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.

Diabetes Care 33:95–97, 2010

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Received 6 July 2009 and accepted 21 September 2009. Published ahead of print at http://care.diabetesjournals.org on 6 October 2009. DOI: 10.2337/dc09-1227.

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A1C, fasting glucose, and diabetes

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/m²)      | 27.9 ± 0.1* | 31.2 ± 0.6 | 34.1 ± 2.5  | 32.7 ± 0.8     |
| Triglycerides (mg/dl)§ | 198.8 ± 4.8 | 196.5 ± 6.7 | 215.2 ± 5.7 | 215.2 ± 5.7    |
| C-reactive protein (mg/l)§ | 49.1 ± 1.3 | 47.7 ± 3.7 | 44.3 ± 1.1  |                |
| Estimated glomerular filtration rate <60 ml/min per 1.73 m² | 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 (77–233) | 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 (units/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 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

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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.

Acknowledgments—No potential conflicts of interest relevant to this article were reported.

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