Relationship of Depression and Diabetes Self-Care, Medication Adherence, and Preventive Care

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OBJECTIVE — We assessed whether diabetes self-care, medication adherence, and use of preventive services were associated with depressive illness.

RESEARCH DESIGN AND METHODS — In a large health maintenance organization, 4,463 patients with diabetes completed a questionnaire assessing self-care, diabetes monitoring, and depression. Automated diagnostic, laboratory, and pharmacy data were used to assess glycemic control, medication adherence, and preventive services.

RESULTS — This predominantly type 2 diabetic population had a mean HbA_{1c} level of 7.8 ± 1.6%. Three-quarters of the patients received hypoglycemic agents (oral or insulin) and reported at least weekly self-monitoring of glucose and foot checks. The mean number of HbA_{1c} tests was 2.2 ± 1.3 per year and was only slightly higher among patients with poorly controlled diabetes. Almost one-half (48.9%) had a BMI >30 kg/m^2, and 47.8% of patients exercised once a week or less. Pharmacy refill data showed a 19.5% nonadherence rate to oral hypoglycemic medicines (mean 67.4 ± 74.1 days) in the prior year. Major depression was associated with less physical activity, unhealthy diet, and lower adherence to oral hypoglycemic, antihypertensive, and lipid-lowering medications. In contrast, preventive care of diabetes, including home-glucose tests, foot checks, screening for microalbuminuria, and retinopathy was similar among depressed and nondepressed patients.

CONCLUSIONS — In a primary care population, diabetes self-care was suboptimal across a continuum from home-based activities, such as healthy eating, exercise, and medication adherence, to use of preventive care. Major depression was mainly associated with patient-initiated behaviors that are difficult to maintain (e.g., exercise, diet, medication adherence) but not with preventive services for diabetes.

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The World Health Organization estimates that at least 170 million individuals suffer from diabetes globally, and this figure is likely to double by 2030 (1). Diabetes-related complications are major causes of morbidity and mortality. Optimal outcomes in diabetes require diligent and daily self-management, including eating a healthy diet, exercising, and regular glucose monitoring (2–4). The American Diabetes Association publishes standards of medical care yearly to promote the importance of achieving optimal glycemic control (HbA_{1c} <7%) (2). Comprehensive treatment includes lifestyle modifications; pharmacological control of hyperglycemia, hypertension, and hyperlipidemia; and preventive care such as monitoring for glycemic control or retinopathy. Depression not only affects mood but compromises functioning as well (5,6). Among diabetic patients, depression is twice as common as compared with matched control subjects without diabetes (7,8). When depression accompanies diabetes, there is evidence of poorer glycemic control, decreased physical activity, higher obesity, and potentially more diabetes end-organ complications and impaired function (9–14). There is also evidence that depression is associated with decreased adherence to oral hypoglycemic prescriptions (15).

However, studies of the relationship between depression and diabetes self-care have been based on smaller samples of patients or have assessed limited aspects of diabetes management in primary care. Little is known about how depression influences the spectrum of diabetes management, ranging from home-based activities (e.g., diet, exercise, glucose monitoring) and medication adherence to preventive clinical services (e.g., HbA_{1c} testing or retinal examinations). This population-based study used self-report and automated clinical data to identify gaps in diabetes management. We also assessed how diabetic patients with depression differ from counterparts without depression to better understand the relationship of depression with specific aspects of self-management and preventive care.

RESEARCH DESIGN AND METHODS

— A population survey of health maintenance organization enrollees with diabetes was carried out to assess associations of major depression with self-care and other clinical outcomes. A multidisciplinary team from the Center

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Abbreviations: GHC, Group Health Cooperative; SDSCA, summary of diabetes self-care activity.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

for Health Studies at Group Health Cooperative (GHC) and the Department of Psychiatry at the University of Washington conducted this study. Institutional review boards from the GHC and University of Washington approved the study protocol.

The study was conducted between 2001 and 2003 at GHC, a prepaid health plan serving ~450,000 members in western Washington state. GHC enrollees reflect the demographic composition of Seattle and western Washington state, which is predominantly Caucasian (88%) with 6% Asian Americans, 4% African Americans, and 3% Latino and other minorities. Nine of the 30 staff-model primary care clinics were selected based on three criteria: *1*) a large number of diabetic patients; *2*) within a 40-mile geographic radius of Seattle; and *3*) racial and ethnic diversity.

In this epidemiologic survey, we assessed presence of major depression in ~4,500 primary care patients with diabetes. A GHC population-based diabetes registry that supported clinical care also facilitated case identification (16). Inclusion criteria for the diabetes registry were *1*) currently taking any diabetic agent, *2*) a fasting glucose ≥126 mg/dl confirmed by a second out-of-range test within 1 year, *3*) a random plasma glucose ≥200 mg/dl also confirmed by a second test within 1 year, or *4*) a hospital discharge diagnosis of diabetes at any time during GHC enrollment or two outpatient diagnoses of diabetes (16). Individuals aged ≥18 years in the diabetes registry received a mailed questionnaire that included a $3.00 gift certificate. If the patient did not return the survey in 4 weeks, we sent a second questionnaire. If the latter was not returned in 2 weeks, our research assistant made a reminder telephone call. This resulted in an overall response rate of 62%. Methods and recruitment are described further in an earlier publication (17).

Self-management for diabetes

We used a recently revised version of the Summary of Diabetes Self-Care Activities (SDSCA) (18) to assess diabetes self-management behaviors for diet, exercise, blood glucose testing, foot checks, and smoking status. The SDSCA is a brief, reliable, valid, and multidimensional measure of diabetes self-management behaviors based on self-report. Patients reported how many days in the prior week she/he engaged in a certain activity. SDSCA data can be reported as mean days of activity in the prior week as well as percent of patients with a specific number of days of activity in the prior week. We intended our results to focus on patients with the highest need of clinical interventions. Therefore, we report findings in reference to patients who infrequently performed specific self-care activities (once a week or less) instead of mean days in the prior week for that activity.

Adherence to oral hypoglycemic medicines

The GHC automated pharmacy database records all prescriptions filled by its enrollees since 1976. Computerized pharmacy refill data were used to assess adherence to oral hypoglycemic agents and antihypertensive and lipid-lowering medications for the year before each patient's interview date. The observation window, i.e., number of days prescribed oral hypoglycemic agents in the year, was estimated to be either: *1*) 365 for patients already using these medications at the beginning of the year or *2*) the number of days between the first prescription and the interview date for patients started on these medications during the year. Patients whose first oral hypoglycemic agent prescription had not been exhausted by the interview date were excluded.

The days that a patient lacked oral hypoglycemic, lipid-lowering, or antihypertensive medicines were labeled as nonadherent days. For each prescription, the days supplied was added to the date the prescription was filled. This is considered the expected refill date. If the next refill was obtained after the expected refill date, then the number of days between the expected refill date and the next refill date are counted as nonadherent days. The percent of nonadherent days is then estimated by the ratio of the total number of nonadherent days in the prior year (numerator) divided by the total number of days prescribed oral hypoglycemic agents, including the nonadherent days (denominator). The percent of nonadherent days allows us to combine information across patients with various lengths of follow-up. A similar measure, using automated pharmacy data, was used by a prior study to evaluate noncompliance with antihypertensive medications (19).

Clinical measures and use of diabetes services

Automated diagnostic, laboratory, and pharmacy data were used to assess glycemic control, diabetes complications, and treatment intensity. Diabetes complications were captured by ICD-9 codes indicating retinopathy; nephropathy; neuropathy; cerebrovascular, cardiovascular, and peripheral vascular disease; and ketoacidosis. This diabetes complication measure, based on an automated data prediction rule for complications (20), was also similar to one developed and validated in a tertiary care diabetes center (21). Computerized pharmacy records were used to measure medical comorbidity based on prescription drug use over the previous 12 months (22). Use of physician-initiated preventive care for diabetes included: HbA_{1c} testing, screening for microalbuminuria, and dilated retinal examinations.

Depression assessment

The Patient Health Questionnaire was used to assess depressive illness. This questionnaire yields a major depression diagnoses according to DSM-IV criteria and a continuous severity score (23). The Patient Health Questionnaire diagnosis has high agreement with major depression diagnosis based on structured interviews (78% sensitivity and 98% specificity) (23,24).

Statistical analyses

We checked for nonresponse bias by examining differences between survey respondents and nonrespondents using deidentified data and propensity score analysis. Nonrespondents are more likely to be younger, use insulin, have higher HbA_{1c}, have comorbid heart disease, and are less likely to use specialty care. There was some evidence of variability in response across service centers. Analysis of nonresponse is described further by Katon et al. (17) in an earlier publication. Differences in estimates based on weighted and unweighted data were negligible in initial analyses, so we report results of analyses based on observed data in this study. The first analytic step described clinical characteristics, self-care behaviors, medication adherence, and preventive services among the sample that completed the questionnaire and allowed access to automated data. Next, we modeled the probability of self-care activ-

Table 1—*Clinical characteristics*

Clinical characteristics	*n*	Means ± SD or percent
Type 2 diabetes		95.6
Treatment intensity		
Diet		25.4
Oral hypoglycemic		59.0
Insulin, alone, or plus oral medications		30.1
Number of HbA_{1c} tests in prior year		2.2 ± 1.3
HbA_{1c} level (%)		7.8 ± 1.6
Number of diabetes complications		1.4 ± 1.5
Major depression		12.0
BMI >30 kg/m^2		48.9
Smoker		8.7
General self-care activities (days performed in the past week)	4,463	
Healthy eating once weekly or less		9.8
Five servings of fruits/vegetables once weekly or less		21.6
High-fat foods ≥6 days		12.4
Physical activity once weekly or less (≥30 min)		29.3
Specific exercise session once weekly or less		47.8
Diabetes-specific self-care (patients on hypoglycemic medications or insulin)	3,439	
Tested blood sugar once weekly or less		17.9
Tested recommended times once weekly or less		24.8
Checked feet once weekly or less		20.1
Checked inside of shoes once weekly or less		59.9
Medication adherence	2,655	
Nonadherence to oral hypoglycemic medicines in prior year		19.5 (64.7 days)

ities, adherence to oral hypoglycemic medicines, and use of preventive services using a generalized estimating equation approach to adjust for clustering of patients within physicians (25). We modeled the continuous adherence outcome using the identity link and the probability of dichotomous outcomes using a logit link. Because one of our primary interests is in the association between major depression and diabetes self-care, including medication adherence and use of preventive services, all models include a covariate indicating major depression (yes/no). Other covariates included are: age, sex, marital status, education, race/ethnicity, medical comorbidity, diabetes complications, treatment intensity, and primary care physician.

RESULTS — A total of 9,063 questionnaires were mailed to patients on the diabetes registry from nine Group Health primary care clinics. Among these, 1,222 were not eligible for the study due to plans for disenrollment (444), spurious diagnosis of diabetes (259), too ill to participate (202), deaths (128), language problems or hearing impairment (99), cognitive impairment (80), gestational diabetes (8), and other miscellaneous reasons (2). A total of 3,002 questionnaires were not returned. Among the 4,839 participants who returned questionnaires (61.7% of eligible patients), 4,463 completed the Patient Health Questionnaire and gave us their consent to review automated records. The sample with HbA_{1c} results included 4,385 subjects, because 78 had no HbA_{1c} test in the prior 18 months.

Approximately one-half of the sample were men (51.3%), and the mean age was 63.3 ± 13.4 years. Approximately one-fifth were minorities, including 8.3% African Americans and 9.3% Asian Americans; three-quarters of the sample received some college education. Table 1 shows that the majority of patients had type 2 diabetes (95.6%). Approximately one-quarter of patients did not receive any hypoglycemic agents, 59.0% received oral agents, and 30.1% received insulin alone or in addition to oral agents. The mean HbA_{1c} level was 7.8 ± 1.6%, with an average of 1.4 ± 1.5 complications per patient. One-half of the patients were obese, and <9% were smokers.

Self-management, medication adherence, and preventive care

Table 1 highlights findings for patients who reported infrequent self-care activities (once weekly or less). Approximately one-half (47.8%) of the sample engaged in exercise sessions only once a week or less, whereas 10% reported that they rarely followed a healthy diet plan. Among patients receiving medication to control hyperglycemia, infrequent self-monitoring of blood glucose was reported by one-quarter of patients, and one-fifth checked their feet once or less in the prior week.

Nonadherence was common among patients prescribed oral hypoglycemic medications. On average, patients were nonadherent 64.7 ± 74.1 days during the prior year, and the average proportion of nonadherent days across patients was 19.5%. More than one-half (59.8%) lacked more than a 1-month supply of hypoglycemic medication, and more than one-quarter (27.0%) lacked more than a 3-month supply of medicines in the prior year.

Overall clinical monitoring of diabetes and use of preventive services were lower than American Diabetes Association recommendations. The mean number of HbA_{1c} tests in the prior year (2.2 tests) was lower than the American Diabetes Association recommendation of four tests per year. Among patients with poor control (HbA_{1c} ≥8%), the mean number of HbA_{1c} tests per year was also low as well (2.4 tests per year). Only one-half of the patients received annual clinical screening for microalbuminuria. In contrast, almost 90% of patients received a retinal examination in the prior year.

Major depression and diabetes self-care

Major depression was present among 12% of this primary care sample with diabetes and was more prevalent among women with diabetes than men (14.4 vs.

Table 2—*Diabetes self-care and depression

Self-care activities (past 7 days)	*n*	No major depression	Major depression	Odds ratio†	95% CI	*P*
Diet						
Healthy eating once weekly or less		8.8%	17.2%	2.1	1.59–2.72	<0.0001
Five servings of fruits/vegetables once weekly or less		21.1%	32.4%	1.8	1.43–2.17	<0.0001
High-fat foods ≥6 times weekly		11.9%	15.5%	1.3	1.01–1.73	<0.04
Exercise						
Physical activity (≥30 min) once weekly or less		27.3%	44.1%	1.9	1.53–2.27	<0.0001
Specific exercise session once weekly or less		45.8%	62.1%	1.7	1.43–2.12	<0.0001
Smoking						
Yes		7.7%	16.1%	1.9	1.42–2.51	<0.0001
Glucose monitoring (patients on medications)	3,439					
Test blood glucose less than once weekly		17.8%	18.2%	1.1	0.80–1.44	NS
Test blood glucose as recommended less than once weekly		24.5%	26.7%	1.1	0.89–1.47	NS
Foot check (patients on medications)	3,439					
Checked feet less than once weekly		20.1%	19.7%	1.0	0.76–1.29	NS
Checked inside of shoes less than once weekly		59.7%	61.4%	1.1	0.88–1.36	NS
Total		3,927	536			

*Percentages are unadjusted; †Odds ratios are adjusted for the covariates age, sex, marital status, education, race/ethnicity, medication risk, complications, treatment intensity, clinic, and physician generalized estimating equation (GEE).

9.8%). Focusing on patients with infrequent self-care activities (once weekly or less), patients with major depression were more likely to lack self-care activities when compared with patients without major depression (Table 2). Major depression was associated with infrequent fruit and vegetable intake (32.4 vs. 21.1%) and more frequent fat intake (15.5 vs. 11.9%). Depressed patients were also more sedentary than nondepressed patients, with almost two-thirds (62.1%) reporting an exercise session once or less in the prior week. Smoking was twice as prevalent among depressed patients than nondepressed patients. In contrast, there was no difference between depressed and nondepressed patients with regard to frequency of self-monitoring of blood glucose or foot checks for ulcers or infections. Parallel analyses using mean scores for SDSCA variables also attained nearly identical results.

Major depression: medication adherence and preventive care

Diabetic patients with major depression showed less adherence than diabetic patients without major depression with the three classes of medications examined: oral hypoglycemic, antihypertensive, and lipid-lowering agents. On average, depressed patients were nonadherent to oral hypoglycemic medicines 80 days in the prior year compared with 62 days for nondepressed patients, and the average percent of nonadherent days was 24.5% in depressed patients compared with 18.8% in nondepressed patients. Adjusting for covariates reduced but did not eliminate differences in adherence for depressed and nondepressed patients (adjusted difference 3.62 [95% CI 1.18–6.06], $P < 0.005$). In a similar manner, depressed patients were less adherent with antihypertensive and lipid-lowering medicines when compared with nondepressed patients with diabetes (Table 3). A slightly higher proportion of patients with depression received no HbA_{1c} test in the prior year (6.3 vs. 4%, $P < 0.005$). Otherwise, there was no difference between the depressed and nondepressed patients in use of diabetes monitoring and preventive services (Table 3).

CONCLUSIONS — In a large population of primary care patients (n = 4,463) with diabetes, both self-report and automated clinical data showed suboptimal levels of diabetes care across a continuum from self-management and medication adherence to preventive care. This study highlights three notable deficiencies in diabetes management—lack of physical activity, high nonadherence rates to oral hypoglycemic medicines, and inadequate clinical monitoring of glycemic control. Interestingly, even among patients with poor control (HbA_{1c} ≥8%), the mean number of HbA_{1c} tests per year was low (2.4 tests per year).

Coexisting major depression was associated with smoking, lack of exercise, and unhealthy eating. Depressed patients adhered less to oral hypoglycemic agents and antihypertensive and lipid-lowering medications. For example, depressed patients used ~20 less days of hypoglycemic agents in the prior year than nondepressed patients. Surprisingly, depression was not related to self-monitoring of blood glucose or daily foot checks. Clinical monitoring and preventive care for diabetes were also similar for patients with and without major depression. Depression did not influence use of physician-initiated services, such as tests for HbA_{1c}, microalbuminuria, and retinopathy.

Findings indicating suboptimal diabetes management across the spectrum of self-care, adherence to medication, and clinical recommendations are not new (26,27). However, effective disease management interventions exist for the three key deficiencies this study identified—lack of physical activity, very high rates of nonadherence to oral hypoglycemic medicines, and inadequate clinical monitoring of glycemic control (28–30). These results can guide quality improvement in-

Table 3—*Medication adherence and use of preventive diabetes services

	Unadjusted means/proportions		Model-based (adjusted) estimates			
	No major depression	Major depression	Mean difference	Odds ratio	95% CI	*P* (*n*)
Nonadherence to medication						
Oral hypoglycemic	18.8%	24.5%	3.62	—	1.18–6.06	<0.005
Lipid lowering	19.3%	27.2%	6.79	—	3.11–10.46	<0.0005
ACE inhibitors	21.6%	27.9%	5.59	—	1.41–9.78	0.01
Preventive diabetes services						
No HbA_{1c} test within the last year	4.0%	6.3%	—	1.9	1.27–2.87	<0.005 (4,347)
Fewer than three HbA_{1c} tests per year among patients with HbA_{1c} >8%	55.1%	55.5%	—	0.9	0.70–1.21	NS (1,922)
No retinal examination within the last year	19.4%	17.2%	—	1.0	0.74–1.24	NS (4,347)
Less than two examinations within 2 years among patients with retinopathy	24.8%	22.5%	—	0.8	0.55, 1.31	NS (1,179)
No microalbumin urine test within the last year among patients not taking ACE inhibitors	47.0%	45.6%	—	1.0	0.80–1.33	NS (1,831)

*Nonadherence to medication outcomes are continuous measures of the percentage of nonadherent days for each individual. Preventive diabetes services outcomes are dichotomous, indicating use or no use. Model-based estimates of percentage point difference in adherence and odds ratios with corresponding CIs and *P* values are adjusted for age, sex, marital status, education, race/ethnicity, medication risk (a pharmacy-based comorbidity measure), diabetes complications, and treatment intensity. Models also adjust for clustering by clinic and physician.

terventions to target diabetic patients at highest risk of complications (e.g., HbA_{1c} ≥8%) and reach those in most need of self-management support (31,32).

The finding that patients lacked oral hypoglycemic medicines for a total of ≥2 months in the prior year underscores a critical shortcoming in diabetes care that has not received adequate notice. Optimal glycemic control and favorable diabetes outcomes cannot be achieved with low adherence to hypoglycemic medicines. Knowledge on adherence to diabetes medication has mainly been based on self-report data, which can be prone to overestimating adherence (18). A large British study using pharmacy refill data reported even lower levels of adherence than our study findings (33).

The addition of mood disorder assessment in the 2004 American Diabetes Association standards of medical care reflects a growing recognition of depression's influence on diabetes care and outcomes (2). This study identified specific gaps in diabetes management that are associated with concurrent depression—medication adherence and self-care activities such as exercise or healthful diet. A meta-analysis on adherence to pharmacotherapy in a variety of illnesses found that depressed patients adhered less to prescribed medicines than nondepressed patients (34). This study showed that coexisting depression was associated with higher nonadherence to all three types of long-term pharmacotherapy examined: oral hypoglycemic, antihypertensive, and lipid-lowering medicines.

A better understanding of specific self-care activities that are compromised in depression can shed light on the relationship between depression and unfavorable diabetes outcomes, such as higher HbA_{1c} levels and more diabetes complications (35). It is noteworthy that depression was not associated with less self-monitoring activities for diabetes such as home glucose or foot checks. However, higher proportions of depressed patients reported very infrequent exercise and healthful diet and more smoking. Even though higher rates of obesity and smoking are not unique to diabetic patients with depression (36,37), unfortunately, smoking and lack of exercise or healthy diet can lead to dire complications such as blindness, heart failure, or renal failure among patients with diabetes. Behavioral changes to increase exercise and healthy nutrition and decrease smoking require motivation, energy, confidence, and sustained effort, which are the exact attributes that depressed people lack. These results suggest much need for interventions that support and sustain specific lifestyle modifications among diabetic patients, especially those who suffer concurrent depression.

Existing research shows that, in general, patients with depression use more medical services when compared with patients without depression (38,39). It would be logical to expect that depressed patients with diabetes may have more visits and would use more preventive care services as well. Our study found that physician-initiated services, such as HbA_{1c} testing and monitoring for nephropathy or retinopathy, were not higher among depressed as compared with nondepressed patients. Depression appears to influence patient-initiated activities more than physician-initiated services.

The cross-sectional design of this survey cannot shed light on possible causes or mechanisms of the observed relationships. Other limitations of the study include the potential overestimation of self-care activities such as healthy diet, exercise, and glucose monitoring by self-report. These findings may be less generalizable in locales with fewer Asian Americans or more Hispanic or African Americans. Data on blood pressure measurement and foot examinations were not available via automated clinical data. Although use of pharmacy prescription data

to assess medication adherence is imperfect, these results avoid the error of overreporting of medication use or ceiling effect seen in self-report data (18). The number of lapsed refill days reported here was a conservative estimate of the nonadherence because we are assuming that patients consumed all oral hypoglycemic medications they refilled.

Recent research illustrates that applying a chronic care model (40) to diabetes care, such as reorganizing services to monitor patient progress regularly, and support for patient self-management can achieve better quality of care (e.g., HbA_{1c} monitoring) and clinical outcomes (16,41). However, the observed links between depression and big gaps in patient-initiated self-care activities such as regular exercise and adherence to oral hypoglycemic medicines imply a need to integrate depression screening and treatment into quality improvement programs for diabetes. In particular, diabetic patients with depression need support for self-management activities such as lifestyle modifications and medication adherence. Further research is needed to evaluate whether integrating depression screening and treatment into comprehensive care of diabetes could enhance self-management, adherence, and patient outcomes.

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