Chapter 2
Psychological Issues in Adults with Type 2 Diabetes

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2.1 Introduction

The global epidemic of type 2 diabetes is a major public health problem, with the world prevalence among adults estimated to be 6.4% for 2010. By 2030, it is expected that the burden of diabetes will affect more than 439 million adults worldwide or 7.7% of the global population. Over the next 20 years, the developed world will see an increase of 20% in the number of adults living with diabetes and developing countries will see an increase of 69% (Shaw, Sicree, & Zimmet, 2010). As the prevalence of diabetes rises, so too does the importance of improving the treatment outcomes and the prevention of complications among those affected.

In this chapter, we focus on type 2 diabetes mellitus (T2DM) in adult populations, although we occasionally draw on data from the literature on type 1 diabetes mellitus (T1DM) where literature is lacking for patients with T2DM. T2DM is the most common type of diabetes, accounting for approximately 90% of diabetes cases in the United States and is usually diagnosed in adulthood, although child and adolescent cases are becoming more common. While T1DM involves an absolute insulin deficiency caused by an autoimmune response that destroys pancreatic beta cells, resulting in a total insulin deficiency, T2DM involves a combination of insulin resistance and relative insulin deficiency (Fowler, 2007) and may not require treatment...
with external insulin, especially at early stages. In either case, the goal of treatment of diabetes is to achieve strict control of blood sugar (glucose) levels. Obesity is associated with insulin resistance and this may be the reason that obesity is more common among patients with T2DM and is associated with worse diabetes control and treatment outcomes. As such, lifestyle factors related to diet and exercise are important in the management of glucose levels in T2DM in addition to treatment adherence to prescribed medications that act to lower blood sugar levels. The ability to successfully manage T2DM is largely dependent upon patient adherence to an intensive set of self-care behaviors (Anderson, 1995) involving adherence to prescribed medications, monitoring of blood glucose, adherence to dietary and physical activity recommendations, preventive foot care, attendance at medical appointments, and regular screening for complications. Self-care in diabetes is extremely important in the prevention of poor health outcomes. Adherence to treatment guidelines helps achieve good diabetes control, reduces cardiovascular risk, and decreases risk of complications and mortality (American Diabetes Association [ADA], 2009; Hartz et al., 2006; Ho et al., 2006). Self-care activities, such as increasing physical activity and maintaining healthy nutrition, can slow disease progression (Glasgow, Boles, McKay, Feil, & Barrera, 2003; Newman, Steed, & Mulligan, 2004; Norris, Engelgau, & Venkat Narayan, 2001). However, diabetes self-care places a significant burden of time and effort on patients; it has been estimated that approximately 2 h/day are required to meet the ADA-recommended guidelines for self-care for patients taking oral medications for diabetes (Russell, Suh, & Safford, 2005). A meta-analysis by DiMatteo, Lepper, and Croghan (2000) demonstrated that patients with diabetes, like patients with other chronic illnesses, exhibit suboptimal adherence to medical recommendations (Ingersoll & Cohen, 2008). Deficiencies in self-care often result from patients’ inability to appreciate the long-term benefits of adherence, such as a reduction in the risk of diabetes-related complications and a tendency to focus on the short-term disadvantages of self-care activities, such as medication side effects and lifestyle disruption (Rubin, 2005). Nationally representative data show that less than half of patients with diabetes are able to meet goals for glycemic control, and when control of blood pressure and cholesterol is also taken into account, fewer than 10% of patients are achieving recommended levels of glycemic control and optimal control over cardiovascular disease risk factors as recommended by the ADA (Saydah, Fradkin, & Cowie, 2004).

We emphasize the importance of treatment adherence in determining the health outcomes of patients with T2DM and highlight the difficulties that many patients have in achieving diabetes treatment goals as a context in which to consider the role of psychopathology in patients with T2DM. Below we review: (1) the evidence for higher prevalence of various psychological problems in patients with diabetes as compared to the general population, (2) the association between various psychological problems and diabetes treatment outcomes, including an examination of potential mechanisms, and (3) assessment and treatment issues related to addressing these psychological problems and the impact they may have on diabetes outcomes. At the outset of this review, we would like to urge clinicians to bear in mind
that the treatment of diabetes requires changes in health behavior and intensive self-management of treatment. These are difficult tasks for most patients with T2DM, and those who are suffering from psychological problems are likely to have even greater difficulty. Therefore, clinicians have an important opportunity to address health behavior and treatment adherence in their approaches to psychopathology in patients with diabetes. Such an approach may improve not only the psychological outcomes of treatment, but may also have a beneficial impact on health outcomes.

2.2 Depression

2.2.1 Epidemiology

Major depressive disorder (MDD) is a highly prevalent and serious illness, with lifetime prevalence of 17% and a point prevalence of 7% in the general US population (Kessler, Berglund, et al., 2005; Kessler, Chiu, Demler, & Walters, 2005). It is among the most serious health problems in the country, associated with substantial suffering, lost productivity, and loss of life (Klerman & Weissman, 1989, 1992; Stewart, Ricci, Chee, Hahn, & Morganstein, 2003). Individuals with MDD experience reduced functioning and decreased quality of life, as well as higher health care utilization and costs, and disability (Bijl & Ravelli, 2000; Eren, Erdi, & Mehmet, 2008; Katon et al., 2003; Katz, 1996; Pennix et al., 1998; Pennix, Leveille, Ferrucci, van Eijk, & Guralnik, 1999; Spitzer et al., 1995). Furthermore, depression is more prevalent in patients with chronic illness in general and diabetes in particular; meta-analyses of the available literature suggest that the point prevalence of depression in diabetes patients is nearly twice as high as the prevalence found in nondiabetic adults (Ali, Stone, Peters, Davies, & Khunti, 2006; Anderson, Freedland, & Clouse, 2001). Most of the studies included in these meta-analyses did not focus on the assessment of MDD, but rather on elevated symptoms of depression. Those studies that used structured diagnostic interviews tended to find somewhat lower prevalence rates (Ali et al.; Anderson et al.). A large scale, international, population-based survey of diabetes patients in 17 countries used a structured diagnostic interview to assess the presence of various mental disorders and found the overall odds of MDD to be 40% greater in participants with diabetes compared to those without diabetes. The overall odds of dysthymia were approximately 30% greater, but this difference did not reach statistical significance (Lin et al., 2008). Fisher et al. (2008) evaluated over 500 T2DM patients with a structured clinical interview and found prevalence rates of MDD and dysthymia to be 60% and 7% higher, respectively, relative to community adults assessed with the same diagnostic interview. The results reported by Fisher et al. also show that the prevalence of elevated depressive affect and distress was much higher than the prevalence of any mood disorder and these subclinical conditions tended to be more persistent over time.
Although aggregate studies tend to find that the point prevalence of clinically significant depression is twice as high in diabetes patients as in patients without diabetes, studies using the strongest methods of assessment suggest that the prevalence of MDD is more likely to be on the order of 40–60% more prevalent. Differences in prevalence rates for dysthymia, though less often evaluated, appear to be less significant. Meta-analyses of the literature have shown that depression is consistently associated with hyperglycemia (Lustman, Anderson, et al., 2000), risk of diabetes complications (de Groot, Anderson, Freedland, Clouse, & Lustman, 2001), and diabetes treatment nonadherence (Gonzalez, Peyrot, et al., 2008). Several studies have also linked depression to increased risk for mortality (Black, Markides, & Ray, 2003; Katon et al., 2005, 2008; Zhang et al., 2005). Importantly, subclinical symptoms of depression and distress tend to be very common in patients with diabetes, are persistent over time, and are more closely related to diabetes control than mood disorders per se (Fisher et al., 2008). Subclinical symptoms of depression are also associated with treatment nonadherence (Gonzalez et al., 2007) and risk of complications and mortality (Black et al., 2003) in patients with T2DM.

2.2.2 Pathophysiology

Diabetes and depression appear to have a consistent bidirectional relationship, with depression often preceding the development of T2DM in adults (Mezuk, Eaton, Albrecht, & Golden, 2008). If these relationships are causal, it is possible that depression and diabetes may be related through either biological or behavioral pathways. Biological pathways through which depression may impact diabetes and its complications include hormonal abnormalities, alterations in glucose transport function, and increased immuno-inflammatory activation (Golden, 2007; Musselman, Betan, Larsen, & Phillips, 2003). The available literature does not yet provide definitive answers about whether biological processes associated with depression may mediate the relationship between depression and diabetes outcomes or whether negative health behaviors associated with depression such as inactivity, poor diet, smoking, and nonadherence to treatment recommendations and self-care may be important explanatory factors. These same biobehavioral factors may be involved in explaining the risk of developing T2DM in depressed individuals. An additional important health behavior that may be implicated in the relationship between depression and diabetes is cigarette smoking; individuals with depression and other mood disorders smoke at higher rates than the general population (McClave et al., 2009; Mueser & McGurk, 2004; Spangler, Summerson, Bell, & Konen, 2001; Ziedonis, Williams, Smelson, 2003) and smoking is associated with insulin resistance, reduced insulin secretion responses, increased central adiposity, and the development of T2DM (ADA, 2004; Willi, Bodenmann, Ghali, Faris, & Cornuz, 2007). At this point, it is not clear whether the relationship between diabetes
and depression is causal or whether the association may be explained by shared environmental and genetic factors, confounding between depression and severity of diabetes or other co-morbid illnesses, etc. Nevertheless, the consistency of the relationship between depression and worse diabetes treatment outcomes has led to an increased focus on improving the recognition and treatment of depression in patients with diabetes in the hopes that such treatment may also improve health outcomes of patients with T2DM.

2.2.3 Clinical Care

2.2.3.1 Assessment and Diagnostic Issues

Assessment of depression in diabetes patients can be challenging both to mental health professionals and medical staff. Confounding between physical symptoms known to be associated with diabetes and those that are part of the diagnostic criteria for MDD (e.g., concentration difficulties, appetite disturbance and weight changes, sleep disturbance, fatigue) complicates the diagnosis of MDD in patients with diabetes and may lead to mistakenly identifying diabetes-related symptoms as symptoms of depression. Various self-report measures have been used to assess depression in patients with diabetes including the Beck Depression Inventory (Beck, Steer, & Brown, 1996), the Centers for Epidemiologic Studies Depression Scale (CESD; Radloff, 1977), and the PHQ-9 (Kroenke, Spitzer, & Williams, 2001). While the potential for confounding between diabetes-related symptoms and scores on these scales has not often been examined, an early study did suggest that the BDI could effectively discriminate between diabetes patients with and without MDD, regardless of whether the total score, the somatic items, or the cognitive items were used (Lustman, Clouse, Griffith, & Carney, 1997). It is recommended that a careful assessment of depression in diabetes should include the use of a structured clinical interview as data have shown that approximately 70% of T2DM patients who score above the cutoff for clinically significant depression on the CESD do not meet criteria for MDD or dysthymia based on a structured clinical interview. Furthermore, 34% of those who met criteria based on a structured clinical interview did not reach the CESD cutoff (Fisher et al., 2007). It is important to note that even those patients who fall short of meeting criteria for a formal diagnosis of a mood disorder, but who nevertheless report significant symptoms of depression may be at elevated risk for worse diabetes outcomes (Black et al., 2003; Fisher et al., 2007; Gonzalez et al., 2007). Therefore, recognizing and providing treatment for subclinical presentations of depression is recommended.

An additionally important assessment issue is differentiating symptoms of depression that are directly associated with living with the burden of diabetes from those that may be more independent of diabetes. Fisher and colleagues have published several studies suggesting that diabetes-specific distress may be more
closely related to problems with diabetes treatment adherence and worse diabetes control than distress assessed by generic depression instruments, such as the CESD (Fisher et al., 2007, 2008, 2010). Thus, measuring symptoms of distress that are specific reactions to living with diabetes may have clinical importance. Even general symptoms of depression are closely tied to aspects of living with diabetes. For example, patients on insulin therapy consistently report higher levels of depression than those who are not taking insulin (e.g., Gonzalez et al., 2007; Katon, Von Korff, et al., 2004). Two studies of patients with diabetic peripheral neuropathy have compellingly demonstrated how aspects of the illness itself, including objective indicators of neuropathy severity, symptoms such as unsteadiness and pain, limitations in activities of daily living, and changes in role functioning, are linked to generic symptoms of depression, both cross-sectionally and longitudinally (Vileikyte et al., 2005, 2009). These findings underscore the importance of a comprehensive assessment of depressive symptoms that carefully evaluates the relationship between these symptoms and important aspects of living with diabetes. The patient’s perspective on these relationships may have implications for the selection of treatments that address the burden of diabetes vs. those that treat depression with less focus on the context of diabetes.

2.2.3.2 Evidence-Based Treatment

Various randomized trials of treatments for depression have been conducted in patients with diabetes (for a review see Markowitz, Gonzalez, Wilkinson, & Safren, 2011). These interventions have included cognitive-behavioral therapy (CBT) and a variety of other approaches and, while overall these interventions have shown promise in successfully reducing the severity of depression, results on glycemic control and treatment adherence have been much less promising. However, there is good reason to suspect that treating depression may be necessary, but not sufficient in order to improve diabetes outcomes for depressed diabetes patients. Meta-analyses of depression’s relationship to hyperglycemia (Lustman, Anderson, et al., 2000), diabetes complications (de Groot et al., 2001), and diabetes treatment nonadherence (Gonzalez, Peyrot, et al., 2008) suggest that while the relationships between depression and these important diabetes outcomes are robust, they are also in the small to medium range. Thus, even if the relationships between depression and these outcomes are causal, amelioration of depression may result in only modest improvements in these diabetes-related outcomes. It is clear that treatment adherence and lifestyle modifications are perhaps the strongest determinants of diabetes treatment outcomes and interventions aimed at improving self-management of diabetes patients have consistent effects on glycemic control (Norris et al., 2004). Patients with diabetes and depression may need comprehensive treatment that targets adherence to this demanding regimen in addition to treatment for their depression. Intervention approaches that integrate adherence training and support for changing health behaviors with strategies aimed at treating depression may capitalize on the consistent relationship between
depression and nonadherence and may result in greater improvements in diabetes control than interventions that focus on depression alone.

Safren and colleagues have developed a psychological treatment model for the integration of CBT with adherence counseling for patients with chronic illness, CBT for adherence and depression (CBT-AD; Safren, Gonzalez, & Soroudi, 2008a, 2008b; Soroudi et al., 2008). The integration of adherence training with cognitive-behavioral techniques in CBT-AD is based on the belief that the strategies employed in CBT for depression (e.g., activity scheduling and mood monitoring, cognitive restructuring) have important applications in facilitating successful treatment adherence in patients with chronic illness (e.g., increasing physical activity, monitoring behavior change, correcting maladaptive beliefs about the illness, and treatment). It is also based on the belief that there is often a bidirectional relationship between depression and the management of medical illness and interventions that improve patients’ ability to successfully manage their illness that will result in an improved sense of self-efficacy and mastery, which will in turn improve patients’ cognitions and underlying negative mood states. Each session of the treatment focuses on the difficulties that the patient is having with disease management, the symptoms of depression that the patient is experiencing, and how these two problems influence each other. The strategies employed are presented to the patient as equally applicable to the difficulties of illness management as to the symptoms of depression.

CBT-AD is an individually delivered program consisting of six modules addressing motivational enhancement and orientation to the program, adherence counseling, behavioral activation, cognitive restructuring, problem solving, and relaxation training. The sequencing of modules and the number of sessions spent on each module is flexible, though it is intended to take approximately 10–12 sessions in total. This approach has been shown to be successful in a recent two-arm randomized crossover trial comparing CBT-AD to enhanced usual care in 45 depressed individuals with HIV/AIDS. Results showed that those who received CBT-AD achieved significantly greater improvements in medication adherence and depression relative to the control group, with control participants who crossed-over to CBT-AD after the acute outcome assessment achieving similar improvements in both depression and adherence outcomes. Treatment gains for those in the intervention group were generally maintained at 6- and 12-month follow-up assessments (Safren et al., 2009).

CBT-AD is currently being evaluated in an ongoing randomized controlled trial in depressed patients with T2DM (NIH 1R01 MH078571). While outcome data are not yet available, data from an open phase pilot of five depressed T2DM patients have been completed (Gonzalez et al., 2010). This study provides preliminary evidence for a successful adaptation of CBT-AD, originally developed for patients with HIV, for patients with T2DM. CBT-AD appears to have been acceptable to all patients and successful in improving diabetes self-care and depression. All participants experienced an improvement in depressive symptoms and four of five patients demonstrated improvements in both depression and glycemic control. All participants reported improvement in self-reported glucose testing and all participants reported either a maintenance or improvement in self-reported
medication adherence. These results are promising in suggesting that interventions that target both adherence and depression may maximize treatment benefits for diabetes patients.

Pharmacological interventions for depression have been recommended for patients with diabetes, both to reduce depression and improve glycemic control. Selective serotonin reuptake inhibitors (SSRIs) are the most commonly prescribed antidepressants because of their safety profile and their efficacy (MacGillivray et al., 2003; Sclar, Robinson, Skaer, & Galin, 1998). They have been recommended in depressed patients with diabetes, because they may lower glucose levels and result in weight loss in addition to their antidepressant properties (Goodnick, Henry, & Buki, 1995). Fluoxetine, for example, can improve glycemic control (Goodnick, 2001), but not all studies are supportive of this (Lustman, Freedland, et al., 2000). Bupropion, a norepinephrine/dopamine reuptake inhibitor, is as effective for in the treatment of depression as the SSRIs (Thase et al., 2005) and has shown favorable effects on weight in patients with obesity and depressive symptoms (Jain et al., 2002) and may improve glycemic control in patients with diabetes (Lustman, Williams, Sayuk, Nix, & Clouse, 2007). Other effective antidepressant medications, however, have been linked to side effects that are particularly undesirable in patients with diabetes. For example, monoamine oxidase inhibitors (MAOIs) can cause weight gain and tricyclic antidepressants (TCAs) can cause hyperglycemia, both of which can be problematic in individuals without diabetes but are especially counterproductive and even dangerous in patients with diabetes (Goodnick et al., 1995). Atypical antipsychotics, some of which are now approved for and have been shown to be effective in the treatment of depression (Philip, Carpenter, Tyrka, & Price, 2008), cannot only cause weight gain (Allison et al., 1999), but can worsen glycemic control in patients with diabetes and cause glycemic abnormalities (including the development of diabetes) in patients without a preexisting diagnosis (Haddad & Sharma, 2007).

2.2.3.3 Issues in Treatment Decision-Making

The current literature supports the utility for both psychosocial and pharmacological interventions for depression in patients with diabetes. Clinical intervention with depressed diabetes patients may be strengthened by an integrative approach that simultaneously treats depression and diabetes treatment nonadherence from a behavioral perspective. Accumulating evidence suggests that even subclinical presentations of depression and distress can be associated with worse treatment outcomes; therefore, approaches that target symptoms of depression that fall short of a formal diagnosis appear warranted. In these cases, it may be especially helpful to evaluate whether a conceptualization that considers these symptoms secondary to the burden of diabetes (e.g., diabetes distress) is clinically useful.
2.3 Anxiety Disorders

2.3.1 Epidemiology

Nationally representative surveys suggest that the prevalence of anxiety disorders may be as high as 18.1%, affecting approximately 40 million US adults (Kessler, Berglund, et al., 2005; Kessler, Chiu, et al., 2005). While there appears to be a higher prevalence of anxiety disorders in patients with diabetes than the general population, prevalence estimates are not well established and anxiety has received much less research attention than depression in diabetes patients. The available literature gives varying estimates, most probably due to differences in measurement methods and sampling. One large-scale study including more than 200,000 participants from the United States Behavioral Risk Factor Surveillance System assessed for lifetime prevalence of anxiety diagnosis by asking patients whether a healthcare provider had ever diagnosed them with an anxiety disorder. Results showed that the age-adjusted prevalence of lifetime diagnosis of anxiety was 19.5% in people with either type 1 or 2 diabetes and 10.9% in those without diabetes respectively. After adjustment for educational level, marital status, employment status, current smoking, leisure-time physical activity, and body mass index, people with diabetes still had a 20% higher prevalence of lifetime diagnosis of anxiety than those without (Li et al., 2008). While the measurement methods used to assess lifetime prevalence of anxiety disorders in this study were rather limited, similar estimates finding increased 12-month prevalence relative to those without diabetes were found using a structured clinical interview in a large community sample from 17 countries: patients with diabetes were 20% more likely to have an anxiety disorder in the last 12 months than those without diabetes (Lin et al., 2008). Generalized Anxiety Disorder (GAD) appears to be the most common anxiety disorder in patients with diabetes with reviews suggesting point-prevalence rates between 13 and 14% (Grigsby, Anderson, Freedland, Clouse, & Lustman, 2002; Mitsonis, Dimopoulous, & Psarra, 2009). This is markedly higher than the 3% rate found in community studies (e.g., Kessler, Chiu, et al., 2005). Grigsby et al. (2002) also found that the prevalence of specific phobia was substantially higher than the rates found in community samples – 21.6% vs. 8.7%, but this estimate was based on only two studies. Reviews suggest that the rates of other anxiety disorders in patients with diabetes are comparable to those found in the general population, though few studies are available (Grigsby et al., 2002; Mitsonis et al., 2009). However, some recent studies report significantly elevated rates of other anxiety disorders. For example, Lin et al. (2008), using a structured clinical interview in a large sample, showed that patients with diabetes are 50% more likely to have Panic Disorder and 30% more likely to have Post-Traumatic Stress Disorder (PTSD) or Social Phobia than those without the disease. Fisher et al. (2008) found 85% higher rates of Panic Disorder and 123% higher rates of GAD relative to national estimates, using structured clinical interviews (Fisher et al.).
Research also suggests elevated prevalence of symptoms of anxiety. For example, Friedman, Vila, Timsit, Boitard, and Mouren-Simeoni (1998) reported that 48.6% of its sample of 69 outpatients had anxiety symptoms, and that two thirds had at least one episode of anxiety (Friedman et al.). Another study of 1,458 attendees of a diabetes education program determined that 49% of its sample reported anxiety symptoms (Peyrot & Rubin, 1997). Finally, two recent reviews, which included studies that used mixed type 1 and 2 diabetes samples, found elevated rates of anxiety symptoms in 40–42% of patients (Grigsby et al., 2002; Mitsonis et al., 2009). This increased prevalence may be related to fears of self-injecting or self-testing. One study found that approximately 9% of insulin-treated diabetes patients reported self-injecting-related anxiety symptoms (Mollema, Snoek, Heine, & van der Ploeg, 2001). Another study of 115 type 1 and 2 patients found that 28% of its sample reported elevated injection anxiety scores on a self-report questionnaire. In addition, 14% avoided injections because of anxiety (Zambanini, Newson, Maisey, & Feher, 1999). Thus, specific features of diabetes treatment and self-management may be associated with increased symptoms of anxiety.

While exact prevalence is unknown, fear of hypoglycemia, or low blood sugars, is another common fear in patients taking insulin (Polonsky, Davis, Jacobson, & Anderson, 1992; Pramming, Thorsteinsson, Bendtson, & Binder, 1991; Weinger & Lee, 2006). Hypoglycemia is often associated with unpleasant symptoms, such as tremors, profuse sweating, cognitive dysfunction, and irritability. If blood glucose drops to dangerously low levels, loss of consciousness, seizures, and death can occur. Patients sometimes try to avoid hypoglycemia at all costs and may prefer to keep blood glucose at high levels to avoid the risk of low blood sugars (Weinger & Lee). Fear of hypoglycemia is especially prevalent in patients with past hypoglycemic experiences (Green, Feher, & Catalan, 2000; Polonsky, 2002; Weinger & Lee, 2006) and can reach levels of intensity that have led some investigators to draw parallels to PTSD. For example, one study found that 25% of its sample of T1DM patients met criteria for PTSD related to hypoglycemia because of avoidance and intrusive thoughts related to hypoglycemia (Myers, Boyer, Herbert, Barakat, & Scheiner, 2007). Patients may also present with subclinical symptoms of anxiety related to hypoglycemia that may not represent disorder, but may still negatively impact diabetes self-management (Myers et al.; Wild et al., 2007).

There is also evidence to suggest that anxiety is associated with problems with disease management, worse clinical outcomes, and decreased functioning and quality of life, even at subclinical levels. For example, a meta-analysis of 11 studies showed a nonsignificant trend for an overall relationship between anxiety and hyperglycemia. When the analysis was limited to studies that used diagnostic interviews for anxiety, the effect size between anxiety and hyperglycemia was in the medium range and significant (Anderson et al., 2002). Panic episodes have been associated with worse diabetes control, increased diabetic complications and symptoms, greater disability, and lower self-rated health and functioning in a sample of over 4,000 patients with diabetes, even after controlling for the effects of co-morbid depression (Ludman et al., 2006). Diabetes-specific manifestations of anxiety may also be associated with worse outcomes. For example, insulin-treated adult
diabetes patients with severe fear of self-injecting or self-testing had higher levels of diabetes-related distress, poorer general well-being, and poorer treatment adherence than those who did not have such fears (Mollema, Snoek, Ader, Heine, & van der Ploeg, 2001).

2.3.2 Pathophysiology

The development of anxiety symptoms in patients with diabetes may arise from a number of underlying causes. While research on the biobehavioral mechanisms between anxiety and diabetes is generally lacking, plausible mechanisms linking anxiety and diabetes include reactions to the stress associated with the self-management of diabetes and underlying biological changes that may be associated with both anxiety and glycemic control.

Diabetes-related stress, including feeling overwhelmed by diabetes and its care, feeling discouraged with the treatment plan, and feeling fearful of the future, may contribute to symptoms of anxiety (Weinger & Lee, 2006). The stress of dealing with diabetes may impact patients’ psychosocial functioning and quality of life, which may also increase the risk for developing anxiety symptoms (Weinger & Jacobson, 2001). Certain aspects of the diabetes self-care regimen, such as frequent self-testing of blood glucose and insulin injections, may also lead to the development or exacerbation of anxiety symptoms, such as phobias, intrusive worry, and avoidance (Green et al., 2000; Mollema, Snoek, Ader, et al., 2001; Mollema, Snoek, Heine, & van der Ploeg, 2001; Polonsky et al., 1992; Pramming et al., 1991; Zambanini et al., 1999). For example, the anticipation before or avoidance of activities such as self-testing may contribute to problematic anxiety, panic disorder, or GAD. Diabetes patients may experience short-term, episodic stress related to self-care activities, or more long-term, chronic stress related to living with a chronic illness, which may eventually develop into anxiety symptoms or a chronic anxiety disorder (Petrak et al., 2005).

Further, patients may develop anxiety symptoms due to fears of hypoglycemia, complications, or mortality. Some patients may be able to better manage diabetes-related stress or general life stress than others, based on their coping skills: use of maladaptive coping could increase the risk for anxiety in patients with diabetes (Sultan, Epel, Sachon, Vaillant, & Hartemann-Heurtier, 2008; Tuncay, Musabak, Gok, & Kutlu, 2008; Weinger & Lee, 2006). Studies suggest that patients who use a variety of coping mechanisms, including both task-based coping and emotion-based coping, have better emotion regulation and diabetes control (Sultan et al., 2008). Conversely, emotion-based coping, such as anxious and angry styles, is associated with poor glycemic control (Peyrot, McMurry, & Kruger, 1999; Yi, Yi, Vitaliano, & Weinger, 2008). Patients who experience diabetes-related stress may become entrenched in a vicious cycle – anxiety and avoidance related to their self-care may cause them to be less adherent to their treatment regimen, which may in turn affect their blood glucose control or cause complications – thus leading to even
greater levels of anxiety. Finally, psychiatric illness such as anxiety disorders often co-occurs with tobacco and other substance use, highlighting a potential pathway between anxiety and worse diabetes outcomes (Spangler et al., 2001).

Physiological mechanisms are also plausible in explaining the link between diabetes and anxiety and the principal candidate is overactivation of the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system. Models that have been proposed to account for neuroendocrine pathways between depression and diabetes also have relevance for anxiety (Golden, 2007). Studies have suggested that co-morbid anxiety may play an important role in the HPA-axis dysregulation seen in patients with depression (Young, Abelson, & Cameron, 2004). Elevated cortisol has been shown to inhibit insulin function (Ehlert, Gaab, & Heinrichs, 2001) and cortisol levels appear to be dysregulated in patients with anxiety disorders (e.g., Chaudieu et al., 2008).

As with depression, there is little understanding of these mechanisms and questions remain as to the directionality and causal nature of the relationships between anxiety and diabetes. However, as anxiety seems to be a risk factor for potential problems with diabetes management and worse treatment outcomes, clinical intervention has the potential to result in mental and physical health benefits for patients.

### 2.3.3 Clinical Care

#### 2.3.3.1 Assessment and Diagnostic Issues

Proper identification and diagnosis of anxiety is necessary so that appropriate treatments may be implemented, but the task of accurate assessment of problems with anxiety is complicated by the context of diabetes. Problems with anxiety may be undertreated or misdiagnosed because they may resemble physiologic changes associated with hypoglycemic episodes, for example (Boyle, Allan, & Millar, 2004; Jacobson, 1996; Polonsky et al., 1992). Both patients and clinicians may have difficulty distinguishing between hypoglycemia and anxiety symptoms such as dizziness, shakiness, lack of coordination, and heart palpitations. Other physiological explanations for anxiety, such as a thyroid disorder, should be ruled out and consultation with the patient’s healthcare provider(s) should be sought (Aina & Susman, 2006). If physical symptoms are present, providers should be sure to ask about behavioral and emotional issues, as these should distinguish diabetes-related physical symptoms from an anxiety disorder (Jacobson, 1996). In addition, anxiety disorders often co-occur with other psychiatric disorders – the co-morbidity between anxiety and depression, for example, appears to be higher in people with diabetes than in the general population (Fisher et al., 2008).

Given the potential difficulty in assessing anxiety in patients with diabetes, several assessment tools should be used, including structured clinical interviews, diabetes-specific anxiety measures, as well as the patient’s self-report, to make an accurate diagnosis. It is important to note that anxiety poses a significant risk for
suicide and co-morbid anxiety and depression is associated with an even greater risk (Keller & Hanks, 1995; Kessler, Borges, & Walters, 1999). For example, panic disorder is associated with a 7% risk of suicide in the general population, but if co-morbid depression exists, this risk increases to 23.6%. Likewise, MDD without anxiety was associated with a 7.9% risk of suicide, but when co-morbid anxiety was present, this risk increased to 19.8% (Keller & Hanks, 1995).

A number of formal screening tools may have utility in working with diabetes patients. These include the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) and Generalized Anxiety Disorder (GAD-7) Scale (Spitzer, Kroenke, Williams, & Lowe, 2006). Given the relatively high rates of anxiety disorders in patients with diabetes, formal evaluation using structured clinical interviews may be warranted for those patients who report symptoms of anxiety. The focus on psychopathology should be supplemented with an assessment of diabetes-specific distress and screening for fears related to hypoglycemia, self-monitoring of blood glucose, and self-injection with insulin. Standardized scales may facilitate this diabetes-focused assessment, including the Diabetes Distress Scale (Polonsky et al., 2005), the Diabetes Quality of Life questionnaire (Burroughs, Desikan, Waterman, Gilin, & McGill, 2004), the Hypoglycemia Fear Survey (Cox, Irvine, Gonder-Frederick, Nowacek, & Butterfield, 1987), and the Diabetes Fear of Injection and Self-Testing Questionnaire (Snoek, Mollema, Heine, Bouter, & van der Ploeg, 1997). It is also recommended to assess the frequency of patients’ self-monitoring blood glucose levels and adherence to insulin regimens, if prescribed, as well as any barriers to adherence. Consultation with diabetes care providers is important in order to identify problems with treatment adherence.

2.3.3.2 Evidence-Based Treatment

A meta-analysis of the literature on psychological interventions in patients with T2DM suggests that a variety of psychological interventions have been utilized, and overall, these interventions have been effective in reducing symptoms of psychological distress and in improving glycemic control (Ismail, Winkley, & Rabe-Hesketh, 2004). While this overall evaluation is promising, important questions as to which approaches are likely to be most effective remain unanswered. We review a variety of approaches below, but note that the empirical literature provides little guidance at this time as to which approaches are likely to be most effective with which patient presentations.

Education programs such as those focused on self-care or living with a diabetes diagnosis may reduce the risk for anxiety symptoms or help to alleviate existing symptoms. Group education programs including a coping skills component have been shown to be useful in reducing stress and improving both coping skills and diabetes control (Grey, Boland, Davidson, Li, & Tamborlane, 2000; Karlsen, Idsoe, Dirdal, Hanestad, & Bru, 2004; Rubin, Peyrot, & Saudek, 1993).

A recent review of ten studies evaluating the efficacy of stress management interventions in adults with diabetes suggests that, overall, these approaches may not
only be helpful in reducing stress, anxiety, and related negative emotions, but may also be effective in improving glycemic control (Soo & Lam, 2009). While results across studies were variable, several studies showed promise in improving diabetes control. For example, T2DM patients who completed a program consisting of five group-based sessions involving training in progressive muscle relaxation, guided imagery, and instruction in behavioral and cognitive skills to recognize and reduce stress showed improvement in glycemic control over 12 months, relative to control patients. Surprisingly, no differences in stress or anxiety were observed (Surwit et al., 2002). Individually delivered, biofeedback-assisted relaxation training was found to reduce symptoms of anxiety and depression, muscle tension, and improve diabetes control in a small trial of 30 patients with diabetes with T2DM (McGinnis, McGrady, Cox, & Grower-Dowling, 2005). Henry, Wilson, Bruce, Chisholm, and Rawling (1997) tested a group-based 6-session program including relaxation training, cognitive restructuring, and training in problem-solving skills and found improvements in anxiety symptoms, stress, and some evidence of a small effect on diabetic control in a small sample of 19 adults with T2DM (Henry et al.). There is also early evidence that mindfulness-based stress management may be successfully applied in patients with T2DM (Whitebird, Kreitzer, & O’Connor, 2009). The one trial of mindfulness-based stress management conducted to date involved an uncontrolled pilot study of 14 patients with T2DM and found improvements in diabetes control, decreased symptoms of depression, anxiety, and general psychological distress after completion of a mindfulness program (Rosenzweig, Reibel, Greeson, Jasser, & McMearty, 2007).

Given the association between hypoglycemia, self-injecting, and anxiety symptoms, providers may need to focus on self-monitoring and self-injecting routines with patients on insulin. Cognitive distortions regarding self-monitoring of blood glucose or injections, avoidance of these behaviors, and associated feelings of worry and fear may be effectively addressed using a cognitive-behavioral approach. This could involve challenging maladaptive and inaccurate beliefs through the provision of education and cognitive restructuring and addressing behavioral avoidance through exposure, self-monitoring, and other in-session and at home “behavioral experiments” to improve patient adherence to the self-care regimen while at the same time reducing avoidance and anxiety. Clinicians should collaboratively review blood glucose records with patients at each clinic visit, in order to determine patterns of how eating and physical activity are related to blood glucose levels. They may also wish to discuss physical symptoms and glycemic control in order to help the patient better recognize how physical symptoms are related to high or low blood glucose levels. Clinicians should also be prepared to evaluate whether patients are becoming maladaptively focused or obsessive about glucose monitoring as too great of an emphasis on blood glucose monitoring has actually been linked with increased anxiety (O’Kane, Bunting, Copeland, & Coates, 2008). In this work, it is crucial to consult with the patient’s diabetes care provider(s) to become thoroughly familiar with the patient’s individual self-management plan and the rationale for the frequency of monitoring of blood glucose.
The relationship between patients and their social support system (including their healthcare team) may also play a role in the prevention or amelioration of anxiety symptoms (Harris & Lustman, 1998; Jacobson, 1996; Weinger, 2007; Weinger & Lee, 2006). Patient satisfaction with the support obtained from family members, and the patients’ relationships with their treatment providers, should be evaluated and strategies for strengthening these relationships should be applied. These may include role-plays to assist the patient in rehearsing questions for their care providers, assertiveness training, and psychoeducation about effective communication. Group-based patient groups may be available to the patient at local diabetes treatment centers and the clinician should explore these options for augmenting treatment.

Regarding specific psychotherapy approaches to anxiety disorders in the context of diabetes, very little is known. Case reports have suggested possible efficacy of cognitive-behavioral interventions for anxiety disorders such as specific phobias relating to hypoglycemia and panic disorders in patients with diabetes (Boyle et al., 2004; Green et al., 2000), but randomized clinical trials are lacking. Boyle et al. (2004), found that an intervention consisting of behavioral experiments, reduction of safety behaviors, and reframing of maladaptive/irrational thoughts and beliefs led to reductions in both a fear of hypoglycemia and panic attacks in a 37-year-old woman with a diabetes-related anxiety disorder. Green et al. (2000) described the treatment of an adult male with T1DM who had poor diabetes control due to an excessive fear of hypoglycemia and who was diagnosed with agoraphobia and panic disorder. He also developed increasing fears of diabetes complications and death as his diabetes control deteriorated and these fears often led to anxious rumination at night and difficulty sleeping. Treatment consisted of graded exposure exercises, self-monitoring of episodes of hypoglycemia and panic, instruction in the use of relaxation techniques, and cognitive restructuring. The authors do not report the length of treatment, but did report that the patient became able to cope with feared situations, became less fearful of hypoglycemia and was better able to differentiate these episodes from panic attacks, became less anxious, and achieved improved glycemic control. After treatment, he no longer exhibited avoidance behaviors related to fear of hypoglycemia (Green et al.).

As with psychotherapy interventions, we are unaware of any randomized trial testing the efficacy of pharmacological agents in treating anxiety disorders in patients with diabetes. However, fludiazepam was shown to be successful in reducing anxiety symptoms and improving lipid profiles in 20 patients with T2DM (Okada et al., 1994). One randomized trial reported an evaluation of alprazolam and found a benefit in glycemic control in poorly controlled patients with diabetes, but relatively few participants had an anxiety disorder and no treatment effects were found on symptoms of anxiety (Lustman et al. 1995). It should be noted that patients with diabetes should be closely monitored on psychotropic medications that may cause weight gain as this may complicate their diabetes control and increase their risks for complications. Also, beta-blockers are useful to reduce some symptoms of anxiety, but should be used with great caution in patients on insulin because they block the adrenergic symptoms of hypoglycemia (Jacobson, 1996).
2.3.3.3 Issues in Treatment Decision-Making

Patients with T2DM may present with a variety of problems related to anxiety and each presentation may require a distinct treatment approach. Subclinical symptoms may need to be treated differently than formal disorders, co-morbid anxiety and depression may need to be treated differently than anxiety alone, and patients for whom problems with anxiety are secondary to problems with diabetes may need interventions that focus on diabetes self-management with an interdisciplinary approach, including collaboration with diabetes educators, dietitians, and physicians providing diabetes care. A careful comprehensive assessment and case conceptualization that addresses the interplay between anxiety, diabetes, and other psychological or physical co-morbidities is an essential first part of treatment. Based on this initial conceptualization, clinicians can choose a tailored set of treatment elements from a variety of interventions that may be effective, including educational, behavioral, supportive, psychotherapeutic, and psychopharmacological approaches. Although there is little information available regarding treatment sequencing and appropriate blending of therapeutic approaches, we emphasize that treatments that target problems with anxiety and problems with diabetes self-management are likely to have a greater impact than those that target these problems in isolation.

2.4 Eating Disorders

2.4.1 Epidemiology

Disordered patterns of eating appear to be more prevalent in individuals with diabetes than nondiabetic individuals but it should be noted that few investigations have been conducted and most have been based on either small or nonrepresentative samples, or both. Therefore, statements about prevalence must be made with caution. Most of the literature has focused on the co-morbidity in adolescent female populations with T1DM (Papelbaum et al., 2005); we extrapolate from this literature when appropriate.

Data from the National Co-morbidity Survey Replication (NCS-R) suggest the prevalence of binge-eating disorder (BED) is 2.0% in the national population (Hudson, Hiripi, Pope, & Kessler, 2007). One study of 3,000 primary care patients from family practice and internal medicine clinics found that individuals with diabetes were 2.4 times more likely to have either bulimia nervosa or BED than those without diabetes. Post-hoc analyses revealed that diabetes was associated with significantly increased odds of BED, but the relationship to bulimia nervosa was not significant. No other medical illness was associated with increased risk of these eating disorders, but the overall prevalence of these disorders was high (7%) in this primary care sample (Goodwin, Hoven, & Spitzer, 2003). Other estimates on the prevalence of BED in patients with T2DM vary considerably. In a small
convenience sample \((n=43)\) of adult T2DM patients, the prevalence of BED was 25.6% based on the Structured Clinical Interview for the DSM-IV \((\text{Crow, Kendall, Praus, \\& Thuras, 2001})\). A Brazilian study examining prevalence of eating disorders using structured clinical interviews in a sample \((n=70)\) of adult T2DM patients found that 10% had BED \((\text{Papelbaum et al., 2005})\). Other studies found low rates of prevalence. One study of overweight patients with T2DM found that the prevalence of BED in females \((n=80)\) was 2.5%, and that no men \((n=76)\) met criteria for BED. This study also compared the prevalence of BED in the diabetes sample to that of a sample of patients without diabetes. The prevalence of BED was also no different between the two samples \((\text{Mannucci et al., 2002})\). A study of 215 women found no difference in bingeing between T2DM patients and controls. However, a nonsignificant trend towards more bingeing in the diabetes group was found \((\text{Carroll, Tiggemann, \\& Wade, 1999})\). Similarly, in a study of 845 older adult T2DM patients, the prevalence of BED was only 1.4% \((\text{Allison et al., 2007})\). Although another study found that BED was the most diagnosed eating disorder in overweight and obese sample of people with diabetes, the prevalence rates were still relatively low. The lifetime prevalence of BED in the female sample \((n=168)\) was 7.1% and 4.5% in the male sample \((n=154; \text{Herpertz, Albus, et al., 1998})\). In a study of more than 5,000 overweight and obese T2DM middle-aged and older patients, 11.7% reported at least one bingeing episode, as assessed by self-report questionnaire. These patients were younger and more likely to be female, white, and college-educated than their nonbinge-eating counterparts. However, only 123 \((2.6\%)\) met diagnostic criteria for BED \((\text{Gorin et al., 2008})\). One study of female T2DM patients found that 21% reported engaging in binge eating at least weekly, but did not assess BED, per se \((\text{Kenardy, Mensch, Bowen, Green, \\& Walton, 2002})\). In contrast, another study of 125 women with T2DM found that bingeing was endorsed by 9.4% of patients \((\text{Carroll et al., 1999})\). Finally, a French study of adult T2DM patients \((n=51)\) found that 27% of men and 11% of women exhibited binge eating or overeating \((\text{Ryan, Gallanagh, Livingstone, Gaillard, \\& Ritz, 2008})\). Due to the small sample sizes of most studies and the variability of methods used to assess binge eating, questions remain about the heterogeneity and generalizability of these estimates.

Data from the NCS-R suggest the prevalence of anorexia to be 0.6% in the US population \((\text{Hudson et al., 2007})\) and the presence of anorexia nervosa in adults with T2DM appears to be minimal \((\text{Herpertz, Albus, et al., 1998})\). Prevalence estimates for bulimia in type 2 patients also appear to be similar to those in the national population. In the NCS-R sample, lifetime bulimia prevalence is 1.1% \((\text{Hudson et al., 2007})\), and reports have found similar prevalence estimates in people with T2DM \((\text{Herpertz, Albus, et al., 1998})\). However, the prevalence of these disorders is especially understudied.

Insulin omission is designated as “misuse of medications for weight loss” in the DSM-IV and, depending on the severity, may qualify as eating disorder-NOS \((\text{American Psychiatric Association [APA], 2000})\). Omitting or reducing insulin to induce glycosuria, where glucose is excreted through the urine causing weight loss, is a form of calorie purging and has significant health consequences for diabetes patients. A study of 8,484 adult T2DM patients on insulin found that nearly 25% of
patients exhibited insulin nonadherence based on outpatient pharmacy refill data (Cramer & Pugh, 2005). While relatively little attention has been paid to reasons for intentional insulin nonadherence, concerns about weight gain represent one possible factor associated with nonadherence. For example, in a sample of 100 adults with T2DM, 22% reported that they feared that taking insulin would cause weight gain and would therefore be unwilling to take insulin (Larkin et al., 2008). Insulin omission also appears to be more common among patients with eating disorders than those without, based on research in T1DM adolescent females (Nielsen, Emborg, & Molbak, 2002; Takii et al., 2008).

Another eating disorder prevalent among people with diabetes is Night-Eating Syndrome, which is characterized by greater than 25% of caloric intake occurring after the evening meal, and/or waking up at least 3 times/week to eat at night (Schenck, 2006). In a study of 714 type 1 and type 2 patients, Morse, Ciechanowski, Katon, and Hirsch (2006) found that 9.7% reported night-eating behaviors and these patients were more likely to be less adherent with diet, exercise, and glucose monitoring. They were also more likely to be obese, to have worse diabetes control, and to have more diabetes complications than patients without night-eating behaviors (Morse et al.).

Negative health outcomes also appear to be associated with other types of eating disorders and related problems in patients with diabetes. For example, studies show that patients who restrict their insulin have poorer metabolic control (Battaglia, Alemzadeh, Katte, Hall, & Perlmutter, 2006; Daneman et al., 2002) and higher rates of nephropathy (Crow, Keel, & Kendall, 1998; Kelly, Howe, Hendler, & Lipman, 2005; Takii et al., 2008). Furthermore, retinopathy (Crow et al., 1998; Daneman et al., 2002; Kelly et al., 2005; Takii et al., 2008), diabetic ketoacidosis (DKA) (Kelly et al., 2005) and other microvascular complications (Kelly et al.; Peveler et al., 2005; Takii et al., 2008) are more prevalent and more severe in people who deliberately restrict their insulin intake. Moreover, insulin omission was shown to increase the relative risk of mortality by 3.2-times in a study of 234 adult women with T1DM. Women who restricted their insulin use were also more likely to die younger than women who did not and were more likely to experience nephropathy and foot problems over the follow-up (Goebel-Fabbri et al., 2008). The relationship between BED and worse diabetes outcomes is less clear. Crow et al. (2001) found that BED was not related to poor diabetes outcome, but Carroll et al. (1999) found BED to be a significant predictor of poor glucose control. Further research may be needed given the few studies examining the effects of BED in diabetes.

Subthreshold variants of eating disorders, such as occasional binge-eating episodes, engaging in extreme dietary restraint or excessive exercise, and when self-evaluation is greatly influenced by shape and weight, appear to be more common in people with diabetes than people without (Colton, Olmsted, Daneman, Rydall, & Rodin, 2004). They are also associated with poorer glycemic control (Mannucci et al., 2002; Peveler et al., 2005) and higher rates of retinopathy and nephropathy (Cantwell & Steel, 1996; Rydall, Rodin, Olmsted, & Devenyi, 1997) as compared to individuals with diabetes who exhibit normal eating behavior. In addition, maladaptive eating attitudes, such as excessive concern with eating, weight, and
body shape, have also been shown to significantly correlate with poorer glycemic control (Mannucci et al., 2002). These studies suggest that diabetes control can be affected by poor body image issues and eating behaviors, even in patients without a diagnosable eating disorder.

### 2.4.2 Pathophysiology

There are various possible explanations for the relationship between eating disorders and diabetes. Several studies have shown that family dysfunction predicts the development of maladaptive eating behaviors in females with and without T1DM (Neumark-Sztainer et al., 2002; Rodin et al., 2002). One study of adolescent females with T1DM studied the relationship between family dysfunction and maladaptive eating behaviors in diabetes. Family dysfunction, as defined by negative familial communication regarding weight and shape, was related to maladaptive eating attitudes and behaviors. Notably, this relationship was moderated by body image dissatisfaction (Kichler, Foster, & Opipari Arrigan, 2008). Moreover, in a review of the relevant literature, Daneman et al. (2002) found that eating disturbances were associated with self-reported family functioning, and more severe eating problems were linked to greater levels of family dysfunction in girls with T1DM. Those with eating disturbances reported significantly poorer relationships and that their parents were not responsive to their needs, leading to greater feelings of anger and hopelessness toward their parents. Additionally, they found that family environment and maternal weight and shape concerns were interrelated with eating disturbances in young women with T1DM. Daneman et al. postulate that individual, family, and societal factors interact with diabetes-specific vulnerabilities and lead to core features of eating disorders, such as body dissatisfaction, drive for thinness, and dietary restraint. These features then lead to disordered eating behaviors, resulting in diabetes-specific outcomes (such as hyperglycemia and complications). The extent to which these etiological factors may be relevant for adults with T2DM is not clear, but Ismail (2008) suggests a theoretical model of potential pathways between disordered eating behaviors and T2DM. She postulates that cultural factors (such as beliefs about diabetes, insulin, and body image) and vulnerability factors (such as social adversity) may lead to overeating and obesity, which is a risk factor for developing diabetes. Overweight people with diabetes often suffer from depression, which is associated with poor diabetes self-care, further increasing the risk of suboptimal diabetes control.

Furthermore, various aspects of diabetes and its treatment may increase the risk of eating disorders, such as dietary restraint and a focus on portion control, calorie monitoring, and carbohydrate counting (Papelbaum et al., 2005; Rodin & Daneman, 1992). Chronic dieting, rigid restraint of eating, and perceptions of “forbidden foods” may also contribute to the development of eating disorders (Polivy & Herman, 1985). Other maladaptive behaviors, such as vomiting, using laxatives, or omitting insulin, also have important clinical implications (Rodin, Craven,
Littlefield, & Murray, 1991; Rydall et al., 1997; Steel, Young, Lloyd, & Clarke, 1987) and may compromise adherence to treatment, self-management, and result in worse treatment outcomes.

2.4.3 Clinical Care

2.4.3.1 Assessment

Diabetes management often includes careful focus on the quality and quantity of food eaten. This may complicate the evaluation of abnormal behaviors and concerns used to diagnose eating disorders (Rubin & Peyrot, 2001). Possible diabetes-related clues to underlying eating disorder include unexplained episodes of DKA (when there is no glucose for the body to use as energy so it begins to break down fat and muscle, changing the body’s chemical balance, which has potentially life-threatening consequences), frequent episodes of hypoglycemia, or easy control in inpatient settings of blood glucose levels that were previously difficult to manage in outpatient settings (Tierney, Deaton, & Whitehead, 2009). Additionally, clinicians should note when patients frequently request changing meal plans to accommodate low-fat, low-carbohydrate, or other diets, refuse to be weighed at clinic visits, exhibit anxiety upon being weighed, or frequently complain about their body weight or shape. These behaviors may have important implications in the context of diabetes management.

There are a variety of tools to assess for eating disorders in the general population. Several generic tools for the assessment of eating disorders have been modified for specific use in people with diabetes (Neumark-Sztainer et al., 2002). The Eating Disorder Examination (EDE) is a standardized interview, designed to measure the current level of eating disorder psychopathology (Cooper & Fairburn, 1987). It is commonly used to assess eating disorders in populations with diabetes (Allison et al., 2007; Gorin et al., 2008; Kenardy et al., 2002; Mannucci et al., 2002) and is the gold standard for assessing binge eating (Fairburn & Beglin, 1994; Grilo, Masheb, & Wilson, 2001). Another screening tool commonly used in populations with diabetes is the Eating Attitudes Test (EAT). The EAT is a 40-question measure of eating attitudes and is predictive of disordered eating behaviors (Garner & Garfinkel, 1979). A shortened form of the EAT-40, the EAT-26, is often used because it minimizes responder burden and is still has high validity and reliability (Berland, Thompson, & Linton, 1986). The Eating Disorder Inventory (Garner, Olmsted, & Polivy, 1983) is a 64-item self-report questionnaire that assesses psychological and behavioral traits common in anorexia and bulimia and has been used in patients with diabetes (Herpertz, Wagener, et al., 1998; Kenardy et al., 2002).

Assessment of insulin misuse and nonadherence is also important for T2DM patients treated with insulin. Some indicators of insulin misuse may include poor metabolic control in spite of adequate diet and insulin regimen or episodes of DKA. Clinically, it would be important to assess patient concerns about insulin and the associated risk of weight gain, especially in cases where the patient reports less than
optimal adherence to the insulin regimen. Such an assessment should include evaluation of frequency of missed or skipped doses, modifying doses to take fewer units than recommended by the patient’s physician, and patient reported reasons for omission or nonadherence. Specific probing for concerns about weight gain may be clinically useful, especially in the context of already reported concern about body weight or shape or other maladaptive attitudes toward eating. Patients who are not taking insulin and have resisted the prescription of insulin by a provider should also be interviewed about their perceptions regarding the negative consequences of insulin, as fears of weight gain have been shown to be a possible reason for resistance to insulin therapy (Larkin et al., 2008). In each of these cases, consultation with the patient’s diabetes care provider(s) would be important.

2.4.3.2 Evidence-Based Treatment

It has been suggested that eating disorders in women with diabetes may be more difficult to treat than in those without diabetes but this view is speculative and based on select cases reported in the literature (Daneman et al., 2002). Although many studies have investigated the efficacy of weight-loss programs in people with T2DM, few interventions for treating eating disorders in people with diabetes have been investigated (Snoek & Skinner, 2002). Additionally, of the limited published psychotherapy intervention studies addressing disordered eating in patients with diabetes, most lack methodological rigor (Rubin & Peyrot, 2001).

One study investigated the efficacy of CBT and nonprescriptive therapy (NPT), a treatment designed to have no theoretical or empirical support in eating disorders, as interventions for binge eating in patients with diabetes. The study was a 10-week randomized control trial of 24 women with T2DM and BED. Assessments were done at posttreatment and at 6-month follow-up. CBT and NPT both appeared to effective treatments, though CBT appeared to provide more sustained change, as there were significantly fewer relapses in CBT condition. Across treatments, decreases in bingeing were associated with improved diabetes control (Kenardy et al., 2002). While this investigation shows promise for the successful treatment of BED in patients with diabetes, no other studies were found investigating other possible treatments for people with T2DM and other eating disorders. Until more research is conducted in this area, it is appropriate to apply the current literature on treating eating disorders in the general population to that of the diabetic population.

Various treatments for anorexia nervosa, including psychotherapeutic and pharmacological interventions, are available and have empirical support for their efficacy. While a review of these treatments is beyond the scope of the present chapter, recent reviews are available (Bulik, Berkman, Brownley, Sedway, & Lohr, 2007) and suggest that cognitive-behavioral, interpersonal, and pharmacological approaches can be helpful. In the context of T2DM, it is important to modify the application of these interventions to take into consideration the importance of weight loss to improve treatment outcomes. Thus, weight loss should be incorporated as a goal of treatment in work with patients with BED, for example. The importance of
treatment adherence and careful attention to the possible relationship between insulin restriction or omission and disordered eating should also be given important consideration. Consultation with the diabetes treatment provider(s) should be sought and collaboration with a dietitian with expertise in the management of diabetes may be beneficial.

2.4.3.3 Issues in Treatment Decision-Making

The current literature gives little guidance for the selection of the most appropriate treatments for eating disorders in the context of T2DM. Interventions that have been empirically supported in nondiabetes populations appear applicable, but there may be a further need to consider even subclinical presentations of maladaptive eating behaviors and attitudes as necessitating treatment given their association with worse treatment outcomes in the context of T2DM. As in the treatment of other psychological problems in patients with T2DM, consideration of the associations between maladaptive patterns of eating behaviors and attitudes about weight and body image on the one hand and insulin omission and other aspects of diabetes treatment adherence on the other may result in more accurate case conceptualizations and more effective treatments.

2.5 Psychotic Disorders and Bipolar Disorders

2.5.1 Epidemiology

T2DM is more prevalent among individuals with serious and persistent mental illnesses such as bipolar disorder and schizophrenia than in the general population (Citrome et al., 2005; Parks, Svendsen, Singer, Foti, & Mauer, 2006). Estimates from a range of national and international epidemiological studies have shown the prevalence of diabetes in patients with schizophrenia to be 1.5–2.5 times greater than that found in the general population, with the difference being particularly striking among younger patients (Parks et al.; Rouillon & Sorbara, 2005). The point prevalence of schizophrenia itself is estimated at 0.5%, lifetime prevalence at around 1%, and annual incidence around 0.2% (APA, 2000; Eaton et al., 2008; Mueser & McGurk, 2004). Due to the comparative rarity of the diagnoses, individuals with schizoaffective, schizophreniform, and other psychotic illnesses are often included as part of a larger sample of individuals with psychotic disorders. The true prevalence of diabetes among individuals with psychotic disorders may be grossly underestimated due to the silent nature of diabetes and the myriad of other, more immediately pressing medical, economic, and social problems people with psychotic disorders face (Bushe & Holt, 2004; Mueser & Gingerich, 2006; Mueser & McGurk, 2004; Parks et al., 2006).
A number of studies have shown that the prevalence of T2DM is also increased among patients with bipolar disorders. For example, a retrospective chart review study of patients between the ages of 50 and 74 found T2DM in 26% of patients with bipolar I (Regenold, Thapar, Marano, Gavirneni, & Kondapavuluru, 2002). An examination of a sample of more than 4,000 VA patients with bipolar disorder found the prevalence of diabetes to be over 17% (Kilbourne et al, 2004). According to the NCS-R, the 12-month prevalence of bipolar I and II disorders is 2.6% (Kessler, Chiu, et al., 2005). Bipolar patients with diabetes have been found to be older, more chronically ill, present with rapid cycling, and have an overall lower level of global functioning than patient with bipolar disorder but without diabetes; they were also found to have higher rates of long-term disability and were also more likely to have higher BMIs (Ruzickova, Slaney, Garnham, & Alda, 2003). Individuals with serious and persistent mental illnesses die on average 25 years younger than the general population due to illnesses such as diabetes and cardiovascular disease (American Diabetes Association, American Psychiatry Association, & American Association of Clinical Endocrinologists, 2006; Parks et al., 2006; Pratt, Dey, & Cohen, 2007).

2.5.2 Pathophysiology

There are many possible reasons for the co-morbidity of serious and persistent mental illness and T2DM, reasons that are likely interactive and interconnected (Rouillon & Sorbara, 2005). Antipsychotic medication, particularly newer atypical antipsychotics, have been associated with metabolic disturbance and higher rates of diabetes (Bushe & Holt, 2004; Mueser & McGurk, 2004). This is particularly important given the dramatic increase in the prescription of atypical antipsychotics over the last decade (Domino & Swartz, 2008). Some atypical antipsychotics as well as conventional antipsychotics have been associated with higher rates of diabetes and metabolic dysregulation both independently and through certain medication side effects, such as weight gain, insulin resistance, decreased physical activity, and metabolic syndrome (Barnett et al., 2007; Basu & Meltzer, 2006; Bushe & Holt, 2004; Folnegovic-Smalec, Jukic, Kozumplik, Mimica, & Uzun, 2004; Kohen, 2004; Mueser & McGurk, 2004; Parks et al., 2006; Sernyak, Leslie, Alarcon, Losonczy, & Rosenheck, 2002; but see Holt & Peveler, 2006; Koro et al., 2002; Smith et al., 2008). However, the association between schizophrenia, diabetes, and diabetic risk appears to be independent of medication regimen, which could be explained by physiological abnormalities co-occurring with the disease, socio-economic and other environmental correlates of schizophrenia, or a combination of these factors (Bushe & Holt, 2004; Holt, Peveler, & Byrne, 2004).

Individuals receiving medication for the treatment of bipolar disorder also frequently experience weight gain (Elmslie, Silverstone, Mann, Williams, & Romans, 2000). Mood stabilizers such as lithium and anticonvulsants are often the first line of pharmacological treatment for bipolar disorder. Numerous studies have found associations between lithium treatment and weight gain, but how lithium
precipitates weight gain is unclear (Kupka et al., 2002). Lithium may stimulate the hypothalamus and thus appetite, which can increase caloric consumption, and may may increase thirst, which can increase fluid retention. Lithium has also been associated with reduced thyroid functioning, which can effect glucose regulation (Kupka et al., 2002). Among individuals taking lithium, thyroid dysfunction has been found to be as high as 47%, with females 5 times more likely to develop this side effect than males (Kupka et al.; Livingstone & Rampes, 2006). Hypothyroidism may also be related to increased likelihood of rapid mood cycling between manic and depressive episodes and severity of depression among patients with bipolar disorder (APA, 2002; Livingstone & Rampes, 2006). Valproic acid can increase levels of testosterone in women and increase the likelihood of developing polycystic ovary syndrome, which can result in obesity as well as endocrine disruption (Joffe et al., 2006).

Poor diet, physical inactivity, smoking, and poor treatment adherence – independent risk factors for T2DM and its complications – are also more common among individuals with schizophrenia (Barnett et al., 2007; Dinan, 2004; El-Mallakh, 2006, 2007; Holt et al., 2004; Kohen, 2004; Kreyenbuhl et al., 2008; McIntyre et al., 2005; Peet, 2004; Piette, Heisler, Ganoczy, McCarthy, & Valenstein, 2007; Rouillon & Sorbara, 2005; Weiss et al., 2006). Risk factors for T2DM and schizophrenia may overlap, including obesity, sedentary lifestyle, lower socioeconomic status, a family history of diabetes, race/ethnicity, poverty, and excess stress (Black, 2002; Centers for Disease Control [CDC], 2005; Kreyenbuhl et al., 2008; Mueser & McGurk, 2004). Individuals with schizophrenia may have impaired glucose metabolism even before they develop schizophrenia, and historical surveys of the co-morbidity literature show an association between schizophrenia and diabetes before the use of neuroleptics and antipsychotics became common among treatments for schizophrenia (Bushe & Holt, 2004; Citrome et al., 2005; Dixon et al., 2000; Kohen, 2004). Individuals with schizophrenia have been found to have more than 3 times the intra-abdominal fat as matched healthy controls and are also at higher risk for developing features of metabolic syndrome – both risk factors for insulin resistance and diabetes (ADA, 2004; Thakore, 2005). Citrome et al. (2005) note that patients with schizophrenia often have increased visceral fat even in the absence of antipsychotic treatment, and visceral and intra-abdominal fat is associated with insulin resistance and metabolic syndrome, both significant risk factors for T2DM. In addition, researchers involved in the National Institute of Mental Health Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study, which recruited 1,460 participants from over 57 catchment areas, found that metabolic syndrome was present in over 40% of the sample. Men and women from the CATIE sample were 138 and 251% more likely to develop metabolic syndrome than a matched sample, respectively (McEvoy et al., 2005). The frequency of metabolic syndrome among people with schizophrenia could be related to blood glucose increases, central abdominal obesity, and disordered lipid metabolism (increasing cortisol production), and any or all of these could be influenced by medication effects, physiological traits concurrent with schizophrenia, or health behaviors such as sedentary lifestyle, food choice, and smoking (Holt et al., 2004; McEvoy et al., 2005). Seventy- to ninety-percent of patients with schizophrenia smoke, compared to less than 30%
of the overall population, and smoking has been implicated in insulin dysregulation (Diwan et al. 1998; Mueser & McGurk, 2004).

People with bipolar disorder are also more likely to be overweight or obese than the general population and are 2–3 times more likely to experience the metabolic syndrome (Elmslie, Silverstone, Mann, Williams, & Romans, 2000; Livingstone & Rampes, 2006; Pendlebury & Holt, 2008). Wang et al. (2006) examined overweight and obesity in 377 participants enrolled in the Systematic Treatment Enhancement Program for Bipolar Disorder study and the majority (55%) of participants were overweight or obese. Eating disorders such as BED are also more prevalent among individuals with bipolar disorder than the overall population and may also increase risk for the development of metabolic disturbances and diabetes (McIntyre et al., 2005). Socioeconomic factors that may increase the risk of diabetes and worse diabetes outcomes among individuals with bipolar disorder include poverty, limited access to health care, and higher rates of unemployment (McIntyre et al.).

Chronic and severe physical and psychological stress resulting from the hardships of serious mental illness may contribute to insulin resistance (Musselman et al., 2003). Stress results in the release of hormones such as glucocorticoids, growth hormone, catecholamines, and glucagon, which raise levels of blood glucose through a variety of metabolic pathways. The impact of stress and hormones, as well as increased immune system activation on glucose metabolism, has been more extensively studied in major depression than in bipolar or psychotic disorders, but as major depressive episodes are a central feature of bipolar and highly co-morbid with schizophrenia, similar risks may be present.

Both schizophrenia and T2DM have been found to have familial inheritance traits, and researchers who study individuals with T2DM and schizophrenia have found multiple links between the two conditions (Bellivier, 2005; Fernandez-Egea, Bernardo, et al., 2008; Fernandez-Egea, Miller, Bernardo, Donner, & Kirkpatrick, 2008; Rouillon & Sorbara, 2005). Research has also found that specific genetic loci and alleles may increase risk of developing bipolar disorder or schizophrenia, indicating that the polygenetic bases of schizophrenia are substantially shared with bipolar disorder, which is itself highly hereditable (Carroll & Owen, 2009; McGuffin et al., 2003; Purcell et al., 2009). This shared genetic risk for both bipolar disorder and schizophrenia is intriguing, as schizophrenia has been found to present an independent risk factor for the development of diabetes, controlling for multiple physiologic and behavioral risk factors, implicating a shared genetic risk for both illnesses (Bellivier, 2005; Fernandez-Egea, Miller, et al., 2008; Rouillon & Sorbara, 2005). Indeed, some researchers have found defects on genes that influence both neurochemicals implicated in schizophrenia as well as metabolic control (Bellivier, 2005).

Individuals with serious mental illnesses such as bipolar disorder or psychotic disorders also have higher rates of tobacco usage than the general population (Diaz et al., 2009; Diwan, Castine, Pomerleau, Meador-Woodruff, & Dalack, 1998). Additionally, the rate of substance and alcohol use among individuals with schizophrenia or bipolar disorder is higher than the general population; individuals with schizophrenia have been found to be more than 7.5 times more likely to report
current or past substance abuse (Phillips & Johnson, 2001). These behaviors can compromise diabetes control and increase the risk for cardiovascular complications of diabetes (Haire-Joshu, Glasgow, & Tibbs, 2004; Himelhoch et al., 2009; McCreadie, 2003; Mueser & McGurk, 2004). Diseases of the pancreas and liver from alcohol abuse can also contribute to the risk of developing diabetes as well as the development of diabetic complications (McIntyre et al., 2005).

### 2.5.3 Clinical Care

#### 2.5.3.1 Assessment

Up to 60–70% of cases of T2DM in individuals with serious and persistent mental illness may go undiagnosed (Pendlebury & Holt, 2008). Thus, screening for diabetes and diabetes risk factors is important in these patients, even when diabetes is not identified as part of the medical history. Mental health providers should be aware of the risk for T2DM in the patients they treat and whether T2DM is part of the patient’s medical history. In the treatment of patients with co-morbid psychotic or bipolar disorders and T2DM, health behaviors should be carefully assessed, including lifestyle factors such as activity level, diet, smoking, drug and alcohol use, eating disorders, and treatment adherence. Adherence to dietary and exercise recommendations should be carefully assessed with the context of the client’s resources and limitations in mind; many clients may not have adequate resources and assessing vulnerabilities and matching patients with the appropriate supportive services may be beneficial (El-Mallakh, 2006, 2007).

Although it seems reasonable to expect that patients with severe mental illness may have more problems with diabetes treatment adherence, few studies have examined this relationship and the existing literature suggests that this may not be the case. For example, adherence to medications for T2DM was better among diabetic individuals with schizophrenia as compared to those without schizophrenia in a study of diabetes patients in ongoing care in a VA health system. However, overall adherence was quite low in this sample (Kreyenbuhl et al., 2008). Piette et al. (2007) assessed treatment adherence in individuals with co-morbid schizophrenia, diabetes, and hypertension and found that adherence was better for oral medications for diabetes and hypertension than for antipsychotic medications. While little is known about the role of depressed mood in explaining the relationship between severe mental illness and worse diabetes outcomes, research documenting that depression symptoms are consistently associated with diabetes treatment nonadherence (Gonzalez, Peyrot, McCarl, et al., 2008) suggests that depressed mood should be carefully assessed in patients with psychotic or bipolar disorders. Supporting this, Kreyenbuhl et al. (2008) found that although schizophrenia was associated with better diabetes medication adherence, depression was associated with worse adherence. Individuals with schizophrenia have been found to have difficulties with treatment adherence for schizophrenia (Mueser & Gingerich, 2006; Parks, Svendsen, Singer,
Foti, & Mauer, 2006; Piette et al., 2007); thus, treatment adherence to psychotropic medications should also be carefully assessed, as control of the psychotic disorder will likely be a necessary condition for addressing diabetes risk. Knowledge about diabetes and its management should also be carefully assessed as patients may have not received adequate education about diabetes because of other treatment priorities or may have been less able to process information because of cognitive deficits.

Careful attention to diabetes risk factors is particularly important in patients treated with atypical antipsychotic medications. These patients should be referred for evaluation of blood glucose levels 4 months after starting an antipsychotic medication, then yearly if no problems are found (ADA, 2004; Gough and Peveler, 2004; Marder et al., 2002; McEvoy et al., 2005). As lithium treatment poses risk for reduction in thyroid function and weight gain, these patients should also be referred for evaluation of T2DM risk. After baseline assessment, thyroid function should be monitored after 3 months of lithium treatment and every 6–12 months after (Goldberg, 2008).

2.5.3.2 Evidence-Based Treatment

Preventing weight gain and reducing weight in those who are already overweight are two important priorities in the management of diabetes in patients suffering from psychotic or bipolar disorders. Education should be provided regarding nutrition and exercise and appropriate patients should be referred to programs to facilitate healthy lifestyle change, particularly if they are starting on atypical antipsychotics or lithium. Clients may be encouraged to chart and monitor their own weight over time. Family members or other caregivers should be made aware of the additional risks the patient faces for metabolic and cardiovascular illness (ADA, 2004; Marder et al., 2002; McEvoy et al., 2005). Lifestyle therapies tailored to individuals with schizophrenia addressing such issues as exercise, portion control, nutritional interventions, and other nonpharmacological interventions have been shown to be effective in controlled clinical trials of individuals with schizophrenia (Citrome & Vreeland, 2008).

Thomas, Raymondet, Charbonnel, and Vaiva (2005) offered a series of recommendations developed by psychiatrists and endocrinologists, encouraging collaboration between endocrinologists and mental health providers in the treatment of their patients. Diabetes information should be tailored to the family and the patient, with a focus on capitalizing on family support for lifestyle changes and treatment adherence. Concrete steps, such as articulating weight loss goals and developing specific behavioral modification strategies, should be outlined for patients and their families. Even modest improvements in nutrition can be beneficial for the metabolic health outcomes of individuals with schizophrenia (Thomas et al.).

Treatment for individuals with bipolar disorder is not significantly different than that for those with psychotic disorders – increased monitoring of risk factors and emphasis on prevention and lifestyle interventions are recommended (McIntyre et al., 2005). Primary goals for treatment of individuals with bipolar disorder are to reduce psychiatric symptoms, improve functioning, and reduce overall risk of
mortality. Much of the weight gained by individuals with bipolar disorder during treatment may be gained during depressive stages, which may indicate that stabilizing mood symptoms is a first priority in controlling risk factors for diabetes and diabetic complications (Fagiolini et al., 2002). Again, we note that symptoms of depression have been associated with worse treatment adherence in diabetes and, thus, difficulty with treatment adherence should be carefully monitored in these patients, especially during depressive episodes. Pretreatment diet and exercise counseling are preferred for preventing treatment-related weight gain (Livingstone & Rampes, 2006).

While there are few well-controlled studies on weight management for individuals with schizophrenia which would allow for concrete guidelines for behavioral treatment of diabetes and modifiable diabetes risk factors, a variety of behavioral and supportive interventions including nutritional education, weight-loss counseling, group support and activities, and psychoeducation regarding challenges to dietary adherence have repeatedly been found to either result in weight loss or reduce or prevent weight gain compared to individuals not receiving similar interventions (Bushe, Haddad, Peveler, & Pendlebury, 2005; Loh, Meyer, & Leckband, 2008).

McKibbin et al. (2006) conducted a randomized controlled trial to examine the feasibility and efficacy of their Diabetes Awareness and Rehabilitation Training (DART) group lifestyle intervention for adults over 40 years of age with co-morbid schizophrenia and diabetes. The DART intervention is a 24-week manualized intervention based on social learning theory that addresses comprehensive diabetes self-care (nutrition, exercise, monitoring blood sugar, physician communication, foot care) and utilized behavioral techniques to assess and reinforce achievable lifestyle goals. Measures of diabetes knowledge as well as physiological assessments were taken at baseline and at 6 months. Comparing outcomes to a usual care plus information control group, they found that intervention was both feasible (90% adherence rate) and resulted in positive health outcomes. Patients in the DART group lost an average of 5 lb, while those in the control group gained a mean of 6 lb; significant interactions were also found for reductions in triglycerides, improvements in diabetes knowledge, diabetes self-efficacy, and self-reported physical activity but not for fasting plasma glucose or HbA1c.

In their review of behaviorally based interventions for weight management among individuals with schizophrenia, Loh et al. (2008) found that the average length of treatment for studies that resulted in either significant weight loss or significant between-group differences was 6 months. Successful interventions consisted of behavioral modification, caloric restriction, and/or psychoeducation. Interventions with external incentives such as token systems were the most intensive in terms of utilization of resources and also most effective (Loh et al.).

The 2009 Schizophrenia Patient Outcomes Research Team (PORT) recommendations for weight loss interventions for individuals with schizophrenia recommend that comprehensive weight loss efforts should persist for at least 3 months to result in weight loss, which is likely to be small in size (Kreyenbuhl, Buchanan, Dickerson, & Dixon, 2010). Research including individuals with bipolar disorder has found similar results, namely that attendance at programs that involve social support, regular weigh-ins, as well as educational components can lead to weight loss and
the prevention of weight gain (Pendlebury & Holt, 2008). Metformin, an oral medication used in the treatment of T2DM, has also been used to facilitate weight loss among individuals on antipsychotic treatment and improve weight loss outcomes on its own as well as for individuals engaged in healthy lifestyle interventions. Focusing on treatment adherence to metformin in these patients could result in multiple health benefits (Carrizo et al., 2009; Wu et al., 2008).

Regarding smoking cessation, the most recent PORT guidelines recommend bupropion therapy for 10–12 weeks (Kreyenbuhl et al., 2010) as a first-line treatment. As bupropion may also result in weight loss, decrease depression, and improve glucose control in T2DM, multiple benefits may be derived from this treatment for patients (Lustman et al., 2007). Smoking cessation programs that offer psychosocial support and nicotine replacement therapy should also be considered, although high attrition rates from many studies reflect the challenge of smoking cessation in general and especially among individuals with a co-morbid psychiatric illness (Kreyenbuhl et al., 2010; Lucksted, McGuire, Postrado, Kreyenbuhl, & Dixon, 2004; McEvoy & Allen, 2003; Weinberger & George, 2009; Ziedonis & George, 1997). Motivation has been found to be a key barrier to smoking cessation and psychoeducation regarding the risks of smoking is important to enhance motivation for quitting.

2.5.3.3 Issues in Treatment Decision-Making

Careful attention to the potential risks and benefits related to diabetes risk for medication regimens, monitoring of metabolic symptoms, integrative and comprehensive patient care, improving treatment adherence, and therapeutic lifestyle change are all key components of care for individuals with psychotic and bipolar disorders who are either at high risk for diabetes or who are already diagnosed with T2DM. Improved efficacy of and adherence to psychotropic medication may be essential for the ability to sustain lifestyle changes necessary to impact metabolic risks for these patients. These medications often prevent a lifetime of severe disability and their benefits may outweigh even serious metabolic risks (Llorente & Uruita, 2006). Thus, treatment adherence to psychotropic medications and to treatment for T2DM should be included as targets of behavioral interventions.

2.6 Substance Use Disorders

2.6.1 Epidemiology

While it does not appear that substance abuse or alcohol abuse rates are higher in T2DM patients than in the general population, it is important to briefly mention these disorders for at least three reasons. First, substance and/or alcohol use disorders complicate diabetes care, increase the risk of complications, and increase health care costs (Banerjea et al., 2008). Second, substance use disorders are commonly co-morbid with other psychological problems and may be prevalent in diabetes
patients seeking psychological care. Third, these disorders are quite prevalent in the US population – more than 22 million people (8.9% of the population) aged 12 or older met DSM-IV criteria for substance dependence or abuse in 2008 (Substance Abuse and Mental Health Services Administration [SAMHSA], 2009). Of them, 3.1 million had alcohol and drug abuse disorders, 3.9 million had a substance use disorder but not an alcohol use disorder, and 15.2 million had alcohol use disorders but not substance use disorders. Furthermore, cigarette smoking is the leading cause of preventable death in the United States, and in 2008, 20.6% of adults were current smokers (CDC, 2008).

2.6.2 Pathophysiology

Substance use can impact diabetes self-care, interfering with treatment adherence and blood glucose monitoring (especially dangerous for those with insulin-dependent diabetes), and also by masking the symptoms of poor diabetes control and complications such as severe hyperglycemia (Lee, Greenfield, & Campbell, 2009). Specific substances may have metabolic impacts. For example, ecstasy can precipitate ketoacidosis in users through its antidiuretic effects; heroin can result in alterations in glucose metabolism and hyperinsulinaemia; cocaine can result in elevated levels of cortisol and corticotropin (Lee et al., 2009; Seymour, Gilman, & Quin, 1996; Sheldon & Quin, 2005). Marijuana’s effects on increased appetite may also indirectly influence glycemic control (Lee et al., 2009). Cigarette smoking increases the likelihood of developing diabetic risk factors, T2DM, and poorer diabetes treatment outcomes (ADA, 2004; CDC, 2008; Haire-Joshu et al., 2004; Willi et al., 2007). Cigarette smoking has also been associated with increased morbidity among diabetes due to cardiovascular disease and macrovascular complications, as well as increased likelihood of diabetic complications such as peripheral neuropathy (Haire-Joshu et al., 2004).

The impact of alcohol consumption on diabetes is complex, both metabolically and behaviorally. Moderate alcohol use has been associated with decreased risk of T2DM, but heavy alcohol use has been associated with increased risks (Banerjea et al., 2008; Ravert, 2009). When blood sugar levels are low, alcohol can induce hypoglycemia; as alcohol can impair judgment and reduce an individual’s awareness of low blood sugar, heavier drinking can greatly increase the risk of negative diabetic consequences and complications (Ravert). Heavy alcohol use has been associated with higher rates of T2DM among lean men and with increased prevalence of diabetes overall, and also been linked to higher levels of abdominal obesity, controlling for BMI (Johnson, Bazargan, & Cherpitel, 2001; Risérus & Ingelsson, 2007). The association between alcohol intake and abdominal obesity specifically, as opposed to overall obesity, reflects the particular risk central adiposity poses for the development of diabetes in heavy alcohol drinkers. Long-term alcohol abuse can also result in pancreatitis, a disease of the pancreas and which can present as acute or chronic progressive disease in which the pancreas is irreversibly damaged, resulting in impaired endocrine and exocrine function as well as disabling pain
In adults, alcoholism is the cause of 70% of all cases of chronic pancreatitis and more than 40% of individuals with chronic pancreatitis will develop T2DM. Most adults who develop chronic pancreatitis will develop diabetes within 5 years of onset (Nair et al.). In addition, some treatments for chronic pancreatitis, such as surgical removal of portions or the entire pancreas, may lead to the development of diabetes.

### 2.6.3 Clinical Care

#### 2.6.3.1 Assessment

Among individuals with alcohol and/or substance disorders, less than 10% received the treatment they required for their disorder in a given year (SAMHSA, 2009). Indeed, among a population drawn for the Veterans Health Administration, disparities in diabetes care were found to be more pronounced when patients had a substance use disorder, increasing in a dose response effect with the addition of additional co-morbid mental health diagnoses (Clark, Weir, Ouellette, Zhang, & Baxter, 2009). Patients with T2DM that use alcohol and/or drugs have been found to receive lower quality of care, above and beyond patient underutilization of preventative and primary care resources of increased ER visits (Frayne et al., 2005). Clinicians should thoroughly assess for current and past substance and alcohol use as part of standard diabetes care, especially in those who are in poor control or have other co-morbid mental health illnesses (ADA, 2004). Recognition of the potential unhealthy effects on glycemic control associated with even moderate use is important in assessing treatment adherence and health behaviors that may impact diabetes treatment. Adolescents and young adults may be at greater risk for engaging in substance use, as are individuals with a former history of drug, alcohol, or tobacco use/misuse, and clinicians are advised to remain aware of the possibility of relapse and provide support and resources if relapse or initiation of use occurs (ADA).

#### 2.6.3.2 Evidence-Based Treatment

Psychoeducation regarding the impact of tobacco, substance, and alcohol use on physical health may motivate patients to address their substance use issues and significant positive health benefits for both metabolic and psychiatric well-being can occur when patients are successful in reducing or discontinuing use (de Leon, Susce, Diaz, Rendon, & Velásquez, 2005). Among clients struggling with alcohol or substance misuse, treatment, especially insulin regimens, should be tailored to fit client’s actual lifestyle to the extent feasible so as to maximize the likelihood of treatment adherence and reduce the risk of life-threatening complications (Lee et al., 2009).

As per the ADA's review of smoking and diabetes (2004), a number of specific recommendations can be made. Intensive smoking cessation interventions, such as
attendance of cessation group or counseling, have been found to be most effective, but patients are less likely to engage in these treatments, due to factors such as time, cost, resources, and motivation (ADA, 2004; Haire-Joshu et al., 2004). All interventions regarding smoking cessation and diabetes should highlight the impact of cigarette smoking on diabetes management and quit aids, such as appropriate prescriptions for pharmacologic interventions and supportive community resources should be available to assist interested patients in cutting down or quitting. The patient’s cessation attempts should be monitored and follow-up care, particularly within the first 2 weeks of the quit date, has also been found to improve cessation outcomes among individuals with diabetes (Haire-Joshu et al.). Finally, while fear of gaining weight may present an unfortunate deterrent to quitting smoking, actual weight gain following smoking cessation can pose at least an increased short-term risk of developing diabetes. Weight gain often occurs during and after a smoking cessation attempt, and smokers, especially heavier smokers, tend to have greater central adiposity than nonsmokers (Healton, Vallone, McCausland, Xiao, & Green, 2006; Willi et al., 2007).

2.6.3.3 Issues in Treatment Decision-Making

A large body of research has explored best practices for treating substance or alcohol use disorders and co-morbid illness in psychiatric illness, the details of which are beyond the scope of this chapter (Riggs, Levin, Green, & Voccì, 2008). As other psychiatric disorders are frequently co-morbid with substance use and have been found to co-occur at higher rates among diabetics than the general population, healthcare practitioners faced with these multiple co-morbidities should consider the implications for psychiatric treatment on diabetes outcomes when planning treatment, as serious mental health issues may often need to be addressed first or in tandem with substance or alcohol use cessation. In a National Epidemiologic Survey on Alcohol and Related Conditions, during the same 12-month period almost 20% of participants with any substance use disorder had at least one mood disorder and almost 18% had at least one anxiety disorder, with rates higher for dependence than abuse (Grant et al., 2003). Even more prevalent were co-morbid alcohol use and psychiatric illness; 40.7% of those with an alcohol use disorder had at least one current mood disorder during the same 12-month time period, and more than 33% had at least one anxiety disorder. Treatment of psychological issues may be essential to both successful substance or alcohol misuse treatment and improvement and stabilization of co-morbid diabetes.

As stated previously, smoking and psychiatric illness often co-occur; individuals with mental illness are approximately twice as likely to smoke as those without mental illness (Lasser et al., 2000). As psychiatric illness may have particular implications for individuals with diabetes and its care, including presenting an increased risk factor for the development of diabetes, metabolic disturbance, and complications from diabetes, it is of vital importance that healthcare professionals attend to co-morbid psychological issues that may underlie an individual’s tobacco use when addressing
smoking cessation and diabetes self-care (Kreyenbuhl et al., 2010; Lucksted et al., 2004; McEvoy & Allen, 2003; Ziedonis et al., 2003). As psychological issues often fuel substance use disorders and compromise both substance cessation and diabetes self-care and predict increased risk of relapse after quitting, it is vital to address mental health as a part of drug, alcohol, or smoking cessation as well as diabetes care (Haire-Joshu et al., 2004; Spangler et al., 2001).

2.7 Cultural Considerations: Diabetes, Race, and Ethnicity

2.7.1 Epidemiology

The problem of racial disparities in the US healthcare system is well documented. Approximately 14% of Hispanics and 12% of African Americans are affected by diabetes compared with 7% of non-Hispanic Whites (Bonds et al., 2003; Harris et al., 1998). Ethnic and racial disparities are also seen in rates of diabetes complications – African Americans and Hispanics have more diabetes-associated nephropathy, retinopathy, and diabetes-related amputations than non-Hispanic Whites (Bonds et al., 2003). Bonds et al. utilized data from the Insulin Resistance Atherosclerosis Study and compared process and outcome measures of diabetes care among African Americans, Hispanics, and non-Hispanic Whites; although the rates of treatment for diabetes and its associated co-morbidities were found to be similar across all three ethnic groups, African Americans and Hispanics had significantly worse control of hypertension and African Americans had worse control of diabetes than non-Hispanic Whites.

The literature is sparse regarding diabetes and mental illness in ethnic and racial minority populations. Studies have shown that greater than 25% of ethnic or racial minority individuals with diabetes reach criteria for MDD, and far more display high levels of depressive symptoms at rates above those found in non-Hispanic Whites (Fisher, Chesla, Mullan, Skaff, & Kanter, 2001; Lustman, Anderson, et al., 2000). Risk factors for increased incidence of depression often overlap with those for developing T2DM. These factors may be more common among individuals more likely to experience disparities in healthcare access and quality, including ethnic/racial minority status, lower SES, unemployment, multiple medical co-morbidities, complications from diabetes, female gender, lower quality of life, and the experience of negative life events or chronic stress (Fisher et al., 2001).

A recent epidemiologic study by Li et al. (2009) utilized a general measure of nonspecific psychological distress to estimate the prevalence of serious psychological distress (SPD) among US adults and found the prevalence of SPD highest among Hispanics (11.8%) and Native Americans (14.7%), individuals with low levels of income (17.3%) and education (15.6%), as well as individuals with T1DM (11.1%) or T2DM (11.5%) who are currently using insulin (Li et al.). Hispanics are also more likely to report higher levels of anxiety compared with Whites and higher levels of diabetes-related distress when compared with African Americans (Li et al.,
The diabetes distress-anxiety association among Hispanics may be especially concerning for both mental and physical health outcomes, as the incidence of type 2 diabetes is projected to increase in the coming years among this rapidly growing segment of the US population (Li et al., 2008).

As discussed previously, risk factors for the development of T2DM and schizophrenia may overlap, including obesity, sedentary lifestyle, lower socioeconomic status, a family history of diabetes, race/ethnicity, poverty, and stress (Black, 2002; CDC, 2005; Mueser & McGurk, 2004). For example, African Americans are more likely to fall into lower economic brackets and rates of both diabetes and schizophrenia diagnoses are found to be higher among African Americans compared to Whites (Black, 2002; CDC, 2005; El-Mallakh, 2006; Mueser & McGurk, 2004). The overrepresentation of socioeconomic burdens among ethnic minority populations may also play a role in the expression of other types of disorders and distress in minority patients with diabetes.

The literature regarding the prevalence of eating disorders and T2DM in minority populations, to our knowledge, is nonexistent. In the general population, cultural beliefs and attitudes have been identified as significant contributing factors in the development of eating disorders (Ismail, 2008). Rates of these disorders appear to vary among different racial/ethnic and national groups, change across time as cultures evolve, and some, such as BED, may be more prevent among individuals who experience social adversity and depression (Ismail; Miller & Pumariega, 2001). As poor diet is a key component in overweight and obesity and increased dietary vigilance is an essential component of self-care for diabetes, research into the ways race, ethnicity, and culture interact with diabetes to impact eating attitudes and disordered eating would help to bridge this knowledge gap.

### 2.7.2 Clinical Care

Racial, ethnic, and socioeconomic disparities in treatment access, utilization, and quality exist in both mental health and diabetes care. In their examination of data from the Behavioral Risk Factor Surveillance System, Li et al. (2010) found that people with diabetes were less likely to be treated for mental health issues than those without. Among adults with diabetes and mental health problems, individuals who were of a non-White race/ethnicity, 65 years of age or older, lacked health insurance, had less than a high school education, or were unemployed were also less likely to receive treatment for mental health needs (Li et al.). The high prevalence of undertreatment may be due to the lack of recognition of mental health problems among these populations and disparities in availability of care or quality of care. The National Co-morbidity Study found that lack of perceived need, situational barriers, financial barriers, perceived lack of effectiveness, thinking the problem would get better by itself, and wanting to solve the problem on one’s own are the major reasons for failing to seek treatment for serious mental illness (Kessler et al., 2001). In a prospective
epidemiological cohort study of 69,068 patients regarding the use of antidepressants, African Americans with diabetes were much less likely to report taking antidepressant medication than Whites (Osborn et al., 2010). The high prevalence of undertreatment among African Americans and Hispanics with diabetes may suggest racial/ethnic disparities in access to medical care or quality of care.

Reducing medical and mental health treatment disparities is a goal of many state and national public health initiatives, as well as Healthy People 2020 (U.S. Department of Health and Human Services, 2010). As in all facets of diabetes care, screening and treatment of diabetes patients with mental illnesses should be culturally sensitive. Including evaluative components in diabetes and mental health interventions targeted to assess the effectiveness of these programs for diverse patient populations may help improve overall quality of care for patients experiencing mental and physical health disparities. Ultimately, there is no one “cookie cutter” approach to diabetes care or mental health treatment – mental health intervention programs should take into account patients’ cultural backgrounds, access to health care, social and economic resources, native languages, as well as health and illness beliefs. There remains a paucity of evidence-based information regarding the treatment of mental health problems in ethnic/racial minority patients in general (Schraufnagel, Wagner, Miranda, & Roy-Byrne, 2006) and even less of this work has been done in patients with diabetes in particular. However, the few studies that have been conducted suggest that empirically supported approaches can be successfully adapted for minority groups. For example, one notable, well-controlled, randomized trial of 267 low-income, English- and Spanish-speaking, White and minority women (Blacks and Latinas) with current major depression demonstrated compared three conditions of treatment: antidepressant medication, manual-guided CBT, or referral to community mental health services (Miranda et al., 2003). Both the medication intervention and the CBT intervention reduced depressive symptoms significantly more than the community referral. Each intervention also had impacts on role functioning, and English- and Spanish-speaking patients responded equally well to each of the treatments. Results of this trial showed that augmentation of treatment with case management resulted in improved retention across all ethnic groups. Interestingly, augmenting the CBT intervention with supplemental case management was shown to improve response for Spanish-speaking depressed patients, but not for English-speaking patients. A recent preliminary report also suggests that a case-management approach to diabetes and depression can be effective in improving depression, self-management, and glycemic outcomes in elderly African Americans with depression and type 2 diabetes (Bogner & de Vries, 2010). This approach included an individualized program to improve adherence to oral hypoglycemic agents and antidepressants and employed a care-manager to facilitate communication between patients and physicians and to address depression and problems with diabetes self-management with sensitivity to cultural issues. Patients randomized to this intervention demonstrated improvements in depression symptom severity, adherence to oral hypoglycemics, adherence to antidepressants, and HbA1c post-intervention as compared to those receiving usual care.
2.8 General Conclusion

The literature reviewed in this chapter highlights the potential for worse treatment outcomes in T2DM patients with co-morbid psychological problems. We have emphasized the importance of careful assessment of psychological disorders in patients with attention to the context of the goals and challenges of living with T2DM. Interventions for psychological problems, even those that may not meet diagnostic thresholds, have the potential to not only improve the mental health and quality of life of patients with T2DM, but may also have important impacts on diabetes treatment outcomes, health, and longevity. For these interventions to be maximally effective, we believe a comprehensive approach that integrates the treatment of psychological problems with interventions aimed at improving health behaviors and diabetes treatment adherence is necessary. Thus far, remarkably few examples of these types of interventions are available in the literature. We sincerely hope that this chapter will encourage clinicians to think carefully about their ability to address the tremendous behavioral challenges facing individuals with co-morbid T2DM and psychopathology and look forward to future research on such integrative interventions that can more thoroughly evaluate the empirical support for our recommendations.

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