

Screening, diagnosis, and management of type II diabetes: A review of the 2014 American Diabetes Association guidelines

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ABSTRACT

Individuals with schizophrenia and schizoaffective disorders are at higher risk than the general population for the development of chronic medical conditions, such as type II diabetes. This review article will focus on the 2014 recommendations from the American Diabetes Association for diagnosis, management, and assessment of glycemic control in patients with type II diabetes

KEYWORDS

Diabetes, treatment, screening, guidelines

The prevalence of type II diabetes among individuals suffering from schizophrenia or schizoaffective disorders is higher than that of the general population. In 2005, the American Diabetes Association along with the American Psychiatric Association, the American Association of Clinical Endocrinologists, and the American Association for the Study of Obesity developed consensus guidelines regarding monitoring of metabolic complications associated with second-generation antipsychotics in this patient population; however, these recommendations do not identify diagnosis and management of type II diabetes in individuals with these conditions. To fill this gap, this review article will focus on the 2014 recommendations from the American Diabetes Association for diagnosis, management, and assessment of glycemic control in patients with type II diabetes. These recommendations should be implemented for management of new onset type II diabetes and prevention of diabetes-related complications in patients with schizophrenia and schizoaffective disorders.

INTRODUCTION

Diabetes mellitus is a chronic disease that is strongly associated with microvascular and macrovascular complications including retinopathy, neuropathy, nephropathy, ischemic heart disease, peripheral vascular

disease, and cerebrovascular disease. These complications result in organ and tissue damage in approximately one-third to one-half of people with diabetes.¹ Diabetes mellitus can be classified into 4 clinical cases: type I diabetes, type II diabetes, gestational diabetes mellitus (GDM), and other specific types of diabetes due to other causes.

In 2005, the World Health Organization (WHO) predicted that the prevalence of type II diabetes will double by 2030, to affect 366 million people globally.² Not everyone is at equal risk for the development of this chronic illness. Studies have shown that individuals suffering from schizophrenia or schizoaffective disorders are at a greater risk of type II diabetes, with prevalence rates 1.5 to 2 times higher than those of the general population.³ While it has been reported that people with schizophrenia may be genetically pre-disposed to type II diabetes, several other risk factors could contribute to disease development in this patient population.⁴ One of the major risk factors is the use of current antipsychotic medications. Despite their notable benefits in the management of psychiatric illnesses, their use has been associated with metabolic complications such as weight gain, dyslipidemia, type II diabetes mellitus and cardiovascular diseases.³

Evaluation and management of psychiatric illnesses is just as important as that of chronic medical conditions caused by the utilization of antipsychotic medications. Since individuals with schizophrenia and schizoaffective disorders are more prone to new-onset type II diabetes, this review article will primarily focus on recommendations from the American Diabetes Association (ADA) for evaluation and management of type II diabetes.

SCREENING

Table 1 describes the ADA screening recommendations for children, adolescents, pregnant women, and adults for type II diabetes.^{3,5} Additionally, it also describes the consensus guidelines developed by the ADA, the American Psychiatric Association, the American Association of Clinical Endocrinologists, and the American Association for the Study of Obesity regarding monitoring of metabolic complications associated with second generation antipsychotics (SGAs).³

DIAGNOSIS

Table 2 describes various diagnostic criteria for diabetes. The ADA guidelines do not prefer one testing method to the other. They do recommend that a "test result diagnostic of diabetes should be repeated to rule out laboratory error unless the diagnosis is clear on clinical grounds. It is preferable that the same test be repeated for confirmation. If two different tests' results are both above the diagnostic threshold, the diagnosis of diabetes is confirmed. If two different tests are available and the results are discordant, the test whose result is above the diagnostic cut point should be repeated, and the diagnosis is made based on the confirmed test."⁵

NON-PHARMACOLOGIC THERAPY

Medical nutrition therapy (MNT) is an integral part of diabetes prevention, management, and self-management education.⁵ In clinical trials and outcome studies, MNT has produced decreases in A1c at 3-6 months ranging from 0.25 to 2.9% with higher reductions seen in new onset type II diabetes.⁶⁻⁸ In addition to its role in preventing and controlling diabetes, the ADA recognizes the importance of nutrition as an essential component of an overall healthy lifestyle. For individuals with type II diabetes, or in individuals who are overweight or obese, with or at risk for diabetes, moderate weight loss (5-7% of body weight) is associated with decreased insulin resistance, improved measures of glycemia and lipemia, and reduced blood pressure.⁶⁻⁸ U.S. Department of Agriculture recommends consumption of 14 g of dietary fiber per 1,000 kcal to prevent insulin resistance in

individuals at high risk for developing type II diabetes. Additionally, the ADA recommends adjustment in daily carbohydrate consumption to achieve glycemic control in individuals with type II diabetes.

Table 1. Current criteria for diabetes screening in different patient populations^{3,5}

Patient Population	Diabetes Screening	Additional Risk Factors
Pediatrics	-Every 3 years in children ≥ 10 years or onset of puberty (if occurs at age < 10 years) + overweight (BMI $> 85^{\text{th}}$ percentile for age and sex, weight for height $> 85^{\text{th}}$ percentile, or weight $> 120\%$ ideal for height) + ≥ 2 additional risk factors	-Family history of type II diabetes in 1 st or 2 nd degree relative -High risk race/ethnicity (African American, Latino, Native American, Asian American, or Pacific Islander) -Conditions associated with insulin resistance -Maternal history of pre-existing diabetes or GDM
Adults	-Every 3 years in all adults with BMI ≥ 25 kg/m ² + ≥ 1 additional risk factor -Every 3 years starting at the age of > 45 years if no risk factors present	-Physical inactivity -First-degree relative with diabetes -High risk race/ethnicity -Women who delivered a baby weighing > 9 lb or had GDM -High-density lipoprotein cholesterol (HDL-C) < 35 mg/dL +/- triglycerides (TG) > 250 mg/dL -BP $\geq 140/90$ mm Hg or on therapy -History of cardiovascular disease -Conditions associated with insulin resistance -A1c $\geq 5.7\%$
Pregnant women	-24-28 weeks of gestation in all pregnant women -6-12 weeks postpartum and then every 3 years if diagnosed with GDM	N/A
Individuals on SGA therapy*	-Baseline, 12 weeks after initiation of a SGA, and then every year regardless of patient's age	N/A

*SGA = second generation anti-psychotic

Table 2. ADA's diagnosis criteria for pre-diabetes, diabetes, and gestational diabetes⁵

Testing method	Pre-diabetes	Diabetes	Gestational diabetes
A1c, %	5.7-6.4	≥ 6.5	N/A
Fasting plasma glucose (FPG), mg/dL	100-125	≥ 126	≥ 92
2-hour plasma glucose during an oral glucose tolerance test (OGTT), mg/dL	140-199	≥ 200	1 hr: ≥ 180 2 hr: ≥ 153
Random plasma glucose in individuals with classic hyperglycemia symptoms, mg/dL	N/A	≥ 200	N/A

Exercise, in addition to MNT, is an important component of the diabetes management plan. Regular exercise has been shown to improve blood glucose control, reduce cardiovascular risk factors, contribute to weight loss, and improves overall well-being.⁵ Evidence suggests that "structured exercise interventions of at least 8 weeks of duration have been shown to lower A1c by an average of 0.66% in individuals with type II diabetes."^{5,9-12} The ADA recommends ≥ 150 minutes per week of moderate-intensity aerobic activity, spread over ≥ 3 days per week with no more than 2 consecutive days without exercise. Additionally, it also recommends resistance training to be performed ≥ 2 times per week. In individuals taking insulin or insulin secretagogues, physical activity can cause hypoglycemia. Individuals taking these agents should be

Table 3. Treatment options for type II diabetes¹³

Drug class	Physiological action	A1c reduction	Advantages	Disadvantages
Biguanide (metformin)	-↓ hepatic glucose production -↑ insulin sensitivity -↓ intestinal glucose absorption	1-2%	-Extensive experience -↓ microvascular risk -↓ macrovascular risk -↓ fasting glucose -No hypoglycemia -No weight gain -↓ LDL-C and TG -↓ cost	-Gastrointestinal side effects (abdominal cramping, diarrhea) -Lactic acidosis (rare) -Multiple contraindications
Sulfonylureas (glyburide, glipizide, glimepiride)	-↑ insulin secretion (glucose independent)	1-2%	-Extensive experience -↓ microvascular risk -↓ fasting and prandial glucose -↓ cost	-Hypoglycemia -Weight gain -↓ durability (hastens β cell dysfunction)
Meglitinides (repaglinide, nateglinide)	-↑ insulin secretion	0.5-1.5%	-↓ prandial glucose	-Hypoglycemia -Weight gain -Frequent dosing

educated to eat a carbohydrate-rich snack, if the pre-exercise glucose levels are <100 mg/dL.⁵

PHARMACOLOGIC THERAPY

A patient-centered approach including individual preferences, cost and potential side effects of each class, effects on body weight, and hypoglycemia risk should be implemented when choosing pharmacological therapy for management of diabetes. Table 3 describes the current treatment options for type II diabetes.¹³ The ADA recommends metformin as the preferred initial agent, barring no contraindications or intolerance, either in addition to MNT and exercise or when lifestyle efforts alone have not achieved or maintained glycemic goals. Metformin has a long-standing evidence base for efficacy and safety, is inexpensive, and reduces risk of cardiovascular events.¹⁴ When 3 months of metformin therapy fails to achieve or maintain glycemic goals, another agent should be added. "Comparative effectiveness meta-analyses suggest that overall each new class of non-insulin agents added to initial metformin therapy lowers A1c around 0.9 to 1.1%."¹⁵ Many individuals with type II diabetes eventually benefit from insulin therapy. Providing individuals with an algorithm for self-titration of insulin doses based on self-monitoring of blood glucose (SMBG) readings improves glycemic control in type II diabetic individuals initiating insulin.¹⁶

ASSESSMENT OF GLYCEMIC CONTROL

Two primary techniques are recommended to assess the effectiveness of the management plan on glycemic

Drug class	Physiological action	A1c reduction	Advantages	Disadvantages
Thiazolidinedione (pioglitazone)	-↑ insulin sensitivity	0.5-1.5%	-↓ fasting and prandial glucose -↓ risk of hypoglycemia -↑ HDL-C and ↓ TG -Possible CV benefit -↓ cost	-Weight gain -Edema -Risk of heart failure -Risk of osteoporosis -Possible bladder cancer risk
α glucosidase inhibitors (acarbose, miglitol)	-Slows intestinal glucose absorption	0.5-0.8%	-↓ prandial glucose -No systemic absorption -No hypoglycemia	-Gastrointestinal side effects (flatulence, diarrhea) -Frequent dosing
DPP-IV inhibitors (sitagliptin, saxagliptin, linagliptin)	-↑ insulin secretion and ↓ glucagon secretion (glucose dependent) -Slows gastric emptying -↑ satiety	0.5-0.8%	-↓ prandial glucose -Well tolerated -Weight neutral -No hypoglycemia	-Possible risk of pancreatitis -↑ cost
SGLT-2 inhibitor (canagliflozin)	-↑ renal excretion of glucose	0.5-0.8%	-↓ fasting and prandial glucose -Weight reduction	-↑ urogenital infections -Questionable long-term safety -↑ cost
Bile-acid sequestrants (colesevelam)	-Unknown: may ↓ hepatic glucose production or ↑ incretin	0.3-0.5%	-↓ prandial glucose -No systemic absorption -No hypoglycemia -↓ LDL-C	-Constipation -↑ TG -May ↓ absorption of other medications -↑ cost
Dopamine-2 agonists (bromocriptine)	-Modulates hypothalamic regulation of metabolism	0.1-0.6%	-↓ fasting and prandial glucose -No hypoglycemia -↓ cost	-CNS adverse effects (dizziness, syncope) -Nausea, fatigue
GLP-1 agonists (exenatide, exenatide XR, liraglutide)	-↑ insulin secretion and ↓ glucagon secretion (glucose dependent) -Slows gastric emptying -↑ satiety	0.5-1.1%	-↓ prandial glucose -↓ fasting glucose (exenatide XR only) -No hypoglycemia -Weight reduction	-Gastrointestinal side effects (nausea, vomiting) -Injectable/ site reactions -Questionable pancreatitis or thyroid cancer risk -↑ cost
Amylin analogs (pramlintide)	-↓ glucagon secretion -Slows gastric emptying -↑ satiety	0.5-1%	-↓ prandial glucose -Modest weight reduction	- Gastrointestinal side effects (nausea, vomiting) -Injectable/ site reactions -↑ risk of hypoglycemia -Must be taken with insulin -Frequent dosing -↑ cost
Insulin (human NPH, human regular, lispro, aspart, glulisine, glargine, detemir, pre-mixed: several)	-↑ glucose disposal -↓ hepatic glucose production	> 1%	-Significant A1c reduction -Basal: ↓ fasting glucose -Bolus: ↓ prandial glucose -Flexibility in dosing strategies and titration -↓ cost for some formulations	-Weight gain -Hypoglycemia -Injectable/site reactions -"Stigma" for patients -↑ cost for some formulations

control; SMBG readings and A1c. SMBG is useful to monitor for and prevent asymptomatic hypo- and hyperglycemia in insulin-treated individuals. The ADA recommends that “individuals on intensive insulin regimens such as multi-dose insulin (MDI) or insulin pump therapy should perform SMBG 6-8 times daily, which includes prior to meals and snacks, occasionally postprandially, at bedtime, prior to exercise, after treating low blood glucose until they are normoglycemic, and prior to critical tasks such as driving.”⁵ On the other hand, the ADA does not provide any recommendations for optimal frequency of SMBG for individuals on non-intensive regimens, such as basal insulin monotherapy or oral hypoglycemic therapies.

Since A1c reflects average glycemia over several months, it serves as a check on the accuracy of the individual's glucometer. Additionally, A1c testing has a strong predictive value for diabetes complications and therefore, it should be performed routinely as part of continuing care.¹⁷⁻¹⁸ Table 4 presents correlation of A1c with mean plasma glucose. The ADA recommends performing A1c at least 2 times a year in individuals who are meeting treatment goals and quarterly in individuals whose therapy has changed or who are not meeting glycemic goals.

Table 4. Correlation of A1c with mean plasma glucose⁵

A1c, %	Mean plasma glucose, mg/dL
6	126
7	154
8	183
9	212
10	240
11	269
12	298

Lowering A1c to around or below 7% has been shown to reduce microvascular complications of diabetes and if implemented soon after the diagnosis of diabetes is associated with long-term reduction in macrovascular disease.^{14,19-21} Therefore, the ADA recommends < 7% as a reasonable A1c goal for many non-pregnant adults. For individuals with short duration of diabetes, long-life expectancy, and no significant CVD, the ADA suggests a more stringent A1c of < 6.5% if it can be achieved without significant hypoglycemia or other adverse effects of treatment. On the other hand, less stringent A1c goal of < 8% may be considered in individuals with history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive

co-morbid conditions, and history of long-standing diabetes⁵. Other glycemic goals recommended by the ADA can be found in Table 5.

Table 5. Current glycemic goals⁵

Testing method	Diabetes	Gestational diabetes	Diabetes in pregnant women
A1c, %	< 7.0	< 7.0	< 6.0
Fasting plasma glucose (FPG), mg/dL	70-130	≤ 95	60-99
2-hour post-prandial plasma glucose (2-hr PPPG), mg/dL	< 180	1 hr: ≤ 140 2 hr: ≤ 120	100-129

PREVENTION AND MANAGEMENT OF DIABETES COMPLICATIONS

CVD is the major cause of morbidity and mortality for individuals with diabetes and the largest contributor to the direct and indirect costs of diabetes. The common conditions co-existing with type II diabetes (hypertension and dyslipidemia) and diabetes by itself confer independent risks for CVD⁵. Numerous studies have shown the efficacy of controlling individual cardiovascular risk factors in preventing or slowing CVD in people with diabetes.²² Large benefits are seen when multiple risk factors are addressed globally.²²⁻²³ Table 6 describes screening, goals, and treatment of CVD risk factors.

Optimization of blood glucose and blood pressure control is recommended in order to reduce the risk or slow the progression of nephropathy, retinopathy, and neuropathy. The ADA recommends performing an annual test to assess urine albumin excretion in all patients with type II diabetes starting at diagnosis. In non-pregnant individuals with evidence of albuminuria, either ACE inhibitors or ARBs are recommended. Individuals with type II diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist shortly after the diagnosis of diabetes. Subsequent examinations should be repeated annually if there is evidence of retinopathy or every 2 years if there is no evidence of retinopathy. The ADA recommends that all individuals should be screened for distal symmetric polyneuropathy starting at diagnosis of type II diabetes and at least annually thereafter, using simple clinical tests. Finally, for all patients with diabetes, an annual comprehensive foot examination should be performed to identify risk factors predictive of ulcers and amputations as well as daily foot checks performed by individuals to assess cuts and bruises.⁵

Table 6. Screening, goals, and treatment of CVD risk factors⁵

Risk factor	Screening	Goals	Treatment
Hypertension	-Every routine visit	-BP < 140/80 mm Hg -BP < 130/80 mm Hg in individuals with CKD, CAD, non-coronary atherosclerotic diseases -BP < 120/80 mm Hg in patients with systolic CHF	-Lifestyle therapy (weight loss, moderation of alcohol intake, increased physical activity) -Drug regimen that include ACE inhibitor or ARB -Administer 1 or more anti-hypertensive at bedtime
Dyslipidemia	-Annually -Every 2 years if LDL-C < 100 mg/dL, HDL-C > 50 mg/dL, TG < 150 mg/dL	-LDL-C < 100 mg/dL in individuals without overt CVD and < 70 mg/dL in individuals with overt CVD -Reduction in LDL-C of ~30-40% from baseline if individuals do not reach below targets on maximal tolerated statin therapy -TG < 150 mg/dL and HDL-C > 40 mg/dL in men and > 50 mg/dL in women	-Lifestyle therapy (reduction in fat and cholesterol intake, weight loss, and increased physical activity) -Statin therapy should be added to lifestyle therapy regardless of baseline lipid levels -Combination therapy – shown not to provide additional cardiovascular benefit above statin therapy alone – not recommended
Anti-platelet agents	N/A	N/A	Primary CVD prevention: -Aspirin therapy (75-162 mg/day) for increased cardiovascular risk (10-year CVD risk > 10%) -Aspirin not recommended for 10-year CVD risk < 5% -Clinical judgment is recommended for 10-year CVD risk 5-10% Secondary CVD prevention: -Aspirin therapy (75-162 mg/day) with history of CVD -If documented allergy to aspirin, clopidogrel should be used

PREVENTION OF INFECTIOUS DISEASES

Table 7 describes the current immunization recommendations for individuals with type II diabetes. It also includes the 2012 recommendation from the Advisory Committee on Immunization Practices of the Centers of Disease Control and Prevention for vaccinating this patient population with Hepatitis B virus (HBV) secondary to increased incidence of HBV-related outbreaks in long-term care facilities and hospitals.⁵

CONCLUSION

Individuals with schizophrenia and schizoaffective disorders are at higher risk for development of chronic medical conditions such as type II diabetes and hyperlipidemia. New onset of these conditions should be monitored, especially when an individual is using a SGA as part of their treatment. The ADA guidelines should be used as the starting point for management of new onset type II diabetes in this patient population.

Table 7. Immunization Recommendations⁵

Type of Vaccination	Age of Administration	Frequency
Influenza	-Individuals ≥ 6 months	-Annually
Pneumococcal	-Individuals ≥ 2 years	-Once -One time revaccination for individuals > 65 years who have been immunized > 5 years ago
Hepatitis B	-Unvaccinated individuals between 19-59 years: recommended -Unvaccinated individuals ≥ 60 years: considered	-Once for a total of 3 shot series

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