Comparison of Diabetes Diagnostic Categories in the U.S. Population According to 1997 American Diabetes Association and 1980–1985 World Health Organization Diagnostic Criteria

MAUREEN I. HARRIS, PHD, MPH
RICHARD C. EASTMAN, MD
CATHERINE C. COWIE, PHD, MPH
KATHERINE M. FLEGAL, PHD
MARK S. EBERHARDT, PHD

OBJECTIVE — To compare the 1997 American Diabetes Association (ADA) and the 1980–1985 World Health Organization (WHO) diagnostic criteria in categorization of the diabetes diagnostic status of adults in the U.S.

RESEARCH DESIGN AND METHODS — Analyses are based on a probability sample of the U.S. population age 40–74 years in the 1988–1994 Third National Health and Nutrition Examination Survey (NHANES III). People with diabetes diagnosed before the survey were identified by questionnaire. For 2,844 people without diagnosed diabetes, fasting plasma glucose was obtained after an overnight 9 to <24-h fast, HbA_{1c} was measured, and a 2-h oral glucose tolerance test was administered.

RESULTS — Prevalence of diagnosed diabetes in this age-group is 7.9%. Prevalence of undiagnosed diabetes is 4.4% by ADA criteria and 6.4% by WHO criteria. The net change of −2.0% occurs because 1.0% are classified as having undiagnosed diabetes by ADA criteria but have impaired or normal glucose tolerance by WHO criteria, and 3.0% are classified as having impaired fasting glucose or normal fasting glucose by ADA criteria but have undiagnosed diabetes by WHO criteria. Prevalence of impaired fasting glucose is 10.1% (ADA), compared with 15.6% for impaired glucose tolerance (WHO). For those with undiagnosed diabetes by ADA criteria, 62.1% are above the normal range for HbA_{1c} compared with 47.1% by WHO criteria. Mean HbA_{1c} is 7.07% for undiagnosed diabetes by ADA criteria and 6.58% by WHO criteria.

CONCLUSIONS — The number of people with undiagnosed diabetes by ADA criteria is lower than that by WHO criteria. However, those individuals classified by ADA criteria are more hyperglycemic, with higher HbA_{1c} values and a greater proportion of values above the normal range. This fact, together with the simplicity of obtaining a fasting plasma glucose value, may result in the detection of a greater proportion of people with undiagnosed diabetes in clinical practice using the new ADA diagnostic criteria.

In 1996–1997, an expert committee of the American Diabetes Association (ADA) reviewed and revised the classification and diagnostic criteria for diabetes that had been promulgated by the National Diabetes Data Group (NDDG) in 1979 (1) and by the World Health Organization (WHO) in 1980 and 1985 (2,3). The findings of this committee have recently been published (4). The committee notes that for patients with symptoms of diabetes, only a casual plasma glucose value ≥200 mg/dl is required for diagnosis of diabetes. However, for clinical diagnosis in asymptomatic individuals and for epidemiologic studies, the committee recommends that diabetes should be defined by a fasting plasma glucose of ≥126 mg/dl. Two other diagnostic classes are delineated: impaired fasting glucose, defined as a fasting plasma glucose of 110–125 mg/dl, and normal fasting glucose, defined as a fasting plasma glucose of <110 mg/dl. The oral glucose tolerance test and its postchallenge glucose values, which form the core of the 1979 NDDG and the 1980–1985 WHO diagnostic criteria, are not advocated for use in either clinical diagnosis or epidemiologic research.

In the Third National Health and Nutrition Examination Survey (NHANES III), information on medical history of diabetes was obtained and fasting and 2-h postchallenge plasma glucose values were measured in a national sample of people age 40–74 years. We analyzed data from this survey to evaluate the effect of the new ADA diagnostic criteria versus the WHO criteria on categorization of the diagnostic status of adults in the U.S. Because a 1-h postchallenge plasma glucose value was not obtained in NHANES III, comparison with the NDDG criteria was not possible.

RESEARCH DESIGN AND METHODS

— NHANES III was conducted in 1988–1994 by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (5). The survey was designed to examine a nationally representative sample of the U.S. civilian noninstitutionalized population, based on a complex stratified multistage probability cluster sampling design. The protocol included a home interview followed by a physical examination in a

From the National Institute of Diabetes and Digestive and Kidney Diseases (M.I.H., R.C.E., C.C.C.), Bethesda; and the National Center for Health Statistics (K.M.F., M.S.E.), Centers for Disease Control and Prevention, Hyattsville, Maryland.

Address correspondence and reprint requests to Maureen I. Harris, PhD, MPH, NIDDK/NIH, Building 45, Room 5AN24, Bethesda, MD 20892. E-mail: harrism@ep.niddk.nih.gov.

Received for publication 11 July 1997 and accepted in revised form 27 August 1997.

Abbreviations: ADA, American Diabetes Association; NCHS, National Center for Health Statistics; NDDG, National Diabetes Data Group; NHANES III, Third National Health and Nutrition Examination Survey; WHO, World Health Organization.

Table 1—*Prevalence of diabetes diagnostic categories for U.S. adults age 40–74 years, using 1997 ADA criteria and 1980–1985 WHO criteria, and mean HbA_{1c} values for each category, NHANES III, 1988–1994*

Fasting plasma glucose (mg/dl)	2-h plasma glucose (mg/dl)	1997 ADA category	1985 WHO category	Prevalence %	Prevalence Millions	Mean HbA_{1c}
≥140	≥200	Undiagnosed diabetes	Undiagnosed diabetes	2.2	2.0	8.20
≥140	140 to <200	Undiagnosed diabetes	Undiagnosed diabetes	0.1	0.1	*
≥140	<140	Undiagnosed diabetes	Undiagnosed diabetes	0.1	0.1	*
126 to <140	≥200	Undiagnosed diabetes	Undiagnosed diabetes	1.0	0.9	6.14
126 to <140	140 to <200	Undiagnosed diabetes	Impaired glucose tolerance	0.7	0.7	5.86
126 to <140	<140	Undiagnosed diabetes	Normal glucose tolerance	0.3	0.3	*
110 to <126	≥200	Impaired fasting glucose	Undiagnosed diabetes	1.8	1.7	5.85
110 to <126	140 to <200	Impaired fasting glucose	Impaired glucose tolerance	3.9	3.7	5.53
110 to <126	<140	Impaired fasting glucose	Normal glucose tolerance	4.4	4.2	5.52
<110	≥200	Normal fasting glucose	Undiagnosed diabetes	1.2	1.2	5.20
<110	140 to <200	Normal fasting glucose	Impaired glucose tolerance	11.0	10.5	5.45
<110	<140	Normal fasting glucose	Normal glucose tolerance	65.4	62.3	5.27
Previously diagnosed diabetes	—	—	—	7.9	7.5	—
Total	—	—	—	100.0	95.2	—

*Value not shown because sample size is <20. ADA criteria are based on fasting plasma glucose values only; WHO criteria are based on fasting and 2-h plasma glucose values.

mobile examination center. For the age-group 40–74 years, 11,060 people were selected to take part in the survey. Of these, 8,737 people (79%) completed a household interview that included questions to determine whether they had diabetes that had been diagnosed by a physician before the survey. Based on the answers to these questions, 1,056 people were categorized as having previously diagnosed diabetes and 7,681 people were categorized as not having diagnosed diabetes.

Each household in which someone was interviewed was randomly assigned to either a morning examination session or an afternoon/evening session. There were 3,833 people age 40–74 years without diagnosed diabetes who were assigned to the morning session and instructed to fast overnight. In the examination, a fasting blood sample was taken, a 75-g glucose-equivalent oral glucose challenge (Dextol or Trutol) was given, and a blood sample was drawn 2 h (± 15 min) later. Both the fasting and the 2-h postchallenge plasma glucose values were obtained for 2,844 individuals (74%). The glucose values were not available for people who did not participate in the examination (n = 336), who were examined at home where fasting was not required (n = 51) or were examined in the afternoon/evening (n = 141), who fasted for <9 h or >24 h or had an unknown fasting time (n = 204), who had an unsuccessful venipuncture (n = 39), who refused the glucose challenge (n = 54), who became ill (n = 21), and who had other reasons (n = 143). There were no statistically significant differences between individuals with and without glucose values for a wide variety of demographic and health-related variables.

The procedures for blood collection and processing have been described (5). For glucose analysis, venous whole blood was collected into a vacuum tube containing the glycolytic inhibitors potassium oxalate and sodium fluoride and was centrifuged immediately at 1,500g for 10 min. For glycated hemoglobin, whole blood was collected into a vacuum tube containing the anticoagulant EDTA and refrigerated at 4–8°C. Frozen plasma and refrigerated whole blood specimens were shipped to the University of Missouri Diabetes Diagnostic laboratory via overnight courier. Plasma glucose was measured using a modified hexokinase enzymatic method. HbA_{1c} was measured by a high-performance liquid chromatographic assay as used in the Diabetes Control and Complications Trial (6).

Statistical analyses were carried out using SAS software (7). NHANES III used stratified cluster sampling to select participating subjects (i.e., certain age, race, and other sociodemographic groups were included in the survey at rates greater than their proportions in the U.S. population). It was thus necessary to use weights in the statistical analyses to adjust for this discrepancy, to produce estimates that were representative of the U.S. population. Rates using fasting and postchallenge glucose computed in the subsample of people without diagnosed diabetes were adjusted by the prevalence of diagnosed diabetes such that the sum represented the total population. To compute numbers of people in the ADA/WHO diagnostic categories, the NHANES III prevalence rates for people age 40–74 years were applied to U.S. Census Bureau estimates of the U.S. population age 40–74 years as of 1 July 1997 (8). Standard errors were calculated using SUDAAN (9), a program that takes into account the nonrandom cluster sample design in calculating variance estimates.

RESULTS — Prevalence of previously diagnosed diabetes is 7.9%, as based on medical history interview data and independent of the diagnostic criteria system used. Table 1 shows the prevalence of these diagnostic categories according to the two sets of criteria. Prevalence of undiagnosed diabetes is 4.4% by ADA criteria (4.1 million people) and 6.4% by WHO criteria (6.0 million people). The net change of −2.0% occurs because 1.0% are classifed as having undiagnosed diabetes in the ADA system who have impaired glucose tolerance or normal glucose tolerance by WHO criteria, and 3.0% are classified as having impaired fasting glucose or normal fasting glucose in the ADA system who have undiagnosed diabetes by WHO criteria.

Prevalence of impaired fasting glucose by ADA criteria is 10.1% (9.6 million people), and prevalence of impaired glucose

Table 2—*Percent distribution according to the normal range for HbA_{1c} and mean HbA_{1c} values for U.S. adults age 40–74 years categorized by ADA and WHO diagnostic criteria*

Diagnostic category	Percent distribution of HbA_{1c}			
	Below normal	Within normal	Above normal	Mean HbA_{1c}
ADA criteria (fasting glucose)				
Undiagnosed diabetes	0.1	37.8	62.1	7.07
Impaired fasting glucose	1.8	84.9	13.3	5.58
Normal fasting glucose	2.9	94.3	2.7	5.30
WHO criteria (fasting and 2-h glucose)				
Undiagnosed diabetes	3.8	49.1	47.1	6.58
Impaired glucose tolerance	2.3	89.7	8.0	5.49
Normal glucose tolerance	2.6	94.6	2.8	5.29

The normal range for HbA_{1c} in this study (4.41–6.13) is defined by the mean (5.27) and 2 SD (0.86) above and below the mean for the group of people with fasting plasma glucose <110 mg/dl and 2-h plasma glucose <140 mg/dl.

tolerance (WHO) is 15.6% (14.9 million). The difference occurs primarily because most individuals with impaired glucose tolerance have fasting plasma glucose <110 mg/dl and are classified as having normal fasting glucose by ADA. Prevalence of normal fasting glucose (ADA) and of normal glucose tolerance (WHO) are 77.6 and 66.8%, respectively.

Also shown in Table 1 are mean HbA_{1c} values for each group. The mean value is lowest for those with fasting plasma glucose <110 mg/dl (mean value of 5.30) and is slightly higher for those with fasting plasma glucose of 110 to <126 mg/dl (5.59) and 126 to <140 mg/dl (5.98). The mean value is greatest (8.20) for those with both fasting plasma glucose ≥140 mg/dl and 2-h glucose ≥200 mg/dl.

Mean HbA_{1c} of the group with both normal fasting plasma glucose (<110 mg/dl) and normal 2-h plasma glucose (<140 mg/dl) is 5.27, with a standard deviation of 0.43. Based on these values, the normal range for HbA_{1c} in this study may be considered to be 4.41–6.13 (mean ± 2 SDs). By this statistical definition, 95% of subjects are expected to have values within this range. Table 2 shows the proportion of subjects in the ADA and WHO diagnostic categories who are below, within, and above this range. For undiagnosed diabetes, a smaller proportion of those defined by ADA criteria have HbA_{1c} values ≤6.13 as compared with WHO criteria (37.9 vs. 52.9%). Conversely, a larger proportion are above the normal range (62.1 vs. 47.1%). Small proportions of those defined as having impaired fasting glucose or impaired glucose tolerance are above the normal range (13.3 and 8.0%, respectively). The proportions above (and below) the normal range for those with normal fasting glucose or normal glucose tolerance are similar to the 2.5% expected by the statistical definition of the normal range.

Mean HbA_{1c} values for each of the ADA and WHO diagnostic categories are shown in Table 2. Values are similar for normal fasting glucose and normal glucose tolerance, and for impaired fasting glucose and impaired glucose tolerance. Mean HbA_{1c} is slightly higher for undiagnosed diabetes defined by ADA compared with undiagnosed diabetes defined by WHO.

CONCLUSIONS — The new ADA diagnostic criteria, requiring only a fasting plasma glucose value for people without overt clinical symptoms of diabetes, provide a much simpler method to diagnose diabetes than the oral glucose tolerance test required by WHO. The fasting value can be routinely obtained during physician visits, and it is much less subject to intraindividual variation and more reproducible than an oral glucose challenge value (10,11). As a result, the diagnosis of diabetes is no more difficult than the diagnosis of other conditions that require a fasting blood sample, such as hypertriglyceridemia.

Fewer people are classified as having undiagnosed diabetes by the ADA system than by the WHO system. However, because of the simplicity of obtaining a fasting plasma glucose value, it is likely that a greater proportion of undiagnosed diabetes cases will be detected in clinical practice than is currently the case using the oral glucose tolerance test. Fewer people are also classified as having impaired fasting glucose by ADA criteria than as having impaired glucose tolerance by WHO. Again, however, the ease of detecting impaired fasting glucose may heighten the clinician's interest in this condition. Impaired glucose tolerance is known to be a strong risk factor for development of clinical diabetes. The prognostic significance of impaired fasting glucose has yet to be defined but is likely to also be a prediabetic condition because elevated fasting glucose in general is known to predict subsequent type 2 diabetes (12–14).

Mean HbA_{1c} is higher for individuals classified as having undiagnosed diabetes by ADA versus WHO criteria, and the proportion above the normal range for HbA_{1c} is also higher. Thus, the ADA system defines a group of individuals with diabetes whose glycemia is more severe than those defined by the WHO system. This fact provides a further clinical basis for physicians to adopt the new diagnostic criteria.

The ADA expert committee report states that "in the absence of unequivocal hyperglycemia with acute metabolic decompensation, the fasting plasma glucose should be measured to confirm the diagnosis on a different day" (3). This was not possible in the NHANES III survey. If repeat testing had been done, it is likely that the diagnostic category of some individuals would have changed because of the phenomenon of regression to the mean.

In summary, the new ADA criteria provide a simple method for detection of the many people in the U.S. who have diabetes and are at risk for diabetic complications but who remain undiagnosed. Even though fewer people are categorized as having undiagnosed diabetes by these criteria compared with WHO criteria, these individuals are more hyperglycemic with higher mean HbA_{1c} and a greater percentage above the normal range. It is likely that implementation of the new criteria will result in a more complete discovery of the many people with undiagnosed diabetes in the U.S. and in the detection of diabetes at an earlier stage. Providing effective treatment for glycemic control and for reduction of cardiovascular risk factors (15–18), particularly when instituted early in the course of diabetes, should have a major effect on decreasing the morbidity and mortality of this all too common disease.

References

1. National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and

other categories of glucose intolerance. *Diabetes* 28:1039–1057, 1979
2. World Health Organization: *Second Report of the WHO Expert Committee on Diabetes Mellitus*. Geneva, World Health Org., 1980 (Tech. Rep. Ser., no. 646)
3. World Health Organization: *Diabetes Mellitus: Report of a WHO Study Group*. Geneva, World Health Org., 1985 (Tech. Rep. Ser., no. 727)
4. American Diabetes Association: Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 20:1183–1197, 1997
5. U.S. Department of Health and Human Services, National Center for Health Statistics: *Third National Health and Nutrition Examination Survey, 1988–1994, Reference Manuals and Reports: Manual for Medical Technicians and Laboratory Procedures Used for NHANES III (CD-ROM)*. Hyattsville, MD, Centers for Disease Control and Prevention, 1996
6. DCCT Research Group: The relationship of glycemic exposure (HbA_{1c}) to the risk of development and progression of retinopathy in the Diabetes Control and Complications Trial. *Diabetes* 44:968–983, 1995
7. SAS Institute: *SAS Procedures Guide, Version 6*. 3rd ed. Cary, NC, SAS Institute, 1990
8. Day JC: *Population Projections of the United States by Age, Race, and Hispanic Origin: 1995 to 2050*. Washington, DC, U.S. Bureau of the Census, Current Population Reports, U.S. Govt. Printing Office, 1996 (P25-1130)
9. Shah BV, Barnwell BG, Bieler GS: *SUDAAN User's Manual, Release 6.40*. Research Triangle Park, NC, Research Triangle Institute, 1995
10. Olefsky JM, Reaven GM: Insulin and glucose responses to identical oral glucose tolerance tests performed forty-eight hours apart. *Diabetes* 23:449–453, 1974
11. Cummings ST, Fraser CG: Variability of capillary plasma glucose in healthy individuals in repeated 75 g oral glucose tolerance tests. *Ann Clin Biochem* 25:634–637, 1988
12. McPhillips JB, Barrett-Connor E, Wingard DL: Cardiovascular disease risk factors prior to the diagnosis of impaired glucose tolerance and non-insulin-dependent diabetes mellitus in a community of older adults. *Am J Epidemiol* 131:443–453, 1990
13. Haffner SM, Stern MP, Mitchell BD, Hazuda HP, Patterson JK: Incidence of type II diabetes in Mexican Americans predicted by fasting insulin and glucose levels, obesity, and body-fat distribution. *Diabetes* 39:283–288, 1990
14. Saad MF, Knowler WC, Pettitt DJ, Nelson RG, Mott DM, Bennett PH: The natural history of impaired glucose tolerance in Pima Indians. *N Engl J Med* 319:1500–1506, 1988
15. U.K. Prospective Diabetes Study Group: U.K. Prospective Diabetes Study 16: overview of 6 years' therapy of type II diabetes: a progressive disease. *Diabetes* 44:1249–1258, 1995
16. Eastman RC, Javitt JC, Herman WH, Dasbach EJ, Copley-Merriman C, Maier W, Dong F, Manninen D, Zbrozek AS, Kotsanos J, Garfield SA, Harris M: Model of complications of NIDDM. II. Analysis of the health benefits and cost-effectiveness of treating NIDDM with the goal of normoglycemia. *Diabetes Care* 20:735–744, 1997
17. Sowers JR: Impact of lipid and ACE inhibitor therapy on cardiovascular disease and metabolic abnormalities in the diabetic and hypertensive patient. *J Hum Hypertens* 11:9–16, 1997
18. Savage PJ: Cardiovascular complications of diabetes mellitus: what we know and what we need to know about their prevention. *Ann Intern Med* 124:123–126, 1996