REVIEW

Diabetes Management

Double jeopardy: diabetes and severe mental illness. Addressing the special needs of this vulnerable group

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Practice points

- Severe mental illness is associated with a 20-year shortening of life expectancy through premature cardiac disease.
- The risk of diabetes is increased two- to four-fold with antipsychotic and antidepressant medications.
- Both antipsychotic and antidepressant medications cause weight gain.
- Lifestyle and metformin interventions are effective and can reduce obesity and cardiometabolic risk in people with severe mental illness.
- The diabetes care model can be translated to physical health care in severe mental illness for early intervention to prevent future physical disease.
- Increased communication and collaboration between diabetologists and psychiatrists and their allied health professionals will improve physical health outcomes in this vulnerable patient group.

SUMMARY Severe mental illness (schizophrenia, bipolar disorder and severe depression) carry a substantial physical health burden, unmet health needs and a 20-year mortality gap. Severe mental illness is also characterized by significantly higher rates of incident diabetes with poorer glycemic, lipid and hypertension control. Treatment disparities are also evident. This review examines the double jeopardy of severe mental illness and diabetes mellitus, which together promote premature vascular mortality and additional physical health burden in this vulnerable population. The review considers the guidelines, models of care and evidence to support early intervention in this vulnerable group, to either prevent diabetes or optimize its management when present.

KEYWORDS
• antipsychotics • antidepressants • cardiometabolic • cardiovascular • depression • diabetes mellitus • mental health • mental illness • metabolic • schizophrenia

Severe mental illness, defined as schizophrenia, bipolar disorder and severe depression, carry a significant physical health burden and increased mortality risk. Severe mental illness is characterized by substantially higher risk of incident diabetes [1–3], which adds to or compounds the physical disease burden and comorbidities suffered. Severe mental illness, such as schizophrenia and bipolar disorder, carry a 20-year reduction in life expectancy [4], through premature cardiometabolic disease due to a number of factors.

This review examines the intersection of severe mental illness with diabetes mellitus, as diabetes is a major promoter or contributor to the premature vascular mortality experienced by this population. Specifically, the review examines the following questions:

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- Why is there a mortality gap in people with severe mental illness?
- What is the risk of diabetes in severe mental illness and what are the metabolic sequelae of medications used to treat severe mental illness?
- How does severe mental illness negatively impact diabetes care?
- How might we address the special needs for diabetes care in this vulnerable group?
- Can the diabetes model of care be transported to mental health to improve physical health care in severe mental illness?

Systematic reviews of national and international documents were undertaken to examine current literature available. Searches of PubMed and Cochrane databases were performed and the literature was extensively reviewed.

The 'scandal of premature mortality' in people with severe mental illness: physical health culprits & our current health dilemmas

Despite efforts to improve health service delivery to people with severe mental illness, recent data show this alarming mortality gap not only remains [5] but appears to be widening [6]. There is a common perception that, in this vulnerable population of people with severe mental illness, suicide is a major cause of death. While suicide rates are up to 20-times higher in people with severe mental illness compared with the general population, the excess mortality is however mainly attributable to premature cardiovascular disease [7,8]. This disparity in life expectancy has been attributed to disparities in physical care of people with severe mental illness, what has been described as a 'scandal of premature mortality that contravenes international conventions for the "right to health"' [9]. The cardiometabolic disease burden in severe mental illness has been termed 'an epidemic within an epidemic' to highlight the unmet treatment needs of this patient population but also to highlight the multitude of missed opportunities to prevent physical disease in this vulnerable population [10].

Western medicine in the last three centuries has dichotomised mental and physical illness, a separation promulgated by the philosopher Rene Descartes in his theories of mind–body dualism. The influence of this thinking permeates the medical system: clinicians will often treat mental illness as a separate entity to a patient's physical illness. Mental health professionals will treat mental illnesses but have mostly not addressed physical health needs. Similarly, physical health facilities will often treat physical illnesses, but will neglect mental illnesses, which in fact should be treated at the same time [11]. The evolving clinical approach is to consider physical and mental health as components of the whole, that one influences the other. This bidirectionality might seem obvious, since mental illness adversely affects physical health and physical illness adversely affects mental health.

To effectively manage diabetes and mental illnesses, and particularly where they overlap requires a change in the way clinicians think about illnesses and how we practice diabetes care. [11]. In medical and nursing schools, mental and physical illness are taught independently, with little attention to how these two affect each other or how they should be treated simultaneously. Modern medicine is now highly specialized with clinicians trained to identify and treat only select disease, thus leaving the potential for lots of comorbidities to be neglected. For example, the Dialogue on Diabetes and Depression is an initiative recently developed by a number of professional organizations, consumers, institutions, research institutes and individuals to increase awareness about the frequent comorbidity of diabetes and depression as well as to increase research into this area and promote models of care [12]. Further research to improve current knowledge about these comorbidities and how to better treat these is clearly warranted.

What is the risk of diabetes in severe mental illness & why?

The standard of care in people with severe mental illness typically involves long-term medication in addition to multidisciplinary psychological interventions [13,14]. Broadly, medications fall into several categories of antipsychotics, mood stabilizers (which include anticonvulsants) and antidepressants. Medications frequently used are listed in **Table 1**.

Antipsychotic medications are classified as first and second generation **(Table 1)**. First-generation antipsychotic medications can have severe adverse motor effects, including as tardive dyskinesia, dystonia and extrapyramidal symptoms. Second-generation antipsychotic medications less frequently have these effects, though long-term data are not available. Both

Table 1. Medications frequently used to treat severe mental illness.

Antipsychotics		Antidepressants		Mood stabilizers
First generation	**Second generation**	**Tricyclics**	**SSRI/NSRI**	
Haloperidol	Aripiprazole	Amitriptyline	Citalopram	Anticonvulsants:
Chloropromazine	Clozapine	Amoxapine	Escitalopram	– Carbamazepine
Perphenazine	Risperidone	Doxepin	Fluoxetine	– Topiramate
Fluphenazine	Quetiapine	Imipramine	Paroxetine	– Valproic acid
Thioridazine	Olanzapine	Nortriptyline	Sertaline	– lamotrigine
	Ziprasidone	Trimipramine	Venlafaxine	Others:
	Amisulpride		Duloxetine	– Lithium

NSRI: Noradrenaline-selective reuptake inhibitor; SSRI: Serotonin-selective reuptake inhibitor (some medications are dual action SSRI/NSRI).

antipsychotic generations are associated with weight gain, obesity and metabolic complications [15,16]. These adverse health complications significantly contribute to the health burden of people with mental illness, directly and negatively impacting on an individual's cardiometabolic health and sense of self. The obligation for clinicians is to prevent, detect and treat and these adverse metabolic complications in order to prevent cardiovascular sequelae.

• Antipsychotics: diabetes risk & their metabolic consequences

Numerous studies have documented higher risk of incident diabetes risk in people receiving antipsychotic medications, with a two- to five-fold increased risk **(Table 2)** [17–24]. Readers are referred to comprehensive reviews for detailed discussion of diabetes risk [19,25]. Glucose screening in a cohort receiving antipsychotics found 5–14% of participants had previously undiagnosed diabetes and 33–53% had prediabetes.

Of concern, a recent study of children and youth showed a threefold higher incidence of diabetes in antipsychotic recipients, compared with other children and youth receiving other psychotropic medications [24]. The onset of diabetes was rapid, within 12 months of antipsychotic initiation. Study limitations included likely lower rates of diabetes ascertainment due to lack of glucose screening and higher diabetes risk in the controls, together suggesting risk was underestimated [28].

Together these data highlight the necessity for regular glucose screening in all antipsychotic recipients, which has been part of international psychiatry initiatives to improve physical health in people with severe mental illness [25,29–31].

All antipsychotics can cause weight gain. **Table 3** shows frequently prescribed antipsychotics and their potential for weight gain and metabolic complications. It is important not to make any distinction between first- and second-generation antipsychotic medications for class effects for weight and metabolic risk, since both classes have adverse risks.

A difficulty in interpreting the literature is that older observational studies of people with severe mental illness on long-term antipsychotic medications suggest high rates of obesity, but no substantive, continued weight gain. These data have perhaps been incorrectly interpreted to suggest antipsychotic therapies does not cause obesity and that patient factors are the cause. Evidence from longitudinal, controlled studies following antipsychotic initiation in treatment-naive patients with severe mental illness show the opposite. Substantial weight gain occurs in up to 60% of treatment-naive individuals with first episode psychosis in the first 10–16 weeks, increasing to 60–100% after 1–2 years of antipsychotic therapy [33]. A prospective study of 505 antipsychotic-naive youth showed significant weight gain over approximately 11 weeks for all four antipsychotic medications studied: aripiprazole, olanzapine, quetiapine and risperidone [15]. Weight gain ranged from 4.4 kg (3.7–5.2) on aripiprazole to 8.5 kg (7.4–9.7) on olanzapine, significantly higher than the 0.2 kg weight gained in the control group [15]. Other studies conform these findings: another study of 400 treatment-naive participants reported an average 12-week weight gain after antipsychotic treatment initiation of 3.9 kg (3.8–3.9) with risperidone, 3.6 kg (3.5–3.7) with quetiapine and 7.1 kg (7.0–7.2) with olanzapine [34]. Another large study of treatment-naive people with first-episode psychosis reported high rates of clinically adverse weight gain (>7%) from baseline weight by 12 months: in 86% of olanzapine

Table 2. Prevalence of preventable metabolic risk factors in severe mental illness.

Risk factor	Prevalence (%)	Relative risk
Obesity	75	1.5–2
Metabolic syndrome	54	2–3
Smoking	67	2–3
Hyperglycemia	29	2–3
Hyperlipidemia	33–50	≤5
Hypertension	54	2–3

Data taken from [26,27].

recipients, 65% of quetiapine recipients, 53% of haloperidol recipients and 37% of all ziprasidone recipients [35].

Of concern, these rapid weight gain effects are also observed in treatment-naive pediatric populations [15,36]. Greater metabolic disturbances including weight gain and hyperglycemia are observed with clozapine and olanzapine [37,38].

The literature also shows rapid onset of other metabolic disturbances induced within as short a period of 12 weeks after antipsychotic initiation in lipids [39], and insulin resistance emerging in the first year of treatment with antipsychotic medications [40]. Other studies have also shown insulin resistance, predicted by the gain in adiposity after treatment initiation [41,42]. Antipsychotics have also been shown to induce fasting and postprandial hyperinsulinemia within 12 days and before any weight gain [43]. Importantly, this study was conducted in healthy participants without psychiatric disease, indicating that adverse metabolic effects are independent of psychiatric disease itself – an argument previously used to mitigate the observed disease associations with these medications. Rates of obesity in youth receiving antipsychotics are alarming: 55% of males and 42% of females in an Australian first-episode psychosis youth cohort were overweight or obese after a median of 8 months of antipsychotic medication, with body mass index directly related to the length of exposure to medication [44]. Higher rates of metabolic syndrome were also observed [44], as shown in numerous other studies [45–47].

The effects of obesity on seeding future diseases is well known – particularly where its onset is in relative youth – for dyslipidemia, dysglycemia and hypertension [48]. Early-onset obesity predicts adult coronary artery disease [49]. The early and adverse effects of these medications on weight, obesity, lipids and insulin metabolism are major contributors to the seeding of diseases such as cardiovascular disease, diabetes and, possibly, future cancer.

• Depression & antidepressants, diabetes risk & metabolic consequences

This section considers the fascinating bidirectional association that exists between depression and diabetes,. It examines the published literature on pathophysiological and psychosocial factors that increases diabetes risk in people with depression and reviews the literature on the potential diabetes-promoting effects of medications used to treat depression.

For example, depression is a common comorbidity of diabetes [50]. Studies show that at least one in three people with diabetes also suffer from a subthreshold or major depressive disorder [51–53]. On the other hand, people with depression also appear to have higher rates of diabetes [54]. The combination of both diabetes and depression augurs for poorer outcomes due, at least in part, to associations with sub-optimal management and self-care [55], increased financial healthcare burden [56] and increased days missed from the workplace [57]. A recent study documented a 15-year life expectancy short fall in people with depressive disorders, excluding more severe forms of depression that are characterized by psychosis [6]. The combination of diabetes and depression also heightens mortality risk [58].

Depression is associated with lifestyle choices that are associated with increased Type 2 diabetes risk, including smoking, increased caloric intake and reduced physical activity [59]. Depression is also associated with a range of physiological defects that increase insulin resistance and diabetes risk including activation of the hypothalamic–pituitary–adrenal axis, the adrenal medulla, sympathetic system and proinflammatory cytokines [60]. Diabetes in itself can increase the risk of depression [61], which may, in part, be due to the sense of loss associated with diabetes diagnosis, as well as in response to the substantial dietary and lifestyle changes necessary to avoid complications.

There is a paucity of data on how to best treat depression in people with diabetes, as well as the

optimal pharmacological treatment. For example, people with diabetes are often omitted from randomized control trials, including those on the efficacy of antidepressants [62]. It is, however, clear that undertaking depression treatment in people with diabetes is effective and beneficial [63]. Data indicate that psychotherapy that includes education on diabetes self-management is effective and should be considered as the first line of treatment [64]. While pharmacological treatment may be useful to treat depression, its impact on glycemic control is variable depending on the type of antidepressant used, with the impact of antidepressants on glucose levels remaining unclear [64].

Collaborative care between different healthcare professionals is emphasized in people with diabetes and depression as a way of delivering appropriate and effective pharmacotherapy and psychotherapy [64]. Crucially, evidence shows that early detection of depression is needed and that physicians have an important role in monitoring and treating physiological abnormalities as well as psychiatric disorders [61]. Moreover, in people with diabetes, depression has been associated with less regular medication adherence [65], which might undermine achievement of diabetes treatment goals.

Antidepressant medications are associated with both weight gain and insulin resistance [66], thereby increasing diabetes risk. Commonly used antidepressant medications fall into at least three categories: serotonin-selective re-uptake inhibitors (SSRIs), noradrenaline-selective reuptake inhibitors (NSRIs) and tricyclics **(Table 1)**. A systematic review of the literature has reported associations between antidepressant medication use and diabetes but could not establish causality, due to the nature of the studies, which were cross-sectional or observational case–controlled or cohort studies [67]. One cross-sectional study showed antidepressant use was associated with elevated 2-h glucose and higher lipids, blood pressure and waist circumference [68]. Another large cross-sectional observation study reported a 40% higher rate of diabetes in people receiving antidepressant medications [69].

Amongst case–controlled studies, a number have consistently shown at least doubling of diabetes risk in people receiving antidepressant medications. Analyses from the UK General Practice Research Database of more than 165,000 people receiving antidepressants, diabetes risk was increased by 80% overall, compared with healthy controls [70]. Diabetes ascertainment was either by recorded diabetes diagnosis, abnormal HbA1c or antidiabetic medication prescription; glucose levels were not examined. Diabetes risk was similar between SSRIs and tricyclic antidepressants, and mitigated by short treatment duration.

Another study compared antidepressant use among people who developed diabetes compared with people free of diabetes, with careful matching of confounders including age, sex, socioeconomic and occupational status, and region [71]. This study reported that antidepressant use was associated with a doubling of diabetes risk

Table 3. The weight-promoting effect and lipid and/or glucose metabolism dysfunction of antipsychotic medications used to treat severe mental illness.

Antipsychotic medication	Weight gain potential	Risk of glucose and/or lipid dysfunction
Chlorpromazine	Substantial	High (with limited data)
Clozapine	Substantial	High
Olanzepine	Substantial	High
Paliperidone	Intermediate	Mild
Quietapine	Intermediate	Moderate
Risperidone	Intermediate	Mild
Thioridazine	Intermediate	High (with limited data)
Amisulpride	Low	Mild
Aripiprazole	Low	Low
Ziprasidone	Low	Low
Fluphenazine	Low	Low (with limited data)
Perphenazine	Low	Low
Haloperidol	Low	Low

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in those with milder forms of depression and a near threefold increase in diabetes risk in those with severe depression. This compared with an incident diabetes risk that was only increased by 20% in depressed people who did not receive antidepressant medication.

Data from the Diabetes Prevention Program has been examined to determine whether antidepressant therapy modulated incident diabetes rates within the randomization framework of intensive lifestyle intervention ± metformin, standard lifestyle intervention ± metformin or metformin alone [72]. Participants taking antidepressant medications that were randomized to lifestyle intervention alone (either intensive or standard) had incident diabetes rates two- to fourfold higher than participants in the same lifestyle intervention. However, no increase in incident diabetes risk was observed in participants taking antidepressant medications randomized to any metformin-containing intervention arm [72]. A 10-year follow-up of 82% of participants found that continuous antidepressant medication use was associated with a more than doubling of incident diabetes risk in participants on lifestyle intervention alone; this risk was mitigated in participants who receiving metformin [73]. In considering these interesting findings, it is important to recall that the Diabetes Prevention Program actively excluded participants with more severe forms of depression.

Pooled data from the Nurses Health Study I, Nurses Health Study II and the Health Professionals Study (amounting to in excess of 1.6 million person-year follow-up, found an almost tripling of incident diabetes risk in women receiving antidepressant medications, attenuated by adjusting for metabolic risk factors such as BMI, lipids and hypertension [74].

Why does the presence of severe mental illness negatively impact diabetes care?

Severe mental illness impacts on diabetes care execution and service delivery in multiple ways that can be considered in several paradigms: individual-specific, psychiatric medication-specific (as discussed above) and service/system-specific.

• Individual-specific factors

Severe mental illness may affect an individual in ways that may reduce capability to ensure the objective of independent diabetes self-care is achieved, or diminish the efficacy of diabetes interventions or prescriptions. For example, people with severe mental illness may be characterized by behaviors that adversely influence intermediate and long-term health outcomes, including sedentariness, lower physical activity, lower quality diet and higher smoking rates [75–78]. For example, less than 30% of adults with schizophrenia take part in regular physical activities compared with 62% of those without schizophrenia [79]. Furthermore, fewer than 25% of adults treated with antipsychotic medications meet the recommended 150 min of moderate intensity exercise per week [80].

While these might be considered 'lifestyle choices' it is necessary for health professionals to examine underlying factors that promote these behaviors or barriers that prevent ready change, but are critical in addressing the foundations of good health. These include the sedating effects of many antipsychotic medications, lesser education around healthy eating patterns, which are often transmitted down generations, interrupted education and socioeconomic disadvantage, if not poverty, and the tolerance of smoking, if not neglect in amending this behavior. These lifestyle factors not only diminish the efficacy of antidiabetic medications, but also increase cardiovascular risk long term. As diet and exercise form the cornerstones of diabetes management, these factors must be addressed, considering each individual's unique situation and tailor-making a lifestyle intervention that addresses some of these barriers to healthier lifestyle. One barrier in this situation is access to individualized dietetic services and basic domestic management (managing on a limited budget, where to purchase healthy food, how to select it and healthy cooking techniques).

Encouraging physical activity may also be challenging. Many antipsychotics induce substantial, even profound sedation, associated with reduced incidental activity, late wakening and fatigue. Added to this, many people with severe mental illness feel uncomfortable in noisy busy environments such as gyms or other health facilities. Individuals with paranoia may feel unsafe outside their homes and finding even a walk confronting. Identifying these factors is helpful and discourse with the psychiatry team about minimizing the sedative effects of prescribed medications (when appropriate) is important.

• System-specific: recognizing disparities in health service access & delivery

Evidence exists to show widespread disparities in health service delivery to people with severe

mental illness over a number of domains [81,82]. It may be a useful self-check of our own practice and that of the services we work within to objectively consider the following questions.

- In our clinics, do people with severe mental illness meet the standards of care promulgated in the St Vincent's Declaration or the American Diabetes Association Standards of Care as frequently as people without mental illness?
- Do our patients with diabetes and severe mental illness equally frequently receive services from dietitians, educators and ophthalmologists?
- Do our patients with severe mental illness have the highest HbA1c levels, most frequent missed appointments, or more frequent amputations?

There is no doubt that people with severe mental illness and diabetes present unique treatment challenges. Disparities in physical health delivery and achievement of benchmarked standards of diabetes care exist. These disparities have been termed 'a disgrace' [9], particularly in health systems where access to healthcare is considered equitable and a human right. People with severe mental illness less frequently achieve physical health benchmarks in diabetes, with higher rates of suboptimal glycosylated hemoglobin levels [83] and higher blood lipid levels and blood pressure despite medical attendance [81].

A number of factors may contribute, listed in **Box 1**. These include the impact of severe mental illness on the capacity to follow physical health advice, the pluripotent metabolic effects of medications prescribed for severe mental illness in decompensating glucose and lipid control or worsening obesity, irregular attendance and nonengagement with physical health services, disparities in health service delivery (a form of discrimination), lack of access to medical services [82], homelessness and poverty. Perhaps a lack of interdisciplinary collaboration and cohesiveness also contributes [84].

People with severe mental illness and diabetes might be seen as a vulnerable group with a double disability: the effects of mental illness plus the effects of diabetes in an individual who is perhaps least capable to manage of the complexities of diabetes self-care. These include the challenges of diet rigor, glucose monitoring, multiple medications, hypoglycemia detection and management, the stress of attending busy, noisy diabetes outpatient services.

Given the described less frequent achievement of the diabetes care benchmarks of glycemic control, lipids and blood pressure, this group is also at greater risk of additional disability from diabetes complications, such as retinopathy and blindness, nephropathy and neuropathy. As smoking rates are higher, with increased risk peripheral vascular disease, amputation risk is also inflated.

Discrepancies in the quality of care given to individuals with mental illness compared with the general population have also been reported [85,86]. For example, people with severe mental illness are less likely to receive appropriate fundamental clinical evaluations such as weight

Box 1. Factors that may contribute to diabetes and other physical health risks in people with severe mental illness.

Weight gain effects on medication (antipsychotics and antidepressants)

- Sedentary lifestyle
- Symptoms of psychosis (delusions and hallucinations may limit activities)
- Impaired and reduced motivation (illness and medication)
- Sedating effects of medication
- Social exclusion and isolation
- Poor nutrition
- Restricted access to fresh food and cooking facilities
- Lack of knowledge on healthy eating
- Impaired and reduced motivation (illness or medication)
- Financial restraint
- Smoking
- Limited access to primary and secondary healthcare
- Disparities in access and provision of preventative healthcare, early intervention or standard physical health
- Disparities in receiving benchmark health services

or blood pressure measurements, despite their higher metabolic risk [87]. Studies have shown that despite some individuals with severe mental illness having limited access to healthcare [88,89], even those that do have access to healthcare and diabetes services may receive poorer quality of care than individuals without severe mental illness [86]. Furthermore, studies have reported that individuals with diabetes and a mental illness were less likely to be prescribed cholesterol-lowering medication or other medication to reduce cardiovascular complications than their counterparts without mental illness.

With this knowledge, it is critical for health professionals involved in diabetes care to more aggressively seek to ensure that their services meet benchmarked standards of care in diabetes for all. In this regard, people with severe mental illness may require clinical attention above and beyond that provided within standard clinical pathways. Our patients with severe mental illness may require additional services, additional referrals, reminder phone calls to attend, the same clinician at every appointment and other levels of advocacy to achieve their physical healthcare. The role of diabetes health professionals may not involve health service delivery, but problem solving and confronting barriers that have prevented achieving diabetes standards of care. This may involve considering the issues of poverty and homelessness. Imagine the challenges of insulin therapy in the homeless, for example.

How might we address the special needs for diabetes care in this vulnerable group?

In the setting of severe mental illness, the complexities of diabetes care including lifestyle changes, glucose monitoring and additional medication adds a further burden to this susceptible population. Individuals with mental illness are arguably the least able to deal with the self-care requirements for optimal diabetes management. Diabetes is a complex disease that requires precise attention and initiative from an individual in their self-care, as well as regular medical attendance. Strategies to improve attendance in people with severe mental illness may include reminder telephone calls prior to the scheduled clinic visit, considering offering later morning appointments (since the sedative effect of many antipsychotics create challenges for early waking), managing waiting areas to be peaceful, uncrowded and less confronting or challenging.

Furthermore, it is known that people with mental illness have not only significantly less knowledge about diabetes but also perform less in neuropsychological tests than their counterparts without mental illness [90]. It is therefore probable that people with mental illness require at least more time with their clinicians and educators to grasp a better understanding of their diabetes management, a special need that is not yet specified. Education and management advice may require repetition, with perhaps visual supports or specific summary handouts to reinforce treatment, education points and self-care requirements.

The special needs of people with mental illness require considering when prescribing dietary and lifestyle change. For example, the impact of social isolation, educational status, income, cognitive limitations, cooking skills (life skills) and so on. Many people experience their first episode of severe mental illness in late adolescence or in youth, when life skills acquisition is in development. Just as formal school or tertiary education can often be abruptly interrupted by severe mental illness, so can life skills acquisition, compounded by social isolation and unemployment. Diabetes allied health professionals as well as mental healthcare workers are aptly placed to assist people with severe mental illness and diabetes address barriers to healthy eating patterns for diabetes and weight management and healthy levels of physical activity. Furthermore, smoking cessation is crucial, as is the management of alcohol and other illicit substance use.

Health professionals involved in diabetes care can also play an important role in advocacy for the patient by requesting review of antipsychotic and antidepressant medications, where mental health appears stable or has substantially improved. It is not uncommon that the fear of mental illness recurrence prevents clinicians from considering lower doses or medications with fewer metabolic complications. In this regard, psychotropic medications can become enduring, with enduring adverse effects. Diabetologists are not trained to make these clinical decisions but, importantly, we can raise the question with our psychiatrist colleagues and promote discourse on the risk/benefit balance for better physical and mental health outcomes in our shared patients. For example, we recently reported a case where a very careful and gradual antipsychotic switch in a man with chronic

schizophrenia led to optimization of very poorly controlled Type 2 diabetes [91]. The patient had received clozapine for many years and had been free of psychotic symptoms for a long time, but endured adverse effects including developing poorly controlled diabetes despite large doses of insulin and frequent contact with diabetes services (medical and education). Diabetes complications had developed. Antipsychotic switch was staggered over a 2-year period with regular and careful psychiatry review, since clozapine withdrawal can precipitate psychosis; a significant and enduring reduction in HbA1c and weight were observed [91]. The case highlights the importance of interdisciplinary collaboration, especially between diabetologists and psychiatrists in the care of people with mental illness and diabetes. It has been suggested that under appropriate and careful supervision, a change in antipsychotic medication to a more metabolically-neutral one is recommended in some patients with mental illness. When switching antipsychotic medications, regular psychiatry monitoring is warranted, and the transition must be gradual.

Preventing diabetes & other physical diseases in people with severe mental illness

The high prevalence of preventable complications including Type 2 diabetes, obesity and metabolic abnormalities in people with mental illness clearly warrants the concern and attention of clinicians [25]. The key to reducing the risk of cardiometabolic complications in people with mental illness seems to be in preventing or reducing the weight gain that occurs on initiation of antipsychotic medication, for which a number of guidelines now exist for early intervention [29–30,92–94].

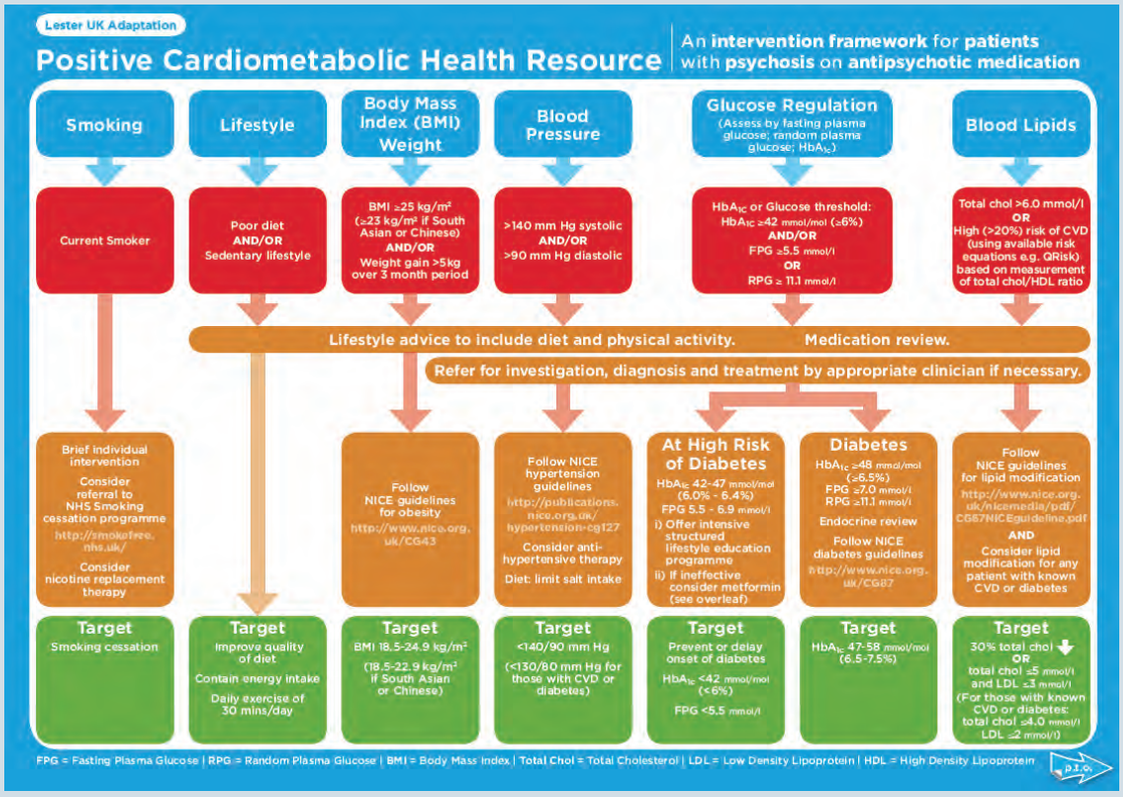
Programs for weight loss have been shown to be efficacious in people with severe mental illness. An 18-month tailored behavioral intervention with weight management counseling and group exercise significantly reduced weight in obese participants with predominantly schizophrenia or bipolar disorder [95]. Interestingly and in contrast with weight loss programs in the general population, weight loss was less rapid initially and continued steadily over the study duration. Furthermore, the weight loss achieved was comparable to that observed in the general population. Another study compared weight loss between obese participants with psychotic illness against that of participants without psychiatric disease [96]. The cognitive behavioral weight management intervention was associated with greater weight loss success in those with psychotic illness. Other weight loss interventions in patients with severe mental illness have been limited to less than 6 months duration [97–102]. Taken together, these studies consistently support that there is a return on effort for weight loss interventions in this high-risk patient subgroup.

In addition to the benefits of lifestyle programs, interventions with metformin have also shown weight and metabolic benefits. A randomized controlled trial with metformin at initiation of antipsychotic medication has shown a 4-kg weight gain difference compared with placebo [103]. Metformin and lifestyle intervention appear to have additive benefits. For example, a randomized controlled trial of people with schizophrenia on long-term antipsychotic medications found that placebo was associated with weight gain over 12 weeks (2.4–3.8 kg); by contrast, participants randomized to metformin lost 2.5–3.9 kg and participants receiving metformin plus lifestyle intervention 3.4–5.7 kg weight loss on [102]. A systematic review of metformin use for prevention of weight gain in psychiatric cohorts found strong evidence of benefit [104].

These data support that lifestyle intervention should be implemented in all individuals receiving antipsychotic therapy as a standard of care. In our view, lifestyle intervention at the time of initiation of psychotropic medications that increase weight and increase diabetes risk is imperative, if not essential, given the strength of the evidence for adverse effects in this vulnerable group. Otherwise, we have lost an opportunity to prevent what can become a downward spiral in physical health. Furthermore, it has been argued by multiple authors internationally that metformin should be considered in all people at the time of initiation of antipsychotic medication, in concert with lifestyle intervention to prevent weight gain and cardiometabolic disease [105–107].

• Models & guidelines

To support cardiometabolic prevention (perhaps even protection) in people with severe mental illness, a clinical algorithm "Positive Cardiometabolic Health Algorithm" was developed by health workers in New South Wales, Australia [29,94]. The algorithm was developed


Lester UK Adaptation
Positive Cardiometabolic Health Resource
An intervention framework for patients with psychosis on antipsychotic medication
Smoking
Lifestyle
Body Mass Index (BMI) Weight
Blood Pressure
Glucose Regulation
(Assess by fasting plasma glucose; random plasma glucose; HbA1c)
Blood Lipids
Current Smoker
Poor diet AND/OR Sedentary lifestyle
BMI ≥25 kg/m² (≥23 kg/m² if South Asian or Chinese) AND/OR Weight gain >5kg over 3 month period
>140 mm Hg systolic AND/OR >90 mm Hg diastolic
HbA1c or Glucose threshold: HbA1c ≥42 mmol/mol (≥6%) AND/OR FPG ≥5.5 mmol/l OR RPG ≥ 11.1 mmol/l
Total chol >6.0 mmol/l OR High (>20%) risk of CVD (using available risk equations e.g. QRisk) based on measurement of total chol/HDL ratio
Lifestyle advice to include diet and physical activity.
Medication review.
Refer for investigation, diagnosis and treatment by appropriate clinician if necessary.
Brief individual intervention
Consider referral to NHS Smoking cessation programme
http://smokefree.nhs.uk/
Consider nicotine replacement therapy
Follow NICE guidelines for obesity
http://www.nice.org.uk/CG43
Follow NICE hypertension guidelines
http://publications.nice.org.uk/hypertension-cg127
Consider anti-hypertensive therapy
Diet: limit salt intake
At High Risk of Diabetes
HbA1c 42-47 mmol/mol (6.0% - 6.4%)
FPG 5.5 - 6.9 mmol/l
i) Offer intensive structured lifestyle education programme
ii) If ineffective consider metformin (see overleaf)
Diabetes
HbA1c ≥48 mmol/mol (≥6.5%)
FPG ≥7.0 mmol/l
RPG ≥11.1 mmol/l
Endocrine review
Follow NICE diabetes guidelines
http://www.nice.org.uk/CG87
Follow NICE guidelines for lipid modification
http://www.nice.org.uk/nicemedia/pdf/CG67NICEguideline.pdf
AND
Consider lipid modification for any patient with known CVD or diabetes
Target
Smoking cessation
Target
Improve quality of diet
Contain energy intake
Daily exercise of 30 mins/day
Target
BMI 18.5-24.9 kg/m² (18.5-22.9 kg/m² if South Asian or Chinese)
Target
<140/90 mm Hg
(<130/80 mm Hg for those with CVD or diabetes)
Target
Prevent or delay onset of diabetes
HbA1c <42 mmol/mol (<6%)
FPG <5.5 mmol/l
Target
HbA1c 47-58 mmol/mol (6.5-7.5%)
Target
30% total chol ↓ OR total chol ≤5 mmol/l and LDL ≤3 mmol/l
(For those with known CVD or diabetes: total chol ≤4.0 mmol/l LDL ≤2 mmol/l)
FPG = Fasting Plasma Glucose | RPG = Random Plasma Glucose | BMI = Body Mass Index | Total Chol = Total Cholesterol | LDL = Low Density Lipoprotein | HDL = High Density Lipoprotein


Don't just SCREEN – INTERVENE for all patients in the "red zone"
Although this clinical resource tool targets antipsychotic medication, many of the principles apply to other psychotropic medicines given to people with long term mental disorders.
The general practitioner and psychiatrist will work together to ensure appropriate monitoring and interventions are provided and communicated. The general practitioner will usually lead on supervising the provision of physical health interventions. The psychiatrist will usually lead on decisions to significantly change antipsychotic medicines.
Primary care's Quality and Outcomes Framework (QOF) includes four physical health indicators in the mental health domain: BMI (MH12); blood pressure (MH13); total to HDL cholesterol ratio (MH14); Blood glucose (MH15). Currently MH14 and MH15 are only for those aged over 40yrs.
History and examination following initiation or change of antipsychotic medication
Frequency: as a minimum review those prescribed a new antipsychotic at baseline and at least once after 3 months.
Ideally weight should be assessed 1-2 weekly in the first 8 weeks of taking a new antipsychotic as rapid early weight gain may predict severe weight gain in the longer term.
Subsequent review should take place annually unless an abnormality of physical health emerges, which should then prompt appropriate action and/or continuing review at least every 3 months.
At review
History: Seek history of substantial weight gain (e.g. 5kg) and particularly where this has been rapid (e.g. within 3 months). Also review smoking, exercise and diet. Ask about family history (diabetes, obesity, CVD in first degree relatives <60 yrs) and gestational diabetes. Note ethnicity.
Examination: Weight, BMI, BP.
Investigations: Fasting estimates of plasma glucose (FPG), HbA1c and lipids (total cholesterol, LDL, HDL, triglycerides). If fasting samples are impractical then non-fasting samples are satisfactory for most measurements except for LDL or triglycerides.
ECG: Include if history of CVD, family history of CVD, or if patient taking certain antipsychotics (see Summary of Product Characteristics) or other drugs known to cause ECG abnormalities (eg erythromycin, tricyclic anti-depressants, anti-arrythmics – see British National Formulary for further information).
Interventions
Nutritional counselling: reduce take away and "junk" food, reduce energy intake to prevent weight gain, stop soft drinks and juices, increase fibre intake.
Physical activity: structured education-lifestyle intervention. Advise physical activity: e.g. Advise a minimum of 150 minutes of 'moderate-intensity' physical activity per week (http://bit.ly/Oe7DeS).
If unsuccessful after 3 months in reaching targets, then consider specific pharmacological interventions (see below).
Specific Pharmacological Interventions
Anti-hypertensive therapy: Normally GP supervised. Follow NICE recommendations http://publications.nice.org.uk/hypertension-cg127.
Lipid lowering therapy: Normally GP supervised. Follow NICE recommendations http://www.nice.org.uk/nicemedia/pdf/CG67NICEguideline.pdf.
Treatment of Diabetes: Normally GP supervised. Follow NICE recommendations http://www.nice.org.uk/CG87.
Treatment of those at high risk of diabetes: FPG 5.5-6.9 mmol/l; HbA1c 42-47 mmol/mol (6.0-6.4%) Follow NICE guideline PH 38 Preventing type 2 diabetes: risk identification and interventions for individuals at high risk (recommendation 19) – http://guidance.nice.org.uk/PH38.
• Where intensive lifestyle intervention has failed consider metformin trial (this would normally be GP supervised).
• Please be advised that off-label use requires documented informed consent as described in the GMC guidelines, http://www.gmc-uk.org/static/documents/content/Good_Practice_in_Prescribing_Medicines_0911.pdf. These GMC guidelines are recommended by the MPS and MDU, and the use of metformin in this context has been agreed as a relevant example by the Defence Unions.
• Adhere to British National Formulary guidance on safe use (in particular ensure renal function is adequate). Start with a low dose e.g 500 mg once daily and build up, as tolerated, to 1500–2000 mg daily.
Review of antipsychotic medication: Normally psychiatrist supervised. Should be a priority if there is:
• Rapid weight gain (e.g. 5kg <3 months) following antipsychotic initiation.
• Rapid development (<3 months) of abnormal lipids, BP, or glucose.
The psychiatrist should consider whether the antipsychotic drug regimen has played a causative role in these abnormalities and, if so, whether an alternative regimen could be expected to offer less adverse effect:
• As a first step prescribed dosages should follow BNF recommendations; rationalise any polypharmacy.
• Changing antipsychotic requires careful clinical judgment to weigh benefits against risk of relapse of the psychosis.
• Benefit from changing antipsychotic for those on the drug for a long time (>1 year) is likely to be minimal.
• If clinical judgment and patient preference support continuing with the same treatment then ensure appropriate further monitoring and clinical considerations.
RC PSYCH
RC GP Royal College of General Practitioners
Royal College of Nursing
HQIP
Royal College of Physicians
DIABETES UK CARE. CONNECT. CAMPAIGN.
Download Lester UK Adaptation: www.rcpsych.ac.uk/quality/NAS/resources
Adapted for use by the RCGP/RCPsych. With permission from Curtis J, Newall H, Samaras K. © HETI 2011

Figure 1. A positive cardiometabolic health intervention algorithm (see facing page).
Reproduced with permission from [111].

as an educational resource to assist mental health workers and psychiatrists in the identification and management of cardiometabolic risk factors, highlight action points, intervention and ultimate health targets for each cardiometabolic risk factor including weight, blood pressure, smoking and glucose levels [29]. The algorithm is now a part of a clinical pathway towards physical health in people with mental illness mandated by the local Department of Health (NSW Health) [108]. This algorithm also formed the template for the Lester Adaption, which is part of the NICE UK Clinical Guidelines for treatment of youth and adults with psychosis [109,110] **(Figure 1)**. Diabetologists are familiar with these principles and targets, since some aspects form of our standard of diabetes care. These algorithms were designed for use by clinicians and allied health professionals across a broad range of specialties that contribute to the management of people with severe mental illness.

Models of care addressing wholistically the mental and physical health of care of people with severe mental illness are gaining traction, as treatment models seek to comprehensively address the health needs of individuals over multiple domains. "RaDiCaL" (Recovery and Discovery in Community and Lifestyle) was recently developed to screen and actively intervene in young people with mental illness to ultimately prevent weight gain via routine metabolic screens and subsequent interventions [29]. The program is individualized and involves the involvement of a multidisciplinary team consisting of clinical nurses, occupational therapists, clinical psychologists and family therapists. Baseline measurements, family history and family history are also an important aspect used to screen and appropriately manage this patient group. The program also aims to perform routine metabolic screens at 3-monthly intervals to evaluate metabolic changes and to support and encourage lifestyle changes. Clearly, healthcare clinicians from many different specialties need to collaborate for best possible health outcomes in people with severe mental illness. Health professionals trained in diabetes are well placed to inform such programs, but also interact and be involved. It is imperative however that research efforts examine the efficacy and cost–effectiveness of different models in the unique setting of people with severe mental illness.

Transporting the diabetes care model to mental health: a way forward for better physical health in severe mental illness

The St Vincent's Declaration has, arguably, illuminated the pathway towards standardization of diabetes treatment objectives that we now apply in diabetes care [112]. When a young person is diagnosed with Type 1 diabetes, our clinical and education efforts are aimed at achieving as normal a life as possible. Our philosophy is that treatment will restore full function and our expectations are that life returns normal, or as near normal as possible. Our expectation is that when a young person is diagnosed with severe mental illness, the philosophical outlook is not nearly so positive, nor are the expectations. It is sobering to consider why this difference exists, when both are biological disorders that start in youth, one affecting insulin-secreting cells, the other the brain. Diabetologists today would have great difficulty in accepting diabetes as an early death sentence and a life of reduced opportunities, discrimination and poor health, as is the current state for people with severe mental illness. With the same rigor in optimization of health and advancing all expectations towards normal life, diabetes health professionals are well placed to share these clinical skills and expertise with people with severe mental illness. These principles have been adapted from what we consider standard philosophical principles in diabetes care, to formulate the Healthy Active Lives Declaration (HeAL), HeAL was recently adopted as an implementation tool by NICE. Advocacy for the special needs for people with severe mental illness [113,114].

Conclusion

People with severe mental illness suffer shortened life expectancy, poor physical health and unmet health needs. The causes of these differences from the general population are multiple and vary from individual factors such as poorer self-care and education, through to system-wide factors that have been called, in the strongest terms, discrimination and neglect. Considering the diverse and specialized skill sets in the different professions that serve people with severe

mental illness and diabetes, workforce engagement, collaboration between and within specialities (including general practitioners and community workers), education of the wider workforce, shared enthusiasm and a measure of tenacity will increase the likelihood that we can systematically, cohesively and effectively improve the physical health and outcomes of our patients with both severe mental illness and diabetes. It is our obligation and a matter of equity and justice.

Future perspective

Imagine a world where a diagnosis of a severe mental illness does not lead to loss of physical health and no longer carries a 20-year premature mortality. Imagine where we might prevent weight gain when a patient with severe mental illness is commenced on an antipsychotic or antidepressant medication. Imagine if diabetes could be prevented in this challenged and vulnerable group.

Evidence-based strategies to prevent weight gain are available, but insufficiently resourced. For antipsychotic medications, long-term research is urgently required to determine if lifestyle intervention and/or metformin translate to diabetes prevention, as known for metformin and antidepressant medications.

Focused research is essential to determine the most efficacious means of preventing obesity, diabetes and premature cardiovascular disease in people with severe mental illness. The development of new antipsychotic and antidepressant medications free from cardiometabolic complications is eagerly awaited.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

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