Screening for Diabetes

AMERICAN DIABETES ASSOCIATION

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Type 2 diabetes, the most prevalent form of the disease, is often asymptomatic in its early stages and can remain undiagnosed for many years.

The chronic hyperglycemia of diabetes is associated with long-term dysfunction, damage, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels. Individuals with undiagnosed type 2 diabetes are also at significantly higher risk for stroke, coronary heart disease, and peripheral vascular disease than the nondiabetic population. They also have a greater likelihood of having dyslipidemia, hypertension, and obesity. Because early detection and prompt treatment may reduce the burden of diabetes and its complications, screening for diabetes may be appropriate under certain circumstances. This position statement provides recommendations for diabetes screenings performed in physicians' offices and in other health care settings.

This position statement does not address screening for type 1 diabetes or gestational diabetes mellitus (GDM). Because of the acute onset of symptoms, most cases of type 1 diabetes are detected soon after symptoms develop. Widespread clinical testing of asymptomatic individuals for the presence of autoantibodies related to type 1 diabetes cannot be recommended at this time as a means to identify persons at risk. Reasons for this include the following: *1*) cutoff values for some of the immune marker assays have not been completely established in clinical settings; *2*) there is no consensus as to what action should be taken when a positive autoantibody test result is obtained; and *3*) because the incidence of type 1 diabetes is low, testing of healthy children will identify only a very small number (<0.5%) who at that moment may be "prediabetic." Clinical studies are being conducted to test various methods of preventing type 1 diabetes in high-risk individuals (e.g., siblings of type 1 diabetic patients). These studies may uncover an effective means of preventing type 1 diabetes, in which case targeted screening may be appropriate in the future.

For information on screening for GDM, refer to the American Diabetes Association's position statement "Gestational Diabetes Mellitus."

DIABETES PREVALENCE AND RISK FACTORS

— The estimated prevalence of diabetes among adults was 7.4% in 1995; this is expected to rise to ~9% in 2025. However, specific population subgroups have a much higher prevalence of the disease than the population as a whole. These subgroups have certain attributes or risk factors that either directly cause diabetes or are associated with it.

The correlation of a risk factor(s) with development of diabetes is never 100%. However, the greater the number of risk factors present in an individual, the greater the chance of that individual developing or having diabetes. Conversely, the chance of an asymptomatic individual without any risk factors having or developing diabetes is relatively low.

The risk of developing type 2 diabetes increases with age, obesity, and lack of physical activity. Type 2 diabetes is more common in individuals with a family history of the disease and in members of certain racial/ethnic groups. It occurs more frequently in women with prior GDM or polycystic ovary syndrome and in individuals with hypertension, dyslipidemia, impaired glucose tolerance (IGT), or impaired fasting glucose (IFG).

PRINCIPLES TO ASSESS THE VALUE OF SCREENING FOR TYPE 2 DIABETES

— There is a major distinction between diagnostic testing and screening. When an individual exhibits symptoms or signs of the disease, diagnostic tests are performed, and such tests do not represent screening. The purpose of screening is to identify asymptomatic individuals who are likely to have diabetes. Separate diagnostic tests using standard criteria are required after positive screening tests to establish a definitive diagnosis.

Generally, screening in asymptomatic populations is appropriate when seven conditions are met: *1*) the disease represents an important health problem that imposes a significant burden on the population; *2*) the natural history of the disease is understood; *3*) there is a recognizable preclinical (asymptomatic) stage during which the disease can be diagnosed; *4*) tests are available that can detect the preclinical stage of the disease, and the tests are acceptable and reliable; *5*) treatment after early detection yields benefits superior to those obtained when treatment is delayed; *6*) the costs of case finding and treatment are reasonable and are balanced in relation to health expenditures as a whole, and facilities and resources are available to treat newly diagnosed cases; and *7*) screening will be a systematic ongoing process and not merely an isolated one-time effort.

For diabetes, conditions 1–4 are met. Conditions 5–7 have not been met entirely because there are no randomized clinical trials documenting the effectiveness of screening programs in decreasing mortality and morbidity from diabetes, and some controversy exists regarding the cost-effectiveness of screening and

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Abbreviations: DPP, Diabetes Prevention Program; FPG, fasting plasma glucose; GDM, gestational diabetes mellitus; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test.

Table 1—*Major risk factors for type 2 diabetes*

Family history of diabetes (i.e., parents or siblings with diabetes)
Overweight (BMI ≥25 kg/m^2)
Habitual physical inactivity
Race/ethnicity (e.g., African-Americans, Hispanic-Americans, Native Americans, Asian-Americans, and Pacific Islanders)
Previously identified IFG or IGT
Hypertension (≥140/90 mmHg in adults)
HDL cholesterol ≤35 mg/dl (0.90 mmol/l) and/or a triglyceride level ≥250 mg/dl (2.82 mmol/l)
History of GDM or delivery of a baby weighing >9 lbs
Polycystic ovary syndrome

whether screening as currently carried out is a systematic and ongoing process.

Randomized clinical trials would be the best means to evaluate the benefits and risks of diabetes screening and early treatment. However, rigorous studies that apply currently available treatments to a screened group but not to a control group have not been done and are unlikely to be performed soon because of feasibility, ethical concerns, and costs. Thus, while it is well established that treating diabetes diagnosed through standard clinical practice is effective in reducing diabetic microvascular complications, it is unknown whether the additional years of treatment that might be received by individuals diagnosed through screening would result in clinically important improvements in diabetes-related outcomes. A large clinical trial, the Diabetes Prevention Program (DPP), is underway in the U.S. It is designed to answer the question of whether treatment with lifestyle interventions or metformin for patients with IGT or IFG detected through a screening program will reduce the incidence of type 2 diabetes. If the DPP demonstrates a reduction in the incidence of type 2 diabetes as a result of one or more of the interventions, then more widespread screening for these conditions, which would incidentally detect many cases of asymptomatic diabetes, may be justified.

The effectiveness of screening may also depend on the setting in which it is performed. In general, community screening outside a health care setting may be less effective because of the failure of people with a positive screening test to seek and obtain appropriate follow-up testing and care or, conversely, to ensure appropriate repeat testing for individuals who screen negative. That is, screening outside of clinical settings may yield abnormal tests that are never discussed with a primary care provider, low compliance with treatment recommendations, and a very uncertain impact on long-term health. Community screening may also be poorly targeted, i.e., it may fail to reach the groups most at risk and inappropriately test those at low risk (the worried well) or even those already diagnosed.

GENERAL RECOMMENDATIONS FOR THE EVALUATION OF HIGH-RISK INDIVIDUALS —

Based on the lack of data from prospective studies on the benefits of screening and the relatively low cost-effectiveness of screening suggested by existing studies, the decision to test for diabetes should ultimately be based on clinical judgment and patient preference.

On the basis of expert opinion, evaluation of the general population should be considered by their health care provider at 3-year intervals beginning at age 45. The rationale for this interval is that false negatives will be repeated before substantial time elapses, and there is little likelihood of an individual developing any of the complications of diabetes to a significant degree within 3 years of a negative screening test result. Testing should be considered at a younger age or be carried out more frequently in individuals with one or more of the risk factors shown in Table 1.

Patients presenting to health care providers with symptoms of marked hyperglycemia, including polyuria, polydipsia, weight loss (sometimes with polyphagia) and blurred vision, should receive diagnostic testing for diabetes, as should those with potential complications of diabetes or with any other clinical presentation in which diabetes is included in the differential diagnosis. Such diagnostic testing, however, does not constitute screening.

The incidence of type 2 diabetes in children and adolescents has been shown to be increasing. Consistent with screening recommendations for adults, only children and youth at substantial risk for the presence or the development of type 2 diabetes should be tested. Although there are insufficient data to make definite recommendations, the American Diabetes Association consensus statement titled "Type 2 Diabetes in Children and Adolescents" recommends that overweight (defined as BMI >85th percentile for age and sex, weight for height >85th percentile, or weight >120% of ideal [50th percentile] for height) youths with any two of the risk factors listed below be screened. Testing should be done every 2 years starting at age 10 years or at the onset of puberty if it occurs at a younger age. Testing may be considered in other high-risk patients who display any of the following characteristics:

- Have a family history of type 2 diabetes in first- and second-degree relatives;
- Belong to a certain race/ethnic group

Table 2—*Criteria for the diagnosis of diabetes*

Normoglycemia	IFG or IGT	Diabetes*
FPG <110 mg/dl 2-h PG† <140 mg/dl	FPG ≥110 and <126 mg/dl (IFG) 2-h PG† ≥140 and <200 mg/dl (IGT)	FPG ≥126 mg/dl 2-h PG† ≥200 mg/dl Symptoms of diabetes and casual plasma glucose concentration ≥200 mg/dl

*A diagnosis of diabetes must be confirmed, on a subsequent day, by measurement of FPG, 2-h PG, or random plasma glucose (if symptoms are present). The FPG test is greatly preferred because of ease of administration, convenience, acceptability to patients, and lower cost. Fasting is defined as no caloric intake for at least 8 h. †This test requires the use of a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water. 2-h PG, 2-h postload glucose.

Table 3—*Summary of major recommendations*

Recommendations	Evidence grading*
Evaluation for type 2 diabetes should be performed within the health care setting. Patients should be screened at 3-year intervals beginning at age 45; testing should be considered at an earlier age or be carried out more frequently if diabetes risk factors are present.	E
Diabetes risk factors include a family history of diabetes; overweight defined as BMI $\geq$25 kg/m^2; habitual physical inactivity; belonging to a high-risk ethnic or racial group; previously identified IFG or IGT; hypertension; dyslipidemia; history of GDM or delivery of a baby weighing >9 lbs; and polycystic ovary syndrome.	B
The FPG is the recommended screening test. The OGTT may be necessary for the diagnosis of diabetes when the FPG is normal. The FPG is preferred for screenings because it is faster and easier to perform, more convenient, acceptable to patients, and less expensive.	C
Diagnostic testing should be performed in any clinical situation in which such testing is warranted; health care providers should not consider whether a person meets screening criteria in such cases.	E
Screening outside of health care settings, or community screening, has not been shown to be beneficial and may result in some harm; this type of screening is not recommended.	E

*Scientific evidence was ranked based on the American Diabetes Association's grading system. The highest ranking (A) was assigned when there is supportive evidence from well-conducted generalizable randomized controlled trials that are adequately powered, including evidence from a meta-analysis that incorporated quality ratings in the analysis. An intermediate ranking (B) was given to supportive evidence from well-conducted cohort studies, registries, or case-control studies. A lower rank (C) was assigned to evidence from uncontrolled or poorly controlled studies or when there is conflicting evidence with the weight of the evidence supporting the recommendation. Expert consensus (E) is indicated, as appropriate. For a detailed description of this grading system, refer to *Diabetes Care* 25 (Suppl. 1):S1, 2002.

(Native Americans, African-Americans, Hispanic Americans, Asians/South Pacific Islanders);

- Have signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome).

TESTS — The best screening test for diabetes, the fasting plasma glucose (FPG), is also a component of diagnostic testing. The FPG test and the 75-g oral glucose tolerance test (OGTT) are both suitable tests for diabetes; however, the FPG test is preferred in clinical settings because it is easier and faster to perform, more convenient and acceptable to patients, and less expensive. An FPG $\geq$126 mg/dl (7.0 mmol/l) is an indication for retesting, which should be repeated on a different day to confirm a diagnosis. If the FPG is <126 mg/dl (7.0 mmol/l) and there is a high suspicion for diabetes, an OGTT should be performed. A 2-h postload value in the OGTT $\geq$200 mg/dl (11.1 mmol/l) is a positive test for diabetes and should be confirmed on an alternate day. Table 2 presents the diagnostic criteria for diabetes. Fasting is defined as no consumption of food or beverage other than water for at least 8 h before testing.

Nondiabetic individuals with an FPG $\geq$110 mg/dl (6.1 mmol/l) but <126 mg/dl (7.0 mmol/l) are considered to have IFG, and those with 2-h values in the OGTT $\geq$140 mg/dl (7.8 mmol/l) but <200 mg/dl (11.1 mmol/l) are defined as having IGT. Both IFG and IGT are risk factors for future diabetes. Normoglycemia is defined as plasma glucose levels <110 mg/dl (6.1 mmol/l) in the FPG test and a 2-h postload value <140 mg/dl (7.8 mmol/l) in the OGTT.

If necessary, plasma glucose testing may be performed on individuals who have taken food or drink shortly before testing. Such tests are referred to as casual plasma glucose measurements and are given without regard to time of last meal. A casual plasma glucose level $\geq$200 mg/dl (11.1 mmol/l) with symptoms of diabetes is considered diagnostic of diabetes. A confirmatory FPG test or OGTT should be completed on a different day if the clinical condition of the patient permits.

Laboratory measurement of plasma glucose concentration is performed on venous samples with enzymatic assay techniques, and the above-mentioned values are based on the use of such methods. The A1C test values remain a valuable tool for monitoring glycemia, but it is not currently recommended for the screening or diagnosis of diabetes. Pencil and paper tests, such as the American Diabetes Association's risk test, may be useful for educational purposes but do not perform well as stand-alone tests. Capillary blood glucose testing using a reflectance blood glucose meter has also been used but because of the imprecision of this method, it is better used for self-monitoring rather than as a screening tool.

OTHER CONSIDERATIONS — In screening for disease, it is crucial that an interpretation of the screening test results be provided to the patient and that follow-up evaluation and treatment are made available. Also, it is important to consider that certain drugs, including glucocorticoids and nicotinic acid, may produce hyperglycemia.

COMMUNITY SCREENING — Although there is ample scientific evidence showing that certain risk factors predispose individuals to development of diabetes (Table 1), there is insufficient evidence to conclude that community screening is a cost-effective approach to reduce the morbidity and mortality associated with diabetes in presumably healthy individuals. While community screening programs may provide a means to enhance public awareness of the seriousness of diabetes and its complications, other less costly approaches may be more appropriate, particularly because the potential risks are poorly defined. Thus, based on the lack of scientific evidence, community screening for diabetes, even in high-risk populations, is not recommended.

CONCLUSION — Diabetes is frequently not diagnosed until complications appear, and approximately one-third of all people with diabetes may be undiagnosed. Although the burden of diabetes is well known, the natural history is well characterized, and there is good evidence for benefit from treating cases diagnosed through usual clinical care, there are no randomized trials demonstrating the benefits of early diagnosis through screening of asymptomatic indi-

viduals. Nevertheless, there is sufficient indirect evidence to justify opportunistic screening in a clinical setting of individuals at high risk. Also, clinicians should be vigilant in evaluating clinical presentations suggestive of diabetes.

A summary of screening recommendations is included in Table 3.

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