Cognitive Behavior Therapy for Depression in Type 2 Diabetes Mellitus

A Randomized, Controlled Trial

Patrick J. Lustman, PhD; Linda S. Griffith, MSW; Kenneth E. Freedland, PhD; Sarah S. Kissel, RN, CDE; and Ray E. Clouse, MD

Background: Psychotherapy is the principal nonpharmacologic method for the management of depression, but its usefulness for depressed patients with diabetes remains unknown.

Objective: To assess the efficacy of cognitive behavior therapy (CBT) for depression in patients with diabetes.

Design: Randomized, controlled trial.

Setting: Referral-based academic medical center.

Patients: 51 patients with type 2 diabetes and major depression.

Intervention: Patients were assigned either to a group that received 10 weeks of individual CBT or to a control group that received no specific antidepressant treatment. All patients participated in a diabetes education program to control for the effects of supportive attention and the possible influence of enhanced diabetes control on mood.

Measurements: Degree of depression was measured by using the Beck Depression Inventory; glycemic control was measured by using glycosylated hemoglobin levels. Outcomes were assessed immediately after treatment and 6 months after treatment.

Results: The percentage of patients achieving remission of depression (Beck Depression Inventory score ≤ 9) was greater in the CBT group than in the control group: post-treatment, 85.0% of patients in the CBT group (17 of 20) compared with 27.3% of controls (6 of 22) achieved remission (difference, 57.7 percentage points [95% CI, 33 to 82 percentage points]) ($P < 0.001$); at follow-up, 70.0% of patients in the CBT group (14 of 20) compared with 33.3% of controls (7 of 21) achieved remission (difference, 36.7 percentage points [CI, 9 to 65 percentage points]) ($P = 0.03$). Post-treatment glycosylated hemoglobin levels were not different in the two groups, but follow-up mean glycosylated hemoglobin levels were significantly better in the CBT group than in the control group (9.5% compared with 10.9%; $P = 0.03$).

Conclusions: The combination of CBT and supportive diabetes education is an effective nonpharmacologic treatment for major depression in patients with type 2 diabetes. It may also be associated with improved glycemic control.

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From Washington University School of Medicine and the Veterans Affairs Medical Center, St. Louis, Missouri. For current author addresses, see end of text.

Data from controlled studies (1–8) suggest that depression is more prevalent in diabetic patients than in the general U.S. population and that it is associated with poor glycemic control and decreased compliance with therapy (3, 5, 9–16). Depression has also been associated with an increased risk for complications of diabetes, particularly cardiovascular disease and retinopathy (17–20). The mechanisms of these associations are not fully understood, but it is plausible that alleviation of depression improves glycemic control and thereby decreases the risk for complications. Pharmacotherapy for depression may be poorly tolerated or may be insufficient to produce full remission in as many as 50% of diabetic patients with major depression (21–23). The usefulness of nonpharmacologic approaches to the management of depression, such as psychotherapy, has not been systematically studied.

Approximately two thirds of patients who have both diabetes and major depression do not receive specific antidepressant treatment, in part because their physicians tend to attribute their depression to poorly controlled or advancing diabetes (24, 25). Therapy for these patients still largely centers on medical management, which may include emotional support and diabetes education; this approach is probably suboptimal. Our study was designed to determine the antidepressant efficacy of cognitive behavior therapy (CBT) added to supportive diabetes education. A secondary aim was to determine whether remission of depression is associated with improved glycemic control.

Methods

Patients

Our study was advertised to primary care physicians working within the Washington University School of Medicine and BJC Healthcare System, St. Louis, Missouri, and it was publicized in various

See editorial comment on pp 656-657.

mass media advertisements. The study protocol was reviewed and approved by the Human Studies Committee of Washington University School of Medicine. Patients with type 2 diabetes mellitus who were 21 to 70 years of age were eligible for participation if they were able to answer questions, fill out study forms, and give informed consent. The diagnosis of type 2 diabetes was made according to the criteria developed by the American Diabetes Association (26) and was confirmed by a statement from the patient's primary physician. Patients also had to meet the diagnostic criteria for major depression and had to have a score of at least 14 on the Beck Depression Inventory (BDI). Patients were excluded from participation if they had active suicidal ideation or a history of attempted suicide; had a history of panic disorder, bipolar depression, or any psychotic disorder; had a current substance abuse disorder; or were currently taking psychoactive medications.

Assessment of Depression

The presence of the major Axis I clinical syndromes was assessed by using the National Institute of Mental Health Diagnostic Interview Schedule (DIS) (27), and these syndromes were diagnosed according to the criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (28). The reliability and validity of the DIS in psychiatric and epidemiologic studies have been extensively reported (29). Evidence also indicates that the DIS is sensitive and useful for patients with diabetes, in whom the somatic manifestations of the medical disease (such as fatigue, weakness, sleep disturbances, and sexual dysfunction) mimic the symptoms of a psychiatric disorder (30, 31). Although the DIS is suitable for use by trained lay personnel, diagnostic evaluations in our study were done by a clinical social worker and a psychologist, both of whom had been trained in the use of the DIS by the instrument's developers and the staff of the St. Louis site of the National Institute of Mental Health Epidemiologic Catchment Area Study (27, 32).

The severity of current symptoms of depression was measured by using the BDI (33). This measure asks patients to provide a self-rating from 0 to 3 on each of 21 items; these ratings are added together to produce a total score. The BDI has been studied extensively and has been shown to be a reliable and valid measure of the severity of depression (34). Depression manifests similarly on this instrument in diabetic and psychiatric patients, particularly with regard to the cognitive symptoms of depression (31).

Assessment of Diabetes

Glycosylated hemoglobin (GHb) levels were measured to assess average glycemic control in the 120-day period before testing (35–37). Total GHb levels were measured with the Pierce Glyco-Test (Pierce Chemical, Rockford, Illinois), an affinity assay that removes confounding by hemoglobin variants, such as hemoglobin F. The range of GHb levels for normal, nondiabetic persons in the Barnes-Jewish Hospital outpatient laboratory is 4.4% to 6.3%. In this laboratory, the between-run coefficients of variation for values greater than 6.6% are all 5% or less, the recommended standard (38). The presence of complications of diabetes (neuropathy, retinopathy, and nephropathy) was determined by a physician–investigator on the basis of review of each patient's medical history, current symptoms, physical examination results, and objective test results (which were obtained through review of clinical records).

Assessment of Compliance

Compliance with self-monitoring of blood glucose levels was determined by using electronic memory glucometers (LifeScan, Inc., Milpitas, California), which recorded the date, time, and result of blood glucose testing. Patients were instructed to test their blood glucose levels four times per day on two nonconsecutive days each week. Values for weekly compliance with blood glucose monitoring were computed by dividing the number of samples measured on the two test days by 8 (the number of tests requested) and multiplying the result by 100%.

Study Design

Patients were informed that depression in diabetes can be a cause or a consequence of poor glycemic control and that the study would determine whether focusing on the mental or the physical side of the problem was the most effective way to relieve depression. These concepts were familiar to most patients and were generally well accepted. No patients declined further evaluation because they were unwilling to accept random assignment. Patients who met the inclusion criteria and gave informed consent underwent a 1-week period of glucometer training and baseline assessment, after which they were randomly assigned to study groups. The randomization pattern was determined by a computer algorithm, and assignments were concealed in sealed envelopes. A secretary who was not otherwise involved with the study opened each patient's envelope after the patient had completed the baseline assessment.

During the 10-week treatment period, all patients participated in a diabetes education program by

meeting in 1-hour, biweekly, individual sessions with a certified diabetes educator. A variety of diabetes self-care topics were covered in these sessions, and diet and exercise regimens were systematically reviewed and modified as needed. Patients continued to see their diabetologists during the trial, and these physicians were given GHb and glucometer data from our study to facilitate management. The diabetes education program was designed to control for the nonspecific effects of supportive attention as well as the potential influence of enhanced self-care and glycemic control on mood and ideation.

Patients were randomly assigned to receive CBT or to receive no specific antidepressant treatment other than the diabetes education program. Patients in the CBT group received 1 hour of treatment weekly for 10 weeks from a licensed psychologist who had been the principal cognitive therapist in an early empirical trial of CBT (39). Cognitive behavior therapy treats depression by using 1) behavioral strategies to re-involve patients in pleasurable social and physical activities; 2) problem-solving procedures to resolve stressful circumstances; and 3) cognitive techniques to identify distorted or maladaptive thought patterns and replace them with more accurate, adaptive, and useful views.

Study outcomes were measured immediately after the end of the 10-week treatment period and at a follow-up evaluation 6 months later. At each evaluation, assessments of diabetic control and depression were made and scored independently of one another. The study personnel who monitored patient progress were not involved in treatment, and assessors were blinded to treatment assignments. No additional study protocol treatment was provided after the end of the 10-week treatment period. Patients who remained depressed at that point (BDI score ≥ 10) were referred to their primary physician for antidepressant medication or to a psychotherapist. Glycemic control and severity of depression were measured again at the 6-month follow-up visit, and patients were restudied at that time with an abbreviated psychiatric interview. Self-monitoring of blood glucose levels was not measured after the end of the 10-week treatment period.

Statistical Analysis

Differences in the demographic and clinical characteristics of patients receiving CBT and controls were determined in the intention-to-treat and completer samples by using the Fisher exact test for categorical data and the Student *t*-test for continuous data. The results of an intention-to-treat analysis of the depression outcomes are provided for the purpose of comparison (40, 41). The analyses of study outcomes focused on the completer sample. Analyses of covariance (ANCOVAs) were used to determine the effects of treatment on symptoms of depression and glycemic control after treatment and at 6-month follow-up with beginning levels of the dependent measures (BDI score and GHb level) as the covariates. The post-treatment and follow-up BDI data were not normally distributed. Consequently, the scores were categorized and Fisher exact tests were used to analyze the data. We used ANCOVA for a secondary analysis after the continuous BDI data were transformed into van der Waerden normalized ranks (42). We also studied GHb levels by using *t*-tests of mean change scores over various intervals (for example, from before to after treatment or after treatment to follow-up). A repeated-measures analysis of variance (ANOVA) was used to determine the effects of treatment on compliance with the protocol for self-monitored blood glucose levels.

The clinical significance of individual depression outcomes (per BDI) was judged by using two standard conventions: A post-treatment score of 9 or less was used to denote remission of depression (34), and a post-treatment score equal to 50% or less of the pretreatment score was used to denote improvement (43). The clinical significance of the treatment findings was judged by using the approach described by Braitman (44). In this approach, a 95% CI is calculated around the point estimate (the difference between the percentages of patients responding to the two treatments). A number is specified that indicates the minimum difference between treatment responses needed to conclude that the experimental treatment has a clinically important advantage. This number is then compared with the CI around the point estimate. A claim that a treatment has clinically significant effects is supported if the CI falls entirely above the value representing the smallest important difference. On the basis of meta-analyses of acute-phase trials of treatment for depression, the smallest clinically important point estimate was set at 15% (40, 43, 45). Less is known about the sustained efficacy of different treatments for depression once treatment has been discontinued. Thus, discussion of the clinical significance of CBT was limited to the post-treatment findings.

Results

Participation Data and Demographic and Clinical Characteristics

One hundred thirty-five patients gave informed consent and were evaluated to determine their eli-

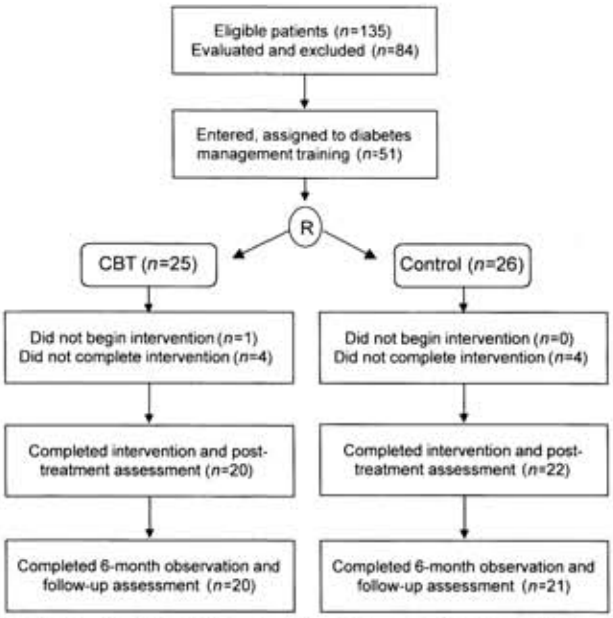

Figure 1. Study participation data. CBT = cognitive behavior therapy; R = randomization.

gibility (**Figure 1**). Eighty-four of these patients (62.2%) were excluded from participation, and 51 (37.8%) satisfied all inclusion criteria and were randomly assigned to study groups after completion of baseline assessment. Of the 84 excluded patients, 37 (44%) had scores lower than 14 on the BDI, 22 (26.2%) had exclusionary comorbid psychiatric conditions, 15 (17.9%) were receiving psychoactive medication and were unwilling or unable to discontinue it, and 10 (11.9%) decided against participation for miscellaneous reasons.

Of the 51 patients who were randomly assigned to treatment, 42 (82.4%) completed the 10 weeks of treatment and 9 (17.6%) discontinued participation prematurely (**Figure 1**). Of the 9 dropouts, 5 (55.6%) were in the CBT group and 4 (44.4%) were in the control group ($P > 0.2$). Only 1 patient withdrew because of assignment to the control group. No differences of more than 15% were seen between dropouts and completers on any of the measured demographic, depression, and clinical characteristics (age, race, sex, marital status, education, previous episodes and treatment of depression, duration of diabetes, type of diabetes treatment, prevalence of complications of diabetes [neuropathy, nephropathy, and retinopathy], and GHb levels and BDI scores before treatment). No evidence of differential attrition was seen. Follow-up data were obtained on all but 1 of the patients who completed treatment (41 of 42 [97.6%]). The patient who was lost to follow-up was in the control group. Only 5 of 18 patients (27.7%) who were depressed after the 10-week treatment period received treatment for their depression during the 6-month follow-up interval. All 5 of these patients had been in the control group, and all 5 took antidepressant medication during the follow-up interval, as prescribed by their primary care physicians.

Selected demographic, depression, and diabetes characteristics of the 42 patients who completed treatment are shown in the **Table**. No statistically significant differences were seen between the study groups in age, race, sex, education, marital status, BDI scores before treatment, history of depression treatment, number of previous episodes of depression, duration of diabetes, type of diabetes treatment (insulin or noninsulin), or GHb levels before treatment. The differences between the study groups in the prevalence of complications of diabetes, use of insulin, and duration of diabetes were not statistically significant but were relatively large. To assess potential confounding of depression treatment, these variables were analyzed in relation to the two depression outcome measures. Complications of diabetes were considered present if the patient had any of the measured complications (neuropathy, nephropathy, or retinopathy). A median split of the values for duration of diabetes was used to sort patients into groups with shorter (<6 years) or longer (≥6 years) duration of diabetes. Of the three variables, only duration of diabetes was associated with a measure of depression outcome. Patients with longer duration of diabetes were not less likely to achieve remission of depression but were less

Table. Selected Characteristics of the Study Sample*

Characteristic	Cognitive Behavior Therapy Group (*n* = 20)	Control Group (*n* = 22)
Mean age ± SD, *y*	53.1 ± 10.5	56.4 ± 9.7
Female sex, *n* (%)	12 (60.0)	13 (59.1)
Race, *n* (%)		
White	17 (85.0)	17 (77.3)
Nonwhite	3 (15.0)	5 (22.7)
Marital status, *n* (%)		
Married	10 (50.0)	12 (54.6)
Not married	10 (50.0)	10 (45.4)
Mean level of education ± SD, *y*	14.5 ± 2.3	13.6 ± 2.2
Mean duration of type 2 diabetes ± SD, *y*	9.9 ± 11.8	7.7 ± 7.0
Mean glycosylated hemoglobin level ± SD, %	10.2 ± 3.6	10.4 ± 3.1
Mean weight ± SD, *lb*	228.8 ± 61.9	211.0 ± 55.5
Complications of diabetes, *n* (%)		
Neuropathy	5 (25.0)	9 (40.9)
Nephropathy	0 (0.0)	0 (0.0)
Retinopathy	2 (10.0)	6 (27.3)
Insulin treatment, *n* (%)	7 (35.0)	11 (50.0)
Mean previous episodes of depression ± SD, *n*	4.1 ± 5.2	4.8 ± 3.5
Previous treatment of depression, *n* (%)	11 (55.0)	9 (40.9)
Mean Beck Depression Inventory score ± SD	24.9 ± 10.2	21.1 ± 6.8

* None of the differences between groups were statistically significant.

likely to realize a reduction in the severity of depression symptoms ($P = 0.03$). For this reason, duration of diabetes was included in all of the multivariable analyses (ANCOVA and ANOVA) of the depression outcome measures.

Effect of Treatment on Depression

Intention-To-Treat Analysis

In this analysis, dropouts were treated as if they did not achieve remission. At the post-treatment evaluation, the percentage of patients achieving remission of depression (BDI score ≤ 9) was greater in the CBT group than in the control group (70.8% [17 of 24] compared with 22.2% [6 of 27]; $P < 0.001$), as was the percentage of patients with clinical improvement (a decrease ≥ 50% in the BDI score) (66.6% [16 of 24] compared with 29.6% [8 of 27]; $P = 0.01$). At the 6-month follow-up evaluation, the percentage of patients in remission was greater in the CBT group than in the control group (58.3% [14 of 24] compared with 25.9% [7 of 27]; $P = 0.03$), as was the percentage of patients with clinical improvement (58.3% [14 of 24] compared with 29.6% [8 of 27]; $P = 0.01$).

Completer Analysis

The effect of treatment on depression at each evaluation point is shown in **Figure 2**. At the post-treatment evaluation, the percentage of patients achieving remission of depression was greater in the CBT group than in the control group (85.0% [17 of 20] compared with 27.3% [6 of 22]; difference, 57.7 percentage points [95% CI, 33 to 82 percentage points]; $P < 0.001$), as was the percentage of patients achieving a clinically significant improvement in symptoms of depression (a decrease ≥ 50% in BDI score) (80.0% [16 of 20] compared with 36.4% [8 of 22]; difference, 43.6 percentage points [CI, 17 to 71 percentage points]); $P < 0.001$). At follow-up, the percentage of patients in remission remained greater in the CBT group than in the control group (70.0% [14 of 20] compared with 33.3% [7 of 21]; difference, 36.7 percentage points [CI, 9 to 65 percentage points]; $P = 0.03$), as did the percentage of patients with clinical improvement (70.0% [14 to 20] compared with 38.1% [8 of 21]; difference, 31.9 percentage points [CI, 3.0 to 60 percentage points]; $P = 0.04$).

Depression outcomes were further studied by using an ANCOVA of the van der Waerden transformed BDI scores. Reduction in depression symptoms was greater, at both post-treatment and follow-up evaluations, in the CBT group than in the control group ($P < 0.001$ for post-treatment comparison and $P = 0.001$ for 6-month comparison).

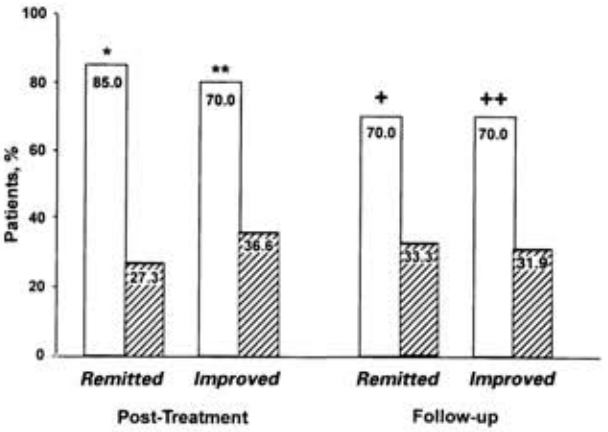

Figure 2. Percentages of patients with depression in remission and those with significantly improved depression at post-treatment and follow-up evaluations. A Beck Depression Inventory score of 9 or less was used to define remission; a score equal to 50% or less of the score before treatment was used to define improvement. A greater percentage of patients receiving cognitive behavior therapy (CBT) had remission or improvement at post-treatment and follow-up evaluations. Forty-two patients (20 in the CBT group and 22 controls) had post-treatment evaluation; 41 patients (20 in the CBT group and 21 controls) had 6-month evaluation. White bars represent the CBT group; striped bars represent controls. *$P < 0.001$; **$P = 0.01$; +$P = 0.03$; ++$P = 0.04$.

Association of Treatment with Glycemic Control

No statistically significant difference was seen in post-treatment GHb levels, adjusted for pretreatment GHb levels, between the CBT group ($n = 20$) and the control group ($n = 22$) (10.2% compared with 9.9%; $P = 0.17$). At follow-up, similarly adjusted mean GHb levels were lower in the CBT group (9.5% compared with 10.9%; $P = 0.03$). Change score analysis confirmed this finding; in the 6 months after treatment, GHb levels decreased by 0.7% in the CBT group and increased by 0.9% in the control group ($P = 0.04$) (**Figure 3**).

Association of Depression Remission with Glycemic Control

An analysis comparing responders with nonresponders was used to estimate the association of change in depression with change in glycemic control. Responders ($n = 18$) were patients whose depression remitted (BDI scores ≤ 9) at both post-treatment and follow-up evaluations. Nonresponders ($n = 11$) were patients with manifest depression (BDI scores ≥ 14) at both evaluation points. Covariate-adjusted mean GHb levels were lower in the nondepressed group at both the post-treatment (8.5% compared with 10.9%; $P = 0.003$) and follow-up (9.2% compared with 12.1%; $P = 0.006$) evaluations.

Association of Treatment with Compliance with Blood Glucose Monitoring

All patients practiced by using a memory glucometer for 1 week before randomization. Analysis of

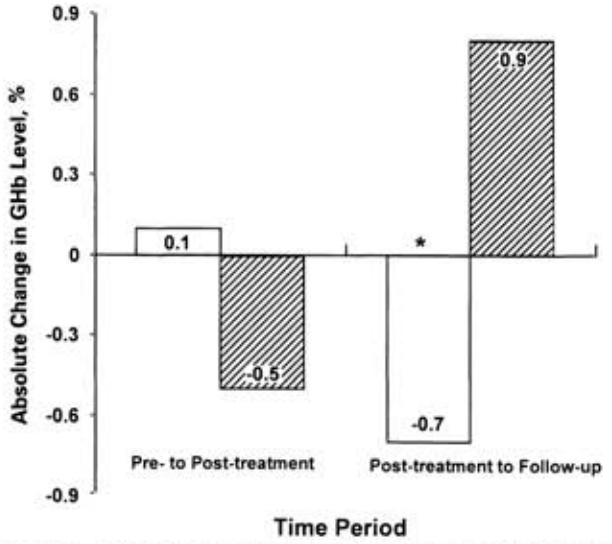

Figure 3. Absolute change in glycosylated hemoglobin (*GHb*) levels from pretreatment to post-treatment evaluations and from post-treatment to follow-up evaluations. Improvement in GHb levels during the follow-up interval was greater in the group receiving cognitive behavioral therapy (CBT) than in controls. Forty-two patients (20 in the CBT group and 22 controls) were evaluated immediately after treatment; 42 patients (20 in the CBT group and 21 controls) were evaluated at 6 months. White bars represent the CBT group; striped bars represent controls. *$P = 0.04$.

the pretreatment data showed no statistically significant differences in compliance with self-monitoring of blood glucose levels in the CBT group and the control group (78.2% compared with 72.7%; $P > 0.2$). A repeated-measures ANOVA was used to determine the association of treatment with weekly compliance over the 10-week treatment period (**Figure 4**). The ANOVA showed no statistically significant main effects (that is, effects of treatment or time). A time-by-treatment-group interaction indicated that over the 10-week treatment period, compliance with self-monitoring of blood glucose levels declined in the CBT group compared with the control group ($P = 0.01$).

Discussion

Our study shows that CBT combined with diabetes education is an effective nonpharmacologic treatment for major depression in patients with diabetes. The finding of depression remission in 70.8% of the intention-to-treat sample and 85.0% of the completer sample compares favorably with the outcomes reported in depressed, medically well outpatients receiving CBT (39, 46–50) and with the response to conventional antidepressant medication seen in the only controlled trial of depression in diabetes available to date (21). In that study, depression remitted in no more than 40% of the intention-to-treat and 57% of the completer sample treated with nortriptyline. Although the brevity of the follow-up interval limits our ability to make long-term projections, the data suggest that CBT combined with diabetes education may produce a more favorable prognosis for patients with depression and diabetes than that seen in earlier follow-up studies of diabetic patients with untreated (10) or nortriptyline-treated depression (51).

The difference in efficacy in the CBT and control groups was also clinically significant. Our 15–percentage point (15%) criterion for the smallest clinically important difference between treatments is based on meta-analyses of the literature on depression treatment (40, 43, 45). The 95% CIs for the difference between the percentage of patients in each study group that were in remission (33 to 82 percentage points) and for the difference between the percentage of patients in each study group that had clinical improvement (17 to 71 percentage points) fell entirely above 15 percentage points. This suggests that the addition of CBT offers a genuine clinical advantage in the management of depression in diabetes compared with the nonspecific intervention used in the controls.

Controls received an educational intervention aimed at improving diabetes self-care. This intervention is frequently used in clinical practice to improve glycemic control, instill feelings of self-control, and thereby create a sense of well-being. During the 10-week treatment period, patients in the control (education-only) group were substantially more compliant with self-monitoring of blood glucose levels and evidenced a mean improvement in GHb levels of 0.5%. Despite increased attention and measurable short-term improvements in diabetes control and compliance, however, only 27.7% of controls achieved remission of depression. This re-

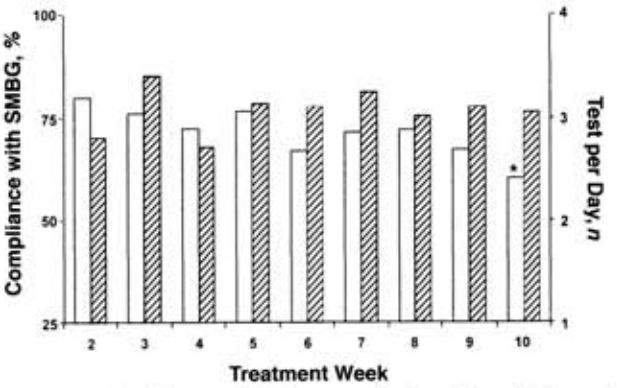

Figure 4. Compliance with the protocol for self-monitoring of blood glucose levels (*SMBG*). Over the 10-week treatment period, compliance declined in the group receiving cognitive behavioral therapy (CBT) compared with controls ($P = 0.01$). White bars represent the CBT group; striped bars represent controls.

sponse rate is no better than the rate reported with placebo and control treatment in meta-analyses of the literature on treatment of depression (40, 43, 45).

Depression is uniquely important in diabetes because its association with poor glycemic control increases the risk for retinopathy and cardiovascular disease. These associations, reported in both cross-sectional and prospective studies (3, 5, 9–14, 17–20), have led to clinical trials designed to determine whether alleviating depression improves medical outcome. In a recent placebo-controlled trial of nortriptyline, remission of depression was associated with clinically important improvements in GHb levels (21). Our study also suggests that remission of depression may favorably affect GHb levels, but it does not reveal the mechanism involved in this association. Improvement in depression may have salutary effects on a variety of behavioral practices (such as sleep practices, dietary practices, and physical activity) or physiologic paths (such as alterations in autonomic tone, hypothalamic–pituitary–adrenal axis activity, or neurotransmitter function) involved in glucose regulation.

An improvement in glycemic control in the CBT group was evident at follow-up but not at the post-treatment evaluation. Improvement in glycemic control may have lagged behind improvement in depression because of the biology of GHb formation and because the interval between GHb measurements taken before and after treatment spanned only 70 days. The GHb level is a "weighted" measure of mean blood glucose levels over the preceding 120-day period (35, 52). Although more recent events contribute relatively more than earlier events to the final result, approximately 25% of the variance in GHb levels is determined by the mean blood glucose level in the third and fourth months (days 60 to 120) before measurement (52). Thus, post-treatment GHb levels reflected points in time before study entry when all patients were depressed, as well as points in time early in treatment when many patients were still depressed. In contrast, follow-up GHb values better captured the beneficial influence of CBT on glycemic control because they reflected a 120-day period during which substantially more of the CBT group remained free of depression. Congruence in the time intervals assessed by measures of GHb and depression (or any psychosocial factor) is methodologically important. Incongruence in these intervals may help explain the inconsistent relation of depression to glycemic control observed in some previous studies (53, 54).

The addition of CBT to diabetes education had a statistically significant adverse effect on compliance with self-monitoring of blood glucose levels during the 10 weeks of treatment, an effect that we had not anticipated and cannot readily explain. We suspect that even though all patients received diabetes education, those who also received CBT viewed the depression intervention as the focus of treatment. As a consequence, their attention to self-monitoring of blood glucose levels decreased. Cognitive behavior therapy routinely included homework assignments directing patients to record their thoughts and increase various physical and social activities. Thus, it is possible that the participation of the CBT group in diabetes education complicated an already complex regimen and was more than the patients could handle. It is a well-established principle of compliance that any action that complicates a treatment regimen (such as adding a medication or using divided rather than single-dose schedules) usually decreases compliance with other components of treatment (55–57).

The generalizability of our findings is uncertain. First, our study was limited to a relatively small number of patients, and the 95% CIs around the point estimates spanned a wide range of plausible true values. When depression was measured in terms of the percentage of patients judged to be clinically improved, the lower limit of the 95% CI was 17%, a value close to that established for the smallest clinically important difference in the percentage of patients responding to the two treatments. Second, our follow-up interval was limited to the 6 months immediately after treatment. Third, we cannot exclude the possibility that CBT and diabetes education interacted in a way that potentiated antidepressant effectiveness; analogous interactions may have occurred in many clinical trials. Further studies comparing CBT and diabetes education, individually and in combination, are needed to answer such questions and to see whether successful CBT alone is sufficient to produce glycemic improvement. Fourth, it is worth noting that patients in the CBT group had education almost a full year longer than controls. The difference in education was not statistically significant, but the extra educational experience may have contributed to improved outcome in the CBT group. Finally, treatment was administered by a single psychologist experienced in the use of CBT (39). Whether treatment would be as effective when administered by other therapists is uncertain.

In conclusion, our study shows that CBT combined with diabetes education is an effective nonpharmacologic treatment for major depression in patients with type 2 diabetes. This therapy was associated with improvement in glycemic control despite its association with a decline in self-monitoring of blood glucose levels. Additional investigations of larger patient samples are needed to fully characterize the covariation of depression and glycemic control. Nevertheless, our study offers further evi-

dence linking health and emotional function by suggesting that improved mental health is related to improved medical outcome. Our findings support the importance of treating depression in patients with comorbid medical illness.

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Requests for Reprints: Patrick J. Lustman, PhD, Department of Psychiatry, Washington University School of Medicine, 4940 Children's Place, St. Louis, MO 63110.

Current Author Addresses: Drs. Lustman and Freedland and Ms. Griffith: Department of Psychiatry, Washington University School of Medicine, 4940 Children's Place, St. Louis, MO 63110.
Dr. Clouse: Department of Internal Medicine, Division of Gastroenterology, Children's Annex, Suite 417, 1 Barnes-Jewish Hospital Plaza, St. Louis, MO 63110.
Ms. Kissel: Department of Internal Medicine, Division of Metabolism, 660 North Euclid, St. Louis, MO 63110.

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