

# Screening for Prediabetes and Type 2 Diabetes

## US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

**IMPORTANCE** An estimated 13% of all US adults (18 years or older) have diabetes, and 34.5% meet criteria for prediabetes. The prevalences of prediabetes and diabetes are higher in older adults. Estimates of the risk of progression from prediabetes to diabetes vary widely, perhaps because of differences in the definition of prediabetes or the heterogeneity of prediabetes. Diabetes is the leading cause of kidney failure and new cases of blindness among adults in the US. It is also associated with increased risks of cardiovascular disease, nonalcoholic fatty liver disease, and nonalcoholic steatohepatitis and was estimated to be the seventh leading cause of death in the US in 2017. Screening asymptomatic adults for prediabetes and type 2 diabetes may allow earlier detection, diagnosis, and treatment, with the ultimate goal of improving health outcomes.

**OBJECTIVE** To update its 2015 recommendation, the USPSTF commissioned a systematic review to evaluate screening for prediabetes and type 2 diabetes in asymptomatic, nonpregnant adults and preventive interventions for those with prediabetes.

**POPULATION** Nonpregnant adults aged 35 to 70 years seen in primary care settings who have overweight or obesity (defined as a body mass index  $\geq 25$  and  $\geq 30$ , respectively) and no symptoms of diabetes.

**EVIDENCE ASSESSMENT** The USPSTF concludes with moderate certainty that screening for prediabetes and type 2 diabetes and offering or referring patients with prediabetes to effective preventive interventions has a moderate net benefit.

**CONCLUSIONS AND RECOMMENDATION** The USPSTF recommends screening for prediabetes and type 2 diabetes in adults aged 35 to 70 years who have overweight or obesity. Clinicians should offer or refer patients with prediabetes to effective preventive interventions. (B recommendation)

JAMA. 2021;326(8):736-743. doi:10.1001/jama.2021.12531

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### Summary of Recommendation

Asymptomatic adults aged 35 to 70 years who have overweight or obesity	The USPSTF recommends screening for prediabetes and type 2 diabetes in adults aged 35 to 70 years who have overweight or obesity. Clinicians should offer or refer patients with prediabetes to effective preventive interventions.	B
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See the Figure for a more detailed summary of the recommendations for clinicians. USPSTF indicates US Preventive Services Task Force.

See the Summary of Recommendation figure.

### Importance

According to the Centers for Disease Control and Prevention 2020 National Diabetes Statistics Report, an estimated 13% of all US adults (18 years or older) have diabetes, and 34.5% meet criteria for prediabetes.<sup>1</sup> The prevalence of prediabetes and diabetes are higher in older adults. Of persons with diabetes, 21.4% were not aware of or did not report having diabetes, and only 15.3% of persons with prediabetes reported being told by a health profes-

sional that they had this condition.<sup>1</sup> Estimates of the risk of progression from prediabetes to diabetes vary widely, perhaps because of differences in the definition of prediabetes or the heterogeneity of prediabetes.<sup>2</sup> A large cohort study of 77 107 persons with prediabetes reported that the risk of developing diabetes increased with increasing hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) level and with increasing body mass index (BMI).<sup>3</sup>

Diabetes is the leading cause of kidney failure and new cases of blindness among adults in the US. It is also associated with increased risks of cardiovascular disease (CVD), nonalcoholic fatty liver

**Table. Summary of USPSTF Rationale**

Rationale	Assessment
Benefits of detection and early intervention	<ul style="list-style-type: none"> <li>The USPSTF found inadequate direct evidence that screening for type 2 diabetes or prediabetes leads to improvements in mortality or cardiovascular morbidity.</li> <li>The USPSTF found adequate evidence that interventions for newly diagnosed diabetes have a moderate benefit in reducing all-cause mortality, diabetes-related mortality, and risk of myocardial infarction after 10 to 20 years of intervention.</li> <li>The USPSTF found convincing evidence that preventive interventions, in particular lifestyle interventions, in persons identified as having prediabetes have a moderate benefit in reducing the progression to type 2 diabetes, as well as reducing other CVD risk factors such as blood pressure and lipid levels. Other preventive interventions are also effective in reducing the progression to type 2 diabetes without necessarily reducing other CVD risk factors.</li> </ul>
Harms of early detection and intervention and treatment	The USPSTF found adequate evidence to bound the harms of screening for prediabetes and type 2 diabetes and treatment of screen-detected or recently diagnosed prediabetes and type 2 diabetes as no greater than small.
USPSTF assessment	The USPSTF concludes with moderate certainty that screening for prediabetes and type 2 diabetes and offering or referring patients with prediabetes to effective preventive interventions has a moderate net benefit.

Abbreviations: CVD, cardiovascular disease; USPSTF, US Preventive Services Task Force.

**Figure. Clinician Summary: Screening for Prediabetes and Type 2 Diabetes**

What does the USPSTF recommend?	Adults aged 35 to 70 years who have overweight or obesity: <ul style="list-style-type: none"> <li>Screen for prediabetes and type 2 diabetes, and offer or refer patients with prediabetes to effective preventive interventions. <b>Grade: B</b></li> </ul>
To whom does this recommendation apply?	Nonpregnant adults aged 35 to 70 years who have overweight or obesity and no symptoms of diabetes.
What's new?	The USPSTF has lowered the starting age of screening from 40 to 35 years.
How to implement this recommendation?	<ol style="list-style-type: none"> <li><b>Assess risk:</b> <ul style="list-style-type: none"> <li>Obtain height and weight measurements to determine whether patient has overweight or obesity. Overweight and obesity are defined as a BMI <math>\geq 25</math> and <math>\geq 30</math>, respectively.</li> </ul> </li> <li><b>Screen:</b> <ul style="list-style-type: none"> <li>If the patient is aged 35 to 70 years and has overweight or obesity. Consider screening at an earlier age if the patient is from a population with a disproportionately high prevalence of diabetes (American Indian/Alaska Native, Black, Hawaiian/Pacific Islander, Hispanic/Latino), and at a lower BMI (<math>\geq 23</math>) if the patient is Asian American.</li> <li>Screening tests for prediabetes and type 2 diabetes include measurement of fasting plasma glucose or HbA<sub>1c</sub> level or an oral glucose tolerance test.</li> </ul> </li> </ol>
How often?	The optimal screening interval for adults with an initial normal glucose test result is uncertain. Screening every 3 years may be a reasonable approach for adults with normal blood glucose levels.
What are other relevant USPSTF recommendations?	The USPSTF has made a recommendation on behavioral weight loss interventions to prevent obesity-related morbidity and mortality in adults with a BMI $\geq 30$ . This recommendation is available at <a href="https://www.uspreventiveservicestaskforce.org">https://www.uspreventiveservicestaskforce.org</a>
Where to read the full recommendation statement?	Visit the USPSTF website ( <a href="https://www.uspreventiveservicestaskforce.org">https://www.uspreventiveservicestaskforce.org</a> ) to read the full recommendation statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others.

*The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or situation.*

BMI indicates body mass index (calculated as weight in kilograms divided by height in meters squared); HbA<sub>1c</sub>, hemoglobin A<sub>1c</sub>; USPSTF, US Preventive Services Task Force.

disease, and nonalcoholic steatohepatitis<sup>4-6</sup> and was estimated to be the seventh leading cause of death in the US in 2017.<sup>1</sup> Screening asymptomatic adults for prediabetes and type 2 diabetes may allow earlier detection, diagnosis, and treatment, with the ultimate goal of improving health outcomes.

### USPSTF Assessment of Magnitude of Net Benefit

The US Preventive Services Task Force (USPSTF) concludes with moderate certainty that screening for prediabetes and type 2

diabetes and offering or referring patients with prediabetes to effective preventive interventions has a **moderate net benefit** (Table).

See the Table for more information on the USPSTF recommendation rationale and assessment and the eFigure in the Supplement for information on the recommendation grade. See the Figure for a summary of the recommendation for clinicians. For more details on the methods the USPSTF uses to determine the net benefit, see the USPSTF Procedure Manual.<sup>7</sup>

## Practice Considerations

### Patient Population Under Consideration

This recommendation applies to nonpregnant adults aged 35 to 70 years seen in primary care settings who have overweight or obesity (defined as a BMI  $\geq 25$  [calculated as weight in kilograms divided by height in meters squared] and  $\geq 30$ , respectively) and no symptoms of diabetes.

### Assessment of Risk

Overweight and obesity are the strongest risk factors for developing prediabetes and type 2 diabetes in adults.<sup>8</sup> Other risk factors include older age, family history, history of gestational diabetes, history of polycystic ovarian syndrome, and dietary and lifestyle factors.<sup>8,9</sup> The prevalence of diabetes is higher among American Indian/Alaska Native (14.7%), Asian (9.2%), Hispanic/Latino (12.5%), and non-Hispanic Black (11.7%) persons than among non-Hispanic White (7.5%) persons.<sup>1</sup> Disparities in diabetes prevalence are the result of a variety of factors. A large body of evidence demonstrates strong associations between prevalence of diabetes and social factors such as socioeconomic status, food environment, and physical environment.<sup>10</sup> The higher prevalence of diabetes in Asian persons may be related to differences in body composition. A difference in body fat composition in Asian persons results in underestimation of risk based on BMI thresholds used to define overweight in the US.<sup>11</sup>

Clinicians should consider screening at an earlier age in persons from groups with disproportionately high incidence and prevalence (American Indian/Alaska Native, Asian American, Black, Hispanic/Latino, or Native Hawaiian/Pacific Islander persons) or in persons who have a family history of diabetes, a history of gestational diabetes, or a history of polycystic ovarian syndrome, and at a lower BMI in Asian American persons.<sup>11,12</sup> Data suggest that a BMI of 23 or greater may be an appropriate cut point in Asian American persons.<sup>13</sup>

### Screening Tests

Prediabetes and type 2 diabetes can be detected by measuring fasting plasma glucose or HbA<sub>1c</sub> level, or with an oral glucose tolerance test. A fasting plasma glucose level of 126 mg/dL (6.99 mmol/L) or greater, an HbA<sub>1c</sub> level of 6.5% or greater, or a 2-hour postload glucose level of 200 mg/dL (11.1 mmol/L) or greater are consistent with the diagnosis of type 2 diabetes. A fasting plasma glucose level of 100 to 125 mg/dL (5.55-6.94 mmol/L), an HbA<sub>1c</sub> level of 5.7% to 6.4%, or a 2-hour postload glucose level of 140 to 199 mg/dL (7.77-11.04 mmol/L) are consistent with prediabetes.<sup>14</sup>

HbA<sub>1c</sub> is a measure of long-term blood glucose concentration and is not affected by acute changes in glucose levels caused by stress

or illness. Because HbA<sub>1c</sub> measurements do not require fasting, they are more convenient than using a fasting plasma glucose level or an oral glucose tolerance test. Both fasting plasma glucose and HbA<sub>1c</sub> levels are simpler to measure than performing an oral glucose tolerance test. The oral glucose tolerance test is done in the morning in a fasting state; blood glucose concentration is measured 2 hours after ingestion of a 75-g oral glucose load. The diagnosis of prediabetes or type 2 diabetes should be confirmed with repeat testing before starting interventions.<sup>14</sup>

### Screening Intervals

Evidence on the optimal screening interval for adults with an initial normal glucose test result is limited. Cohort and modeling studies suggest that screening every 3 years may be a reasonable approach for adults with normal blood glucose levels.<sup>15-17</sup>

### Preventive Interventions

Both lifestyle interventions that focus on diet, physical activity, or both and metformin have demonstrated efficacy in preventing or delaying progression to diabetes in persons with prediabetes.<sup>2</sup> However, metformin has not been approved for this specific indication by the US Food and Drug Administration.

Clinicians and patients may want to consider several other factors as they discuss preventive interventions for prediabetes. In the Diabetes Prevention Program (DPP) study (which serves as a model for many lifestyle intervention programs in the US), lifestyle intervention was more effective than metformin in preventing or delaying diabetes. In addition to preventing progression to diabetes, lifestyle interventions have a beneficial effect on weight, blood pressure, and lipid levels (increasing high-density lipoprotein cholesterol levels and lowering triglyceride levels). Metformin has a beneficial effect on weight, but it does not appear to affect blood pressure, or to consistently improve lipid levels.<sup>2</sup> In post hoc analyses of the DPP, lifestyle intervention was effective in all subgroups, while similar analyses of the DPP and the DPP Outcomes Study (DPPOS) suggest that metformin was effective in persons younger than 60 years, in persons with a BMI of 35 or greater, in persons with a fasting plasma glucose level of 110 mg/dL (6.11 mmol/L) or greater, or in persons with a history of gestational diabetes.<sup>18,19</sup>

### Additional Tools and Resources

The Centers for Disease Control and Prevention has several resources related to the diagnosis, prevention, and treatment of prediabetes and type 2 diabetes available at <https://www.cdc.gov/diabetes/index.html> and <https://www.cdc.gov/diabetes/prevent-type-2/index.html>, as well as information on the National Diabetes Prevention Program at <https://www.cdc.gov/diabetes/prevention/index.html>.

The National Institutes of Health has several resources related to screening, diagnosis, prevention, and management of prediabetes and type 2 diabetes available at <https://www.niddk.nih.gov/health-information/professionals/clinical-tools-patient-management/diabetes>.

The Community Preventive Services Task Force recommends diet and physical activity promotion programs to prevent type 2 diabetes among persons at increased risk (<https://www.thecommunityguide.org/findings/diabetes-combined-diet-and-physical-activity-promotion-programs-prevent-type-2-diabetes>).

### Other Related USPSTF Recommendations

The USPSTF recommends offering or referring adults with a BMI of 30 or greater to intensive, multicomponent behavioral interventions.<sup>20</sup>

### Update of Previous USPSTF Recommendation

This recommendation replaces the 2015 USPSTF recommendation statement on screening for abnormal blood glucose levels and type 2 diabetes in asymptomatic adults. In 2015, the USPSTF recommended screening for abnormal blood glucose levels as part of cardiovascular risk assessment in adults aged 40 to 70 years who have overweight or obesity. The USPSTF also recommended that clinicians should offer or refer patients with abnormal blood glucose levels to intensive behavioral counseling interventions to promote a healthful diet and physical activity.<sup>21</sup> For the current recommendation statement, the USPSTF recommends screening for prediabetes and type 2 diabetes in adults aged 35 to 70 years who have overweight or obesity, and that clinicians should offer or refer patients with prediabetes to effective preventive interventions. Based on data suggesting that the incidence of diabetes increases at age 35 years compared with younger ages<sup>22</sup> and on the evidence for the benefits of interventions for newly diagnosed diabetes (discussed below), the USPSTF has decreased the age at which to begin screening to 35 years.

### Supporting Evidence

#### Scope of Review

To update its 2015 recommendation statement, the USPSTF commissioned a systematic review<sup>2,23</sup> of the evidence on screening for prediabetes and type 2 diabetes in asymptomatic, nonpregnant adults and preventive interventions for those with prediabetes. This review focused on direct evidence on the benefits and harms of screening for prediabetes and type 2 diabetes and the benefits and harms of interventions (such as behavioral counseling focused on diet, physical activity, or both, or pharmacotherapy for glycemic, blood pressure, or lipid control, compared with no treatment or usual care) for screen-detected prediabetes and type 2 diabetes or recently diagnosed type 2 diabetes. The review also looked at the evidence on the effectiveness of interventions for prediabetes to delay or prevent progression to type 2 diabetes.

#### Benefits of Early Detection and Treatment

##### Screening for Diabetes

The USPSTF found 2 randomized clinical trials, the Anglo-Danish-Dutch Study of Intensive Treatment In People with Screen Detected Diabetes in Primary Care (ADDITION)-Cambridge (n = 20 184 participants)<sup>24-26</sup> and the Ely study (n = 4936 participants),<sup>27-29</sup> that evaluated the effect of screening for diabetes on health outcomes. ADDITION-Cambridge was a cluster randomized trial that randomly assigned practices to no screening, screening followed by intensive treatment of screen-detected diabetes (HbA<sub>1c</sub> target <7.0%, blood pressure target ≤135/85 mm Hg, and cholesterol targets, and low-dose aspirin use unless contraindicated), or screening followed by routine care of screen-detected diabetes. In the Ely study, the treatment of persons with screen-

detected diabetes was managed by primary care clinicians as they deemed appropriate. Neither trial found a reduction in all-cause or type-specific mortality with screening compared with no screening over approximately 10 years of follow-up, which notably may have been too short to detect an effect on health outcomes. Neither trial found statistically significant differences in cardiovascular events, quality of life, nephropathy, or neuropathy between screening and control groups, but data collection for these outcomes was limited to a minority of trial participants.

##### Effect of Interventions for Screen-Detected Type 2 Diabetes or Prediabetes on Health Outcomes

One randomized clinical trial (ADDITION-Europe)<sup>30-33</sup> evaluated interventions for persons with screen-detected type 2 diabetes. It found no difference over 5 to 10 years of follow-up between an intensive multifactorial intervention aimed at controlling glucose, blood pressure, and cholesterol levels and routine care in the risk of all-cause mortality, cardiovascular-related mortality, occurrence of a first cardiovascular event, chronic kidney disease, visual impairment, or neuropathy. Follow-up may have been too short in this trial to detect an effect on the health outcomes of interest.

Thirty-eight trials that assessed behavioral or pharmacologic interventions for prediabetes reported on health outcomes.<sup>2,23</sup> Overall, trials found no statistically significant differences in all-cause mortality or CVD events, and no difference or only small improvements in quality of life scores that are not likely clinically significant. Follow-up duration in most of these trials may have been too short to detect an effect on health outcomes. One trial, the Da Qing Diabetes Prevention Study comparing a 6-year lifestyle intervention (diet, exercise, or both) with control, found lower all-cause mortality and CVD-related mortality in the combined intervention groups vs control group at 23 and 30 years of follow-up, though not at 20 years of follow-up (all-cause mortality: 28.1% vs 38.4%; hazard ratio [HR], 0.71 [95% CI, 0.51 to 0.99] at 23 years and 45.7% vs 56.3%; HR, 0.74 [95% CI, 0.61 to 0.89] at 30 years; CVD-related mortality: 11.9% vs 19.6%; HR, 0.59 [95% CI, 0.36 to 0.96] at 23 years and 29.6% vs 22.0%; HR, 0.67 [95% CI, 0.48 to 0.94] at 30 years).<sup>34,35</sup> However, this trial was limited by baseline differences between intervention and control groups that were likely to bias results in favor of the intervention.

##### Effect of Interventions for Newly or Recently Diagnosed Type 2 Diabetes on Health Outcomes

The UK Prospective Diabetes Study (UKPDS) and 2 other studies reported the effect of interventions for newly diagnosed diabetes on health outcomes. The UKPDS found that all-cause mortality, diabetes-related mortality, and myocardial infarction were improved with intensive glucose control with sulfonylureas or insulin over 20 years (10-year posttrial assessment) but not at shorter follow-up. Intensive glucose control was associated with a decreased risk for all-cause mortality (relative risk [RR], 0.87 [95% CI, 0.79 to 0.96]), diabetes-related mortality (RR, 0.83 [95% CI, 0.73 to 0.96]), and myocardial infarction (RR, 0.85 [95% CI, 0.74 to 0.97]) over 20 years.<sup>36,37</sup> For persons who had overweight, intensive glucose control with metformin decreased all-cause mortality (RR, 0.64 [95% CI, 0.45 to 0.91]), diabetes-related mortality (RR, 0.58 [95% CI, 0.37 to 0.91]), and myocardial infarction (RR, 0.61 [95% CI, 0.41 to 0.89]) at the 10-year follow-up, and benefits were maintained during the subsequent 10 years of posttrial follow-up.<sup>37,38</sup>

The other 2 studies found no statistically significant difference between intervention and control groups in all-cause mortality and risk of myocardial infarction; however, these studies were limited by short duration of follow-up, small study size, or both. The Diabetes Education and Self Management for Ongoing and Newly Diagnosed (DESMOND) trial<sup>39,40</sup> found no statistically significant difference in all-cause mortality between persons randomly assigned to group education and those randomly assigned to the control group over 1 and 3 years of follow-up. Another trial (n = 150)<sup>41</sup> found no statistically significant difference in myocardial infarction over 7 years of follow-up.

#### Effect of Interventions for Prediabetes on Progression to Diabetes

Twenty-three trials compared lifestyle interventions with a control group for delaying or preventing the onset of type 2 diabetes.<sup>2,23</sup> In most trials (18 trials), the lifestyle interventions focused on both diet/nutrition and physical activity, and most (18 trials) delivered high-contact lifestyle interventions, defined as intervention contact time of more than 360 minutes. Most of the trials focused on persons with impaired glucose tolerance. Meta-analysis of the 23 trials found that lifestyle interventions were associated with a reduction in progression to diabetes (pooled RR, 0.78 [95% CI, 0.69 to 0.88]; n = 12 915 participants). In post hoc analyses, the DPP reported that lifestyle intervention was effective in all subgroups and treatment effects did not differ by age, sex, race and ethnicity, or BMI after 3 years of follow-up.<sup>18</sup>

Several trials also reported the effects of lifestyle interventions on intermediate outcomes. In pooled analyses, lifestyle interventions were associated with a reduction in weight (pooled weighted mean difference [WMD], -1.2 kg [95% CI, -1.6 to -0.7 kg]) and BMI (pooled WMD, -0.54 [95% CI, -0.76 to -0.33]). In addition, lifestyle interventions were associated with a reduction in both systolic and diastolic blood pressure (pooled WMD, -1.7 mm Hg [95% CI, -2.6 to -0.8 mm Hg] and pooled WMD, -1.2 mm Hg [95% CI, -2.0 to -0.4 mm Hg], respectively), and high-contact lifestyle interventions were associated with reduced triglyceride levels and increased high-density lipoprotein cholesterol levels.<sup>2,23</sup>

Fifteen trials evaluated pharmacologic interventions to delay or prevent diabetes.<sup>2,23</sup> For metformin, meta-analysis of 3 trials found that it was associated with a reduction in the incidence of diabetes (pooled RR, 0.73 [95% CI, 0.64 to 0.83]).<sup>2,23</sup> In post hoc analyses, the DPP reported that the effect associated with use of metformin compared with placebo was not statistically significantly different after 3 years of follow-up for subgroups defined by age, sex, or race and ethnicity. The analysis reported a statistically significant effect modification by BMI, with greater effect on diabetes incidence for persons with a higher BMI (eg, reduction in diabetes incidence, 53% [95% CI, 36% to 65%] for BMI  $\geq 35$  vs 3% [95% CI, -36% to 30%] for BMI of 22 to <30).<sup>18</sup> For both thiazolidinediones and  $\alpha$ -glucosidase inhibitors, meta-analysis of 3 trials each found associations with a reduction in the incidence of diabetes, but the results were limited by imprecision and inconsistency across trials.<sup>2,23</sup> Other pharmacologic interventions seeking to delay or prevent diabetes have been studied, but only in 1 study each.<sup>2</sup>

Two trials reported the effects of metformin on intermediate outcomes. The DPP (n = 2155) reported greater decreases in weight for persons receiving metformin compared with those receiving placebo (-2.0 kg [95% CI, -3.2 to -0.8 kg]).<sup>18</sup> The

Promotora Effectiveness Versus Metformin Trial (PREVENT-DM) of metformin also found that participants in the intervention group had greater decreases in weight and BMI, but the differences were not statistically significant.<sup>42</sup> Both trials reported no significant difference in blood pressure among persons receiving metformin compared with placebo.<sup>42,43</sup> The DPP reported a greater increase in high-density lipoprotein levels for persons receiving metformin compared with those receiving placebo after 3 years (difference between groups, 0.40 [95% CI, 0.15 to 0.65]) but no difference between groups for other lipid levels,<sup>43</sup> whereas the PREVENT-DM study (n = 92) found no statistically significant difference in lipid levels between metformin and control groups at 1 year.<sup>42</sup>

#### Harms of Screening and Treatment

Some of the trials reporting on the benefits of screening and interventions for prediabetes and type 2 diabetes also reported harms. Overall, the ADDITION-Cambridge and Ely trials, and a pilot study of ADDITION-Cambridge,<sup>28,29,44-46</sup> did not find clinically significant differences between screening and control groups in measures of anxiety, depression, worry, or self-reported health. However, the results suggest possible short-term increases in anxiety (at 6 weeks) among persons screened and diagnosed with diabetes compared with those screened and not diagnosed with diabetes.

Harms of interventions for screen-detected or recently diagnosed type 2 diabetes were sparsely reported and, when reported, were rare and not significantly different between intervention and control groups across trials.<sup>2,23</sup> The UKPDS trial reported 1 patient of 911 in the intervention group receiving insulin who died from hypoglycemia, and serious hypoglycemic events requiring medical attention in 6 of 619 participants (1%) receiving chlorpropamide, 9 of 615 (1.5%) receiving glibenclamide, 16 of 911 (1.8%) receiving insulin, and 6 of 896 (0.7%) in the conventional care group.<sup>36</sup>

Several trials reported on harms associated with interventions for prediabetes. Four studies of pharmacotherapy interventions reported on any hypoglycemia and found no difference between interventions and placebo over 8 weeks to 5 years. Three trials found higher rates of gastrointestinal adverse events associated with metformin. Although not reported in studies, lactic acidosis is a rare but potentially serious adverse effect of metformin, primarily in persons with significant renal impairment.<sup>47</sup> In studies of lifestyle interventions that reported on musculoskeletal events, 1 study found no significant difference between groups for rates of joint sprains/strains or muscle or joint aches over 1 year, 1 study found few cases of musculoskeletal problems (<1% per group), and 1 study (the DPP) found higher rates of musculoskeletal symptoms per 100 person-years in the intensive lifestyle intervention group than in the control group (24.1 vs 21.1 events per 100 person-years;  $P < .017$ ).<sup>2,23</sup>

#### Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF website from March 16 to April 12, 2021. Many comments agreed with the USPSTF recommendation. In response to public comment, the USPSTF clarified that disparities in the prevalence of prediabetes and type 2 diabetes are due to social factors and not biological ones, and incorporated person-first language when referring to persons who have overweight or obesity. Some comments requested broadening the eligibility criteria for screening to all adults, or to persons with any risk factor for diabetes, and not

confined to persons who have overweight or obesity. The USPSTF appreciates these perspectives; however, the available evidence best supports screening starting at age 35 years. The USPSTF also added language clarifying that overweight and obesity are the strongest risk factors for developing prediabetes and type 2 diabetes. In response to comments, the USPSTF also noted that metformin appears to be effective in reducing the risk of progression from prediabetes to diabetes in persons with a history of gestational diabetes, based on post hoc analyses of the DPP and DPPOS.

- Clinical trials and additional modeling studies are needed to better elucidate the optimal frequency of screening and the age at which to start and stop screening.
- More research is needed on the natural history of prediabetes, including the identification of factors associated with risk of progression to diabetes or reversion to normoglycemia.

## Research Needs and Gaps

More research is needed to evaluate the following.

- More studies are needed on the effects of screening on health outcomes that enroll populations reflective of the prevalence of diabetes in the US, particularly racial and ethnic groups that have a higher prevalence of diabetes than White persons.
- More US data are needed on the effects of lifestyle interventions and medical treatments for screen-detected prediabetes and diabetes on health outcomes over a longer follow-up period, particularly in populations reflective of the prevalence of diabetes.
- More research is needed on how best to increase uptake of lifestyle interventions, especially among populations at highest risk for progression to diabetes and adverse health outcomes.

## Recommendations of Others

The American Diabetes Association<sup>48</sup> recommends universal screening for prediabetes and diabetes, using a fasting plasma glucose level, 2-hour plasma glucose level during a 75-g oral glucose tolerance test, or HbA<sub>1c</sub> level, for all adults 45 years or older, regardless of risk factors, and screening adults who have overweight or obesity (BMI  $\geq 25$  or  $\geq 23$  in Asian American persons) with 1 or more risk factors, regardless of age. If the results are normal, it recommends repeat screening at a minimum of 3-year intervals. The American Association of Clinical Endocrinology<sup>49</sup> recommends universal screening for prediabetes and diabetes for all adults 45 years or older, regardless of risk factors, and screening persons with risk factors for diabetes (regardless of age). Testing for prediabetes and diabetes can be done using a fasting plasma glucose level, 2-hour plasma glucose level during a 75-g oral glucose tolerance test, or HbA<sub>1c</sub> level. It recommends repeat screening every 3 years.

### ARTICLE INFORMATION

**Accepted for Publication:** July 20, 2021.

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**Author Contributions:** Dr Davidson had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. The USPSTF members contributed equally to the recommendation statement.

**Conflict of Interest Disclosures:** Authors followed the policy regarding conflicts of interest described at <https://www.uspreventiveservicestaskforce.org/Page/Name/conflict-of-interest-disclosures>. All members of the USPSTF receive travel reimbursement and an honorarium for participating in USPSTF meetings.

**Funding/Support:** The USPSTF is an independent, voluntary body. The US Congress mandates that the Agency for Healthcare Research and Quality (AHRQ) support the operations of the USPSTF.

**Role of the Funder/Sponsor:** AHRQ staff assisted in the following: development and review of the research plan, commission of the systematic evidence review from an Evidence-based Practice Center, coordination of expert review and public comment of the draft evidence report and draft recommendation statement, and the writing and preparation of the final recommendation statement and its submission for publication. AHRQ staff had no role in the approval of the final recommendation statement or the decision to submit for publication.

**Disclaimer:** Recommendations made by the USPSTF are independent of the US government. They should not be construed as an official position of AHRQ or the US Department of Health and Human Services.

**Additional Contributions:** We thank Howard Tracer, MD (AHRQ), who contributed to the writing

of the manuscript, and Lisa Nicoletta, MA (AHRQ), who assisted with coordination and editing.

**Additional Information:** The US Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without obvious related signs or symptoms. It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment. The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

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