Development and Validation of a Risk-Score Model for Type 2 Diabetes: A Cohort Study of a Rural Adult Chinese Population

Ming Zhang1*, Hongyan Zhang1,2*, Chongjian Wang2, Yongcheng Ren1,2, Bingyuan Wang1,2, Lu Zhang1,2, Xiangyu Yang1,2, Yang Zhao1,2, Chengyi Han1,2, Chao Pang3, Lei Yin3, Yuan Xue2, Jingzhi Zhao3*, Dongsheng Hu1*

1 Department of Preventive Medicine, Shenzhen University School of Medicine, Shenzhen, Guangdong, People’s Republic of China, 2 Department of Epidemiology and Health Statistics, College of Public Health, Zhengzhou University, Zhengzhou, Henan, People’s Republic of China, 3 Department of Prevention and Health Care, Military Hospital of Henan Province, Zhengzhou, Henan, People’s Republic of China

* These authors contributed equally to this work.
* hud@szu.edu.cn (DH); zhao_jingzhi@126.com (JZ)

Abstract

Some global models to predict the risk of diabetes may not be applicable to local populations. We aimed to develop and validate a score to predict type 2 diabetes mellitus (T2DM) in a rural adult Chinese population. Data for a cohort of 12,849 participants were randomly divided into derivation (n = 11,564) and validation (n = 1285) datasets. A questionnaire interview and physical and blood biochemical examinations were performed at baseline (July to August 2007 and July to August 2008) and follow-up (July to August 2013 and July to October 2014). A Cox regression model was used to weigh each variable in the derivation dataset. For each significant variable, a score was calculated by multiplying $\beta$ by 100 and rounding to the nearest integer. Age, body mass index, triglycerides and fasting plasma glucose (scores 3, 12, 24 and 76, respectively) were predictors of incident T2DM. The model accuracy was assessed by the area under the receiver operating characteristic curve (AUC), with optimal cut-off value 936. With the derivation dataset, sensitivity, specificity and AUC of the model were 66.7%, 74.0% and 0.768 (95% CI 0.760–0.776), respectively. With the validation dataset, the performance of the model was superior to the Chinese (simple), FINDRISC, Oman and IDRS models of T2DM risk but equivalent to the Framingham model, which is widely applicable in a variety of populations. Our model for predicting 6-year risk of T2DM could be used in a rural adult Chinese population.

Introduction

The prevalence of diabetes, especially Type 2 diabetes mellitus (T2DM), is growing at a worrying rate in the world. In 2013, 382 million people had diabetes worldwide, and this number is expected to increase to 592 million by 2035 [1]. About 80% of people with diabetes are in low- and middle-income countries [1]. As a developing country, China is inevitably faced with a
serious prevalence of this disease. In 2013, China had a large burden of diabetes: 1 in 4 people had the disease [2]. This disease may reduce life expectancy by about 10 years [3]. Thus, T2DM is a major public health problem, causing a significant burden on patients, their families, and society.

Although the mechanisms of T2DM remain unclear, people with T2DM are usually asymptomatic in the early period. Several studies have demonstrated that T2DM can be prevented with a vast array of interventions in people at high risk [4–6]. Therefore, prevention among high-risk individuals is an attractive and practical approach to reduce the prevalence of T2DM [7].

A number of diabetes risk-score models have been developed to predict the risk of T2DM [8–11]. These models can be used in clinical practice to identify people at high risk of T2DM and to guide clinical treatment. Some national and international diabetes guidelines have recommended diabetes risk-assessment tools as a simple screening method for identifying people who may be at high risk [12–14]. However, whether these models can be applied to local populations is not ensured. Indeed, the incidence and risk factors of T2DM in a population determine the suitability of a risk score. Some scores developed in a particular population often do not perform well in other populations [15].

Here, we developed and validated a prediction model for T2DM in a cohort of rural adult Chinese people.

Materials and Methods

Study design and participants

In total, 20,194 participants ≥18 years old were recruited from a rural Chinese population from July to August of 2007 and July to August of 2008 (baseline); 17,262 (85.5%) were followed up from July to August 2013 and July to October 2014. The same questionnaire interview and physical and blood biochemical examinations were performed at baseline and follow-up. We excluded people lost to follow-up (n = 2932), who had a diagnosis of T2DM at baseline (n = 1230), had unknown T2DM at follow-up (n = 2083) or died during follow-up (n = 1100). Data for 12,849 participants were selected for this analysis and were randomly divided into derivation (n = 11,564) and validation (n = 1285) datasets to establish and validate the model. Randomization was carried out by use of random numbers generated by computer.

The study was approved by the Ethics Committee of Zhengzhou University School of Medicine, and all participants provided informed written consent.

Data collection

Trained investigators administered a questionnaire (collecting data on demographic characteristics, dietary and lifestyle behaviors, family history of T2DM). Education level was categorized as no education, elementary level, secondary school, high school, and college and above. Marital status was classified as married/cohabitating and unmarried/divorced/widowed. The daily food intake composition was calculated according to the China Food Composition Table [16]. The limits of high-fat and high-vegetable consumption were 30 g/d and 500 g/d, respectively, based on the Dietary Guidelines for Chinese Residents [17]. Smoking was defined as currently smoking and/or having smoked at least 100 cigarettes during the lifetime. Drinking was defined as having consumed at least 30 g of alcohol per week in the previous year. According to the International Physical Activity Questionnaire (IPAQ) [18], physical activity level was classified as low, moderate, or high. Family history of T2DM was considered positive with either parent having a history of T2DM.
Body weight, height and waist circumference (WC) were measured by standard methods [19]. Body mass index (BMI) was calculated by mass in kilograms divided by height in meters squared [20]. An electronic sphygmomanometer (OMRON HEM-7071, Japan) was used to measure blood pressure and heart rate (HR). Pulse pressure (PP) was calculated as systolic blood pressure minus diastolic blood pressure. Overnight fasting blood samples were collected in a vacuum tube with disodium EDTA and centrifuged at 3000 rpm for 10 min, then plasma was transferred to an EP tube and stored at -20°C for blood biochemical examination. Levels of fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG) and high-density lipoprotein-cholesterol (HDL-C) were detected by using an automatic biochemical analyzer (Hitachi 7080, Tokyo) with reagents from Wako Pure Chemical Industries (Osaka, Japan). Low-density lipoprotein-cholesterol (LDL-C) level was calculated by the Freidwald formula [21].

**Definition of T2DM**

According to the Guideline for prevention and treatment of type 2 diabetes in Chinese (2013 edition) [22], T2DM was diagnosed by FPG ≥7.00 mmol/L and/or current treatment with anti-diabetes medication. We excluded subjects with type 1 diabetes, gestational diabetes and other diabetes types.

**Statistical analyses**

We used covariates of T2DM risk ascertained from the literature: gender, age, educational level, marital status, smoking, drinking, high-fat diet, high-vegetable diet, physical activity, family history of T2DM, BMI, WC, PP, HR and levels of TC, TG, HDL-C, LDL-C and FPG. In comparing the derivation and validation datasets at baseline, the Mann-Whitney Wilcoxon test was used for continuous variables because of non-normal distribution and chi-square test for categorical variables. Person-years of follow-up and the incidence density rate were computed.

Disease-free survival was analyzed by the Kaplan-Meier method, with the log-rank test to compare survival curves. A Cox proportional-hazards model with forward selection was used for multivariable survival analysis. Coefficients ($\beta$) and baseline hazard function ($h_0(t)$) were estimated by Cox regression analysis. For each variable significant on Cox regression analysis, a score was calculated by multiplying $\beta$ by 100 and rounding to the nearest integer. The total score was the sum of scores for each factor. ($h_0(t)$) was T2DM-free average survival probability at time $t$ (e.g., $t = 6$ years). The probability ($P$) of T2DM over 6 years was calculated as follows:

$$P(T2DM) = 1 - h_0(t)^{\exp(score/100)}$$

The predictive power of the risk-score model was evaluated to identify the risk of developing T2DM in the derivation and validation datasets. The aggregated scores were divided into four ranges, and the observed 6-year cumulative incidence of T2DM was compared with predicted risk by chi-square test for trend. The model’s accuracy was assessed by the area under the receiver operating characteristic curve (AUC) based on the sum of scores. The AUC performance of the model was compared with that of several prediction models developed in other populations, including the Chinese (simple) [23], FINDRISC [24], Oman [25], IDRS [26] and Framingham [27] models by the DeLong et al. method [28]. The optimal cut-off AUC was defined as having the maximum combination of sensitivity and specificity. Goodness of fit was assessed by the Hosmer-Lemeshow test [29].

Statistical analysis involved use of SAS 9.1 (SAS Institute, Cary, NC) and MedCalc 9.3.1 (Med-Calc, Inc., Mariakerke, Belgium). All statistical tests were two-sided and $P<0.05$ was considered statistically significant.
Results

Characteristics of study participants

From the 12,849 participants, we detected 729 in whom T2DM developed during the 6-year follow-up. Overall, the incidence density rate of T2DM was estimated at 9.79/1000 person-years: 9.57 (n = 659) and 9.15/1000 person-years (n = 70) for the derivation and validation datasets, respectively, with no difference between the datasets ($P = 0.922$). The baseline characteristics of subjects did not differ between the two datasets (Table 1).

Prediction model

Only age, BMI, TG and FPG reached statistical significance and were retained in the Cox regression model with the derivation dataset (Table 2).

Table 1. Baseline characteristics of subjects in the derivation and validation datasets for developing a model of type 2 diabetes mellitus (T2DM).

| Characteristics of subjects                  | Derivation dataset (n = 11,564 subjects) | Validation dataset (n = 1285 subjects) | $P$ value |
|----------------------------------------------|------------------------------------------|----------------------------------------|-----------|
| Gender (female), n (%)*                      | 7190 (62.18)                             | 819 (63.74)                            | 0.274     |
| Age (years), median (IQR) #                  | 51 (42, 59)                              | 50 (41, 59)                            | 0.469     |
| Education, n (%)*                            |                                          |                                        | 0.426     |
| No education                                 | 1715 (14.83)                             | 171 (13.31)                            |           |
| Primary school                               | 3820 (33.03)                             | 452 (35.18)                            |           |
| Middle school                                | 4868 (42.10)                             | 540 (42.02)                            |           |
| High school                                  | 1047 (9.05)                              | 109 (8.48)                             |           |
| College and above                            | 114 (0.99)                               | 13 (1.01)                              |           |
| Marital status, n (%)*                       |                                          |                                        | 0.882     |
| Married/cohabitating                         | 10628 (91.94)                            | 1182 (92.06)                           |           |
| Unmarried/divorced/widowed                   | 932 (8.06)                               | 102 (7.94)                             |           |
| High-fat diet, n (%)*                        | 1487 (12.86)                             | 155 (12.06)                            | 0.417     |
| High-vegetable diet, n (%)*                  | 4663 (40.32)                             | 541 (42.10)                            | 0.218     |
| Smoking, n (%)*                              | 2395 (20.71)                             | 266 (20.70)                            | 0.547     |
| Drinking, n (%)*                             | 1294 (11.19)                             | 134 (10.43)                            | 0.410     |
| Physical activity, n (%)*                    |                                          |                                        | 0.419     |
| Low                                          | 3253 (28.13)                             | 371 (28.87)                            |           |
| Moderate                                     | 2585 (22.35)                             | 302 (23.50)                            |           |
| High                                         | 5726 (49.52)                             | 612 (47.63)                            |           |
| Family history of T2DM, n (%)*               | 607 (5.25)                               | 73 (5.68)                              | 0.531     |
| BMI (kg/m²), median (IQR) #                  | 24.09 (21.76, 26.59)                     | 24.14 (21.78, 26.64)                   | 0.887     |
| WC (cm), median (IQR) #                      | 81.75 (74.90, 89.25)                     | 82.05 (75.10, 89.25)                   | 0.708     |
| PP (mmHg), median (IQR) #                    | 45 (38, 53)                              | 45 (38, 53)                            | 0.750     |
| HR (bpm), median (IQR) #                     | 74 (67, 81)                              | 73 (67, 80)                            | 0.180     |
| TC (mmol/L), median (IQR) #                  | 4.39 (3.83, 5.01)                        | 4.35 (3.81, 5.02)                      | 0.644     |
| TG (mmol/L), median (IQR) #                  | 1.35 (0.96, 1.95)                        | 1.34 (0.95, 1.93)                      | 0.591     |
| HDL-C (mmol/L), median (IQR) #               | 1.14 (0.99, 1.32)                        | 1.14 (0.99, 1.32)                      | 0.898     |
| LDL-C (mmol/L), median (IQR) #               | 2.50 (2.08, 3.00)                        | 2.50 (2.08, 3.00)                      | 0.715     |
| FPG (mmol/L), median (IQR) #                 | 5.32 (4.99, 5.68)                        | 5.31 (4.98, 5.71)                      | 0.540     |

Data are no. (%) for classification variables and median (IQR) for numeric variables because of a non-normal distribution.

IQR, interquartile range; BMI, body mass index; WC, waist circumference; PP, pulse pressure; HR, heart rate; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FPG, fasting plasma glucose.

*chi-square test.
#Mann-Whitney Wilcoxon test.

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Significant variables were assigned a score based on the regression coefficient (Table 2). The total risk score was calculated as follows:

$$\text{Risk score} = 3 \times \text{age (years)} + 12 \times \text{BMI (kg/m}^2\text{)} + 24 \times \text{TG (mmol/L)} + 76 \times \text{FPG (mmol/L)}$$

(rounding to the nearest integer for each variable’s score)

The probability ($P$) of T2DM during the 6-year follow-up was calculated by the baseline hazard function $[h_0(t)]$:

$$P(T2DM) = 1 - 0.999997^{\text{score}/100}$$

The probability of T2DM developing in subjects in the derivation dataset was 0.02% to 100% (score $402$–$1529$).

### Evaluation of the model’s predictive performance

The optimal cut-off value for this risk-score model was $936$. Sensitivity, specificity and AUC were $66.7\%$, $74.0\%$ and $0.768$ (95% CI: $0.760$–$0.776$) with the derivation dataset. To validate the model, we applied this scoring method to the validation dataset. The aggregated scores were divided into 4 ranges (Table 3). For scores of $<800$, $800$–$899$, $900$–$1099$, and $\geq1100$, the cumulative incidence of T2DM was $1.24\%$, $2.20\%$, $9.62\%$, and $33.13\%$, respectively, in the derivation dataset and $1.52\%$, $2.53\%$, $8.29\%$ and $44.44\%$, respectively, in the validation dataset. The observed incidence increased with increasing risk score or estimated probability in the 2 datasets (both $P_{\text{trend}} < 0.001$).

Table 4 compares the performance of our model and the Chinese (simple), FINDRISC, Oman, IDRS, and Framingham models with the validation dataset. The AUC was higher for our model than the Chinese (simple), FINDRISC, Oman and IDRS models ($0.766$ (95% CI: $0.742$–$0.789$) vs $0.630$ (95% CI: $0.603$–$0.657$), $0.638$ (95% CI: $0.611$–$0.664$), $0.673$ (95% CI: $0.651$–$0.695$), respectively).

### Table 2. Risk factors of T2DM in the derivation dataset.

| Risk factor   | β   | HR (95%CI)            | P value | Score allocated |
|---------------|-----|-----------------------|---------|-----------------|
| Age (years)   | 0.027 | 1.027 (1.020–1.034) | <0.001 | 3               |
| BMI (kg/m²)   | 0.124 | 1.132 (1.109–1.156) | <0.001 | 12              |
| TG (mmol/L)   | 0.239 | 1.270 (1.156–1.396) | <0.001 | 24              |
| FPG (mmol/L)  | 0.760 | 1.379 (1.172–1.622) | <0.001 | 76              |

HR, hazard ratio; 95% CI, 95% confidence interval; BMI, body mass index; TG, triglycerides; FPG, fasting plasma glucose.

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### Table 3. Estimated probability and observed incidence of T2DM in the derivation and validation datasets.

| Score range | Probability, % | Derivation dataset | Validation dataset |
|-------------|----------------|---------------------|--------------------|
|             | Non-T2DM, n | T2DM, n | Incidence, % * | Non-T2DM, n | T2DM, n | Incidence, % * |
| <800        | 1830         | 23 | 1.24 | 195 | 3 | 1.52 |
| 800–899     | 4454         | 100 | 2.20 | 501 | 14 | 2.53 |
| 900–1099    | 4435         | 472 | 9.62 | 498 | 45 | 8.29 |
| ≥1100       | 109          | 54 | 33.13 | 10 | 8 | 44.44 |

T2DM, type diabetes mellitus

*P for trend <0.001.

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0.646–0.698) and 0.638 (95% CI: 0.611–0.664)—but not the Framingham model—0.745 (95% CI: 0.720–0.769). Hence, the performance of our model was superior to the Chinese (simple), FINDRISC, Oman, and IDRS models but equivalent to the Framingham model in a rural adult Chinese population. Moreover, both our model and the Framingham model showed high sensitivity (70.0% and 78.6%), but the specificity was lower for the Framingham than our model (63.2% and 72.5%). The Chinese (simple) model had the lowest AUC of 0.630, and specificity of 60.3%. The FINDRISC and IDRS models had similar performance with the validation cohort, with low sensitivity (54.3% and 52.9%) and high specificity (71.1% and 73.7%). The sensitivity and specificity for the Oman model was 67.1% and 62.7%, respectively. Hosmer-Lemeshow $P$ values were non-significant for all models, for satisfactory goodness of fit. Our model had good predicting ability for T2DM (Fig 1).

**Discussion**

We aimed to develop and validate a risk-score model for predicting risk of developing T2DM in a rural adult Chinese population. With the model, age, BMI, TG and FPG were predictors of incident T2DM. With the derivation dataset, sensitivity, specificity and AUC were 66.7%, 74.0% and 0.768 (95% CI 0.760–0.776), respectively. With the validation dataset, the performance of our model was superior to the FINDRISC, Oman and IDRS models of T2DM risk but equivalent to the Framingham model, widely used in a variety of populations. Thus, our model for predicting 6-year risk of T2DM could be used for a rural adult Chinese population.

The growth in diabetes incidence is mainly due to the increase in T2DM prevalence [30]. Even so, many cases are still undiagnosed and thus poorly controlled because T2DM has a prolonged latent phase [31–32]. Lifestyle and pharmacological interventions can delay or prevent T2DM in high-risk populations [33–37]. Several randomized clinical trials have demonstrated that interventions can reduce the rate of onset of T2DM in people at high risk of the disease [38–41]. Three follow-up studies showed the rate of conversion to T2DM decreased with lifestyle intervention: 43% reduction over 7 years in the Finnish Diabetes Prevention Study [36], 34% reduction over 10 years in the US Diabetes Prevention Program Outcomes Study [35], and 43% reduction over 20 years in the China Da Qing Diabetes Prevention Study [34]. These findings suggest a promising window in which effective prediction and intervention can lower the prevalence and disease burden of T2DM. Thus, improved efforts are needed to detect people at high risk of T2DM and implement intervention strategies.

Currently, risk prediction models of T2DM are divided into non-invasive and invasive models. Non-invasive risk models are generally based on data obtained by questionnaire and...
anthropometric measurements for straightforward measurement of T2DM risk. Invasive prediction models are developed on the basis of routine information and laboratory measurements. To obtain sufficient predictive ability, researchers need to include more variables with predictive potential, in some cases even genetic risk factors [42]. A study evaluating the effects of diabetes definitions on diabetes prevalence from a pooled analysis of 96 population-based studies with 331,288 participants, reported that using FPG in population surveys was a strategy for consistent and comparable surveillance [43]. Therefore, we developed an invasive risk-assessment model including FPG.

We established a risk-score model including 4 variables—age, BMI, TG and FPG—based on a rural adult Chinese cohort, to estimate the 6-year probability of developing T2DM (Table 2). The data for these 4 predictors are easy to obtain. The American Diabetes Association (ADA) considers that age is a major risk factor for T2DM and thus recommends the testing of people without other risk factors no later than 45 years old [44]. Age can be used to identify more cases of undiagnosed diabetes when used with the other risk factors in model [45]. However, some researchers suggest that the effect of age on incident T2DM may be mediated by anthropometric measures such as blood pressure, BMI and FPG, which could explain why this factor is not retained in some risk models including these factors [46]. Although age retained in a risk-score model is controversial [11, 27, 47–49], it was a significant factor in our prediction.

![Fig 1. Receiver-operating characteristic (ROC) curves for the Chinese, Chinese (simple), FINDRISC, Oman, IDR and Framingham models with the validation dataset. Area under the ROC curve: Chinese, 0.766; Chinese (simple), 0.630; FINDRISC, 0.638; Oman, 0.673; IDR, 0.638; Framingham, 0.745. doi:10.1371/journal.pone.0152054.g001](image)
However, the association of age and T2DM risk was not overly strong, with an HR of 1.027. Although our risk-score model showed age as a risk factor of T2DM, this finding does not give much guidance for prevention because age is non-modifiable. The other 3 factors included are meaningful for prevention strategies to reduce the incidence of T2DM. Previous studies found that the modifiable risk factor playing a substantial role on T2DM is obesity [50]. The Nurses’ Health Study, which documented 3300 new cases of T2DM, indicated that BMI, measuring obesity, was a major risk factor for T2DM [51]. TG and FPG are components of metabolic syndrome. Kahn et al. reported that adding information about fasting blood tests could preferably identify people at extreme risk of T2DM with sensitivity 74% and specificity 71% [52]. The Atherosclerosis Risk in Communities study showed that adding data on lipid and fasting blood levels for clinical information can increase AUC values from 0.71 to 0.80 in a model [53]. The Framingham Offspring Study found odds ratios of 1.00 and 1.15 for TG and FPG in predicting 7-year incident T2DM [27]. Our findings are in line with previous results, with hazard ratios of 1.270 and 1.379 for TG and FPG, respectively, in our risk score model.

Because a variable should not be a predictor related to outcome assessment in principle, the inclusion of FPG in the model seemed to not be the case. However, the higher level of FPG might sustained for a substantial time of period, for so-called pre-diabetes. Pre-diabetes is associated with high risk of diabetes developing, with a yearly conversion rate of 5% to 10% [54]. It is an intermediate state of hyperglycemia covering impaired glucose tolerance, impaired fasting glucose or glycated hemoglobin level 6.0% to 6.4% [55]. The ADA indicates that pre-diabetes should not be considered a clinical entity but rather a risk factor of diabetes [44]. Therefore, including FPG as an independent predictor in our model was somewhat reasonable.

Lifestyle changes could prevent T2DM. However, we did not find lifestyle factors such as physical activity, smoking and drinking significant predictors of T2DM in our model after adjusting for other factors, perhaps because of their correlation with BMI, TG and FPG or because data for these factors were not sufficiently accurate as compared with that for the included factors. Similarly, lifestyle factors also contributed less to the model than other variables in the FINDRISC model where the odds ratio of daily consumption of fruits and vegetables and physical activity < 4 h/week were 1.18 (95% CI 0.85–1.64) and 1.31 (95% CI 0.88–1.95) [24].

Validation of a risk-score model often involves comparing estimated probability and observed incidence [8, 56]. We found an overlap between estimated probability and observed incidence, with increased incidence occurring with increasing estimated risk. Thus, estimated risk has a certain accuracy. Comparison with previous prediction models of T2DM using the same dataset can verify the performance of a risk score model. We chose the Chinese (simple) [23], FINDRISC [24], Oman [25], IDRS [26], and Framingham [27] models, with data available from our dataset. Of all the variables, WC, age and family history of diabetes were used to construct the Chinese (simple) score model. Age, BMI, WC, use of blood pressure medication and history of high blood glucose were included for the FINDRISC model from a random population sample of 35- to 64-year-old participants. The Oman model, using Oman’s 1991 National Diabetes Survey data (n = 4881), involved age, WC, family history of diabetes, BMI, and presence of hypertension. The IDRS model, based on a cohort of 10,003 people ≥20 years old in India, involved age, positive family history of diabetes, BMI, WC, and physical activity. The Framingham score system, retaining fasting glucose level, BMI, HDL-C level, parental history of diabetes mellitus, TG, blood pressure or receiving treatment is seminal and widely applicable in a variety of populations [57]. The AUC predictive value of the Framingham model was close to that of our model (0.745 vs 0.766). In general, the Framingham model was
more complicated than our model by including seven items. Therefore our model may be more suitable for application in a Chinese population.

Of note, the laboratory variables were not included in the Chinese (simple), FINDRISC, Oman, or IDRS models; therefore, our model having better prediction ability than these models might not be surprising. Similar results were observed in another study [58], finding that the model included both invasive and non-invasive predictors (age, BMI, white blood cell count, TG, HDL-C and FPG) which yielded a higher AUC (0.749) than non-invasive models deriving in America, Europe, or Asia (AUC 0.665–0.703).

Our risk-score model was based on Cox regression for a Chinese rural population. For survival models, the limiting sample size is the number of events if the number of events is smaller than that of nonevents [59]. Peduzzi et al. suggested that a survival model is reasonably stable if the limiting sample size meets a ratio of at least 10 events per variable [60]. The number of T2DM cases was 659 in our derivation dataset. Thus, our sample size is sufficiently large for this type of analysis and limits the problem of over-fitting. Collapsing continuous data into categories results in lost information and power to detect a real relationship, further obtaining optimistic results [59]. Therefore, we retained factors as continuous variables. In addition, our model was developed for a population including young people (≥18 years). T2DM is increasingly common in young people [61], making this an advantage of our model.

Our model has some limitations. First, this is an invasive rather than a non-invasive model, the difficulty and costly for having invasive measurements might restrict its application practically in the rural areas. Second, the cohort study measured only fasting glucose on a single occasion, used to define T2DM at baseline and follow-up. More than three-quarters of the population with impaired glucose tolerance (IGT) and one-third with diabetes with a diagnosis by the 2-h glucose criteria would be classified as normal if they were diagnosed only by fasting glucose [62]. Thus, misclassification bias would be introduced, which would affect estimating the risk of T2DM and hence the performance of model. Future study should aim to develop and validate this risk-score model with 2-h oral glucose tolerance test for diagnosing diabetes. Third, the derivation and validation datasets were from the same cohort. Therefore, the model should undergo external validation for external application. Fourth, a large proportion of participants were lost to follow-up or their diabetic status could not be identified at follow-up. Therefore, the potential bias of lost to follow-up could have been introduced. Finally, it should be noted that the total risk score was larger in our model because a score was calculated by multiplying $\beta$ by 100 for making better use of the information on age.

Conclusions

We developed a risk score model to predict T2DM based on age, BMI, TG and FPG for rural adult Chinese people ≥ 18 years old. This model shows adequate performance and may be useful in China to promote the identification of people at high risk of T2DM.

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Author Contributions

Conceived and designed the experiments: DH. Performed the experiments: HZ YR BW LZ XY YZ CH YX. Analyzed the data: HZ. Contributed reagents/materials/analysis tools: CW CP LY JZ. Wrote the paper: HZ MZ.
1. Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. Global estimates of diabetes prevalence for 2013 and projections for 2035. Diabetes Res Clin Pract. 2014; 103(2):137–49. doi: 10.1016/j.diabres.2013.11.002 PMID: 24630390

2. Chan J, Zhang Y, Ning G. Diabetes in China: a societal solution for a personal challenge. Lancet Diabetes Endocrinol. 2014; 2(12):969–979. doi: 10.1016/S2213-8587(14)70144-5 PMID: 25218728

3. Barber SR, Davies MJ, Khunti K, Gray LJ. Risk assessment tools for detecting those with pre-diabetes: A systematic review. Diabetes Res Clin Pract. 2014; 105(1):1–13. doi: 10.1016/j.diabres.2014.03.007 PMID: 24694663

4. American Diabetes Association. Executive summary: Standards of medical care in diabetes—2012. Diabetes Care. 2012; 35(Suppl 1):S4–10. doi: 10.2337/dc12-s004 PMID: 22187471

5. Salas-Salvado J, Martinez-Gonzalez MA, Bullo M, Ros E. The role of diet in the prevention of type 2 diabetes. Nutr Metab Cardiovasc Dis. 2011; 21(Suppl 2):B32–48. doi: 10.1016/j.numecd.2011.03.009 PMID: 21745730

6. Godino JG, van Sluijs EM, Sutton S, Griffin SJ. Understanding perceived risk of type 2 diabetes in healthy middle-aged adults: A cross-sectional study of associations with modelled risk, clinical risk factors, and psychological factors. Diabetes Res Clin Pract. 2014; 106(3):412–419. doi: 10.1016/j.diabres.2014.10.004 PMID: 25467619

7. Zhang Y, Hu G, Zhang L, Mayo R, Chen L. A novel testing model for opportunistic screening of pre-diabetes and diabetes among U.S. adults. PLOS ONE. 2015; 10(3):e0120382. doi: 10.1371/journal.pone.0120382 PMID: 25790106

8. Buijsse B, Simmons RK, Griffin SJ, Schulze MB. Risk Assessment Tools for Identifying Individuals at Risk of Developing Type 2 Diabetes. Epidemiol Rev. 2011; 33(1):46–62. doi: 10.1093/epirev/mxq019 PMID: 21622851

9. Gray LJ, Taub NA, Khunti K, Gardiner E, Hiles S, Webb DR, et al. The Leicester Risk Assessment score for detecting undiagnosed Type 2 diabetes and impaired glucose regulation for use in a multi-ethnic UK setting. Diabetic Med. 2010; 27(Suppl 8):S87–S95. doi: 10.1111/j.1464-5491.2010.03037.x PMID: 20653746

10. Paulweber B, Valensi P, Lindstrom J, Lalic NM, Greaves CJ, McKee M, et al. A European Evidence-Based Guideline for the Prevention of Type 2 Diabetes. Horm Metab Res. 2010; 42(Suppl 1):S3–36. doi: 10.1055/s-0029-1240928 PMID: 20391306

11. Riaz M, Basit A, Hydrel MZ, Shaheen F, Hussain A, Hakeem R, et al. Risk assessment of Pakistani individuals for diabetes (RAPID). Prim Care Diabetes. 2012; 6(4):297–302. doi: 10.1016/j.pcd.2012.04.002 PMID: 22560662

12. U.S. Preventive Services Task Force. Screening for type 2 diabetes mellitus in adults: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2008; 148(11):846–854. doi: 10.7326/0003-4819-148-11-200806030-00007 PMID: 18519930.

13. Chatterton H, Younger T, Fischer A, Khunti K, Programme Development Group. Risk identification and interventions to prevent type 2 diabetes in adults at high risk: summary of NICE guidance. BMJ. 2012; 345:e6426. doi: 10.1136/bmj.e6426 PMID: 22791792

14. Canadian Task Force on Preventive Health Care, Pottie K, Jaramillo A, Lewin G, Dickinson J, Bell N, et al. Recommendations on screening for type 2 diabetes in adults. CMAJ. 2012; 184(15):1687–1696. doi: 10.1503/cmaj.120732 PMID: 23073674

15. Bhowmik B, Akhter A, Ali L, Ahmed T, Pathan F, Mahtab H, et al. Simple risk score to detect rural Asian Indian (Bangladeshi) adults at high risk for type 2 diabetes. J Diabetes Invest. 2015 Mar 28. doi: 10.1111/jdi.12344 PMID: 26543541

16. Chinese Center for Disease Control and Prevention. China Food Composition Table. 2nd ed. Beijing: Peking University Medical Press; 2009.

17. Chinese Nutrition Society. Chinese Dietary Guidelines. Lhasa: Tibet People Publishing House; 2008.

18. International Physical Activity Questionnaire: Short Last 7 Days Self-Administered Format 2005. 2015; 10: 1. Available: http://www.ipaq.ki.se/downloads.htm.

19. Wang CJ, Li YQ, Wang L, Li LL, Guo YR, Zhang LY, et al. Development and Evaluation of a Simple and Effective Prediction Approach for Identifying Those at High Risk of Dyslipidemia in Rural Adult Residents. PLOS ONE. 2012; 7(8):e43834. doi: 10.1371/journal.pone.0043834 PMID: 22952780

20. Doak CM, Hoffman DJ, Norris SA, Ponce MC, Polman K, Griffiths PL. Is body mass index an appropriate proxy for body fat in children? Global Food Security. 2013; 2(2):65–71. doi: 10.1016/j.gfs.2013.02.003
21. Cantin B, Lamarche B, Despres JP, Dagenais GR. Does correction of the Friedewald formula using lipoprotein(a) change our estimation of ischemic heart disease risk? The Quebec Cardiovascular Study. Atherosclerosis. 2002; 163(2):261–267. doi: 10.1016/S0021-9150(02)00034-5 PMID: 12052472.

22. Chinese Diabetes Society. Guideline for prevention and treatment of type 2 diabetes in Chinese (2013 edition). Chin J Endocrinol Metab. 2014; 30(10):893–942. Chin.ese. doi: 10.3760/cma.j.issn.1000-6699.2014.10.020

23. Gao WG, Dong YH, Pang ZC, Nan HR, Wang SJ, Ren J, et al. A simple Chinese risk score for undiagnosed diabetes[J]. Diabet Med. 2010; 27(3):274–281. doi: 10.1111/j.1464-5410.2010.02943.x PMID: 20536489

24. Lindstrom J, Tuomilehto J. The diabetes risk score: a practical tool to predict type 2 diabetes risk. Diabetes Care. 2003; 26(3):725–731. doi: 10.2337/diacare.26.3.725 PMID: 12610029

25. Al-Lawati JA, Tuomilehto J. Diabetes risk score in Oman: a tool to identify prevalent type 2 diabetes among Arabs of the Middle East. Diabetes Res Clin Pract. 2007; 77(3):438–444. doi: 10.1016/j.diabetres.2007.01.013 PMID: 17306410

26. Ramachandran A, Snehalatha C, Vijay V, Wareham NJ, Colagiuri S. Derivation and validation of diabetes risk score for urban Asian Indians. Diabetes Res Clin Pract. 2005; 70(1):63–70. doi: 10.1016/j.diarres.2005.02.016 PMID: 16126124

27. Wilson PW, Meigs JB, Sullivan L, Fox CS, Nathan DM, D'Agostino RB. Prediction of incident diabetes mellitus in middle-aged adults: the Framingham Offspring Study. Arch Intern Med. 2007; 167(10):1068–1074. doi: 10.1001/archinte.167.10.1068 PMID: 17533210

28. Delong ER, Delong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics. 1988; 44(3):837–845. doi: 10.2307/2531595 PMID: 3203132

29. Chien K, Cai T, Hsu H, Su T, Chang W, Chen M, et al. A prediction model for type 2 diabetes risk among Chinese people. Diabetologia. 2009; 52(4):443–450. doi: 10.1007/s00125-008-1232-4 PMID: 19057891

30. Liu XM, Liu YJ, Zhan J, He QQ. Overweight, obesity and risk of all-cause and cardiovascular mortality in patients with type 2 diabetes mellitus: a dose-response meta-analysis of prospective cohort studies. Eur J Epidemiol. 2015; 30(1):35–45. doi: 10.1007/s10654-014-9973-5 PMID: 25421785

31. Misra A, Ramachandran A, Jayawardena R, Shrivastava U, Snehalatha C. Diabetes in South Asians: Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). Diabetologia. 2006; 49(2):289–298. doi: 10.1007/s00125-005-0097-z PMID: 16391903

32. Yang F, Qian D, Chen J, Hu D, Hou M, Chen S, et al. Prevalence, awareness, treatment and control of diabetes mellitus in rural China: results from Shandong Province. Diabetic Med. 2016; 33(4):454–458. doi: 10.1111/dmbe.12842 PMID: 26108553

33. Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V, et al. The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). Diabetes Care. 2006; 29(1):267–273. doi:10.2337/diacare.29.1.267 PMID: 16126124

34. Li GW, Zhang P, Wang JP, Gregg EW, Yang WY, Gong QH, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. Lancet. 2008; 371(9626):1783–1789. doi: 10.1016/S0140-6736(08)60766-7 PMID: 18502303

35. Diabetes Prevention Program Research Group; Knowler WC, Fowler SE, Hamman RF, Christofi CA, Hoffman HJ, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet. 2009; 374(9707):1677–1686. doi: 10.1016/S0140-6736(09)61475-4 PMID: 19878968

36. Lindstrom J, Ilanez-Parikka P, Peltonen M, Auniola S, Eriksson JG, Hemio K, et al. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. Lancet. 2006; 368(9548):1673–1679. doi: 10.1016/S0140-6736(06)69701-8 PMID: 17098085

37. Gillies CL, Abrams KR, Lambert PC, Cooper NJ, Sutton AJ, Hsu RT, et al. Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. BMJ. 2007; 334(7588):299. doi: 10.1136/bmj.39063.689375.55 PMID: 17237299

38. Chaissong JL, Josse RG, Gomis R, Hanefeld M, Karasik A, Laakso M. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. Lancet. 2002; 359(9323):2072–2077. doi: 10.1016/S0140-6736(02)08903-5 PMID: 12086760

39. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002; 346(6):393–403. doi: 10.1056/NEJMoa012512 PMID: 11832527
40. Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilian-ne-Parikka P, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med. 2001; 344(18):1343–1350. doi: 10.1056/nejm200105033441801 PMID: 11333990

41. Gerstein HC, Yusuf S, Bosch J, Pogue J, Sheridan P, Dincacag N, et al. Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. Lancet. 2006; 368(9541):1096–1105. doi: 10.1016/s0140-6736(06)69420-8 PMID: 16997664

42. Sun F, Tao Q, Zhan S. An accurate risk score for estimation 5-year risk of type 2 diabetes based on a health screening population in Taiwan. Diabetes Res Clin Pract. 2009; 85(2):228–234. doi: 10.1016/j.diabetres.2009.05.005 PMID: 19500871

43. NCD Risk Factor Collaboration. Effects of diabetes definition on global surveillance of diabetes prevalence and diagnosis: a pooled analysis of 96 population-based studies with 331 288 participants. Lancet Diabetes Endocrinol. 2015; 3(8): 624–637. doi: 10.1016/S2213-8587(15)00129-1 PMID: 26109024

44. American Diabetes Association. Standards of medical care in diabetes—2013. Diabetes Care. 2013; 36(Suppl 1):S1–66. doi: 10.2337/dc13-S001 PMID: 23264422

45. Adegbija O, Hoy W, Wang Z. Predicting absolute risk of type 2 diabetes using age and waist circumference values in an aboriginal Australian community. PLOS ONE. 2015; 10(4):e0123788. doi: 10.1371/journal.pone.0123788

46. Bozorgmanesh M, Hadaegh F, Ghaffari S, Harati H, Azizi F. A simple risk score effectively predicted type 2 diabetes in Iranian adult population: population-based cohort study. Eur J Public Health. 2011; 21(5):554–559. doi: 10.1093/eurpub/ckq074 PMID: 20534689.

47. Norberg M, Eriksson JW, Lindahl B, Andersson C, Rolandsson O, Stenlund H, et al. A combination of HbA1c, fasting glucose and BMI is effective in screening for individuals at risk of future type 2 diabetes: OGTT is not needed. J Intern Med. 2006; 260(3):263–271. doi: 10.1111/j.1365-2796.2006.01689.x PMID: 16918624

48. Guasch-Ferre M, Buillo M, Costa B, Martinez-Gonzalez MA, Ibarrola-Jurado N, Estruch R, et al. A Risk Score to predict type 2 diabetes mellitus in an elderly Spanish Mediterranean population at high cardiovascular risk. PLOS ONE. 2012; 7(3):e33437. doi: 10.1371/journal.pone.0033437 PMID: 22442692

49. Muhlener K, Ludwig T, Jeppesen C, Joost HG, Rathmann W, Meisinger C, et al. Update of the German Diabetes Risk Score and external validation in the German MONICA/KORA study. Diabetes Res Clin Pr. 2014; 104(3):459–466. doi: 10.1016/j.diabres.2014.03.013 PMID: 24742930

50. Aekplakorn W, Bunng P, Woodward M, Sritara P, Cheepudomwit S, Yamwong S, et al. A risk score for predicting incident diabetes in the Thai population. Diabetes Care. 2006; 29(8):1872–1877. doi: 10.2337/diacare.2005-2141 PMID: 16873795

51. Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, et al. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. N Engl J Med. 2001; 345(11):790–797. doi: 10.1056/NEJmoa0104922 PMID: 11568298

52. Kahn HS, Cheng YJ, Thompson TJ, Imperatore G, Gregg EW. Two Risk-Scoring Systems for Predicting Incident Diabetes Mellitus in US Adults Age 45 to 64 Years. Ann Inter Med. 2009; 150(11):741–751. doi: 10.7326/0003-4819-150-11-200906020-00002 PMID: 19467709

53. Schmidt MI, Duncan BB, Bang H, Pankow JS, Ballantyne CM, Golden SH, et al. Identifying individuals at high risk for diabetes: The Atherosclerosis Risk in Communities study. Diabetes Care. 2005; 28(8):2013–2018. doi: 10.2337/diacare.28.8.2013 PMID: 16043747

54. Bansal N. Prediabetes diagnosis and treatment: A review. World J Diabetes. 2015; 6(2):296–303. doi: 10.4239/wjd.v6.i2.296 PMID: 25789110

55. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee, Goldenberg R, Punthakee Z. Definition, Classification and Diagnosis of Diabetes, Prediabetes and Metabolic Syndrome. Can J Diabetes. 2013; 37 (Suppl 1):S8–11. doi: 10.1016/j.jcjd.2013.01.011 PMID: 24070969

56. Schulze MB, Hoffmann K, Boeing H, Linseisen J, Rohrmann S, Mohlig M, et al. An accurate risk score based on anthropometric, dietary, and lifestyle factors to predict the development of type 2 diabetes. Diabetes Care. 2007; 30(3):510–515. doi: 10.2337/dc06-2089 PMID: 17327313

57. Mashayekhi M, Prescod F, Shah B, Dong LY, Keshavjee K, Guergachi A. Evaluating the Performance of the Framingham Diabetes Risk Scoring Model in Canadian Electronic Medical Records. Can J Diabetes. 2015; 39(2):152–156. doi: 10.1016/j.jcjd.2014.10.006 PMID: 25577729

58. He S, Chen X, Cui K, Peng Y, Liu K, Lv Z, et al. Validity evaluation of recently published diabetes risk scoring models in a general Chinese population. Diabetes Res Clin Pract. , 2012; 95(2):291–298. doi: 10.1016/j.diabres.2011.10.039 PMID: 22129653
59. Babyak MA. What you see may not be what you get: a brief, nontechnical introduction to overfitting in regression-type models. Psychosom Med. 2004; 66(3):411–421. PMID: 15184705

60. Peduzzi P, Concato J, Feinstein AR, Holford TR. The importance of events per independent variable in multivariable analysis, II: accuracy and precision of regression estimates. J Clin Epidemiol. 1995; 48(12):1503–1510. doi: 10.1016/0895-4356(95)00048-8 PMID: 8543964

61. Mathur R, Noble D, Smith D, Greenhalgh T, Robson J. Quantifying the risk of type 2 diabetes in East London using the QDScore: a cross-sectional analysis. Br J Gen Pract. 2012; 62(603):e663–670. doi: 10.3399/bjgp12X656793 PMID: 23265225

62. Qiao Q, Nakagami T, Tuomilehto J, Borch-Johnsen K, Balkau B, Iwamoto Y, et al. Comparison of the fasting and the 2-h glucose criteria for diabetes in different Asian cohorts. Diabetologia. 2000; 43(12):1470–1475 doi: 10.1007/s001250051557 PMID: 11151755