



Screening for diabetes mellitus

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INTRODUCTION — The following five criteria define the optimal conditions for screening for a particular disorder [1]:

- The disorder should be an important public health problem
- An early asymptomatic stage should exist
- There is a suitable screening test
- An accepted treatment should be available
- There is evidence that early treatment improves long-term outcome

The extent to which these criteria are met for type 1 and type 2 diabetes mellitus is reviewed here, as well as practical recommendations on how to screen for these disorders in clinical practice. Screening of pregnant women for gestational diabetes is discussed separately. ([See "Screening and diagnosis of gestational diabetes mellitus"](#)).

TYPE 1 DIABETES — The prevalence of type 1 diabetes continues to increase around the world, although it still affects less than 0.5 percent of the population [2]. An early asymptomatic phase exists; many subjects in this phase can be identified, but only by a combination of immunologic, genetic, and metabolic tests. ([See "Pathogenesis of type 1 diabetes mellitus"](#) and [see "Prediction of type 1 diabetes mellitus"](#)).

There is no accepted treatment for the asymptomatic phase of type 1 diabetes. In the Diabetes Prevention Trial (DPT), parenteral insulin therapy did not prevent type 1 diabetes in high-risk patients. ([See "Prevention of type 1 diabetes mellitus"](#)).

Thus, routine screening for type 1 diabetes cannot be recommended except for research purposes.

TYPE 2 DIABETES — The arguments for widespread screening to identify undiagnosed cases of type 2 diabetes are much stronger than for type 1 diabetes.

- Type 2 diabetes is a major public health problem affecting approximately 8 percent of the United States (US) population, with probably an equal number of cases being undiagnosed. The global prevalence of type 2 diabetes continues to rise [3]. Data from the Framingham Heart Study indicate that the incidence of type 2 diabetes has doubled over the last 30 years [4]. ([See "Prediction and prevention of type 2 diabetes mellitus"](#)).
- An asymptomatic period exists.
- There is no ideal screening test, but measurement of fasting blood glucose (or, under some circumstances, random blood glucose or 2-hour post-glucose challenge) is adequate for identifying many undiagnosed cases.

- Well-established treatments for type 2 diabetes exist. (See ["Overview of medical care in adults with diabetes mellitus"](#) and see ["Initial management of blood glucose in type 2 diabetes mellitus"](#)).

In addition, undiagnosed diabetes can cause progressive microvascular damage. At the time of diagnosis, approximately 20 percent of newly diagnosed patients with type 2 diabetes have diabetic retinopathy [5] and 10 percent have nephropathy [6]. (See ["Classification and clinical features of diabetic retinopathy"](#) and see ["Microalbuminuria in type 2 diabetes mellitus"](#)).

In addition, adults with undiagnosed diabetes often have other risk factors for macrovascular diabetic complications: 67 percent have hypertension (of whom one-half are uncontrolled); 62 percent have serum low-density lipoprotein cholesterol concentrations >130 mg/dL (3.4 mmol/L); more than 50 percent are overweight; and almost one-third smoke cigarettes [7].

The Diabetes Control and Complications Trial (DCCT) demonstrated that interventions that improve glycemic control in patients with type 1 diabetes reduce the risk of development and slow the progression of diabetic microvascular disease [8]. The United Kingdom Prospective Diabetes Study (UKPDS) showed that strict glycemic control has a similar benefit in patients with type 2 diabetes [9]. (See ["Glycemic control and vascular complications in type 1 diabetes mellitus"](#) and see ["Glycemic control and vascular complications in type 2 diabetes mellitus"](#)).

In addition, [metformin](#) and the combination of diet and exercise reduce the risk of type 2 diabetes in patients with IGT. (See ["Prediction and prevention of type 2 diabetes mellitus"](#)).

Cost-effectiveness — It has not been firmly established that early detection of type 2 diabetes and intervention improve long-term outcome.

A computer simulation model of subjects over age 25 suggested that the increases in costs attributable to screening and early treatment may be acceptable [10]. The benefits of early detection in this model were derived more from postponement of complications and the resulting improvement in quality of life than from additional life-years. Screening was more cost-effective for younger people and for blacks.

There are, however, some concerns about this study. The potential benefits are based upon the assumption that most of the population could be screened; unfortunately, those at greatest risk may well be the most difficult group to screen. In addition, if the standard of care for patients known to have diabetes was better (eg, better screening and management of nephropathy, neuropathy, retinopathy, and glycemic control from the time of diagnosis), then the benefits of screening for undiagnosed cases would fall.

In other cost-effectiveness analyses, screening targeted to individuals with hypertension was more cost-effective than universal screening [11], and screening for impaired glucose tolerance and undiagnosed type 2 diabetes, followed by intervention (lifestyle or pharmacological), was more cost-effective than no screening [12]. In one model, the most cost-effective strategy was targeted screening at age 55 to 75 years [11].

Screening tests — The most commonly used screening tests for type 2 diabetes include measurement of the plasma glucose (FPG), two-hour plasma glucose during an oral glucose tolerance test (2-h OGTT), glycosylated hemoglobin, and the urine dipstick testing for glucose.

Blood glucose — Blood glucose values are distributed over a continuum in the population, although there are some approximate thresholds above which the risk of future adverse events is substantial. An Expert Committee on the Diagnosis and Classification of Diabetes Mellitus has recommend placing individuals in one of three categories based upon the fasting plasma glucose concentration [13,14] or 2-h OGTT (75 gram glucose load) [15]. (see ["Diagnosis of diabetes mellitus"](#)):

- Normal — Fasting plasma glucose (FPG) <100 mg/dL (5.6 mmol/L). The 1997 criteria had been <110 mg/dL (6.1 mmol/L).
- Pre diabetes

- Impaired fasting glucose (IFG) — Fasting plasma glucose between 100 and 125 mg/dL (5.6 to 6.9 mmol/L). The 1997 values were between 110 and 125 mg/dL (6.1 to 6.9 mmol/L).

- Impaired glucose tolerance (IGT) — Two hour plasma glucose value during a 75 gram oral glucose tolerance test between 140 and 199 mg/dl (7.8 to 11.0 mmol/L).

- Diabetes mellitus — FPG at or above 126 mg/dL (7.0 mmol/L), a two-hour value in an OGTT (2-h PG) at or above 200 mg/dL (11.1 mmol/L), or a random (or "casual") plasma glucose concentration \geq 200 mg/dL (11.1 mmol/L) in the presence of symptoms. The diagnosis of diabetes must be confirmed on a subsequent day by measuring any one of the three criteria.

Patients with diabetes mellitus are at increased risk for both macrovascular and microvascular disease. Those with impaired fasting blood glucose are at increased risk for macrovascular disease (myocardial infarction, stroke, peripheral vascular disease), but not for microvascular disease (retinopathy, neuropathy and nephropathy).

In 1997, the Expert Committee lowered the fasting blood glucose value defining the presence of diabetes from 140 mg/dL (7.8 mmol/L) to 126 mg/dL (7.0 mmol/L) because the lower value more accurately reflects the blood glucose concentration at or above which the risk for microvascular disease is increased. This lower value also correlates better with the risk associated with a random (or two-hour post-glucose challenge) blood glucose concentration of 200 mg/dL (11.1 mmol/L), which was retained from the old classification as also being diagnostic for diabetes mellitus [13]. (See "[Diagnosis of diabetes mellitus](#)" for a detailed discussion on the Expert Committee's 2003 updated report).

The sensitivity and specificity of the fasting blood glucose as a screening test vary according to the population tested and the threshold used to define diabetes. Using a 2-hour blood glucose >200 mg/dL (11.1 mmol/L) on an oral glucose tolerance test as the reference standard, the specificity of a fasting blood glucose \geq 126 mg/dL (7.0 mmol/L) is greater than 95 percent; the sensitivity is about 50 percent, and may be lower for people over the age of 65 [16]. Among people ages 40 to 74, the specificity of a fasting blood glucose \geq 140 mg/dL (7.8 mmol/L) is 91 percent; the specificity is 47 percent for a fasting blood glucose between 126 and 140 mg/dL (7.0 to 7.8 mmol/L) [17].

Glycosylated hemoglobin — There has been interest in the use of glycosylated hemoglobin (A1C) values for screening and identification of impaired glucose tolerance and diabetes. In June, 2009, an International Expert Committee recommended using the hemoglobin A1C (A1C) to diagnose diabetes. National and international diabetes organizations, including the American Diabetes Association (ADA), are considering whether and how to implement the recommendations. (See "[Diagnosis of diabetes mellitus](#)", section on Hemoglobin A1C (A1C)).

Urine glucose — Detection of glucose on a semiquantitative urine dipstick (anything regarded as trace positive or more) or Clinitest tablets is an insensitive means of screening for type 2 diabetes [18]. The high rate of false-negative results suggests that the urine dipstick is not adequate as a screening test. Additionally, not all patients with glucosuria have diabetes. Glucosuria can occur with defects in renal tubular function, as seen in Type 2 (proximal) renal tubular acidosis and in familial renal glucosuria, a genetic disorder associated with salt-wasting, polyuria, and volume depletion [19].

Screening recommendations by expert groups — The two approaches to screening that are usually

recommended (and are not mutually exclusive) are either to screen the entire population above a certain age, or to screen certain "high-risk" groups. The ADA recommends testing for diabetes or prediabetes in all adults with BMI ≥ 25 kg/m² and one or more additional risk factors for diabetes (see "Risk factors" below). In individuals without risk factors, testing should begin at age 45 years [15,20]. Either fasting plasma glucose or 2-h OGTT is appropriate for testing.

If the fasting blood glucose concentration is above 100 mg/dL (5.6 mmol/L), the test should be repeated. Two fasting blood glucose values over 125 mg/dL (6.9 mmol/L), two post-glucose values over 200 mg/dL (11.1 mmol/L), or one of each, or a random glucose ≥ 200 mg/dL (11.1 mmol/L) with symptoms of diabetes is required to make the diagnosis of diabetes. (See "Diagnosis of diabetes mellitus").

The United States Preventive Services Task Force concluded that there was insufficient evidence to recommend for or against screening for diabetes in nonpregnant adults without hypertension [21]. This conclusion was based primarily on the lack of evidence that earlier detection of diabetes improves long-term outcomes. However, the task force found that there was moderate evidence for and recommended screening in adults with hypertension (blood pressure $> 135/80$ mmHg) as part of an integrated approach to reduce cardiovascular risk. The USPSTF clinical practice guideline for screening for type 2 diabetes mellitus in adults, as well as other USPSTF guidelines, can be accessed through the website for the Agency for Healthcare Research and Quality at www.ahrq.gov/clinic/uspstfix.htm.

The Canadian Task Force on the Periodic Health Examination recommends screening adults with hypertension and hyperlipidemia for type 2 diabetes [22].

Other predictive models using risk factor assessment have been investigated as a strategy to guide screening, but are not in widespread use [23].

Risk factors — Diabetes risk factors include the following:

- Age ≥ 45 years
- Overweight (body mass index ≥ 25 kg/m²)
- Family history diabetes mellitus in a first-degree relative
- Habitual physical inactivity
- Belonging to a high-risk ethnic or racial group (eg, African-American, Hispanic, Native American, Asian-American, and Pacific Islanders)
- History of delivering a baby weighing > 4.1 kg (9 lb) or of gestational diabetes mellitus
- Hypertension (blood pressure $\geq 140/90$ mmHg)
- Dyslipidemia defined as a serum high-density lipoprotein cholesterol concentration ≤ 35 mg/dL (0.9 mmol/L) and/or a serum triglyceride concentration ≥ 250 mg/dL (2.8 mmol/L)
- Previously identified impaired glucose tolerance or impaired fasting glucose
- Polycystic ovary syndrome
- History of vascular disease

A suggested approach — Consistent with ADA guidelines, we recommend measurement of fasting blood glucose in individuals who are considered high risk (BMI ≥ 25 kg/m² with one or more additional risk factors for diabetes) and everyone aged 45 years or older receiving health care (or maintenance). A value ≤ 100 mg/dL (5.6 mmol/L) should be considered normal and the patient should be retested in three years. If the fasting blood glucose value is above 100 mg/dL (5.6 mmol/L), the test should be repeated and the scheme in Table 1 followed

([show table 1](#)).

Among patients seeking health care who have not fasted overnight, those ages 45 years and older or considered high-risk according to the criteria listed above should have a measurement of nonfasting (random) blood glucose on that visit. A random value less than 125 mg/dL is considered normal and requires no further testing.

Patients with a random value 126 mg/dL (6.9 mmol/L) or greater should have a follow-up fasting blood glucose measured. For patients whose random blood glucose was greater than 200 mg/dL (11.1 mmol/L), a follow-up fasting glucose value \geq 126 mg/dL (6.9 mmol/L) is consistent with a diagnosis of diabetes mellitus. The management of all other individuals should follow the scheme in Table 2 ([show table 2](#)).

Patients classified as having impaired fasting glucose (IFG) should be counseled vigorously on issues related to lowering their risk of macrovascular disease (smoking cessation, use of [aspirin](#), diet, and exercise), and should have measurements of blood pressure and serum lipids. They should also be encouraged to modify their lifestyle with increased exercise (ideally 150 minutes weekly) and weight reduction, targeting a seven percent weight loss if overweight, as these measures have been shown to significantly decrease the risk of developing type 2 diabetes [[24,25](#)]. Screening for diabetes should be repeated annually.

Patients classified as having type 2 diabetes mellitus should be treated using the approach described separately. (See "[Overview of medical care in adults with diabetes mellitus](#)").

INFORMATION FOR PATIENTS — Educational materials on this topic are available for patients. (See "[Patient information: Diabetes mellitus type 1: Overview](#)" and see "[Patient information: Diabetes mellitus type 2: Overview](#)"). We encourage you to print or e-mail these topic reviews, or to refer patients to our public web site, www.uptodate.com/patients, which includes these and other topics.

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GRAPHICS

Scheme for follow-up of fasting plasma glucose screening for diabetes mellitus

First fasting glucose, mg/dL	Second fasting glucose, mg/dL	Diagnosis	Treatment
>125	>125	DM	Treat for DM
>125	101 to 125	IFG	Treat as IFG
>125	<100	Indeterminate	Repeat; if >125 treat as DM; if 101-125 treat as IFG; <100 consider normal
101 to 125	>125	IFG	Treat as IFG
101 to 125	101 to 125	IFG	Treat for IFG
101 to 125	<100	Indeterminate	Repeat; if >125 treat as DM; if 101-125 treat as IFG; <100 consider normal

To correct blood glucose values to mmol/L, multiply by 0.0555.

DM: diabetes mellitus; IFG: impaired fasting glucose.

Scheme for follow-up of random blood glucose screening for diabetes mellitus

Random glucose mg/dL	Fasting glucose mg/dL	Diagnosis	Treatment
≥200	>125	DM	Treat for DM
≥200	101 to 125	Indeterminate	Treat as IFG
≥200	<100	Indeterminate	Repeat; if >125 treat as DM; if 110-125 treat as IFG; <110 consider normal
125 to 200	>125	Indeterminate	Repeat; if >125 treat as DM; otherwise treat as IFG
125 to 200	101 to 125	Indeterminate	Treat for IFG
125 to 200	<100	Normal	Recommend rescreening in three years

To correct blood glucose values to mmol/L, multiply by 0.0555.

DM: diabetes mellitus; IFG: impaired fasting glucose.

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