Increased Mortality Risks of Pre-Diabetes (Impaired Fasting Glucose) in Taiwan

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OBJECTIVE — The objective of this article was to assess mortality risks at different levels of fasting blood glucose (FBG) in Taiwan, with particular attention to those pre-diabetic subjects with impaired fasting glucose (IFG).

RESEARCH DESIGN AND METHODS — Governmental employees and schoolteachers were followed up for an average of 11 years. With the use of Cox regression analyses, mortality risks were calculated for 36,386 subjects, aged 40–69.

RESULTS — FBG ≥110 mg/dl was associated with increased mortality risks for all causes, cardiovascular diseases (CVD), and diabetes. IFG, when defined as 110–125 mg/dl, was associated with a significant increase for CVD and/or diabetes mortality. These mortality risks remained elevated when known CVD risk factors were adjusted for. The IFG group shared risk factor characteristics more with the FBG ≥126 mg/dl group than with the FBG <110 mg/dl group. When IFG was defined as 100–125 mg/dl, the number of subjects quadrupled, but mortality risks diminished substantially because of the inclusion of 100–109 mg/dl group. The lowest FBG group, 50–75 mg/dl, had a significant 2-fold risk from all causes.

CONCLUSIONS — There was an overall J-shaped relationship between all-cause mortality and FBG. IFG, when defined as 110–125 mg/dl, is an independent risk factor and should be aggressively treated as a disease because its subsequent mortality risks for CVD and diabetes were significantly increased. The newly defined IFG at 100–125 mg/dl did not have the predictive power for later increases in CVD or diabetes mortality.

Diabetes Care **28:**2756–2761, 2005

Pre-diabetes, defined as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), has received increasing attention for its propensity to become diabetes and for the potential it presents for prevention (1–4). The definition of IFG, fasting blood glucose (FBG) at 110–125 mg/dl, was lowered to FBG 100–125 mg/dl in 2003 (5). Such a modification provoked controversy and was challenged as to its appropriateness (6–10). It reportedly would more than double the number of those with pre-diabetes in the U.S. (6,11) or in Singapore (10). The basis for such lowering was not made immediately clear (5), but it seems to have come more from theoretical extrapolations from a few studies than from long-term outcome studies. For the purpose of predicting diabetes from pre-diabetes, the lowering of the IFG cut point was an attempt to reduce false-negative results and to increase true-positive results to the maximal extent. However, in so doing, a large number of false-positive results are created. Although the benefits of early intervention have been assumed, whether it is still cost effective to intervene in a much larger population with pre-diabetes, one that more than doubles the original number of subjects with IFG, remains unsettled (6,8). Nevertheless, the recent change reflected the trend to lower the cut point for either diabetes or pre-diabetes by the American Diabetes Association (ADA) and the World Health Organization (WHO) (1,4), with the expectation that progression of pre-diabetes into diabetes or the development of cardiovascular diseases (CVD) can be prevented through earlier awareness and intervention (3, 12,13).

IFG, or pre-diabetes, is "not considered as a clinical entity in its own right, but rather a risk factor for future diabetes" (14). The reason is that, although IFG is associated with elevated mortality risks (2,15–21), these risks could attenuate or lose statistical significance when associated risk factors were adjusted. Because only a few studies assessed the long-term risks of IFG and were based mainly on Caucasian populations with largely inconclusive results (21–29), we evaluated this subject from an on-going large cohort study in Taiwan by calculating the mortality risks at different levels of FBG. Clarifying the predictive value of IFG will have important policy implications and will be useful for clinician's management.

RESEARCH DESIGN AND METHODS — Details of this cohort and its limitation have been reported elsewhere (30,31). The cohort studied in this article (36,386 subjects) was selected from a pool of more than 76,000 individuals, aged ≥40, who went through an employer-sponsored medical examination program between 1989 and 1992. The subjects were mainly white-collar civil servants and teachers, with >75% college graduates. In the course of medical checkups, a medical history detailing, among other facts, the presence of physician-diagnosed diabetes or associated medication was recorded. In addition, a health risk appraisal questionnaire, eliciting lifestyle and health risk factors, was administered to each subject. Anthropometric and blood pressure measurements, collection of

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Table 1—*Comparison of risk factors among male and female subjects classified by FBG at time of recruitment*

	FBG					
	<100 mg/dl (5.6 mmol/l)	100–109 mg/dl (5.6–6.1 mmol/l)	110–125 mg/dl (6.1–6.9 mmol/l) (IFG)	≥126 mg/dl (>7.0 mmol/l) (screened diabetes)	Known diabetes	Total
Men						
n (%)	14,772 (62.2)	5,703 (24.0)	1,857 (7.8)	816 (3.4)	607 (2.6)	23,755 (100)
Person-years observed	163,434	62,395	20,297	8,760	6,400	261,286
Age (years)	51.7 ± 0.07†	52.6 ± 0.11†	54.2 ± 0.18	55.9 ± 0.27†	58.0 ± 0.30†	52.4 ± 0.05
Fasting glucose						
mg/dl	91.4 ± 0.05	103.5 ± 0.04	115.1 ± 0.10	161.3 ± 1.56	164.5 ± 2.37	100.4 ± 0.14
mmol/l	5.1 ± 0.002	5.8 ± 0.002	6.4 ± 0.01	9.0 ± 0.09	9.1 ± 0.13	5.6 ± 0.01
SBP (mmHg)	117.3 ± 0.13†	121.8 ± 0.23†	126.1 ± 0.41	128.4 ± 0.64†	126.2 ± 0.73	119.7 ± 0.11
DBP (mmHg)	76.4 ± 0.08†	79.0 ± 0.14†	80.9 ± 0.25	81.0 ± 0.37	78.1 ± 0.43†	77.6 ± 0.07
Total serum cholesterol (mg/dl)	194.2 ± 0.28†	199.3 ± 0.46*	202.9 ± 0.81	204.4 ± 1.40	194.9 ± 1.37†	196.5 ± 0.22
BMI (kg/m^2)	23.6 ± 0.02†	24.4 ± 0.04*	25.0 ± 0.06	25.3 ± 0.10*	24.7 ± 0.12*	24.0 ± 0.02
Smoking prevalence (%)						
Current smoker	30.1	26.7	27.1	32.8	31.8	29.2
Ex-smoker	14.2	17.0	19.0	20.3	22.4	15.7
Women						
n (%)	9,805 (77.6)	2.032 (16.1)	499 (4.0)	161 (1.3)	134 (1.1)	12,631 (100)
Person-years observed	108,889	22,264	5,449	1,780	1,481	139,864
Age (years)	47.3 ± 0.06†	49.5 ± 0.16†	51.4 ± 0.32	52.8 ± 0.59*	54.8 ± 0.61†	47.9 ± 0.06
Fasting glucose						
mg/dl	90.3 ± 0.06	103.3 ± 0.06	114.8 ± 0.19	160.9 ± 3.31	170.8 ± 5.0	95.1 ± 0.14
mmol/l	5.0 ± 0.003	5.7 ± 0.003	6.4 ± 0.01	8.9 ± 0.18	9.49 ± 0.28	5.3 ± 0.01
SBP (mmHg)	111.8 ± 0.16†	117.5 ± 0.39†	123.2 ± 0.89	129.7 ± 1.97†	125.7 ± 1.73	113.6 ± 0.15
DBP (mmHg)	72.1 ± 0.10†	75.1 ± 0.23†	77.4 ± 0.49	79.9 ± 1.08*	76.8 ± 1.00	73.0 ± 0.09
Total serum cholesterol (mg/dl)	193.0 ± 0.34†	201.6 ± 0.80†	211.1 ± 1.63	214.2 ± 3.27	210.8 ± 3.54	195.5 ± 0.31
BMI (kg/m^2)	22.3 ± 0.03†	23.2 ± 0.06†	24.3 ± 0.15	24.6 ± 0.24	24.4 ± 0.29	22.6 ± 0.03
Smoking, prevalence (%)						
Current smoker	1.3	1.1	1.2	1.2	2.2	1.3
Ex-smoker	0.4	0.7	0.8	0.6	0.8	0.5

Data are means ± SE unless otherwise indicated. Differences from IFG, *$P < 0.05$, †$P < 0.01$.

blood, and laboratory analyses were performed, in addition to hands-on physical examinations by physicians.

Blood analysis

All subjects visited one centrally located clinic in Taipei City in the morning after overnight fasting. Venous blood specimens collected were centrifuged shortly afterward, within 30 min, for analysis. Specimens were then processed with a Hitachi 730-20 AutoAnalyzer using the glucose oxidase method for FBG analysis (Wako, Osaka, Japan). For description of characteristics, the cohort was divided into five groups, those with FBG <100 mg/dl, 100–109 mg/dl, 110–125 mg/dl (IFG), ≥126 mg/dl (screened diabetes), and subjects with known diabetes.

Outcome follow-up

A nationwide mortality computer file has been maintained by the government since 1971. In this study, a search was conducted on data from 1990 to 2001 from this Taiwan mortality file. We limited our mortality analysis to men ($n = 23,755$) because of the small number of female deaths. By the end of 2001, 1,060 male deaths were identified and coded, using the WHO ICD-9 (32).

Statistical analysis

Relative risks were calculated by comparing the age-adjusted mortality rates of different levels of FBG with the reference group, FBG between 90 and 109 mg/dl. In addition, another reference group, defined as FPG 90–99 mg/dl, was used to assess differences in relative risks from the recently revised IFG definition (5). A Cox

proportionate hazard model was used to make adjustments on CVD risk factors, i.e., systolic blood pressure (SBP) (≥140 or <140 mmHg), diastolic blood pressure (DBP) (≥90 or <90 mmHg), smoking (never, ex-smoker, or current smoker), total serum cholesterol (≥240 or <240 mg/dl), and BMI (≥24 or <24 kg/m^2). The cut points selected for cholesterol at 240 mg/dl (33) and BMI at 24 kg/m^2 (34–36) in risk adjustment were based on data from the literature.

RESULTS — IFG 110–125 mg/dl includes 7.8% of men and 4.0% of women (Table 1), and the group is ~3 times the size of the group with "known diabetes" (2.6% of men and 1.1% of women) and twice the size of the additional group with "screened diabetes" (3.4% of men and 1.3% of women). The addition of those

Table 2—Relative mortality risks for different levels of FBG (for IFG at 110–125 mg/dl, using 90–109 and 90–99 mg/dl as reference)

Glucose, mg/dl (mmol/l)	n	All-causes Deaths	RR*	RR†	CVD Deaths	RR*	RR†	Diabetes Deaths	RR*	RR†	CVD and diabetes Deaths	RR*	RR†
90–109 ml/dl as reference													
Total	23,755	1,060			256			53			309		
50–75 (2.8–4.1)	129	12	2.1‡	2.0‡	2	1.5	1.4	0	NA	NA	2	1.4	1.4
76–89 (4.2–4.9)	4,706	205	1.1	1.2	37	0.8	0.9	2	1.3	1.3	39	0.9	0.9
90–109 (5.0–6.0)	15,640	580	1.0	1.0	142	1.0	1.0	5	1.0	1.0	147	1.0	1.0
110–125 (6.1–6.9) (IFG)	1,857	79	1.0	0.9	29	1.5‡	1.3	3	4.4‡	4.3‡	32	1.6‡	1.4
126–139 (7.0–7.7)	371	26	1.4	1.3	4	0.9	0.7	4	24.0‡	22.6‡	8	1.7	1.4
140–179 (7.8–9.9)	270	25	1.8‡	1.6‡	11	3.1‡	2.6‡	3	22.4‡	21.2‡	14	3.8‡	3.2‡
180+ (10.0+)	175	27	3.7‡	3.6‡	8	4.4‡	3.9‡	8	122.2‡	125.6‡	16	8.5‡	7.6‡
Known diabetic subjects	607	106	3.3‡	3.1‡	23	2.9‡	2.6‡	28	99.4‡	95.2‡	51	6.2‡	5.6‡
90–99 mg/dl as reference													
Total	23,755	1,060	—	—	254	—	—	53	—	—	307	—	—
50–75 (2.8–4.1)	129	12	2.1‡	1.9‡	2	1.5	1.4	0	—	—	2	1.4	1.4
76–89 (4.2–4.9)	4,706	205	1.1	1.1	36	0.8	0.9	2	2.0	2.0	38	0.9	1.9
90–99 (5.0–5.5)	9,937	369	1.0	1.0	86	1.0	1.0	2	1.0	1.0	88	1.0	1.0
100–125 (5.6–6.9) (IFG)	7,560	290	1.0	0.9	84	1.2	1.0	6	3.6	3.6	90	1.2	1.1
100–109 (5.6–6.1)	5,703	211	0.9	0.9	55	1.0	1.0	3	2.4	2.5	58	1.1	1.0
110–125 (6.1–6.9)	1,857	79	1.0	0.9	29	1.5‡	1.3	3	6.8‡	7.0‡	32	1.7‡	1.4
126–139 (7.0–7.7)	371	26	1.4	1.2	4	0.9	0.7	4	38.7‡	38.0‡	8	1.8	1.4
140–179 (7.8–9.9)	270	25	1.8‡	1.6‡	11	3.2‡	2.5‡	3	37.9‡	37.7‡	14	4.0‡	3.3‡
180+ (10.0+)	175	27	3.7‡	3.5‡	8	4.5‡	3.8‡	8	197.5‡	209.5‡	16	8.9‡	7.8‡
Known diabetic subjects	607	106	3.1‡	2.9‡	23	2.7‡	2.4‡	28	146.4‡	141.5‡	51	6.0‡	5.4‡

Data are n unless otherwise indicated. *RR adjusted for age only. †RR adjusted for age, SBP (≥140 mmHg), smoking (never, ex-smoker, and current smoker), total serum cholesterol (≥240 mg/dl), and BMI (≥24 kg/m²). ‡P < 0.05. Reference group was based on 90–109 mg/dl for all levels. CVD, ICD-9: 401–448; diabetes, ICD-9: 250.

with FBG 100–109 mg/dl (24.0% of men and 16.1% of women) as a newly defined group with IFG would at least quadruple the number of those with IFG, making the new group with IFG to be 31.8% in men and 20.1% in women. The IFG group showed significantly higher SBP, DBP, cholesterol level, and BMI than those with FBG at <100 mg/dl or 100–109 mg/dl, in both men and women. The means for SBP, DBP, cholesterol level, or BMI for men in the IFG group was closer to that for those with screened diabetes than for those with FBG <109 mg/dl. A similar trend was generally seen for women.

With the use of those with FBG at 90–109 mg/dl as the group to compare with, those with IFG at 50–75, 140–179, and ≥180 mg/dl and those with known diabetes showed significantly increased risks for all-cause mortality (Table 2). For those with the three FBG levels ≥126 mg/dl, i.e., 126–139, 140–179, and ≥180, mortality risks for CVD, diabetes, or CVD and diabetes combined, generally increased with increasing levels of blood glucose. A similar pattern of mortality increases was seen for the known diabetes group, with the magnitude of the increase similar to that for the group at ≥180 mg/

dl. The IFG group, defined as 110–125 mg/dl, had significantly increased mortality risks for CVD, diabetes, and CVD and diabetes. Upon adjustments for CVD risk factors, all increased relative risks (RRs) for IFG remained elevated. Specifically, the adjusted RR for CVD and diabetes at 1.4 was borderline significant, with P = 0.08. With those with FBG 90–99 mg/dl being used as the comparison group in Table 2, the 100–125 mg/dl group, the group recently classified as having IFG by ADA criteria (5), failed to show significant increases in either all-cause or CVD mortality. When this group was split into two, 100–109 mg/dl and 110–125 mg/dl, and examined separately, the latter group, but not the former, had a significantly increased risk for CVD, diabetes, or both.

The relationships between FPG and mortality risks for all causes are graphically presented in Fig. 1. The J-shaped curve reflects increases at both ends of the FBG spectrum and remained similar with the inclusion of known diabetes.

Table 3 shows relative risks at different FBG levels, with those having FBG above each specified level being compared with those having FBG below that level. Four levels were selected: 100, 110,

126, and 140 mg/dl. The all-cause mortality risks increased by 30, 90, and 130% for those with FBG level ≥110, 126, or 140 mg/dl, when compared with those with FBG below that level, respectively. In contrast, the risks among those with FBG above the cut point at 100 mg/dl failed to show significant increases for all-cause or for CVD mortality, although increases were found for diabetes or CVD and diabetes.

CONCLUSIONS — This study found an overall J-shaped relationship between all-cause mortality and levels of FBG in an Asian population, with significant increases in mortality, starting at ≥110 mg/dl as well as ≤75 mg/dl. The higher the FBG ≥110 mg/dl, the more the risks increased. This increased risks at both ends of the FBG spectrum to form a similar J-shaped relationship has been observed in several Caucasian populations (37–39). In the Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe (DECODE) study, an RR = 1.2 for all-cause mortality was seen among those with FBG ≤81 mg/dl (37). Similarly, in the San Antonio Heart Study, those with FBG <70 mg/dl had a 3.3-fold higher risk of CVD mortality compared
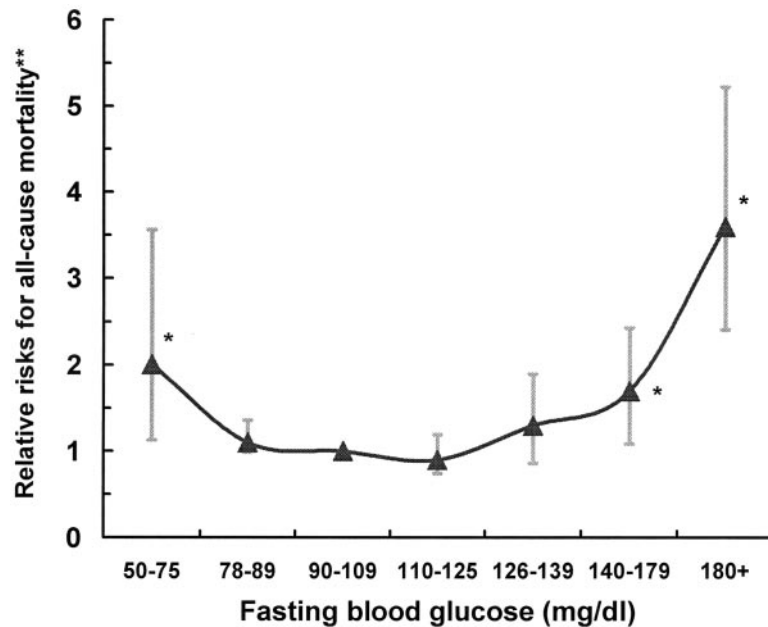
Figure 1—*Relative risks for all-cause mortality by levels of fasting blood glucose on subjects with no history of diabetes. Vertical bars represent 95% CI. *P < 0.05 vs. those at 90–109 mg/dl. **Relative risks adjusted for age, systolic blood pressure (≥140 mmHg), smoking (never, ex-smoker, and current smoker), total serum cholesterol (≥240 mg/dl), and BMI (≥24 kg/m²).*

with those with FBG 80–109 mg/dl (39). With a cutoff at 75 mg/dl, our data substantiated such an increase for all-cause mortality (RR = 2.0) but not for CVD mortality. A recent report from 17 pooled studies in the Asian Pacific region (19), showing a dose-response benefit of reducing CVD burden when FBG was lowered to a level of ≤90 mg/dl, was in line with the findings from this study. A note of caution should be added for those expecting the risk to continue to be reduced as FBG becomes lower and lower. In our study, FBG <75 mg/dl was actually associated with a higher, not lower, risk for all-cause mortality. If validated in other populations and if found not to reflect the presence of other pathologic conditions, this finding of a J-shaped relationship with increased mortality risk at FBG <75 mg/dl may have important implications in the clinical management of glucose control.

This study confirms the tendency of the IFG group, defined as 110–125 mg/dl, to have a severe risk of CVD. The characteristics of subjects with IFG have contributed to the widely held concept that the reason IFG was associated with increased CVD mortality was because subjects with IFG had additional or more severe risk factors, and, therefore, IFG per se is not an independent risk (2,15,17,22–29,40,41). Nevertheless, this study showed for the first time that

the increased risks of IFG remained significantly elevated, even after CVD risk factors were adjusted. In other words, IFG is capable of predicting future mortality independently, and identifying someone with IFG is not an incidental or innocent finding. Contrary to the consensus statement previously reported (2,3), IFG is more than just a risk marker for future diabetes. First, anyone with FBG ≥110 mg/dl (Table 3) was shown to have substantially increased risks for all-cause and CVD mortality, with excess risks as much as 140% for CVD and diabetes. Second, IFG per se caused higher mortality for CVD and/or diabetes (Table 2). Obviously, these individuals were indeed vulnerable, not only because they tended to be associated with additional CVD risk profiles, but also because they had an ad-

ditional unique, independent risk in having FBG at 110–125 mg/dl. Thus, a simple blood test to uncover IFG can predict substantial mortality risks for CVD and diabetes among nondiabetic individuals, hitherto vaguely recognized (2,15,17,22–29). The failure of previous studies to identify such risks may have come more from the inadequate sample size of study cohorts than from a true absence of risks (15,17,18,23–27).

The excess risks of IFG were demonstrated within 11 years, a relatively short time, implying that an urgency exists for preventive actions in those with IFG. In the meantime, a mechanism to identify those in the high-risk IFG group and to retard the progression of IFG should be pursued (2,14). The recent designation of smoking as "a chronic addictive disease" (42) has facilitated the implementation of smoking cessation programs in the clinical setting. Similarly, making IFG a treatable condition or recognizing it as a disease would legitimize early intervention. It should be emphasized that much of the intervention for IFG is to institute sustainable lifestyle changes (43,44).

Even though the results in this study came from a cohort with higher education, the increased risks of IFG seen in this study can be a reasonable estimate for those in the general population because risk estimation was based on internal comparison with persons with similar socioeconomic status. Some practices in this study resulted in consistent quality: collecting a history and examining subjects under one protocol from one single clinic and analyzing blood samples in the same laboratory with the same machine by the same trained staffs using the same methodology. The independently increased risk of IFG found in this study is in contrast to results of published reports of IFG based mostly on pooled studies (19,23,26,28, 37,45,46), which are affected by inconsistent quality or wide variations, including

Table 3—RRs comparing FBG* levels for subsequent mortality in male subjects

Glucose [mg/dl] (mmol/l)]	n (deaths)	All-cause	CVD	Diabetes	CVD and diabetes
≥100 (5.6+)	8,376 (368)	1.0 (0.8–1.1)	1.2 (0.9–1.5)	7.8 (2.6–22.9)	1.4 (1.1–1.7)
≥110 (6.1+)	2,673 (157)	1.3 (1.1–1.5)	1.8 (1.4–2.5)	15.7 (6.5–37.6)	2.4 (1.8–3.1)
≥126 (7.0+)	816 (78)	1.9 (1.5–2.4)	2.3 (1.5–3.5)	29.5 (13.1–66.5)	3.6 (2.5–5.1)
≥140 (7.8+)	445 (52)	2.3 (1.8–3.1)	3.5 (2.2–5.6)	29.0 (12.9–65.2)	5.2 (3.5–7.6)

Data are RRs adjusted for age, SBP (≥140 mmHg), smoking (never, ex-smoker, and current smoker), total serum cholesterol level (≥240 mg/dl), and BMI (≥24 kg/m²). *Each level of FBG indicates a comparison of mortality risks of those at or above the level with those below that level. CVD, ICD-9: 401–448; diabetes, ICD-9: 250.

differences in the age or morbidity distribution of subcohorts.

The cut point for our reference group, FBG 90–109 mg/dl, was selected because of its lowest risk in our study subjects. An identical cut point was chosen by de Vegt et al. (15) and by the Asia Pacific Cohort Studies Collaboration (19). This is because, given the J-shaped relationship of FBG with mortality risk, lower levels of glucose carried some adverse risks in this and other studies. In fact, similar observations were made by the DECODE group, which reported the lowest mortality risks in subjects with FPG at 4.5–5.0 mmol/l (80–90 mg/dl) for all-cause mortality or 5.0–5.5 mmol/l (90–100 mg/dl) for CVD mortality (37) and by Balkau et al. (38), who also concluded that the lowest mortality rate was seen among subjects in the group with FBG 5.25–5.75 mmol/l (95–104 mg/dl). All of these data indicate that the inclusion of any group with FBG <90 mg/dl may not be the best reference group.

Although IFG was reportedly less sensitive in its predictive value for diabetes or CVD than was IGT (2,23,24,26), FBG has been universally recognized as a preferred mode of diabetes screening, with the test being easier to perform, more convenient and acceptable to patients, more reproducible, and, most importantly, less expensive (47). These advantages are further magnified in Asian populations, particularly because the cost of screening has always been an overriding concern.

Most studies examining the mortality outcome of high blood glucose have focused mainly on deaths from CVD and not from diabetes (2,21,23–26,29,41), but in our study, mortality from diabetes as an additional end point was included. First, as shown in this cohort, a strong association between various glucose levels and subsequent deaths coded to diabetes supports their causal relationships: RR as large as 4.3 for 110–125 mg/dl, 22.6 for 126–139 mg/dl, 21.2 for 140–179 mg/dl, and 125.6 for ≥180 mg/dl (Table 2). Second, more deaths were coded to diabetes in Taiwan than elsewhere: Diabetes ranked as the fourth leading cause of deaths in Taiwan, and constituted 7.7% of all deaths (48). This proportion was far larger than its counterparts in the U.S. of 3.0% (49,50) or in Japan of 1.3% (51), even though the prevalence of diabetes in Taiwan was not much higher (52). The age-adjusted mortality rates, 57.7 and 74.0, for men and for women in Taiwan (48) were more than

twice as large than those in the U.S. (28.6 and 23.0) (49,50) or 6–10 times larger than those in Japan (9.1 and 5.9 per 100,000) (51), respectively. This gap between Taiwan and the U.S. or Japan has been widening because the mortality rate for diabetes in Taiwan has been rapidly increasing (53). This higher proportion of deaths from diabetes has been shown not to be due to a coding artifact (53,54) or to a true increase in the prevalence of diabetes (52) but is more reflective of the preference by physicians in assigning diabetes as the underlying cause of death when filling out death certificates. Based on these considerations, we felt these deaths coded to diabetes should be considered along with CVD deaths in accounting for all diabetes-related deaths.

This study shows that the new ADA criteria for IFG, defining IFG as 100–125 mg/dl, instead of as 110–125 mg/dl, have substantially weakened the predictive power of mortality outcome. By including the 100–109 mg/dl group, the new IFG criteria quadrupled the number of subjects in this cohort, from 7.8% to 24.0%. However, this inclusion was found to produce almost no increase in mortality risks. As the new population with IFG becomes statistically not different from those with IFG below this level, mainly because of the inclusion of this 100–109 mg/dl group, the new definition of IFG cannot be justified from the mortality perspective.

In summary, there was an overall J-shaped relationship between all-cause mortality and FBG. IFG, traditionally defined as 110–125 mg/dl, is an independent risk factor and should be aggressively treated as a disease, because it produced a significant increase in combined CVD and diabetes mortality risks in this Asian population. The increase in risk and the predictive value of IFG disappeared when IFG was defined as 100–125 mg/dl, making the necessity of the new IFG definition questionable.

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