

# Screening for Prediabetes and Type 2 Diabetes in Children and Adolescents

## US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

**IMPORTANCE** The Centers for Disease Control and Prevention estimates that 210 000 children and adolescents younger than 20 years had diabetes as of 2018; of these, approximately 23 000 had type 2 diabetes. Youth with type 2 diabetes have an increased prevalence of associated chronic comorbid conditions, including hypertension, dyslipidemia, and nonalcoholic fatty liver disease. Data indicate that the incidence of type 2 diabetes is rising; from 2002-2003 to 2014-2015, incidence increased from 9.0 cases per 100 000 children and adolescents to 13.8 cases per 100 000 children and adolescents.

**OBJECTIVE** The US Preventive Services Task Force (USPSTF) commissioned a review of the evidence on screening for prediabetes and type 2 diabetes in asymptomatic, nonpregnant persons younger than 18 years. This is a new recommendation.

**POPULATION** Children and adolescents younger than 18 years without known diabetes or prediabetes or symptoms of diabetes or prediabetes.

**EVIDENCE ASSESSMENT** The USPSTF concludes that the evidence is insufficient to assess the balance of benefits and harms of screening for type 2 diabetes in children and adolescents. There is a lack of evidence on the effect of screening for, and early detection and treatment of, type 2 diabetes on health outcomes in youth, and the balance of benefits and harms cannot be determined.

**RECOMMENDATION** The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for type 2 diabetes in children and adolescents. (I statement)

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**Group Information:** A complete list of the members of the US Preventive Services Task Force appears at the end of this article.

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### Summary of Recommendation

Population	Recommendation	Grade
Asymptomatic children and adolescents younger than 18 years	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for type 2 diabetes in children and adolescents.	I

See the Practice Considerations section for additional information regarding the I statement. USPSTF indicates US Preventive Services Task Force.

See the Summary of Recommendation figure.

### Importance

The Centers for Disease Control and Prevention estimates that 210 000 children and adolescents younger than 20 years had diabetes as of 2018; of these, approximately 23 000 had type 2 diabetes.<sup>1</sup> Youth with type 2 diabetes have an increased prevalence of associated chronic comorbid conditions, including

hypertension, dyslipidemia, and nonalcoholic fatty liver disease.<sup>2</sup> Data indicate that the incidence of type 2 diabetes is rising; from 2002-2003 to 2014-2015, incidence increased from 9.0 cases per 100 000 children and adolescents to 13.8 cases per 100 000 children and adolescents.<sup>3</sup> Most of the increase in the incidence rate is in American Indian/Alaska Native, Black, and Hispanic/Latino children and adolescents.<sup>3</sup> Approximately 18% of adolescents aged 12 to 18 years had prediabetes during 2005 to 2016.<sup>4</sup>

Table. Summary of USPSTF Rationale

Rationale	Assessment
Benefits of early detection and intervention and treatment	<ul style="list-style-type: none"> <li>• Inadequate evidence, due to a lack of studies, that screening for type 2 diabetes and prediabetes in asymptomatic children and adolescents improves health outcomes.</li> <li>• Inadequate evidence that interventions for screen-detected type 2 diabetes and prediabetes improve health outcomes. Few trials reported on the effect of treatment on health outcomes; all studies were underpowered for included health outcomes.</li> <li>• Inadequate evidence that interventions for prediabetes delay or prevent progression to type 2 diabetes. Limited evidence is available from a single, small trial.</li> </ul>
Harms of early detection and intervention and treatment	<ul style="list-style-type: none"> <li>• Inadequate evidence, due to a lack of studies, to determine the harms of screening for type 2 diabetes and prediabetes in asymptomatic children and adolescents.</li> <li>• Inadequate evidence to determine the harms of interventions for prediabetes, screen-detected type 2 diabetes, or recently diagnosed type 2 diabetes. Limited evidence from 2 trials is available.</li> </ul>
USPSTF assessment	The evidence on screening for type 2 diabetes is lacking, and the balance of benefits and harms cannot be determined.

Abbreviation: USPSTF, US Preventive Services Task Force.

## USPSTF Assessment of Magnitude of Net Benefit

The US Preventive Services Task Force (USPSTF) concludes that the **evidence is insufficient** to assess the balance of benefits and harms of screening for type 2 diabetes in children and adolescents. There is a lack of evidence on the effect of screening for, and early detection and treatment of, type 2 diabetes on health outcomes in youth, and the balance of benefits and harms cannot be determined.

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>5</sup>

## Practice Considerations

### Patient Population Under Consideration

This recommendation applies to children and adolescents younger than 18 years without known diabetes or prediabetes or symptoms of diabetes or prediabetes. Screening in adolescents who are pregnant is outside the scope of this recommendation. The USPSTF has a separate recommendation on screening for gestational diabetes.

### Definitions of Prediabetes and Type 2 Diabetes

*Diabetes* refers to a range of metabolic disorders characterized by hyperglycemia. Type 2 diabetes is characterized by insulin resistance and progressive loss of  $\beta$ -cell insulin secretion.<sup>6</sup> In contrast, type 1 diabetes is the result of autoimmune  $\beta$ -cell destruction, usually leading to absolute insulin deficiency. Prediabetes is the term used for individuals whose blood glucose levels (measured by plasma glucose level or hemoglobin A<sub>1c</sub> [HbA<sub>1c</sub>] level) are considered higher than normal but do not meet criteria for diabetes.<sup>6</sup>

The definitions of prediabetes and diabetes in children and adolescents are the same as in adults.<sup>2,7</sup> A fasting plasma glucose level of 100 to 125 mg/dL (5.6-6.9 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 (7.8-11.0 mmol/L) are consistent with prediabetes.<sup>6</sup> A fasting plasma glucose level of 126 mg/dL (7.0 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.<sup>6</sup> The diagnosis of prediabetes or type 2 diabetes should be confirmed with repeat testing before starting interventions.<sup>6</sup>

### Screening Tests

Although there is insufficient evidence to recommend for or against screening in patients without signs or symptoms, 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.<sup>2,7</sup> HbA<sub>1c</sub> level is a measure of long-term blood glucose concentration and is not affected by acute changes in glucose levels. The oral glucose tolerance test is performed in the morning in a fasting state, with blood glucose concentration measured 2 hours after ingestion of a 75-g oral glucose load.

### Treatment and Preventive Interventions

Lifestyle interventions to achieve weight loss, improve diet, and increase physical activity are often recommended for youth diagnosed with prediabetes and diabetes. The Centers for Disease Control and Prevention recommends programs that increase exercise and improve nutrition; these programs include extensive education on promoting self-management skills and establishing individualized plans for self-monitoring of glycemic targets.<sup>8</sup> Formal programs to improve diet and increase exercise are often paired with pharmacotherapy.<sup>9,10</sup> The US Food and Drug Administration has approved 3 drugs for treatment of type 2 diabetes in children: metformin, insulin, and liraglutide.<sup>2,7</sup> While metformin has demonstrated improvements in body mass index (BMI), fasting glucose level, and insulin resistance, it is not approved by the US Food and Drug Administration to prevent the progression of prediabetes to diabetes.<sup>11</sup>

### Suggestions for Practice Regarding the I Statement

#### Potential Preventable Burden

Diabetes (both type 1 and type 2) is the third most common chronic disease in childhood.<sup>2,7</sup> Many of the diabetes complications experienced by adults (such as kidney failure, non-injury-related lower-limb amputations, and blindness) can begin in childhood.

Compared with non-Hispanic White youth, the type 2 diabetes rate in American Indian/Alaska Native, Black, and Hispanic/Latino youth has been shown to be 5, 4, and 8 times higher, respectively.<sup>12</sup> Causes of these differences are not well understood, but structural factors that disproportionately affect non-White populations, as well as cultural and environmental influences and quality of and access to health care, may contribute significantly to differences by race and ethnicity.<sup>13</sup>

Obesity and excess adipose tissue, especially when centrally distributed, are the most important risk factors for type 2 diabetes in younger persons.<sup>2,7,13</sup> Family history of diabetes (including gestational diabetes) is also a strong risk factor.<sup>2,7,13</sup> Risk assessment tools are also available to help identify children and adolescents at

Figure. Clinician Summary: Screening for Prediabetes and Type 2 Diabetes in Children and Adolescents

What does the USPSTF recommend?	For children and adolescents younger than 18 years who do not have any symptoms of type 2 diabetes: The USPSTF found that the evidence is insufficient to assess the balance of benefits and harms of screening for type 2 diabetes in children and adolescents. <b>Grade: I statement</b>
To whom does this recommendation apply?	<ul style="list-style-type: none"> <li>Children and adolescents younger than 18 years who have no signs or symptoms of diabetes or prediabetes.</li> <li>Screening for diabetes in adolescents who are pregnant is covered in a separate USPSTF recommendation.</li> </ul>
What's new?	This is a new USPSTF recommendation; the USPSTF has not previously released a recommendation on this topic.
How to implement this recommendation?	<ul style="list-style-type: none"> <li>There is insufficient evidence to recommend for or against screening for type 2 diabetes in children and adolescents without symptoms of diabetes or prediabetes.</li> <li>Clinicians should use their clinical judgment to determine if screening is appropriate for individual patients.</li> </ul>
What additional information should clinicians know about this recommendation?	<ul style="list-style-type: none"> <li>Type 2 diabetes disproportionately affects American Indian/Alaska Native, Black, Hispanic/Latino, and Native Hawaiian/Pacific Islander youth.</li> <li>Risk factors for type 2 diabetes include obesity and excess adipose tissue, especially when centrally distributed, as well as a family history of diabetes.</li> <li>Several screening tests (such as fasting plasma glucose level, hemoglobin A<sub>1c</sub> level, or oral glucose tolerance test) can identify type 2 diabetes and prediabetes; however, there is inadequate evidence that screening and early intervention lead to improvements in health outcomes such as renal impairment, cardiovascular morbidity, mortality, and quality of life.</li> <li>Treatment of type 2 diabetes and prediabetes generally includes lifestyle modifications (changes in diet and physical activity), medications to improve glycemic control, or both. However, there is limited evidence that interventions for screen-detected type 2 diabetes and prediabetes improve health outcomes.</li> <li>Approximately 1 in 5 adolescents aged 12 to 18 years has prediabetes, but there is limited evidence on whether interventions for prediabetes delay or prevent progression to type 2 diabetes. Approximately 20% to 50% of children and adolescents with prediabetes return to normal glycemia or normal glucose tolerance without intervention.</li> </ul>
Why is this recommendation and topic important?	<ul style="list-style-type: none"> <li>Type 2 diabetes affects approximately 23 000 children and adolescents in the US. The incidence of type 2 diabetes is on the rise.</li> <li>Youth with type 2 diabetes have an increased prevalence of associated chronic comorbid conditions, including hypertension, dyslipidemia, and nonalcoholic fatty liver disease.</li> </ul>
What are other relevant USPSTF recommendations?	The USPSTF has a recommendation on screening for obesity in children and adolescents, screening for prediabetes and type 2 diabetes in adults, and screening for gestational diabetes in pregnant persons, which can be found on the USPSTF website ( <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/uspstf/">https://www.uspreventiveservicestaskforce.org/uspstf/</a> ) or the JAMA website ( <a href="https://jamanetwork.com/collections/44068/united-states-preventive-services-task-force">https://jamanetwork.com/collections/44068/united-states-preventive-services-task-force</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.

increased risk for prediabetes and type 2 diabetes; however, there is limited evidence on their accuracy.<sup>14,15</sup>

Type 2 diabetes is much more common in older than in younger children, often presenting at the onset of puberty.<sup>16</sup> This timing is likely related to physiologic, but transient, pubertal insulin resistance that can be exacerbated by metabolic challenges related to obesity.<sup>17,18</sup> Twenty-two percent to 52% of children and adolescents with prediabetes return to normal glycemia or normal glucose tolerance without intervention over 6 months to 2 years.<sup>2,7</sup>

#### Potential Harms

Because some youth with prediabetes may revert to normal glycemia without intervention, potential harms of screening include labeling, overdiagnosis, and overtreatment. Potential harms caused by treatment of type 2 diabetes include hypoglycemia and gastrointestinal issues (eg, nausea or vomiting) related to medication use.<sup>2,7</sup>

#### Other Related USPSTF Recommendations

The USPSTF has other recommendations on screening for obesity in children and adolescents (B recommendation) and screening for

prediabetes and type 2 diabetes in adults (B recommendation).<sup>19,20</sup> The USPSTF also has a recommendation on screening for gestational diabetes in pregnant persons (B recommendation).<sup>21</sup>

## Supporting Evidence

### Scope of Review

The USPSTF commissioned a systematic review of the evidence on screening for prediabetes and type 2 diabetes in asymptomatic, non-pregnant persons younger than 18 years.<sup>3</sup> This review focused on evidence of the benefits and harms of screening for prediabetes and type 2 diabetes and the benefits and harms of interventions for screen-detected prediabetes and type 2 diabetes or recently diagnosed type 2 diabetes. The USPSTF focused on effects of screening and interventions on health outcomes, including mortality, cardiovascular morbidity, chronic kidney disease, amputation, skin ulcers, visual impairment, neuropathy, and quality of life. 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

The USPSTF found no studies addressing the direct benefits of screening for type 2 diabetes and prediabetes on health outcomes in asymptomatic children and adolescents.

Two randomized clinical trials examined the benefits of interventions for screen-detected or recently diagnosed type 2 diabetes and prediabetes on health outcomes. The first and larger study was the Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) study (n = 699), which randomly assigned adolescents with obesity (defined as a BMI  $\geq$ 85th percentile for age and sex) and recently diagnosed type 2 diabetes to metformin monotherapy, metformin plus rosiglitazone, or metformin plus a lifestyle intervention.<sup>3,10</sup> No statistically significant differences were found in rates of diabetic ketoacidosis or renal impairment. However, studies were underpowered to detect differences in these health outcomes.<sup>3</sup> The second study was a 16-week trial that compared metformin and placebo in 82 treatment-naïve adolescents aged 10 to 16 years with previous or newly diagnosed type 2 diabetes.<sup>22</sup> It reported that zero participants in the metformin group developed diabetic ketoacidosis and 1 person in the control group developed diabetic ketoacidosis; however, this study was underpowered for this outcome, and this also was not the primary outcome for the study. Neither trial reported on other health outcomes.<sup>3</sup>

One fair-quality randomized clinical trial examined the benefits of interventions to prevent progression to type 2 diabetes. The study (n = 75) compared a lifestyle modification program focused on both diet or nutrition and physical activity with standard care for adolescents aged 10 to 16 years with obesity (defined as a BMI >95th percentile) and prediabetes.<sup>23</sup> The trial reported that no participants developed diabetes during the 6-month trial; however, the overall attrition rate was high (23%), and some participants were withdrawn from the study because they started taking metformin.<sup>23</sup>

### Harms of Screening and Treatment

The USPSTF found no studies addressing the harms of screening for type 2 diabetes and prediabetes in asymptomatic children and adolescents.

Two previously mentioned intervention trials (n = 781)<sup>10,22</sup> reported on harms associated with treatment of youth recently diagnosed with type 2 diabetes. The TODAY study reported that 4 youths had severe hypoglycemia. It also reported that more youths had repeated mild hypoglycemia in the group that received metformin plus rosiglitazone than in the metformin monotherapy or metformin plus lifestyle intervention groups (n = 19 [8.2%] for metformin plus rosiglitazone vs n = 10 [4.3%] for metformin monotherapy vs n = 8 [3.4%] for metformin plus lifestyle intervention; *P* = .05 across the 3 groups).<sup>10</sup> The 16-week trial comparing metformin monotherapy with placebo reported zero hypoglycemic events requiring medical attention in either study group.<sup>22</sup>

Gastrointestinal events were common in both studies. In the TODAY study, lower rates of gastrointestinal symptoms were reported in the metformin plus rosiglitazone group than in the metformin monotherapy or metformin plus lifestyle intervention groups.<sup>10</sup> The 16-week trial reported that more youths treated with metformin than with placebo had abdominal pain (25% vs 12%) and nausea or vomiting (17% vs 10%).<sup>22</sup> Other adverse events were reported in both studies; however, events were varied, and most found

no difference between groups or reported that events were not attributed to study interventions.<sup>3</sup>

### Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF website from December 14, 2021, to January 18, 2022. Several comments noted the connection between excess body weight and impaired glucose tolerance as well as the recent rise in childhood obesity. These comments suggested that a risk-based approach (ie, screening youth with overweight and obesity) may better identify children and adolescents with prediabetes and type 2 diabetes. The USPSTF found no evidence on screening for type 2 diabetes or prediabetes in children and adolescents, including in those with risk factors. The USPSTF is calling for more studies on the benefits and harms of screening in children and adolescents, including those that may be at higher risk. Comments also proposed that the scope of the recommendation should include screening for type 1 diabetes. Given the distinct clinical course of type 1 diabetes, the USPSTF chose to focus on type 2 diabetes and prediabetes.

Additionally, the USPSTF wishes to clarify that the I statement is neither a recommendation for nor against screening. Clinicians should continue to use their clinical judgment to determine if screening is appropriate for individual patients.

## Research Needs and Gaps

More studies are needed that address the following areas.

- The effects of screening on health outcomes in child and adolescent populations reflective of the prevalence of diabetes in the US, particularly American Indian/Alaska Native, Black, Hispanic/Latino, and Native Hawaiian/Pacific Islander youth, who have a higher prevalence of diabetes than White youth.
- The effects of screening on health outcomes in children and adolescents considered to be at higher risk such as those who are overweight, have obesity, or have a family history of diabetes.
- The effects of lifestyle interventions, pharmacotherapy, or both for treatment of screen-detected prediabetes and diabetes on health outcomes in children and adolescents, particularly in racial and ethnic groups who have a higher prevalence of diabetes than White youth.
- Trials (both screening and intervention) focusing on health outcomes such as mortality, cardiovascular morbidity, chronic kidney disease, amputation, visual impairment, neuropathy, and quality of life that are of sufficient duration and sample size.
- The natural history of prediabetes in children and adolescents, including the identification of factors associated with risk of progression to diabetes or reversion to normoglycemia.

## Recommendations of Others

The American Diabetes Association recommends risk-based screening for type 2 diabetes after onset of puberty or age 10 years in children who have overweight (defined as a BMI  $\geq$ 85th percentile) or obesity (defined as a BMI  $\geq$ 95th percentile) and 1 or more additional risk factors for diabetes.<sup>9</sup> In children who are deemed at high risk, it recommends screening every 3 years if tests are normal or more frequently if BMI increases.

## ARTICLE INFORMATION

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**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. Published by JAMA®—Journal of the American Medical Association under arrangement with the Agency for Healthcare Research and Quality (AHRQ). ©2022 AMA and United States Government, as represented by the Secretary of the Department of Health and Human Services (HHS), by assignment from the members of the United States Preventive Services Task Force (USPSTF). All rights reserved.

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