Tangled Up in Blue: Unraveling the Links Between Emotional Distress and Treatment Adherence in Type 2 Diabetes

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OBJECTIVE

We conducted comprehensive assessments of emotional distress to examine relations with diabetes medication adherence over time.

RESEARCH DESIGN AND METHODS

Ethnically and socioeconomically diverse adults treated for type 2 diabetes completed validated self-reports (SRs) for diabetes distress and depression, were administered semistructured depression interviews, and provided blood samples for A1C. Medication adherence among 104 participants was electronically monitored (EM) over the subsequent 3 months; validated SRs of medication adherence were also obtained. Hierarchical linear regression evaluated independent effects of diabetes distress and depression on adherence.

RESULTS

Mean ± SD 3-month medication adherence was 76.1% ± 25.7% for EM and 83.7% ± 21.9% for SR. Higher levels of SR ($P < 0.001$) and interview-based ($P < 0.05$) depressive symptom severity ($P < 0.05$) and diabetes-related distress ($P < 0.01$) showed a significant bivariate association with EM and SR nonadherence. Regression models showed baseline diabetes distress was a significant independent predictor of EM ($\beta = -0.29$; $P = 0.001$) and SR adherence ($\beta = -0.24$; $P < 0.02$) at follow-up. SR depression was an independent predictor of EM and SR adherence and reduced the effects of diabetes distress to nonsignificance. Subsequent models indicated this effect was driven by somatic rather than cognitive-affective symptoms of depression. Results were consistent but weaker for interview-based depressive symptoms.

CONCLUSIONS

Findings support diabetes-related distress and depression symptom severity as risk factors for type 2 diabetes medication nonadherence. Somatic symptoms captured by depression measures, but not cognitive-affective symptoms, independently predict nonadherence and should be further investigated as a potential link between emotional distress and nonadherence.

The prevalence of depression has been estimated to be up to twofold greater in individuals with type 2 diabetes than in those without diabetes (1), and depression may have significant consequences for diabetes treatment outcomes (2–4). If these associations reflect a causal influence of depression on diabetes treatment

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outcomes, that influence may be explained, in part, by treatment nonadherence and suboptimal self-management. Depressive symptoms have been significantly associated with problematic self-management (5), even at low levels of symptom severity that would not warrant a psychiatric diagnosis (6). How to conceptualize these subclinical symptoms of depression has been a matter of debate (7–9). Questions include whether elevated scores on such measures that do not rise to the level of a diagnosable disorder should be thought of as symptoms of depression at all.

Considerable evidence supports the validity of a construct for diabetes-related emotional distress that is distinct from a depressive mood disorder and specific to the stress of living with a chronic illness and a demanding self-management regimen (9). Diabetes-related distress reflects the emotional and psychological reactions to the burden and stress associated with diabetes and its management (10). Diabetes-related distress has been empirically distinguished from depression and depressive symptoms in relation to self-management and glycemic control (9,11–13). The available literature suggests that diabetes distress is more common, more chronic, and more closely associated with diabetes outcomes than major depressive disorder (MDD) (9). Evidence also suggests that diabetes-related distress can often be mischaracterized as MDD in research studies as a result of an overreliance on self-report (SR) screening measures with high rates of false positives (7,8). Thus, there is a need for continued research that differentiates depression from diabetes-related distress in relation to diabetes self-management.

Studies illustrate that the majority of patients with type 2 diabetes who endorse elevated levels of depressive symptoms on screening measures do not qualify for a diagnosis of a depressive mood disorder (see, e.g., ref. 11). The overlap between somatic symptoms of depression and diabetes-associated illness may partially explain this discrepancy. For example, a study of adults with type 2 diabetes showed that much of the overidentification of depression by a commonly used screening instrument (14) was explained by symptoms involving impairments in sleep, appetite, and energy level (15). Results from a large, population-based study showed that differences in depressive symptoms between adults with and without diabetes were limited to somatic symptoms; no significant differences were found for cognitive-affective symptoms of depression (16). Further, qualitative analysis of structured clinical interviews for depression showed that patients with type 2 diabetes often discuss somatic symptoms of depression as being caused by diabetes and diabetes-related medications (17).

The current study sought to examine, using rigorous assessment methods, associations among diabetes distress, depression, and medication adherence. Based on previous research showing a linear relationship between depressive symptom severity and diabetes treatment nonadherence, even at subclinical levels (5,6) and the lack of a significant relationship between MDD and type 2 diabetes treatment nonadherence (11), our analyses focus on severity ratings for emotional distress, rather than a diagnosis of MDD. We hypothesized independent effects of diabetes-related distress and depression in relation to medication nonadherence and explored the possibility of differential effects for somatic versus cognitive-affective symptoms of depression in relation to diabetes nonadherence. We expected that these relationships would be consistent *1*) across SR and interviewer assessments of depressive symptom severity and *2*) across subjective and objective measures of diabetes medication adherence.

RESEARCH DESIGN AND METHODS

Study Sample and Procedures

Participants were recruited from diabetes specialty and primary care clinics affiliated with a large, urban, academic medical center through clinician referral, clinic screening, posted fliers, and mailings as part of a 3-month longitudinal observational study examining treatment adherence and distress. Participants (N = 120) were evaluated for depression, completed SR questionnaires, had blood drawn, received an electronic bottle cap to track their adherence, and were given $50 compensation. Of the 120 participants, 105 completed the electronic medication monitoring portion of the study and returned for a follow-up assessment, for which they were compensated an additional $50. One participant was excluded because their monitored oral medication was discontinued between study visits, leaving 104 participants for these analyses. Entry criteria included age 18 years or older, a diagnosis of type 2 diabetes, an SR ability to read or write in English, and taking oral medication for diabetes or insulin and taking an oral medication for hypertension or hypercholesterolemia. Participants provided informed consent, and the institutional review board at the Albert Einstein College of Medicine approved this study.

Measures

Psychiatric Diagnoses

The Mini International Neuropsychiatric Interview (MINI), a structured and valid diagnostic interview that assesses various psychiatric disorders based on diagnostic criteria, was used to establish baseline current or previous MDD (18). Interviews were administered by doctoral-level clinical psychology students, who were trained and monitored by a licensed clinical psychologist (J.S.G.) through audiotaped supervision.

Diabetes-Related Distress

The 17-item Diabetes Distress Scale (DDS) (10) evaluates distress over the past month, using a scale from 1 (no distress) to 6 (serious distress). A mean score <2.0 indicates little to no distress, 2.0 to 2.9 indicates moderate distress, and ≥ 3 indicates high distress (19). The instrument has four subscales. Here we focus on the five-item emotional burden subscale (DDS-EB) to avoid overlap with reports of adherence to the treatment regimen (i.e., regimen distress items), and to avoid items that are not specifically representative of the experience of emotional distress (e.g., dissatisfaction with providers and support from significant others). The DDS-EB most clearly measures emotional distress related to diabetes (face validity) and has been previously associated with SR medication adherence among adults with type 2 diabetes (20). In this sample, internal reliability was excellent for the DDS total score (α = 0.95) and for the DDS-EB (α = 0.92); scores from these scales were strongly correlated (r = 0.90; $P < 0.001$).

9-Item Patient Health Questionnaire

The 9-item Patient Health Questionnaire (PHQ-9) is a brief, valid, SR depression screening measure assessing the frequency of depressive symptoms over the past 2 weeks (14). The PHQ-9 assesses four somatic (sleep, fatigue, appetite, and psychomotor retardation)

and five cognitive-affective symptoms (lack of interest, depressed mood, negative self-feelings, concentration problems, and suicidal ideation) that are part of the diagnostic criteria for MDD (21). Total scores ≥10 are considered a positive screen for MDD (14). The internal reliability in this sample was adequate for the total (α = 0.88), cognitive-affective (α = 0.83), and somatic (α = 0.75) scales. The two subscales were strongly correlated (r = 0.74; $P < 0.001$).

Montgomery-Åsberg Depression Rating Scale

Doctoral-level clinical psychology students assessed depression symptom severity via a semistructured interview at baseline, with audiorecorded supervision by a licensed clinical psychologist (J.S.G.). The Montgomery-Åsberg Depression Rating Scale (MADRS) probes depressive symptoms experienced during the previous week (22). Additional open-ended follow-up questions elicit information about the severity and frequency of a specific symptom, rated from 0 to 6. Scores between 31 and 34 are considered moderate depression and those ≥35 are considered severe depression (23). The MADRS has fewer somatic symptoms than other measures of depression severity (24). Intraclass correlation between raters has been previously reported as excellent (r = 0.93) (25). The MADRS was also scored as a composite of cognitive-affective symptoms (apparent sadness, reported sadness, inner tension, concentration difficulties, inability to feel, pessimistic thoughts, and suicidal thoughts) and somatic symptoms (reduced sleep, reduced appetite, and lassitude), consistent with previous studies (26,27). Internal reliability for the total scale score in our sample was good (α = 0.85), with lower reliability for the somatic (α = 0.60) than the cognitive-affective (α= 0.82) subscales, which were strongly correlated (r = 0.66; $P < 0.001$).

Electronically Monitored Medication Adherence

Each participant was given a Medication Event Monitoring System bottle cap (MEMS) (AARDEX Group, Zurich, Switzerland) to track one diabetes-related medication for approximately 3 months. Oral antihyperglycemic medications were tracked when available. If a participant was taking insulin and no oral antihyperglycemic medication, a medication for cholesterol or blood pressure was tracked. If multiple medications satisfied these criteria, the oral medication that was taken most frequently or was the most difficult to remember was selected. The percentage of doses taken as prescribed was calculated by dividing the number of times the bottle was opened by the number of openings prescribed during that time period. MEMS data were corrected only when participants could identify a specific day or days on the calendar that they took their medication in a way that would not have been recorded by the MEMS. MEMS readings were corrected for 44 participants for common reasons including medication taken from a pillbox, inpatient hospitalization, or taking multiple doses out of the bottle when leaving home.

SR Medication Adherence

SR adherence ratings were adapted from Lu et al. (28) and were previously validated in adults with type 2 diabetes (29). Participants were asked six separate questions: "What percentage of the time did you take all your diabetes medications as your doctor prescribed?," using past week, month, and 3-month intervals with 11 response categories (0%, 10%, 20%, . . . 100%), and "On average, how would you rate your ability to take all your diabetes medications as your doctor prescribed?," using past week, month, and 3-month intervals with 6 response categories (very poor, poor, fair, good, very good, and excellent). For the current analyses, responses were combined into a composite standardized score (α = 0.97).

Glycemic Control

Diabetes control was assessed by glycated hemoglobin A_{1c} (HbA_{1c}) via a central laboratory. Participants had blood drawn by a research nurse at each study visit. Only 101 participants supplied a valid HbA_{1c} result at the follow-up for reasons including refusal because of a recent blood draw as part of regular clinical care, a research nurse was unavailable during the scheduled visit, and unwillingness to wait or return for a blood draw.

Data Analysis

Descriptive statistics, including distribution normality, were examined for demographic and study-related variables. Bivariate relations among covariates, indicators of emotional distress, SR/electronic monitoring (EM) adherence, and HbA_{1c} values were examined using the Pearson r statistic. Hierarchical linear regression examined independent effects of baseline indictors of emotional distress in predicting 3-month SR/EM adherence. The DDS-EB, total continuous scores from the PHQ-9 and MADRS, and composite scores of cognitive-affective and somatic depressive symptoms were evaluated as independent predictors of EM and SR adherence in separate models. Multicollinearity in the multiple regression models was assessed using the variance inflation factor and tolerance, and no significant multicollinearity among predictors was found. All analyses were completed using SPSS software version 22.0 (IBM Corp., Armonk, NY).

RESULTS

Sample Characteristics

Baseline characteristics of the larger sample were described by Baek et al. (30), and values for baseline variables included in this analysis were not significantly different between those who are included in the current analysis and those who were lost to follow-up. As seen in Table 1, participants were, on average, ethnically diverse, older adults; 51.9% reported at least one diabetes-related complication and 38.5% were prescribed insulin. The average EM percentage of dosage taken as prescribed was 76.1% (SD 25.7%); the average number of days monitored was just over 3 months (96.1 ± 13.4 days). The average DDS score indicated "moderate" diabetes distress. Approximately 46.2% of the sample scored above the threshold for clinically significant diabetes distress (19). Approximately 21% screened positive for MDD on the PHQ-9. However, only five individuals who screened positive on the PHQ-9 met diagnostic criteria for current MDD (22.7%); three positive screens met criteria for previous MDD (13.6%). The small number of participants with current MDD precluded further analysis of the role of diagnosis in this sample.

Bivariate Relationships: Covariates, Medication Adherence, and Emotional Indicators

Among potential covariates, two were associated with greater EM and SR

Table 1—Participant characteristics (*N* = 104)

Age (years)	
Mean (SD)	56.6 (9.2)
Range	29–87
Sex	
Female	64.4 (67)
Male	35.6 (37)
BMI, mean (SD)	35.7 (7.8)
Hispanic ethnicity (*n* = 93)	26.9 (25)
Education level (*n* = 103)	
Less than high school diploma	17.5 (18)
High school diploma	16.5 (17)
Some college	34.0 (35)
College degree	19.4 (20)
Some graduate school or degree	12.6 (13)
Yearly family income (*n* = 98)	
<$10,000	18.4 (18)
$10,000–14,999	14.3 (14)
$15,000–24,999	19.4 (19)
$25,000–49,999	28.6 (28)
$50,000–99,999	18.4 (18)
$100,000–149,999	1.0 (1)
Years since diagnosis (*n* = 102), mean (SD)	12.5 (9.3)
Baseline A1C, mean (SD)	
Percentage	7.8 (1.6)
Millimoles per mole	61.2 (17.1)
Prescribed insulin	38.5 (40)
MDD diagnosis based on the MINI (*n* = 103)	
Current	7.7 (8)
Past	12.5 (13)
Total diabetes distress, mean (SD)	2.3 (1.2)
Clinically significant diabetes distress	46.2 (48)
Emotional burden	2.5 (1.5)
Total PHQ-9 score, mean (SD)	5.9 (5.6)
Screened positive	21.2 (22)
Somatic symptoms	3.4 (2.9)
Cognitive-affective symptoms	2.5 (3.1)
Total MADRS score, mean (SD)	10.1 (9.0)
Somatic symptoms	3.5 (3.5)
Cognitive-affective symptoms	6.6 (6.3)
Self-reported medication adherence	
Percentage-based ratings, mean (SD)	83.7 (21.9)
Categorical ratings	
Very poor	0 (0)
Poor	6.7 (7)
Fair	8.7 (9)
Good	19.2 (20)
Very good	27.9 (29)
Excellent	37.5 (39)

Data are presented as percentage (*n*) unless otherwise indicated.

adherence: older age ($r = 0.33$, $P = 0.001$ and $r = 0.21$, $P = 0.03$, respectively) and fewer days of electronic monitoring ($r = -0.36$, $P < 0.001$ and $r = -0.13$, $P = 0.20$, respectively). Participants taking insulin had significantly lower EM adherence (67.24% ± 27.28%; $P = 0.005$), compared with those taking oral medications only (81.72% ± 23.09%), although their SR adherence was not significantly different ($P = 0.59$). Significant covariates were included in the respective multivariable models presented below.

EM and SR adherence at follow-up were significantly correlated ($r = 0.45$; $P < 0.001$); each was significantly associated with baseline HbA_{1c} ($r = -0.24$, $P = 0.02$ and $r = -0.32$, $P < 0.001$, respectively) and with follow-up HbA_{1c} ($n = 101$; $r = -0.30$, $P = 0.003$ and $r = -0.31$, $P = 0.001$, respectively). DDS-EB was positively correlated with PHQ-9 ($r = 0.62$; $P < 0.001$) and MADRS total scores ($r = 0.45$, $P < 0.001$). DDS-EB was somewhat more closely related to cognitive-affective (PHQ-9: $r = 0.65$, $P < 0.001$; MADRS: $r = 0.46$, $P < 0.001$) than somatic depressive symptoms (PHQ-9: $r = 0.50$, $P < 0.001$; MADRS: $r = 0.32$, $P = 0.001$). MADRS and PHQ-9 total scores were strongly correlated ($r = 0.82$; $P < 0.001$).

Those who screened positive on the PHQ-9 had significantly lower EM adherence (62.52% ± 29.21%; $t = 2.91$; $P = 0.005$) than those who screened negative (79.80% ± 23.49%). This difference was significant for SR adherence as well ($P = 0.010$). Each of the continuous variables for emotional distress was significantly and negatively associated with EM adherence in bivariate analyses, except for MADRS cognitive-affective symptoms ($P = 0.16$); all emotional distress variables were significantly associated with SR adherence (Table 2). No significant bivariate relationships were found between emotional distress variables and HbA_{1c} at baseline (data not shown). Only DDS total scores were significantly associated with follow-up HbA_{1c} ($n = 101$; $r = 0.22$; $P = 0.029$).

Multivariable Regression Analyses

Hierarchical models showed that greater levels of diabetes distress were significantly associated with lower EM and SR adherence after covariate adjustment (Table 3, step 1). When the PHQ-9 total score was added to these models, it accounted for significant additional variance in both EM ($P = 0.021$) and SR adherence ($P = 0.004$), and attenuated the effect of diabetes distress to nonsignificance (Table 3, step 2a). Adding MADRS total scores in separate models did not account for significant additional variance in EM or SR adherence beyond that accounted for by diabetes distress and covariates (Table 3, step 2b).

Next, we examined somatic and cognitive-affective depressive symptom dimensions as predictors of adherence, controlling for covariates. Results showed that only somatic depressive symptoms were independently associated with EM adherence, whereas cognitive-affective symptoms were not independently significant in either model. Neither of the depression symptom components was independently

Table 2—Correlations for indicators of emotional distress and medication adherence

	EM adherence	SR adherence
DDS		
Total	−0.37‡	−0.28†
DDS-EB	−0.38‡	−0.28†
PHQ-9		
Total	−0.39‡	−0.40‡
Somatic symptom scale	−0.45‡	−0.38‡
C/A scale	−0.27†	−0.37‡
MADRS		
Total	−0.22*	−0.26†
Somatic symptom scale	−0.32†	−0.20*
C/A scale	-0.14^{NS}	−0.25†

C/A, cognitive/affective symptom. *$P < 0.05$; †$P < 0.01$; ‡$P < 0.001$; NS, not significant.

predictive of SR adherence; this was consistent for MADRS and PHQ-9 (Table 4, steps 1a and 1b).

Based on these results, we tested a final set of models adding somatic symptoms to covariates and diabetes distress to examine their independence in predicting adherence. PHQ-9 somatic symptoms accounted for additional independent variance in EM and SR nonadherence; diabetes distress was attenuated to nonsignificance in each of these models (Table 4, step 2a). MADRS somatic depressive symptoms accounted for additional independent variance in EM adherence, but not in SR adherence; in each case diabetes distress remained a significant independent predictor of adherence (Table 4, step 2b).

CONCLUSIONS

Our results show that various indicators of depression and diabetes-related emotional distress were bivariately associated over time with both SR and EM medication nonadherence in a diverse sample of adults with type 2 diabetes. Diabetes distress and depression shared between 20% and 38% of their variance in this sample, suggesting substantial overlap in the measurement of these emotional distress constructs. Cognitive-affective symptoms of depression assessed by clinical interview, the gold-standard approach of depression assessment, were the only indicator of emotional distress not significantly associated with EM adherence in bivariate analysis. About 21% of our sample screened positive for MDD, and their adherence was significantly lower than those who did not screen positive. However, only 36% of these positive screens met diagnostic criteria for either current or previous MDD (64% were false positives). Further, total diabetes-related distress was the only indicator of emotional distress that was associated with HbA_{1c} values at follow-up.

Multivariable adjustment showed that diabetes distress, measured by the emotional burden subscale of the DDS, was significantly associated with both EM and SR adherence. Self-reported depression symptom severity was independently significant across adherence measures and attenuated the contribution of diabetes distress to nonsignificance, indicating overlapping variance between these two measures. Effects were weaker for the MADRS, which was not independently predictive of either EM or SR adherence, and did not attenuate the effects of diabetes distress. Importantly, the MADRS interview was designed to be less sensitive to somatic symptom confounding when chronic illness is present (23). Thus somatic symptoms may play a role in explaining differences between MADRS and PHQ-9 findings.

As recommended by authoritative diagnostic systems (21), MADRS interviews involved clinical judgment in the evaluation of symptoms. Also, the MADRS does not assess increases in sleep or appetite, only decreases. The PHQ-9 includes items for fatigue and psychomotor retardation, whereas the MADRS only assesses difficulty in initiating activities (lassitude). Thus the PHQ-9 more fully assesses the symptom criteria for MDD (21) but may also be more vulnerable to confounding by physical illness and illness-related functional impairment (24). PHQ-9 reports of disturbed appetite, fatigue, and psychomotor retardation were the only symptoms that differentiated adults with diabetes from those without diabetes in a recent population-based study (16). Furthermore, problems with appetite, sleep, and fatigue were the only PHQ-9 symptoms that did not discriminate between false-positive and true-positive cases of depressive disorder in a study of adults with type 2 diabetes (15). This suggests these somatic symptoms are less closely associated with true depression in diabetes than

Table 3—Diabetes distress and depression symptoms as predictors of medication adherence

	EM			SR		
	β	*P* value	R^2	β	*P* value	R^2
Step 1			0.32			0.10
Age	**0.18**	**0.04**		0.14	0.15	
Insulin	−0.15	0.09		–	–	
Days monitored	**−0.31**	**<0.001**		–	–	
DDS-EB	**−0.29**	**0.001**		**−0.24**	**0.02**	
Step 2a			0.36			0.17
Age	0.15	0.08		0.10	0.31	
Insulin	−0.11	0.20		–	–	
Days monitored	**−0.35**	**<0.001**		–	–	
DDS-EB	−0.15	0.14		−0.04	0.75	
PHQ-9 total	**−0.25**	**0.02**		**−0.35**	**0.004**	
Step 2b			0.33			0.12
Age	0.17	0.05		0.13	0.20	
Insulin	−0.14	0.10		–	–	
Days monitored	**−0.33**	**<0.001**		–	–	
DDS-EB	**−0.25**	**0.01**		−0.18	0.10	
MADRS total	−0.11	0.27		−0.15	0.16	

P values <0.05 and β values are set in boldface to indicate significance.

Table 4—Somatic and cognitive-affective depressive symptom dimensions as independent predictors of medication adherence

	EM			SR		
	β	*P* value	R^2	β	*P* value	R^2
Step 1a			0.40			0.17
Age	**0.19**	**0.02**		0.10	0.28	
Insulin	−0.08	0.38		—	—	
Days monitored	**−0.34**	**<0.001**		—	—	
PHQ-9 S	**−0.50**	**<0.001**		−0.23	0.10	
PHQ-9 C/A	0.13	0.29		−0.17	0.22	
Step 1b			0.31			0.09
Age	**0.21**	**0.02**		0.16	0.10	
Insulin	−0.14	0.11		—	—	
Days monitored	**−0.33**	**<0.001**		—	—	
MADRS S	**−0.28**	**0.02**		−0.04	0.77	
MADRS C/A	0.03	0.78		−0.20	0.13	
Step 2a			0.40			0.17
Age	0.15	0.07		0.11	0.26	
Insulin	−0.07	0.38		—	—	
Days monitored	**−0.35**	**<0.001**		—	—	
DDS-EB	−0.15	0.11		−0.10	0.36	
PHQ-9 S	**−0.34**	**<0.001**		**−0.30**	**0.006**	
Step 2b			0.36			0.11
Age	0.16	0.07		0.13	0.20	
Insulin	−0.11	0.19		—	—	
Days monitored	**−0.33**	**<0.001**		—	—	
DDS-EB	**−0.24**	**0.01**		**−0.21**	**0.04**	
MADRS S	**−0.20**	**0.03**		−0.11	0.29	

P values <0.05 and β values are set in boldface to indicate significance. C/A, cognitive-affective symptom scale; PHQ-9 C/A, Patient Health Questionnaire, 9-item, cognitive-affective symptom scale; PHQ-9 S, Patient Health Questionnaire, 9-item, somatic symptom scale. S, somatic symptom scale.

cognitive-affective symptoms. These differences warrant further investigation.

Our findings demonstrating an independent role for somatic symptoms of depression in predicting medication adherence in type 2 diabetes are, to our knowledge, novel and require replication. Previous research has repeatedly linked depression to diabetes treatment nonadherence, but these studies have not examined differences between depression symptom dimensions (5). Furthermore, prior studies have predominantly relied on SR screening measures of depression, for which more than half of positive screens would be false positives (11,31), consistent with our findings. When studies assessed depressive disorders using a standardized diagnostic interview, they generally failed to find a relationship with diabetes treatment adherence (see, e.g., ref. 11). Intervention trials that have been successful in treating depression in diabetes have been unsuccessful in improving medication adherence or self-management (see, e.g., ref. 32). Other data demonstrate that relations between depression symptom severity and problems with self-management, including medication nonadherence, persist after the exclusion of nearly all likely cases of MDD (6). The lack of an independent role for cognitive-affective symptoms of depression reported by this study casts further doubt on whether clinical depression is the construct underlying the relationship between elevations on depressive symptom scales and diabetes treatment nonadherence.

Studies that have attempted to identify independent relationships between diabetes distress and depressive symptoms in relation to diabetes self-care have found somewhat mixed results, emphasizing one or the other construct, with variation of effects across aspects of self-management (12,13,20,33). Our study is unique in *1*) using both a clinical interview for depression severity and validated SR; *2*) using EM to assess missed medication doses and validated SR; and *3*) examining somatic and cognitive-affective components of depression. These methods allow us to limit the role of shared measurement error in these effects. We also took a conservative approach of using only the emotional burden subscale of the DDS in our analyses to limit potential confounding with treatment adherence behaviors and to avoid introducing sources of distress, such as dissatisfying relationships with providers, that could influence adherence through pathways other than emotional distress (10,20).

Our design also has limitations. There is no "gold standard" for the assessment of medication adherence and, although our data are consistent with prior research showing that EM captures more nonadherence than SR, EM is also subject to measurement error; both measures were equivalently related to HbA_{1c} in this and previous research (29). Further limitations of EM include a lack of standardization concerning which type of medication was monitored. Thus, we cannot speak to variations across these measures with certainty, despite our attempt to avoid errors related to EM by adjusting values based on compelling participant reports about doses taken in ways that would not be captured by EM. The same is true for our measures of depression: we cannot be certain about which differences between the assessments explain the variations in effects. The MADRS somatic symptom scale also had marginal reliability. We focused on depressive symptom severity rather than diagnosis of a mood disorder in these analyses based on prior evidence (6,11), and results cannot speak directly to the effect of depressive mood disorders. Our relatively small sample may also limit the generalizability of findings and may have limited power for our analyses, especially for more distal HbA_{1c} effects. Given the correlational nature of this study, it is possible that a third variable, such as disease burden (e.g., complications and comorbidities) or complexity of diabetes management, contributed to both increased emotional distress and nonadherence. Finally, although we captured average adherence over a clinically meaningful period of time (i.e., ~3 months), our design also prevents an examination of how these variables change over time. Future longitudinal studies with more than two time points and those that use ecological momentary assessment methods may better evaluate the direction of and capture the dynamic relations among the factors identified here.

Distinguishing between somatic and cognitive-affective aspects of depression

in future research may improve our understanding of the nature and potential explanatory mechanisms for relations between depression and diabetes health outcomes. Studies from the cardiovascular disease (CVD) literature, which also reports consistent evidence linking depression to poor prognosis, suggest that this distinction could be important. For example, population-level data showed that somatic symptoms of depression, but not cognitive-affective symptoms, were independently associated with coronary heart disease and personal and family history of myocardial infarction, among other CVD risk factors (34). Meta-analysis of prospective studies of depressive symptom dimensions in individuals with CVD found that somatic symptoms were significantly associated with mortality and cardiovascular events in fully adjusted analyses; cognitive-affective symptoms were not (35). Other recent studies similarly demonstrate an independent effect of somatic symptoms, rather than cognitive-affective symptoms, in predicting poor CVD outcomes (see, e.g., refs. 35, 36, and 37). Whether this pattern of findings reflects a unique effect of certain depressive symptoms, a particular depression "subtype," or confounding with symptoms of physical illness is unclear. Further investigation of these possibilities is needed in relation to diabetes self-management and health outcomes.

Clinical Implications

One fundamental clinical implication of this study is that providers should be aware that emotional distress can often be associated with risk for type 2 diabetes treatment nonadherence. Our results provide evidence for considerable consistency of effects across measures of emotional distress; they also demonstrate substantial intercorrelation among these indicators of emotional distress. This likely reflects a significant role for shared variance across these measures. While routine screening for depression, an increasingly common standard of diabetes care, identifies patients with more depressive symptoms and who may be at higher risk for treatment nonadherence, it does not separate the larger number of false-positive from true-positive depression cases, nor does it identify the most appropriate intervention. Further evaluation is necessary for screening programs to be effective (7,8). Rather than focusing exclusively on clinical depression—an important but far less prevalent problem than clinically significant diabetes distress in this and other samples (see, e.g., refs. 38 and 39)—evidence suggests that emotional distress that does not rise to the level of a psychiatric diagnosis could nevertheless represent meaningful risk for problems with diabetes treatment adherence. As such, providers should be attuned to emotional distress in their patients during clinical encounters and consider specific depressive symptom presentations and diabetes-related distress as part of their further evaluation of positive screens to more accurately identify the nature of the problem and guide the selection of appropriate interventions (7,9,11).

Consistent evidence across methods of assessment demonstrates that somatic symptoms involving fatigue, sleep, appetite disturbance, and psychomotor changes may warrant particular attention in relation to emotional distress and risk for type 2 diabetes treatment nonadherence. Whether these symptoms represent somatic symptoms of a major depressive episode, residual symptoms between episodes of depression, situational stress, confounding with symptoms of physical illness, or side effects of prescribed medication, or whether they have other explanations can likely only be ascertained through a careful clinical interview. Distinguishing among these explanations for reported "symptoms" should be at least as important as establishing their severity in guiding the selection of appropriate interventions to reduce emotional distress and improve treatment adherence among adults living with type 2 diabetes.

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