Depression in Adults in the T1D Exchange Clinic Registry

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OBJECTIVE

Little is known about the frequency of depression in adults with type 1 diabetes (T1D) or its relationship to diabetes outcomes. The T1D Exchange clinic registry allowed us to explore depression in a large, heterogeneous sample.

RESEARCH DESIGN AND METHODS

Participants ≥18 years old (*N* = 6,172; median age 34 years; median diabetes duration 16 years; 55% female; and 89% non-Hispanic white) completed the eight-item Patient Health Questionnaire (PHQ-8), a validated, reliable measure of current depression. Probable major depression was defined in four ways: PHQ-8 ≥10, PHQ-8 ≥12, per diagnostic algorithm, and as a continuous variable. Characteristics and clinical outcomes of those with and without depression were compared using logistic and linear regression models.

RESULTS

A total of 4.6–10.3% of participants were classified as probable major depression depending on how defined. Participants classified as depressed were more likely female, nonwhite race/ethnicity, to have a lower household income and lower education level, to exercise less often, to miss insulin doses, and to have one or more complications (neuropathy, nephropathy, treatment for retinopathy, or cardiovascular/cerebrovascular disease) (all $P < 0.01$). HbA_{1c} was higher in the depressed versus not depressed groups (8.4 ± 1.7% [68 ± 8.6 mmol/mol] vs. 7.8 ± 1.4% [62 ± 15.3 mmol/mol]; $P < 0.001$). Occurrence of one or more diabetic ketoacidosis events (11 vs. 4%; $P < 0.001$) and one or more severe hypoglycemic events (18 vs. 9%; $P < 0.001$) in the past 3 months was higher among depressed participants.

CONCLUSIONS

In the T1D Exchange clinic registry, adults with probable major depression have worse clinical outcomes than those not depressed. Whether identification and treatment of depression improves diabetes outcomes requires study. Depression is common in T1D, and better identification and treatment of this comorbid condition is needed.

The prevalence of depression is almost two times higher in persons with diabetes than it is in the general population (1–3). Not only do persons with diabetes have an increased risk of developing depression (4), but persons with depression have an increased risk of developing diabetes (5), which may relate to their use of antidepressants (6) or other biological or psychosocial factors associated with diabetes. Depression in diabetes is a particular concern because it is associated with poorer glycemic control (7) and regimen adherence (8), greater morbidity and mortality

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(9–11), greater risk of severe hypoglycemia (SH) (12), higher healthcare costs (13,14), and poorer quality of life (15). Most studies and meta-analyses include only people with type 2 diabetes or combine type 1 and type 2 diabetic participants without reporting data separately for each group. Thus, we do not know if these findings extend to adults with type 1 diabetes (T1D). It is estimated that as many as 3 million Americans have T1D, of which 85% are adults (16), yet little is known about the psychosocial issues that may affect their adherence, glycemic control, and quality of life.

This study had two main goals: *1*) to describe the frequency of depression and the participant characteristics associated with depression in a large, heterogeneous sample of adults with T1D; and *2*) to explore the relationship of depression to diabetes-related clinical (glycemic control, episodes of SH, and diabetic ketoacidosis [DKA]) and behavioral (adherence) outcomes.

RESEARCH DESIGN AND METHODS

The T1D Exchange Clinic Network and registry includes 70 U.S.-based pediatric and adult endocrinology practices. Each clinic received approval from an Institutional Review Board, and informed consent was obtained according to Institutional Review Board requirements. Data were collected at enrollment (baseline) and then annually, as previously described (17). More than 26,000 participants were enrolled in the registry between September 2010 and December 2012. At the 1-year data collection point, participants aged ≥18 years also completed the eight-item Patient Health Questionnaire depression scale (PHQ-8). This report includes data on 6,172 participants from 64 sites, who were ≥18 years of age, and who completed the PHQ-8 at the 1-year registry follow-up visit.

Measures

Depression

The PHQ-8 is a standardized and validated measure of self-reported depression symptoms and their severity (18), a modification of the PHQ-9. The PHQ-9 has been used in several hundred studies to assess both mentally and physically ill patients (19), including studies with patients with diabetes (20). The PHQ-8 consists of eight items that measure how many days in the past 2 weeks the individual has experienced eight of the nine symptoms of depression defined in the DSM-IV (21). The suicidal-thoughts criterion is not included, and research has shown that this does not affect validity of scoring thresholds (18). A severity score of 0–3 is assigned to each item (0, not at all; 1, several days; 2, more than half the days; and 3, nearly every day), with the total score having a possible range of 0–24. There are several ways this measure can be used, and the method used affects one's interpretation of the data. It is most common to use a cutoff score of ≥10 to define a clinically relevant level of major depression symptoms, as it has been demonstrated that this scoring threshold is valid as a measure of depression severity, with a reported sensitivity and specificity of 88% for diagnosing major depression (18,19,22,23). Scores of 10–14 are used to define mild major depression. We used this cutoff score of ≥10 for our first analyses. Twist et al. (20) recently reported that a cutoff of ≥12 (on the PHQ-9, with newly diagnosed type 2 diabetic patients) may be more appropriate for patients with diabetes, as its use decreases the proportion of false positives. They reported a sensitivity of 86.9% and specificity of 80.3% for major depression identified via structured interview. Although our sample is quite different (i.e., adults with T1D of long duration), we also analyzed the data using a cutoff of 12. Third, we looked at depressive symptoms as a continuous variable, not providing a cutoff for major depression, but allowing us to assess any depressive symptoms. Finally, to allow a comparison with the general population data from the Behavioral Risk Factor Surveillance Survey (24), we used their scoring algorithm. This algorithm is based on the symptom profile that is required by the DSM-IV for one to make a diagnosis of major depression on interview. Participants were identified as having probable major depression if they met at least five of the eight criteria for "more than half the days" (i.e., rated that symptom a 2 or 3), and at least one of those criteria was depressed mood or anhedonia (loss of interest). Participants were identified as "other depression" if they met two, three, or four of the eight criteria, and, again, at least one of those was depressed mood or anhedonia. We note, however, that "other depression" is not a DSM diagnostic entity, but we use this label to capture a group with symptoms of depression that are not likely to meet DSM criteria. Sullivan et al. (11) used this algorithm in the ACCORD trial and found that less than half of those defined as depressed using PHQ-9 ≥10 as the cutoff were defined as depressed with the algorithm.

Demographic Data

Demographic data on sex, race/ethnicity, household income, insurance status, education, marital status, and employment status were collected through a participant questionnaire. Information about age, duration of diabetes, type of treatment (pump or injections), BMI (height/weight), and presence of diabetes-related complications was captured from medical chart review.

Diabetes Self-Care

All T1D Exchange clinic registry participants completed an online questionnaire at their 1-year visit. It included specific questions about diabetes self-care: one question about frequency of self-monitoring of blood glucose (SMBG) ("About how many times per day are you checking your blood sugar with a blood glucose meter?"), one question about insulin delivery method ("How do you usually take insulin?"), one question about missed insulin doses ("How often do you miss an insulin dose?"), and one question about activity ("In a typical week, how many days do you spend at least 30 minutes doing any physical activities or exercises such as running, working out, yoga or Pilates, aerobics, sports, gardening, PE in school, or walking for exercise?"). These questions were developed for the Exchange questionnaire, and there are no reliability or validity data available for them.

Diabetes Outcomes

1. HbA_{1c}, widely accepted as a reliable and valid index of metabolic control, was obtained by their treating providers as part of usual care. In most cases, the clinics gathered this information using point-of-care devices, which is accepted as a reliable, pragmatic means of obtaining HbA_{1c} values.

2. Information on the occurrence of SH and DKA in the prior 3 months was obtained by participant self-report on the 1-year questionnaire. SH was defined as an episode of documented or presumed low blood glucose that resulted in seizure or loss of consciousness. DKA was defined as the occurrence of ketoacidosis that resulted in hospitalization.

Statistical Methods

Participants were defined as depressed or not depressed in the three ways defined above (i.e., PHQ-8 ≥10, PHQ-8 ≥12, or per algorithm). Patient characteristics of the depressed versus nondepressed groups were compared using the Wilcoxon rank-sum test for continuous variables and χ^2 tests for categorical variables (Mantel-Haenszel statistics for ordered categories). Logistic regression models were used to identify the demographic (e.g., age and sex) and clinical (e.g., insulin delivery method and duration of diabetes) factors that were associated with the occurrence of depression. Factors with a *P* value <0.10 from individual factor models were included in an initial multivariate model, and then a backward elimination procedure was used to remove variables with a *P* value >0.01. A forward selection process resulted in a similar model. Tests of significance were reported from models using continuous or ordinal variables, and odds ratios (ORs) were reported from models using the categorical variables.

Diabetes-management factors (i.e., frequency of SMBG, frequency of missed insulin doses, and frequency of exercise) and outcomes (most recent HbA_{1c}, SH events, and DKA events) in those with and without depression were compared using linear regression for continuous variables and logistic regression models for the categorical variables.

Patient characteristics, diabetes-management factors, and outcomes were also analyzed using the continuous PHQ-8 depression score. Linear regression models were used to assess the relationship between depression score and patient demographic and clinical factors using the same backward selection approach described above. Least-square means were reported from models using categorical variables, and tests of significance were reported from models using continuous or ordinal variables. The association between depression score and diabetes-management factors and outcomes was assessed using the methods described above, replacing the covariate indicator for depression with the continuous depression score.

Data analyses used SAS software, version 9.3 (SAS Institute Inc., Cary, NC). All *P* values are two-sided. In view of the multiple comparisons and large sample size, only *P* values <0.01 were considered significant.

RESULTS

The 6,172 participants ranged in age from 18–92 years (median 34 years [interquartile range 21–51 years]); 55% were female, and 89% were non-Hispanic white. Median diabetes duration was 16 years (interquartile range 9–28 years). Additional characteristics of the cohort are shown in Table 1. (In the following results, we classify participants are "depressed" or "not depressed" for ease of presentation, but note that we are not able to diagnose depression per DSM standards without a clinical interview.)

Participant Characteristics Associated With Depression

Depression Defined as PHQ-8 ≥10

[Note that Table 2 shows only the data for the PHQ-8 ≥10 analyses for ease of display. The analyses of the other PHQ formulas, which were remarkably similar, are available in the Supplementary Tables.]

Among the 6,172 participants, 638 (10.3%) were classified as depressed, with the frequency being 9.8% in 18 to <26 year olds, 10.9% in 26 to <50 year olds, 11.7% in 50 to <65 year olds, and 6.1% in ≥65 year olds (*P* = 0.006; Table 2). In univariate analyses, the occurrence of depression was more likely in participants who were female, Hispanic, without private health insurance, with a lower household income level and a lower education level, living alone, unemployed, having longer duration of diabetes, and having one or more diabetes-associated complications (*P* < 0.01 for all factors; Table 2). In a multivariate analysis, associations were similar, except there was not a significant association between living alone and depression (*P* = 0.16) and between diabetes duration and depression (*P* = 0.48).

Depression Defined as PHQ ≥12

Among the 6,172 participants, 430 (7.0%) were classified as depressed based on the higher cutoff score, with the frequency being 6.5% in 18 to <26 year olds, 7.7% in 26 to <50 year olds, 7.7% in 50 to <65 year olds, and 3.7% in ≥65 year olds (*P* = 0.01; Supplementary Table 1). The results of the univariate and multivariate analyses were similar to those with the lower cutoff score of 10, except sex is no longer present in the multivariate model (Supplementary Table 1). The absence of sex from the multivariate model is likely due to the reduction in power resulting from the lower frequency of depression using the higher cutoff score; the ORs for sex from the full multivariate model are the same for the lower cutoff score and the higher cutoff score (OR 1.37; Table 2 and Supplementary Table 1).

Depression Defined per Algorithm

Among the 6,172 participants, 283 (4.6%) were classified as probable major depression, with the frequency being 4.1% in 18 to <26 year olds, 5.5% in 26 to <50 year olds, 4.7% in 50 to <65 year olds, and 1.7% in ≥65 year olds (*P* = 0.004; Supplementary Table 2). Also, 267 (4.3%) could be classified as "other depression;" thus, a total of 8.9% can be defined as having any depressive disorder. The univariate and multivariate analyses using the algorithm for probable major depression were similar to those using the lower cutoff score; however, the univariate association with duration was no longer statistically significant (*P* = 0.08), and the multivariate model did not include sex, race/ethnicity, or education level (Supplementary Table 2). The lack of statistical significance for these demographic variables in the univariate and multivariate models is likely due to the decreased power from the reduction in the frequency of depression when defining depression per the algorithm; we note that the ORs for duration, sex, race/ethnicity, and education level are similar between the two methods (Table 2 and Supplementary Table 2).

Depression Using Continuous PHQ-8 Score

The results of the univariate analyses were similar when using continuous (rather than categorical) PHQ-8 depression scores (data not shown); however, the association between living alone

Table 1—Patient characteristics

	All (*N* = 6,172)	Probable major depression: PHQ-8 ≥10		Probable major depression: PHQ-8 ≥12		Probable major depression: per algorithm	
		Depressed (*n* = 638)	Not depressed (*n* = 5,534)	Depressed (*n* = 430)	Not depressed (*n* = 5,742)	Depressed (*n* = 283)	Not depressed (*n* = 5,889)
Age (years)‡							
Median (25th–75th percentile)	34.0 (21.0–51.0)	35.0 (22.0–50.0)	34.0 (21.0–51.0)	36.0 (22.0–50.)	34.0 (21.0–51.0)	36.0 (22.0–48.0)	34.0 (21.0–51.0)
18 to <26 (*n* [%])	2,196 (36)	216 (34)	1,980 (36)	142 (33)	2,054 (36)	91 (32)	2,105 (36)
26 to <50 (*n* [%])	2,314 (37)	253 (40)	2,061 (37)	178 (41)	2,136 (37)	128 (45)	2,186 (37)
50 to <65 (*n* [%])	1,204 (20)	141 (22)	1,063 (19)	98 (22)	1,111 (19)	56 (20)	1,148 (19)
≥65 (*n* [%])	458 (7)	28 (4)	430 (8)	17 (4)	441 (8)	8 (3)	450 (8)
P value		0.98		0.86		0.95	
Sex, female (*n* [%])£	3,380 (55)	395 (62)	2,985 (54)	269 (63)	3,111 (54)	175 (62)	3,205 (54)
P value		<0.001		0.001		0.01	
Race/ethnicity (*n* [%])£							
White non-Hispanic	5,491 (89)	465 (82)	4,964 (90)	349 (81)	5,142 (90)	233 (82)	5,258 (89)
Black non-Hispanic	174 (3)	22 (3)	152 (3)	16 (4)	158 (3)	10 (4)	164 (3)
Hispanic or Latino	316 (5)	57 (9)	259 (5)	40 (9)	276 (5)	24 (8)	292 (5)
Other race/ethnicity	191 (3)	32 (5)	159 (3)	25 (6)	166 (3)	16 (6)	175 (3)
P value		<0.001		<0.001		0.002	
Duration of T1D (years)‡							
Median (25th–75th percentile)	16.0 (9.0–28.0)	18.0 (10.0–29.0)	16.0 (9.0–28.0)	19.0 (10.0–30.0)	16.0 (9.0–28.0)	19.0 (11.0–28.0)	16.0 (9.0–28.0)
<20 (*n* [%])	3,621 (59)	345 (54)	3,276 (59)	227 (53)	3,394 (59)	148 (52)	3,473 (59)
20 to <40 (*n* [%])	1,887 (31)	216 (34)	1,671 (30)	149 (35)	1,739 (30)	103 (36)	1,785 (30)
≥40 (*n* [%])	664 (11)	77 (12)	587 (11)	54 (13)	609 (11)	32 (11)	631 (11)
P value		0.009		0.02		0.03	
BMI (*n* [%])‡§							
Under-/normal weight	2,059 (43)	201 (41)	1,858 (43)	126 (37)	1,933 (43)	81 (37)	1,978 (43)
Overweight	1,659 (35)	140 (29)	1,519 (35)	106 (31)	1,553 (35)	71 (32)	1,588 (35)
Obese	1,078 (22)	150 (31)	928 (22)	108 (32)	970 (22)	67 (31)	1,011 (22)
P value		0.01		0.003		0.02	
Household income (*n* [%])‡							
<$35,000	962 (20)	207 (40)	755 (18)	142 (41)	820 (18)	87 (39)	875 (19)
$35,000 to <75,000	1,449 (30)	144 (28)	1,305 (30)	109 (32)	1,340 (30)	74 (33)	1,375 (30)
≥$75,000	2,392 (50)	164 (32)	2,228 (52)	93 (27)	2,299 (52)	61 (27)	2,331 (51)
P value		<0.001		<0.001		<0.001	
Insurance status (*n* [%])£							
Private insurance	4,636 (80)	403 (68)	4,233 (81)	265 (66)	4,371 (81)	178 (67)	4,458 (81)
Other insurance	1,046 (18)	169 (29)	877 (17)	123 (31)	923 (17)	78 (30)	968 (18)
No insurance	109 (2)	20 (3)	89 (2)	15 (4)	94 (2)	8 (3)	101 (2)
P value		<0.001		<0.001		<0.001	

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Table 1—Continued

	All (*N* = 6,172)	Probable major depression: PHQ-8 ≥10		Probable major depression: PHQ-8 ≥12		Probable major depression: per algorithm	
		Depressed (*n* = 638)	Not depressed (*n* = 5,534)	Depressed (*n* = 430)	Not depressed (*n* = 5,742)	Depressed (*n* = 283)	Not depressed (*n* = 5,889)
Education level (*n* [%])‡							
High school diploma/GED or less	2,879 (47)	345 (55)	2,534 (46)	242 (57)	2,637 (46)	155 (55)	2,724 (47)
Associate's or bachelor's degree	2,171 (35)	208 (33)	1,963 (36)	137 (32)	2,034 (36)	97 (35)	2,074 (36)
Master's, professional, or doctorate degree	1,066 (17)	77 (12)	989 (18)	48 (11)	1,018 (18)	28 (10)	1,038 (18)
P value		<0.001		<0.001		<0.001	
Marital status (*n* [%])£							
Living alone	3,117 (51)	363 (57)	2,754 (50)	252 (59)	2,865 (50)	163 (58)	2,954 (50)
Married/living together	3,017 (49)	270 (43)	2,747 (50)	177 (41)	2,840 (50)	120 (42)	2,897 (50)
P value		<0.001		0.001		0.02	
Employment status (*n* [%])£							
Student	1,371 (22)	113 (18)	1,258 (23)	69 (16)	1,302 (23)	46 (16)	1,325 (23)
Working full-/part-time	3,362 (55)	285 (45)	3,077 (56)	192 (45)	3,170 (56)	121 (43)	3,241 (56)
Not working	1,386 (23)	236 (37)	1,150 (21)	166 (39)	1,220 (21)	115 (41)	1,271 (22)
P value		<0.001		<0.001		<0.001	
Complications (*n* [%])†£							
None	2,754 (65)	203 (47)	2,551 (68)	133 (46)	2,621 (67)	83 (43)	2,671 (66)
≥1	1,461 (35)	233 (53)	1,228 (32)	157 (54)	1,304 (33)	110 (57)	1,351 (34)
P value		<0.001		<0.001		<0.001	

GED, general educational development. †Cardiovascular complications, neuropathy, retinopathy, and renal disease. ‡*P* value from Wilcoxon rank-sum test. Ordinal income and education variables were analyzed. £*P* value from χ^2 test. §For participants <20 years of age, BMI <5th percentile is considered underweight, 5th to <85th percentile normal weight, 85th to <95th percentile overweight, and ≥95th percentile obese. For participants >20 years of age, BMI <18.5 is considered underweight, 18.5 to <25 normal weight, 25 to <30 overweight, and ≥30 obese.

and depression remained in the multivariate model (P = 0.001; data not shown).

Relationship of Aspects of Diabetes Management and Outcomes to Depression

The frequencies of insulin pump use and SMBG testing were similar (i.e., no differences) comparing depressed and nondepressed participants using all three methods of classifying someone as depressed (all P values nonsignificant; adjusted for age, sex, race/ethnicity, and income). (Note that Table 3 shows only the data for the PHQ-8 ≥10 analyses for ease of display. The analyses of the other PHQ formulas are available in the Supplementary Tables.)

Mean HbA_{1c} was higher among those with depression compared with those classified as not depressed (PHQ ≥10: 8.4 ± 1.7% [68 ± 18.6 mmol/mol] vs. 7.8 ± 1.4% [62 ± 15.3 mmol/mol], $P <$ 0.001; PHQ ≥12 and algorithm method: 8.5 ± 1.7% [69 ± 18.6 mmol/mol] vs. 7.8 ± 1.4% [62 ± 15.3 mmol/mol], $P <$ 0.001; adjusted for age, sex, race/ethnicity, and income). Participants with depression were more likely to miss insulin doses (adjusted $P < 0.001$) and exercise less often (adjusted $P <$ 0.001) than those without depression in all analyses (Table 3 and Supplementary Tables 3 and 4).

Compared with the nondepressed participants, the depressed participants had more frequent DKA events (11 vs. 4%; $P < 0.001$ for all three definitions of depression) and SH events (PHQ-8 ≥10 and algorithm method: 18 vs. 9%, $P <$ 0.001; PHQ-8 ≥12: 19 vs. 9%, $P < 0.001$; each adjusted for age, sex, race/ethnicity, income, and HbA_{1c}) in the past 3 months (Fig. 1*A*).

Results for the continuous PHQ-8 depression score were similar to results for the occurrence of depression. The association between depression and HbA_{1c} showed a strong linear pattern when using a continuous depression score; participants that scored high on the PHQ-8 also had higher HbA_{1c} (adjusted $P < 0.001$; Fig. 1*B*). Compared with lower-scoring participants, participants with higher depression scores were more likely to miss insulin doses (adjusted $P < 0.001$), exercise less often (adjusted $P < 0.001$), and experience more frequent DKA ($P < 0.001$) and SH

Table 2—Factors associated with depression†

	Total *N*	Frequency of depression (%)	Unadjusted OR (95% CI)	Univariate *P* value	Full-model OR (95% CI)	Full-model *P* value	Reduced-model OR (95% CI)	Reduced-model *P* value
All	6,172	10.3						
Age (years)[a]				0.006		<0.001		<0.001
18 to <26	2,196	9.8	1.0		1.0		1.0	
26 to <50	2,314	10.9	1.13 (0.93–1.36)		1.00 (0.74–1.36)		0.97 (0.75–1.27)	
50 to <65	1,204	11.7	1.22 (0.97–1.52)		0.81 (0.55–1.17)		0.79 (0.58–1.08)	
≥65	458	6.1	0.60 (0.40–0.90)		0.27 (0.16–0.46)		0.26 (0.16–0.42)	
Sex				<0.001		0.003		0.005
Male	2,790	8.7	1.0		1.0		1.0	
Female	3,380	11.7	1.39 (1.17–1.64)		1.37 (1.14–1.64)		1.36 (1.14–1.63)	
Race/ethnicity				<0.001		0.001		0.002
White non-Hispanic	5,491	9.6	1.0		1.0		1.0	
Black non-Hispanic	174	12.6	1.36 (0.86–2.15)		0.91 (0.55–1.51)		0.94 (0.57–1.54)	
Hispanic or Latino	316	18.0	2.07 (1.54–2.80)		1.68 (1.20–2.35)		1.68 (1.20–2.35)	
Other race/ethnicity	191	16.8	1.90 (1.28–2.80)		1.83 (1.19–2.79)		1.83 (1.20–2.78)	
Duration of T1D (years)				0.006		0.48		
<20	3,621	9.5	1.0		1.0			
20 to <40	1,887	11.4	1.23 (1.03–1.47)		1.17 (0.92–1.48)			
≥40	664	11.6	1.25 (1.00–1.62)		1.12 (0.78–1.61)			
BMI				0.65				
Under-/normal weight	2,059	9.8	1.0					
Overweight	1,659	8.4	0.85 (0.68–1.07)					
Obese	1,078	13.9	1.50 (1.19–1.87)					
Household income				<0.001		<0.0001		<0.001
≥$75,000	2,392	6.9	1.0		1.0		1.0	
$35,000 to <75,000	1,449	9.9	1.50 (1.19–1.89)		1.26 (0.98–1.62)		1.30 (1.02–1.67)	
<$35,000	962	21.5	3.73 (3.00–4.65)		2.44 (1.88–3.17)		2.61 (2.03–3.35)	
Insurance status[b]				<0.001				
Private insurance	4,636	8.7	1.0					
Other/no insurance	1,155	16.4	2.06 (1.71–2.48)					
Education level				0.001		0.005		0.008
High school diploma/GED or less	2,879	12.0	1.0		1.0		1.0	
Associate's or bachelor's degree	2,171	9.6	0.78 (0.65–0.93)		0.84 (0.68–1.04)		0.84 (0.68–1.04)	
Master's, professional, or doctorate degree	1,066	7.2	0.57 (0.44–0.74)		0.74 (0.55–1.01)		0.75 (0.55–1.01)	
Marital status				<0.001		0.16		
Married/living together	3,017	8.9	1.0		1.0			
Living alone	3,117	11.6	1.34 (1.14–1.58)		1.24 (0.99–1.55)			

Continued on p. 1569

Table 2—Continued

	Total *N*	Frequency of depression (%)	Unadjusted OR (95% CI)	Univariate *P* value	Full-model OR (95% CI)	Full-model *P* value	Reduced-model OR (95% CI)	Reduced-model *P* value
Employment status				<0.001		<0.001		<0.001
Student	1,371	8.2	1.0		1.0		1.0	
Working full-/part-time	3,362	8.5	1.03 (0.82–1.30)		1.24 (0.93–1.67)		1.22 (0.91–1.63)	
Not working	1,386	17.0	2.29 (1.80–2.90)		2.41 (1.74–3.35)		2.36 (1.71–3.25)	
Complications				<0.001		<0.001		<0.001
None	2,754	7.4	1.0		1.0		1.0	
≥1	1,461	15.9	2.38 (1.95–2.91)		2.23 (1.75–2.84)		2.28 (1.80–2.89)	

GED, general educational development. †Depression defined using PHQ-8 cutoff score of ≥10. ‡The categorical variable of age was analyzed. §Not included in multivariate analysis because of high correlation with other socioeconomic variables.

events ($P < 0.001$). In contrast to the results for the occurrence of depression, participants with higher depression scores checked their blood glucose less frequently, on average, than participants with lower depression scores (adjusted $P < 0.001$).

CONCLUSIONS

It is well-documented that adults with type 2 diabetes have a higher prevalence of depression than is found in the general population (2,25), but the literature on depression in adults with T1D is much more limited. In a systematic review of studies (26) that have specifically addressed depression in adults with T1D published through 2004 (14 studies, mostly small *N*s), the reported prevalence of depression ranged from 10.7 (27) to 43.3% (28). In this study, 4.6 (algorithm method) to 10.3% (cutoff of 10) of adult participants with T1D could be classified as probable major depression. If we include those whom the algorithm defines as "other depression," this number increases to ~9% who are likely to be diagnosable with a depressive disorder. This compares to a prevalence of major depression of 4.1% and of any depressive disorder of 9.1% in the general population as reported in the Behavioral Risk Factor Surveillance System, which also used the PHQ-8 (24). Our finding is low compared with earlier T1D studies; however, significant differences exist. The other studies assessed small homogenous samples (*N* = 75, 60, and 487), young or old populations, and each used different depression measures (27–29). Our sample was large and heterogeneous and used a measure of depression with reported sensitivity and specificity of 88% (19). Also, by using four different methods of interpreting the PHQ-8 results, we have enhanced the strength of our results. While these results are robust and based on a very large geographically diverse sample, they are still limited to T1D Exchange registrants, and the results may not represent the prevalence of depression in patients with T1D in other populations. Our other findings are consistent with the prior literature. Studies of depression in the general population describe many factors that have been shown to increase one's risk for depression. Of those we assessed, female sex, African American race or Hispanic ethnicity, low education (i.e., less than high school), being unemployed, being without health insurance coverage, low socioeconomic status, and medical illness are consistently viewed as significant risk factors (24,30), as they were shown to be in this study. For patients with type 2 diabetes, the literature shows that those who are poorer, less educated, unemployed, without insurance, and who have more complications are more likely to be depressed (6–11,13,14). We found similar results in our sample of adults with T1D. In patients with type 2 diabetes, depression relates to poorer self-care and glycemic control and to more frequent serious negative events. Again, in this study, similar relationships were found for adults with T1D (i.e., poorer adherence and greater risk of SH and DKA events).

There are several study limitations. First, the data are cross-sectional, and therefore, causality cannot be determined; we do not know if poorer self-care and more complications make people depressed or if being depressed affects self-care that leads to complications. Longitudinal studies are needed to answer these questions. Second, there may be concerns with the use of a self-report questionnaire to define depression. While the PHQ-8 is a valid screening tool, it should not be used to make a clinical diagnosis of major depression. It also has some items (fatigue, difficulty concentrating, and poor appetite) that may reflect symptoms of hypo- or hyperglycemia. If scores do reflect the diabetes, not depression, this would lead to an overestimation of depression in this sample. In a recent review of depression screening tools, Roy et al. (31) raise the concern that these tools have a high rate of false positives, although they conclude that the PHQ-9 is valid and reliable with high sensitivity and specificity for major depression. Twist et al. (20) report similarly high false-positive rates for patients with type 2 diabetes. We believe that we have addressed this concern to the extent possible by analyzing the data with the higher cutoff, as has been recommended for patients with diabetes, and with the algorithm method. While the percentage of participants classified as depressed differs with these three methods, the key findings (i.e., that

Table 3—Diabetes management and outcomes in depressed† versus nondepressed participants

	Depressed (n = 638)	Not depressed (n = 5,534)	P value
Insulin route (n [%])[a]			0.93
Pump	375 (59)	3,380 (62)	
Multiple daily injections	257 (41)	2,086 (38)	
Self-reported SMBG frequency (per day)[b]			0.12
Mean ± SD	4.9 ± 2.9	5.1 ± 2.5	
Times per day (n [%])			
0–2 times	102 (16)	606 (11)	
3 to 4 times	223 (36)	2,090 (38)	
5–9 times	248 (40)	2,400 (44)	
≥10 times	48 (8)	383 (7)	
Self-reported frequency of missing insulin dose (n [%])[b]			<0.001
≥3 times a week	135 (21)	447 (8)	
1 to 2 times a week	103 (16)	635 (12)	
Less than once a week	146 (23)	1,392 (25)	
Almost never	252 (40)	3,043 (55)	
Frequency of exercise, days/week (n [%])[d]			<0.001
0	133 (22)	547 (10)	
1 to 2	156 (26)	1,144 (22)	
3–5	222 (37)	2,647 (50)	
6 to 7	84 (14)	982 (18)	
Most recent HbA_{1c} (%)[c]			<0.001
Mean ± SD	8.4 ± 1.7 (68 ± 18.6 mmol/mol)	7.8 ± 1.4 (62 ± 15.3 mmol/mol)	
≤7.0% (≤53 mmol/mol)	127 (21)	1,705 (32)	
7.1–8.0% (54–64 mmol/mol)	155 (25)	1,893 (36)	
8.1–9.0% (65–75 mmol/mol)	136 (22)	1,007 (19)	
9.1–10.0% (76–86 mmol/mol)	100 (16)	380 (7)	
>10% (>86 mmol/mol)	90 (15)	335 (6)	

†Depression defined using PHQ-8 cutoff score of ≥10. [a]P value from logistic regression, adjusted for age, sex, race/ethnicity, and income. [b]P value from linear regression model with van der Waerden transformed continuous variable as outcome, adjusted for age, sex, race/ethnicity, and income. [c]P value from linear regression model with HbA_{1c} as outcome, adjusted for age, sex, race/ethnicity, and income. [d]P value from multinomial logistic regression model, adjusted for age, sex, race/ethnicity, income, and HbA_{1c}.

depression relates to poorer glycemic control and self-care) are consistently supported. One might argue that these consistent results suggest that we are not, in fact, measuring depression, but instead measuring a dimension of global emotional distress, and it may be that a structured interview assessment would have yielded different findings. Third, the single-item reports of self-care were developed for the T1D Exchange clinic registry questionnaire and do not represent a reliable and validated measurement tool. Thus, self-care, too, may have been over- or underreported, which could also affect our findings. Fourth, we do not have data about whether those we defined as depressed or not depressed differed in terms of whether they have been diagnosed with, or treated for, depression by their healthcare provider. While the PHQ-8 may have identified some depressed individuals without that diagnosis, there may also be some that we defined as not depressed who do have a diagnosis of depression but are being successfully treated. Also, this means that we could not assess whether duration of depression played a role in our results. Fifth, the patient characteristics for all T1D patients are not known, and, while the T1D Exchange provides a very large number of participants from a diverse geographic area, we do not know if they are a representative group. As reported previously, T1D Exchange clinic registry participants are similar to the patient populations from the participating clinics in terms of their race/ethnicity (77 vs. 82% non-Hispanic White), access to private insurance (61 vs. 75%), and insulin pump use (41 vs. 50%). However, differences may exist between patients who did and did not choose to participate in the clinic registry.

Depression in adults with diabetes is a serious concern. Depression itself is a disabling condition, and when it occurs with comorbid diabetes, there can be a marked impact on health and mortality (11) and health-related quality of life (1). For adults with comorbid type 2 diabetes, there are the added concerns that depression relates to poorer self-care, poorer glycemic control, serious negative health outcomes, and higher healthcare costs (7–14). Depression treatment for diabetic patients can result in improved mental health, but the evidence is less clear that intervention will lead to improved glycemic control or improvement in other diabetes-related outcomes (32,33), although interventions that integrate both depression and diabetes treatment appear to hold promise (34,35).

Much less is known for adults with T1D. In the current study, probable major depression was related to a higher incidence of SH and DKA, and both are very serious, and costly, complications of the disease. There may be physiological mechanisms that relate to both depression and hypoglycemia for adults with T1D. A recent review (36) outlines plausible biologic mechanisms that might explain the relationship of T1D

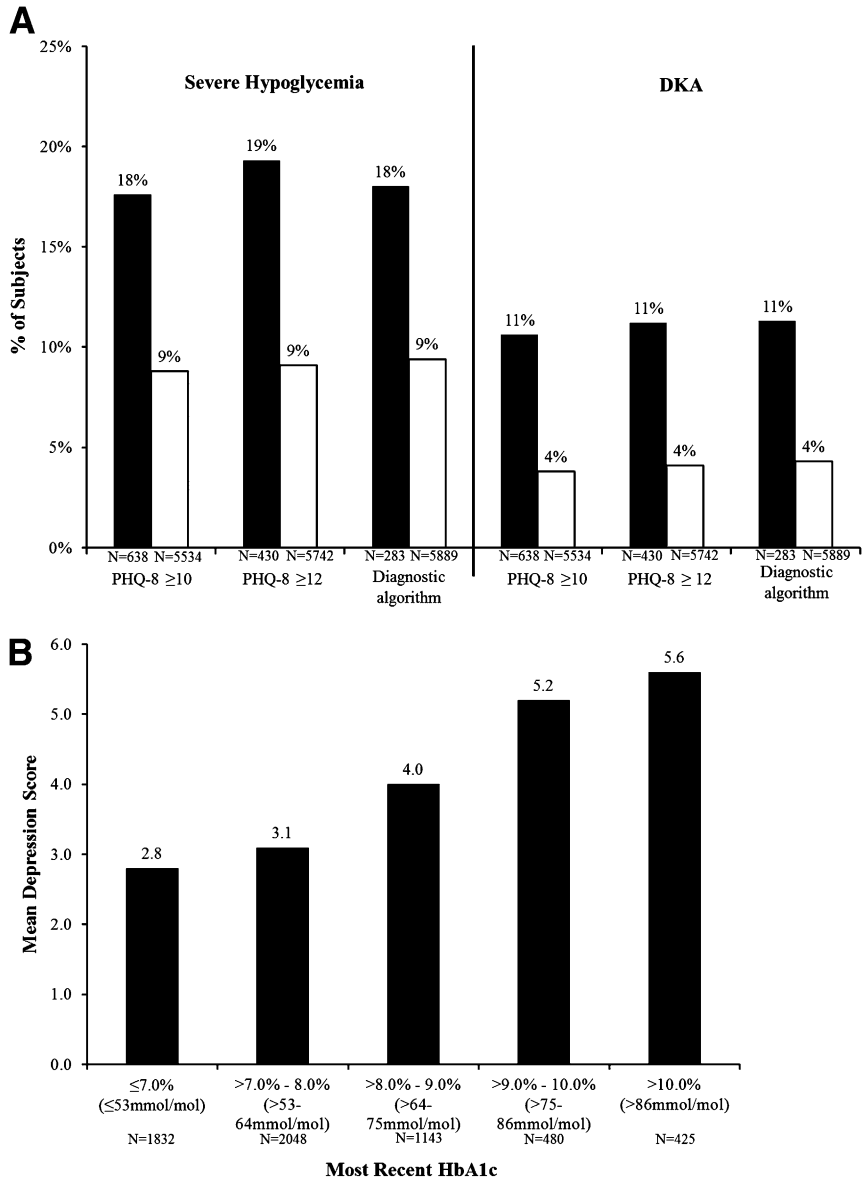

Figure 1—*A*: Frequency of one or more severe hypoglycemic and DKA events in prior 3 months. Black bars, depressed; white bars, not depressed. *B*: Mean PHQ-8 depression score vs. most recent HbA_{1c}.

and depression. Proposed mechanisms suggest shared biologic vulnerability and include the effects of increased circulating cytokines, insulin deficiency on neurogenesis/neurotransmitter metabolism, chronic hyperglycemia and/or iatrogenic hypoglycemia, and basal hyperactivity of the hypothalamic–pituitary–adrenal axis (36). Further study is needed to elucidate these potential biological mechanisms linking depression to poor glycemic control for adults with T1D, as well as potential psychosocial mechanisms that have not been defined.

This paper represents an important step in better defining the prevalence of depression in adults with T1D and highlights its relationship to poorer self-care and negative health outcomes. We believe that these findings are quite significant, as they are based on a very large and diverse sample of individuals with a wide range in age, socioeconomic status, and geographic location across the U.S. We do not know if the treatment of depression will lead to better T1D-related outcomes, as measured by glycemic control, complications, and episodes of hypoglycemia. If it does, this could translate into very significant savings in healthcare costs for patients with T1D, as well as improved quality of life. Whether or not identification and treatment of depression in adults with T1D will improve diabetes outcomes or reduce acute or chronic diabetes complications requires further study.

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companies for his services, and no personal income goes to R.M.B. He has inherited Merck stock and has been a volunteer officer of the American Diabetes Association. R.W.B.'s nonprofit employer has received consultant payments on his behalf from Sanofi and Animas and a research grant from Novo Nordisk with no personal compensation to R.W.B. R.S.W.'s nonprofit employer has received grant money as the site for multicenter clinical trials sponsored by Eli Lilly, Medtronic, AstraZeneca, GlaxoSmithKline, and Johnson & Johnson. No other potential conflicts of interest relevant to this article were reported.

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