The Effect of a Diabetes-Specific Cognitive Behavioral Treatment Program (DIAMOS) for Patients With Diabetes and Subclinical Depression: Results of a Randomized Controlled Trial

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OBJECTIVE

Subclinical depression is one of the most frequent mental comorbidities in patients with diabetes and is associated with a poorer long-term prognosis. Since there is a lack of specific intervention concepts for this patient group, a self-management–oriented group program (DIAMOS [Diabetes Motivation Strengthening]) was newly developed and evaluated in a randomized trial.

RESEARCH DESIGN AND METHODS

DIAMOS is composed of cognitive behavioral interventions aiming at the reduction of diabetes distress. The active control group (CG) received diabetes education. The primary outcome was depressive symptoms. Secondary outcomes were diabetes distress, well-being, self-care behavior, diabetes acceptance, diabetes treatment satisfaction, HbA_{1c}, and subclinical inflammation.

RESULTS

Two hundred fourteen participants (mean age 43.3 ± 13.3 years, female sex 56.5%, type 2 diabetes 34.1%, mean diabetes duration 14.2 ± 10.5 years, HbA_{1c} 8.9 ± 1.8%, BMI 28.7 ± 71 kg/m^2) were randomized. The 12-month follow-up revealed a significantly stronger reduction of depressive symptoms (Center for Epidemiologic Studies Depression Scale score) in the DIAMOS group compared with the CG (Δ3.9 [95% CI 0.6–7.3], *P* = 0.021). Of the secondary variables, the Patient Health Questionnaire-9 (Δ1.7 [95% CI 0.2–3.2], *P* = 0.023), Problem Areas in Diabetes scale (Δ8.2 [95% CI 3.1–13.3], *P* = 0.002), and Diabetes Distress Scale scores (Δ0.3 [95% CI 0.1–0.5], *P* = 0.012) displayed significant treatment effects. Moreover, the risk of incident major depression in the DIAMOS group was significantly reduced (odds ratio 0.63 [95% CI 0.42–0.96], *P* = 0.028). Inflammatory variables were not substantially affected.

CONCLUSIONS

DIAMOS is more effective in lowering depressive symptoms and diabetes-related distress in diabetic patients with subclinical depression. DIAMOS also has a preventive effect with respect to the incidence of major depression.

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A slide set summarizing this article is available online.

Depression prevalence is roughly doubled in patients with diabetes compared with people without diabetes. A meta-analysis (1) based on cross-sectional studies showed that 11.4% of patients with diabetes fulfilled criteria for major or clinical depression according to DSM or ICD criteria. A more recent study (2) observed a point prevalence of clinical depression of 10.7%. If depressive symptoms were merely assessed by self-report measures (questionnaires), a greater proportion of people with diabetes ranging from 22.0% to 38.0% would be affected by elevated depressive symptoms (1–3). Thus, ~10% of diabetic patients would meet the criteria of major or clinical depression, whereas ~20% of people with diabetes are affected by subclinical depression, as defined by reporting elevated depressive symptoms without fulfilling diagnostic criteria for clinical depression according to the DSM or the ICD.

There is substantial evidence that depression in diabetes is associated with a broad range of adverse outcomes. Patients with diabetes and comorbid depression report a poorer quality of life (4), reduced well-being (5), higher levels of diabetes-related distress (6,7), lower satisfaction with diabetes treatment (8), reduced diabetes self-care (9), and higher nonacceptance of diabetes treatment measures (10). In the long term, depression in diabetes is associated with a poorer prognosis with regard to microvascular or macrovascular diabetes complications (11), disability (12), and early mortality (13,14). Remarkably, the adverse effects of depression in individuals with diabetes do not occur only in people with clinical depression, but are also observed in people with subclinical depression (9,11,13,14).

The mechanisms translating depression into increased morbidity and mortality are currently not fully understood. Besides behavioral factors such as poor self-care (9), proinflammatory mechanisms are discussed. A meta-analysis by Howren et al. (15) in community and hospital settings demonstrated that depression is associated with elevated circulating levels of the proinflammatory mediators CRP and interleukin (IL)-6 as well as increased levels of the counter-regulatory IL-1 receptor antagonist (IL-1RA) (16,17). Because these inflammatory markers are also associated with diabetes complications (18), subclinical inflammation may be an additional mechanism converting depression in individuals with diabetes into a poorer prognosis. Given these epidemiological findings, it is also of interest to analyze whether a reduction of depression could also normalize systemic concentrations of diabetes-related immune mediators.

Given these negative sequelae of even subclinical depression and the fact that the majority of depressed patients with diabetes are experiencing a subclinical rather than a clinical depression, there is clearly a need for addressing subclinical depression in clinical care adequately. However, whereas the management of moderate-to-severe clinical depression commonly involves pharmacological treatment with antidepressant drugs or psychotherapy within collaborative care settings or mental health units (19,20), the treatment of subclinical depression is less clearly defined.

There is evidence that subclinical depression in people with diabetes should be understood in the context of living with a chronic disease rather than as an independent comorbidity of diabetes. Elevated depressive symptoms are regarded as an indication that living with diabetes and its treatment exceeds the patients' ability to cope with the task of integrating the demands of diabetes into daily life (6,21–23).

This understanding has implications for intervention programs in diabetic patients with subclinical depression. We developed a cognitive behavioral group intervention program (DIAMOS [Diabetes Motivation Strengthening]). This new intervention program focused on integrating diabetes into life by reducing diabetes-related distress and establishing better coping abilities regarding diabetes distress. Besides better coping with diabetes-specific distress, the intervention also helped people to identify and manage stress unspecific for diabetes.

In a randomized controlled trial, the efficacy of this newly developed program was evaluated after a 12-month follow-up period. The primary objective of this study was to test whether DIAMOS was superior in reducing depressive symptoms compared with standard diabetes education, which served as a control treatment. Since DIAMOS also focuses on coping with diabetes-related distress, the impact of the program on diabetes distress was evaluated as a secondary outcome variable. Further positive effects of DIAMOS were expected regarding the following secondary outcome variables: improved glycemic control, higher treatment adherence, higher diabetes acceptance, greater treatment satisfaction, and better well-being. As growing evidence suggests an association between inflammatory markers and depression, the impact of DIAMOS on CRP, IL-6, IL-1RA, and adiponectin as biomarkers of subclinical inflammation were tested as additional secondary outcomes.

RESEARCH DESIGN AND METHODS

Design

The study was a monocenter, prospective, randomized trial with two treatment groups. The participants were recruited at a German inpatient diabetes center. People with diabetes and subclinical depression were randomly assigned to either the group undergoing the newly developed intervention program DIAMOS or the control group (CG).

This trial is registered at ClinicalTrials.gov with identification number NCT01009138.

Sample Size

Based on previous studies about the efficacy of diabetes education (3) and cognitive behavioral treatment (24) in reducing depressive symptoms, an effect size of $d = 0.5$ was expected by comparing the DIAMOS group with the CG. Given this assumption, a two-sided therapeutic superiority could be shown with an error of $\alpha = 0.05$ (two-sided) and $\beta = 0.1$ (power $1 - \beta = 0.90$) with 86 participants per group (total of 172 participants). Given an expected nonevaluable rate of 20%, a total of 214 individuals were needed, with 107 participants in each group.

Randomization

The randomization occurred externally through the Coordination Centre for Clinical Trials, Düsseldorf, Germany. A patient pool was established with patients having provided their written informed consent to participate in the study. Once the patient pool reached a size between 4 and 16 patients, the study center contacted the Coordination Centre for Clinical Trials, and a person independent from the recruitment

process randomized the patients to the two treatment groups with a 1:1 allocation.

Participants

The eligibility criteria for study participation were as follows: diabetes mellitus; elevated depressive symptoms (Center for Epidemiologic Studies Depression Scale [CES-D] score ≥16); age ≥18 and ≤70 years; sufficient German language skills; and written informed consent. The study exclusion criteria were as follows: major depression; current schizophrenia/psychotic disorder, eating disorder, bipolar disorder, addictive disorder, or personality disorder; current use of antidepressant medication or ongoing psychotherapy; being bedridden; and under guardianship.

Patients were recruited at a tertiary diabetes center. The most frequent reasons for referral to this center are poor glycemic control despite optimized treatment in outpatient settings, treatment of late complications, hypoglycemia problems, or psychosocial problems. The average stay in the tertiary care unit is 10–14 days.

Clinical Ethics

This study was approved by the Ethics Committee of the State Medical Chamber of Baden-Württemberg, Germany. All patients included in the baseline examination signed a written informed consent form.

Interventions

The patients in the CG participated in a standard group-based diabetes education program, consisting of five lessons (90 min each) that included topics such as healthy diet in diabetes, diabetes and exercise, and diabetes and legal issues. The program was conducted by diabetes educators (for detailed content, see Supplementary Table 1).

The DIAMOS program is based on a self-management/empowerment approach. DIAMOS was delivered by certified psychologists in small groups with three to six members. It comprised five lessons of 90 min each (for detailed content, see Supplementary Table 1). The mean attendance rate was 4.6 of 5 sessions. Overall, 76.2% of the participants attended all five group sessions, and an additional 18.1% attended four sessions. In summary, 94.3% of the participants attended four or five group lessons, while only six persons (5.7%) attended three or fewer lessons. After hospital discharge and during the follow-up period, four intended phone visits were performed. On average, 3.3 phone visits were attended; 88.6% attended three or four phone visits, 3.8% attended only two phone visits, and eight participants who withdrew their informed consent did not attend any phone visit.

A key topic of DIAMOS is diabetes-related distress originating from living with a chronic condition and the distress caused by treatment-related factors. Another focus is the discrimination between diabetes-related and unrelated problems and problem-solving strategies addressing both issues. The replacement of dysfunctional attitudes about diabetes, its treatment, or sequelae is a further therapeutic objective of DIAMOS. Another important aim is to prevent relapses in dysfunctional attitudes toward diabetes. A key element of this treatment approach is the exchange between group members about living with diabetes and the use of master models for successfully coping with the challenges associated with diabetes and its treatment. After the lessons, the participants completed entries in a booklet in which they recorded personally important topics and individual problem-solving strategies that emerged from the lesson (e.g., a personal distress model or development of personal coping strategies). At the beginning of each lesson, the entries recorded in this booklet were discussed.

Outcomes

The outcome variables were assessed at four measurement time points. There were four measurement points (baseline, immediately after the intervention, 6 months after the intervention, and 12 months after the intervention). The baseline and 12-month measurements were performed at the study center, and the other two measurements were performed by phone and mail.

The primary outcome was the reduction of depressive symptoms at the time of the 12-month follow-up session. Depressive symptoms were assessed using the German version of the CES-D (25).

The secondary outcome measures were assessed as follows: the Patient Health Questionnaire-9 (PHQ-9) is a depression scale assessing the frequency of each of the nine symptoms of major depression as defined by the DSM-IV from "0" (not at all) to "3" (nearly every day). In addition to measuring the frequency of depressive symptoms, the PHQ-9 is also able to make a criteria-based diagnosis of major depression (26).

Diabetes-related distress was assessed by the German version of the Diabetes Distress Scale (DDS). The DDS is a well-validated and widely applied 17-item self-report scale covering the current level of diabetes-related emotional distress both in individuals with type 1 and type 2 diabetes (7). Participants also completed the Problem Areas in Diabetes (PAID) scale, a questionnaire consisting of 20 items, which also assesses the amount of diabetes-related distress (27).

Self-care activities were measured using the German version of the Summary of Diabetes Self-Care Activities Measure (SDSCA) (28). In this questionnaire, patients are asked to indicate how many days of the week they engaged in several specific diabetes self-care activities (healthy diet, physical exercise, self-monitoring of blood glucose, and foot care). The answers range between "0" and "7."

Psychological well-being was assessed using the World Health Organization five-item (WHO-5) Well-Being Index. Each of the five items is rated on a 6-point Likert scale from "0" (at no time) to "5" (all of the time). Higher scores indicate better well-being.

The EuroQol (EQ-5D) is a standardized measure of health-related quality of life and provides a generic measure of health for clinical and economic appraisal. The EQ-5D three-level descriptive system comprises the following five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has the following three levels: no problems, some problems, and extreme problems (29).

Diabetes acceptance was assessed using the Acceptance and Action Diabetes Questionnaire (AADQ) (30). The six-item German version of the AADQ measures acceptance of diabetes-related thoughts and feelings and the degree to which they interfere with valued action (10). A higher score indicates greater acceptance.

Diabetes treatment satisfaction was assessed by the Diabetes Treatment Satisfaction Questionnaire (DTSQ) (31).

Medical Data

Information about comedication was taken from medical records. Information about the occurrence of complications was based on a thorough entry examination, including laboratory analysis and recorded complications in the medical files. Diagnosis of cardiovascular disease, stroke, or peripheral arterial disease was based on a previous event or previous revascularization measures. The diagnosis of diabetic nephropathy was based on a measured glomerular filtration rate of $<$60 mL/min. Diabetic retinopathy was established by an ophthalmologic examination resulting in a diagnosis of proliferative retinopathy or previous laser coagulation treatment. Diabetic neuropathy was based on the neuropathy deficit score. This score is based on the sensitivity for pain, vibration, and temperature, as well as the Achilles tendon reflex. A neuropathy deficit score of $\geq$3 was regarded as indicative for diabetic neuropathy.

Laboratory Measurements

Serum levels of hs-CRP were determined on a Roche/Hitachi cobas c 311 analyzer (Basel, Switzerland). Serum levels IL-1RA, IL-6, and total adiponectin were measured using Quantikine (IL-1RA, adiponectin) or Quantikine HS (IL-6) ELISA kits (R&D Systems, Wiesbaden, Germany). All measurements were performed in a blinded fashion with respect to group assignment. In addition, baseline and follow-up samples from each individual were measured in the same assay in order to reduce bias due to interassay variability. Case patients with a white blood cell count of $>$10,000 cells/μL (DIAMOS group n = 9, CG n = 10) were excluded from analyses because of the possibility of acute inflammation.

Statistical Analyses

The statistical analyses of the study outcomes were performed with repeated-measures ANOVAs. The differences in the outcome parameter data between baseline and 12-month follow-up ($data_{follow\text{-}up} - data_{baseline}$) were the dependent variables. The independent variables were treatment group and diabetes type. The baseline values of the dependent variables, the presence of macrovascular complications, baseline BMI, and baseline CES-D and PHQ-9 scores were used as covariates because of the significant baseline differences between the groups in these variables despite randomization. Paired-samples t tests were used for within-group comparisons.

Statistical tests of inflammatory variables were performed with log-transformed values because of skew distributions of the raw scores, whereas in the descriptive statistics median raw scores and interquartile ranges are reported. The following additional covariates were used for the analysis of inflammatory variables: intake of medications (statins, anticoagulants, thyroid medication, cortisone, and nonsteroidal anti-inflammatory drugs), age, sex, diabetes duration, and the presence of macrovascular complications (coronary heart disease, stroke, and peripheral arterial disease) or microvascular complications (retinopathy, nephropathy, and diabetic neuropathy).

For the main outcome, an intention-to-treat analysis was performed, using the last observation carried forward method. Statistical testing was conducted at a significance level of α = 0.05, since secondary variables were exploratory rather than for hypothesis testing. The statistical software program SYSTAT version 12.0 (Systat Software, Inc., Chicago, IL) was used for the statistical analysis.

RESULTS

Recruitment started in December 2009 and ended in February 2011. In the recruitment period, 3,156 patients were screened for depressive symptoms. From these, 1,261 subjects were screened positive, and 710 subjects did not meet the inclusion criteria. A total of 214 of 551 eligible patients (38.8% provided informed consent) were then randomized to either the CG (n = 108) or DIAMOS group (n = 106). A total of 33 patients (15.4%) were lost to follow-up. The flow of patients through each stage of the trial is depicted in Fig. 1.

Baseline characteristics of the sample are presented in Table 1 for both the CG and DIAMOS group. Patients were rather young. The sex distribution in both groups was similar. People with type 1 diabetes were rather frequent in both groups; however, in the CG group the proportion of people with type 1 diabetes was significantly higher than in the DIAMOS group. Diabetes duration was identical in both groups. Moderate overweight was present in both groups, but BMI was significantly lower in the CG than in the DIAMOS group. Glycemic control was comparably poor in both groups. The prevalence of microvascular complications did not differ significantly between groups, whereas the prevalence of macrovascular complications was significantly higher in the DIAMOS group.

Participants of the DIAMOS group reported significantly more depressive symptoms and a considerably lower status of well-being than participants of the CG group. Diabetes-related distress, health-related quality-of-life scores, self-care behavior, and diabetes acceptance did not differ at baseline between both groups. Inflammatory markers were also highly comparable between both groups. There were high correlations between the CES-D score and the PAID (r = 0.43) and DDS (r = 0.38) scores, and between the PHQ-9 score and PAID (r = 0.51) and DDS (r = 0.46) scores (Table 1).

Comparing the randomized and the analyzed samples, no significant difference in drop-out rates between the DIAMOS group and CG (13.9% vs. 22.7%, P = 0.205) was observed. A drop-out analysis showed that patients who dropped out of the study were significantly younger (33.8 $\pm$ 14.9 vs. 45.0 $\pm$ 13.6 years of age, P = 0.01) and had a lower BMI (24.8 $\pm$ 6.0 vs. 29.5 $\pm$ 7.0 kg/m^2, $P < 0.01$) and poorer glycemic control (HbA_{1c} 9.6 $\pm$ 2.0% vs. 8.8 $\pm$ 1.7%; P = 0.01).

Primary Outcome

The primary outcome was the reduction of depressive symptoms. The per protocol analysis showed that the CES-D score was reduced by 2.7 in the CG, whereas a significantly greater reduction (by 7.4) was observed in the DIAMOS group. Adjustment for diabetes type, baseline scores of CES-D and PHQ-9, BMI, and macrovascular complications resulted in a significant difference between the groups of the per protocol analysis (P = 0.021). The intention-to-treat analysis also showed a significant difference between the CG and DIAMOS group (P = 0.016) (Fig. 2).

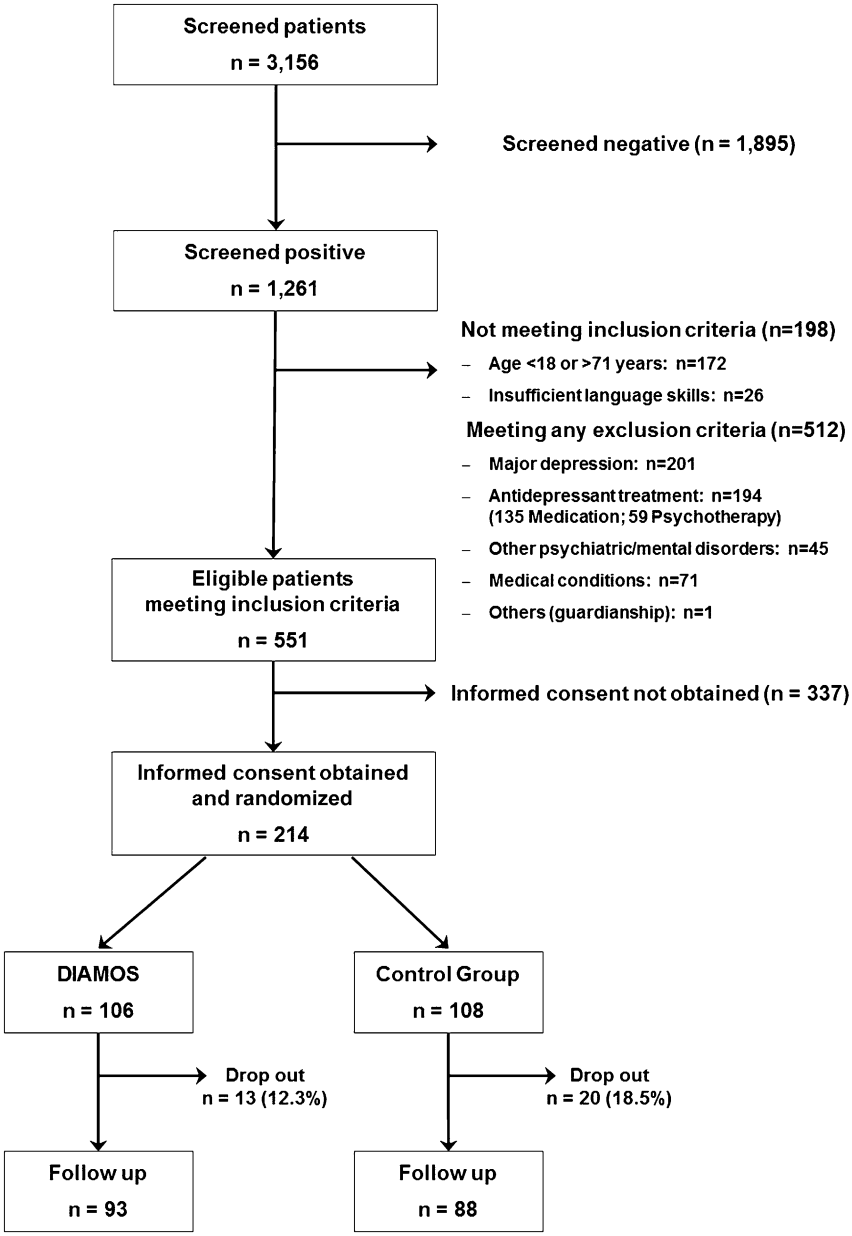

Figure 1—Study flowchart.

Secondary Outcomes

Table 2 illustrates the results of the primary outcome and all secondary outcome variables. In the analysis stratified by diabetes type, no significant interaction effects were observed, except for diabetes acceptance (see Supplementary Table 2).

Patients in the DIAMOS group showed a significant reduction of the PHQ-9 depression score, corroborating the finding of a significant reduction of depressive symptoms measured by the CES-D. The PHQ-9 also allows a categorical assessment of major depression according to DSM-IV criteria. Based on this analysis, 10 participants of the DIAMOS group (10.8%) compared with 20 participants of the CG (22.7%) fulfilled the criteria for major depression at follow-up (P = 0.030), resulting in a 37% reduction of the incidence of major depression after participation in the DIAMOS (adjusted odds ratio 0.63 [95% CI 0.42–0.96], P = 0.028).

Participants in the DIAMOS group also exhibited a significant reduction in diabetes-related distress as measured by the PAID or the DDS.

Improved well-being was reported in the DIAMOS group as well as in the CG; however, the difference of improvement in well-being between the groups did not reach significance.

Apparently, neither the DIAMOS group nor the CG had a significant impact on self-reported self-care behavior, as assessed by the SDSCA, or on generic health-related quality of life, as assessed by the EQ-5D. Acceptance of diabetes and diabetes treatment satisfaction improved in both groups but without significant differences between the groups. Interestingly, there was also a significant improvement in glycemic control in both groups, yet no significant difference between the DIAMOS group and the CG.

In both the DIAMOS group and the CG, we observed decreases in IL-1RA, but without difference between the groups. Serum levels of hs-CRP, IL-6, or total adiponectin did not change significantly within or between both groups.

CONCLUSIONS

One year after participating in both programs, subjects in the DIAMOS program showed a significantly greater reduction of depressive symptoms as assessed by the CES-D, which was confirmed in a secondary depression measurement using the PHQ-9. The PHQ-9 assesses all depressive symptoms required for a categorical diagnosis of major depression according to the DSM-IV (26). This categorical evaluation revealed a 37% lower probability of an exacerbation of depressive symptoms at the 12-month follow-up in the DIAMOS group compared with the CG. Since subclinical depression is an established risk factor for clinical depression (32), this result indicates that effective treatment of subclinical depression may yield a preventive effect for the exacerbation of depressive symptoms. Given that major depression in individuals with diabetes is associated with more adverse outcomes (11,14), more intensive depression treatment requirements, and higher healthcare costs (33), the prevention of an exacerbation of subclinical depressive symptoms is of high clinical relevance.

There was also a significant impact of DIAMOS on the reduction of diabetes-related distress. The finding that an intervention reducing diabetes distress also reduced depressive symptoms supports epidemiological findings of a close relationship between diabetes-related distress and subclinical depression

Table 1—Demographics and baseline characteristics of the study population

	DIAMOS group (n = 106)	CG (n = 108)	P
Demographic variables			
Age (years)	43.2 ± 14.9	43.4 ± 13.8	0.911
Female sex	60 (56.6)	61 (56.5)	0.986
Years of education (years)	11.3 ± 3.0	10.8 ± 2.7	0.232
Type 1 diabetes	63 (59.4)	78 (72.2)	0.049
Diabetes duration (years)	14.2 ± 10.3	14.2 ± 10.7	0.992
HbA_{1c}			
%	8.9 ± 1.8	8.9 ± 1.8	0.722
mmol/mol	64.5 ± 10.2	67.4 ± 12.4	0.722
BMI (kg/m^2)	29.8 ± 7.7	27.7 ± 6.3	0.029
Patients with microvascular complications[1]	57 (53.8)	49 (45.4)	0.219
Patients with macrovascular complications[2]	18 (17.0)	7 (6.5)	0.017
Psychological variables			
CES-D (depression score)	24.7 ± 7.6	22.4 ± 8.6	0.049
PHQ-9 (depressive symptoms)	10.8 ± 4.4	9.6 ± 3.9	0.043
WHO-5 (emotional well-being)	8.5 ± 4.3	9.6 ± 4.8	0.091
DDS (diabetes-related distress)	2.7 ± 0.9	2.7 ± 0.8	0.445
PAID (diabetes-related distress)	39.7 ± 19.6	37.5 ± 17.0	0.385
EQ-5D (health-related quality of life)	0.86 ± 0.21	0.88 ± 0.20	0.479
AADQ (diabetes acceptance)	28.8 ± 7.1	28.2 ± 7.2	0.532
DTSQ (treatment satisfaction)	21.9 ± 7.0	22.8 ± 7.3	0.350
SDSCA (self-care behavior)	4.1 ± 1.1	4.3 ± 1.1	0.430
Inflammation-related biomarkers			
hs-CRP (mg/dL)	0.2 (0.1–0.6)	0.2 (0.1–0.5)	0.346
IL-6 (pg/mL)	1.6 (0.8–2.9)	1.3 (0.9–2.3)	0.123
IL-1RA (pg/mL)	492.0 (332.8–776.1)	438.2 (300.0–669.6)	0.706
Adiponectin (ng/mL)	6,713.0 (3,815.5–14,714.8)	7,954.5 (4,504.0–13,960.0)	0.722

Values are reported as mean ± SD, n (%), or median (interquartile range), unless otherwise indicated. [1]Including diabetic neuropathy, retinopathy, or nephropathy. [2]Including cardiovascular disease, stroke, or peripheral arterial disease.

from the intervention side. The baseline PAID and DDS scores indicate that participants originally experienced moderate-to-severe diabetes distress (6,34). Compared with the REDEEM (Reducing Distress and Enhancing Effective Management) study (35), an intervention trial designed to reduce diabetes-related distress, the observed reduction in this study was slightly greater. However, it has to be taken into account that the baseline distress values were also slightly lower in the REDEEM study.

Psychological well-being was observed to improve in the DIAMOS group as well as in the CG, indicating that the DIAMOS intervention affected well-being only partially.

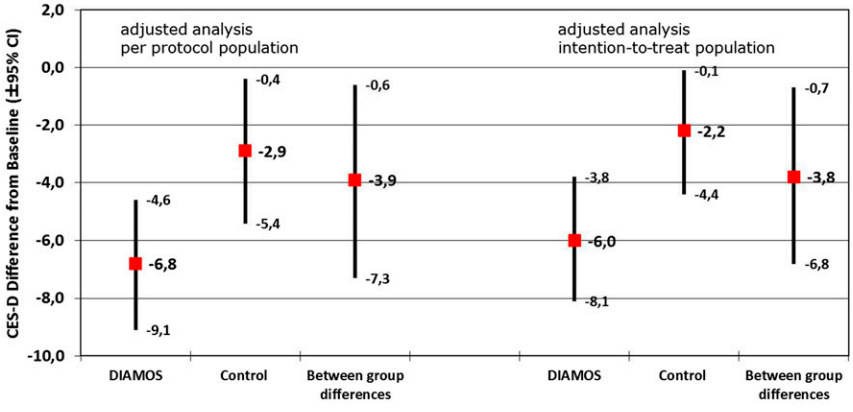

Figure 2—Reduction of depressive symptoms (CES-D score) in per protocol and intention-to-treat analyses. Data are reported as adjusted mean differences (95% CIs).

Despite a significant reduction in depressive symptoms and diabetes distress, we observed, surprisingly, no positive effect on self-reported self-care behavior in either the CG or the DIAMOS group. However, the associations between depression and self-care activities are generally rather weak. In the meta-analysis by Gonzalez et al. (9), the overall correlation between depression and self-care was r = 0.21, which represents a small effect on depression explaining only 4.4% of the variance. Furthermore, the SDSCA (28) is the only available validated measure for diabetes self-care and is primarily designed to measure self-care behavior in individuals with type 2 diabetes, where lifestyle modification is an essential part of the treatment regimen. In this sample, all persons with type 1 diabetes and most of those with type 2 diabetes were receiving therapy with multiple daily insulin injections or insulin infusions. For these people, self-care behaviors (e.g., insulin dose adaptation before each meal) other than those measured by the SDSCA were more

Table 2—Changes in primary and secondary outcomes from baseline to follow-up

	DIAMOS group (n = 93)	CG (n = 88)	Adjusted between-group change from baseline to end point	Adjusted P values between groups
Primary outcome—depressive symptoms[1,2]				
CES-D score			3.9 ± 1.7 (0.6–7.3)	0.021
Baseline	24.4 ± 7.5	22.1 ± 8.6		
End point	17.0 ± 10.0	19.4 ± 11.8		
Baseline to end point change	−7.4 ± 11.4 ($P < 0.001$)	−2.7 ± 11.7 ($P = 0.036$)		
Secondary outcomes[1,2]				
Psychological variables				
PHQ-9 score			1.7 ± 0.8 (0.2–3.2)	0.023
Baseline	10.9 ± 4.3	9.6 ± 3.8		
End point	7.5 ± 4.8	8.4 ± 5.0		
Baseline to end point change	−3.3 ± 5.1 ($P < 0.001$)	−1.2 ± 5.7 ($P = 0.050$)		
WHO-5 score			−1.5 ± 0.9 (−3.2 to 0.3)	0.097
Baseline	8.2 ± 4.0	9.6 ± 4.9		
End point	12.7 ± 5.5	12.1 ± 6.1		
Baseline to end point change	4.5 ± 6.1 ($P < 0.001$)	2.5 ± 6.3 ($P < 0.001$)		
DDS score			0.3 ± 0.1 (0.1–0.5)	0.012
Baseline	2.8 ± 0.9	2.6 ± 0.8		
End point	2.1 ± 0.8	2.3 ± 0.8		
Baseline to end point change	−0.7 ± 1.0 ($P < 0.001$)	−0.4 ± 0.7 ($P < 0.001$)		
PAID score			8.2 ± 2.6 (3.1–13.3)	0.002
Baseline	41.1 ± 19.1	37.9 ± 17.5		
End point	28.1 ± 18.4	33.7 ± 19.7		
Baseline to end point change	−13.0 ± 18.9 ($P < 0.001$)	−4.2 ± 16.9 ($P = 0.022$)		
EQ-5D score			0.03 ± 0.03 (−0.03 to 0.01)	0.751
Baseline	0.84 ± 0.21	0.85 ± 0.21		
End point	0.84 ± 0.23	0.85 ± 0.21		
Baseline to end point change	−0.01 ± 0.23 ($P = 0.628$)	−0.01 ± 0.25 ($P = 0.654$)		
AADQ score			−1.6 ± 1.0 (−3.5 to 0.3)	0.098
Baseline	28.4 ± 7.2	28.5 ± 7.1		
End point	30.9 ± 7.3	30.5 ± 6.9		
Baseline to end point change	2.5 ± 7.7 ($P = 0.002$)	2.0 ± 6.6 ($P = 0.005$)		
DTSQ score			0.01 ± 1.34 (−2.63 to 2.65)	0.997
Baseline	21.6 ± 6.9	23.2 ± 7.1		
End point	24.6 ± 6.9	26.0 ± 6.9		
Baseline to end point change	3.0 ± 8.7 ($P = 0.001$)	2.8 ± 7.8 ($P = 0.001$)		
SDSCA score			0.2 ± 0.2 (−0.1 to 0.5)	0.243
Baseline	4.2 ± 1.1	4.3 ± 1.1		
End point	4.1 ± 1.1	4.3 ± 1.0		
Baseline to end point change	−0.1 ± 1.1 ($P = 0.504$)	0.0 ± 1.0 ($P = 0.931$)		

Continued on p. 558

Table 2—Continued

	DIAMOS group (n = 93)	CG (n = 88)	Adjusted between-group change from baseline to end point	Adjusted P values between groups
Glycemic control				
HbA_{1c} (%)			−0.3 ± 0.2 (−0.7 to 0.2)	0.230
Baseline	8.8 ± 1.7	8.7 ± 1.7		
End point	8.3 ± 1.7	7.9 ± 1.2		
Baseline to end point change	−0.5 ± 2.0 (P = 0.018)	−0.7 ± 1.7 ($P < 0.001$)		
Inflammation-related biomarkers[3,4,5]				
hs-CRP (mg/dL)			−0.3 ± 0.1 (−0.5 to 0.0)	0.061
Baseline	0.2 (0.1; 0.5)	0.1 (0.1; 0.4)		
End point	0.2 (0.1; 0.4)	0.2 (0.1; 0.3)		
Baseline to end point change	0.0 (−0.1; 0.2) (P = 0.062)	0.0 (−0.1; 0.1) (P = 0.283)		
IL-6 (pg/mL)			0.0 ± 0.1 (−0.3 to 0.2)	0.792
Baseline	1.6 (0.8; 2.7)	1.3 (0.8; 1.9)		
End point	1.5 (1.0; 2.4)	1.5 (1.0; 2.4)		
Baseline to end point change	0.0 (−0.6; 0.4) (P = 0.780)	0.1 (−0.6; 0.5) (P = 0.711)		
IL-1RA (pg/mL)			0.0 ± 0.1 (−0.1 to 0.1)	0.910
Baseline	552.3 (340.8; 786.8)	422.5 (300.0; 642.7)		
End point	455.8 (333.7; 564.8)	349.7 (246.0; 451.3)		
Baseline to end point change	−100.5 (−261.9; 28.8) (P = 0.001)	−70.8 (−171.8; 11.8) (P = 0.006)		
Adiponectin (ng/mL)			0.0 ± 0.1 (−0.2 to 0.1)	0.452
Baseline	5,352.5 (3,443.0; 14,288.5)	7,695.0 (4,384.0; 12,970.0)		
End point	5,578.0 (4,062.0; 14,270.0)	8,224.0 (5,187.0; 12,610.0)		
Baseline to end point change	449.0 (−691.0; 1,818.7) (P = 0.529)	738.0 (−802.0; 1,434.0) (P = 0.251)		

[1]Baseline and end point data are shown as the mean ± SD; values for within-group baseline and end point changes are unadjusted differences. [2]Values for between-group differences in baseline and end point changes, reported as the mean ± SEM (95% CI), are adjusted for BMI, diabetes type, macrovascular complications, baseline CES-D score, baseline PHQ-9 score, and baseline values. [3]Baseline and end point data for inflammatory markers are shown as the median (interquartile range); values for within-group baseline and end point changes are unadjusted differences. [4]Values for between-group differences in baseline and end point changes, reported as the mean ± SEM (95% CI), for inflammation-related biomarkers are adjusted for age, sex, BMI, diabetes type, diabetes duration, microvascular and macrovascular complications, intake of medications (statins, anticoagulants, thyroid medication, cortisone, and nonsteroidal anti-inflammatory drugs), baseline CES-D score, baseline PHQ-9 score, and baseline values. [5]Statistical tests for inflammation-related biomarkers were performed with log-transformed values due to skewed distributions of the raw data.

relevant. Therefore, the SDSCA may not be sensitive to those self-care behaviors relevant to the studied sample.

The DIAMOS had a significant impact on diabetes acceptance, but there was a significant interaction effect, which indicates that DIAMOS increases diabetes acceptance more in persons with type 2 diabetes than in those with type 1 diabetes. This might be due to the construction of the acceptance scale by Gregg et al. (30), which mainly covers the acceptance of different aspects of diabetes treatment, which may be different between type 1 and type 2 diabetic patients. Also, diabetes acceptance is not a well-defined construct. More research is needed to determine the degree of acceptance that is be desirable and what differentiates diabetes acceptance from fatalism.

The participants' satisfaction with their diabetes treatment significantly improved in both groups, but there was no significant difference between the groups. However, since the patients were treated by their diabetologists in an outpatient setting during the 1-year follow-up phase, medical diabetes treatment was not systematically influenced, explaining the lack of group differences regarding treatment satisfaction.

Both groups showed significant improvements in glycemic control. It has also been considered that the CG received education about diabetes treatment–related topics. As mentioned above, the medical treatment was under the responsibility of the local physician. Thus, patients might have undergone similar medical treatment, which was recommended by the German diabetes guidelines. The aforementioned REDEEM study (35) also did not observe treatment effects on HbA_{1c} in any of the three treatment arms. In the literature, the impact of depression reduction to improve glycemic control is also controversial (36,37). Clearly, more research is required to identify mediating pathways linking improvement in depression to improvements in glycemic control.

Among the inflammatory parameters, there were no significant between-group differences. It should be considered that the effect sizes of the association between depression and inflammatory markers commonly range between d = 0.11 and d = 0.24 (Cohen d statistic), representing small to medium effects (20). Given these effect sizes, it is possible that the observed reduction of depressive symptoms was too small to have a significant impact on the analyzed inflammatory markers. The reduction in IL-1RA in both groups is interesting because lowered IL-1RA levels may reflect attenuated IL-1β–related processes, which have been implicated in the development of macrovascular and microvascular complications of diabetes (38). Therefore, study participants from both intervention arms appeared to have benefited with respect to subclinical inflammation as a risk factor of diabetes complications.

Some limitations should be taken into account. The CG received diabetes education, which has been shown to produce a beneficial impact on diabetes-related distress (39,40). Furthermore, the study included high proportions of patients with type 1 or type 2 diabetes, who were treated primarily with insulin and had diabetes for a rather long time. The transferability of results to other subgroups of patients with type 2 diabetes (e.g., treated exclusively with oral medication) is therefore uncertain. Finally, the intervention was delivered by trained psychologists, which has the potential to impair cost-efficiency.

The strength of this study is that the efficacy of the DIAMOS was evaluated in a randomized controlled trial. The new intervention was tested against an active CG (who received diabetes education). Therefore, attention bias is unlikely. The measurement of inflammatory parameters as a secondary outcome of an intervention aiming at the reduction of depressive symptoms is also novel.

In summary, the DIAMOS program has proven its efficacy in treating subthreshold depression and elevated diabetes distress more efficiently and specifically than diabetes education alone. Furthermore, subsequent analyses showed that DIAMOS has the effect of preventing a deterioration of subclinical depression into major depression. Given the negative sequelae of subclinical depression on the prognosis of diabetes, this new program has the potential to close an important gap in the management of subclinical depression in diabetes care.

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