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# Patient education: Type 2 diabetes: Treatment (Beyond the Basics)

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All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: Nov 2024.

This topic last updated: May 20, 2024.

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# **TYPE 2 DIABETES OVERVIEW**

Type 2 diabetes mellitus is a disorder that is known for disrupting the way your body uses glucose (sugar); it also causes other problems with the way your body stores and processes other forms of energy, including fat.

All the cells in your body need glucose to work normally. Glucose gets into the cells with the help of a hormone called insulin. In type 2 diabetes, the body stops responding to normal or even high levels of insulin, and over time, the pancreas (an organ in the abdomen) does not make enough insulin to keep up with what the body needs. Having excess body weight or extra fat stored in the liver and abdomen (even if body weight is within a healthy range) increases the body's demand for insulin. This can cause high blood glucose levels, which can lead to problems if untreated. (See "Patient education: Type 2 diabetes: Overview (Beyond the Basics)".)

People with type 2 diabetes require regular monitoring and ongoing treatment to maintain blood sugar levels at goal. Treatment includes lifestyle changes (including dietary changes and exercise to promote weight loss), self-care measures, and often medications, which can minimize the risk of diabetes-related and cardiovascular (heart-related) complications.

This topic review will discuss the medical treatment of type 2 diabetes.

#### TYPE 2 DIABETES TREATMENT GOALS

The main goals of treatment in type 2 diabetes are to keep your blood sugar levels within your goal range and treat other medical conditions that go along with diabetes (like high blood pressure and high cholesterol); it is also very important to stop smoking if you smoke. These measures will reduce your risk of complications.

**Blood sugar management** — It is important to keep your blood sugar levels at goal. This can help prevent long-term complications that can result from poorly managed blood sugar (including problems affecting the eyes, kidneys, nervous system, and cardiovascular system).

**Home blood sugar testing** — Your doctor may ask you to check your blood sugar at home, especially if you take insulin or certain oral diabetes medicines that can cause low blood sugar. Home blood sugar testing is not usually necessary for people who manage their diabetes through diet only or with diabetes medications that do not cause low blood sugar.

A **random** blood sugar test is based on blood drawn at any time of day, regardless of when you last ate. A **fasting** blood sugar test is a blood test done after not eating or drinking for 8 to 12 hours (usually overnight). A normal fasting blood sugar is more than 70 mg/dL (3.9 mmol/L) but less than 100 mg/dL (5.6 mmol/L), although people with diabetes may have a different goal. Your doctor or nurse can help you set a blood sugar goal and show you exactly how to check your level. (See "Patient education: Glucose monitoring in diabetes (Beyond the Basics)".)

**A1C testing** — Blood sugar management can also be estimated with a blood test called glycated hemoglobin, or "A1C." The A1C blood test measures your average blood sugar level over the past two to three months. The goal A1C for most young people with type 2 diabetes is less than 7 percent (53 mmol/mol), which corresponds to an average blood sugar of approximately 150 mg/dL (8.3 mmol/L) ( table 1). Lowering your A1C level reduces your risk for kidney, eye, and nerve problems. For some people, a different A1C goal may be more appropriate. Your health care provider can help determine your A1C goal.

**Reducing the risk of cardiovascular complications** — The most common, serious, long-term complication of type 2 diabetes is cardiovascular disease, which can lead to problems like heart attack, stroke, and even death. On average, people with type 2 diabetes have twice the risk of cardiovascular disease as people without diabetes.

However, you can substantially lower your risk of cardiovascular disease by:

- Quitting smoking, if you smoke
- Managing high blood pressure and high cholesterol with diet, exercise, and medicines
- Taking a low-dose aspirin every day, if you have a history of heart attack or stroke or if your health care provider recommends this

Some studies have shown that lowering A1C levels with certain medications may also reduce your risk for cardiovascular disease. (See 'Type 2 diabetes medicines' below.)

A detailed discussion of ways to prevent complications is available separately. (See "Patient education: Preventing complications from diabetes (Beyond the Basics)".)

## **DIET AND EXERCISE IN TYPE 2 DIABETES**

Diet and exercise are the foundation of diabetes management.

Changes in diet can improve many aspects of type 2 diabetes, including helping to manage your body weight, blood pressure, and your body's ability to produce and respond to insulin. The single most important thing most people can do to improve diabetes and body weight management is to avoid all sugary beverages, such as soft drinks or juices, or if this is not possible, to significantly limit consumption. Limiting overall food portion size is also very important. Detailed information about type 2 diabetes and diet is available separately. (See "Patient education: Type 2 diabetes and diet (Beyond the Basics)".)

Regular exercise can also help manage type 2 diabetes, even if you do not lose weight. Exercise lowers blood sugar because it improves your body's response to insulin. (See "Patient education: Exercise and medical care for people with type 2 diabetes (Beyond the Basics)".)

## **TYPE 2 DIABETES MEDICINES**

A number of medications are available to treat type 2 diabetes.

**Metformin** — Most people who are newly diagnosed with type 2 diabetes will immediately begin a medicine called metformin (sample brand names: Glucophage, Glumetza, Riomet, Fortamet). Metformin improves your body's response to insulin and, as a result, lowers blood sugar levels.

Metformin is a pill that is usually started with a once-daily dose with dinner (or your last meal of the day); a second daily dose (with breakfast) is added one to two weeks later. The dose may be increased every one to two weeks thereafter.

**Side effects** — Common side effects of metformin include nausea, diarrhea, and gas. These are usually not severe, especially if you take metformin along with food. The side effects usually improve after a few weeks.

People with severe kidney, liver, and heart disease and those who drink alcohol excessively should not take metformin. You should stop taking metformin in certain situations, including

if you develop acute or unstable heart failure, get a serious infection causing low blood pressure, become dehydrated, or have severely decreased kidney function. You will also need to stop your metformin before having surgery of any kind.

Adding a second medicine — Your doctor or nurse might recommend a second medication in addition to metformin. This may happen within the first two to three months if your blood sugar and A1C levels are still higher than your goal; otherwise, many people need to add a second glucose-lowering medication later (after several years of having diabetes). Many available classes of medications can be used with metformin or in combination with each other if metformin is contraindicated or not tolerated. (See "Patient education: Type 2 diabetes: Insulin treatment (Beyond the Basics)".)

If your blood sugar levels are still high after two to three months but your A1C is fairly close to goal, a second oral medicine might be added. If your A1C is higher than 9 percent, however, your doctor might recommend insulin (usually as a single daily injection) or a glucagon-like peptide-1 (GLP-1) or dual receptor agonist (a daily or weekly injection). The most appropriate second medicine depends upon several different factors, including your body weight, risk of low blood sugar, other medical problems, and preferences, in addition to the efficacy, side effects, and cost of the medication.

**Sulfonylureas** — Sulfonylureas have been used to treat type 2 diabetes for many years. They work by increasing the amount of insulin your body makes and can lower blood sugar levels by approximately 20 percent. They are reasonable second agents because they are inexpensive, effective, universally available, and have a long-term track record. Side effects can include low blood sugar (hypoglycemia) and weight gain. Most patients can take sulfonylureas even if they have an allergy to "sulfa" drugs. You should be very cautious taking a sulfonylurea if you have kidney failure.

Usually shorter-acting sulfonylureas are preferred due to a lower risk of hypoglycemia. These include glipizide and glimepiride (brand names: Glucotrol, Amaryl).

If you take a sulfonylurea, you can develop low blood sugar, known as hypoglycemia. Low blood sugar symptoms can include:

- Sweating
- Shaking
- Feeling hungry
- Feeling anxious
- Feeling confused

Low blood sugar must be treated quickly by eating 10 to 15 grams of fast-acting carbohydrate (eg, fruit juice, hard candy, glucose tablets). It is possible to pass out if you do not treat low blood sugar quickly enough. If you know you are going to miss a meal, you can

skip the sulfonylurea tablet you would usually take before eating to reduce the risk of low blood sugar. A full discussion of low blood sugar is available separately. (See "Patient education: Hypoglycemia (low blood glucose) in people with diabetes (Beyond the Basics)".)

**DPP-4 inhibitors** — Dipeptidyl peptidase-4 (DPP-4) inhibitors include sitagliptin (brand name: Januvia), saxagliptin (brand name: Onglyza), linagliptin (brand name: Tradjenta), alogliptin (brand name: Nesina), and vildagliptin (brand name: Galvus). Vildagliptin is available in some countries but not in the United States. These medicines lower blood sugar levels by increasing insulin release from the pancreas in response to a meal. They can be given alone in people who cannot tolerate metformin or other medicines, or they can be given together with other oral medicines if blood sugar levels are still higher than the goal. These medicines usually do not cause hypoglycemia or changes in body weight. There have been rare reports of joint pain, pancreatitis, and severe skin reactions.

**SGLT2 inhibitors** — The sodium-glucose co-transporter 2 (SGLT2) inhibitors, canagliflozin (brand name: Invokana), empagliflozin (brand name: Jardiance), dapagliflozin (brand name: Farxiga), and ertugliflozin (brand name: Steglatro), lower blood sugar by increasing the excretion of sugar in the urine. They are variably effective in lowering blood sugar, but on average, they are similar in potency to the DPP-4 inhibitors (see 'DPP-4 inhibitors' above). SGLT2 inhibitors may be a good choice for people with heart failure or chronic kidney disease because they have been shown to have heart, kidney, and mortality benefits.

SGLT2 inhibitors usually do not cause low blood sugar unless they are combined with sulfonylureas or insulin. They promote modest reductions in body weight and blood pressure. Side effects include genital yeast infections in males and females and dehydration. Some medicines in this class have been associated with an increased risk of bone fracture, amputation, or urinary tract infections. An uncommon but deadly infection of the tissue in the perineum (the area between the genitals and the anus) has also been reported in men and women.

SGLT2 inhibitors can increase the risk of diabetic ketoacidosis (DKA); this is a serious problem that can happen when acids called "ketones" build up in the blood in the setting of dehydration. DKA can happen even when blood sugar is only mildly elevated. SGLT2 inhibitors should be stopped three to four days before procedures, during illness with nausea and vomiting, and during periods of fasting.

**GLP-1 receptor agonists** — The glucagon-like peptide-1 (GLP-1) receptor agonists are medications given by injection that increase insulin release in response to a meal and slow digestion. They include exenatide, dosed twice daily (brand name: Byetta); exenatide extended release, dosed weekly (brand name: Bydureon); liraglutide, dosed daily (brand name: Victoza); dulaglutide, dosed weekly (brand name: Trulicity); lixisenatide in combination with insulin, dosed daily (brand name: LixiLan); and semaglutide, dosed weekly as an

injection (brand name: Ozempic) or daily as a tablet (brand name: Rybelsus). There is also a "dual" agonist, tirzepatide (brand name: Mounjaro). These medications are useful for people whose blood sugar is not adequately managed on the highest dose of one or two oral medicines. They may be especially helpful for people with excess body weight who are gaining weight or struggling to lose weight on other diabetes medicines. Liraglutide, dulaglutide, or semaglutide injections are recommended for people who have, or are at high risk for, cardiovascular disease, as they have been shown to have cardiovascular benefits in these groups.

GLP-1 receptor agonists do not usually cause low blood sugar when used without other medications that cause low blood sugar. They promote loss of appetite and a sense of feeling full after eating a smaller amount of food, which helps with weight loss but can also cause bothersome side effects, including nausea, vomiting, and diarrhea. Gastrointestinal side effects usually improve with time. Pancreatitis (inflammation of the pancreas) has been reported rarely in people taking GLP-1 receptor agonists, but it is not known if these medications caused the pancreatitis. They have also been associated with gall bladder disease. You should stop taking these medications if you develop severe abdominal pain. Exenatide and lixisenatide should not be used in people with abnormal kidney function, and liraglutide and dulaglutide should be used with caution in this situation. These drugs are generally expensive. They should be stopped before procedures or surgery.

Meglitinides — Meglitinides include repaglinide (brand name: Prandin) and nateglinide (brand name: Starlix). They work to lower blood sugar levels, similar to the sulfonylureas, but they act more quickly than sulfonylureas and should be taken right before a meal; they might also be recommended in people who are allergic to sulfonylureas. They are taken in pill form. Meglitinides are not generally used as a first-line treatment, because they are more expensive than sulfonylureas and must be taken three times per day. Repaglinide can be used in patients with kidney failure.

**Thiazolidinediones** — This class of medicines includes pioglitazone (brand name: Actos) and rosiglitazone (brand name: Avandia, which is no longer available in many regions including the United States), which work to lower blood sugar levels by increasing the body's sensitivity to insulin. They are taken in pill form and usually in combination with other diabetes medicines.

Common side effects of thiazolidinediones include:

- · Weight gain.
- Swelling of the feet and ankles, which sometimes can be a sign of new or worsening heart failure. The risk of heart failure is small but serious. An early sign of heart failure

is swelling of the feet and ankles. People who take thiazolidinediones should monitor for swelling.

- A small but serious increased risk of developing fluid retention at the back of the eyes (macular edema).
- An increased risk of bone fractures.
- A possible risk of developing certain types of cancer (like bladder cancer).

**Alpha-glucosidase inhibitors** — These medicines, which include acarbose (brand name: Precose) and miglitol (brand name: Glyset), work by interfering with the absorption of carbohydrates in the intestine. This helps to lower blood sugar levels but not as effectively as metformin or the sulfonylureas. They can be combined with other medicines if the first medicine does not lower blood sugar levels enough.

The main side effects of alpha-glucosidase inhibitors are gas (flatulence), diarrhea, and abdominal pain; starting with a low dose may minimize these side effects. The medicine is usually taken three times per day with the first bite of each meal.

**Insulin** — In the past, insulin treatment was reserved for patients with type 2 diabetes whose blood sugar was not adequately managed with oral medicines and lifestyle changes (ie, diet and exercise). However, increasing evidence suggests that insulin treatment at earlier stages may improve overall diabetes management over time. Side effects include low blood sugar, if you take more insulin than your body needs, and weight gain. Adjusting the dose of insulin to the body's needs can minimize the risk of these side effects. It may be necessary to change your dose frequently.

In some situations, insulin injections (shots) can be used as a first-line treatment for type 2 diabetes. In other cases, insulin can be added to or substituted for oral medicines. If you take insulin, you will need to get comfortable giving yourself the injections or have a family member or housemate learn how to do it for you. More detailed information about insulin treatment is available separately. (See "Patient education: Type 2 diabetes: Insulin treatment (Beyond the Basics)".)

# LIVING WITH TYPE 2 DIABETES

Living with type 2 diabetes can be stressful. It is a lot of responsibility to have to monitor your blood sugar (if you need to do this), watch your diet, exercise regularly, keep all your appointments, and take your medications every day. It can also be scary to think about the potential complications of diabetes. It can help to involve your family and friends and make

sure you have a solid support system in place to provide encouragement, reminders, and help as you need it.

It is not uncommon for stress to lead to burnout or even depression, and this can make taking care of yourself more difficult. Having an open and honest discussion with your doctor, nurse, or other health care provider can help you to understand your diagnosis, treatment plan, and what to do if you are overwhelmed. Some people also benefit from talking with a counselor or social worker to help them cope with their responsibilities and worries.

## WHERE TO GET MORE INFORMATION

Your health care provider is the best source of information for questions and concerns related to your medical problem.

This article will be updated as needed on our website ( www.uptodate.com/patients).

Related topics for patients, as well as selected articles written for health care professionals, are also available. Some of the most relevant are listed below.

**Patient level information** — UpToDate offers two types of patient education materials.

**The Basics** — The Basics patient education pieces answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials.

Patient education: Treatment for type 2 diabetes (The Basics)

Patient education: Type 2 diabetes (The Basics)
Patient education: Using insulin (The Basics)

Patient education: Low blood sugar in people with diabetes (The Basics)

Patient education: Metabolic dysfunction-associated steatotic liver disease (The Basics)

Patient education: Exercise and movement (The Basics)

Patient education: Carb counting for adults with diabetes (The Basics)

Patient education: Lowering your risk of prediabetes and type 2 diabetes (The Basics)

Patient education: Diabetic ketoacidosis (The Basics)

Patient education: Hyperosmolar hyperglycemic state (The Basics)

Patient education: How to give an insulin shot (The Basics)
Patient education: How to use an insulin pen (The Basics)

**Beyond the Basics** — Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are best for patients who want in-depth information and are comfortable with some medical jargon.

Patient education: Type 2 diabetes: Overview (Beyond the Basics)

Patient education: Type 2 diabetes: Insulin treatment (Beyond the Basics)

Patient education: Type 2 diabetes and diet (Beyond the Basics)

Patient education: Glucose monitoring in diabetes (Beyond the Basics)

Patient education: Hypoglycemia (low blood glucose) in people with diabetes (Beyond the

Basics)

Patient education: Exercise and medical care for people with type 2 diabetes (Beyond the

Basics)

Patient education: Preventing complications from diabetes (Beyond the Basics)

**Professional level information** — Professional level articles are designed to keep doctors and other health professionals up-to-date on the latest medical findings. These articles are thorough, long, and complex, and they contain multiple references to the research on which they are based. Professional level articles are best for people who are comfortable with a lot of medical terminology and who want to read the same materials their doctors are reading.

Alpha-glucosidase inhibitors for treatment of diabetes mellitus

Measurements of chronic glycemia in diabetes mellitus

Glycemic management and vascular complications in type 2 diabetes mellitus

Insulin therapy in type 2 diabetes mellitus

Management of persistent hyperglycemia in type 2 diabetes mellitus

Metformin in the treatment of adults with type 2 diabetes mellitus

Overview of general medical care in nonpregnant adults with diabetes mellitus

Sodium-glucose cotransporter 2 inhibitors for the treatment of hyperglycemia in type 2 diabetes mellitus

Sulfonylureas and meglitinides in the treatment of type 2 diabetes mellitus Thiazolidinediones in the treatment of type 2 diabetes mellitus

The following organizations also provide reliable health information.

National Library of Medicine

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( www.nlm.nih.gov/medlineplus/healthtopics.html)
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American Diabetes Association (ADA)

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(800)-DIABETES (800-342-2383)
( www.diabetes.org)
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Canadian Diabetes Associates

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( www.diabetes.ca)
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• US Center for Disease Control and Prevention

www.cdc.gov/diabetes)

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Topic 1737 Version 36.0

## **GRAPHICS**

# A1C level and average blood sugar

If your A1C level is (percent):	That means your average blood sugar level during the past 2 to 3 months was about:	
	If you live <i>in the US</i> , use these values.  Your blood sugar is measured in milligrams/deciliter (mg/dL).	If you live <i>outside the US</i> , use these values.  Your blood sugar is measured in millimoles/liter (mmol/L).
6	126	7
7	154	8.6
8	183	10.2
9	212	11.8
10	240	13.3
11	269	15
12	298	16.5
13	326	18.1
14	355	19.7

The A1C blood test tells you what your average blood sugar level has been for the past 2 to 3 months. This table lists which A1C levels go with which average blood sugar levels. Blood sugar is measured differently in the US than it is in most other countries. The column in the middle is for people in the US. The column on the right is for people who live outside the US.

A1C: glycated hemoglobin.

Graphic 76310 Version 5.0

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