Screening and Diagnosis of Prediabetes and Diabetes in US Children and Adolescents

Amelia S. Wallace, MS,[a,b] Dan Wang, MS,[a,b] Jung-Im Shin, MD, PhD,[a,b] Elizabeth Selvin, PhD, MPH[a,b]

abstract

BACKGROUND: The optimal approach to screening and diagnosis of prediabetes and diabetes in youth is uncertain.

METHODS: We conducted a cross-sectional analysis of 14 119 youth aged 10 to 19 years in the 1999–2016 NHANES. First, we examined the performance of American Diabetes Association risk-based screening criteria. Second, we evaluated the performance of current clinical definitions of prediabetes and diabetes based on hemoglobin A1c (HbA1c), fasting plasma glucose (FPG), either HbA1c or FPG, or both HbA1c and FPG (confirmatory definition) to identify youth at high cardiometabolic risk.

RESULTS: Overall, 25.5% of US youth (10.6 million in 2016) were eligible for screening. Sensitivity and specificity of the screening criteria for detecting any hyperglycemia were low for both HbA1c ≥5.7% (sensitivity = 55.5%, specificity = 76.3%) and FPG ≥100 mg/dL (sensitivity = 35.8%, specificity = 77.1%). Confirmed undiagnosed diabetes (HbA1c ≥6.5% and FPG ≥126 mg/dL) was rare, <0.5% of youth. Most (>85%) cases of diabetes were diagnosed. Associations with cardiometabolic risk were consistently stronger and more specific for HbA1c-defined hyperglycemia (specificity = 98.6%; sensitivity = 4.0%) than FPG-defined hyperglycemia (specificity = 90.1%; sensitivity = 19.4%).

CONCLUSIONS: One-quarter of US youth are eligible for screening for diabetes and prediabetes; however, few will test positive, especially for diabetes. Most cases of diabetes in US youth are diagnosed. Regardless of screening eligibility, we found that HbA1c is a specific and useful nonfasting test to identify high-risk youth who could benefit from lifestyle interventions to prevent diabetes and cardiovascular risk in adulthood.

[a]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, John Hopkins University, Baltimore, Maryland; and [b]Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins University, Baltimore, Maryland

Address correspondence to Elizabeth Selvin, PhD, MPH; Department of Epidemiology, Welch Center for Prevention, Epidemiology and Clinical Research and the Johns Hopkins Bloomberg School of Public Health; 2024 E Monument St, Suite 2-639, Baltimore, MD 21287. E-mail: eselvin@jhu.edu

WHAT'S KNOWN ON THIS SUBJECT: The American Diabetes Association and American Academy of Pediatrics recommend screening for type 2 diabetes and prediabetes in asymptomatic youth. It is unknown how many US youth are eligible and which screening tests are most useful for identifying high-risk youth.

WHAT THIS STUDY ADDS: We found that one-quarter of US children would be eligible for screening for type 2 diabetes, but few would meet diagnostic criteria for diabetes. Regardless of screening eligibility, the hemoglobin A1c test was an efficient approach to identify high-risk youth.

To cite: Wallace AS, Wang D, Shin J, et al. Screening and Diagnosis of Prediabetes and Diabetes in US Children and Adolescents. *Pediatrics.* 2020;146(3):e20200265

ARTICLE

Childhood obesity in the United States has increased dramatically since the late 1980s, with corresponding increases in prediabetes and type 2 diabetes mellitus.[1–3] Although there is limited evidence on the long-term effects of hyperglycemia in children,[4] researchers of studies in adults have shown that earlier onset of diabetes and longer duration of the disease are associated with worse outcomes.[5] Evidence from adults reveals that early interventions can delay or prevent complications.[6] There is evidence that intensive lifestyle modification in obese children with prediabetes can improve markers of insulin resistance.[7]

In 2000, the American Diabetes Association (ADA) and American Academy of Pediatrics first recommended[8] general screening for type 2 diabetes in asymptomatic youth ages 10 and older (or after onset of puberty). Until 2018, these recommendations were to screen only in high-risk youth, defined as being overweight and with at least 2 of the following risk factors: non-white race, family history of type 2 diabetes, maternal gestational diabetes, or signs of insulin resistance. Beginning in 2018,[9] the ADA expanded this recommendation to include all overweight youth with one or more of these risk factors. The implications of this change are uncharacterized; it is unknown how many US children and adolescents are eligible for screening by these new guidelines.

Among those who are eligible for screening, there are multiple criteria used to define diabetes and prediabetes in clinical practice. It is unclear which approach might be optimal in children and adolescents. Hemoglobin A1c (HbA1c), fasting plasma glucose (FPG), and 2-hour plasma glucose are all recommended for screening for diabetes in youth and adults.[10] The 3 tests do not always identify the same

subpopulations, particularly in younger age groups.[11] The use of HbA1c in pediatric populations is particularly controversial,[12,13] with at least one major guideline organization recommending against its use in children and adolescents.[14]

Our objectives were to evaluate the performance of current ADA guidelines for screening of diabetes and prediabetes in youth and characterize the performance of clinical definitions of prediabetes and diabetes on the basis of HbA1c and/or fasting glucose to identify US children and adolescents at high cardiometabolic risk.

METHODS

Study Population

The NHANES is a cross-sectional, nationally representative sample of the civilian noninstitutionalized US population conducted by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention. The surveys, which have been conducted in 2-year cycles since 1999, consist of interviews and standardized physical examinations in-home and at a mobile examination center, including laboratory tests. The health questionnaires are answered by an adult proxy for children under age 16. A random subsample of participants ages 12 and older who attended the morning examination are asked to fast the night before. Detailed information on the protocols and procedures for NHANES are available elsewhere.[15]

All protocols for NHANES were approved by the research ethics board of the NCHS. Written informed consent was obtained from all participants or their parents or guardians if <18 years old.

We combined data from 9 cycles (1999–2016) of NHANES. For estimates of screening eligibility (full sample), we included the population for whom the ADA guidelines would

be applicable. There were 19 714 children and adolescents ages 10 to 19 years who attended the medical examination session. There were 94 individuals aged 10 to 19 with diagnosed diabetes who were excluded from our main analyses. We also excluded individuals missing HbA1c (n = 5051), leaving us with a sample of 14 119 youth. For analyses incorporating any of the fasting laboratory tests (plasma glucose, triglycerides, or low-density lipoprotein cholesterol [LDL-C]), we were limited to the random subsample of participants ages 12 to 19 without diagnosed diabetes who attended the morning fasting examination (n = 7426). Of these, we excluded participants who fasted for <9 hours (n = 839) or who were missing data on glucose (n = 352) or HbA1c (n = 10). This left us with 6225 participants in the fasting subsample.

Diabetes and Prediabetes Screening Criteria

Current ADA guidelines recommend screening for type 2 diabetes of prediabetes in all asymptomatic children and adolescents ages 10 and older (or after the onset of puberty) who are overweight or obese who have at least one of the following risk factors for diabetes: maternal history of gestational diabetes during the child's gestation; family history of type 2 diabetes in first or second degree relatives; American Indian, African American, Latino, Asian American, or Pacific Islander race or ethnicity; or signs of insulin resistance or conditions associated with insulin resistance, specifically acanthosis nigricans, hypertension, dyslipidemia, polycystic ovarian syndrome, or small-for-gestational-age birth weight.[10]

Based on the available data in NHANES, we used the following risk factors to determine eligibility for screening: (1) non-white race and ethnicity, (2) self-report of being told

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by a health professional that the participant had medical or family history that put them at increased risk for diabetes, or (3) hypertension (systolic or diastolic blood pressure ≥95th percentile for age, sex, and height [ages 10–12] or systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥80 mm Hg [ages 13–19])[16] or dyslipidemia (total cholesterol ≥200 mg/dL, LDL-C ≥130 mg/dL, triglycerides ≥130 mg/dL, or high-density lipoprotein cholesterol [HDL-C] <40 mg/dL).[17] Screening eligibility was defined as being overweight or obese (BMI ≥85th percentile for age and sex, based on Centers for Disease Control and Prevention growth charts[18]) and having ≥1 of the 3 risk factors for diabetes.

Definitions of Undiagnosed Diabetes and Prediabetes

We evaluated the performance of current clinically used definitions of prediabetes and undiagnosed diabetes to identify youth at high cardiometabolic risk. We considered 4 definitions of prediabetes: HbA1c 5.7% to 6.4%, fasting glucose 100 to 125 mg/dL, elevations in either test, or elevations in both tests. We evaluated 4 definitions for undiagnosed diabetes: HbA1c ≥6.5%, fasting glucose ≥126 mg/dL, elevations in either test, or elevations in both tests. Because the number of adolescents with undiagnosed diabetes was small, we also evaluated total hyperglycemia (prediabetes plus undiagnosed diabetes), defined as HbA1c ≥5.7%, fasting glucose ≥100 mg/dL, elevations in either test, or elevations in both tests.

To account for changes in laboratory methods over the study period, plasma glucose measurements were calibrated by using regression equations recommended by the NCHS[15] and HbA1c measurements were calibrated by using an equipercentile equating approach.[19]

Cardiometabolic Risk

We evaluated the metabolic syndrome and its components to characterize cardiometabolic risk in this population of children and adolescents. To define high cardiometabolic risk, we used a modification of the pediatric International Diabetes Federation definition of the metabolic syndrome[20]: waist circumference ≥90th percentile for age, sex, and ethnicity, and one of (1) triglycerides ≥150 mg/dL, (2) HDL-C <40 mg/dL (HDL-C <50 mg/dL for girls 16–19), or (3) systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg.

Statistical Analyses

We calculated the percentage of US youth without diagnosed diabetes who were eligible for screening by current ADA criteria and used US Census counts from 2016 to estimate the number of US children and adolescents. We then calculated the percentage of US youth who met each definition of prediabetes and undiagnosed diabetes, according to screening eligibility, and calculated the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the screening criteria to identify youth with undiagnosed diabetes or prediabetes in the population.

We evaluated the prevalence of cardiometabolic risk factors, comparing those with and without prediabetes or diabetes according to each clinical definition. We used multivariable logistic regression to estimate the age-sex-race–adjusted prevalence odds ratios (ORs) for the associations of definitions of hyperglycemia with each risk factor. We also calculated the sensitivity, specificity, PPV, and NPV to evaluate the performance of each definition to identify youth at high cardiometabolic risk based on metabolic syndrome criteria.

All statistical analyses were conducted by using survey estimation procedures and sampling weights recommended by the NCHS to account for the complex sample design and nonresponse.[15] Analyses were performed in 2019 by using Stata version 15.0 and the svy suite of commands (StataCorp, College Station, TX). The P values <.05 were considered statistically significant, and all tests were 2 sided. Estimates with poor precision (SE >30% of the estimate) were not reported.

RESULTS

Approximately one-quarter of US children and adolescents, 10.6 million in 2016, were overweight or obese and had at least one risk factor for diabetes, making them eligible for screening for diabetes by the 2018 criteria (Table 1). In comparison, <10% of US children and adolescents, 3.6 million in 2016, would have been eligible for screening by the pre-2018 criteria. Undiagnosed diabetes was uncommon, regardless of screening eligibility (2018 criteria) or the definition of diabetes used. Unconfirmed cases of undiagnosed diabetes, defined by a single HbA1c ≥6.5%, were seen in 0.3% (95% confidence interval [CI]: 0.1%–0.5%) of screening eligible youth and <0.1% in nonscreening eligible youth. The prevalence of undiagnosed diabetes using a single elevated FPG, elevations in either test, or the clinical confirmatory definition (both tests elevated) in the screening eligible population, and prevalence by all definitions in the nonscreening eligible population were too small to estimate with precision. Diagnosed diabetes was seen in 0.5% (95% CI: 0.4%–0.7%) of youth (0.2 million), equating to >85% of total confirmed diabetes cases.

The prevalence of prediabetes varied depending on the definition used, ranging from 1.5% to 17.5% in the

TABLE 1 Prevalence of Prediabetes and Undiagnosed Diabetes by Screening Eligibility in US Children and Adolescents Aged 10 to 19 Years, NHANES 1999–2016

	Screen Eligible, Weighted % = 25.5%, US Population = 10.5 Million			Not Screen Eligible, Weighted % = 74.5%, US Population = 31.1 Million			Diagnostic Performance of Screening			
	Unweighted *n*	Weighted % (95% CI)	US Population *n*, Millions	Unweighted *n*	Weighted % (95% CI)	US Population *n*, Millions	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
Diagnosed diabetes[a]	—	—	—	94	0.5 (0.4–0.7)	0.2				
Undiagnosed diabetes										
HbA1c ≥6.5%[b]	17	0.3 (0.1–0.5)	0.03	4	<0.1[d]	—[d]	85.7 (71.0–100.0)	74.6 (73.4–75.8)	~0	~100
HbA1c ≥6.5%[c]	7	<0.5[d]	—[d]	1	<0.1[d]	—[d]	90.7 (72.5–100.0)	75.8 (74.2–77.4)	~0	~100
FPG ≥126 mg/dL[c]	8	<0.5[d]	—[d]	4	<0.1[d]	—[d]	78.4 (55.1–100.0)	75.8 (74.2–77.4)	~0	~100
Either[c]	9	<0.5[d]	—[d]	4	<0.1[d]	—[d]	78.7 (55.8–100.0)	75.8 (74.2–77.4)	~0	~100
Both[c]	6	<0.5[d]	—[d]	1	<0.1[d]	—[d]	90.5 (71.9–100.0)	75.8 (74.2–77.4)	~0	~100
Prediabetes										
HbA1c 5.7%–6.4%[b]	226	3.8 (3.1–4.5)	0.4	166	1.1 (0.9–1.3)	0.3	54.5 (47.3–61.7)	75.1 (73.9–76.3)	3.8 (3.1–4.5)	98.9 (98.7–99.1)
HbA1c 5.7%–6.4%[c]	84	3.4 (2.3–4.6)	0.3	70	1.0 (0.7–1.3)	0.2	53.2 (41.8–64.5)	76.3 (74.7–77.8)	3.4 (2.3–4.6)	99.0 (98.7–99.3)
FPG 100–125 mg/dL[c]	300	15.6 (13.0–18.3)	1.3	401	9.2 (7.8–10.5)	2.3	35.2 (29.6–40.9)	77.1 (75.6–78.7)	15.6 (13.0–18.3)	90.8 (89.5–92.2)
Either[c]	350	17.5 (14.7–20.4)	1.4	458	9.9 (8.6–11.3)	2.5	36.0 (30.6–41.5)	77.4 (75.9–78.9)	17.5 (14.7–20.4)	90.1 (88.7–91.4)
Both[c]	34	1.5 (0.8–2.2)	0.1	13	<0.5[d]	—[d]	71.1 (54.1–88.0)	76.0 (74.5–77.6)	1.5 (0.8–2.2)	~100
Total hyperglycemia (prediabetes or undiagnosed diabetes)										
HbA1c ≥5.7% (full sample)[b]	243	4.1 (3.4–4.9)	0.4	170	1.1 (0.9–1.3)	0.3	56.2 (49.2–63.2)	75.1 (73.9–76.3)	4.1 (3.4–4.9)	98.9 (98.7–99.1)
HbA1c ≥5.7%[c]	91	3.8 (2.7–5.0)	0.3	71	1.0 (0.7–1.3)	0.2	55.5 (44.7–66.3)	76.3 (74.7–77.8)	3.8 (2.7–5.0)	99.0 (98.7–99.3)
FPG ≥100 mg/dL[c]	308	16.0 (13.4–18.6)	1.3	405	9.2 (7.9–10.6)	2.3	35.8 (30.2–41.5)	77.1 (75.6–78.7)	16.0 (13.4–18.6)	90.8 (89.4–92.1)
Either[c]	359	17.9 (15.1–20.8)	1.5	461	10.0 (8.6–11.3)	2.5	36.6 (31.2–42.0)	77.4 (75.9–78.9)	17.9 (15.1–20.8)	90.0 (88.7–91.4)
Both[c]	40	1.9 (1.1–2.7)	0.2	15	<0.5[d]	—[d]	73.6 (59.1–88.1)	76.0 (74.5–77.6)	1.9 (1.1–2.7)	~100

—, not estimated.

[a] Estimates are based on sample of all participants ages 10 to 19, *n* = 19 620.

[b] Estimates are based on sample of nondiabetic participants ages 10 to 19 with nonmissing HbA1c data, *n* = 14 119.

[c] Estimates are based on participants ages 12 to 19 who attended the morning fasting examination with nonmissing HbA1c and FPG data, *n* = 6225.

[d] Sample size was too small to estimate with precision (SE ≥30% of estimate).

screening eligible population and from <0.5% to 9.9% in the noneligible population. Similarly, the prevalence of total hyperglycemia (prediabetes plus undiagnosed diabetes) among screen eligible youth was higher than prevalence among nonscreen eligible youth, but the yield varied substantially by hyperglycemia definition. Approximately 4% of the overall screening eligible population had HbA1c-defined hyperglycemia (≥5.7%), whereas 17.9% of the screening eligible population had hyperglycemia defined by either HbA1c or FPG, which were higher than the rates in the nonscreening eligible population. However, a larger absolute number of youth not eligible for screening had FPG ≥100 mg/dL as compared with screen eligible youth: 2.3 million vs 1.3 million, respectively (Fig 1).
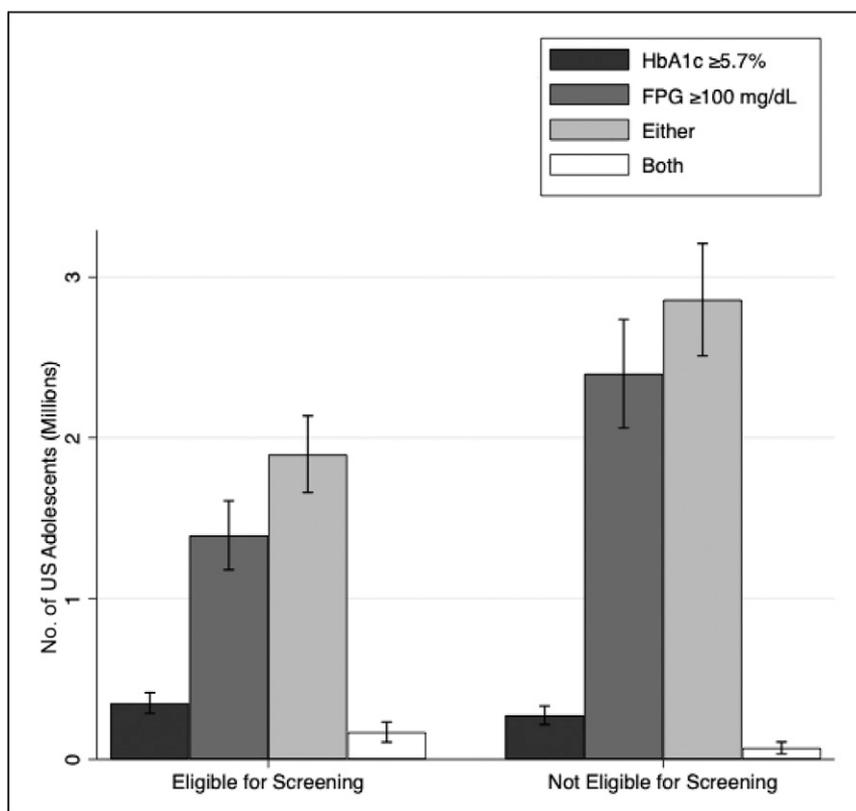
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FIGURE 1
Number (in millions) of US adolescents with hyperglycemia (prediabetes or undiagnosed diabetes) in 2016, by diabetes screening eligibility status.

The performance of current ADA screening criteria to identify youth with prediabetes or diabetes was poor. The sensitivity and specificity for detecting HbA1c-defined hyperglycemia (≥5.7%) were 55.5% and 76.3%, respectively; the sensitivity for detecting FPG-defined hyperglycemia (≥100 mg/dL) was 35.8%, and the specificity was 77.1% (Table 1).

In the total population (ignoring screening eligibility), cardiometabolic risk factors (obesity, metabolic syndrome, and hypercholesterolemia) were common in youth with hyperglycemia by either single-test definition (HbA1c ≥5.7% or FPG ≥100 mg/dL) (Table 2) or for the combined definition (Supplemental Table 4). However, risk factor associations were consistently stronger for HbA1c-defined hyperglycemia, with ORs ranging

from 2.6 to 4.1, compared with FPG-defined hyperglycemia, in which ORs ranged from 1.5 to 3.0. The prevalence of obesity and abdominal obesity were higher in youth with HbA1c-defined hyperglycemia than in youth with FPG-defined hyperglycemia, 50.7% vs 28.5% and 52.6% vs 35.0%, respectively. Risk factor associations were strongest when hyperglycemia was defined by using a confirmatory definition (HbA1c ≥5.7% and FPG ≥100 mg/dL) (Supplemental Table 5). Diagnostic performance of hyperglycemia definitions for detecting metabolic syndrome was more specific for HbA1c ≥5.7% (specificity = 98.6%) than for FPG ≥100 mg/dL (specificity = 90.1%) (Table 3), but sensitivity was higher for FPG-defined hyperglycemia (19.4%) than HbA1c-defined hyperglycemia (4.0%) (Table 3). The confirmatory definition (HbA1c

≥5.7% and FPG ≥100 mg/dL) had the highest specificity, 99.6%, (Supplemental Table 7), whereas hyperglycemia by either single-test definition had the highest sensitivity, 20.9% (Supplemental Table 6).

DISCUSSION

Guidelines from the ADA for screening of prediabetes and diabetes apply to a substantial proportion of the US youth population, but rates of hyperglycemia in these screening eligible youth was relatively low and varied considerably by the definition of prediabetes or diabetes used. Undiagnosed diabetes was rare; most cases of diabetes in US youth were diagnosed (>85% of total diabetes). Based on data from the SEARCH for Diabetes in Youth Study, ~80% to 90% of prevalent cases in youth 10 to 19 are likely to be type 1 diabetes.[21] Although the prevalence of prediabetes and undiagnosed diabetes were higher in the population eligible for ADA screening, there were also a substantial number of youth with hyperglycemia in the nonscreening eligible population; in fact, the absolute number of youth with elevated FPG was larger in the nonscreening eligible population, and the majority (88.5%) of these youth were of normal weight. Current screening criteria are not highly sensitive or specific and may miss high-risk youth who should be targeted for diabetes prevention.

There is controversy regarding optimal approaches to define diabetes and prediabetes in adults and youth.[10,12–14,22] We observed substantial variability in the prevalence of undiagnosed diabetes and prediabetes depending on the definition used. This is consistent with the variation in findings from other reports using NHANES data with differing definitions of hyperglycemia.[3,23] In most epidemiological studies, researchers define undiagnosed diabetes based on

TABLE 2 Prevalence of Cardiometabolic Risk Factors and ORs (95% CIs) According to HbA1c Category (<5.7% vs ≥5.7%) and FPG Category (<100 vs ≥100 mg/dL), US Children and Adolescents Without Diagnosed Diabetes, NHANES 1999–2016

	HbA1c <5.7%	HbA1c ≥5.7%	Adjusted[a] OR (95% CI) (HbA1c ≥5.7% vs <5.7%)	FPG <100 mg/dL, %	FPG ≥100 mg/dL, %	Adjusted[a] OR (95%) (FPG ≥100 vs <100 mg/dL)
Obese, ≥95th percentile for age or sex	18.5 (17.0–20.0)	50.7 (38.6–62.8)	4.1 (2.5–6.6)*	17.9 (16.4–19.5)	28.5 (23.2–33.8)	1.8 (1.4–2.4)*
Metabolic syndrome[b]	10.6 (9.5–11.7)	25.7 (16.1–35.2)	3.5 (2.1–5.9)*	9.8 (8.7–10.8)	19.5 (14.9–24.2)	2.2 (1.6–3.0)*
Waist circumference ≥90th percentile	31.7 (29.9–33.5)	52.6 (40.7–64.5)	3.3 (1.9–5.7)*	31.7 (29.8–33.5)	35.0 (29.6–40.4)	1.6 (1.2–2.0)*
Hypertension, ≥130/≥85	3.6 (2.9–4.4)	14.4 (6.4–22.5)	3.5 (1.7–6.9)*	3.0 (2.2–3.7)	10.7 (7.1–14.3)	3.4 (2.2–5.5)*
Triglycerides ≥150 mg/dL	9.1 (8.0–10.2)	17.3 (7.5–27.1)	—[c]	8.4 (7.4–9.5)	15.9 (12.0–19.7)	2.0 (1.4–2.7)*
HDL-C <40 mg/dL	13.8 (12.6–15.1)	26.1 (15.1–37.0)	2.6 (1.5–4.5)*	12.9 (11.6–14.3)	23.1 (18.8–27.4)	1.8 (1.3–2.3)*
LDL-C ≥130 mg/dL	7.4 (6.4–8.3)	—[c]	—[c]	7.2 (6.2–8.1)	9.9 (6.4–13.4)	—[c]

—, not estimated.

[a] Adjusted for age, sex, and race.

[b] Metabolic syndrome is defined as waist circumference ≥90th percentile for age, sex, and race and 1 of hypertension, hypertriglyceridemia, or hypoalphalipoproteinemia.

[c] Sample size was too small to estimate with precision (SE ≥30% of estimate).

* $P < .05$

a single elevation in fasting glucose or HbA1c, without confirmation. In clinical practice, confirmation of any elevation of a biomarker of hyperglycemia is recommended for making a diagnosis of diabetes.[10] This approach enhances specificity and reduces the possibility of a false-positive diagnosis. No current guidelines recommend a confirmatory definition for prediabetes. Given the biological variability of glycemic markers[24] especially FPG, a larger number of

individuals will always be identified as having hyperglycemia on the basis of a single test than would be identified by using a confirmatory approach (repeat testing or using a combination of elevated FPG and A1C in a single blood sample).[25] There will continue to be substantial variability in estimates of undiagnosed diabetes and the prevalence of prediabetes across populations as long as multiple definitions are in use.

Adolescents with ≥1 elevated measure of hyperglycemia have been previously shown to have higher prevalence of cardiometabolic risk factors.[26,27] We demonstrated in this study that there are substantial differences in cardiometabolic risk profiles depending on how hyperglycemia was defined. HbA1c-defined hyperglycemia identifies a smaller, but higher-risk, population than FPG-defined hyperglycemia; this is consistent with previous studies in adults,[22] limited studies in children,[4]

TABLE 3 Diagnostic Performance of HbA1c ≥5.7% and FPG ≥100 mg/dL for Detecting Cardiometabolic Risk Factors, US Children and Adolescents Without Diagnosed Diabetes, NHANES 1999–2016

	HbA1c ≥5.7%				FPG ≥ 100 mg/dL			
	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
Obese, ≥95th percentile for age and sex	4.4 (2.9–6.0)	99.0 (98.7–99.3)	50.7 (38.6–62.8)	81.5 (80.0–83.0)	16.2 (13.1–19.3)	90.4 (89.1–91.7)	28.5 (23.2–33.8)	82.1 (80.5–83.6)
Metabolic syndrome[a]	4.0 (2.3–5.7)	98.6 (98.3–98.9)	25.7 (16.1–35.2)	89.4 (88.3–90.5)	19.6 (15.4–23.9)	90.2 (88.9–91.5)	19.5 (14.9–24.2)	90.2 (89.2–91.3)
Waist circumference ≥90th percentile	2.8 (1.8–3.7)	98.8 (98.5–99.2)	52.6 (40.7–64.5)	68.3 (66.5–70.1)	11.9 (9.9–14.0)	89.5 (88.1–91.0)	35.0 (29.6–40.4)	68.3 (66.5–70.2)
Hypertension, ≥130/≥85	6.2 (2.9–9.6)	98.5 (98.2–98.9)	14.4 (6.4–22.5)	96.4 (95.6–97.1)	30.6 (21.7–39.4)	90.0 (88.7–91.2)	10.7 (7.1–14.3)	97.0 (96.3–97.8)
Triglycerides ≥150 mg/dL	—[b]	—[b]	17.3 (7.5–27.1)	90.9 (89.8–92.0)	18.8 (14.3–23.3)	89.8 (88.6–91.0)	15.9 (12.0–19.7)	91.6 (90.5–92.6)
HDL-C <40 mg/dL	3.1 (1.6–4.6)	98.6 (98.2–98.9)	26.1 (15.1–37.0)	86.2 (84.9–87.4)	18.0 (14.2–21.9)	90.2 (88.9–91.5)	23.1 (18.8–27.4)	87.1 (85.7–88.4)
LDL-C ≥130 mg/dL	—[b]	—[b]	—[b]	92.6 (91.7–93.6)	14.5 (9.5–19.4)	89.4 (88.1–90.6)	9.9 (6.4–13.4)	92.8 (91.9–93.8)

—, not estimated.

[a] Metabolic syndrome is defined as waist circumference ≥90th percentile for age, sex, or race and 1 of hypertension, hypertriglyceridemia, or hypoalphalipoproteinemia.

[b] Sample size was too small to estimate with precision (SE ≥30% of estimate).

and the known specificity of current HbA1c cut-points[28]

In previous reports, authors have stated that HbA1c is not appropriate in children, largely because of limited research on long-term prognostic value of HbA1c in this population and the discordance between HbA1c and glucose measures in youth.[12–14] Regardless of screening eligibility, both FPG- and HbA1c-defined hyperglycemia identified youth with a high burden of cardiometabolic risk factors, but using a confirmatory definition (elevations in both FPG and HbA1c) provided the highest discrimination for cardiometabolic risk. HbA1c also has practical advantages; it does not require fasting, which can be difficult in children, has lower within person variability as compared with glucose,[29] and is the basis for diabetes treatment decisions in clinical practice. Our results suggest that HbA1c is a specific and useful test in children and adolescents.

Limitations of our study include the lack of repeat measurements and a limited sample size in certain subgroups. However, the small numbers are a function of the low prevalence of undiagnosed diabetes in the general population of adolescents and children in the US. We did not have information on all variables that make up current diabetes screening criteria in youth; in particular, although we have

information on general family history or medical risk for diabetes, we do not have explicit information on history of maternal gestational diabetes and family history of type 2 diabetes or on presence of acanthosis nigricans or polycystic ovarian syndrome. Because of this imprecision, it is likely that we underestimated the number of US youth who would be eligible for diabetes screening. The NHANES questions also did not allow us to distinguish diabetes type (type 1 or type 2) in those with diagnosed diabetes. The cross-sectional design is an inherent limitation; we relied on existing cardiometabolic risk factors to identify high-risk youth. Additional studies with long-term follow-up for clinical outcomes are needed to evaluate prognosis among children and adolescents meeting criteria for prediabetes. This is a major gap in the pediatric diabetes literature. Strengths of our study include the large, nationally representative sample of children and adolescents and rigorous and standardized measurements of both FPG and HbA1c and important cardiometabolic risk factors.

CONCLUSIONS

Our results suggest that new screening guidelines may pose a high burden on the health care system given the large number of children and adolescents who are now eligible.

The current screening approach targets a large number of children and adolescents, whereas few will test positive for diabetes or prediabetes, and a substantial number of children with hyperglycemia may be missed. Targeted approaches to diabetes screening in certain settings may be warranted. We also provided evidence that HbA1c is a useful nonfasting test in children and adolescents, regardless of screening eligibility. Youth with prediabetic levels of HbA1c or fasting glucose had a high burden of other cardiometabolic risk factors, suggesting that intensive lifestyle interventions in this high-risk population could help prevent future diabetes and cardiovascular risk in adulthood.

ABBREVIATIONS

ADA: American Diabetes Association
CI: confidence interval
FPG: fasting plasma glucose
HbA1c: hemoglobin A1c
HDL-C: high-density lipoprotein cholesterol
LDL-C: low-density lipoprotein cholesterol
NCHS: National Center for Health Statistics
NPV: negative predictive value
OR: odds ratio
PPV: positive predictive value

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Pediatrics originally published online August 10, 2020;

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