Lowering the Criterion for Impaired Fasting Glucose

Impact on disease prevalence and associated risk of diabetes and ischemic heart disease

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OBJECTIVE — To determine the effect of lowering the fasting plasma glucose (FPG) criterion for impaired fasting glucose (IFG) on the prevalence of IFG, the risks of diabetes, and cardiovascular disease (CVD) associated with IFG.

RESEARCH DESIGN AND METHODS — Three studies were used: *1*) the 1998 National Health Survey (NHS98), a randomly selected cross-sectional sample of 4,723 subjects; *2*) the Singapore Impaired Glucose Tolerance (IGT) Follow-up Study, a cohort study comprising 295 IGT and 292 normal glucose tolerance subjects (frequency matched for age, sex, and ethnic group) followed up from 1992 to 2000; and *3*) the Singapore CVD Cohort Study, comprising 5,920 subjects from three cross-sectional studies in whom the first ischemic heart disease (IHD) event was identified through linkage to registry databases. Risk of diabetes (Singapore IGT Follow-up study) was estimated using logistic regression adjusted for age, sex, and ethnicity. Risk of IHD (Singapore CVD cohort) was estimated using stratified (by study, from which data were derived) Cox's proportional hazards models adjusted for age, sex, and ethnicity.

RESULTS — Lowering the criterion for diagnosing IFG to 5.6 mmol/l increased the prevalence of IFG from 9.5 to 32.3% in the NHS98. The lower cutoff identified more subjects at risk of diabetes and IHD, but the relative risk was lower than that for IGT.

CONCLUSIONS — Greater efforts to identify those with IGT, or a group at similar risk of diabetes and CVD, may be a more efficient public health measure than lowering the FPG criterion for diagnosing IFG.

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Abbreviations: 2-h PG, 2-h postchallenge glucose; CVD, cardiovascular disease; FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; IHD, ischemic heart disease; NGT, normal glucose tolerance; NHS92, 1992 National Health Survey; NHS98, 1998 National Health Survey; NNT, number needed to treat; OGTT, oral glucose tolerance test; ROC, receiver operating characteristic.

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

The American Diabetes Association had previously recommended (1) the recognition of impaired fasting glucose (IFG) as a category of glucose tolerance analogous to impaired glucose tolerance (IGT). It was recommended that IFG be diagnosed in those with fasting plasma glucose (FPG) between 6.1 and 6.9 mmol/l. Since then, many analyses have examined the equivalence of FPG and 2-h postchallenge glucose (2-h PG) in predicting both diabetes and cardiovascular disease (CVD). Several key findings have emerged from these studies. First, the association between IGT and CVD events and mortality is stronger than that for IFG (2,3). Second, although IFG and IGT identify some of the same individuals, the degree of overlap is variable (4,5). As a consequence of the recommendations to use FPG rather than 2-h PG for the diagnosis of diabetes, many subjects with IGT, who are at risk of future CVD events, would not be identified.

On the basis of the aforementioned findings, the American Diabetes Association has recently recommended (6) that the lower limit for the diagnosis of IFG be changed from 6.1 to 5.6 mmol/l. However, the need for this change has been questioned by others (7,8). Singapore is a small country in Asia with a high prevalence of diabetes and IGT. As in Europe and the U.S., we have found that IFG and IGT often identify different individuals. Only 26% of subjects with IGT had IFG (as defined by the older criteria of FPG 6.1–6.9 mmol/l), and 50% of those with IFG had IGT (9). We have also recently reported that IGT is associated with increased risk of all-cause mortality (10) and diabetes (11). The majority of these IGT subjects also had FPG <6.1 mmol/l.

The aims of this study were: *1*) to identify the optimal level of fasting glucose that would allow the identification of those with IGT and those at risk of incident diabetes, *2*) to determine the effect of lowering the criterion for the diagnosis of

IFG on disease prevalence, and 3) to determine the risk of future diabetes and CVD associated with the different levels of FPG and compare them against those associated with IGT.

RESEARCH DESIGN AND METHODS

— To conduct this study, we utilized data from three large studies conducted in Singapore: the 1998 National Health Survey (NHS98), the Singapore IGT Follow-up Study, and the Singapore CVD Cohort Study.

The NHS98 was a study conducted to determine the prevalence of risk factors for the major noncommunicable diseases in Singapore, including diabetes, CVD, stroke, and hypertension (12). The two minority ethnic groups, Malays and Asian Indians, were oversampled to give an ethnic distribution of 64% Chinese, 21% Malay, and 15% Asian Indian to ensure sufficient numbers for statistical analysis. A total of 4,723 subjects were studied. FPG was determined in all subjects in the morning following a 10-h fast. Those who were not on oral hypoglycemic agents or insulin underwent a 75-g oral glucose tolerance test (OGTT). Only one measure of glucose tolerance was performed.

In 1992, another cross-sectional sample comprising 3,568 subjects was selected and examined using identical methodology (13). This was the 1992 National Health Survey (NHS92). As in the NHS98, all subjects who were not on oral hypoglycemic agents or insulin underwent a 75-g OGTT in the morning, on a single occasion, following a 10-h fast. A total of 469 subjects with IGT were identified in the NHS92. In the year 2000, all subjects with IGT were frequency matched by strata of age, sex, and ethnic group with 468 subjects with normal glucose tolerance (NGT). The discrepancy of one subject arose due to the unavailability of sufficient Chinese women in the age range of 65–69 years with NGT. Among the 937 NGT and IGT subjects selected, 1 died, 1 was mentally ill, and 20 could not be traced. Of the remaining 915 subjects, 595 of them attended a follow-up examination, giving a response rate of 65.0%. In a manner identical to the baseline examination, all subjects who were not on insulin or oral hypoglycemic agents underwent a 75-g OGTT following a 10-h fast on a single occasion. These formed the study population for the Singapore IGT Follow-up Study (11).

Table 1—*Cross-tabulation of subjects from the NHS98 by categories according to fasting or 2-h PG*

Glucose tolerance according to FPG	Glucose tolerance according to 2-h PG: NGT	IGT	Total
FPG < 5.6 mmol/l	2,456 (91.6)	225 (8.4)	2,681 (100)
FPG 5.6–6.0 mmol/l	879 (80.0)	220 (20.0)	1,099 (100)
FPG 6.1–6.9 mmol/l	283 (61.1)	180 (38.9)	646 (100)

Glucose tolerance according to 2-h PG	Glucose tolerance according to FPG: <5.6 mmol/l	5.6–6.0 mmol/l	6.1–6.9 mmol/l	Total
NGT	2,456 (67.9)	879 (24.3)	283 (7.8)	3,618 (100)
IGT	225 (36.0)	220 (35.2)	180 (28.8)	625 (100)

Data are *n* (%). Percentages in parentheses represent the percentage of subjects in each row who fall into the category of glucose tolerance defined by the column. Results are weighted to take into account the oversampling of minority ethnic groups.

The Singapore CVD Cohort Study (14,15) was composed of participants from three previous cross-sectional surveys: the Thyroid and Heart Study 1982–1984 (16), the NHS92 (described in the preceding paragraph), and the National University of Singapore Heart Study 1993–1995 (17). A total of 5,920 individuals comprised the cohort. The demographic characteristics of the participants of the three studies are presented in the supplemental Table 1 (online appendix [http://care.diabetesjournals.org]). The study populations of the Thyroid and Heart Study and the NHS92 were similar in terms of age and the distribution of sex and ethnic groups. However, the National University of Singapore Heart Study population was older and had a greater proportion of Malays and Asian Indians. Outcomes were obtained by linking individual records (using unique national registry identity card numbers) to three national registries. These were: *1*) the Registry of Births and Deaths; *2*) the Central Claims Processing System and its predecessor, the Hospital Inpatient Discharge System (these databases capture inpatient discharge information from all hospitals in Singapore, both public and private); and 3) the Singapore Myocardial Infarct Registry, a population-based registry with comprehensive coverage of acute myocardial infarction occurring in Singapore. All obtained outcome measures were in coded form using the 9th revision of the *International Classification of Diseases* (ICD-9). An ischemic heart disease (IHD) event was defined as the occurrence of acute myocardial infarction or IHD (ICD-9 410-414) recorded in the aforementioned registries. The first IHD event was used for analysis. Subjects were censored as of 1 March 1999 or their date of event occurrence or death, whichever occurred first. This analysis excluded those with diabetes and preexisting IHD at baseline.

The assessment of glucose tolerance for the Thyroid Heart Study and the National University of Singapore Heart Study differed somewhat from that for the NHS92 and NHS98. In both of the former studies, FPG was determined in all subjects after a 10-h overnight fast. However, in the Thyroid Heart Study, an OGTT was only performed in those with fasting glucose ≥6.0 mmol/l. In the National University of Singapore Heart Study, an OGTT was performed in those with FPG ≥5.5 mmol/l. These methods, although reasonably effective for the identification of those with diabetes, resulted in significant misclassification of those with IGT. Therefore, we utilized data from the entire cohort in the assessment of CVD risk associated with varying levels of FPG only. We felt that these data were relevant because it reflects the clinical scenario, in which the recommended test is the FPG evaluation and not an OGTT. However, we felt that it was also important to compare the predictive value of the FPG and 2-h PG tests, and this was carried out by limiting the analysis to those subjects

from the NHS92. In this study, all subjects had an OGTT.

In accordance with the American Diabetes Association (1) and World Health Organization (18) recommendations, diabetes was diagnosed if the subject was taking medication for diabetes or if the FPG was ≥7.0 mmol/l or the 2-h PG ≥11.1 mmol/l. IGT was diagnosed if the FPG was <7.0 mmol/l and 2-h PG ≥7.8 mmol/l and <11.1 mmol/l.

To assess the likelihood that those with FPG 5.6–6.0 mmol/l would already be steered toward lifestyle intervention for the prevention of CVD, we estimated the prevalence of other features of the metabolic syndrome among this subgroup of the population using data from the NHS98. For this purpose, we utilized the National Cholesterol Education Program Adult Treatment Panel III definition for the metabolic syndrome (19) with one variation. The waist circumference we used to identify those with central obesity was lowered from 102 cm in men and 88 cm in women to 90 cm in men and 80 cm in women. This is in line with our recent work (20) showing that these cutoffs would be more appropriate when applied to an Asian population.

Statistical analyses were performed using SPSS version 11.2 for Windows (SPSS, Chicago, IL). We performed receiver operating characteristic (ROC) analysis in two of the study populations. For NHS98, which was a cross-sectional survey of the Singapore population, we determined the level of fasting glucose closest to the ideal of 100% sensitivity and 100% specificity for predicting glucose intolerance. The analysis was performed with any hyperglycemia (diabetes or IGT) as the outcome and also with IGT as the outcome after excluding those with diabetes. We carried out a similar analysis using the Singapore IGT Follow-up Study. In this instance, the outcome was the presence of diabetes after 8 years of follow-up.

The impact of lowering the criterion for IFG from 6.1 to 5.6 mmol/l on the prevalence of IFG in Singapore was assessed using the NHS98 population. To ensure that the survey findings were representative of the Singapore population, all subjects were assigned a weight to correct for the different age, sex, and ethnic distribution between the survey sample and the actual Singapore population at the time of the survey. Weighted prevalences and 95% CIs, taking into account stratification and oversampling of minority ethnic groups, were calculated using the svy set of commands in Stata software (Statacorp, College Station, TX).

To determine the impact of lowering the criterion for IFG from 6.1 to 5.6 mmol/l on the risk of future diabetes, we examined data from the Singapore IGT Follow-up Study. We utilized logistic regression analysis to estimate the odds ratio of developing diabetes associated with each category of glucose tolerance. Subjects were classified according to glucose tolerance at baseline. Those with fasting glucose <5.6 mmol/l and 2-h PG <7.8 mmol/l were taken as the reference group.

To determine the impact of lowering the criterion for IFG from 6.1 to 5.6 mmol/l on the risk of IHD, we utilized data from the Singapore CVD Cohort Study. For these analyses, subjects with IHD or diabetes at baseline were excluded from the analysis. We tested for homogeneity of effect of glucose tolerance on the risk of IHD in the three study populations. This was carried out by introducing the interaction terms FPG category × study into the model. No statistically significant interaction was noted between the FPG category, study, and risk of IHD. Therefore, the three datasets were combined. Hazard ratios for each category of glucose tolerance were calculated using stratified Cox's proportional hazards regression (stratified by the study from which the data were derived) and adjusted for age and ethnicity. This allowed the baseline hazard function to differ for subjects from each of the three studies in order to take into account any period effects on CVD incidence. A separate analysis was conducted utilizing only subjects from the NHS92, with subjects in each category of fasting glucose further subcategorized according to the presence of IGT.

RESULTS — The results of ROC analyses are shown in supplemental Fig. 1 (online appendix). When the presence of either IGT or diabetes was considered as the outcome, the level of fasting glucose closest to the ideal of 100% sensitivity and 100% specificity was 5.8 mmol/l. However, in terms of identifying those with IGT (those with diabetes having been excluded), it was 5.6 mmol/l. When ROC analysis was applied to the Singapore IGT Follow-up Study, the ideal level of FPG to predict future diabetes was also 5.6 mmol/l.

Based on data from the NHS98, the lowering of the diagnostic criterion increased the prevalence of IFG from 9.5% (95% CI 8.7–10.3) to 32.3% (31.0–33.6). In comparison, the prevalence of IGT was 13.3% (12.3–14.2). IFG, irrespective of the definition used, did not identify the same individuals as IGT (Table 1). Only 28.8% of those with IGT had FGP 6.1–6.9 mmol/l. This was increased to 64% by lowering the criterion for IFG from 6.1 to 5.6 mmol/l. However, this new definition also included a large number of subjects with normal 2-h PG.

One hundred eighteen subjects in the Singapore IGT Follow-up Study had diabetes at the follow-up examination in 2000, 8 years after the initial examination in 1992 (Table 2). Those with FPG 5.6–6.0 mmol/l at baseline were at increased risk of diabetes, even after adjustment for age, sex, and ethnic group. However, the risk was lower than that for those with FPG 6.1–6.9 mmol/l (odds ratio 55.1 vs. 12.4). In addition, the risk of diabetes was not homogenous within each category of FPG. Those with IGT had higher risk than those without IGT within each category of FPG. Furthermore, even among subjects with FPG <5.6 mmol/l, those with IGT were at greater risk of diabetes than those with FPG 5.6–6.0 mmol/l and without IGT.

We also estimated the risk of IHD in the Singapore CVD cohort for each category of glucose intolerance. First, we determined the risk of IHD associated with glucose tolerance as determined by FPG alone. Table 3 shows the age and the IHD risk associated with each category of FPG. Subjects with FPG 5.6–6.0 mmol/l were younger than those with FPG 6.1–6.9 mmol/l. To assess the effect of age on the risk of IHD associated with FPG, analyses were carried out before and after adjustment for age. Compared with those with FPG <5.6 mmol/l, subjects with FPG 6.1–6.9 mmol/l were at increased risk of IHD. Those with FPG 5.6–6.0 mmol/l exhibited an intermediate level of risk.

As with the risk of diabetes, significant heterogeneity was present within each category of FPG (Table 4). Based on data from the NHS92, those with IGT were at higher risk of IHD events irrespective of FPG category, even in those with FPG <5.6 mmol/l.

Finally, we found that the majority of

Table 2—*Risk of development of diabetes according to FPG in the Singapore Impaired Glucose Tolerance Follow-up Study*

Glucose tolerance based on FPG criteria	*n*	Percentage who developed diabetes	Odds ratio (95% CI)
Analyses with subjects pooled within categories of FPG if FPG 5.6–6.9 mmol/l			
FPG < 5.6 mmol/l			
NGT*	200	2.4	1
IGT*	89	19.1	9.7 (3.5–26.3)
FPG 5.6–6.0 mmol/l	137	22.2	12.4 (4.7–32.8)
FPG 6.1–6.9 mmol/l	43	55.2	55.1 (20.4–148.7)
Analyses with study subjects stratified by both FPG and 2-h PG criteria			
FPG < 5.6 mmol/l			
NGT*	200	2.4	1
IGT*	89	19.1	9.7 (3.5–26.8)
FPG 5.6–6.0 mmol/l			
NGT*	66	9.6	4.4 (1.3–14.6)
IGT*	71	31.1	19.8 (7.4–53.5)
FPG 6.1–6.9 mmol/l			
NGT*	10	28.6	17.6 (4.0–77)
IGT*	33	59.8	66.2 (24.1–182.1)

Odds ratios of future diabetes were estimated using logistic regression analysis and were adjusted for age, sex, and ethnic group. Data are presented for glucose tolerance determined by FPG with and without stratification by 2-h PG following a 75-g OGTT. *Glucose tolerance based on 2-h PG criteria.

subjects in the NHS98, who had FPG 5.6–6.0 mmol/l, also exhibited other features of the metabolic syndrome (Table 5). At least one feature of the metabolic syndrome, other than glucose intolerance, was observed in 63.5% of subjects with FPG 5.6–6.0 mmol/l. Central obesity, high plasma triglycerides, and high blood pressure were the most common abnormalities detected.

CONCLUSIONS — In the follow-up report on the diagnosis of diabetes, the American Diabetes Association cites epidemiologic data suggesting that, using the 1997 definitions, IFG did not connote the same degree of risk of diabetes or CVD as IGT. These differences in predictive abilities represented an area of concern that the expert committee felt could be addressed by lowering the cut point for the diagnosis of IFG from 6.1 to 5.6 mmol/l. In line with these recommendations, our study has found that, statistically speaking, an FPG of 5.6 mmol/l represents an appropriate cutoff for the Singapore population (supplemental Fig. 1 [online appendix]). First, adopting this cutoff would enhance the identification of those with IGT (Table 1). The identification of individuals with IGT is desirable now that several randomized controlled trials have shown significant reduction in the risk of diabetes following interventions using lifestyle measures or drug therapy in those with IGT (21–24). Second, in line with the findings in the U.S. (6) and in Mauritius (25), lowering the FPG criterion to 5.6 mmol/l identified a greater number of individuals at risk for future diabetes (Table 2). In further support of the recommendations of the American Diabetes Association to lower the FPG criterion for diagnosis IFG from 6.1 to 5.6 mmol/l, we have shown that an FPG of 5.6–6.0 mmol/l is associated with increased risk of diabetes (Table 2) and IHD (Table 3).

Although it is true that those with FPG 5.6–6.0 mmol/l were at increased risk of diabetes and IHD, our data suggest that this increased risk resided primarily within the subgroup that also had IGT (Tables 2 and 4). The odds ratio for diabetes in those with FPG 5.6–6.0 mmol/l and 2-h PG <7.8 mmol/l was lower than that in those with IGT, irrespective of FPG category. The situation was similar in relation to IHD. As in previous studies (2,3), those with FPG 5.6–6.0 were at increased risk of IHD (Table 3). However, within this category, no increased risk was detected in those with 2-h PG <7.8 mmol/l, whereas those with IGT were at substantially increased risk of IHD (Table 4). In fact, IGT was associated with a greater risk of both diabetes and IHD, even when the FPG was <5.6 mmol/l. Thus, lowering the FPG criteria to 5.6 mmol/l did not make IFG equivalent to IGT as a predictor of future disease.

In addition to the different predictive values for diabetes and CVD, IFG and IGT also differ in terms of the individuals identified. Lowering the diagnostic crite-

Table 3—*Age and risk of IHD events among nondiabetic subjects of the Singapore CVD Cohort Study according to FPG*

Category of fasting glucose	Age (years)	*n*		Person-years	Hazard ratio (95% CI)	
		Total	Cases		Adjusted for ethnic group and sex	Adjusted for age, ethnic group, and sex
<5.6 mmol/l	35.9 ± 12.3	4,160	94	39,052.6	1	1
5.6–6.0 mmol/l	42.3 ± 12.4*	708	23	5,568.1	1.92 (1.20–3.01)	1.13 (0.70–1.81)
6.1–6.9 mmol/l	45.3 ± 12.9†	223	11	1,736.2	3.12 (1.65–5.90)	1.51 (0.79–2.90)

Data are means ± SD, unless noted otherwise. Comparison of age between categories was carried out by ANOVA. Pair-wise comparisons were carried out using the least significant difference method. Hazard ratios are estimated using the stratified Cox proportional hazards model (stratified by the study from which the data were derived) and adjusted for age, sex, and ethnic group. *$P < 0.005$ compared with those with FPG < 5.6 mmol/l; †P value = 0.002 compared with those with FPG = 5.6–6.0 mmol/l.

Table 4—*Risk of IHD events among nondiabetic subjects in the NHS92 according to glucose tolerance stratified by both FPG and 2-h PG after a 75-g OGTT*

Glucose tolerance based on FPG criteria	*n*		Person-years	Hazard ratio (95% CI)
	Total	Cases		
Analyses with subjects pooled within categories of FPG if FPG 5.6–6.9 mmol/l				
FPG <5.6 mmol/l				
NGT*	—	14	13,633.7	1
IGT*	—	8	1,226.9	3.00 (1.22–7.38)
FPG 5.6–6.0 mmol/l	—	12	3,463.6	1.42 (0.65–3.14)
FPG 6.1–6.9 mmol/l	—	6	1,096.1	1.60 (0.60–3.14)
Analyses with study subjects stratified by both FPG and 2-h PG criteria				
FPG <5.6 mmol/l				
NGT*	2,137	14	13,633.7	1
IGT*	289	8	1,226.9	3.07 (1.26–7.56)
FPG 5.6–6.0 mmol/l				
NGT*	388	4	2,458.9	0.69 (0.22–2.12)
IGT*	154	8	1,004.4	3.08 (1.26–7.52)
FPG 6.1–6.9 mmol/l				
NGT*	85	2	540.5	1.09 (0.24–4.90)
IGT*	86	4	555.6	2.09 (0.67–6.49)

Hazard ratios were estimated using Cox proportional hazards models and adjusted for age, sex, and ethnic group. *Glucose tolerance based on 2-h PG criteria.

rion does not make IFG any more equivalent in this regard either. Although the new criteria doubled the number of those with IGT detected (Table 1), it identified an even larger group of individuals with 2-h PG <7.8 mmol/l. These latter individuals are at relatively low risk of diabetes and IHD and, among those with FPG 5.6–6.0 mmol/l, outnumber those at high risk (IGT) by a factor of four to one (Table 1). For this reason, the lowering of the criterion of IFG lowers the CVD risk associated with this category of glucose intolerance. It has also been suggested that lowering the IFG criterion brings a larger proportion of younger individuals into the IFG population, thereby lowering the predictive nature of IFG for development of IHD. Our data support that hypothesis. Subjects with FPG 5.6–6.0 mmol/l were younger than those with FPG 6.1–6.9 (Table 3).

We need to bear in mind that a cut point that is statistically "ideal" may not be optimal from a public health point of view. The assessment of the public health benefits of lowering the criterion for FPG needs to take into account the benefits, or harm, that may accrue from such a change. Unfortunately, the data to make such an assessment are not currently available. All subjects in existing randomized controlled trials for diabetes prevention had IGT (21–24). Thus, there is currently no evidence to suggest that effective prevention of diabetes is available for those with FPG 5.6–6.9 mmol/l and normal 2-h PG. These represent the majority of those diagnosed with IFG under the new definition. It has also been suggested that many of the individuals with FPG 5.6–6.0 mmol/l may already have a reason to modify their lifestyle due to the presence of other CVD risk factors (8). In our study, 63.5% of those with FPG between 5.6 and 6.0 mmol/l exhibited at least one other feature of the metabolic syndrome (Table 5), which would have been sufficient reason for therapeutic lifestyle modification. There is no evidence that adding the label of IFG to the existing risk factors will enhance their adherence to a healthy lifestyle.

Even if it could be shown that intensive lifestyle modification prevented diabetes in those with FPG 5.6–6.0 mmol/l as effectively as it does in those with IGT, the cost of intensive lifestyle modification for such a large proportion of the population may be prohibitive for less economically developed countries. To illustrate this, we have utilized data from this study and from the lifestyle modification arm of the Diabetes Prevention Program (23). In the latter study, the relative risk reduction for diabetes over the 3 years of the study among those with IGT was 58% compared with the placebo group.

In the Singapore IGT Follow-up Study, 35.1% of those with IGT developed diabetes over 8 years (11). If we assume a constant rate of conversion over the 8 years, this amounts to a cumulative incidence of 13.2% over 3 years (the duration of intervention in the Diabetes Prevention Program). With a relative risk reduction of 58%, the absolute risk reduction would be 7.66% and number needed to treat (NNT) to prevent one case of diabetes would be 13. We compared these estimates with those for subjects with FPG 5.6–6.0 mmol/l. Within this range of FPG, 3.6% of those with normal 2-h PG and 11.7% of those with IGT would develop diabetes over 3 years (Table 2). The absolute risk reductions associated with lifestyle modification, assuming similar efficacy as in those with IGT, would be 2.1% (NNT = 48) and 6.8% (NNT = 15), respectively.

The number of individuals aged 20–69 years (a similar age distribution of the NHS98 study population) and residing in Singapore was 2,202,647 in the year 2000 (data from the Singapore Department of Statistics, www.singstat.gov.sg, accessed 15 March 2004). From the NHS98, we estimated that 13.3% of

Table 5—*Prevalence of other features of the metabolic syndrome among those with fasting glucose 5.6–6.0 mmol/l: the NHS98*

Feature of the metabolic syndrome	Prevalence (%)
Triglycerides >1.7 mmol/l	32.3
HDL, cholesterol <1.0 mmol/l in men or <1.3 mmol/l in women	15.4
Waist >90 cm in men or >80 cm in women	32.2
Hypertension or blood pressure ≥130/85 mmHg	36.0
No. of other features of the metabolic syndrome	
0	36.5
1	27.3
2	22.7
3	10.5
4	2.9

the population would have IGT. This amounts to 292,952 individuals. Treatment of these individuals with an intensive lifestyle modification program akin to that used in the Diabetes Prevention Program would prevent 22,534 cases of diabetes over 3 years. In contrast, we would expect that 22.8% (502,204 individuals) of the population aged 20–69 years would have FPG 5.6–6.0 mmol/l. Of these, 80% would have NGT (401,763 individuals), and treatment of these individuals would prevent 8,370 cases of diabetes over 3 years. The other 20% would have IGT (100,441 individuals), and their treatment would prevent 6,696 cases of diabetes over 3 years. Overall, intensive lifestyle modification among those with FPG 5.6–6.0 mmol/l would prevent 15,066 cases of diabetes over 3 years for 502,204 patients treated. It can be seen that the treatment of those with IGT would result in a larger number of cases of diabetes prevented for a substantially smaller number of cases treated.

In addition to the public health implications, concerns have also been expressed with regard to the impact of these changes at an individual level. The psychological impact of diagnosing a subject with IFG when he or she was previously considered normal is not known. As pointed out by Davidson et al. (7), there is the added potential that insurance companies could raise life insurance premiums or medical insurance premiums for these individuals. To have such a large proportion of the population diagnosed as having abnormal glucose tolerance would also put considerable strain on public health systems.

Our study has several limitations. First, glucose tolerance was determined on only one occasion. This could lead to misclassification of glucose tolerance. We believe that such misclassification would affect all categories of glucose tolerance equally. Such nondifferential misclassification could reduce the absolute measures of risk associated with the various categories of glucose tolerance. However, it should not alter the conclusions that we have drawn. Second, the ascertainment of IHD events in the Singapore CVD cohort was carried out using data from several registries, which could be unreliable. We are currently unable to provide direct evidence as to the reliability of the registry data. However, we can say that data from the myocardial infarction registry were derived using the World Health Organization Monitoring Trends and Determinants of CVD (MONICA) protocol. The methodology is therefore well established. Furthermore, submissions to the Central Claims Processing System and its predecessor, the Hospital Inpatient Discharge System, are regulatory requirements for all hospitals in Singapore, and most, if not all, hospital admissions are represented. The discharge diagnoses are completed by doctors directly involved in the management of the patients admitted to the hospital, and we believe that they are reasonably accurate. We concede that patients who are overseas at the time of their IHD event would be missed. However, our own experience as clinicians suggests that these would be small in number. Third, the Singapore IGT Follow-up Study was not a representative sample of the Singapore population. Specifically, those with NGT in the study were older than those with NGT in the general population due to the matching process. The mean age of those with FPG 5.6–6.9 selected as control subjects in the Singapore IGT Follow-up Study was 47 years, whereas the mean age for those with the same level of FPG was 42 years in the entire NHS92 (data not shown). Given that the risk of diabetes increases with age, it is likely that our study overestimates the risk of diabetes associated with IFG. Therefore, the odds ratio for future diabetes in those with IFG is likely to be even lower than that found in our study, supporting our conclusions that IFG is associated with a lower risk of diabetes than IGT.

The greater reproducibility of the FPG compared with the 2-h PG is one of the reasons the FPG has been favored for the diagnosis of glucose intolerance. However, the presence of IGT connoted a greater risk of diabetes and IHD than IFG. Unfortunately, lowering the criterion for IFG from 6.1 to 5.6 mmol/l did not seem to improve the predictive value of IFG in our population. Based on the findings in this study, one could argue that our focus should be to identify individuals with IGT or a group with a risk of diabetes or IHD similar to those with IGT, whose FPG levels are $<$6.1 mmol/l. This may prove a more efficient strategy for identifying those at risk of diabetes or IHD than lowering the diagnostic criteria for IFG to encompass a much larger number of individuals at lower risk. We are not suggesting that the OGTT is required to identify those at risk of diabetes or CVD. Other means of assessing risk may be available. For example, models incorporating variables such as sex, obesity, age, ethnic group, FPG, lipids, blood pressure, and family history have been shown to outperform the 2-h PG in the identification of those at risk of diabetes (26) and CVD (27). Alternatively, we could consider other measures of glycemia (such as HbA_{1c}) or markers of systemic inflammation.

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