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Incidence Rates and Predictors of Diabetes in Those with Prediabetes: The Strong Heart Study

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Abstract

Background—The association between prediabetes as currently defined and incident diabetes in populations with widespread obesity, insulin resistance syndrome, and diabetes is not well defined. In this article, diabetes risk factors and incidence rates in American Indians (AI) with prediabetes are examined.

Methods—1677 AI who were nondiabetic at baseline were examined during a median 7.8-year follow up as part of the Strong Heart Study (SHS). Risk factors for incident diabetes were measured. Prediabetes was defined according to American Diabetes Association 2003 criteria as having impaired glucose tolerance (IGT) (2-h plasma glucose [2-h PG] ≥140 mg/dL but <200 mg/dL) and/or impaired fasting glucose (IFG) (fasting plasma glucose [FPG] ≥100 mg/dL but <126 mg/dL).

Results—Prediabetes was identified by FPG alone in 87.5%. Diabetes incidence in those with baseline prediabetes was 66.1/1,000 person-years, with a hazard ratio of 2.35 (95% conference interval: 1.84-3.01), compared with participants with normal glucose tolerance (NGT) at baseline. Elevated A1c, 2-h PG, and fasting insulin (FI); albuminuria; and obesity were significantly associated with conversion from prediabetes to diabetes. Younger age, elevated FI (or BMI in models without FI), and less physical activity were significantly associated with conversion from NGT.

Conclusions—Prediabetes is an independent predictor of conversion to type 2 diabetes in AI, and most can be identified through a fasting glucose measure. Measures of obesity, A1c, FPG, 2-h PG, FI, albuminuria, and insulin resistance help predict this conversion. Obesity is a modifiable risk factor. Strategies to reduce obesity should be emphasized in individuals with prediabetes.

Keywords

prediabetes; type 2 diabetes; risk factors

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Introduction

Prediabetes is an increasingly common condition, in which blood glucose concentrations are higher than normal but not in the diabetic range. This condition is defined as having either impaired glucose tolerance (IGT) with 2-h plasma glucose (2-h PG) ≥140 mg/dL (7.8 mmol/l) but <200 mg/dl (11.1 mmol/l) and/or impaired fasting glucose (IFG) with fasting plasma glucose (FPG) ≥100 mg/dL (5.6 mmol/l) but <126 mg/dL (7.0 mmol/l) [1]. Data from the 3rd and 4th National Health and Nutrition Examination surveys (NHANES) indicate IGT and IFG prevalence as approximately 26% and 15%, respectively, among U.S. adults [2,3]. Several longitudinal studies support the hypothesis that prediabetes is a risk factor for diabetes and cardiovascular disease (CVD) [4,5,6,7,8,9], but few studies have examined rates of prediabetes and risk factors for conversion to diabetes in populations with widespread obesity and diabetes.

Obesity [10], insulin resistance syndrome [11], and type 2 diabetes [12] are prevalent among American Indians (AI); thus evaluation of prediabetes and risk factors for conversion to diabetes would be useful to health providers caring for this population. An earlier analysis reported that AI with IGT had a higher risk of developing diabetes than individuals with normal glucose tolerance (NGT) [13]. However, the association of IFG and prediabetes with incident diabetes has not been explored in AI. This population has been valuable as a model for other populations with high prevalence of obesity, insulin resistance, and type 2 diabetes. In this article, diabetes incidence rates in individuals with prediabetes will be reported and predictors of conversion to diabetes among those with prediabetes compared to those with NGT at baseline will be examined.

Materials and Methods

Study Population

The Strong Heart Study (SHS) is a population-based longitudinal study of CVD and its risk factors among AI in 13 tribes and communities in Oklahoma, Arizona, and North and South Dakota. A total of 4,549 AI, ages 45-74 years, was examined in the SHS baseline examination (1989-1991). The SHS design and selection criteria have been described [14,15,16,17]. Of the 4,549 participants, those who had undetermined diabetes status at baseline (n=211), had no follow-up exam (n=679, 413 [60.8% of whom died before their first follow-up examination]), had diabetes at baseline (n=2297), had received a kidney transplant but reported no diabetes (n=1), and those who reported receiving dialysis therapy but no diabetes (n=2) were excluded, leaving 1677 participants (716 men and 961 women) for this analysis. Median follow up was 7.8 years (range 2.5-10.1 years).

Examination

The baseline examination consisted of a personal interview and a physical examination, including collection of fasting blood samples for laboratory measures and a 75-g oral glucose tolerance test (OGTT). Two follow-up examinations were conducted, one during 1993-1995 and the other during 1996-1999, with response rates of 89% and 88%, respectively.

Clinical and laboratory measures for body mass index (BMI), waist circumference (WC), waist-to-hip ratio, fasting plasma glucose (FPG), 2-h plasma glucose (2-h PG), A1c, fasting insulin, triglycerides, low-density lipoprotein-cholesterol (LDL-C), high density lipoprotein-cholesterol (HDL-C), blood pressure, urine albumin, and urine creatinine have been described [14,15,16,18]. Data on smoking status, alcohol consumption, and parental history of diabetes were collected during the personal interview. Physical activity was assessed at baseline via a physical activity questionnaire designed for AI [19]. Hypertension was

defined as self-report of using antihypertension medication, systolic blood pressure ≥140mmHg, or diastolic blood pressure ≥90mmHg. Microalbuminuria and macroalbuminuria were defined as urinary abuminuria/creatinine ratios of 30-299 mg/g and ≥300 mg/g, respectively. Because few participants had macroalbuminuria, micro- and macroalbuminuria were combined as albuminuria. Overweight and obesity were defined as BMI of 25-30 kg/m^2 and ≥30 kg/ m^2, respectively. Insulin resistance was estimated by homeostasis model calculation (HOMA): [fasting glucose (mmol/l) × fasting insulin (μU/ml)]/22.5.

Diabetes Assessment

ADA diagnostic criteria (2003) were used to classify participants by category of glucose intolerance. Diabetes, NGT, IFG, isolated IFG, IGT, isolated IGT, and prediabetes were defined as follows:

- **Diabetes** – FPG ≥ 126 mg/dL, 2-h PG ≥ 200 mg/dL, or receiving insulin and/or hypoglycemic agent treatment, or history of diabetes indicated via questionnaire.
- **NGT** – FPG < 100 mg/dL, 2-h PG < 140 mg/dL, and no diagnosis of diabetes.
- **IFG** – FPG ≥ 100 mg/dL but < 126 mg/dL and no diagnosis of diabetes.
- **Isolated IFG** – IFG without IGT.
- **IGT** – 2-h PG ≥ 140 mg/dL but < 200 mg/dL and no diagnosis of diabetes.
- **Isolated IGT** – IGT without IFG.
- **Prediabetes** – IFG and/or IGT.

Incident diabetes was defined as new diabetes cases identified between the baseline and third examinations. Because all participants were ≥45 years old at baseline, all incident diabetes was assumed to be type 2.

Statistical Analysis

The baseline characteristics are presented as means and standard deviations for continuous variables with normal distribution, as median and interquartile range for continuous variables with highly skewed distribution, and as percentages for categorical variables, by gender and glucose tolerance categories. T tests, Wilcoxon rank-sum tests, and chi-square tests were used to examine differences in means, medians, and proportions, respectively.

Diabetes incidence rates during follow up were determined by gender for each category of baseline glucose tolerance (i.e., NGT, IFG, IGT, and prediabetes). For those who developed diabetes, time of onset was assumed to be the midpoint between the last examination without diabetes and the examination when diabetes was diagnosed. For those who did not develop diabetes, diabetes-free time was defined as the time between the baseline and final available examination. A Cox proportional hazards model was used to estimate the hazard ratio (HR) of developing diabetes for each category of glucose intolerance, compared with NGT. Univariate models and multivariate models adjusted for age, BMI, WC, parental history of diabetes, physical activity, smoking status, albuminuria, and gender were tested, with the reference group consisting of the participants with NGT.

Diabetes incidence also was calculated according to category of potential risk factors, including BMI, WC, albuminuria, hypertension, A1c, HOMA-insulin resistance (IR), LDL-C, HDL-C, and level of physical activity. Cox proportional hazards models were used to assess the association between potential risk factors and incident diabetes. Linear trends were assessed using ordered categories in the Cox model. We tested the significance of

potential interaction terms by including the product of factors in the Cox model, adjusting for other risk factors.

A natural log transformation was applied to highly skewed variables, such as fasting insulin. P values <0.05 were considered statistically significant. Data were analyzed using SAS version 9.1 (SAS Institute, Cary, NC).

Results

Baseline Characteristics

Men and women with prediabetes were significantly older; had significantly higher BMI, WC, waist-to-hip ratio, triglycerides, fasting insulin, and A1c; had lower HDL-C; and more albuminuria, hypertension, and obesity than participants with NGT (Table 1). Participants with prediabetes reported significantly less smoking than participants with NGT and were significantly more likely to be past smokers. Participants with prediabetes reported physical activity, parental history of diabetes, and alcohol use that were similar to participants with NGT. No significant difference was observed in LDL-C between those with prediabetes and those with NGT.

Proportion of Baseline Prediabetes as Measured by Isolated IFG, Isolated IGT, and Both IFG and IGT

Most participants with prediabetes were identified by fasting glucose (Figure 1). Only 6.5% of men and 16.7% of women had isolated IGT (12.5% for men and women combined). Among participants with IGT, some (81.2% of men and 68.5% of women) also had IFG that was identified by FPG alone (72.5% for men and women combined). Some (93.5% of men and 83.3% of women) had isolated IFG or both IFG and IGT that were identified by FPG alone (87.5% for men and women combined).

Incidence of Type 2 Diabetes

Compared to those with NGT, men and women with baseline prediabetes had a higher diabetes incidence (unadjusted HRs 2.77 and 2.88, respectively) (Table 2). Participants with both IFG and IGT at baseline had the highest diabetes incidence rate upon follow up. After adjusting for potential confounders, including age, BMI, WC, albuminuria, family history of diabetes, smoking status, and physical activity in a Cox proportional hazards model, and comparing with participants with NGT, HRs for participants with IFG, IGT, both IFG and IGT, and prediabetes were 2.10, 3.82, 4.44, and 2.11, respectively, for men and 2.46, 3.16, 3.80, and 2.41, respectively, for women.

Risk Factors for Diabetes in Individuals with Prediabetes

Diabetes incidence rates in those with baseline prediabetes were significantly higher in women and in persons with albuminuria; higher BMI, WC, A1c, and HOMA-IR; lower LDL-C; and less physical activity (Table 3). Hypertension and HDL-C were not significantly related to diabetes incidence (data not shown).

In a multivariate Cox proportional hazards model (Table 4) in men and women, combined obesity (BMI≥30), central adiposity (WC≥120cm/88cm for men/women), elevated A1c, fasting insulin, 2-h PG; and albuminuria were significant risk factors for diabetes in those with prediabetes. Age, gender, FPG, HOMA-IR, LDL-C, and physical activity were not independent risk factors after adjustment for other covariates.

Predictors differed in those with NGT. In the multivariate Cox proportional hazards model younger age, elevated fasting insulin, and physical inactivity were independent predictors.

When fasting insulin was removed from the model, BMI was significantly associated with conversion from NGT to diabetes.

No significant interaction was observed between the risk factors for conversion to diabetes in those with prediabetes. Nor was there a significant interaction between the risk factors for conversion to diabetes in those with NGT.

Discussion

This article provides the first assessment of diabetes incidence rates among those with prediabetes as currently defined by the ADA and risk factors for conversion from prediabetes to diabetes among AI, a population that serves as a model for other populations with high rates of obesity and diabetes. Of those with prediabetes, 87.5% were identified by FPG alone and 36.3% developed diabetes within 8 years. Participants with prediabetes were more than twice as likely to develop diabetes as those with baseline NGT in adjusted models. Individuals with prediabetes and those with IFG had a similar risk for developing diabetes; this risk, however, was lower than for those with IGT or with both IGT and IFG. BMI; WC; elevated A1c, 2-h PG, and fasting insulin; and presence of albuminuria were independent predictors of diabetes incidence in individuals with baseline prediabetes. For those with NGT at baseline, younger age, elevated fasting insulin (or BMI in models without fasting insulin), and less physical activity were significant predictors for incident diabetes.

Diabetes Incidence in Individuals with Prediabetes

A number of studies have reported diabetes incidence among those with prediabetes; however, there are differences in the definitions used for prediabetes and diabetes. Incidence rates for diabetes in individuals with prediabetes observed in this report are comparable with those reported for Pima Indians [8] and South-African Indians [20], but higher than those reported for many other populations [21,22,23,24,25].

Our findings support previous studies from other populations showing that individuals with both IFG and IGT have the highest risk of conversion to diabetes, indicating that elevated fasting glucose and 2-h PG are both strongly related to development of diabetes [7,20,21,22,23,24]. Because fasting glucose concentrations reflect hepatic glucose output and thus are crude reflectors of insulin resistance, while 2-h PG concentrations also reflect insulin secretion capacity, the higher predictive value of IGT may reflect a more advanced stage in the progression to diabetes. However, fasting glucose alone identified most of the individuals with prediabetes, thus confirming glucose tolerance testing would not be cost-effective.

Predictors of Diabetes in Individuals with Prediabetes

Consistent with findings in other studies, diabetes incidence among those with prediabetes as well as most other categories of glucose tolerance, including NGT, was higher in women than in men [13,24]. Explanations as to why women are more likely to develop diabetes include higher adiposity and less physical activity. Our findings regarding the prognostic significance of overall obesity, central adiposity, elevated fasting insulin and 2-h PG, and albuminuria in incident diabetes confirm early reports that these factors are predictors of diabetes in individuals with prediabetes [20,22,26,27,28,29,30,31]. Our data indicate that in AI with prediabetes, both measurements of BMI and WC are useful in estimating risk of incident diabetes.

In our study, we observed that the association between FPG and incident diabetes was attenuated and no longer significant after adjustment for A1c and other covariates. A1c measures the chronic glycemic level by capturing the average glucose values over the

previous 2-3 months. Compared with FPG testing, A1c testing is convenient because it does not require a fasting sample and the samples are more stable. Our data show that the risk of progression to diabetes significantly increased as A1c rose, suggesting that A1c measurement is a good tool for predicting diabetes risk in those with prediabetes, as well as for monitoring long-term glycemic control and predicting future diabetes complications in those with diabetes.

The inverse association between physical activity and incident diabetes was attenuated after adjustment for BMI and other obesity-related covariates. This finding is consistent with an early SHS report in nondiabetic individuals and a study of Niue Island residents with IGT [32]. A similar association was observed between LDL-C and incident diabetes. Several studies also found that higher triglycerides and blood pressure at baseline in those with prediabetes were associated with progression to diabetes [33,34,35]. However, these variables were not independent predictors in the current analyses. Because these variables are highly correlated with obesity, the effects of these risk factors may have been represented by the measure of obesity. The San Luis Valley Diabetes Study reported that the higher dietary fat intake at baseline in those with IGT was a predictor for incident diabetes, after controlling for obesity and markers of glucose metabolism [21,36]. Dietary fat intake at baseline, however, was not measured in the SHS.

Risk factors for diabetes in those with prediabetes differed from those with NGT. In NGT, fasting insulin (or BMI) and less physical activity were independent predictors. These may both reflect the fact that insulin resistance is a major determinant of type 2 diabetes and may be present for several years before the appearance of hyperglycemia [37]. During this period, pancreatic β-cells secrete more insulin in response to the increasing insulin resistance and thus normoglycemia is maintained. In contrast, once glycemia begins to deteriorate (i.e., prediabetes), other factors such as the level of glycemia and the resultant albuminuria emerge as predictors. Age had a weak negative association with risk of incident diabetes in those with NGT at baseline. This finding may be due to the survival effect in older people and higher prevalence of obesity in younger people [10]. The lack of statistical significance of BMI in the model including fasting insulin probably reflects the strong association between obesity and fasting insulin. However, our findings suggest that in persons with NGT, obesity is the most valuable clinically available measure of future diabetes risk.

Strengths and Limitations

Strengths of this study include the large, well-characterized, population-based cohort, long follow up, and use of the ADA 2003 definitions of prediabetes. This research was limited by the absence of data in adults <age 45. The single ethnic group studied further limits this research. However, our results may be applicable to other ethnic groups with widespread obesity, insulin resistance syndrome, and type 2 diabetes.

Conclusions

Our analyses in a population with high rates of obesity and diabetes confirm that prediabetes is an independent predictor of diabetes. Only 12.5% of individuals with prediabetes could not be identified by FPG alone. Although determination of IGT identifies persons as having a higher risk of developing diabetes, the additional number of cases found does not seem to warrant the expense and inconvenience of glucose tolerance testing in the SHS population. Our findings suggest that in follow up of individuals with prediabetes, measures of A1c and albuminuria may help identify those at greatest risk of conversion to diabetes. Lifestyle intervention, including increased physical activity and weight loss, will address these abnormalities.

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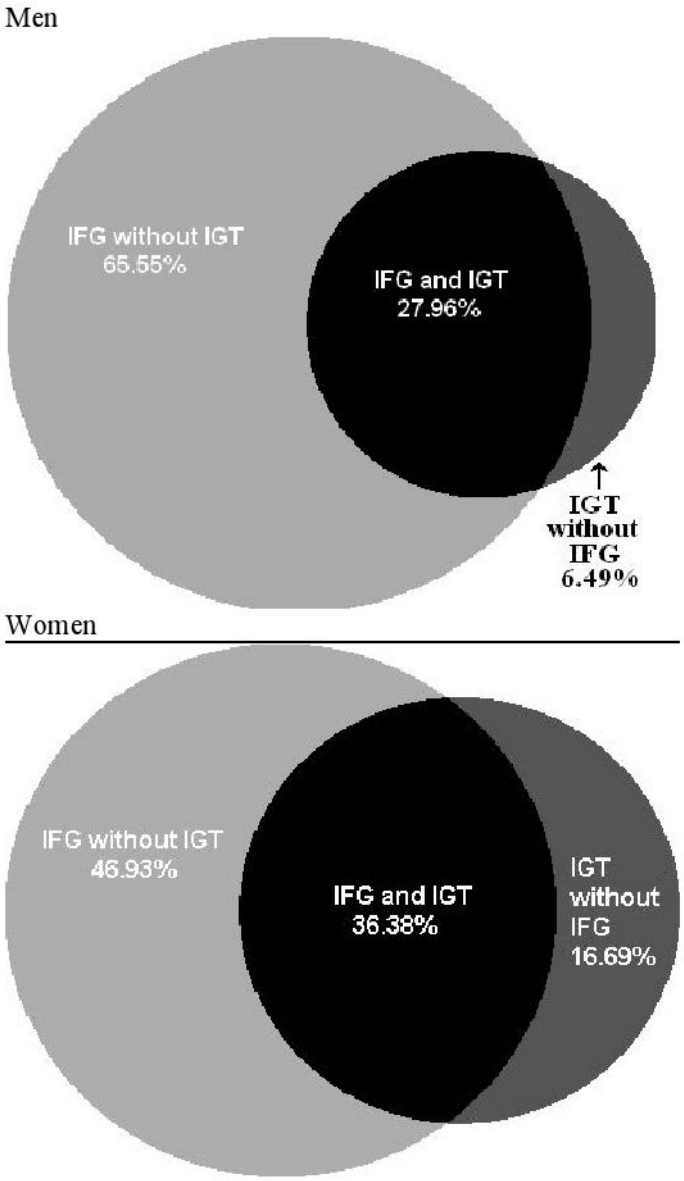

Figure 1. Venn diagram with true proportion of Isolated IFG, Isolated IGT, and Both IFG and IGT among Men and Women with Prediabetes

IFG = impaired fasting glucose; IGT = impaired glucose tolerance.

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Table 1

Baseline Characteristics by Gender and Glucose Tolerance

	Men			Women		
	NGT	Prediabetes*	P †	NGT	Prediabetes	P †
N	269	447	---	326	635	---
Age (years)	53.9±7.40	55.6±7.94	.0051	54.3±7.47	55.5±7.86	.0018
BMI (kg/m^2)	27.0±4.23	30.1±4.93	<.0001	27.9±5.88	31.5±6.27	<.0001
Waist circumference (cm)	96.5±10.49	103.2±11.95	<.0001	95.8±15.23	105.3±14.52	<.0001
Waist-to-hip ratio	0.95±0.06	0.97±0.06	<.0001	0.90±0.07	0.93±0.06	<.0001
Fasting glucose (mg/dL)	92.1±7.14	107.9±7.86	<.0001	91.8±5.76	106.4±8.79	<.0001
2-h glucose (mg/dL)	95.9±25.01	124.0±33.53	<.0001	102.1±21.14	139.0±30.60	<.0001
A1c (%)	4.9±0.60	5.2±0.55	<.0001	4.9±0.49	5.2±0.57	<.0001
Fasting insulin (uU/mL)	8.4(5.2-13.1)	13.8(8.0-21.2)	<.0001	9.3(5.9-13.1)	15.0(9.9-21.7)	<.0001
Triglycerides (mg/dL)	92.0(66.0-126.0)	117.0(83.0-166.0)	<.0001	97.0(67.0-138.0)	114.0(80.0-154.0)	<.0001
LDL-C (mg/dL)	123.3±33.55	123.9±32.43	0.7938	120.1±33.12	119.0±32.74	0.6284
HDL-C (mg/dL)	46.6±15.45	43.0±11.51	0.0012	53.7±15.28	49.5±12.88	<.0001
Albuminuria (%)	6.02	10.34	0.0481	7.38	11.67	0.0380
Current smoking (%)	50.56	38.48	0.0018	48.16	30.39	<.0001
Past smoking (%)	30.11	43.40	0.0005	19.02	30.71	0.0001
Current alcohol use (%)	59.85	55.73	0.3102	42.94	39.37	0.2984
Past alcohol use (%)	36.80	40.45	0.3433	39.88	39.37	0.8893
Overweight (%)	47.01	40.27	0.0859	34.36	32.91	0.6652
Obese (%)	20.90	47.65	<.0001	30.67	55.75	<.0001
Parental history of diabetes (%)	33.09	36.91	0.3332	37.42	40.94	0.2973
Physical activity (MET-hours/week)	86.4(29.3-153.2)	81.3(22.6-171.6)	0.8958	59.2(10.8-127.5)	41.8(10.6-111.4)	0.0946
Hypertension (%)	26.39	34.23	0.0306	17.48	32.60	<.0001

Abbreviations: NGT: normal glucose tolerance; A1c = HbA1c; BMI = body mass index; MET = metabolic equivalent.

Data are means ± STD or median (IQR) or %.

*Impaired glucose tolerance (IGT) with 2-h plasma glucose (2-h PG) of ≥140 mg/dL (7.8 mmol/l) but <200 mg/dL (11.1 mmol/l) and/or impaired fasting glucose (IFG) with fasting plasma glucose (FPG) of ≥100 mg/dL (5.6 mmol/l) but <126 mg/dL (7.0 mmol/l).

† T tests were used for continuous variables with normal distribution, Wilcoxon rank-sum tests were used for continuous variable that were highly skewed, and chi-square tests were used for categorical variables.

Table 2

Incidence Rate of Type 2 Diabetes (per 1000 person-years) During 8-Year Follow Up, by Gender and Baseline Glucose Tolerance

	Using ADA 2003 criteria				
	NGT	**IFG**	**IGT**	**IFG and IGT**	**Prediabetes**
Men					
N	269	418	154	125	447
No. with type 2 diabetes	34	137	75	66	146
%	12.64	32.78	48.70	52.80	32.66
Person-Years	1613.3	2373.9	764.8	605.3	2533.4
Incidence rate‡	21.1	57.7	98.1	109.0	57.6
Univariate HR†	1	2.78(1.91-4.04)	4.72(3.15-7.09)	5.28(3.49-7.99)	2.77(1.91-4.03)
Multivariate HR*	1	2.10(1.40-3.15)	3.82(2.41-6.04)	4.44(2.75-7.15)	2.11(1.41-3.16)
Women					
N	326	529	337	231	635
No. with type 2 diabetes	50	208	158	119	247
%	15.34	39.32	46.88	51.52	38.90
Person-Years	1969.2	2834.9	1666.5	1091.5	3409.9
Incidence rate	25.4	73.4	94.8	109.0	72.4
Univariate HR	1	2.92(2.15-3.98)	3.74(2.72-5.14)	4.30(3.09-5.99)	2.88(2.13-3.91)
Multivariate HR*	1	2.46(1.78-3.39)	3.16(2.26-4.43)	3.80(2.66-5.42)	2.41(1.76-3.30)
Both sexes					
N	595	947	491	356	1082
No. with type 2 diabetes	84	345	233	185	393
%	14.12	36.43	47.45	51.97	36.32
Person-Years	3582.5	5208.8	2431.3	1696.7	5943.4
Incidence rate	23.4	66.2	95.8	109.0	66.1
Univariate HR	1	2.86(2.25-3.63)	4.11(3.20-5.27)	4.68(3.62-6.07)	2.85(2.25-3.61)
Multivariate HR*	1	2.38(1.85-3.05)	3.47(2.64-4.55)	4.06(3.05-5.40)	2.35(1.84-3.01)

Abbreviations: IFG = impaired fasting glucose; IGT = impaired glucose tolerance; prediabetes = IFG and/or IGT; NGT = normal glucose tolerance.

[*] Multivariate model: adjusted for age, body mass index (BMI), waist circumference, albuminuria (yes/no), smoking (current, past and never), family history of diabetes (yes/no), and quartiles of physical activity; additionally adjusted for gender for both sexes.

[†] Hazard ratio (95% confidence limits).

[‡] Incidence rate (per 1000 person-years).

Table 3

Diabetes Incidence (per 1000 person-year) in Persons with Pre-Diabetes at Baseline, by Categories of Risk Factors

	N	No. with type 2 diabetes	%	Incidence	Hazard ratio* (95% CI)
Gender					0.0246£
Men	447	146	32.7	57.629	1
Women	635	247	38.9	72.435	1.26(1.03-1.55)
Albuminuria					0.0008£
Absent	959	335	34.9	62.363	1
Present	120	56	46.7	100.964	1.63(1.23-2.18)
BMI, kg/m^2					<.0001£
<25	126	23	18.3	30.537	1
[25,30)	389	103	26.5	45.394	1.50(0.96-2.36)
≥30	567	267	47.1	91.402	2.97(1.94-4.55)
Waist circumference, cm					<.0001£
<102,88(m,w)	258	46	17.8	29.343	1
≥102,88(m,w)	818	344	42.1	79.151	2.87(2.07-3.98)
HOMA-IR†					<.0001£
[0.3-2.8)	360	69	19.2	31.688	1
[2.8-5.0)	361	135	37.4	66.739	2.06(1.54-2.75)
[5.0,54.2)	360	188	52.2	108.323	3.39(2.57-4.47)
LDL-C, mmol/L					0.0177£
<100	285	112	39.3	73.250	1
[100,130)	364	150	41.2	76.711	1.06(0.83-1.36)
≥130	407	122	30.0	52.856	0.75(0.58-0.96)
A1c, %					<.0001£
<5	335	87	26.0	45.708	1
[5, 5.5)	360	132	36.7	65.392	1.48(1.13-1.94)
[5.5, 6.5)	309	144	46.6	89.950	2.05(1.57-2.68)
≥6.5	9	6	66.7	208.357	5.10(2.22-11.70)
Physical activity, METS/wk ‡					0.0327£

	N	No. with type 2 diabetes	%	Incidence	Hazard ratio* (95% CI)
[0, 9.5]	208	91	43.8	86.153	1
[9.6, 33.2]	208	72	34.6	61.579	0.72(0.53-0.98)
[33.3, 64.6]	209	72	34.4	64.493	0.75(0.55-1.02)
[84.7, 152]	208	88	42.3	80.103	0.93(0.69-1.24)
[152.4, 522.7]	208	62	29.8	49.541	0.58(0.42-0.81)

Abbreviations: BMI = body mass indes; HDL-C = high-density lipoprotein cholesterol; HOMA-IR= homeostasis model calculation insulin resistance; LDL-C = low-density lipoprotein cholesterol; METS = metabolic equivalents.

*Adjusted for age and gender;

†Tertiles of HOMA-IR;

‡Quintiles of physical activity;

£p for linear trend

Table 4

Significant Predictors of Incident Type 2 Diabetes in Those With Baseline Prediabetes and those with NGT

Variable	HR(95% CI)	P*
In those with prediabetes		
Age, yrs	0.99(0.979-1.006)	0.2476
Gender, women vs. men	0.92(0.730-1.161)	0.4845
Obesity, BMI≥30/BMI<30	1.31(1.000-1.708)	0.0502
WC, ≥120, 88cm/<120, 88 cm (men, women)	1.54(1.038-2.269)	0.0317
A1c, %	1.26(1.038-1.539)	0.0197
2h PG, mg/dL	1.01(1.007-1.015)	<.0001
Ln(fasting insulin), μU/ml	1.67(1.386-2.014)	<.0001
Albuminuria (yes/no)	1.46(1.084-1.977)	0.0129
In those with NGT		
Age, yrs	0.96(0.925-0.990)	0.0114
Gender, women vs. men	1.28(0.808-2.024)	0.2932
Ln(fasting insulin), μU/ml	2.12(1.527-2.947)	<.0001
Physical activity		
Quantile 1	0.67(0.355-1.255)	0.2097
Quantile 2	0.43(0.206-0.894)	0.0238
Quantile 3	0.23(0.093-0.572)	0.0016
Quantile 4	0.94(0.513-1.720)	0.8395
BMI (instead ln(insulin))	1.06(1.026-1.103)	0.0009

Abbreviations: BMI = body mass index; Ln(insulin)= natural log transformation of fasting insulin; WC=waist circumference.

*P value of multivariate Cox proportional hazards model.