**Prevention of type 2 diabetes mellitus**

**Authors**  
David K McCulloch, MD

R Paul Robertson, MD

…

**Section Editor**  
David M Nathan, MD

**Deputy Editor**  
Jean E Mulder, MD

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

**Literature review current through:** May 2017. | **This topic last updated:** Jun 19, 2017.

**INTRODUCTION** — Type 2 diabetes mellitus is characterized by hyperglycemia, insulin resistance, and relative impairment in insulin secretion. Although the lifetime risk of type 2 diabetes is high, our ability to predict and prevent type 2 diabetes in the general population is limited. However, individuals at high risk, including those with impaired fasting glucose (IFG), impaired glucose tolerance (IGT), obesity, close relatives with type 2 diabetes, or who are members of certain ethnic groups (Asian, Hispanic, African American), are appropriate candidates for preventive interventions [[1](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/1)].

The prevention of type 2 diabetes mellitus will be reviewed here. The prevalence, risk factors, and screening for type 2 diabetes are discussed elsewhere. (See "Risk factors for type 2 diabetes mellitus" and "Screening for type 2 diabetes mellitus".)

**GOALS OF DIABETES PREVENTION** — The goals of diabetes prevention include:

●Delaying the onset of diabetes

●Preserving beta cell function

●Preventing or delaying microvascular and perhaps cardiovascular complications

As a therapeutic target, preservation of beta cell function may be particularly important as beta cell failure largely underlies the transition from prediabetic states to diabetes (as well as worsening of glycemic control once diabetes has developed).

**OUR APPROACH**

**Identify individuals for preventive measures** — In order to identify individuals who are appropriate candidates for preventive interventions, we measure glycated hemoglobin (A1C) or fasting plasma glucose (FPG) in adults at high risk for diabetes:

●Individuals >45 years of age with body mass index (BMI) >25 kg/m2 who have one or more additional risk factors for diabetes:

•Family history of diabetes mellitus in a first-degree relative

•Sedentary lifestyle

•Gestational diabetes

•Hypertension

•Dyslipidemia

Although oral glucose tolerance testing (OGTT) has been used to identify people at high risk to develop type 2 diabetes in almost all of the clinical trials, in practice, we usually use the A1C or FPG as more practical (and as recommended for diagnosis of diabetes by the American Diabetes Association [ADA]). (See "Risk factors for type 2 diabetes mellitus" and "Clinical presentation and diagnosis of diabetes mellitus in adults", section on 'Diagnostic criteria'.)

●**FPG ≥126 mg/dL or A1C ≥6.5 percent** – If FPG is ≥126 mg/dL (7 mmol/L) or A1C ≥6.5 percent (48 mmol/mol), the individual has met the criteria for the diagnosis of diabetes mellitus. The initial test should be repeated to confirm the diagnosis (table 1). Appropriate management of patients with diabetes is reviewed separately. (See "Overview of medical care in adults with diabetes mellitus" and "Initial management of blood glucose in adults with type 2 diabetes mellitus".)

●**FPG 100 to 125 mg/dL or A1C 5.7 to 6.4 percent** – If the FPG or A1C value is abnormal, the initial test should be repeated to confirm abnormal glucose metabolism (table 2). For patients with impaired fasting glucose (IFG) or A1C of 5.7 to 6.4 percent (39 to 46 mmol/mol), we promote lifestyle changes (healthy diet, exercise) (see 'Lifestyle modification' below). We repeat testing annually.

Although the risk for developing diabetes follows a continuum across all levels of subdiabetic, abnormal glucose metabolism, when classified categorically, people with IFG, impaired glucose tolerance (IGT), or an A1C level of 5.7 to 6.4 percent (39 to 46 mmol/mol) are at increased risk of developing type 2 diabetes compared with those with lower levels (table 2). Individuals with additional diabetes clinical risk factors, including obesity and family history, are even more likely to develop diabetes (see "Risk factors for type 2 diabetes mellitus"). Lifestyle changes can be endorsed for patients at all risk levels.

●**FPG <100 mg/dL or A1C <5.7 percent** – If glycemic indices are normal (FPG is <100 mg/dL [5.6 mmol/L] or A1C <5.7 percent [39 mmol/mol]), we retest (A1C or FPG) high-risk individuals at two- to three-year intervals (see "Screening for type 2 diabetes mellitus", section on 'A suggested approach'). We promote lifestyle changes (healthy diet and regular exercise) to all patients.

**Lifestyle modification** — All patients with IGT, IFG, or an A1C of 5.7 to 6.4 percent (39 to 46 mmol/mol) (table 2) should be provided with a comprehensive lifestyle modification program that includes:

●Behavior modification

●Dietary therapy

●Physical activity

●Smoking cessation

The goal of the lifestyle intervention is weight loss with return to normal glycemia. Regular reinforcement of the program is important for successful compliance.

Although insulin resistance and impaired insulin secretion in type 2 diabetes have a substantial genetic component, they can also be influenced, both positively and negatively, by environmental and behavioral factors. Changes in lifestyle, including diet modification, weight loss, and exercise, slow progression of IGT to overt diabetes [[2-4](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/2-4)]. The beneficial effects of such intervention appear to continue after the original intervention [[5-9](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/5-9)]. Although neither lifestyle changes nor pharmacologic therapy have been shown to reduce morbidity or mortality in patients at high risk for developing diabetes [[10](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/10)], lifestyle changes are generally beneficial and do not have adverse effects. (See 'Lifestyle intervention' below.)

**Assess response to lifestyle intervention** — For patients with abnormal glucose metabolism (FPG 100 to 125 mg/dL or A1C 5.7 to 6.4 percent) participating in a lifestyle modification program, we reassess fasting glucose or A1C annually.

●**Management if lifestyle intervention unsuccessful**– For select patients (age <60 years and/orBMI ≥35 kg/m2, women with a history of gestational diabetes) in whom lifestyle interventions fail to improve glycemic indices, we suggest metformin for diabetes prevention (table 3). (See 'Metformin' below.)

This suggestion is based upon the findings of the Diabetes Prevention Program (DPP), in which metformin was particularly effective for diabetes prevention in those at highest risk for developing diabetes (individuals who were younger, more obese [BMI >35 kg/m2], and in women with a history of gestational diabetes). In older individuals (≥60 years of age at baseline), the lifestyle intervention was particularly effective (72 percent reduction in diabetes compared with placebo), while metformin was relatively less effective. (See 'Diabetes Prevention Program' below and 'Pharmacologic therapy' below.)

Patients treated with metformin require at least annual monitoring (A1C or FPG) for the development of diabetes. (See "Clinical presentation and diagnosis of diabetes mellitus in adults".)

Patients who are not treated with metformin should also be followed, with repeat examination and annual measurements of FPG or A1C, as well as serum lipids. If FPG increases to ≥126 mg/dL (7 mmol/L) or A1C ≥6.5 percent (48 mmol/mol), appropriate management of diabetes is necessary. (See "Clinical presentation and diagnosis of diabetes mellitus in adults", section on 'Diagnostic criteria' and "Overview of medical care in adults with diabetes mellitus" and "Initial management of blood glucose in adults with type 2 diabetes mellitus".)

●**Management if lifestyle intervention successful**– Patients who improve or maintain their glycemic indices with lifestyle interventions should continue diet and exercise with repeat examination and measurements of fasting blood glucose or A1C and serum lipids on an annual basis.

**LIFESTYLE INTERVENTION** — We promote lifestyle changes (healthy diet and regular exercise) to all patients.

**Efficacy** — Lifestyle intervention (combined diet and exercise aimed at weight loss and increasing activity levels) can improve glucose tolerance and prevent progression from impaired glucose tolerance (IGT) to type 2 diabetes, as illustrated by meta-analyses of trials comparing exercise plus diet with standard therapy (risk ratio [RR] with intervention compared with control 0.59, 95% CI 0.51-0.66) [[2-4](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/2-4)]. The beneficial effect of the original lifestyle intervention appears to persist for years after the end of the study [[5-9](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/5-9)].

Some of the individual trials (table 4) in the meta-analyses are described below.

The glycemic benefit of sustained weight reduction in patients already diagnosed with type 2 diabetes is reviewed separately. (See "Initial management of blood glucose in adults with type 2 diabetes mellitus", section on 'Intensive lifestyle modification'.)

**Finnish Diabetes Prevention Study** — The Finnish Diabetes Prevention Study randomly assigned 522 middle-aged patients with IGT (mean age 55 years, mean body mass index [BMI] 33.2 kg/m2) to a weight-reduction and exercise program or a control group [[11](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/11)].

●The mean weight loss in the intervention group was 3.5 kg at the end of two years compared with 0.8 kg in the control group. At the end of four years, the cumulative incidence of diabetes was significantly lower in the intervention group (11 versus 23 percent).

●The effect of the original lifestyle intervention appears to persist for at least three years after the end of the study. Patients who were diabetes free at four years were followed for an additional three years [[5](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/5)]. No further lifestyle intervention was provided through the study during the extended follow-up. The reduction in diabetes incidence associated with the original intensive lifestyle group continued, although not as powerfully during the three-year follow-up (58 percent reduction during the trial; 36 percent reduction during the three-year follow-up). Over the extended seven-year follow-up, comparing intervention and control groups, the hazard ratio (HR) for diabetes was 0.57 (95% CI 0.43-0.76), with cumulative incidence of diabetes 23 versus 38 percent at the end of year 6 (43 percent reduction over the entire period).

**Diabetes Prevention Program** — The results of a second trial, the Diabetes Prevention Program (DPP), were similar [[12](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/12)]. In this trial, 3234 obese (average BMI 34 kg/m2) subjects aged 25 to 85 years (average 51 years) at high risk for diabetes (based on BMI ≥24 kg/m2, and fasting and two-hour plasma glucose concentrations of 96 to 125 mg/dL [5.3 to 6.9 mmol/L] and 140 to 199 mg/dL [7.8 to 11.1 mmol/L], respectively) were randomly assigned to one of the following groups:

●Intensive lifestyle changes with the aim of reducing weight by 7 percent through a behavioral modification program aimed at a low-fat diet and exercise for 150 minutes per week. Details of the lifestyle intervention have been published [[13](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/13)].

●Treatment with metformin (850 mg twice daily) plus information on diet and exercise.

●Placebo plus information on diet and exercise.

The study was terminated one year ahead of schedule when the independent data safety monitoring board determined that the study hypotheses had been answered: at an average follow-up of three years, fewer patients in the intensive lifestyle group developed diabetes, as diagnosed by fasting plasma glucose (FPG) and two-hour post-load glucose concentrations (14 versus 22 and 29 percent in the metformin and placebo groups, respectively). The intensive lifestyle and metformin interventions reduced the cumulative incidence of diabetes by 58 and 31 percent, respectively [[12](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/12)]. Lifestyle intervention was effective in men and women in all age groups, in all ethnic groups, and across all risk levels [[14](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/14)].

The diet and exercise group lost an average of 15 pounds (6.8 kg; 7 percent) of weight in the first year, most of which was sustained for the duration of the study. An analysis of patients in the intensive lifestyle group found that, within the three components of the intervention (weight loss, diet change, and exercise), diabetes prevention correlated most strongly with weight loss; there was a 16 percent reduction in diabetes risk for every kilogram reduction in weight [[15](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/15)].

●**History of gestational diabetes** – In contrast to the findings in the entire DPP cohort (lifestyle intervention more effective than metformin therapy), metformin and lifestyle intervention were similarly effective in reducing the incidence of diabetes in women with a history of gestational diabetes [[16](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/16)].

In a preplanned subset analysis of women with a history of gestational diabetes and IGT, the incidence of diabetes was reduced by 50 and 53 percent in subjects assigned to metformin and lifestyle intervention, respectively, compared with placebo. In parous women with IGT and without a history of gestational diabetes, risk reductions with metformin and lifestyle (compared with placebo) were 14 and 49 percent, respectively. The discrepancy is due, in part, to the higher cumulative incidence of diabetes during the three-year trial in women assigned to placebo with versus without gestational diabetes (38.4 versus 25.7 percent) and in part due to the inability of women with a history of gestational diabetes randomly assigned to intensive lifestyle intervention to sustain physical activity and maintain weight loss.

●**Diabetes defined by A1C** – Metformin and lifestyle intervention were similarly effective in reducing the incidence of diabetes when diabetes was defined by A1C criteria (≥6.5 percent) rather than FPG or post-load glucose concentrations [[17](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/17)]. Although A1C was measured at baseline and throughout the DPP, it was not used for study eligibility or outcomes. In a subsequent analysis of data from the DPP, 2765 patients without diabetes at baseline according to FPG (<126 mg/dL [7.0 mmol/L]), two-hour post-load glucose (<200 mg/dL [11.1 mmol/L]), and A1C criteria (<6.5 percent) were included in the analysis [[17](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/17)]. The reduction in the incidence of diabetes defined by A1C ≥6.5 percent was similar in the metformin and lifestyle intervention groups (reduced by 44 and 49 percent, respectively [compared with reductions of 31 and 58 percent in diabetes diagnosed by FPG and two-hour post-load glucose criteria]). The long-term health (microvascular disease, cardiovascular risk factors) implications of the interventions and the diagnostic differences in defining them are uncertain.

●**Persistent benefit after intervention** – In a follow-up observational study, the Diabetes Prevention Program Outcomes (DPPOS), the benefit of the lifestyle intervention persisted over 10 years. In this study, 85 percent of patients originally enrolled in DPP joined the long-term follow-up and were offered group-implemented lifestyle intervention [[6](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/6)]. Patients originally assigned to metformin continued receiving it (unblinded). During a cumulative 10 years of follow-up, the incidence of diabetes in the lifestyle and metformin groups was significantly reduced by 34 and 18 percent, respectively, compared with placebo. In a subsequent analysis of participants with IGT who completed the DPP without developing diabetes, participants who reverted to normal glucose tolerance at least once during the DPP had a lower risk of diabetes during DPPOS than those who consistently had prediabetes (HR 0.44, 95% CI 0.37-0.55) [[7](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/7)]. This finding was unaffected by previous group assignment and suggests that reversion to normal glucose tolerance, even if brief, is associated with an enduring reduction in the risk of developing diabetes.

Follow-up after 15 years showed a continued benefit in the original lifestyle intervention and metformin groups (cumulative incidence of diabetes 55, 56, and 62 percent in the lifestyle, metformin, and placebo groups, respectively) [[18](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/18)].

Both lifestyle interventions and metformin therapy are effective prevention strategies (with similar efficacy in the subset of women with a history of gestational diabetes and when diabetes is defined by A1C ≥6.5 percent). In older individuals (≥60 years of age at baseline), the lifestyle intervention was particularly effective (72 percent reduction in diabetes compared with placebo), while metformin was relatively less effective. Conversely, metformin was particularly effective in individuals who were younger (<60 years of age), more obese (body mass index [BMI] >35 kg/m2), and at highest risk for developing diabetes.

Whether the DPP lifestyle intervention is practical for implementation on a national level is not known. A cost-effectiveness analysis using data from the DPP (three years) and the DPPOS (seven years) showed that lifestyle intervention was cost-effective compared with placebo [[19](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/19)]. Moreover, metformin was actually cost-saving. Numerous lifestyle intervention programs based upon the DPP, including one implemented through YMCAs, have been successfully initiated nationwide and demonstrated comparable weight loss results as in the original DPP. Long-term compliance with previous dietary interventions has been poor, and new behavioral strategies, like those used in the DPP, need to be identified to promote cost-effective and long-term weight loss. (See "Obesity in adults: Dietary therapy".)

**Exercise** — Although there is no one exercise prescription for all individuals, adults at high risk for diabetes are encouraged to perform 30 to 60 minutes of moderate-intensity, aerobic activity on most days of the week (at least 150 minutes of moderate-intensity, aerobic exercise per week).

The benefit of exercise in preventing diabetes has been demonstrated in several studies [[12,20-24](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/12,20-24)]. A meta-analysis of 28 prospective cohort studies of physical activity and type 2 diabetes reported a lower risk of developing diabetes with 150 min/week of moderate physical activity, including brisk walking, compared with being sedentary (relative risk 0.74, 95% CI 0.69-0.80) [[25](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/25)]. Additional benefits were seen with higher levels of activity (300 min/week, relative risk 0.64, 95% CI 0.56-0.73). The changes in glucose metabolism that can occur with exercise are discussed elsewhere. (See "Effects of exercise in adults with diabetes mellitus".)

In a subsequent prospective cohort study in men, either weight training or aerobic exercise for at least 150 minutes per week was associated with a lower risk of developing type 2 diabetes than no physical activity (relative risk 0.66, 95% CI 0.46-0.93 for weight training and relative risk 0.48, 95% CI 0.42-0.55 for aerobic exercise) [[26](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/26)]. Men who combined aerobic and weight training exercise had the greatest reduction in diabetes risk.

**Diet** — We suggest choosing a dietary pattern of healthful foods, such as the Dietary Approaches to Stop Hypertension (DASH) or Mediterranean-style diet, rather than focusing on a specific nutrient. This approach allows greater flexibility and personal preference in diet and may improve long-term adherence [[27](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/27)].

There are few trials examining the effects of diet alone (without weight loss) for the prevention of diabetes. In one trial, a Mediterranean diet appeared to reduce the incidence of diabetes independent of weight loss [[28-30](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/28-30)]. This trial, which included 7447 men and women, examined the effects of two different Mediterranean diets (one supplemented with extra virgin olive oil, the other with mixed nuts) versus a low-fat control diet on cardiovascular outcomes in men and women at high risk for cardiovascular disease (CVD) (eg, type 2 diabetes or three or more cardiovascular risk factors, such as smoking, hypertension, dyslipidemia, BMI ≥25 kg/m2, or family history of premature CVD) [[31](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/31)]. The incidence of diabetes could be ascertained (fasting plasma glucose [FPG] or two-hour oral glucose tolerance test [OGTT] during follow-up, and if results consistent with diabetes, a repeat measurement within three months) in a subgroup of 3541 individuals without diabetes at baseline [[29](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/29)]. After a median follow-up of four years, there was a decreased risk of developing diabetes in the groups assigned to the Mediterranean diets (80, 92, and 101 new cases of diabetes in the groups assigned to the Mediterranean diet supplemented with olive oil, Mediterranean diet supplemented with nuts, and the control diet, respectively [HRs 0.60, 95% CI 0.43-0.85 and 0.82, 95% CI 0.61-1.10 for the olive oil and nut groups, respectively, compared with controls]). Changes in weight and physical activity did not differ among the three groups.

Although these results suggest that a Mediterranean diet reduces the incidence of diabetes independent of weight loss, they should be interpreted with caution, as this was an exploratory analysis of a trial in which randomization was not stratified by diabetes status and which was stopped early due to benefit. These limitations combined with the small number of events (273) and the greater losses to follow-up in the control group may have resulted in overestimation of benefit. In addition, it remains uncertain which components of the Mediterranean diet offer the protective benefit or if the benefits result from an aggregation of effects. There is no single definition of a Mediterranean diet, but such diets are typically high in fruits, vegetables, whole grains, beans, nuts, and seeds; include olive oil as an important source of monounsaturated fat; and allow low to moderate wine consumption. There are typically low to moderate amounts of fish, poultry, and dairy products, with little red meat (see "Healthy diet in adults", section on 'Mediterranean diet'). Randomized trials of Mediterranean diets with diabetes as a primary endpoint are needed before they can be recommended for the prevention of diabetes.

In another trial, the Women's Health Initiative Dietary Modification Trial (WHI DMT), a low-fat diet (20 percent of caloric intake) did not reduce the incidence of diabetes compared with a usual diet (approximately 7 percent in each group) [[32](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/32)]. The difference in weight between the two groups was less than 2 kg. These results, which suffer from the absence of uniform glucose testing in the study, suggest that in average-risk women, a low-fat diet without weight reduction does not prevent diabetes.

**Smoking** — Several large, prospective, observational studies have shown that cigarette smoking increases the risk of type 2 diabetes. The effect of smoking cessation on diabetes risk is variable and may depend upon individual patient factors. Smoking cessation may reduce diabetes risk by reducing systemic inflammation. On the other hand, smoking cessation is often associated with weight gain, which will increase the risk of diabetes. This topic is reviewed in detail separately. (See "Risk factors for type 2 diabetes mellitus", section on 'Smoking'.)

**PHARMACOLOGIC THERAPY** — Drug therapy may be helpful in preventing type 2 diabetes in high-risk patients for whom lifestyle interventions fail or are not sustainable. However, the impact on cardiovascular disease (CVD) risk factors is less clear and varies with the individual drug. In addition, the long-term effects on cardiovascular events are unknown [[33](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/33)]. Furthermore, the long-term benefits and cost effectiveness of early pharmacologic treatment versus withholding treatment until diabetes develops are unproven [[34](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/34)].

Lifestyle changes, which are at least as effective and may be cheaper than most drugs used in prevention trials, are considered first-line preventive therapy [[35](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/35)]. Although lifestyle changes have not been shown to reduce morbidity or mortality thus far, lifestyle changes are generally beneficial and do not have adverse effects. (See 'Our approach' above and 'Lifestyle intervention' above and 'Guidelines' below.)

**Choice of drug therapy** — For select patients (age <60 years and/or body mass index [BMI] ≥35 kg/m2, women with a history of gestational diabetes) with impaired glucose tolerance (IGT), impaired fasting glucose (IFG), or A1C of 5.7 to 6.4 percent (39 to 46 mmol/mol), in whom lifestyle interventions fail to improve glycemic indices, we suggest metformin for diabetes prevention (table 3). (See 'Metformin' below.)

This is in agreement with the American Diabetes Association (ADA) guidelines [[36,37](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/36,37)]. (See 'Guidelines' below.)

**Metformin** — Metformin appears to be effective in reducing the risk of type 2 diabetes in patients with IGT, although it is less effective than lifestyle intervention (diet and exercise). This was illustrated in the Diabetes Prevention Program (DPP) of obese patients with IGT described above [[12](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/12)] (see 'Diabetes Prevention Program' above). Metformin reduced the rate of progression to diabetes (22 versus 29 percent with placebo at an average follow-up of three years). Metformin was effective in men and women and in all ethnic groups but was relatively ineffective in older patients and in those who were less overweight. Metformin was most effective in reducing the risk of diabetes in younger, obese subjects, and particularly in women with a history of gestational diabetes [[16](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/16)]. Metformin is relatively inexpensive and has no long-term, serious side effects. (See "Metformin in the treatment of adults with type 2 diabetes mellitus", section on 'Side effects'.)

In addition, a meta-analysis of randomized trials of metformin for the prevention of diabetes in individuals at high risk for diabetes showed that metformin decreased new-onset diabetes compared with placebo (odds ratio [OR] 0.6, 95% CI 0.5-0.8) [[38](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/38)]. Additional benefits of metformin included reductions in fasting plasma glucose (FPG), fasting insulin, and modest improvements in BMI, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides.

There has been concern that the diabetes prevention benefit of metformin might represent a delaying of the development of diabetes rather than true prevention since follow-up oral glucose tolerance testings (OGTTs) in most studies were done while patients were still taking the medication. In one follow-up study of 1247 subjects in the DPP metformin group (who had not developed diabetes), follow-up OGTTs after stopping metformin (on average 11 days) showed that approximately 75 percent of the metformin benefit persisted [[39](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/39)]. Although the authors suggested that this finding is consistent with prevention, longer drug-free trials are needed to firmly draw this conclusion.

Patients treated with metformin require at least annual monitoring (A1C or fasting glucose).

**Drugs not recommended for prevention** — Longer follow-up studies (at least 10 years) of pharmacologic therapy, as has been done with metformin in the DPP, with demonstration of reduced morbidity and mortality, are needed before other drugs can be recommended for the majority of patients at high risk for diabetes.

We do not administer the following drugs for prevention of diabetes in patients with IGT and/or IFG, given the modest benefit in reducing the incidence of diabetes in the short term, the side effects, and/orthe absence of proven cardiovascular benefit:

●Insulin [[40](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/40)]

●Liraglutide [[33,41](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/33,41)]

●Pioglitazone [[42](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/42)]

●Rosiglitazone [[43,44](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/43,44)]

●Orlistat [[45,46](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/45,46)]

●Alpha-glucosidase inhibitors (eg, acarbose, voglibose) [[47-49](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/47-49)]

●Vitamin D [[50](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/50)]

Other drugs that are not recommended for diabetes prevention, because of lack of preventive efficacy or limited efficacy, include nateglinide, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), and estrogen [[51-55](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/51-55)]. However, ACE inhibitors and ARBs are appropriate agents for initial treatment of hypertension in patients at high risk for diabetes. (See "Choice of drug therapy in primary (essential) hypertension".)

In addition to metformin, thiazolidinediones, alpha-glucosidase inhibitors, orlistat, and liraglutide have demonstrated preventive efficacy [[3,33,35,41,56](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/3,33,35,41,56)]. Although these drugs delay the onset of diagnosis of diabetes and therefore reduce the length of exposure of hyperglycemia, the benefit or harm of the intervention, independent of the effect on hyperglycemia, must be considered. As an example, thiazolidinediones are limited by adverse effects (fluid retention, weight gain, heart failure, possibly myocardial infarction [MI] for rosiglitazone, and possibly bladder cancer for pioglitazone) and alpha-glucosidase inhibitors by gastrointestinal side effects and poor long-term compliance. The use of thiazolidinediones, in particular, for the prevention of diabetes, may cause more net harm than benefit. In contrast, metformin is relatively inexpensive and safe and is especially effective in younger, more obese individuals [[34](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/34)]. (See "Thiazolidinediones in the treatment of diabetes mellitus", section on 'Safety' and "Alpha-glucosidase inhibitors and lipase inhibitors for treatment of diabetes mellitus", section on 'Adverse effects'.)

Although liraglutide has been shown to decrease cardiovascular outcomes in patients with type 2 diabetes and coexisting CVD (or at high risk for CVD), there are few data on cardiovascular outcomes in lower-risk patients and those without diabetes. (See "Glucagon-like peptide-1 receptor agonists for the treatment of type 2 diabetes mellitus", section on 'Cardiovascular effects'.)

**BARIATRIC SURGERY** — Surgical treatment of obese patients with diabetes results in a large degree of sustained weight loss and, in parallel, large improvements in blood glucose control (see "Bariatric operations for management of obesity: Indications and preoperative preparation" and "Management of persistent hyperglycemia in type 2 diabetes mellitus", section on 'Surgical treatment of obesity'). There are few data evaluating the ability of bariatric surgery to prevent diabetes in obese individuals. The Swedish Obese Subjects trial, a nonrandomized trial comparing bariatric surgery with usual care, was initiated in 1987. Among the 4047 obese individuals enrolled in the study, 2010 chose to undergo surgery for obesity (gastric banding, gastroplasty, or gastric bypass) while 2037 chose conventional treatment [[57](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/57)]. After 15 years, type 2 diabetes developed in 110 and 392 patients in the surgery and control groups, respectively (incidence rates of 6.8 and 28.4 cases per 1000 person-years) [[58](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/58)]. Baseline body mass index (BMI) did not influence the effect of bariatric surgery on the incidence of diabetes. The study had several limitations, including a lack of randomization and a high loss to follow-up rate (36 percent at 15 years). In addition, 31 percent of patients had not yet been followed for 15 years. Thus, the unadjusted 15-year participation rate was only 32.9 percent. The potential mechanisms for improvement in insulin resistance and beta cell function after bariatric surgery are uncertain and include a reduction in caloric intake, weight loss, and anatomic changes as a result of malabsorptive procedures. Additional studies are warranted.

**GUIDELINES**

●**American Diabetes Association (ADA)** – The ADA recommends lifestyle modification as the primary intervention in subjects with impaired glucose tolerance (IGT), impaired fasting glucose (IFG), or an A1C of 5.7 to 6.4 percent (39 to 46 mmol/mol) [[36,37](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/36,37)].

Specific goals include:

•Modest weight loss (5 to 10 percent of body weight)

•Moderate-intensity exercise (30 minutes daily)

•Smoking cessation

Because of its effectiveness, low cost, and long-term safety, the ADA recommends consideration of metformin for prevention of diabetes in individuals at highest risk for developing diabetes, such as those with IGT, IFG, or an A1C of 5.7 to 6.4 percent, particularly for those who benefited most from metformin during the Diabetes Prevention Program (DPP) (<60 years of age, body mass index [BMI] ≥35 kg/m2, women with a history of gestational diabetes) (table 3) [[37](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/37)]. In addition, assessment for and treatment of modifiable cardiovascular risk factors, such as hypertension and dyslipidemia, is important to reduce cardiometabolic risk.

Patients treated with metformin require at least annual monitoring (A1C or fasting glucose) for the development of diabetes.

The ADA recommendations for diabetes screening are reviewed separately. (See "Screening for type 2 diabetes mellitus", section on 'Screening recommendations by expert groups'.)

●**Community Preventive Services Task Force**– The task force recommends combined diet and physical activity programs for individuals at increased risk for type 2 diabetes [[59](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/59)]. An economic evaluation of 28 studies showed that such lifestyle programs were cost effective [[60](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/60)]. Costs were lower when lifestyle modification programs were delivered to groups in community or primary care settings. The use of pharmacologic therapy was not addressed.

●**National Institute for Health and Care Excellence (NICE)** – In the United Kingdom, NICE guidelines suggest metformin for patients with elevated fasting plasma glucose (FPG) (100 to 125 mg/dL [5.6 to 6.9 mmol/L]) or A1C (6 to 6.5 percent [42 to 47 mmol/mol]) who are unable to participate in lifestyle interventions or in whom FPG or A1C values deteriorate despite participation in a lifestyle intervention program [[61](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/61)]. They also suggest orlistat for those with a BMI >28 kg/m2whose FPG or A1C show deterioration, as part of an overall strategy to reduce weight. (See "Obesity in adults: Drug therapy", section on 'Orlistat'.)

**SOCIETY GUIDELINE LINKS** — Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Diabetes mellitus in adults" and "Society guideline links: Diabetes mellitus in children".)

…

**INFORMATION FOR PATIENTS** — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they 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. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

●Basics topics (see "Patient education: Type 2 diabetes (The Basics)" and "Patient education: Preventing type 2 diabetes (The Basics)")

●Beyond the Basics topics (see "Patient education: Diabetes mellitus type 2: Overview (Beyond the Basics)")

**SUMMARY AND RECOMMENDATIONS**

●The goals of diabetes prevention include delaying the onset of diabetes, preserving beta cell function, and preventing or delaying microvascular and perhaps cardiovascular complications. (See 'Goals of diabetes prevention' above.)

●In order to identify individuals who are appropriate candidates for preventive interventions, we measure glycated hemoglobin (A1C) or fasting plasma glucose (FPG) in adults at high risk for diabetes, including individuals >45 years of age with body mass index (BMI) >25 kg/m2 who have one or more additional risk factors for diabetes (eg, family history of diabetes mellitus in a first-degree relative, sedentary lifestyle, gestational diabetes, hypertension, dyslipidemia). (See 'Our approach' above.)

●Lifestyle modification (predominantly exercise and weight loss) successfully decreases the development of diabetes (table 4). Thus, we promote lifestyle changes (healthy diet and regular exercise) to all patients. Regular reinforcement of these benefits is important for successful compliance. Patients should also be encouraged to stop smoking. Patients who are at high risk (table 2) should be followed closely, with repeat examination and measurements of fasting blood glucose or A1C on an annual basis. (See 'Our approach' above and 'Lifestyle modification' above.)

●For select patients (age <60 years and/or BMI ≥35 kg/m2, women with a history of gestational diabetes) with impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or A1C of 5.7 to 6.4 percent, in whom lifestyle interventions fail to improve glycemic indices, we suggest metformin for diabetes prevention (table 2 and table 3) (**Grade 2B**). (See 'Our approach' above and 'Pharmacologic therapy' above.)

●Patients treated with metformin require at least annual monitoring (A1C or fasting glucose). (See 'Metformin' above and 'Guidelines' above.)

…

Use of UpToDate is subject to the [Subscription and License Agreement](https://www.uptodate.com/contents/license).

**REFERENCES**

|  |  |
| --- | --- |
| 1 | [Brancati FL, Kao WH, Folsom AR, et al. Incident type 2 diabetes mellitus in African American and white adults: the Atherosclerosis Risk in Communities Study. JAMA 2000; 283:2253.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/1) |
| 2 | [Gillett M, Royle P, Snaith A, et al. Non-pharmacological interventions to reduce the risk of diabetes in people with impaired glucose regulation: a systematic review and economic evaluation. Health Technol Assess 2012; 16:1.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/2) |
| 3 | [Selph S, Dana T, Blazina I, et al. Screening for type 2 diabetes mellitus: a systematic review for the U.S. Preventive Services Task Force. Ann Intern Med 2015; 162:765.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/3) |
| 4 | [Balk EM, Earley A, Raman G, et al. Combined Diet and Physical Activity Promotion Programs to Prevent Type 2 Diabetes Among Persons at Increased Risk: A Systematic Review for the Community Preventive Services Task Force. Ann Intern Med 2015; 163:437.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/4) |
| 5 | [Lindström J, Ilanne-Parikka P, Peltonen M, et al. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. Lancet 2006; 368:1673.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/5) |
| 6 | [Diabetes Prevention Program Research Group, Knowler WC, Fowler SE, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet 2009; 374:1677.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/6) |
| 7 | [Perreault L, Pan Q, Mather KJ, et al. Effect of regression from prediabetes to normal glucose regulation on long-term reduction in diabetes risk: results from the Diabetes Prevention Program Outcomes Study. Lancet 2012; 379:2243.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/7) |
| 8 | [Li G, Zhang P, Wang J, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. Lancet 2008; 371:1783.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/8) |
| 9 | [Li G, Zhang P, Wang J, et al. Cardiovascular mortality, all-cause mortality, and diabetes incidence after lifestyle intervention for people with impaired glucose tolerance in the Da Qing Diabetes Prevention Study: a 23-year follow-up study. Lancet Diabetes Endocrinol 2014; 2:474.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/9) |
| 10 | [Naci H, Ioannidis JP. Comparative effectiveness of exercise and drug interventions on mortality outcomes: metaepidemiological study. BMJ 2013; 347:f5577.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/10) |
| 11 | [Tuomilehto J, Lindström J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001; 344:1343.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/11) |
| 12 | [Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002; 346:393.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/12) |
| 13 | [Diabetes Prevention Program (DPP) Research Group. The Diabetes Prevention Program (DPP): description of lifestyle intervention. Diabetes Care 2002; 25:2165.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/13) |
| 14 | [Sussman JB, Kent DM, Nelson JP, Hayward RA. Improving diabetes prevention with benefit based tailored treatment: risk based reanalysis of Diabetes Prevention Program. BMJ 2015; 350:h454.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/14) |
| 15 | [Hamman RF, Wing RR, Edelstein SL, et al. Effect of weight loss with lifestyle intervention on risk of diabetes. Diabetes Care 2006; 29:2102.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/15) |
| 16 | [Ratner RE, Christophi CA, Metzger BE, et al. Prevention of diabetes in women with a history of gestational diabetes: effects of metformin and lifestyle interventions. J Clin Endocrinol Metab 2008; 93:4774.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/16) |
| 17 | [Diabetes Prevention Program Research Group. HbA1c as a predictor of diabetes and as an outcome in the diabetes prevention program: a randomized clinical trial. Diabetes Care 2015; 38:51.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/17) |
| 18 | [Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol 2015; 3:866.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/18) |
| 19 | [Diabetes Prevention Program Research Group. The 10-year cost-effectiveness of lifestyle intervention or metformin for diabetes prevention: an intent-to-treat analysis of the DPP/DPPOS. Diabetes Care 2012; 35:723.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/19) |
| 20 | [Helmrich SP, Ragland DR, Leung RW, Paffenbarger RS Jr. Physical activity and reduced occurrence of non-insulin-dependent diabetes mellitus. N Engl J Med 1991; 325:147.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/20) |
| 21 | [Lynch J, Helmrich SP, Lakka TA, et al. Moderately intense physical activities and high levels of cardiorespiratory fitness reduce the risk of non-insulin-dependent diabetes mellitus in middle-aged men. Arch Intern Med 1996; 156:1307.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/21) |
| 22 | [Hu FB, Sigal RJ, Rich-Edwards JW, et al. Walking compared with vigorous physical activity and risk of type 2 diabetes in women: a prospective study. JAMA 1999; 282:1433.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/22) |
| 23 | [Eriksson KF, Lindgärde F. Prevention of type 2 (non-insulin-dependent) diabetes mellitus by diet and physical exercise. The 6-year Malmö feasibility study. Diabetologia 1991; 34:891.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/23) |
| 24 | [Hu G, Lindström J, Valle TT, et al. Physical activity, body mass index, and risk of type 2 diabetes in patients with normal or impaired glucose regulation. Arch Intern Med 2004; 164:892.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/24) |
| 25 | [Smith AD, Crippa A, Woodcock J, Brage S. Physical activity and incident type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of prospective cohort studies. Diabetologia 2016; 59:2527.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/25) |
| 26 | [Grøntved A, Rimm EB, Willett WC, et al. A prospective study of weight training and risk of type 2 diabetes mellitus in men. Arch Intern Med 2012; 172:1306.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/26) |
| 27 | [Mozaffarian D. Dietary and Policy Priorities for Cardiovascular Disease, Diabetes, and Obesity: A Comprehensive Review. Circulation 2016; 133:187.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/27) |
| 28 | [Salas-Salvadó J, Bulló M, Babio N, et al. Reduction in the incidence of type 2 diabetes with the Mediterranean diet: results of the PREDIMED-Reus nutrition intervention randomized trial. Diabetes Care 2011; 34:14.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/28) |
| 29 | [Salas-Salvadó J, Bulló M, Estruch R, et al. Prevention of diabetes with Mediterranean diets: a subgroup analysis of a randomized trial. Ann Intern Med 2014; 160:1.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/29) |
| 30 | [Bloomfield HE, Koeller E, Greer N, et al. Effects on Health Outcomes of a Mediterranean Diet With No Restriction on Fat Intake: A Systematic Review and Meta-analysis. Ann Intern Med 2016; 165:491.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/30) |
| 31 | [Estruch R, Ros E, Salas-Salvadó J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. N Engl J Med 2013; 368:1279.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/31) |
| 32 | [Tinker LF, Bonds DE, Margolis KL, et al. Low-fat dietary pattern and risk of treated diabetes mellitus in postmenopausal women: the Women's Health Initiative randomized controlled dietary modification trial. Arch Intern Med 2008; 168:1500.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/32) |
| 33 | [Hemmingsen B, Sonne DP, Metzendorf MI, Richter B. Dipeptidyl-peptidase (DPP)-4 inhibitors and glucagon-like peptide (GLP)-1 analogues for prevention or delay of type 2 diabetes mellitus and its associated complications in people at increased risk for the development of type 2 diabetes mellitus. Cochrane Database Syst Rev 2017; 5:CD012204.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/33) |
| 34 | [Nathan DM, Berkwits M. Trials that matter: rosiglitazone, ramipril, and the prevention of type 2 diabetes. Ann Intern Med 2007; 146:461.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/34) |
| 35 | [Gillies CL, Abrams KR, Lambert PC, et al. Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. BMJ 2007; 334:299.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/35) |
| 36 | [Nathan DM, Davidson MB, DeFronzo RA, et al. Impaired fasting glucose and impaired glucose tolerance: implications for care. Diabetes Care 2007; 30:753.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/36) |
| 37 | [Standards of Medical Care in Diabetes-2016: Summary of Revisions. Diabetes Care 2016; 39 Suppl 1:S4.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/37) |
| 38 | [Salpeter SR, Buckley NS, Kahn JA, Salpeter EE. Meta-analysis: metformin treatment in persons at risk for diabetes mellitus. Am J Med 2008; 121:149.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/38) |
| 39 | [Diabetes Prevention Program Research Group. Effects of withdrawal from metformin on the development of diabetes in the diabetes prevention program. Diabetes Care 2003; 26:977.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/39) |
| 40 | [ORIGIN Trial Investigators, Gerstein HC, Bosch J, et al. Basal insulin and cardiovascular and other outcomes in dysglycemia. N Engl J Med 2012; 367:319.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/40) |
| 41 | [le Roux CW, Astrup A, Fujioka K, et al. 3 years of liraglutide versus placebo for type 2 diabetes risk reduction and weight management in individuals with prediabetes: a randomised, double-blind trial. Lancet 2017; 389:1399.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/41) |
| 42 | [DeFronzo RA, Tripathy D, Schwenke DC, et al. Pioglitazone for diabetes prevention in impaired glucose tolerance. N Engl J Med 2011; 364:1104.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/42) |
| 43 | [DREAM (Diabetes REduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators, Gerstein HC, Yusuf S, et al. Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. Lancet 2006; 368:1096.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/43) |
| 44 | [DREAM Trial Investigators. Incidence of diabetes following ramipril or rosiglitazone withdrawal. Diabetes Care 2011; 34:1265.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/44) |
| 45 | [Torgerson JS, Hauptman J, Boldrin MN, Sjöström L. XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. Diabetes Care 2004; 27:155.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/45) |
| 46 | [Heymsfield SB, Segal KR, Hauptman J, et al. Effects of weight loss with orlistat on glucose tolerance and progression to type 2 diabetes in obese adults. Arch Intern Med 2000; 160:1321.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/46) |
| 47 | [Chiasson JL, Josse RG, Gomis R, et al. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. Lancet 2002; 359:2072.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/47) |
| 48 | [Kirkman MS, Shankar RR, Shankar S, et al. Treating postprandial hyperglycemia does not appear to delay progression of early type 2 diabetes: the Early Diabetes Intervention Program. Diabetes Care 2006; 29:2095.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/48) |
| 49 | [Kawamori R, Tajima N, Iwamoto Y, et al. Voglibose for prevention of type 2 diabetes mellitus: a randomised, double-blind trial in Japanese individuals with impaired glucose tolerance. Lancet 2009; 373:1607.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/49) |
| 50 | [Pittas AG, Chung M, Trikalinos T, et al. Systematic review: Vitamin D and cardiometabolic outcomes. Ann Intern Med 2010; 152:307.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/50) |
| 51 | [NAVIGATOR Study Group, Holman RR, Haffner SM, et al. Effect of nateglinide on the incidence of diabetes and cardiovascular events. N Engl J Med 2010; 362:1463.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/51) |
| 52 | [DREAM Trial Investigators, Bosch J, Yusuf S, et al. Effect of ramipril on the incidence of diabetes. N Engl J Med 2006; 355:1551.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/52) |
| 53 | [NAVIGATOR Study Group, McMurray JJ, Holman RR, et al. Effect of valsartan on the incidence of diabetes and cardiovascular events. N Engl J Med 2010; 362:1477.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/53) |
| 54 | [Kanaya AM, Herrington D, Vittinghoff E, et al. Glycemic effects of postmenopausal hormone therapy: the Heart and Estrogen/progestin Replacement Study. A randomized, double-blind, placebo-controlled trial. Ann Intern Med 2003; 138:1.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/54) |
| 55 | [Margolis KL, Bonds DE, Rodabough RJ, et al. Effect of oestrogen plus progestin on the incidence of diabetes in postmenopausal women: results from the Women's Health Initiative Hormone Trial. Diabetologia 2004; 47:1175.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/55) |
| 56 | [Padwal R, Majumdar SR, Johnson JA, et al. A systematic review of drug therapy to delay or prevent type 2 diabetes. Diabetes Care 2005; 28:736.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/56) |
| 57 | [Sjöström L, Lindroos AK, Peltonen M, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med 2004; 351:2683.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/57) |
| 58 | [Carlsson LM, Peltonen M, Ahlin S, et al. Bariatric surgery and prevention of type 2 diabetes in Swedish obese subjects. N Engl J Med 2012; 367:695.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/58) |
| 59 | [Pronk NP, Remington PL, Community Preventive Services Task Force. Combined Diet and Physical Activity Promotion Programs for Prevention of Diabetes: Community Preventive Services Task Force Recommendation Statement. Ann Intern Med 2015; 163:465.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/59) |
| 60 | [Li R, Qu S, Zhang P, et al. Economic Evaluation of Combined Diet and Physical Activity Promotion Programs to Prevent Type 2 Diabetes Among Persons at Increased Risk: A Systematic Review for the Community Preventive Services Task Force. Ann Intern Med 2015; 163:452.](https://www.uptodate.com/contents/prevention-of-type-2-diabetes-mellitus/abstract/60) |
| 61 | NICE public health guidance. <http://publications.nice.org.uk/preventing-type-2-diabetes-risk-identification-and-interventions-for-individuals-at-high-risk-ph38/recommendations#recommendation-3-risk-identification-stage-1>(Accessed on May 02, 2013). |

Topic 1774 Version 33.0