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Prevalence of Prediabetes Among Adolescents and Young Adults in the United States, 2005-2016

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IMPORTANCE Individuals with prediabetes are at increased risk of developing type 2 diabetes, chronic kidney disease, and cardiovascular disease. The incidence and prevalence of type 2 diabetes in the US adolescent population have increased in the last decade. Therefore, it is important to monitor the prevalence of prediabetes and varying levels of glucose tolerance to assess the future risk of type 2 diabetes in the youngest segment of the population.

OBJECTIVE To examine the prevalence of impaired fasting glucose (IFG), impaired glucose tolerance (IGT), and increased glycated hemoglobin A_{1c} (HbA_{1c}) levels in US adolescents (aged 12-18 years) and young adults (aged 19-34 years) without diabetes.

DESIGN, SETTING, AND PARTICIPANTS This cross-sectional analyses of the 2005-2016 National Health and Nutrition Examination Survey assessed a population-based sample of adolescents and young adults who were not pregnant, did not have diabetes, and had measured fasting plasma glucose, 2-hour plasma glucose after a 75-g oral glucose tolerance test, and HbA_{1c} levels. Analysis began in April 2017.

MAIN OUTCOMES AND MEASURES Impaired fasting glucose was defined as fasting plasma glucose of 100 mg/dL to less than 126 mg/dL, IGT as 2-hour plasma glucose of 140 mg/dL to less than 200 mg/dL, and increased HbA_{1c} level as HbA_{1c} level between 5.7% and 6.4%. The prevalence of IFG, isolated IFG, IGT, isolated IGT, increased HbA_{1c} level, isolated increased HbA_{1c} level, and prediabetes (defined as having IFG, IGT, or increased HbA_{1c} level) were estimated. Fasting insulin levels and cardiometabolic risk factors across glycemic abnormality phenotypes were also compared. Obesity was defined as having age- and sex-specific body mass index (calculated as weight in kilograms divided by height in meters squared) in the 95th percentile or higher in adolescents or 30 or higher in young adults.

RESULTS Of 5786 individuals, 2606 (45%) were adolescents and 3180 (55%) were young adults. Of adolescents, 50.6% (95% CI, 47.6%-53.6%) were boys, and 50.6% (95% CI, 48.8%-52.4%) of young adults were men. Among adolescents, the prevalence of prediabetes was 18.0% (95% CI, 16.0%-20.1%) and among young adults was 24.0% (95% CI, 22.0%-26.1%). Impaired fasting glucose constituted the largest proportion of prediabetes, with prevalence of 11.1% (95% CI, 9.5%-13.0%) in adolescents and 15.8% (95% CI, 14.0%-17.9%) in young adults. In multivariable logistic models including age, sex, race/ethnicity, and body mass index, the predictive marginal prevalence of prediabetes was significantly higher in male than in female individuals (22.5% [95% CI, 19.5%-25.4%] vs 13.4% [95% CI, 10.8%-16.5%] in adolescents and 29.1% [95% CI, 26.4%-32.1%] vs 18.8% [95% CI, 16.5%-21.3%] in young adults). Prediabetes prevalence was significantly higher in individuals with obesity than in those with normal weight (25.7% [95% CI, 20.0%-32.4%] vs 16.4% [95% CI, 14.3%-18.7%] in adolescents and 36.9% [95% CI, 32.9%-41.1%] vs 16.6% [95% CI, 14.2%-19.4%] in young adults). Compared with persons with normal glucose tolerance, adolescents and young adults with prediabetes had significantly higher non–high-density lipoprotein cholesterol levels, systolic blood pressure, central adiposity, and lower insulin sensitivity ($P < .05$ for all).

CONCLUSIONS AND RELEVANCE In the United States, about 1 of 5 adolescents and 1 of 4 young adults have prediabetes. The adjusted prevalence of prediabetes is higher in male individuals and in people with obesity. Adolescents and young adults with prediabetes also present an unfavorable cardiometabolic risk profile, putting them both at increased risk of type 2 diabetes and cardiovascular diseases.

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Supplemental content

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The American Diabetes Association has defined prediabetes as the presence of impaired fasting glucose (IFG; fasting plasma glucose [FPG] concentration between 100 mg/dL to <126 mg/dL; to convert to millimoles per liter, multiply by 0.0555), impaired glucose tolerance (IGT; a 2-hour plasma glucose [2hrPG] concentration after a 75-g oral glucose tolerance test of 140 mg/dL to 199 mg/dL), or glycated hemoglobin A_{1c} (HbA_{1c}) levels between 5.7% and 6.4% (to convert to proportion of total hemoglobin, multiply by 0.01).[1] In adults, these 3 phenotypes increase the risk of developing type 2 diabetes[2] as well as cardiovascular diseases.[3] In 2011 to 2012, the overall prevalence of prediabetes among US adults, defined as the presence of any of the 3 glucose metabolism dysregulation phenotypes, was 38% and it increased to about 50% in persons 65 years and older.[4] In 2005 to 2014, in the US adolescent population aged 12 to 19 years, the prevalence of prediabetes was 17.4% when measured as any of the 3 glucose metabolism phenotypes[5]; more recent estimates of the prevalence of the 3 glucose abnormality phenotypes in US adolescents are lacking. A study among American Indian adolescents demonstrated that IFG, elevated HbA_{1c} levels, and IGT performed equally well in predicting the incidence of type 2 diabetes.[6] Given the observed recent increase in the incidence and prevalence of type 2 diabetes in US adolescents[7,8] and the projected more than 4-fold increase[9] in the next decades, it is important to monitor the prevalence of these phenotypes of glucose dysregulation at the population level. This will help guide prevention strategies and identify subgroups at higher risk for early-onset type 2 diabetes.

This study assessed the prevalence of IFG, IGT, increased HbA_{1c} level, and prediabetes (IFG, IGT, or increased HbA_{1c} levels) among US adolescents (aged 12-18 years) and young adults (aged 19-34 years) by sex, race/ethnicity, and body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) status. We also compared insulin sensitivity and cardiometabolic risk factors across these categories of glucose tolerance.

Key Points

Question What is the prevalence of prediabetes in US adolescents and young adults?

Findings In this survey study of 5786 US adolescents and young adults, the prevalence of prediabetes was lower among adolescents than young adults and significantly higher in male than female individuals and in those with obesity overall. Participants with prediabetes in both age groups had significantly higher non–high-density lipoprotein cholesterol levels, systolic blood pressure, central adiposity, and lower insulin sensitivity than individuals with normal glucose tolerance.

Meaning Adolescents and young adults with prediabetes present an unfavorable cardiometabolic risk profile and are therefore at increased risk of not only developing type 2 diabetes, but also cardiovascular diseases.

Methods

Data Source

We combined data from six 2-year cycles of the National Health and Nutrition Examination Surveys (NHANES; 2005-2006 through 2015-2016). NHANES is a cross-sectional, nationally representative survey that includes household interviews and standardized medical examinations plus blood sample collections in mobile examination centers.[10] Participants are randomly assigned to a morning or afternoon/evening session for their mobile examination centers appointment. Participants assigned to the morning sessions and who are scheduled for the oral glucose tolerance test are instructed to fast for at least 9 hours. The overall response rates among the examined samples were 77.4%, 75.4%, 77.3%, 69.5%, 68.5%, and 58.7% for the 2005-2006, 2007-2008, 2009-2010, 2011-2012, 2013-2014, and 2015-2016 surveys, respectively. Analysis began in April 2017.

Study Population

The study included participants aged 12 to 34 years who had fasted 8 to 24 hours and had valid results for FPG, 2hrPG, and HbA_{1c} tests. Participants were excluded if they reported receiving a diagnosis of diabetes by a health care professional (n = 199) or had undiagnosed diabetes (FPG, >125 mg/dL; 2hrPG, ≥200 mg/dL; or HbA_{1c}, ≥6.5%) (n = 100). Also excluded were pregnant women (n = 558) and those with missing values for FPG, 2hrPG, or HbA_{1c} levels (n = 639). The study received approval for human subjects research from the National Center for Health Statistics Institutional Review Board. All NHANES adult and emancipated minor participants provided written informed consent; a parent or guardian gave permission for minors to participate.

Measurements and Glucose Status Definitions

NHANES survey instruments and protocols have been previously published.[11] Laboratory analyses for biochemical indicators followed standard protocols and are described in detail.[12] Owing to changes in methodology for measuring FPG, 2hrPG, and insulin, all glucose measures were backward calibrated to the methodology used before the initial change in 2003,[13,14] as were fasting insulin levels.[14-16] Participants' glucose metabolism statuses were defined by 4 phenotypes: (1) IFG defined as FPG of 100 mg/dL to less than 126 mg/dL; (2) IGT defined as 2hrPG of 140 mg/dL to less than 200 mg/dL; (3) increased HbA_{1c} level determined by HbA_{1c} of 5.7% to less than 6.5%; or (4) prediabetes defined as having any of IFG, IGT, or increased HbA_{1c} level. Normal glucose tolerance (NGT) was defined as FPG less than 100 mg/dL; 2hrPG less than 140 mg/dL; and HbA_{1c} level less than 5.7%.

Total cholesterol and high-density lipoprotein (HDL) cholesterol levels were measured enzymatically. Non-HDL cholesterol levels were calculated as total cholesterol minus HDL cholesterol.

The Single Point Insulin Sensitivity Estimator was used as a surrogate measure of insulin sensitivity and calculated from HDL cholesterol, triglyceride level, and BMI.[17] Anthropometric measurements included barefoot standing height (with a stadiometer), weight with minimal clothing (on a digital, electronic scale), and waist circumference (in the horizontal plane

Table 1. Demographic and Clinical Characteristics of the US Population Aged 12 to 34 Years Using Data From the National Health and Nutrition Examination Survey, 2005-2016

Characteristic	Age Group, Mean (95% CI)		P Value for Difference
	12-18 y	19-34 y	
Sample size (population size)	2606 (10.0 million)	3180 (21.2 million)	NA
Male, %	50.6 (47.6-53.6)	50.6 (48.8-52.4)	.99
Age, y	15.1 (14.9-15.2)	26.4 (26.2-26.6)	NA
Race/ethnicity, %			
Non-Hispanic			
White	58.2 (53.8-62.4)	58.9 (55.1-62.6)	.68
Black	14.6 (12.5-17.0)	13.5 (11.5-15.8)	.25
Hispanic	19.6 (16.6-22.9)	19.5 (17.0-22.2)	.95
Obesity, %[a]	16.2 (14.2-18.5)	29.8 (27.7-32.1)	<.001
BMI	23.8 (23.5-24.2)	27.7 (27.3-28.1)	<.001
Waist to height ratio >0.5, %	36.0 (33.3-38.9)	64.0 (61.2-66.7)	<.001
Non-HDL cholesterol, mg/dL	103.0 (101.6-104.4)	125.8 (124.2-127.5)	<.001
Systolic blood pressure, mm Hg	109.2 (108.6-109.9)	114.2 (113.6-114.8)	<.001
Fasting insulin, μU/mL[b]	3.7 (3.5-3.9)	3.4 (3.3-3.5)	.01
Insulin sensitivity (SPISE)[c]	8.5 (8.3-8.7)	6.6 (6.5-6.7)	<.001

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HDL, high-density lipoprotein; NA, not applicable; SPISE, Single Point Insulin Sensitivity Estimator.

SI conversion factors: To convert HDL cholesterol to mmol/L, multiply by 0.0259; insulin to pmol/L, multiply by 6.945.

[a] Defined as age- and sex-specific BMI in the 95th percentile or higher for participants aged 12 to 18 years and as BMI of 30 or higher in participants aged 19 to 34 years.

[b] Values represent geometric means (95% CI).

[c] SPISE = $600 \times \text{HDL cholesterol}^{0.185}/(\text{triglycerides}^{0.2} \times \text{BMI}^{1.338})$.

at a point marked just above the right ilium on the midaxillary line at minimal respiration). Height and waist circumference were recorded to the nearest 0.1 cm. We used waist-to-height ratio greater than 0.5 as a measure of central adiposity. Body mass index was categorized as normal or underweight, overweight, or obesity. In participants aged 19 to 34 years, normal weight was defined as BMI less than 25, overweight as 25 to less than 30, and obesity as BMI of 30 or less. For participants aged 12 to 18 years, BMI was compared with age- and sex-specific growth norms.[18] Participants with BMI in less than the 85th percentile of their age- and sex-specific group were considered to have normal weight, 85th percentile to less than 95th percentile to have overweight, and 95th percentile or higher to have obesity.

Up to 3 blood pressure measurements were taken by a physician after a 5-minute rest following the NHANES standard protocol and the mean of the measurements was used for the analysis. Interview data included sex and race/ethnicity, classified as non-Hispanic white (NHW), non-Hispanic black (NHB), Hispanic, or other. Owing to small sample size, the other race/ethnicity group was suppressed in all tables.

Data Analysis

Data were analyzed using SAS version 9.4 (SAS Institute) and SAS-callable SUDAAN 11.0 to account for the complex sampling design of NHANES, including unequal probabilities of selection, nonresponse adjustments, and a stratified, clustered sample design. Because our sample included only participants with valid measures for both FPG and 2hrPG, we used the sample weights for the oral glucose tolerance test subsample of NHANES to make results representative of the civilian, noninstitutionalized US population. Distributions of FPG, 2hrPG, and HbA_{1c} level were plotted using unweighted kernel probability density estimation of the probability density function to show the shape of the overall distributions.[19] The distribution plots were right-truncated because people with diabetes (either diagnosed or undiagnosed) were excluded from the analysis. We compared the medians and confidence intervals for each distribution by age group and sex.

To compare the prevalence of each glycemic status category or prediabetes across groups within the sample, we calculated the predictive margins, ie, covariate-adjusted percentages, for each of the prediabetes phenotypes using logistic regression models.[20,21] Results were stratified by age in years, sex, race/ethnicity, and BMI category. We used linear regression models to calculate predictive margins, ie, covariate-adjusted means, for cardiometabolic continuous variables across glycemic status categories. Results were adjusted by age in years, sex, and race/ethnicity. Because of the skewed distributions of fasting insulin levels, this variable was log-transformed for the analyses. Statistical significance was defined as 2-sided *P* value less than .05.

Results

The final analytic sample consisted of 5786 participants. Of these, 2606 (45%) were adolescents aged 12 to 18 years and 3180 (55%) were young adults aged 19 to 34 years. The distribution of sex and race/ethnicity were similar across age groups of adolescents and young adults (50.6% [95% CI, 47.6%-53.6%] vs 50.6% [95% CI, 48.8%-52.4%] male; 58.2% [95% CI, 53.8%-62.4%] vs 58.9% [95% CI, 55.1%-62.6%] NHW; 14.6% [95% CI, 12.5%-17.0%] vs 13.5% [95% CI, 11.5%-15.8%] NHB; 19.6% [95% CI, 16.6%-22.9%] vs 19.5% [95% CI, 17.0%-22.2%] Hispanic) (Table 1). However, there were significant differences in many of the metabolic indicators. A larger proportion of young adults had waist-to-height ratios greater than 0.5 (36.0% [95% CI, 33.3%-38.9%] vs 64.0% [95% CI, 61.2%-66.7%]; $P < .001$) and had higher non-HDL cholesterol (103.0 [95% CI, 101.6-104.4] vs 125.8 [95% CI 124.2-127.5]; $P < .001$).

Table 2. Distribution of Glucose Metabolism Abnormalities in US Adolescents and Young Adults by Age[a]

Characteristic	% (95% CI)	
	Adolescents	Young Adults
Age, y	12-18	19-34
Normal glucose	82.0 (79.9-84.0)	76.0 (73.9-78.1)
IFG only	9.2 (7.8-10.7)	11.4 (9.7-13.4)
IGT only	2.8 (2.0-3.8)	3.2 (2.6-4.0)
Increased HbA_{1c} level only	3.7 (3.0-4.7)	4.6 (3.9-5.4)
IFG + IGT	0.7 (0.3-1.6)	1.3 (0.9-1.9)
IFG + increased HbA_{1c} level	1.0 (0.7-1.6)	2.2 (1.7-2.8)
IGT + increased HbA_{1c} level	0.3 (0.2-0.5)	0.3 (0.2-0.6)
IFG + IGT + increased HbA_{1c} level	0.2 (0.1-0.5)	0.9 (0.5-1.4)
All IFG	11.1 (9.5-13.0)	15.8 (14.0-17.9)
All IGT	4.0 (3.1-5.2)	5.8 (4.9-6.8)
All increased HbA_{1c} level	5.3 (4.3-6.4)	8.0 (7.0-9.2)
Any prediabetes	18.0 (16.0-20.1)	24.0 (21.9-26.1)

Abbreviations: HbA_{1c}, glycated hemoglobin A_{1c}; IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

[a] Impaired fasting glucose is defined as a blood glucose level of 100 mg/dL to less than 126 mg/dL (to convert to mmol/L, multiply by 0.0555). Impaired glucose tolerance is defined as 2-hour plasma glucose level of 140 mg/dL to less than 200 mg/dL after oral glucose tolerance test. Increased HbA_{1c} level defined as 5.7% to less than 6.5% (to convert to proportion of total hemoglobin, multiply by 0.01). Prediabetes is defined as having any of IFG, IGT, or increased HbA_{1c} level.

Fasting insulin levels and insulin sensitivity were significantly higher in adolescents than in young adults (3.7 [95% CI, 3.5-3.9] vs 3.4 [95% CI, 3.3-3.5]; $P = .01$ and 8.5 [95% CI, 8.3-8.7] vs 6.6 [95% CI, 6.5-6.7]; $P < .001$, respectively).

The probability density estimates for FPG, 2hrPG, and HbA_{1c} level by age group and sex are shown in the eFigure in the Supplement; medians and confidence intervals are reported in eTable 1 in the Supplement. For FPG, there was a significant difference between male and female individuals in both age groups, with male individuals having significantly higher medians. There were no significant differences in FPG by age group. In addition, there were no significant differences in 2hrPG or HbA_{1c} level between male and female individuals or by age group.

There was very little overlap among IFG, IGT, and increased HbA_{1c} level categories (**Table 2**). For example, among the 11.1% (95% CI, 9.5%-13.0%) of the population aged 12 to 18 years affected by IFG, 9.2% (95% CI, 7.8%-10.7%) had isolated IFG. There were significant differences by age group in the percentage with IFG (11.1% [95% CI, 9.5%-13.0%] among adolescents vs 15.8% [95% CI, 14.0%-17.9%] among young adults; $P < .001$), with IGT (4.0% [95% CI, 3.1%-5.2%] among adolescents vs 5.8% [95% CI, 4.9%-6.8%] among young adults; $P = .015$), and with increased HbA_{1c} levels (5.3% [95% CI, 4.3%-6.4%] among adolescents vs 8.0% [95% CI, 7.0%-9.2%] among young adults; $P < .001$). Overall, the percentage with prediabetes (any of IFG, IGT, or increased HbA_{1c} level) was significantly lower for individuals aged 12 to 18 years than for those aged 19 to 34 years (18.0% [95% CI, 16.0%-20.1%] vs 24.0% [95% CI, 21.9%-26.1%]; $P < .001$) (eTable 2 in the Supplement provides distributions by age group and race/ethnicity).

In girls aged 12 to 18 years, after adjusting for age in years, race/ethnicity, and BMI, the prevalence of IFG was significantly lower than for boys (7.0% [95% CI, 5.1%-9.4%] vs 15.2% [95% CI, 13.0%-17.8%]; $P < .001$) (**Table 3**). The prevalence of IFG was significantly lower in NHB than Hispanic adolescents (7.8 [95% CI, 5.5%-11.0%] vs 16.5% [95% CI, 13.5%-19.9%]; $P < .001$) while increased HbA_{1c} levels were significantly more prevalent in NHB adolescents than in Hispanic or NHW adolescents (16.7% [95% CI, 13.1%-21.1%] vs 6.8% [95% CI, 4.7%-9.9%] and 1.9% [95% CI, 1.0%-3.4%] for all increased HbA_{1c} level; both $P < .001$). Among individuals aged 12 to 18 years, the adjusted prevalence of prediabetes (any of IFG, IGT, or increased HbA_{1c} level) was significantly lower in girls than in boys (13.4% [95% CI, 10.8%-16.5%] vs 22.5% [95% CI, 19.8%-25.4%]; $P < .001$), as well as in adolescents with normal weight compared with adolescents with obesity (16.4% [95% CI, 14.3%-18.7%] vs 25.7% [95% CI, 20.0%-32.4%]; $P = .004$).

The results for young adults aged 19 to 34 years were similar (**Table 4**). The adjusted prevalence of IFG was significantly lower in women than in men (10.1% [95% CI, 8.1%-12.5%] vs 21.5% [95% CI, 18.9%-24.3%]; $P < .001$). There were also significant differences in the percentage with IFG between NHB and Hispanic young adults (19.0% [95% CI, 16.0%-22.3%] vs 10.7% [95% CI, 8.2%-13.7%]; $P < .001$), but the prevalence of increased HbA_{1c} level was significantly greater in NHB young adults compared with Hispanic young adults (18.2% [95% CI, 15.4%-21.3%] vs 10.6% [95% CI, 8.7%-12.8%]; $P < .001$) and NHW individuals (4.8% [95% CI, 3.5%-6.4%]; $P < .001$). The adjusted prevalence for prediabetes among individuals aged 19 to 34 years varied by BMI, with highest prevalence among people with obesity, intermediate in those with overweight, and lowest in those with normal weight or underweight (36.9% [95% CI, 32.9%-41.1%], 20.7% [95% CI, 17.9%-23.7%], and 16.6% [95% CI, 14.2%-19.4%], respectively).

Among adolescents aged 12 to 18 years, systolic blood pressure was significantly higher among all with IFG, IGT, increased HbA_{1c} level, or prediabetes than in those with NGT (*P* values shown in **Table 5**). Non-HDL cholesterol levels in adolescents were significantly higher among all with IFG, IGT, or prediabetes compared with those with NGT. The groups of all adolescents with IFG, all with increased HbA_{1c} level or prediabetes also presented significantly higher waist-to-height ratio compared with those with NGT. All adolescents with IFG, with increased HbA_{1c} level, or prediabetes had a significantly higher BMI and lower insulin sensitivity when compared with those with NGT.

Among young adults aged 19 to 34 years, systolic blood pressure and non-HDL cholesterol were significantly higher for all those with IFG, all with IGT, all with increased HbA_{1c} level, or prediabetes compared with NGT (*P* values shown in Table 5). Young adults with any of the glucose abnormal phenotypes had significantly higher waist-to-height ratio than the NGT group and were also significantly less insulin sensitive than those with NGT.

Table 3. Crude and Adjusted Prevalence of IFG, IGT, Increased HbA_{1c}, and Prediabetes in US Adolescents Aged 12 to 18 Years by Sex, Race/Ethnicity, and BMI Status[a]

	% (95% CI)						
	Isolated			All			
Characteristic	IFG	IGT	Increased HbA_{1c} Level	IFG	IGT	Increased HbA_{1c} Level	Prediabetes
Unadjusted							
All youth aged 12-18 y	9.2 (7.8-10.8)	2.8 (2.0-3.8)	3.7 (3.0-4.7)	11.1 (9.5-13.0)	4.0 (3.1-5.2)	5.3 (4.4-6.5)	18.0 (16.0-20.1)
Adjusted by Age, Sex, Race/Ethnicity, and BMI[b]							
Sex							
Male	12.9 (10.8-15.4)	2.4 (1.4-4.1)	4.5 (3.5-5.9)	15.2 (13.0-17.8)	3.5 (2.4-5.2)	6.6 (5.3-8.1)	22.5 (19.8-25.4)
Female	5.4 (4.0-7.1)	3.1 (1.9-4.9)	2.9 (2.0-4.2)	7.0 (5.1-9.4)	4.5 (3.0-6.6)	4.0 (2.8-5.6)	13.4 (10.8-16.5)
Race/ethnicity							
Non-Hispanic							
White	9.7 (7.7-12.2)	3.4 (2.2-5.1)	1.7 (0.9-3.2)	10.7 (8.3-13.6)	4.3 (2.9-6.2)	1.9 (1.0-3.4)	15.8 (12.9-19.1)
Black	4.7 (3.2-7.0)	0.8 (0.3-1.8)	13.0 (10.4-16.1)	7.8 (5.5-11.0)	2.6 (1.6-4.3)	16.7 (13.1-21.1)	22.7 (19.0-26.8)
Hispanic	12.5 (10.1-15.4)	2.3 (1.4-3.5)	3.2 (2.0-5.2)	16.5 (13.5-19.9)	4.2 (2.9-6.2)	6.8 (4.7-9.9)	22.5 (19.0-26.3)
BMI[c]							
Normal or underweight	8.2 (6.6-10.2)	2.8 (1.9-4.1)	3.8 (2.9-4.9)	9.6 (7.7-12.0)	3.7 (2.6-5.2)	4.8 (3.7-6.2)	16.4 (14.3-18.7)
Overweight	10.6 (6.8-16.2)	1.5 (0.7-3.4)	2.8 (1.6-4.7)	12.4 (8.4-17.8)	2.4 (1.2-5.0)	4.2 (2.6-6.5)	16.6 (12.7-21.5)
Obesity	12.3 (8.5-17.5)	3.6 (1.7-7.4)	4.2 (2.3-7.5)	16.8 (12.3-22.4)	6.6 (4.1-10.6)	8 (5.7-11.1)	25.7 (20.0-32.4)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HbA_{1c}, glycated hemoglobin A_{1c}; IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

[a] Impaired fasting glucose is defined as a blood glucose level of 100 mg/dL to less than 126 mg/dL (to convert to mmol/L, multiply by 0.0555). Impaired glucose tolerance is defined as 2-hour plasma glucose level of 140 mg/dL to less than 200 mg/dL after oral glucose tolerance test. Increased glycated HbA_{1c} is defined as 5.7% to less than 6.5% (to convert to proportion of total hemoglobin, multiply by 0.01). Prediabetes is defined as having any of IFG, IGT, or increased HbA_{1c} level.

[b] Predictive margins were obtained from logistic regression.

[c] Normal or underweight was defined as BMI less than 85th percentile, overweight as 85th percentile to less than 95th percentile, and obesity as BMI of 95th percentile or higher.

Discussion

Using a nationally representative data set comprising 12 years of NHANES data (2005-2016), we estimated the overall prevalence of prediabetes (IFG, IGT, or increased HbA_{1c} level) to be about 1 in 5 for adolescents aged 12 to 18 years and 1 in 4 for young adults aged 19 to 34 years. In both age groups, of the phenotypes of glucose homeostasis dysregulation, IFG was the most prevalent. In addition, we found very little overlap across the subgroups having IFG, IGT, and increased HbA_{1c} level, indicating that the prevalence of prediabetes varies depending on the method used to identify this condition. In adults, it has been demonstrated that the pathophysiology of IFG and IGT differ[22-28] with IFG characterized by reduced basal insulin secretion and increased hepatic and renal insulin resistance, while IGT was associated with impaired postprandial insulin secretion and increased peripheral insulin resistance.[27,29-31] Very few data are available on the natural history and rate of progression to type 2 diabetes of these different phenotypes of glucose metabolism abnormalities in adolescence, as studies are usually limited to populations at very high risk for diabetes.[6] In adolescents with obesity, the predominant defect in IFG or IGT is impaired insulin secretion associated, as in adults, with insulin resistance. However, compared with adults, decline in β-cell function seems to occur at an accelerated rate resulting in relative insulin deficiency and progression to overt type 2 diabetes[32-34] with insulin treatment needed to control hyperglycemia within a few years after diagnosis. Large longitudinal studies are needed to examine the natural history of these different phenotypes of glucose metabolism abnormalities in adolescents.

This study found that isolated IFG represented the most common glucose dysregulation in adolescents and young adults. While individuals with IFG are at increased risk for type 2 diabetes,[2] few primary prevention trials have included individuals selected for the presence of IFG[35,36] and none have been conducted in adolescents with IFG or IGT, to our knowledge. A Japanese study in persons without diabetes but with IFG, regardless of their 2hrPG or HbA_{1c} levels, found that lifestyle intervention significantly reduced the incidence of type 2 diabetes but only in individuals who had, in addition to IFG, either IGT or elevated HbA_{1c} levels. In individuals with isolated IFG, there was no significant reduction in diabetes incidence (hazard ratio, 1.17 [95% CI, 0.50-2.74]).[36] On the other hand, a systematic review and meta-analysis of randomized trials of structured lifestyle interventions in adults without IGT found significant improvements in FPG, HbA_{1c} level, fasting insulin levels, and insulin resistance.[37] A simulation model showed that applying the magnitude of changes observed in the meta-analysis in FPG (−2.5 mg/dL [95% CI, −3.4 mg/dL to −1.6 mg/dL]) or HbA_{1c} level (−0.05% [95% CI, −0.08% to

Table 4. Crude and Adjusted Prevalence of IFG, IGT, Increased HbA_{1c}, and Prediabetes in US Young Adults Aged 19 to 34 Years by Sex, Race/Ethnicity, and BMI Status[a]

Characteristic	% (95% CI)						
	Isolated			All			
	IFG	IGT	Increased HbA_{1c} Level	IFG	IGT	Increased HbA_{1c} Level	Prediabetes
Unadjusted							
All young adults aged 19-34 y	11.4 (9.7-13.4)	3.3 (2.6-4.0)	4.6 (3.9-5.4)	15.8 (14.9-17.9)	5.8 (4.9-6.8)	8.0 (7.0-9.2)	24.0 (22.0-26.1)
Adjusted by Age, Sex, Race/Ethnicity, and BMI[b]							
Sex							
Male	16.9 (14.4-19.8)	2.3 (1.6-3.3)	5.0 (4.0-6.4)	21.5 (18.9-24.3)	4.5 (3.4-5.8)	8.6 (7.2-10.3)	29.1 (26.4-32.1)
Female	5.8 (4.4-7.7)	4.2 (3.2-5.5)	4.1 (3.3-5.1)	10.1 (8.1-12.5)	7.1 (5.8-8.7)	7.4 (6.1-9.0)	18.8 (16.5-21.3)
Race/ethnicity							
Non-Hispanic							
White	12.4 (9.9-15.3)	3.4 (2.5-4.7)	2.3 (1.6-3.4)	15.4 (12.8-18.5)	5.1 (4.0-6.6)	4.8 (3.5-6.4)	21.4 (18.5-24.5)
Black	6.4 (4.4-9.2)	1.4 (0.7-2.8)	14.5 (11.9-17.6)	10.7 (8.2-13.7)	3.5 (2.4-5.2)	18.2 (15.4-21.3)	26.9 (23.5-30.5)
Hispanic	11.4 (9.4-13.8)	3.7 (2.4-5.6)	5.4 (4.1-7.2)	19.0 (16.0-22.3)	8.3 (6.4-10.5)	10.6 (8.7-12.8)	28.7 (25.1-32.5)
BMI[c]							
Normal or underweight	9.2 (7.3-11.5)	2.1 (1.3-3.6)	3.5 (2.6-4.9)	10.9 (9.0-13.1)	2.9 (1.9-4.3)	4.8 (3.7-6.1)	16.6 (14.2-19.4)
Overweight	10.1 (8.0-12.7)	2.8 (1.7-4.6)	4.4 (3.2-6.1)	13.2 (10.6-16.2)	4.9 (3.4-7.0)	6.5 (5.0-8.3)	20.7 (17.9-23.7)
Obesity	15.9 (12.8-19.7)	5.3 (3.9-7.2)	5.8 (4.3-7.8)	25.2 (21.7-29.0)	10.6 (8.5-13.2)	13 (10.5-15.9)	36.9 (32.9-41.1)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HbA_{1c}, glycated hemoglobin A_{1c}; IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

[a] Impaired fasting glucose is defined as a blood glucose level of 100 mg/dL to less than 126 mg/dL (to convert to mmol/L, multiply by 0.0555). Impaired glucose tolerance is defined as 2-hour plasma glucose level of 140 mg/dL to less than 200 mg/dL after oral glucose tolerance test. Increased glycated HbA_{1c} is defined as 5.7% to less than 6.5% (to convert to proportion of total hemoglobin, multiply by 0.01). Prediabetes is defined as having any of IFG, IGT, or increased HbA_{1c} level.

[b] Predictive margins were obtained from logistic regression.

[c] Normal or underweight was defined as BMI less than 25, overweight as 25 to less than 30, and obesity as BMI of 30 or higher.

−0.02%]) to the US adult population could reduce the prevalence of prediabetes by 29%.[37]

We found that in adolescents and young adults, the prevalence of prediabetes in male individuals was almost twice that in female individuals, which was driven by a 2-fold difference in the percentage of IFG in male individuals compared with female individuals. Female individuals, on the other hand, were more likely to have IGT than male individuals, but this difference was not statistically significant. These findings are consistent with those of other studies in adults[26,38-43]; however, the underlying mechanisms for explaining this discrepancy are still unclear. Hormone replacement therapy in postmenopausal women has been associated with reduced fasting glucose levels, reduced insulin resistance, and increased risk of isolated IGT,[43,44] suggesting that female sex hormones, primarily estrogen, may contribute to the differences in the prevalence of IFG and IGT between male and female individuals. The finding that IFG and IGT prevalence differs by sex also highlights the fact that screening programs based solely on fasting glucose value may miss women at high risk for developing type 2 diabetes.

In our study, NHB adolescents and young adults had higher rates of increased HbA_{1c} levels compared with Hispanic and NHW individuals. Similarly, black participants with prediabetes enrolled in the US Diabetes Prevention Program research study had higher levels of HbA_{1c} levels compared with white participants, after adjustment for glucose concentration.[45] This difference was also found in individuals with normal glucose levels.[46] Studies have shown that HbA_{1c} levels overestimate mean glucose concentrations in NHB compared with NHW individuals, which may be due to differences in hemoglobin glycation among children and adults[47] or red cell survival among adults.[48] In NHB participants of the Atherosclerosis Risk in Communities study with a mean age of 55 to 56 years and adjusted for age and sex, a 1% increase in HbA_{1c} level at baseline was associated with a 4-fold increase in the incidence of type 2 diabetes after 20 years of follow-up.[49] Among individuals with HbA_{1c} level of 5.7% or higher, the incidence of diabetes in NHB was similar to that of NHW individuals (30.5 events per 1000 person-years [95% CI, 28.6-32.5]) and 29.4 events per 1000 person-years [95% CI, 26.8-32.1], respectively). However, in young adults, a type 2 diabetes risk prediction model that included HbA_{1c} level performed better among NHW than NHB individuals at predicting 5-year diabetes incidence.[50] These findings highlight the need for additional studies on the long-term consequences and preventive strategies of abnormal glucose metabolism as measured by HbA_{1c} levels in adolescents and young adults, especially of minority racial/ethnic groups.

Obesity is a strong predictor of increased risk for type 2 diabetes in adults[51,52] and probably also plays a major role in the development of the disease at younger ages. Obesity is highly prevalent among US adolescents and young adults.[53] The finding that a large proportion of adolescents and young adults with obesity already present glucose metabolism abnormalities is of great public health concern given the sharp increase in type

Table 5. Metabolic Characteristics by Glucose Tolerance Status in US Adolescents and Young Adults Adjusted by Age, Sex, and Race/Ethnicity[a,b]

Characteristic	Mean (95% CI)							
		Isolated			All			
	NGT	IFG	IGT	Increased HbA_{1c} Level	IFG	IGT	Increased HbA_{1c} Level	Prediabetes
Adolescents, Aged 12-18 y								
Systolic blood pressure, mm Hg	108.5 (107.8-109.1)	113.1 (111.3-114.9)[c]	112 (108.7-115.2)	111.5 (109.3-113.8)	113.1 (111.2-115.1)[c]	111.6 (108.7-114.6)[c]	112.2 (110.9-114.5)[c]	112.6 (111.1-114.0)[c]
Non-HDL cholesterol, mg/dL	101.6 (100.0-103.2)	110.5 (104.8-116.1)[c]	110.2 (98.6-121.7)	103.2 (95.8-110.6)	110.9 (105.6-116.3)[c]	112.6 (103.1-122)[c]	105.8 (100.1-111.5)	109.3 (104.7-113.9)[c]
Waist-to-height ratio	0.49 (0.48-0.49)	0.50 (0.48-0.52)	0.50 (0.46-0.54)	0.52 (0.49-0.54)	0.52 (0.50-0.53)[c]	0.52 (0.48-0.55)	0.54 (0.52-0.57)[c]	0.51 (0.50-0.53)[c]
BMI	23.5 (23.2-23.9)	24.4 (23.1-25.6)	23.3 (20.7-25.9)	25.3 (23.3-27.3)	25.3 (24.0-26.6)[c]	24.7 (22.5-26.9)	27.2 (25.4-29.0)[c]	25.1 (24.0-26.1)[c]
Fasting insulin, μU/mL[d]	4.4 (4.2-4.7)	4.9 (4.4-5.5)	4.1 (3.3-4.8)	5.5 (4.4-6.7)	5.1 (4.5-5.7)[c]	4.4 (3.7-5.1)	5.8 (4.8-6.9)[c]	5.0 (4.5-5.5)[c]
Insulin sensitivity (SPISE)[e]	8.6 (8.4-8.8)	8 (7.4-8.6)	8.9 (7.6-10.2)	8.1 (7.4-8.9)	7.7 (7.0-8.3)[c]	8.4 (7.2-9.6)	7.3 (6.7-8.0)[c]	7.9 (7.4-8.5)[c]
Young Adults, Aged 19-34 y								
Systolic blood pressure, mm Hg	113.4 (112.8-113.9)	116.9 (115.4-118.3)[c]	115.7 (113.2-118.2)	115.1 (113.1-117.1)	117.6 (116.5-118.8)[c]	117.6 (116.5-118.8)[c]	117.6 (116.5-118.8)[c]	117.0 (116.0-118.0)[c]
Non-HDL cholesterol, mg/dL	101.6 (100.0-103.2)	128.9 (125-132.9)[c]	136.3 (129.5-143.1)[c]	126.3 (119.6-132.9)	132.8 (129.4-136.3)[c]	112.6 (103.1-122)[c]	133.7 (127.7-139.7)[c]	132.8 (129.6-136.0)[c]
Waist-to-height ratio	0.53 (0.53-0.54)	0.58 (0.57-0.60)[c]	0.58 (0.56-0.61)[c]	0.58 (0.55-0.60)[c]	0.60 (0.58-0.61)[c]	0.6 (0.59-0.63)[c]	0.61 (0.59-0.62)[c]	0.59 (0.58-0.61)[c]
BMI	26.7 (26.4-27.1)	30.2 (29-31.3)[c]	29.1 (27.4-30.7)[c]	29.5 (27.8-31.2)[c]	31.2 (30.2-32.2)[c]	31.2 (30-32.5)[c]	31.6 (30.4-32.8)[c]	30.8 (29.9-31.6)[c]
Fasting insulin, μU/mL[d]	4.0 (3.8-4.1)	5.0 (4.3-5.7)[c]	5.0 (4.1-5.9)[c]	4.3 (3.7-5.0)	5.4 (4.9-5.9)[c]	5.4 (4.6-6.1)[c]	5.2 (4.7-5.7)[c]	5.1 (4.7-5.6)[c]
Insulin sensitivity (SPISE)[e]	6.9 (6.8-7.0)	5.8 (5.6-6.1)[c]	5.8 (5.2-6.5)[c]	6.2 (5.6-6.7)[c]	5.5 (5.3-5.7)[c]	5.3 (4.8-5.7)[c]	5.6 (5.2-5.9)[c]	5.6 (5.4-5.9)[c]

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HbA_{1c}, glycated hemoglobin A_{1c}; HDL, high-density lipoprotein; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; NGT, normal glucose tolerance; SPISE, Single Point Insulin Sensitivity Estimator.

SI conversion factors: To convert HDL cholesterol to mmol/L, multiply by 0.0259; insulin to pmol/L, multiply by 6.945.

[a] Predictive margins were obtained from linear regression.

[b] Impaired fasting glucose is defined as a blood glucose level of 100 mg/dL to less than 126 mg/dL (to convert to mmol/L, multiply by 0.0555). Impaired glucose tolerance is defined as 2-hour plasma glucose level of 140 mg/dL to less than 200 mg/dL after oral glucose tolerance test. Increased HbA_{1c} level is defined as 5.7% to less than 6.5% (to convert to proportion of total hemoglobin, multiply by 0.01). Prediabetes is defined as having any of IFG, IGT, or increased HbA_{1c} level.

[c] $P < .05$ vs NGT.

[d] Dependent variable is the logarithm of fasting insulin.

[e] SPISE = $600 \times \text{HDL-cholesterol}^{0.185}/(\text{triglycerides}^{0.2} \times \text{BMI}^{1.338})$.

2 diabetes in adolescence.[7] In an obesity clinic population of adolescents with overweight or obesity with IGT during a median follow-up of 2.9 years, 65% reverted to NGT and 8% progressed to overt type 2 diabetes.[54] In adults, primary prevention intervention trials have demonstrated that in individuals at high risk, type 2 diabetes can be prevented or delayed with lifestyle modifications[55-59]; similar studies have not been conducted in the adolescent population. Therefore, future studies are needed to assess whether these interventions with demonstrated efficacy in adults are similarly effective in adolescents with different phenotypes of glucose metabolic dysregulations.

Limitations

Our results are subject to several limitations. First, FPG, 2hrPG, and HbA_{1c} levels were only measured once at the same time as all other biometric indicators, which may be problematic. Because of the poor reproducibility of IGT and IFG,[60] some individuals may have been misclassified. Furthermore, a large population-based screening program of people at high risk for type 2 diabetes reported that 21% of persons with elevated HbA_{1c} levels and 36% of those with IFG at first measurement regressed to normal range at a second confirmatory testing.[61] Second, our analyses are cross-sectional in design and causality cannot be inferred from our results. Third, we used Single Point Insulin Sensitivity Estimator as a surrogate measure of insulin sensitivity rather than direct measures of glucose disposal. However, Single Point Insulin Sensitivity Estimator has been shown to have good agreement with M values from the euglycemic hyperinsulinemic clamp test and has been validated among juveniles and white adults.[17] Fourth, we were not able to differentiate between participants with one of the glucose tolerance statuses and those with preclinical type 1 diabetes. Finally, some of the glucose tolerance statuses had relatively few participants, although combining 10 years of NHANES data helps to counter this problem. However, combining multiple years of data to represent the entire period assumes that prevalence is relatively constant across time.[62] If the prevalence of prediabetes has risen, as has the prevalence of type 2 diabetes, our prevalence estimates may be lower than the true current prevalence levels.

Conclusions

Our study found that prediabetes is highly prevalent in US adolescents and young adults, especially in male individuals and in people with obesity. Moreover, adolescents and young adults with prediabetes also present an unfavorable cardiometabolic risk profile and are therefore at increased risk of not only developing type 2 diabetes, but also cardiovascular diseases. These findings together with the observed increase in the prevalence of type 2 diabetes in US adolescents[7] and in diabetes-related complications in young adults[63] highlight the need for primary and secondary prevention efforts tailored to the young segment of the US population.

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