The 1997 American Diabetes Association and 1999 World Health Organization Criteria for Hyperglycemia in the Diagnosis and Prediction of Diabetes

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OBJECTIVE — The 1997 American Diabetes Association (ADA) and the 1985 and 1999 World Health Organization (WHO) criteria for diabetes and hyperglycemia differ. The appropriateness of these diagnostic criteria in terms of individuals identified as abnormal and their prognosis has been debated. The purpose of this study is to compare the classifications of people by these criteria and to compare fasting and postload plasma glucose concentrations in the prediction of diabetes.

RESEARCH DESIGN AND METHODS — The frequencies of diabetes by the 3 sets of criteria were compared in 5,023 adult Pima Indians not taking hypoglycemic drugs. Among nondiabetic subjects, fasting plasma glucose (FPG) and 2-h postload plasma glucose (2-h PG) concentrations and categories of impaired glucose regulation or diabetes were evaluated as predictors of diabetes defined by 1999 WHO criteria.

RESULTS — The frequency of diabetes was 12.5% by 1997 ADA criteria, 14.6% by 1985 WHO criteria, and 15.3% by 1999 WHO criteria. The incidence of diabetes was strongly related to higher FPG and 2-h PG, each of which had very similar predictive powers. Impaired glucose tolerance (IGT) was more common than impaired fasting glucose (IFG) (15 vs. 5%), but the 5-year incidence of diabetes was higher in IFG than IGT (37 vs. 24%).

CONCLUSIONS — The prevalence and incidence of diabetes are somewhat lower with the ADA criteria than with the 1985 or 1999 WHO criteria. The intermediate categories of glycemia differ substantially. IFG defines a smaller number of people who are at higher risk of developing diabetes than those with IGT. More people at high risk of diabetes could be identified by using either IFG or IGT, as recommended by the 1999 WHO criteria, or by using the FPG concentration alone, but with a lower cutoff value.

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Abbreviations: 2-h PG, 2-h postload plasma glucose; ADA, American Diabetes Association; FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test; ROC, receiver operator characteristic; WHO, World Health Organization.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

In 1997, the American Diabetes Association (ADA) published criteria for the diagnosis of diabetes (1). They were introduced to facilitate wider recognition of diabetes and to minimize the need for oral glucose tolerance testing to identify people with undiagnosed asymptomatic diabetes. The diagnostic level for fasting plasma glucose (FPG) was set at ≥7.0 mmol/l to minimize the discrepancy in the 1985 WHO criteria, by which diabetes was diagnosed by either FPG ≥7.8 mmol/l or 2-h postload plasma glucose (2-h PG) ≥11.1 mmol/l during a 75-g oral glucose tolerance test (OGTT) (2). In participants in the second National Health and Nutrition Examination Survey, only 23% of those with newly diagnosed diabetes by the 1985 WHO criteria had FPG ≥7.8 mmol/l, whereas 97% had 2-h PG ≥11.1 mmol/l (3). Thus, most people being tested for diabetes would not be diagnosed without an OGTT, a procedure not routinely performed in clinical practice unless diabetes is suspected.

The ADA criteria are based primarily on FPG, which, if ≥7.0 mmol/l, is provisionally diagnostic of diabetes. A clinical diagnosis requires confirmation on repeat testing. Although the ADA recommendations do allow for diagnosis by OGTT (if the 2-h PG is ≥11.1 mmol/l) or by high casual plasma glucose in the presence of symptoms, the ADA recommends using only the fasting level with the FPG criterion of FPG ≥7.0 mmol/l for determining the prevalence or incidence of diabetes (1). The prevalence of undiagnosed diabetes by ADA criteria is lower than by the 1985 WHO criteria (1,4), but implementation of the ADA recommendations in clinical practice and screening will likely result in a more complete discovery of people with undiagnosed diabetes and detection at an earlier stage (1). Yet, there is concern that the diagnosis of diabetes by FPG alone using the ADA criteria will fail to identify people who would be diagnosed by glucose tolerance testing using the 1985

Table 1—*Number of subjects and percentage (%) of the total distribution by fasting and 2-h PG concentrations and WHO and ADA diagnostic groups in 5,023 Pima Indians at baseline*

	2-h PG (mmol/l)			
FPG (mmol/l)	<7.8	7.8–11.0	≥11.1	Total
<6.1				
n	3,499 (69.7)	537 (10.7)	60 (1.2)	4,096 (81.5)
WHO-1985	Normal	IGT	Diabetes	ADA = Normal
WHO-1999	Normal	IGT	Diabetes	
6.1–6.9				
n	93 (1.9)	126 (2.5)	79 (1.6)	298 (5.9)
WHO-1985	Normal	IGT	Diabetes	ADA = IFG
WHO-1999	IFG	IFG + IGT	Diabetes	
7.0–7.7				
n	14 (0.3)	21 (0.4)	85 (1.7)	
WHO-1985	Normal	IGT	Diabetes	
WHO-1999	Diabetes	Diabetes	Diabetes	629 (12.5)
≥7.8				ADA = Diabetes
n	2 (<0.1)	8 (0.2)	499 (9.9)	
WHO-1985	Diabetes	Diabetes	Diabetes	
WHO-1999	Diabetes	Diabetes	Diabetes	

Data are *n* (%). WHO-1985, classification by WHO (1985) criteria; WHO-1999, classification by WHO (1999) criteria; ADA, classification by ADA (1997) criteria for fasting plasma glucose only.

WHO criteria (5–7). In 1999, the WHO made further recommendations regarding criteria for diagnosis of diabetes and other categories of impaired glucose regulation (8). They incorporate the change in the FPG diagnostic level to ≥7.0 mmol/l but retain the recommendation for the OGTT and diagnosis of diabetes if the 2-h PG is ≥11.1 mmol/l.

In this article, the characteristics of the 3 sets of criteria (ADA, and 1985 and 1999 WHO) are compared using longitudinal data on fasting and 2-h PG concentrations from the Pima Indian population. FPG and 2-h PG are compared as predictors of diabetes defined by each set of criteria.

RESEARCH DESIGN AND METHODS

Subjects and measures

A longitudinal study of diabetes and its complications in Pima Indian residents of the Gila River Indian Community in Arizona has been conducted since 1965 (9). Every 2 years, all residents of a defined area of the community aged ≥5 years are invited to participate in a standardized medical examination including a medical history and physical examination. At each examination, an OGTT is performed with determination of venous plasma glucose, fasting and 2 h after the ingestion of 75 g glucose. Data are presented from examinations of people ≥15 years of age conducted since 1975, when routine testing of participants in the fasting state began.

The following diagnostic criteria for diabetes were used:

- ADA criteria: FPG ≥7.0 mmol/l (i.e., the criterion recommended for determining the prevalence and incidence of the disease);
- 1985 WHO criteria: FPG ≥7.8 mmol/l or 2-h PG ≥11.1 mmol/l; and
- 1999 WHO criteria: FPG ≥7.0 mmol/l or 2-h PG ≥11.1 mmol/l.

Although clinical diagnosis requires a confirmatory test, in this article, these classifications were made, as in epidemiologic studies, on the basis of single examinations. Note that anyone meeting either of the first 2 criteria for diabetes also meets the 1999 WHO criterion.

Among people determined nondiabetic by each criterion, impaired glucose tolerance (IGT) is defined by 2-h PG ≥7.8 to <11.1 mmol/l, and in the ADA and 1999 WHO criteria, impaired fasting glucose or glycemia (IFG) is defined by FPG ≥6.1 to <7.0 mmol/l.

Statistical analysis

Prevalence of diabetes. At the first examination at which FPG and 2-h PG were measured, the presence of diabetes diagnosed by the ADA or the 1985 or 1999 WHO criteria was determined among subjects not taking oral hypoglycemic agents or insulin.

Incidence of diabetes. Incidence rates of diabetes by the ADA or the 1985 or 1999 WHO criteria were calculated in longitudinal data from people who at baseline were nondiabetic by the criterion in question. Individuals taking oral hypoglycemic agents or insulin during follow-up were considered to have diabetes by each of these criteria. Incidence rates were expressed as the number of patients divided by person-years from baseline until the development of diabetes or until the last examination (9). The 5-year cumulative incidence of diabetes was calculated by the Kaplan-Meier method (10). For simplicity, most of the results of incidence calculations are shown only for diabetes defined by the 1999 WHO criteria, since this set of criteria is the most recent and is the same as the ADA criteria if the 2-h PG result is included.

Sensitivity and specificity for predicting diabetes. The ability of FPG or 2-h PG to predict the development of diabetes by 1999 WHO criteria at the first follow-up examination was determined by computing sensitivity and specificity and plotting them in a receiver operating characteristic (ROC) curve (11). Among 2,743 people

Table 2—*Number of subjects and percentage in each category of glucose according to the ADA and WHO diagnostic categories*

Classification	ADA	WHO-1985	WHO-1999
Normal	4,096 (81.5)	3,606 (71.8)	3,499 (69.7)
IGT	—	684 (13.6)	663 (13.2)*
IFG	298 (5.9)	—	219 (4.4)*
Diabetes	629 (12.5)	733 (14.6)	768 (15.3)

Data are *n* (%). *Includes 126 individuals with IFG and IGT. ADA, classification by ADA (1997) criteria for fasting plasma glucose only; WHO-1985, classification by WHO (1985) criteria; WHO-1999, classification by WHO (1999) criteria.

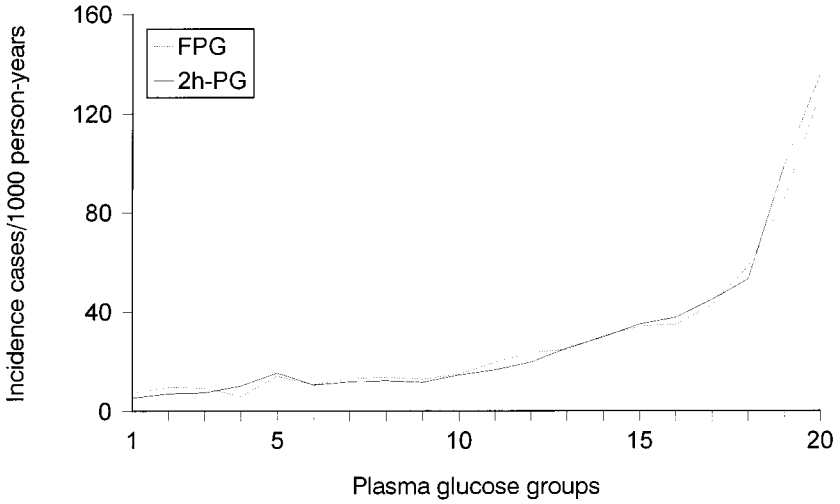
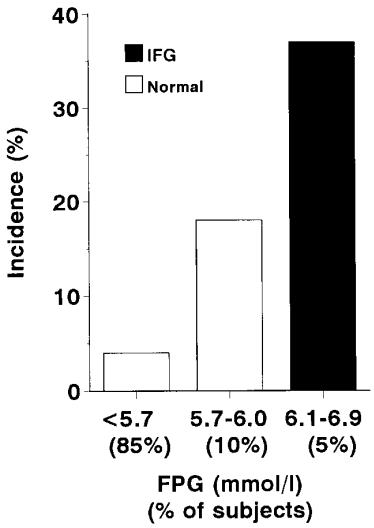


Figure 1—*The incidence rate of diabetes by 1999 WHO criteria according to baseline FPG and 2-h PG. FPG and 2-h PG distributions are divided from low to high (1–20) in 5th-percentile intervals.*



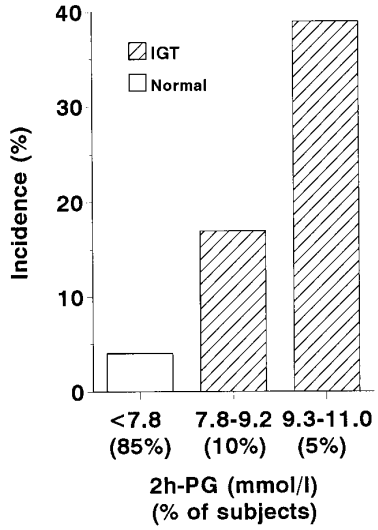


Figure 2—*The cumulative incidence of diabetes by the 1999 WHO criteria in normal fasting and 2-h PG, IFG, and IGT.*

determined nondiabetic by 1999 WHO criteria at baseline and with a follow-up examination, the sensitivity for a given cut-point value was computed as the number with a baseline glucose of at least that cut-point value divided by the number with diabetes at follow-up. The specificity was the number with baseline glucose below the cut-point value divided by the number remaining nondiabetic. The sensitivity and specificity were computed over a wide range of FPG values and, for comparison, with selected values of 2-h PG or FPG combined with 2-h PG. The area under an ROC curve represents the probability that a subject chosen at random from the group who developed the outcome of interest had a higher test value than one from those who did not.

RESULTS

Prevalence of diabetes

The distribution of the 5,023 subjects by glucose concentrations and their classifications according to the 3 sets of criteria are shown in Tables 1 and 2. For 97.5% of the subjects, the WHO-1985 and WHO-1999 classifications were the same. They differed only in the 93 nondiabetic subjects who met the 1999 definition of IFG and the 35 (14 + 21) who were diabetic by having FPG 7.0–7.7 mmol/l and 2-h PG <11.1 mmol/l. The prevalence of diabetes was 14.6% by the 1985 or 15.3% by the 1999 WHO criteria. By contrast, 629 people (12.5%) had diabetes by the ADA criteria (FPG ≥7.0 mmol/l). This was fewer than the 768 diabetic by the 1999 WHO criteria because of the 139 people (60 + 79) with 2-h PG ≥11.1 mmol/l but FPG <7.0 mmol/l. Thus, among the 768 subjects with diabetes by the 1999 WHO criterion, 82% met the ADA criteria and 95% met the 1985 WHO criteria.

Incidence of diabetes

The incidence of diabetes by each criterion was determined among those not diabetic by the corresponding criterion at baseline. There were 678 new cases of diabetes diagnosed by ADA criteria in 27,586 person-years of follow-up, 749 new cases of diabetes diagnosed by 1985 WHO criteria in 26,743 person-years, and 767 new cases of diabetes diagnosed by 1999 WHO criteria in 26,386 person-years of follow-up. By the ADA criteria, the incidence of diabetes was 12% lower than by the 1985 WHO criteria and 15% lower than by the 1999 WHO criteria.

Figure 1 shows the incidence rates of diabetes by 1999 WHO criteria in 5th-percentile groups of baseline FPG or 2-h PG. Both FPG and 2-h PG were strong predictors of diabetes, in that incidence rates increased gradually over most of the distribution but were markedly higher in the upper 10% of the distribution of the glycemic measure. The curves for FPG and 2-h PG were nearly indistinguishable.

Figure 2 shows 5-year cumulative incidence of diabetes by 1999 WHO criteria among 2,743 individuals grouped by FPG or 2-h PG at baseline. The first group, containing the lower 85% of each glucose distribution, is considered normal by ADA or WHO criteria. The next 10% of each distribution had normal FPG by ADA criteria but abnormal 2-h PG (IGT) by WHO criteria. The upper 5% of each distribution had IFG by ADA criteria and IGT by WHO criteria. The 5-year cumulative incidence of diabetes was similar whether subjects were divided into 3 groups according to FPG (4, 18, or 37%) or 2-h PG (4, 17, or 39%). The cumulative incidence in the 15% of the subjects with IGT was 24%. By contrast, only 5% of the subjects had IFG, but their diabetes cumulative incidence was higher (37%). The greater predictive value of IFG than IGT simply reflects the fact that IFG

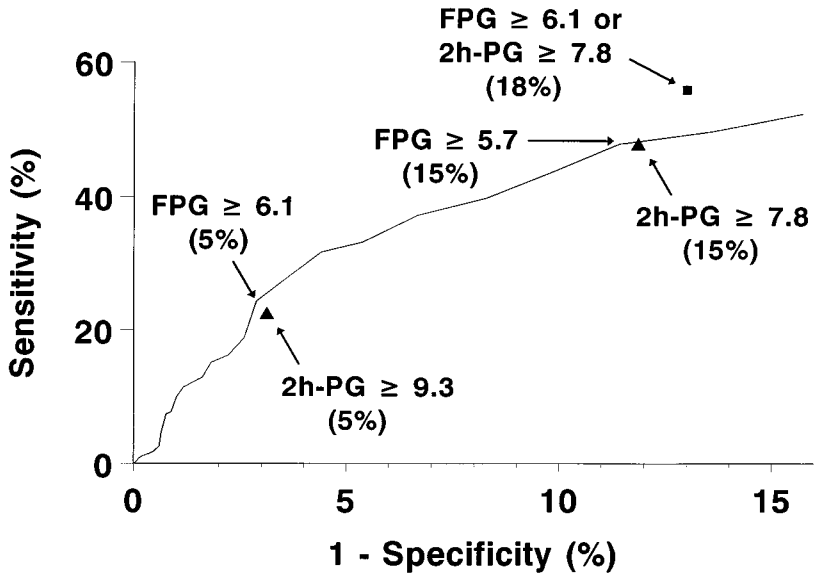


Figure 3—*The ROC curve for FPG in predicting diabetes by the 1999 WHO criteria in the first follow-up examination. The sensitivity is plotted as a function of 1 − specificity. The points on the curve representing the 2 FPG values of 5.7 and 6.1 mmol/l are marked with arrows. The percentages of the baseline population with values at or above these points are shown in parentheses. For comparison, the 2 points corresponding to 2-h PG of 7.8 or 9.3 mmol/l are shown (▲). ■, The combined category of IFG or IGT (i.e., FPG ≥6.1 mmol/l or 2-h PG ≥7.8 mmol/l).*

includes a smaller, but more extreme, part of the glucose distribution.

Among subjects with normal FPG and 2-h PG, IGT alone (FPG <6.1 mmol/l and 2-h PG 7.8–11.0 mmol/l), IFG alone (FPG 6.1–6.9 mmol/l and 2-h PG <7.8 mmol/l), or both IFG and IGT (FPG 6.1–6.9 and 2-h PG = 7.8–11.0 mmol/l), the 5-year cumulative incidences of diabetes were 3.6, 19.9, 31.0, and 41.2%, respectively. Thus, IFG defines a higher risk category than IGT. Nevertheless, individuals with IGT but not IFG had a cumulative incidence of diabetes 5.5 times as high as those with "normal" FPG and 2-h PG.

Sensitivity and 1 − specificity of FPG for predicting diabetes by 1999 WHO criteria are plotted as an ROC curve in Fig. 3. Points representing the FPG values of 5.7 and 6.1 mmol/l are indicated along with the percentage of the baseline population with values at or above these points in parentheses. FPG ≥5.7 mmol/l, defining a group representing the same percentage of the population (15%) as IGT (Fig. 2), has sensitivity and specificity almost identical to those of IGT, as indicated in Fig. 3 by the point for 2-h PG ≥7.8 mmol/l. IFG (FPG ≥6.1 mmol/l) is much less common (5%), and as a result, its sensitivity for prediction of diabetes is lower, but its specificity is higher. The 2 triangles on the curve represent 2-h PG ≥7.8 and ≥9.3 mmol/l. These cutoff points define parts of the baseline population including the same percentages as the FPG values of ≥5.7 and ≥6.1 mmol/l. These 2 points lie almost on the ROC curve for FPG, indicating that the predictive values of these 2 points are almost identical to the corresponding FPG values. The category impaired glucose regulation (IFG or IGT, i.e., FPG ≥6.1 mmol/l or 2-h PG ≥7.8 mmol/l) is also shown as a square. This point lies above the curve, indicating a higher sensitivity for a given specificity than obtained with FPG alone.

Similar results were obtained for prediction of diabetes by 1985 WHO or by ADA criteria (not shown).

CONCLUSIONS — The 1997 ADA and 1999 WHO criteria lowered the FPG value for the diagnosis of diabetes from ≥7.8 to ≥7.0 mmol/l to facilitate identification of undiagnosed diabetes (and thereby identify more people at risk for complications of diabetes at an earlier stage in their disease) and to reduce the discrepancy between FPG and 2-h PG cutoff points used in an OGTT. Use of FPG was advocated by the ADA because it is a much simpler test than an OGTT and can be widely applied in clinical practice and because its predictive value for microvascular complications is nearly the same as that of 2-h PG (1). The WHO in 1999, however, advocated retention of the OGTT for the diagnosis of diabetes and staging of impaired glucose regulation.

Despite the lower FPG diagnostic level, the overall prevalence and incidence rates of diabetes by ADA criteria (using FPG alone) are lower than those by either 1985 or 1999 WHO criteria applied to an OGTT. These findings are consistent with those of the third National Health and Nutrition Examination Survey, in which the prevalence of undiagnosed diabetes was 4.4% by ADA criteria, 6.4% by 1985 WHO criteria, and 7.1% by 1999 WHO criteria (4).

When the population is ranked by FPG or 2-h PG, both are equivalent predictors of diabetes. Nevertheless, in the ADA and 1999 WHO classifications, the category of IFG includes substantially fewer people than the category of IGT. The 5-year cumulative incidence of diabetes is lower in IGT than IFG, but more people at risk are identified when IGT is used. If categories of FPG and 2-h PG are defined to include similar percentages of their respective distributions, their predictive values for diabetes are equivalent. The difference in IGT and IFG reflects the fact that they represent different proportions of the glucose distributions rather than that FPG or 2-h PG per se are inherently different in their sensitivity, specificity, or predictive value. Among the Pima Indians, the FPG cutoff point of ≥5.7 mmol/l had similar sensitivity and positive predictive value as IGT for predicting subsequent diabetes, although the choice of such a cutoff point might differ among populations. It is, therefore, not necessary to perform an OGTT to obtain the same sensitivity for predicting future diabetes as is obtained by IGT; this can be accomplished simply by using a lower level of FPG.

When it is feasible to perform glucose tolerance testing, the combination of FPG and 2-h PG provides somewhat more information than either alone. In practice, however, glucose tolerance testing is not usually performed unless diabetes is suspected. Measurement of FPG alone provides considerable information, and its widespread use could identify many more people who could benefit from intervention.

Diagnostic criteria cannot be based only on comparison of the resultant prevalence and incidence rates of the disease, but should also be based on their abilities to predict specific complications of diabetes (12) and other serious outcomes, such as

cardiovascular disease (13,14) or mortality. Differences in outcome according to the different diagnostic criteria are examined in a companion article (15).

In summary, most Pima Indians with diabetes by either the 1985 or 1999 WHO or the ADA criteria met all 3 criteria simultaneously. The prevalence of intermediate categories of glycemia differed, however, with the ADA category of IFG defining a smaller proportion of the population who are at higher risk of developing diabetes than those with IGT. Using a cutoff FPG level lower than that currently used to define IFG could identify a greater proportion of the population at high risk of diabetes but at the cost of lower specificity and predictive value.

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