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Motivational Enhancement Therapy with and without Cognitive Behavior Therapy to Treat Type 1 Diabetes

A Randomized Trial

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Background: Although psychological issues can interfere with diabetes care, the effectiveness of psychological treatments in improving diabetes outcomes is uncertain.

Objective: To determine whether motivational enhancement therapy with or without cognitive behavior therapy improves glycemic control in type 1 diabetes compared with usual care.

Design: Randomized, controlled trial.

Setting: 8 diabetes centers in London and Manchester, United Kingdom.

Patients: 344 adults with type 1 diabetes for longer than 2 years, with hemoglobin A_{1c} levels of 8.2% to 15%, and without complications or severe comorbid disease.

Intervention: Nurse-delivered motivational enhancement therapy (4 sessions over 2 months), motivational enhancement therapy plus cognitive behavior therapy (12 sessions over 6 months), or usual care.

Measurements: 12-month change in hemoglobin A_{1c} levels (primary outcome), hypoglycemic events, depression, quality of life, fear of hypoglycemia, diabetes self-care activities, and body mass index (secondary outcomes).

Results: In an analysis including all randomly assigned patients, the 12-month change in hemoglobin A_{1c} levels compared with usual care was −0.46% (95% CI, −0.81% to −0.11%) in the motivational enhancement therapy plus cognitive behavior therapy group and −0.19% (CI, −0.53% to 0.16%) in the motivational enhancement therapy group alone. There was no evidence of treatment effects on secondary outcomes.

Limitations: Of 1659 screened patients, only 507 were eligible and 344 participated. Data on the primary outcome were unavailable for 11.3% of the participants. Study design did not permit distinction of the additive effect of cognitive behavior therapy plus motivational enhancement therapy from the effect of greater intensity and duration of the combined intervention compared with the motivational enhancement therapy alone.

Conclusion: Nurse-delivered motivational enhancement therapy and cognitive behavior therapy is feasible for adults with poorly controlled type 1 diabetes. Combined therapy results in modest 12-month improvement in hemoglobin A_{1c} levels compared with usual care, but motivational enhancement therapy alone does not.

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Suboptimal glycemic control in type 1 diabetes is common, despite the effectiveness of intensive insulin therapies, continuous subcutaneous insulin infusion pumps, and structured education programs (1–3). Depression, anxiety, and disordered eating patterns are common in persons with diabetes and are associated with suboptimal glycemic control, complications, and death (4–12). Diabetes-related anxieties related to hypoglycemia, complications, self-injections, and glucose self-testing are also well recognized (13, 14). The effectiveness of psychological treatments in improving glycemic control in adults with type 1 diabetes has not been established (15). One reason may be that previous trials have not specifically targeted the broad range of diabetes-related problems (15).

See also:

Print
Editors' Notes 709
Summary for Patients I-48

Web-Only
Appendix Table
Conversion of graphics into slides

Evidence in substance misuse settings suggests that adding cognitive behavior therapy to motivational enhancement therapy may increase efficacy (16). Motivational enhancement therapy is a brief (usually 1 to 4 sessions) counseling method for enhancing motivation to change problematic health behaviors by exploring and resolving the ambivalence about change (17). Motivational enhancement therapy is effective in improving alcohol misuse and smoking, and preliminary evidence suggests that it may be effective in diabetes (18, 19). Cognitive behavior therapy is a longer therapy (usually a minimum of 6 to 12 sessions) that aims to enable the patient to identify, challenge, and substitute unhelpful cognitions and behaviors with more constructive ones (20, 21). In diabetes, several trials have predominantly used behavioral techniques (22–25) and, more recently, cognitive techniques (26–28), but this novel method of integrating motivational enhancement therapy and cognitive behavior therapy has yet to be tested in diabetes settings.

One question we examined when we designed the trial was whether diabetes nurses could be trained to deliver

psychological treatments, because such a model of intervention could be used more widely than one that relied on psychologists. We added cognitive behavior therapy to motivational enhancement therapy as 1 of the interventions, rather than cognitive behavior therapy alone, because we aimed to reach a group of patients who had persistent problems with diabetes control and were more likely to be ambivalent about change. Our objective of this randomized, controlled trial (RCT) was to determine whether motivational enhancement therapy plus cognitive behavior therapy was more effective than usual care in improving glycemic control in adults with type 1 diabetes and persistent, suboptimal glycemic control and whether motivational enhancement therapy alone was more effective than usual care in improving glycemic control. The secondary objective was to assess whether either psychological intervention was more effective than usual care in improving depressive symptoms, fear of hypoglycemia, diabetes self-care behaviors, body mass index, and diabetes quality of life.

Context

Psychological issues can interfere with behavior modification that is necessary to manage type 1 diabetes, so psychological therapy might improve diabetes control.

Contribution

This randomized, controlled trial compared motivational enhancement therapy with and without cognitive behavior therapy with usual care in 344 adults with type 1 diabetes (average baseline hemoglobin A_{1c} level, 9.4%). Patients who received motivational enhancement therapy plus cognitive behavior therapy had a greater decrease in hemoglobin A_{1c} over 12 months than patients who received usual care (difference between groups, −0.46%). No other improvements were observed.

Implication

Motivational enhancement therapy plus cognitive behavior therapy led to only small improvements in diabetes control, despite a total of 16 therapy sessions prescribed over 6 months.

—The Editors

METHODS

Design

We followed the CONSORT (Consolidated Standards of Reporting Trials) guidelines (29). The Clinical Trials Unit, Institute of Psychiatry, King's College London, London, United Kingdom, sponsored the trial. The South West Multi-Centre Research Ethics Committee and the ethics committees of all participating hospitals approved the trial. A trial steering committee and data monitoring and ethics committee oversaw the conduct of the study. All participants provided signed informed consent.

Setting

Five hospitals in southeast London (King's College Hospital, Guy's and St Thomas' Hospitals, Lewisham Hospital, and Mayday University Hospital), and 3 hospitals in Greater Manchester (Manchester Royal Infirmary, North Manchester General, and Stockport General Hospital/Stepping Hill Hospitals), United Kingdom, served as the recruiting centers.

Participants

Local clinicians screened their hospital databases or lists to identify patients with type 1 diabetes. Adults (age 18 to 65 years) with type 1 diabetes for at least 2 years who had persistent, suboptimal glycemic control were candidates for inclusion into the study. Type 1 diabetes was defined as onset at age younger than 35 years and onset of insulin therapy within 6 months of diagnosis or ketones in the urine. Persistent, suboptimal glycemic control was defined as having at least 2 records of hemoglobin A_{1c} levels between 8.2% and 15%: one measurement in the past 12 months and the second being the current (in other words, at recruitment) hemoglobin A_{1c} level. We excluded participants if they did not speak English, were pregnant, had a short-term or serious medical illness defined by the treating physician, had advanced diabetes complications (registered blind, serum creatinine levels >300 μmol/L [>3.39 mg/dL]), had known hemaglobinopathy, had psychotic disorders, had alcohol dependence, were in psychotherapy, or had been in a structured diabetes education program less than 3 months previously. We did not exclude persons with major depression unless they were receiving antidepressant therapy initiated less than 2 months prior. Before patients were randomly assigned, they had at least 1 session of nurse-delivered diabetes education and received a fact sheet containing the minimum accepted level of diabetes knowledge (30). The hemoglobin A_{1c} level was measured by ion-exchange, high-pressure liquid chromatography by using analyzers at each participating clinic: Menarini HA-8140, HA-8121, or HA-8160 (Menarini Diagnostics, Florence, Italy); Tosoh 2.2 Plus (Tosoh Medics, Foster City, California); or Variant II HPLC System (Bio-Rad Laboratories, Hercules, California), by using methods aligned with the Diabetes Control and Complications Trial (1, 31).

Baseline Measures

We collected data on the following baseline characteristics: sociodemographic factors (age, sex, employment status, educational level, ethnicity, marital status); lifestyle factors (current smoking status and units of alcohol intake per week); physical health (hemoglobin A_{1c} level); resting blood pressure (mm Hg), body mass index (kg/m^2); total random cholesterol level (μmoL/L [mg/dL]); duration of diabetes (years); presence of diabetes complications (early morning albumin–creatinine ratio level); peripheral neu-

ropathy (screened using the 10-g monofilament); retinopathy status coded as none or any (treated, non–sight-threatening, and sight-threatening) from retinal color photographs or fundoscopy assessments; and depressive symptoms assessed on the well-validated and reliable self-reported Patient Health Questionnaire-9 (score range, 0 to 27; scores ≥10 represent major depressive disorder) (32). We measured diabetes-related cognitions and behaviors on the revised Hypoglycaemia Fear Survey (33, 34), which consists of 10 behavior items (score range, 0 to 40) and 13 worry items (score range, 0 to 52) self-rated on 5-point Likert scales. The revised Summary of Diabetes Self-Care Activities asks how many days in the last 7 days the participant engaged in diet, exercise, and blood sugar testing (score range, 0 to 7 days) (35). Higher scores denote a greater tendency to maintain high blood glucose levels and fear of hypoglycemia, respectively. Quality of life was measured by satisfaction and impact subscales of the Diabetes Quality of Life scale (score range per subscale, 1 to 5) (36).

Randomization

We prepared a computer-generated randomization list, stratified by hospital site, which used blocks of random sizes (3, 6, 9, and 12) in advance. The database manager of the Clinical Trials Unit, who was independent of the study, held the list electronically in a password-protected database. Allocation could only be revealed to the recruiting researcher, who then assigned each participant after obtaining consent. We collected all baseline measures before randomization. The laboratory technicians, who were blinded to the allocation throughout the study and the self-reported psychological measures, assessed hemoglobin A_{1c} levels, which was the main outcome. The researchers, study participants, and nurse therapists were not blinded to allocation after randomization because of the nature of delivering psychological treatments.

Interventions

Usual Care

All 3 groups continued to receive usual diabetes care. The participating hospitals agreed to a protocol of minimum standards of diabetes care for persons with suboptimal glycemic control on the basis of national guidelines aiming toward hemoglobin A_{1c} levels of 7% or less with no problematic hypoglycemia (30). The frequency of clinic attendance was expected to vary depending on patient and clinic factors, but all patients were offered a minimum of 2 to 4 clinic appointments per year. At the time of the study, 2 hospital centers offered basal–bolus intensive insulin therapy in combination with structured education programs and continuous, subcutaneous insulin infusion pumps (King's College Hospital and Guy's and St Thomas' Hospitals) (3). Treatment protocols did not substantially change during the study.

Usual Care with Motivational Enhancement Therapy

We developed a diabetes-specific motivational enhancement therapy manual for therapists and an accompanying patient workbook (available on request). Over 2 months, we offered participants 4 individual face-to-face sessions that lasted 50 minutes each. The first session was a standardized, computerized self-assessment of behaviors relevant to diabetes (exercise, smoking, diet, diabetes medication, blood sugar, and testing) followed by feedback and an assessment of the rating of the level of importance, confidence, and readiness to change (37). The remaining sessions included discussion of obstacles and options to change behaviors, with an emphasis on patients' own problem-solving skills and the collaborative formulation of a plan to change. Homework writing tasks designed to increase motivation supplemented the therapy (17).

Usual Care with Motivational Enhancement Therapy plus Cognitive Behavior Therapy

We offered participants 4 sessions of motivational enhancement therapy over 2 months, followed by 8 sessions of cognitive behavior therapy for an additional 4 months. We developed a diabetes-specific cognitive behavior therapy manual (available on request) for patients on the basis of Lang's (20) 3 systems model and Beck's (21) cognitive model of emotional disorders. We developed a collaborative, individualized program for each participant. We structured each session around agenda setting, homework planning, and feedback. We included such strategies as normalizing dietary, exercise, and diabetes-related self-monitoring and lifestyle-related behaviors; anxiety, worry, and stress management; challenging diabetes-specific, negative automatic thoughts; improving impulse control; behavioral experiments; activity scheduling; strategies for eliciting social support; and assertiveness training.

Training of Diabetes Nurses

We trained 6 nurses over 3 months. Training consisted of an introductory workshop followed by self-directed learning from transcription of recorded sessions and a syllabus of reading material, audiovisual feedback, weekly group and individual supervision for a training caseload of 10 patients with type 1 diabetes, and problematic diabetes control of persons who did not participate in the trial. We used progressive ratings of competency and skill, and nurses did not take on study participants until they were competent and skilled in motivational enhancement therapy and cognitive behavior therapy using the quality assurance criteria. We delivered all sessions in the diabetes clinics at times separate from clinic visits for usual care.

Assessment of Quality Assurance

To check therapists' adherence to the treatment protocol, we rated a random sample of 20 tapes of session 3 from all patients who were randomly assigned to either therapy group and 20 tapes of session 7 from the motivational enhancement therapy plus cognitive behavior ther-

apy group for procedures considered specific to each treatment. We used the Motivational Interviewing Treatment Integrity Code, version 2.0, to score a range of motivational enhancement therapy skills, such as empathy, spirit, and collaboration (score range, 1 to 7 on a Likert scale; score ≥5 defined as minimum for adherence) (38, 39). We used the Cognitive Therapy Rating Scale-Revised to score a range of cognitive behavior therapy skills (score range, 0 to 72; score ≥40 defined as minimum for adherence) (40). The acceptable mean scores for the 6 nurses for motivational enhancement therapy (such as empathy, acceptance, and collaboration) were 5.1 (range, 4.0 to 6.5), 5.3 (range, 4.5 to 7.0), and 5.1 (range, 2.5 to 6.5), respectively, and the mean total of the Cognitive Therapy Rating Scale-Revised score was 52.1 (range, 41 to 62) for cognitive behavior therapy. Therapist competency was supported by adherence to the manuals and by weekly individual and group supervision during the trial.

Outcomes

The main outcome was change in hemoglobin A_{1c} levels from baseline to 12 months from randomization. We also measured hemoglobin A_{1c} levels at quarterly intervals. The secondary outcomes were changes from baseline to 12 months in the Patient Health Questionnaire-9 score, Hypoglycaemia Fear Survey score, Summary of Diabetes Self-Care Activities score, body mass index, and the Diabetes Quality of Life score.

We calculated the unit costs for motivational enhancement therapy and cognitive behavior therapy in pounds sterling at 2005 to 2006 prices. Indications in U.S. dollars are based on a 2006 purchasing power conversion rate of £1 = $1.534 (41). Costs include contact and noncontact time inputs of the nurse therapists and the specialists who trained and supervised them, appropriate overheads, salary costs, and materials.

Harmful Events Monitoring

We asked all participants about the number of severe hypoglycemia episodes (that is, events requiring third-party assistance) in the 12 months before randomization and during the 12-month follow-up.

Sample Size Calculation

This was based on a hypothesized 0.8% difference in hemoglobin A_{1c} levels in the motivational enhancement therapy plus cognitive behavior therapy group (or motivational enhancement therapy alone group) compared with usual diabetes care. We assumed that the SD of the changes was approximately 1.65 (15). At a power of 90%, a type I error rate of 0.05 (2-tailed), a randomization ratio of 1:1:1, and a 20% withdrawal rate, we estimated a sample size of 339 participants (n = 113 in each group).

Statistical Analysis

We analyzed data by using Stata, version 9 (StataCorp, College Station, Texas); SAS software, version 9.1 (SAS Institute, Cary, North Carolina); and R, version 2.7.1 (www.R-project.org). We compared baseline characteristics to assess the effectiveness of randomization.

We used a linear mixed model to analyze the hemoglobin A_{1c} levels (main outcome) from all follow-up intervals as repeated-measures data using fixed effects of time, group, baseline hemoglobin A_{1c} levels, and interactions between group and baseline hemoglobin A_{1c} levels with time by using SAS Proc Mixed (42). We entered time as a categorical variable to avoid making a parametric assumption for the evolution of hemoglobin A_{1c} levels over time. An unstructured residual variance–covariance matrix was used to allow for the correlations between hemoglobin A_{1c} levels within patients.

We examined which baseline variables, including those that were subject to be missing, and postrandomization variables, such as therapy completion, were associated with missing a hemoglobin A_{1c} measurement. Those variables found to be associated with missing a hemoglobin A_{1c} measurement or were predictive of hemoglobin A_{1c} were used to impute the missing measurements by using a multivariate imputation model, fitted using SAS Proc Mixed (42). Multiple imputation gives unbiased estimates under the missing-at-random assumption (43). We fitted the linear mixed model for a hemoglobin A_{1c} level (previously described) to each imputed data set and combined the results using Rubin rules (43).

To assess sensitivity of these results to the missing-at-random assumption, we conducted a simple sensitivity analysis. We used multiple imputations to impute the missing 12-month hemoglobin A_{1c} measurements, using the same imputation model as we did for the main analysis, except that intermediate measurements of hemoglobin A_{1c} levels were not used because dropout bias is likely to vary according to the availability of intermediate measurements (44). For various scenarios of nondifferential nonresponse and differential nonresponse, a fixed amount was added to the imputed 12-month hemoglobin A_{1c} levels, and the results were reanalyzed by using analysis of covariance and combined by using Rubin rules.

We analyzed the baseline and 12-month measurements of secondary outcomes (change in depressive symptoms, fear of hypoglycemia, diabetes self-care behaviors, body mass index, and quality of life) as repeated measures in a linear mixed model with no random effects and an unstructured residual variance–covariance matrix. We included all patients with either a baseline or 12-month follow-up measurement available in the analyses. We specified a common baseline mean so that estimated differences between groups at 12 months were adjusted for baseline (45). We analyzed the number of severe hypoglycemia events in the previous 12 months (reported at 12 months) by using the same linear mixed model.

Role of the Funding Source

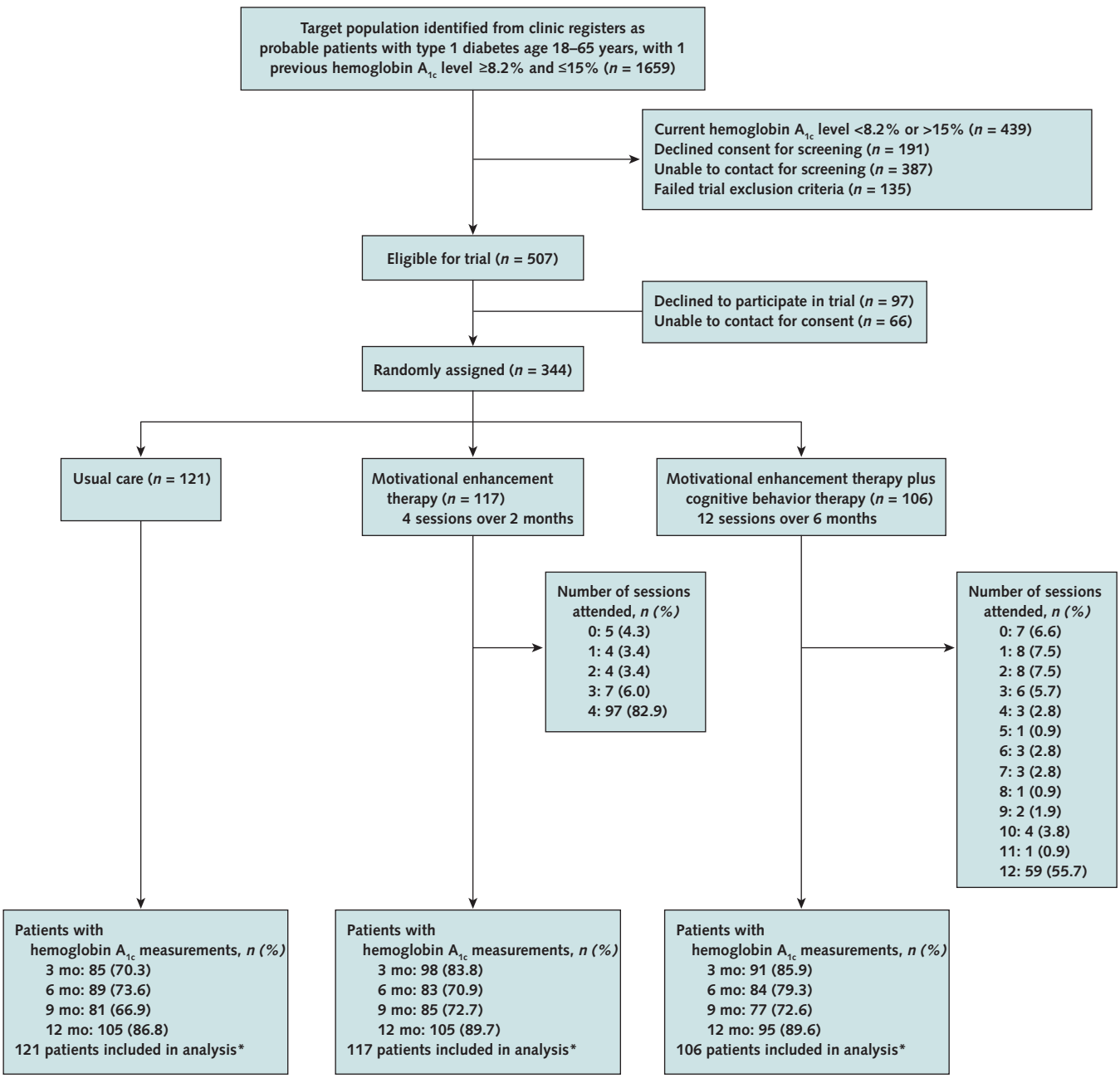
The United Kingdom Department of Health's Health Technology Assessment Programme funded the study

(project no. 01/17/05). The funding source had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

RESULTS

Figure 1 shows the study flow diagram. We identified a total of 1659 persons with a diagnosis of type 1 diabetes from clinic registers. We deemed 507 adults eligible, 344 of whom consented to participate. We recruited participants from September 2003 to August 2005 and followed them until November 2006. The proportion of participants allocated to motivational enhancement therapy ($n = 117$) and motivational enhancement therapy plus cognitive behavior therapy ($n = 106$) who completed their planned therapy (and

Figure 1. **Study flow diagram.**



* Primary analysis was based on linear mixed models using data from all participants since all participants had at least baseline hemoglobin A_{1c} levels measured.

Table 1. **Baseline Characteristics of Participants Randomly Assigned to Receive Motivational Enhancement Therapy plus Cognitive Behavior Therapy Compared with Motivational Enhancement Therapy Alone or Usual Care***

Explanatory Variable	Motivational Enhancement Therapy plus Cognitive Behavior Therapy (*n* = 106)	Motivational Enhancement Therapy (*n* = 117)	Usual Care (*n* = 121)
Mean age (IQR), *y*	36.6 (29.9–44.4)	35.7 (28.4–42.3)	36.0 (25.8–44.5)
Women, *n (%)*	66 (62.3)	76 (65.0)	66 (54.6)
Ethnicity, *n (%)*			
White	84 (79.2)	88 (75.2)	104 (86.0)
Black or other	22 (20.8)	29 (24.8)	17 (14.1)
Marital status, *n (%)*			
Single	38 (36.2)	51 (43.6)	61 (50.4)
Married or cohabiting	56 (53.3)	55 (47.0)	47 (38.8)
Separated, divorced, or widowed	11 (10.5)	11 (9.4)	13 (10.7)
Education level, *n (%)*			
No formal qualifications	14 (13.9)	17 (15.0)	14 (11.7)
High school qualifications (age 16 years)	30 (29.7)	39 (34.5)	37 (30.8)
College qualifications or more (age ≥18 years)	57 (56.4)	57 (50.4)	69 (57.5)
Smoking status, *n (%)*			
Current	37 (36.3)	32 (28.3)	30 (25.2)
Former	11 (10.8)	17 (15.0)	22 (18.5)
Never	54 (52.9)	64 (56.6)	67 (56.3)
Median alcohol intake (IQR), *units/wk*	3 (0–10)	4 (0–10)	2 (0–12)
Median duration of diabetes (IQR), *y*	18.6 (12.0–24.6)	16.4 (10.2–23.0)	18.7 (10.6–26.8)
Median hemoglobin A_{1c} level (IQR), %	9.25 (8.6–10.3)	9.4 (8.8–9.9)	9.4 (8.8–10.2)
Median body mass index (IQR), kg/m^2	25.3 (22.9–28.0)	25.8 (22.9–28.6)	25.4 (22.9–28.6)
Median blood pressure (IQR), *mm Hg*			
Systolic	127.5 (114–138)	126 (115–136)	125 (117–135)
Diastolic	75 (70–81.5)	76 (70–82)	77 (71–81)
Median cholesterol level (IQR)			
mmol/L	5.05 (4.5–5.6)	4.75 (4.3–5.4)	4.7 (4.1–5.4)
mg/dL	195.00 (173.75–216.22)	183.40 (163.02–208.50)	181.47 (158.30–208.50)
Neuropathy (screened by using the 10-g monofilament), *n (%)*	19 (25.7)	21 (22.3)	16 (17.8)
Median albumin–creatinine ratio (IQR)	1.5 (0.6–2.9)	1.5 (0.6–3.4)	1.9 (0.7–5.2)
Retinopathy, *n (%)*			
None	28 (29.8)	32 (32.7)	29 (28.7)
Any	66 (70.2)	66 (67.3)	72 (71.3)
Depressive symptoms			
Patient Health Questionnaire-9 score (IQR) (score range, 0–27)†	6 (3–12)	6 (3–10)	6 (3–10)
Hypoglycaemia Fear Survey score (IQR)†			
Behavior subscale (score range, 0–40)	29 (24.5–32)	28 (24–32)	29.5 (26–33)
Worry subscale (score range, 0–52)	32 (25–39)	33 (26–42)	30 (25–37.5)
Summary of Diabetes Self-Care Activities score (IQR)†			
Diet subscale (score range, 0–7 d/wk)	4.2 (2.6–5)	3.8 (2.2–5.2)	4 (2.8–5.2)
Exercise subscale (score range, 0–7 d/wk)	2.5 (1–4.5)	2.5 (0.5–3.5)	2.5 (1–4.5)
Self-monitoring blood glucose subscale (score range, 0–7 d/wk)	5 (2.5–7)	4.5 (1.5–7)	5.5 (2–7)
Diabetes Quality of Life score (IQR) (score range, 1–5)†			
Satisfaction subscale	2.67 (2.2–3.0)	2.87 (2.33–3.2)	2.57 (2.3–3)
Impact subscale	2.25 (1.95–2.75)	2.23 (1.9–2.65)	2.15 (1.85–2.75)
Severe hypoglycemia episodes in past 12 mo, *n (%)*			
0	59 (66.3)	76 (73.8)	75 (77.3)
1–5	26 (29.2)	21 (20.4)	18 (18.6)
>5	4 (4.5)	6 (5.8)	4 (4.1)

IQR = interquartile range.
* Values were missing for marital status (*n* = 1), education (*n* = 10), smoking status (*n* = 10), alcohol intake (*n* = 25), body mass index (*n* = 13), blood pressure (*n* = 14), cholesterol (*n* = 33), neuropathy (*n* = 86), albumin–creatinine ratio (*n* = 157), retinopathy (*n* = 51), Patient Health Questionnaire-9 score (*n* = 29), Hypoglycaemia Fear Survey score (behavior [*n* = 14] and worry [*n* = 70]), Summary of Diabetes Self-Care Activities score (diet [*n* = 17], exercise [*n* = 9], and self-monitoring blood glucose levels [*n* = 17]), Diabetes Quality of Life score (satisfaction [*n* = 50] and impact [*n* = 56]), and hypoglycemia episodes (*n* = 55).
† Higher scores on Patient Health Questionnaire-9, Hypoglycaemia Fear Survey, and Diabetes Quality of Life indicate worse health, and higher scores on Summary of Diabetes Self-Care Activities indicate increased frequency of self-care activities.

the average time to do so) was 90% (3 months [SD, 1.8]) and 55% (6.8 months [SD, 1.8]), respectively (**Figure 1**).

Protocol Violations

After randomization, 2 study participants did not meet the criteria for type 1 diabetes: One received a diagnosis of gestational diabetes and later type 2 diabetes and required insulin therapy, and the other received a diagnosis of steroid-induced diabetes. A third participant should have been excluded because we discovered that this participant had manic depression. All 3 patients remained in the study and are included in the analyses.

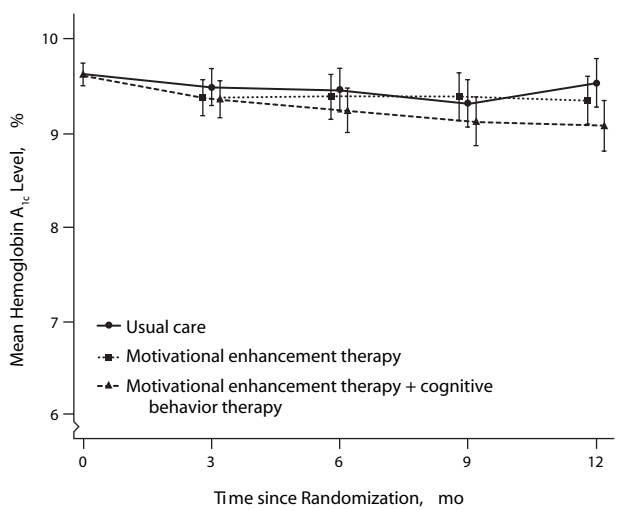
Baseline Characteristics

Table 1 shows the baseline characteristics. There were no statistically significant differences between groups at baseline. There were slightly more women, and most participants were in their mid-30s, were employed, and had either high school qualifications (age 16 years) or above. One fifth of women were nonwhite, and most had clinically significant depressive symptoms. The median duration of diabetes was nearly 18 years (interquartile range, 10.6 to 24.8 years), and the baseline median hemoglobin A_{1c} level was 9.4% (interquartile range, 8.8% to 10.2%) (**Table 1**).

Change in Hemoglobin A_{1c} Levels

Of the 344 randomly assigned patients, 39 (11.3%) did not have a 12-month hemoglobin A_{1c} measurement. At the 3-, 6-, and 9-month follow-ups, 70 (20.3%), 88 (25.6%), and 101 (29.4%) patients did not have hemoglobin A_{1c} measurements, respectively. A larger proportion of the usual care group missed their hemoglobin A_{1c} measurement than in the 2 intervention groups at 3, 9, and 12 months, although the difference was only significant at 3 months ($P = 0.007$). Within the interventions groups, strong evidence suggested that not completing all therapy sessions was associated with missing a hemoglobin A_{1c} measurement at 3 ($P < 0.001$), 6 ($P < 0.001$), 9 ($P = 0.001$), and 12 ($P = 0.006$) months. Age, hospital, baseline depression Patient Health Questionnaire-9 score, and ethnicity were all statistically significantly associated with missing values of hemoglobin A_{1c} levels at at least 1 quarterly interval. No evidence suggested that either baseline hemoglobin A_{1c} levels or therapist (within the intervention groups) was associated with missing a hemoglobin A_{1c} measurement at any interval.

Figure 2. **Estimated quarterly mean hemoglobin A_{1c} levels (95% CI), by intervention group.**



Results based on 1000 imputed data sets generated by using a multivariate imputation model.

Figure 2 and the **Appendix Table** (available at www.annals.org) show the estimated baseline adjusted mean hemoglobin A_{1c} level at each interval. At 3 months, the motivational enhancement therapy alone and the motivational enhancement therapy plus cognitive behavior therapy groups had a minimal decrease in hemoglobin A_{1c} levels (about 0.1%) compared with usual care. At 6 months, the effect of motivational enhancement therapy compared with usual care was slightly less, whereas that of motivational enhancement therapy plus cognitive behavior therapy compared with usual care increased further. At 9 months, hemoglobin A_{1c} levels increased by 0.07% in the motivational enhancement group compared with usual care, whereas for motivational enhancement therapy plus cognitive behavior therapy, the hemoglobin A_{1c} level was, on average, 0.19% less than that in the usual care group. At 12 months, an increase in the hemoglobin A_{1c} level in the usual care group led to a larger effect of both therapy groups, with the motivational enhancement therapy plus cognitive behavior therapy versus usual care difference increasing to nearly 0.5% (**Figure 2** and **Table 2**).

The estimated differences in time-averaged treatment effects of change in hemoglobin A_{1c} levels were −0.07% (95% CI, −0.31% to 0.16%) for motivational enhancement therapy versus usual care and −0.25% (CI, −0.49% to −0.01%) for motivational enhancement therapy plus cognitive behavior therapy versus usual care (**Appendix Table**, available at www.annals.org).

Missing Data Sensitivity Analysis for the Main Outcome

The results based on multiple imputations that did not use intermediate measurements of hemoglobin A_{1c} levels were similar to those that did. The baseline adjusted mean hemoglobin A_{1c} level at 12 months in the motivational enhancement therapy plus cognitive behavior therapy group was 0.48% less (CI, 0.12% to 0.84% less) than that in the usual care group, whereas it was 0.19% less (CI, 0.17% greater to 0.54% less) in the motivational enhancement therapy than that in the usual care group.

The analysis for assessing the sensitivity of the results to the missing-at-random assumption showed that the results were largely unchanged if nonresponse bias is nondifferential (that is, the same in each treatment group). This is to be expected because the proportion of patients with missing 12-month hemoglobin A_{1c} levels was similar in all 3 treatment groups. When we assumed a differential nonresponse bias, the estimates of motivational enhancement therapy plus cognitive behavior therapy versus usual care difference ranged from 0.28% (CI, −0.11% to 0.66%) to 0.74% (CI, 0.36% to 1.13%) less in the motivational enhancement therapy plus cognitive behavior therapy group. Similarly, the estimates of the motivational enhancement therapy versus usual care difference ranged from 0.02%

Table 2. **Estimated Differences in Hemoglobin A_{1c} Levels between Groups at Quarterly Intervals (Primary Outcome), Adjusted for Baseline Hemoglobin A_{1c} Levels and Secondary Outcomes at 12 Months***

Outcome	Participants with Baseline or Follow-up Measurements, *n*†	Participants with Baseline and Follow-up Measurements, *n*	Estimated Mean Difference: Motivational Enhancement Therapy vs. Usual Care (95% CI)	Estimated Mean Difference: Motivational Enhancement Therapy plus Cognitive Behavior Therapy vs. Usual Care (95% CI)
Primary				
Hemoglobin A_{1c} level measured at follow-up, %‡				
3 mo	344	274	−0.11 (−0.35 to 0.14)	−0.13 (−0.38 to 0.12)
6 mo	344	256	−0.07 (−0.38 to 0.24)	−0.22 (−0.52 to 0.09)
9 mo	344	243	0.07 (−0.27 to 0.41)	−0.19 (−0.53 to 0.15)
12 mo	344	305	−0.19 (−0.53 to 0.16)	−0.46 (−0.81 to −0.11)
Time-averaged hemoglobin A_{1c} level, %§	344	164	−0.07 (−0.31 to 0.16)	−0.25 (−0.49 to −0.01)
Secondary				
Body mass index, kg/m^2	331	263	−0.35 (−0.77 to 0.07)	−0.21 (−0.62 to 0.20)
Reported severe hypoglycemia episodes in past 12 mo, *n*	311	233	−0.79 (−1.76 to 0.17)	−0.62 (−1.61 to 0.38)
Hypoglycaemia Fear Survey score‖				
Behavior subscale (score range, 0–40)	339	241	0.07 (−1.21 to 1.35)	−0.35 (−1.56 to 0.85)
Worry subscale (score range, 0–52)	304	176	0.66 (−1.90 to 3.22)	−1.79 (−4.31 to 0.72)
Depression status‖				
Patient Health Questionnaire-9 score (score range, 0–27)	337	235	0.02 (−1.18 to 1.21)	1.10 (−0.28 to 2.48)
Diabetes Quality of Life score‖				
Satisfaction subscale (score range, 1–5)	331	225	−0.08 (−0.20 to 0.05)	0.04 (−0.10 to 0.18)
Impact subscale (score range, 1–5)	326	206	−0.04 (−0.14 to 0.05)	−0.04 (−0.14 to 0.07)
Summary of Diabetes Self-Care Activities score¶				
Diet (score range, 0–7 d/wk)	336	244	−0.06 (−0.40 to 0.28)	0.05 (−0.31 to 0.42)
Exercise (score range, 0–7 d/wk)	339	255	−0.04 (−0.57 to 0.49)	0.00 (−0.55 to 0.56)
Blood glucose testing (score range, 0–7 d/wk)	335	244	0.14 (−0.44 to 0.71)	−0.06 (−0.60 to 0.49)

*Adjusted for their respective baseline values.
† 12-month measurement for secondary end points are included in linear mixed-model analysis.
‡ Estimates based on linear mixed-model analysis with fixed effects of time (categorical), treatment, and baseline glycated hemoglobin A_{1c} levels; their interactions with time; and an unstructured residual variance–covariance matrix. Results based on 1000 imputed data sets generated by using a multivariate imputation model.
§ Average results of 3-, 6-, 9-, and 12-month glycated hemoglobin A_{1c} measurements.
‖ Negative change score represents improvement in symptoms.
¶ Positive change score represents increase in frequency of self-care activities.

greater (CI, −0.36% to 0.40%) to 0.45% less (CI, 0.07% to 0.82%) (**Table 3**).

Secondary Outcomes

Statistically, neither motivational enhancement therapy alone nor motivational enhancement therapy plus cognitive behavior therapy were effective in improving any of the secondary outcomes (**Table 2**).

Adverse Events (Severe Hypoglycemia Events)

Thirty-three participants had missing baseline and 12-month values for the number of severe hypoglycemia events. Based on a linear mixed model analysis of data from the 311 participants with data at either baseline or 12 months, the estimated mean number of reported severe hypoglycemia events at 12 months was 0.79 (CI, −0.17 to 1.76) less in the motivational enhancement therapy group than in the usual care group and 0.62 (CI, −0.38 to 1.61) less in the motivational enhancement therapy plus cognitive behavior therapy group than in the usual care group, but the data were statistically consistent with no effects.

Cost of Intervention

The unit costs, including training and supervision, for the motivational enhancement therapy and the motivational enhancement therapy plus cognitive behavior therapy interventions were £49 ($75) and £81 ($124) per session, respectively.

DISCUSSION

Our RCT in adults with type 1 diabetes tested whether psychological treatments delivered by nurses could improve glycemic control over 12 months. Motivational enhancement therapy plus cognitive behavior therapy was associated with a decrease in hemoglobin A_{1c} levels by half compared with usual diabetes care. Although the effect of motivational enhancement therapy did not differ statistically from that of usual care, the upper CI limit for its effect reached a 0.5% reduction in hemoglobin A_{1c} levels, and thus the results about motivational enhancement therapy alone are not definitive. We achieved high follow-up rates for the 12-month outcome assessments. No evidence

Table 3. **Sensitivity to Missing Values of Estimated Intervention Effects on Hemoglobin A_{1c} Levels at 12 Months**

Nonresponse Scenario*			Mean Estimated Difference in 12-Month Hemoglobin A_{1c} Level If Nonresponse Bias Was Assumed (95% CI), %	
Usual Care	Motivational Enhancement Therapy	Motivational Enhancement Therapy plus Cognitive Behavior Therapy	Motivational Enhancement Therapy vs. Usual Care	Motivational Enhancement Therapy plus Cognitive Behavior Therapy vs. Usual Care
Scenario 1: No bias due to nonresponse†				
0	0	0	−0.19 (−0.54 to 0.17)	−0.48 (−0.84 to −0.12)
Scenario 2: Nondifferential nonresponse bias‡				
+1	+1	+1	−0.22 (−0.58 to 0.15)	−0.51 (−0.88 to −0.14)
+2	+2	+2	−0.24 (−0.64 to 0.15)	−0.54 (−0.94 to −0.13)
−1	−1	−1	−0.16 (−0.51 to 0.20)	−0.45 (−0.82 to −0.09)
Scenario 3: Differential nonresponse bias§				
0	+1	+1	−0.08 (−0.45 to 0.28)	−0.38 (−0.75 to −0.01)
0	+2	+2	0.02 (−0.36 to 0.40)	−0.28 (−0.66 to 0.11)
+1	0	0	−0.32 (−0.68 to 0.04)	−0.61 (−0.98 to −0.25)
+2	0	0	−0.45 (−0.82 to −0.07)	−0.74 (−1.13 to −0.36)

* The amount of hemoglobin A_{1c} measurements in percentage units that was added to multiply imputed missing 12-month hemoglobin A_{1c} measurements (%).
† Scenario 1: Assumed 0 nonresponse bias and is based on analyzing values imputed under the missing-at-random assumption.
‡ Scenario 2: Sensitivity analyses that assumed nondifferential nonresponse and assumed all participants with missing 12-month hemoglobin A_{1c} measurements were either 1% or 2% systematically greater or 1% less than their imputed value, regardless of intervention group. For example, a participant with an imputed missing 12-month hemoglobin A_{1c} level of 8.5% would be given a value of 9.5% (+1, +1, +1).
§ Scenario 3: Sensitivity analyses assuming differential nonresponse and assumed that participants' missing 12-month hemoglobin A_{1c} measurements were either 1% or 2% greater than their values imputed under the missing-at-random assumption (in the intervention groups [motivational enhancement therapy or motivational enhancement therapy plus cognitive behavior therapy]) or were 1% or 2% greater (in the usual care group).

indicated that the interventions affected the secondary outcomes (body mass index, depressive symptoms, fear of hypoglycemia, diabetes self-care behaviors, or quality of life). Nurses can be trained to competently deliver diabetes-specific psychological treatments. These findings support the case that a combination of motivational enhancement therapy plus cognitive behavior therapy may be an adjunct to medical regimens in type 1 diabetes, but the modest improvements observed are of limited clinical significance because many patients did not meet target levels of hemoglobin A_{1c}.

We targeted a vulnerable group of persons with diabetes, most of whom had had diabetes for nearly 2 decades, who were struggling to optimize their glycemic control. They had a higher prevalence of depression than other samples with type 1 diabetes (46, 47) and increased rates of early microvascular complications. We used a multicenter, consecutive screening of diabetes registers to minimize selection biases, and this ensured a diverse socioeconomic and multiethnic sample.

We compared 2 psychological treatments rather than 1 with usual care, which partially controlled for the effects of attention. The initial effects of motivational enhancement therapy in both interventions were equally small but increased over time in the motivational enhancement therapy plus cognitive behavior therapy group. This may be because of techniques specific to cognitive behavior therapy, but we could not test this. In clinical settings, cognitive behavior therapy is most effective when patients are motivated to change their behaviors. The Combining Medications and Behavioral Interventions study shows that motivational enhancement strategies to enhance intrinsic motivation and resolve ambivalence for change as a prelude to cognitive behavior therapy may optimize psychotherapy effectiveness (16, 48). We used motivational enhancement therapy to formulate the problems in diabetes self-care that the patient wanted to change that could then be the focus during cognitive behavior therapy.

An alternative explanation is that longer rather than shorter treatment, in terms of number of sessions, is required to improve glycemic control. We could not test the possibility that treatment effect is confounded by treatment dose.

This study was not powered to examine moderators or mediators. There were no significant changes in secondary outcome variables. Given the lack of change in depression, an improvement in mood seems unlikely to have mediated the effect on glycemic control.

The interim quarterly results were not as impressive as the 12-month results. It is not clear why this occurred, but the therapeutic process in psychological treatments is gradual and accumulative.

A meta-analysis of previous RCTs of psychological treatments found a 0.22% decrease in hemoglobin A_{1c} levels (15). We observed a slightly greater decrease. Several possible reasons explain this.

First, we used an individualized approach tailored to patient's self-identified needs and problems by using a computerized agenda-setting program, whereas most of the studies in the review used group approaches. One study

found that 14 sessions of individual cognitive behavior therapy did substantially decrease hemoglobin A_{1c} levels in adults with type 1 diabetes (26). Other RCTs using group cognitive behavior therapy techniques found that these techniques were not associated with substantial changes in hemoglobin A_{1c} levels (24, 25, 27, 28, 49).

Second, we trained nurses to moderate levels of skills in psychotherapy. One RCT trained diabetes nurses in counseling skills, but the primary aim was to improve psychological well-being, and the sample at baseline had good glycemic control (50).

Our study differs from another RCT that used similar criteria for persistent, suboptimal glycemic control. They found that cognitive analytical therapy delivered by an experienced psychotherapist was more effective than nurse-delivered education sessions in 1 hospital (51). Our study focused on training nurses and on recruiting a representative sample of persons with type 1 diabetes and suboptimal glycemic control from a range of hospital settings.

We did not have an attention control group, so meeting with a nurse on 12 occasions over 6 months with no psychological intervention might result in the same improvement in hemoglobin A_{1c} levels, but previous trials suggest that this is not the case (51). We achieved excellent 12-month follow-up rates, but the quarterly follow-up rates were not as good. This may have biased the quarterly effect sizes because persons who do not attend have worse glycemic control (52), but we hope our analysis methods mitigated this by accounting for variables, such as ethnicity, that were predictive of missingness. The long-term effectiveness of the intervention and whether these findings translate to reduction in risk for diabetes complications is not known. We may have underestimated the rates of hypoglycemia because we asked patients to recall episodes at 2 intervals only, but severe hypoglycemia includes third-party assistance in its definition, and this is less likely to be underreported than milder forms of hypoglycemia. The small proportion of participants with missing values for severe hypoglycemia events may have been those with better diabetes control.

Using qualitative techniques to examine the active ingredients of the psychotherapeutic process will help inform future generations of RCTs (53). The long-term effectiveness of psychological treatments in diabetes is underresearched; the average follow-up is 7 months (15). Adding psychotherapy components to structured education programs for type 1 diabetes is underevaluated.

There are many clinical implications of our study. First, we achieved a clinically meaningful decrease in hemoglobin A_{1c} levels. In the Diabetes Control and Complications Trial (1), any decrease in glucose levels was associated with a decrease in the development of microvascular complications. Second, with appropriate manual skills training, diabetes nurses can deliver behavior change strategies that improve glycemic control. Third, the focus on patient-identified problems rather than on general psychological distress may inform translating these findings into practice.

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Appendix Table. **Further Results: Standardized Estimates of Quarterly Mean Hemoglobin A_{1c} Levels in Each Group**

Hemoglobin A_{1c} Level	Usual Care, %	Motivational Enhancement Therapy, %	Motivational Enhancement Therapy Plus Cognitive Behavior Therapy, %
Measured at follow-up			
Baseline	9.63 (9.51–9.75)	–	–
3 mo	9.49 (9.29–9.70)	9.39 (9.19–9.58)	9.37 (9.17–9.57)
6 mo	9.47 (9.24–9.70)	9.40 (9.15–9.64)	9.25 (9.01–9.49)
9 mo	9.32 (9.07–9.57)	9.40 (9.14–9.65)	9.13 (8.88–9.39)
12 mo	9.54 (9.29–9.80)	9.36 (9.10–9.61)	9.08 (8.81–9.359)
Time-averaged*	9.46 (9.27–9.64)	9.38 (9.19–9.57)	9.21 (9.01–9.40)

* Average results of the 3-, 6-, 9-, and 12-month hemoglobin A_{1c} measurements.