ADA Updates Standards of Medical Care for Patients with Diabetes Mellitus

Key Points for Practice

- All adults should be tested for diabetes beginning at 45 years of age.
- Overweight or obese patients with one or more risk factors for diabetes should be screened at any age.
- Persons who use continuous glucose monitoring and insulin pumps should have continued access after 65 years of age.
- Aspirin therapy should be considered for women with diabetes who are 50 years and older.
- The addition of ezetimibe to statin therapy should be considered for eligible patients who can tolerate only a moderate-dose statin.

From the AFP *Editors*

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Ongoing patient self-management education and support are critical to preventing acute complications of diabetes mellitus and reducing the risk of long-term complications. The American Diabetes Association (ADA) recently updated its standards of care to provide the components of diabetes care, general treatment goals, and tools to evaluate the quality of care. Key changes in the 2016 update include new screening recommendations, clarification of diagnostic testing, and recommendations on the use of new technology for diabetes prevention, the use of continuous glucose monitoring devices, cardiovascular risk management, and screening for hyperlipidemia in children with type 1 diabetes. General recommendations for treatment of type 2 diabetes are shown in *Figure 1*.

Classification and Diagnosis

In the 2016 update, the ADA revised the order and discussion of diagnostic tests to make it clear that no one test is preferred over others. Diabetes may be diagnosed based on results of random plasma glucose testing (200 mg per dL [11.1 mmol per L] or greater), fasting plasma glucose testing (126 mg per dL [7 mmol per L] or greater after no caloric intake for at least eight hours), two-hour 75-g oral glucose tolerance testing (OGTT; 200 mg per dL or greater), or an A1C level of 6.5% or greater. Studies have confirmed that, compared with fasting plasma glucose and A1C testing, two-hour OGTT diagnoses more persons with diabetes. A1C testing has several advantages compared with fasting plasma glucose testing and OGTT, including greater convenience, greater preanalytical stability, and less day-to-day variation during stress and illness. However, these advantages may be offset by the lower sensitivity of A1C testing at the designated cutoff, greater cost, limited availability in certain regions, and the imperfect correlation between A1C and average glucose levels in certain persons.

The ADA revised screening recommendations in the 2016 update to clarify the relationship between age, body mass index (BMI), and risk of type 2 diabetes and prediabetes. It now recommends that all adults be tested beginning at 45 years of age, regardless of weight. Testing is also recommended for asymptomatic adults of any age who are overweight or obese (BMI of 25 kg per m^2 or greater, or 23 kg per m^2 or greater in Asian Americans) and who have at least one additional risk factor for diabetes (A1C of 5.7% or greater; first-degree relative with diabetes; high-density lipoprotein cholesterol level less than 35 mg per dL [0.90 mmol per L] and/or triglyceride level of 250 mg per dL [2.8 mmol per L] or greater; high-risk race/ethnicity [e.g., black, Hispanic, Native American, Asian American, Pacific Islander]; history of cardiovascular disease [CVD]; hypertension; impaired glucose tolerance or impaired fasting glucose on previous testing; other clinical conditions associated with insulin resistance [e.g., severe obesity, acanthosis nigricans]; physical inactivity; women who delivered a baby weighing more than 9 lb (4.1 kg) or who were diagnosed with gestational diabetes; and women with polycystic

Antihyperglycemic Therapy for Type 2 Diabetes Mellitus

Healthy eating, weight control, increased physical activity, and diabetes education

Monotherapy	Metformin
Effectiveness	High
Hypoglycemia risk	Low
Weight	Neutral/loss
Adverse effects	Gastrointestinal/lactic acidosis
Costs	Low

If A1C target not achieved after three months of monotherapy, proceed to two-drug combination (order not meant to denote any specific preference; choice dependent on a variety of patient- and disease-specific factors):

Dual therapy*	Metformin + sulfonylurea	Metformin + TZD	Metformin + DPP-4 inhibitor	Metformin + SGLT2 inhibitor	Metformin + GLP-1 receptor agonist	Metformin + insulin (basal)
Effectiveness	High	High	Intermediate	Intermediate	High	Highest
Hypoglycemia risk	Moderate	Low	Low	Low	Low	High
Weight	Gain	Gain	Neutral	Loss	Loss	Gain
Adverse effects	Hypoglycemia	Edema, fractures, heart failure	Rare	Dehydration, genitourinary	Gastrointestinal	Hypoglycemia
Costs	Low	Low	High	High	High	Variable

If A1C target not achieved after three months of dual therapy, proceed to three-drug combination (order not meant to denote any specific preference; choice dependent on a variety of patient- and disease-specific factors):

Triple therapy	Metformin + sulfonylurea + TZD *or* DPP-4 inhibitor *or* SGLT2 inhibitor *or* GLP-1 receptor agonist *or* Insulin†	Metformin + TZD + Sulfonylurea *or* DPP-4 inhibitor *or* SGLT2 inhibitor *or* GLP-1 receptor agonist *or* Insulin†	Metformin + DPP-4 inhibitor + Sulfonylurea *or* TZD *or* SGLT2 inhibitor *or* Insulin†	Metformin + SGLT2 inhibitor + Sulfonylurea *or* TZD *or* DPP-4 inhibitor *or* Insulin†	Metformin + GLP-1 receptor agonist + Sulfonylurea *or* TZD *or* Insulin†	Metformin + insulin (basal) + TZD *or* DPP-4 inhibitor *or* SGLT2 inhibitor *or* GLP-1 receptor agonist

If A1C target not achieved after three months of triple therapy and patient (1) receiving oral combination, move to injectables; (2) receiving GLP-1 receptor agonist, add basal insulin; or (3) receiving an optimally titrated basal insulin, add GLP-1 receptor agonist or mealtime insulin. In refractory cases, consider adding TZD or an SGLT2 inhibitor:

Combination injectable therapy‡	Metformin + basal insulin + mealtime insulin + GLP-1 receptor agonist

**—Consider starting at this stage when A1C is ≥ 9%.*

†—Usually a basal insulin.

‡—Consider starting at this stage when blood glucose is ≥ 300 to 350 mg per dL (16.7 to 19.4 mmol per L) and/or A1C is ≥ 10% to 12%, especially if symptomatic or catabolic features are present, in which case basal insulin plus mealtime insulin is the preferred initial regimen.

Figure 1. Antihyperglycemic therapy in type 2 diabetes: general recommendations. The order in the chart was determined by historical availability and the route of administration, with injectables to the right; it is not meant to denote any specific preference. Potential sequences of antihyperglycemic therapy for patients with type 2 diabetes are displayed, with the usual transition moving vertically from top to bottom, although horizontal movement within therapy stages is also possible, depending on the circumstances. (DPP-4 = dipeptidyl peptidase 4; GLP-1 = glucagon-like peptide 1; SGLT2 = sodium–glucose cotransporter 2; TZD = thiazolidinedione.)

Adapted with permission from Inzucchi SE, Bergenstal RM, Buse JM, et al. Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach: update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care. *2015;38(1):145.*

ovary syndrome). If test results are normal, repeat testing at a minimum of three-year intervals is reasonable.

Technology for Prevention or Delay of Diabetes

Randomized controlled trials have shown that persons at high risk of developing type 2 diabetes can significantly decrease the rate of diabetes onset with intensive lifestyle modification programs. Follow-up of these studies has shown sustained reduction in the rate of conversion to type 2 diabetes. Given these results and the known risks of progression from prediabetes to diabetes, persons with an A1C of 5.7% to 6.4%, impaired glucose tolerance, or impaired fasting glucose should be counseled on lifestyle changes to achieve 7% weight loss and moderate-intensity physical activity of at least 150 minutes per week.

To reflect the changing role of technology in the prevention of type 2 diabetes, the ADA added a recommendation encouraging the use of new technology (e.g., mobile apps, text messaging) to promote lifestyle modifications. Initial studies have validated DVD-based content delivery, and this has been corroborated in a primary care patient population. Recent studies support content delivery through virtual small groups, Internet-driven social networks, cellular phones, and other mobile devices. Mobile apps for weight loss and diabetes prevention have been validated for their ability to reduce A1C in the setting of prediabetes. The Centers for Disease Control and Prevention has started to certify electronic and mobile health-based modalities that may be considered in addition to more traditional face-to-face and coach-driven diabetes prevention programs.

Continuous Glucose Monitoring

Two primary techniques are available for clinicians and patients to assess glycemic control: patient self-monitoring of blood glucose levels and A1C. Continuous glucose monitoring may be a useful adjunct to self-monitoring in select patients. Real-time continuous glucose monitoring devices measure interstitial glucose levels (which correlate with plasma glucose levels) and include alarms for hypo- and hyperglycemia. However, the U.S. Food and Drug Administration has not approved these devices as a sole agent to monitor glucose levels.

A meta-analysis suggests that, compared with patient self-monitoring, continuous glucose monitoring is associated with short-term A1C lowering of approximately 0.26%. This technology may be particularly useful in patients who are not aware of hypoglycemia or who have frequent hypoglycemic episodes, and may reduce severe hypoglycemia in patients with a history of nocturnal hypoglycemia. Because of the growing number of older adults with insulin-dependent diabetes, the ADA now recommends that persons who use continuous glucose monitoring and insulin pumps should have continued access after 65 years of age.

CVD Risk Management

In all patients with diabetes, cardiovascular risk factors should be systematically assessed at least annually. These risk factors include dyslipidemia, hypertension, smoking, a family history of premature coronary disease, and the presence of albuminuria. Atherosclerotic CVD, defined as acute coronary syndromes, a history of myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, stroke, transient ischemic attack, or peripheral arterial disease presumed to be of atherosclerotic origin, is the leading cause of morbidity and mortality in persons with diabetes. Conditions that commonly coexist with type 2 diabetes (e.g., hypertension, dyslipidemia) are clear risk factors for atherosclerotic CVD, and diabetes itself confers independent risk. Studies have shown that controlling cardiovascular risk factors helps prevent or slow atherosclerotic CVD in persons with diabetes.

Aspirin has been shown to be effective in reducing cardiovascular morbidity and mortality in high-risk patients with previous myocardial infarction or stroke. In 2010, the ADA, the American Heart Association, and the American College of Cardiology Foundation recommended that low-dose aspirin for primary prevention is reasonable in adults with diabetes and no history of vascular disease who are at increased risk of atherosclerotic CVD and do not have an increased risk of bleeding. This recommendation included most men older than

50 years and women older than 60 years who also have one or more of the following major risk factors: smoking, hypertension, dyslipidemia, family history of premature atherosclerotic CVD, and albuminuria. However, multiple recent well-conducted studies and meta-analyses reported a risk of heart disease and stroke that is equivalent if not higher in women compared with men who have diabetes. Thus, the ADA's previous recommendation to consider aspirin therapy in women older than 60 years has been changed to include women 50 years and older.

A recommendation was also added to address antiplatelet use in patients younger than 50 years who have multiple risk factors. Aspirin is not recommended for persons at low risk of atherosclerotic CVD, including those younger than 50 years who have diabetes and no other major risk factors; the low benefit is likely to be outweighed by the risks of significant bleeding. Clinical judgment should be used for those at intermediate risk (younger patients with one or more risk factors or older patients with no risk factors; those with 10-year risk of 5% to 10%) until further research is available. Aspirin use in patients younger than 21 years is contraindicated because of the risk of Reye syndrome.

A randomized controlled trial comparing the combination of ezetimibe/simvastatin (Vytorin) vs. simvastatin (Zocor) alone enrolled persons 50 years and older who experienced an acute coronary syndrome within the preceding 10 days and had a low-density lipoprotein cholesterol level of 50 mg per dL (1.29 mmol per L) or greater. In those with diabetes, the combination of moderate-dose ezetimibe/simvastatin showed a significant reduction in major adverse cardiovascular events. Based on this evidence, the ADA now recommends considering the addition of ezetimibe to statin therapy for persons who meet eligibility criteria and who can tolerate only a moderate-dose statin.

Screening for Hyperlipidemia in Children with Type 1 Diabetes

Although pediatric lipid guidelines provide some guidance relevant to children with type 1 diabetes, there are few studies on modifying lipid levels in this population. The American Heart Association categorizes children with type 1 diabetes in the highest tier for cardiovascular risk and recommends lifestyle and pharmacologic treatment for those with elevated low-density lipoprotein cholesterol levels. For children with a significant family history of CVD, the National Heart, Lung, and Blood Institute recommends obtaining a fasting lipid panel beginning at two years of age. However, statins are not approved for patients younger than 10 years and should generally not be used in children with type 1 diabetes before this age. Therefore, the recommendation to obtain a fasting lipid profile in children starting at two years of age has been changed to 10 years of age.

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