Here is a strong positive association between obesity and risk of diabetes in both women and men (1, 2), and both obesity and type 2 diabetes have increased at staggering rates in the United States in the last 15 years. Older adults are particularly susceptible to diabetes; approximately one-third of the population over 60 years of age has diagnosed or undiagnosed diabetes (3). Weight loss in obese persons with diabetes leads to long-term improvements in metabolic control and reduces mortality risks by 25% (4), but sustained significant weight loss is difficult to achieve.

Depression may contribute to the difficulty of behavior change and weight loss among persons with diabetes (5). The strong association between depression and obesity that has been well documented in community respondents (6) has more recently been demonstrated in older adult patients with diabetes (7). Multiple reciprocal biopsychosocial influences are thought to be at play (8) with depression increasing risk for obesity and type 2 diabetes and the social stigma associated with obesity and diabetes complications increasing risk for depression.

The purpose of this research was to use the Pathways longitudinal cohort study to investigate the longitudinal associations between depressive symptom changes and weight change among 2,600 patients with diabetes. Previous research has

**How Does Change in Depressive Symptomatology Influence Weight Change in Patients With Diabetes? Observational Results From the Pathways Longitudinal Cohort**

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**Background.** Little is known about how change in depressive symptoms over time is associated with change in weight.

**Methods.** Longitudinal associations between change in depression (Patient Health Questionnaire-9 [PHQ-9]) and weight (self-reported and chart abstracted) were examined in 2,600 patients with type 2 diabetes (mean age 62, \( SD = 11.6 \)) who were surveyed by telephone in 2001–2002 and 5 years later as part of the Pathways study. Mixed effects regression analyses compared a) patients with persistently low depression symptoms with those whose depression worsened (increased at least 5 points on PHQ-9) over 5 years and b) patients with persistently high depression symptoms with those who improved (decreased at least 5 points on PHQ-9) over 5 years.

**Results.** Those who worsened in comparison to those with persistently low depression symptoms did not differ in their pattern of weight change (\( z = 1.54, p = .12 \)). Both groups weighed approximately 92 kg at baseline and lost approximately 2 kg. A significantly different pattern of change over time was observed for those with persistently high depression symptoms in comparison to those whose depression improved (\( z = 1.98, p = .04 \)). Although the groups had almost identical weight at baseline (approximately 100 kg), at the 5-year assessment, those with persistently high depression symptoms had about half the weight loss (\( M = -1.71, SD = 9.08 \)) in comparison to those whose depression improved (\( M = -3.62, SD = 19.93 \)).

**Conclusion.** In persons with diabetes who have clinically significant levels of depressive symptoms, improvement in depression is accompanied by significantly greater, clinically significant weight loss.

**Key Words:** Depression—Obesity—Diabetes.
demonstrated a cross-sectional association between weight and depression in people with diabetes (7); here, we examine whether change in depressive symptoms is associated with change in weight. If improvements in depression are associated with steeper weight loss trajectories among persons with diabetes, perhaps proactively and optimally treating depression in older adults could ultimately reduce the complications and functional impairment attendant to obesity.

METHODS

Study Setting and Participants

The Pathways study is a population-based study of adult enrollees with diabetes within Group Health Cooperative (GHC), a health maintenance organization serving approximately 600,000 persons in the U.S. Pacific Northwest. The study protocol was reviewed and approved by institutional review boards at the University of Washington and GHC. We described the recruitment procedures in detail in previous publications (7,9).

Mailed questionnaires were sent to 9,064 primary care patients identified as having diabetes through GHC’s population-based diabetes registry. Of potentially eligible patients, 1,222 were considered ineligible for reasons such as death, disenrollment, erroneous diabetes diagnosis, or cognitive impairment. Of 7,841 eligible participants, 4,839 participants returned the baseline questionnaire, for a response rate of 61.7%. These 4,839 participants comprised the Pathways cohort. Of these, 329 participants who were depressed were also enrolled in a randomized controlled trial of a nurse-delivered intervention to improve care for depression.

Approximately 5 years after enrollment, between 2005 and 2007, surviving members of the cohort were asked to complete a 30-minute survey and for permission to review their electronic and paper medical records for information on medical conditions. Of 2,909 participants who completed the follow-up survey, we excluded living participants who did not consent to medical record review (n = 139) and participants with type 1 diabetes (n = 132), missing depression status (n = 11), or prior bariatric surgery (n = 27) (Figure 1).

Measures

The Patient Health Questionnaire-9 (PHQ-9) was used to assess depressive symptoms at baseline and 5-year follow-up (10,11). The PHQ-9 diagnosis of major depression has been found to have an adequate sensitivity (73%) and high specificity (98%) in relation to a diagnosis of major depression based on structured interviews (10–12). A score of at least 10 of a possible 27 points has been recommended as an optimal cutoff for major depression (11).

The baseline questionnaire included questions on age, sex, years of education, employment, race/ethnicity, marital status and weight, age of onset and duration of diabetes, and type of treatment at onset of disease. The intensity of diabetes treatment was determined using automated pharmacy data on the use of oral hypoglycemic agents and insulin. Patients were classified as having type 1 diabetes if onset was prior to 30 years of age, insulin was the first treatment prescribed, and they were currently taking insulin.

Computerized pharmacy records were used to compute a chronic disease score (RxRisk), a measure of medical comorbidity based on prescription drug use in the previous 12 months (12). A measure using automated data was used to code for seven types of diabetes complications present at baseline: retinopathy, neuropathy, nephropathy, cerebrovascular, cardiovascular, peripheral vascular, and metabolic (ketoacidosis, hyperosmolar coma) (13). This diabetes complication measure has been shown to predict mortality and hospitalization rates over the next 2-year period (13).

During the 5-year period between the baseline and follow-up surveys, weight was ascertained from medical chart review. Weight measures routinely obtained in clinical care are highly correlated (.99) with those obtained by trained research staff (14).

Evidence of macrovascular and microvascular complications and coronary procedures (coronary artery bypass surgery, angioplasty, or stent placement), cerebrovascular procedures (carotid endarterectomy), and peripheral vascular procedures (angioplasty or major vascular surgery of the aorta or peripheral vasculature) was identified both before baseline and during follow-up from automated medical records data using International Classification of Diseases, 9th Revision, and Current Procedural Terminology (CPT) codes. Macrovascular events including myocardial infarction, stroke, and peripheral vascular disease were verified by chart review. The specific codes and definitions for myocardial infarction, stroke, and coronary procedures were adopted from the Women’s Health Initiative study, with the addition of CPT codes that have come into use during the period of follow-up (15,16).

Statistical Analysis

We stratified the sample on participants’ PHQ score at baseline, forming two groups, those with a PHQ score of at least 10 (probable major depression) at baseline and those with a PHQ score of less than 10 (no depression) at baseline. Within these two groups, those who had a substantial change in their level of depression symptoms over the 5-year follow-up period were compared to those who did not have a substantial change. Substantial change was defined as a change of at least 5 points on the PHQ (11), specifically, a decrease of at least 5 points for the group with depression at baseline (improving depression symptoms) and an increase of at least 5 points for the group without depression at baseline (worsening depression symptoms). All other participants in the group with depression at baseline were said to have persistently high depression symptoms, and all other
participants in the group without depression at baseline were said to have persistently low depression symptoms. Thus, in the group with a PHQ score of less than 10 at baseline, those with worsening depression symptoms were compared to those with persistently low depression symptoms, and in the group with a PHQ score of 10 or greater at baseline, those with improving depression symptoms were compared to those with persistently high depression symptoms.

Within each group (probable major depression at baseline and no major depression at baseline), we conducted bivariate analyses to compare the demographic and clinical characteristics of the substantially changed or unchanged groups using chi-square analyses and t tests for categorical and continuous covariates, respectively. To examine bivariate relationships between baseline weight and the covariates, Pearson correlation coefficients and t tests were used for the continuous and dichotomous covariates, respectively.

Using kilograms as our dependent variable, we conducted intent-to-treat analyses of repeated measures with six yearly time points (baseline and 5 years of assessment). Mixed effects regression analyses were used to determine if the groups had significantly different patterns of change in weight over the next 5 years. A significant group-by-time interaction is interpreted as having significantly different trends in weight over time depending upon group status.

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Although we had complete data at the baseline and 5-year assessments, 13–16 percent of the weights were missing for years one to four. The pattern of missing weights across the six time points was examined by an analysis of variance on the number of missing weights for the four depression groups. The four depression groups did not differ in the number of missed weights over the six assessments [F(2596) = 1.39]. We employed multiple imputation to impute item-level missing weights using a method of multiple imputations by iterative-chained regression equations. All analyses were performed using STATA 10.0 and SPSS 15.0.

RESULTS

Table 1 shows all covariates in the analyses and their relationships to the depression groups.

Those who worsened over time in comparison to those with low symptoms at both time points did not differ in their pattern of weight change over the 5-year period (Figure 2), that is, for those without major depression at baseline, there was not a significant time-by-group interaction (z = 1.54, p = .12). The addition of the covariates barely changed this coefficient (z = 1.52). In other words, both groups had baseline weights of
about 92 kg and both groups lost approximately 2 kg over the 5-year period.

For those with probable major depression at baseline, there was a significant time-by-group interaction ($z = 1.98, p = .04$). The addition of the covariates did not change this coefficient or its significance. There was a significantly different overall pattern of change over time for those with persistently high depressive symptoms in comparison to those with improving depression symptoms over the 5-year period (Figure 3). Overall, those with major depression at baseline lost a mean of 3.03 kg ($SD = 10.43$). Additional post hoc regression analysis showed that those with improving depression symptoms had a significantly greater change in weight over the 5 years ($M = -3.62, SD = 19.93$) than those with persistently high depression symptoms ($M = -1.71, SD = 9.08$). Although the groups had almost identical weight at baseline of approximately 100 kg, at the 5-year assessment, those with persistent symptoms had about half the weight loss in comparison to those whose symptoms were improved at the 5-year assessment.

**DISCUSSION**

In this 5-year prospective cohort study investigating the longitudinal associations between depression symptomatology and weight change among 2,600 older adult patients with diabetes, we found that all participants lost some weight over time. It is likely that some amount of weight loss in this cohort was due to age-related decline in muscle mass (17,18). Among those without probable major depression at baseline, there was no difference in the pattern of weight change between those who remained nondepressed at 5 years and those whose depression worsened at the 5-year follow-up. Among those who began the study with probable major depression, there was a significantly steeper pattern of weight loss among those whose depression improved over the 5 years as compared to those whose depression symptoms were present at both time periods. On average, participants whose depression symptoms improved lost close to 4% of their body weight; modest weight loss of this magnitude can improve cardiovascular risk factors such as lipid profiles (19) and blood pressure (20). Parallel research by our group found that at 5-year

### Table 1. Baseline Characteristics of Participants by Baseline and 5-Year PHQ-9 Scores

<table>
<thead>
<tr>
<th>5-Year depression</th>
<th>Baseline PHQ&lt;10 (n=2075)</th>
<th>Baseline PHQ≥10 (n=525)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total sample (N=2600)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Persistently low depression symptoms (n=1873)</td>
<td>Worsening depression symptoms (n=202)</td>
</tr>
<tr>
<td>Age (y), M (SD)</td>
<td>62.2 (11.6)</td>
<td>63.1 (11.3)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Women (n)</td>
<td>48.8 (1269)</td>
<td>45.4 (850)</td>
</tr>
<tr>
<td>Race</td>
<td>80.5 (2093)</td>
<td>81.3 (1523)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% College graduation or more (n)</td>
<td>40.0 (1041)</td>
<td>42.8 (801)</td>
</tr>
<tr>
<td>Years with diabetes, M (SD)</td>
<td>8.1 (7.7)</td>
<td>8.0 (7.9)</td>
</tr>
<tr>
<td>Height in feet, M (SD)</td>
<td>5.6 (0.3)</td>
<td>5.6 (0.3)</td>
</tr>
<tr>
<td>RxRisk medical comorbidity, M (SD)</td>
<td>2758.3 (2081.2)</td>
<td>2737.4 (2066.7)</td>
</tr>
<tr>
<td>No. of diabetes complications, M (SD)</td>
<td>1.2 (1.1)</td>
<td>1.1 (1.1)</td>
</tr>
<tr>
<td>Insulin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Using insulin (n)</td>
<td>24.8 (646)</td>
<td>22.1 (413)</td>
</tr>
<tr>
<td>Years of exposure to antidepressants (0–5), M (SD)</td>
<td>1.0 (1.8)</td>
<td>0.7 (1.5)</td>
</tr>
<tr>
<td>% With at least one cardiovascular event prior to study (n)</td>
<td>21.4 (557)</td>
<td>20.5 (384)</td>
</tr>
<tr>
<td>% With at least one microvascular event prior to study (n)</td>
<td>16.4 (426)</td>
<td>15.3 (287)</td>
</tr>
<tr>
<td>% With at least one cardiovascular event during the study (n)</td>
<td>17.6 (458)</td>
<td>16.4 (307)</td>
</tr>
<tr>
<td>% With at least one microvascular event during the study (n)</td>
<td>17.6 (458)</td>
<td>12.1 (227)</td>
</tr>
<tr>
<td>Randomization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% in RCT (n)</td>
<td>7.7 (201)</td>
<td>0.2 (3)</td>
</tr>
</tbody>
</table>

Notes: PHQ = Patient Health Questionnaire, RCT = Randomized Controlled Trial.

* $p<.05$.

† $p<.01$.

‡ $p<.001$.
follow-up, patients with a substantial improvement in depressive symptoms over the 5-year period had a similar number of days per week of adherence to diet and exercise regimens at 5-year follow-up as patients with few or no depressive symptoms at both time points (21). Combined, these results suggest that improvement in depression symptoms may be accompanied not only by improved self-care (dietary change, physical activity) but also by significantly greater and clinically significant weight loss.

There is a high burden of self-care among those who have type 2 diabetes. In persons with diabetes, depression is associated with more bothersome diabetes symptoms (22), less physical activity, less healthy diet, and lower adherence to oral hypoglycemic, antihypertensive, and lipid-lowering medications; all patient-initiated behaviors that are difficult to maintain (5). The current study provides hope that improvements in depression symptoms may be accompanied by greater weight loss, which may be due to more successful sustained behavior change. However, the longitudinal relationship we observe most likely goes in both directions (improvement in depression leads to more success in weight loss and greater weight loss leads to more improvement in depression). This area is worthy of further investigation.

These results are important because type 2 diabetes is an emerging epidemic among older adults (23) and weight loss among those with diabetes has both short- and long-term benefits. Even minor or moderate weight loss in obese persons with diabetes is associated with improvements in insulin sensitivity and glucose tolerance (24). In a prospective study of 4,970 overweight individuals with 12-year mortality follow-up, Williamson and colleagues found that intentional weight loss was associated with a 25% reduction in total mortality and a 28% reduction in cardiovascular disease and diabetes mortality (25). The Diabetes Prevention Program trial found that weight loss following intensive lifestyle modification was significantly more effective than metformin in preventing diabetes with increasing participant age (26).

The strengths of this study include the large sample size, the use of well-validated and reliable depression questionnaires, and the ability to use medical chart data to ascertain interval body weights. We were also able to control for severity of diabetes, comorbid medical illnesses, and diabetes treatment intensity. Limitations include that the sample was drawn from one large health care organization in the U.S. Pacific Northwest, which may limit generalizability of the results. Only 70% of the eligible sample participated in the 5-year follow-up study. Depression diagnosis was not confirmed by structured diagnostic interview. Initial and follow-up depressive symptom measures were assessed at only two points over a relatively long 5-year period, and it is not known how depressive symptoms may have fluctuated during the interim years.

Summary

In persons with diabetes who had clinically significant levels of depressive symptoms, improvement in depressive symptomatology was accompanied by significantly greater weight loss over 5 years. Combined with previous research by our group, these results suggest that depressive symptom improvement may be accompanied by improved self-care (dietary change, physical activity) leading to greater weight loss. One clinical implication may be that proactively and optimally treating depression could ultimately reduce the complications and functional impairment associated with obesity and diabetes.

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CONFLICT OF INTEREST

No authors have any financial involvement or affiliation with any organization whose financial interests may be affected by material in the manuscript or which might potentially bias it.

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