Diabetes Distress in Young Adults With Youth-Onset Type 2 Diabetes: TODAY2 Study Results

Diabetes Care 2022;45:529–537 | https://doi.org/10.2337/dc21-1689

Paula M. Trief,[1] Diane Uschner,[2] Melinda Tung,[2] Marsha D. Marcus,[3] Maria Rayas,[4] Sarah MacLeish,[5] Ryan Farrell,[5] Joyce Keady,[6] Lily Chao,[7] and Ruth S. Weinstock,[1] on behalf of the TODAY Study Group*

OBJECTIVE

To assess the prevalence of high diabetes distress and associated factors in the Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY2) study cohort of young adults with youth-onset type 2 diabetes.

RESEARCH DESIGN AND METHODS

Participants completed the Diabetes Distress Scale (DDS) at end-of-study visits. Factors examined for association with high distress were demographic (sex, race/ethnicity, age, education, income), medical (HbA_{1c}, BMI, complications), psychological (depressive and anxiety symptoms), and social (number in household, offspring, health care coverage, established with diabetes care provider). Univariate logistic regression identified factors associated with high distress that were controlled for in multivariate logistic regressions.

RESULTS

Of 438 participants, 66% were female (mean age 26.8 years, 18% non-Hispanic White, 37% non-Hispanic Black, 38% Hispanic). High distress (DDS ≥2) was reported by 105 (24%) participants. Subscales identified 40% with high regimen distress and 29.7% with high emotional burden. A greater percentage of those with high distress were female ($P = 0.002$), diagnosed with hypertension ($P = 0.037$) and retinopathy ($P = 0.005$), treated with insulin, had higher HbA_{1c}, and had moderate to severe depressive and anxiety symptoms (all $P < 0.001$). In multivariate analyses, female sex ($P < 0.001$), HbA_{1c} ($P < 0.001$), anxiety symptoms ($P = 0.036$), and lack of health care coverage ($P = 0.019$) were associated with high distress, after controlling for potential confounders. Moderate to severe depressive symptoms were associated with high regimen distress ($P = 0.018$) and emotional burden ($P < 0.001$); insulin treatment was associated with high emotional burden ($P = 0.027$).

CONCLUSIONS

Future research should identify modifiable factors associated with high diabetes distress in young adults with youth-onset type 2 diabetes that may inform distress interventions with this medically vulnerable group.

Diabetes distress is defined as the negative feelings and emotional burdens associated with living with the challenges and demands of diabetes, including feeling burned out, overwhelmed, anxious, defeated, and depressed (1,2). In a meta-analysis, significant diabetes distress was identified in ∼36% of adults with type 2

[1]State University of New York Upstate Medical University, Syracuse, NY
[2]The Biostatistics Center, George Washington University, Rockville, MD
[3]University of Pittsburgh School of Medicine, Pittsburgh, PA
[4]University of Texas Health Science Center at San Antonio, San Antonio, TX
[5]Case Western Reserve University School of Medicine, Cleveland, OH
[6]Joslin Diabetes Center, Boston, MA
[7]Children's Hospital Los Angeles, Los Angeles, CA

Corresponding author: Paula M. Trief, triefp@upstate.edu

Received 11 August 2021 and accepted 29 November 2021

Clinical trial reg. nos. NCT00081328, NCT01364350, and NCT02310724, clinicaltrials.gov

This article contains supplementary material online at https://doi.org/10.2337/figshare.17136365.

*A complete list of the TODAY Study Group can be found in the supplementary material online.

diabetes (3). In a diverse community sample, 45.4% reported at least moderate distress (4). Diabetes distress persists over time and is associated with poor glycemic control, self-care, and health-related quality of life (4–7). Factors associated with high distress are female sex (3), younger age, and shorter diabetes duration (8); low social support (9); and being a member of a minority racial or ethnic group (10). These findings are from middle- to older-aged adults who developed type 2 diabetes as adults or people with type 1 diabetes. There has been a concerning increase in the incidence of type 2 diabetes in youth (11), but nothing is known about diabetes distress in younger adults or those with youth-onset type 2 diabetes. The Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) study (2004–2011) examined the relative efficacy of three treatment regimens in a large, diverse sample of youth and adolescents with youth-onset type 2 diabetes (12). Participants ($N = 699$) who were 10 to <18 years old, diagnosed with type 2 diabetes (American Diabetes Association [ADA] 2002 criteria) <2 years earlier, and had a BMI ≥85th percentile, negative pancreatic antibodies, and fasting C-peptide levels >0.6 ng/mL were recruited at 15 U.S. centers.

After the intervention trial, an observational follow-up study (TODAY2, 2011–2020) assessed changes in various factors over time, and the relationship of these changes to comorbidities/complications durng young adulthood (13). A measure of diabetes distress was completed by TODAY2 participants at end-of-study (EOS) visits.

The objectives of our analyses were to *1*) assess the prevalence of high diabetes distress in the TODAY2 cohort; *2*) identify key sources of distress; *3*) identify individual factors (e.g., sex, race/ethnicity) associated with diabetes distress; and *4*) determine whether medical (HbA_{1c}, insulin use, complications, BMI), psychological (depressive symptoms, anxiety symptoms), or social (lack of health care coverage, lack of health care provider) factors were associated with high diabetes distress. TODAY2 was an observational study; this report is exploratory with no specific a priori hypotheses.

TODAY

A detailed description of the TODAY protocol (Clinicaltrials.gov identifier: NCT0008132) and primary outcome results have been published (12). Briefly, participants were eligible if they were 10 to <18 years old and had type 2 diabetes (ADA 2002 criteria) of <2 years duration. Other inclusion criteria were BMI ≥85th percentile, fasting C-peptide level >0.6 ng/mL, and negative for pancreatic autoantibodies. The primary aim (2004–2011) was to compare the effects of three treatments on time to treatment failure, defined as loss of glycemic control (i.e., HbA_{1c} ≥8% [64 mmol/mol]) for 6 months or inability to wean from temporary insulin after acute metabolic decompensation. Youth and adolescents ($N = 699$) from 15 U.S. clinical centers were enrolled and randomly assigned to one of three treatment arms: metformin monotherapy, metformin + rosiglitazone, or metformin + intensive lifestyle intervention. Participants were followed longitudinally for 2–6 years. After an average 3.9 years of follow-up, 319 (45.6%) participants reached the primary outcome. The metformin + rosiglitazone group demonstrated a significantly lower rate of treatment failure than the metformin-alone group (12).

TODAY2

At the end of TODAY, 572 participants enrolled in a follow-up study, TODAY2. In phase 1 (2011–2014), participants were assessed quarterly and received standard-of-care diabetes treatment from the TODAY team, using metformin and/or insulin as needed. In phase 2 (2014–2020), 518 remaining TODAY participants transitioned to an observational study involving annual assessments; diabetes care was managed by community providers. Average total length of follow-up was 10.2 years after randomization. The composition of cohorts in each phase was highly consistent with the original TODAY cohort (13). TODAY and TODAY2 were approved by the institutional review boards at all 15 centers. Participants and guardians provided written informed assent and/or consent, as appropriate.

RESEARCH DESIGN AND METHODS

Design

This cross-sectional study used data gathered in the TODAY2 study. TODAY2 participants completed the Diabetes Distress Scale (DDS) at EOS visits (April 2019–January 2020). Of the 458 TODAY2 participants who completed EOS visits, 457 completed the DDS. After removing 19 diagnosed with maturity-onset diabetes of the young, 438 were included in these analyses (Fig. 1).

At EOS visits, participants also completed depressive and anxiety symptom questionnaires and a health care usage survey asking whether they had a routine diabetes care provider and health care coverage. Other EOS assessments included HbA_{1c}, BMI, blood pressure (BP), and diagnoses of retinopathy, nephropathy, neuropathy, and dyslipidemia. EOS data gathered from the TODAY2 database included age, sex, race/ethnicity, years of education, income, number of people in household, and number of offspring. All assessment procedures were defined per the TODAY2 study protocol (13).

Measures

Diabetes Distress

The DDS is a 17-item self-report questionnaire with good internal reliability and validity (4,14). It lists emotions and stressors associated with living with type 2 diabetes. The respondent rates how much of a problem each has been over the past month (1 = not a problem, 6 = very significant problem). There are four subscales that explore type of distress: emotional burden (feeling overwhelmed, fearful), regimen distress (feeling badly about not managing diabetes well), interpersonal distress (receiving insufficient support from family/friends), and physician distress (worries about health care provider expertise and support). Mean item scores are calculated to yield overall and subscale mean scores. Per recommendation, a score ≥2 defines clinically significant distress, here labeled high diabetes distress, and a score <2 defines low diabetes distress (4).

Depressive Symptoms

The Patient Health Questionnaire 8 (PHQ-8) is an eight-item self-report questionnaire that assesses presence and severity of depressive symptoms over the past 2 weeks (15,16). It assesses eight symptoms of depression (a ninth symptom, suicidal ideation, was omitted, as is common in research protocols). Respondents indicate whether they have experienced symptoms (i.e., low level of interest in doing things,

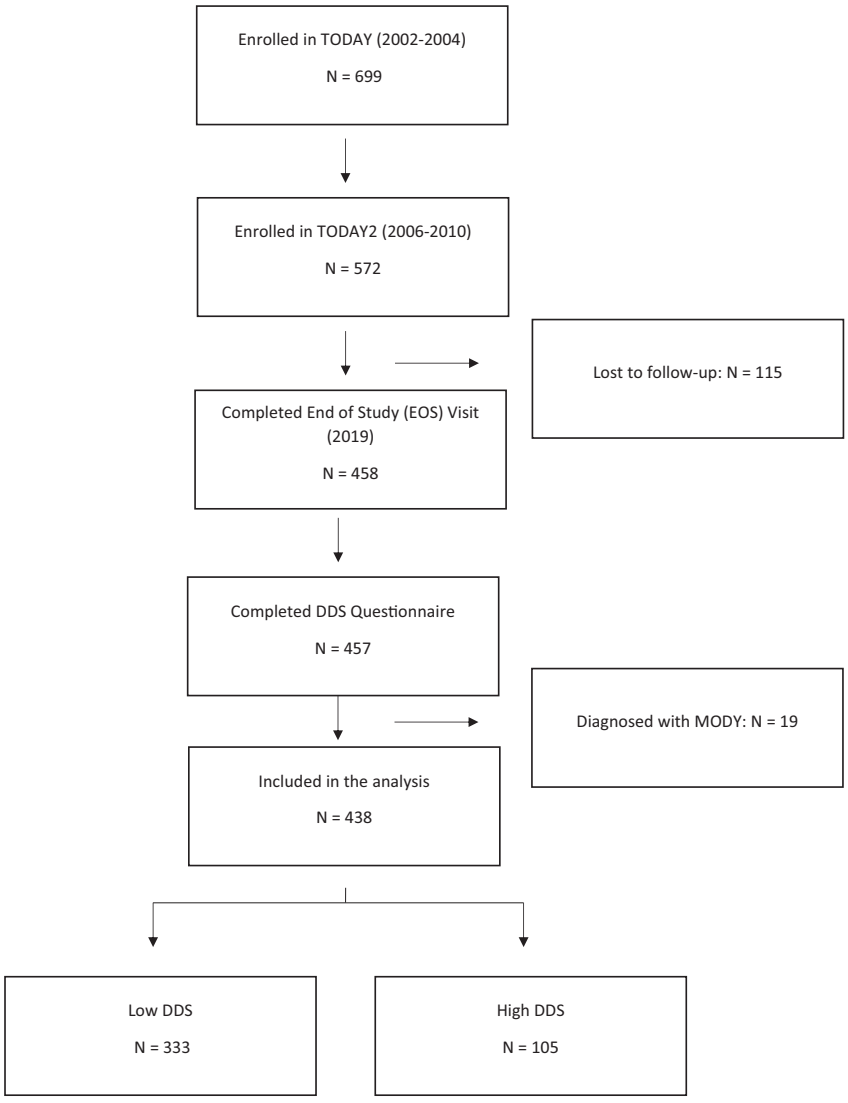

Figure 1—Flowchart depicting participant enrollment and retention. MODY, maturity-onset diabetes of the young.

feeling down/depressed, difficulty sleeping, low energy, disrupted eating, feeling badly about oneself, inability to concentrate, sluggishness/agitation) from 0 = not at all to 3 = nearly every day. The PHQ-8 has shown excellent reliability and validity and is widely used as a tool to screen for probable major depressive disorder, defined as DDS score ≥10 (17). We used this cutoff to define moderate to severe depressive symptoms.

Anxiety Symptoms

Generalized Anxiety Disorder 7 (GAD-7) is a seven-item self-report questionnaire that assesses the presence and severity of symptoms of generalized anxiety disorder over the past 2 weeks. Respondents indicate whether they have experienced symptoms (e.g., anxiety, restlessness, irritability) from 0 = not at all to 3 = nearly every day. It has excellent reliability and validity (18,19) and is recommended for anxiety disorder screening (20), using a score of ≥10 to define moderate to severe anxiety symptoms.

Medical Measures

All medical assessments were completed at annual visits. Fasting blood samples were processed according to standard protocols; assays (HbA_{1c}, dyslipidemia) were performed at the Northwest Lipids Research Laboratory. BMI was determined with standardized anthropometric measurements. Diabetes complications/comorbidities (retinopathy, nephropathy, neuropathy, dyslipidemia) were diagnosed as previously described (12), as briefly defined below.

Hypertension

BP was measured at every visit. Hypertension was diagnosed if BP was ≥95th percentile for age, sex, and height; if systolic BP was ≥130 mm Hg and/or diastolic BP was ≥80 mm Hg at three consecutive visits; or if the participant was being treated with antihypertensive medication.

Dyslipidemia

LDL cholesterol dyslipidemia was diagnosed if the participant had consecutive values ≥130 mg/dL (3.37 mmol/L). Triglyceride dyslipidemia was diagnosed if consecutive values were ≥150 mg/dL (1.69 mmol/L) or if there was a single elevated lipid value followed by treatment with lipid-lowering medications.

Nephropathy

Urine was collected annually, and if the sample showed abnormal albuminuria values, the test was repeated on a first-morning sample. A urine albumin-to-creatinine ratio ≥30 mg/g defined moderately increased albuminuria; ≥300 mg/g on at least two of three assessments defined severely increased albuminuria.

Neuropathy

Participants completed the Michigan Neuropathy Screening Instrument and underwent a monofilament examination, at annual visits. A screening score >2 on at least two consecutive assessments was defined as abnormal. The monofilament examination was abnormal if <8 of 10 responses were correct on at least two consecutive assessments.

Retinopathy

Fundus photography was performed; masked examiners graded photos at a central reading center. Eye disease was diagnosed according to the Early Treatment Diabetic Retinopathy Study scale or if clinically significant macular edema was present in either eye.

Statistical Analyses

Descriptive statistics and univariate logistic, multivariate logistic, and linear regression analyses were used. Continuous variables are reported as

mean ± SD and categorical data as frequency counts and percentages. Descriptive statistics were calculated to describe participants' characteristics for the overall group and by high (DDS ≥2) versus low (DDS <2) diabetes distress, high versus low regimen distress, and high versus low emotional burden. Regimen distress and emotional burden subscales had a significant percentage of respondents who scored ≥2; thus, their data were included in analyses. Interpersonal distress and physician distress subscales had low endorsement rates (15.3% and 8.3%, respectively) and were not considered further; scores on these subscales are included in the overall DDS. Trajectories of selected continuous variables that had been collected longitudinally were summarized using a time-weighted average, considering the duration when the participant was ≥19 years of age. Outcome variables were considered present if the condition had been diagnosed at any point since the age of 19 years (early adulthood). Groups (high vs. low diabetes distress, regimen distress, and emotional burden) were compared on these variables using *t* tests (continuous) and χ^2 tests (categorical). $P < 0.05$ was considered statistically significant. Univariate logistic regression ($n = 438$) was used to identify factors associated with high diabetes distress, regimen distress, and emotional burden. Those found to be significant in univariate models and some characteristics selected a priori were adjusted for in multivariate logistic regression models. Thus, multivariate logistic regression analyses were adjusted for sex, HbA_{1c}, insulin treatment, hypertension, race/ethnicity, education, health care coverage, anxiety symptoms, depressive symptoms, and retinopathy. Nine participants lacked a retinopathy measure and 1 lacked the anxiety measure; data of those 10 participants were not included in multivariate analyses ($n = 428$). Associations are expressed using odds ratios with the corresponding 95% CIs. Associations with diabetes distress as a continuous outcome were assessed using linear regression models. Statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC) and R 3.6.0 software.

RESULTS

Participant characteristics ($n = 438$) are provided in Table 1. The diverse sample was predominantly female (66%) and low income (62% with an annual income of <$25,000). Participant health characteristics are provided in Table 2. On average, the group had poor glycemic control (mean ± SD HbA_{1c} 9.2 ± 2.5% [77 ± 4 mmol/mol]), and more than one-half (52%) were treated with insulin.

In this group of young adults with youth-onset type 2 diabetes, 105 (24.0%) reported high diabetes distress (DDS ≥2). Subscale scores showed that 40.0% had high regimen distress and 29.7% high emotional burden. Of those in the high diabetes distress group, 92.4% reported

Table 1—Participant characteristics

		TODAY2 EOS visits							
	Overall ($n = 438$)	DDS <2 ($n = 333$)	DDS ≥2 ($n = 105$)	*P*	RD <2 ($n = 263$)	RD ≥2 ($n = 175$)	*P*	EB <2 ($n = 308$)	EB ≥2 ($n = 130$)	*P*
Female	287 (66)	205 (62)	82 (78)	0.002	163 (62)	124 (71)	0.055	192 (62)	95 (73)	0.031
Race/ethnicity				0.677			0.011			0.744
Non-Hispanic Black	160 (37)	121 (36)	39 (37)		99 (38)	61 (35)		113 (37)	47 (36)	
Non-Hispanic White	79 (18)	64 (19)	15 (14)		57 (22)	22 (13)		59 (19)	20 (15)	
Hispanic	167 (38)	125 (38)	42 (40)		94 (36)	73 (42)		115 (37)	52 (40)	
Other	32 (7)	23 (7)	9 (9)		13 (5)	19(11)		21 (7)	11 (8)	
Age (years)	26.8 ± 2.5	26.8 ± 2.4	27.0 ± 2.8	0.554	26.8 ± 2.4	26.9 ± 2.6	0.746	26.9 ± 2.4	26.8 ± 2.7	0.736
Education				0.501			0.305			0.938
Less than HS	51 (12)	36 (11)	15 (14)		31 (12)	20 (11)		34 (11)	17 (13)	
HS, GED, business, technical	273 (62)	214 (64)	59 (56)		172 (65)	101 (58)		194 (63)	79 (61)	
College no degree	46 (11)	33 (10)	13 (12)		24 (9)	22 (13)		32 (10)	14 (11)	
College degree	68 (16)	50 (15)	18 (17)		36 (14)	32 (18)		48 (16)	20 (15)	
Income				0.439			0.628			0.754
<$25,000	273 (62)	212 (64)	61 (58)		168 (64)	105 (60)		191 (62)	82 (63)	
$25,000–$49,999	129 (30)	96 (29)	33 (31)		75 (29)	54 (31)		93 (30)	36 (28)	
≥$50,000	35 (8)	24 (7)	11(10)		19 (7)	16 (9)		23 (7)	12 (9)	
Duration of diabetes (years)	13.6 ± 1.5	13.6 ± 1.5	13.6 ± 1.5	0.959	13.6 ± 1.5	13.7 ± 1.4	0.728	13.6 ± 1.5	13.6 ± 1.5	0.928
Number of people in household	3.5 ± 1.8	3.5 ± 1.8	3.5 ± 1.8	0.850	3.6 ± 1.9	3.4 ± 1.7	0.511	3.4 ± 1.8	3.7 ± 1.7	0.227
Have offspring	137 (31)	100 (30)	37 (35)	0.316	84 (62)	53 (30)	0.715	97 (31)	40 (31)	0.881
Have health care coverage	381 (87)	295 (89)	86 (82)	0.076	234 (89)	147 (84)	0.130	272 (88)	109 (84)	0.204
Have a routine diabetes care provider	327 (75)	248 (74)	79 (75)	0.875	190 (72)	137 (78)	0.154	224 (73)	103 (79)	0.153
Treated with insulin	227 (52)	157 (47)	70 (67)	<0.001	114 (43)	113 (65)	<0.001	134 (44)	93 (72)	<0.001

Data are *n* (%) or mean ± SD. EB, emotional burden; GED, General Educational Development; HS, high school; RD, regimen distress. *P* values shown reflect significance when groups were compared on these characteristic variables using *t* test (continuous) and χ^2 test (categorical).

Table 2—Participant health characteristics

	TODAY2 EOS visits									
	Overall (n = 438)	DDS <2 (n = 333)	DDS ≥2 (n = 105)	P	RD <2 (n = 263)	RD ≥2 (n = 175)	P	EB <2 (n = 308)	EB ≥2 (n = 130)	P
HbA_{1c} (%)*	9.2 ± 2.5	8.8 ± 2.5	10.4 ± 2.2	<0.001	8.6 ± 2.5	10.1 ± 2.3	<0.001	8.7 ± 2.5	10.4 ± 2.2	<0.001
SBP (mmHg)*	120.7 ± 10.2	120.4 ± 10.1	121.7 ± 10.3	0.410	120.1 ± 9.9	121.5 ± 10.5	0.441	120.6 ± 10.0	120.8 ± 10.6	0.888
DBP (mmHg)*	75.0 ± 8.0	74.7 ± 7.9	76.2 ± 8.1	0.376	74.4 ± 7.8	76.0 ± 8.3	0.141	74.8 ± 8.0	75.6 ± 7.9	0.676
BMI (kg/m^2)*	36.5 ± 8.2	36.8 ± 8.3	35.5 ± 7.9	0.159	36.8 ± 8.4	36.1 ± 8.0	0.355	37.2 ± 8.3	34.9 ± 7.7	0.005
Hypertension§	284 (65)	207 (62)	77 (73)	0.037	163 (62)	121 (69)	0.124	197 (64)	87 (67)	0.553
Dyslipidemia§	257 (59)	193 (58)	64 (61)	0.587	149 (57)	108 (62)	0.292	182 (59)	75 (58)	0.786
Neuropathy§	138 (32)	108 (32)	30 (29)	0.458	82 (31)	56 (32)	0.856	99 (32)	39 (30)	0.659
Nephropathy§	210 (48)	157 (47)	53 (50)	0.552	122 (46)	88 (50)	0.424	141 (46)	69 (53)	0.163
Retinopathy†	198 (46)	139 (42)	59 (58)	0.005	106 (41)	92 (54)	0.010	122 (40)	76 (60)	<0.001
Number of microvascular complications				0.048			0.321			0.001
0	113 (26)	94 (28)	19 (18)		75 (29)	38 (22)		92 (30)	21 (16)	
1	150 (34)	112 (34)	38 (36)		91 (35)	59 (34)		105 (34)	45 (35)	
2	129 (29)	89 (27)	40 (38)		72 (27)	57 (33)		76 (25)	53 (41)	
3	46 (11)	38 (11)	8 (8)		25 (10)	21 (12)		35 (11)	11 (8)	
Depression symptoms (PHQ-8)‡				<0.001			<0.001			<0.001
None to mild	392 (90)	315 (95)	77 (73)		250 (95)	142 (81)		295 (96)	97 (75)	
Moderate to severe	45 (10)	17 (5)	28 (27)		12 (5)	33 (19)		12 (4)	33 (25)	
Anxiety symptoms (GAD-7)‡				<0.001			<0.001			<0.001
None to mild	388 (89)	312 (94)	76 (72)		245 (94)	143 (82)		289 (94)	99 (76)	
Moderate to severe	49 (11)	20 (6)	29 (28)		17 (6)	32 (18)		18 (6)	31 (24)	

Data are mean ± SD or n (%). EB, emotional burden; DBP, diastolic BP; RD, regimen distress; SBP, systolic BP. P values shown reflect significance when groups were compared on these characteristic variables using t test (continuous) and χ^2 test (categorical). *Time-weighted average taking into account the duration when the participant was ≥19 years of age. §Present if condition had been present at any point since early adulthood. †Nine missing scores for retinopathy because of missing/incomplete data. ‡One missing score for PHQ-8 and GAD-7.

high emotional burden and 93.3% high regimen distress.

Overall Diabetes Distress

Comparing low versus high diabetes distress groups, we found that a greater percentage of participants with high distress were female (78% vs. 62%, $P = 0.002$), diagnosed with hypertension (73% vs. 62%, $P = 0.037$) and retinopathy (58% vs. 42%, $P = 0.005$), treated with insulin (67% vs. 47%, $P < 0.001$), had moderate to severe depressive (27% vs. 5%, $P < 0.001$) and anxiety (28% vs. 6%, $P < 0.001$) symptoms, and had higher HbA_{1c} (10.4 ± 2.2% [90 ± 1 mmol/mol] vs. 8.8 ± 2.5% [73 ± 4 mmol/mol], $P < 0.001$) (Tables 1 and 2). Univariate logistic regression analyses identified factors associated with high diabetes distress (Supplementary Table 1) that were controlled for in multivariate analyses (Table 3). Multivariate logistic regression models ($n = 428$) found that female sex ($P < 0.001$), HbA_{1c} ($P < 0.001$), and moderate to severe anxiety symptoms ($P = 0.036$) remained associated with high diabetes distress, as was lack of health care coverage ($P = 0.019$), after adjusting for race/ethnicity, education, BMI, insulin use, hypertension, retinopathy, and depressive symptoms (Table 3). Specifically, females were 3.3 times more likely, participants who lacked health care coverage 2.4 times more likely, and participants with moderate to severe anxiety symptoms 3.2 times more likely to report high diabetes distress. HbA_{1c} was also associated with diabetes distress; for every 1 unit increase in HbA_{1c}, there was a 30% increase in the odds of having high diabetes distress. When we analyzed distress as a continuous variable, female sex ($P < 0.001$), lack of health care coverage ($P = 0.030$), HbA_{1c} ($P < 0.001$), and moderate to severe anxiety symptoms ($P = 0.026$) were again associated with higher levels of distress. In addition, BMI ($P < 0.001$) and moderate to severe depressive symptoms ($P < 0.001$) were associated with higher distress (Supplementary Tables 2 and 3).

Regimen Distress

A greater percentage of participants with high regimen distress versus low regimen distress were treated with insulin (67% vs. 47%), had higher HbA_{1c} (10.1 ± 2.3% [87 ± 2 mmol/mol] vs. 8.6 ± 2.5% [70 ± 4 mmol/mol]), had moderate to severe

Table 3—Predictors of diabetes distress, RD, and EB on the basis of logistic regression models

	Multivariate analysis					
	DDS ≥2		RD ≥2		EB ≥2	
Predictor	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Male vs. female	0.30 (0.16, 0.55)	<0.001	0.57 (0.35, 0.92)	0.022	0.49 (0.28, 0.85)	0.012
Race/ethnicity						
Non-Hispanic Black vs. Hispanic	0.72 (0.39, 1.30)	0.275	0.62 (0.37, 1.03)	0.065	0.80 (0.46, 1.41)	0.446
Non-Hispanic White vs. Hispanic	0.81 (0.37, 1.73)	0.598	0.56 (0.29, 1.05)	0.075	1.03 (0.50, 2.08)	0.924
Non-Hispanic Black vs. non-Hispanic White	0.88 (0.41, 1.96)	0.748	1.12 (0.58, 2.19)	0.740	0.78 (0.38, 1.62)	0.492
Education						
HS, GED, business, or technical degree vs. less than HS	0.93 (0.42, 2.14)	0.856	1.19 (0.59, 2.44)	0.631	1.19 (0.55, 2.66)	0.668
College no degree vs. less than HS	1.98 (0.69, 5.74)	0.205	2.52 (1.01, 6.41)	0.050	1.83 (0.66, 5.13)	0.245
Any college degree vs. less than HS	2.14 (0.80, 5.91)	0.134	3.16 (1.34, 7.70)	0.010	2.05 (0.79, 5.50)	0.144
Have health care coverage	0.41 (0.19, 0.87)	0.019	0.44 (0.22, 0.86)	0.017	0.48 (0.23, 0.99)	0.046
Treated with insulin	1.35 (0.72, 2.58)	0.351	1.60 (0.93, 2.75)	0.089	1.96 (1.09, 3.60)	0.027
HbA_{1c}*	1.30 (1.13, 1.49)	<0.001	1.25 (1.11, 1.40)	<0.001	1.28 (1.12, 1.45)	<0.001
BMI (per 5 kg/m^2 increase)*	0.93 (0.77, 1.11)	0.411	1.00 (0.86, 1.15)	0.989	0.86 (0.72, 1.02)	0.096
Hypertension†	1.80 (1.01, 3.28)	0.051	1.35 (0.83, 2.22)	0.232	1.08 (0.63, 1.87)	0.768
Retinopathy	1.06 (0.61, 1.87)	0.828	0.94 (0.58, 1.51)	0.793	1.11 (0.66, 1.87)	0.701
Depressive symptoms (PHQ-8)						
Moderate to severe vs. none to mild	2.80 (0.91, 8.62)	0.070	3.91 (1.30, 12.88)	0.018	7.31 (2.37, 25.22)	0.001
Anxiety symptoms (GAD-7)						
Moderate to severe vs. none to mild	3.19 (1.06, 9.47)	0.036	1.29 (0.42, 3.71)	0.644	1.36 (0.42, 4.06)	0.589

n = 428. EB, emotional burden; GED, General Educational Development; HS, high school; OR, odds ratio; RD, regimen distress. *Time-weighted average taking into account the duration when the participant was ≥19 years of age. †Present if condition had been present at any point since early adulthood.

depressive (19% vs. 5%) and anxiety (18% vs. 6%) symptoms (all $P < 0.001$), and were diagnosed with retinopathy (54% vs. 41%, $P = 0.010$). Compared with the low regimen distress group, the high regimen distress group had a higher percentage of Hispanic participants (42% vs. 36%, $P = 0.011$) (Tables 1 and 2). Multivariate analyses (Table 3) controlled for factors associated with high regimen distress in univariate analyses (Supplementary Table 1) and found that female sex ($P = 0.022$), higher HbA_{1c} ($P < 0.001$), and moderate to severe depressive symptoms ($P = 0.018$) remained associated with high regimen distress. Lack of health care coverage was also associated with high regimen distress ($P = 0.017$); participants lacking health care coverage were 2.3 times more likely to report high regimen distress. Education showed an association, with participants with a college degree being more likely than those with less than a high school education to have high regimen distress ($P = 0.010$). Analysis of regimen distress as a continuous variable again found an association with female sex ($P = 0.013$), college versus no high school degree ($P = 0.003$), lack of health care coverage ($P = 0.008$), higher HbA_{1c} ($P < 0.0001$), and moderate to severe depressive symptoms ($P = 0.001$), as well as with moderate to severe anxiety symptoms ($P = 0.024$) (Supplementary Tables 2 and 3).

Emotional Burden

A greater percentage of participants with high emotional burden were female (73% vs. 62%, $P = 0.031$), had lower BMI (34.9 ± 7.7 kg/m^2 vs. 37.2 ± 8.3 kg/m^2, $P = 0.005$), were treated with insulin (72% vs. 44%), had higher HbA_{1c} (10.4 ± 2.2% [90 ± 1 mmol/mol] vs. 8.7 ± 2.5% [72 ± 4 mmol/mol]), and had moderate to severe depressive (25% vs. 4%) or anxiety (24% vs. 6%) symptoms (all $P < 0.001$) (Tables 1 and 2). After controlling for all factors identified through univariate analyses (Supplementary Table 1), multivariate analyses found that female sex ($P = 0.012$), HbA_{1c} ($P < 0.001$), and lack of health care coverage ($P = 0.046$) remained associated with high emotional burden (Table 3). Report of moderate to severe depressive symptoms was also associated with high emotional burden; participants with moderate to severe depressive symptoms were 7.3 times more likely to report high emotional burden ($P = 0.001$). Insulin treatment was uniquely associated with emotional burden; participants treated with insulin were two times more likely to report high emotional burden ($P = 0.027$). Analysis of distress as a continuous variable again found that female sex ($P = 0.046$), HbA_{1c} ($P = 0.007$), insulin treatment ($P = 0.003$), and moderate to severe depressive symptoms ($P < 0.0001$) were associated with higher emotional burden (Supplementary Tables 2 and 3).

CONCLUSIONS

In this large and diverse cohort of young adults with youth-onset type 2 diabetes, 24% reported that they were experiencing

a clinically significant level of diabetes distress, with females and participants with higher HbA_{1c}, those who lacked health care coverage, and with moderate to severe anxiety symptoms being at increased risk of high diabetes distress. This is comparable to the finding that 20% of participants had elevated diabetes distress in a study of adults with type 1 diabetes (21). Comparing these findings with studies of adults with type 2 diabetes is challenging because the other studies assessed middle- and older-aged adults who developed type 2 diabetes as adults and because estimates of high diabetes distress vary depending on the sample and measure. Given these issues, 24% of the current cohort is lower than the 36% reported in a recent meta-analysis of studies in older adults (3). Two caveats with our study are that *1*) the overall distress scores were probably lower because of low physician and interpersonal distress scores, noting that 40% had high regimen distress and 30% high emotional burden, and *2*) the cohort is unique. Participants have maintained involvement in a long-running clinical study, which provided extensive diabetes education and support, frequent contact, and providers who were skilled in provider-patient communication. Even though contact decreased during TODAY2, the average total length of follow-up was 10.2 years after randomization, thus still unique and important. Poor patient-provider communication, feeling ignored, and limited opportunities to discuss the challenges of living with diabetes all relate to higher diabetes distress (22–24); these factors were likely lessened in this TODAY-involved cohort.

Prior research found that the most common cause of distress in adults with type 2 diabetes is managing the disease (25); this was also highly salient in the current cohort. Distress related to the emotional burdens of diabetes (feeling overwhelmed, burned out) was also high, especially for those being treated with insulin. These emotional strains may be particularly stressful for young adults, as many are only recently managing diabetes independently while also dealing with common challenges of young adulthood (e.g., new jobs, relationships, living situations, financial independence); some have termed this a developmental phase of "emerging adulthood" (26).

Females were more likely to report high diabetes distress (including regimen distress and emotional burden) and to have higher levels of distress (overall, regimen and emotional burden), consistent with other studies (3). We did not find distress differences by race/ethnicity in this highly diverse cohort. In a prior study of a combined type 1 and type 2 diabetes cohort, members of racial/ethnic minority groups had higher distress than non-Hispanic Whites (10). Similarly, while a lack of social support was associated with high diabetes distress in a Scandinavian sample (9), we did not find that number of people in household was associated with distress, although this is likely not an adequate proxy for social support.

High HbA_{1c} was associated with high diabetes distress and higher levels of distress (including high regimen distress and emotional burden). This is consistent with the older adult literature (5); a recent meta-analysis reported a consistent, though modest, relationship between high HbA_{1c} and high diabetes distress (27). Given that high distress consistently relates to poor self-care (2), one hypothesis is that the relationship between diabetes distress and HbA_{1c} is mediated by self-care. If this hypothesis is supported, interventions to lower diabetes distress may not result in improved glycemic control unless the individual can engage in effective self-care behaviors. Of course, health care coverage and access to medications and care are also needed to achieve good glycemic control. In general, HbA_{1c} levels were very high in this cohort, reflecting difficulties in attaining optimal glycemic control in this socioeconomically disadvantaged population. The role that diabetes distress may play in these concerning outcomes needs further attention.

Moderate to severe anxiety symptoms were associated with high diabetes distress and higher levels of overall and regimen distress. Anxiety symptoms (e.g., feeling nervous, worrying) may reflect diabetes distress. Additionally, those with anxiety, who already feel overwhelmed, may find it more difficult to cope with diabetes-related stressors. Depressive symptoms were associated with regimen distress and emotional burden, a relatively frequent finding (25). Depressive symptoms were also associated with higher levels of overall distress (and regimen distress and emotional burden). As with anxiety, it is not surprising that those who are struggling with depressive symptoms, perhaps major depressive disorder, feel highly challenged by the emotional strains of living with diabetes. Prior evidence suggests that in adults with type 2 diabetes, elevated depression scores are capturing diabetes distress, with ~2–30% shared variance (5). However, there was a relatively small number of participants with moderate to severe depressive symptoms. Future studies of those with youth-onset type 2 diabetes, including more individuals with significant depressive symptoms, are needed.

Lack of health care coverage was associated with high diabetes distress (including regimen distress and emotional burden) and higher levels of overall and regimen distress. We are unaware of studies that explored a link between having health care coverage and diabetes distress, but previously, we observed that TODAY participants without health care coverage and living in states without Medicaid expansion had higher HbA_{1c} levels (28). It is not surprising that these young adults who are managing their diabetes independently would identify lack of health care coverage as contributing to their regimen challenges and emotional burden, as it reflects less access to needed treatments and medications, thus fueling fears about the future.

Finally, insulin treatment was associated with high emotional burden. Insulin treatment adds unique challenges to self-care, such as needing to self-inject and to pay closer attention to timing of eating and activity. Anecdotally, patients who start insulin often state that doing so makes them feel as if their disease has progressed and heightens their fears about developing complications.

There has been a call to develop interventions to decrease diabetes distress, and doing so may have a positive impact on self-care, glycemic control, and quality of life (29). The evidence suggests that the most effective interventions focus on diabetes and emotions (i.e., psychoeducation) (2). In the clinic, this means routine screening for diabetes distress, especially at key transition points (e.g., when treatment changes, when complications develop), as recommended by the

ADA (30). Those patients identified as having high distress might be referred to social workers to identify and address barriers to care and to provide mental health referrals when needed (31). The literature suggests that there are emotional benefits from peer support (32) (e.g., online or group support programs, group medical visits). Research in young adults with type 1 diabetes suggests that programs to build individual resilience (33) and address "diabetes-specific loneliness" through a social network of people who understand diabetes challenges (34) may be beneficial for this group.

These and other interventions typically focus on the individual, yet our data suggest that greater attention should be paid to ways that the health care system may contribute to diabetes distress, since interactions with providers and the health care system play a significant role in how one copes (2). This may be especially relevant to young adults with youth-onset type 2 diabetes who are highly vulnerable to early onset of poor health outcomes (13, 35). Importantly, accessibility of health care coverage must be addressed. In addition, health care systems have incorporated programs for young adults with type 1 diabetes to help them to transition from pediatric to adult health care systems (36). Young adults with youth-onset type 2 diabetes are likely to also benefit from this approach.

Limitations

While the cohort's size and diversity are strengths, the fact that participants were involved in a long-running study is a limitation because their involvement may have ameliorated diabetes distress. If this is the case, the prevalence of high diabetes distress would be greater in a comparable community sample. In addition, the data are cross-sectional, and thus, causal relationships, and specifically the direction of the associations, cannot be assessed. Finally, a large percentage of the cohort was female, and women often report higher levels of distress than men, so we might have found a lower prevalence of diabetes distress if the cohort included more men.

Summary and Directions for Future Research

Approximately one-quarter of young adults with youth-onset type 2 diabetes in the TODAY2 cohort experienced clinically significant diabetes distress, with 30–40% experiencing high distress related to regimen challenges and emotional burdens. This number might be higher if those with youth-onset type 2 diabetes in nonresearch, community settings were assessed. Women and participants with high HbA_{1c}, moderate to severe anxiety symptoms, and without health care coverage were at greater risk for high diabetes distress. Participants with moderate to severe depressive symptoms were at higher risk for regimen distress and emotional burden, and those treated with insulin were more likely to experience high levels of emotional burden.

Future longitudinal research should explore other psychosocial factors that might have an impact on distress (e.g., fear of hypoglycemia, especially for those using insulin). Data are also needed on the relationship of diabetes distress with health care behaviors (e.g., blood glucose testing, missed health care visits) to develop interventions that have an impact on distress and key behaviors that affect diabetes outcomes. This article represents a first step in learning about sources of diabetes distress and factors that may contribute to high distress in this vulnerable group of young adults with youth-onset type 2 diabetes. Much more needs to be learned.

Acknowledgments. We gratefully acknowledge the participation and guidance of the American Indian partners associated with the clinical center located at the University of Oklahoma Health Sciences Center, including members of the Absentee Shawnee Tribe, Cherokee Nation, Chickasaw Nation, Choctaw Nation of Oklahoma, and Oklahoma City Area Indian Health Service. The opinions expressed in this article are those of the authors and do not necessarily reflect the views of the respective tribes and the Indian Health Service.

Funding. This work was completed with funding from the National Institute of Diabetes and Digestive and Kidney Diseases and National Institutes of Health Office of the Director grants U01-DK-61212, U01-DK-61230, U01-DK-61239, U01-DK-61242, and U01-DK-61254.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The National Institute of Diabetes and Digestive and Kidney Diseases project office was involved in all aspects of the study, including the design and conduct, collection, management, analysis, and interpretation of the data; review and approval of the manuscript; and decision to submit the manuscript for publication.

Duality of Interest. The TODAY Study Group acknowledges the following companies for donations in support of the study's efforts: Becton Dickinson, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, LifeScan, Pfizer, and Sanofi. No other potential conflicts of interest relevant to this article were reported.

Author Contributions. P.M.T., D.U., M.T., M.D.M., M.R., S.M., R.F., J.K., L.C., and R.S.W. critically reviewed and edited the submitted manuscript. P.M.T. and R.S.W. wrote the manuscript. D.U. and M.T. conducted the statistical analyses and wrote sections of the manuscript. P.M.T. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Prior Presentation. Parts of this study were presented in poster form at the 81st Scientific Sessions of the American Diabetes Association, 25–29 June 2021.

References

1. Polonsky WH, Anderson BJ, Lohrer PA, et al. Assessment of diabetes-related distress. Diabetes Care 1995;18:754–760
2. Skinner TC, Joensen L, Parkin T. Twenty-five years of diabetes distress research. Diabet Med 2020;37:393–400
3. Perrin NE, Davies MJ, Robertson N, Snoek FJ, Khunti K. The prevalence of diabetes-specific emotional distress in people with type 2 diabetes: a systematic review and meta-analysis. Diabet Med 2017;34:1508–1520
4. Fisher L, Hessler DM, Polonsky WH, Mullan J. When is diabetes distress clinically meaningful? Establishing cut points for the Diabetes Distress Scale. Diabetes Care 2012;35:259–264
5. Fisher L, Mullan JT, Arean P, Glasgow RE, Hessler D, Masharani U. Diabetes distress but not clinical depression or depressive symptoms is associated with glycemic control in both cross-sectional and longitudinal analyses. Diabetes Care 2010;33:23–28
6. Fisher L, Skaff MM, Mullan JT, et al. Clinical depression versus distress among patients with type 2 diabetes: not just a question of semantics. Diabetes Care 2007;30:542–548
7. Fisher L, Mullan JT, Skaff MM, Glasgow RE, Arean P, Hessler D. Predicting diabetes distress in patients with type 2 diabetes: a longitudinal study. Diabet Med 2009;26:622–627
8. Fisher L, Polonsky WH, Hessler DM, et al. Understanding the sources of diabetes distress in adults with type 1 diabetes. J Diabetes Complications 2015;29:572–577
9. Schiøtz ML, Bøgelund M, Almdal T, Jensen BB, Willaing I. Social support and self-management behaviour among patients with type 2 diabetes. Diabet Med 2012;29:654–661
10. Peyrot M, Egede LE, Campos C, et al. Ethnic differences in psychological outcomes among people with diabetes: USA results from the second Diabetes Attitudes, Wishes, and Needs (DAWN2) study. Curr Med Res Opin 2014;30:2241–2254
11. Tamborlane WV, Klingensmith G. Crisis in care: limited treatment options for type 2 diabetes in adolescents and youth. Diabetes Care 2013;36:1777–1778

12. Zeitler P, Hirst K, Pyle L, et al.; TODAY Study Group. A clinical trial to maintain glycemic control in youth with type 2 diabetes. N Engl J Med 2012;366:2247–2256
13. Bjornstad P, Drews KL, Caprio S, et al.; TODAY Study Group. Long-term complications in youth-onset type 2 diabetes. N Engl J Med 2021; 385:416–426
14. Polonsky WH, Fisher L, Earles J, et al. Assessing psychosocial distress in diabetes: development of the diabetes distress scale. Diabetes Care 2005;28:626–631
15. Kroenke K, Spitzer RL. The PHQ-9: a new depression diagnostic and severity measure. Psychiatr Ann 2002;32:509–515
16. Kroenke K, Strine TW, Spitzer RL, Williams JBW, Berry JT, Mokdad AH. The PHQ-8 as a measure of current depression in the general population. J Affect Disord 2009;114:163–173
17. Corson K, Gerrity MS, Dobscha SK. Screening for depression and suicidality in a VA primary care setting: 2 items are better than 1 item. Am J Manag Care 2004;10:839–845
18. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006; 166:1092–1097
19. Swinson RP. The GAD-7 scale was accurate for diagnosing generalised anxiety disorder. Evid Based Med 2006;11:184
20. Löwe B, Decker O, Müller S, et al. Validation and standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the general population. Med Care 2008;46:266–274
21. Sturt J, Dennick K, Due-Christensen M, McCarthy K. The detection and management of diabetes distress in people with type 1 diabetes. Curr Diab Rep 2015;15:101
22. Peimani M, Nasli-Esfahani E, Sadeghi R. Patients' perceptions of patient-provider communication and diabetes care: a systematic review of quantitative and qualitative studies. Chronic Illn 2020;16:3–22
23. Hajos TR, Polonsky WH, Twisk JW, Dain MP, Snoek FJ. Do physicians understand type 2 diabetes patients' perceptions of seriousness; the emotional impact and needs for care improvement? A cross-national survey. Patient Educ Couns 2011;85:258–263
24. Bohlen K, Scoville E, Shippee ND, May CR, Montori VM. Overwhelmed patients: a videographic analysis of how patients with type 2 diabetes and clinicians articulate and address treatment burden during clinical encounters. Diabetes Care 2012;35:47–49
25. Fisher L, Polonsky WH, Hessler D. Addressing diabetes distress in clinical care: a practical guide. Diabet Med 2019;36:803–812
26. Arnett JJ. Emerging adulthood. A theory of development from the late teens through the twenties. Am Psychol 2000;55:469–480
27. Schmidt CB, van Loon BJP, Vergouwen ACM, Snoek FJ, Honig A. Systematic review and meta-analysis of psychological interventions in people with diabetes and elevated diabetes-distress. Diabet Med 2018;35:1157–1172
28. TODAY Study Group. Health care coverage and glycemic control in young adults with youth-onset type 2 diabetes: results from the TODAY2 study. Diabetes Care 2020;43:2469–2477
29. Sturt J, Dennick K, Hessler D, Hunter BM, Oliver J, Fisher L. Effective interventions for reducing diabetes distress: systematic review and meta-analysis. Int Diabet Nurs 2015;12:40–55
30. Young-Hyman D, de Groot M, Hill-Briggs F, Gonzalez JS, Hood K, Peyrot M. Psychosocial care for people with diabetes: a position statement of the American Diabetes Association. Diabetes Care 2016;39:2126–2140
31. Yared Z, Blunden S, Stotland S. Addressing a care gap in type 1 diabetes management: using the Diabetes Distress Scale in a community care setting to address diabetes-related treatment challenges. Can J Diabetes 2020;44:514–520
32. Dale JR, Williams SM, Bowyer V. What is the effect of peer support on diabetes outcomes in adults? A systematic review. Diabet Med 2012; 29:1361–1377
33. Housden L, Wong ST, Dawes M. Effectiveness of group medical visits for improving diabetes care: a systematic review and meta-analysis. CMAJ 2013;185:E635–E644
34. Joensen LE, Filges T, Willaing I. Patient perspectives on peer support for adults with type 1 diabetes: a need for diabetes-specific social capital. Patient Prefer Adherence 2016;10:1443–1451
35. TODAY Study Group. Longitudinal changes in cardiac structure and function from adolescence to young adulthood in participants with type 2 diabetes mellitus: the TODAY follow-up study. Circ Heart Fail 2020;13:e006685
36. Agarwal S, Raymond JK, Schutta MH, Cardillo S, Miller VA, Long JA. An adult health care-based pediatric to adult transition program for emerging adults with type 1 diabetes. Diabetes Educ 2017;43:87–96