Unadjusted and Adjusted Prevalence of Diagnosed Depression in Type 2 Diabetes

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OBJECTIVE — To estimate the prevalence of diagnosed depression in a large population of individuals with type 2 diabetes, compared to a matched control group, and to estimate the extent of depression that is independently associated with diabetes.

RESEARCH DESIGN AND METHODS — We compared the prevalence of diagnosed depression in all 16,180 full-year health maintenance organization members who had been diagnosed with type 2 diabetes and in 16,180 comparison members without diabetes matched for age and sex. We ascertained diagnoses from the Kaiser Permanente Northwest Region’s electronic medical record. Using multiple logistic regression, we adjusted the prevalence estimates for the presence of cardiovascular disease, age, sex, and body weight.

RESULTS — Depression was more common in individuals with type 2 diabetes than among matched control subjects (17.9% vs. 11.2%; P < 0.001). Women in both groups were nearly twice as likely to be depressed as men; however, the relative difference in depression prevalence between subjects with and without diabetes was greater in men. In the multivariate model for women, body weight was a much stronger predictor of depression than diabetes status.

CONCLUSIONS — This study further documents the association between depression and diabetes, providing unadjusted population-based estimates in a large sample. Depression remained associated with diabetes after adjustment for several other possible causes. The association among diabetes, cardiovascular disease, depression, and obesity are multifaceted and differ for men and women.

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A growing body of literature has established a strong association between depression and type 2 diabetes (1–15). Although the published studies base their conclusions on relatively small sample sizes, the consistency of the relation leaves little doubt that depression and diabetes are closely linked. A recent meta-analysis examined as many as 42 such studies and concluded that the presence of diabetes doubles the odds of comorbid depression (16). However, those authors noted that the stability of this estimate was questionable because of the relatively small number of controlled studies, the small sample sizes of the studies, and the fact that many of the included studies were not population based (16). Depression prevalence estimates in diabetes would be more precise in a population-based study, and comparisons would be strengthened by the inclusion of similar subjects without diabetes. Egede et al. (17) recently published such a study based on respondents to the 1996 Medical Expenditure Panel Survey (MEPS); however, only 825 of the ~21,500 subjects reported having diabetes, and of those, just 85 reported having depression.

Other comorbidities further complicate estimates of depression in diabetes. In particular, cardiovascular disease and obesity are both highly prevalent and strongly associated with both depression and diabetes (18–27). Whether depression is truly associated with diabetes or is merely a by-product of the association with these other conditions has not been studied. Adjusting depression prevalence estimates for these and other potential moderators would strengthen comparative estimates of depression in diabetic and non diabetic individuals.

In this study, we provided prevalence rates of diagnosed depression in a very large population of patients with type 2 diabetes in comparison to an age- and sex-matched control group. We also adjusted those comparative estimates of depression for moderators known to be associated with both depression and diabetes, including age, sex, presence of cardiovascular disease, and body weight.

RESEARCH DESIGN AND METHODS

Research setting and patients

The study site was Kaiser Permanente Northwest (KPNW), a not-for-profit group-model health maintenance organization (HMO) with ~440,000 members during the study period (1999). Subscribers’ demographics are similar to the area population as a whole, with ~90% of the population comprised of non-Hispanic whites and 10% comprised of African Americans, Asians/Pacific Islanders, Native Americans, and those of Hispanic descent (28). KPNW has 18.5% members eligible for Medicare (age > 64 years) and ~8% Medicaid members. KPNW and the 14-year-old diabetes registry used in this report have been described elsewhere (29,30).
TABLE 1—Characteristics of diabetes and control groups by depression status

<table>
<thead>
<tr>
<th></th>
<th>Diabetic subjects</th>
<th>Control subjects</th>
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<tbody>
<tr>
<td></td>
<td>With depression</td>
<td>With no depression</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td></td>
</tr>
<tr>
<td>Female sex (%)</td>
<td>2,844</td>
<td>13,336</td>
</tr>
<tr>
<td></td>
<td>63.6</td>
<td>45.2</td>
</tr>
<tr>
<td>Mean age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>60.5</td>
<td>64.1</td>
</tr>
<tr>
<td>Men</td>
<td>61.8</td>
<td>63.8</td>
</tr>
<tr>
<td>Total</td>
<td>61.0</td>
<td>65.5</td>
</tr>
<tr>
<td>Presence of cardiovascular disease (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>28.2</td>
<td>27.0</td>
</tr>
<tr>
<td>Men</td>
<td>42.8</td>
<td>33.8</td>
</tr>
<tr>
<td>Total</td>
<td>33.5</td>
<td>30.7</td>
</tr>
<tr>
<td>Mean weight (lbs)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>208</td>
<td>192</td>
</tr>
<tr>
<td>Men</td>
<td>224</td>
<td>216</td>
</tr>
<tr>
<td>Total</td>
<td>214</td>
<td>205</td>
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For this study, we selected all 16,180 members in the diabetes registry who had type 2 diabetes and who had 12 full months of HMO eligibility in 1999. Using a method that assured random assignment, we used age and sex to match these subjects to 16,180 control members without diabetes who also had 12 full months of HMO eligibility in 1999.

Data

The organization maintains administrative and clinical electronic databases containing information on inpatient admissions, pharmacy dispenses, outpatient visits, laboratory tests, and outside claims and referrals. All of these databases are linked through the unique health record number that each member receives at the time of his or her first enrollment in the health plan.

The cornerstone of these databases is the electronic medical record system. When a clinician decides to code depression, he or she enters “depression” into a text field. The clinician is then offered a list of ICD-9-CM codes from which to choose, and 311.0 (depression NOS) heads that list. Because of the apparent imprecision in coding, we did not differentiate among specific types of depression in this study. Instead, we defined any qualifying code as diagnosed depression. We also defined diagnosed depression as the receipt of an antidepressant medication if 1) the average daily dosage of all such dispenses in 1999 was ≥100% of the minimum therapeutic dosage for depression (31), and 2) the subject did not have a diagnosis of peripheral neuropathy, posttraumatic stress disorder, anxiety disorder, obsessive-compulsive disorder, or social phobia.

We also used the electronic medical record to ascertain body weight, calculating the mean of all available measurements in 1999, and to establish cardiovascular comorbidity (ICD-9-CM codes 410.xx–414.xx, and 420.9–429.xx).

Statistical analyses

Univariate comparisons were performed using the $\chi^2$ test for categorical variables and Student’s t test for continuous variables. We then used multiple logistic regression models to estimate the unique association between diabetes and diagnosed depression by calculating the probability of a depression diagnosis, controlling for age, sex, presence of cardiovascular disease, and body weight. Separate models were then estimated for men and women. Based on these models, we estimated the amount of diagnosed depression uniquely associated with diabetes by applying the multivariate parameter estimates to the mean values of the control group and recalculating the probability of a depression diagnosis.

RESULTS—The characteristics of individuals with and without diabetes and with and without diagnosed depression are displayed in Table 1. Patients with diagnosed depression were younger and more likely to be female regardless of diabetes status. Except among diabetic women, a greater proportion of those with a depression diagnosis also had cardiovascular disease. Mean body weight was greater in patients with diagnosed depression, but the difference was greater among women. In subjects diagnosed as depressed, both with and without diabetes, those identified as depressed by having received a diagnosis in the medical record did not differ from those who were identified as depressed by receipt of an antidepressant drug (data not shown).

The prevalence of diagnosed depression was significantly greater in subjects with type 2 diabetes than in an age- and sex-matched control subjects (Fig. 1). Overall, diabetic subjects had 1.5 times greater prevalence than nondiabetic subjects (17.6 vs. 11.9%; $P < 0.001$). However, after adjusting for age, sex, presence of cardiovascular disease, and body...
weight, diagnosed depression prevalence in diabetic subjects declined to 15.0% and the risk ratio declined to 1.26. Diagnosed depression was approximately twice as likely in women as in men, regardless of diabetes status (Fig. 2). The unadjusted depression diagnosis rates were 23.1% in diabetic women and 16.2% in nondiabetic women, and 12.4% in diabetic men and 7.8% in nondiabetic men. The calculation of the unique association between diabetes and diagnosed depression resulted in a 3.5 percentage point reduction in diagnosed depression prevalence in women, to 19.5%. In men, however, the adjusted prevalence fell just over 1 percentage point to 11.3%.

The multiple logistic regression models used to adjust diagnosed depression rates are reported in Table 2. Age performed similarly in models for men and women, but the variables for presence of diabetes, cardiovascular disease, and body weight did not. The presence of cardiovascular disease was the strongest predictor of a depression diagnosis in men, whereas body weight was the strongest predictor in women.

**CONCLUSIONS** — The estimation of the unique association between diagnosed depression and type 2 diabetes is complicated by many factors known to be individually linked to each of these conditions. To improve on previously published estimates, we studied a large population-based sample, simultaneously accounting for other potential causes.
Table 2—Multiple logistic regression models of depression

<table>
<thead>
<tr>
<th></th>
<th>Model for men</th>
<th>Model for women</th>
<th>Combined model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \beta ) (SE)</td>
<td>Odds ratio (95% CI)</td>
<td>( \beta ) (SE)</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.105 (0.002)</td>
<td>0.984 (0.980–0.989)</td>
<td>0.096 (0.002)</td>
</tr>
<tr>
<td>Age</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Presence of diabetes</td>
<td>0.065 (0.037)</td>
<td>1.269 (1.134–1.420)</td>
<td>0.033 (0.046)</td>
</tr>
<tr>
<td>Presence of cardiovascular disease</td>
<td>0.105 (0.061)</td>
<td>1.506 (1.337–1.696)</td>
<td>0.055 (0.054)</td>
</tr>
<tr>
<td>Weight (per 10 lbs)</td>
<td>0.059 (0.001)</td>
<td>1.024 (1.012–1.037)</td>
<td>0.133 (0.001)</td>
</tr>
</tbody>
</table>

Previous studies of depression have relied on diagnostic interviews or self-report scales to define depression (16). The current study used a definition of either an ambulatory visit diagnosis of depression or evidence of antidepressant drug therapy when no other indication (i.e., neuropathy, stress disorders, social phobias) for an antidepressant could explain the therapy. Inclusion of patients with antidepressant therapy captures those subjects identified as depressed but not charted as such—a common occurrence in primary care record keeping. Because the current study focused exclusively on diagnosed depression, our results must be viewed in a somewhat different light than those of previous studies. Unlike studies using diagnostic interviews, our results did not include individuals who met diagnostic criteria for depression, but were undiagnosed. However, similar to studies using self-reported depression, our results might have included individuals who did not meet Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) (34) diagnostic criteria. It should be noted that our definition included individuals who, in their clinicians’ opinion, had sufficient depressive symptoms to warrant chart notation or antidepressant treatment. Depression screening instruments typically have false positive rates that result in overdiagnosis. On the other hand, before the selective serotonin reuptake inhibitor era, depression was notoriously underdiagnosed in clinical settings (32); our data could not account for undiagnosed depression. Whether depression remains either undiagnosed or treated at different rates in patients with and without diabetes is an important question for further study.

In both diabetic and nondiabetic subjects, those identified as depressed from charted diagnoses did not differ from those identified from dispensed antidepressant drugs. Moreover, the logistic regression models yielded similar results regardless of the method used to identify diagnosed depression (data not shown). This suggests that our inclusion of both methods of defining diagnosed depression resulted in a homogeneous set of cases. Furthermore, the characteristics of those cases, such as a disproportionate number of women and relatively younger age, were similar to other published reports of depression prevalence. Thus our definition of depression likely produced a similar set of individuals as would diagnostic interviews and self-report scales. If so, then the relative adjustment to depression prevalence that we calculated may be generalized to prevalence rates based on other definitions of depression.

We cannot assess the degree to which clinicians applied DSM-IV criteria in diagnosing depression. We suspect that clinicians were not rigorous in their use of DSM-IV criteria, choosing instead the depression code first offered by the electronic medical record system used in the study setting. This does not mean that subjects were not depressed; symptoms were sufficient for the busy clinician to take time to code some form of depression. However, it does mean that we could not accurately estimate separate prevalence rates of MDD, dysthymia, and other forms of depression. We found an unadjusted prevalence of diagnosed depression of 17.6% in diabetic subjects compared to 11.9% in control subjects, showing that in a representative population, diabetic individuals were nearly 50% more likely to have diagnosed depression than nondiabetic individuals (relative risk 1.48, 95% CI 1.41–1.56). This risk ratio is considerably lower that the doubling of comorbid depression reported in the recent Anderson et al. (16) meta-analysis and in the recent study using MEPS data (17). The difference can likely be accounted for in part by our use of diagnosed depression rather than self-reported symptom scales or diagnostic interviews. As Anderson et al. (16) noted, the prevalence of depression varies systematically as a function of the method used to identify depression cases. Because the current study employed a previously unused method, it is not surprising that the results differed from those of previous studies. Nonetheless, despite the lower relative risk in our results, the unadjusted prevalence rates used to calculate the risk ratio were similar to previously published estimates. In controlled studies, Anderson et al. (16) found depression prevalence rates of 9.0–26.1% in subjects with diabetes and 5.0–14.4% in control subjects. Our unadjusted depression prevalence for subjects with and without diabetes were 17.6 and 11.9%, respectively, well within these ranges.

Our data showed that even after controlling for cardiovascular disease and obesity, two conditions that are highly prevalent in patients with depression and diabetes, a strong association between depression and diabetes remained. However, our data also suggest that the relation among depression, diabetes, cardiovascular disease, and obesity differs between men and women. In the multivariate model of the probability of diagnosed depression in men, younger age and the presence of cardiovascular disease were the strongest predictors of a depression diagnosis, followed by diabetes. Body weight, although statistically significant, was the least important variable. In women, however, body weight was by far the strongest predictor of depression, with a standardized parameter estimate four times greater than the standardized

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estimate for diabetes. Although we did not directly assess the interaction of these variables and sex, our results suggest that diabetes and depression treatment preferences may differ for men and women. For example, men may be more willing to undertake treatment regimens that reduce cardiac risk, whereas women may prefer treatments that reduce weight or minimize weight gain. Selecting treatments with which patients will comply is an important consideration when multiple treatment options are available.

A potential limitation to the current study was that diabetic subjects had a greater opportunity to be diagnosed with depression because of their increased contact with the medical care system. At-face visits proved problematic because of the high correlation between diabetes and medical utilization. Instead, we examined other mental health conditions (stress disorders, obsessive-compulsive disorder, and social phobias) and found that the diabetic and control groups did not differ in the prevalence of these conditions. Had our estimates of depression been biased by opportunity, we would have expected a similar bias in these other diagnoses. We also might have found relative depression rates equal to or greater than the approximate doubling reported in the literature (16), but our relative rates were, in fact, lower.

Another potential limitation was the exclusion of demographic characteristics that may have also contributed to the relationship between depression and diabetes. In particular, we were unable to control for ethnicity, socioeconomic status, or education level because these variables were not available in our data. Although these characteristics may not be related to depression prevalence in either the general population (32) or in diabetic individuals (17), a more fully specified model with these factors included might have strengthened our conclusions.

Although association does not prove causation, the motivation for attempting to isolate the unique association between diabetes and depression was to get a more precise estimate of how large such a causal association could be, if it exists. Our results showed that the magnitude of a possible causal association was considerably lower than previous publications of unadjusted data from unrepresentative populations would lead us to believe. Adjustment for age, sex, presence of cardiovascular disease, and body weight reduced the estimated prevalence of depression in diabetes from 17.6 to 15.0%. Nonetheless, a unique association still remained. The adjusted prevalence of depression in diabetic individuals was still >26% greater than in control subjects. To the extent that causality underlies this association, it may well be bidirectional; that is, the experience and perhaps the physiological changes of diabetes may trigger depression, and the experience, behaviors, and physiological changes of depression may cause diabetes.

References