Curr Diab Rep (2016) 16:16
DOI 10.1007/s11892-015-0704-4

Diabetes and Schizophrenia

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Abstract People with schizophrenia have 2- to 5-fold higher risk of type 2 diabetes than the general population. The traditional risk factors for type 2 diabetes, especially obesity, poor diet, and sedentary lifestyle, are common in people with schizophrenia already early in the course of illness. People with schizophrenia also often have low socioeconomic status and income, which affects their possibilities to make healthy lifestyle choices. Antipsychotic medications increase the risk of type 2 diabetes both directly by affecting insulin sensitivity and indirectly by causing weight gain. Lifestyle modification interventions for prevention of diabetes should be an integral part of treatment of patients with schizophrenia. In the treatment of type 2 diabetes in patients with schizophrenia, communication and collaboration between medical care and psychiatric treatment providers are essential.

Keywords Schizophrenia · Diabetes · Risk factors · Prevention · Treatment

This article is part of the Topical Collection on *Other Forms of Diabetes*

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Introduction

Schizophrenia is a psychotic disorder that is often chronic and leads to difficulties in everyday functioning. The main symptoms of schizophrenia are delusions and hallucinations which are called positive symptoms, symptoms of disorganization such as odd behavior and speech that is difficult to understand, and negative symptoms such as lack of motivation and withdrawal. In addition, cognitive impairments are common in patients with schizophrenia. Patients typically have psychotic episodes during which delusions and hallucinations are present and residual symptoms, like negative symptoms, between these episodes. Sometimes, positive psychotic symptoms are continuous or there is full remission between the psychotic episodes. The lifetime prevalence of schizophrenia is 1.0–1.5 % [1, 2].

People with schizophrenia have an elevated risk for diabetes [3••]. This applies particularly to type 2 diabetes which is highly prevalent in people with schizophrenia, but the risk of type 1 diabetes may also be elevated [3••, 4].

In this article, we review current knowledge about the epidemiology of diabetes in schizophrenia, risk factors that contribute to the substantial risk of type 2 diabetes in people with schizophrenia, possibilities for prevention, and treatment recommendations.

Published online: 23 January 2016

Epidemiology of Diabetes in People With Schizophrenia

As in the general population, the prevalence of type 2 diabetes in people with schizophrenia rises with age [5], and the risk of type 2 diabetes in people with schizophrenia is 2- to 5-fold higher than in the general population across age groups [3••]. Reported prevalence, ranging from 1.3 to 50 %, in individual studies has been highly variable due to differences in age, study design, and method of detection of diabetes [3••]. Although some studies have found increased prevalence of impaired glucose tolerance even in patients with first episode psychosis not exposed to antipsychotic medication [6–8], the prevalence of type 2 diabetes is not increased at the onset of schizophrenia. People with schizophrenia have 11–20 years shorter life expectancy than the general population [9], and type 2 diabetes is among the major causes of increased mortality risk [10].

Some recent register-based studies suggest that type 1 diabetes may increase the risk of schizophrenia about 1.5- to 2-fold [4, 11], and people diagnosed with schizophrenia or who have a family history of schizophrenia have increased risk of type 1 diabetes [12]. Many autoimmune diseases show similar associations, suggesting that there is general vulnerability to autoimmune diseases in people with schizophrenia or that these diseases may share etiological mechanisms [11, 12]. However, one previous study found that people with type 1 diabetes had decreased risk of schizophrenia [13]. Therefore, further studies are needed on the link between type 1 diabetes and schizophrenia. In the following, we will focus on type 2 diabetes.

Risk Factors for Type 2 Diabetes in People With Schizophrenia

The traditional risk factors for type 2 diabetes (obesity, especially abdominal obesity, sedentary lifestyle, hypertension, and hyperlipidemia) are common in people with schizophrenia already early in the course of illness. In a study of 394 patients with first episode schizophrenia spectrum disorders, averaging only 47 days of lifetime antipsychotic treatment, 48.3 % of patients were obese or overweight, 56.5 % had dyslipidemia, 39.9 % had prehypertension, 10.0 % had hypertension, and 13.2 % had metabolic syndrome [14]. According to a review of 25 studies on first episode psychosis patients, patients had increased waist-hip ratio and more intra-abdominal fat at treatment onset, while weight, BMI, and waist circumference did not differ from healthy controls [15]. After the treatment is initiated with antipsychotic medication, weight gain, increase in waist circumference, and hyperlipidemia are common [15, 16].

Most important of the modifiable risk factors for diabetes is obesity, especially visceral obesity. It is estimated that in the general population, one third of new cases of diabetes can be attributed to obesity [17], and obesity is among the most important risk factors for type 2 diabetes also in people with schizophrenia. Obesity (body mass index (BMI) over 30) is over 2-fold more common in people with schizophrenia than in the general population [18]. Moreover, the body composition of schizophrenia patients is metabolically unfavorable, comprising abdominal obesity, high fat percentage, and low muscle mass [18]. Several factors contribute to the high risk of obesity, including both medication and lifestyle-related factors.

In comparison to general population, the lifestyle of patients with psychotic disorders tends to include more risk factors of diabetes. Patients have unhealthier diet, with a high intake of saturated fat and low consumption of fruit and fiber [19]. Sedentary lifestyle is common among people with schizophrenia. Patients exercise less and tend to be more passive in everyday activities in comparison to general population [20, 21]. The negative symptoms of schizophrenia and sedative effects of antipsychotics may contribute to the lower activity level.

Cigarette smoking has been recognized as an independent risk factor for type 2 diabetes [22]. Smoking is common among patients with schizophrenia. For example, the prevalence of smoking in a large first episode psychosis study was 50.8 % [14]. Several other recent large-scale clinical studies have reported that over 50 % of people with schizophrenia are current smokers [23, 24], and the prevalence of smoking is not decreasing, in contrast to the general population [24].

People with schizophrenia often have low socioeconomic status and income [25]. This affects their possibilities to make healthy lifestyle choices. For example, many cannot afford physical activity facilities and equipment and high-quality food.

Antipsychotic medications increase the risk of type 2 diabetes [26], and the risk may be especially high for children and adolescents [27].

Antipsychotic use related risk for type 2 diabetes is partly mediated by weight gain. All antipsychotics may increase weight. Among second-generation antipsychotics (SGA), weight gain is the most common and of greatest magnitude with clozapine and olanzapine and intermediate with quetiapine, risperidone, paliperidone, and iloperidone, while aripirazole, amisulpride, ziprasidone, asenapine, and lurasidone have least effect on weight [26, 28]. Of first-generation antipsychotics, low-potency antipsychotics like chlorpromazine cause more weight gain than high-potency antipsychotics like haloperidol [26]. Weight gain tends to be rapid during the first weeks of treatment and reaches a plateau after the first year of treatment [26]. Antipsychotics increase appetite and food intake and delay satiety signal [26, 29]. Serotonin 5-HT_{2C} and histamine H1 receptor antagonism are among the contributing mechanisms [26, 29]. In animal studies, olanzapine has also elevated the expression of appetite-stimulating agouti-related peptide and neuropeptide Y [29]. However, regardless of the prescribed antipsychotic, there are marked individual variations in weight gain [26].

Antipsychotics may increase the risk of diabetes also irrespective of weight gain and obesity [26, 29]. Chronic treatment with antipsychotics, particularly olanzapine and clozapine, is associated with insulin resistance, reduction in insulin sensitivity, and glucose dysregulation [29]. This may be mediated by the muscarinic M_3 receptor antagonism [29]. A rare adverse effect of several SGAs is type 2 diabetes manifesting as diabetic ketoacidosis (DKA). A recent review summarized all published case reports of DKA associated with antipsychotic treatment [30]. The incidence of DKA in patients with schizophrenia treated with antipsychotics was reported to be 0.15–0.2 % per year [30]. The most commonly used antipsychotic in cases with DKA had been olanzapine, followed by clozapine, risperidone, and quetiapine, and the mean duration of antipsychotic treatment 9 months (range 4 days–4 years) [30]. In 39 % of the reported cases, antipsychotic use had been associated with no weight gain or even weight loss. Of the DKA cases, 68 % were male and 41 % were of African American or African Caribbean origin [30]. Very few cases were associated with infection [30].

Several family studies have found that a family history of diabetes is more common in people with schizophrenia than in the general population or in other psychiatric disorders [31, 32]. It has been suggested that this is due to shared genetic risk factors, but it might also be related to environmental factors like shared dietary habits. Several studies have tried to identify this putative shared genetic background, and there are some positive findings. For example, transcription factor 7-like 2 (TCF7L2), an established risk gene for type 2 diabetes [33], has been associated with schizophrenia in several studies [34–36]. A pathway analysis of genes with reported associations to schizophrenia and type 2 diabetes found shared pathways in the two disorders related to insulin, AKT, and adipocytokine signaling [37]. However, there have also been negative findings [38]. A thorough cross-disorder analysis utilizing large genome-wide association dataset, as has been performed in psychiatric disorders [39], would be warranted to verify the genetic overlap between schizophrenia and type 2 diabetes.

Prevention

Screening and Monitoring Risk of Diabetes

In 2004, the American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, and North American Association for the Study of Obesity (hereafter referred to as the "ADA/APA consensus panel") released expert consensus guidelines for screening and monitoring of somatic conditions among users of antipsychotics [40], which has been the basis for later guidelines (reviewed in [41]). The ADA/APA consensus panel guidelines recommend more frequent screening for and monitoring of cardiovascular risk factors among antipsychotic users than recommended for the overall population (Table 1) [42].

The diabetes risk scores have not been validated in schizophrenia patients. Instead, routine measurement of fasting glucose should be done [17] (Table 1 and Fig. 1). After recent treatment onset, measuring fasting blood glucose is the best indicator for rapidly rising blood glucose due to antipsychotic treatment. Later, HbA1c indicates need for intensive intervention [17]. After onset of a new antipsychotic medication, HbA1c should be monitored after 3 months and then annually [42]. Some guidelines recommend laboratory measurement at 6 weeks after treatment onset [41], the utility of which has not been tested, but this might be relevant for those at the highest risk. The use of HbA1c instead of or in addition to fasting glucose has been validated in patients receiving antipsychotics [43].

For antipsychotic users, the ADA/APA consensus panel recommends monitoring weight at time of antipsychotic initiation and 4, 8, and 12 weeks after initiation of a new antipsychotic medication, and four times per year thereafter [42]. Monitoring waist circumference, smoking habits, and other lifestyle factors affecting the risk of diabetes is also recommended. Waist circumference might be a more sensitive measure for reduced risk than change in BMI [44]. Annual follow-up of lipids is recommended by most guidelines [41].

Nonpharmacological Prevention Interventions

Interventions on reducing the risk of diabetes aim at reducing the modifiable risk factors of diabetes. Most important of these is obesity, especially visceral obesity [17]. The single most important factor in reducing diabetes incidence is weight loss [42]. It is important to focus on prevention of increased weight, which is easier than loss of weight [45]. Other modifiable risk factors for diabetes are diet and physical inactivity. Both nonpharmacological and pharmacological interventions on these risk factors have been tested in schizophrenia.

Several studies show positive results in reducing weight of severely mentally ill patients. For example, in a sample of 291 participants with severe mental illness, including 58 % with schizophrenia or a schizoaffective disorder, a behavioral intervention led to a mean −3.2 kg more decrease of weight during 18 months in the intervention group, and 37.8 % in the intervention group vs. 22.7 % in the nonintervention group lost 5 % or more of their initial weight [46].

Some specific components of interventions focusing diet, exercise, and elements of behavioral therapy increase the effect of nonpharmacological interventions. Successful programs in the general population have employed multiple components, personalization, duration of at least 4 months of active intervention, more frequent contact, and trained, multidisciplinary treatment teams [47••]. Including peer community

Table 1 Recommendations for monitoring of type 2 diabetes risk in patients with schizophrenia according to different guidelines

Risk factor assessment	At treatment onset	4 weeks	6 weeks	8 weeks	3 months	Every 3 months	Annually
Personal history	x				x		x
Familial history	x						
Physical examination	x				x		x
Alcohol	x				x		x
Substance use	x				x		x
Smoking	x				x		x
Physical activity	x				x		x
Diet	x				x		x
Body mass index	x	x		x	x	x	x
Waist circumference	x	x		x	x	x	x
Blood pressure	x				x	x	x
Fasting glucose[a]	x		(x)		(x)		x
HbA1c					x		x
Cholesterol, triglycerids, HDL, LDL	x						x[b]
Metabolic syndrome	x				(x)		X
Additional evaluations							
Electrocardiogram	Despite the risk of QT prolongation, the APA practice guidelines do not suggest routine monitoring of healthy individuals before starting most antipsychotic medication. The recommendations of guidelines and features of specific medications are summarized in Shulman et al. [54]						
Liver, renal, and thyroid function	No specific recommendations for schizophrenia except for some medications						
Oral glucose tolerance test	No specific recommendations for schizophrenia						
Diabetic ketoacidosis	According to symptoms						
Prolactin	According to symptoms						
COPD	According to symptoms						
Myocarditis	The majority of clozapine-induced myocarditis occurs within the first 4 weeks of treatment, usually between days 14 and 21, although cases have been reported more than a year after treatment initiation, see [54].						

CHOL cholesterol, *COPD* chronic obstructive pulmonary disease, *TRIG* triglycerides, *HDL* high-density lipoprotein. *LDL* low- density lipoprotein, *HbA1c* glycosylated haemoglobin

[a] No consensus whether fasting glucose should be measured in addition to HbA1c during follow-up

[b] No consensus; several guidelines recommend testing every 2 years

providers in addition to professionals in teams shows the best outcomes [47••]. Combination of diet and exercise is more effective than either alone [17]. Personalizing diet by addressing personal food preferences, occupation, social support, and family environment leads to more change in eating habits than generic nutrition advice [47••].

The typical challenges for an intervention in severely mentally ill patients include this population's low socioeconomic status, psychiatric symptoms, barriers to accessing healthy lifestyle options, and medication side effects [47••]. Suggestions to overcome these difficulties with exercise include using stairs of the residence instead of gyms, distributing exercise videos or handouts, providing gym memberships, in-clinic exercise sessions, and use of outdoor recreational activities in small groups. To improve diet, providing groceries and meal replacements may temporarily address the problem, but shopping trips to local grocery stores or nearby fast food and other restaurants to highlight healthy choices is recommended, as is focusing on reduction of food intake instead of complicated or expensive food substitution [47••]. Also, associating lifestyle interventions into visits with established case managers, use of familial locations, and use of peer leader may improve therapeutic alliance [17, 47••]. Focusing on increasing motivation is important in schizophrenia. Several means have proved effective, including use of group settings, incentives, engagement of friends, family, and facilitator [47••].

Smoking is highly prevalent, and a significant but challenging modifiable lifestyle factor, among people with mental illness. Patients with schizophrenia need specific consideration for their worry about deteriorating mental health and weight gain related to smoking cessation [48, 49]. A recent review on interventions aiming at smoking cessation notes a paucity of studies in schizophrenia [50]. Based on the current preliminary evidence, smoking cessation interventions are effective and should be actively offered to patients with schizophrenia [50]. A careful monitoring of antipsychotic medication dose (especially of clozapine), psychiatric symptoms, and weight is

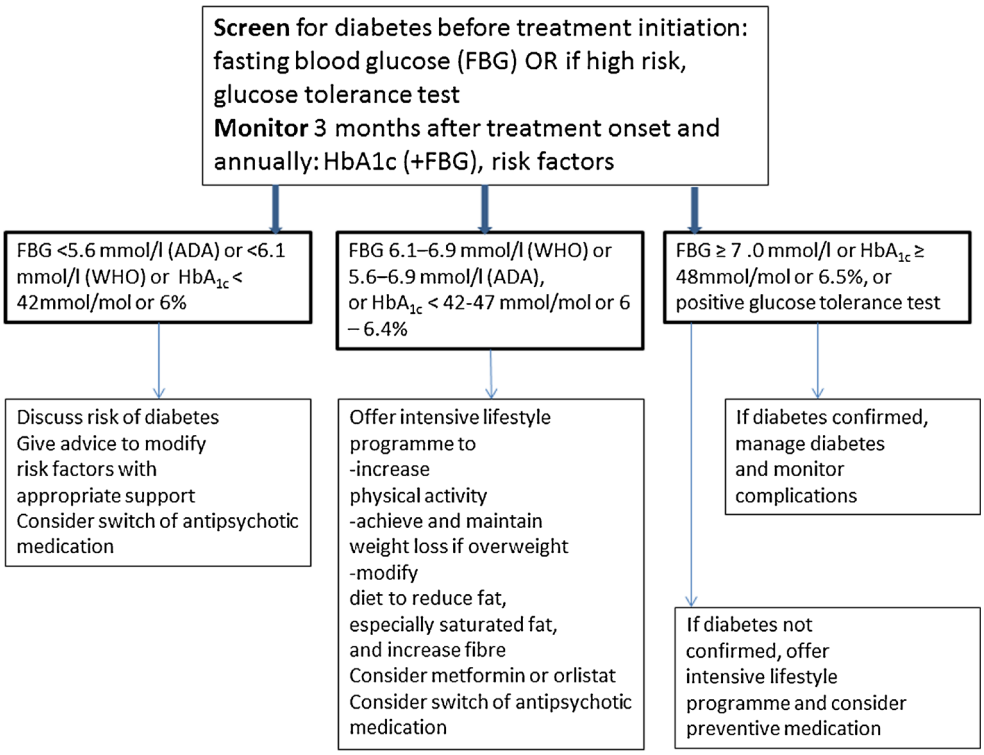

Fig. 1 Clinical algorithm for the management of diabetes risk in people with schizophrenia

needed during cessation. NICE guideline recommends as first-line treatment nicotine replacement therapy, usually a combination of transdermal patches with a short-acting product such as an inhalator, gum, lozenges, or spray [51]. Of pharmacological interventions, a positive effect of bupropion is best evaluated and of nicotine replacement therapy and varenicline preliminary [50, 52••]. Some interventions (best evidence for bupropion) in the general population prevent an increase in weight. However, risk for adverse neuropsychiatric symptoms especially in patients using clozapine due to drug interactions restricts the use. A pilot study from an ongoing randomized controlled trial in schizophrenia reported encouraging results about the applicability and effectiveness of the smoking cessation intervention: 36 % in the intervention group vs. 23 % in the nonintervention group managed in the cessation during the 12 months follow-up, while 48 vs. 19 % were using pharmacological add-on treatment [53].

Pharmacological Prevention of Diabetes

Every selection of antipsychotic treatment should be done noting the risk for diabetes. For patients who already are overweight or have signs of impaired glucose tolerance, an antipsychotic with lower tendency for metabolic side effects is considered. However, while a switch in antipsychotic medication is possible, it must be made after considering the effect on mental health and under careful psychiatric follow-up [54]. Research suggests that switching to a metabolically more favorable antipsychotic medication reduces risk of diabetes in longer term, but the evidence is not of high quality [17].

Pharmacological interventions to prevent diabetes in general population consist of two groups of drugs: drugs currently used to treat diabetes (e.g., metformin), and drugs against obesity (orlistat) [17]. In a meta-analysis of pooled pharmacological trials in the general population, the risk of diabetes was reduced by 36 % [17]. In patients with schizophrenia, no reports on the effectiveness of pharmacological interventions to prevent diabetes are available but positive outcomes include reduction in body weight, BMI, and insulin resistance [55]. In a recent meta-analysis on double-blind randomized placebo-controlled trials focusing on patients with schizophrenia [56], metformin was the most extensively studied drug in regard to body weight, the mean difference amounting to −3.17 kg (95 % CI −4.44 to −1.90 kg) as compared to placebo. Pooled effects for topiramate, sibutramine, aripiprazole, and reboxetine were also different from placebo. Furthermore, metformin and rosiglitazone improved insulin resistance, while aripiprazole, metformin, and sibutramine decreased blood lipids. As treatment guidelines propose for general population, those at high risk of diabetes who are unable to participate in an intensive lifestyle-change program, or whose blood glucose measure shows they are, despite participation, still progressing toward type 2 diabetes, should be considered metformin treatment [51]. The NICE guidelines also recommend that adults who have a BMI of 28.0 kg/m^2 or more who after intervention are progressing towards type 2 diabetes should be considered orlistat treatment [51]. However, given

the limited evidence for the effectiveness, tolerance, and adverse effects in schizophrenia, no strict recommendations can currently be made to target specific interventions. Also, apparently for several both clinician and patient dependent factors, the current clinical practice is far from above recommendations [3••].

Selection of Interventions Based on the Risk of Diabetes and Evidence of Effect

Information about possible metabolic side effects should be offered to every patient with antipsychotic treatment (Fig. 1.). This should include information and help in finding ways to improve diet and sufficient physical exercise. Preventive intervention at onset of antipsychotic treatment seems more effective than treatment after metabolic change [45]. The intensity of follow-up of weight and lifestyle should increase according to the risk. For people confirmed as being at high risk of diabetes (fasting plasma glucose of 5.5–6.9 mmol/l or HbA1c of 42–47 mmol/mol [6.0–6.4 %]), a referral to a lifestyle-change program after a discussion about risks and ways to modify them is recommended [51]. If this is not possible or does not prevent progression toward type 2 diabetes, pharmacological intervention is considered.

To date, no evidence-based interventions to prevent diabetes specifically in patients with schizophrenia are available. Some of the interventions to reduce risk factors can be recommended based on the evidence. A recent review concluded that the strength of the evidence was high for four interventions: metformin and behavioral interventions had beneficial effects on weight loss, and bupropion and varenicline reduced tobacco smoking [52••]. Due to insufficient specific evidence in patients with schizophrenia, recommendations are mostly based on the results from general population. This might be problematic due to some specific features associating with schizophrenia (see above and Table 2) and antipsychotic medication. The effectiveness of patient education and general suggestions of lifestyle change without more intensive interventions have not been fully determined [54]. Research on the effect of interventions on reducing risk of diabetes is lacking. Based on several excellent reviews and meta-analyses as reviewed in [57], estimated from studies without strict quality criteria, effect of lifestyle interventions on diabetes risk factors is small in schizophrenia. However, based on the studies fulfilling the quality criteria that in general population interventions are known to be central for effectiveness, results are equal to general population [47••].

While reading the results in interventions aiming at reducing cardiometabolic risk in psychiatric patients, it is important to note that some key elements found effective in general population studies were not utilized in most of the studies done on severely mentally ill patients [47••, 57]. Interventions in schizophrenia had mean duration of 18 weeks, low intensity in some studies with less than weekly contact, and meeting with one professional without specific training instead of multidisciplinary teams. Furthermore, higher intensity exercise, structured curricula, and multiple components intervention were seldom used. Also, common group interventions can reduce the possibility to tailor personalized interventions [47••]. On the other hand, groups can have specific advantages when treating schizophrenia as described above.

The cost-effectiveness ratio specifically in schizophrenia of a pharmacological treatment as compared to nonpharmacological prevention cannot be determined based on the current evidence. One meta-analysis has found that individual nonpharmacological interventions had a larger effect size on weight than pharmacologic interventions in independent studies [45], but in the only head-to-head comparison trial, metformin was more effective at producing weight loss than behavioral interventions [58]. Paucity of research prevents interpretations of differences in effect of individual pharmacological compounds. Some studies like the smoking cessation study by Peckham et al. [53] suggest that a combination of nonpharmacological and pharmacological treatment might be more effective than either alone.

Treatment

The special needs of people with schizophrenia need to be taken into account in the treatment of type 2 diabetes (Table 2). In practice, successful treatment requires collaboration between mental health and primary care practitioners and other professionals who are responsible for the diabetes care.

Cognitive difficulties are common in people with schizophrenia, including problems in abstract thinking, memory, and executive functioning [59]. Negative and disorganized symptoms and difficulties in social functioning may impair communication further. Therefore, people with schizophrenia may need to receive treatment recommendations in a simplified form, and they need longer medical visits [60•].

As outlined previously, antipsychotic medications differ in their propensity to cause weight gain and impair glucose tolerance. Unfortunately, clozapine and olanzapine, which are metabolically the most unfavorable antipsychotics, are also the most effective antipsychotic medications [28]. However, medication changes may be possible and antipsychotics with low risk of metabolic side effects are preferred for people with schizophrenia with comorbid type 2 diabetes [60•]. Besides antipsychotics, people with schizophrenia may also have other medications that have metabolic side effects, for example valproic acid and some antidepressants [26, 61], and possibilities to change these medications should also be evaluated. The treating psychiatrist should be responsible and monitor any changes made to antipsychotic and other psychotropic medication.

Table 2 Problems and needs that have to be taken into account in the treatment of type 2 diabetes in patients with schizophrenia

Problem	Solutions
Cognitive deficits	Reserve more time
	Provide recommendations and counseling in plain language
	Engage family members and caregivers in the treatment
Negative symptoms and difficulties in everyday functioning	Reserve more time to motivation
	Motivate and monitor adherence to treatment and lifestyle changes
	Pay attention to glucose self-monitoring
	Pay attention to patient's hygiene, address foot, and skin care
	Arrange home nursing services or other assistance if needed
Disorganized symptoms	If there are problems in communicating with the patient, arrange visits together with family members or psychiatric case manager
Antipsychotic medication	Consult psychiatrist about the possibility to change to medication with lower metabolic side effects
Low socioeconomic status	Take low income into account in recommendations and counseling
Comorbidities	Patients with schizophrenia have increased risk of many medical diseases, and these may be undiagnosed. Make careful medical examination and arrange treatment.
Dental care	Patients often have poor dental health; arrange dental care
Polypharmacy	Consider possible drug-drug and drug-disease interactions
Substance abuse	Ask about alcohol and other substance abuse. Alcohol abuse needs to be taken into account in medication choices (e.g., varenicline, metformin). Inform the treating psychiatrist.
Treatment fragmentation	Collaboration with mental health services

Physical activity and other lifestyle changes should be an integral part of the treatment of type 2 diabetes in people with schizophrenia, and patients should be referred to a structured treatment program [60•]. If such programs are available, even small improvements in diet and physical activity are beneficial [60•, 62]. Health care professionals should encourage small but incremental lifestyle changes and monitor them in patient visits.

In the pharmacotherapy of type 2 diabetes, antidiabetic agents with lesser likelihood of weight gain are preferred. If the patient needs help in glucose self-monitoring, this should be arranged. Monitoring treatment adherence is also important, but according to previous studies patients with schizophrenia have usually better adherence to diabetes medication than other patients with diabetes [63]. Trials comparing metformin and novel antidiabetic agents (DPP-4- or SGLT2-inhibitors, GLP-1 receptor agonists) in the treatment of type 2 diabetes in patients with schizophrenia have not been published. A German register-based study found that novel antidiabetic drugs were used less often in patients with schizophrenia who had type 2 diabetes than in other patients with type 2 diabetes, but this was associated with lack of private insurance in patients with schizophrenia [64]. Target HbA1c goals should be set, and if these cannot be reached with appropriate pharmacotherapy and lifestyle interventions, insulin should be started. Insulin regimens should be kept as simple as possible. Patients need education on the treatment of diabetes, and often multiple sessions are needed. Many patients need help in glucose self-monitoring and insulin treatment, and it must be ensured that they receive it. If family members or caregivers are supporting the patient in the treatment of type 2 diabetes, they should receive education on type 2 diabetes, including monitoring and treatment. Home nursing services can be often used as well. It is important that all professionals and other people involved in the care of the patient are aware of the diabetes treatment plan [60•].

Prevention of complications is an essential part of treatment. Dyslipidemias and hypertension are common in patients with schizophrenia and should be treated adequately [60•]. Smoking cessation should be strongly encouraged, and effective interventions should be used to achieve it [65••]. Special attention should be paid to foot care, since many patients have problems in adequate hygiene [60•]. Cardiovascular diseases are common in patients with schizophrenia, and they should be identified early and treated adequately. Dental health care is also important [60•]. People with schizophrenia often have poor dental health [66], which contributes to their increased cardiovascular disease risk. Gastrointestinal symptoms and renal functioning should also be monitored [60•]. Unfortunately, there is currently very limited information on the prevalence and treatment of diabetic complications in patients with schizophrenia. One study which was based on self-report found them quite common [67].

Patients with schizophrenia often have psychotropic polypharmacy. For example, a recent nationwide register-based study from Finland found that 46 % of patients

with schizophrenia were currently using more than one antipsychotic, and 56 % had been using antidepressants and 69 % benzodiazepines at some point of their illness [68]. This means that potential drug disease and drug-drug interactions need to be taken into account in the treatment of diabetes in these patients [69].

Conclusions

The fragmented health care system complicates the treatment of comorbid diabetes and schizophrenia both for the patient and for health care professionals [70••]. Collaborative care models can improve the medical care of patients with schizophrenia [70••]. More research is needed on the outcome of type 2 diabetes in patients with schizophrenia, especially on cost-effectiveness ratio as comparing intensive psychosocial intervention to pharmacological interventions and concerning complications. Trials that would investigate specifically in patients with schizophrenia treatments and interventions that have been shown to be effective in the general population are needed [70••]. Such information would be essential for guidelines and treatment programs tailored to the needs of patients with schizophrenia.

Acknowledgments Jaana Suvisaari reports grants from the Academy of Finland (#278181), the Sigrid Juselius Foundation, and the Finnish Cultural Foundation. Outi Mantere reports grants from the Helsinki University Central Hospital and the University of Helsinki. The funding organizations had no role in the design and conduct of the work; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Compliance with Ethical Standards

Conflict of Interest Jaakko Keinänen owns shares in the pharma company Orion. Saana Eskelinen has worked as a consultant for Janssen-Cilag and received lecture fees from Janssen-Cilag, Otsuka, and Lundbeck. Jaana Suvisaari and Outi Mantere declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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