Once considered a disease of aging, type 2 diabetes is now observed at increasing rates in young people. The prevalence of type 2 diabetes in children and adolescents has increased substantially over the last 2 decades; among youth aged 10 to 19 years, the prevalence increased from 0.34/1000 in 2001 to 0.67/1000 in 2017, a relative increase of 95% over 16 years. The highest rates of type 2 diabetes occur among American Indian, Black, and Hispanic youth. The COVID-19 pandemic has further magnified the trend of increased numbers of youth developing type 2 diabetes, likely due to multiple reasons, including unhealthy lifestyle risk factors of increased sedentary behavior, decreased physical activity, and weight gain.

Well-recognized contributors to youth-onset type 2 diabetes include obesity, high-fat/high-carbohydrate diets, physical inactivity, and family history of diabetes, factors that tend to cluster in the US by socioeconomic status. Moreover, mounting evidence indicates that type 2 diabetes diagnosed in childhood is associated with higher morbidity and premature mortality, likely due to the accelerated onset and progression of microvascular and macrovascular complications. These complications are evident at higher rates and at younger ages in those with youth-onset type 2 diabetes than those with youth-onset type 1 diabetes or in adults diagnosed with type 2 diabetes. Thus, prevention and early identification of type 2 diabetes in children is a key public health priority.

Unlike type 1 diabetes, which has typically been described as having a rapid onset secondary to loss of beta cell mass due to autoimmune destruction, type 2 diabetes usually has a more indolent course and may come to clinical attention after a prolonged period of dysglycemia not meeting criteria for diabetes. This period of dysglycemia, or “prediabetes,” includes the presence of either impaired fasting glucose or impaired glucose tolerance, defined as glucose levels of 100 to 125 mg/dL and 140 to 199 mg/dL, respectively. This period of prediabetes provides an opportunity for identification of at-risk individuals, allowing for targeted preventive interventions. Such secondary prevention approaches are best exemplified by the Diabetes Prevention Program (DPP) study, which randomized 3234 adults with impaired glucose tolerance to either placebo, metformin, or a lifestyle intervention. After 10 years, the incidence rate of type 2 diabetes was reduced by 34% and 18% in the original lifestyle and metformin groups, respectively, compared with the placebo group despite introduction of the lifestyle intervention to all participants during the latter 7 years of follow-up. After the initial 3 years, the lifestyle intervention significantly reduced progression to type 2 diabetes by 58% while metformin reduced progression by 31% compared with placebo (absolute incidence rates of 11.0, 7.8, and 4.8 per 100 person-years in the placebo, metformin, and lifestyle groups, respectively).

However, it is unclear that preventive interventions validated in adults are efficacious in youth, as many studies have suggested substantial pathophysiologic and metabolic differences according to age at diagnosis. In the TODAY study, a trial designed to identify treatment options and understand the natural history of type 2 diabetes in 699 youth (mean age of onset, 13 years), an intensive lifestyle intervention combined with metformin did not diminish the time to glycemic failure vs metformin alone. While the DPP and TODAY studies tested lifestyle interventions at different stages of disease progression (prediabetes and diabetes, respectively), such intensive efforts for weight management through lifestyle efforts appear to be less effective in youth than in adults. Moreover, in the Restoring Insulin Secretion (RISE) study, which compared youth (aged 10-19 years; n = 91) with adults (aged 20-65 years; n = 355) with impaired glucose tolerance or recently diagnosed type 2 diabetes, the youth participants had substantially higher body mass index (BMI), lower insulin sensitivity, greater beta cell hypersecretion at baseline, and more rapid loss of beta cell function than adults. In the TODAY study, about half the participants did not maintain glycemic control without the addition of insulin after only 12 months.

Together, these studies highlight the important and substantial differences in pathophysiology and treatment responses in children and adults with prediabetes and type 2 diabetes, and consequent differences in screening and treatment guidelines. Moreover, given the increased occurrence of type 2 diabetes in young people, coupled with the growing awareness that type 2 diabetes in children and adolescents can be an aggressive and potentially devastating disease with onset in childhood, the role of screening in this population requires careful evaluation.

In this issue of JAMA, the US Preventive Services Task Force (USPSTF) addresses this important issue with a new Recommendation Statement on screening for prediabetes and type 2 diabetes in children and adolescents based on an Evidence Report and Systematic Review of the evidence on screening for prediabetes and type 2 diabetes in asymptomatic, nonpregnant persons younger than 18 years. The Evidence Report examined several key questions that addressed the following topics: Is there direct evidence that screening for prediabetes and type 2 diabetes in asymptomatic children and adolescents improves health outcomes? What are the harms and benefits of screening? Does early initiation of treatment for screen-detected prediabetes and type 2 diabetes improve health outcomes, vs initiating treatment later? What are the potential harms of treatment? Do interventions for prediabetes delay or prevent progression to type 2 diabetes?
After providing interventions for prediabetes, how do health outcomes change from reducing progression to type 2 diabetes?

After reviewing the recent literature on these topics, the Task Force could not identify relevant pediatric studies that addressed the majority of these questions. Furthermore, there was no available literature to answer the overarching question related to potential benefits of screening for prediabetes or type 2 diabetes among asymptomatic youth. Moreover, there were no studies that compared individuals with screen-detected diabetes vs those who presented with clinical symptoms. With respect to the question as to whether interventions for prediabetes prevent progression to type 2 diabetes in youth, the Task Force identified a single randomized trial of 75 obese youth, aged 10 to 16 years, that compared an intensive lifestyle intervention with standard care in a pediatric obesity clinic. Overall, this small, 6-month study was deemed of only fair quality due to attrition and initiation of metformin in some participants. Notably, no cases of progression from prediabetes to type 2 diabetes were identified in either group, although the authors concluded that the lifestyle intervention may be more effective than routine care in reducing risk for type 2 diabetes, given more favorable reductions in the 2-hour glucose levels following oral glucose tolerance testing. In addition, the Evidence Report identified some potential harms, mainly related to reports of gastrointestinal symptoms with metformin.

The USPSTF concluded 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).” This conclusion stems from insufficient evidence of potential benefits, harms, or both from screen-detected prediabetes and type 2 diabetes in asymptomatic youth as well as from insufficient evidence that interventions for screen-detected prediabetes and type 2 diabetes improve health outcomes. Thus, this report highlights important gaps in the literature and underscores the need for large-scale studies in youth at risk for prediabetes and type 2 diabetes.

Future research could consider following a standard pediatric approach to health care with development of studies that address primary, secondary, and tertiary prevention. Primary prevention studies could begin in early childhood with focused attention on healthy lifestyle around family dietary behaviors and exercise, potentially targeting families with obesity, diabetes, or both, with outcomes related to childhood weight gain. Secondary prevention studies might focus on pubertal youth at risk for diabetes due to overweight or obese status with frequent screening for prediabetes. Tertiary prevention studies could include youth with either clinically identified or screen-detected type 2 diabetes for evaluation in medication trials utilizing combination therapies in efforts to reduce insulin resistance while preserving residual beta cell function. All such efforts would require lengthy follow-up to answer the questions posed in the USPSTF report regarding potential benefits and harms on long-term health outcomes, including those beyond the pediatric period.

For now, while awaiting more data and definitive guidelines, pediatricians and primary care clinicians can continue to emphasize the importance of healthy lifestyles for children and their families, maintain a watchful approach to detect clinical symptoms of hyperglycemia, and continue to follow risk-based screening recommendations for type 2 diabetes in overweight (BMI 85th to <95th percentile) or obese (BMI ≥95th percentile) youth with at least 1 additional risk factor (eg, family history of type 2 diabetes or signs of insulin resistance, such as acanthosis nigricans or polycystic ovary syndrome).