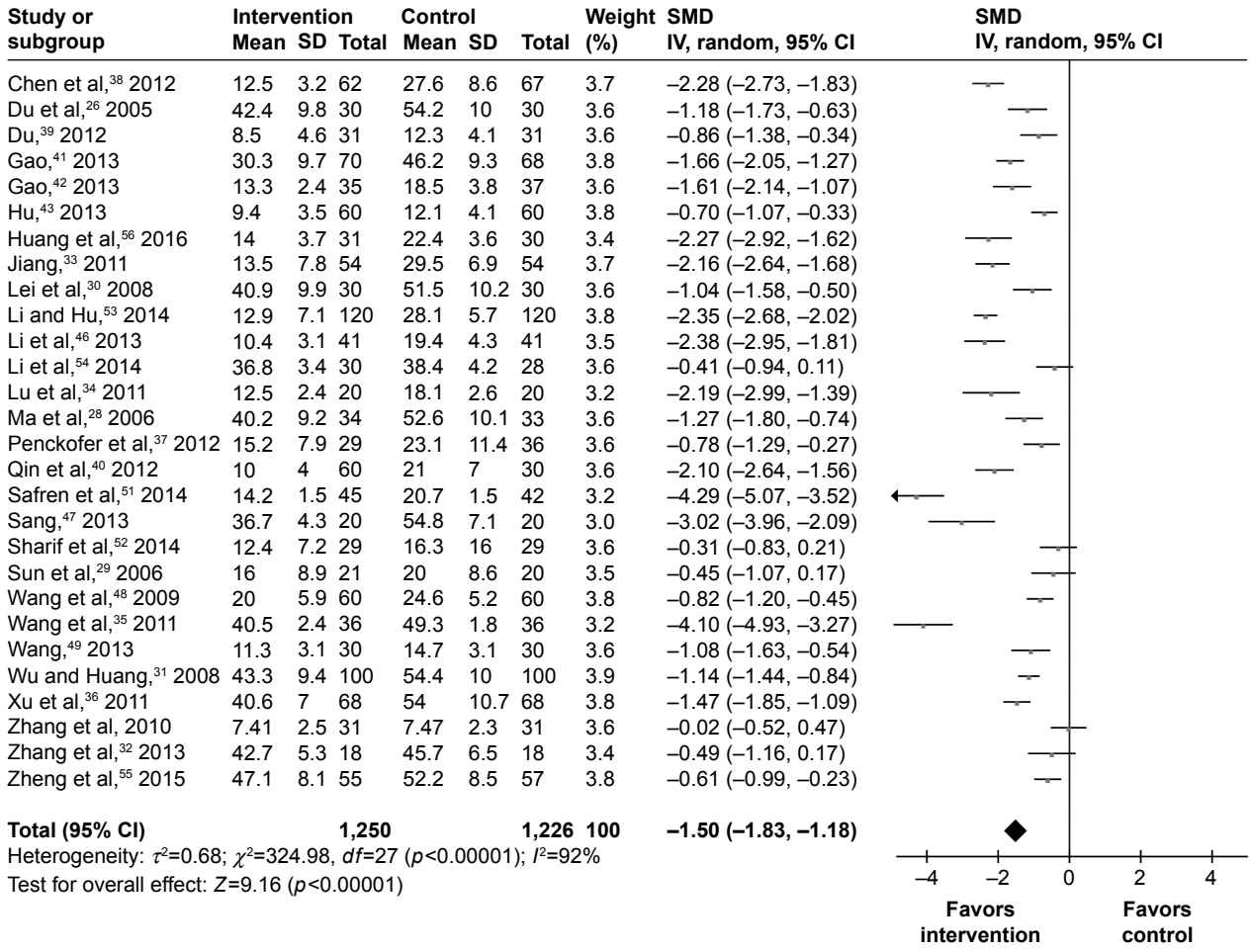

Figure 2 Meta-analysis of depressive symptoms after treatment.
Abbreviation: SMD, standardized mean difference.

had no effect, two studies had a small effect, five studies had a moderate effect, and seven studies had a large effect. Finally, the pooled SMD was –0.84 (95% CI =–1.13, –0.56) for the random-effects model (Figure 5), which indicated a large effect of psychosocial intervention on the 2hPPG of T2DM patients.

The values of HbA1c at the end of trial were available for 22 studies. Among the 1,765 T2DM patients, there

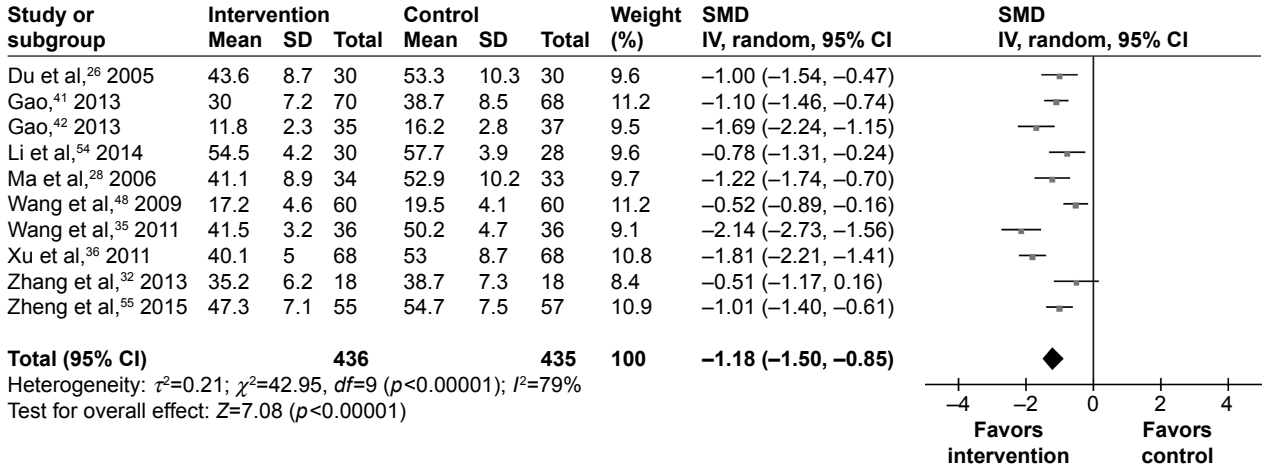

Figure 3 Meta-analysis of anxiety symptoms after treatment.
Abbreviation: SMD, standardized mean difference.

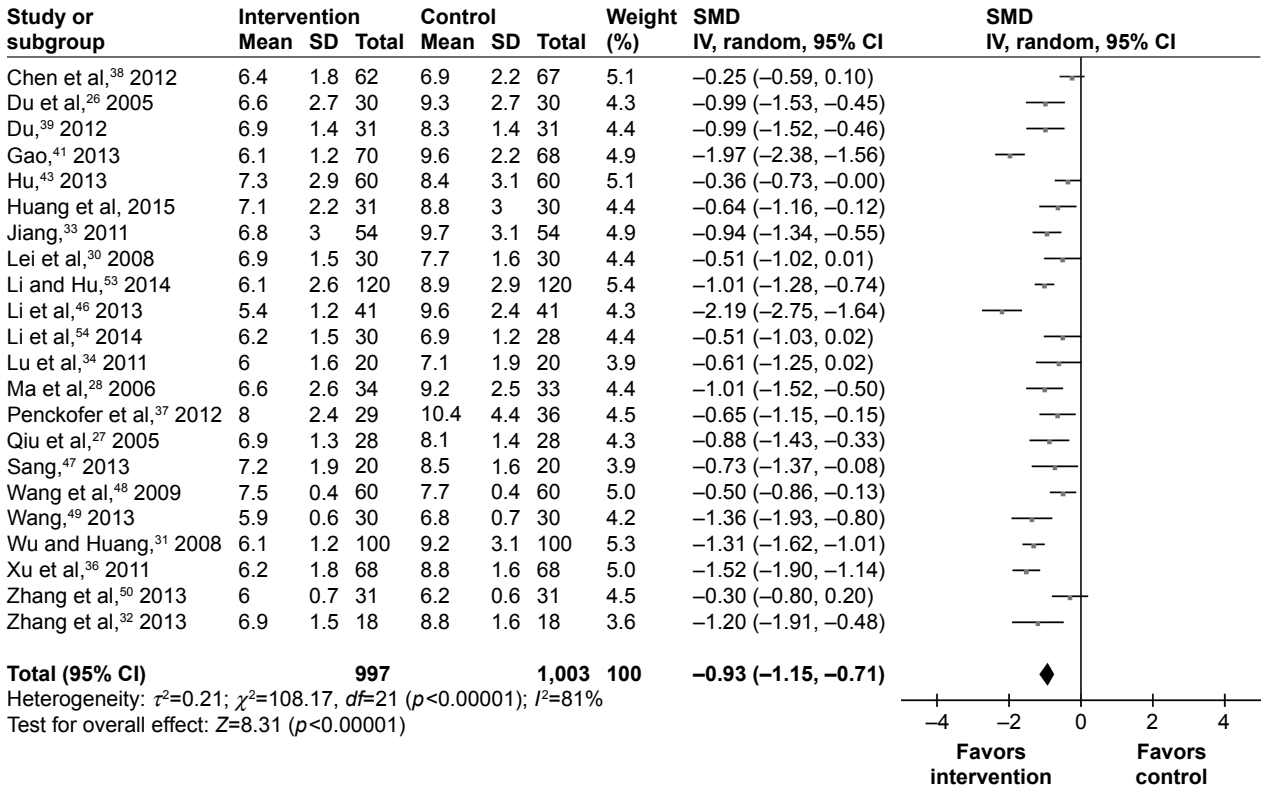

Figure 4 Meta-analysis of FPG after treatment.
Abbreviations: FPG, fasting plasma-glucose; SMD, standardized mean difference.

were 882 T2DM patients receiving psychosocial intervention. The SMD was calculated for these studies: one study had no effect, four studies had a small effect, four studies had a moderate effect, and eight studies had a large effect. Finally, the pooled SMD was –0.81 (95% CI =–1.10, –0.53) for the random-effects model (Figure 6), which indicated a large effect of psychosocial intervention on the HbA1c of T2DM patients.

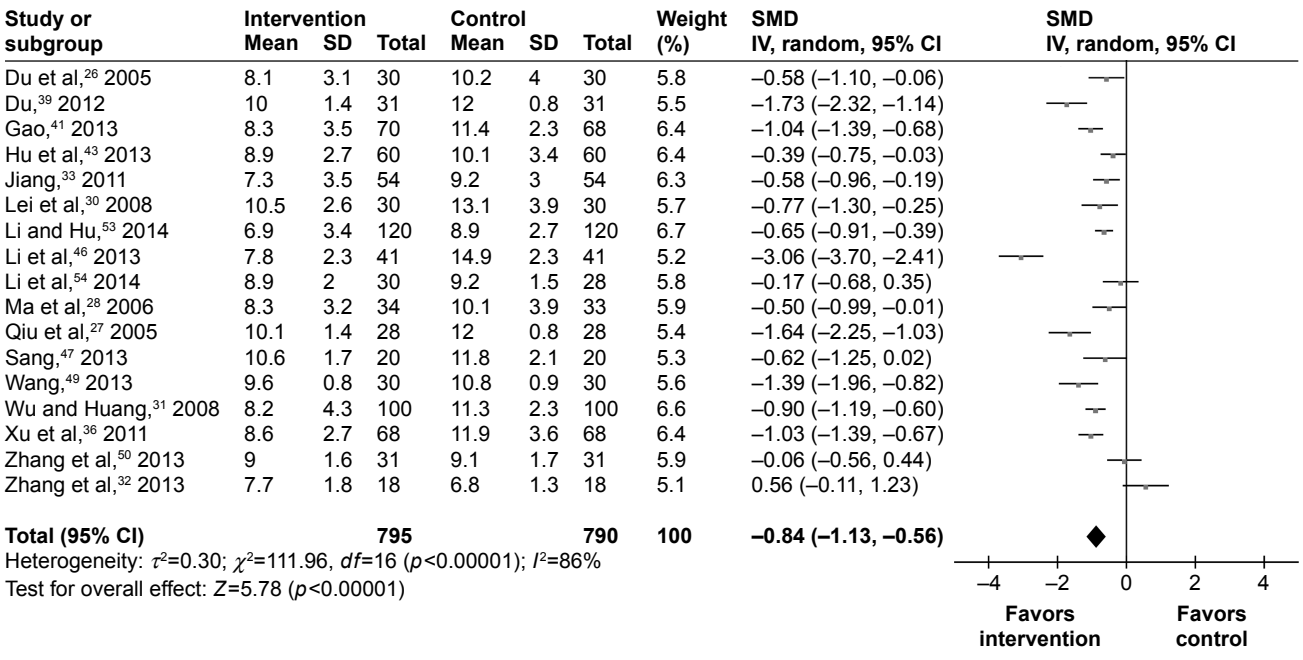

Figure 5 Meta-analysis of 2hPPG after treatment.
Abbreviations: 2hPPG, 2-hour postprandial plasma glucose; SMD, standardized mean difference.

Study or subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight (%)	SMD IV, random, 95% CI
Du et al,[26] 2005	6.5	1.3	30	7.8	1.4	30	4.5	–0.95 (–1.49, –0.41)
Du,[39] 2012	7.2	2.2	31	8.3	2.4	31	4.5	–0.47 (–0.98, 0.03)
Hu,[43] 2013	6.3	1.9	60	7.2	2.1	60	4.9	–0.45 (–0.81, –0.08)
Huang et al,[56] 2016	6.2	0.9	31	7.5	1.8	30	4.5	–0.91 (–1.44, –0.38)
Jiang,[33] 2011	6.3	1.2	54	7.9	1.3	54	4.8	–1.27 (–1.68, –0.86)
Lan et al,[44] 2013	6.1	1.2	42	7.2	1	42	4.7	–0.99 (–1.44, –0.53)
Lei et al,[30] 2008	7.5	1.5	30	8.6	1.8	30	4.5	–0.66 (–1.18, –0.13)
Li,[45] 2013	6.1	1.3	35	7.2	1	35	4.6	–0.94 (–1.43, –0.44)
Li and Hu,[53] 2014	6.3	1.5	120	8.7	1.2	120	5.0	–1.76 (–2.06, –1.46)
Li et al,[46] 2013	6.6	1.4	41	8	2.2	41	4.7	–0.75 (–1.20, –0.30)
Li et al,[54] 2014	8.5	1.2	30	9.1	0.8	28	4.5	–0.58 (–1.10, –0.05)
Lu et al,[34] 2011	6.5	1.5	20	7	1.7	20	4.2	–0.31 (–0.93, 0.32)
Ma et al,[28] 2006	6.3	1.2	34	7.9	1.3	33	4.5	–1.26 (–1.79, –0.74)
Penckofer et al,[37] 2012	7.4	1.3	29	7.8	1.8	36	4.6	–0.25 (–0.74, 0.24)
Qiu et al,[27] 2005	7	2.1	28	8.4	2.6	28	4.5	–0.58 (–1.12, –0.05)
Safren et al,[51] 2014	7.9	0.2	45	8.6	0.2	42	4.1	–3.47 (–4.14, –2.79)
Sharif et al,[52] 2014	8.2	1	29	8.1	1.4	29	4.5	0.08 (–0.43, 0.60)
Sun et al,[29] 2006	8	1.3	21	8.3	1.2	20	4.3	–0.23 (–0.85, 0.38)
Xu et al,[36] 2011	6.2	1.6	68	7.8	1.8	68	4.9	–0.93 (–1.29, –0.58)
Zhang et al,[50] 2013	6	1.1	31	5.9	1.5	31	4.6	0.08 (–0.42, 0.57)
Zhang et al,[32] 2013	3.3	1.6	18	5.3	1.3	18	3.9	–1.34 (–2.07, –0.61)
Zheng et al,[55] 2015	6.3	1.1	55	6.5	1.4	57	4.9	–0.16 (–0.53, 0.21)
Total (95% CI)			**882**			**883**	**100**	**–0.81 (–1.10, –0.53)**

Heterogeneity: τ^2=0.39; χ^2=163.70, df=21 (p<0.00001); I^2=87%
Test for overall effect: Z=5.63 (p<0.00001)

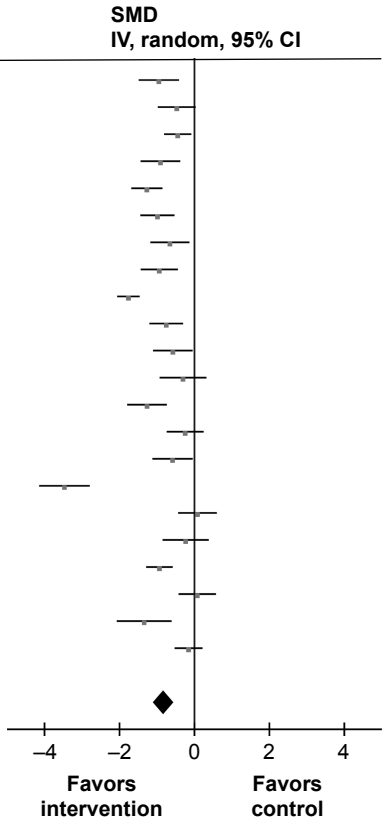

Figure 6 Meta-analysis of HbA1c after treatment.
Abbreviations: HbA1c, hemoglobin A1c; SMD, standardized mean difference.

Discussion

This meta-analysis was based on 31 studies. The 2,616 T2DM patients with depression were randomly assigned to either receiving psychosocial intervention during diabetes management or not. The results demonstrated that the addition of psychosocial intervention could improve the depressive (SMD =–1.50, 95% CI =–1.83, –1.18) and anxiety (SMD =–1.18, 95% CI =–1.50, –0.85) symptoms of T2DM patients. Moreover, this method could also produce a significant effect on glycemic control. After treatment with psychosocial intervention, there was a significant improvement in the mean score of FPG (SMD =–0.93, 95% CI =–1.15, –0.71), 2hPPG (SMD =–0.84, 95% CI =–1.13, –0.56), and HbA1c (SMD =–0.81, 95% CI =–1.10, –0.53). These results demonstrated that the psychosocial intervention was very effective in treatment of T2DM patients with depression.

Heterogeneity is common because of the difference of included studies, methodological or clinical heterogeneity.[57] Heterogeneity existed in this meta-analysis. In order to find the source of heterogeneity, subgroup analysis was conducted according to the different depression rating scales, treatment time, age, DM duration, and mean score of depression at baseline. Meanwhile, sensitivity analysis was conducted by excluding studies with unbalanced sex ratios. However, heterogeneity still existed in our outcomes. Although the detail of the psychosocial intervention in the different studies might be different, this method, on the whole, was about conversation between patients and doctors. Thus, the heterogeneity might not be induced by the methodological or clinical heterogeneity. Actually, the SMD of these included studies ranged from –0.02 to –4.29, which indicated that the heterogeneity was likely to come from the diverse true treatment effects. Therefore, in this meta-analysis, to obtain a robust conclusion in the presence of heterogeneity, we used the random-effects model in this study.

Kok et al conducted a systematic review to assess the effect of psychosocial interventions on patients with diabetes and comorbid depression.[2] But they could not determine whether or not this method had a good effect on diabetes patients with depression. Meanwhile, several limitations existed in this study: i) only studies written in English were included; ii) the included studies recruited patients with type 1 or T2DM; iii) the relatively small number of included studies, and only five of the included studies were RCTs. Also, due to the disparate intervention types, DM duration and delivery method of the included studies, they did not conduct a meta-analysis. But these limitations were also the general problems for study of meta-analysis.[58] Here, 31 RCTs written

in English and Chinese were included to do meta-analysis. The obtained results determined that this method could be very effective in treating T2DM patients with depression.

Limitations of this meta-analysis should be mentioned here: i) most of the included RCTs were conducted in China, which possibly limited the generalizability of our conclusion; ii) all of the included studies recruited patients with T2DM only, thus, whether our conclusion is appropriate for patients with type 1 diabetes needs to be clarified by future studies; iii) although the total number of the included T2DM patients with depression was more than 2,500, only eleven studies recruited more than 100 patients; iv) only the effects of psychosocial intervention in acute treatment phase were assessed; v) heterogeneity, probably caused by the diverse true treatment effects of the included studies, existed; vi) many included studies did not provide details of conventional therapy, so there is no way to analyze the confounding effect of conventional therapy. Therefore, future large-scale RCTs with follow-up assessments after the intervention are still needed to further investigate the effects of psychosocial intervention on treating T2DM patients with depression.

Conclusion

These results obtained by the meta-analysis of 31 RCTs determined that the psychosocial intervention was effective in improving depressive and anxiety symptoms of T2DM patients with depression. Moreover, the addition of psychosocial intervention during diabetes management could improve glycemic control in those patients. However, future studies are still needed to verify and support our conclusion.

Acknowledgments

The project was supported by Cultivation Project of Chongqing Youth Medical High-end Reserve Talents and Technology Foresight and System Innovation of Chongqing Science and Technology Commission for Wuquan Deng and Yu Ma. Our sincere gratitude is extended to Jian-jun Chen and Qian-ping Wei from Chongqing Medical University for their efforts in extracting data and proofreading the manuscript. We also thank Dr He Zhou and Joel George for editing and proofreading the manuscript.

Disclosure

The authors report no conflicts of interest in this work.

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