



# Diabetes Mellitus (DM)

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Reviewed/Revised Oct 2023 | Modified Mar 2025

Diabetes mellitus is impaired insulin secretion and variable degrees of peripheral insulin resistance leading to hyperglycemia. Early symptoms are related to hyperglycemia and include polydipsia, polyphagia, polyuria, and blurred vision. Later complications include vascular disease, peripheral neuropathy, nephropathy, and predisposition to infection. Diagnosis is by measuring plasma glucose. Treatment is diet, exercise, and medications that reduce glucose levels, including insulin, oral antihyperglycemic medications, and non-insulin injectable medications. Complications can be delayed or prevented with adequate glycemic control; heart disease remains the leading cause of mortality in diabetes mellitus.

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There are 2 main categories of diabetes mellitus (diabetes)

- Type 1
- Type 2

The two types of diabetes can be distinguished by a combination of features (see table [General Characteristics of Types 1 and 2 Diabetes Mellitus](#)). Terms that describe the age of onset (juvenile or adult) or type of treatment (insulin-dependent or non-insulin-dependent) are no longer used because of overlap in age groups and treatments between disease types.

## Overview of Diabetes

VIDEO

## DIABETIC KETOACIDOSIS (DKA)

### Treatment

- FLUIDS for DEHYDRATION
- INSULIN to lower

**Impaired glucose regulation** (impaired glucose tolerance, or impaired fasting glucose—see table [Diagnostic Criteria for Diabetes Mellitus and Impaired Glucose Regulation](#)) is an intermediate, possibly transitional, state between normal glucose metabolism and diabetes mellitus that becomes more common with aging. It is a significant risk factor for diabetes and may be present for many years before onset of diabetes. It is associated with an increased risk of cardiovascular disease, but typical diabetic [microvascular complications](#) are not very common (albuminuria and/or retinopathy develop in 6 to 10% of patients).

## Complications

Years of poorly controlled hyperglycemia lead to multiple, primarily vascular complications that affect small vessels (microvascular), large vessels (macrovascular), or both. (For additional detail, see [Complications of Diabetes Mellitus](#).)

**Microvascular disease** underlies 3 common and severe complications of diabetes mellitus:

- [Retinopathy](#)
- [Nephropathy](#)
- [Neuropathy](#)

Microvascular disease may also impair wound healing, so that even minor breaks in skin integrity can develop into deeper ulcers and easily become infected, particularly in the lower extremities. Intensive control of plasma glucose can prevent or delay many of these complications but will not reverse them once established.

**Macrovascular disease** involves [atherosclerosis](#) of large vessels, which can lead to

- [Angina pectoris](#) and [myocardial infarction](#)
- [Transient ischemic attacks](#) and [strokes](#)
- [Peripheral arterial disease](#)

**Immune dysfunction** is another major complication and develops from the direct effects of hyperglycemia on cellular immunity. Patients with diabetes mellitus are particularly susceptible to bacterial and fungal infections.

## Etiology of Diabetes Mellitus

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### Type 1 diabetes

- Autoimmune pancreatic beta-cell destruction and absent insulin production

Type 1 accounts for < 10% of all cases of diabetes mellitus.

In type 1 diabetes mellitus (previously called juvenile-onset or insulin-dependent), insulin production is absent because of autoimmune pancreatic beta-cell destruction possibly triggered by an environmental exposure in people who are genetically susceptible. Destruction progresses subclinically over months or years until beta-cell mass decreases to the point that insulin concentrations are no longer adequate to control plasma glucose levels. Type 1 diabetes generally develops in childhood or adolescence and until recently was the most common form diagnosed before age 30; however, it can also develop in adults.

Autoimmune diabetes that develops in adulthood is often more slowly progressive than childhood type 1 diabetes. Some adults do not need insulin when dysglycemia first develops. This form of diabetes, called latent autoimmune diabetes of adulthood (LADA), may initially be diagnosed as type 2 diabetes.

Some cases of type 1 diabetes do not appear to be autoimmune in nature and are considered idiopathic.

The pathogenesis of the autoimmune beta-cell destruction involves incompletely understood interactions between susceptibility genes, autoantigens, and environmental factors.

**Susceptibility genes** include those within the major histocompatibility complex (MHC)—especially HLA-DR3,DQB1\*0201 and HLA-DR4,DQB1\*0302, which are present in > 90% of patients with type 1 diabetes mellitus—and those outside the MHC, which seem to regulate insulin production and processing and confer risk of diabetes mellitus in concert with MHC genes. Susceptibility genes are more common among some populations than among others and explain the higher prevalence of type 1 diabetes in people with ancestry from certain areas (eg, Scandinavians, Sardinians).

**Autoantigens** include glutamic acid decarboxylase, insulin, proinsulin, insulinoma-associated protein, zinc transporter ZnT8, and other proteins in beta cells. It is thought that these proteins are exposed or released during normal beta-cell turnover or beta-cell injury (eg, due to infection), activating primarily a T cell-mediated immune response that results in beta-cell destruction (insulitis). Glucagon-secreting alpha cells remain unharmed. Antibodies to autoantigens, which can be detected in serum, seem to be a response to (not a cause of) beta-cell destruction.

Several **viruses** (including coxsackievirus, rubella virus, cytomegalovirus, Epstein-Barr virus, SARS-CoV-2 (1,2), and retroviruses) have been linked to the onset of type 1 diabetes. Viruses may directly infect and destroy beta cells, or they may cause beta-cell destruction indirectly by exposing autoantigens.

activating autoreactive lymphocytes, mimicking molecular sequences of autoantigens that stimulate an immune response (molecular mimicry), or other mechanisms.

**Diet** may also be a factor. Exposure of infants to dairy products (especially cow's milk and the milk protein beta casein), high nitrates in drinking water, and low vitamin D consumption have been linked to increased risk of type 1 diabetes. Early (< 4 months) or late (> 7 months) exposure to gluten and cereals increases islet cell autoantibody production. Mechanisms for these associations are unclear.

## Type 2 diabetes

- Resistance to insulin

In type 2 diabetes mellitus (previously called adult-onset or non-insulin-dependent), insulin secretion is inadequate because patients have developed resistance to insulin. Hepatic insulin resistance leads to an inability to suppress hepatic glucose production, and peripheral insulin resistance impairs peripheral glucose uptake. This combination gives rise to fasting and postprandial hyperglycemia. Often insulin levels are very high, especially early in the disease. Later in the course of the disease, insulin production may fall, further exacerbating hyperglycemia.

The disease generally develops in adults and becomes more common with increasing age; up to one third of adults > age 65 years have impaired glucose tolerance. In older adults, plasma glucose levels reach higher levels after eating than in younger adults, especially after meals with high carbohydrate loads. Glucose levels also take longer to return to normal, in part because of increased accumulation of visceral and abdominal fat and decreased muscle mass.

Type 2 diabetes has become more common among children because childhood obesity has become epidemic. More than 90% of adults with diabetes have type 2 disease. There are clear genetic determinants, as evidenced by the high prevalence of the disease in relatives of people with the disease. Although several genetic polymorphisms have been identified, no single gene responsible for the most common forms of type 2 diabetes has been identified.

Pathogenesis is complex and incompletely understood. Hyperglycemia develops when insulin secretion can no longer compensate for insulin resistance. Although insulin resistance is characteristic in people with type 2 diabetes and those at risk of it, evidence also exists for beta-cell dysfunction and impaired insulin secretion that progresses over time, including

- Impaired first-phase insulin secretion
- A loss of normally pulsatile insulin secretion
- An increase in proinsulin secretion signaling, indicating impaired insulin processing
- An accumulation of islet amyloid polypeptide (a protein normally secreted with insulin)

Hyperglycemia itself may impair insulin secretion, because high glucose levels desensitize beta cells, cause beta-cell dysfunction (glucose toxicity), or both.

Obesity and weight gain are important determinants of insulin resistance in type 2 diabetes. They have some genetic determinants but also reflect diet, exercise, and lifestyle. An inability to suppress lipolysis in adipose tissue increases plasma levels of free fatty acids that may impair insulin-stimulated glucose

transport and muscle glycogen synthase activity. Adipose tissue also functions as an endocrine organ, releasing multiple factors (adipocytokines) that favorably (adiponectin) and adversely (tumor necrosis factor-alpha, interleukin-6, leptin, resistin) influence glucose metabolism.

Intrauterine growth restriction and low birth weight have also been associated with insulin resistance in later life and may reflect adverse prenatal environmental influences on glucose metabolism.

## Miscellaneous types of diabetes

Miscellaneous types of diabetes mellitus account for a small proportion of cases. Causes include

- Monogenic diabetes due to genetic defects affecting beta-cell function, insulin action, or mitochondrial DNA (eg, maturity-onset diabetes of youth, neonatal diabetes)
- Conditions that affect the pancreas (eg, [cystic fibrosis](#), [pancreatitis](#), [hemochromatosis](#), pancreatectomy)
- Endocrinopathies (eg, [Cushing syndrome](#), [acromegaly](#))
- Medications, most notably glucocorticoids, beta-blockers, protease inhibitors, atypical antipsychotics, immune checkpoint inhibitors, and calcineurin inhibitors

Pregnancy causes some insulin resistance in all women, but only a fraction will develop [gestational diabetes](#).

TABLE

**General Characteristics of Types 1 and 2 Diabetes Mellitus**

Characteristic	Type 1	Type 2
Age at onset	Most commonly < 30 years	Most commonly > 30 years
Associated obesity	Uncommon	Very common
Propensity to ketoacidosis requiring insulin treatment for control	Yes	No
Plasma levels of endogenous insulin	Extremely low to undetectable	Variable; may be low, normal, or elevated depending on degree of insulin resistance and insulin secretory defect
Twin concordance	≤ 50%	> 90%
Associated with specific HLA-D antigens	Yes	No
Pancreatic autoantibodies at diagnosis	Yes, but may be absent	No
Islet pathology	Insulitis, selective loss of most beta cells	Smaller, normal-appearing islets; amyloid (amylin) deposition common
Prone to develop diabetic complications (retinopathy, nephropathy, neuropathy, atherosclerotic cardiovascular disease)	Yes	Yes
Hyperglycemia responds to non-insulin antihyperglycemic medications	No	Yes, initially in many patients

**Etiology references**

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## Symptoms and Signs of Diabetes Mellitus

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The most common symptoms of diabetes mellitus are those of hyperglycemia. The mild hyperglycemia of early diabetes is often asymptomatic; therefore, diagnosis may be delayed for many years if routine screening is not done.

More significant hyperglycemia causes glycosuria and thus an osmotic diuresis, leading to urinary frequency, polyuria, and polydipsia that may progress to [orthostatic hypotension](#) and [dehydration](#). Severe dehydration causes weakness, fatigue, and mental status changes. Symptoms may come and go as plasma glucose levels fluctuate.

Polyphagia may accompany symptoms of hyperglycemia but is not typically a primary patient concern. Hyperglycemia can also cause weight loss, nausea and vomiting, and blurred vision, and it may predispose to bacterial or fungal infections.

**Patients with type 1 diabetes** typically present with symptomatic hyperglycemia and sometimes with [diabetic ketoacidosis](#) (DKA). However, they develop diabetes-related autoantibodies and dysglycemia before becoming symptomatic.

Type 1 diabetes mellitus progresses in stages:

- Stage 1: Presence of  $\geq 2$  islet autoantibodies with normal blood sugar and no symptoms
- Stage 2: Glucose intolerance or dysglycemia but no symptoms
- Stage 3: Clinical symptoms

Some patients in stage 3 experience a long but transient phase of near-normal glucose levels after acute onset of the disease (honeymoon phase) due to partial recovery of insulin secretion.

**Patients with type 2 diabetes** may present with symptomatic hyperglycemia but are often asymptomatic, and their condition is detected only during routine testing. In some patients, initial symptoms are those of [diabetic complications](#), suggesting that the disease has been present for some time. In some patients, [hyperosmolar hyperglycemic state](#) occurs initially, especially during a period of stress or when glucose metabolism is further impaired by medications, such as corticosteroids.

## Diagnosis of Diabetes Mellitus

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- Fasting plasma glucose (FPG) levels
- Glycosylated hemoglobin (HbA1C)
- Sometimes oral glucose tolerance testing

Diabetes mellitus is suggested by typical symptoms and signs and confirmed by measurement of plasma glucose ([1](#), [2](#)). It is often detected through screening.

Measurement after an 8- to 12-hour fast (FPG) or 2 hours after ingestion of a concentrated glucose solution (oral glucose tolerance testing [OGTT]) is preferred (see table [Diagnostic Criteria for Diabetes](#)

Mellitus and Impaired Glucose Regulation). OGTT is more sensitive for diagnosing diabetes and impaired glucose tolerance but is less convenient and reproducible than FPG. It is therefore rarely used routinely, except for diagnosing gestational diabetes and for research purposes.

In practice, diabetes mellitus or impaired fasting glucose regulation is often diagnosed using random measures of plasma glucose or of HbA1C. A random glucose value  $> 200$  mg/dL ( $> 11.1$  mmol/L) may be diagnostic, but values can be affected by recent meals and must be confirmed by repeat testing; testing twice may not be necessary in the presence of symptoms of diabetes.

HbA1C is a form of hemoglobin that is chemically attached to a sugar that increases with blood glucose and has a validated relationship with average glucose level over the preceding 3 months. HbA1C measurements are now included in the diagnostic criteria for diabetes:

- HbA1C  $\geq 6.5\%$  = diabetes
- HbA1C 5.7 to 6.4% = prediabetes or at risk of diabetes

However, HbA1C is an indirect measure of blood glucose; values may be falsely high or low (see Monitoring) and can vary with race/ethnicity. Tests must be done in a certified clinical laboratory with an assay that is certified and standardized to a reference assay. Point-of-care finger-stick HbA1C measurements should not be used for diagnostic purposes, although they can be used for monitoring diabetes control.

Urine glucose measurement, once commonly used, is no longer used for diagnosis or monitoring because it is neither sensitive nor specific.

### Pearls & Pitfalls

- Point-of-care fingerstick HbA1C tests are not accurate enough to be used for initial diagnosis of diabetes.

TABLE

## Diagnostic Criteria for Diabetes Mellitus and Impaired Glucose Regulation\*

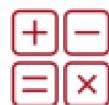
Test	Normal	Impaired Glucose Regulation	Diabetes
FPG (mg/dL [mmol/L])	< 100 (< 5.6)	100–125 (5.6–6.9)	≥ 126 (≥ 7.0)
OGTT (mg/dL [mmol/L])	< 140 (< 7.8)	140–199 (7.8–11.0)	≥ 200 (≥ 11.1)
HbA1C (%)	< 5.7	5.7–6.4	≥ 6.5
Random glucose (mg/dL [mmol/L])	< 200 (< 11.1)	—	> 200 (> 11.1) in a patient with symptoms

\* See also [American Diabetes Association](#): Standards of Medical Care in Diabetes. *Diabetes Care* 46 (Supplement 1): S1–S291, 2023.

FPG = fasting plasma glucose; HbA1C = glycosylated hemoglobin; OGTT = oral glucose tolerance test, 2-hour glucose level.

### CLINICAL CALCULATORS

#### [Glycemic Assessment](#)



## Monitoring for complications of diabetes

All patients with type 1 diabetes mellitus should begin screening for diabetic complications 5 years after diagnosis. For patients with type 2 diabetes, screening begins at diagnosis. Typical monitoring for complications includes

- Foot examination
- Funduscopic examination
- Urine testing for albuminuria
- Measurement of serum creatinine and lipid profile

**Foot examination** should be done at least annually for impaired sense of pressure, vibration, pain, or temperature, which is characteristic of peripheral neuropathy. Pressure sense is best tested with a monofilament esthesiometer (see figure [Diabetic Foot Screening](#)). The entire foot, and especially skin

beneath the metatarsal heads, should be examined for skin cracking and signs of ischemia or infection, such as ulcerations, gangrene, fungal nail infections, deceased pulses, and hair loss.

**Funduscopic examination** should be done by an ophthalmologist; the screening interval is typically annually for patients with any retinopathy to every 2 years for those without retinopathy on a prior examination. If retinopathy shows progression, more frequent evaluation may be needed.

**Spot or 24-hour urine testing** is indicated annually to detect albuminuria, and serum creatinine should be measured annually to assess kidney function.

**Testing for cardiovascular disease** is needed. Many physicians consider baseline ECG important given the risk of heart disease. Lipid profile should be checked at least annually and more often when abnormalities are present. Blood pressure should be measured at every examination.

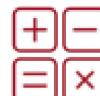
## Calculators for Managing Patients With Diabetes

### CLINICAL CALCULATORS

[Cardiovascular Risk](#)

[Assessment \(10-year, Revised\)](#)

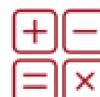
[Pooled Cohort Equations 2018](#)



### CLINICAL CALCULATORS

[5-Year Risk of Cardiovascular](#)

[Disease in Type I Diabetes](#)



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## Treatment of Diabetes Mellitus

- Diet and exercise
- For type 1 diabetes, insulin
- For type 2 diabetes, oral antihyperglycemics, non-insulin injectable medications such as glucagon-like peptide-1 (GLP-1) receptor agonists, insulin, or a combination
- To prevent complications, often renin-angiotensin-aldosterone system blockers (angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers), and statins

Key elements of treatment for all patients are patient education, diet, exercise, weight loss, and monitoring of glucose control. Patients with type 1 diabetes require insulin. Some patients with type 2 diabetes may be able to avoid or cease treatment with medications if they are able to maintain plasma glucose levels with diet and exercise alone. For detailed discussion, see [Medication Treatment of Diabetes](#).

## Overview of pharmacotherapy

(See also [Medication Treatment of Diabetes](#).)

All patients with **type 1 diabetes** require [insulin therapy](#). The goal is to try to replicate the pattern of insulin secretion of a person who does not have diabetes by using basal-bolus insulin therapy. In basal-bolus therapy, a longer-acting insulin (or a continuous subcutaneous infusion of rapid-acting insulin delivered by a pump) is used to simulate basal insulin production that suppresses hepatic glucose production, especially in the fasting state, and a shorter-acting insulin is used before meals to control postprandial glucose excursions.

Sliding-scale insulin is a strategy in which varying doses of rapid-acting insulin are given before meals and at bedtime depending on the patient's plasma glucose level. However, a sliding scale insulin regimen on its own is not an effective strategy for maintaining euglycemia in patients with type 1 diabetes or in most patients with type 2 diabetes.

Patients with **type 2 diabetes** and mildly elevated plasma glucose may be prescribed a trial of diet and exercise, followed by a [non-insulin antihyperglycemic medication](#) (often metformin) if lifestyle changes are insufficient. Early combination therapy and/or insulin therapy should be initiated in patients with more significant glucose elevations at diagnosis or with HbA1C levels 1.5 to 2.0% above target. There is evidence that early combination medication therapy leads to superior and more durable blood glucose control than a stepwise approach to adding diabetes pharmacotherapy (1). [Goals and monitoring](#) are discussed below.

In patients without atherosclerotic cardiovascular disease, heart failure, or chronic kidney disease, selection of therapy often involves consideration of adverse effects, convenience, cost, and patient preference. Metformin is usually the first oral medication used due to its cost-effectiveness and safety profile. Glucagon-like peptide-1 (GLP1) receptor agonists are an effective second-line therapy after metformin and may be more effective than insulin, or as an add-on to insulin therapy in type 2 diabetes. Patients with obesity can also benefit from the weight-lowering effects of GLP-1 receptor agonist therapy or from the use of tirzepatide, a dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptor agonist.

In patients with atherosclerotic cardiovascular disease, a sodium/glucose cotransporter 2 (SGLT2) inhibitor or a GLP-1 receptor agonist may be recommended because of evidence that these medication classes decrease major adverse cardiovascular events (eg, myocardial infarction, stroke) and mortality. In patients with chronic kidney disease (2, 3) or heart failure (4) without contraindications, SGLT2-inhibitors are recommended because they have been shown to decrease disease progression and mortality. GLP-1 receptor agonists and pioglitazone can be used in patients with [metabolic associated](#)

steatotic liver disease (formerly nonalcoholic fatty liver disease) or metabolic associated steatohepatitis (formerly nonalcoholic steatohepatitis).

Insulin is indicated as initial therapy for women with type 2 diabetes who are pregnant and for patients who present with acute metabolic decompensation, such as hyperosmolar hyperglycemic state or diabetic ketoacidosis (DKA). Insulin should be considered in patients with evidence of ongoing catabolism (weight loss) or symptoms of hyperglycemia (ie, polyuria, polydipsia) and/or with HbA1C levels > 10% and blood glucose levels  $\geq 300$  mg/dL (16.7 mmol/L). Patients with severe hyperglycemia may respond better to therapy after glucose levels are normalized with insulin treatment.

## Patient education

Education is crucial to optimizing care. Education should include information about the following:

- Causes of diabetes
- Diet
- Exercise
- Medications
- Self-monitoring with fingerstick testing or continuous glucose monitoring
- Monitoring HbA1C
- Symptoms and signs of hypoglycemia, hyperglycemia, and diabetic complications

Most patients with type 1 diabetes can be taught how to adjust their insulin doses based on blood glucose levels and carbohydrate intake. Education should be reinforced at every physician visit and hospitalization. Formal diabetes education programs, generally conducted by diabetes nurses and nutrition specialists, are often very effective and have been shown to improve diabetes outcomes.

## Diet

Adjusting diet to individual circumstances can help patients control fluctuations in their glucose level and, for patients with type 2 diabetes mellitus, lose weight. Dietary recommendations should be individualized based on patient tastes, preferences, culture, and goals and should be formulated to accommodate requirements posed by comorbid conditions. There are no recommendations on the percentages of calories that should come from carbohydrate, protein, or fat. Patients should be educated on consuming a diet rich in whole foods rather than processed foods. Carbohydrates should be high quality and should contain adequate amounts of fiber, vitamins, and minerals and be low in added sugar, fat, and sodium. Some adults can reduce blood glucose levels and decrease antihyperglycemic medications by following a low- or very-low-carbohydrate eating plan, although maintaining such a diet can be challenging and the benefits may not be sustained long-term.

Patients with type 1 diabetes should use carbohydrate counting or the carbohydrate exchange system to match insulin dose to carbohydrate intake and facilitate physiologic insulin replacement. "Counting" the amount of carbohydrate in the meal is done to calculate the preprandial insulin dose. For example, if a carbohydrate-to-insulin ratio (CIR) of 15 gram:1 unit is used, a patient will require 1 unit of rapid-acting insulin for each 15 g of carbohydrate in a meal. These ratios can vary significantly between patients, depending on their degree of insulin sensitivity and must be tailored to the patient and

adjusted over time. Patients should also be educated that meals with higher protein or fat content can increase insulin requirements and dose adjustments may be necessary. This approach requires detailed patient education and is most successful when guided by a dietitian experienced in working with patients with diabetes. Some experts have advised use of the glycemic index (a measure of the impact of an ingested carbohydrate-containing food on the blood glucose level) to delineate between rapid and slowly metabolized carbohydrates, although there is little evidence to support this approach.

For both type 1 diabetes and type 2 diabetes, nutrition consultation with a dietitian should complement physician counseling; the patient and any person who prepares the patient's meals should be present.

## Exercise

Physical activity should increase incrementally to whatever level a patient can tolerate. Both aerobic exercise and resistance exercise have been shown to improve glycemic control in type 2 diabetes, and several studies have shown a combination of resistance and aerobic exercise to be superior to either alone (5, 6, 7). In type 1 diabetes, exercise has been shown to decrease mortality although the effect on HbA1C lowering is less clear (8, 9, 10). Adults with diabetes and without physical limitations should exercise for a minimum of 150 minutes/week (divided over at least 3 days). Exercise has a variable effect on blood glucose, depending on the timing of exercise in relation to meals and the duration, intensity, and type of exercise. In patients with type 1 diabetes in particular, exercise can lead to hypoglycemia. Therefore, blood glucose should be monitored immediately before and after exercise. The target range for blood glucose prior to exercise should be between 90 mg/dL and 250 mg/dL (5 mmol/L to 14 mmol/L).

Patients who experience hypoglycemic symptoms during exercise should be advised to test their blood glucose and ingest carbohydrates or lower their insulin dose as needed to get their glucose slightly above normal just before exercise. Hypoglycemia during vigorous exercise may require carbohydrate ingestion during the workout period, typically 5 to 15 g of sucrose or another simple sugar.

Patients with known or suspected cardiovascular disease may benefit from [exercise stress testing](#) before beginning an exercise program. Activity goals may need to be modified for patients with complications of diabetes such as [neuropathy](#) and [retinopathy](#).

## Weight loss

In people with diabetes and [obesity](#), physicians should prescribe antihyperglycemic medications that promote weight loss (eg, GLP1 receptor agonists, SGLT-2 inhibitors, or a dual incretin agonist) or are weight-neutral (eg, dipeptidyl peptidase-4 inhibitors, metformin), if possible (for details, see [Medication Treatment of Diabetes](#)). Two GLP-1 receptor agonists that are used for weight loss at higher doses (semaglutide 2.4 mg, liraglutide 3 mg) are associated with significant weight loss even at doses used for diabetes treatment.

Other weight loss medications, including orlistat, phentermine/topiramate, and naltrexone/bupropion, may be useful in selected patients as part of a comprehensive weight loss program. Orlistat, an intestinal lipase inhibitor, reduces dietary fat absorption; it reduces serum lipids and helps promote weight loss. Phentermine/topiramate is a combination medication that reduces appetite through

multiple mechanisms in the brain. Many of these medications also have been shown to decrease HbA1C.

An oral hydrogel containing cellulose and citric acid that causes patients to feel full and eat less can induce modest weight loss in patients with prediabetes and diabetes.

Medical devices, including implanted gastric balloons, a vagus nerve stimulator, and gastric aspiration therapy, are also available, but their use remains limited due to high cost and limited data in patients with diabetes.

Surgical treatment for obesity, such as sleeve gastrectomy or gastric bypass, also leads to weight loss and improvement in glucose control (independent of weight loss) and decreased cardiovascular risk in patients who have diabetes mellitus and should be recommended for appropriately selected patients.

## Foot care

Regular professional podiatric care, including trimming of toenails and calluses, is important for patients with sensory loss or circulatory impairment. Such patients should be advised to inspect their feet daily for cracks, fissures, calluses, corns, and ulcers. Feet should be washed daily in lukewarm water, using mild soap, and dried gently and thoroughly. A lubricant (eg, lanolin) should be applied to dry, scaly skin. Nonmedicated foot powders should be applied to moist feet. Toenails should be cut, preferably by a podiatrist, straight across and not too close to the skin. Adhesive plasters and tape, harsh chemicals, corn cures, water bottles, and electric pads should not be used on skin. Patients should change socks or stockings daily and not wear constricting clothing (eg, garters, socks, or stockings with tight elastic tops).

Shoes should fit well, be wide-toed without open heels or toes, and be changed frequently. Special shoes should be prescribed to reduce trauma if the foot is deformed (eg, previous toe amputation, hammer toe, bunion). Walking barefoot should be avoided.

Patients with neuropathic foot ulcers should avoid weight bearing until ulcers heal. If they cannot, they should wear appropriate orthotic protection. Because most patients with these ulcers have little or no macrovascular occlusive disease, debridement and antibiotics frequently result in good healing and may prevent major surgery. After the ulcer has healed, appropriate inserts or special shoes should be prescribed. In refractory cases, especially if osteomyelitis is present, surgical removal of the metatarsal head (the source of pressure), amputation of the involved toe, or transmetatarsal amputation may be required. A neuropathic joint can often be satisfactorily managed with orthopedic devices (eg, short leg braces, molded shoes, sponge-rubber arch supports, crutches, prostheses).

## Vaccination

All patients with diabetes mellitus should be vaccinated against Streptococcus pneumoniae, influenza virus, hepatitis B, varicella, and SARS-CoV-2 as per standard recommendations.

## Pancreas transplantation

Pancreas transplantation and transplantation of pancreatic islet cells are alternative means of insulin delivery ([11](#), [12](#)); both techniques effectively transplant insulin-producing beta-cells into patients who

are insulin deficient (have type 1 diabetes mellitus).

## Treatment references

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## Monitoring Diabetes Treatment

The goal of diabetes treatment is control of hyperglycemia to relieve symptoms and prevent complications while minimizing hypoglycemic episodes. Diabetes mellitus control can be monitored by measuring blood levels of

- Glucose
- HbA1C
- Fructosamine

**Goals for glycemic control** for most people are

- Preprandial blood glucose between 80 and 130 mg/dL (4.4 and 7.2 mmol/L)
- Peak postprandial (1 to 2 hours after beginning of the meal) blood glucose < 180 mg/dL (< 10 mmol/L)
- With continuous glucose monitoring (CGM), 14-day time in range (TIR) > 70% (target blood glucose range 70 to 180 mg/mL [3.9 to 9.9 mmol/L])
- HbA1C levels < 7%

These goals may be adjusted to be less strict for patients in whom strict glucose control may be inadvisable, such as

- Frail older patients
- Patients with a short life expectancy
- Patients who experience repeated episodes of [hypoglycemia](#), especially those who do not develop symptoms of hypoglycemia (hypoglycemia unawareness)
- Patients who cannot communicate the presence of hypoglycemia symptoms (eg, young children, patients with dementia)

Clinicians may also recommend stricter glycemic goals (eg HbA1C < 6.5%) in select patients if these goals can be achieved without hypoglycemia. Potential candidates for tighter glycemic control include

- Patients not being treated with medications that induce hypoglycemia
- Patients who have had a shorter duration (< 10 years) of diabetes mellitus
- Patients who have a long life expectancy
- Patients who have no cardiovascular disease

Glucose levels are typically determined by [home monitoring](#) of capillary blood glucose (eg, from a fingerstick) or continuous glucose monitoring. Both of these monitoring modalities help patients adjust dietary intake and insulin dosing and help physicians recommend adjustments in the timing and doses of medications. Patients using fingerstick glucose meters or CGMs may need to self-monitor 1 to ≥ 5 times a day (first measurement is usually morning fasting). The frequency depends on blood glucose levels, the patient's needs and abilities, and the complexity of the treatment regimen. Most patients with type 1 diabetes benefit from testing at least 4 times a day ([1](#)). More frequent self-monitoring is

recommended when blood glucose levels are suboptimal or when there are changes in the medication regimen.

HbA1C levels measured in venous plasma are monitored every 3 months or, for patients with consistently good control, every 6 months.

## Fingerstick glucose monitoring

Fingerstick glucose monitors measure capillary blood glucose. Many different glucose meters are available. Nearly all require test strips and a means for pricking the skin and obtaining a blood sample. Choice among devices is usually based on patient preferences for features such as time to results (usually 5 to 30 seconds), size of display panel (large screens may benefit patients with poor eyesight), voice readout (for those with visual impairment), and smartphone app connectivity (2).

## Continuous glucose monitoring

Continuous glucose monitoring (CGM) systems estimate capillary blood glucose from interstitial glucose detected by a subcutaneous sensor. They can either provide glucose measurements continuously (real-time CGM) or intermittently when scanned with a device (intermittently scanned CGM). CGMs provide real-time glucose data including an alarm to warn of hypoglycemia, hyperglycemia, or rapidly changing glucose levels.

Although CGMs have less stringent accuracy requirements than capillary blood glucose monitors, they allow users and clinicians to assess for patterns of hyperglycemia and hypoglycemia that are not identified with fingerstick glucose monitoring. Use of CGMs has been shown to increase patients' time in target range (TIR) and decrease HbA1C (3,4,5). Use of CGMs is recommended for all patients who are treated with intensive insulin therapy and can use the devices safely (6).

For patients with diabetes who use CGMs, TIR is defined as the percentage of time blood glucose measurement on CGM is within the target blood glucose range (70 to 180 mg/mL [3.9 to 9.9 mmol/L]) over 14 days. A 14-day TIR > 70% is associated with decreased risk of diabetes complications and is inversely correlated with HbA1C level (7). To decrease risk of severe hypoglycemia, time below range (< 70 mg/dL [< 3.9 mmol/L]) should be < 4%, and time below 54 mg/L (< 3.0 mmol/L) should be < 1% (7,8). As with all glycemic targets, CGM targets should be individualized depending on age, comorbidities, and risk of hypoglycemia.

CGM systems can be integrated with insulin pumps to provide real-time adjustment of insulin doses based on blood glucose levels. Such systems, known as automated insulin delivery (AID) systems or hybrid closed-loop systems, are expensive; however, they are recommended for all patients who take multiple daily injections of insulin and have been shown to lower HbA1C levels and decrease hypoglycemia (6,9,10). They are becoming more commonly used, and some versions do not require daily fingerstick glucose testing to calibrate the glucose monitor. They are especially useful in patients with type 1 diabetes and for those with hypoglycemia unawareness or nocturnal hypoglycemia. Some CGM sensors can be used for up to 2 weeks before they need to be replaced. Clinicians can review the recorded data to determine whether the patient is experiencing undetected hyperglycemia or hypoglycemia.

## Hemoglobin A1C

HbA1C levels reflect glucose control over the preceding 3 months and hence assess control between physician visits. HbA1C should be assessed quarterly in patients with type 1 diabetes and at least twice a year in patients with type 2 diabetes when plasma glucose appears stable and more frequently when control is uncertain. For most patients, the goal HbA1C is < 7%; however, this goal should be individualized. Home testing kits are available but are used infrequently.

Control suggested by HbA1C values sometimes appears to differ from that suggested by daily glucose readings because of falsely elevated or normal HbA1C values. False elevations of HbA1C may occur with low red blood cell turnover (as occurs with iron, folate, or vitamin B12 deficiency anemia), high-dose aspirin, and high blood alcohol concentrations. Falsely normal HbA1C values occur with increased red blood cell turnover, as occurs with [hemolytic anemias](#) and [hemoglobinopathies](#) (eg, HbS disease, HbC disease), or during treatment of deficiency anemias. In patients with [cirrhosis](#) or [chronic kidney disease stages 4 and 5](#), correlation between HbA1C and glycemic levels is poor, and HbA1C can be falsely decreased in these patients. Pregnancy also falsely decreases HbA1C values.

## Fructosamine

Fructosamine, which is mostly glycosylated albumin but also comprises other glycosylated proteins, reflects glucose control in the previous 1 to 2 weeks. Fructosamine monitoring may be used during intensive treatment of diabetes and for patients with hemoglobin variants or high red blood cell turnover (which cause false HbA1C results), but it is mainly used in research settings.

## Urine glucose

Urine glucose monitoring is too inaccurate to be recommended. Self-measurement of **urine ketones** is recommended for patients with type 1 diabetes if they experience symptoms, signs, or triggers of ketoacidosis, such as nausea or vomiting, abdominal pain, fever, cold or flu-like symptoms, or unusual sustained hyperglycemia (> 250 to 300 mg/dL [> 13.9 to 16.7 mmol/L]) during glucose self-monitoring.

## Monitoring references

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## Special Populations and Settings

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Diabetes care requires careful adjustment for patient factors, including those related to age and lifestyle, comorbid conditions, and need for treatment of other acute or chronic conditions.

### Patients with difficulty maintaining goal glucose levels

The term brittle diabetes has been used to refer to patients who have dramatic, recurrent swings in glucose levels, often for no apparent reason. Labile plasma glucose levels are more likely to occur in patients with type 1 diabetes because endogenous insulin production is almost completely absent, and in some patients, counter-regulatory response to hypoglycemia is impaired. Other causes of labile plasma glucose levels include occult infection, gastroparesis (which leads to erratic absorption of dietary carbohydrates), and endocrine disorders (eg, Addison disease).

Patients with chronic difficulty maintaining acceptable glucose levels should be evaluated for situational factors that affect glucose control. Such factors include inadequate patient education or understanding that leads to errors in insulin administration, inappropriate food choices, and psychosocial stress that expresses itself in erratic patterns of medication use and food intake.

The initial approach is to thoroughly review self-care techniques, including insulin preparation and injection and glucose testing. Increased frequency of self-testing may reveal previously unrecognized patterns and provides the patient with helpful feedback. A thorough dietary history, including timing of

meals, should be taken to identify potential contributions to poor control. Underlying disorders should be ruled out by physical examination and appropriate laboratory tests.

For some insulin-treated patients, changing to a more intensive regimen that allows for frequent dose adjustments (based on glucose testing) is helpful. Continuous glucose monitoring with alarms and sensor-augmented or hybrid closed-loop insulin pump therapy are useful tools in individuals who fluctuate between hypoglycemia and hyperglycemia.

## Children

[Diabetes in children](#) is discussed in more detail elsewhere.

**Children with type 1 diabetes** require physiologic insulin replacement as do adults, and similar treatment regimens, including [insulin pumps](#), are used. However, the risk of hypoglycemia, because of unpredictable meal and activity patterns and limited ability to report hypoglycemic symptoms, may require modification of treatment goals. Most young children can be taught to actively participate in their own care, including glucose testing and insulin injections. School personnel and other caregivers must be informed about the disease and instructed about the detection and treatment of hypoglycemic episodes. [Monitoring for microvascular complications](#) can generally be deferred until after puberty.

**Children with type 2 diabetes** require the same attention to diet and weight control and recognition and management of dyslipidemia and hypertension as do adults. Most children with type 2 diabetes have obesity, so lifestyle modification is the cornerstone of therapy. Medication therapy may also be indicated.

## Adolescents

[Diabetes in adolescents](#) is discussed in more detail elsewhere.

Glucose control typically deteriorates as children with diabetes enter adolescence. Multiple factors contribute, including

- Pubertal and insulin-induced weight gain
- Hormonal changes that decrease insulin sensitivity
- Psychosocial factors that lead to insulin nonadherence (eg, mood and anxiety disorders, hectic schedules, irregular meals, family conflict)
- Experimentation with cigarette, alcohol, and substance use
- [Eating disorders](#) that lead to insulin omission as a means of controlling weight

For these reasons, some adolescents experience recurrent episodes of hyperglycemia, [diabetic ketoacidosis](#), and hypoglycemia requiring emergency department visits and hospitalization.

Treatment often involves intensive medical supervision combined with psychosocial interventions (eg, mentoring or support groups), individual or family therapy, and psychopharmacology when indicated. Patient education is important so that adolescents can safely enjoy the freedoms of early adulthood. Rather than judging personal choices and behaviors, clinicians must continually reinforce the need for

careful glycemic control, especially frequent glucose monitoring and use of frequent, low-dose, fast-acting insulins as needed.

## Hospitalization

Diabetes mellitus may be a primary reason for hospitalization or may accompany other illnesses that require inpatient care. All patients with [diabetic ketoacidosis](#), [hyperosmolar hyperglycemic state](#), or prolonged or severe [hypoglycemia](#) should be hospitalized. Patients with hypoglycemia induced by sulfonylureas, poorly controlled hyperglycemia, or acute worsening of diabetic complications may benefit from brief hospitalization. [Children and adolescents with new-onset diabetes](#) may also benefit from hospitalization. Control may worsen on discharge when insulin regimens developed in controlled inpatient settings prove inadequate to the uncontrolled conditions outside the hospital. In patients with newly diagnosed diabetes, insulin doses used in the inpatient setting are often too high and can cause hypoglycemia if not adjusted when discharged from the hospital.

When other illnesses mandate hospitalization, some patients can continue on their home diabetes treatment regimens. However, glucose control often proves difficult, and it is often neglected when other diseases are more acute. Restricted physical activity and acute illness worsen hyperglycemia in some patients, whereas dietary restrictions and symptoms that accompany illness (eg, nausea, vomiting, diarrhea, anorexia) precipitate hypoglycemia in others—especially when antihyperglycemic medication doses remain unchanged. In addition, it may be difficult to control glucose adequately in patients who are hospitalized because usual routines (eg, timing of meals, medications, and procedures) are inflexibly timed relative to diabetes treatment regimens.

In patients who are hospitalized, oral antihyperglycemic medications often need to be stopped. Metformin can cause [lactic acidosis](#) in patients with renal insufficiency and has to be stopped if contrast agents need to be given. Therefore, metformin is withheld in all but the most stable patients who are hospitalized. Sulfonylureas can cause hypoglycemia and should also be stopped.

Most inpatients can be appropriately treated with basal insulin without or with supplemental short-acting insulin. Dipeptidyl peptidase-4 inhibitors are relatively safe, even in patients with kidney disease, and they may also be used for postprandial glucose lowering.

Sliding-scale insulin should not be the only intervention to correct hyperglycemia; it is reactive rather than proactive, and it leads to poor glycemic control compared to basal-bolus insulin. Longer-acting insulins should be adjusted to prevent hyperglycemia rather than just using short-acting insulins to correct it.

Inpatient hyperglycemia is associated with increased infection rate and mortality. Critical illness causes insulin resistance and hyperglycemia even in patients without known diabetes mellitus. Such stress-induced hyperglycemia is associated with poor outcomes, including increased mortality. Insulin infusion to maintain plasma glucose between 140 and 180 mg/dL (7.8 and 10.0 mmol/L)

- Prevents adverse outcomes such as organ failure
- Possibly enhances recovery from stroke
- Leads to improved survival in patients requiring prolonged (> 5 days) critical care

Previously, glucose target levels were lower; however, it appears that the less stringent targets as described above may be sufficient to prevent adverse outcomes. Severely ill patients, especially those treated with glucocorticoids or pressors and those receiving total parenteral nutrition (TPN), may need very high doses of insulin (> 5 to 10 units/hour) because of insulin resistance. In critically ill patients or postsurgical patients who are in an intensive care unit, insulin infusion protocols and/or computerized algorithms can be used to titrate insulin drips to maintain euglycemia.

## Surgery

The physiologic stress of surgery can increase plasma glucose in patients with diabetes and induce diabetic ketoacidosis in those with type 1 diabetes. For shorter procedures, subcutaneous insulin can be used. In patients with type 1 diabetes, one half to two thirds of the usual morning dose of intermediate-acting insulin or 70 to 80% of the dose of long-acting insulin (glargine or detemir) can be given the night or morning before surgery (at the usual time of long-acting insulin administration).

Patients with type 2 diabetes who are taking insulin should be given 50% of their basal insulin dose the night or morning before surgery. An IV infusion of a dextrose solution can be started before surgery at a rate of 75 to 150 mL/hour and titrated to maintain euglycemia.

During and after surgery, plasma glucose (and ketones if hyperglycemia suggests the need) should be measured at least every 2 hours. Dextrose infusion can be continued, and regular or short-acting insulin can be given subcutaneously every 4 to 6 hours as needed to maintain the plasma glucose level between 100 and 200 mg/dL (5.5 and 11.1 mmol/L) until the patient can be switched to oral feedings and resume the usual insulin regimen. Additional doses of intermediate- or long-acting insulin should be given if there is a substantial delay (> 24 hours) in resuming the usual regimen. This approach may also be used for insulin-treated patients with type 2 diabetes, but frequent measurement of ketones may be omitted.

Some physicians prefer to withhold subcutaneous or inhaled insulin on the day of surgery and to give insulin by IV infusion. For patients undergoing a long procedure or major surgery, a continuous insulin infusion is preferable, especially since insulin requirements can increase because of the stress of surgery. IV insulin infusion can be given at the same time as intravenous dextrose solution to maintain blood glucose. One approach is to combine glucose, insulin, and potassium in the same bag (GIK regimen), for example, by combining 10% dextrose with 10 mEq (10 mmol) potassium, and 15 units of insulin in a 500-mL bag. The insulin doses are adjusted in 5-unit increments. This approach is not used at many institutions because of the frequent remixing and changing of bags needed to adjust to the patient's level of glycemia. A more common approach in the United States is to infuse insulin and dextrose separately. Insulin can be infused at a rate of 1 to 2 U/hour with 5% dextrose infusing at 75 to 150 mL/hour. The insulin rate may need to be decreased for patients with more insulin-sensitive type 1 diabetes and increased for patients with more insulin-resistant type 2 diabetes. Ten percent dextrose may also be used. It is important, especially in patients with type 1 diabetes, to continue insulin infusion to avoid development of diabetes ketoacidosis. Insulin adsorption onto IV tubing can lead to inconsistent effects, which can be minimized by preflushing the IV tubing with insulin solution. Insulin infusion is continued through recovery, with insulin dose adjusted based on the plasma glucose levels obtained in the recovery room and at 1- to 2-hour intervals thereafter.

Most patients with type 2 diabetes who are treated only with oral antihyperglycemic medications maintain acceptable glucose levels when fasting and may not require insulin in the perioperative period. Most oral medications, including sulfonylureas and metformin, should be withheld on the day of surgery, and plasma glucose levels should be measured preoperatively and postoperatively and every 6 hours while patients receive IV fluids. Oral medications may be resumed when patients are able to eat, but metformin should be withheld until normal renal function is confirmed 48 hours after surgery.

## Screening for Diabetes Mellitus

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Screening for diabetes mellitus should be conducted for people at increased risk of the disease.

### Type 1 diabetes

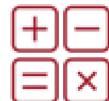
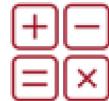
People at high risk of type 1 diabetes (eg, siblings and children of people with type 1 diabetes) can be tested for the presence of islet cell or anti-glutamic acid decarboxylase antibodies, which precede onset of clinical disease ([1](#)).

### Type 2 diabetes

**Risk factors for type 2 diabetes** include

- Age  $\geq$  35 years
- Overweight or [obesity](#)
- Sedentary lifestyle
- Family history of type 2 diabetes mellitus
- History of impaired glucose regulation (prediabetes)
- [Gestational diabetes mellitus](#) or delivery of a baby  $> 4.1$  kg
- [Hypertension](#)
- [Dyslipidemia](#) (high-density lipoprotein [HDL] cholesterol  $< 35$  mg/dL [0.9 mmol/L] or triglyceride level  $> 250$  mg/dL [2.8 mmol/L])
- History of cardiovascular disease
- [Polycystic ovary syndrome](#)
- African, Hispanic, Asian, or American Indian ancestry
- [Steatotic liver disease](#) (formerly fatty liver disease)
- [HIV infection](#)

People  $\geq$  age 35 years and all adults with the additional risk factors described above should be screened for diabetes with an FPG level, HbA1C, or a 2-hour value on a 75-g OGTT at least once every 3 years as long as plasma glucose measurements are normal and at least annually if results reveal impaired fasting glucose levels (see table [Diagnostic Criteria for Diabetes Mellitus and Impaired Glucose Regulation](#)).

**CLINICAL CALCULATORS**[Diabetes Risk Self-Assessment](#)**CLINICAL CALCULATORS**[Body Mass Index \(Quetelet's index\)](#)

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## Prevention of Diabetes Mellitus

### Type 1 diabetes

There are no current therapies to completely prevent type 1 diabetes.

Progression of type 1 diabetes from preclinical to symptomatic disease can be delayed with pharmacologic therapy. Teplizumab is a monoclonal antibody that binds to CD3 cell surface antigens on T cells, which leads to an increase in the proportion of regulatory T cells and exhausted CD8+ T cells and attenuates the autoimmune response that leads to beta-cell destruction. In a phase 2 randomized trial in people with stage 2 type 1 diabetes (presence of  $\geq 2$  autoantibodies and elevated glucose without symptoms) who had a relative with type 1 diabetes ( $n = 76$ ), the use of teplizumab (14-day course) versus placebo resulted in a median 24-month delay in time to diagnosis of type 1 diabetes in the initial trial (1) and 33 months in a follow-up study (2). In addition, in the follow-up study, after a median of 923 days, stage 3 type 1 diabetes was diagnosed at lower rates in participants treated with teplizumab versus placebo (22% vs. 50%).

Other treatments that target the autoimmune inflammatory response, including azathioprine, corticosteroids, and cyclosporine, induce remission of early type 1 diabetes in some patients, but longer term studies have not shown benefits (3).

Antithymocyte globulin (ATG), TNF- alpha (tumor necrosis factor- alpha) inhibitors, and abatacept (CTLA-4-Ig) have shown some promise in preserving beta-cell function in recent-onset type 1 diabetes and are being investigated (3, 4). Some data suggest that verapamil may preserve beta-cell function in patients with newly diagnosed diabetes (5).

### Type 2 diabetes

Patients with impaired glucose regulation should receive counseling addressing their risk of developing diabetes and the importance of lifestyle changes for preventing diabetes. They should be monitored closely for development of diabetes symptoms or elevated plasma glucose. Ideal follow-up intervals have not been determined, but annual or biannual checks are probably appropriate.

Type 2 diabetes usually can be prevented with lifestyle modification. Weight loss of as little as 7% of baseline body weight, combined with moderate-intensity physical activity (eg, walking 30 minutes/day), may reduce the incidence of diabetes in high-risk people by > 50% ([6](#)).

Various medications have been evaluated for diabetes prevention, including metformin, acarbose, liraglutide, thiazolidinediones, valsartan, testosterone, orlistat, and phentermine/topiramate. Metformin is safe and cost-effective and has the strongest evidence for the prevention of diabetes. It can be considered if diet and lifestyle are not successful, especially in patients who are at highest risk for developing diabetes (body mass index  $\geq$  35 or history of gestational diabetes) ([7](#), [8](#)).

In patients with obesity, pharmacotherapy for weight loss, medical devices, and weight loss surgery can be used as adjuncts to diet and physical activity (see [weight loss in diabetes](#)). Metabolic surgery ([bariatric surgery](#)) has been shown to decrease the risk of progression to diabetes ([9](#)).

## Complications

Risk of [complications of diabetes](#) can be decreased by strict control of plasma glucose, defined as HbA1C < 7%, and by control of [hypertension](#) and [lipid levels](#). For most patients with diabetes, blood pressure should be maintained at < 130/80 mm Hg, although blood pressure targets may need to be individualized with consideration of adverse effects of antihypertensive medications. Specific measures for prevention of progression of complications once detected are described under [Complications](#) and [Treatment](#).

## Prevention references

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## Key Points

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- Type 1 diabetes is caused by an absence of insulin production due to autoimmune-mediated inflammation in pancreatic beta cells.
- Type 2 diabetes is caused by hepatic insulin resistance (causing an inability to suppress hepatic glucose production) and peripheral insulin resistance (which impairs peripheral glucose uptake), in combination with a pancreatic beta cell secretory defect.
- Diagnose by elevated fasting plasma glucose level and/or elevated hemoglobin A1C and/or elevated 2-hour value on oral glucose tolerance test.
- Do regular screening for complications.
- Microvascular complications include nephropathy, neuropathy, and retinopathy.
- Macrovascular complications involve atherosclerosis resulting in coronary artery disease, transient ischemic attack/stroke, and peripheral arterial insufficiency.
- Treat with diet, exercise, weight loss, and insulin, and/or oral or injectable antihyperglycemic medications.
- Often, give renin-angiotensin-aldosterone system blockers, and statins to prevent complications.

## More Information

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The following English-language resources may be useful. Please note that THE MANUAL is not responsible for the content of these resources.

[American Diabetes Association: Standards of Medical Care in Diabetes](#) *Diabetes Care* 46 (Supplement 1): 1-291, 2023.

[Davies MJ, Aroda VR, Collins BS, et al.](#). Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care* 2022;45(11):2753-2786. doi:10.2337/dci22-0034

[Endocrine Society: Clinical Practice Guidelines](#): provides guidelines on evaluation and management of patients with diabetes as well as links to other information for clinicians

[Holt RIG, DeVries JH, Hess-Fischl A, et al](#): The management of type 1 diabetes in adults. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetologia* 64(12):2609–2652, 2021. doi: 10.1007/s00125-021-05568-3

[Powers MA, Bardsley JK, Cypress M, et al](#). Diabetes Self-management Education and Support in Adults With Type 2 Diabetes: A Consensus Report of the American Diabetes Association, the Association of Diabetes Care & Education Specialists, the Academy of Nutrition and Dietetics, the American Academy of Family Physicians, the American Academy of PAs, the American Association of Nurse Practitioners, and the American Pharmacists Association. *Diabetes Care* 2020;43(7):1636-1649. doi:10.2337/dci20-0023

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