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Development of a clinical risk score for incident diabetes: A 10-year prospective cohort study

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ABSTRACT

Aims/Introduction: We developed a self-assessable Korean Diabetes Risk score using the data of the Korean Genome and Epidemiology Study.

Materials and Methods: A total of 8,740 participants without diabetes at baseline were followed up biannually over a period of 10 years. We included variables that were significantly different between participants who developed diabetes mellitus and those who did not in the development cohort at baseline. We assigned a maximum score of 100 to the selected variable in each gender group. Next, the 10-year probability of incident diabetes was calculated and validated in the validation cohort. Finally, we compared the predictive power of Korean Diabetes Risk score with models including fasting plasma glucose or glycated hemoglobin and other cohort models of Atherosclerosis Risk in Communities and Korea National Health and Nutrition Examination Survey.

Results: During a median follow-up period of 9.7 years, 22.7% of the participants progressed to diabetes. The Korean Diabetes Risk score included age, living location (urban or rural area), waist circumference, hypertension, family history of diabetes and smoking history. The developed risk score yielded acceptable discrimination for incident diabetes (area under the curve 0.657) and the predictive power was improved when the model included fasting plasma glucose (area under the curve 0.690) or glycated hemoglobin (area under the curve 0.746). In addition, our model predicted incident diabetes more accurately than previous Western or Korean models.

Conclusions: This newly developed self-assessable diabetes risk score is easily applicable to predict the future risk of diabetes even without the necessity for laboratory tests. This score is useful for the Korean diabetes prevention program, because high-risk individuals can be easily screened.

INTRODUCTION

As incident type 2 diabetes is greatly affected by lifestyle, the occurrence of type 2 diabetes can be reduced by lifestyle modifications. The Diabetes Prevention Program already showed that drastic lifestyle modifications can prevent and delay diabetes as much as 58% compared with control groups[1]. However, the adherence to lifestyle modifications is generally poor when it is unsupervised[2]. Therefore, it is critical to identify high-risk individuals, and targeted healthcare services should be provided to them to effectively reduce the risk of diabetes[3].

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Risk factors for diabetes can be categorized into two groups: (i) modifiable factors, such as smoking, bodyweight, diet and exercise habits; and (ii) non-modifiable factors, such as family history, age and sex. Modifiable factors are important when personalized and targeted treatment is used to reduce the individual risk of diabetes. In contrast, non-modifiable factors, such as age and genetic susceptibility, are also important for risk assessment of individuals; however, they are not manageable. There are several prediction models for incident type 2 diabetes[4] using diverse combinations of modifiable and non-modifiable risk factors. From the layperson's perspective, it would be more practical if the risk calculation or risk scores included only non-laboratory variables that could be either modifiable

(e.g., bodyweight) or non-modifiable (e.g., age). Risk calculation, including non-laboratory data, will allow people to check the dynamic change of their risks frequently and motivate them to prevent type 2 diabetes. In fact, the prevalence of diabetes will be increasing[5], and 29.3% of participants with diabetes were not aware of their condition according to the data from the Korean National Health and Nutrition Examination Survey for 2013 to 2014[6]. Globally, the prevalence of undiagnosed diabetes was >50% of individuals with diabetes[7]. The majority of undiagnosed diabetes were in low- and middle-income countries. Therefore, we need an easy tool to detect individuals at high risk for type 2 diabetes.

It is evident from the various cohort studies that individuals in Asia, including Korea, seemed to develop diabetes with a lesser degree of obesity[8]. Regional fat distribution could be an important risk factor of type 2 diabetes from the data of Korean National Health and Nutrition Examination Surveys[9]. In that study, trunk fat, but not leg fat, was associated with an increased risk of type 2 diabetes[9]. Therefore, it would be necessary to incorporate a parameter that shows abdominal obesity (waist circumference) rather than a parameter of total fatness, such as body mass index (BMI), for developing diabetes risk score, especially in the Korean population.

The objective of the present study was to enhance the prediction of diabetes in Korean populations by: (i) deriving a clinical risk score for incident type 2 diabetes using non-laboratory variables; (ii) enhancing this risk score with fasting plasma glucose (FPG) or glycated hemoglobin (HbA1c); and (iii) compare the ability of these new risk scores to predict incident type 2 diabetes with two established risk scores. At first, we developed a clinical risk score for incident type 2 diabetes using non-laboratory variables and compared it with a model, including a simple laboratory test of FPG or HbA1c. We further compared our new clinical risk score with the Atherosclerosis Risk in Communities study, which included clinical parameters, such as age, parental history of diabetes, ethnicity, smoking history, waist circumference, height, weight, hypertension and resting heart rate, but did not include laboratory data[10]. We also compared our model with Korean Diabetes Score, which was developed using cross-sectional Korea National Health and Nutrition Examination Survey data of non-laboratory variables, which were age, family history of diabetes, hypertension, waist circumference, smoking and alcohol[11]. Previous studies already showed that obesity[12], high blood pressure[13] and smoking status[14] increased the risk of diabetes. Therefore, we evaluated these variables and incorporated them into our model.

METHODS

Participants

The detailed design of the Korean Genome and Epidemiology Study was published elsewhere[15,16]. Individuals aged 40–69 years were enrolled and follow up examination was carried out, and this cohort continued in order to evaluate non-communicable disease and its related risk factors. The baseline examination of 10,038 participants was carried out during 2001 and 2002, and participants were followed up biannually for 10 years. Cohort participants lived in the Ansung (rural) and Ansan (urban) areas. We enrolled 8,740 participants who were not diagnosed with diabetes at baseline. During the 10-year follow up, 35% of the participants were not followed up and we excluded this population. We developed the type 2 diabetes risk score using 70% of the participants (development cohort, n = 3,973), and then validated the model using the remaining 30% of the participants (validation cohort, n = 1,700). The study protocol was approved by the ethics committee of the Korean Center for Disease Control and the institutional review board of the Ajou University School of Medicine (IRB No. AJIRB-CRO-07-012). All participants provided their written informed consent.

Baseline evaluation

The clinical evaluation was carried out by trained examiners, and included anthropometric measurements, 12-h fasting laboratory tests and a questionnaire. Systolic and diastolic blood pressures (SBP and DBP, respectively) were obtained using mercury sphygmomanometers (Baumanometer-Standby; W.A. Baum Co., Inc, Copiague, NY, USA) after 10 min of rest. Hypertension was defined when the SBP was ≥140 mmHg or the DBP was ≥90 mmHg, or when antihypertensive medication was used[17]. Prehypertension was defined as an SBP of 120–139 mmHg or a DBP of 80–89 mm Hg. Height and bodyweight were measured using a digital scale to the nearest 0.1 cm or 0.1 kg, respectively. BMI was calculated as bodyweight (kg) / height^2 (m^2). Waist circumference was measured at the midline between the lowest rib margin and the highest point of the iliac crest. A family history of diabetes was defined when the participants' first-degree relatives had diabetes. The education level was categorized into three groups: (i) <6 years; (ii) 6–12 years; and (iii) >12 years, because the Korean education system consists of 6 years of elementary school, and another 6 years of middle and high school. The monthly personal income was categorized as <$1,000 (approximately 1,000,000 Korean Won), $1,000–2,000 and >$2,000. The smoking status was categorized as follows: current, former and never smoker[18]. The definition of a never smoker was an individuals who had smoked <400 cigarettes. When persons consumed alcohol more than once a month, they were defined as alcohol drinkers[19]. If the participants did not drink during the past 1 year, they were defined as a former drinker. Regular exercise was defined as physically exercising once per week or more, each time for at least 30 min.

Assessment of type 2 diabetes

We carried out a 75-g oral glucose tolerance test and checked HbA1c levels every 2 years. Incident type 2 diabetes was defined as FPG levels ≥126 mg/dL or 2-h postprandial levels ≥200 mg/dL or HbA1c levels ≥6.5% according to the clinical practice recommendations of the American Diabetes

Association[20]. When data for 2-h postprandial were missing, we diagnosed type 2 diabetes using FPG and HbA1c levels.

Predictors

We used age, SBP, DBP, bodyweight, waist circumference, FPG levels and BMI as continuous variables, and compared the baseline characteristics between participants who developed type 2 diabetes and those who did not. Then, we divided participants into age groups of <45, 45–49, 50–54, 55–59, 60–64 and 65–69 years, and waist circumference groups of <90 and ≥90 cm for men, and <85 and ≥85 cm for women[21].

Development of type 2 diabetes risk scores

First, we assessed variables at baseline that were significantly different between participants with incident type 2 diabetes and participants without type 2 diabetes. Next, we sorted variables that had similar clinical characteristics. For example, SBP, DBP and the presence of hypertension were included in the same category. Similarly, bodyweight, waist circumference, and BMI were summarized in a marker for obesity. The scores of each variable were allocated according to the beta-coefficient, and the total maximum sum of Korean Diabetes Risk (KDR) score was 100. Finally, we calculated the 10-year probability of incident diabetes associated with each score in the validation cohort.

Statistical analysis

Continuous variables are shown as the mean ± standard deviation, and categorical variables are presented as numbers and percentages. We used the Student's *t*-test and χ^2-test to compare the clinical characteristics between participants with incident type 2 diabetes (during the 10-year follow-up period) and those without type 2 diabetes at the end of the observation period. A logistic regression analysis was carried out to estimate the odds ratio (OR) and 95% confidence interval (CI) for the development of type 2 diabetes. The area under the ROC curve (AUC) was calculated to test the predictive power of the developed risk score system in the validation cohort. We recalculated the diabetes risk using the equation of diabetes risk of the Atherosclerosis Risk in Communities study, which just included non-laboratory data[10] and the Korean Diabetes Score[11] using the data of the validation cohort. To compare the AUCs, we used DeLong's method[22]. All analyses were carried out using IBM SPSS Statistics (Windows version 22.0; IBM Corporation, Armonk, NY, USA) and SAS (version 9.4; SAS Institute, Cary, NC, USA) software. Two-sided *P*-values <0.05 were considered significant.

RESULTS

Clinical characteristics of study participants

Among 8,740 participants without diabetes at baseline, we assessed diabetes in 5,675 participants (2,658 men and 3,017 women) at 10 years of follow up. A total of 35% of the population were not followed up, and Table S1 shows the different parameters between participants who were followed up or not. Participants who were not followed up were older than those who were followed up continuously (52.1 ± 9.4 vs 51.5 ± 8.5 years, $P = 0.005$) and had lower BMI, waist circumference and HbA1c levels. Among the participants in the whole cohort, 25.7% of men and 20.1% of women developed type 2 diabetes. The 2-h postprandial data were missing in 1,617 (28.5%) at the second follow up, 535 (9.4%) at the third follow up, 782 (13.8%) at the 4th follow-up, and 702 (12.4%) at the 5th follow-up. The baseline characteristics are shown in Table 1. In the development cohort, subjects who developed type 2 diabetes were older than those who did not develop type 2 diabetes both in the male (52.6 ± 8.7 vs 50.7 ± 8.2 years, $P < 0.001$) and the female groups (54.1 ± 8.8 vs 51.3 ± 8.5 years, $P < 0.001$). Participants with incident type 2 diabetes more frequently had a family history of type 2 diabetes and prehypertension or hypertension, increased BMI and waist circumference than participants without incident type 2 diabetes in both gender groups. A difference of education and income levels between participants with and without incident type 2 diabetes was only observed in women. More female participants with incident type 2 diabetes had low education and income levels compared with participants without type 2 diabetes. More participants with incident type 2 diabetes were ex-smokers or current smokers, but there was no difference in regular exercise among the groups.

Risk scoring including significant risk factors

The means and standard deviations of the KDR scores were 36.9 ± 14.5 in men and 30.5 ± 15.4 in women, respectively. Table 2 presents the logistic regression analysis results and corresponding scores. In men, the highest OR of incident type 2 diabetes was related with older age (OR 2.90, 95% CI 1.61–2.64, $P < 0.001$) and increased blood pressure (OR 2.27, 95% CI 1.71–3.01, $P < 0.001$). In women, the highest OR of incident type 2 diabetes was also related with older age (OR 2.47, 95% CI 1.61–3.78, $P < 0.001$) and increased blood pressure (OR 2.44, 95% CI 1.82–3.07, $P < 0.001$). Tables S2 and S5 show the results of the logistic regression analysis and risk scores including FPG levels or HbA1c.

Ten-year risk of type 2 diabetes

During a median follow-up period of 9.7 years, 22.7% of all participants progressed to diabetes. Table 3 represents the diabetes risk score-card to calculate the score in an easy way. As the KDR scores increased, the probability of incident type 2 diabetes increased from 8.9% to 34.9% in men, and 10.8 to 38.3% in women (Table 4). The estimated risk of type 2 diabetes in each score category seemed to be higher when the KDR scores were calculated including FPG or HbA1c levels (Tables S3, S4, S6, S7) compared with KDR scores not including these laboratory data. The AUC of the KDR score was 0.657 (95% CI 0.626–0.715), the KDR score including FPG levels was 0.690 (95% CI 0.660–0.720) and the KDR score

Table 1 | Clinical characteristics of participants at baseline

	Development cohort						Validation cohort					
	Men			Women			Men			Women		
	Non-T2D (n = 1,359)	T2D (n = 484)	P-value	Non-T2D (n = 1,704)	T2D (n = 426)	P-value	Non-T2D (n = 613)	T2D (n = 200)	P-value	Non-T2D (n = 706)	T2D (n = 181)	P-value
Age (years)	50.7 ± 8.2	52.6 ± 8.7	<0.001	51.3 ± 8.5	54.1 ± 8.8	<0.001	50.8 ± 8.1	52.1 ± 8.7	0.051	51.2 ± 8.4	54.2 ± 8.9	<0.001
Age group			<0.001			<0.001			0.300			0.004
40–44 years	397 (29.2%)	110 (22.7%)		491 (28.8 %)	77 (18.1%)		174 (28.3%)	50 (25.0%)		194 (27.5%)	34 (18.8%)	
45–49 years	344 (25.3%)	109 (22.5%)		384 (22.5%)	80 (18.8%)		157 (25.5%)	43 (21.5%)		173 (24.5%)	33 (18.2%)	
50–54 years	200 (14.7%)	70 (14.5%)		237 (13.9%)	65 (15.3%)		99 (16.1%)	32 (16.0%)		93 (13.2%)	26 (14.4%)	
55–59 years	172 (12.7%)	67 (13.8%)		212 (12.4%)	54 (12.7%)		63 (10.2%)	29 (14.5%)		101 (14.3%)	29 (16.0%)	
60–64 years	131 (9.6%)	57 (11.8%)		212 (12.4%)	79 (18.5%)		70 (11.4%)	22 (11.0%)		81 (11.5%)	29 (16.0%)	
65–69 years	115 (8.5%)	71 (14.7%)		168 (9.9%)	71 (16.7%)		52 (8.5%)	24 (12.0%)		64 (9.1%)	30 (16.6%)	
Family history of T2D	128 (9.4%)	62 (12.8%)	0.037	180 (10.6%)	69 (16.2%)	0.002	57 (9.3%)	25 (12.5%)	0.223	88 (12.5%)	24 (13.3%)	0.802
SBP (mm Hg)	115.2 ± 15.0	120.6 ± 17.6	<0.001	114.6 ± 18.1	122.8 ± 19.9	<0.001	115.7 ± 16.2	119.3 ± 15.1	0.006	115.2 ± 17.4	121.7 ± 19.3	<0.001
DBP (mm Hg)	75.5 ± 10.8	78.1 ± 11.6	<0.001	72.8 ± 11.4	76.8 ± 12.1	<0.001	76.1 ± 11.2	78.1 ± 10.5	0.028	72.8 ± 10.8	75.9 ± 11.8	0.001
Blood pressure			<0.001			<0.001			0.002			<0.001
Normal	756 (55.6%)	190 (39.3%)		1056 (62.0%)	178 (41.8%)		342 (55.6%)	84 (42.0%)		433 (61.3%)	81 (44.8%)	
Prehypertension	369 (27.2%)	151 (31.2%)		351 (20.6%)	102 (23.9%)		166 (27.0%)	63 (31.5%)		140 (19.8%)	48 (26.5%)	
Hypertension	234 (17.2%)	143 (29.5%)		296 (17.4%)	146 (34.3%)		107 (17.4%)	53 (26.5%)		133 (18.8%)	52 (28.1%)	
Bodyweight (kg)	67.6 ± 9.5	69.1 ± 9.9	<0.001	58.4 ± 7.9	61.0 ± 8.7	<0.001	67.1 ± 8.9	69.0 ± 10.7	0.020	58.8 ± 8.3	61.2 ± 8.5	0.001
BMI (kg/m^2)	24.1 ± 2.8	24.9 ± 3.0	<0.001	24.6 ± 3.1	25.8 ± 3.2	<0.001	24.1 ± 2.6	24.7 ± 3.2	0.015	24.7 ± 3.1	26.1 ± 3.4	<0.001
Waist circumference (cm)	83.1 ± 7.4	85.6 ± 7.7	<0.001	80.6 ± 9.3	84.7 ± 9.3	<0.001	82.8 ± 7.2	84.9 ± 7.9	<0.001	81.0 ± 9.2	84.8 ± 9.7	<0.001
FPG (mg/dL)	85.1 ± 8.5	91.8 ± 10.1	<0.001	82.3 ± 7.7	87.5 ± 10.5	<0.001	85.0 ± 8.1	91.6 ± 10.9	<0.001	82.1 ± 7.3	87.1 ± 10.0	<0.001
HbA1c (%)	5.5 ± 0.3	5.8 ± 0.4	<0.001	5.5 ± 0.3	5.9 ± 0.5	<0.001	5.5 ± 0.3	5.8 ± 0.4	<0.001	5.5 ± 0.3	5.9 ± 0.5	<0.001
Urban	688 (50.6%)	281 (58.1%)	0.005	783 (46.0%)	220 (51.6%)	0.039	334 (54.3%)	119 (59.5%)	0.219	297 (42.1%)	95 (52.5%)	0.015
Education group			0.203			0.001			0.080			0.003
<6 years	224 (16.6%)	97 (20.1%)		679 (40.2%)	210 (49.9%)		114 (18.6%)	26 (13.0%)		274 (39.1%)	96 (53.0%)	
6–12 years	825 (61.1%)	285 (59.1%)		900 (53.3%)	185 (43.9%)		356 (58.1%)	133 (66.5%)		386 (55.1%)	77 (42.5%)	
>12 years	302 (22.4%)	100 (20.7%)		111 (6.6%)	26 (6.2%)		143 (23.3%)	41 (20.5%)		41 (5.8%)	8 (4.4%)	
Income group			0.180			0.043				0.041		0.195
<$1,000	360 (26.6%)	136 (28.4%)		624 (37.6%)	187 (44.2%)		123 (20.2%)	56 (28.3%)		270 (39.5%)	81 (45.5%)	
1,000–2,000 dollars	407 (30.1%)	159 (33.2%)		495 (29.8%)	115 (27.2%)		202 (33.2%)	53 (26.8%)		205 (30.0%)	42 (23.6%)	
>$2,000	584 (43.2%)	184 (38.4%)		541 (32.6%)	121 (28.6%)		283 (46.5%)	89 (23.9%)		209 (30.6%)	55 (30.9%)	
Smoking status			0.024			0.049			0.325			0.004
Never	298 (22.1%)	78 (16.3%)		1615 (96.5%)	396 (93.8%)		144 (23.7%)	37 (18.6%)		666 (96.4%)	167 (93.3%)	
Former	438 (32.5%)	168 (35.0%)		18 (1.1%)	8 (1.9%)		195 (32.1%)	69 (34.7%)		12 (1.7%)	1 (0.6%)	
Current	611 (45.4%)	234 (48.8%)		41 (2.4%)	29(4.3%)		269 (44.2%)	93 (46.7%)		13 (1.9%)	11 (6.1%)	
Alcohol group			0.852			0.033			0.092			0.978

Table 1 | (*Continued*)

	Development cohort						Validation cohort					
	Men			Women			Men			Women		
	Non-T2D (n = 1,359)	T2D (n = 484)	*P*-value	Non-T2D (n = 1,704)	T2D (n = 426)	*P*-value	Non-T2D (n = 613)	T2D (n = 200)	*P*-value	Non-T2D (n = 706)	T2D (n = 181)	*P*-value
Never	248 (18.7%)	83 (17.6%)		1176 (70.9%)	304 (71.9%)		127 (21.3%)	28 (14.5%)		499 (72.2%)	126 (71.6%)	
Former	129 (9.8%)	46 (9.7%)		42 (2.5%)	20 (4.7%)		58 (9.7%)	24 (12.4%)		18 (2.6%)	5 (2.8%)	
Current	946 (71.5%)	343 (72.7%)		441 (26.6%)	99 (23.4%)		412 (69.0%)	141 (73.1%)		174 (25.2%)	45 (20.5%)	
Regular exercise	535 (39.4%)	173 (35.7%)	0.174	558 (32.7%)	147(34.5%)	0.490	243 (39.5%)	80 (40.0%)	0.934	236 (33.4%)	55 (30.4%)	0.478

Data are the mean ± standard deviation or numbers (%). *P*-values were determined using a Student's *t*-test and χ^2-test. BMI, body mass index; DBP, diastolic blood pressure; FPG, fasting plasma glucose; SBP, systolic blood pressure; T2D, type 2 diabetes.

including HbA1c levels was 0.746 (95% CI 0.717–0.775; Table 5). The difference between the models was significant. Additionally, compared with previous models based on Western[10] and Korean data[11], the AUC was significantly higher in the KDR model.

DISCUSSION

In the present study, we developed clinical risk scores for incident diabetes that can be calculated by the general population. We included modifiable or non-modifiable parameters. We created a KDR score-card and a 10-year diabetes risk table for clinical use. In addition, we compared our model with previous models, and showed that our model could predict incident diabetes more accurately.

The present study showed a higher risk of type 2 diabetes in people living in urban areas compared with those in rural areas. This location difference has also been reported in an Indian observational study[23]. However, in adults living in the USA, a higher prevalence of type 2 diabetes was observed in rural than in urban areas[24,25]. This discrepancy might be driven by the difference of obesity status according to urbanization. Previous studies[24,25] showed a higher prevalence of obesity in rural areas than urban areas. In contrast, the present study showed that obesity was not different between urban areas and rural areas in the whole cohort (43.6% vs 41.7%, $P = 0.198$). To determine the contributing factors of urbanization on increasing diabetes risk, nutritional factors and physical activity should be considered.

Prediction models that include laboratory data generally predicted type 2 diabetes risk more sensitively than prediction models that exclude laboratory data (Table 6). In fact, we observed that the prediction power was improved when we included FPG or HbA1c data in the KDR scores. However, a blood test and doctor's visit are necessary to obtain them. Therefore, some high-risk people might easily remain undiagnosed. In the present data, women with a lower education level and lower income had a relatively higher risk of type 2 diabetes than those with a higher education level and higher income. In line with this, self-assessable risk scores excluding laboratory tests might be more practical than those including laboratory data. Furthermore, our model had an acceptable prediction level of AUC (0.657) compared with previous large cohort studies, such as the Framingham Heart Study and the Atherosclerosis Risk in Communities study[10]. Lee *et al.*[11] published a Korean Diabetes Score, including self-assessable variables, using cross-sectional national data. This prediction model had been validated using Korean Genome and Epidemiology Study data, and the AUC of the Korea Diabetes Score was 0.641[26]. When we validated this model in the validation cohort, the AUC was 0.624, which was lower than the AUC of KDR scores. Compared with the Korea Diabetes Score, which did not consider sex difference, but included alcohol history, we made risk scores differently between the sexes, and did not include alcohol history, which might be inaccurate[27]. The

Table 2 | Beta-coefficients, odds ratios and corresponding risk scores of new-onset type 2 diabetes in the development cohort

	Men				Women			
	β	OR (95% CI)	*P*-value	Score	β	OR (95% CI)	*P*-value	Score
Age								
40–44 years		Reference				Reference		
45–49 years	0.175	1.19 (0.87–1.63)	0.274	4	0.235	1.27 (0.89–1.80)	0.195	5
50–54 years	0.299	1.35 (0.93–1.95)	0.112	7	0.469	1.60 (1.09–2.36)	0.018	10
55–59 years	0.503	1.65 (1.13–2.42)	0.009	12	0.373	1.45 (0.96–2.20)	0.080	8
60–64 years	0.712	2.04 (1.35–3.08)	0.001	17	0.796	2.22 (1.48–3.32)	<0.001	18
65–69 years	1.063	2.90 (1.61–2.64)	<0.001	25	0.904	2.47 (1.61–3.78)	<0.001	20
Region								
Rural		Reference				Reference		
Urban	0.723	2.06 (1.61–2.64)	<0.001	17	0.870	2.39 (1.84–3.10)	<0.001	19
Smoking								
Never smokers		Reference				Reference		
Former smokers	0.354	1.43 (1.04–1.98)	0.028	8	0.386	1.47 (0.61–3.55)	0.389	9
Current smokers	0.598	1.82 (1.34–2.47)	<0.001	14	0.589	1.80 (1.00–3.26)	0.051	13
Blood pressure								
Normotensive		Reference				Reference		
Prehypertension	0.445	1.56 (1.20–2.03)	0.001	11	0.472	1.60 (1.19–2.15)	0.002	10
Hypertension	0.818	2.27 (1.71–3.01)	<0.001	20	0.890	2.44 (1.82–3.07)	<0.001	19
Family history of T2D								
None		Reference				Reference		
Yes	0.493	1.64 (1.17–2.30)	0.004	12	0.688	1.99 (1.44–2.75)	<0.001	15
Waist circumference								
Men<90 cm, women <85 cm		Reference				Reference		
Men ≥90 cm, women≥85 cm	0.491	1.64 (1.27–2.11)	<0.001	12	0.638	1.89 (1.48–2.43)	<0.001	14

CI, confidence interval; T2D, type 2 diabetes; OR, odds ratio.

Table 3 | Diabetes risk score-card

	Men		Women	
1. Age group	40–44 years	0	40–44 years	0
	45–49 years	+4	45–49 years	+5
	50–54 years	+7	50–54 years	+10
	55–59 years	+12	55–59 years	+8
	60–64 years	+17	60–64 years	+18
	65–69 years	+25	65–69 years	+20
2. Living area	Rural	0	Rural	0
	Urban	+17	Urban	+19
3. Smoking	Never	0	Never	0
	Former	+8	Former	+9
	Current	+14	Current	+13
4. Hypertension	Normotensive	0	Normotensive	0
	Prehypertension	+11	Prehypertension	+10
	Hypertension	+20	Hypertension	+19
5. Family history of T2D	No	0	No	0
	Yes	+12	Yes	+15
6. Waist circumference	<90 cm	0	<85 cm	0
	≥90 cm + 12	+12	≥85 cm	+14

performance of our prediction model is also acceptable when we compared it with other Asian cohort studies (Table 6). Furthermore, we included just seven variables to calculate the risk of type 2 diabetes, which is relatively easy to calculate. Therefore, this new type 2 diabetes risk prediction algorithm is more practical.

There were several limitations to the present study. First, this prediction model was not validated in an independent cohort. We hope that other Korean cohort studies will adopt our prediction model to validate the usefulness of the KDR score. Second, we did not repeat the oral glucose tolerance test or HbA1c, but used a single measurement to diagnose type 2 diabetes. From the previous report, approximately 75% of participants with diagnosed type 2 diabetes in epidemiological studies were confirmed to have clinical diabetes[28]. Therefore, there could be some dilution with the prediabetic state in newly diagnosed type 2 diabetes. In addition, 35% of the population were not followed up, which could influence the accuracy of the model. Among participants who were lost to follow up during the 10 years, 24.5% of participants did not attend follow-up visits because of personal issues, such as being farming season, going on a business trip and moving to another location. An additional 16.2% and 10.3% of participants became severely ill and died, respectively, therefore it was impossible to carry out a follow-up evaluation. In total, annually, approximately 3.5% of participants failed to follow up. In the present cohort, there were significantly different parameters between participants who were followed up and those who were lost to follow up.

Table 4 | Estimated 10-year risk of new-onset type 2 diabetes (30% validation cohort)

Score	Men (%)	Women (%)
≤24	8.9	10.8
25–29	20.6	24.1
30–34	24.3	21.5
35–39	23.4	27.4
40–44	34.8	26.9
45–49	28.8	28.6
≥50	34.9	38.3

Table 5 | Area under the receiver operating characteristic curves for previous models and Korean Diabetes Risk scores (30% validation cohort)

	ROC area (95% CI)	*P*-value compared with KDR
KDR	0.657 (0.626–0.715)	Referent
KDR plus FPG	0.690 (0.660–0.720)	<0.001
KDR plus HbA1c	0.746 (0.717–0.775)	<0.001
ARIC	0.604 (0.571–0.637)	0.002
Korea Diabetes Score	0.624 (0.593–0.656)	0.038

ARIC, atherosclerosis risk in communities; CI, confidence interval; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; KDR, Korean Diabetes Risk; ROC, receiver operating characteristic curve.

Some of the risk factors were higher, and some of them were lower in participants who were lost to follow up compared with participants who were followed up. However, the difference in KDR score was minimal between groups (33.4 vs 34.4 in the follow-up group and follow-up loss group, respectively). Even though the magnitude of difference was minimal, we should consider the limitations of our model.

This newly developed self-assessable diabetes risk score did not include laboratory test data, but did include clinical parameters, including three modifiable risk factors: smoking status, hypertension and waist circumference. This risk prediction model can be used in the general population, and the KDR risk score-card makes it easy to calculate a person's risk. Further studies will be required to validate the model, and to test its feasibility in real clinical settings.

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Table 6 | Characteristics of the diabetes prediction model from prospective cohort studies in Asian countries

Author (Year)	Country	Population	Sample size	Non-laboratory parameters (1)	Added laboratory parameters (2)	Predictive ability
Aekplakorn (2006)[29]	Thailand	Employees of a state enterprise	2,677 (development) 2,420 (validation)	Age, BMI, WC, HTN and family history of diabetes	Status of IFG and IGT, HDL, TG	(1) AUC: 0.74 (2) AUC: 0.78
Chien (2009)[30] Liu (2011)[31]	China China	Middle-aged and elderly participants Health checkup-based population	2,960 1,457 (development) 394 (validation)	Age and BMI Age, BMI, HTN, history of hyperglycemia	WBC, FPG, HDL, TG FPG, HDL, TG	(2) AUC: 0.702 (2) AUC: 0.734
Doi (2012)[32]	Japan	Suburb population	1,935 (development) 1,147 (validation)	Age, sex, BMI, WC, HTN, family history of diabetes, smoking and exercise	FPG	(1) AUC: 0.700 (2) AUC: 0.772
Yatsuya (2018)[33]	Japan	Male workers	3,540	Age, BMI, smoking, alcohol, exercise, medication of dyslipidemia and family history of diabetes	FPG, HDL, TG	(2) C-statistics: 0.77
Ha (2018)[34]	Korea	National Health Insurance Service-National Health Screening Cohort (development) KoGES (validation)	359,349 (development) 6,660 (validation)	Age, BMI, SBP, family history of diabetes, alcohol, smoking, physical activity, medication of hypertension and statin therapy	FPG, TC, GGT	(2) C-statistics: 0.63 (men) and 0.66 (women)

AUC, area under the receiver-operating characteristic curve; BMI, body mass index; FPG, fasting plasma glucose; HTN, hypertension; IFG, fasting plasma glucose; IGT, impaired glucose tolerance; KoGES, Korean Genome and Epidemiology Study; NHIS-HEALS, National Health Insurance Service-National Health Screening Cohort; TG, triglyceride; WBC, white blood cell count; WC, waist circumference.

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DISCLOSURE

The authors declare no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1 | Difference in clinical characteristics between participants who were followed up and those who were not followed up.

Table S2 | Beta-coefficients, odds ratios and corresponding risk scores including fasting plasma glucose levels of new-onset type 2 diabetes.

Table S3 | Diabetes risk score-card including fasting plasma glucose.

Table S4 | Estimated 10-year risk of new-onset type 2 diabetes using models including fasting plasma glucose.

Table S5 | Beta-coefficients, odds ratios and corresponding risk scores including glycated hemoglobin levels of new-onset type 2 diabetes.

Table S6 | Diabetes risk score-card including glycated hemoglobin.

Table S7 | Estimated 10-year risk of new-onset type 2 diabetes using models including glycated hemoglobin.