Clinical Depression Versus Distress Among Patients With Type 2 Diabetes

Not just a question of semantics

LAWRENCE FISHER, PHD[1]
MARILYN M. SKAFF, PHD[1]
JOSEPH T. MULLAN, PHD[2]
PATRICIA AREAN, PHD[3]

DAVID MOHR, PHD[3]
UMESH MASHARANI, MD[4]
RUSSELL GLASGOW, PD[5]
GRACE LAURENCIN, MD[1]

OBJECTIVE — We sought to determine differences between structured interviews, symptom questionnaires, and distress measures for assessment of depression in patients with diabetes.

RESEARCH DESIGN AND METHODS — We assessed 506 diabetic patients for major depressive disorder (MDD) by a structured interview (Composite International Diagnostic Interview [CIDI]), a questionnaire for depressive symptoms (Center for Epidemiological Studies Depression Scale [CESD]), and on the Diabetes Distress Scale. Demographic characteristics, two biological variables (A1C and non-HDL cholesterol), and four behavioral management measures (kilocalories, calories of saturated fat, number of fruit and vegetable servings, and minutes of physical activity) were assessed. Comparisons were made between those with and without depression on the CIDI and the CESD.

RESULTS — Findings showed that 22% of patients reached CESD ≥16, and 9.9% met a CIDI diagnosis of MDD. Of those above CESD cut points, 70% were not clinically depressed, and 34% of those who were clinically depressed did not reach CESD scores ≥16. Those scoring ≥16, compared with those <16 on the CESD, had higher A1C, kilocalories, and calories of saturated fat and lower physical activity. No differences were found using the CIDI. Diabetes distress was minimally related to MDD but substantively linked to CESD scores and to outcomes.

CONCLUSIONS — Most patients with diabetes and high levels of depressive symptoms are not clinically depressed. The CESD may be more reflective of general emotional and diabetes-specific distress than clinical depression. Most treatment of distress, however, is based on the depression literature, which suggests the need to consider different interventions for distressed but not clinically depressed diabetic patients.

P atients with diabetes and comorbid depressive symptoms, compared with patients with diabetes alone, have increased functional impairment, more hospital days and days off of work (1,2), poorer glycemic control (3), poorer self-management behavior (4), increased health care use and costs (5), and a higher risk of morbidity and mortality (6,7). Clearly, the co-occurrence of diabetes and depression has significant implications for clinical outcomes, disease management, health care costs, and patient health and well-being.

The way depression is measured in clinical studies of diabetes, however, takes a number of different forms, and it is not at all clear whether each method similarly assesses depression and whether different methods uniformly classify patients. We may be identifying very different groups of patients by each method.

The gold standard for assessment of clinical depression is a standardized, structured patient interview that yields clinical diagnoses that conform with Diagnostic and Statistical Manual of Psychiatric Disorders, 4th edition (DSM-IV) criteria. The most frequently used interview schedules are the Structured Clinical Interview for DSM (8), the Composite International Diagnostic Interview (CIDI) (9), and the Mini International Neuropsychiatric Interview (10). Unfortunately, these interviews are time-consuming and expensive to administer, which often adds to patient burden, and, because of cost, they are rarely used to screen for depression among patients with diabetes.

The most widely used method of depression assessment is self-administered questionnaires, e.g., Beck Depression Inventory (11), the Center for Epidemiological Studies Depression (CESD) scale (12), and the Patient Health Questionnaire-9 (13). These scales are easy to use, inexpensive, and user-friendly. However, most do not directly address clinical diagnostic criteria; rather, they consist of a list of emotional symptoms that are endorsed by the respondent as present or absent during a specified time period. The time period, however, varies across scales: The CESD and the Beck Depression Inventory ask about symptoms occurring during the last week, and the Patient Health Questionnaire-9 refers to the last 2 weeks. Most scales have cut points based on summed symptom scores, above which "likely depression" is suggested. However, studies (14,15) employed different cut points: ≥16 or ≥22 on the CESD.

Many studies (14,16) add diagnostic interviews to confirm DSM-IV diagnoses for those patients who reach clinical cri-

teria on questionnaire measures, but this method can create a verification bias (17): A patient who is false negative on the questionnaire never reaches the interview stage. Also, the number of patients diagnosed with a depressive disorder using an interview is far lower than the number who reach a cut point on a questionnaire (3), although many studies (18) rely on questionnaire methods alone when linking depression to poor diabetes outcomes. For example, in a recent meta-analysis (19), 11.4% of patients reached criteria for a depressive disorder using interview methods, whereas 31.0% had significantly elevated depressive symptoms using questionnaire methods.

Although there are considerable data (14) about the sensitivity and specificity of questionnaire and diagnostic interview measures of depression, two related questions of clinical concern remain and are the subject of this study. First, among patients with diabetes, are there differences between those with positive scores only on depression symptom questionnaires versus only on diagnostic interviews? Second, are the clinical implications of high symptom scores the same as clinical depression with respect to their linkages with diabetes distress, self-management, and biological markers? If not, what do symptom questionnaires actually measure? Given the importance of depression in diabetes care, these questions address what the two methods of assessment actually measure and the clinical implications of each.

RESEARCH DESIGN AND METHODS — This report is based on the first of a three-wave longitudinal study of diabetes and depression. To assure a diverse, multiethnic community sample, patients were recruited from several San Francisco Bay area medical groups and diabetes education centers. Inclusion criteria included patients with type 2 diabetes who were aged 21–75 years, could fluently read and speak English or Spanish, and had no severe diabetes complications and no diagnosis of active psychosis or dementia. All patients received a letter from their respective health facilities, cosigned by a facility and project representative, informing them of the project and that they would receive a phone call from the project office if one of the following two opt-out procedures was not initiated: return postcard or 800-number phone call. A screening phone call followed, and, for eligible patients, an

appointment was made in the patient's home, our office, or a community setting to explain the project in detail, collect informed consent, and begin assessment. Patients received a 1.5-h home visit that included questionnaires, physical measurements, interviews, a 150-item mail-back questionnaire, and a visit to a community laboratory for collection of blood and urine specimens. All materials were prepared in English and Spanish, and research assistants were fluent in both languages. The project was approved by the Committee on Human Research at the University of California San Francisco and at each participating facility.

The following patient characteristics were included: age, sex, education, BMI, number of comorbidities (from a list of 25), self-identified ethnicity, years since diagnosis, diabetes treatment (i.e., diet/exercise, oral medication, or insulin), and use of psychotropic medication.

Two measures of depression were used for all patients. The CIDI is a structured interview including a set of modules that assess different groups of DSM-IV psychiatric diagnoses (9). We included the depressive disorders module that yields time of last diagnosis of major depressive disorder (MDD) being within the last month (Dx1), between 1 and 6 months (Dx2), or between 6 and 12 months (Dx3). Research assistants were trained by a registered CIDI trainer to criterion, and they scored standardized protocols over time to prevent drift. The CESD is a 20-item questionnaire ($\alpha = 0.89$) that assesses depressive symptoms over the previous 7 days (12). Cut points of ≥16 and ≥22 were used to define "likely depression" (14,15). Prevalence comparisons between our sample and community rates were based on data from the National Comorbidity Survey Replication (20,21). Also using the CIDI, the National Comorbidity Survey Replication study assessed a stratified national sample of 9,090 community respondents in 2001 and 2002. Last, we included a measure of diabetes-specific emotional distress. The Diabetes Distress Scale (DDS) is a 17-item scale that assesses distress associated with emotional burden, care regimen, interpersonal factors, and physician care ($\alpha = 0.93$) (22,23). Each item is rated on a six-point scale, ranging from "not a problem" to "a very serious problem."

Six dependent variables were included. Two diabetes-related biological measures were A1C and non-HDL cholesterol. Four behavioral management mea-

sures included three dietary indexes, derived from the Block 2000 Brief Food Frequency Questionnaire (Block Dietary Data Systems, Berkeley, CA): average kilocalories consumed per day, average calories of saturated fat as a percentage of total calories consumed per day, and average number of fruit and vegetable servings per day (see Block et al. [24] for psychometric data). Physical activity was assessed by the International Physical Activity Questionnaire (IPAQ) (25). This scale reflects the number of minutes of activity per week at each of three activity levels (walking, moderate, or vigorous), each weighted by a measure of energy expenditure with multiples of resting metabolic rate for each activity for a 60-kg person (light = 3.3, moderate = 4.0, and vigorous = 8.0).

Data analysis
Univariate comparisons between patients with and without a CIDI diagnosis of a MDD and by CESD of likely depression were undertaken using χ^2 tests and Student's t tests. ANCOVA was used to estimate the effects of CIDI, CESD scores ≥16, and their interaction on the six dependent variables. The effects of nine covariates, and their interactions with the primary variables, were evaluated to prevent their potential effects from obscuring the relationships among the primary variables. Multiple regression was used to assess the impact of distress on these relationships, and tests for multicolinearity and corrections for multiple statistical tests were also undertaken. The analyses were completed using SPSS 11.0 and SAS 9.1.

RESULTS — Screening identified 640 eligible patients, and 506 patients completed data collection (79.0%). There were no significant differences between eligible patients who participated and eligible patients who initially refused or later dropped out in terms of age, sex, ethnicity, marital status, education, years since diagnosis, and number of comorbidities.

The sample was ethnically and socially diverse, with large SDs around most mean values (Table 1). Average age was 57.8 years, average time since diabetes diagnosis was 8.2 years, and average A1C was 7.2%. Nineteen patients (4.0%) received a CIDI Dx1, 16 (3.0%) a Dx2, and 15 (2.9%) a Dx3 diagnosis of MDD (total $n = 50$, 9.9%). The comparable past-year National Comorbidity Survey Replication rate was 6.6%, suggesting a 50% higher

Table 1—Sample description

	Total sample	Patients with CESD scores ≥16		Patients with CESD scores ≥22		CIDI	
	n = 506	n = 113		n = 75		n = 50	
		≥16	<16	≥22	<22	MDD	No MDD
Male/female subjects	218 (43)/288 (57)	41 (36)/72 (64)	176 (45)/212 (55)	25 (33)/50 (67)	192 (45)/239 (55)	20 (40)/30 (60)	198 (43)/258 (57)
Age (years)	57.83 ± 9.86	55.38 ± 10.13*	58.4 ± 9.7	55.53 ± 0.96†	58.1 ± 9.8	56.90 ± 9.11	57.9 ± 9.9
Education (years)	14.57 ± 3.33	13.72 ± 3.62*	14.8 ± 3.2	13.49 ± 3.71*	14.8 ± 3.2	14.56 ± 3.62	14.6 ± 3.3
Family income ($1,000)	52.68 ± 36.37	42.11 ± 38.28*	55.4 ± 35.0	40.23 ± 39.93*	54.6 ± 35.1	52.89 ± 40.91	52.8 ± 35.9
BMI (kg/m^2)	32.73 ± 7.74	33.80 ± 8.11	32.5 ± 7.6	33.95 ± 8.55	32.6 ± 7.6	35.52 ± 8.81*	32.4 ± 7.6
Psychiatric medications	105 (20.8)	48 (42.7)*	57 (14.8)	35 (46.7)*	70 (16.5)	31 (62)*	74 (16.3)
Comorbidities	3.8 ± 2.5	4.9 ± 2.97*	3.6 ± 2.3	5.3 ± 2.85*	3.6 ± 2.4	5.6 ± 2.79*	3.7 ± 2.4
Years with diabetes	8.1 ± 7.5	8.7 ± 7.3	7.9 ± 7.6	8.0 ± 6.6	8.2 ± 7.7	8.4 ± 7.0	8.1 ± 7.6
Medication							
Diet/exercise	84 (16.6)	13 (11.6)	72 (18.0)	10 (13.0)	75 (17.1)	6 (12.0)	77 (16.9)
Oral	346 (68.2)	78 (68.8)	267 (68.3)	51 (67.0)	294 (68.5)	36 (72)	311 (68.1)
Insulin	76 (15.0)	22 (19.6)	54 (13.7)	14 (19.0)†	62 (14.8)	8 (16)‡	68 (15.0)
Ethnicity							
Asian American	85 (16.8)	15 (18.1)	69 (81.9)	7 (8.4)†	77 (91.6)	3 (3.5)‡	82 (96.5)
African American	104 (20.5)	21 (20.6)	82 (79.4)	15 (14.7)	88 (85.3)	5 (4.9)	98 (95.1)
Hispanic	98 (19.3)	29 (29.3)	71 (70.7)	24 (24.2)	76 (75.8)	11 (11.1)	88 (88.9)
Non-Hispanic white	185 (36.7)	42 (22.7)	144 (77.3)	24 (13.0)	162 (87.0)	25 (13.4)	161 (86.6)
Other	34 (6.7)	6 (18.8)	27 (81.3)	5 (15.6)	28 (84.4)	6 (18.2)	27 (81.8)

Data are means ± SD or n (%). Significance levels based on Student's t test or χ^2 test compared between those with and without a diagnosis on the designated scale. *$P < 0.001$; †$P < 0.05$; ‡$P < 0.01$.

rate of past-year MDD for patients with diabetes than suggested by community samples.

Because the recency of diagnosis of the last MDD episode might have been related to the primary study variables, we conducted a time-trend analysis among the three CIDI time-of-diagnosis groups (Dx1, Dx2, and Dx3), with demographic, disease status, control, and outcome variables. A priori estimates of differences among the three groups found that to detect an average difference of 0.5 SD required an $n = 17$ per group for a power = 0.80. No analysis reached statistical significance, although there was a nonsignificant trend on the IPAQ: Dx1 patients reported a lower level of physical activity than Dx2 and Dx3 patients. Patients in all three CIDI groups were highly symptomatic on the CESD, with 78, 63, and 53% scoring ≥16 in groups Dx1–3, respectively, compared with patients without MDD (18%). Because we noted no significant differences among these three patient groups, we combined them into a single group of MDD patients who had an episode within the last year. This combined group was used in subsequent analyses.

Of the 506 patients, 113 (22.0%) scored ≥16, and 75 (15.0%) scored ≥22 on the CESD. Among the 113 patients with CESD scores ≥16, only 33 (29.2%) received a past-year CIDI diagnosis of MDD; among the 75 patients with CESD scores ≥22, only 23 (30.7%) received a similar CIDI diagnosis. Conversely, of the 50 patients receiving a CIDI MDD diagnosis, 33 (66.0%) scored ≥16, and 23 (46.0%) scored ≥22 on the CESD. This means that 70% of patients above the CESD cut points did not meet CIDI criteria for MDD and that 30–50% of those with a CIDI diagnosis were not above CESD cut points.

Of the 50 patients with MDD, 31 (62.0%) were taking psychotropic medication; of those scoring ≥16 and ≥22 on the CESD, the rates were 48 (42.5%) and 35 (46.7%), respectively (90% antidepressants, 8% anti-anxiety, and 2% antipsychotics). Thus, far more patients with a CIDI diagnosis were taking psychotropic medications compared with those above the CESD cut points.

Among the patient characteristics listed in Table 1, differences between those with MDD and those without occurred for ethnicity, BMI, number of comorbidities, and psychotropic medication. Far fewer Asian- and African-

Table 2—*Student's* t *test compared between those who reached and did not reach criteria on the CIDI or score ≥16 or ≥22 on the CESD*

	CESD score (cut point 16)		CESD score (cut point 22)		CIDI	
	≥16	<16	≥22	<22	MDD	No MDD
A1C	7.58 ± 1.73	7.16 ± 1.33	7.55 ± 1.7†	7.20 ± 1.38	7.06 ± 1.30	7.28 ± 1.45
Non-HDL cholesterol	144.85 ± 52.95	136.50 ± 45.37	138.80 ± 54.43	138.24 ± 45.98	144.54 ± 53.79	137.74 ± 46.80
Kilocalories	1,636.30 ± 819.74‡	1,294.40 ± 608.54	1,661.10 ± 844.38‡	1,317.40 ± 627.15	1,385 ± 632.13	1,367.10 ± 678.64
Saturated fat calories (%)	12.7 ± 3.54*	11.86 ± 3.54	13.0 ± 3.97§	11.86 ± 3.46	12.75 ± 4.07	11.9 ± 3.49
Fruit and vegetable servings (*n*)	5.45 ± 3.39	5.39 ± 3.32	5.25 ± 3.27	5.43 ± 3.34	5.63 ± 3.47	5.38 ± 3.31
Exercise level (IPAQ)	1,970.80 ± 2,637.1*	2,565.80 ± 2,704.2	1,732.40 ± 2,622.7§	2,695.50 ± 2,697.60	2,280.40 ± 2,591.0	2,432.30 ± 2,701.8

Data are means ± SD. $*P < 0.05$; $†P < 0.10$; $‡P < 0.001$; $§P < 0.01$.

American patients had MDD than members of other ethnic groups, and those with MDD had a higher BMI, more comorbidities, and took psychotropic medication more often than those without MDD. Significant differences between those with and without likely depression in patients with CESD scores ≥16 and ≥22 occurred for five variables: patients with elevated CESD scores were significantly younger, less educated, of lower income, had more comorbid conditions, and were more likely to take psychotropic medications.

Relationships with behavioral and biological markers
Student's *t* tests compared those who met versus those who did not meet CESD scores ≥16 or ≥22 and CIDI criteria on each of the six biological and behavioral variables (Table 2). Results for the patients with CESD scores ≥16 and ≥22 were quite similar, with four of the six comparisons statistically significant: those who scored above the CESD cut points had higher A1C, higher kilocalories and saturated fat calories, and less physical activity (IPAQ). No significant differences occurred for any of the six tests comparing those with and without MDD. Thus, CESD scores ≥16 and ≥22 were significantly linked to biological and behavioral markers, whereas a CIDI diagnosis of MDD was not.

To assess the main and interactive effects of CESD and CIDI diagnoses on each of the six dependent variables, two-by-two ANCOVAs were used. Controls for patient sex, years since diagnosis, age, BMI, number of comorbid conditions, education, ethnicity, diabetes medications, and use of psychotropic medication were included because of the significant findings reported in Table 1. Since results for patients with CESD scores ≥16 and ≥22 were similar, we reviewed only those with CESD scores ≥16 (yes/no) by CIDI (yes/no) findings. Controlling both for covariates and CIDI diagnosis, scoring ≥16 on the CESD was significantly and independently related to higher A1C ($F = 10.93$, $P < 0.001$), higher kilocalories ($F = 23.66$, $P < 0.001$), and lower IPAQ scores ($F = 4.26$, $P = 0.04$). Conversely, controlling for both the covariates and patients with CESD scores ≥16, having a CIDI diagnosis of MDD yielded nonsignificant findings in each analysis. With the covariates included, and controlling for both the CESD and the CIDI, we then tested the interaction between having a CESD score ≥16 and CIDI diagnoses on the six dependent variables. None of the six interaction terms were statistically significant. We also tested interaction terms for patient sex and use of psychotropic medication in all equations. None reached statistical significance.

Relationships with diabetes-specific distress
The differences between the CIDI and CESD findings led us to hypothesize that the CESD may be measuring something other than clinical depression, perhaps something akin to a general level of emotional distress. To explore this hypothesis, we constructed six multiple regression equations. Each included the same nine control variables used in the two-by-two ANCOVAs described above (to assure that any between-group differences were not due to differences in the proportion of patients within the control subgroups), as well as CIDI diagnosis of MDD (yes/no), the continuous CESD score, and the DDS continuous score. Continuous CESD and

DDS scores were used because negative mood and emotional distress were considered continuous and not dichotomous variables. The dependent variable in each equation was one of the six behavioral or biological markers. Our goal in these equations was to observe the independent associations of MDD, CESD, and DDS with respect to each of the six diabetes markers. Tests for multicolinearity were negative.

The zero-order correlation between DDS versus CESD and MDD was 0.48 ($P < 0.001$) and 0.16 ($P < 0.001$), respectively. No CIDI-MDD regression coefficient reached significance in any of the six equations, nor was the interaction between DDS and CESD or DDS and MDD significant in any equation (Table 3). DDS scores independently reached or approached significance in four of the six equations: A1C ($B = 0.23$, $P < 0.001$), non-HDL cholesterol ($B = 4.94$, $P < 0.06$), kilocalories ($B = 168.10$, $P < 0.001$), and fruit and vegetable servings ($B = 0.41$, $P < 0.03$). CESD scores reached or approached significance in only two equations: fruit and vegetable servings ($B = -0.04$, $P < 0.04$) and IPAQ (-37.90, $P < 0.04$). Both CESD and DDS coefficients were significant only in the equation with fruit and vegetable servings. Thus, once DDS was added to these analyses, the initial univariate associations between CESD and the dependent variables (A1C, kilocalories, and saturated fat calories) were no longer significant. The independent and shared associations of the CESD and DDS with each other and with diabetes management variables (from both the ANCOVAs and multiple regression analyses) suggested that the CESD reflected diabetes-specific and perhaps other forms of

Table 3—*Unstandardized regression coefficients in MR equations*

Independent variables	Dependent variables					
	A1C	Non-HDL cholesterol	Kilocalories	Saturated fat calories (%)	Fruit and vegetable servings	IPAQ
Controls						
MDD	−0.19	4.24	−200.9*	0.13	0.24	35.86
CESD	0.00	−0.21	5.73	0.02	−0.04†	−37.90‡
DDS	0.23§	4.63*	168.1§	0.25	0.41†	−33.45
R	0.46	0.26	0.37	0.43	0.28	0.30
P	0.001	0.01	0.001	0.001	0.002	0.001

Controls included sex, years with diabetes, age (years), BMI, number of comorbidities, years of education, ethnicity (non-Hispanic white versus other), diabetes medications (diet/exercise, oral, insulin), and psychotropic medication (yes/no). *$P < 0.10$; †$P < 0.05$; ‡$P < 0.01$; §$P < 0.001$.

general emotional distress but not clinical depression.

CONCLUSIONS — The analyses yielded five major findings. First, we found CIDI prevalence rates of last diagnosis of MDD within the past year and CESD likely depression similar to other studies of diabetes (19,26,27) that used diverse, community samples: 9.9% for MDD and 22.0% for likely depression. This suggests substantive differences in the prevalence of depression based on assessment measure: CESD rates of likely depression are twice as high as CIDI rates of MDD, and rates of MDD are 50% higher than those found among community samples (20,21). Second, >70% of those with CESD scores ≥16 or ≥22 are not clinically depressed, according to the CIDI, whereas about one-third of those receiving a CIDI diagnosis of MDD do not score above a CESD cut point. Thus, a substantial number of patients who receive a diagnosis on one depression measure do not receive a diagnosis on the other. These results are unrelated to use of psychotropic medication, even though 62% of patients with MDD and 42% of those who met criteria on the CESD take psychotropic medication (27).

Third, among patients with diabetes, there were relatively few significant differences between those with MDD and those without in terms of patient characteristics: far fewer Asian- and African-American patients and more non-Hispanic white patients received a CIDI diagnosis of MDD compared with patients from other ethnic groups, and those with MDD had a higher BMI, more comorbidities, and more often take psychotropic medications. However, patients who met criteria on the CESD, compared with those who did not, were younger,

less educated, had a lower family income, and had more comorbidities. Thus, the CESD, compared with the CIDI, seems to be more sensitive to or reflective of the stresses associated with other interrelated chronic health conditions, socioeconomic factors, and, perhaps, access to care issues.

Fourth, being above a cut point on the CESD was more strongly associated with deficits in diabetes-related behavioral and biological variables than receiving a CIDI diagnosis of MDD. This finding occured in comparisons that included other potentially confounding covariates. These findings suggest that patients with diabetes who reach criteria for MDD may be considerably different from those who report elevated levels on the CESD; the CESD discriminates between patients based on demographic and diabetes-related behavioral and biological variables, whereas the CIDI alone does not. Fifth, the CESD was significantly associated with the DDS, and the CESD and DDS displayed both shared and independent linkages with behavioral and biological markers.

Three factors may explain the discrepancy between our findings and those of some other studies. First, regarding the relatively low rates of clinical depression found in this study, we used a diverse community sample, not one gathered at a specialty clinic or health facility. Recent meta-analyses (19) suggest that the prevalence of MDD among patients with diabetes is substantially lower in community settings, closely matching the level found in this report. Community samples may also have lower rates of severity than other samples. The percentage of patients who scored above CESD cut points (22.0%) is also at levels reported in other studies (18,19).

Second, our depression assessment was not staged, thus reducing potential sampling bias. Third, there are differences between the time frames covered by the two measures: past-year time of diagnosis for the CIDI and past-week time of diagnosis for the CESD. It may have been that patients who met criteria on the CIDI experienced their depression earlier in the previous year and were no longer depressed at time of assessment. However, a trend analysis for time of diagnosis within the past year showed no differences in patient demographics, disease status, behavioral, or biological variables for Dx1, Dx2, and Dx3. Furthermore, Dx1, Dx2, and Dx3 patients remained highly symptomatic at time of assessment, and 62% remained on medication. Thus, time of diagnosis within the last year is a possible but unlikely explanation for our findings.

What is particularly striking among the current findings is that the 70% of patients who scored above CESD cut points but who were not clinically depressed displayed significant deficits in behavioral and biological markers, deficits often considered to be a function of clinical depression. What, then, does the CESD measure if it is not a screening surrogate for DSM-IV MDD? Our results suggest that the CESD may be a broader, more heterogeneous measure of negative mood or emotional distress than a measure of depressive affect alone. Findings from two previous meta-analytic reports (3,19) suggest that the items of the CESD reflect symptoms of anxiety, subclinical depression, substance use, and general distress. Another report (28) demonstrated that the CESD is as good a screening tool for other Axis I disorders as it is for dysphoria. Items such as fatigue and irritability also may be symptoms of hyperglycemia. Others outside the diabetes

arena (29,30) have long argued that scales like the CESD are really measures of emotional distress, not clinical depression. They have shown that even when severity is controlled those with and without clinical depression differ on the CESD in significant ways: The clinically depressed endorse items reflecting depressed mood, anhedonia, and suicidality, whereas the nonclinically depressed but distressed score high on items reflecting hypochondriasis and insomnia. Future research should explore how reliable and coherent subsets of CESD items are linked to diabetes-specific outcomes.

Given the significant correlation between the CESD and the DDS ($r = 0.48$) and the findings from the analyses with behavioral and biological markers, we suggest that the CESD may, at least in part, reflect both general psychological distress and diabetes-specific distress in ways that are qualitatively different from clinical depression and are more related to struggles with life circumstances, including dealing with a demanding chronic disease like diabetes. The diabetes-specific component of negative mood and emotional distress may reflect not only general dysphoria around the disease and its management, but also distress associated with general health, comorbidities, regimen adherence, and other diabetes-related health care, economic, social, and family difficulties.

This is not to say that the prevalence of clinical depression is not elevated in diabetes or that depression among these patients is not a serious clinical condition worthy of concern and treatment in its own right; rather, we suggest only that a far larger number of other, nonclinically depressed patients display a high level of distress and that a significant amount of this distress is related to diabetes and its management. In fact, scoring high on the CESD is more related to these markers than receiving a diagnosis of MDD alone. This may explain why even successful treatments for clinical depression among patients with diabetes have little or no effect on diabetes management (16,27,31); they were based on studies of MDD, and the distress substantively linked to biological and behavioral disease management variables may not have been directly addressed.

Our proposed distinction between clinical depression, general emotional distress, and diabetes-specific distress has two major implications for clinical care. First, considerable research (32) has iden-

tified a highly differentiated subset of negative emotions that are linked to coronary artery disease and often co-occur with diabetes: hopelessness, pessimism, rumination, anxiety, and anger/hostility. Understanding patients' qualitative experiences of general and diabetes-specific distress should provide a greater understanding of the specific affective processes that are involved with poor behavioral disease management, rather than generically labeling the culprit as depression when, in fact, most of these patients are not clinically depressed.

A second implication is that patients with diabetes who are significantly distressed but who are not clinically depressed, and this includes 70% of those who score ≥16 on the CESD, may not profit from interventions that are derived from studies of the clinically depressed. Instead, addressing the personal, health-related, and social causes of their distress, including diabetes-specific distress with problem-solving or coping interventions, may be more meaningful and effective than initiating treatments specifically directed at clinical depression.

Several limitations may affect these findings. First, the diversity of the sample prevented a full examination of subgroup variations among the relationships reported. Second, the data reported are cross sectional, and implications about causation can only be inferred. Third, we did not explore the potential impact of other Axis I disorders, such as general anxiety or panic disorders, which have additional implications for treatment.

We have shown that 70% of patients with diabetes who reach high levels of negative mood and psychological distress, as measured by the CESD, are not clinically depressed. Yet, both general and diabetes-specific distress are significantly related to behavioral and biological diabetes outcomes, and distress is more common and more impactful than clinical depression alone. Most treatments for general and disease-specific distress, however, are derived from the depression treatment literature. New research should focus on identifying the impact of specific negative emotions, such as has been done in the coronary artery disease literature, and on clarifying the roles of both general and diabetes-specific distress so that the mechanisms of influence can be more fully understood and appropriate interventions developed.

References
1. Pouwer F, Beekman AT, Nijpels G, Dekker JM, Snoek FJ, Kostense PJ, Heine RJ, Deeq DJ: Rates and risks for co-morbid depression in patients with type 2 diabetes mellitus: results from a community-based study. *Diabetologia* 46:892–898, 2003
2. Egede LE: Effects of depression on work loss and disability bed days in individuals with diabetes. *Diabetes Care* 27:1751–1753, 2004
3. Lustman PJ, Anderson RJ, Freedland KE, de Groot M, Carney RM, Clouse RE: Depression and poor glycemic control. *Diabetes Care* 23:934–942, 2000
4. Ciechanowski PS, Katon WJ, Russo JE: Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. *Arch Int Med* 160:3278–3285, 2000
5. Egede L, Zheng D, Simpson K: Comorbid depression is associated with increased health care use and expenditures in individuals with diabetes. *Diabetes Care* 25:464–470, 2002
6. Katon WJ, Rutter C, Simon G, Lin EHB, Ludman E, Ciechanowski P, Kinder L, Young B, Von Korff M: The association of comorbid depression with mortality in patients with type 2 diabetes. *Diabetes Care* 28:2668–2672, 2005
7. Black SA, Markides KS, Ray LA: Depression predicts increased incidence of adverse health outcomes in older Mexican Americans with type 2 diabetes. *Diabetes Care* 26:2822–2828, 2003
8. First MB, Spitzer RL, Gibbon M, Williams JB: The structured clinical interview for DSM-III-R personality disorders (SCID-II). Part I. Description. *J Person Dis* 9:2–12, 1995
9. Wittchen HU: Reliability and validity studies of the WHO–Composite International Diagnostic Interview (CIDI): a critical review. *J Psychiatr Res* 28:57–84, 1994
10. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar GC: The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric

interview for DSM-IV and ICD-10. *J Clin Psychiatry* 59 (Suppl. 20):22–33, 1998

11. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J: An inventory for measuring depression. *Arch Gen Psychiatry* 4:561–571, 1961

12. Radloff LS: The CES-D scale: a self-report depression scale for research in the general population. *Applied Psychol Meas* 3:385–401, 1977

13. Spitzer RL, Kroenke K, Williams JB: Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study: Primary Care Evaluation of Mental Disorders: Patient Health Questionnaire. *JAMA* 282:1737–1744, 1999

14. Hermanns N, Kulzer B, Krichbaum M, Kubiak T, Haak T: How to screen for depression and emotional problems in patients with diabetes: comparison of screening characteristics of depression questionnaires, measurement of diabetes-specific emotional problems and standard clinical assessment. *Diabetologia* 49:469–477, 2006

15. Zich JM, Attkisson CC, Greenfield TK: Screening for depression in primary care clinics: the CES-D and the BDI. *Int J Psychiatry Med* 20:259–277, 1990

16. Katon WJ, Von Korff M, Lin EH: The Pathways Study: a randomized trial of collaborative care in patients with diabetes and depression. *Arch Gen Psychiatry* 61:1042–1049, 2004

17. Reid MC, Lachs MS, Feinstein AR: Use of methodological standards in diagnostic test research: getting better but still not good. *JAMA* 274:645–651, 1995

18. Fisher L, Chesla CA, Mullan JT, Skaff MM, Kanter RA: Contributors to depression in Latino and European-American patients with type 2 diabetes. *Diabetes Care* 24:1751–1757, 2001

19. Anderson RJ, Freedland KE, Clouse RE, Lustman PJ: The prevalence of comorbid depression in adults with diabetes. *Diabetes Care* 24:1069–1078, 2001

20. Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, Rush AJ, Walters EE, Wang PS: The epidemiology of major depressive disorder: tesults from the National Comorbidity Survey Replication. *JAMA* 289:3095–3105, 2003

21. Kessler RC, Chiu WT, Demler O, Walters MSP: Prevalence, severity and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiat* 62:617–627, 2005

22. Mullan JT, Fisher L, Skaff MM, Polonsky WH: The diabetes distress scale: a replication. *Diabetes* 55 (Suppl. 1):A426–A427, 2006

23. Polonsky WH, Fisher L, Earles J, Dudl RJ, Lees J, Mullan JT, Jackson RA: Assesing psychosocial stress in diabetes. *Diabetes Care* 28:626–631, 2005

24. Block G, Hartman AM, Naughton D: A reduced dietary questionnaire: development and validation. *Epidemiology* 1:58–64, 1990

25. Ainsworth BE, Haskell WL, Whitt MC: Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc* 32:S498S504, 2000

26. Fisher L, Laurencin G, Chesla CA, Skaff MM, Mullan JT, Gardiner PS, Chun KM: Depressive affect among four ethnic groups of male patients with type 2 diabetes. *Diabetes Spectrum* 17:215–218, 2004

27. Lin EH, Katon WJ, Rutter C, Simon GE, Ludman EJ, Von Korff M, Young B, Oliver M, Ciechanowski PS, Kinder L, Walker E: Effects of enhanced depression treatment on diabetes self-care. *Ann Fam Med* 4:46–53, 2006

28. Fechner-Bates S, Coyne JC, Schwenk TL: The relationship of self-reported distress to depressive disorders and other psychopathology. *J Clin Consult Psychol* 62:550–559, 1994

29. Coyne JC: Self-reported distress: analog or Ersatz depression? *Psychol Bull* 116:29–45, 1994

30. Coyne JC, Thompson R, Racioppo MW: Validity and efficiency of screening for history of depression by self-report. *Psychol Assess* 13:163–170, 2001

31. Williams JW, Katon WJ, Lin EH: The effectiveness of depression care management on diabetes-related outcomes in older patients. *Ann Int Med* 140:1015–1049, 2004

32. Kubzansky LD, Davidson KW, Rozanski A: The clinical impact of negative psychological states: expanding the spectrum of risk for coronary artery disease. *Psychosom Med* 67:S10–S14, 2005