

Managing diabetes in people with severe mental illness

John Pendlebury, Richard IG Holt

Article points

1. Diabetes is two to three times more common in people with severe mental illness (SMI) than in the general population.
2. The reasons for this are multifactorial, and include genetic and environmental risk factors as well as disease and treatment factors.
3. There is a need for screening, diabetes prevention and strategies to manage the diabetes if this occurs.
4. Psychiatric and diabetes services need to work together to improve communication pathways and collaboration to ensure that people with SMI and diabetes enjoy a long and healthy life.

Key words

- Antipsychotics
- Bipolar illness
- Schizophrenia
- Severe mental illness

Authors' details can be found at the end of the article.

Diabetes and other metabolic abnormalities, as well as an unhealthy lifestyle, are more prevalent in people with severe mental illness (SMI), increasing their risk of cardiovascular disease (CVD). The most common cause of death in people with schizophrenia and bipolar illness is CVD, accounting for up to 60% of all deaths. There are many different causes of diabetes in people with SMI, as in the general population; arguably the most important are potentially modifiable lifestyle factors. People with SMI are more likely to be unemployed, have low incomes, live in rented accommodation, have a poor diet and be more physically inactive. Mental illness itself further contributes to the risk of developing diabetes. Antipsychotic medications have been implicated in the aetiology of diabetes. The increased prevalence of diabetes in people with SMI has clinical implications for care, including screening, diabetes prevention and strategies to manage the diabetes if this occurs. Healthcare professionals working in psychiatry and diabetes care need to collaborate closely to provide the integrated care that people with SMI need. The DSN has a pivotal role in this.

The connection between diabetes and the two main severe mental illnesses (SMIs) – schizophrenia and bipolar illness – was recognised more than a century ago. In 1879, Sir Henry Maudsley, in *The Pathology of Mind*, commented that:

“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.”

The prevalence of diabetes in people with schizophrenia or bipolar illness (10–15%) is two to three times that in the general population (3.5–5%) (Holt et al, 2005). Diabetes and other metabolic risk factors may explain, to a large extent, the increased rates of cardiovascular disease (CVD) in people with SMI. CVD is the most common cause of death in people with SMI and is partially responsible for the reduction in life expectancy (by 10–15 years) in

Table 1. Positive and negative symptoms of schizophrenia.

Positive symptoms

- Delusions.
- Hallucinations.
- Thought disorder.

Negative symptoms

- Lack of energy.
- Social withdrawal.
- Lack of motivation.
- Flattening of affect.
- Anhedonia.

people with schizophrenia compared with the general population (Brown et al, 2000).

Severe mental illness

SMI, here taken to mean the psychotic illnesses schizophrenia and bipolar illness, is associated with a lack of insight by the sufferer. Schizophrenia affects around 1% of the population and occurs equally in men and women (Jablensky, 2000; Goodwin et al, 2008). Onset of psychosis before the age of 15 years is rare, but can occur at any time after this, most often between 15 and 35 years of age. Symptoms of schizophrenia are often described as positive or negative (*Table 1*), but schizophrenia may also be associated with mood disorders and cognitive impairment.

Bipolar disorder, previously known as manic depression, involves cycles of mania and depression, but those affected may also have times when mood is normal.

The lives of many people with SMI were transformed in the 1950s, following the development of antipsychotic medications (*Table 2*). This markedly reduced the number of psychiatric inpatients in the UK from approximately half a million in the pre-antipsychotic era to the current figure of less than 100 000. This figure is continuing to fall with the introduction of early intervention, crisis resolution, home treatment and liaison services.

Although this meant that SMI could be treated effectively for the first time, conventional or “typical” antipsychotics were found to have a number of stigmatising side-effects, such as extrapyramidal movement disorders, including tardive dyskinesia, parkinsonism, dystonia and akathisia. Second-

Box 1. NICE (2009) Schizophrenia guideline: recommendation 1.4.1.3.

People with schizophrenia at increased risk of developing cardiovascular disease and/or diabetes (e.g. with elevated blood pressure, raised lipid levels, smokers, increased waist measurement) should be identified at the earliest opportunity.

generation or “atypical” antipsychotics were developed and introduced in the 1990s, with the prospect of more effective treatment for SMI and fewer side-effects (*Table 2*).

Metabolic abnormalities

Cardiovascular risk factors other than diabetes are also more common in people with SMI than in the general population, and so it is important that these are considered in addition to diabetes (*Box 1; Table 3*) (De Hert et al, 2009).

Detailed guidelines about the management of these risk factors may be found in the joint European Psychiatric Association, European Association for the Study of Diabetes, and European Society of Cardiology position statement (De Hert et al, 2009).

Aetiology of diabetes in SMI

Understanding why diabetes and other metabolic comorbidities are more common in people with SMI is vital if we are to develop appropriate holistic strategies to meet the clinical challenges that this presents.

There are multiple risk factors for diabetes in the general population, and similarly these contribute to the increased risk of diabetes in people with SMI (Holt and Peveler, 2006a; 2006b). Lifestyle factors are arguably the most important, as these are potentially modifiable. Poverty, urbanisation, poor diet and physical inactivity are all important risk factors for diabetes and occur more frequently in people with SMI. People with schizophrenia tend to have diets that contain higher amounts of fat and refined sugar, but lower amounts of fibre, mainly because of inadequate fruit and vegetable intake

Table 2. Currently available antipsychotic medication.

Conventional or “typical” antipsychotics	Second-generation or “atypical” antipsychotics
Chlorpromazine, haloperidol, thioridazine, trifluoperazine, flupentixol, fluphenazine, pipotiazine, zuclopenthixol.	Amisulpride, aripiprazole, clozapine, olanzapine, paliperidone, quetiapine, risperidone, sertindole, zotepine.

Table 3. Estimated prevalence of modifiable cardiovascular risk factors in people with schizophrenia and bipolar illness and relative risk compared with the general population.

Modifiable risk factor	Schizophrenia		Bipolar illness	
	Prevalence	Relative risk	Prevalence	Relative risk
Smoking	50–80%	2–3	54–68%	2–3
Dyslipidaemia	25–69%	≤5	23–38%	≤3
Diabetes	10–15%	2–3	8–17%	1.5–3
Hypertension	19–58%	2–3	35–61%	2–3
Obesity	45–55%	1.5–2	21–49%	1–2
Metabolic syndrome	37–63%	2–3	30–49%	2–3

Adapted from: De Hert et al (2009)

(McCreadie et al, 1998; Brown et al, 1999) compared with the general population.

Genetic factors are also important, as demonstrated by the high number of people with SMI (17–50%) who have a first-degree relative with type 2 diabetes (Gough and O’Donovan, 2005). Also, first-degree relatives have a high frequency of other glucose abnormalities (Spelman et al, 2007).

The mental illness is likely to contribute further to the risk of diabetes, as illustrated by studies of drug-naïve people during their first episode of psychosis. One study of 26 people with “first-episode” psychosis found that more than 15% had impaired fasting glucose levels compared with none of the healthy controls (Ryan et al, 2003). Individuals with “first-episode” psychosis also had three times as much intra-abdominal fat as controls (Thakore et al, 2002).

Some more recent studies (Cohn et al, 2005; Saddichha et al, 2008), but not all (Arranz et al, 2004; Graham et al, 2008), have confirmed these findings, raising the possibility of biological links between diabetes and SMI. One putative mechanism is the change in neuroendocrine function seen during acute episodes of psychosis: people with SMI have higher concentrations of cortisol and catecholamines (Ryan and Thakore, 2002; Dantzer et al, 2008). As both these hormones are insulin antagonists and elevations of these hormones have been associated with the

development of diabetes, they may provide a link between diabetes and SMI.

Antipsychotics have also been implicated in the development of diabetes. The first reports appeared in the 1950s following the introduction of conventional antipsychotics (Hiles, 1956), when the term “phenothiazine diabetes” appeared in the medical literature. This side-effect seems to have been first ignored and then forgotten, as there were no alternatives to antipsychotic treatment. The issue of treatment-emergent diabetes only returned after the introduction of the newer second-generation antipsychotics (SGAs).

There are many reported cases of people developing diabetes after starting treatment with SGAs, some of which remit after cessation of treatment (Jin et al, 2002). In these cases, it seems likely that the antipsychotic played a major role in the development of diabetes, but what is less clear is how far this can be extrapolated to the wider body of people receiving antipsychotics (Holt and Peveler, 2006a).

Observational studies have suggested that people receiving antipsychotics are more likely to develop diabetes than those who are not, but these data may be biased by the confounding effect of the mental illness and its associated genetics and lifestyle (Holt and Peveler, 2006a).

Observational studies have also suggested that treatment with SGAs is associated with a small increase in the risk of diabetes, compared with treatment with a first-generation antipsychotic (Smith et al, 2008). Some studies have suggested a higher risk of diabetes with clozapine and olanzapine compared with other SGAs, but these reports are inconsistent (Citrome et al, 2007).

Around 20 prospective studies have reported glucose abnormalities but none found any significant differences between different antipsychotics, or indeed between antipsychotic and placebo. This suggests that the main factors responsible for the development of diabetes are the illness and associated genetics and environment, as opposed to the medication (Bushe and Leonard, 2007) (*Figure 1*).

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Implications for the clinical care of people with SMI

The higher prevalence of diabetes among people with SMI has a number of clinical implications for care for those working in diabetes and psychiatry services. First, we need to screen for diabetes, then we need to implement strategies to reduce the risk of diabetes, and finally care plans should be developed to manage those individuals who develop diabetes.

Screening

The high rates of undiagnosed diabetes and long duration between onset of diabetes and development of symptoms support the need to screen for diabetes in the general population. This, coupled with the higher prevalence of both diagnosed and undiagnosed diabetes in people with SMI, provides a stronger imperative for screening in this group.

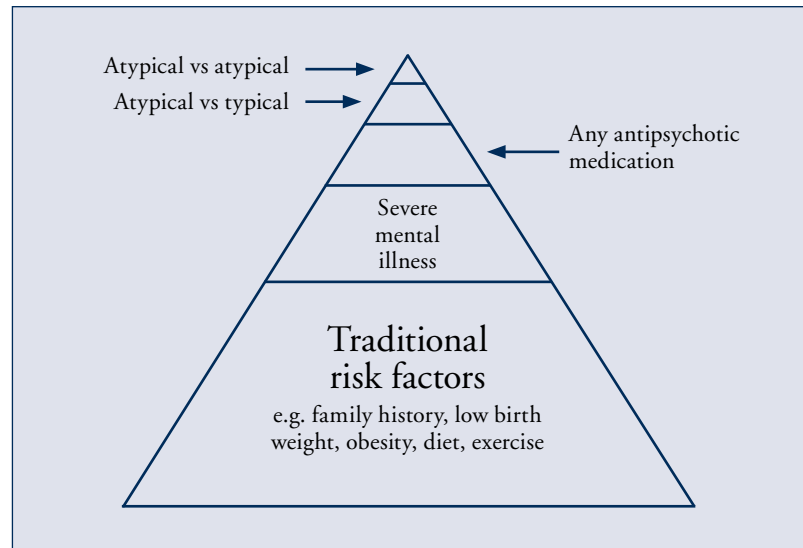
As many as 60–70% of all cases of diabetes in those with SMI are undiagnosed (Subramaniam et al, 2003; Taylor et al, 2005; Voruganti et al, 2007), not least because of possible diagnostic uncertainty as people with SMI may have negative symptoms and side-effects that mimic the symptoms of diabetes. Furthermore, opportunities for screening may be limited for those people with SMI, who attend their GP surgery less frequently than the general population.

For these reasons, a number of national and international bodies, including NICE (2009), Diabetes UK, the Joint European Societies (De Hert et al, 2009), the American Diabetes Association, Canadian Diabetes Association and Australian Diabetes Association, have recommended screening for diabetes in people with SMI irrespective of their treatment (Citrome and Yeomans, 2005).

It is recommended that symptoms of diabetes and blood glucose concentration should be assessed at baseline, 3–4 months after initiation of, or changes in, antipsychotic medication, and annually thereafter.

While a fasting blood glucose concentration is probably the ideal screening test, a pragmatic view is needed because people with SMI may find it difficult to attend fasted for a blood test.

Figure 1. Schematic representation of the reasons why people with severe mental illness develop diabetes. Most of the excess prevalence can be explained by an increase in traditional risk factors, while the illness itself conveys a further risk. Antipsychotic medication increases the risk, but this is small compared with the overall risk. Adapted from Holt and Peveler (2006b).



In such circumstances a random blood glucose level is a reasonable alternative (Holt et al, 2005). In due course, it may also be reasonable to screen by HbA_{1c} as, at the time of writing, the World Health Organization is considering the use of HbA_{1c} as a diagnostic test.

Although much of this work will be undertaken by the psychiatry team or healthcare professionals in primary care, DSNs may be needed to provide advice about screening and interpretation of blood test results (Box 2).

Prevention of diabetes

There are studies from China, Finland, India and the USA demonstrating the effectiveness of lifestyle modification in preventing,

Box 2. NICE (2009) Schizophrenia guideline: recommendation 1.4.1.5.

Healthcare professionals in secondary care should ensure, as part of the Care Programme Approach, that people with schizophrenia receive physical healthcare from primary care as described in recommendations 1.4.1.1.–1.4.1.4.

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2. One reason for this is diagnostic uncertainty as people with SMI may have negative symptoms and side-effects that mimic the symptoms of diabetes.
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or at least delaying the onset of, diabetes (Pan et al, 1997; Tuomilehto et al, 2001; Knowler et al, 2002; Ramachandram et al, 2006). It has now been recognised that the physical health needs of people with SMI have been ignored for too long and opportunities for lifestyle modification have been missed. Several studies challenge the view that lifestyle modification is impossible in those with SMI (Alvarez-Jiménez et al, 2008; Holt et al, 2010); indeed, the results achieved in people with SMI may be even better than those seen in the general population.

One example of a lifestyle intervention programme for people with SMI is the Cromwell House clinic set up by Pendlebury in May 2000 (Holt et al, 2010). The clinic was established at the request of a small group of people with SMI and is the longest running service in the world. The programme is available to individuals receiving psychotropic medications, who are concerned about their weight and are able to refer themselves to this clinic. Patients attend a weekly group session, held on Thursday lunchtime; this time was chosen to make the clinic accessible for people with SMI.

Attendance at the sessions is voluntary and participants may attend as few or as many sessions as they chose. Weight is measured in private using imperial measures to the nearest half pound at the request of the patients at all visits.

After the weighing there is a 15-minute period for discussion and feedback within the group. During this time the group voluntarily shares details of their weight change, together with personal dietary experiences from the previous week. Patients are asked to keep a dietary record, which is used individually or within the group to negotiate a single change, such as a switch to non-sugary soft drinks, in the person's diet for the following week.

The final 30 minutes is used for a series of eight rotational topics, which address issues such as healthy eating, exercise, self-esteem, meal planning and demonstrations, motivation, and evaluation. Written materials are not used within the clinic.

Ninety-two per cent of the people who attended the clinic lost some weight, 4% maintained their initial weight while only 4% gained weight.

Several pharmacological agents have been tried in an attempt to reverse or prevent antipsychotic-induced weight gain (Baptista et al, 2008). No drug has been found to be particularly effective, but a systematic review in 2009 showed that there was preliminary evidence that metformin may attenuate weight gain in both adult and adolescent patients taking atypical antipsychotics (Bushe et al, 2009). As metformin has been shown to prevent diabetes in the general population, this may be considered in people with SMI, particularly those with additional risk factors such as

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1. Following a diagnosis of diabetes, the psychiatric care coordinator and DSNs should work together to outline a care plan for both severe mental illness (SMI) and diabetes within the Care Programme Approach meetings.
2. It is imperative that people with SMI receive sufficient education and medical and nursing input to allow the person with diabetes to take control of their illness for the majority of the time when they have no contact with the professional diabetes team.
3. The first priority for the person with SMI and diabetes is to treat the psychosis adequately, even if this involves using an antipsychotic that may have an adverse effect on glycaemic control.
4. Without adequate control of the psychosis, patient education and management are likely to be futile.

Box 3. NICE (2009) Schizophrenia guideline: recommendations 1.4.1.2, 1.4.1.4.

Treat people with schizophrenia who have diabetes and/or cardiovascular disease in primary care according to the appropriate NICE guidance (1.4.1.4). A copy of the results should be sent to the care coordinator and/or psychiatrist, and put in the secondary care notes (1.4.1.2).

a personal or family history of metabolic dysfunction (Knowler et al, 2002). Specific trials of longer duration in people with SMI, however, are needed (De Hert et al, 2009).

Management of the person with diabetes and SMI

The management of diabetes in people with SMI is complex and requires a multidisciplinary team approach involving healthcare professionals working in both psychiatry and diabetes services in both primary and secondary care. The DSN has a key role in the delivery of care.

Following a diagnosis of diabetes, the psychiatric care coordinator and DSNs should work together to outline a care plan for both SMI and diabetes within the Care Programme Approach meetings. Good communication is essential and copies of the results and care offered by the diabetes team should be sent to the care coordinator and/or psychiatrist.

Box 4. Case history.

A 19-year-old man with a history of schizophrenia presented to A&E with a short history of malaise, weight loss and polyuria. He had elevated blood glucose concentrations and ketones in his urine. He was diagnosed with type 1 diabetes and commenced on insulin. His schizophrenia was difficult to control and he had frequent episodes of persecutory delusions and hallucinations. When he was seen at the diabetes clinic, he described how, when these occurred, he was unable to concentrate on his diabetes and frequently missed his injections. He was unable to test his blood glucose and consequently his HbA_{1c} level was 11.2% (99 mmol/mol). His psychiatry team recommended switching his antipsychotic medication to clozapine. This not only improved his mental state but also led to an improvement in his glycaemic control.

It is imperative that people with SMI receive sufficient education and medical and nursing input to allow the person with diabetes to take control of their illness for the majority of the time when they have no contact with the professional diabetes team. For this reason, the authors believe that it is vital that the diabetes of a person with SMI is managed by someone with expertise in the management of diabetes, either within primary care or secondary care diabetes services (Consensus Group, 2005; NICE, 2009).

Despite this imperative, the authors recognise that most diabetes clinics are not set up to manage the multiple health needs of people with concomitant SMI. For this reason, it is vital that there is a strong interaction between physical and mental health services to ensure that both these aspects of the health care needs of people with SMI and diabetes are addressed (*Box 3*).

The first priority for the person with SMI and diabetes is to ensure that the psychosis is adequately treated, even if this involves using an antipsychotic that may have an adverse effect on glycaemic control. Without adequate control of the psychosis, patient education and management are likely to be futile.

Individual needs may change throughout a person's psychiatric illness. For example, positive symptoms of schizophrenia may interfere with the person's ability to engage with the management of their diabetes, as will cognitive impairment (*Box 4*). Negative symptoms of schizophrenia and depression in bipolar illness may adversely affect motivation to self-manage the diabetes. By contrast, over-confidence with mania can lead to minimisation of the consequences of poor diabetes control.

It is therefore important to adapt one's approach during different phases of the psychosis accordingly. For similar reasons, interactions between DSNs may be different when working with inpatient or community-based mental health teams. With good control of the mental state, however, the diabetes may be managed using the same principles as for management of diabetes in the general population.

Page points

1. Although mental healthcare professionals are becoming increasingly aware of the physical health issues of people with severe mental illness (SMI), these health issues lie outside the traditional realm of psychiatric services.
2. DSNs have a vital role in educating healthcare professionals working in psychiatry as well as people with SMI. In some settings, DSNs have taken a lead in ensuring that people with SMI receive the screening and advice about diabetes prevention they deserve.
3. There is an opportunity and challenge for psychiatric and diabetes services. We need to work together to improve communication pathways and collaboration to ensure that vulnerable people with SMI and diabetes are able to enjoy a long and healthy life.

Role of the DSN

Although mental healthcare professionals are becoming increasingly aware of the physical health issues of people with SMI, these health issues lie outside the traditional realm of psychiatric services. This should provide an opportunity and challenge for healthcare professionals to increase the liaison between psychiatric and diabetes services.

DSNs have a vital role in educating healthcare professionals working in psychiatry as well as people with SMI. In some settings, DSNs have taken a lead in ensuring that people with SMI receive the screening and advice about diabetes prevention they deserve.

Conclusion

The prevalence of diabetes in people with SMI is two to three times that in the general population; in most developed countries, therefore, 10–15% of those with SMI will have diabetes. The underlying reasons for this increase are multifactorial, and include genetic and environmental risk factors as well as disease and treatment factors. There is a need for screening, diabetes prevention and strategies to manage the diabetes if this occurs.

Finally, there is an opportunity and challenge for psychiatric and diabetes services. We need to work together to improve communication pathways and collaboration to ensure that vulnerable people with SMI and diabetes are able to enjoy a long and healthy life. ■

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Conflict of interest

JP has received fees for lecturing, advisory boards and attendance at conferences from AstraZeneca, Bristol-Myers Squibb, Eli Lilly & Co, Janssen-Cilag Ltd and Novartis. RIGH has received fees for lecturing, consultancy work and attendance at conferences from Eli Lilly & Co, Bristol-Myers Squibb, GlaxoSmithKline and MSD.

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