Depression in Diabetes: Have We Been Missing Something Important?

Jeffrey S. Gonzalez, phd[1,2]
Lawrence Fisher, phd[3]
William H. Polonsky, phd, cde[4,5]

An extensive literature has developed to suggest that depression is more common in patients with diabetes than in the general population (1) and is associated with chronic hyperglycemia (2), risk for diabetes complications (3), and mortality (4). Although the causal linkages among these relationships have not been demonstrated, their consistency has led to calls for intensive efforts to identify and treat clinical depression in patients with diabetes, with the reasonable presumption that this will contribute to better diabetes outcomes. Recent studies, however, suggest a more complicated picture and cast doubt on this presumption.

Although research has suggested that the prevalence of clinical depression, or major depressive disorder (MDD), among adults with diabetes may be two to three times greater than among community adults (1), recent studies—which have used structured clinical interviews, the gold standard in the diagnosis of MDD—suggest that it is only about 60% more common (5). More importantly, diabetes-related distress, or significant negative emotional reactions to the diagnosis of diabetes, threat of complications, self-management demands, unresponsive providers, and/or unsupportive interpersonal relationships, has been found to be far more common, more chronic, and more closely related to diabetes self-care and glycemic control than MDD (5–7).

Symptoms of depression, such as depressed mood, diminished interest, loss of energy, and concentration difficulties, that are elevated but do not meet severity criteria for MDD (referred to here as depressive symptoms) are also quite common among patients with diabetes and are associated with poor self-care (8). Furthermore, increased risk of complications and early mortality is not limited to those with MDD but also extends to those with elevated depressive symptoms, even when these elevations are quite modest (4). This suggests an incremental relationship between the severity of depressive symptoms and poorer diabetes outcomes rather than an effect of MDD per se.

There is minimal evidence for a longitudinal relationship between MDD and hyperglycemia over time, and changes in one over time do not appear to be associated with changes in the other (7). Numerous treatment studies have shown positive effects for the improvement of MDD in diabetic patients, but evidence for resulting glycemic benefit is, at best, weak (9).

The current commentary seeks to shed light on the discontinuity among these findings. First, we suggest that there has been considerable confusion among MDD, diabetes-related distress, and depressive symptoms. We argue that this confusion has been exacerbated by measurement problems that stem from the lack of a clear distinction between MDD and nonpsychiatric emotional distress. Second, we suggest that this has led to a narrow focus on potential intervention approaches, originally developed for MDD, that may be limited in their ability to address diabetes-related distress and depressive symptoms. Although we do not deny the importance of true psychiatric presentations of MDD among those with diabetes, traditional approaches to MDD treatment may be unlikely to improve diabetes outcomes unless they also incorporate strategies to address important relationships between MDD and chronic illness (rev. in 10). Finally, we suggest an alternative approach to understanding the common experience of emotional distress in diabetes that emphasizes the demanding experience of diabetes and requires diabetes-specific measurement and treatment approaches.

Have we been using the wrong assessment approach?

There is a recurrent disconnect in the diabetes literature between the conceptual basis of emotional distress and the measurement methods we use. The predominant conceptual model that underlies the current understanding of emotional distress in diabetes, whether explicit or implicit, is the psychiatric diagnosis of MDD. However, the vast majority of studies rely on self-report questionnaires that assess symptoms of distress that are often only loosely associated with the diagnostic criteria for MDD. These self-report measures have been shown to be more reflective of general emotional distress than MDD (11). Furthermore, they may fully capture but inappropriately pathologize diabetes distress and depressive symptoms. The physical symptoms associated with diabetes further complicate distress assessment because they may be mistaken for symptoms of MDD. Even though many self-report measures have been developed with acceptable psychometric properties for detecting MDD, they often achieve a satisfactory level of sensitivity at the expense of yielding a high percentage of false-positives (12). Thus, diabetic patients experiencing depressive symptoms and/or diabetes distress may be misclassified as having MDD, especially when self-report measures are used.

Studies that have used both self-report questionnaires for depressive symptoms and structured interviews based on MDD diagnostic criteria suggest that these measures tap into different constructs that have independent associations with diabetes. For example, 70% of diabetic patients with elevated self-reported depressive symptom scores did not meet diagnostic criteria for MDD on

From the [1]Ferkauf Graduate School of Psychology, Yeshiva University, Bronx, New York; the [2]Einstein Diabetes Research Center, Albert Einstein College of Medicine, Bronx, New York; the [3]Department of Family and Community Medicine, University of California, San Francisco, San Francisco, California; the [4]Department of Psychiatry, University of California, San Diego, San Diego, California; and the [5]Behavioral Diabetes Institute, San Diego, California.
Corresponding author: Jeffrey S. Gonzalez, jeffrey.gonzalez@einstein.yu.edu.
Received 18 October 2010 and accepted 18 October 2010.
DOI: 10.2337/dc10-1970

the basis of a structured clinical interview (6). More importantly, depressive symptoms and diabetes distress, which shared only 23% of their variance, were each associated with problematic diabetes self-management, whereas MDD was not (6). A subsequent study further demonstrated that diabetes distress covaried with hyperglycemia over time, but depressive symptoms and MDD did not (7). Thus, it appears that MDD, depressive symptoms, and diabetes distress are distinct constructs with independent relationships to diabetes.

We believe that much of the overapplication of the MDD conceptual model to the problem of distress in diabetes is linked to the fact that the contemporary diagnostic system for MDD is based only on symptom assessment (number, duration, and degree of impairment) and ignores the life context in which these symptoms occur. As Horowitz and Wakefield (13) compellingly argue, this represents a departure from a long-standing history of thought, from Hippocrates to Kraepelin, that emphasizes the importance of situational context in the diagnosis of clinical depression. Evaluating symptoms only, regardless of their derivation (e.g., diabetes, job loss, divorce), may improve the reliability of diagnosis, but it sacrifices validity and obfuscates the great heterogeneity of presentations that are, in our view, often misclassified as MDD (leading inexorably, as we discuss below, to inappropriate treatments).

This symptom-based and context-neutral approach to conceptualizing and assessing MDD is particularly problematic for patients with diabetes, leading to both an overpathologizing of patients and an underappreciation of the role of chronic illness in explaining emotional symptoms. For example, in a well-defined sample of patients with diabetic peripheral neuropathy, investigators showed that objective indicators of neuropathy severity, neuropathy-related symptoms, impairment in daily activities due to neuropathy and neuropathy-related changes in important roles were predictive of increases in depressive symptoms over time (14). Thus, a cascade of disease-related factors, from objective indicators of severity to subjective ratings of functional impairment, contributed to the development of depressive symptoms in these patients. Applying the label of MDD to the outcome of these studies would not only inaccurately pathologize the observed level of depressive symptoms, it would also ignore the disease-associated factors that explain them.

The importance of disease-associated functional impairment, in particular, as a contributor to distress in chronic illness has strong empirical support. For example, disease-related physical limitations predict changes in subsequent depressive symptoms over time, but depressive symptoms do not predict corresponding changes in physical limitations (15). Furthermore, although epidemiological data consistently link MDD and physical illness, the strength of this association diminishes with age; impairments at young ages of adulthood are more strongly associated with MDD than those occurring at advanced ages, when some loss in functioning is normative and expected (16). The link between chronic illness and depressive symptoms similarly diminishes with age, as does the association between functional disability and depressive symptoms (17). Thus, life context (e.g., expectations of functioning in important roles) is crucial for explaining the link between disease and significant emotional distress. The current MDD-focused model ignores this context and when applied to patients with diabetes leads to an underappreciation of the impact of demanding treatment regimens, ongoing threats of serious complications, and associated functional impairment that may contribute to the experience of distress.

Have we been using the wrong treatment approach?

The implications of this argument go far beyond questions of semantics; the overapplication of the MDD-model to the problem of distress in people with diabetes has also led to a narrow focus on treatments for clinical depression that may not be appropriate for the majority of distressed patients. For example, meta-analysis has demonstrated that antidepressants, though widely prescribed as a treatment for MDD, may be no more effective than placebo for mild to moderate levels of symptom severity; clinically significant benefits are only observed at "very severe" levels of impairment (18). Thus, exporting existing treatments for MDD to the greater population of diabetic patients experiencing disease-related distress or depressive symptoms may be ill advised. Interventions that have attempted this among those with diabetes have focused rather narrowly on reducing the severity of MDD with antidepressants or psychotherapy and, for the most part, have not attended to the co-occurring, linked problems of living with and managing the stress of diabetes. Moreover, they have failed to show compelling evidence that amelioration of MDD leads to improved diabetes management or glycemic control (9).

Newer intervention approaches reflect an evolution in MDD-focused treatment by concurrently addressing co-occurring problems with diabetes management. These include interventions that integrate psychological treatments with exercise training (20), nurse-led self-management support (21), and nurse-, dietitian-, and mental health-specialist–delivered self-management interventions (22). In contrast to previous intervention studies that focused solely on the amelioration of MDD, these studies also address the behavioral barriers to successful diabetes treatment and, therefore, may be more successful in improving diabetes health outcomes. Novel approaches to the emotional aspects of diabetes management are clearly needed for the far larger population of patients struggling with diabetes-related distress and/or depressive symptoms but who are not clinically depressed.

Although very few intervention studies have targeted diabetes distress directly, several trials have attempted to integrate behavioral and distress-related changes into a single, comprehensive intervention. For example, a small trial of cognitive behavioral therapy adapted to address diabetes-relevant behavior change improved both glycemic control and diabetes distress in adults with poorly controlled type 1 diabetes, compared with a control condition, with benefits maintained over 1 year of follow-up (23). Similar benefits were seen from a peer-delivered self-management intervention in Spanish-speaking type 2 diabetic patients: both glycemic control and diabetes-related distress improved relative to control subjects, and improvements were maintained over 18 months (24). These studies suggest that co-occurring improvements in disease management and diabetes distress can be achieved through interventions that target both of these linked problems.

Recommendations for clinical practice: toward a new model of care

It is time to recognize that the marked emotional distress commonly seen in patients with diabetes may not be a traditional depressive disorder, no matter the

elevated score on a self-reported depression questionnaire nor the presentation of recognizable MDD symptoms. A new treatment model to understand and address the emotional concomitants of diabetes is needed. Diabetes-related distress and depressive symptoms are clearly associated with problems of poor diabetes self-management and clinical outcomes and, therefore, should be recognized as important indicators of diabetes self-management. This is consistent with dominant theories on the functional implications of emotion, which argue that emotions, both positive and negative, serve to indicate how well a behavior is leading to a desired outcome or goal (25). Conceptualizing emotional distress within the context of the self-regulation of diabetes management supports intervention approaches that target problems with self-management, including addressing dysfunctional beliefs about diabetes and reducing the tendency to disengage from the pursuit of goals when experiencing emotional distress, rather than treatments that focus exclusively on reducing symptoms of distress disconnected from the diabetes-relevant issues that prompt them (10).

This comprehensive approach to the management of diabetes and nonpsychiatric emotional distress (including depressive symptoms and diabetes-related distress) requires several changes to how we deliver care to patients with diabetes. First, emotional distress should be considered a common component of the experience of diabetes; it falls within the spectrum of diabetes management and is not a comorbid disorder. Second, because of the reciprocal influences between emotional distress and diabetes self-management, distress can indicate increased risk for poor treatment outcomes; interventions that focus on addressing both distress and diabetes management are likely to have stronger effects than those that focus on either in isolation (21). Understanding the diabetes-related factors that drive the experience of distress is crucial to the development of appropriate interventions. Third, levels of distress can vary considerably over time, following or preceding changes in diabetes status, and should be evaluated regularly as part of ongoing, comprehensive diabetes care. Fourth, there are major advantages to treating the large number of distressed patients within the diabetes practice environment rather than referring them to other health care providers: comprehensive approaches to care that recognize the bidirectional relationship between distress and diabetes management are likely to have maximal effects.

Although validated and easy-to-use screening instruments for diabetes-related distress are presently available (25,26), an ongoing clinical conversation about distress may be the most effective and time-sensitive clinical approach. It avoids false-positives and over-pathologizing common nonpsychiatric distress that can occur with many screening instruments designed to detect MDD and allows for the evaluation of the context that might explain any distress that is reported. The results of a brief conversation can also guide the selection of appropriate intervention. Patients reporting distress secondary to frustration about chronic hyperglycemia or fear of complications (i.e., diabetes-related distress) will likely need different interventions than patients who report being distressed because of life circumstances unrelated to diabetes. Although antidepressants are unlikely to be effective in most presentations of distress (18), physical activity, psychotherapeutic approaches, and discussions with diabetes team members can be effective. Patients are often relieved when health care providers initiate discussions about their distress. Even brief conversations that label feelings, link them to difficulties with self-management and normalize emotional reactions to diabetes issues can be re-assuring; indeed, even the patient's verbalization and expression of emotional experiences of diabetes can be therapeutic.

While this comprehensive approach to the assessment and management of distress in diabetes has clear advantages over the current fragmented model of care in the U.S., it may conflict with the existing realities of treatment delivery. The time pressures of clinical care may leave practitioners unwilling to add tasks to an already densely packed clinical encounter. Furthermore, many diabetes team members may be uncomfortable addressing the emotional components of diabetes care, and may be concerned about opening a Pandora's Box that they fear will be difficult to close. We believe that addressing the emotional aspects of living with diabetes does not require extensive mental health training, although some patients, especially those who are experiencing MDD or profound and longstanding depressive symptoms or diabetes distress, may require a referral for specialized care. Rather, all team members should be skilled in attentive and empathic listening, sensitive verbal inquiry, and use of thoughtful and reflective comments—skills that are the hallmarks of good clinical care. Documentation of the content and level of distress that include summaries of discussions among team members as part of clinical care requires only a small shift in perspective. A comprehensive approach that distinguishes clinical depression from disease-related distress and that offers support for the management of emotional distress as an integral part of providing support for the behavioral management of diabetes will have the greatest likelihood of clinical benefit for the vast majority of patients with diabetes.

Acknowledgments— J.S.G is supported by a Grant DK 020541from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). L.F. is supported by grant 2 R01 DK 061937 from NIDDK.

No potential conflicts of interest relevant to this article were reported.

References

1. Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. Diabetes Care 2001;24:1069–1078
2. Lustman PJ, Anderson RJ, Freedland KE, de Groot M, Carney RM, Clouse RE. Depression and poor glycemic control: a meta-analytic review of the literature. Diabetes Care 2000;23:934–942
3. de Groot M, Anderson R, Freedland KE, Clouse RE, Lustman PJ. Association of depression and diabetes complications: a meta-analysis. Psychosomatic Medicine 2001;63:619–630
4. Black SA, Markides KS, Ray LA. Depression predicts increased incidence of adverse health outcomes in older Mexican Americans with type 2 diabetes. Diabetes Care 2003;26:2822–2828
5. Fisher L, Skaff MM, Mullan JT, Arean P, Glasgow R, Masharani U. A longitudinal study of affective and anxiety disorders, depressive affect and diabetes distress in adults with type 2 diabetes. Diabet Med 2008;25:1096–1101
6. Fisher L, Skaff MM, Mullan JT, Arean P, Mohr D, Masharani U, Glasgow R, Laurencin G. 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, 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 longi-

tudinal analyses. Diabetes Care 2010;33:23–28
8. Gonzalez JS, Safren SA, Cagliero E, Wexler DJ, Delahanty L, Wittenberg E, Blais MA, Meigs JB, Grant RW. Depression, self-care, and medication adherence in type 2 diabetes: relationships across the full range of symptom severity. Diabetes Care 2007;30:2222–2227
9. Markowitz S, Gonzalez J, Wilkinson J, and Safren S. Treating depression in diabetes: emerging findings. Psychosomatics. In Press
10. Detweiler-Bedell JB, Friedman MA, Leventhal H, Miller IW, Leventhal EA. Integrating co-morbid depression and chronic physical disease management: identifying and resolving failures in self-regulation. Clin Psychol Rev 2008;28:1426–1446
11. Coyne JC. Self-reported distress: Analog or Ersatz depression? Psychol Bull 1994;116:29–45
12. Thombs BD, de Jonge P, Coyne JC, Whooley MA, Frasure-Smith N, Mitchell AJ, Zuidersma M, Eze-Nliam C, Lima BB, Smith CG, Soderlund K, Ziegelstein RC. Depression screening and patient outcomes in cardiovascular care: a systematic review. JAMA 2008;300:2161–2171
13. Horowitz AV, Wakefield JC. *The Loss of Sadness: How Psychiatry Transformed Normal Sorrow into Depressive Disorder*. New York, Oxford University Press, 2007
14. Vileikyte L, Peyrot M, Gonzalez JS, Rubin RR, Garrow AP, Stickings D, Waterman C, Ulbrecht JS, Cavanagh PR, Boulton AJ. Predictors of depressive symptoms in persons with diabetic peripheral neuropathy: a longitudinal study. Diabetologia 2009;52:1265–1273
15. Gayman MD, Turner RJ, Cui M. Physical limitations and depressive symptoms: exploring the nature of the association. J Gerontol B Psychol Sci Soc Sci 2008;63:S219–S228
16. Kessler RC, Birnbaum H, Bromet E, Hwang I, Sampson N, Shahly V. Age differences in major depression: results from the National Comorbidity Survey Replication (NCS-R). Psychol Med 2010;40:225–237
17. Schnittker J. Chronic illness and depressive symptoms in late life. Soc Sci Med 2005;60:13–23
18. Fournier JC, DeRubeis RJ, Hollon SD, Dimidjian S, Amsterdam JD, Shelton RC, Fawcett J. Antidepressant drug effects and depression severity: a patient-level meta-analysis. JAMA 2010;303:47–53
19. de Groot M, Kushnick M, Doyle T, Merrill J, McGlynn M, Shubrook J, Schwartz F. A model of community-based behavioral intervention for depression in diabetes: program ACTIVE. Diabetes Spectr 2010;23:18–25
20. Katon W, Lin EH, Von Korff M, Ciechanowski P, Ludman E, Young B, Rutter C, Oliver M, McGregor M. Integrating depression and chronic disease care among patients with diabetes and/or coronary heart disease: the design of the TEAMcare study. Contemp Clin Trials 2010;31:312–322
21. Gonzalez JS, McCarl LA, Wexler DJ, Cagliero E, Delahanty L, Soper TD, Goldman V, Knauz R, Safren SA. Cognitive-behavioural therapy for adherence and depression (CBT-AD) in type 2 diabetes. J Cogn Psychother 2010;24:329–343
22. Amsberg S, Anderbro T, Wredling R, Lisspers J, Lins PE, Adamson U, Johansson UB. A cognitive behavior therapy-based intervention among poorly controlled adult type 1 diabetes patients–a randomized controlled trial. Patient Educ Couns 2009;77:72–80
23. Lorig K, Ritter PL, Villa F, Piette JD. Spanish diabetes self-management with and without automated telephone reinforcement: two randomized trials. Diabetes Care 2008;31:408–414
24. Carver CS. Affect and the functional bases of behavior: on the dimensional structure of affective experience. Pers Soc Psychol Rev 2001;5:345–356
25. Polonsky WH, Fisher L, Earles J, Dudl RJ, Lees J, Mullan J, Jackson RA. Assessing psychosocial stress in diabetes: development of the Diabetes Distress Scale. Diabetes Care 2005;28:626–631
26. Polnsky WH, Anderson BJ, Lohrer PA, Welch G, Jacobson AM, Schwarz C (1995). Assessment of diabetes-specific distress. Diabetes Care, 18, 754–760