The Relation of Fasting and 2-h Postchallenge Plasma Glucose Concentrations to Mortality

Data from the Baltimore Longitudinal Study of Aging with a critical review of the literature

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OBJECTIVE — Under the auspices of the National Institutes of Health, American Diabetes Association, and World Health Organization, expert committees lowered the fasting plasma glucose (FPG) concentration diagnostic for diabetes from 7.8 to 7.0 mmol/l and defined 6.1–6.9 mmol/l as impaired fasting glucose (IFG) and <6.1 mmol/l as normal fasting glucose. In 2003, IFG was lowered to 5.6–6.9 mmol/l and normal fasting glucose to <5.6 mmol/l. Reports of the relationship between glucose concentration and all-cause mortality have been inconsistent. It is not known if the 2-h plasma glucose (2hPG) concentration from an oral glucose tolerance test (OGTT) adds to the predictive power of FPG.

RESEARCH DESIGN AND METHODS — We followed 1,236 men for an average of 13.4 years to determine the relationship between both FPG and 2hPG and all-cause mortality.

RESULTS — Risk for mortality did not increase until the FPG exceeded 6.1 mmol/l. Risk increased by ~40% in the 6.1–6.9 mmol/l range and doubled when FPG ranged from 7.0 to 7.7 mmol/l. A combination of the 2hPG and FPG allowed better estimation of risk than the FPG alone. Within any category of FPG, risk generally increased as the 2hPG increased, and within any category of 2hPG, risk generally increased as the FPG increased.

CONCLUSIONS — These data support the decision to lower the FPG diagnostic for diabetes from 7.8 to 7.0 mmol/l, show that both IFG and impaired glucose tolerance have risks between the normal and diabetic ranges, and show that the OGTT adds predictive power to that of FPG alone and should not be abandoned. The lowering of IFG to 5.6 mmol/l from 6.1 mmol/l, at least for mortality, is, however, not supported by our results.

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From 1979 to 2004, reports appeared on standards for the classification of subjects based upon fasting plasma glucose (FPG) concentration and plasma glucose 2 h after the ingestion of a standard glucose load (2hPG). American reports were issued in 1979 (1), 1997 (2), and 2003 (3). World Health Organization (WHO) reports were issued in 1980 (4), 1985 (5), and 1999 (6). Over this 25-year period, standards for interpreting the oral glucose tolerance test (OGTT) were identical and unchanged in the U.S. and WHO reports; an impaired zone was defined as 140–199 mg/dl (7.8–11.0 mmol/l) and the diabetic cut point was defined as 200 mg/dl (11.1 mmol/l). The standards for interpreting the FPG changed over the years. In the early reports, no impaired zone was defined (1,4,5). Both the U.S. and WHO committees recommended that the cut point for diabetes be 140 mg/dl (7.8 mmol/l). In subsequent reports, the U.S. (2) and WHO (6) recommended that an impaired fasting glucose (IFG) zone of 110–125 mg/dl (6.1–6.9 mmol/l) be created and also that the diabetic cut point be lowered to 126 mg/dl (7.0 mmol/l). Most recently (3), the U.S. committee changed the IFG zone to 100–125 mg/dl (5.6–6.9 mmol/l). Inevitably, data from population studies have become difficult to compare and to interpret because the definitions of impaired and diabetic test results have changed.

The purpose of the present study is to examine the risks of mortality from these variously defined categories of glucose metabolism, to evaluate whether the OGTT adds power to the FPG value as a predictor of risk, and to examine the literature critically with respect to these questions.

RESEARCH DESIGN AND METHODS

— The 1,236 men included in this study are participants in the Baltimore Longitudinal Study of Aging (BLSA). Participants are middle to upper-middle class, highly educated, healthy, ambulatory, community-dwelling Caucasian (94%) men aged 17–102 years (7). The BLSA, a continuing study of normative aging, was established in 1958 and initially included only men. Women were added to the study in 1978. Because of the shorter follow-up time and the lower mortality rate in women, there were only 43 deaths, too few to draw meaningful conclusions at this time; therefore, this study includes data from men only.

BLSA subjects were continuously re-

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Abbreviations: 2hPG, plasma glucose concentration 2 h after oral glucose challenge; ADA, American Diabetes Association; BLSA, Baltimore Longitudinal Study on Aging; FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test; WHO, World Health Organization.

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

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Table 1—*Relation between FPG and all-cause mortality in 1,236 men*

	Glucose (mmol/l)		Glucose (mg/dl)		Subjects		RR for mortality*		
	Range	Median	Range	Median	At risk	Deaths	RR	95% CI	*P*
N	4.1–5.2	5.1	74–94	91	390	115	1.00	—	—
	5.3–5.5	5.4	95–99	97	307	100	1.06	0.81–1.39	0.69
I	5.6–6.0	5.7	100–109	103	415	155	1.03	0.80–1.32	0.83
	6.1–6.9	6.3	110–125	113	108	54	1.41	1.01–1.97	0.05
D	7.0–7.7	7.3	126–139	132	16	12	2.02	1.09–3.73	0.03

*Adjusted for age, BMI, BMI^2, sagittal abdominal diameter, and smoking. Median follow-up 13.4 years. D, diabetic; I, impaired; N, normal.

cruited to replace subjects who died or who withdrew from the study. Initially, men ≤70 of age were examined every 18 months, and men >70 years of age were examined annually. In 1970, the schedule was changed to every 2 years for men 20–59 years, every 18 months for those 60–69 years, and annually for those men ≥70 years old. Since 1978, all subjects have been scheduled to return every 2 years. At each visit, subjects spend 2.5 days at the Gerontology Research Center. Subjects undergo a battery of medical, physiological, psychological, and functional tests including assessments of glucose metabolism and a history and physical examination. This report is based on the first FPG and OGTT provided by each subject. BLSA studies are approved by an institutional review board.

Exclusions

Subjects treated with insulin or oral hypoglycemic agents, had a documented history of diabetes, or had an FPG concentration ≥140 mg/dl (7.8 mmol/l) at entry were excluded. Subjects with diseases or taking medications known to have an important effect on glucose metabolism were excluded. Data from OGTTs during which a subject experienced significant nausea, emesis, or diarrhea were excluded.

Medical records from the personal physician and from hospitalizations were obtained. Two physicians examined these records to determine whether the history of a previous diagnosis of diabetes was justified.

FPG and 2hPG determination

FPG measurements started in 1963, and OGTT measurements started in 1965. Blood was obtained in the morning after a 9- to 12-h fast. Subjects spent the night before the test at the Gerontology Research Center. No significant physical activity or smoking was allowed from the night before metabolic testing until the end of the test. Subjects were semireclining in bed during the test. An antecubital blood sample was drawn immediately before and 2 h after glucose ingestion.

Several methods have been used to measure plasma glucose concentration. Ferricyanide reduction (Technicon AutoAnalyzer) was used from 1963 through 1977, at which time glucose oxidase was adopted (Beckman Glucose Analyzer 1977–1983, Abbott Laboratories ABA 200 ATC Series II Bichromatic Analyzer 1983–1992, and Abbott Spectrum CCX 1992-present). Before changing assay methods, glucose concentrations were measured using the old and new assays. There were no systematic differences in glucose concentrations among the assays.

From August 1965 through June 1977, subjects received a 1.75-g glucose/kg body wt OGTT (8,9). The average man weighed 79 kg; the average glucose dose was 138 g. In 1969, the Statistical Committee of the American Diabetes Association (ADA) recommended the glucose dose be changed to 40 g/m^2 body surface area (10). From July 1977 forward, BLSA men received an average glucose dose of 78 g (mean surface area 1.96 m^2). In 1979, the National Diabetes Data Group (1) and in 1980 the WHO (4) recommended a dose of 75 g regardless of body size. Because the difference between our average dose of 78 g and the 75-g dose recommended by the National Diabetes Data Group and the WHO is small, it seemed appropriate to us to adjust the glucose dose for body size. Since we wished to minimize changes in this long-term study, we continued to use the 40-g/m^2 body surface area dose.

2hPG concentrations from the older 1.75-g/kg test (g_{old}) were converted to values that would have been obtained from the newer 40-g/m^2 dose (g_{new}) according to the formula:

$$g_{new} = -1.75 + 1.02 g_{old}$$

The conversion formula was obtained by perpendicular least squares, properly weighted (11) of 2hPG from the 1.75-g/kg test on concentrations from the 40-g/m^2 test. Detailed information about the conversion is available upon request. The data used in the conversion came from 322 men who received both tests.

Mortality follow-up

Follow-up of BLSA subjects is close to 100%. We become aware of deaths by information supplied by family members, the participant's physician of record, response to mailings and phone calls we make to the participant's family for those who stop or do not report for periodic return visits, and searching the National Death Index.

Statistical methods

Cox's proportional hazards regression (12), adjusted for age, BMI, BMI^2, abdominal sagittal diameter (an index of abdominal adiposity), and smoking, was used to relate FPG and 2hPG to outcome. Abdominal sagittal diameter was measured at end expiration with a caliper placed midway between the lower rib margin and the iliac crest while the subject was standing. BMI^2 was entered into the models because many studies have reported a curvilinear relation between mortality and BMI.

FPG concentration was entered in the models as a series of dummy variables (Table 1 and Table 2). Relative risks (RRs) were computed using the lowest concentration category as the reference group. Cut points were chosen to include the recommended cut points for defining IFG and diabetic fasting glucose, 100, 110, and 126 mg/dl (5.6, 6.1, and 7.0 mmol/l).

2hPG concentration was entered as a series of dummy variables representing the three diagnostic categories defined by the ADA (1) and the WHO (4): normal <140 mg/dl (7.7mmol/l), impaired 140–199 mg/dl (7.8–11.0 mmol/l), and diabetic ≥200 mg/dl (11.1 mmol/l), as well

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Table 2—*Relation between 2hPG and all-cause mortality in 1,064 men*

	Glucose (mmol/l)		Glucose (mg/dl)		Subjects		RR for mortality*		
	Range	Median	Range	Median	At risk	Deaths	RR	95% CI	*P*
N	2.4–6.6	5.7	43–119	102	449	90	1.00	—	—
	6.7–7.7	7.2	120–139	129	220	65	1.06	0.77–1.46	0.73
I	7.8–9.4	8.4	140–169	151	200	87	1.38	1.03–1.86	0.03
	9.5–11.0	10.1	170–199	181	115	66	1.51	1.08–211	0.02
D	11.1–18.8	12.6	200–338	227	80	61	1.48	1.08–2.03	0.02

*Adjusted for age, BMI, BMI^2, sagittal abdominal diameter, and smoking. Median follow-up 12.4 years. D, diabetic; I, impaired; N, normal.

as the reference category (≤139 mg/dl). In some analyses, the number of deaths in the normal and impaired zones allowed these zones to be further subdivided into smaller groups: normal ≤119 mg/dl (6.6 mmol/l) (the reference category) and 120–139 mg/dl (6.7–7.7 mmol/l) and impaired 140–169 mg/dl (7.8–9.4 mmol/l) and 170–199 mg/dl (9.5–11.0 mmol/l).

RESULTS

Baseline characteristics

The mean age of the subjects was 53 years (range 17–102); median follow-up was 13.4 years. The mean BMI of the men was 25.1 ± 2.8 kg/m^2 (mean ± SD). The mean abdominal sagittal diameter was 23.8 ± 3.9 cm.

FPG and all-cause mortality

During follow-up, 35% of the men died. Men in the new diabetic zone of 126–139 mg/dl (7.0–7.7 mmol/l) and in the original impaired zone of 110–125 mg/dl (6.1–6.9 mmol/l) had a significantly increased RR for mortality compared with the reference group (74–94 mg/dl [4.1–5.2 mmol/l]). There was, however, no increase in mortality among men with FPG 100–109 mg/dl (5.6–6.0 mmol/l). FPG, entered as a continuous covariate, was a statistically significant predictor of all-cause mortality (Table 1). The RRs associated with a 1-mg/dl (0.056 mmol/l) concentration difference in FPG was 1.014 (95% CI 1.003–1.025, $P < 0.006$).

2hPG and all-cause mortality

Men in the lower and upper portions of the impaired zones of 140–169 and 170–199 mg/dl (7.8–9.4 and 9.5–11.0 mmol/l) and men with diabetic glucose tolerance, ≥200 mg/dl (11.1 mmol/l), had significantly increased risk for all-cause mortality. There was no increased risk in the upper portion of the normal zone (120–139 mg/dl [6.7–7.7 mmol/l]) (RR 1.06, 95% CI 0.77–1.46, $P < 0.73$) (Table 2). The RR associated with a 1-mg/dl (0.056 mmol/l) difference in glucose concentration was 1.003 (1.001–1.005, $P < 0.006$).

RR for all-cause mortality based upon both FPG and 2hPG

Men with IFG and normal glucose tolerance had the same risk for all-cause mortality, RR 1.0 (95% CI 0.5–2.1), as men with both normal FPG and normal 2hPG (the reference category) (Table 3). In contrast, men with impaired FPG and diabetic 2hPG had a significantly increased risk for all-cause morality, 1.7 (1.0–2.8). The RR for men with impaired glucose tolerance (IGT) and IFG, 1.5, was of borderline significance ($P \leq 0.07$). The RR for all-cause mortality in men with IFG increased progressively as the 2hPG concentration worsened, from normal (1.0) to impaired (1.5) to diabetic (1.7).

CONCLUSIONS — Clinical diabetes is associated with a wide variety of diseases (13) and all-cause mortality. This report does not deal with clinically unequivocal diabetes but rather with subclinical disease diagnosed by measuring the FPG or 2hPG.

A number of studies have examined the relation of FPG or 2hPG to mortality. In preparing the summary below, we considered those studies that report the risk of one or more concentration categories compared with a reference category. There is great variance in methods across the papers. The reference concentration category varies as do the cut points defining the concentration categories, the size and age of the populations, and the length of the follow-up. Inclusion and exclusion rules also vary. Recognizing the impor-

Table 3—*RR for mortality in 1,064 men by FPG and 2hPG concentration*

	FPG											
	Normal ≤109 mg/dl (6.1 mmol/l)				Impaired 110–125 mg/dl (6.1–6.9 mmol/l)				Diabetic 126–139 mg/dl (7.0–7.7 mmol/l)			
2hPG	RR	95% CI	*P*	Deaths/ subjects	RR	95% CI	*P*	Deaths/ subjects	RR	95% CI	*P*	Deaths/ subjects
Diabetes: ≥200 mg/dl (≥11.1 mmol/l)	1.3	0.9–1.9	0.21	31/44	1.7	1.0–2.8	0.05	20/23	1.7	0.8–3.5	0.15	8/10
Impaired: 140–199 mg/dl (7.8–11.1 mmol/l)	1.4	1.1–1.8	0.01	132/276	1.5	0.9–2.5	0.07	21/39	*	—	—	1/1
Normal: <140 mg/dl (<7.7 mmol/l)	1.0	Reference	—	148/643	1.0	0.5–2.1	0.98	8/28	†	—	—	0/0

*RR and 95% not computed; only one subject was classified as diabetic by fasting and impaired by 2-h concentrations. †There were no subjects whose fasting glucose concentration was classified as diabetic and whose 2-h concentration was classified as normal.

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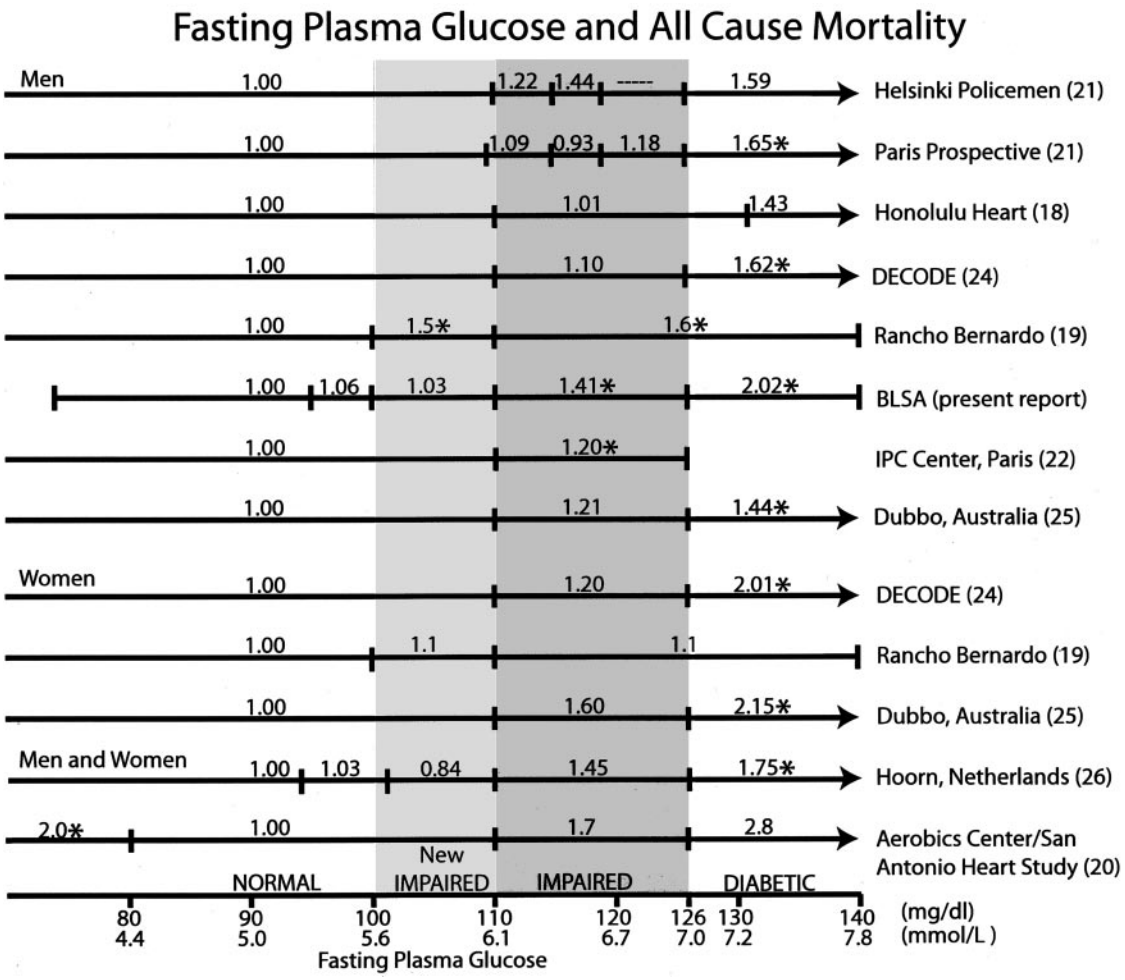

Figure 1—*Summary of reports on the relation of FPG concentration to mortality. The vertical ticks on each line represent the cut points between glucose categories. The numbers above each line represent the RR, odds ratio, or standardized mortality ratio for the glucose concentration categories. *Risk is statistically significantly different from the reference category. An arrow at the end of a line indicates that the upper concentration limit of the highest glucose concentration category was not given. The "New Diabetic" zone represents that portion of the diabetic zone that was previously considered normal, i.e., 126–139 mg/dl (7.0–7.8 mmol/l). See* APPENDIX *for further details of the construction of the figure.*

tance of placing the results of our study in perspective, we have produced Figs. 1 and 2, which summarize data about FPG, 2hPG, and all-cause mortality.

Some conclusions emerge from the figures. Only the present BLSA report (Fig. 1) has examined the FPG zone 126–140 mg/dl (7.0–7.8 mmol/l), a range that became designated as the "diabetes zone" in the ADA 1997 (1) and WHO 1999 reports (6). In the BLSA, the RR for mortality in the diabetic zone is 2.02. The other reports (Fig. 1) analyze mortality risk for FPG concentrations ranging from 126 mg/dl (7.0 mmol/l) to levels far greater than 140 mg/dl (7.8 mmol/l). These reports cannot be used as evidence that the 126–140 mg/dl (7.0–7.8 mmol/l) diabetic zone carries an increased mortality risk. However, it is clear that the IFG zone of 110–125 mg/dl (6.1–6.9 mmol/l) defined in the 1997 and 1999 reports (1,6) is a zone of intermediate risk for mortality and is also justified. Very few studies allow evaluation of the newest extension of IFG down from 110 to 100 mg/dl (6.1–5.6 mmol/l) (3). Although the Rancho Bernardo men (20) showed a significant increase in mortality in that zone, the Rancho Bernardo women (18) and the Hoorn Study of men and women (27) did not. In the BLSA, we did not find an increased RR for mortality in men with FPG from 100–110 mg/dl (5.6–6.1 mmol/l). Thus, with respect to all-cause mortality, the few reports that are available do not consistently support extension of the IFG zone down to 100 mg/dl (5.6 mmol/l).

The OGTT results (Fig. 2) are not easily summarized. The recommendations in the reports of 1979 (1) and 1985 (5) setting the cut points diagnostic for diabetes for the 2hPG concentration at 200 mg/dl (11.1 mmol/l) are clearly supported. The IGT zone of 140–199 mg/dl (7.8–11.0 mmol/l) also shows an increased RR for mortality; the Honolulu Heart Study (19) and the Rancho Bernardo men (20) are exceptions. Mortality risk in subjects in the normal glucose tolerance zone of <140 mg/dl (7.8 mmol/l) are quite variable. It is of importance to know whether individuals in the upper part of the normal range (e.g., 120–139 mg/dl, 6.7–7.7 mmol/l) consistently show an increase in mortality risk. It appears that in most cases, an increase in mortality is seen even within the normal glucose tolerance zone (22,20,18,27) but not in the current BLSA report. Two of the studies that we summarized in Fig. 2 (19,25) did not examine individuals in the upper and lower portions of the normal zone. Some of the results of mortality risk with increasing glucose concentration are not smoothly progressive (22,20). It can be concluded,

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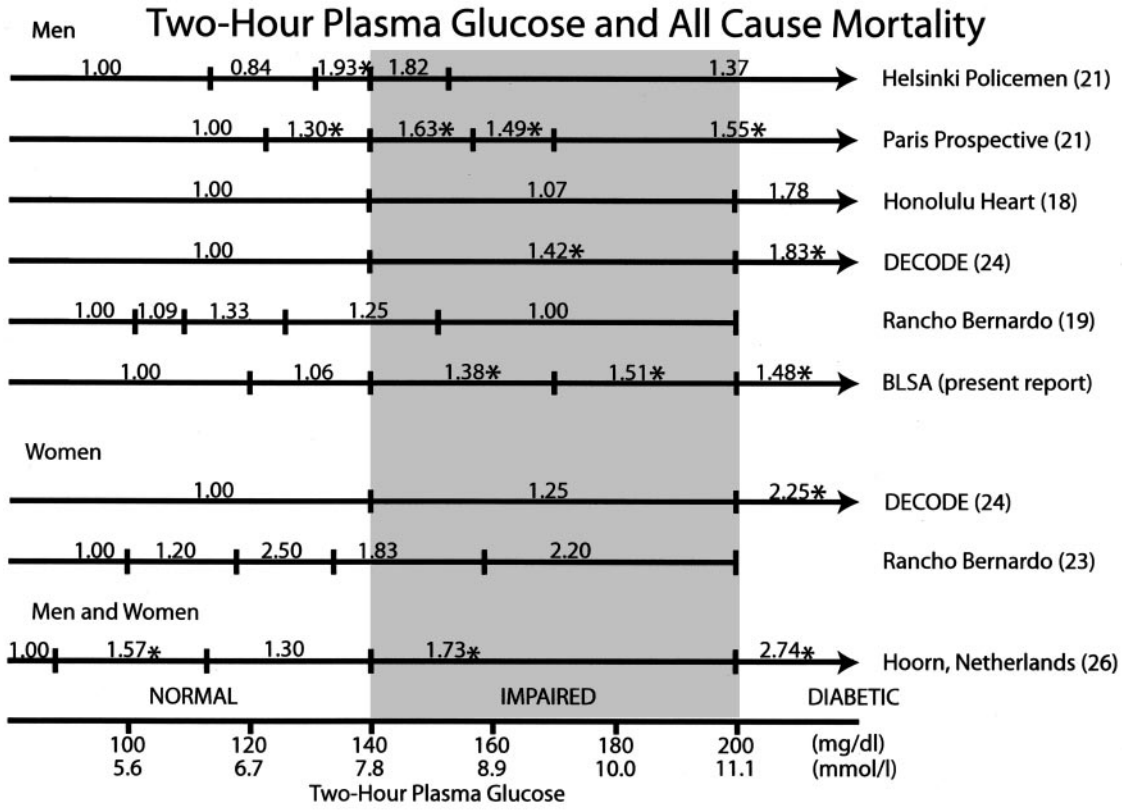

Figure 2—*Summary of reports on the relation of 2hPG after an OGTT and mortality. See Fig. 1 legend. The cut points given for the Rancho Bernardo Study (23) represent the 95% CI for each concentration category.*

however, that the diabetic and impaired zones definitely carry increased mortality risk, and the risk for mortality in the diabetic zone is higher than in the impaired zone. An important unanswered question is, does the relation between glucose concentration and mortality differ by sex? In order to address this question, it would be helpful if future studies would report sex-specific results.

A combination of the FPG and the 2hPG provided better evaluation of mortality risk than did the FPG alone. In men, categorization of risk based only upon FPG concentration suggests that risk for all-cause mortality among men with impaired FPG is intermediate to that of men with normal and diabetic fasting concentrations (Table 1). Characterization of men by FPG and 2hPG concentrations indicates that *1*) there is no increased all-cause mortality risk for men with IFG and a normal 2hPG and *2*) risk increases progressively in men with IFG as the 2hPG becomes progressively worse (Table 3).

We are aware of three studies (14–16) in which subjects have been crossclassified by their FPG and 2hPG and were followed to determine whether the 2hPG added to the predictive power of the FPG. These studies do not allow evaluation of IFG cut points; subjects with normal or impaired FPG were combined into a single nondiabetic group. In the DECODE (Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe) study (14), men, but not women, with nondiabetic FPG and a diabetic 2hPG did worse than those men with nondiabetic FPG and 2hPG concentrations. A study of subjects from Mauritius, Fiji, and Nauru (15) reached a similar conclusion, but rather than being significant only for men, the study found significant relations for both men and women. The study from Japan (16) is difficult to compare to the other reports. Subjects received a 50-g OGTT, and the cut points for normal fasting glucose were 140 mg/dl (7.8 mmol/l), while the cut point for the 2hPG was 200 mg/dl (11.1 mmol/l). Thus, impaired zones were not evaluated.

In its 1997 report (2), the ADA Expert Committee stated, ". . . although the OGTT is an acceptable diagnostic test and has been an invaluable tool in research, it is not recommended for routine use. Because of its inconvenience to patients and the perception by many physicians that it is unnecessary, the OGTT is already not widely used for diagnosing diabetes. . ." The report further states that ". . . simultaneous measurement of both FPG and 2hPG will inevitably lead to some diagnostic discrepancies and dilemmas." The data from the present report suggest that simultaneous measurement of FPG and 2hPG concentrations can lead to more precise classification of subjects. Rather than placing subjects into one of three categories, normal, impaired, or diabetic, it may prove to be useful, despite the increased complexity, to place subjects into one of nine categories: normal fasting with normal 2 h, normal fasting with impaired 2 h, normal fasting with diabetic 2-h concentrations, etc. It would also be important to explore the accuracy of HbA_{1c} to improve the prognostic ability of the fasting (17) and 2-h glucose concentrations. Furthermore, longitudinal follow-up of subjects in these multiple diagnostic categories is needed to gain a clearer understanding of the prognostic significance of these tests.

Limitations of the present study should be noted. The BLSA consists of community volunteers, largely Caucasian, and only men provided enough deaths to allow analysis. However, we

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Appendix Table 1—*The tables and figures from which data were obtained*

Study (reference)	FPG source	2hPG source	Age range (years)
Helsinki Policemen (21)	Table 6	Table 4	44–55
Paris Prospective (21)	Table 6	Table 4	44–55
Honolulu Heart (18)	Fig. 1	Fig. 1	71–93
DECODE (24)	Table 4	Table 4	30–89
Rancho Bernardo (19)	Table 4	—	40–79
Rancho Bernardo (23)	—	Fig. 1	55–92
IPC Center, Paris (22)	Table 4	—	21–60
Dubbo, Australia (25)	Table 1	—	60+
Hoorn, Netherlands (26)	Table 3 (model 1)	Table 4 (model 1)	50–75
Aerobics Center/ San Antonio Heart (20)	Fig. 1 (right panel)	—	20–82

summarize results from women (and men) from the literature. Our end point, all-cause mortality, is only one of many that can be related to the fasting and 2-h glucose concentrations. Diagnostic cut points cannot be determined solely by statistically significant associations with harmful outcomes, such as mortality. The labeling of individuals as having a disease (or as being at high risk) has harmful as well as beneficial effects. Nevertheless, data such as those in this report provide information that must be taken into account when establishing or modifying diagnostic standards.

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APPENDIX

Construction of Figs. 1 and 2 (summaries of published studies)

The current study and 10 previous reports present data on the relation of FPG to all-cause mortality (Fig. 1). In addition to the present study, six studies report the relation of 2hPG to mortality (Fig. 2). Many of the studies present multiple analyses of their data. We therefore present the figure or table from which we have obtained the risk estimates presented in our figures (APPENDIX, Table 1). In Fig. 1, there are eight reports in men and three in women. Two reports present data on both sexes combined. In Fig. 2, there are six studies in men, two in women, and one report of data on both sexes combined.

Only studies that presented mortality data on subjects whose glucose values were in the impaired zones for FPG and 2hPG were included. The sole exception was the Rancho Bernardo Study (Fig. 1) in which the upper FPG limit extended to 140 mg/dl (7.8 mmol/l).

The horizontal lines for each study are segmented by vertical bars showing the ranges of the glucose concentrations reported. Lines that end in an arrow indicate that the upper extent of the glucose concentration was not given. The lower limits of the glucose lines almost always extend beyond the lower extent of the glucose scale, i.e., <70 mg/dl (3.9 mmol/l) for FPG and <80 mg/dl (4.4 mmol/l) for 2hPG.

RRs were not presented but were computed by us from other data for reports (18–20). For example, if mortality rates were given, an RR could be computed by comparing mortality in the several glucose categories to the mortality in the lowest glucose concentration. We did not attempt to determine statistical significance when we computed the RR. In two reports, the Honolulu Heart Study (18) and the Aerobics Center and San Antonio Heart Study (20), we estimated the mortality rates from data presented in figures. Some of the number of events/subjects are so large that significance is nearly certain, but no indication of significance was given in the figures. Examples of such high RRs in our Fig. 1 are seen in the Honolulu Heart Study (1.43) and the Aerobics Center and San Antonio Heart Study (1.7 and 2.8). In Fig. 2, examples are the Honolulu Heart Study (1.78) and the Rancho Bernardo Women (2.50, 1.83, and 2.20). For the Helsinki Policemen Study (22), we omitted the RR in Fig. 1 for the 124–139 mg/dl (6.9–7.7 mmol/l) area since there were only two deaths in this category.

The reports were inconsistent in the covariates included in the analyses. All studies adjusted for age; the two studies that combined the data for men and women adjusted for sex and two studies that combined diverse populations appropriately adjusted for that fact. There was no consistency in adjustment for such variables as BMI, blood pressure, lipid concentrations, and cigarette smoking. Five studies adjusted for BMI, three for blood pressure, four for cholesterol, and five for smoking. Other isolated examples of adjustments included administrative grade (Paris Prospective [21] and Helsinki Policemen [21]), estrogen use (Rancho Bernardo women [19]), and presence of cardiovascular disease (Paris Prospective [21] and Helsinki Policemen [21]), triglycerides (IPC Center, Paris [22]), and abdominal sagittal diameter (BLSA).

For the glucose tolerance test results (Fig. 2), only studies that administered a glucose dose of 75 g were included; exceptions include the BLSA (see RESEARCH DESIGN AND METHODS) and the Helsinki Study (75 or 90 g were given depending on surface area; 11% of the men received the larger dose) (21).

All data in the figures are presented in terms of plasma glucose concentration. In the Helsinki Study (21), glucose was measured and reported in whole blood. We converted these values to the equivalent plasma concentrations by multiplying the blood concentration by 1.15.

For the Aerobics Center and the San Antonio Heart Study (20), results are reported for seven concentration zones: the diabetic zone (≥126 mg/dl, 7.0 mmol/l), the impaired zone (110–125 mg/dl, 6.1–6.9mmol/l), and five categories in the normal zone. The mortality rates for the three categories, 80–89, 90–99, and 100–110 mg/dl (4.4–4.9, 5.0–5.5, and 5.6–6.0 mmol/l), were essentially identical; we grouped them together as the reference category. The mortality rates in the <70 mg/dl (3.8 mmol/l) and 70–79 mg/dl (3.9–4.3 mmol/l) zones had high mortality. For ease of presentation, we grouped them together in one category in our figure. For Rancho Bernardo, we have included the report of Park et al. (23) for the 2hPG since these were not reported in the earlier study by Barrett-Connor et al. (19). The cut points for the FPG were more informative for this report in the earlier study (19) than in the later study (23).

A large number of reports have been published from the Paris Prospective Study. We selected a report that had cut

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points for the fasting plasma glucose concentration that allowed conclusions to be drawn about the IFG zone (21). Similarly, for the 2hPG, we selected a report that allowed conclusions to be drawn about the IGT zone (21). The locations from which our data was obtained are indicated (APPENDIX, Table 1).

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