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Correlates of depression among people with diabetes: The Translating Research Into Action for Diabetes (TRIAD) study

Beth Waitzfelder[a,b], **Robert B. Gerzoff**[c], **Andrew J. Karter**[d], **Stephen Crystal**[e], **Mathew J. Bair**[f], **Susan L. Ettner**[g,h], **Arleen F. Brown**[g], **Usha Subramanian**[i], **Shou-En Lu**[j], **David Marrero**[k], **William H. Herman**[l], **Joseph V. Selby**[d], and **R. Adams Dudley**[m]

[a]Pacific Health Research Institute, Honolulu, HI, United States

[b]Kaiser Permanente Center for Health Research Hawaii, Honolulu, HI, United States

[c]Centers for Disease Control and Prevention (CDC), Atlanta, GA, United States[1]

[d]The Division of Research, Kaiser Permanente, Oakland, CA, United States

[e]Institute for Health, Health Care Policy, and Aging Research, Rutgers University, New Brunswick, NJ, United States

[f]Roudebush Veterans Affairs Center for Implementing Evidence Based Practice Indiana, University School of Medicine Indianapolis, IN, United States

[g]David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA, United States

[h]Department of Health Services, UCLA School of Public Health, Los Angeles, CA, United States

[i]Roudebush Veterans Affairs Medical Center, Indianapolis, IN, United States

[j]University of Medicine and Dentistry of New Jersey, School of Public Health, Piscataway, NJ, United States

[k]Division of Endocrinology & Metabolism, Indiana University School of Medicine, Indianapolis, IN, United States

[l]Department of Internal Medicine, Division of Endocrinology, Metabolism and Diabetes, University of Michigan, Ann Arbor, MI, United States

[m]Department of Medicine and Institute for Health Policy Studies, University of California, San Francisco, San Francisco, CA, United States

Abstract

Correspondence to: Beth Waitzfelder.

Conflict of interest: Two co-authors have served as consultants for pharmaceutical companies (Herman – Amylin Pharmaceuticals, Eli Lilly and Company, GlaxoSmithKline, Merck and Co., Sanofi-Aventis; and Marrero – Eli Lilly and Company, Sun Pharmaceuticals). Two have received grants (Karter – an unrestricted grant to study therapy effectiveness from Novartis; and Herman – Sanofi-Aventis). Dr. Herman has also received honoraria from several pharmaceutical companies and Dr. Ettner and Bair have served on pharmaceutical company advisory boards. One co-author (Crystal) has stock ownership in two pharmaceutical companies.

Aim—The broad objective of this study was to examine multiple dimensions of depression in a large, diverse population of adults with diabetes. Specific aims were to measure the association of depression with: (1) patient characteristics; (2) outcomes; and (3) diabetes-related quality of care.

Methods—Cross-sectional analyses were performed using survey and chart data from the Translating Research Into Action for Diabetes (TRIAD) study, including 8790 adults with diabetes, enrolled in 10 managed care health plans in 7 states. Depression was measured using the Patient Health Questionnaire (PHQ-8). Patient characteristics, outcomes and quality of care were measured using validated survey items and chart data.

Results—Nearly 18% of patients had major depression, with prevalence 2-3 times higher among patients with low socioeconomic status. Pain and limited mobility were strongly associated with depression, controlling for other patient characteristics. Depression was associated with slightly worse glycemic control, but not other intermediate clinical outcomes. Depressed patients received slightly fewer recommended diabetes-related processes of care.

Conclusions—In a large, diverse cohort of patients with diabetes, depression was most prevalent among patients with low socioeconomic status and those with pain, and was associated with slightly worse glycemic control and quality of care.

1. Introduction

Depression is a common co-morbid condition among adults with diabetes with prevalence estimates ranging from 8.3% to over 30% – as much as three times higher than in non-diabetic populations [1–5]. Depression has been associated with worse diabetes-related outcomes including poorer glycemic control, other cardiovascular disease risk factors, a greater diabetes symptom burden and poorer quality of life [6–9]. Patients with diabetes and co-morbid depression have been found to be at an increased risk of death from all causes, including those unrelated to diabetes [10–12]. Depression has been associated with suboptimal self-care and poor treatment adherence, thus contributing to adverse outcomes [13–16]. Co-morbid depression also results in higher utilization for both medical and mental health care, and higher health care costs [15,17,18]. Furthermore, previous studies have shown that co-morbid depression may often be unrecognized and untreated in individuals with diabetes [19–21]. With emerging evidence that depression treatment improves patient outcomes [22–25], it is important to clarify which diabetes patients are at risk for depression, and the relationships between depression, quality of care and outcomes for diabetes.

Estimates of the prevalence of co-morbid depression with diabetes vary widely. A number of methodological factors affecting these estimates have been identified, including differences in depression measures, population size and characteristics, study design and the inclusion of confounding variables [1,2,26]. These methodological issues are further compounded in studies of outcomes associated with co-morbid depression. Health systems factors can directly and indirectly affect quality of care for diabetes, depression and associated outcomes [27–29], but have received very little attention. Few previous diabetes studies have been designed to include sufficient diversity in patient characteristics and health system factors, as well as an adequate sample size, to assess the independent

association of a broad range of patient characteristics and outcomes associated with depression.

The Translating Research Into Action for Diabetes (TRIAD) study, with nearly 12,000 diabetes patients varying in age, race/ethnicity and socioeconomic position, receiving care under many different health care plans across the U.S., offers the opportunity to better elucidate the relationships of depression with patient characteristics, quality, and outcomes. The three specific aims of this diabetes study were to measure the association of co-morbid depression with: (1) patient characteristics; (2) outcomes; and (3) diabetes-related quality of care.

2. Methods

The main objective of the TRIAD study was to measure quality of care and outcomes among a diverse population of people with diabetes receiving care under varying managed health care systems located throughout the U.S. The TRIAD study design, key hypotheses and sampling frame have been described elsewhere [30]. Six centers (Pacific Health Research Institute, Hawaii; University of California, Los Angeles; Kaiser Permanente Northern California; University of Michigan; Indiana University; and the University of Medicine and Dentistry of New Jersey) partnered with ten managed care plans in seven states for this study. A standard algorithm was used to identify all adult (age 18 and older) patients with diabetes in each health plan with continuous enrollment for at least 18 months. Patients were randomly selected within each health plan and recruited to participate in a computer assisted telephone interview (CATI) or mailed survey. The surveys included measures of a broad range of domains, including socio-demographic information, measures of quality of care, self-care, mental and physical health and quality of life. Surveys were conducted in English and Spanish. Medical records were reviewed to collect information on medications, lab results and co-morbid conditions. We excluded patients who denied having diabetes; were pregnant at the time of the survey; lived in a non-community setting; did not use the health plan for the majority of their diabetes care; or were unable to give informed consent. The study protocol was reviewed and approved by all relevant Institutional Review Boards.

A follow-up patient survey was conducted between July 2002 and June 2003, 18 months after the baseline survey, among all surviving members of the baseline survey cohort. A total of 8790 (74%) patients completed this survey and medical records were reviewed for 6072 (69%). Results reported in this paper use data from the follow-up survey, corresponding chart review data and baseline demographics.

2.1. Measures

Depression was measured using the 8-item version of the Patient Health Questionnaire (PHQ)[31]. The PHQ is based on *DSM-IV* criteria and has a sensitivity of 88% and a specificity of 88% for major depression (PHQ score ≥10) in comparison to interviews by mental health professionals. The PHQ-8 excludes the suicidality item of the PHQ-9, making it a more appropriate instrument to use for survey research, while still retaining the psychometric properties of the original instrument as a brief and valid measurement of depression [31].

We used validated cut points indicating levels of depression (minimal to none [PHQ score 0–4], mild [PHQ score 5–9], moderate [PHQ score 10–14], moderate-severe [PHQ score 15–19] and severe [PHQ score >19])[31]. The Charlson Index was calculated from co-morbid conditions recorded in the medical record [32]. A diabetes symptom score was calculated using eight questions about the frequency of hyperglycemic symptoms, with a score range of 8 (low) to 40 (high)[33]. Pain was measured by the single item pain measure of the EQ-5D [34], and a single item rating of the quality of diabetes care received (scale of 1–5, with 1=excellent and 5=poor), were included in the follow-up patient survey.

Seven dichotomous quality of care indicators were measured, receipt of a dilated eye examination, A1c test, foot examination, proteinuria assessment, lipid profile, advice to take aspirin and an influenza vaccine during the prior 12 months, based on American Diabetes Association recommendations. Analyses included a composite measure of these seven indicators. Evidence of eye examinations, foot examinations and advice to take aspirin came from survey data and/or chart review data. Evidence of A1c tests and proteinuria assessments came from chart review data only. Evidence of influenza vaccines was obtained solely from the patient survey.

2.2. Analytic approach

The prevalence of depression was measured for the overall TRIAD study population and for patient subgroups using a validated PHQ cut point of ≥10, indicating major depression [31] without adjusting for other variables.

Regression models were then developed to measure the association of depression using the PHQ score as a continuous variable, with key variables within each of the four areas of interest: patient characteristics; outcomes (intermediate clinical outcomes and other outcomes of interest); quality of care; and self-care behavior. In the first model, a series of patient characteristics, including demographic variables, BMI, pain, mobility, diabetes treatment, Charlson index, and diabetes duration, were treated as predictors of depression (PHQ score) in a single multiple regression model.

In subsequent regression models predicting outcomes, quality of care and self-care behaviors; depression (PHQ score) was treated as the main independent variable, with adjustment for selected patient characteristics – age, sex, education, income, race/ethnicity, diabetes treatment and co-morbid conditions. Individual regression models were then used to calculate predicted means (least square means) for each of the four intermediate clinical outcomes (A1c, systolic blood pressure, diastolic blood pressure, and LDL), three other outcomes of interest (diabetes symptom score, outpatient visits during the prior year, and rating of diabetes care quality), two measures of self-care behavior (percentage of non-smokers and self-monitoring of blood glucose (SMBG)) and each of the seven quality of care measures, individually and as a summary measure, by severity of depression (category of PHQ score).

Hierarchical random effects models were used to account for clustering of patients within health plans and provider groups. The model for the diabetes symptom score was additionally adjusted for most recent A1c value, and models for quality of care measures

were additionally adjusted for number of outpatient visits in the prior year. The model for SMBG included only patients using insulin.

Dichotomous outcomes (quality of care indicators), were modeled using logistic regression, and continuous outcomes (intermediate clinical outcomes), were modeled using linear regression. Predicted values included in the tables are predicted marginal mean values. Analyses were performed using the General Linear Model for Mixture Distributions (GLIMMIX) procedure in SAS V9.1. Missing data were imputed using Imputation and Variance Estimation Software (IVEware) and results were based on five imputations. Synthesis of the multiple imputation results was performed using the "MIAnalyze" procedure in SAS [35,36].

3. Results

3.1. Sample characteristics

The mean age of the 8790 TRIAD study follow-up participants was 61.8 years, 53% were female, and more than 90% had type 2 diabetes. Mean duration of diabetes was 13.5 years. Among study participants, 44% were white, non-Hispanic, 16% were Asian/Pacific Islander, 16% were Hispanic, 15% were African American and 9% belonged to other racial or ethnic groups.

3.2. Prevalence of depression and patient characteristics

3.2.1. Unadjusted results—Unadjusted results showed an overall rate of major depression (PHQ score >10) of 18% (Table 1). Depression rates were highest among women, younger patients, those with lower socioeconomic status and patients who reported experiencing pain.

Nearly 21% of women met the criteria for major depression, compared to 14% of men. Younger patients (age 18–44 years) had the highest rate of major depression (22%), compared to those ages 45–64 years (21%) and those age 65 years and older (14%). The prevalenceof major depression was highest among African American patients (24%) and lowest among Asian/Pacific Islander patients (12%), with rates of 19% and 18% for Hispanic participants and white, non-Hispanic participants respectively.

Socioeconomic status indicators were strongly associated with the unadjusted prevalence of major depression. The rate of major depression was more than three times higher among participants earning less than $15,000 annually (29%), compared with those earning more than $75,000 (9%). Similarly, the rate of major depression was 14% among those with more than a high school education, compared to 26% among those who did not complete high school. Nearly half of participants who reported being unemployed due to health reasons or other reasons had major depression (48% and 33% respectively).

Pain and limited mobility had the greatest impact on depression scores of all the patient characteristics studied. Nearly half (49%) of the participants who reported having extreme pain met the criteria for major depression, compared to 8% of participants who reported having no pain. Similarly, 44% of the participants who reported being bedridden met the

criteria for major depression, compared to 10% of those who reported having no trouble walking.

3.2.2. Results of multivariate models—Combining all patient characteristics into a single multivariate model enabled us to measure the independent association of each characteristic with depression (PHQ score). Results of this model (Table 1) showed that most patient characteristics remained independently and significantly associated with depression ($P<.05$). Exceptions included race/ethnicity, which was no longer significantly associated with depression after controlling for other patient characteristics ($P = .079$). Diabetes treatment ($P = .079$), other co-morbid conditions ($P = .119$) and diabetes duration ($P = .230$) were also not significantly associated with depression in this multivariate model (Table 1).

Socioeconomic status indicators remained strongly associated with depression in multivariate results. Individuals reporting an annual income of less than $15,000 had a mean PHQ score of 5.9, compared to a mean score of 4.3 among participants with an annual income greater than $75,000 ($P<.0001$). Similarly, patients reporting the lowest education had the highest mean PHQ score (5.7 for patients who did not complete high school compared to 4.9 among those with more than a high school education, $P<.0001$). Patients who were unemployed, particularly for health reasons, had a higher mean PHQ score (7.1 compared to 4.8 for those employed by others).

Controlling for all other variables in the model, we found that self-reported pain had the greatest impact on PHQ score. Participants reporting extreme pain had a predicted mean PHQ score of 7.9 compared to 4.2 for those reporting no pain. Results for limited mobility were similar.

3.3. Outcomes

Results of adjusted models did not show a strong association between depression and intermediate clinical outcomes (Table 2). The mean A1c value was 7.9 for patients with severe depression, compared to 7.7 for those with minimal or no depression ($P<.02$). Depression was not significantly associated with blood pressure or LDL levels.

We did observe strong associations between the severity of depression and other diabetes outcomes (Table 2). The adjusted mean diabetes symptom score was 14.6 among patients with minimal or no depression compared to 21.6 among patients with severe depression ($P<.0001$). Outpatient visits during the prior year increased with PHQ score, with 5.8 visits among patients with minimal or no depression compared to 6.9 among those with severe depression ($P< .002$). Patients with severe depression also rated the quality of their diabetes care lower with a mean adjusted score of 2.5 in a range of 1 (excellent) to 5 (poor), compared to 2.0 among those with minimal or no depression ($P<.0001$).

3.4. Quality of care and self-care

The adjusted summary measure of diabetes-related quality of care indicated that patients with depression received slightly fewer of the seven recommended processes of care (Table

3). Patients with severe depression received 5.1 services on average, compared to 5.3 among patients with minimal or no depression ($P < .001$).

Patients with depression received significantly fewer ($P < .02$) dilated eye examinations, A1c tests, and foot examinations in particular (90% among patients with minimal or no depression compared to 84% among those with severe depression). The lowest rates of eye examinations and A1c testing were among patients with moderate depression, and not among patients with severe depression. Patients with severe depression also received fewer proteinuria and lipid assessments, and influenza vaccinations, although not to a statistically significant degree.

Eighty-nine percent of patients with minimal or no depression were current non-smokers compared to 80%of those with severe depression ($P < .0001$). Rates of SMBG were not associated with depression severity.

4. Discussion

4.1. Depression prevalence and important correlates

Methodological issues associated with previous studies have resulted in large differences in estimates of co-morbid depression prevalence rates, as well as conflicting results about the impact of depression upon outcomes. The most frequently identified issues are limited sample size, the use of different measures of depression, the lack of a control group, and the failure to adequately include important confounding variables [1,26]. Health system factors in particular have received very little attention for their potential direct and indirect effects upon diabetes and depression treatment, quality of care and outcomes. The impact of these potentially confounding factors, such as benefit structure, co-pay amounts, requirements for pre-approval of specialist care, and the use of electronic medical record systems [27–29,37,38] are difficult to take into consideration in studies of single health care plans.

The use of meta-analysis has overcome some of these methodological issues [1,26]. However, meta-analyses are limited in the assessment of important confounding variables. For example, a number of studies have estimated depression prevalence among racial/ethnic subgroups with diabetes, but few have controlled for differences in socioeconomic status, known to be correlated with depression [39–42]. The study most comparable to ours (Li et. al.) used the PHQ-8 with a large, geographically varied community sample [43]. The overall prevalence of co-morbid major depression (PHQ ≥ 10) reported by this study was 14.4%, somewhat lower than our finding (17.9%), and likely due to study population differences. While results from this study report as much as a 25 fold difference in the rates of major depression across racial/ethnic groups, we found that after adjusting for income, education and other relevant covariates, there were no statistically significant differences in the rates of major depression across racial/ethnic groups.

Two other important correlates of depression were identified in our study were pain and limited mobility. Pain has been associated with suboptimal self-care [44], particularly a lack of exercise, and may negatively affect outcomes.

4.2. Outcomes

We did not find a strong relationship between intermediate clinical outcomes for diabetes and depression. Our study confirmed a link between glycemic control and depression [6,45,46], but the difference in adjusted A1c levels between non-depressed and severely depressed patients was small.

We found strong associations between depression and health care utilization, rating of diabetes care quality, and reported symptoms of hyperglycemia. The finding of poorer quality of diabetes care among depressed patients is consistent with previous studies [16,47]. This finding is noteworthy since depressed patients saw health care providers more often, presenting more opportunities for care, yet they did receive slightly fewer recommended diabetes services. Higher health care utilization could be related to clinical complexity and physicians may have spent more time discussing depression or related symptoms, leaving less time for standard diabetes care.

4.3. Limitations

A limitation of our study is that we did not have a control group of people without diabetes. In addition, the results of our study may not be comparable to results measuring depression using more in-depth interviews by mental health professionals. Finally, as across-sectional study, we cannot describe with confidence the causal pathways among diabetes, depression, other patient characteristics, and outcomes.

5. Conclusions

While there are many previous studies of diabetes and co-morbid depression, the results of this study are based on the largest and most diverse sample of patients and health care systems ever undertaken. The TRIAD study sampling design, and the collection of comprehensive covariate data, enabled the independent assessment of a broad range of correlates and outcomes associated with depression.

The strong association of socioeconomic status and co-morbid depression was clear. The association of race/ethnicity and socioeconomic status may result in findings of higher depression rates in minority groups, as shown by the high unadjusted rates of depression we found among some groups. However, the more important risk factors were income and education, not race/ethnicity, as shown in adjusted analyses. Although minority and low income patients may be at higher risk for depression, other studies have reported that these patient groups are significantly less likely to be screened and treated for depression [20,21,48]. Effective depression treatments are available [22,24,25,49,50], and the continuity of health care to optimally manage diabetes presents an opportunity to detect and treat depression in populations at risk.

The relationship between depression and pain is complicated, however, recent studies suggest that antidepressant medication may reduce the pain experienced by patients with diabetes [23,24]. Evidence-based pain management strategies should be considered for patients with diabetes, depression and pain.

Finally, there is increasing evidence that treatment for depression is effective in patients with diabetes and may help improve diabetes-related outcomes including mortality, quality of life and reduce health care costs [11,22,25,49].

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Table 1

Patient characteristics as predictors of PHQ score and unadjusted percentage of patients with major depression.

***N*=8790**	**Unadjusted % Major depression (PHQ ≥ 10)**	**Adjusted[a] mean PHQ score**	**95% CI**
Total	17.9	–	–
Sex			
Female (53%)	20.9	5.3	5.1–5.5
Male (47%)	14.2	5.0	4.8–5.2
Age			
18–44 (10%)	22.2	6.4	6.1–6.8
45–64 (48%)	20.5	5.6	5.3-5.8
65+ (42%)	13.7	4.4	4.1-4.6
Education			
<High school grad. (21%)	26.0	5.7	5.5–6.0
High school grad. (30%)	18.6	5.1	4.9–5.4
>High school grad. (49%)	14.0	4.9	4.7–5.2
Marital status			
Married (60%)	15.0	5.1	4.9–5.3
Living as couple (3.0%)	23.2	6.0	5.4–6.6
Never married (7.6%)	24.7	5.4	5.0–5.9
Widowed (15.8%)	18.4	4.9	4.6–5.3
Divorced or separated (13.4%)	24.7	5.2	4.9–5.5
Annual income			
<$15,000 (19%)	29.1	5.9	5.6–6.2
$15,000–40,000 (37%)	19.7	5.4	5.1–5.7
$40,000–75,000 (25%)	13.0	4.8	4.6–5.1
>$75,000 (18%)	8.8	4.3	3.9–4.6
Employment			
Employed by others (35%)	13.8	4.8	4.6–5.1
Self-employed (7%)	12.0	4.9	4.5–5.4
Retired (40%)	14.6	4.9	4.7–5.2
Homemaker (6%)	20.2	5.2	4.7–5.6
Student (<1%)	25.6	5.8	3.6–8.1
Unempl. – health (8%)	48.3	7.1	6.7–7.5
Unempl. – other (3%)	33.4	6.6	5.9–7.2
BMI			
<25 (16%)	14.7	5.2	4.9–5.5
≥25 and <30 (32%)	13.0	4.9	4.6–5.1
≥30 (52%)	21.7	5.3	5.1–5.5
Pain			
None (39%)	8.4	4.2	3.9–4.4
Moderate (54%)	20.5	5.5	5.3–5.7

***N*=8790**	**Unadjusted % Major depression (PHQ ≥ 10)**	**Adjusted[a] mean PHQ score**	**95% CI**
Extreme (7%)	49.2	7.9	7.5–8.4
Mobility			
No prob. walking (56%)	9.6	4.3	4.1–4.6
Some prob. walking (44%)	28.1	6.1	5.9–6.4
Bedridden (<1%)	44.4	7.5	6.1–8.9

[a]Results from multivariate model including all variables shown plus co-morbidity, diabetes treatment, race/ethnicity and diabetes duration (non-significant) with adjustment for clustering within health plans and provider groups.

All variables shown in the table were significant in this model at $P < .01$, except marital status ($P < .05$).

Table 2

Predicted mean intermediate clinical outcomes values and other outcomes by category of PHQ depression score (*N*= 8790).

PHQ category	None/minimal 0–4	Mild 5–9	Moderate 10–14	Moderate to severe 15–19	Severe >19	*P*
Intermediate clinical outcomes						
A1c	7.7	7.8	7.9	8.0	7.9	.02
Systolic blood pressure	135.3	135.2	136.0	135.5	137.3	.77
Diastolic blood pressure	74.7	74.4	74.9	75.2	75.6	.63
Low density lipids (LDL)	108.5	107.8	109.2	108.5	107.7	.96
Other outcomes						
Diabetes symptom score	14.6	17.3	19.4	20.9	21.6	<.001
Outpatient visits	5.8	6.0	6.2	6.3	6.9	.005
Quality of care rating	2.0	2.3	2.4	2.6	2.5	<.001

Adjusted for age, gender, education, income, race/ethnicity, diabetes treatment and co-morbidity, health plan and provider group, plus A1c level for DM symptoms.

P-values are multiple imputation type III tests that effects at all levels of depression are zero.

Table 3

Mean rates of processes of care received during the past 12 months by categories of PHQ depression scores (*N*=8790).

PHQ category	None/minimal 0–4	Mild 5–9	Moderate 10–14	Moderate/severe 15–19	Severe >19	*P*
Eye exam	79	77	73	74	78	.002
A1C test	89	86	86	85	87	.02
Foot exam	90	88	87	84	84	<.001
Proteinuria assessed	82	81	81	79	78	.68
Lipids assessed	69	66	66	66	64	.23
Aspirin advised	53	54	51	53	54	.46
Influenza vaccination	74	72	71	70	71	.47
Mean summary measure	5.3	5.2	5.1	5.1	5.1	<.001

Adjusted for age, sex, education, race/ethnicity, co-morbid conditions, diabetes treatment, diabetes duration, income, clustering within health plan and provider group and number of outpatient visits.

P-values are multiple imputation type III tests that effects at all levels of depression are zero.