A growing awareness of the physical health needs of people with psychotic disorders has led to concern about their high prevalence of diabetes and “subclinical” abnormalities of glucose metabolism, such as impaired glucose tolerance. Concern has been expressed in recent years that the newer antipsychotic medications may have accelerated the development of diabetes in these people. The dilemma facing medical practitioners relates, on the one hand, to the high rate of medical comorbidity in people with psychosis, perhaps amplified by antipsychotic treatment, and, on the other hand, to the enhanced benefits of the newer agents in the management of the psychosis. Complicating the issue is the fact that people with psychosis are not very good advocates for their own medical health, and may face many barriers to adequate screening and treatment of medical problems, including diabetes.

To facilitate the optimal medical care of hyperglycaemia-related illness in people with psychosis in Australia, an expert group was convened to develop a consensus statement. The group was drawn from the disciplines of psychiatry, endocrinology, epidemiology, general practice, mental health nursing, and pharmacy, along with representatives of community and non-government organisations (see Acknowledgements). The group reviewed the relevant literature, developed a series of draft statements and subjected these to peer review by external consultants to arrive at a broadly accessible set of guidelines. After this process, representatives from the peak consumer and carer organisations across Australia met to develop a consumer-based initiative extending from the consensus document. The aim was to provide the impetus for change in the care of people with psychosis and potential metabolic-related medical comorbidity using simultaneous top-down and bottom-up approaches.

A number of important principles emerged. First, successful and optimal treatment of the psychotic disorder has priority. The advent of second-generation antipsychotic medications has allowed more effective and better-tolerated treatment of psychotic illnesses. Second, all people taking antipsychotic medication should be screened for diabetic risk. Protocols were suggested to help clinicians ensure that people with psychiatric disorders receive appropriate and timely management of their physical disorders. This may sometimes require a more assertive approach than is currently the case. Finally, all health professionals involved in the care of a patient with a psychotic disorder, including the psychiatrist in charge, can contribute to the care of physical disorders, including diabetes and obesity. Consistent advice should be provided on diet, exercise and smoking, and the psychiatric team should assume responsibility for ensuring appropriate screening is undertaken, in close liaison with other healthcare providers.

Here, we outline the main findings of the consensus group. The full consensus statements for professionals and for consumers and carers are available at www.psychiatry.unimelb.edu.au/open/diabetes_consensus/

### Antipsychotic therapy and diabetes

Many case reports and series and a few larger studies based on administrative databases have described associations between antipsychotic treatment and the onset or exacerbation of diabetes. However, there are no long-term, randomised controlled trials to guide clinical practice in this area. The existing evidence suggests that the introduction of first-generation antipsychotic medications (FGAs, see Box 1) was associated with a two- to threefold increase in the prevalence of diabetes among treated patients (Level III evidence [derived from pseudorandomised controlled trials, comparative studies, single-arm studies or interrupted time series without a parallel control group]). It also suggests that the obesity rate (and, by inference, potential for diabetes) is much higher in patients treated with depot FGAs than in the general population.
Antipsychotic medication can be both life-enhancing and life-saving for sufferers of psychosis. The Australian consensus group recognised that successful treatment of the psychotic disorder has priority over concerns about potential metabolic consequences. The latter need to be dealt with in their own right after the total risks and benefits of antipsychotic therapy have been estimated. Thus, selection of an antipsychotic medication for a particular patient should be driven more by its capacity to reduce psychiatric symptoms than its diabetic potential alone, particularly in the absence of definitive information about causality and risk.

The consensus group considered that pre-existing diabetes may be a relative contraindication, as effective treatment of the psychosis should be the primary aim. Because of the high prevalence of hyperglycaemia, informed consent should be obtained from patients or their guardians, with acknowledgement of the requirement to monitor for diabetes.

Mechanisms for links between psychosis and diabetes

The importance of weight gain to the development of type 2 diabetes is detailed in the recent American Diabetes Association position statement. A hierarchy of potential short-term weight gain exists among antipsychotic medications (Level II evidence [obtained from at least one properly designed randomised controlled trial]). The advent of new SGAs might lead to fewer adverse metabolic consequences, but long-term “real world” data are lacking.

In the longer term, obesity seems to be less related to specific medications and more to behavioural factors, including diet and exercise. These relationships have been described in the “hare and tortoise” theory of antipsychotic-mediated weight gain. This theory suggests that some medications have the propensity to drive weight gain rapidly (the “hares”), while most others have a lesser potential that nonetheless results in weight gain in the longer term because of the interactions with the disease process itself and its social consequences (the “tortoises”). However, non-controlled descriptions of cross-sectional weight gain cannot be used to test hypotheses, and a prospective study of a controlled cohort from inception of antipsychotic treatment is required. People with psychosis are undoubtedly at risk of diabetes, but factors other than medication contribute to adverse metabolic outcomes. There is no evidence that people with psychosis are less vulnerable to the effects of obesity, and some evidence that they may be more vulnerable.

2 Estimated prevalence of diabetes before and after development of antipsychotic medications

<table>
<thead>
<tr>
<th>Era</th>
<th>Rate in people with psychosis</th>
<th>Population rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-antipsychotic medications</td>
<td>2.5%–4.2%6,7</td>
<td>Unknown</td>
</tr>
<tr>
<td>First-generation antipsychotics</td>
<td>17%6</td>
<td>3.4%</td>
</tr>
<tr>
<td>(since 1952)</td>
<td></td>
<td>(Busselton, 1981)11</td>
</tr>
<tr>
<td>Second-generation antipsychotics</td>
<td>19%10</td>
<td>7.5%</td>
</tr>
<tr>
<td>(since 1990)</td>
<td></td>
<td>(Australia, 2000)12</td>
</tr>
</tbody>
</table>
More research is required on the hypothesis that amelioration of psychiatric symptoms during treatment with medications such as clozapine and olanzapine is associated with the extent of weight gain. A proposed mechanism for a link involves a direct interaction between orexin peptides and dopamine systems in the prefrontal cortex. This suggests that, at least for some medications, weight gain may be a marker of decrease in symptoms.

A recent study found that, compared with a control group (without psychiatric illness, who were matched on parameters such as exercise level), people with unmedicated schizophrenia had an increased incidence of central obesity (a risk factor for cardiovascular disease and diabetes) and higher levels of plasma cortisol. Previous exposure to antipsychotic medications did not appear to influence the findings, as both medication-naïve and medication-free patients had equally high levels of visceral fat. The findings suggested that the schizophrenic illness itself influenced fat distribution and associated risks.

There is no evidence that the natural history of diabetes differs between people with psychotic disorders or other mental illness and those without such disorders. However, people living with a psychotic disorder have a higher rate of other cardiovascular risk factors, including smoking and features of the metabolic syndrome, which are associated with weight gain and include hypertension and dyslipidaemia. These factors may contribute to a high rate of cardiovascular mortality. Premature mortality from medical disorders is well described among people with psychosis.

### Economic and public health approaches to diabetes in people with psychotic illness

The World Health Organization Global Burden of Disease Study estimated that, in 1990, psychotic disorders accounted for five of the leading 10 causes of disability-adjusted life-years lost in people aged 15–44 years. Direct healthcare costs and indirect costs associated with schizophrenia are estimated at 0.3%–2% of gross domestic product in developed countries. People with diabetes are four times more costly to the national health system than those without the disorder. Therefore, the high prevalence of diabetes in psychotic disorders suggests that, from an economic perspective alone, particular attention is needed to this form of comorbidity.

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### 3 Screening for hyperglycaemia in people treated with antipsychotic medication

<table>
<thead>
<tr>
<th>Patient taking antipsychotic medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assess risk factors for diabetes</td>
</tr>
<tr>
<td>• Older age</td>
</tr>
<tr>
<td>• Family history of diabetes</td>
</tr>
<tr>
<td>• Cardiovascular disease or other cardiovascular risk factors</td>
</tr>
<tr>
<td>• Personal history of gestational diabetes or polycystic ovary syndrome</td>
</tr>
<tr>
<td>• Ethnic predisposition (eg, Indigenous Australian, Pacific Islander, Asian, African American)</td>
</tr>
<tr>
<td>• Lack of exercise</td>
</tr>
<tr>
<td>• Poor diet</td>
</tr>
<tr>
<td>• Obesity</td>
</tr>
</tbody>
</table>

**Measure body mass index and waist – hip ratio every visit or every 3 months**

**Measure blood glucose level (random or fasting)**
- Immediately on starting or changing antipsychotic medication and then every 3-6 months (ideally every month for 6 months, by fingerprick or venepuncture)
- Then minimum of twice yearly
- Reassess earlier or more frequently if rapid weight gain, polydipsia or polyuria

**> 7.0 mmol/L (fasting) or > 11.0 mmol/L (random) on two occasions, or once with diabetic symptoms**

**2h blood glucose level > 11.1 mmol/L**

**Diagnosis of diabetes**

**HbA1c every 3-6 months to monitor glycaemic control (HbA1c is not used to diagnose diabetes)**

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* Medicare covers up to four assessments per year.
In Australia, mental health is identified as a National Health Priority Area in its own right and as a major theme across all other National Health Priority Areas, which include diabetes and vascular disease. The National Health priorities Area Action Council has commissioned programs to ensure not only that the common mental health needs of those with physical conditions such as diabetes are recognised, but also that the physical health needs of those with specific mental illnesses such as schizophrenia are identified. Key non-government groups, such as the Mental Health Council of Australia, have also prioritised the need to improve the physical healthcare of those with mental illness.2,4

Recent reforms in mental health service delivery under the Better Outcomes in Mental Health Care initiative (2001–2004) provide new opportunities for promoting integrated physical and mental healthcare, based largely on expanded services and improved quality of mental healthcare by Australian general practitioners. The recognition and active management of diabetes in people with psychotic illness could be specifically targeted for attention under this strategy. Obesity and diabetes continue to increase in the general population, despite the efforts of the healthcare system to alter dietary and exercise habits. Barriers to healthcare in people with psychotic illness accentuate this.1

Monitoring for the metabolic syndrome and diabetes

The National Health and Medical Research Council has developed draft guidelines on population screening for diabetes.25 These recommend more intensive screening of some groups within the population known to be at higher risk, for example on the basis of family history, ethnicity, age, a history of gestational diabetes, or other risk factors.

People with psychotic illnesses are such a high-risk group.1 They should be monitored for the metabolic syndrome (also known as metabolic syndrome X, comprising obesity, hyperinsulinemia, dyslipidaemia, and hypertension)26 and for diabetes. Monitoring is required when initiating antipsychotic treatment, increasing the dose or changing antipsychotic medication and also during continuing treatment.

An algorithm for monitoring glucose metabolism in people treated with antipsychotic medication is shown in Box 3. Ideally, fasting or random blood glucose levels should be assessed monthly for 6 months after initiating or changing antipsychotic therapy, then at least twice yearly. In cases where there are repeated changes in the antipsychotic medication or dose, clinical judgement on appropriate glucose monitoring will be required. In any case, blood glucose measurements should be obtained a minimum of twice yearly. Laboratory blood glucose measurements or finger-prick measurements using a blood glucose meter are acceptable.

Treating diabetes in people with psychosis

All health professionals involved in the care of patients with psychotic disorders, including the psychiatrist in charge, can contribute to the care of physical disorders, including diabetes and obesity. They should provide consistent advice on diet, exercise and smoking. General practitioners will probably be best placed to coordinate physical healthcare with the support of appropriate specialists and other agencies, but “shared care” can sometimes lead to a failure of care unless responsibilities are clearly defined for each patient. Assertive community-care models are ideal for coordinating physical and mental healthcare if they are adequately resourced. Effective partnerships, not just with the patient but also with family members and other key carers, can contribute to monitoring and treatment.

Principles of treating diabetes in people with psychotic disorders are similar to those in the general population, although some additional issues could be considered that take into account the particular disabilities and barriers presented by psychotic illnesses. Treatment options are discussed more fully in the consensus document.

Preventing diabetes and its complications

The consensus statement recognises the importance of early identification of abnormal glucose metabolism to assist in targeting preventive measures. Improved diet and increased physical activity in middle-aged, overweight members of the general population can reduce the progression of pre-diabetic states to diabetes,27 and the United Kingdom Prospective Diabetes Study demonstrated that appropriate treatment of diabetes reduces complications.28 There is little evidence on the effects of such interventions in people with psychotic disorders, but pilot studies indicate that exercise programs and dietary counselling can lead to healthier behaviours and improve a range of health outcomes.29

Exercise and dietary change can improve metabolic parameters even in the absence of weight loss. Thus, prevention of diabetes can be adopted as an objective which is independent of efforts to prevent or treat obesity. Practically, a range of approaches could be adopted for preventing diabetes in people with psychotic illness, from a “top down” approach within mental health services, through to approaches to individual patients by members of multidisciplinary teams. Medicare Benefits Schedule item numbers for enhanced primary care by general practitioners can facilitate an integrated approach to physical healthcare at the patient level. Modalities such as patient-held medical records could assist with monitoring of diabetes and coordination of preventive interventions.

Research directions

Whether psychosis itself increases the risk of diabetes, and whether specific antipsychotic medications have differential effects on glucose metabolism during long-term use, remains uncertain, and the mechanisms of any such links remain obscure. Evidence on the effects of diabetes, the benefits of treatment and the benefits of preventive activities are derived almost entirely from the general population. Even when specific evidence is derived from people with psychotic disorders, those recruited into trials are not necessarily representative of those in the community. Given the very substantial public health consequences of diabetes in those with psychotic disorders, programs evaluating relative risks, strategies for improving outcomes, and the development of education and training programs for service providers, consumers and carers, remain a high priority.

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**Carer and consumer groups:** Association of Relatives and Friends of the Mentally III (ARAFMI), GROW Self Help/Mutual Help Groups, Australian Mental Health Consumer Network (AMHCN), Carers Australia, Consumers Mentally Ill (ARAFMI), GROW Self Help/Mutual Help Groups, Australian Council of Australia, Fremantle.

**Competing interests:**

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**References**


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