ORIGINAL ARTICLE

The Pathways Study

A Randomized Trial of Collaborative Care in Patients With Diabetes and Depression

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Background: There is a high prevalence of depression in patients with diabetes mellitus. Depression has been shown to be associated with poor self-management (adherence to diet, exercise, checking blood glucose levels) and high hemoglobin A_{1c} (HbA_{1c}) levels in patients with diabetes.

Objective: To determine whether enhancing quality of care for depression improves both depression and diabetes outcomes in patients with depression and diabetes.

Design: Randomized controlled trial with recruitment from March 1, 2001, to May 31, 2002.

Setting: Nine primary care clinics from a large health maintenance organization.

Participants: A total of 329 patients with diabetes mellitus and comorbid major depression and/or dysthymia.

Intervention: Patients were randomly assigned to the Pathways case management intervention (n=164) or usual care (n=165). The intervention provided enhanced education and support of antidepressant medication treatment prescribed by the primary care physician or problem-solving therapy delivered in primary care.

Main Outcome Measures: Independent blinded assessments at baseline and 3, 6, and 12 months of depression (Hopkins Symptom Checklist 90), global improvement, and satisfaction with care. Automated clinical data were used to evaluate adherence to antidepressant regimens, percentage receiving specialty mental health visits, and HbA_{1c} levels.

Results: When compared with usual care patients, intervention patients showed greater improvement in adequacy of dosage of antidepressant medication treatment in the first 6-month period (odds ratio [OR], 4.15; 95% confidence interval [CI], 2.28-7.55) and the second 6-month period (OR, 2.90; 95% CI, 1.69-4.98), less depression severity over time (z=2.84, P=.004), a higher rating of patient-rated global improvement at 6 months (intervention 69.4% vs usual care 39.3%; OR, 3.50; 95% CI, 2.16-5.68) and 12 months (intervention 71.9% vs usual care 42.3%; OR, 3.50; 95% CI, 2.14-5.72), and higher satisfaction with care at 6 months (OR, 2.01; 95% CI, 1.18-3.43) and 12 months (OR, 2.88; 95% CI, 1.67-4.97). Although depressive outcomes were improved, no differences in HbA_{1c} outcomes were observed.

Conclusion: The Pathways collaborative care model improved depression care and outcomes in patients with comorbid major depression and/or dysthymia and diabetes mellitus, but improved depression care alone did not result in improved glycemic control.

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APPROXIMATELY 10% TO 15% of patients with diabetes mellitus meet criteria for comorbid major depression.[1,2] Depression is a risk factor for development of diabetes mellitus,[3,4] it is associated with adverse diabetes outcomes,[5-9] and diabetes may worsen the course of depression.[10] Research suggests that the presence of comorbid chronic physical disease, such as diabetes mellitus, is a negative prognostic factor for depression treatment outcomes.[11,12] Patients with diabetes mellitus and major depression, compared with those with diabetes mellitus alone, have been shown to have higher symptom burden[5]; increased functional impairment[5,6]; poorer adherence to diet, exercise, and taking medications[2,5,6]; higher hemoglobin A_{1c} (HbA_{1c}) levels[7]; and more diabetes complications.[8,9] Given the high comorbidity of depression and diabetes mellitus and the potential reciprocal adverse impact of these conditions, there is a need for treatment trials to assess whether enhancing recognition and treatment of depression improves diabetes and depression outcomes.

Several small tertiary care–based trials have shown that antidepressant medica-

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tion was more effective than placebo in treating major depression in patients with diabetes mellitus.[13,14] One tertiary care–based trial[15] also found that cognitive behavior therapy was more effective than a diabetes educational intervention in relieving depressive symptoms and significantly decreased HbA_{1c} levels in patients with comorbid major depression and diabetes mellitus. A more recent, larger trial[16] among elderly, depressed, diabetic patients with relatively low baseline mean HbA_{1c} levels did not find improvement in glycemic control resulting from improved depression outcomes. These studies may not have been adequately powered to detect effects on glycemic control due to the sample size or low baseline HbA_{1c} levels.

Most patients with diabetes mellitus and major depression are treated within primary care rather than specialty care. Primary care diabetic patients are more likely to have type 2 diabetes mellitus, less likely to be treated with insulin, and likely to have fewer diabetic complications and medical comorbidities.[2,5,6,17] Health services research in primary care systems has improved the quality of diabetes care with telephone or in-person case management interventions.[18,19] However, these studies have not addressed treatment of comorbid major depression.[18,19] Only a minority of patients with diabetes mellitus and major depression receive adequate treatment for depression.[20] Population-based strategies to improve quality of care and outcomes in patients with diabetes mellitus in primary care have found depression to be an important barrier to enhancing diabetes self-management.[21] The present randomized controlled trial tested the effect of a health services intervention aimed at improving quality of depression care on both depression and glycemic control outcomes among primary care patients with diabetes mellitus and depression.

METHODS

The Pathways Study was developed by a multidisciplinary team in the Department of Psychiatry and Behavoiral Sciences at the University of Washington and the Center for Health Studies at Group Health Cooperative (GHC), Seattle. The GHC is a nonprofit health maintenance organization with 30 primary care clinics in western Washington State. The study protocol was reviewed and approved by institutional review boards at the University of Washington and the GHC. All participants gave written informed consent.

STUDY SETTING

Nine GHC primary care clinics in western Washington were selected for the study. We estimated that 150 participants in both the intervention and usual care arms (assuming 15% patient attrition) were required to have 80% power to detect as significant a 0.23 (SD, 0.7) difference in the mean score of the 20 depression items from the Hopkins Symptom Checklist-90 (SCL-90).[22] We estimated that 162 participants in both the intervention and control arms (assuming 15% patient attrition) were required to have 80% power to detect as significant a 0.5% (SD, 1.65%) mean difference in HbA_{1c} values.

SAMPLE RECRUITMENT

Case identification was facilitated by prior development by the GHC of a population-based diabetes registry[23] that supports patient care. A survey mailed to patients on the diabetes registry assessed age, sex, years of education, employment status, race, and marital status. Questions about clinical status included the following: age at onset of diabetes, duration of diabetes, current diabetic treatments, and diabetes treatment at onset of disease. When surveys were not returned, second and third mailings and telephone reminders were used to achieve a final response rate of 61.7%.

Eligible patients were ambulatory, were English speaking, had adequate hearing to complete a telephone interview, and planned to continue to be enrolled in GHC during the next year. Psychiatric exclusions were as follows: (1) currently in care with a psychiatrist; (2) a diagnosis based on GHC's automated diagnostic data of bipolar disorder or schizophrenia; (3) use of antipsychotic or mood stabilizer medication based on GHC's automated pharmacy data; and (4) mental confusion on interview, suggesting significant dementia.

The Patient Health Questionnaire 9 (PHQ-9) was used to screen for depression.[24,25] The PHQ-9 (at a cutting score of $\geq$10 with $\geq$5 symptoms scored as being present more than half of the days) has been found to have high agreement with structured interview in establishing a diagnosis of major depression.[24,25] Although we did not require patients to meet criteria for major depression, they were required to have a score of 10 or greater on the PHQ-9 in the initial screening and persistent symptoms, as evidenced by an SCL-90 depression[22] mean item score of higher than 1.1 at a second telephone screen 2 weeks later. Patients were not excluded if they were taking antidepressants in the prior 3 months as long as they had persistent symptoms.

A total of 9063 questionnaires were mailed, and 7841 patients were found to meet initial eligibility criteria (**Figure 1**); 4839 questionnaires (61.7% of those eligible) were returned, and 1038 were eligible for baseline screening based on a PHQ-9 score of 10 or greater. A total of 851 (82.0%) of the 1038 respondents were successfully reached by telephone for baseline screening, and 375 met criteria for the randomized trial (based on a second screening SCL-90 score of >1.1). Only 46 (12%) of 375 eligible patients refused to participate.

MEASURES

For measuring change in depression, the SCL-90 depression scale[22] was chosen as the primary dependent variable, based on previous studies that showed the high reliability, validity, and sensitivity to change of this measure.[16,22,26] Given the higher percentage of patients with dysthymia than with major depression, response to treatment at 6 and 12 months was defined as 40% or greater reduction in SCL-90 scores, based on a National Institutes of Health consensus panel recommendation regarding measurement of outcomes in dysthymia.[27] We also report 50% or greater reduction in SCL-90 scores at 6 and 12 months. We used the Patient Global Impression[28] score at 6 and 12 months as a subject-rated global assessment of improvement in depression since baseline. Patients rated their satisfaction with depression care at baseline and 6 and 12 months on a 5-point ordinal scale that rated treatment from poor to excellent.[26]

Hemoglobin A_{1c} measures exposure of red blood cells to glucose during a 90-day period.[29] Study participants agreed to blood draws at their GHC primary care clinic to measure HbA_{1c} at baseline and 6 and 12 months.

The GHC's computerized pharmacy and utilization records were used to measure the number of specialty mental health visits, for examination of refills of antidepressant medications, and to determine whether the patient received an adequate dosage based on evidence-based guideline standards for 90 days or more within each 6-month period.[30] The lowest doses in the ranges recommended in the Agency for Health Care Policy

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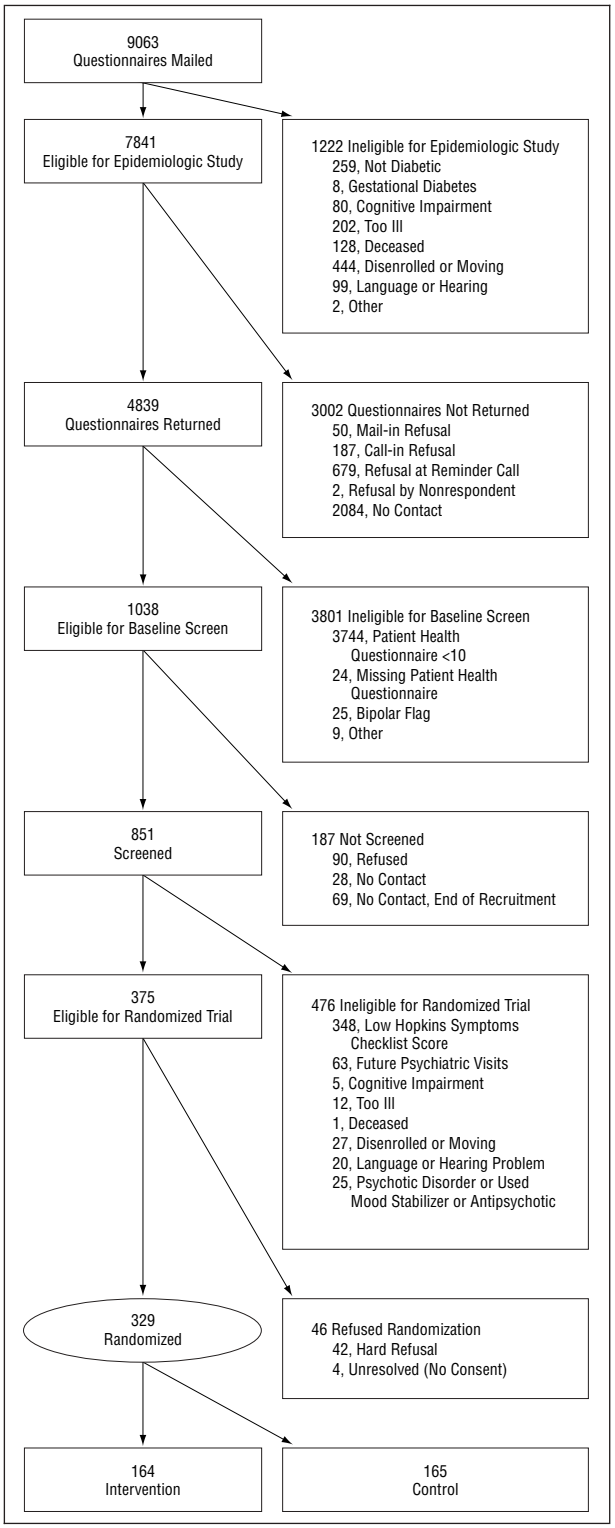

Figure 1. Recruitment for the randomized controlled trial. Patients were eligible for baseline screening based on a Patient Health Questionnaire 9 score of 10 or higher. Patients were categorized as "ineligible–other" if (1) they were enrolled in another study, (2) their spouse was enrolled in the Pathways Study, (3) they were at high risk for self-harm or they refused a self-harm assessment, or (4) they fulfilled other special circumstances (ie, there was 1 case in which the team deemed someone ineligible owing to a recent hospitalization for drug overdose).

and Research Guidelines and in guidelines developed for newer agents were used to define minimum dosage standards.[31,32]

Computerized pharmacy records were used to compute a chronic disease comorbidity score known as RxRisk.[33] The RxRisk has been found to be comparable to using ambulatory care groups[34] in predicting total future health costs.

A measure was developed based on previous literature[35] to define 2 aspects of diabetes using automated diagnostic, pharmacy, and laboratory data: (1) diabetes complications and (2) treatment intensity required. *International Classification of Diseases, Ninth Revision,* codes were used to identify 7 potential types of diabetic complications (retinopathy, nephropathy, neuropathy, cerebrovascular, cardiovascular, peripheral vascular, and ketoacidosis).[35] Pharmacy data regarding the use of oral hypoglycemic agents and insulin indicated treatment intensity.

RANDOMIZATION

Using a computerized algorithm, patients were randomized to the intervention or usual care group. After completion of the baseline interview, intervention patients were called by a nurse within 1 week to set up an appointment. Usual care patients were given recommendations to work with their primary care physician on issues related to depression. After randomization, telephone interviews were provided at 3, 6, and 12 months by a telephone survey team who were blinded to intervention status.

INTERVENTION DESIGN

The intervention was designed to improve quality of care and outcomes of depression but not to directly improve diabetes education or care. The intervention was an individualized, stepped-care depression treatment program provided by a depression clinical specialist nurse in collaboration with the primary care physician.

TRAINING

Three half-time registered nurses were hired to implement collaborative care treatment. Nurses received an initial 1-week training course on diagnosis and pharmacotherapy and an introduction to problem-solving treatment methods based on the intervention developed for the Improving Mood–Promoting Access to Collaborative Treatment (IMPACT) study.[36,37] A psychiatrist (W.J.K.), primary care physician (E.H.B.L.), and psychologist (E.L.) participated in the training. An intervention manual from the IMPACT trial was used to train nurses on collaborative care, stepped-care principles, pharmacology, and problem-solving treatment.[38]

Nurses were also trained using the manual for problem-solving treatment of depressive disorders in primary care (PST-PC) following the protocol described by Hegel and colleagues,[39] which included didactics, role play, observation of a videotaped demonstration, and review of the PST-PC treatment manual.[40] Each nurse was required to treat at least 4 depressed patients with 6 sessions of PST-PC during a 2-month period. Each session was audiotaped, and sessions 1, 3, and 5 were rated using the PST-PC Adherence and Competency Rating Scale.[39,40] Nurses were required to have at least 3 audiotaped treatment sessions from different patients rated as satisfactory by the team psychologist (E.L.).

COLLABORATIVE CARE

Patients were offered an initial choice of 2 evidence-based treatments: antidepressant medication or PST. Treatment included an initial 1-hour visit followed by twice-a-month, half-hour appointments (telephone and in person) in the acute phase of treatment (0 to 12 weeks).

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STEPPED-CARE ALGORITHM

A stepped-care approach was used in which patients received different types and intensities of services tailored to their observed outcomes.[41] If patients still had persistent depressive symptoms (<50% decrease in severity based on the PHQ-9) 10 to 12 weeks after initial treatment with either PST or antidepressant medication, they could (1) switch to a second antidepressant with a different mechanism or side effect profile; (2) switch to the alternative treatment (from PST to medication or vice versa); (3) receive augmentation with PST or antidepressant medication with the first treatment they had received; or (4) receive a psychiatric consultation. This change in treatment at 10 to 12 weeks was labeled step 2 care. In situations where patients received 1 or more step 2 interventions, where symptoms persisted (<50% improvement), or where there was a lack of patient and clinician satisfaction with outcome after a second treatment (8 to 12 weeks), referral to specialty care by the GHC mental health system for longer-term follow-up was made (step 3).

Once patients reached a significant decrease in clinical symptoms (≥50% decrement in symptoms), the nurse began continuation phase treatment, which consisted of monthly scheduled telephone contacts. For patients with persistent symptoms or social isolation, nurses offered monthly continuation groups instead of monthly telephone calls.

SUPERVISION

Each nurse had supervision twice a month with a team that included a psychiatrist (W.J.K., G.S., or E.W.), psychologist (E.L.) (pertaining to PST), and family physician (E.H.B.L.) to review new cases and patient progress. Nurses interacted regularly (via written notes and verbally) with the primary care physician treating the patient. On alternate weeks, nurses reviewed cases by telephone with the psychiatrist supervisor. The psychiatrist supervisor regularly reviewed choices and dosages of medication and clinical response and recommended changes, which the nurse discussed with the primary care physician and patient. During the study, 45 audiotapes were reviewed by the team psychologist to provide ongoing feedback to nurses and to assess treatment fidelity.

USUAL CARE

Usual care patients were advised to consult with their primary care physician regarding depression. Primary care physicians at the GHC frequently prescribe antidepressant medication and can refer patients to the GHC Mental Health Services. Both intervention and usual care patients could also self-refer to a GHC mental health care provider. Usual care for diabetes mellitus in the GHC is provided by the primary care physician, with occasional support from diabetes nurses for patients with persistently high HbA_{1c} levels.

STATISTICAL ANALYSIS

χ^2 Analyses with correction for continuity and 2-tailed independent group *t* tests were used to examine differences between the intervention and usual care groups on demographic and clinical variables. Group differences in the adequacy of dosage of antidepressants, patient global improvement, and percentage of patients with at least a 40% and 50% decrease in depression were examined using logistic analyses to account for baseline group differences and to calculate odds ratios and 95% confidence intervals (CIs). To examine treatment group trends over time (baseline and 3, 6, and 12 months) in antidepressant medication use, we used mixed-effect longitudinal logistic regression models with 2 random effects (intercept and time) and 2 fixed effects (treatment group and its interaction with time). We initially tested models with time as both a random and a fixed effect. In both models, the intercept was always assumed to be random. The 2 models had similar levels of significance for their main effects and interaction. Comparing the log likelihoods for the 2 models revealed a better fit for the model with time as a random effect (eg, slopes of the line over time being random effects). For the clinical outcomes of the continuous SCL-90 depression scale scores and HbA_{1c} values, mixed-effect continuous longitudinal models were used, following the same strategy described herein. In the event of significant effects, planned post hoc analyses were performed using F tests to elucidate the findings (adjusted for baseline values).

Effect modification of the pattern of change in depression over time between the treatment groups was examined for patient subgroups with major depression, patients with dysthymia, and those taking antidepressants at baseline. This was tested by individually examining the 3-way interaction of group by time by effect modifier (major depression, dysthymia, or antidepressant use).

RESULTS

Figure 1 illustrates the flow of patient selection for the study, including reasons for exclusion at various points. Of the 329 patients enrolled (164 intervention patients and 165 usual care patients), the following percentages completed 3-, 6-, and 12-month assessments: 3-month assessment, 151 (91.5%) intervention patients and 154 (93.3%) usual care patients; 6-month assessment, 143 (87.8%) intervention patients and 149 (90.9%) usual care patients; and 12-month assessment, 146 (88.5%) intervention patients and 142 (86.1%) usual care patients. A total of 132 intervention patients (80.5%) and 131 usual care patients (79.4%) completed all 3 assessments.

PATIENTS

There were no significant differences between groups in any variable (**Table 1**). The population was middle-aged to elderly, with approximately 1 patient in 5 from a racial/ethnic minority population. Most patients had type 2 diabetes mellitus, and approximately two fifths were treated with insulin. The mean glycosylated hemoglobin level was 8.0%, and the mean number of complications was 1.5. This population had a high rate of lifetime dysthymia (approximately 70%), and approximately two thirds met criteria for major depression. Only 13% of patients did not meet major depression or dysthymia criteria at baseline. Approximately half were treated with an antidepressant medication within the last 3 months.

INTERVENTION IMPLEMENTATION

Most (97.6%) of the 164 intervention patients completed an initial visit with a nurse. Intervention patients had a mean ± SD of 5.06 ± 3.43 in-person visits and 5.87 ± 4.32 telephone contacts with a nurse, and 4.9% were seen for a consultation by a team psychiatrist. A total of 84 intervention patients (51.3%) took medication and underwent PST, 13 (7.9%) underwent PST only, 53 (32.3%)

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Table 1. Baseline Demographic and Clinical Comparisons

Characteristic	Usual Care (n = 165)	Intervention (n = 164)
Age, mean ± SD, y	58.1 ± 12.0	58.6 ± 11.8
Female, No. (%)	107 (64.8)	107 (65.2)
Married, No. (%)	90 (54.9)	94 (58.4)
Education (≥1 year of college), %	77.6	79.9
Working full or part time, No. (%)	71 (45.2)	84 (54.2)
White, No. (%)	133 (81.1)	115 (75.2)
Type 2 diabetes, No. (%)	158 (95.8)	157 (96.3)
HbA_{1c}, mean ± SD, %	8.0 ± 1.5	8.0 ± 1.6
Taking insulin, No. (%)	71 (43.0)	63 (38.4)
Diabetes complications, mean ± SD, No.	1.5 ± 1.4	1.5 ± 1.3
Duration of diabetes, mean ± SD, y	10.2 (10.1)	9.6 (8.8)
Age at onset of diabetes, mean ± SD, y	47.9 (13.4)	49.0 (13.9)
Major depression, No. (%)	114 (69.1)	102 (62.6)
Lifetime dysthymia, No. (%)	116 (70.3)	110 (67.5)
Baseline SCL-20 score, mean ± SD	1.6 ± 0.45	1.7 ± 0.51
Panic disorder, No. (%)	35 (23.0)	39 (25.2)
Taking an antidepressant in 3 mo before study, No. (%)	101 (54.0)	86 (46.0)
Three or more prior depression episodes, No. (%)	92 (60.5)	107 (68.6)

Abbreviations: HbA_{1c}, hemoglobin A_{1c}; SCL-20, 20 depression items from the Hopkins Symptoms Checklist 90.

took medications only, and only 14 (8.5%) did not take medication or undergo PST. Of the 97 patients receiving PST, 62 (64%) had 4 or more in-person treatment sessions.

PROCESS OF CARE

Patients receiving the intervention were more likely to receive 4 or more specialty mental health treatment visits (including nurse intervention visits and GHC specialty mental health visits) compared with patients receiving usual care (67.7% vs 6.7%). Controlling for prebaseline 6-month rate of adequacy, the intervention group had significantly higher rates of adequate dosage in the first 6-month period (57.3% for intervention vs 40% in the usual care group) and the second 6-month period (53.0% for intervention vs 38.2% in the usual care group) (**Table 2**).

A mixed-effect logistic regression model using baseline and 3-, 6-, 9-, and 12-month refills of antidepressant medication based on automated data was performed. The 2 random-effects models (slope and intercept) showed a significant time × treatment group interaction (z=3.30, P<.001) and nonsignificant main effects of time (z=0.29) and intervention group (z=1.08). At baseline, the usual care and intervention groups did not differ in adherence (43.6% vs 35.4%, χ^2_1=2.02, P=.16). At each of the follow-up assessments, the intervention group had significantly greater medication adherence than the usual care group, controlling for baseline adherence, with the odds ratios ranging from 2.18 to 3.20 (Table 2).

At baseline, rates of satisfaction in the intervention and usual care groups were very similar, but at 6 and 12 months, the intervention group reported significantly greater satisfaction (Table 2) than the usual care group.

CLINICAL OUTCOMES

Mixed-effect regression models using baseline and 3-, 6-, and 12-month follow-up SCL-90 continuous data were performed. The 2 random-effects models (slope and intercept) showed a significant group × time interaction (z=2.84, P=.004); both the main effects of time (z=8.92, P<.001) and intervention group (z=2.14, P=.03) were statistically significant. **Figure 2** shows the depression means over time for the treatment groups (all follow-up means adjusted for the baseline SCL-90 score). The baseline SCL-90 depression mean scores ($F_{1,327}$=2.21, P=.14) and the 3-month assessment ($F_{1,302}$=1.45, P=.23) did not differ significantly between the groups. However, by 6 months, the intervention group had a significantly lower adjusted mean than the usual care group ($F_{1,290}$=4.11, P=.04), and this difference continued to be statistically significant at the 12-month assessment ($F_{1,285}$=4.96, P=.03). The average change from baseline to 6 months was 0.39 (95% CI, 0.28-0.49) for the usual care group and 0.56 (95% CI, 0.46-0.67) for the intervention group. The average change between baseline and 12 months was 0.44 (95% CI, 0.33-0.56) for the usual care group and 0.65 (95% CI, 0.54-0.76) for the intervention group.

Results of our effect modification analyses showed trend-level effect modification for patients treated with an antidepressant in the 3 months before randomization (z=1.59, P=.11) and nonsignificant modification for major depression (z=0.65, P=.52) or dysthymia (z=0.45, P=.65). The trend-level modification by antidepressants showed a greater intervention vs usual care treatment effect over time for those who had not had previous exposure to antidepressants.

Table 3 shows significant differences in the percentage of patients with a 40% decrease in SCL-90 depression scores between the intervention and usual care groups at 12 months and similar but nonsignificant trends at 6 months. Approximately 10% more intervention vs usual care patients also improved 50% or more from baseline on SCL-90 scores at 6 and 12 months, but these trends were not statistically significant.

At 6 months, a significantly higher percentage of the intervention patients reported improvement on the Patient Global Impression measure from baseline, compared with usual care patients. These differences were greatest at the 12-month assessment, when 71.9% of the intervention group reported improvement in their depression from baseline, compared with 42.3% of the usual care patients (Table 3).

A mixed-effect regression model compared HbA_{1c} values at baseline and 6 and 12 months. There was no statistically significant group × time interaction (z=0.60, P=.55) and no main effect of intervention; however, the time effect was statistically significant. We refit the model without the interaction term, and there was no statistically significant treatment group effect (z=0.89, P=.37), but there was a statistically significant time effect (z=3.65, P<.001). **Figure 3** shows that HbA_{1c} levels decreased over time for both groups: baseline (overall mean ± SD), 7.99% ± 1.55%; 6-month assessment, 7.58% ± 1.47%; and 12-month assessment, 7.64% ± 1.57%. The follow-up means were adjusted for baseline HbA_{1c} levels. There were no statistically significant group differences at any of the

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Table 2. Intervention vs Control Differences in Quality of Care

Variable	Total No. of Patients	Patients, No. (%) Usual Care (n = 165)	Patients, No. (%) Intervention (n = 164)	OR (95% CI)
4 or more specialty mental health visits at 12 mo	329	11 (6.7)	111 (67.7)	29.31 (14.65-58.66)
Adequate dosage				
First 6 mo*	329	66 (40.0)	94 (57.3)	4.15 (2.28-7.55)
Second 6 mo*	329	63 (38.2)	87 (53.0)	2.90 (1.69-4.98)
Any (adherence) antidepressant refills (automated data)				
Baseline	329	72 (43.6)	58 (35.4)	0.71 (0.45-1.10)
3 mo*	329	76 (46.1)	101 (61.6)	3.20 (1.84-5.58)
6 mo*	329	80 (48.5)	99 (60.4)	2.29 (1.38-3.82)
9 mo*	329	76 (46.1)	98 (59.8)	2.78 (1.62-4.76)
12 mo*	329	76 (46.1)	94 (57.3)	2.18 (1.32-3.62)
Satisfaction with treatment for depression (very or moderately satisfied)				
Baseline	325	106 (65.0)	101 (62.3)	0.89 (0.57-1.40)
6 mo*	291	89 (60.1)	104 (72.7)	2.01 (1.18-3.43)
12 mo*	287	76 (53.9)	106 (72.6)	2.88 (1.67-4.97)

Abbreviations: CI, confidence interval; OR, odds ratio.
*The ORs and CIs are adjusted for baseline values.

time points: baseline, $F_{1,315}=0.24$, $P=.62$; 6 months, $F_{1,282}=0.67$, $P=.41$; and 12 months, $F_{1,274}=0.61$, $P=.44$.

COMMENT

Compared with usual care patients, the Pathways intervention patients received more adequate depression treatment, were more satisfied with their care for depression, and showed significantly greater improvements in depressive symptoms during a 12-month period. These results add to the expanding literature that shows that depression can be effectively treated in the context of major chronic medical illness.[42]

Unlike many trials in younger adults, where differences between intervention and control patients in depressive outcomes at 4 to 6 months tended to decrease by 9 to 12 months,[26,43] the data from this trial suggest sustained intervention effects at longitudinal follow-up for 1 year. A similar pattern of sustained benefits during a 12-month period was also seen in the recently published IMPACT trial, which tested a similar nurse intervention vs usual care in elderly patients.[36] These results may reflect the fact that both the current study and the IMPACT trial[36] built in a continuation phase of the intervention in which nurses continued to monitor adherence and outcomes by telephone during a 1-year period.

An extremely high rate of dysthymia (approximately 70%) and prior depression treatment was found in these patients. In contrast, we found rates of dysthymia of 20% to 30%[26,43] in primary care studies that tested collaborative care depression interventions with mixed-age populations in the same health maintenance organization. The data that show high rates of chronic depression are consistent with other data that have shown that chronic medical illness is a negative prognostic factor in recovering from depression.[11,12] Although a higher percentage of intervention patients compared with controls improved during the 12 months, approximately 45% of intervention patients still had significant depressive symptoms, suggesting continued need for improved intervention models. The high rates of coexisting chronic depression in this population suggest that many patients may benefit from longer-term interventions that combine medication and evidenced-based psychotherapy.[44] A recently reported trial that enrolled patients with 2 or more years of depression found that a combined antidepressant medication and cognitive behavior analysis therapy intervention was more effective than either medication or cognitive behavior analysis therapy alone in improving outcomes.[44]

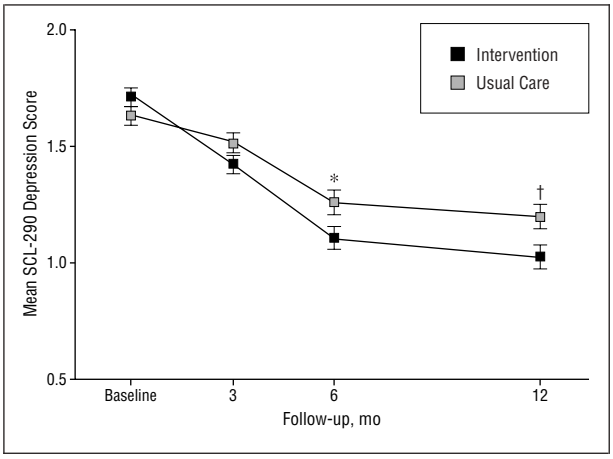

Figure 2. Intervention vs control differences on mean depression scores (range, 0-4) from the 20 depression items from the Hopkins Symptoms Checklist-90 (SCL-90). Error bars indicate standard errors. The 3-, 6-, and 12-month means were adjusted for baseline. Asterisk indicates $P=.04$; dagger, $P=.03$.

In this trial, the enhancement in quality of care and outcomes of depression was not accompanied by significant differences in HbA_{1c} levels between intervention and control patients during a 12-month period. Only 1 of 4 prior trials with patients with depression and diabetes

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Table 3. Intervention vs Control Differences in Recovery From Depression

Variable	Total No. of Patients	Patients, No. (%) Usual Care (n = 165)	Patients, No. (%) Intervention (n = 164)	OR (95% CI)
Response (≥40% decrease in SCL-90 depression score from baseline)				
6-mo follow-up*	293	51 (34.2)	61 (42.4)	1.40 (0.87-2.25)
12-mo follow-up*	288	54 (38.0)	79 (54.1)	1.89 (1.18-3.02)
Response (≥50% decrease in SCL-90 depression score from baseline)				
6-mo follow-up*	293	39 (26.2)	53 (36.8)	1.62 (0.98-2.67)
12-mo follow-up*	288	45 (31.7)	60 (41.1)	1.47 (0.90-2.39)
Patient global improvement (change from baseline)				
6-mo follow-up	293	59 (39.3)	100 (69.4)	3.50 (2.16-5.68)
12-mo follow-up	288	60 (42.3)	105 (71.9)	3.50 (2.14-5.72)

Abbreviations: CI, confidence interval; OR, odds ratio; SCL-90, 20 depression items from the Hopkins Symptoms Checklist-90.
*The ORs and CIs were adjusted for baseline values.

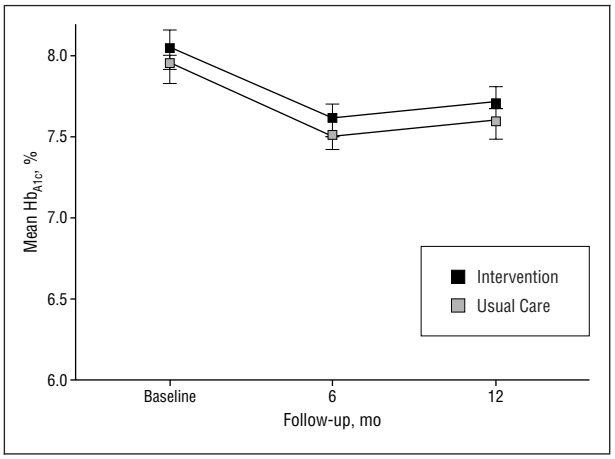

Figure 3. Intervention vs control differences in mean hemoglobin A_{1c} (HbA_{1c}) levels. Error bars indicate standard errors. The 3-, 6-, and 12-month means were adjusted for baseline.

mellitus has found that an effective depression intervention was associated with improved HbA_{1c} levels.[13-16] However, the mean baseline HbA_{1c} level in that efficacy study was approximately 10.0% vs approximately 8.0% in the current trial.[15] Also, the controls in that trial received diabetes education only,[15] whereas approximately half of the usual care controls in this study received antidepressant treatment, which probably decreased intervention vs usual care differences in depression outcomes. Similar to research showing that focusing only on biomedical aspects of diabetes is not an optimal treatment for patients with comorbid diabetes mellitus and depression,[21] our results suggest that the alternative approach of focusing on depression care only is not likely to achieve optimal diabetes outcomes. Given that depressed patients with diabetes mellitus have more severe disease[2] and higher numbers of behavioral risk factors (obesity, smoking, and sedentary lifestyle) than diabetic patients without depression,[2,45] an integrated biopsychosocial intervention program that focuses on improving both depression and diabetes mellitus management may be needed to improve clinical outcomes in both of these chronic illnesses.

This randomized trial was completed in 1 large health care system in the Pacific Northwest, limiting generalizability. Participants had enhanced usual care, since routine care patients were encouraged to discuss depression with their primary care physician. Primary care physicians treated both intervention and control patients, leaving room for a spillover effect due to potential physician improvements in knowledge and skills in treating depression. The relatively low baseline HbA_{1c} levels in this primary care population may have limited the effectiveness of the intervention on glycemic control. These potential biases would tend to result in underestimation of the effectiveness of the intervention, not overestimation.

In conclusion, the collaborative care model used in this study seems to be a feasible and effective approach for improving the quality of care and outcomes of depression in primary care patients with diabetes mellitus. Enhanced depression care did not result in improved glycemic control. Further research is needed to determine how to improve diabetes outcomes in patients with depression and diabetes mellitus.

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