ORIGINAL INVESTIGATION

Glucose Tolerance and Cardiovascular Mortality

Comparison of Fasting and 2-Hour Diagnostic Criteria

The DECODE Study Group, on behalf of the European Diabetes Epidemiology Group

Background: New diagnostic criteria for diabetes based on fasting blood glucose (FBG) level were approved by the American Diabetes Association. The impact of using FBG only has not been evaluated thoroughly. The fasting and the 2-hour glucose (2h-BG) criteria were compared with regard to the prediction of mortality.

Methods: Existing baseline data on glucose level at fasting and 2 hours after a 75-g oral glucose tolerance test from 10 prospective European cohort studies including 15 388 men and 7126 women aged 30 to 89 years, with a median follow-up of 8.8 years, were analyzed. Hazards ratios for death from all causes, cardiovascular disease, coronary heart disease, and stroke were estimated.

Results: Multivariate Cox regression analyses showed that the inclusion of FBG did not add significant information on the prediction of 2h-BG alone ($P>.10$ for various causes), whereas the addition of 2h-BG to FBG criteria significantly improved the prediction ($P<.001$ for all causes and $P<.005$ for cardiovascular disease). In a model including FBG and 2h-BG simultaneously, hazards ratios (95% confidence intervals) in subjects with diabetes on 2h-BG were 1.73 (1.45-2.06) for all causes, 1.40 (1.02-1.92) for cardiovascular disease, 1.56 (1.03-2.36) for coronary heart disease, and 1.29 (0.66-2.54) for stroke mortality, compared with the normal 2h-BG group. Compared with the normal FBG group, the corresponding hazards ratios in subjects with diabetes on FBG were 1.21 (1.01-1.44), 1.20 (0.88-1.64), 1.09 (0.71-1.67), and 1.64 (0.88-3.07), respectively. The largest number of excess deaths was observed in subjects who had impaired glucose tolerance but normal FBG levels.

Conclusion: The 2h-BG is a better predictor of deaths from all causes and cardiovascular disease than is FBG.

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NEW DIAGNOSTIC criteria for diabetes mellitus based on the fasting blood glucose level alone (fasting plasma glucose ≥7.0 mmol/L [126 mg/dL]) were approved by the American Diabetes Association (ADA) Expert Group.[1] For epidemiological purposes, the ADA recommended the use of fasting glucose level alone and did not recommend the 2-hour 75-g oral glucose tolerance test. The choice of the cutoff point was based on bimodalities in the fasting glucose distribution[1] and on the association between fasting glucose level and risk of diabetic retinopathy. The World Health Organization) adopted the same fasting glucose level as the ADA, but retained the use of the 2-hour glucose tolerance test for the diagnosis of diabetes in population studies.[2] The 2-hour 75-g oral glucose tolerance test has been the international standard for diabetes diagnosis since 1985[3] and the basis of much epidemiological data in the medical literature about risks of complications associated with diabetes.

To evaluate the prognostic impact of the new fasting glucose criteria, the DECODE (Diabetes Epidemiology: Collaborative analysis Of Diagnostic criteria in Europe) Study was initiated. We have previously reported that there was a high degree of disagreement in the fasting and 2-hour glucose classifications in European populations.[4] Among subjects with diabetes diagnosed by a fasting glucose level of 7.0 mmol/L or more, only 46% also had 2-hour glucose level of 11.1 mmol/L or more (≥200 mg/dL), the 2-hour glucose diagnostic criterion for diabetes.[2,3] Furthermore, analyses of the DECODE database showed that abnormalities in 2-hour glucose levels were better predictors of all-cause mortality than fasting glucose alone.[5] A high 2-hour glucose concentration was found to be associated with an increased risk of death, independent of the level of fasting blood glucose, whereas mortality associated with the fasting glucose con-

Members of the DECODE Group are listed in a box on page 410.

PARTICIPANTS AND METHODS

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The study populations and the methods used to recruit the participants have been reported previously.[4-6] Briefly, researchers in Europe who had performed population-based studies or large studies in occupational groups using the standard 2-hour 75-g oral glucose tolerance test were invited to participate in the DECODE Study. Individual data on fasting and 2-hour glucose concentrations and several other variables were sent to the Diabetes and Genetic Epidemiology Unit of the National Public Health Institute in Helsinki, Finland, for collaborative data analyses. In this article, only the studies with prospective data on cause-specific mortality and all required confounding variables (cholesterol, blood pressure, smoking habits, and body mass index) were included.

A total of 13 centers provided cause-specific mortality data for the DECODE Study, 10 of which provided data with all the covariates required. All 10 studies included men (n = 15 388) and 6 included women (n = 7126). Among the 22 514 subjects, aged 30 to 89 years, 796 subjects were previously diagnosed as having diabetes. For the other 21 718 subjects who had no previous history of diabetes, the median duration of follow-up was 8.8 years (5.8 and 20.6 years for the 25th and the 75th quartiles, respectively), and 208 203 person-years in men and 52 536 person-years in women were accumulated.

Subjects who had not previously been diagnosed as having diabetes were classified according to the following criteria: (1) *2-hour glucose criteria alone:* 2-hour plasma glucose concentrations of 11.1 mmol/L or more (≥10.0 mmol/L [≥180 mg/dL] for whole blood) for diabetes, 7.8 to 11.0 mmol/L (140-198 mg/dL) (6.7-9.9 mmol/L [121-178 mg/dL] for whole blood) for impaired glucose tolerance (IGT), and less than 7.8 mmol/L (<140 mg/dL) (<6.7 mmol/L [<121 mg/dL] for whole blood) for normal glucose tolerance; and (2) *fasting glucose criteria alone:* fasting plasma glucose level of 7.0 mmol/L or more (≥126 mg/dL) (≥6.1 mmol/L [≥110 mg/dL] for whole blood) for diabetes, 6.1 to 6.9 mmol/L (110-124 mg/dL) (5.6-6.0 mmol/L [101-108 mg/dL] for whole blood) for impaired fasting glucose (IFG), and less than 6.1 mmol/L (<110 mg/dL) (<5.6 mmol/L [<101 mg/dL] for whole blood) for normal fasting glucose.

Vital status information was recorded for each of the subjects attending the baseline examination in all of the studies. Subjects who emigrated, for whom the vital status could not be confirmed, were treated as censored at the time of emigration. Follow-up was complete, ranging from 95.2% in the Paris Prospective Study to 100% in most of the other studies.[5] Causes of death were classified using the *International Classification of Diseases, Eighth and Ninth Revision*, codes 401-448 (CVD), 410-414 (coronary heart disease [CHD]), and 430-438 (stroke).

Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Subjects were classified as nonsmokers, ex-smokers, and current smokers.

STATISTICAL ANALYSIS

Age-standardized mortality was calculated using 10-year age groups, separately for men and women, and direct standardization for a European standard population.[7] Age- and center-standardized means were compared using analysis of variance according to the diabetic status defined by the fasting and by the 2-hour glucose criteria. Hazard ratios of cause-specific and all-cause mortality were estimated for the various glucose categories, using the Cox proportional hazards model, and adjusting for age, center, BMI, systolic blood pressure, serum cholesterol level, smoking status, and sex if men and women were combined. Results are presented as mortality hazards ratios and 95% confidence intervals, with respect to the given reference groups. Cumulative mortality curves were estimated by the same Cox proportional hazards model. Nested models were compared using a χ^2 log-likelihood ratio test to determine whether men and women had significantly different hazards ratios and whether the fasting glucose criteria or the 2-hour glucose criteria were independent of each other in predicting mortality from cardiovascular causes and from all causes. The absolute number of excess deaths from all cardiovascular causes was calculated by comparison with the group determined to be strictly normal using both the fasting and the 2-hour glucose criteria.

centration depended on the level of 2-hour glucose, in all categories of fasting glucose.

Because most patients with type 2 diabetes mellitus die of cardiovascular diseases (CVD) and not of microvascular complications, cardiovascular mortality and morbidity should be considered in defining the diagnostic criteria for diabetes. Herein we report on cardiovascular deaths as well as all-cause deaths in the DECODE Study population.

RESULTS

The number of men and women and the percentage of deaths due to cardiovascular and all causes, according to the fasting and the 2-hour glucose criteria, by DECODE study centers, are shown in **Table 1** and **Table 2**, respectively, for subjects not previously known as diabetic. Age-standardized death rates from all causes and cardiovascular causes were higher in diabetic subjects than in those not meeting diabetic criteria (Tables 1 and 2). Increased mortality was also observed in subjects with IGT (Table 2), whereas there was no difference between subjects with IFG and those with normal fasting glucose (Table 1). Mortality from the various causes was higher in men than in women (Tables 1 and 2).

Subjects who had 2-hour glucose levels of 11.1 mmol/L or more (whole blood, ≥10.0 mmol/L) and fasting glucose levels less than 7.0 mmol/L (whole blood, <6.1mmol/L) were older and had higher serum cholesterol levels than those whose fasting glucose levels were ≥7.0 mmol/L (whole blood, ≥6.1 mmol/L) and 2-hour glucose levels less than 11.1 mmol/L (whole blood, <10.0 mmol/L). The latter group was more obese (**Table 3**).

Multivariate-adjusted Cox proportional hazards model analyses showed that diabetic subjects by either the fasting or the 2-hour glucose criteria had an in-

Table 1. Number of Subjects and Percentage of Deaths From Cardiovascular Disease (CVD), Coronary Heart Disease (CHD), Stroke, and All Causes According to Fasting Glucose Categories, by DECODE Study Centers in Subjects Not Previously Diagnosed as Diabetic*

	Fasting Plasma (Whole Blood) Glucose Category, mmol/L†														
	Normal Fasting Glucose <6.1 (5.6)					Impaired Fasting Glucose 6.1-6.9 (5.6-6.0)					Diabetes ≥7.0 (6.1)				
Center	No.	CVD	CHD	Stroke	All	No.	CVD	CHD	Stroke	All	No.	CVD	CHD	Stroke	All
Men															
Paris Prospective Study, France	**5532**	5.7	2.5	1.3	26.4	**1129**	6.0	2.4	1.3	29.1	**237**	10.1	3.4	3.4	48.1
FIN MONICA, Finland	**1813**	4.1	3.3	0.5	8.4	**183**	2.2	1.6	0.5	3.8	**40**	7.5	5.0	0.0	10.0
Helsinki Policemen Study, Finland	**1055**	18.0	11.5	4.0	36.4	**48**	27.1	20.8	4.2	47.9	**17**	41.2	29.4	11.8	64.7
MONICA Study, Northern Sweden	**923**	0.9	0.5	0.0	2.5	**89**	0.0	0.0	0.0	2.2	**20**	5.0	0.0	0.0	10.0
Hoorn Study, the Netherlands	**880**	3.2	0.5	0.7	9.7	**155**	5.2	1.9	1.3	14.8	**63**	6.3	0.0	3.2	20.6
Glostrup Study, Denmark	**878**	17.9	12.6	3.4	39.2	**78**	10.3	10.3	0.0	23.1	**45**	20.0	17.8	0.0	40.0
Cremona Study, Italy	**670**	2.5	0.7	0.3	8.4	**47**	6.4	0.0	2.1	19.1	**17**	11.8	0.0	11.8	23.5
Zutphen Study, the Netherlands	**320**	10.6	5.3	2.2	22.5	**90**	12.2	6.7	1.1	27.8	**32**	6.3	6.3	0.0	31.3
East and west Finland	**265**	13.2	10.2	2.3	30.6	**61**	19.7	14.8	3.3	36.1	**28**	14.3	10.7	3.6	42.9
POL-MONICA, Poland	**133**	7.5	5.3	0.8	10.5	**27**	0.0	0.0	0.0	0.0	**7**	0.0	0.0	0.0	0.0
Total															
Unstandardized	**12 469**	7.0	4.0	1.4	21.4	**1907**	6.7	3.5	1.3	24.0	**506**	11.1	5.5	3.0	37.2
Age standardized	. . .	7.2	4.3	1.2	19.7	. . .	7.3	4.6	1.0	19.5	. . .	9.0	4.6	2.2	27.5
Women															
FIN MONICA, Finland	**2268**	0.6	0.4	0.2	2.6	**98**	2.0	1.0	1.0	4.1	**27**	7.4	7.4	0.0	7.4
MONICA Study, Northern Sweden	**1027**	0.1	0.0	0.1	1.1	**49**	0.0	0.0	0.0	0.0	**13**	0.0	0.0	0.0	0.0
Hoorn Study, the Netherlands	**1089**	1.3	0.0	0.5	5.3	**131**	1.5	0.0	0.0	9.9	**57**	1.8	0.0	1.8	10.5
Glostrup Study, Denmark	**872**	11.6	6.3	3.0	25.6	**52**	13.5	3.8	7.7	19.2	**34**	26.5	20.6	5.9	35.3
Cremona Study, Italy	**887**	1.6	0.3	0.2	4.1	**31**	0.0	0.0	0.0	3.2	**16**	0.0	0.0	0.0	12.5
POL-MONICA, Poland	**171**	0.6	0.0	0.0	2.9	**11**	0.0	0.0	0.0	0.0	**3**	0.0	0.0	0.0	0.0
Total															
Unstandardized	**6314**	2.3	1.0	0.6	6.2	**372**	3.0	0.8	1.3	7.5	**150**	8.0	6.0	2.0	14.7
Age standardized	. . .	3.2‡	1.2‡	0.9‡	7.5‡	. . .	3.0§	0.4§	2.2‖	5.8‡	. . .	4.2‖	3.3‖	0.9‖	9.2‡

*DECODE indicates Diabetes Epidemiology: Collaborative analysis Of Diagnostic criteria in Europe; MONICA, Monitoring of Trends and Determinants in Cardiovascular Disease.

†To convert glucose to milligrams per deciliter, divide by 0.05551.

‡$P<.001$, men vs women.

§$P<.01$, men vs women.

‖$P>.05$, men vs women.

creased hazards ratio of death from cardiovascular causes and from all causes compared with those normal on the corresponding criteria (**Table 4**). The hazards ratios for the various causes of death tended to be higher in diabetic women than in diabetic men, but these differences in hazards ratios were significant only for CHD mortality ($\chi^2=11.57$ for fasting glucose criteria and $\chi^2=11.35$ for 2-hour glucose criteria, 3 *df*, $P<.01$). Increased hazards ratios for deaths from all-cause, CVD, and CHD mortality were also observed in subjects with IGT, but not in subjects with IFG (Table 4). In a model including the fasting and the 2-hour glucose criteria simultaneously, the hazards ratios for death from the various causes were only slightly reduced in individuals with IGT or diabetes for the 2-hour glucose (**Table 5**), but decreased significantly in subjects with IFG and diabetes for the fasting glucose. Comparing nested models, inclusion of the fasting glucose categories did not significantly improve the prediction of the 2-hour glucose alone, in contrast, addition of the 2-hour categories to the fasting glucose categories significantly improved the prediction (except in the case of stroke mortality) (Table 5).

The cumulative hazards curves (**Figure 1**) further illustrate the differences between the 2 diagnostic criteria. Previously known diabetic subjects had worse survival profiles for fatal CVD and CHD events than those observed in the newly diagnosed diabetic subjects according to either the fasting or the 2-hour glucose criteria. The survival curves for known and screened diabetic subjects were similar for fatal stroke events and for all-cause mortality. The subjects with IGT had a survival profile in between the diabetic and the normal subjects according to the 2-hour glucose criteria and clearly worse than the normal subjects for fatal cardiovascular events and for all-cause mortality. The subjects with IFG had a survival curve similar to that of the subjects nor-

Table 2. Number of Subjects and Percentage of Deaths From Cardiovascular Disease (CVD), Coronary Heart Disease (CHD), Stroke, and All Causes According to 2-Hour Glucose Categories, by DECODE Study Centers in Subjects Not Previously Diagnosed as Diabetic*

	2-h Plasma (Whole Blood) Glucose Category, mmol/L†														
	Normal Glucose Tolerance <7.8 (6.7)					Impaired Glucose Tolerance 7.8-11.0 (6.7-9.9)					Diabetes ≥11.1 (10.0)				
Center	No.	CVD	CHD	Stroke	All	No.	CVD	CHD	Stroke	All	No.	CVD	CHD	Stroke	All
Men															
Paris Prospective Study, France	**6102**	5.6	2.4	1.3	25.6	**638**	7.5	3.3	2.2	39.7	**158**	10.1	3.8	3.2	55.7
FIN MONICA, Finland	**1766**	3.5	2.8	0.5	7.3	**236**	7.6	5.5	0.8	11.9	**34**	8.8	5.9	0.0	17.6
Helsinki Policemen Study, Finland	**1067**	18.1	11.7	3.8	36.5	**43**	32.6	20.9	9.3	53.5	**10**	30.0	20.0	10.0	60.0
MONICA Study, Northern Sweden	**944**	0.8	0.5	0.0	2.6	**72**	1.4	0.0	0.0	2.8	**16**	0.0	0.0	0.0	0.0
Hoorn Study, the Netherlands	**938**	3.4	0.5	0.9	9.8	**107**	6.5	1.9	0.9	15.9	**53**	1.9	0.0	1.9	22.6
Glostrup Study, Denmark	**629**	19.4	13.7	3.8	44.4	**292**	14.0	11.0	1.7	26.0	**80**	13.8	11.3	1.3	31.3
Cremona Study, Italy	**657**	2.1	0.8	0.2	7.8	**61**	9.8	0.0	3.3	23.0	**16**	12.5	0.0	12.5	25.0
Zutphen Study, the Netherlands	**356**	11.0	5.6	2.2	23.3	**50**	6.0	2.0	0.0	26.0	**36**	13.9	11.1	0.0	30.6
East and west Finland	**216**	14.8	11.1	3.2	29.6	**105**	13.3	9.5	1.9	33.3	**33**	15.2	15.2	0.0	48.5
POL-MONICA, Poland	**131**	6.1	5.3	0.8	9.2	**29**	6.9	0.0	0.0	6.9	**7**	0.0	0.0	0.0	0.0
Total															
Unstandardized	**12 806**	6.7	3.7	1.4	21.0	**1633**	9.4	5.4	1.8	28.4	**443**	10.4	6.3	2.3	37.9
Age standardized	. . .	7.0	4.2	1.2	19.3	. . .	8.3	4.9	1.4	22.8	. . .	8.1	4.9	1.7	28.2
Women															
FIN MONICA, Finland	**2047**	0.5	0.3	0.1	2.2	**304**	1.6	1.0	0.3	4.3	**42**	7.1	4.8	2.4	14.3
MONICA Study, Northern Sweden	**954**	0.1	0.0	0.1	0.8	**110**	0.0	0.0	0.0	1.8	**25**	0.0	0.0	0.0	4.0
Hoorn Study, the Netherlands	**1066**	1.1	0.0	0.5	4.9	**153**	2.0	0.0	0.0	10.5	**58**	3.4	0.0	1.7	15.5
Glostrup Study, Denmark	**690**	10.9	5.7	3.0	24.9	**216**	13.0	6.5	3.7	24.1	**52**	26.9	21.2	5.8	40.4
Cremona Study, Italy	**813**	1.4	0.4	0.2	3.2	**91**	3.3	0.0	0.0	12.1	**30**	0.0	0.0	0.0	6.7
POL-MONICA, Poland	**129**	0.8	0.0	0.0	3.1	**50**	0.0	0.0	0.0	2.0	**6**	0.0	0.0	0.0	0.0
Total															
Unstandardized	**5699**	1.9	0.8	0.6	5.4	**924**	4.2	1.8	1.0	10.3	**213**	8.9	6.1	2.3	18.3
Age standardized	. . .	3.2‡	1.1‡	1.1‡	6.9‡	. . .	3.7‡	1.2‡	1.0§	9.6‡	. . .	5.1§	3.7§	1.2§	11.2‡

**DECODE indicates Diabetes Epidemiology: Collaborative analysis Of Diagnostic criteria in Europe; MONICA, Monitoring of Trends and Determinants in Cardiovascular Disease.*

†To convert glucose to milligrams per deciliter, divide by 0.05551.

‡P<.001, men vs women.

§P>.05, men vs women.

moglycemic on the fasting glucose criteria alone. Overall, the cumulative hazard curves were better separated for the three 2-hour glucose categories than for the 3 fasting glucose categories, indicating that the former classification provides a better discrimination for cardiovascular fatal events and for all-cause death.

The highest absolute number of excess cardiovascular deaths attributable to the fasting and the 2-hour glucose criteria was for subjects with IGT, particularly those who had normal fasting glucose levels (**Figure 2**).

COMMENT

Diabetes is an important independent risk factor for CVD mortality.[8-15] Hyperglycemia, in the absence of clinically diagnosed diabetes, has also been associated with an increased risk of CVD and all-cause mortality in some, but not all studies.[8-11,16-38] The lack of adjustment for the established risk factors, applying unstandardized methods for the glucose test and the small number of events obtained during follow-up might have contributed to these inconsistencies. Our analyses, based on a large European population with more than 260 000 person-years of follow-up, show that asymptomatic diabetes as well as IGT defined by the 2-hour glucose criteria alone, increased the risk of death from cardiovascular causes and all causes, independent of other known risk factors and the level of fasting glucose. In contrast, mortality associated with the fasting glucose concentration depended largely on the level of 2-hour glucose.

This study is a collaborative study based on the data collected from 10 different centers in different countries in Europe. There is no uniform approach to the quality control in the glucose measurements. This was not possible in such a large collaborative study based on retrospective data. Also, as in other population studies, fasting status could not always be assured. It is possible that failure to report prior energy (calorie)

Table 3. Characteristics of Diabetic Subjects at Baseline According to Fasting and 2-Hour Glucose Criteria in Subjects Not Previously Diagnosed as Diabetic in the DECODE Study*

Characteristic	Plasma (Whole) Blood Glucose Category, mmol/L†				*P*
	Fasting <7.0 (6.1) and 2-h <11.1 (10.0), Nondiabetic (n = 20 707)	Fasting ≥7.0 and 2-h <11.1, Diabetic on Fasting (n = 355)	Fasting <7.0 and 2-h ≥11.1, Diabetic on 2-h (n = 355)	Fasting ≥7.0 and 2-h ≥11.1, Diabetic on Both (n = 301)	
Age, y	53 (0.1)	54 (0.5)	56 (0.5)	60 (0.5)	<.001
Body mass index, kg/m^2	26.2 (0.03)	28.4 (0.2)	26.9 (0.2)	29.3 (0.2)	.02
Blood pressure, mm Hg					
Systolic	140 (0.1)	152 (1.1)	150 (1.1)	155 (1.2)	.02
Diastolic	82 (0.1)	87 (0.6)	86 (0.6)	88 (0.7)	.007
Serum cholesterol, mmol/L‡	6.1 (0.01)	6.2 (0.1)	6.3 (0.1)	6.2 (0.1)	.001

*Data are given as age- and center-standardized mean (SE). DECODE indicates Diabetes Epidemiology: Collaborative analysis Of Diagnostic criteria in Europe.
†To convert glucose to milligrams per deciliter, divide by 0.05551.
‡To convert cholesterol to milligrams per deciliter, divide by 0.02586.

Table 4. Multivariate-Adjusted Hazards Ratios for Deaths From Cardiovascular Disease (CVD), Coronary Heart Disease (CHD), Stroke, and All Causes According to Fasting and 2-Hour Glucose Criteria: The DECODE Study*

	Plasma (Whole Blood) Glucose Category, mmol/L [Subjects Not Known as Diabetic]				
	Fasting Glucose Criteria†		2-h Glucose Criteria‡		
	IFG 6.1-6.9 (5.6-6.0)	Diabetes ≥7.0 (6.1)	IGT 7.8-11.0 (6.7-9.9)	Diabetes ≥11.1 (10.0)	Known Diabetes‡
Men					
CVD	1.03 (0.85-1.25)	1.29 (0.98-1.71)	1.34 (1.12-1.60)	1.25 (0.92-1.70)	1.93 (1.53-2.44)
CHD	1.05 (0.80-1.37)	1.14 (0.77-1.68)	1.29 (1.02-1.64)	1.22 (0.82-1.81)	1.90 (1.41-2.57)
Stroke	0.89 (0.57-1.38)	1.64 (0.95-2.85)	1.26 (0.84-1.88)	1.37 (0.71-2.64)	2.08 (1.25-3.45)
All causes	1.10 (0.99-1.22)	1.62 (1.39-1.88)	1.42 (1.28-1.57)	1.83 (1.56-2.15)	1.76 (1.52-2.05)
Women					
CVD	1.53 (0.81-2.90)	3.50 (1.89-6.47)	1.28 (0.88-1.86)	3.10 (1.87-5.15)	1.85 (1.30-2.63)
CHD	1.25 (0.39-4.03)	6.22 (2.97-13.01)	1.22 (0.69-2.15)	5.10 (2.66-9.79)	2.11 (1.27-3.48)
Stroke	3.02 (1.11-8.21)	4.57 (1.31-15.88)	1.21 (0.56-2.59)	3.30 (1.23-8.82)	1.05 (0.45-2.42)
All causes	1.20 (0.81-1.79)	2.01 (1.29-3.13)	1.25 (0.98-1.58)	2.25 (1.60-3.17)	1.88 (1.48-2.20)
All					
CVD	1.09 (0.90-1.30)	1.48 (1.15-1.91)	1.34 (1.14-1.57)	1.55 (1.20-2.01)	1.96 (1.62-2.37)
CHD	1.07 (0.83-1.39)	1.43 (1.02-2.02)	1.28 (1.02-1.59)	1.64 (1.18-2.28)	1.94 (1.51-2.50)
Stroke	1.04 (0.70-1.56)	1.92 (1.16-3.17)	1.26 (0.88-1.79)	1.74 (1.01-2.99)	1.72 (1.11-2.66)
All causes	1.11 (1.00-1.23)	1.65 (1.43-1.91)	1.40 (1.27-1.54)	1.92 (1.66-2.22)	1.81 (1.60-2.05)

*Data are given as hazards ratios (95% confidence intervals), adjusted for age, center, total cholesterol, body mass index, systolic blood pressure, smoking, and sex when men and women are combined (all). DECODE indicates Diabetes Epidemiology: Collaborative analysis Of Diagnostic criteria in Europe; IFG, impaired fasting glucose; and IGT, impaired glucose tolerance.
†Using fasting plasma (whole blood) glucose <6.1 (5.6) mmol/L as reference group. To convert glucose to milligrams per deciliter, divide by 0.05551.
‡Using 2-hour postload plasma (whole blood) glucose <7.8 (6.7) mmol/L as reference group.

Table 5. Adjusted Hazards Ratios for Deaths From Cardiovascular Disease (CVD), Coronary Heart Disease (CHD), Stroke, and All Causes With Fasting and 2-Hour Glucose Categories in the Same Model: The DECODE Study*

	Plasma (Whole Blood) Glucose Category, mmol/L [Subjects Not Known as Diabetic]						
	Fasting Glucose Criteria†			2-h Glucose Criteria‡			
Mortality	IFG 6.1-6.9 (5.6-6.0)	Diabetes ≥7.0 (6.1)	χ^2 (*P*)§	IGT 7.8-11.0 (6.7-9.9)	Diabetes ≥11.1 (10.0)	χ^2 (*P*)‖	Known Diabetes†
CVD	1.01 (0.84-1.22)	1.20 (0.88-1.64)	1.34 (>.10)	1.32 (1.12-1.56)	1.40 (1.02-1.92)	12.09 (<.005)	1.96 (1.62-2.37)
CHD	1.01 (0.77-1.31)	1.09 (0.71-1.67)	0.15 (>.10)	1.27 (1.01-1.58)	1.56 (1.03-2.36)	6.81 (<.05)	1.94 (1.51-2.50)
Stroke	1.00 (0.66-1.51)	1.64 (0.88-3.07)	2.35 (>.10)	1.21 (0.84-1.74)	1.29 (0.66-2.54)	1.23 (>.10)	1.73 (1.12-2.68)
All causes	1.03 (0.93-1.14)	1.21 (1.01-1.44)	4.32 (>.10)	1.37 (1.25-1.51)	1.73 (1.45-2.06)	61.35 (<.001)	1.82 (1.60-2.06)

*Data are given as hazards ratios (95% confidence intervals), adjusted for age, sex, center, total cholesterol, body mass index, systolic blood pressure, and smoking. DECODE indicates Diabetes Epidemiology: Collaborative analysis Of Diagnostic criteria in Europe; IFG, impaired fasting glucose; and IGT, impaired glucose tolerance.
†Using fasting plasma (whole blood) glucose <6.1 (5.6) mmol/L as reference group. To convert glucose to milligrams per deciliter, divide by 0.05551.
‡Using 2-hour postload plasma (whole blood) glucose <7.8 (6.7) mmol/L as reference group.
§Compared with the models in Table 4, with only the 2-hour glucose criteria, 2 df.
‖Compared with the models in Table 4, with only the fasting glucose criteria, 2 df.

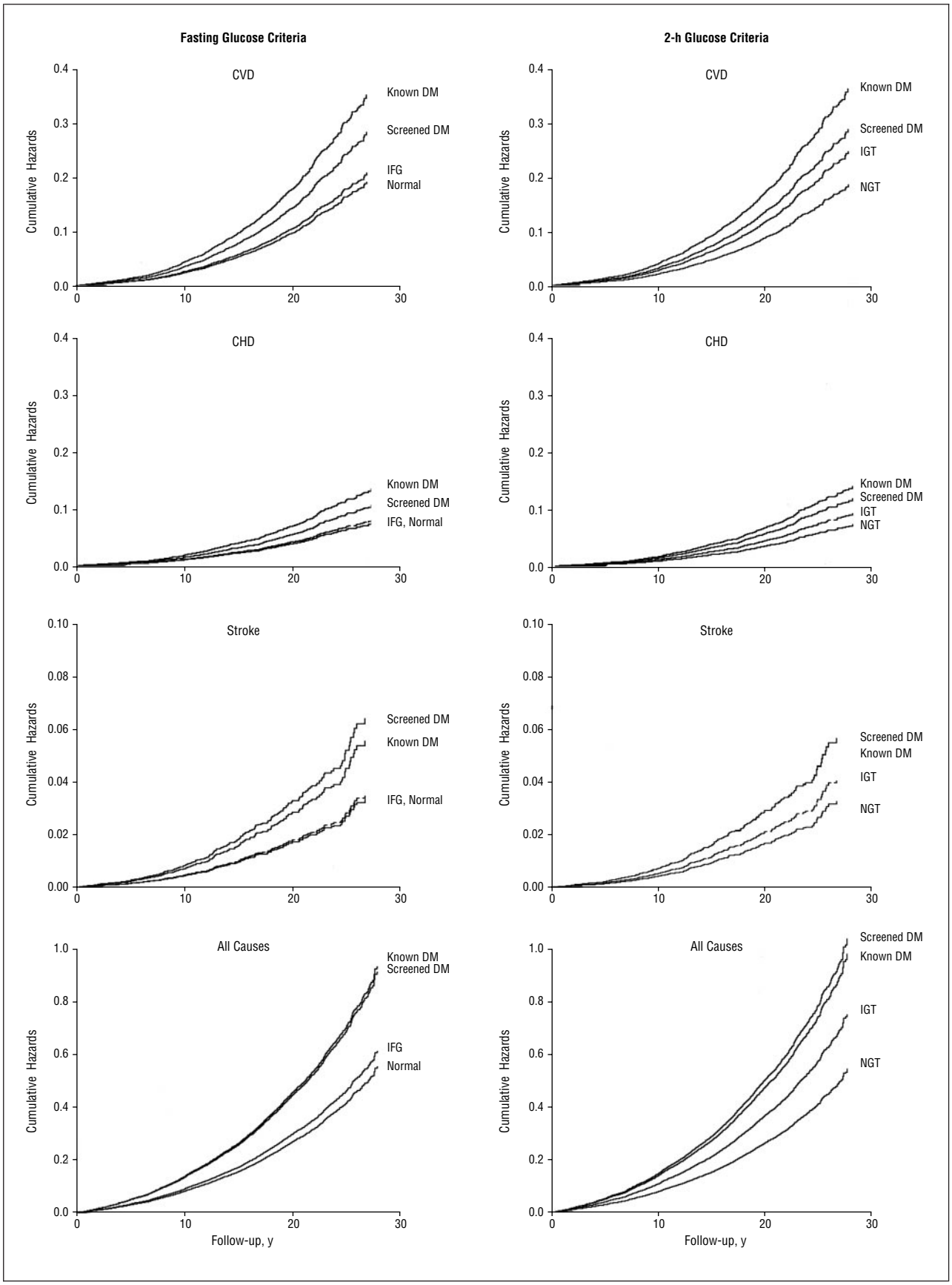

Figure 1. *Cumulative hazards curves for deaths from cardiovascular disease (CVD), coronary heart disease (CHD), stroke, and all causes, according to fasting and 2-hour glucose criteria. The cumulative hazards are estimated from Cox proportional hazards models and adjusted for age, center, sex, body mass index, blood pressure, serum cholesterol levels, and smoking status. DM indicates diabetes mellitus; IFG, impaired fasting glucose; and NGT, normal glucose tolerance.*

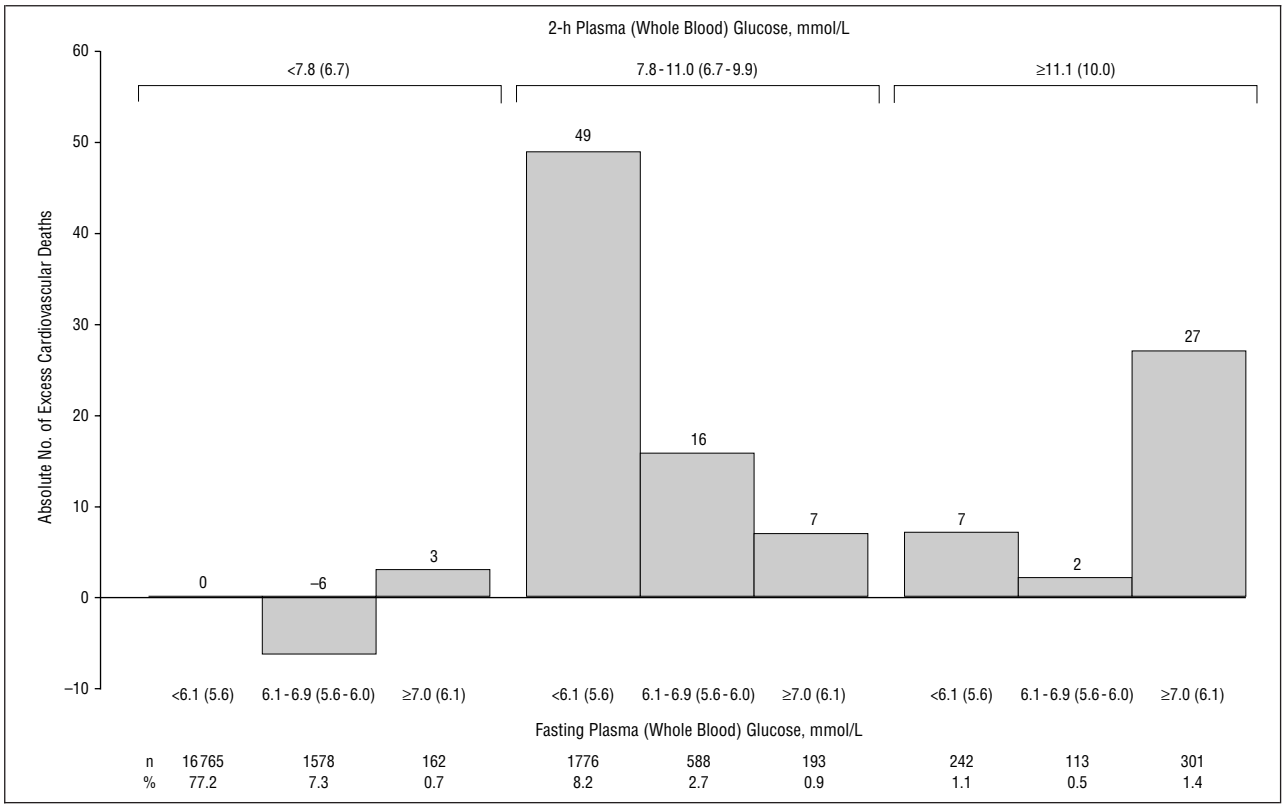

Figure 2. *Estimated absolute number of excess cardiovascular deaths according to the duration of follow-up, with reference to the fasting and the 2-hour glucose categories in subjects not previously known as diabetic. Number (n) and the total percentage of subjects in each glucose category are presented. To convert glucose to milligrams per deciliter, divide by 0.05551.*

consumption resulted in false elevated fasting glucose concentrations in some individuals, and these subjects might have been misclassified as diabetic or IFG. However, the fasting status must also have had an influence on 2-hour glucose values because fasting and 2-hour glucose concentrations were correlated in subjects with higher fasting glucose concentrations.[3] Moreover, the excess risk of CVD deaths observed among subjects with normal fasting glucose levels but who were diabetic or IGT according to the 2-hour glucose criteria could not be explained by the failure to fast.

The fasting glucose concentration has been considered to have good reproducibility, small variability, and easy application in clinical practice. However, the fasting state is difficult to assure in a population study,[3] and it has been found that fasting glucose level was not more reliable than postload glucose level when measurements were repeated in an elderly population.[39] For epidemiological studies, the ADA did not recommend the use of the 2-hour glucose measurement.[1] However, in our study, the 2-hour glucose value certainly gave additional prognostic information on the risk of death from various causes. In our study, about one third of the men (148 of 443) and 44% of the women (94 of 213) who were diabetic according to the 2-hour glucose criteria were classified as normal according to the fasting glucose criteria. These subjects carried a 50% higher risk for CVD mortality and 100% higher risk for all-cause mortality compared with subjects who had strictly normal levels for both glucose criteria. The fact that inclusion of the 2-hour glucose with the fasting glucose criteria significantly improved the prediction indicates that the predictive ability of the fasting glucose largely depended on the levels of 2-hour glucose. Conversely, that fasting glucose levels did not add statistically significant information on the prediction of deaths once the 2-hour value was included in the model demonstrated that the relation between the 2-hour glucose level and the risk of deaths was independent of the fasting glucose levels.

A new category, IFG, based on fasting glucose level alone was introduced by the ADA Expert Group.[1] It was claimed that IFG and IGT, based on the 2-hour glucose concentration, were metabolic stages intermediate between normal glucose homeostasis and diabetes, and both were risk factors for future diabetes and CVD. It is clear from our study that people with IFG and IGT do not have a similar prognosis with regard to CVD risk. We failed to show any independent association of IFG with risk of death from CVD and CHD; however, IFG was associated with stroke mortality in women. In contrast, the IGT category based on the 2-hour glucose concentration predicted mortality from all causes, CVD, and CHD. The largest number of excess CVD deaths was found in subjects with IGT who had a normal fasting glucose level, which also indicates that the IGT classification has prognostic importance and cannot be replaced by IFG.

Diabetic women had a higher hazards ratio of death from the CVD causes than the diabetic men, although the difference in the hazards ratio between men and women was statistically significant only for CHD mortality. This

The DECODE Study Participants

The DECODE Study (*D*iabetes *E*pidemiology: *C*ollaborative analysis *O*f *D*iagnostic *C*riteria in *E*urope) was undertaken in 1997 on the initiative of the European Diabetes Epidemiology Group (chairman: Knut Borch-Johnsen; vice-chairman: Andrew Neil; secretary: Beverley Balkau).

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finding was compatible with women's greater relative risk of CVD associated with diabetes, as reported in other studies.[40] In this study, age-standardized mortality from various causes was higher in men than in women in each glucose category, especially in the normal glucose category. In men, the increase in mortality in the normal glucose category reduced the relative risk of death observed in diabetic men and indicates that men are at higher risk of death from risk factors other than hyperglycemia.

Age was an important confounding factor. It could be argued that the excess risk of death in diabetic subjects on the 2-hour glucose criteria could have been attributed to the older age in this group. However, age has been adjusted for in the data analyses, and the age difference was too small (only 2 years) to have any serious impact on mortality. Other known CVD risk factors were also taken into account and are unlikely to have influenced the observed difference between the fasting and the 2-hour glucose criteria.

In conclusion, diabetes and IGT determined by the 2-hour glucose criteria predicted mortality from the various causes, independent of the level of fasting glucose, whereas the association between mortality and diabetes and IFG based on fasting glucose depended largely on the 2-hour glucose categories. With regard to the prediction of death, classification by 2-hour glucose concentration is better than that by fasting glucose.

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