Comparison of A1C and Fasting Glucose Criteria to Diagnose Diabetes Among U.S. Adults

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OBJECTIVE — To compare A1C and fasting glucose for the diagnosis of diabetes among U.S. adults.

RESEARCH DESIGN AND METHODS — This study included 6,890 adults (≥20 years of age) from the 1999–2006 National Health and Nutrition Examination Survey without a self-reported history of diabetes who had fasted ≥9 h. A1C ≥6.5% and fasting glucose ≥126 mg/dl were used, separately, to define diabetes.

RESULTS — Overall, 1.8% of U.S. adults had A1C ≥6.5% and fasting glucose ≥126 mg/dl, 0.5% had A1C ≥6.5% and fasting glucose <126 mg/dl, and 1.8% had A1C <6.5% and fasting glucose ≥126 mg/dl. Compared with individuals with A1C <6.5% and fasting glucose ≥126 mg/dl, individuals with A1C ≥6.5% and fasting glucose <126 mg/dl were younger, more likely to be non-Hispanic black, had lower Hb levels, and had higher C-reactive protein.

CONCLUSIONS — A1C ≥6.5% demonstrates reasonable agreement with fasting glucose for diagnosing diabetes among U.S. adults.

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In June 2009, the International Expert Committee released a report that recommended the use of A1C to diagnose diabetes (1). Previously, A1C had been used primarily to monitor glycemic control among individuals with diabetes. However, over the last decade, the A1C measurement has become standardized (2,3), facilitating its recognition as an acceptable diagnostic method for diabetes.

Before the release of this report, diabetes was mainly defined using a fasting plasma glucose ≥126 mg/dl (≥7.0 mmol/l) in the U.S (4). Using A1C (≥6.5%) to diagnose diabetes may identify different individuals than fasting plasma glucose because the two methods assess different elements of glucose metabolism (1). The purpose of this study was to compare A1C ≥6.5% and fasting plasma glucose ≥126 mg/dl for the identification of undiagnosed diabetes among participants in the U.S. National Health and Nutrition Examination Survey (NHANES). Additionally, we calculated the demographic characteristics and cardiovascular risk profile for individuals diagnosed with diabetes by each of these methods.

RESEARCH DESIGN AND METHODS

— NHANES 1999–2000, 2001–2002, 2003–2004, and 2005–2006 are serial cross-sectional surveys including nationally representative samples of the noninstitutionalized civilian U.S. population identified through a stratified, multistage probability sampling design. Methods for pooling these datasets have been published (5). The current analysis was limited to 6,890 participants without self-reported diabetes who attended a morning examination, fasted for ≥9 h at the time of their blood collection, and had valid plasma glucose and A1C values.

Data were collected through questionnaires (demographics, medical history), a physical examination (blood pressure), and blood collection (lipids, plasma glucose, A1C). Plasma glucose was measured using a modified hexokinase enzymatic method and A1C using high-performance liquid chromatography. The coefficient of variation was <3% in each 2-year period for glucose and <2% for A1C.

Participants were categorized into one of four mutually exclusive groups by the presence or absence of fasting plasma glucose ≥126 mg/dl and A1C ≥6.5%. The distribution of the population into these groupings was determined. The κ statistic was calculated as a measure of agreement. Characteristics of the study population were calculated for each group with the statistical significance of differences determined using least squares and maximum likelihood estimation for continuous and categorical variables, respectively. In secondary analyses, the distribution of U.S. adults by fasting glucose and different A1C cut-points (6.0–6.7%) were calculated. Also, sensitivity, specificity, positive and negative predictive values, and number of U.S. adults misclassified were calculated using different A1C cut-points. Analyses were weighted to represent the U.S. population and conducted using SUDAAN (version 9; Research Triangle Institute) to account for the complex survey design.

RESULTS

— Among U.S. adults, the prevalence of undiagnosed diabetes was 2.3% using A1C and 3.6% using fasting glucose. Moderate agreement existed for A1C and fasting glucose diagnoses (κ = 0.60; 95% CI 0.55–0.64). Diabetes classification was consistent for the majority of the study participants, with 95.9% classified as not having diabetes by both A1C and fasting glucose and 1.8% classified as having diabetes by both A1C and fasting glucose (Table 1). Discordant classifications occurred for 0.5% of participants who had an A1C ≥6.5% and fasting glucose <126 mg/dl and for 1.8% who

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Table 1—*Characteristics of NHANES participants (1999–2006) without self-reported diabetes, by A1C and fasting plasma glucose*

	A1C <6.5%		A1C ≥6.5%	
	FPG <126 mg/dl	FPG ≥126 mg/dl	FPG <126 mg/dl	FPG ≥126 mg/dl
n	6,541	142	45	162
Prevalence (95% CI)	95.9 (95.3–96.5)	1.8 (1.5–2.2)	0.5 (0.4–0.7)	1.8 (1.5–2.1)
Age (years)	44.7 ± 0.4†	60.0 ± 1.6*	53.1 ± 2.7	57.2 ± 1.5
Women (%)	52.9	36.3	39.8	38.7
Race/ethnicity				
Non-Hispanic white (%)	76.2*	81.9	64.9	59.5
Non-Hispanic black (%)	10.7†	7.4‡	25.9	14.9
Hispanic (%)	13.0	10.6	9.3	25.6
Current smoker (%)	23.8	15.1	16.5	22.8
Systolic blood pressure (mmHg)	121.3 ± 0.3	137.6 ± 1.9	130.0 ± 4.5	132.3 ± 2.6
Diastolic blood pressure (mmHg)	71.1 ± 0.3	72.0 ± 1.4	75.8 ± 3.7	71.2 ± 1.7
Hypertension (%)	25.3	65.2	52.7	56.7
BMI (kg/m^2)	27.9 ± 0.1*	31.2 ± 0.6	34.1 ± 2.5	32.7 ± 0.8
Waist circumference (cm)	95.5 ± 0.3*	107.5 ± 1.2	112.9 ± 6.5	110.1 ± 1.6
Total cholesterol (mg/dl)	200.9 ± 0.8	198.8 ± 4.8	196.5 ± 6.7	215.2 ± 5.7
HDL cholesterol (mg/dl)	53.4 ± 0.3	49.1 ± 1.3	47.7 ± 3.7	44.3 ± 1.1
Triglycerides (mg/dl)§	112 (78–164)	147 (106–214)	127 (88–151)	178 (128–257)‡
Estimated glomerular filtration rate <60 ml/min per 1.73 m^2	7.4	21.6	17.0	15.6
Microalbuminuria (%)	7.0	24.2	14.7	29.6
Hb (g/dl)	14.6 ± 0.1	15.0 ± 0.2†	14.3 ± 0.2	15.1 ± 0.1†
Serum albumin (g/dl)	4.29 ± 0.01	4.25 ± 0.04	4.17 ± 0.08	4.18 ± 0.03
Ferritin (ng/ml)§	67 (31–136)†	137 (77–253)	122 (57–139)	219 (96–293)*
Aspartate aminotransferase (units/l)	24.9 ± 0.2	28.3 ± 1.8	30.0 ± 3.3	27.7 ± 1.8
Alanine aminotransferase (unites/l)	25.6 ± 0.3†	30.7 ± 2.0	36.2 ± 3.7	33.6 ± 2.6
C-reactive protein (mg/l)§	1.9 (0.7–4.4)†	2.2 (1.2–6.2)*	4.2 (2.1–12.9)	4.1 (2.5–9.0)
FPG (mg/dl)	95.5 ± 0.3	136.9 ± 1.1	110.6 ± 2.2	199.9 ± 7.7
A1C (%)	5.26 ± 0.01	5.82 ± 0.05	6.92 ± 0.14	8.34 ± 0.19

Data are means ± SE or percent, except variables denoted by §, which are medians (25th to 75th percentiles). *$P < 0.05$; †$P < 0.01$; ‡$P < 0.001$ compared with individuals with A1C ≥6.5% and fasting plasma glucose (FPG) <126 mg/dl (after age adjustment).

had an A1C <6.5% and fasting glucose ≥126 mg/dl. Among individuals with an A1C ≥6.5% and fasting glucose <126 mg/dl, 82% had impaired fasting glucose (100–125 mg/dl). Among individuals with an A1C <6.5% and a fasting glucose ≥126 mg/dl, 45% had an A1C value ≥6.0% but <6.5% (i.e., elevated risk for diabetes using the new A1C guidelines).

The demographic and cardiovascular profile differed for participants with A1C ≥6.5% and fasting glucose <126 mg/dl compared with individuals with A1C <6.5% and fasting glucose ≥126 mg/dl. Specifically, participants with A1C ≥6.5% and fasting glucose <126 mg/dl were younger, more likely to be non-Hispanic black, had lower Hb, and higher C-reactive protein values.

The distribution of adults by fasting glucose and different A1C cut points are available in Table S1 (which is located in an online-only appendix at http://care.diabetesjournals.org/cgi/content/full/dc09-1227/DC1). Overall, lower A1C cut points resulted in higher sensitivity and lower specificity (Table S2).

CONCLUSIONS — The results of the current study indicate the new recommendation by the International Expert Committee to use A1C to diagnose diabetes would result in the same classification as fasting glucose for 97.7% of U.S. adults. For those with discordant results, 0.5% of U.S. adults had A1C ≥6.5% and fasting glucose <126 mg/dl, whereas 1.8% had A1C <6.5% and fasting glucose ≥126 mg/dl. Discordance in the diagnosis of diabetes using A1C and fasting glucose was expected and is likely due to the assessment of different aspects of glucose metabolism (1). For example, participants with an A1C ≥6.5% and fasting glucose <126 mg/dl may have been diagnosed by an oral glucose tolerance test, which was not available for the majority of participants in this study.

About 1.8% of U.S. adults had A1C <6.5% and fasting glucose ≥126 mg/dl and would not be classified as having diabetes using the new recommendation. However, as defined using the report's guidelines, almost half of these individuals would be identified as high risk for diabetes based on A1C values between 6.0 and 6.4%. Although these adults would not satisfy the new A1C recommendation for the diagnosis of diabetes, they would be targeted for preventive therapy to reduce diabetes risk, which may also prompt a fasting glucose measurement. Using a lower A1C cut point would result in more diabetes diagnoses among this group; however, there would also be a tradeoff with substantially more diabetes diagnoses among individuals who would have previously been classified as not having diabetes using fasting glucose alone.

Subgroup differences were noted in this study, with a higher percentage of individuals diagnosed with diabetes via

A1C versus with fasting glucose being non-Hispanic black and of younger age. These differences are similar to previous reports (6–8), but caution should be used when comparing estimates across subgroups because of the limited sample size in this study.

In summary, A1C may be an appropriate method for diagnosing diabetes, although clinical implications for using different A1C cut points warrant further investigation.

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