

Behavioral and Clinical Factors Associated With Depression Among Individuals With Diabetes

WAYNE KATON, MD¹
MICHAEL VON KORFF, SCD²
PAUL CIECHANOWSKI, MD, MPH¹
JOAN RUSSO, PHD¹
ELIZABETH LIN, MD, MPH²

GREGORY SIMON, MD, MPH²
EVETTE LUDMAN, PHD²
EDWARD WALKER, MD¹
TERRY BUSH, PHD²
BESSIE YOUNG, MD, MPH³

OBJECTIVE — The goal of this study was to determine the behavioral and clinical characteristics of diabetes that are associated with depression after controlling for potentially confounding variables.

RESEARCH DESIGN AND METHODS — A population-based mail survey was sent to patients with diabetes from nine primary care clinics of a health maintenance organization. The Patient Health Questionnaire was used to diagnose depression, and automated diagnostic, pharmacy, and laboratory data were used to measure diabetes treatment intensity, HbA_{1c} levels, and diabetes complications.

RESULTS — Independent factors that were associated with a significantly higher likelihood of meeting criteria for major depression included younger age, female sex, less education, being unmarried, BMI ≥ 30 kg/m², smoking, higher nondiabetic medical comorbidity, higher numbers of diabetes complications in men, treatment with insulin, and higher HbA_{1c} levels in patients <65 years of age. Independent factors associated with a significantly higher likelihood of meeting criteria for minor depression included younger age, less education, non-Caucasian status, BMI ≥ 30 kg/m², smoking, longer duration of diabetes, and a higher number of complications in older (≥ 65 years) patients.

CONCLUSIONS — Smoking and obesity were associated with a higher likelihood of meeting criteria for major and minor depression. Diabetes complications and elevated HbA_{1c} were associated with major depression among demographic subgroups: complications among men and HbA_{1c} among individuals <65 years of age. Older patients with a higher number of complications had an increased likelihood of minor depression.

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A recent meta-analysis of 39 studies in patients with diabetes reported an estimate of major depression in 11% of patients based on structured psychiatric interviews and elevated depression symptoms in 31% based on

depression-rating scales (1). Prior research on sociodemographic predictors of depression in patients with diabetes has shown high risk for female sex (2–4), younger age (2–4), less education (2–6), and less income (1,3,4,7). Depression has

also been found in two recent meta-analyses to have significant associations with increased HbA_{1c} levels (8) and diabetes complications (9). Most of the studies included in these meta-analyses had small, nonrepresentative samples and did not fully characterize the depressed versus the nondepressed patients in terms of the number of complications, type of diabetes, insulin dependence, behavioral risk factors (i.e., smoking, obesity), medical comorbidity, socioeconomic variables, race, or ethnicity (1,8,9). The lack of reporting of sociodemographic and clinical variables in most studies is a significant limitation, as analyses of the association between depression and diabetes severity and HbA_{1c} have often not controlled for potentially important confounding variables (1,8,9).

The small sample sizes also precluded the study of potentially important interactions such as the effect of age and sex on glycemic control and complications. Studies have suggested that younger and older patients with type 2 diabetes may represent distinct cohorts (10). Younger patients with poor self-management and glycemic control may not survive to geriatric years, and diabetes has no effect on longevity in patients who develop diabetes after age 75 years (10). Sex interactions are important to explore because lower quality of care for heart disease and diabetes has been documented in women (11) and greater cardiac mortality has been shown in women with diabetes (12).

In this report, we describe the results of a population-based study of individuals with diabetes enrolled in one health plan in western Washington State. Our study goals are to answer three questions after controlling for sociodemographic factors. 1) Are behavioral factors that are known to increase the risk for development of diabetes (i.e., smoking, obesity) more likely to be present in patients with major and minor depression versus nondepressed patients with diabetes? 2) Do patients with adverse clinical characteristics of diabetes (i.e., higher HbA_{1c} levels and higher number of diabetes complica-

From the ¹Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, Seattle, Washington; the ²Center for Health Studies, Group Health Cooperative, Seattle, Washington; and the ³Department of Medicine, Veterans Administration Hospital, University of Washington, Seattle, Washington.

Address correspondence and reprint requests to Wayne J. Katon, MD, Department of Psychiatry and Behavioral Sciences, Box 356560, University of Washington School of Medicine, 1959 NE Pacific, Seattle, WA 98195-6560. E-mail: wkaton@u.washington.edu.

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Abbreviations: GHC, Group Health Cooperative; HMO, health maintenance organization; PHQ, Patient Health Questionnaire.

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

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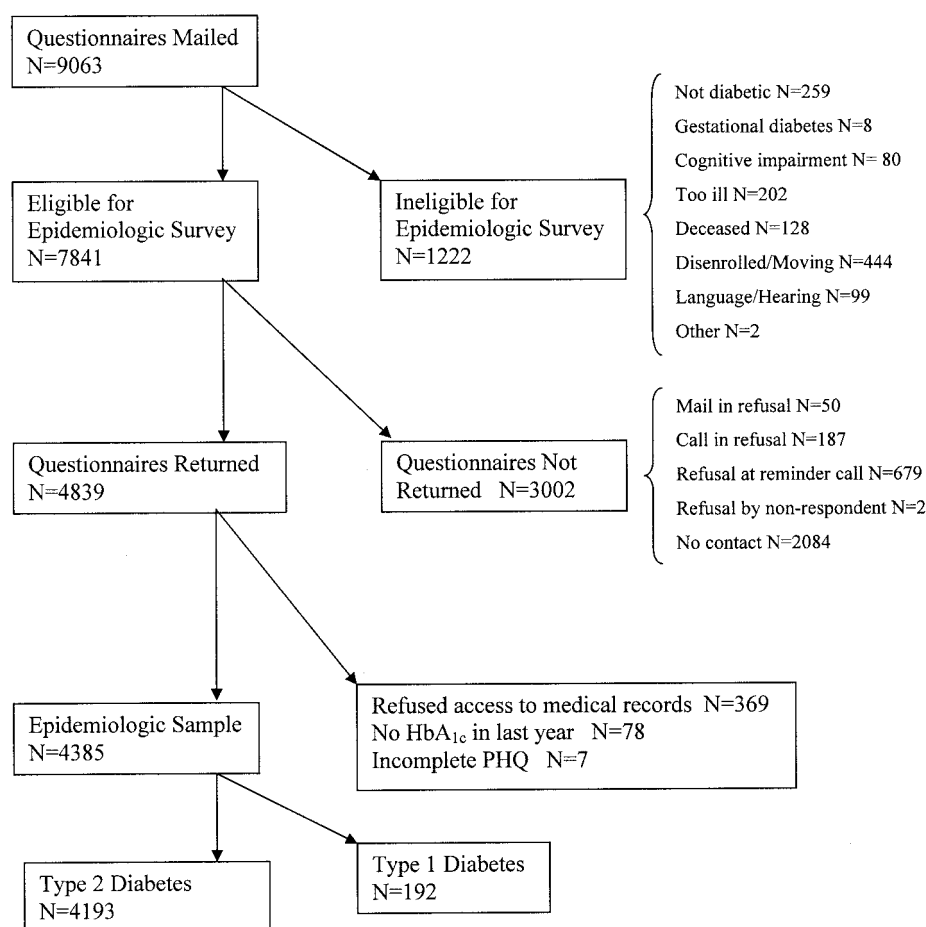


Figure 1—Recruitment for epidemiological study.

tions) have an increased likelihood of meeting criteria for major and minor depression? 3) Are there potential interactions of age and sex with behavioral and clinical factors that are associated with an increased likelihood of meeting criteria for major and minor depression?

RESEARCH DESIGN AND METHODS

The Pathways Study was developed by a multidisciplinary team in the Department of Psychiatry at the University of Washington and the Center for Health Studies at Group Health Cooperative (GHC). GHC is a nonprofit health maintenance organization (HMO) 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 GHC.

Nine GHC primary care clinics in western Washington were selected for the study based on three criteria: 1) clinics with the largest number of diabetic patients; 2) clinics within a 40-mile geo-

graphic radius of Seattle; and 3) clinics with the greatest amount of racial and ethnic diversity.

Case identification was facilitated by GHC's prior development of a population-based diabetes registry that supports patient care (13). Listing in the registry is based on: 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 (13).

Patients were screened in two sequential mailings with ~ 700 questionnaires sent per month. A potential third contact was by telephone, resulting in a 61.7% response rate (Fig. 1).

The Patient Health Questionnaire (PHQ)-9 was used to screen for depression. This questionnaire provides both a dichotomous diagnosis of major and minor depression and a continuous severity

score (14,15). The PHQ-9 diagnosis of major depression has been found to have high sensitivity (73%) and specificity (98%) to the diagnosis of major depression based on structured psychiatric interview (14). The criteria for major depression required the patient to have for at least 2 weeks five or more depressive symptoms present for more than one-half of the days, with at least one of these symptoms being either depressed mood or anhedonia (14,15). The criteria for minor depression requires two to four depressive symptoms for at least 2 weeks, with at least one of these symptoms being either depressed mood or anhedonia (16).

The questionnaire also included demographics on age, sex, years of education, employment, race, and marital status. Questions about clinical status included: age of onset and duration of diabetes, treatment at onset of disease, smoking, height, and weight. Patients were diagnosed as having type 1 diabetes

if onset was <30 years of age and insulin was the first treatment prescribed.

Computerized pharmacy records were used to compute a chronic disease comorbidity score known as Rx Risk, which was a measure of medical comorbidity based on prescription drug use over the previous 12 months (17). The Rx Risk has been found to be comparable with using ambulatory care groups (18) in predicting total future health care costs (17). A measure using automated diagnostic, pharmacy, and laboratory data was developed to indicate three aspects/domains of diabetes: 1) diabetes complications; 2) treatment intensity required; and 3) glycemic control. ICD-9 codes for seven types of diabetes complications (retinopathy, nephropathy, neuropathy, cerebrovascular, cardiovascular, peripheral vascular, and metabolic) were used to identify the presence of specific complications. Pharmacy data regarding the use of oral hypoglycemic agents and insulin indicated the intensity of treatment. Our diabetes complication measure was similar to one previously developed based on automated data using ICD-9 codes and clinical data that correlated with medical costs in a tertiary diabetes center (19). GHC automated data on HbA_{1c} levels for the 18 months before screening were used for this study. The HbA_{1c} level closest in time before the return date of the screening questionnaire was used.

Statistical analysis

After obtaining institutional review board approval, we examined differences in deidentified data between survey respondents and nonrespondents using automated health care data. We excluded 369 survey participants who did not give permission to use automated medical records data. We estimated response propensity scores (probability of being a respondent) as a function of the following variables (all of these within the prior year): age, sex, most recent HbA_{1c} value, treatment with insulin, use of oral hypoglycemic medicines, received specialty mental health care, depression diagnosis in primary or specialty care, any prescriptions filled for antidepressant medication, hospitalization, Rx Risk score omitting diabetes and psychiatric medications, number of primary and specialty care visits, patient inclusion on the GHC heart disease registry, and patient primary care clinic. We predicted response/nonresponse status as a

function of these variables using PROC LOGISTIC of SAS (20). Using these predictors, we estimated a response probability for each survey respondent (response propensity score). We used a weighted analysis (weights inversely proportional to estimated probability of response) rescaled to sum to the observed sample size (i.e., the number of survey respondents). In a weighted analysis, individuals with a low probability of responding would be given a higher weight in the analysis to represent the larger number of nonrespondents with similar characteristics. We then compared weighted and unweighted analyses to see if postsurvey adjustment for factors related to nonresponse resulted in meaningful differences in survey estimates. Differences in weighted and unweighted data were negligible; therefore, we report analyses based on observed data.

We examined group differences in type 2 diabetic patients regarding sociodemographic, behavioral, and clinical variables between patients with major depression, minor depression, and those without depression using χ^2 tests for categorical variables. Analyses of variance were used for continuous measures.

Logistic regression models were constructed to model the odds of having major depression versus no depression and minor depression versus no depression. In these models, 14 variables were examined for association with depression, including sociodemographic characteristics, behavioral risk factors for diabetes, and diabetes clinical factors. The full model contained: six sociodemographic factors (age, sex, education, marital status, employment, and race); two behavioral risk factors (BMI and smoking); five diabetes clinical factors (Rx Risk score, HbA_{1c}, duration of diabetes, treatment intensity, and number of complications); and an indicator variable for clinic site. We examined potential for effect modification by testing the significance of interactions between age and sex with behavioral risk and diabetes factors. Only statistically significant interaction terms were retained in the final models. Odds ratios and their 95% CIs were estimated for all variables in the models.

RESULTS — Figure 1 describes the recruitment and eligibility requirement for the study sample. Of the 4,193 study patients, 79.5% ($n = 3,335$) had diabetes

alone, 12% ($n = 501$) met the *Diagnostic and Statistical Manual of Mental Disorders* (4th edition) criteria for major depression, and 8.5% ($n = 357$) had minor depression. The group with major depression was significantly more likely to be younger, female, and unmarried compared with the group without depression (Table 1). The group with minor depression was significantly less educated and less likely to be Caucasian than the group without depression. The major depression group was associated with significantly higher medical comorbidity, numbers of diabetes complications, higher HbA_{1c} levels, BMI ≥ 30 kg/m², higher percentage of smokers, higher frequency of treatment with insulin, and longer duration of diabetes compared with the no depression group. The minor depression group had the same pattern of results except that HbA_{1c} levels were not associated with depression status.

Clinic type was retained in the logistic models. Demographic characteristics associated with significantly higher likelihood of having major depression included younger age, female sex, less education, and being unmarried (Table 2). Behavioral and clinical factors associated with a significantly higher likelihood of major depression included: BMI ≥ 30 kg/m², smoking, higher medical comorbidity, number of diabetes complications, treatment with insulin, and higher HbA_{1c} levels. Two interactions were statistically significant: age with HbA_{1c} level and sex with complications. Age modified the relationship between major depression and HbA_{1c} such that for individuals <65 years of age, there is a strong relationship between major depression and HbA_{1c} ($\chi^2 [1] = 24.19, P < 0.001$), with 54.4% of those <65 years of age with major depression having HbA_{1c} $\geq 8.0\%$ compared with only 37.3% of those without depression. For subjects age ≥ 65 years, 36.4 and 32.3% of those with major depression and without depression had HbA_{1c} levels $\geq 8.0\%$, respectively ($\chi^2 [1] = 1.12, NS$). Younger patients in the study sample had significantly higher HbA_{1c} levels than older patients (8.0 ± 1.7 vs. 7.6 ± 1.3 , $F [2, 4,385] = 106.5, P < 0.001$).

Sex modified the relationship between complications and major depression, such that the association between complications and major depression is statistically significant for men ($\chi^2 [4] = 44.85, P < 0.001$) but not for women (χ^2

Table 1—Depression and demographic characteristics by depression grouping

Variables	Total sample	No depression	Minor depression	Major depression	Overall test statistics (χ^2 , df = 2)	Minor vs. none (χ^2 , df = 1)	Major vs. none (χ^2 , df = 1)
n (%)	4,193*	3,335 (79.5)	357 (8.5)	501 (12)			
Women	2,042 (48.7)	1,567 (47.0)	182 (51.0)	293 (58.5)	23.86†	1.91	22.59†
High school or less	1,047 (25.3)	801 (24.3)	112 (31.7)	134 (27.2)	10.33‡	8.94‡	1.74
Unmarried and not living as married	1,403 (33.7)	1,068 (32.3)	132 (37.2)	203 (41.0)	14.89†	3.30	14.41†
Employment: full or part time	1,677 (41.2)	1,339 (41.2)	126 (36.8)	212 (44.6)	4.99	2.22	1.91
Caucasian	3,196 (77.7)	2,561 (78.2)	255 (72.2)	380 (77.9)			
African American	338 (8.2)	256 (7.8)	34 (9.6)	48 (9.8)	21.66†	10.14§	13.14‡
Asian	369 (9.0)	306 (9.3)	36 (10.2)	27 (5.3)	df = 6	df = 3	
Other	212 (5.2)	151 (4.6)	28 (7.9)	33 (6.8)			
Age in years	64.9 ± 12.6	64.9 ± 12.3	64.7 ± 13.3	59.7 ± 13.0	F(2, 4,190)	t(3,690)	t(3,834)
Rx Risk score					37.54†	0.22	8.69†
First quartile	1,024 ± 24.4	810 ± 24.3	89 ± 24.9	125 ± 25.0			
Second quartile	1,077 ± 25.7	895 ± 26.8	66 ± 18.5	116 ± 23.1	25.02†	14.10‡	12.99‡
Third quartile	1,040 ± 24.8	838 ± 25.2	95 ± 26.6	107 ± 21.4	df = 6	df = 3	df = 4
Fourth quartile	1,052 ± 25.1	792 ± 23.7	107 ± 30.0	153 ± 30.5			
Diabetes complications							
0	1,312 ± 31.3	1,094 ± 32.8	91 ± 25.5	127 ± 25.3			
1	1,333 ± 31.8	1,078 ± 32.3	106 ± 29.7	149 ± 29.7	51.51†	25.96†	33.58†
2	802 ± 19.1	619 ± 18.6	80 ± 22.4	103 ± 20.6	df = 8	df = 4	df = 2
3	423 ± 10.1	329 ± 9.9	35 ± 9.8	59 ± 11.8			
4+	323 ± 7.7	215 ± 6.4	45 ± 12.6	63 ± 12.6			
HbA _{1c} level groups					27.06†	1.79	25.94†
<8.00%	2,667 ± 63.6	2,179 ± 65.3	220 ± 61.6	268 ± 53.5			
≥8.00%	1,526 ± 36.4	1,156 ± 34.7	137 ± 38.4	233 ± 46.5			
Duration of diabetes in years							
>5	1,541 ± 36.8	1,269 ± 38.1	107 ± 30.1	165 ± 33.0			
>5–9.9	1,097 ± 26.2	872 ± 26.2	103 ± 28.9	122 ± 24.4	16.84‡	9.00‡	9.21‡
>10.0	1,548 ± 37.0	1,189 ± 35.7	146 ± 41.0	213 ± 42.6	df = 4	df = 2	df = 2
BMI					72.02†	7.95‡	67.38†
<30.0 kg/m ²	2,055 ± 49.7	1,736 ± 52.8	157 ± 44.7	162 ± 32.9			
>30.0 kg/m ²	2,077 ± 50.3	1,552 ± 47.2	194 ± 55.3	331 ± 67.1			
Smoking currently	357 ± 8.7	238 ± 7.3	37 ± 10.5	82 ± 16.7	49.66†	4.44§	47.63†
Treatment intensity							
None or diet	1,076 ± 25.7	910 ± 27.3	79 ± 22.1	87 ± 17.4	74.48†	13.21†	68.10†
Oral hypoglycemic	1,973 ± 47.0	1,607 ± 48.2	160 ± 44.8	206 ± 41.1	df = 4	df = 2	df = 2
Insulin or insulin+ oral hypoglycemic	1,144 ± 27.3	818 ± 24.5	118 ± 33.1	208 ± 41.5			

Data are n (%) or mean ± SD. *Sample size may vary with 10% missing data. df = 1 unless otherwise indicated; †P > 0.001; ‡P < 0.01; §P < 0.05.

[4] = 6.62). Male patients with major depression had almost twice the rate of having three or more complications (33.6%) in comparison with men with no depression (17.4%). For women, the rate of three or more complications was 17.7% for those with major depression and 15.1% for those with no depression.

Patients with minor depression were significantly younger, less educated, more

likely to be non-Caucasian, to have BMIs ≥ 30 kg/m², to smoke, and to have a longer duration of diabetes than those patients with diabetes only (Table 2). The only significant effect modification was that the relationship between minor depression and complications was modified by age. The association between complications and minor depression is statistically significant for patients ≥ 65 years old

(χ^2 [4] = 39.92, P < 0.001) but not for those <65 years of age (χ^2 [4] = 3.86). Among older patients with minor depression, 37.4% had three or more complications in comparison with 22.5% of the older patients with no depression. For younger patients, the rate of three or more complications was 7.3% for those with minor depression and 9.3% for those with no depression.

Table 2—Logistic regression models for major and minor depression versus no depression

Independent variables*	Major depression		Minor depression	
	Odds ratio	95% CI	Odds ratio	95% CI
Demographics				
Age (years)	0.96	0.95–0.98	0.97	0.95–0.99
Female sex	2.29	1.47–3.55	0.99	0.77–1.28
High school or less	1.34	1.04–1.72	1.44	1.10–1.88
Unmarried and not living as married	1.41	1.13–1.77	1.16	0.90–1.50
Employed	0.78	0.60–1.02	0.85	0.62–1.18
Racial ethnicity				
African American vs. Caucasian	1.21	0.80–1.80	1.11	0.70–1.75
Asian vs. Caucasian	0.85	0.54–1.34	1.52	1.01–2.30
Other vs. Caucasian	1.24	0.79–1.02	1.82	1.13–2.92
Risk factors				
BMI ≥ 30.0 kg/m ²	1.76	1.39–2.22	1.57	1.21–2.03
Smoking	2.15	1.56–2.95	1.61	1.08–2.38
Clinical factors				
Rx Risk score				
Second vs. first quartile	1.35	0.98–1.87	0.70	0.48–1.04
Third vs. first quartile	1.69	1.19–2.40	1.17	0.77–1.77
Fourth vs. first quartile	2.28	1.58–3.30	1.09	0.70–1.70
Duration of diabetes				
5–9.9 years vs. <5 years	0.88	0.74–1.30	1.39	1.01–1.90
≥ 10 years vs. <5 years	0.54	0.82–1.46	1.30	0.93–1.80
Diabetes complications				
1 vs. 0	1.45	0.90–2.33	0.30	0.06–1.34
2 vs. 0	2.04	1.23–3.41	0.34	0.06–2.14
3 vs. 0	2.63	1.50–4.62	0.03	0.001–0.67
4+ vs. 0	3.08	1.67–5.69	0.003	.0001–0.09
Treatment intensity				
Oral hypoglycemic vs. none or diet	1.04	0.78–1.40	1.00	0.73–1.37
Insulin vs. none or diet	1.54	1.08–2.19	1.22	0.83–1.79
HbA_{1c} level groups				
$\geq 8.0\%$	3.72	1.30–10.71	1.39	0.42–4.68
Age HbA _{1c} $\geq 8.0\%$ †	0.98	0.97–0.99		
Sex complications†				
1 vs. 0	0.63	0.35–1.13		
2 vs. 0	0.46	0.24–0.87		
3 vs. 0	0.24	0.11–0.52		
4 vs. 0	0.38	0.17–0.84		
Age complications†				
1 vs. 0			1.02	1.00–1.05
2 vs. 0			1.02	1.00–1.05
3 vs. 0			1.06	1.01–1.10
4 vs. 0			1.10	1.05–1.16

*Adjusted for clinic type. † $P < 0.05$.

CONCLUSIONS— Our data suggest an association of both major and minor depression with higher BMI and smoking. Obesity has become substantially more common in the U.S. and is correlated with the increasing prevalence of type 2 diabetes (21). There may be bidirectional effects between obesity and depression. Several longitudinal studies of adolescents report that depression in teenage

years was associated with a higher risk of developing obesity in early adulthood (22,23). Depression also is associated in cross-sectional studies with obesity in women but not men (22). Depression earlier in life has also been shown in prospective studies to increase the risk of type 2 diabetes by twofold (24,25). The comorbidity between depression and obesity may worsen the course of diabetes be-

cause both factors are associated with increased risk of adverse cardiac outcomes (26). In addition, depression has been shown to decrease adherence to diabetes diet (27) and predict dropout from weight loss programs (28).

The association between both major and minor depression and cigarette smoking is especially worrisome among people with diabetes. Smoking has been found to be associated with increased insulin resistance (29,30) and is a risk factor for macrovascular disease in patients with diabetes (31). National epidemiological studies have also found higher rates of smoking in patients with major depression compared with those without depression (32). A longitudinal study in teenagers found that depression increased susceptibility to peer pressure to begin smoking (33). Diabetes guidelines strongly recommend that patients with diabetes stop smoking, but Anda et al. (34) showed that over a 9-year period, smokers with depression were 40% less likely to quit than nondepressed smokers. Smokers with a history of depression versus those without a history of affective disorders were found to be more likely to develop a major depressive episode when they tried to quit smoking (35). Improving smoking cessation success rates in diabetic patients may require improving screening for and treatment of depression.

Our multivariate data suggest that after controlling for sociodemographic, behavioral, and clinical factors, having an HbA_{1c} level $\geq 8.0\%$ was associated with significantly increased odds of having major depression in younger but not older (>65 years) patients. There was no association between HbA_{1c} levels and minor depression. The fact that higher HbA_{1c} levels are associated with major depression in younger but not older patients may be because there are significant differences in these two populations (10). There may be a survivorship effect such that younger patients who do not follow self-care regimens or who have a more severe disease do not live to be older (10). The endocrine physiology of developing diabetes in later life may also differ from younger onset patients. For example, the onset of diabetes occurring in patients >75 years of age has little effect on longevity (10). Differences in endocrine physiology in younger versus older patients with diabetes are supported by the significantly higher HbA_{1c} levels in younger

versus older (>65 years) patients in our study. Two of three randomized controlled trials in mixed-age patients with depression and diabetes have shown that improving depression outcomes was associated with a significant decrease or a trend level decrease in HbA_{1c} levels (36–38). The only trial in depressed elderly patients with diabetes found that an intervention that improved depression outcomes was not associated with a difference between interventions and controls in HbA_{1c} levels (39).

After controlling for sociodemographic and behavioral factors, an increased number of diabetes complications was associated with a higher likelihood of meeting criteria for major depression for men but not women. Also, a higher number of complications increased the likelihood of meeting criteria for minor depression for patients >65 years of age but not for younger patients. We are not aware of other studies reporting sex and age differences in the association of complications with depression. There may be a reciprocal relationship between depression and diabetes complications. Women may be less likely to develop depression in the face of increasing diabetes complications because of having a wider and more flexible range of coping strategies compared with men (40). Depression is often caused by psychosocial as well as medical life stressors. Men have been shown to react to stressors with larger and more consistent increase in stress hormones, neurotransmitter metabolites, and blood pressure, which may worsen diabetes outcomes (41). The increase in older versus younger patients in risk of minor depression may be because older patients may have more problems coping physically and psychologically with higher numbers of diabetes complications because they likely already have more nondiabetic medical comorbidity.

Patients with major and minor depression in our sample were significantly younger, patients with major depression had an earlier age of onset of diabetes, and patients with minor depression had a longer duration of diabetes compared with nondepressed diabetes patients. The earlier onset of type 2 diabetes, higher BMI and smoking rates, and the association with higher HbA_{1c} levels in younger patients could explain the higher probability of diabetes complications that was found among male patients with major

depression and diabetes. The longer duration of diabetes in patients with minor depression and higher BMI and smoking rates may also explain the higher probability of complications in older patients with minor depression. A recent longitudinal study also found that depression was associated over time with increased risks of microvascular and macrovascular complications in type 2 patients (31). It is also possible that diabetes complications precipitated depressive episodes in some patients. Recent longitudinal epidemiological data have found that patients with chronic illness are at a higher risk for depression when they develop new functional limitations due to chronic illness (42).

Strengths of this study include the fact that it is the largest population-based survey of depression in a representative primary care population with diabetes. Because it was conducted in an HMO, it was possible to use automated data to identify medical comorbidity, diabetes complications, and intensity of treatment. Limitations include that the data are from a single geographically located HMO and the data are cross-sectional, which limited analyses concerning direction of causation. There was only a 61.7% response rate, and although analysis using weights for propensity to respond to the survey showed few differences from unweighted analysis, other unmeasured differences between nonrespondents and respondents may have influenced study findings. The use of the patient-rated PHQ-9 may have been associated with an overestimation of the prevalence of major depression because diabetes and other medical comorbidities may cause somatic symptoms that were attributed to depression. However, the 12% rate of major depression found in this sample is very similar to the 11% rate of major depression found in the prior meta-analysis of 39 studies (1).

Both obesity and tobacco use were associated with a higher likelihood of meeting criteria for major and minor depression. Younger patients with higher HbA_{1c} levels and male patients with an increased number of diabetes complications had an increased likelihood of major depression, and older patients with a higher number of complications had an increased likelihood of meeting criteria for minor depression. Improving outcomes for patients with diabetes may

need to address depressive illness to improve diabetes self-care (losing weight and quitting smoking) and prevent adverse medical outcomes.

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References

1. Anderson RJ, Freedland KE, Clouse RE, Lustman PJ: The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care* 24:1069–1078, 2001
2. Blazer DG, Moody-Ayers S, Craft-Morgan J, Burchett B: Depression in diabetes and obesity: racial/ethnic/gender issues in older adults. *J Psychosom Res* 53:913–916, 2002
3. Egede L, Zheng D: Independent factors associated with major depressive disorder in a national sample of individuals with diabetes. *Diabetes Care* 26:104–111, 2003
4. Egede L, Zheng D, Simpson K: Comorbid depression is associated with increased health care use and expenditures in individuals with diabetes. *Diabetes Care* 25:464–470, 2002
5. Cowie CC, Eberhardt MS: Sociodemographic characteristics of persons with diabetes. In *Diabetes in America*. 2nd ed. National Diabetes Data Group, Eds. Bethesda, MD, National Institutes of Health, 1995 (NIH publ. no. 95-1468)
6. Leonetti DL, Tsunehara CH, Wahl PW, Fujimoto WY: Educational attainment and the risk of non-insulin-dependent diabetes or coronary heart disease in Japanese American men. *Ethn Dis* 2:326–336, 1992
7. Marmot MG, Smith GD, Stansfeld S, Patel C, North F, Head J, White I, Brunner E, Feeney A: Health inequalities among British civil servants: the Whitehall II study. *Lancet* 337:1387–1393, 1991
8. Lustman PJ, Anderson RJ, Freedland KE, de Groot M, Carney RM, Clouse RE: Depression and poor glycemic control. *Diabetes Care* 23:934–942, 2000
9. De Groot M, Anderson R, Freedland KE, Clouse RE, Lustman PJ: Association of depression and diabetes complications: a meta-analysis. *Psychosom Med* 63:619–630, 2001
10. Panzani G, Zabel-Langhenning R: Prognosis of diabetes mellitus in a geographically defined population. *Diabetologia* 20:587–591, 1981
11. Bird CE, Fremont A, Wickstrom S, Beirman AS, McGlynn E: Improving women's quality of care for cardiovascular disease

- and diabetes: the feasibility and desirability of stratified reporting of objective performance measures. *Womens Health Issues* 13:150–157, 2003
12. Gu K, Cowie C, Harris M: Diabetes and decline in heart disease mortality in U.S. adults. *JAMA* 281:1291–1297, 1999
 13. McCulloch D, Price M, Hindmarsh M, Wagner E: A population-based approach to diabetes management in a primary care setting: early results and lessons learned. *Eff Clin Pract* 1:12–22, 1998
 14. Spitzer R, Kroenke K, Williams J: Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study: Primary Care Evaluation of Mental Disorders: Patient Health Questionnaire. *JAMA* 282:1737–1744, 1999
 15. Kroenke K, Spitzer RL, Williams JBW: The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 16:606–613, 2001
 16. American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed, text revision. Washington, DC, American Psychiatric Association, 2002, p. 775–776
 17. Fishman P, Goodman M, Hornbrook M, Meenan RT, Bachman DJ, O'Keefe Rosetti MC: Risk adjustment using automated pharmacy data: the Rx Risk Model. *Med Care* 41:84–99, 2003
 18. Starfield B, Weiner J, Mumford L, Steinwachs D: Ambulatory care groups: a categorization of diagnoses for research and management. *Health Serv Res* 26:53–74, 1999
 19. Rosenzweig JL, Weinger K, Poirier-Solomon L, Rushton M: Use of a disease severity index for evaluation of health care costs and management of comorbidities of patients with diabetes mellitus. *Am J Manag Care* 8:950–958, 2002
 20. SAS: *SAS/Statistics Software: Changes and Enhancements*. SAS technical release. Cary, NC, SAS, 1994
 21. Pi-Sunyer FX: The obesity epidemic: pathophysiology and consequences of obesity. *Obes Res* 10 (Suppl. 2):97S–104S, 2002
 22. Goodman E, Whitaker R: A prospective study of the role of depression in the development and persistence of adult obesity. *Pediatrics* 110:497–504, 2002
 23. Richardson L, David R, Poulton R, McCauley E, Moffitt TE, Caspi A, Connell F: A longitudinal evaluation of adolescent depression and adult obesity. *Arch Pediatr Adolesc Med* 157:739–745, 2003
 24. Eaton W, Armenian H, Gallo J, Pratt L, Ford D: Depression and risk for onset of type 2 diabetes: a prospective population-based study. *Diabetes Care* 19:1097–1102, 1996
 25. Kawakami N, Takatsuka N, Shimizu H, Ishibashi H: Depressive symptoms and occurrence of type II diabetes among Japanese men. *Diabetes Care* 22:1071–1076, 1999
 26. Joynt K, Whellan D, O'Connor C: Depression and cardiovascular disease: mechanisms of interaction. *Biol Psychiatry* 54:248–261, 2003
 27. Ciechanowski P, Katon W, Russo J: Depression and diabetes: impact of depressive symptoms on adherence, function and costs. *Arch Intern Med* 160:3278–3285, 2000
 28. Marcus M, Wing R, Guare J, Blaire E, Jawad A: Lifetime prevalence of depression and its effect on treatment outcome in obese type 2 diabetic patients. *Diabetes Care* 15:253–255, 1992
 29. Facchini FS, Hollenbeck CB, Jeppesen J, Chen YD, Reaven GM: Insulin resistance and cigarette smoking. *Lancet* 339:1619–1620, 1992
 30. Ronnema T, Ronnema EM, Puukka P, Pyorala K, Laakso M: Smoking is independently associated with high plasma insulin levels in nondiabetic men. *Diabetes Care* 19:1229–1232, 1996
 31. Black S, Markides K, Ray L: Depression predicts increased incidence of adverse health outcomes in older Mexican Americans with type 2 diabetes. *Diabetes Care* 26:2822–2828, 2003
 32. Glassman A, Helzer J, Covey L, Cottler L, Stetner F, Tipp JE, Johnson J: Smoking, smoking cessation and major depression. *JAMA* 264:1546–1549, 1990
 33. Patton G, Carlin J, Coffey C, Wolfe R, Hibbert M, Bowes G: Depression, anxiety, and smoking initiation: a prospective study over 3 years. *Am J Public Health* 88:1518–1522, 1998
 34. Anda R, Williamson D, Escobedo L, Most E, Giovino G, Remington P: Depression and dynamics of smoking. *JAMA* 264:1541–1543, 1990
 35. Dierker L, Avenevoli S, Stolar M, Merikangas K: Smoking and depression: an examination of mechanisms of comorbidity. *Am J Psychiatry* 159:947–953, 2002
 36. Lustman PJ, Griffith LS, Clouse RE, Freedland KE, Eisen SA, Rubin EH, Carney RM, McGill JB: Effects of nortriptyline on depression and glycemic control in diabetes: results of a double-blind, placebo-controlled trial. *Psychosom Med* 59:241–250, 1997
 37. Lustman PJ, Freedland KE, Griffith LS, Clouse RE: Fluoxetine for depression in diabetes: a randomized double-blind placebo-controlled trial. *Diabetes Care* 23:618–623, 2000
 38. Lustman PJ, Griffith LS, Freedland KE, Kissel SS, Clouse RE: Cognitive behavior therapy for depression in type 2 diabetes mellitus: a randomized controlled trial. *Ann Intern Med* 129:613–621, 1998
 39. Williams Jr J, Katon W, Lin E, et al: Effectiveness of depression case management on depression and diabetes-related outcomes in older patients with both conditions. *Ann Intern Med*. In press
 40. Unruh J, Ritchie J, Merskey H: Does gender affect appraisal of pain and coping strategies? *Clin J Pain* 15:31–40, 1999
 41. Vitaliano P, Zhang J, Scanlan J: Is care giving hazardous to one's physical health: a meta-analysis. *Psychol Bull* 129:946–972, 2003
 42. Prince M, Harwood H, Thomas A, Mann A: A prospective population-based cohort study of the effects of disablement and social milieu on the onset and maintenance of late-life depression: the Gospel Oak Project VII. *Psychol Med* 28:334–350, 1998