3. Prevention or Delay of Type 2 Diabetes and Associated Comorbidities: *Standards of Medical Care in Diabetes—2022*

*American Diabetes Association Professional Practice Committee**

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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/dc22-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/dc22-SINT). Readers who wish to comment on the Standards of Care are invited to do so at 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/dc22-S002). For guidelines related to screening, diagnosis, and management of type 2 diabetes in youth, please refer to Section 14, "Children and Adolescents" (https://doi.org/10.2337/dc22-S014).

Recommendation

3.1 Monitor for the development of type 2 diabetes in those with prediabetes at least annually, modified based on individual risk/benefit assessment. **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/dc22-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. The utility of A1C screening for prediabetes and diabetes may be limited in the presence of hemoglobinopathies and conditions that affect red blood cell turnover. See

**A complete list of members of the American Diabetes Association Professional Practice Committee can be found at https://doi.org/10.2337/dc22-SPPC.*

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Section 2, "Classification and Diagnosis of Diabetes" (https://doi.org/10.2337/dc22-S002), and Section 6, "Glycemic Targets" (https://doi.org/10.2337/dc22-S006), for additional details on the appropriate use and limitations of A1C testing.

LIFESTYLE BEHAVIOR CHANGE FOR DIABETES PREVENTION

Recommendations

3.2 Refer adults with overweight/obesity at high risk of type 2 diabetes, as typified by the Diabetes Prevention Program (DPP), to an intensive lifestyle behavior change program consistent with the DPP to achieve and maintain 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 Given the cost-effectiveness of lifestyle behavior modification programs for diabetes prevention, such diabetes prevention programs should be offered to patients. **A** Diabetes prevention programs should be covered by third-party payers and inconsistencies in access should be addressed.

3.5 Based on patient preference, certified technology-assisted diabetes prevention programs may be effective in preventing type 2 diabetes and should be considered. **B**

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 with individualized reduced-calorie meal plan is highly effective in preventing or delaying 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 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 progression 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 achieving the weight loss goal, 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. Further analysis suggests maximal prevention of diabetes with at least 7–10% weight loss (9). The recommended pace of weight loss was 1–2 lb/week. Calorie goals were calculated by estimating the daily calories needed to maintain 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 flexible maintenance program of individual counseling, group sessions, motivational campaigns, and restart opportunities. The 16-session core curriculum was completed within the first 24 weeks of the program and included sessions on lowering calories, increasing physical activity, self-monitoring, maintaining healthy lifestyle behaviors, and guidance on managing psychological, social, and motivational challenges. Further details are available regarding the core curriculum sessions (8).

Nutrition

Dietary counseling for weight loss in the DPP lifestyle intervention arm included a reduction of total dietary fat and calories (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 habitually 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 (18,20–22). 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/dc22-S005, for more detailed information) is effective in lowering A1C in individuals diagnosed with prediabetes (23).

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 (24,25). 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 (8,26,27). Breaking up prolonged sedentary time may also be encouraged, as it is associated with moderately lower postprandial glucose levels (28,29). The preventive effects of exercise appear to extend to the prevention of gestational diabetes mellitus (GDM) (30).

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 among 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 (31–35). 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 (36–40).

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). This online resource includes locations of CDC-recognized diabetes prevention lifestyle change programs (available at www.cdc.gov/diabetes/prevention/find-a-program.html). 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, a previous diagnosis of GDM, or a positive risk test (available at 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 (41). The CDC has also developed the Diabetes Prevention Impact Tool Kit (available at nccd.cdc.gov/toolkit/diabetesimpact) to help organizations assess the economics of providing or covering the National DPP lifestyle change program (42). 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 (at innovation.cms.gov/innovation-models/medicare-diabetes-prevention-program). The locations of Medicare DPPs are available online at innovation.cms.gov/innovation-models/medicare-diabetes-prevention-program/mdpp-map. To qualify for Medicare coverage, patients must have BMI >25 kg/m^2 (or BMI $>$23 kg/m^2 if self-identified as Asian) 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 behavioral counseling programs, including Medicare DPP services, have met minimum quality standards and are reimbursed by many payers, there have been lower retention rates reported for younger adults and racial/ethnic minority populations (43). Therefore, other programs and modalities of behavioral counseling 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 and cost-effective (44,45) (see Section 1, "Improving Care and Promoting Health in Populations," https://doi.org/10.2337/dc22-S001, for more information). The use of community health workers may facilitate adoption of behavior changes for diabetes prevention while bridging barriers related to social determinants of health, though coverage by third-party payers remains problematic. Counseling by registered dietitians/registered dietitian nutritionists (RDNs) has been shown to help individuals with prediabetes improve eating habits, increase physical activity, and achieve 7–10% weight loss (10,46–48). Individualized medical nutrition therapy (see Section 5, "Facilitating Behavior Change and Well-being to Improve Health Outcomes," https://doi.org/10.2337/dc22-S005, for more detailed information) is also effective in improving glycemia in individuals diagnosed with prediabetes (23,46). Furthermore, trials involving medical nutrition therapy for patients with prediabetes found significant reductions in weight, waist circumference, and glycemia. Individuals with prediabetes can benefit from referral to an RDN for individualized medical nutrition therapy upon diagnosis and at regular intervals throughout their treatment regimen (48,49). Other allied health professionals, such as pharmacists and diabetes care and education specialists, may be considered for diabetes prevention efforts (50,51).

Technology-assisted programs may effectively deliver the DPP program (52–57). 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 (52,58–60). The CDC Diabetes Prevention Recognition Program (DPRP) (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 DPP 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 adults with prediabetes, as typified by the Diabetes Prevention Program, especially those aged 25–59 years with BMI ≥35 kg/m^2, higher fasting plasma glucose (e.g., ≥110 mg/dL), and higher A1C (e.g., ≥6.0%), and in 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, α-glucosidase inhibitors, liraglutide, thiazolidinediones, testosterone (61), and insulin have been shown to lower the incidence of diabetes in specific populations (62–67), whereas diabetes prevention was not seen with nateglinide (68). In addition, several weight loss medications like orlistat and phentermine 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 in preventing diabetes with ramipril or anti-inflammatory drugs (71–74). Although the Vitamin D and Type 2 Diabetes (D2d) prospective randomized controlled trial showed no significant benefit of vitamin D versus placebo on the progression to type 2 diabetes in individuals at high risk (75), post hoc analyses and meta-analyses suggest a potential benefit in specific populations (75–78). Further research is needed to define patient characteristics and clinical indicators where vitamin D supplementation may be of benefit (61).

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 (79). For other drugs, cost, side effects, treatment goals, 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 (33). During initial follow-up in the DPP, metformin was as effective as lifestyle modification in participants with BMI ≥35 kg/m^2 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 (80), and both interventions remained highly effective during a 10-year follow-up period (81). By the time of the 15-year follow-up (DPPOS), exploratory analyses demonstrated that participants with a higher baseline fasting glucose (≥110 mg/dL vs. 95–109 mg/dL), those with a higher A1C (6.0–6.4% vs. <6.0%), and women with a history of GDM (vs. women without a history of GDM) experienced higher risk reductions with metformin, identifying subgroups of participants that benefitted the most from metformin (82). In the Indian Diabetes Prevention Program (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 (83). 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 ≥35 kg/m^2). Consider periodic monitoring of vitamin B12 levels in those taking metformin chronically to check for possible deficiency (84,85) (see Section 9, "Pharmacologic Approaches to Glycemic Treatment," https://doi.org/10.2337/dc22-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 (86), and are at increased risk for cardiovascular disease (87,88). 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 (89–91), 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/dc22-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 (92,93). 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 (7,94). 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 (95).

PATIENT-CENTERED CARE GOALS

Recommendation

3.9 In adults with overweight/obesity at high risk of type 2 diabetes, care goals should include weight loss or prevention of weight gain, minimizing progression of hyperglycemia, and attention to cardiovascular risk and associated comorbidites. **B**

Individualized risk/benefit should be considered in screening, intervention, and monitoring for the prevention or delay of type 2 diabetes and associated comorbidities. Multiple factors, including age, BMI, and other comorbidities, may influence risk of progression to diabetes and lifetime risk of complications (96,97). In the DPP, which enrolled high-risk individuals with impaired glucose tolerance, elevated fasting glucose, and elevated BMI, the crude incidence of diabetes within the placebo arm was 11.0 cases per 100 person-years, with a cumulative 3-year incidence of diabetes of 28.9% (1). In the community-based Atherosclerosis Risk in Communities (ARIC) study, observational follow-up of older adults (mean age 75 years) with laboratory evidence of prediabetes (based on A1C 5.7–6.4% and/or fasting glucose 100–125 mg/dL) but not meeting specific BMI criteria found much lower progression to diabetes over 6 years: 9% of those with A1C-defined prediabetes, 8% with impaired fasting glucose (97).

Thus, it is important to individualize the risk/benefit of intervention and consider person-centered goals. Risk models have explored risk-based benefit, in general finding higher benefit of intervention in those at highest risk (9). Diabetes prevention and observational studies highlight several key principles, which may guide patient-centered goals. In the DPP, which enrolled a high-risk population meeting criteria for overweight/obesity, weight loss was an important mediator of diabetes prevention or delay, with greater metabolic benefit generally seen with greater weight loss (9,98). In the DPP/DPPOS, progression to diabetes, duration of diabetes, and mean level of glycemia were important determinants of development of microvascular complications (7). Furthermore, ability to achieve normal glucose regulation, even once, during the DPP was associated with a lower risk of diabetes and lower risk of microvascular complications (99). Observational follow up of the Da Qing study also showed that regression from impaired glucose tolerance to normal glucose tolerance or remaining with impaired glucose tolerance rather than progressing to type 2 diabetes at the end of the 6-year intervention trial resulted in significantly lower risk of cardiovascular disease and microvascular disease over 30 years (100). Prediabetes is associated with increased cardiovascular disease and mortality (88), emphasizing the importance of attending to cardiovascular risk in this population.

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