International Criteria for the Diagnosis of Diabetes and Impaired Glucose Tolerance

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International agreement on classification and criteria for the diagnosis of diabetes is highly desirable. Two systems promulgated in 1979–80 and widely used today are those of the NIH National Diabetes Data Group (NDDG) and of the World Health Organization (WHO). Although these systems are similar in many ways, certain discrepancies between them result in different classifications of oral glucose tolerance test (OGTT) results and different estimates of prevalence of the various glucose tolerance groups. Analysis of 3704 OGTTs performed during a survey of a national probability sample of U.S. residents without known diabetes and aged 20–74 yr shows that the two systems agreed in classification of 87.7% of OGTTs. For the remainder, the NDDG and WHO classifications differed, primarily because nondiagnostic OGTTs occur in the NDDG system but not in the WHO system. The differences resulted in the prevalence of impaired glucose tolerance (IGT) using WHO criteria (11.6%) being more than twice that using NDDG criteria (4.9%), although prevalence rates of diabetic OGTTs were similar in both systems (3.6%, 3.4%). The WHO system represents a simpler, inclusive classification scheme, and there is insufficient evidence from longitudinal studies of prognostic differences that would justify the more complicated NDDG diagnostic criteria. In situations where multiple venipunctures or retesting are not possible, the venous plasma glucose concentration at 2 h after 75 g glucose appears to be the most appropriate single value to use to designate whether a person has diabetes, IGT, or neither. The use of this value alone placed 97% of diabetic subjects and all other subjects, in the same class they were in when the full WHO criteria were used. DIABETES CARE 1985; 8:562–67.

The NIH National Diabetes Data Group (NDDG)[1] and the World Health Organization (WHO)[2] have both promulgated recommendations regarding methodology and criteria for making the diagnoses of diabetes and impaired glucose tolerance (IGT) in nonpregnant subjects and for classifying a person as "normal." These recommendations are similar in several ways. Both permit the diagnosis of diabetes in symptomatic individuals with unequivocally elevated plasma glucose concentrations. To establish a diagnosis of diabetes or IGT in asymptomatic individuals, both recommend a 2-h, 75-g oral glucose tolerance test (OGTT) if the fasting plasma glucose (FPG) is <140 mg/dl. However, there are two main differences between the sets of diagnostic criteria (Table 1) that lead to discrepancies in how individuals are classified based on OGTT results: (1) to class an OGTT as normal, NDDG requires an FPG <115 mg/dl, whereas WHO does not stipulate an upper limit of normal but implies that it may not exceed 140 mg/dl, as levels >140 mg/dl constitute diabetes; (2) NDDG recommends five plasma glucose values, whereas WHO requires only two. Both require the fasting and 2-h postglucose values, but NDDG also recommends that plasma glucose values at ½ h, 1 h, and 1½ h after the challenge be used in determining a person's diagnostic class. If the glucose concentration of one of these midtest samples does not meet certain specific values, the OGTT is considered "nondiagnostic" in the NDDG schema. To classify a person using WHO criteria, midtest glucose concentrations are not considered and need not be obtained. A third difference between the criteria arises from the WHO rounding, to the nearest whole integer, the mil-

TABLE 1
NDDG and WHO diagnostic criteria

	Plasma glucose mg/dl (mmol/L)*				
			Oral glucose tolerance test		
Class	Fasting		Midtest		2-h
NDDG					
Normal	<115 (<6.4)	and	<200 (<11.1)	and	<140 (<7.8)
IGT	<140 (<7.8)	and	≥200 (≥11.1)	and	140–199 (7.8–11.1)
Diabetes†	≥140 (≥7.8)	or	≥200 (≥11.1)	and	≥200 (≥11.1)
Nondiagnostic	all other combinations of fasting, midtest, and 2-h values				
WHO					
Normal‡	<140 (<7.8)		—	and	<140 (<7.8)
IGT	<140 (<7.8)		—	and	140–199 (7.8–11.1)
Diabetes†	≥140 (≥7.8)		—	or	≥200 (≥11.1)

*The mmol/L values were computed by dividing mg/dl values by 18.016 (the number of milligrams of glucose in 1 dl of a 1-mM solution) and rounding to the nearest 0.1 mmol/L. WHO obtained mmol/L values by dividing mg/dl values by 18 and rounding to the nearest 1 mmol/L.
†NDDG and WHO require both the fasting and 2-h values to classify a subject, except when the fasting is ≥140 mg/dl, which by itself is diagnostic of diabetes.
‡Although WHO does not define a "normal" OGTT, the term is used here to include subjects who do not meet criteria for diabetes or IGT.

limole per liter equivalent of the NDDG milligram per deciliter values. This problem could be readily resolved by defining the millimole per liter criteria more precisely (Table 1), as recommended by the WHO Study Group on Diabetes in February 1985.

METHODS

We examined the results of applying the NDDG and WHO criteria in determining prevalence of the various diagnostic classes in persons without a medical history of diabetes using OGTTs from a population-based survey of U.S. civilian, noninstitutionalized residents aged 20–74 yr. This survey, the Second National Health and Nutrition Examination Survey (NHANES II),[3] was conducted by the U.S. National Center for Health Statistics with support from the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases and other agencies from February 1976 to February 1980. Household interviews were conducted by U.S. Bureau of the Census interviewers. Persons were selected for the survey using a stratified, multistage, probability design with some oversampling of children and poor and elderly persons. The analyses in this report do not include children, but oversampling of the poor and elderly have been corrected for by using statistical weights. These weights were adjusted for nonresponse and were poststratified to produce prevalence estimates representing the 1978 U.S. resident population aged 20–74 yr.

Of 27,809 persons aged 6 mo to 74 yr selected for the survey, 17,390 were aged 20–74 yr; 88.3% of these adults participated in the household medical history interview component of the survey. One-half (7688 persons) were allocated to receive an OGTT; from their interview data, 381 had a medical history of physician-diagnosed diabetes and are excluded from the present analysis. Losses from the other 7307 sample persons were due to nonparticipation in the examination component of the survey (1677 subjects), nonattendance at the exam center in the morning (877), not fasting for 10–16 h (442) or length of fast unknown (128), refusal of the OGTT (178), illness (46), and technical errors including lost or mislabeled samples, unsuccessful venipunctures, or 2-h blood samples not being taken at 120 ± 10 min (255 subjects). This article analyzes the OGTT results of the remaining 3704 persons. Their OGTTs were those that met NDDG recommendations,[1] which require that the subject fast overnight for 10–16 h, the OGTT be performed in the morning, a fasting blood sample be taken, and the subject ingest 75 g oral glucose or carbohydrate equivalent. In the present study, Glucola (Ames, Elkhart, Indiana) was used. In this voluntary survey, obtaining multiple midtest venipunctures was not attempted but fasting, single midtest (at 1 h), and 2-h blood samples were obtained in 3689 of the 3704 OGTTs; only fasting and 2-h values were obtained in 15 OGTTs. Over 95% of 1-h and 2-h samples were taken within 5 min of the specified times and 99% were within 10 min. Venous blood samples were obtained, and plasma glucose concentration was measured using a microadaptation of the glucose-oxidase reference method.[4]

Losses of sample persons from the group allocated to receive an OGTT have been examined by us[5] and in an independent report.[6] Persons with valid OGTT data differed little or not at all from the complete NHANES II interviewed sample in a number of demographic, clinical, and medical history factors (Table 2). Furthermore, the existing differences should not affect the conclusions regarding the NDDG and WHO classification systems in this report.

TABLE 2
Investigation of bias in NHANES II OGTT data: characteristics of persons aged 20–74 yr in the full NHANES II interviewed sample and of those for whom valid OGTT data were obtained

Characteristic	Total sample interviewed	Fasting subsample, valid OGTT data
U.S. region	(percent distribution)	
Northeast	23.0	22.3
Midwest	24.6	24.7
South	25.6	24.0
West	26.8	29.0
Area		
Outside Standard Metropolitan Statistical Area	37.1	37.3
Inside Standard Metropolitan Statistical Area	62.9	62.7
Segment type		
Nonpoverty	65.7	66.5
Poverty	34.3	33.5
Age (yr)		
20–44	56.7	54.1
45–54	17.2	18.5
55–64	15.2	16.1
65–74	10.8	11.3
Sex		
Men	47.6	45.9
Women	52.4	54.1
Race		
Not Black	89.8	91.0
Black	10.2	9.0
Family income (dollars)		
<6,000	14.5	13.5
6,000–9,999	20.2	20.0
10,000–14,999	18.3	18.8
15,000–24,999	27.3	28.7
≥25,000	15.4	16.0
Unknown	4.3	3.1
Health status		
Excellent	27.5	26.5
Very good	26.8	29.2
Good	28.2	27.9
Fair	12.4	11.8
Poor	5.1	4.5
Unknown	0.1	0.1
Body mass index		
<23	32.9	32.0
23–27	44.3	44.7
>27	21.2	21.8
Unknown	1.6	1.5
Selected medical conditions reported in the interview	(percent with condition)	
Mother with diabetes	10.3	11.5
Father with diabetes	6.9	7.7
Hospital stay in past 12 mo	14.1	13.7
Rheumatic heart disease	0.7	0.6
Heart murmur	7.4	7.8
Heart failure	.9	1.0
Heart attack	3.0	3.0
Other heart trouble	5.0	5.1
Hardening of arteries	2.4	2.2
Stroke	1.5	1.4
Hypertension	24.6	24.3
Cataracts	2.7	2.9
Glaucoma	0.8	0.8
Currently smokes cigarettes	37.8	34.7
Cannot read newspaper	1.2	1.0
Trouble hearing	8.9	9.2
Selected exam variables	(mean ± SD)	
Height (cm)	168.3 ± 9.7	168.3 ± 9.8
Weight (kg)	71.8 ± 15.5	72.0 ± 15.7
Body mass index (kg/m^2)	25.3 ± 4.9	25.3 ± 5.0
Serum cholesterol (mg/dl)	213.2 ± 48.4	213.0 ± 47.3
Systolic blood pressure (mm Hg)	126.4 ± 23.2	124.6 ± 22.1
Diastolic blood pressure (mm Hg)	80.6 ± 14.3	79.2 ± 13.9

RESULTS

Table 3 summarizes the OGTT results by possible combinations of the three venipunctures and presents reasons for discrepancies between NDDG and WHO classification of OGTTs. All OGTTs that were classified as normal, IGT, or diabetes by NDDG have the same classification in the WHO system (87.7% of OGTTs). The WHO, by using only the fasting and 2-h postglucose challenge values, can classify all persons for whom these values are obtained. However, NDDG, by requiring a specific midtest value, resulted in 11.3% of OGTTs being nondiagnostic. An additional 1.0% could not be classified by NDDG because of elevated FPG values (115–139 mg/dl) without diagnostic postload values.

NDDG requirements for fasting and 1-h values resulted in 222 of 2981 subjects being nondiagnostic or unclassifiable, while they were normal in the WHO system. Of the 3.6% of persons with diabetes by WHO criteria, the majority (180/191) also had diabetes by NDDG criteria. The major discrepancy occurred in the class IGT: while 532 OGTTs were classified as IGT by WHO, 303 of these were designated nondiagnostic by NDDG because the midtest value was <200 mg/dl. The nondiagnostic and unclassifiable OGTTs resulted in prevalence of the classes normal, diabetes, and IGT being lower using NDDG criteria, most notably for IGT, where prevalence was less than half that using WHO criteria (Table 4). One hundred eighty-six of 191 diabetic individuals, and all of the other subjects, would have been classified identically to their WHO designations if only their 2-h glucose value had been considered.

TABLE 3
Reasons for discrepancies between WHO and NDDG in classifying OGTTs of persons with no medical history of diabetes

Glucose concentration (mg/dl)	Number	Weighted %*	WHO class	NDDG class	Reason for difference due to NDDG criteria
FPG <115, 2 h <140					
1 h <200	2759	79.4	Normal†	Normal	—
1 h ≥200	172	4.2	Normal	Nondiagnostic	1 h too high‡
1 h missing	12	0.2	Normal	Unclassifiable	1 h missing
FPG <115, 2 h 140–199					
1 h <200	291	6.5	IGT	Nondiagnostic	1 h too low§
1 h ≥200	184	4.0	IGT	IGT	—
1 h missing	1	0	IGT	Unclassifiable	1 h missing
FPG <115, 2 h ≥200					
1 h <200	10	0.2	Diabetes	Nondiagnostic	1 h too low
1 h ≥200	83	1.4	Diabetes	Diabetes	—
1 h missing	0	0	Diabetes	Unclassifiable	1 h missing
FPG 115–139, 2 h <140					
1 h <200	17	0.5	Normal	Nondiagnostic	FPG too high
1 h ≥200	20	0.4	Normal	Nondiagnostic	FPG too high
1 h missing	1	0	Normal	Unclassifiable	1 h missing
FPG 115–139, 2 h 140–199					
1 h <200	12	0.2	IGT	Nondiagnostic	1 h too low‡
1 h ≥200	43	0.9	IGT	IGT	—
1 h missing	1	0	IGT	Unclassifiable	1 h missing
FPG 115–139, 2 h ≥200					
1 h <200	1	0	Diabetes	Nondiagnostic	1 h too low
1 h ≥200	53	1.0	Diabetes	Diabetes	—
1 h missing	0	0	Diabetes	Unclassifiable	1 h missing
FPG ≥140	44‖	0.9	Diabetes	Diabetes	—
Total	3704	99.8			

*Percentages are adjusted according to the sampling scheme of the survey to the estimated 1978 U.S. civilian noninstitutionalized resident population aged 20–74 yr with no medical history of diabetes. 3.4% of persons aged 20–74 yr had a medical history of physician-diagnosed diabetes and are excluded from this table.
†Although WHO does not define a normal OGTT, the term is used here to include subjects who do not meet criteria for diabetes or IGT.
‡Fifty-seven percent had 1-h values of 200–219 mg/dl.
§Forty-nine percent had 1-h values of 175–199 mg/dl.
‖The 1-h and 2-h values of 39 persons were ≥200 mg/dl; for five persons, 1-h values ranged from 249 to 320, but 2-h values fell below 200 (range 153–181).

DISCUSSION

The major reason for discrepancies between NDDG and WHO was use of the 1-h value by NDDG. Although the 1-h and 2-h postglucose challenge values are correlated, we are unaware of data indicating that a particular midtest value is a better predictor of the development of diabetes or its complications than are the fasting and 2-h values, both of which have been shown to predict the development of nephropathy and retinopathy.[7] We are also unaware of longitudinal data supporting the NDDG upper limit of normal for FPG at 115 mg/dl, although there is evidence that the acute-phase insulin response is absent at levels above this value.[8]

In addition to creating discrepancies in prevalence rates, the nondiagnostic and unclassifiable OGTTs have practical significance. The NDDG could not place one in eight (12.3%) OGTTs in a diagnostic class. Data from two independent studies indicate the same phenomenon (Table 5). Among 2040 members of an Israeli Jewish population (where rates of undiagnosed diabetes and IGT were about twice those in the present study)[9] and among 543 subjects attending a Paris diabetes screening clinic (a population selected for risk factors for diabetes in which rates of undiagnosed diabetes and IGT were about three times the U.S. rates),[10] the prevalence of diabetes was 5% and 10% lower, respectively, using NDDG rather than WHO criteria and IGT rates were 63% and 41% lower. In comparing these three populations, as the prevalence of diabetes and IGT increased, there was greater discrepancy between NDDG and WHO diagnostic class rates

TABLE 4
Classification of persons with no medical history of diabetes using NDDG and WHO diagnostic criteria for the oral glucose tolerance test

Class	NDDG		WHO	
	N	Weighted %*	N	Weighted %*
Normal†	2759	79.4	2981	84.8
IGT	227	4.9	532	11.6
Diabetes	180	3.4	191	3.6
Nondiagnostic	523	12.1	—	—
Unclassifiable	15	0.2	—	—
Total	3704	100.0	3704	100.0

*Percentages are adjusted according to the sampling scheme of the survey to the estimated 1978 U.S. civilian noninstitutionalized resident population aged 20–74 yr with no medical history of diabetes. 3.4% of persons aged 20–74 yr had a medical history of physician-diagnosed diabetes and are excluded from this table. A detailed analysis of the U.S. prevalence of diagnosed and undiagnosed diabetes and of IGT can be found in ref. 5.
†Although WHO does not define a normal OGTT, the term is used here to include subjects who do not meet criteria for diabetes or IGT.

due to a higher proportion of OGTTs being nondiagnostic or unclassifiable by NDDG.

In the present study, the ability of the 2-h value to detect diabetes is indicated by the following: of 180 OGTTs classified as diabetic by NDDG criteria and 191 by WHO criteria, 175 and 186, respectively (97%), had 2-h values ≥200 mg/dl. Thus, diagnoses of diabetes made in studies where only the 2-h postglucose challenge value can be obtained (e.g., epidemiologic field studies) would be virtually congruent with diagnoses made where the complete set of plasma glucose values were ascertained (e.g., studies of clinical subjects). In contrast, estimates based on the fasting value alone would seriously underestimate the prevalence of diabetes, as only 44 of 180 (28%) subjects meeting NDDG criteria for diabetes, and 44 of 191 (26%) meeting WHO criteria, had FPG ≥140 mg/dl. The NDDG recommendation that the FPG be <115 mg/dl to conform to normality had little effect on classification. The fasting value might even be considered superfluous in diagnosing diabetes based on the present study, since 39 of 44 subjects with FPG ≥140 mg/dl also exhibited 1-h and 2-h values ≥200 mg/dl.

CONCLUSIONS

The NDDG criteria present difficulties of application because: (1) a large proportion of OGTTs are in a nondiagnostic or unclassifiable category and (2) five venipunctures are recommended even in situations where this may be impractical or unfeasible. In contrast, the WHO criteria are inclusive, can classify all subjects, and require only two venipunctures. However, it remains to be determined whether the WHO or the NDDG criteria for diabetes are more predictive of diabetic complications, and if the respective criteria for IGT are predictive of the development of diabetes per se.

There is at present insufficient evidence from longitudinal studies to justify the more complicated classification scheme of the NDDG, especially in large-scale field research or screening programs where performing additional venipunctures may be impractical. The FPG concentration seems to be of little value in diagnosis in these situations and might be omitted. A 2-h postload glucose determination appears to be the most appropriate single value to designate whether a subject has diabetes, IGT, or neither.

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TABLE 5
Comparison of three studies using WHO and NDDG criteria for OGTTs in groups of persons with no medical history of diabetes

Population sample	Age (yr)	N	Diabetes		IGT		Normal		Nondiagnostic/ unclassifiable	
			WHO	NDDG	WHO	NDDG	WHO	NDDG	WHO	NDDG
U.S.	20–74	3704	3.6	3.4	11.6	4.9	84.8	79.4	—	12.3
Israeli Jewish	40–70	2040	6.7	6.4	19.6	7.2	73.7	66.6	—	19.9
Paris diabetes screening clinic	44 ± 12 (mean ± SD)	543	11.2	10.1	28.9	17.1	60.0	42.4	—	30.4

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