



### 3. Prevention or Delay of Type 2 Diabetes: Standards of Medical Care in Diabetes—2021

American Diabetes Association

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The American Diabetes Association (ADA) “Standards of Medical Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee, a multidisciplinary expert committee (<https://doi.org/10.2337/dc21-SPPC>), are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations, please refer to the Standards of Care Introduction (<https://doi.org/10.2337/dc21-SINT>). Readers who wish to comment on the Standards of Care are invited to do so at [professional.diabetes.org/SOC](https://professional.diabetes.org/SOC).

For guidelines related to screening for increased risk for type 2 diabetes (prediabetes), please refer to Section 2 “Classification and Diagnosis of Diabetes” (<https://doi.org/10.2337/dc21-S002>). For guidelines related to screening, diagnosis, and management of type 2 diabetes in youth, please refer to Section 13 “Children and Adolescents” (<https://doi.org/10.2337/dc21-S013>).

#### Recommendation

**3.1** At least annual monitoring for the development of type 2 diabetes in those with prediabetes is suggested. **E**

Screening for prediabetes and type 2 diabetes risk through an informal assessment of risk factors (**Table 2.3**) or with an assessment tool, such as the American Diabetes Association risk test (**Fig. 2.1**), is recommended to guide providers on whether performing a diagnostic test for prediabetes (**Table 2.5**) and previously undiagnosed type 2 diabetes (**Table 2.2**) is appropriate (see Section 2 “Classification and Diagnosis of Diabetes,” <https://doi.org/10.2337/dc21-S002>). Testing high-risk patients for prediabetes is warranted because the laboratory assessment is safe and reasonable in cost, substantial time exists before the development of type 2 diabetes and its complications during which one can intervene, and there is an effective means of preventing type 2 diabetes in those determined to have prediabetes with an A1C 5.7–6.4% (39–47 mmol/mol), impaired glucose tolerance, or impaired fasting glucose. Using A1C to screen for prediabetes may be problematic in the presence of certain hemoglobinopathies or conditions that affect red blood cell turnover. See Section 2 “Classification and Diagnosis of Diabetes” (<https://doi.org/10.2337/dc21-S002>) and Section 6 “Glycemic Targets” (<https://care.diabetesjournals.org/lookup/doi/10.2337/dc21-S006>) for additional details on the appropriate use of the A1C test.

#### LIFESTYLE BEHAVIOR CHANGE FOR DIABETES PREVENTION

##### Recommendations

**3.2** Refer patients with prediabetes to an intensive lifestyle behavior change program modeled on the Diabetes Prevention Program to achieve and maintain

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7% loss of initial body weight and increase moderate-intensity physical activity (such as brisk walking) to at least 150 min/week. **A**

- 3.3** A variety of eating patterns can be considered to prevent diabetes in individuals with prediabetes. **B**
- 3.4** Based on patient preference, certified technology-assisted diabetes prevention programs may be effective in preventing type 2 diabetes and should be considered. **B**
- 3.5** Given the cost-effectiveness of lifestyle behavior modification programs for diabetes prevention **A**, such diabetes prevention programs should be covered by third-party payers.

### The Diabetes Prevention Program

Several major randomized controlled trials, including the Diabetes Prevention Program (DPP) (1), the Finnish Diabetes Prevention Study (DPS) (2), and the Da Qing Diabetes Prevention Study (Da Qing study) (3), demonstrate that lifestyle/behavioral therapy featuring an individualized reduced-calorie meal plan is highly effective in preventing type 2 diabetes and improving other cardiometabolic markers (such as blood pressure, lipids, and inflammation) (4). The strongest evidence for diabetes prevention in the U.S. comes from the DPP trial (1). The DPP demonstrated that an intensive lifestyle intervention could reduce the risk of incident type 2 diabetes by 58% over 3 years. Follow-up of three large studies of lifestyle intervention for diabetes prevention has shown sustained reduction in the risk of conversion to type 2 diabetes: 39% reduction at 30 years in the Da Qing study (5), 43% reduction at 7 years in the Finnish DPS (2), and 34% reduction at 10 years (6) and 27% reduction at 15 years (7) in the U.S. Diabetes Prevention Program Outcomes Study (DPPOS).

The two major goals of the DPP intensive lifestyle intervention were to achieve and maintain a minimum of 7% weight loss and 150 min of physical activity per week similar in intensity to brisk walking. The DPP lifestyle intervention was a goal-based intervention: all participants were given the same weight loss and physical activity goals, but individualization was permitted in the specific methods used to achieve the goals (8). Although weight loss was the most important factor to reduce the risk of

incident diabetes, it was also found that achieving the target behavioral goal of at least 150 min of physical activity per week, even without weight loss, reduced the incidence of type 2 diabetes by 44% (9).

The 7% weight loss goal was selected because it was feasible to achieve and maintain and likely to lessen the risk of developing diabetes. Participants were encouraged to achieve the 7% weight loss during the first 6 months of the intervention. However, longer-term (4-year) data reveal maximal prevention of diabetes observed at about 7–10% weight loss (9). The recommended pace of weight loss was 1–2 lb/week. Calorie goals were calculated by estimating the participant's initial weight and subtracting 500–1,000 calories/day (depending on initial body weight). The initial focus was on reducing total dietary fat. After several weeks, the concept of calorie balance and the need to restrict calories as well as fat was introduced (8).

The goal for physical activity was selected to approximate at least 700 kcal/week expenditure from physical activity. For ease of translation, this goal was described as at least 150 min of moderate-intensity physical activity per week similar in intensity to brisk walking. Participants were encouraged to distribute their activity throughout the week with a minimum frequency of three times per week and at least 10 min per session. A maximum of 75 min of strength training could be applied toward the total 150 min/week physical activity goal (8).

To implement the weight loss and physical activity goals, the DPP used an individual model of treatment rather than a group-based approach. This choice was based on a desire to intervene before participants had the possibility of developing diabetes or losing interest in the program. The individual approach also allowed for tailoring of interventions to reflect the diversity of the population (8).

The DPP intervention was administered as a structured core curriculum followed by a more flexible maintenance program of individual sessions, group classes, motivational campaigns, and restart opportunities. The 16-session core curriculum was completed within the first 24 weeks of the program and included sections on lowering calories, increasing physical activity, self-monitoring, maintaining healthy lifestyle behaviors, and psychological, social, and motivational challenges.

Further details are available regarding the core curriculum sessions (8).

### Nutrition

The dietary counseling for weight loss in the DPP intervention included a reduction of total dietary fat and calories to prevent diabetes for those at high risk for developing type 2 diabetes with an overweight or obese BMI (1,8,9). However, evidence suggests that there is not an ideal percentage of calories from carbohydrate, protein, and fat for all people to prevent diabetes; therefore, macronutrient distribution should be based on an individualized assessment of current eating patterns, preferences, and metabolic goals (10). Based on other intervention trials, a variety of eating patterns characterized by the totality of food and beverages consumed (10,11) may also be appropriate for patients with prediabetes (10), including Mediterranean-style and low-carbohydrate eating plans (12–15). Observational studies have also shown that vegetarian, plant-based (may include some animal products), and Dietary Approaches to Stop Hypertension (DASH) eating patterns are associated with a lower risk of developing type 2 diabetes (16–19). Evidence suggests that the overall quality of food consumed (as measured by the Healthy Eating Index, Alternative Healthy Eating Index, and DASH score), with an emphasis on whole grains, legumes, nuts, fruits, and vegetables and minimal refined and processed foods, is also associated with a lower risk of type 2 diabetes (18,20–23). As is the case for those with diabetes, individualized medical nutrition therapy (see Section 5 “Facilitating Behavior Change and Well-being to Improve Health Outcomes,” <https://doi.org/10.2337/dc21-S005>, for more detailed information) is effective in lowering A1C in individuals diagnosed with prediabetes (24).

### Physical Activity

Just as 150 min/week of moderate-intensity physical activity, such as brisk walking, showed beneficial effects in those with prediabetes (1), moderate-intensity physical activity has been shown to improve insulin sensitivity and reduce abdominal fat in children and young adults (25,26). On the basis of these findings, providers are encouraged to promote a DPP-style program, including a focus on physical activity, to all individuals who have been identified to be at an increased risk of

type 2 diabetes. In addition to aerobic activity, an exercise regimen designed to prevent diabetes may include resistance training (8,27,28). Breaking up prolonged sedentary time may also be encouraged, as it is associated with moderately lower postprandial glucose levels (29,30). The preventive effects of exercise appear to extend to the prevention of gestational diabetes mellitus (GDM) (31).

### Delivery and Dissemination of Lifestyle Behavior Change for Diabetes Prevention

Because the intensive lifestyle intervention in the DPP was effective in preventing type 2 diabetes for those at high risk for the disease and lifestyle behavior change programs for diabetes prevention were shown to be cost-effective, broader efforts to disseminate scalable lifestyle behavior change programs for diabetes prevention with coverage by third-party payers ensued (32–36). Group delivery of DPP content in community or primary care settings has demonstrated the potential to reduce overall program costs while still producing weight loss and diabetes risk reduction (37–41).

The Centers for Disease Control and Prevention (CDC) developed the National Diabetes Prevention Program (National DPP), a resource designed to bring such evidence-based lifestyle change programs for preventing type 2 diabetes to communities ([www.cdc.gov/diabetes/prevention/index.htm](http://www.cdc.gov/diabetes/prevention/index.htm)). This online resource includes locations of CDC-recognized diabetes prevention lifestyle change programs (available at [https://nccd.cdc.gov/DDT\\_DPRP/Programs.aspx](https://nccd.cdc.gov/DDT_DPRP/Programs.aspx)). To be eligible for this program, patients must have a BMI in the overweight range and be at risk for diabetes based on laboratory testing or a positive risk test (available at [www.cdc.gov/prediabetes/takethetest/](http://www.cdc.gov/prediabetes/takethetest/)). Results from the CDC's National DPP during the first 4 years of implementation are promising and demonstrate cost-efficacy (42). The CDC has also developed the Diabetes Prevention Impact Tool Kit (available at <https://nccd.cdc.gov/toolkit/diabetesimpact>) to help organizations assess the economics of providing or covering the National DPP lifestyle change program (43). In an effort to expand preventive services using a cost-effective model that began in April 2018, the Centers for Medicare & Medicaid Services expanded Medicare reimbursement coverage for the National DPP lifestyle intervention to organizations

recognized by the CDC that become Medicare suppliers for this service (online at <https://innovation.cms.gov/innovation-models/medicare-diabetes-prevention-program>). The locations of Medicare DPPs are available online at <https://innovation.cms.gov/innovation-models/medicare-diabetes-prevention-program/mdpp-map>. To qualify for Medicare coverage, patients must have a BMI in the overweight range and laboratory testing consistent with prediabetes in the last year. Medicaid coverage of the DPP lifestyle intervention is also expanding on a state-by-state basis.

While CDC-recognized lifestyle change programs and Medicare DPP services have the advantages of having met minimum quality standards and being reimbursed by various payers, there have been lower retention rates in such programs reported for younger adults and racial/ethnic minority populations (44). Therefore, other programs and modalities of lifestyle behavior changes for achieving the goals for diabetes prevention may also be appropriate and efficacious based on patient preferences and availability. The use of community health workers to support DPP efforts has been shown to be effective with cost savings (45,46) (see Section 1 “Improving Care and Promoting Health in Populations,” <https://doi.org/10.2337/dc21-S001>, for more information). The use of community health workers may facilitate adoption of lifestyle behavior changes for diabetes prevention while bridging barriers related to social determinants of health, though coverage by third-party payers sometimes remains problematic. Registered dietitian nutritionists (RDN) can help individuals with prediabetes reach their goals of improving eating habits, increasing moderate-intensity physical activity, and achieving 7–10% loss of initial body weight (10,47–49). Individualized medical nutrition therapy (see Section 5 “Facilitating Behavior Change and Well-being to Improve Health Outcomes,” <https://doi.org/10.2337/dc21-S005>, for more detailed information) is also effective in improving glycemia in individuals diagnosed with prediabetes (24,47). Furthermore, these trials involving medical nutrition therapy for patients with prediabetes found significant reductions in weight, waist circumference, and glycemia. Individuals with prediabetes can benefit from being referred to an RDN for individualized medical nutrition

therapy upon diagnosis and at regular intervals throughout their treatment regimen (49,50). Other allied health professionals, like pharmacists and diabetes care and education specialists, also have the capability of delivering lifestyle behavior change programs and may be considered for diabetes prevention efforts (51,52).

Technology-assisted programs may effectively deliver the DPP lifestyle program, reducing weight and, therefore, diabetes risk (53–58). Such technology-assisted programs may deliver content through smartphone, web-based applications, and telehealth, and may be an acceptable and efficacious option to bridge barriers particularly for low-income and rural patients; however, not all programs are effective in helping people reach targets for diabetes prevention (53,59–61). The CDC Diabetes Prevention Recognition Program (DPRP) ([www.cdc.gov/diabetes/prevention/requirements-recognition.htm](http://www.cdc.gov/diabetes/prevention/requirements-recognition.htm)) certifies technology-assisted modalities as effective vehicles for DPP-based programs; such programs must use an approved curriculum, include interaction with a coach, and attain the DPRP outcomes of participation, physical activity reporting, and weight loss. Therefore, providers should consider referring patients with prediabetes to certified technology-assisted DPP programs based on patient preference.

## PHARMACOLOGIC INTERVENTIONS

### Recommendations

- 3.6** Metformin therapy for prevention of type 2 diabetes should be considered in those with prediabetes, especially for those with BMI  $\geq 35$  kg/m<sup>2</sup>, those aged <60 years, and women with prior gestational diabetes mellitus. **A**
- 3.7** Long-term use of metformin may be associated with biochemical vitamin B12 deficiency; consider periodic measurement of vitamin B12 levels in metformin-treated patients, especially in those with anemia or peripheral neuropathy. **B**

Because weight loss through behavior changes in diet and exercise alone can be difficult to maintain long term (6), people

being treated with weight loss therapy may benefit from support and additional pharmacotherapeutic options, if needed. Various pharmacologic agents used to treat diabetes have been evaluated for diabetes prevention. Metformin,  $\alpha$ -glucosidase inhibitors, liraglutide, thiazolidinediones, and insulin have been shown to lower the risk of diabetes in those with prediabetes (62–67); whereas diabetes prevention was not seen with nateglinide (68). In addition, several weight loss medications like orlistat and phenteramine-topiramate have also been shown in research studies to decrease the incidence of diabetes to various degrees in those with prediabetes (69,70). Studies of other pharmacologic agents have shown some efficacy in diabetes prevention with valsartan but no efficacy with ramipril, anti-inflammatory drugs, or vitamin D in preventing diabetes (71–75). However, no pharmacologic agent has been approved by the U.S. Food and Drug Administration specifically for diabetes prevention. The risk versus benefit of each medication must be weighed. Metformin has the strongest evidence base (1) and demonstrated long-term safety as pharmacologic therapy for diabetes prevention (76). For other drugs, cost, side effects, and durable efficacy require consideration.

Metformin was overall less effective than lifestyle modification in the DPP, though group differences declined over time in the DPPOS (7), and metformin may be cost-saving over a 10-year period (34). During initial follow-up in the DPP, metformin was as effective as lifestyle modification in participants with BMI  $\geq 35$  kg/m<sup>2</sup> and in younger participants aged 25–44 years (1). In the DPP, for women with a history of GDM, metformin and intensive lifestyle modification led to an equivalent 50% reduction in diabetes risk (77), and both interventions remained highly effective during a 10-year follow-up period (78). By the time of the 15-year follow-up (DPPOS), exploratory analyses demonstrated that participants with a higher baseline fasting glucose ( $\geq 110$  mg/dL vs. 95–109 mg/dL) and women with a history of GDM (vs. women without a history of GDM) experienced higher risk reductions with metformin (compared with the placebo arm) (79). In the Indian Diabetes Prevention Programme (IDPP-1), metformin and the lifestyle intervention reduced diabetes risk similarly at 30 months; of note, the lifestyle intervention in IDPP-1 was less intensive

than that in the DPP (80). Based on findings from the DPP, metformin should be recommended as an option for high-risk individuals (e.g., those with a history of GDM or those with BMI  $\geq 35$  kg/m<sup>2</sup>). Consider monitoring vitamin B12 levels in those taking metformin chronically to check for possible deficiency (81,82) (see Section 9 “Pharmacologic Approaches to Glycemic Treatment,” <https://doi.org/10.2337/dc21-S009>, for more details).

## PREVENTION OF VASCULAR DISEASE AND MORTALITY

### Recommendation

**3.8** Prediabetes is associated with heightened cardiovascular risk; therefore, screening for and treatment of modifiable risk factors for cardiovascular disease are suggested. **B**

People with prediabetes often have other cardiovascular risk factors, including hypertension and dyslipidemia (83), and are at increased risk for cardiovascular disease (84,85). Evaluation for tobacco use and referral for tobacco cessation, if indicated, should be part of routine care for those at risk for diabetes. Of note, the years immediately following smoking cessation may represent a time of increased risk for diabetes (86–88), a time when patients should be monitored for diabetes development and receive the concurrent evidence-based lifestyle behavior change for diabetes prevention described in this section. See Section 5 “Facilitating Behavior Change and Well-being to Improve Health Outcomes” (<https://doi.org/10.2337/dc21-S005>) for more detailed information. The lifestyle interventions for weight loss in study populations at risk for type 2 diabetes have shown a reduction in cardiovascular risk factors and the need for medications used to treat these cardiovascular risk factors (89,90). In longer-term follow-up, lifestyle interventions for diabetes prevention also prevented the development of microvascular complications among women enrolled in the DPPOS and in the study population enrolled in the China Da Qing Diabetes Prevention Outcome Study (7,91). The lifestyle intervention in the latter study was also efficacious in preventing cardiovascular disease and mortality at 23 and 30 years of follow-up (3,5). Treatment goals and

therapies for hypertension and dyslipidemia in the primary prevention of cardiovascular disease for people with prediabetes should be based on their level of cardiovascular risk, and increased vigilance is warranted to identify and treat these and other cardiovascular risk factors (92).

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