5. Prevention or Delay of Type 2 Diabetes

American Diabetes Association

For guidelines related to screening for increased risk for type 2 diabetes (prediabetes), please refer to Section 2 "Classification and Diagnosis of Diabetes."

Recommendations

- At least annual monitoring for the development of diabetes in those with prediabetes is suggested. **E**
- Patients with prediabetes should be referred to an intensive behavioral lifestyle intervention program modeled on the Diabetes Prevention Program 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**
- Technology-assisted tools including Internet-based social networks, distance learning, DVD-based content, and mobile applications may be useful elements of effective lifestyle modification to prevent diabetes. **B**
- Given the cost-effectiveness of diabetes prevention, such intervention programs should be covered by third-party payers. **B**

Screening for prediabetes and type 2 diabetes 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 2.4**) and previously undiagnosed type 2 diabetes (**Table 2.2**) is appropriate (see Section 2 "Classification and Diagnosis of Diabetes"). Those determined to be at high risk for type 2 diabetes, including people with A1C 5.7–6.4% (39–47 mmol/mol), impaired glucose tolerance, or impaired fasting glucose, are ideal candidates for diabetes prevention efforts. At least annual monitoring for the development of diabetes in those with prediabetes is suggested.

LIFESTYLE INTERVENTIONS

The Diabetes Prevention Program

The strongest evidence for diabetes prevention comes from the Diabetes Prevention Program (DPP) (1). The DPP demonstrated that an intensive lifestyle intervention could reduce the incidence of 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 rate of conversion to type 2 diabetes: 43% reduction at 20 years in the Da Qing study (2), 43% reduction at 7 years in the Finnish Diabetes Prevention Study (DPS) (1), and 34% reduction at 10 years in the U.S. Diabetes Prevention Program Outcomes Study (DPPOS) (3).

The two major goals of the DPP intensive, behavioral, 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 (4).

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. 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 (4).

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 with 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 (4).

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 (4).

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. For further details on the core curriculum sessions, refer to ref. 4.

Nutrition

Reducing caloric intake is of paramount importance for those at high risk for developing type 2 diabetes, though recent evidence suggests that the quality of fats consumed in the diet is more important than the total quantity of dietary fat (5–7). For example, the Mediterranean diet, which is relatively high in monounsaturated fats, may help to prevent type 2 diabetes (8–10).

Whereas overall healthy low-calorie eating patterns should be encouraged, there is also some evidence that particular dietary components impact diabetes risk. Data suggest that whole grains may help to prevent type 2 diabetes (11). Higher intakes of nuts (12), berries (13), yogurt (14), coffee, and tea (15) are associated with reduced diabetes risk. Conversely, red meats and sugar-sweetened beverages are associated with an increased risk of type 2 diabetes (6).

As is the case for those with diabetes, individualized medical nutrition therapy (see Section 4 "Lifestyle Management" for more detailed information) is effective in lowering A1C in individuals diagnosed with prediabetes (16).

Physical Activity

Just as 150 min/week of moderate-intensity physical activity, such as brisk walking, showed beneficial effects in those with prediabetes (17), moderate-intensity physical activity has been shown to improve insulin sensitivity and reduce abdominal fat in children and young adults (18,19). On the basis of these findings, providers are encouraged to promote a DPP-style program, including its 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 (1,20). Breaking up prolonged sedentary time may also be encouraged, as it is associated with moderately lower postprandial glucose levels (21,22). The preventative effects of exercise appear to extend to the prevention of gestational diabetes mellitus (GDM) (23).

Technology Assistance to Deliver Lifestyle Interventions

New information technology platforms may effectively deliver the core components of the DPP (24–26). Initial studies have validated DVD-based content delivery (27). This has been corroborated in a primary care patient population (28). Recent studies support content delivery through virtual small groups (29), Internet-driven social networks (30,31), cellular phones, and other mobile devices. Mobile applications for weight loss and diabetes prevention have been validated for their ability to reduce A1C in the setting of prediabetes (31). The Centers for Disease Control and Prevention (CDC) Diabetes Prevention Recognition Program (DPRP) (http://www.cdc.gov/diabetes/prevention/recognition/index.htm) has begun to certify electronic and mobile health-based modalities as effective vehicles for DPP-based interventions that may be considered alongside more traditional face-to-face and coach-driven programs. A recent study showed that an all-mobile approach to administering DPP content can be effective as a prevention tool, at least over the short term, in overweight and obese individuals at high risk for diabetes (32).

Cost-effectiveness

A cost-effectiveness model suggested that the lifestyle intervention used in the DPP was cost-effective (33). Actual cost data from the DPP and DPPOS confirmed this (34). Group delivery of DPP content in community settings has the potential to reduce overall program costs while still producing weight loss and diabetes risk reduction (35,36). The CDC helps to coordinate the National Diabetes Prevention Program, a resource designed to bring evidence-based lifestyle change programs for preventing type 2 diabetes to communities (http://www.cdc.gov/diabetes/prevention/index.htm). On 7 July 2016, the Centers for Medicare and Medicaid Services (CMS) proposed expanded Medicare reimbursement coverage for DPP programs in an effort to expand preventive services using a cost-effective model (https://www.cms.gov/site-search/search-results.html?q=diabetes%20prevention).

PHARMACOLOGIC INTERVENTIONS

> *Recommendations*
> - Metformin therapy for prevention of type 2 diabetes should be considered in those with prediabetes, especially for those with BMI ≥35 kg/m^2, those aged <60 years, women with prior gestational diabetes mellitus, and/or those with rising A1C despite lifestyle intervention. **A**
> - Long-term use of metformin may be associated with biochemical vitamin B12 deficiency, and periodic measurement of vitamin B12 levels should be considered in metformin-treated patients, especially in those with anemia or peripheral neuropathy. **B**

Pharmacologic agents including metformin, α-glucosidase inhibitors, orlistat, glucagon-like peptide 1 (GLP-1) receptor

agonists, and thiazolidinediones have each been shown to decrease incident diabetes to various degrees in those with prediabetes. Metformin has the strongest evidence base and demonstrated long-term safety as pharmacologic therapy for diabetes prevention (37). For other drugs, cost, side effects, and durable efficacy require consideration.

Metformin was less effective than lifestyle modification in the DPP and DPPOS but may be cost-saving over a 10-year period (34). It was as effective as lifestyle modification in participants with BMI $\geq$35 kg/m^2 but not significantly better than placebo in those over 60 years of age (17). In the DPP, for women with history of GDM, metformin and intensive lifestyle modification led to an equivalent 50% reduction in diabetes risk (38), and both interventions remained highly effective during a 10-year follow-up period (39). Metformin should be recommended as an option for high-risk individuals (e.g., those with a history of GDM, those who are very obese, and/or those with relatively more hyperglycemia) and/or those with rising A1C despite lifestyle intervention. Consider monitoring B12 levels in those taking metformin chronically to check for possible deficiency (see Section 8 "Pharmacologic Approaches to Glycemic Treatment" for more details).

PREVENTION OF CARDIOVASCULAR DISEASE

Recommendation
- Screening for and treatment of modifiable risk factors for cardiovascular disease is suggested for those with prediabetes. **B**

People with prediabetes often have other cardiovascular risk factors, including hypertension and dyslipidemia, and are at increased risk for cardiovascular disease (40). Although treatment goals for people with prediabetes are the same as for the general population, increased vigilance is warranted to identify and treat these and other cardiovascular risk factors (e.g., smoking).

DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT

Recommendation
- Diabetes self-management education and support programs may be appropriate venues for people with prediabetes to receive education and support to develop and maintain behaviors that can prevent or delay the development of diabetes. **B**

As for those with established diabetes, the standards for diabetes self-management education and support (see Section 4 "Lifestyle Management") can also apply to people with prediabetes. Currently, there are significant barriers to the provision of education and support to those with prediabetes. However, the strategies for supporting successful behavior change, and the healthy behaviors recommended for people with prediabetes are comparable to those for diabetes. Although reimbursement remains a barrier, studies show that providers of diabetes self-management education and support are particularly well equipped to assist people with prediabetes in developing and maintaining behaviors that can prevent or delay the development of diabetes (16,41).

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