KEY MESSAGES

- The experience of living with diabetes is often associated with concerns specific to the illness and can cause conditions, such as diabetes distress, psychological insulin resistance and the persistent fear of hypoglycemic episodes.
- A wide range of psychiatric disorders, including major depressive disorder, bipolar and related disorders, schizophrenia spectrum and other psychotic disorders, anxiety disorders, sleep disorders, eating disorders and stress-related disorders are more prevalent in people with diabetes compared to the general population.
- People living with diabetes and depressive disorders are at increased risk for earlier all-cause mortality compared to people living with diabetes without a history of depression.
- All individuals with diabetes should be regularly screened for the presence of diabetes distress, as well as symptoms of common psychiatric disorders.
- Compared to those with diabetes only, individuals with diabetes and mental health concerns have decreased participation in diabetes self-care, a decreased quality of life, increased functional impairment, increased risk of complications associated with diabetes, and increased health-care costs.
- Cognitive behaviour therapy, patient-centred approaches (e.g. motivational interviewing), stress management, coping skills training, family therapy and collaborative case management should be incorporated into primary care. Self-management skills, educational interventions that facilitate adaptation to diabetes, addressing co-occurring mental health issues, reducing diabetes-related distress, fear of hypoglycemia, and psychological insulin resistance are all helpful.
- Individuals taking psychiatric medications, particularly (but not limited to) atypical antipsychotics, benefit from regular screening of metabolic parameters to identify glucose dysregulation, dyslipidemia and weight gain throughout the course of the illness so that appropriate interventions can be instituted.

KEY MESSAGES FOR PEOPLE WITH DIABETES

- Living with diabetes can be burdensome and anxiety provoking, with the constant demands taking a psychological toll. As a result, many people experience distress, decreased mood and disabling levels of anxiety. Diabetes is often associated with a significant emotional burden, distress over the self-care regimen and stress in relationships (with family and friends, as well as health-care providers).
- It is important to recognize your emotions and talk to your friends, family and members of your diabetes health-care team about how you are feeling. Your team can help you to learn effective coping skills and direct you to support services that can make a difference for you.

Introduction

Research has shown an increasingly clear relationship between diabetes and a variety of mental health issues. These include diagnosable psychiatric disorders, and other problems that are specific to the experience of living with diabetes. “Diabetes distress” refers to the negative emotions and burden of self-management related to living with diabetes. This term is used to describe the despondency and emotional turmoil specifically related to living with diabetes, in particular the need for continual monitoring and treatment, persistent concerns about complications, and the potential erosion of personal and professional relationships (1,2). “Psychological insulin resistance” is the reluctance or refusal to initiate insulin therapy, which may delay the start of a necessary treatment for a period of time (3). Fear of hypoglycemia is another common diabetes-specific concern. The presence of psychiatric and diabetes-specific psychosocial issues is associated with reduced participation in self-management activities and can lead to a decrease in quality of life. Psychiatric disorders among individuals with diabetes increases the risk of diabetes complications and early mortality (4).

Psychological Effects of Diabetes in Adults

Diabetes is a demanding chronic disease for both individuals and their families (5). It is associated with a number of challenges, including adjusting to a new diagnosis, diabetes distress impairing self-management, psychological insulin resistance, and fear of hypoglycemia. In addition, a range of psychiatric disorders can arise that contributes to greater complexity in both assessment and treatment. For instance, distinguishing between diabetes distress, major depressive disorder (MDD) and the presence of depressive symptoms...
is important. Although these constructs have some shared symptomatology, diabetes distress has been most shown to have the strongest effect in causing adverse diabetes outcomes (6–9) (Table 1).

**Diabetes distress** is comprised of 4 interconnected domains, which include: 1) the emotional burden of living with diabetes; 2) the distress associated with the diabetes self-management regimen; 3) the stress associated with social relationships; and 4) the stress associated with the patient-provider relationship. Diabetes distress is associated with elevated glycated hemoglobin (A1C levels), higher diastolic blood pressure (BP) and increased low-density lipoprotein cholesterol (LDL-C) levels (10–12). Furthermore, individuals with higher levels of diabetes distress were found to have a 1.8-fold higher mortality rate, a 1.7-fold increased risk of cardiovascular (CV) disease (13), and have lower quality of life (14). Risk factors for developing diabetes distress include being younger, being female, having lower education, living alone, having a higher body mass index (BMI), lower perceived self-efficacy, lower perceived provider support, poorer quality diet, greater perceived impact of glycemic excursions and greater number of diabetes complications (15,16).

**Psychological insulin resistance** refers to a strong negative response to the recommendation from health-care providers that a person may benefit from adding insulin to his or her diabetes regimen. This can be a common reaction, particularly for individuals with type 2 diabetes who may have previously been successfully managed with noninsulin antihyperglycemic agents. Individuals may hold maladaptive beliefs that requiring insulin is a sign of personal failure in their self-management, or that their illness has become much more serious. Further, many people report fear and anxiety about having to self-administer injections, or have a low level of confidence in their ability to manage their blood glucose with insulin (17,18).

**Fear of hypoglycemia** is a common occurrence. Hypoglycemic experiences, especially serious or nocturnal episodes, can be traumatic for both individuals and their family members. A common strategy to minimize fears of hypoglycemia is compensatory hyperglycemia, where individuals either preventatively maintain a higher blood glucose (BG) level, or treat hypoglycemia in response to perceived somatic symptoms without objective confirmation by capillary blood glucose concentrations (19–22). Over time, this maladaptive process, if left unmanaged, can negatively impact diabetes control, increase the risk of CV complications, and reduce quality of life.

Challenges accompanying the diagnosis of diabetes include adjustment to the illness, participation in the treatment regimen and psychosocial difficulties at both a personal and an interpersonal level (23,24). Stress, deficient social supports and negative attitudes toward diabetes can impact on self-care and glycemic control (25–29). Diabetes management strategies ideally incorporate a means of addressing the psychosocial factors that impact on individuals and their families. Both symptom measures (e.g. self-report measures of various symptoms) and methods to arrive at psychiatric diagnoses (e.g. structured interviews leading to Diagnostic and Statistical Manual of Mental Disorders Fifth Edition [DSM-5 diagnoses] [30] have been assessed. Given that the person with diabetes is directly responsible for 95% of diabetes management (31), identifying significant psychological reactions in diabetes is important since depressive symptoms are a risk factor for poor diabetes self-management (32–34) and outcomes, including early mortality (35,36).

**Psychiatric Conditions in Adults**

Individuals with serious mental illnesses, particularly those with depressive symptoms or syndromes, and people with diabetes share reciprocal susceptibility and a high degree of comorbidity (Figure 1). The mechanisms behind these relationships are multifactorial, complicated and presently only partially understood. Some evidence shows that treatment for mental health disorders may actually increase the risk of diabetes, particularly when second- and third-generation (atypical) antipsychotic agents are prescribed (37). Biochemical changes due to psychiatric disorders themselves also may play a role (38). Symptoms of mental health disorders and their impact on lifestyle are also likely to be contributing factors (39).

**Major Depressive Disorder**

The prevalence of clinically relevant depressive symptoms among people with diabetes is approximately 30% (40–42). The prevalence of MDD is approximately 10% (43,44), which is double the overall prevalence in people without a chronic medical illness. The risk of developing MDD increases the longer a person has diabetes (45). Clinically identified diabetes was associated with a doubling of the prescriptions for antidepressants, but undiagnosed diabetes was not, consistent with the hypothesis that the relationship between diabetes and depression may be attributable to factors related to diabetes management (46). Individuals with depression have an approximately 40% to 60% increased risk of developing type 2 diabetes (46–48). The prognosis for comorbid depression and diabetes is worse than when each illness occurs separately (3). Depression in people with diabetes amplifies symptom burden by a factor of about 4 (49). Episodes of depression in individuals with diabetes are likely to last longer and have a higher chance of recurrence compared to those without diabetes (50). Episodes of severe hypoglycemia have been correlated with the severity of depressive symptoms (51,52). Major depressive disorder has been found to be underdiagnosed in people with diabetes (53).

Studies examining differential rates for the prevalence of depression in type 1 vs. type 2 diabetes have yielded inconsistent results (40,54). One study found that the requirement for insulin was the factor associated with the highest rate of depression,
regardless of the type of diabetes involved (55). Treatment with metformin may enhance recovery from MDD (56).

Risk factors for developing depression in individuals with diabetes are as follows (57–61):

- Female sex
- Adolescents/young adults and older adults
- Poverty
- Few social supports
- Stressful life events
- Poor glycemic control, particularly recurrent hypoglycemia
- Higher illness burden
- Longer duration of diabetes
- Presence of long-term complications.

Intensive lifestyle intervention for people with type 2 diabetes with overweight or obesity reduced the risk of depressive symptoms by 15% (62).

Risk factors (with possible mechanisms) for developing diabetes in people with depression are as follows:

- Physical inactivity (63) and overweight/obesity, which leads to insulin resistance
- Psychological stress leading to chronic hypothalamic-pituitary-adrenal dysregulation and hyperactivity stimulating cortisol release, also leading to insulin resistance (64–69)
- Hippocampal atrophy and decreased neurogenesis (70).

Some of the mechanisms underlying this association have been found to be: autonomic and neurohormonal dysregulation, hippocampal structural changes, inflammatory processes and oxidative stress (70).

Comorbid depression worsens clinical outcomes in diabetes, possibly because the accompanying lethargy lowers motivation for self-care, resulting in lowered physical and psychological fitness, higher use of health-care services and reduced participation in medication regimens (71,72). Depression also appears to worsen CV mortality (73–75). Treating depressive symptoms more reliably improves mood than it does glycemic control (76–79).

**Bipolar Disorder**

One study demonstrated that over half of people with bipolar disorder were found to have impaired glucose metabolism, which was found to worsen key aspects of the course of the mood disorder (80). In this same study, impaired glucose tolerance (IGT) was deemed to be an etiologic factor in the development of bipolar disorder (80). People with bipolar disorder have been found to have prevalence rates estimated to be double that of the general population for metabolic syndrome and triple for diabetes (81–84). Insulin resistance is associated with a less favourable course of bipolar illness, more cycling between mood states, and a poorer response to lithium (85).

**Schizophrenia Spectrum Disorders**

Schizophrenia and other psychotic disorders may contribute an independent risk factor for diabetes. People diagnosed with psychotic disorders were reported to have had insulin resistance/glucose intolerance prior to the advent of antipsychotic medication, although this matter is still open to debate (86–88). The Clinical Antipsychotic Trials for Intervention Effectiveness (CATIE) study found that of the individuals with schizophrenia who participated in the study, 11% had diabetes at baseline (type 1 and 2 combined) (37). The prevalence of metabolic syndrome was approximately twice that of the general population (89). Diabetes and schizophrenia together lead to more CV complications and all-cause mortality compared to people with diabetes alone (90). Whether the increased prevalence of diabetes is due to the effect of the illness (such as advanced glycation end products), antipsychotic medications or other factors, individuals with psychotic disorders represent a particularly vulnerable population (91).
Personality Traits/Disorders

Personality traits or disorders that put people in constant conflict with others or engender hostility have been found to increase the risk of developing type 2 diabetes (92). People with chronic, significantly negative mood states and social inhibition were less likely to follow a healthy diet or to consult health-care professionals in case problems developed with their diabetes management. They report more barriers surrounding medication use, diabetes-specific social anxiety, loneliness and symptoms of depression and anxiety (93).

Stress, Trauma, Abuse and Neglect

A history of significant adversity/trauma, particularly early in life, increases the risk of obesity, diabetes and CV disease (94). Higher BMI, leptin, BP, fibrinogen and decreased insulin sensitivity have been found (95). Post-traumatic stress disorder (PTSD) was found to cause a 40% increased risk of developing type 2 diabetes; those with sub-syndromal traumatic stress symptoms had a 20% increased risk (96).

Anxiety

Anxiety is commonly comorbid with depressive symptoms (97). One study estimated that 14% of individuals with diabetes suffered from generalized anxiety disorder, with double this figure experiencing a subclinical anxiety disorder and triple this figure having at least some anxiety symptoms (98). Anxiety disorders were found in one-third of people with serious mental illnesses and type 2 diabetes, and were associated with increased depressive symptoms and decreased level of function (99). Long-term anxiety has been associated with an increased risk of developing type 2 diabetes (100).

Feeding and Eating Disorders

Anorexia nervosa, bulimia nervosa and binge-eating disorder have been found to be more common in individuals with diabetes (both type 1 and type 2) than in the general population (101). Eating disorders are common and persistent, particularly in females with type 1 diabetes (102,103). Elevated BMI is a risk factor for developing type 2 diabetes and MDD (104). Depressive symptoms are highly comorbid with eating disorders, affecting up to 50% of individuals (105). Night eating syndrome is characterized by the consumption of >25% of daily caloric intake after the evening meal and waking at night to eat, on average, at least 3 times per week. Night eating syndrome has been noted to occur in individuals with type 2 diabetes and depressive symptoms. Night eating syndrome can result in weight gain, poor glycemic control and an increased number of diabetes complications (106).

Sleep-Wake Disorders

People with sleep apnea develop diabetes at higher rates than those without the condition (107).

Substance Use Disorders

The exact prevalence of substance use disorders among individuals with diabetes is not well established, and the presence of substance use disorders may contribute to unique challenges in this population. Recreational substance abuse was associated with increased rates of hospitalization and readmissions for DKA (108). Furthermore, substance abuse and psychosis among individuals with type 1 and type 2 diabetes increases the risk of all-cause mortality (109).

Children and Adolescents with Diabetes

For children, and particularly adolescents, there is a need to identify mental health disorders associated with diabetes and to intervene early to minimize the impact over the course of development. Children and adolescents with type 1 diabetes have significant risks for mental health problems, including depression, anxiety, eating disorders and disruptive behaviour disorders (110–112). The risks increase significantly during adolescence (113,114). Studies have shown that mental health disorders predict poor diabetes management and control (115–118) and worsen medical outcomes (32,119–121). Conversely, as glycemic control worsens, the probability of mental health problems increases (122). Adolescents with type 1 diabetes have been shown to have generally comparable rates for diabetes distress compared to adults with type 1 diabetes (1).

The presence of psychological symptoms and diabetes problems in children and adolescents with type 1 diabetes are often strongly affected by caregiver/family distress. It has been demonstrated that while parental psychological issues are often related to poor psychological adjustment and diabetes control (123–126), they also distort perceptions of the child’s diabetes control (127). Maternal anxiety and depression are associated with poor diabetes control in younger adolescents with type 1 diabetes and with reduced positive effects and motivation in older teens (128).

Feeding and Eating Disorders in Pediatric Diabetes

Ten per cent of adolescent females with type 1 diabetes met the Diagnostic and Statistical Manual of Mental Disorders (5th Edition) criteria for eating disorders (30), compared to 4% of their age-matched peers without diabetes (128). Eating disorders are also associated with poorer metabolic control, earlier onset and more rapid progression of microvascular complications (103). In adolescent and young adult females with type 1 diabetes who are unable to achieve and maintain glycemic targets, particularly if insulin omission is suspected, an eating disorder may be a potential cause. Individuals with eating disorders may require different management strategies to optimize glycemic control and prevent microvascular complications (129). Type 1 diabetes in young adolescent women appears to be a risk factor for development of an eating disorder, both in terms of an increased prevalence of established eating disorder features as well as through deliberate insulin omission or underdosing (called diabulimia) (130,131).

Other Considerations in Children and Adolescents

The prevalence of anxiety disorders in children and adolescents with type 1 diabetes in 1 study was found to be 15.5%, and mood disorders was 3.5%, with one-third having a lifetime prevalence of at least one psychiatric condition (132). The presence of psychiatric disorders was related to elevated A1C levels and a lowered health-related quality of life score in the general pediatric quality of life inventory. In the diabetes mellitus-specific pediatric quality of life inventory, children with psychiatric disorders revealed more symptoms of diabetes, treatment barriers and lower adherence than children without psychiatric disorders (132). Adolescents with type 1 diabetes ranked school as their number 1
Prevention and Intervention

Children and adolescents with diabetes, along with their families, should be screened throughout their development for mental health disorders (134). Given the prevalence of mental health issues, screening in this area is just as important as screening for microvascular complications in children and adolescents with diabetes (135).

Psychological interventions with children and adolescents, as well as families, have been shown to improve mental health (136), including overall well-being and perceived quality of life (137), along with reducing depressive symptoms (138). In addition, there is evidence to show that psychosocial interventions can positively affect glycemic control (139,140). Most importantly, some studies have demonstrated that psychological interventions can increase both diabetes treatment adherence and glycemic control, as well as psychosocial functioning (141,142).

Type 2 Diabetes in Children and Adolescents

Atypical antipsychotic medications are associated with significant weight gain, insulin resistance, IFG and type 2 diabetes in children (143). Psychiatric disorders and the use of psychiatric medications are more common in children with obesity at diagnosis of type 2 diabetes compared to the general pediatric population (144). Children and adolescents prescribed an atypical antipsychotic have double the risk of developing diabetes (145). The risk of developing diabetes may be higher in adolescents taking concomitant antipsychotic and antidepressant medications (146).

Considerations in Pregnancy

One study found that gestational diabetes was strongly associated with increased risk for postpartum depression (PPD), regardless of prior depression history, whereas gestational diabetes increased risk only for those with a prior history of depression. It was also found that for those with a history of depression, diabetes adds a 1.5-fold increased risk for PPD (147). Optimized glycemic control in pregnancy has been shown to have numerous benefits for pregnancy outcomes and may also be protective against PPD (148,149). In another study, the presence of depressive symptoms in early pregnancy was associated with preterm delivery in women with pregestational diabetes (150). Thus, there may be a role for improved screening and treatment of depression in optimizing pregnancy outcomes in women with diabetes (151).

Considerations for Older People with Diabetes

Type 2 diabetes does not appear to be more common in geriatric psychiatric patients than similarly aged controls. MDD and the use of antidepressants, cholinesterase inhibitors and valproate may increase fasting glucose levels (152). The risk of developing a dementing illness in people is increased with those who have MDD (hazard ratio [HR 1.83], type 2 diabetes [HR 1.20] or both [HR 2.17]) (153). The presence of depressive symptoms in elderly people with type 2 diabetes is associated with increased mortality risk (154).

Suicide

A review article found that people with both type 1 and type 2 diabetes had increased rates of suicidal ideation, suicide attempts and completed suicide compared to the general population (155). Another study found that people with newly diagnosed type 2 diabetes had a rate of past suicide attempts of almost 10%, which is twice the rate estimated in the general population. The rate of past suicide attempts in currently depressed patients with diabetes was reported at over 20% (156).

Psychiatric Disorders and Adverse Outcomes

Two independent systematic reviews with meta-analyses showed that MDD significantly increases the risk of all-cause mortality among individuals with diabetes compared to those with diabetes without it (157,158). Older adults with diabetes and depression may be at particular risk (109). Individuals with bipolar disorder, schizophrenia or other psychotic disorders, and who have comorbid diabetes, are at increased risk of rehospitalization following medical-surgical admissions (159).

Screening and Assessment of Mental Health Symptoms

Because of the prevalence of diabetes distress and psychiatric comorbidity and the negative impact that these factors have on glycemic control, early morbidity and quality of life, it is recommended that individuals with diabetes should be regularly screened with validated questionnaires or clinical interviews. The available data does not currently support the superiority of any particular depression screening tool (160). Currently available screening instruments have a sensitivity of between 80% and 90% and a specificity of 70% to 85% (160). Scales that are in the public domain are available at www.outcometracker.org/scales_library.php. Patient Health Questionnaire (PHQ) Screeners are available at www.phqscreeners.com. PHQ-9 (for MDD) scores of ≥10 and Generalized Anxiety Disorders (GAD)-7 scores ≥10 have been associated with increased diabetes complications (161,162).

Screening instruments fall into 3 categories:

- Diabetes-specific measures, such as the Problem Areas in Diabetes (PAID) Scale or the Diabetes Distress Scale (DDS) (163,164)
- Quality of life measures, such as the WHO-5 screening instrument (165)
- Depressive/anxiety symptoms, such as the Hospital Anxiety and Depression Scale (HADS) (166), the Patient Health Questionnaire (PHQ-9) (167,168), the Centre for Epidemiological Studies-Depression Scale (CES-D) (169) or the Beck Depression Inventory (BDI) (170).

Table 1 outlines the principal features and assessment methods to differentiate diabetes distress from MDD.

Psychosocial (Non-Pharmacological) Treatments

Efforts to promote well-being to mitigate distress should be incorporated into diabetes management for all individuals (171). Motivational interventions (172,173), coping skills, self-efficacy enhancement, stress management (174,175) and family interventions (176–179) all have been shown to be helpful. Care management by a nurse working with the patient’s primary care provider and providing guideline-based, patient-centred care resulted in improved A1C, lipid levels, BP and depression scores (172,180–182). Individuals with diabetes distress and/or psychiatric disorders benefit from professional interventions, either some form of psychotherapy or prescription medication. Evidence from systematic reviews of randomized controlled trials supports cognitive behaviour
with type 2 diabetes shown to be helpful. diabetes care providers can enhance successful behaviour changes through motivational and behavioural change strategies can be effective. Diabetes outcomes are heavily dependent on the susceptibility to treatment, such as with the behavioural desensitization therapies (CBT) and antidepressant medication, both solely or in combination (138,183,184). No evidence presently shows that the combination of CBT and medication is superior to these treatments given individually. A pilot study of 50 people with type 2 diabetes who initially had a moderate level of depression at baseline showed an improvement in the severity of their depression (moving to the mild range) with a 12-week intervention of 10 CBT sessions combined with exercise in the form of 150 minutes of aerobic activity weekly. This effect was sustained at 3 months (138).

Table 2 illustrates some of the major features of CBT as applied to diabetes care. Gains from treatment with psychotherapy are more likely to benefit psychological symptoms and glycemic control in adults than will psychiatric medications (which usually reduce psychological symptoms only) (185). Meta-analyses of psychological interventions found that they improved glycemic control (A1C) in children and adolescents with type 1 diabetes (186), and adults with type 2 diabetes (187). Furthermore, evidence suggests interventions are best implemented in a collaborative fashion and when combined with self-management interventions (185). Recent evidence also supports the effectiveness of mindfulness-based CBT (188,189).

Among adults with type 2 diabetes and subclinical depression, CBT resulted in reductions in diabetes distress and depressive symptoms compared to controls (190). Lower diabetes regimen distress (produced by an intervention combining education, problem solving and support for accountability) led to improvements in medication adherence, physical activity and decreased A1C over 1 year (191,192).

Recent research suggests that CBT can be used to address psychological insulin resistance by specifically addressing the beliefs that underlie it (3,193–195) (Figure 2). Fear of hypoglycemia is amenable to treatment, such as with the behavioural desensitization process illustrated in Figure 3 (21,22,195,196).

Pharmacological Treatments

Psychiatric medications have the capacity to affect metabolic parameters and cause changes in weight, glycemic control, lipid profile and can have immunomodulating effects (202–205). A systematic review estimated and compared the effects of antipsychotics, both novel and conventional, and noted variable effects on weight gain (206). The weight gain potential of clozapine and olanzapine has been established (207,208). Children and adolescents using antipsychotics had a 2- to 3-fold increased risk of type 2 diabetes (209,210), which was apparent within the first year of follow up. Metformin has been shown to have a modest ability to reduce weight gain due to antipsychotic medication (211).

A comprehensive review and meta-analysis looked at the effect of antidepressants on body weight (212). Serotonin-norepinephrine reuptake inhibitors (SNRIs) are generally more active on the serotonergic component, with levomilnacipran having the strongest preference among the group for blocking norepinephrine reuptake. Desipramine is the tricyclic antidepressant (TCA) with the strongest action in blocking norepinephrine reuptake (213), and has the potential to affect glucose homeostasis.

The CATIE study investigated 4 aspects of the effectiveness of antipsychotic medications: efficacy, tolerability, emergence of

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**Table 2**

<table>
<thead>
<tr>
<th>Cognitive Component</th>
<th>Behavioural Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>Record keeping to identify distressing automatic thoughts</td>
<td>Strategies to help get the person moving (behavioural activation)</td>
</tr>
<tr>
<td>Understanding the link between thoughts and feelings</td>
<td>Scheduling pleasant and meaningful events</td>
</tr>
<tr>
<td>Learning the common “thinking errors” that mediate distress (e.g. all-or-nothing thinking, personalization, magnification, minimization, etc.)</td>
<td>Learning assertive and effective communication skills</td>
</tr>
<tr>
<td>Analyzing negative thoughts and promoting more functional ones</td>
<td>Focusing on feelings of mastery and accomplishment</td>
</tr>
<tr>
<td>Identifying basic assumptions about oneself (e.g. “unless I am very successful, my life is not worth living) and being encouraged to adopt healthier ones (e.g. “when I am doing my best, I should be proud of myself”)</td>
<td>Exposure to new experiences</td>
</tr>
<tr>
<td>Shaping behaviours by breaking them down into smaller steps to develop skills</td>
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</tbody>
</table>

CBT, cognitive behavioural therapy.

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**Figure 2.** Features of psychological insulin resistance.

**Figure 3.** Suggested cognitive behaviour therapy for fear of hypoglycemia.
medical problems and patient choice (67). The results did indicate that some antipsychotic medications were more likely to cause weight gain, worsen glycemic control and induce unfavourable changes in lipid profile. However, when these effects were considered in the context of efficacy, tolerability and patient choice, no conclusive statements could be made about which medications to clearly use or avoid. Consequently, all 4 aspects are important and reinforce the need for regular and comprehensive metabolic monitoring. Non-pharmacological interventions can be effective in reducing antipsychotic-associated weight gain and glucose changes (214).

Should medical problems arise while a person is taking psychiatric medications, clinical judgement will dictate on a case-by-case basis whether healthy behaviour interventions, such as diet or exercise, adding a medication to address the emergent issue (e.g. side effect or medical complication) or changing the psychiatric prescription is the most reasonable step (215,216). Resources are available to help clinicians quickly review the major side effect profiles of psychiatric medications (217,218).

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### Monitoring Metabolic Risks

Metabolic syndrome is found at higher rates in individuals with psychiatric illnesses than in the general population (84,219). Patients with diabetes and comorbid psychiatric illnesses are at an elevated risk for developing metabolic syndrome, possibly due to a combination of the following factors (220):

- **Patient factors** (e.g. health behaviour choices, diet, tobacco consumption, substance use, exercise, obesity, low degree of implementation of education programs)
- **Illness factors** (e.g. pro-inflammatory states from MDD or depressive symptoms, possible disease-related risks for developing diabetes) (221,222)
- **Medication factors** (e.g. psychiatric medications have variable effects on glycemic control, weight and lipids)
- **Environmental factors** (e.g. access to health care, availability of screening and monitoring programs, social supports, education programs).

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### Table 3

<table>
<thead>
<tr>
<th>Anticholinergics</th>
<th>Unlikely</th>
<th>Likely</th>
<th>Very Likely</th>
<th>Highly Likely</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benztropine</td>
<td>Trihexyphenidyl</td>
<td>Procyclidine</td>
<td>Amitriptyline, Clomipramine, Desipramine, Doxepin, Fluvoxamine, Imipramine, Maprotiline, Mirtazapine, Nortriptyline, Phenelzine, Trimipramine, Diphenhydramine</td>
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### Table 4

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>1 month</th>
<th>2 months</th>
<th>3 months</th>
<th>Every 3 to 6 months</th>
<th>Annually</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (BMI)</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Waist circumference</td>
<td>x</td>
<td></td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td>x</td>
<td></td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting lipid profile</td>
<td>x</td>
<td></td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personal history, particularly alcohol, tobacco and recreational substance use</td>
<td>x</td>
<td></td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history</td>
<td>x</td>
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</tbody>
</table>

A1C, glycated hemoglobin; BMI, body mass index.
Many psychiatric medications (primarily second- and third-generation or atypical antipsychotics), have the potential to affect weight, lipids and glycemic control even in patients without diabetes (37,223). A weight gain of between 2 to 3 kg was found within a 1-year time frame with the antidepresants amisulpride, ziprasidone, risperidone, paliperidone (212). A study of people with type 2 diabetes and schizophrenia who were treated with antipsychotic medications also showed worsening glycemic control, requiring the addition of insulin therapy over a 2.5-year period with a HR of 2.0 (224). The reported weight gain over a 1-year period ranges from <1 kg to >4 kg for various antipsychotic medications. The main impact on lipid profile is an increase in triglyceride and total cholesterol levels, especially with clozapine, olanzapine and quetiapine (37,225).

Table 3 lists the likelihood for weight gain with use of psychiatric medications.

Regular, comprehensive monitoring of metabolic parameters is recommended for all persons who receive antipsychotic medications, whether or not they have diabetes. A1C was shown to be a more stable parameter in identifying psychiatric patients with diabetes (226). Table 4 outlines a Psychiatric Medication Metabolic Monitoring Protocol.

**RECOMMENDATIONS**

1. Individuals with diabetes should be regularly screened for diabetes-related psychological distress (e.g. diabetes distress, psychological insulin resistance, fear of hypoglycemia) and psychiatric disorders (e.g. depression, anxiety disorders) by validated self-report questionnaire or clinical interview [Grade D, Consensus]. Plans for self harm should be asked about regularly as well [Grade C, Level 155].

2. The following groups of people with diabetes should be referred to specialized mental health-care professionals [Grade D, Consensus for all of the following]:
   - Significant distress related to diabetes management
   - Persistent fear of hypoglycemia
   - Psychological insulin resistance
   - Psychiatric disorders (i.e. depression, anxiety, eating disorders).

3. Collaborative care by interprofessional teams should be provided for individuals with diabetes and depression to improve:
   - Depressive symptoms [Grade A, Level 1 (181,182)]
   - Adherence to antidepressant and noninsulin antihyperglycemic medications [Grade A, Level 1 (181)]
   - Glycemic control [Grade A, Level 1 (182)].

4. Psychosocial interventions should be integrated into diabetes care plans, including:
   - Motivational interventions [Grade D, Consensus]
   - Stress management strategies [Grade C, Level 3 (175)]
   - Coping skills training [Grade A, Level 1A (227) for type 2 diabetes; Grade B, Level 2 (228) for type 1 diabetes]
   - Family therapy [Grade A, Level 1B (176,178,229)]
   - Case management [Grade B, Level 2 (192)].

5. Antidepressant medication should be used to treat acute depression in people with diabetes [Grade A, Level 1 (78)] and for maintenance treatment to prevent recurrence of depression [Grade A, Level 1A (77)]. Cognitive behaviour therapy (CBT) can be used to treat depression in individuals with depression alone [Grade B, Level 2 (79)] or in combination with antidepressant medication [Grade A, Level 1 (138,184)].

6. Because of the risk of adverse metabolic effects of many antipsychotic medications (especially atypical/second and third generation) [Grade A, Level 1 (37)], regular metabolic monitoring should be performed in people with and without diabetes who are treated with these medications [Grade D, Consensus].

7. Children and adolescents with diabetes should be screened at diagnosis for major depressive disorder [Grade D, Consensus] and regularly for psychosocial difficulties, family distress or mental health disorders [Grade D, Consensus]. An expert in mental health and/or psychosocial issues should provide intervention when required; this individual may be part of the pediatric diabetes health-care team or enlisted by referral [Grade D, Consensus]. Individual and family educational interventions should be included to address stress or diabetes-related conflict when indicated [Grade D, Consensus].

8. Adolescents with type 1 diabetes should be regularly screened using non-judgemental questions about weight and body image concerns, dieting, binge eating and insulin omission for weight loss [Grade D, Level 2 (131)].

** Abbreviations:**

- A1C, glycated hemoglobin; BMI, body mass index; BP, blood pressure; CBT, cognitive behaviour therapy; CV, cardiovascular; DKA, diabetic ketoacidosis; HR, hazard ratio; IGF, impaired fasting glucose; LDL-C, low density lipoprotein; MDD, major depressive disorder; PPD, postpartum depression; PTSD, post-traumatic stress disorder.

**Other Relevant Guidelines**

Nutrition Therapy, p. S64

Glycemic Management in Adults With Type 1 Diabetes, p. S80

Pharmacologic Glycemic Management of Type 2 Diabetes in Adults, p. S88

Type 1 Diabetes in Children and Adolescents, p. S234

Type 2 Diabetes in Children and Adolescents, p. S247

**Author Disclosures**

Dr. Robinson reports personal fees from Janssen, Otsuka, Lundbeck, and Allergan, outside the submitted work. Dr. Coons has received honoraria from the Canadian Medical and Surgical Knowledge Translation Working Group. Dr. Vallis reports personal fees from Novo Nordisk, Valeant, Sanofi, Pfizer, CSL Behring, Merck, and Abbvie, outside the submitted work. Dr. Yale reports grants and personal fees from Eli Lilly Canada, Sanofi, Merck, AstraZeneca, Boehringer Ingelheim, Janssen, and Medtronics; personal fees from Novo Nordisk, Takeda, Abbott, and Bayer; and grants from Mylan. No other author has anything to disclose.

**References**

5. Snoek FJ, Kersch NY, Eldrup E, et al. A weight gain of between 2 to 3 kg was found for various antipsychotic medications. The main impact on lipid profile is an increase in triglyceride and total cholesterol levels, especially with clozapine, olanzapine and quetiapine (37,225).
6. The following groups of people with diabetes should be referred to specialized mental health-care professionals [Grade D, Consensus for all of the following]:
   - Significant distress related to diabetes management
   - Persistent fear of hypoglycemia
   - Psychological insulin resistance
   - Psychiatric disorders (i.e. depression, anxiety, eating disorders).
7. Collaborative care by interprofessional teams should be provided for individuals with diabetes and depression to improve:
   - Depressive symptoms [Grade A, Level 1 (181,182)]
   - Adherence to antidepressant and noninsulin antihyperglycemic medications [Grade A, Level 1 (181)]
   - Glycemic control [Grade A, Level 1 (182)].
8. Adolescents with type 1 diabetes should be regularly screened using non-judgemental questions about weight and body image concerns, dieting, binge eating and insulin omission for weight loss [Grade D, Level 2 (131)].
9. The reported weight gain over a 1-year period ranges from <1 kg to >4 kg for various antipsychotic medications. The main impact on lipid profile is an increase in triglyceride and total cholesterol levels, especially with clozapine, olanzapine and quetiapine (37,225).
10. Table 3 lists the likelihood for weight gain with use of psychiatric medications.
11. Regular, comprehensive monitoring of metabolic parameters is recommended for all persons who receive antipsychotic medications, whether or not they have diabetes. A1C was shown to be a more stable parameter in identifying psychiatric patients with diabetes (226).
12. Table 4 outlines a Psychiatric Medication Metabolic Monitoring Protocol.
13. Many psychiatric medications (primarily second- and third-generation or atypical antipsychotics), have the potential to affect weight, lipids and glycemic control even in patients without diabetes (37,223).
14. A weight gain of between 2 to 3 kg was found within a 1-year time frame with the antidepresants amisulpride, ziprasidone, risperidone, paliperidone (212).
15. A study of people with type 2 diabetes and schizophrenia who were treated with antipsychotic medications also showed worsening glycemic control, requiring the addition of insulin therapy over a 2.5-year period with a HR of 2.0 (224).
16. The reported weight gain over a 1-year period ranges from <1 kg to >4 kg for various antipsychotic medications. The main impact on lipid profile is an increase in triglyceride and total cholesterol levels, especially with clozapine, olanzapine and quetiapine (37,225).
17. Table 3 lists the likelihood for weight gain with use of psychiatric medications.
18. Regular, comprehensive monitoring of metabolic parameters is recommended for all persons who receive antipsychotic medications, whether or not they have diabetes. A1C was shown to be a more stable parameter in identifying psychiatric patients with diabetes (226).
19. Table 4 outlines a Psychiatric Medication Metabolic Monitoring Protocol.


with diabetes: Results of a randomized controlled trial. Diabetes Care 2014;37:2427–34.


