Depression and Diabetes

Impact of Depressive Symptoms on Adherence, Function, and Costs

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Background: Depression is common among patients with chronic medical illness. We explored the impact of depressive symptoms in primary care patients with diabetes on diabetes self-care, adherence to medication regimens, functioning, and health care costs.

Methods: We administered a questionnaire to 367 patients with types 1 and 2 diabetes from 2 health maintenance organization primary care clinics to obtain data on demographics, depressive symptoms, diabetes knowledge, functioning, and diabetes self-care. On the basis of automated data, we measured medical comorbidity, health care costs, glycosylated hemoglobin (HbA1c) levels, and oral hypoglycemic prescription refills. Using depressive symptom severity tertiles (low, medium, or high), we performed regression analyses to determine the impact of depressive symptoms on adherence to diabetes self-care and oral hypoglycemic regimens, HbA1c levels, functional impairment, and health care costs.

Results: Compared with patients in the low-severity depression symptom tertile, those in the medium- and high-severity tertiles were significantly less adherent to dietary recommendations. Patients in the high-severity tertile were significantly distinct from those in the low-severity tertile by having a higher percentage of days in nonadherence to oral hypoglycemic regimens (15% vs 7%); poorer physical and mental functioning; greater probability of having any emergency department, primary care, specialty care, medical inpatient, and mental health costs; and among users of health care within categories, higher primary (51% higher), ambulatory (75% higher), and total health care costs (86% higher).

Conclusions: Depressive symptom severity is associated with poorer diet and medication regimen adherence, functional impairment, and higher health care costs in primary care diabetic patients. Further studies testing the effectiveness and cost-effectiveness of enhanced models of care of diabetic patients with depression are needed.

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Identification and effective treatment of comorbid depression increasingly is considered an essential component of high-quality clinical care of patients with chronic medical illness in the specialty medical setting. This is in response to a number of studies in specialty settings demonstrating the high prevalence of depression in the medically ill1,2 and the major adverse impact of affective illness on symptom burden, functional impairment, and self-management of illness.3-9 For example, it has been shown that, compared with nondepressed medically ill patients, those who are depressed are more likely to experience a higher burden of disease-specific symptoms10 and social and vocational impairment when controlling for severity of medical illness.9 Other researchers have shown that depression is associated with poorer adherence to medication and self-care regimens (eg, diet, exercise, and quitting smoking),11-14 potentially leading to worse medical outcomes. These factors and the propensity for depressed medical patients to utilize more health care lead to higher direct and indirect health care costs.15-17

Most patients with chronic medical illness are treated in primary rather than specialty care settings. However, few studies have examined the impact of depression on a specific medical illness in primary care–based populations. There are likely important differences between these 2 populations, such as increased severity of medical illness in specialty care patients. In ongoing development of health care policies and clinical guidelines about treatment of depression in medically ill primary care patients, it will be important to have at hand research from primary care settings. Research demonstrating that depression is associated with additive medical costs due to a specific chronic medical illness and increased indirect costs (eg, days off work) may lead to pressure from national credentialing committees such as the National Com-
PATIENTS AND METHODS

We conducted a secondary analysis of data obtained in 2 primary care clinics of the Group Health Cooperative (GHC), a large staff-model health maintenance organization (HMO) in Puget Sound, Wash. The clinics were staffed by 22 board-certified family physicians. The GHC has developed a diabetes improvement program, the primary feature of which is an automated diabetes registry that tracks diabetic patients and includes demographic, pharmacy, laboratory, cost, and health care utilization data. All English-speaking patients with types 1 and 2 diabetes older than 18 years and enrolled for at least 2 years at these primary care clinics were eligible to participate in the study. Patients with severe cognitive or language deficits were excluded. In November 1998, using the GHC diabetes registry, we sent the population base of 588 study-eligible diabetic patients an approach letter. The letter described the primary study, which explored diabetes treatment adherence and the quality of the patient–provider relationship, and offered the option of declining further involvement. Two weeks later, participating subjects were sent a questionnaire, a request for consent to review their registry data, and a compensation of $10 for their time in filling out the questionnaire. After a complete description of the study to the subjects, written informed consent was obtained. Mailed reminders were sent to nonrespondents 2 and 4 weeks after the initial questionnaire. This project was reviewed by the institutional review boards of the University of Washington, Seattle, and GHC.

SELF-REPORT INSTRUMENTS COMPLETED BY PATIENTS

The Hopkins Symptom Checklist-90, Revised (HSCL-90-R) is a self-report instrument that has been validated in previous studies with medical patients and has been found to be highly reliable. The 20 items from the depression and additional symptom subscales (HSCL-20) were used as the main independent variable in these analyses, and each item is scored on a 0-to-4 range of severity. The Diabetes Knowledge Assessment is a valid and reliable 15-item instrument that assesses patient knowledge about diabetes and its treatment. Scores were expressed as a percentage of correct answers.

The Summary of Diabetes Self-Care Activities is a 12-item questionnaire that measures absolute levels of self-care behavior and the percentage of activities recommended by the physician that were actually performed. This questionnaire has been shown to be a valid and reliable measure of diabetes self-management in multiple trials. In this study, diet amount, diet type, exercise, and glucose testing were assessed, and since items within each domain have different scales, raw scores for each were converted to standard scores having a mean of 0 and an SD of 1. Standardized scores were averaged to form a composite z score for each regimen behavior. A higher z score indicates better adherence to the self-care behavior.

General health and functional impairment were measured using the Short-Form 12 Health Survey (SF-12). The SF-12 is a generic measure of health status that is a shorter and valid alternative to the SF-36. The SF-12 measures functioning in medical populations and assesses physical functioning, role limitations due to physical health problems, bodily pain, general health, and social functioning, which are represented in mental and physical component scores.

A composite score of diabetes severity was derived for use as a covariate in analyses. Raw data from the following 3 domains were transformed and combined with the use of z scores: (1) a count of current diabetes complications including nephropathy, neuropathy, and retinopathy, which has been shown to be highly correlated with severity of diabetes from independent physician raters (r = 0.72; P < .001); (2) duration of diabetes in years; and (3) whether subjects were initially prescribed insulin around the time of diagnosis.

AUTOMATED DATA

Demographic and clinical data (eg, number of years with diabetes, insulin use at diagnosis, number of diabetes complications, type of diabetes treatment) were determined from questionnaire responses and automated data. Also, the following variables were determined from automated data.

Ratings of medical comorbidity were derived from the Chronic Disease Score (CDS), which is an index based on medications used to treat chronic medical conditions derived from automated pharmacy data. The CDS has been shown to correlate with physician ratings of physical disease severity and to predict mortality and hospital utilization. Diabetes medications were excluded in determination of the CDS in this study.

Health care costs were determined using data from the GHC cost and utilization system. Costs were expressed as 1999 dollars and were assessed for a period of 6 months after the time the research questionnaire was completed and...
included total, ambulatory (total costs less all inpatient costs), primary care, specialty care, emergency department, inpatient, mental health, and prescription costs. These analyses assessed only direct costs from the perspective of the HMO.

A measure of nonadherence to treatment regimens was derived by determining interruptions of medication treatment for the 200 patients using oral hypoglycemics (glyburide, metformin, glipizide [Glucotrol], tolazamide, and tolbutamide sodium). Based on the methods of Unutzer and colleagues,29 we defined an interruption as an episode in which a refill or subsequent prescription of oral hypoglycemics was overdue by more than 15 days and by more than 25% of the intended duration of use. For each subject, we calculated the percentage of days in interruption by summing all days in interruption and dividing by the total number of days of intended treatment with oral hypoglycemics in 12 months, including a period of 6 months before until 6 months after administration of the study questionnaire. Twelve months was used to allow a sufficient number of refill events to occur given an upper range of prescription duration of 120 days in the study sample, with 43% of prescriptions written for 60 or more days.

Mean HbA1c values for the same 12-month period were obtained. Serum level of HbA1c is an objective measure of glucose control. The GHC laboratory uses an immunoinhibition assay (Roche-Boehringer Mannheim, Hitachi-Naka, Japan) performed on a blood chemistry analyzer (Hitachi 917; Hitachi, San Jose, Calif) to analyze HbA1c level, which is a method certified by the Diabetes Complications and Control Trial. This 12-month period was chosen to optimize the number of patients undergoing at least 1 HbA1c blood test. In this naturalistic study, only 74% patients underwent at least 1 HbA1c test in a 6-month period, compared with 92% of patients in a 12-month period.

**STATISTICAL ANALYSIS**

Data were analyzed with the use of commercially available software (SPSS 8.0 for Windows; SPSS Inc, Chicago, Ill). Two-tailed t tests or \( \chi^2 \) tests with corrections for continuity were used to compare respondents and nonrespondents by age, sex, HbA1c level, and CDS. The total respondent sample then was grouped into tertiles for all remaining analyses based on HSCL-90-R depression subscale scores (HSCL-20). The HSCL score ranges for depressive symptom severity tertiles were as follows: less than 0.5 indicates low severity; 0.5 to 1.0, medium severity; and greater than 1.0, high severity. Demographic and clinical variables were compared between depressive symptom severity tertiles using analyses of variance or \( \chi^2 \) tests with corrections for continuity.

Given the large SDs of cost data, the relatively small sample size, and the proportion of patients with no health care costs in some cost categories, a 2-part model was used30 to determine if health care costs varied as a function of depressive symptom severity. In the first part, logistic regression was used to derive odds ratios (ORs) of the probability of having any health care costs, for those cost categories in which some subjects may not have had costs. Subjects in both the medium- and high-severity tertiles were compared with subjects in the low-severity tertile. In the second part, differences in the level of costs for users of health care between tertiles were predicted based on ordinary least squares regression using dummy variables31 (in which the low-severity tertile was the reference group). To satisfy the requirements of a normal distribution for the ordinary least squares regression, health care cost data, which are highly skewed to the right, were log-transformed. Tests for heteroscedasticity of log-transformed data were performed. Cost ratios of estimated median health care costs (with 95% confidence intervals [CIs]) between the high- or medium-severity depression symptom tertile and the low-severity tertile were obtained by exponentiating the regression coefficients for each dummy variable.31 This was performed for those cost categories where at least 20% of patients had at least some costs. Covariates for both parts of the model (and for all subsequent regression analyses in this study) included age, sex, diabetes severity (composite score), medical comorbidity (CDS), and diabetes knowledge.

To determine if HbA1c levels, functional status, and adherence to diabetes self-care and oral hypoglycemic regimens were associated with depressive symptom severity, analysis of covariance was used to test for differences among depressive symptom severity tertiles within each of these domains. Dependent variables included self-reported standardized (z scores) adherence outcomes in the domains of exercise, glucose monitoring, diet type, and diet amount; interruptions in prescriptions of oral hypoglycemics as determined from automated prescription data; mean HbA1c values; and physical and mental component scores from the SF-12. In the event of any significant main effects involving depressive symptom severity tertiles, post hoc analyses of covariance were used to determine which levels of depressive symptom severity demonstrated significant differences among the analyses involving self-care, adherence, and functioning.

### RESULTS

**DEMOGRAPHIC AND CLINICAL CHARACTERISTICS**

Of 588 subjects receiving questionnaires, 367 (62%) returned them and consented to the release of their automated data. There were no significant differences in age, sex, HbA1c levels, or CDS between respondents and nonrespondents.

Demographic and clinical characteristics of respondents by depressive symptom severity are shown in
Table 1. Baseline Characteristics of Subjects by Depressive Symptom Severity Tertiles*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Low (n = 119)</th>
<th>Medium (n = 119)</th>
<th>High (n = 121)</th>
<th>Statistical Test†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>63.5 (10.9)</td>
<td>61.4 (11.9)</td>
<td>59.0 (12.2)</td>
<td>F, 4.30‡</td>
</tr>
<tr>
<td>Chronic Disease Score, mean (SD)</td>
<td>1985 (2381)</td>
<td>2175 (1528)</td>
<td>2294 (2501)</td>
<td>F, 0.61</td>
</tr>
<tr>
<td>Years with diabetes mean (SD)</td>
<td>9.0 (7.9)</td>
<td>10.9 (8.4)</td>
<td>11.2 (10.7)</td>
<td>F, 0.12</td>
</tr>
<tr>
<td>Diabetes Knowledge Score, mean (SD)</td>
<td>68.2 (19.0)</td>
<td>74.8 (17.4)</td>
<td>78.2 (16.1)</td>
<td>F, 10.00§</td>
</tr>
<tr>
<td>HSC-20 score, mean (SD)</td>
<td>0.24 (0.13)</td>
<td>0.15 (0.15)</td>
<td>1.65 (0.59)</td>
<td>F, 469.61‖</td>
</tr>
<tr>
<td>Female</td>
<td>60 (50)</td>
<td>71 (60)</td>
<td>70 (58)</td>
<td>x², 2.32</td>
</tr>
<tr>
<td>White race</td>
<td>104 (87)</td>
<td>106 (89)</td>
<td>100 (83)</td>
<td>x², 2.27</td>
</tr>
<tr>
<td>At least 1 y of college</td>
<td>78 (66)</td>
<td>81 (68)</td>
<td>81 (68)</td>
<td>x², 0.11</td>
</tr>
<tr>
<td>Married</td>
<td>82 (69)</td>
<td>78 (66)</td>
<td>87 (72)</td>
<td>x², 1.13</td>
</tr>
<tr>
<td>Type 1 diabetes</td>
<td>3 (3)</td>
<td>5 (4)</td>
<td>6 (5)</td>
<td>x², 1.00</td>
</tr>
<tr>
<td>One or more complications</td>
<td>41 (37)</td>
<td>59 (55)</td>
<td>67 (62)</td>
<td>x², 14.13¶</td>
</tr>
<tr>
<td>Diabetes treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin only</td>
<td>26 (22)</td>
<td>17 (15)</td>
<td>14 (12)</td>
<td>x², 4.95</td>
</tr>
<tr>
<td>Oral hypoglycemics only</td>
<td>66 (56)</td>
<td>58 (50)</td>
<td>61 (52)</td>
<td>x², 1.03</td>
</tr>
<tr>
<td>Diet only</td>
<td>8 (7)</td>
<td>13 (11)</td>
<td>18 (15)</td>
<td>x², 4.22</td>
</tr>
<tr>
<td>Insulin and hypoglycemics</td>
<td>17 (15)</td>
<td>28 (24)</td>
<td>25 (21)</td>
<td>x², 3.54</td>
</tr>
</tbody>
</table>

* A total of 259 subjects satisfactorily completed the Hopkins Symptom Checklist (HSCL-20). Unless otherwise indicated, data are given as number (percentage) of patients. Denominators for percentages vary due to missing data for some items.
† Range of df for F is 2,352 to 2,358.
‡ Post hoc testing, P<.01 (high-severity tertile is significantly greater than low-severity tertile).
§ Post hoc testing, P<.001 (high-severity tertile is significantly greater than low-severity tertile) and P=.01 (medium-severity tertile is significantly greater than low-severity tertile).
¶ Post hoc testing, P<.001 (high- and medium-severity tertiles are both significantly greater than low-severity tertile; high-severity tertile is significantly greater than medium-severity tertile).
‖ Post hoc testing, P<.001 (high-severity tertile is significantly greater than low-severity tertile) and P=.01 (medium-severity tertile is significantly greater than low-severity tertile).

Table 2. Diabetes Adherence Variables by Depressive Symptom Severity Tertiles*

<table>
<thead>
<tr>
<th>Adherence Domain</th>
<th>Low (n = 119)</th>
<th>Medium (n = 119)</th>
<th>High (n = 121)</th>
<th>Analysis†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-care domains, (z scores)‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td>0.20 (0.90)</td>
<td>−0.02 (0.84)</td>
<td>−0.15 (0.87)</td>
<td>(2.69)</td>
</tr>
<tr>
<td>Glucose monitoring</td>
<td>0.14 (0.94)</td>
<td>0.08 (0.91)</td>
<td>−0.02 (0.95)</td>
<td>(1.05)</td>
</tr>
<tr>
<td>Diet amount</td>
<td>0.28 (0.74)</td>
<td>−0.07 (0.87)</td>
<td>−0.18 (0.93)</td>
<td>(8.05)§</td>
</tr>
<tr>
<td>Diet type</td>
<td>0.14 (0.63)</td>
<td>−0.03 (0.66)</td>
<td>−0.15 (0.75)</td>
<td>(4.36)‖</td>
</tr>
<tr>
<td>Days in oral hypoglycemic therapy interruption, % SD¶</td>
<td>7.1 (12.0)</td>
<td>9.3 (15.5)</td>
<td>14.9 (20.0)</td>
<td>(4.33)#</td>
</tr>
<tr>
<td>Glycosylated hemoglobin, %∗∗</td>
<td>7.4 (1.4)</td>
<td>7.6 (1.4)</td>
<td>7.9 (1.5)</td>
<td>2.05</td>
</tr>
</tbody>
</table>

* Adjusted for age, sex, medical comorbidity, diabetes severity and diabetes knowledge. A total of 356 subjects satisfactorily completed the Summary of Diabetes Self-Care Activities.
† Range of df for F is 7,352 to 7,358; for percentage of days, df for analysis is 7,192; for glycosylated hemoglobin, df for analysis is 7,315.
‡ Post hoc testing, P<.001 (high- and medium-severity tertiles are significantly greater than low-severity tertile).
§ Post hoc testing, P<.05 (high- and medium-severity tertiles are significantly greater than low-severity tertile).
¶ Post hoc testing, P<.05 (high-severity tertile is significantly greater than low-severity tertile).
‖ Post hoc testing, P<.05 (high-severity tertile is significantly greater than low-severity tertile).
# Post hoc testing, P<.05 (high-severity tertile is significantly greater than low-severity tertile).
** For low-severity tertile, n = 65; medium-severity, n = 67; and high-severity, n = 68.

Table 1. Age, diabetes knowledge, and diabetes complications were significantly different between depressive symptom severity tertiles and were included as covariates in subsequent analyses.

ADHERENCE TO TREATMENT

Diabetes self-care was shown to be significantly associated with depressive symptom severity in the domains of diet amount and diet type (Table 2). Post hoc analyses showed that for diet amount, high- and medium-severity tertiles had significantly worse adherence than low-severity tertile (F1,214 = 12.71 [P<.001] and F1,208 = 10.99 [P<.001], respectively). Similarly, for diet type, high- and medium-severity tertiles had significantly worse adherence than low-severity tertile (F1,212 = 4.01 [P=.046] and F1,217 = 6.69 [P=.01], respectively). The medium- and high-severity tertiles did not significantly differ from each other for diet type or amount.
Other tertiles in this regard. Depressive symptom severity tertile did not significantly differ from the low-severity tertile having a significantly greater percentage of interruptions in their use of oral hypoglycemics compared with the low-severity tertile (F1,211 = 28.50 [P < .001] and F1,211 = 7.62 [P = .006], respectively). The medium-severity depression symptom tertile was significantly different from the low-severity tertile in the physical functioning domain (F1,207 = 21.69 [P < .001]) and from the high-severity tertile in the mental functioning domain (F1,209 = 17.29 [P < .001]).

**FUNCTIONAL STATUS**

Depressive symptom severity had a significant effect on physical (F2,316 = 18.15 [P < .001]) and mental (F2,316 = 11.58 [P < .001]) functioning (Figure). For physical and mental functioning, post hoc analyses demonstrated significant differences between the low- and high-severity depression symptoms tertiles (F1,211 = 28.50 [P < .001] and F1,211 = 7.62 [P = .006], respectively). The medium-severity depression symptom tertile was significantly different from the low-severity tertile in the physical functioning domain (F1,207 = 21.69 [P < .001]) and from the high-severity tertile in the mental functioning domain (F1,209 = 17.29 [P < .001]).

**HEALTH CARE COSTS**

Unadjusted mean 6-month health care costs are presented in Table 3. Health care costs increased as depressive symptom severity increased. The probability of having any health care costs for 6 of the 8 cost categories (for 2 categories, total and ambulatory costs, all subjects had some costs) was determined after adjusting for covariates. Patients in the high-severity depression symptom tertile were significantly more likely than those in the low-severity tertile to have costs in the following categories: primary care (96% vs 84% [OR, 4.69; 95% CI, 1.59-13.83]), emergency department (19% vs 13% [OR, 2.48; 95% CI, 1.08-5.73]), medical inpatient (17% vs 9% [OR, 2.70; 95% CI, 1.11-6.38]), and mental health (14% vs 6% [OR, 3.63; 95% CI, 1.22-10.80]). No significant differences were found between the medium- and low-severity depression symptom tertiles.

For specialty care, patients in the medium- and high-severity depression symptom tertiles were significantly more likely to have any health care costs compared with those in the low-severity tertile (82% vs 64% [OR, 2.65; 95% CI, 1.36-5.16] and 79% vs 64% [OR, 2.38; 95% CI, 1.21-4.65], respectively). The probability of having any pharmacy costs was not significantly different between depressive symptom severity tertiles.

Cost ratios for health care utilizers were calculated for those cost categories where at least 20% of patients had at least some costs (total, ambulatory, primary care, and specialty care) and are presented in Table 4. These ratios and significance tests are based on log-transformed cost data. We observed no significant heteroscedasticity that may have invalidated results of log-transformed analyses. Total and ambulatory costs in patients among the high- and medium-severity depression symptom tertiles were 51% to 86% higher than those of patients in the low-severity tertile. Primary care costs were significantly higher (51% higher; P = .002) only in patients in the high-severity compared with the low-severity tertile. Depressive symptom severity was not significantly associated with specialty care costs among utilizers of specialty care.

### Table 3. Unadjusted Six-month Health Care Costs by Depressive Symptom Severity Tertiles

<table>
<thead>
<tr>
<th>Depressive Symptom Severity Tertiles</th>
<th>Low (n = 115)</th>
<th>Medium (n = 117)</th>
<th>High (n = 118)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costs, $</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2094 ± 3052</td>
<td>2663 ± 2864</td>
<td>3654 ± 4258</td>
</tr>
<tr>
<td>Primary care</td>
<td>356 ± 367</td>
<td>484 ± 444</td>
<td>641 ± 730</td>
</tr>
<tr>
<td>Specialty care</td>
<td>253 ± 686</td>
<td>396 ± 779</td>
<td>431 ± 954</td>
</tr>
<tr>
<td>Emergency department</td>
<td>81 ± 375</td>
<td>128 ± 479</td>
<td>185 ± 548</td>
</tr>
<tr>
<td>Prescription</td>
<td>561 ± 481</td>
<td>710 ± 453</td>
<td>918 ± 778</td>
</tr>
<tr>
<td>Inpatient</td>
<td>379 ± 1523</td>
<td>353 ± 1680</td>
<td>777 ± 2620</td>
</tr>
<tr>
<td>Ambulatory care</td>
<td>1638 ± 1682</td>
<td>2276 ± 1869</td>
<td>2830 ± 2439</td>
</tr>
<tr>
<td>Mental health</td>
<td>10 ± 70</td>
<td>15 ± 88</td>
<td>55 ± 187</td>
</tr>
</tbody>
</table>

*Data are given as mean ± SD.

### Table 4. Adjusted Cost Ratios of 6-Month Median Health Care Costs by Depressive Symptom Severity Tertiles

<table>
<thead>
<tr>
<th>Depressive Symptom Severity Tertiles</th>
<th>Cost Ratio (95% Confidence Interval)$^\dagger$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costs, $</td>
<td>Medium-Low</td>
</tr>
<tr>
<td>Total</td>
<td>1.54 (1.20-1.97)</td>
</tr>
<tr>
<td>Ambulatory</td>
<td>1.51 (1.21-1.89)</td>
</tr>
<tr>
<td>Primary care</td>
<td>1.23 (0.96-1.58)</td>
</tr>
<tr>
<td>Specialty care</td>
<td>1.32 (0.88-1.97)</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, medical comorbidity, diabetes severity, and diabetes knowledge.

$^\dagger$At least 1.00, equivalent to P < .05.

The percentage of days in oral hypoglycemic therapy interruptions was significantly associated with depressive symptom severity (Table 2). Post hoc analyses showed that this association was accounted for by patients in the high-severity tertile having a significantly greater percentage of interruptions in their use of oral hypoglycemics compared with the low-severity tertile (F1,126 = 4.13 [P = .04]). The medium-severity tertile did not significantly differ from the other tertiles in this regard. Depressive symptom severity was associated with a nonsignificant increase in HbA1c level (Table 2).
In a primary-care–based sample of patients with types 1 and 2 diabetes in a staff-model HMO, we found that depressive symptom severity was significantly associated with less adherence to dietary recommendations and approximately twice as many interruptions in refills of oral hypoglycemics. Depressive symptom severity was associated with a nonsignificant increase in HbA1c level. After controlling for demographics, medical comorbidity, and diabetes severity, higher levels of depressive symptom severity were associated with significantly worse mental and physical functioning and a significantly greater probability of having any emergency department, primary care, specialty care, medical inpatient, and mental health costs compared with patients with low-severity depressive symptoms. Among those patients with health care utilization among the various cost categories, depressive symptom severity was associated with significantly higher ambulatory, primary care, and total costs. 

There was a significant association between depression severity and decreased age, which is consistent with a higher reported prevalence of depression in younger compared with older patients in the large Epidemiological Catchment Area Study. There was also a significant association between depression severity and greater diabetes knowledge. We suspect that knowledge was related to depression through confounding by severity of diabetes, ie, patients with more severe diabetes are more knowledgeable about diabetes and more likely to be depressed. In fact, after controlling for diabetes severity, we found that the correlation between knowledge and depression severity decreased from 0.16 (P = .004) to 0.09 (P = .08).

The medium-severity depressive symptom tertile range in this study (HSCL-20 scores, 0.5-1.0) corresponds to subdiagnostic ranges of depressive symptom severity. Even in the high-severity depressive symptom tertile, an HSCL-20 depression score of greater than 1.0 represents a mixture of patients with dysthymia and minor or major depression. For example, the mean HSCL score of the highest severity tertile (1.65; SD, 0.59) (Table 1) is higher than the mean HSCL score of 1.4 in a recent large sample of 417 primary care patients with dysthymia and minor depression. It is impressive, therefore, that we had such robust results with respect to the adverse impact of depressive symptom severity, given the relatively low level of depressive symptom severity among many of these primary care diabetic patients. However, previous studies have shown that patients with minor depression or dysthymia have significant functional impairment and higher medical costs compared with non-depressed control subjects. The major outcomes of this study may be even more clinically relevant when one considers the probable impact of more serious depressive episodes on adherence, functioning, and medical costs in diabetic patients. An estimated 10% to 15% of patients with diabetes have been found to have major depression.

The finding of higher health care costs among more depressed patients in this study corresponds with data showing that, among aging primary care patients with diverse medical illnesses, depression makes a significant independent contribution to increased health care utilization. We have shown increased health care costs among depressed diabetic patients to be largely the result of increased medical, not mental health, utilization. Lustman et al have shown that in diabetes, depression is a better predictor of symptoms commonly associated with worsening glucose control (ie, polyphagia and polydipsia) than HbA1c levels. In addition, depressive symptoms have been shown to be associated with a perception of more impaired physical health and may mimic worsening diabetes symptoms (eg, fatigue or appetite change). It is possible that the perception of worse control of diabetes and general poor physical health by the patient (and, in turn, by the provider) prompted increases in health care utilization and subsequent medical testing in this study sample.

Medical utilization in depressed diabetic patients also may be increased as a result of objective worsening of glucose control, which may result from changes in the autonomic nervous system, the hypothalamic-pituitary adrenal axis, or neurotransmitters. Winokur et al have shown that depressed patients have increased insulin resistance after oral glucose testing compared with non-depressed patients. Changes in glucose control may also be related to poorer adherence to treatment among depressed diabetic patients. In this study, we have shown that depressive symptom severity was associated with significantly worse adherence to type and amount of diet (even in patients in the medium-severity tertile) and to use of oral hypoglycemics. Although HbA1c level was not associated significantly with depressive symptom severity, the trends were in a similar direction (eg, as depressive symptom severity increased, HbA1c levels tended to increase). Previous researchers have reported the effect of depression on worsening adherence to various self-care strategies (glucose monitoring, exercise, diet, or medications) in diabetes. The importance of improving adherence to treatment of diabetes has been emphasized in the Diabetes Control and Complications Trial and the United Kingdom Prospective Diabetes Study, both of which showed that strict adherence to diabetes treatment regimens (and lowering of blood glucose levels) in patients with type 1 and 2 diabetes, resulted in a decreased risk of long-term complications. Other studies have shown that depression is directly associated with an increased risk of diabetic complications, especially retinopathy and macrovascular complications. The implications of untreated depression on long-term complications are even more significant when one considers that depression tends to be recurrent in diabetes, ie, 79% of patients reporting a history of major depression relapsed during a 5-year follow-up period, with an average of 4 episodes per patient.

There are several limitations of this study. Although this was a population-based study of diabetic patients from 2 large primary care clinics, there was a relatively small sample size, especially for assessing costs. Despite this, our results remain relatively robust. Furthermore, despite being a primary care sample, findings of this predominantly white, educated, employed, and insured HMO population may not be generalizable to
other settings. Particularly at issue may be the smaller degree of socioeconomic barriers to treatment in this sample. Another possible limitation of this study is the use of self-report questionnaires to derive levels of depressive symptom severity rather than structured interviews to make a diagnosis of major depression. Because this study reports cross-sectional observational data, causal inferences about depressive symptoms on the reported outcomes cannot be made. Alternative explanations, such as the depressive symptoms resulting from poorer diabetes outcomes or the possibility that unmeasured third factors may be responsible for this relationship, must be considered. Clinically, causality may be in both directions, with possible interactions, and only further prospective longitudinal studies will help resolve these issues.

An implication of the findings of this study is that because depressive symptom severity is associated with increased costs, decreased adherence to treatment regimens (potentially worsening the course of the illness), and additional functional impairment in diabetic patients, it is highly probable that much of the adverse impact of depressive symptoms may be reduced significantly by effective treatment of depression. Although ours is not a treatment study, 2 recent randomized control trials have shown antidepressants and cognitive-behavioral therapy to be more effective than placebo or an educational group in reducing depressive symptoms in diabetic patients from specialty clinics. The cognitive behavioral trial also reported that patients in the cognitive-behavior therapy arm of the trial had improvement in HbA1c levels during the course of the 6-month follow-up compared with controls. However, studies have also shown that roughly 2 of 3 depressed diabetic patients seen in primary care receive no specific antidepressant treatment. Our data suggest that studies are needed to screen a population base of primary care patients with diabetes for depression and to test health service interventions aimed at improving outcomes. Stepped or collaborative care programs in which rigorous screening, proper identification, and effective multimodal treatment of depression are performed have been shown to improve symptom and functional outcomes of mixed age groups of primary care patients but have not been tested in a large group of patients with depression and the same medical illness.

Although these collaborative care programs in primary care have not shown a cost offset effect, they have been shown to be moderately cost-effective. For an additional cost of $400 to $500 per patient per year, response rates improved from approximately 40% recovery in usual primary care to 70% response rates in collaborative care. This study, diabetic patients with HbA1c depressive symptom severity scores of at least 0.5 had total annual costs of greater than $2100 above those with HbA1c depressive symptom severity scores below 0.5 (mean±SD, $6382±$7232 vs $4208±$6178, respectively). Intervention studies are needed to test the cost-effectiveness (and possible cost offset) of models of care that screen for depression and randomize primary care diabetic patients to a collaborative care program of depression treatment compared with usual care.

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