55 Psychiatric Disorders and Diabetes

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Keypoints

- The interactions between diabetes and psychiatric disorders are complex: physical illness raises the risk of psychiatric disorder, but mental illness and its treatment also impact on the risks and outcomes of diabetes.
- Because mental health problems are common among people with diabetes, good levels of awareness and knowledge are vital for the health professionals who work with them.
- A strong case has been made for implementation of screening for mental health problems in a range of care settings.
- Increased availability of mental health expertise in the settings where people with diabetes are treated is required.

Introduction

The interaction between mind and body is central to the management and outcome of all chronic diseases, but is perhaps particularly complex and fascinating in the case of diabetes. Diabetes is no longer an invariably fatal condition; however, in order to maintain good health, many patients face high behavioral demands. Psychiatric disorders may significantly compromise the ability of the patient to perform self-care to the required standard for optimum health, leading to increased risks of poor outcomes including complications and premature mortality.

Both diabetes and psychiatric disorders are common conditions, and therefore a degree of co-occurrence would be expected purely by chance; however, there is a considerable body of evidence that diabetes is associated more frequently than expected with a range of psychiatric morbidity. In particular, it appears that patients with mood and psychotic disorders are at increased risk of developing diabetes, and people with diabetes go on to develop a range of psychologic problems at increased rates compared to healthy controls. This was first noted over a century ago; as Henry Maudsley said in his celebrated textbook, *Pathology of Mind*, when discussing the increased rates of diabetes observed among psychiatric patients [1]:

> "*Diabetes is a disease which often shows itself in families in which insanity prevails. Whether one disease predisposes in any way to the other or not, or whether they are independent outcomes of a common neurosis, they are certainly found to run side by side, or alternately with one another more often than can be accounted for by accidental coincidence or sequence*".

Knowledge of the special problems that occur when diabetes and a psychiatric disorder coincide is essential if optimum care is to be provided. Unfortunately, in most countries, services are not well organized to deliver good quality care for both the physical and psychologic needs of patients in the same setting. Clinicians need to be aware of the increased risks of co-morbidity, and the need for screening. Diabetes health care professionals should be able to provide "first response" management, and recognize the needs of those more complex patients for whom specialist management is essential. The topic of co-morbidity is also attracting interest from researchers, and there is the potential for considerable progress in understanding the epidemiology and psychobiologic mechanisms involved. The increased availability of objective measures of glycemic control and diabetes outcomes over the past few decades has opened up the possibility of a wide range of psychobiologic research. This chapter provides an overview of the current state of knowledge of these topics, and highlights needs for further research.

Mood disorders

Until quite recently, any discussion of mood disorders and diabetes would have concentrated solely on the increased rates of depression observed in cohorts of patients with diabetes, and is

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likely to have viewed such co-morbidity mainly as an "understandable" reaction to the difficulties resulting from living with a demanding and life-limiting chronic physical illness. We now understand that the interaction between the two conditions is more complex than this:

- Depression may itself be a risk factor for the development of diabetes;
- Biologic aspects of diabetes may contribute to the development of depression;
- Other antecedent factors, such as the early nutritional environment, may have a "common soil effect," thereby contributing to the risks of both conditions.

Depression can also impact on the clinical course of the diabetes, increasing the risk of poor glycemic control and complications. People with both diabetes and depression have been found to have higher symptom burden, poorer functional status, poorer self-care and higher health care costs [2].

Case definition

Depressive symptoms exist on a continuum of severity. Standard definitions of "clinical" depression are based on symptom count and duration; the most widely used diagnostic criteria in current practice are those of the American Psychiatric Association's DSM-IV "major" depression (Table 55.1) [3].

This definition is to some degree arbitrary; however, it approximates to a level of symptomatology that is associated with significant disability and dysfunction, and is very widely accepted as a standard in both clinical practice and research. It is important to note that depressive disorders of lesser severity may still compromise self-care and outcomes in people with diabetes.

The clinical category of mood disorders includes both unipolar depression and bipolar ("manic-depressive") illness. This section focuses on unipolar depression; bipolar illness is included in the section on psychotic disorders.

Table 55.1 DSM-IV "major" depressive episode.

Five or more of the listed symptoms should be present nearly every day, for at least 2 weeks, and should represent a change from normal functioning; at least one of the first two symptoms in the list must be present

Symptoms

1. **Depressed mood for most of the day**
2. **Markedly diminished interest or pleasure in all, or almost all, activities for most of the day**
3. Significant weight loss when not dieting, or weight gain (change of 5%), or decrease or increase in appetite
4. Insomnia or hypersomnia
5. Psychomotor agitation or retardation
6. Fatigue or loss of energy
7. Feelings of worthlessness or excessive or inappropriate guilt
8. Diminished ability to think or concentrate
9. Recurrent thoughts of death or suicidal ideation

Epidemiology

Unipolar depression is one of the most common mental health problems in the general population, affecting 3–5% of the population at any time, and its prevalence appears to be increasing, such that the World Health Organization have estimated that it will be the second leading cause of disability (after heart disease) in the world by 2020 [4].

There have been many studies of the prevalence of depressive symptoms and disorders in people with diabetes over the past 40 years. Most of the early studies, however, had significant methodologic shortcomings.

First, they lacked standardized definitions of depressive disorders, mainly using rating scales of unknown reliability and validity in a diabetic population. The "gold standard" for ascertainment of case status is a research diagnostic interview; most rating scales can only give a probabilistic estimate of caseness. In addition, there may be an overlap between symptoms of diabetes and those of depression (e.g. fatigue, weight loss).

Second, studies have tended to ignore the heterogeneity of people with diabetes, studying mixed populations of patients with different forms of diabetes (e.g. type 1 [T1DM] and type 2 [T2DM]). It is important to distinguish between these groups for several reasons:

- Although there is increasing overlap, people with T2DM are older and depression prevalence varies with age;
- There may be differences in pathologic mechanisms;
- The rates of diabetic complications and other co-morbid conditions (e.g. obesity, heart disease) differ; and
- The demands of management are different.

Third, studies have often been based on "convenience" samples of patients, usually drawn from diabetic clinics, where the operation of referral and other biases in sample composition was of unknown effect. Ethnicity is also an important confounder for rates of both depression and diabetes.

Finally, studies have had low or unknown response rates, and because the presence of depressive symptoms may reduce the likelihood of responding in such studies, this biases prevalence estimates further. Not surprisingly, as a result the range of prevalence figures that can be found in the literature is very wide.

More recent studies, using better methods, and meta-analyses, have led to lower estimates of prevalence. For example, one recent review of the prevalence of co-morbid depression in people with T1DM [5] concluded that clinical depression was present in 12%, compared with 3.2% in control subjects without diabetes. Caution is still needed in the interpretation of this finding, because it was based on only 14 studies, of which only four included control groups and only seven were based on interview methods. Excluding studies without control groups and interview ascertainment led to a fall in estimated prevalence to 7.8%, a figure that, although still raised, is no longer statistically significantly different from that found in healthy controls (odds ratio [OR] 2.4; 95% confidence interval [CI] –0.7 to 5.4).

Studies of depression in people with T2DM tend to be based on larger samples, given that around 85% of patients have this

disease subtype. A recent study based on clinical diagnoses from a US Health Maintenance Organization [6] concluded that depression was more common in people with T2DM (17.9%) than in matched controls (11.2%), with marked sex differences: depression was nearly twice as common in women, but the effect of the presence of diabetes was greater in men. The effect remained after adjustment for covariates such as cardiovascular disease and obesity.

Depressive disorders as a risk factor for diabetes

The suggestion that emotional factors, such as grief or sadness, could lead to the onset of diabetes was first raised by Thomas Willis in 1684. It is a common clinical observation that the onset of diabetes may follow a depressive episode, although because T2DM often goes undiagnosed for years, the apparent association may be at least partly the result of ascertainment bias – patients with depression are more likely to have a screening test for diabetes than those without.

A recent systematic review has addressed the question of the direction of the association between these conditions, and summarized the evidence that depression may be a risk factor for diabetes [7]. Unfortunately, the vast majority of existing studies are cross-sectional and therefore uninformative about this issue. The reviewers were able to identify nine longitudinal studies, and the analysis suggested that depressed adults have an increased risk of developing T2DM of around 37%; however, this must be regarded as a preliminary finding, and further large well-designed longitudinal studies are needed.

Proposed mechanisms linking depression and diabetes

Psychosocial factors

Most studies confirm that risk factors for depression in otherwise healthy individuals operate equally in people with diabetes. Thus, socioeconomic hardship, poor education, stressful life events and lack of social support are all important [8]. Gender differences are also important. There is relatively little evidence that people with diabetes differ greatly with respect to these types of risk factors, and it can be concluded that much depression in people with diabetes may be "independent" of the presence of the disease, an issue that may be particularly important when it comes to management planning.

Early nutrition

One putative common risk factor that may increase the risks of both of diabetes and depression is that of disrupted nutrition during fetal life. There are now over 38 reports linking poor fetal growth with impaired glucose metabolism in later life [9]. Most of these studies report an inverse relationship or J-shaped relationship between birth weight and plasma glucose and insulin concentrations, the prevalence of T2DM and measures of insulin resistance and secretion. Similarly, the risk of depression has been found to be associated with low birth weight for both young and older adults [10]. Furthermore, data from the Dutch Hunger Winter study showed that exposure to famine during the second or third trimester of fetal life is associated with increased risk of hospital treatment for major affective disorder [11].

The mechanism underlying this association is not clear but one hypothesis proposes that fetal programming of the hypothalamic-pituitary-adrenal (HPA) axis may play a part.

Shared genetic risk

Another suggested mechanism that may link diabetes and psychiatric disorder is that of shared genetic variance. There is some evidence that close relatives of people with some forms of psychiatric disorder have an increased incidence of diabetes [12], and known loci for the disorders occur in overlapping positions within chromosomes [13]. Investigation of this intriguing possibility is in its infancy and further research is needed.

Inflammatory mechanisms

It has been hypothesized that inflammation and increased production of proinflammatory cytokines by activated immune cells may mediate the association between depression and diabetes, with associated perturbation of the HPA axis [14]. Parallels have been noted between depression and so-called "sickness behavior" seen in response to the elevation of cytokines, interleukin 1 (IL-1), IL-6 and tumor necrosis factor α (TNF-α). It is thought that such cytokines may be released in increased amounts from adipose tissue in conditions including diabetes and obesity as people age, and this may interfere with insulin action.

Counter-regulatory hormones

Acute psychologic stress is known to increase circulating concentrations of counter-regulatory hormones including noradrenaline, glucocorticoids and growth hormone (GH), which antagonize the hypoglycemic action of insulin. Although the effects of chronic stress on the HPA axis are somewhat less well understood, the view of depression as a maladaptive prolonged stress reaction has some empirical support.

Loss of normal diurnal variation in cortisol levels together with non-suppression of cortisol release in response to exogenous steroid administration have long been noted as hallmarks of depressive illness, particularly the "melancholic" subtype. It is suggested that this may lead to increased glycogenolysis, gluconeogenesis, lipolysis and inhibition of peripheral glucose transport and utilization [15]. Non-diabetic patients with depression have been shown to have increased insulin resistance, but further investigation of this mechanism is warranted. Glucose transport in the brains of people with depression has also been shown to be abnormal [15].

Depression and glycemic control

Several studies have demonstrated an association between the severity of depressive symptoms and the level of glycemic control as assessed by glycosylated hemoglobin level (HbA_{1c}) [16], although the size of this effect has been generally modest, and may be explained by confounders such as the presence of microvascular complications. Most studies have been cross-sectional in

nature, although some treatment studies have suggested that improvements in glycemic control are associated with reduction of depressive symptoms.

Depression and complications

There seems to be little doubt that the risk of depression increases as microvascular and macrovascular complications accrue over the course of the disease [17]. The evidence is less strong that the presence of depression increases the risk of developing complications, although the fact that self-care and resulting glycemic control are impaired would lead to this expectation. One longitudinal cohort study of 66 people with T1DM found that depression was an independent risk factor for retinopathy at 10 years [18], but other studies have had negative results. The meta-analysis of de Groot *et al.* [17] supports a positive association.

One complication that may have a particular association with depression is that of peripheral neuropathic pain. Recent studies suggest that not only is chronic pain a risk factor for depression, but the presence of depression may itself worsen the experience of pain. Common neurotransmitters appear to be involved in both depression and pain [19].

Management of people with diabetes and depression

At present, advice for the management of patients with co-morbid depression and diabetes is based on evidence derived from populations without diabetes because the number of treatment studies in people with diabetes is as yet too small to lead to robust conclusions. Nevertheless, some inroads into this problem are now being made.

The main aims of treatment are to reduce depressive symptoms and to improve self-care, glycemic control and diabetes outcomes. A major difficulty for most clinics is the lack of readily available specialist mental health input, and this has been a disincentive for services to engage actively in tackling this important clinical problem. By contrast, guidelines are now including the issue of psychologic well-being, increasing the need for attention to be paid to it. It should be possible for most clinics to provide "first response" management for simple depressive disorders, although specialist help will still be required for more complex cases, where there is diagnostic uncertainty or lack of response to initial treatment. Assessment and management of suicide risk is a particularly important issue, although fortunately rare in most clinic settings.

Screening for depression

Given the high prevalence of depression in people with diabetes, it is recommended [20] that screening and case finding is worthwhile and this is now recommended by the National Institute for Health and Clinical Excellence (NICE) in the UK [21]. NICE recommends that health care professionals who care for or advise adults with diabetes should be alert to the development or presence of clinical or subclinical depression and anxiety. This is particularly the case where someone reports or appears to be having difficulties with self-management. Health care professionals should ensure they have appropriate diagnostic and management skills for non-severe psychologic disorders in people from different cultural backgrounds. Knowledge of appropriate counseling techniques and appropriate drug therapy is important, as well as an awareness of the need for prompt referral to specialists of those in whom psychologic difficulties continue to interfere significantly with well-being or diabetes self-management.

In the UK, GPs are now reimbursed specifically for carrying out screening in populations with chronic illness, including diabetes. There are several short screening questionnaires that can be used for this purpose including the Patient Health Questionnaire (PHQ-9) [22], Hospital Anxiety and Depression Scale (HADS) [23] and Beck Depression Inventory (BDI) [24], although none of these have been specifically validated for use in diabetic populations, and scores may be inflated by the presence of diabetes-related symptoms. It may be better to use a very brief clinical interview using three questions [25]. Initially, the patient is asked:

- During the past month, have you been bothered by having little interest or pleasure in doing things?
- During the past month, have you been bothered by feeling down, depressed, or hopeless?

If the answer to either of these is "yes," the patient should then be asked if they want help with this problem. If the answer to this is also "yes," then it is reasonable to offer treatment.

Case history 1: A woman with diabetes and depression

Joan is a 62-year-old married woman who has had type 2 diabetes for 15 years, which is treated by diet and oral hypoglycemic medication. She has a body mass index of 32 kg/m^2, and at interview was noticeably low in mood. On direct questioning, she gave a history of significant depressive symptoms lasting for several months, and had a history of previous intermittent depressive episodes dating back to the birth of her first child at the age of 24. She had low self-esteem, and admitted to bouts of "comfort eating" (mainly chocolate) to try to treat her low mood. There was no disturbance of body image. In addition, she was socially isolated, and complained of receiving little support from her husband, who was usually busy at work. Management consisted of antidepressant medication, augmented with advice and support focused on increasing socialization and resumption of pleasurable and rewarding activities, such as spending more time with her grandchildren.

Pharmacotherapy

Many treatment guidelines exist, including those from NICE [26], and similar ones from bodies such as the American Psychiatric Association. Drug treatment is the mainstay of depression management. Effective and well-tolerated antidepressant drugs are widely available and affordable. Choice of agent tends to be based on side effect profile because evidence of differential efficacy is poor. Older families of compounds such as tricyclic antidepressants and monoamine oxidase inhibitors have

decreased in popularity because of their toxicity, particularly in patients who might be at increased risk of heart disease.

Selective serotonin reuptake inhibitors are relatively safe and very widely used as first choice agents; however, caution is needed because there are important drug–drug interactions with some members of this class and oral hypoglycemic agents through inhibition of the cytochrome P450 3A4 and 2C9 isoenzymes (see Chapter 26). For example, the use of fluoxetine may lead to hypoglycemia [15]. Weight gain, which occurs with some antidepressants including mirtazepine, is particularly undesirable in overweight people with T2DM.

It is important to have a clear treatment target, and most guidelines now recommend that this should be complete remission of depressive symptoms. To achieve this, treatment must be sustained at an adequate dosage for a sufficient period of time. Once remission has been attained, treatment should be continued for at least 4–6 months to consolidate recovery. There is an increased risk of relapse and recurrence if the course of treatment is given at too low a dosage or for insufficient duration.

In addition to possible direct pharmacologic effects, it should be remembered that treating depression may lead to a change in the patient's behavior and routine that may require adjustment of the diabetic regimen. For example, if the patient's appetite improves, insulin requirements may increase; if the patient becomes more active, they may decrease. It is likely, however, that improvement in depressive symptoms alone will not translate automatically into improved self-care and diabetes outcomes. Additional attention to diabetes management is required as the depression improves.

Clinical management

In most health care systems, depression is managed mostly within primary care by family physicians or GPs. Much emphasis has been placed in recent years on the delivery of evidence-based practice, and this has led to a proliferation of guidelines and educational support designed to improve quality of primary care. In the USA, a case management model known as "collaborative care" has been pursued, whereby family physicians are supported in case management by specialist mental health teams. This approach has been shown to be clinically useful and cost-effective [27,28]. Recently, a large study, the Pathways study [29], has attempted to address the question of whether or not this approach can improve outcomes for patients with both diabetes and depression. In this study over 300 patients were randomly allocated to receive the intensified case management approach or usual care. Contrary to expectations, although depression outcomes were improved, no concomitant improvements in glycemic control were observed over a 12-month period. This finding suggests that when treating depression in people with diabetes, attention also needs to be paid to modifications that are needed in the diabetes regimen such as adjustment of diet, activity and medication if the best possible outcomes are to be attained. Such integrated approaches to management are all too rare at the present time.

Psychologic treatment

The other important aspect of management for depression that has been widely evaluated in diabetic populations is psychologic treatment, which can take a variety of forms. There is some confusion in the literature between approaches that could be broadly described as "educational" – that is, largely based on improving knowledge and understanding of diabetes management – and those with a more psychologic or behavioral basis, such as cognitive–behavior therapy. For most patients with suboptimal self-care, it appears that lack of knowledge of their condition is not the most important cause; rather there are more complex causes, which may have their origins in early life experiences or in current stressful events or circumstances, and it is these that psychologic treatments seek to address.

Educational approaches could be broadly divided into "didactic" and "enhanced"; in the latter form the giving of information and advice is supplemented with behavioral instruction, development of skills such as problem-solving and a range of other techniques such as biofeedback or relaxation. Thus, the boundary between educative approaches and formal psychotherapy has become blurred, and this creates difficulties in evaluating the available literature. The consensus from systematic reviews is that such interventions can improve glycemic control, albeit with a modest effect size of about 0.3 – equivalent to a reduction in HbA_{1c} of around 0.6% (7 mmol/mol) – and can also reduce psychologic distress [30].

There are few trials that have set out to test directly the efficacy of psychologic treatment in treating depression in people with diabetes. Studies of otherwise healthy subjects with depression show that several forms of treatment including cognitive–behavioral therapy, interpersonal psychotherapy and cognitive–analytic therapy can all be of benefit. A recent systematic review evaluated the efficacy of psychologic interventions aimed primarily at improving glycemic control in people with T2DM [30], and found that benefits were seen in terms of reduced psychologic distress and improved long-term glycemic control.

Given that psychologic treatments are potentially very effective, but expensive and limited in availability, there is an urgent need for more evaluation of their benefits and applicability. In the UK, there is currently a large program evaluating the benefits of widening access to psychologic treatment for depression, and a similar initiative in the case of diabetes is warranted. Unfortunately, it appears as if availability of such treatments to people with diabetes is actually decreasing within the UK [31].

Psychotic disorders

Psychotic disorders are the most serious forms of illness within the mental health field, and are often also known as "severe mental illness" (SMI). (Although this term is imprecise because it is perfectly possible for patients to have equally serious forms of other non-psychotic types of illness.) The two main forms of psychotic disorder in working age adults are schizophrenia and

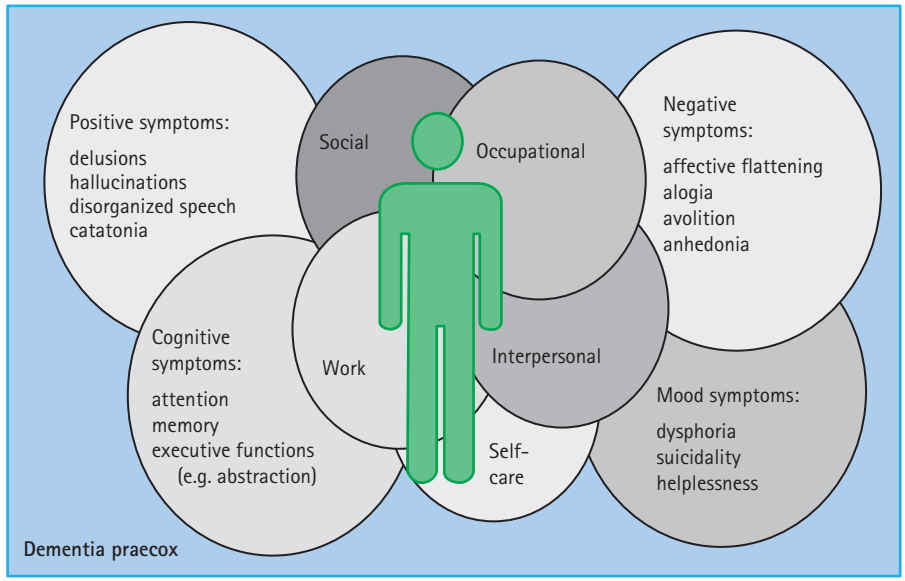

Figure 55.1 Impact of schizophrenia on overall functioning.

bipolar mood disorder or "manic depression." The impact of these disorders on patients' well-being and functioning is particularly severe because of the presence of psychotic symptoms including delusions and hallucinations which have a profound effect on any or all aspects of daily life (Figure 55.1). When they co-occur with a chronic physical illness, they can create significant management challenges, and such patients are amongst the most complex that health care systems encounter.

It has been noted for over a century that abnormalities of glucose metabolism are more common in those with this type of mental illness [32], although only in recent years have efforts been made to establish the precise nature of this association. The situation is complicated by the fact that some forms of treatment for these disorders may also affect metabolic health. It is known that patients with such disorders have reduced life expectancy, and much of the excess early mortality results from physical disease including diabetes and cardiovascular disease. Intensified efforts to improve the physical health of people with long-term mental illness are now underway in most countries, with detection and management of metabolic and cardiovascular risk factors and diabetes at their core [33].

Case definitions

Diagnostic criteria for schizophrenia are shown in Table 55.2. It can be seen that the illness is characterized by psychotic symptoms (delusions, hallucinations), disorganization of speech and other behavior, and so-called "negative" symptoms which include loss of drive and blunting of affect. In the longer term, schizophrenia is also associated with cognitive decline. The illness has marked effects on daily functioning, tends to run a chronic clinical course and most patients with the condition will be under the long-term care of specialist mental health services.

Bipolar disorder is characterized by the occurrence of one or more episodes of mania (elevated mood), with or without a previous history of depressive episodes. Criteria for a manic episode are shown in Table 55.3. The strict diagnostic criteria for bipolar disorders are complex, and there is a degree of overlap with schizophrenia, such that some patients may be characterized as having a "schizo-affective" disorder.

Table 55.2 DSM-IV schizophrenia.

1	Two or more of the following symptoms:
	(i) Delusions
	(ii) Hallucinations
	(iii) Disorganized speech
	(iv) Grossly disorganized or catatonic behavior
	(v) Negative symptoms (affective flattening, alogia or avolition)
2	Social/occupational dysfunction
3	Features continuously present for at least 6 months

Epidemiology

Schizophrenia is estimated to have a point prevalence of 1–7/1000 in the general population, with an annual incidence of 13–70/100 000 and a lifetime risk of 1–2%. Strikingly, this varies very little across the countries of the world. The clinical course of the illness is variable, ranging from a single brief episode (rarely) to a lifelong illness with marked deterioration over time. There are many theories about the causation of schizophrenia. It has a marked genetic risk profile, but is also associated with early cerebral insults (e.g. birth anoxia) and environmental stress.

Bipolar disorder is much less common than unipolar depression, with an estimated lifetime prevalence of 0.5–1.0%. Again, genetic factors are thought to have an important role in the etiology of bipolar disorders, which are among the most heritable of psychiatric disorders.

Table 55.3 DSM-IV manic episode.

1 A distinct period of abnormally and persistently elevated, expansive or irritable mood, lasting at least 1 week
2 During the period of mood disturbance, three or more of the following symptoms have persisted (four if mood only irritable):
(i) Inflated self-esteem or grandiosity
(ii) Decreased need for sleep
(iii) More talkative than usual or pressure to keep talking
(iv) Flight of ideas or subjective experience that thoughts are racing
(v) Distractibility
(vi) Increase in goal-directed activity or psychomotor agitation
(vii) Excessive involvement in pleasurable activities that have high potential for painful consequences (e.g. spending, sexual activity)
3 Marked impairment in occupational functioning or in usual social activities or relationships with others, or need for hospitalization to prevent harm to self or others, or psychotic symptoms

Mortality of people with psychotic illnesses

The fact that people with psychotic disorders have premature mortality has long been known. A landmark study in this area was that by Brown *et al.* [34], who showed that the standardized mortality ratio of psychiatric patients was increased threefold, and life expectancy reduced by 10–20 years. Although suicide and accidents were important causes of death, "natural causes" accounted for the majority of the excess mortality in this population.

A difficulty in the interpretation of this finding arises from the fact that patients with long-term mental illness are exposed to a wide range of different risk factors from those of the general population. Older studies suggested that hospitalization itself may have been a risk. Most patients are now cared for in community settings, but there are still marked differences in lifestyle, with psychiatric patients being more likely to smoke, being less active and having different diets from the general population, as well as being exposed to a range of pharmacologic agents. Disentangling risks associated with the disease, its treatment and genetic and lifestyle factors has proved to be particularly challenging [35].

As is the case for schizophrenia, there is growing evidence that patients with bipolar illness also have increased all-cause mortality, and evidence of increased cardiovascular disease, when compared with the general population. Again the findings of longitudinal studies in the face of confounders such as lifestyle differences and the effects of treatments can be difficult to interpret. It is likely that those patients with bipolar illness who are exposed to long-term use of antipsychotic drugs (the majority) will have similar outcomes to those of patients with schizophrenia. Other drugs used in bipolar patients such as lithium and sodium valproate are also associated with weight gain, but there has been much less research on their wider metabolic effects to date.

Psychotic disorders and their treatment as a risk factor for diabetes

Papers commenting on the association between schizophrenia and diabetes date back to at least the early part of the 20th century, but the volume of literature exploded in the early years of the 21st century, largely driven by marketing claims related to different antipsychotic drugs. Of course, the early papers demonstrating the association date from the period before the availability of these agents, and provide some of the best evidence we have of an association with the disease alone [32]. This has been supplemented more recently by a small number of studies of drug-naïve patients, but such studies are now very difficult to undertake because of the ethical difficulties of leaving people untreated [36]. Another boost to publication rates occurred when the first antipsychotic agents, the phenothiazines, came into widespread clinical use in the 1950s and 1960s, with many reports of "phenothiazine diabetes" appearing. Unfortunately, interpretation of older studies is hampered by the different diagnostic practices in use for both diabetic and psychotic disorders.

Case history 2: The interaction of schizophrenia and diabetes

Timothy is a 30-year-old man who was admitted to a hospital with an acute psychotic illness. Following a diagnosis of schizophrenia, he was treated with an atypical antipsychotic and after this remained well both physically and mentally. He had a family history of diabetes. He disliked exercise and he tended to eat snacks and smoke 20 cigarettes per day. After 7 years, he developed diabetes. His psychiatrist was concerned that the antipsychotic may have been involved in the development of his diabetes and switched him to an alternative antipsychotic. Unfortunately, the psychosis relapsed and the patient was readmitted to hospital. His diabetes did not resolve and proved more difficult to control until the original medication was restarted and his mental state improved.

A particular difficulty in establishing whether schizophrenia and its treatment increase the risks of diabetes results from the fact that important known risk factors differ between populations, leading to a high degree of confounding in most epidemiologic studies.

The risk factors with large effect sizes include:

- Overweight and obesity;
- Family history;
- Age; and
- Ethnicity.

It is likely that the disease and its treatment have effects that are of smaller size than these, and so failure to match adequately for these confounders can easily yield results that are uninterpretable (Figure 55.2). Added to this is the fact that most studies are retrospective, and that patients tend to be exposed to a wide range of different antipsychotic drugs over the course of their illness. Prospective studies using single agents are much fewer in number,

although reviews of such studies are now beginning to appear. Consequently, we are faced with many studies that give inconsistent and often contradictory results.

In order to overcome some of these difficulties, studies in drug naïve, first-episode patients have been instructive in determining the possibility of an underlying abnormality in glucose metabolism associated with schizophrenia. In two small cross-sectional studies of first-episode drug naïve individuals in Ireland, 10–15% of participants had impaired fasting glycemia and were more insulin resistant than healthy control subjects [36,37]. First-episode patients were also found to have significantly higher waist:hip ratios, and over three times as much visceral fat (a predictor of insulin resistance) when assessed by computed tomography scanning [38]. A study from India found that non-fasting blood glucose concentrations were higher in those with first-episode psychosis than healthy controls [39], while other studies have found differences in body composition between first-episode patients and healthy control subjects but without glucose changes [40]. These findings have not been replicated in all studies [41–43].

The consensus that emerges from the current literature is that having schizophrenia is associated with a two- to fourfold increase in risk of developing diabetes, which leads to an overall prevalence of diabetes of 10–15% in Western populations. Most patients have T2DM and there is some evidence that the rates of T1DM are in fact reduced in people with schizophrenia. Studies conducted in clinical populations suffer from the limitation of screening bias, in that T2DM is often asymptomatic for many years, and ascertainment rates are highly sensitive to such bias. Although subjected to much less systematic study to date, there is a suggestion in the literature that patients with bipolar disorder are also at increased risk of developing diabetes, with a relative risk estimated at two- to threefold. Similar caveats about the effects of treatments and lifestyle differences to those for schizophrenia apply.

By comparing the rates of diabetes at different age groups (Figure 55.3), it is also possible to see that the onset of diabetes appears to occur around 10–20 years earlier in people with SMI than the general population. There are significant numbers of people with diabetes under the age of 40 years and therefore this issue should not be ignored even in those with a recent diagnosis of mental illness.

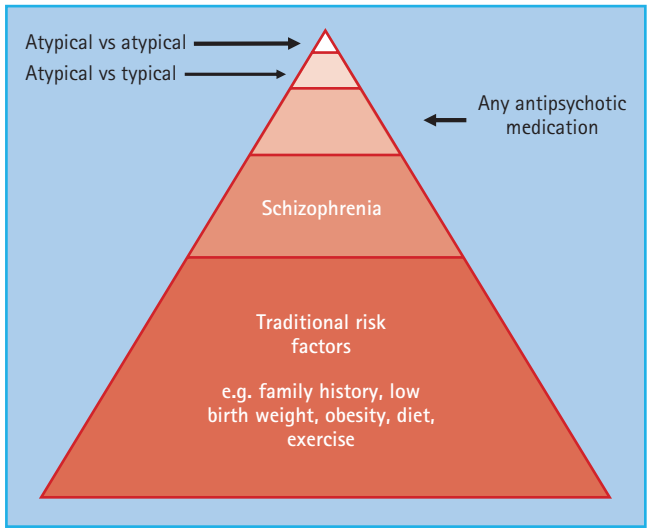

Figure 55.2 The relative contributions of traditional diabetic risk factors, schizophrenia and antipsychotic medication to the development of diabetes in people with serious mental illness. Adapted from Holt RI, Peveler RC. Association between antipsychotic drugs and diabetes. *Diabetes Obes Metab* 2006; **8**:125–135.

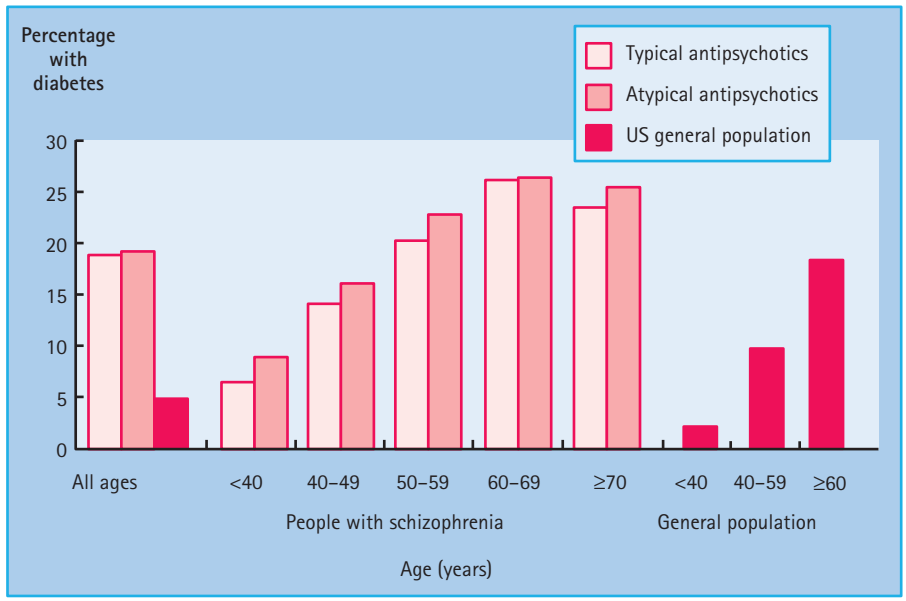

Figure 55.3 Age-specific prevalence rates of diabetes in people with schizophrenia compared with the general US population. Data from Sernyak MJ, Leslie DL, Alarcon RD, Losonczy MF, Rosenheck R. Association of diabetes mellitus with the use of atypical neuroleptics in the treatment of schizophrenia. *Am J Psychiatry* 2002; **159**:561–566 and National Health and Nutritional Examination Survey 2001–2002.

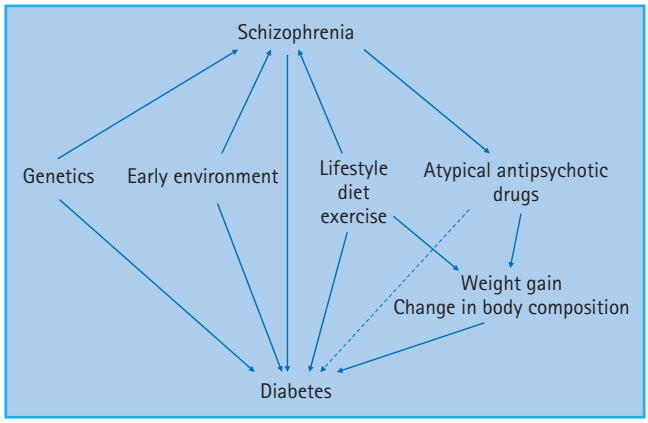

Figure 55.4 The possible mechanisms linking schizophrenia to diabetes. Reproduced from Holt RI, Peveler RC, Byrne CD. Schizophrenia, the metabolic syndrome and diabetes. *Diabet Med* 2004; **21**:515–523.

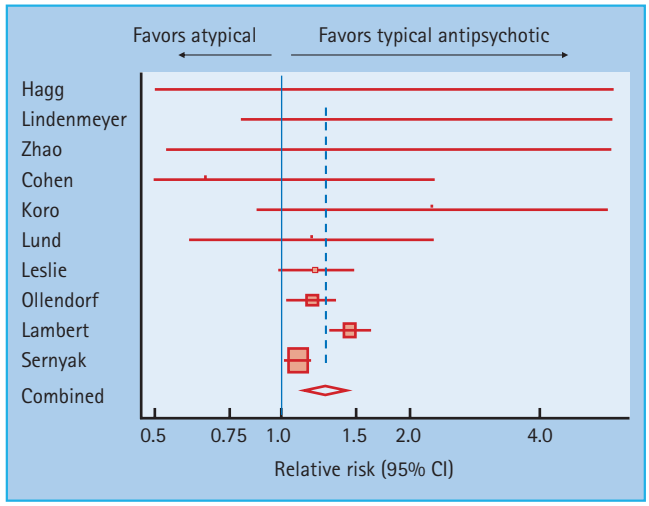

Figure 55.5 Forest plot of relative risks and 95% confidence intervals for diabetes in patients with schizophrenia receiving first-generation antipsychotics compared with second-generation antipsychotics. Adapted from Smith M, Hopkins D, Peveler RC, Holt RI, Woodward M, Ismail K. First- v. second-generation antipsychotics and risk for diabetes in schizophrenia: systematic review and meta-analysis. *Br J Psychiatry* 2008; **192**:406–411.

Mechanisms of the association

There are many difficulties in disentangling the possible mechanisms underlying the apparent associations between psychotic illness and diabetes. Diabetes, schizophrenia and bipolar illness all appear to be strongly heritable, and genetic associations appear to be likely (Figure 55.4). It has been reported that up to 50%, although more commonly 15–30%, of individuals with schizophrenia have a family history of T2DM, compared to 5% of healthy adult controls [12]. Shared susceptibility loci are now being investigated using linkage and candidate gene approaches [13].

Other factors that may underlie the association include a poorer diet, with lower intake of fruit and vegetables and much higher intake of fat, lower levels of physical activity, urbanization and higher rates of smoking among patients [44]. These findings have been documented consistently in several studies; however, it is difficult to assess the size of the effect that they may contribute to the observed association.

Another suggested mechanism involves activation of the HPA axis by stress associated with mental illness, leading to chronic hypercortisolemia and hence an increased risk of diabetes.

The role of antipsychotic medication in contributing to the association remains under debate. There is reasonably strong evidence that most antipsychotic drugs are associated with an increase in risk of developing diabetes, but proof of causation has not been firmly established. Making distinctions between different classes of drug is challenging, and distinguishing between individual agents is extremely difficult. The current consensus is that newer agents (the so-called atypical or second-generation drugs) may have increased propensity to cause diabetes compared to older drugs, although the differences are modest, amounting to perhaps a 10–30% increase in risk (Figure 55.5) [45]. Of the newer agents, clozapine is probably associated with the highest risk but this is not found universally (Figure 55.6). Most antipsychotic drugs induce weight gain, and observational studies suggest that there is a general trend for the drugs with the highest potential for weight gain to also have the highest risk for diabetes, although this is not true in every case. This is in contrast to randomized trials that show no difference in diabetes rates between drugs despite often marked differences in weight gain. Both observational and randomized studies have their pitfalls, which mean that the true risk is difficult to determine [35].

Metabolic syndrome

In recent years investigations in this field have broadened their scope to include assessment of intermediate hyperglycemia and the metabolic syndrome. It appears at this early stage that almost all of the wider range of cardiovascular risk factors, with the possible exception of hypertension, that make up this syndrome are elevated in patients with psychotic disorders, increasing yet further the emphasis on the importance of cardiovascular health promotion in these populations [46].

Management

From the foregoing review it can be seen that the metabolic health of people with psychotic disorders is a wide-ranging public health issue. Historically, it appears that such patients have experienced considerable disadvantage at a time when health promotion as an approach to cardiovascular risk factors in the general population has been developing rapidly. Consideration needs to be given to lifestyle advice, early detection of risk factors, screening for clinical disease and treatment for established disease.

Lifestyle advice and health promotion

National guidelines [33] now stress the importance of physical health promotion for people with long-term mental illness, rec-

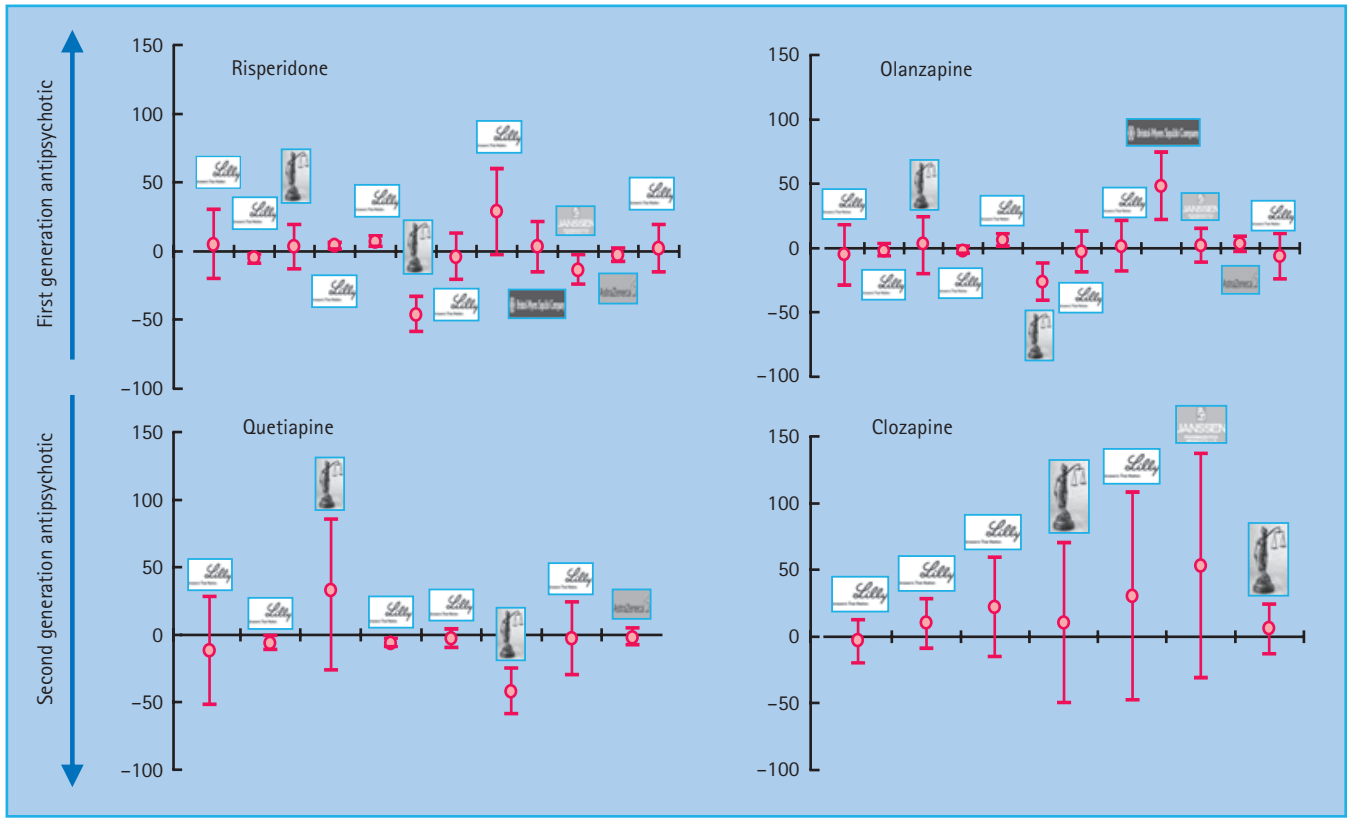

Figure 55.6 Number of cases of diabetes estimated to occur beyond those expected with first-generation antipsychotics per 1000 patients treated with a second-generation antipsychotic, 95% confidence intervals and study sponsorship. Pharmaceutical company sponsorship indicated by figure above or below the upper limit bar in each graph. Independent studies are represented by the scales of justice. Numbers represent additional numbers of cases of diabetes per 1000 treated.

ognizing the health disadvantage that they have experienced in the past. There is still debate about how this is best achieved, with responsibility in many health care systems being split between specialist services and primary care. Primary care is probably the best source of health promotion in most cases, and in many countries this role attracts remuneration, but many patients with long-term mental health problems see their GPs less frequently and depend on the mental health team for most of their health needs. Unfortunately, many such teams have not considered physical health promotion to be part of their remit in the past.

However, there are now signs that this is changing, at least in some countries, and many services are integrating such health promotion into their routine care pathways. Appropriately tailored advice is needed on diet, exercise, weight management, smoking and drug use, supplemented by environmental initiatives such as provision of alternatives to sweetened beverages and "institutional" food in hospital settings, and support for increased activity and body weight monitoring. Contrary to expectation, people with SMI, irrespective of diagnosis or treatment, may well be able to modify their lifestyles with appropriate education and support, and this may result in significant weight loss. Several models to deliver lifestyle education have been proposed but group sessions appear to be both clinically useful and cost-effective. The most important issue is to engage people with mental illness as engagement with the program was the only predictor of long-term weight loss in the longest running program in the UK [47]. A Cochrane review of lifestyle interventions showed modest weight reduction for those currently treated with antipsychotics and a reduction in antipsychotic-induced weight gain in those about to start treatment [48].

Prevention of diabetes

The principles of lifestyle modification have been well established as a means of preventing or at least delaying the onset of diabetes. The lifestyle programs described in the preceding section should provide an effective framework to reduce the incidence of diabetes. These programs are not suitable for all and pharmacologic treatments should be considered for those unable to adapt their lifestyles.

The Diabetes Prevention Program (DPP) has established that the use of metformin is associated with a 31% reduction in the incidence of diabetes. Metformin has been shown to lead to modest reductions in weight in several small studies of people receiving antipsychotics. In one study, metformin treatment

Table 55.4 Drugs that have been tested as potential agents to prevent or reduce weight gain.

Amantadine	Fluoxetine
Nizatidine	Reboxetine
Topiramate	Sibutramine
Metformin	Exenatide
Betahistine	Orlistat

prevented the deterioration in insulin resistance as assessed by homeostasis model assessment in patients treated with antipsychotics [49].

Several other drugs have been tried to prevent or reduce antipsychotic-induced weight gain (Table 55.4). A Cochrane review found that none of the treatments was particularly effective [48] and so none can be recommended without reservation; however, given the long experience with metformin and an understanding of its safety and tolerability, together with its modest cost and proven benefit in reducing incident diabetes, this seems a logical choice for those unable to modify their diet. Further long-term trials are needed, however, to prove that metformin is an effective agent in preventing diabetes in this patient group.

Screening

We now know enough about the scale of risk involved to suggest that patients with psychotic disorders should undergo routine screening for the presence of diabetes. This should be carried out at least annually and possibly more frequently if other risk factors are present. There is debate about the best method of screening – a fasting blood glucose estimation is clearly the ideal, but not easy to obtain in all cases. A random glucose alone, or in combination with an HbA_{1c} test, may be an acceptable substitute, and while its sensitivity and specificity may be lower, it is still preferable to no test at all.

Patients with established diabetes

There are considerable challenges in managing the patient with both a psychotic disorder and established diabetes. The key to success lies in close liaison between the diabetes and mental health services involved with the patient. Management of the mental illness will follow established guidelines, and deploy drug and psychologic treatment, family work, hospital admission and community support as appropriate. It is important to note that most health professionals working in mental health teams are not medically qualified, and will probably have little familiarity with the principles of management of diabetes.

The goals of treating the diabetes should be no different from those in otherwise healthy patients, although achieving these is likely to be much more difficult. Communication with patients with psychotic disorders can be challenging for those with little experience of such work, and patients may find it difficult to report symptoms or extent of self-care to health professionals as clearly as non-psychotic patients might. Extra time and additional training may be needed for health professionals in diabetes teams who are to work with such patients.

Pharmacotherapy

Given what we know about the relative risks of metabolic problems associated with antipsychotic drugs, this aspect of safety must be considered when treatments are being chosen. Unfortunately, there is marked individual variation in clinical response to different antipsychotic agents, and for some patients it will be necessary to continue to use an agent for the sake of obtaining the best result in terms of the patient's mental state, even though metabolic risks may be higher than would be ideal. It is never advisable to discontinue an antipsychotic drug on the grounds that it may be contributing to a metabolic problem without careful consideration of the choices available for treating the psychotic disorder and without discussion with the psychiatric team.

Eating disorders

Case definitions

Three main forms of eating disorder are currently recognized: anorexia nervosa, bulimia nervosa and a residual category of eating disorder not otherwise specified (EDNOS) [3]. The first two conditions have been the subject of much research for many decades; however, the latter category is much less well studied, but is important from a public health perspective as it tends to be more prevalent, and in many cases equally disabling, as the better known forms. As with depressive symptoms, eating disorders exist on a continuum of severity, and there is a lack of good evidence on which to establish a formal boundary or cut-off for "clinical" significance. When an eating disorder co-occurs with a chronic disease such as diabetes, its significance may be increased by the potential for harm resulting from impaired self-care and glycemic control – thus, eating disorders that may be seen as "mild" in an otherwise healthy individual take on increased clinical importance. Because eating disorders are most common in adolescents and young adults, there has been much more research on the co-occurrence of eating disorders and T1DM; far less is known about such problems in the larger population with T2DM [50].

Diagnostic criteria for the common forms of eating disorder are given in Table 55.5 [3].

Clinical features

Anorexia nervosa

The hallmark of anorexia nervosa is weight loss, usually achieved by a combination of extreme dieting, exercise and, less commonly, self-induced vomiting. Misuse of laxatives and other weight-reducing substances (e.g. diuretics, thyroxine) also occurs.

Table 55.5 DSM-IV diagnostic criteria for anorexia nervosa, bulimia nervosa and eating disorder not otherwise specified (EDNOS).

Anorexia nervosa

- A refusal to maintain body weight at or above a minimally normal weight for age and height (e.g. weight loss leading to a maintenance of body weight less than 85% of that expected, or failure to make expected weight gain during period of growth, leading to body weight less than 85% of that expected)
- Intense fear of gaining weight or becoming fat, even though underweight
- Disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or denial of the seriousness of the current low body weight
- In postmenarchal females, amenorrhea (i.e. the absence of at least three consecutive cycles)

Bulimia nervosa

- Recurrent episodes of binge eating. An episode of binge eating is characterized by:
  - (i) eating, in a discrete period of time (e.g. within any 2-hour period), an amount of food that is definitely larger than most people would eat during a similar period of time and under similar circumstances; and
  - (ii) a sense of lack of control over eating during the episode
- Recurrent inappropriate compensatory behavior in order to prevent weight gain, such as: self-induced vomiting; misuse of laxatives, diuretics, enemas or other medications; fasting or excessive exercise
- The binge eating and inappropriate compensatory behaviors both occur, on average, at least twice a week for 3 months
- Self-evaluation is unduly influenced by body shape and weight
- The disturbance does not occur exclusively during episodes of anorexia nervosa

Eating disorder not otherwise specified

- All the criteria for anorexia nervosa are met except that the individual's current weight is in the normal range or, for females, regular menstruation continues
- All of the criteria for bulimia nervosa are met, except that the binge eating and inappropriate compensatory mechanisms occur at a lower frequency than that required for a full diagnosis
- Use of inappropriate compensatory behaviors by an individual of normal body weight after eating small amounts of food
- Repeatedly chewing and spitting out, but not swallowing, large amounts of food
- Binge eating disorder

Patients have a characteristic set of attitudes and values concerning body shape and weight. They complain of intense feelings of fatness, and extreme fear of loss of control over eating and consequent weight gain. They express a level of dissatisfaction with their shape and weight that is far beyond that seen in the normal population, and tend to judge their self-worth almost solely in terms of weight, shape and ability to control food intake. This is described as the "core psychopathology" of the condition. In some cases there is true body shape misperception, when a thin body shape is actually experienced as fat, although this is not a universal feature.

Anorexia nervosa usually begins in adolescence, although prepubertal and adult onset may occur. For some the natural body changes of adolescence appear to be a risk factor; it has also been reported that weight gain and then loss associated with a diagnosis of T1DM and then commencement of insulin treatment may act as a trigger.

The low weight of patients with anorexia gives rise to the physiologic and psychologic features of starvation, including ritualized eating habits, cognitive rumination about eating, irritability, poor concentration, constant feelings of cold and misery, and decreased activity. Social withdrawal and isolation is common, and anxiety, obsessional features and suicidal thoughts sometimes occur. Foods viewed as fattening are typically avoided and the diet contains an average daily intake of calories in the region of 600–900 kcal/day, with very low fat and mineral intake. In spite of this most patients continue to feel hungry, and as such the term "anorexia" is a misnomer.

Common physical symptoms include gastrointestinal complaints (constipation, fullness after eating, bloating and abdominal pain), lack of energy, reduced libido, early waking and postural dizziness. In postmenarchal females not receiving oral contraceptives, amenorrhoea is often present, with infertility and osteopenia a significant risk. Those with prepubertal onset are often small in stature and show failure of breast development. Bradycardia, hypotension and peripheral neuropathy are also reported, and a range of endocrine abnormalities may be found on investigation, including low sex hormone and tri-iodothyronine levels (with normal thyroxine and thyroid-stimulating hormone), and raised growth hormone and cortisol.

Bulimia nervosa

Bulimia nervosa is characterized by recurrent episodes of binge eating in which large amounts of food are consumed (typically 2000 kcal or more), and the individual has a feeling of being unable to control the eating. This behavior is accompanied by a range of "compensatory" behaviors designed to prevent weight gain, including dietary restriction, vomiting, exercise and misuse of laxatives or diuretics. People with bulimia seem to have broadly the same set of attitudes and beliefs to those seen in anorexia. Although most patients fall within the normal weight range, some will have a past history of underweight and may have met the diagnostic criteria for anorexia in the past, and some are overweight. The vicious cycle of dieting, bingeing, purging and fear of weight gain invariably has a detrimental impact on other aspects of functioning, such as work and social relationships, and can have financial implications resulting from the cost of the food. For some, binge eating seems to serve an important function as a means of regulating unpleasant emotional states. Some individuals also have other impulse control problems and a history of interpersonal difficulties. Depression and self-harming behaviors such as cutting, overdosing or substance misuse may occur.

Physical complications of bulimia include enlargement of the parotid glands, erosion of dental enamel and hypokalemia resulting from vomiting, laxative or diuretic misuse.

Eating disorder not otherwise specified

There is still debate about the best set of criteria to use to define this "residual" category of eating disorder. Patients may either have "partial syndromes" (they may have some but not all the features of anorexia or bulimia) or they may be "subthreshold cases" (they have a full set of clinical features, which fall below the severity threshold currently in use).

The best characterized group of patients are those with recurrent binge eating but no compensatory behavior – usually described as "binge eating disorder." Patients with this syndrome describe:

- Eating rapidly;
- Eating until uncomfortably full;
- Eating when not hungry; and
- Feeling disgusted or guilty after overeating.

Binge eating disorder is associated with obesity, and it appears to affect 5–10% of obese patients in weight loss treatment programs. Physical complications may occur as for anorexia or bulimia, depending on the precise symptom pattern of the presentation and its severity.

Impact on diabetes outcome

In addition to the clinical picture described above, patients who have both an eating disorder and diabetes manifest additional features. Early case reports in the 1970s and 1980s highlighted the fact that people with T1DM have available to them an additional means of weight control in the form of the under-use or omission of insulin. Such "self-induced glycosuria" is common but not universal in patients with eating disorders, and is now known not to be confined to patients with a frank eating disorder, being more widely observed as an occasional phenomenon in a range of weight conscious patients, mostly females. As a means of weight control, the behavior produces rapid but often not sustained weight loss, the main effect being via acute dehydration. Not surprisingly, this behavior is associated with impaired glycemic control, and probably a higher risk of microvascular and macrovascular complications if it persists. Such patients are particularly likely to be admitted to hospital with ketoacidosis [51].

Epidemiology

Estimates of prevalence for eating disorders in the general population remain imprecise because of a lack of systematic study. It is thought that about 1 in 250 females and 1 in 1000 males will experience anorexia, usually during adolescence or early adult life. Bulimia is thought to be much more common: in community studies 0.5–1% of young women have been found to be affected. EDNOS appears to be much more common than anorexia or bulimia, and is the most common presentation seen in routine clinical practice.

Diabetes as a risk factor for the development of an eating disorder

The causes of eating disorders are incompletely understood. Dieting appears to be an important risk factor, although only a small proportion of all those who diet go on to develop a disorder. Other known risk factors include a history of obesity, and premorbid traits including perfectionism and low self-esteem. Family relationships are often disturbed, although this may be either a cause or consequence of the disorder, or both. Genetic risks have also been identified.

Case history 3: Eating disorders and diabetes

Helen is a 20-year-old student with a 3-year history of disturbed eating habits and attitudes. She developed type 1 diabetes at the age of 11. She displayed extreme concerns about her shape and weight, despite have a body mass index well within the normal range. She had experienced weight gain during puberty, which she had found distressing, and had managed by reducing her insulin dosage, diet and exercise. She had continued to reduce or omit her insulin dosage intermittently since, and in the last 3 years had begun to vomit food occasionally, and to have episodes of binge eating. Details of these clinical features remained hidden from the diabetes team until a specialist nurse noticed that she seemed upset at a clinic visit, and arranged a follow-up home visit for a lengthy discussion about her diabetes management. It was subsequently noticed at the next clinic visit that Helen had developed mild retinopathy and proteinuria. Referral to the eating disorder services was made, and a course of cognitive–behavior therapy was offered in an outpatient setting.

There has been a strong clinical impression for many years that eating disorders are over-represented in people with diabetes, and several studies have been conducted to address this. Although both diabetes and eating disorders are common conditions, and so a degree of co-occurrence by chance is expected, there are some theoretical grounds to expect eating disorders to occur more commonly in people with diabetes. The following have been suggested as risk factors:

- The stress of living with a chronic disease;
- The availability of a means of rapid weight control via insulin misuse;
- Prescription of a rigid dietary regimen; and
- The experience of marked weight fluctuation around the time of diagnosis of diabetes.

Insulin treatment itself can lead to weight gain and adjustment of insulin dose through the pubertal period in females is notoriously difficult. In contrast, there may also be protective factors that operate; most notable of these is close medical and family surveillance during the period of highest risk of behaviors such as vomiting and bingeing.

Early studies appeared to support the contention that prevalence was raised in people with diabetes, but these studies had many methodologic shortcomings including use of non-validated assessment measures, recruitment of highly selected populations from specialist diabetes clinics (mainly in the USA) and the absence of well-matched control groups. More recent studies and

analyses using better methods of assessing the full range of diagnoses, including EDNOS, have indicated that there may be a slightly raised prevalence in diabetic populations, although the increase in risk appears to be modest if assessed by cross-sectional prevalence comparisons (around a threefold increase for bulimia and a doubling for EDNOS) [50].

Longitudinal studies have now shown that for most patients eating disorder diagnoses are unstable over time, and cross-sectional studies underestimate the proportion of the population that may be affected in the long run. Incidence rates in adolescent and young adult patients are higher than previously estimated, and it is clear that such disorders, especially if persistent, are a major cause of poor outcome in people with diabetes [51]. Rates of serious microvascular and macrovascular complications and mortality are significantly increased in these cohorts, even in those patients whose eating disorder features are relatively short-lived. It appears that adolescence and young adulthood is a particularly vulnerable time for people with T1DM, and even short periods of poor control can have serious consequences in middle and later adult life.

Questions to ask to establish possible eating disorder features

- What is your current weight?
- What would be your ideal weight?
- Are you happy with the shape of your body?
- If not, why not?
- Would you prefer to be a different weight or shape?
- If so, what would you wish to change?
- Do you do anything to control your weight or body shape?
- If so, what do you do?

If appropriate:

- Do you diet?
- Are there any foods that you particularly avoid?
- Do you ever feel that your eating is out of control?
- Have you ever vomited food to avoid weight gain?

Management

Detection

Although some people with diabetes may volunteer information about eating problems, many will be secretive as a result of factors including denial, guilt or shame. Thus, an essential first step in management is successful detection of the problem. It is important to note that, although eating disorders are generally associated with poor self-care and erratic glycemic control, alternating periods of hypoglycemia and hyperglycemia may be undetected by a screening test such as HbA_{1c}. Warning symptoms include the following:

- Marked weight fluctuation or loss;
- Symptoms of hyperglycemia (thirst or tiredness);
- Frequent episodes of ketoacidosis (often requiring hospital admission) or hypoglycemia leading to loss of consciousness;
- Growth retardation and pubertal delay may be seen in younger patients with T1DM.

Unfortunately, most of these features are not specific for eating disorders and are only indicative of poor self-care. The only way to establish a diagnosis of an eating disorder is by means of a clinical interview, although brief self-report scales do exist and may be a useful means of screening. Unfortunately, none have been validated specifically for use with people with diabetes, and many contain items (e.g. "I always avoid foods with sugar in them") that may be contaminated by the presence of diabetes. Sensitive but direct questions related to eating habits and attitudes, concerns about body weight and methods of weight control should be asked.

Principles of treatment

There is a lack of primary research to guide the treatment of patients with an eating disorder and diabetes, and advice is therefore based on existing guidelines for patients without diabetes such as the one by NICE [52]. Dietary counseling by a dietitian or specialist nurse may be a helpful first step, especially for those with milder disorders, but most cases will require specialist help. Guided self-help appears to be a viable option as a first step for patients with bulimia. In all cases, close liaison between the therapist managing the eating disorder and the team managing the diabetes will be required. Eating disorder treatment needs to be enhanced with attention to the following:

- Insulin or medication use;
- Glycemic control;
- Diabetes-related dietary restrictions;
- Relationships with family and medical staff; and
- Feelings about having diabetes.

Although most patients can be managed on an outpatient basis, the risk of impaired physical health necessitating inpatient admission is increased in people with diabetes. Regular physical monitoring is needed to manage the high risk of complications and mortality [53].

Anorexia nervosa

The evidence base for the treatment of anorexia remains surprisingly weak. A necessary first step for all patients is restoration of weight towards normal levels. During this process it is usually necessary to accept that glycemic control may not be perfect, but severe hypoglycemia or hyperglycemia must be avoided. The patient will need to monitor insulin dose and blood glucose levels as eating habits and weight change. It is essential that the eating disorder therapist has a good knowledge of the principles of treatment for diabetes.

Bulimia nervosa

Treatment for bulimia, particularly by means of cognitive–behavioral therapy (CBT) has been widely researched, although

the suitability of CBT for people with diabetes has been subjected to much less study. The coexistence of diabetes with bulimia inevitably complicates management. Successfully engaging patients in treatment may itself be more difficult, and approaches such as motivational interviewing may have a role in future [54]. Modification to the standard treatment approach includes the monitoring of self-care behaviors, and it is desirable that the eating disorder therapist has knowledge and experience of the standard management of diabetes. Conflict may arise between the modifications to eating behavior usually advocated for the treatment of bulimia (promoting a more flexible approach to eating) and the dietary advice often given for management of diabetes (regular controlled eating and avoidance of certain food groups). The development of the approach known as DAFNE (diabetes adjusted for normal eating) may offer a solution to this dilemma [55].

Other forms of treatment for bulimia include interpersonal psychotherapy, and the use of antidepressant drugs. Although clinical trials are lacking, there is a clinical impression that medication may be a useful adjunct to psychologic treatment for some patients. A group educational program for patients with bulimia and T1DM was shown to be better than "standard care" in improving eating behavior, but did not lead to improvements in glycemic control [56]. Inpatient treatment has also been evaluated for this group, and appeared to be successful, although the applicability of this approach in most health care systems remains to be tested.

Eating disorder not otherwise specified

Little is known about the optimum management of patients with these more prevalent but less severe forms of eating disturbance. Similar approaches to those used for anorexia and bulimia are usually tried.

Treatment of children and adolescents

Cross-sectional studies investigating the association between family environment, eating problems and diabetes outcomes suggest that family factors have a particularly important role in younger patients. Family-based interventions addressing issues such as limit setting, communication skills and development of self-esteem may be particularly appropriate and helpful for this group. Family interventions in young people without diabetes are known to be more effective in treating eating disorders than individual therapy.

Other disorders

Several other forms of psychiatric or psychological disorder may be important in the management of people with diabetes (see Chapter 49). Needle phobia fortunately appears to be rare among insulin-treated patients, although if it does occur (usually early in treatment) it can create considerable difficulties. It appears to be usually relatively easy to treat using behavioral principles.

Sexual dysfunction is common, and differential diagnosis between organic and psychologic factors can sometimes be difficult, but psychologic factors are usually important and again relatively easy to address using psychologic treatment.

Substance misuse and dependence, and personality disorder, can prove resistant to treatment and create considerable management challenges. Historically, the term "brittle diabetes" has been used to describe patients with unexplained poor metabolic control. It is now recognized that psychologic and behavioral factors are usually the most important causes of this.

Conclusions

This chapter has highlighted the many and various ways in which diabetes and psychiatric disorders can interact. It is clear that such disorders can have a major impact on diabetes outcomes, and health professionals who work with patients with diabetes require good knowledge and awareness of these issues to be able to provide optimal care. There is clearly also a great need for closer working between diabetes services and mental health services. Further research on these topics is clearly required.

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