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Development and validation of a non-invasive assessment tool for screening prevalent undiagnosed diabetes in middle-aged and elderly Chinese

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ABSTRACT

To develop a non-invasive assessment tool and compare it to other assessment tools among middle-aged and elderly Shanghainese, 15,309 individuals, who were 45–70 years old, not previously diagnosed with diabetes, and from a cross-sectional survey conducted between April 2013 and August 2014 in Shanghai, were selected into this study. The participants were randomly assigned to either the exploratory group or the validation group. Undiagnosed diabetes was defined according to the American Diabetes Association diagnostic criteria, and score points were generated according to the logistic regression coefficients. Age, family history of diabetes, hypertension, overweight/obesity, and central obesity all contributed to the constructed model, the Shanghai Nicheng diabetes screening score, with the area under the receiver-operating characteristic curve (AUC) being 0.654 (95% CI 0.637–0.670) in the exploratory group and 0.669 (95% CI 0.653–0.686) in the validation group. The score value of 6 was the optimal cut-point with the largest Youden's index. When applied to the validation group, our model had a similar discriminative ability to the New Chinese Diabetes Risk Score (AUC: 0.669 vs. 0.662, $p = 0.187$), and performed better than other screening scores for Chinese. However, our model was inferior to fasting plasma glucose, 2-hour plasma glucose, and glycosylated hemoglobin in detecting prevalent undiagnosed diabetes (AUC: 0.669 (0.653–0.686) vs. 0.881 (0.868–0.894), 0.934 (0.923–0.944), and 0.834 (0.819–0.848), all $p < 0.001$). Although non-invasive models, based on demographic and clinical information, are advisable in resource-scarce developing areas, regular blood glucose screening is still necessary among those aged 45 or older.

1. Introduction

Diabetes is prevalent worldwide, and as many as half (50.0%) of the population with diabetes went undiagnosed according to the 2017 International Diabetes Federation report (International Diabetes Federation, 2017). The China Chronic Disease and Risk Factors Surveillance study conducted in 2013 showed that the prevalence of diabetes was 10.4% in China and that 63.5% of participants with diabetes were unaware that they had this disease (Wang et al., 2017). The previous study revealed that up to half of people with undiagnosed diabetes exhibited one or more macrovascular or microvascular complications at the time of diagnosis (Harris, 1993) and that the identification and treatment of diabetes at an earlier stage would have greatly reduced the risk of cardiovascular morbidity and mortality (Herman et al., 2015). Therefore, practical screening tools to detect diabetes early in the general population or in some certain populations at high risk of diabetes would be of great value, in light of the scarce health resources and heavy public health burden that diabetes brings to China.

As is shown in many epidemiology studies and clinical trials, timely intervention and treatment could delay the development and progression of microvascular and macrovascular complications in participants

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with newly diagnosed diabetes (Knowler et al., 2009; Pan et al., 1997). There were some established multi-risk scoring systems and models to assess the risk of incident diabetes (Aekplakorn et al., 2006; Balkau et al., 2008; Chen et al., 2010; Heianza et al., 2012; Hippisley-Cox et al., 2009; Kahn et al., 2009; Lindstrom and Tuomilehto, 2003; Wen et al., 2017) or undiagnosed diabetes (Al-Lawati and Tuomilehto, 2007; Bang et al., 2009; Gao et al., 2010; Glumer et al., 2004; Lee et al., 2012; Zhou et al., 2017; Zhou et al., 2013) for different ethnicities. The tools used in screening for diabetes could usually be divided into three categories: (1) non-invasive self-assessment tools; (2) routine clinical biochemical tests; (3) new-type biomarkers and genetic markers. The latter two methods are invasive, time-consuming, and inconvenient. Although fasting plasma glucose (FPG), 2-hour plasma glucose (2-h PG) after 75 g oral glucose tolerance test (OGTT), and glycosylated hemoglobin (HbA1c) are most appropriate for diagnosing diabetes (American Diabetes Association, 2017), blood glucose tests are not easy to perform on the general population due to their cost and inconvenience. Despite lower accuracy than clinical diagnosis methods, non-invasive screening models are more practical and economically effective for the general population. Currently, most screening score models have been built for Caucasians (Balkau et al., 2008; Bang et al., 2009; Chen et al., 2010; Glumer et al., 2004; Hippisley-Cox et al., 2009; Kahn et al., 2009; Lindstrom and Tuomilehto, 2003), while some models have been developed for Asians (Aekplakorn et al., 2006; Heianza et al., 2012; Lee et al., 2012), and a few models have been established in China (Gao et al., 2010; Wen et al., 2017; Zhou et al., 2017; Zhou et al., 2013). Note that the efficacy of different models was affected by their study population characteristics, such as race/ethnicity, age range of study population, exposure features of risk factors, all of which led to each screening score model performing better in their study population than in others and limited these models' generalizability to other populations. Therefore, it is important to explore different screening tools for different populations. Also, evaluating these screening models in the target population is the first step of population intervention.

In this study, we aimed to develop a non-invasive, convenient, and inexpensive assessment tool, i.e., the Shanghai Nicheng diabetes screening score, to identify prevalent cases of undiagnosed diabetes among middle-aged and elderly Shanghainese, and to compare the efficacy of different screening tools for undiagnosed prevalent diabetes in our validation group.

2. Methods

2.1. Study population

As described elsewhere (Chen et al., 2018; Hou et al., 2018), the Shanghai Nicheng Cohort Study was designed to investigate the prevalence, incidence and related factors of cardiometabolic diseases in the residential population aged 45–70 years in Nicheng suburb, a new industrial zone developing from a rural county located in the east of Shanghai. We conducted the baseline survey between April 2013 and August 2014. The target population covered 23,375 residents, of which 21,408 residents were invited to participate in this survey. A total of 17,212 people finished the baseline survey. We excluded participants without data for body mass index (BMI) or waist circumference (n = 175), FPG, 2-h PG or HbA1c (n = 103), blood pressure (n = 4), history of hypertension (n = 5), family history of diabetes (n = 8), participants with previous diagnosis of diabetes (n = 1426), and participants with severe liver and kidney diseases (n = 131). Finally, 15,309 participants with BMI and waist circumference between the 0.1th and 99.9th percentiles ($16.2\,kg/m^2 \le BMI \le 37.3\,kg/m^2$ and $57.0\,cm \le$ waist circumference $\le 116.0\,cm$) were included; see Fig. 1 for the participation flowchart. The independent ethics committee of the Shanghai Sixth People's Hospital has approved the study. Written informed consent was obtained from each participant before the start of the study.

2.2. Data collection and definition of variables for statistical analysis

All participants were invited to the health center of each block or village at around 6:00 am to participate in this survey. The medical staff of the Nicheng community health center was trained to be qualified as investigative staff for this survey. Participants were interviewed about their demographic information, lifestyle (smoking, drinking, physical activities at leisure time), medical history of diabetes, cardiovascular disease (CVD), and family history of diabetes using a standard questionnaire. We classified participants as current smokers if they had smoked at least one cigarette per day for the past year, and as current drinkers if they had consumed at least 1 g of alcohol per week for the past year. Family history of diabetes was defined as having one or more first-degree relatives with diabetes (parents, siblings, or offspring). History of CVD was defined as having a medical diagnosis of coronary heart disease or stroke (Yang et al., 2012). Low education level was defined as primary school or lower, and high education level was defined as middle school or above.

Height and weight were measured without shoes and in light clothes, and BMI (kg/m^2) was calculated as weight in kilograms divided by height in meters squared. Blood pressure was measured twice by mercury sphygmomanometer and the average was calculated. Waist circumference was measured at the midpoint between the lowest rib and the iliac crest on the mid-axillary line.

After an overnight fast of at least 10 h, venous blood samples were obtained for measuring FPG, HbAlc, total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C). Individuals without known diabetes underwent a 75 g OGTT and venous blood samples were drawn at 120 min. Plasma glucose level was determined by glucose oxidase method (7600-120 Hitachi automatic analyzer, Hitachi Inc., Tokyo, Japan), HbA1c was assayed by high-performance liquid chromatography (VARIANT II, Bio-Rad Laboratories, Inc., Hercules, USA), and TC, TG, and HDL-C were measured with the colorimetry method (7600-120 Hitachi automatic analyzer, Hitachi Inc., Tokyo, Japan).

According to the 2010 American Diabetes Association (ADA) criteria, prevalent undiagnosed diabetes was defined as FPG ≥ 7.0 mmol/L and/or 2-h PG ≥ 11.1 mmol/L, and/or HbAlc ≥6.5% among those participants without previously diagnosed diabetes (American Diabetes Association, 2010). Hypertension was defined as systolic blood pressure/diastolic blood pressure ≥ 140/90 mm Hg (≥18.7/12.0 kPa) or having a history of hypertension (Liu, 2011). Elevated TG was TG ≥ 150 mg/dL (1.7 mmol/L) and reduced HDL-C was HDL-C < 40 mg/dL (1.0 mmol/L) in men and 50 mg/dL (1.3 mmol/L) in women. Dyslipidemia was defined as elevated TG and/or reduced HDL-C (Alberti et al., 2009). Central obesity was defined as waist circumference ≥ 90 cm in men or ≥ 85 cm in women (Alberti et al., 2009). Overweight or obesity was defined as BMI ≥ 25 kg/m^2.

2.3. Statistical analysis

Statistical analyses were performed using Stata/MP (version 14.0, StataCorp LP, College Station, Texas, USA), SPSS (version 22.0, SPSS Inc., Chicago, Illinois, USA) and MedCalc (version15.2.2, Med-Calc, Inc., Mariakerke, Belgium). Descriptive statistics were presented as means (standard deviations) for continuous variables or numbers (percentages) for categorical variables. Multivariable logistic regression analysis was used to compare the difference in means or percentages between the two groups with and without undiagnosed diabetes and to calculate the corresponding odds ratio (OR). A two-tailed p-value < 0.05 was considered to be statistically significant.

Participants were stratified by gender and age group (with a 5-year interval); participants at each stratum were then randomly allocated to the exploratory group (n = 7658) or the validation group (n = 7651). The model was then developed in the exploratory group and the efficacy of the model was evaluated in the validation group. First, we

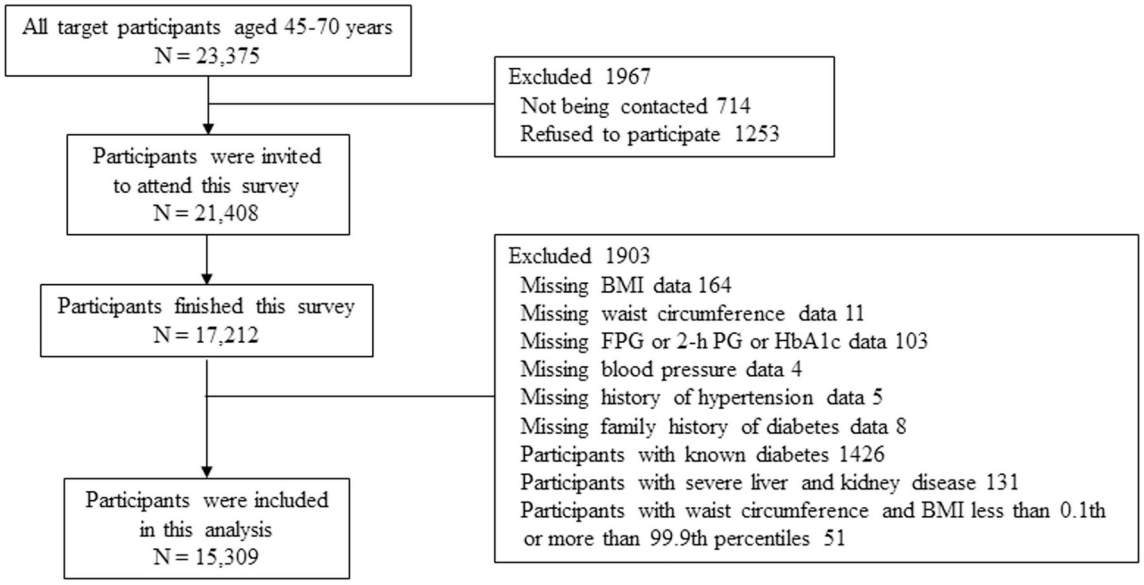


Fig. 1. Participation flowchart.
FPG, fasting plasma glucose; 2-h PG, 2-hour plasma glucose; HbAlc, glycosylated hemoglobin; BMI, body mass index.

assessed potential factors (non-laboratory variables) associated with prevalent undiagnosed diabetes using the binary logistic regression analysis after adjustment for age and sex. Then, the variables associated with undiagnosed diabetes with a two-tailed p-value < 0.2 were selected to construct the final model using the multivariable logistic regression model with the backward stepwise method. Finally, of the 11 variables tested (sex, age group, education level, physical activity, drinking status, smoking status, history of CVD, hypertension, family history of diabetes, overweight/obesity, and central obesity), age, family history of diabetes, hypertension, overweight/obesity, and central obesity were retained in the final model, i.e., the Shanghai Nicheng diabetes screening score. Additionally, we assessed the interaction effect between overweight/obesity and central obesity on the undiagnosed diabetes.

The performance of the screening tools was evaluated according to the area under the curve (AUC) using a receiver operating characteristics curve. The final model with the least variables and the best goodness of fit was derived according to the Hosmer-Lemeshow (HL) goodness-of-fit test (a measure of calibration, where an HL $\chi 2$ statistic < 20 represents good calibration with a p-value ≥0.01), Akaike's information criterion and Bayesian information criterion (measures of goodness of fit). The score points associated with each variable in the final model were calculated according to the logistic regression coefficients with the minimum value of the logistic regression coefficient being 1 and the other logistic regression coefficients divided by the minimum value in round numbers. The optimal cut-point was determined on the basis of the maximum of the Youden's index (sensitivity plus specificity minus 1) (Al-Lawati and Tuomilehto, 2007), with approximately equal weight being given to sensitivity and specificity.

We compared the performance of the Shanghai Nicheng diabetes screening score with other screening scores for Chinese in the validation group using AUC. We also compared the AUC of our model with those of FPG, 2-h PG, and HbA1c in the validation group.

We performed two sensitivity analyses. First, the performance of the screening score was tested for men and women separately. Second, when undiagnosed diabetes was defined according to the OGTT test (1999 WHO criteria: FPG ≥ 7.0 mmol/L and/or 2-h PG ≥ 11.1 mmol/L), another screening score was derived and validated.

3. Results

Table 1 presents the characteristics of participants with prevalent undiagnosed diabetes and without diabetes. Among the 15,309 participants, 54.6% were female and 15.3% had undiagnosed diabetes. After adjustment only for age, there was no difference in gender proportions between two groups (p = 0.921). After adjustment for sex, participants with undiagnosed diabetes tended to be older than those without diabetes. After adjustment for both age and sex, compared to those without diabetes, the participants with undiagnosed diabetes had higher proportions of family history of diabetes, hypertension, and current drinkers but a lower proportion of current smokers (p < 0.05). Participants with undiagnosed diabetes had higher FPG, 2-h PG, HbA1c, BMI, waist circumference, TG, and reduced HDL-C (all p < 0.001) than those without diabetes.

Table 2 shows the logistic regression coefficients and score points of the final model constructed with the non-laboratory variables. The final model included 5 variables: age, family history of diabetes, hypertension, overweight/obesity, and central obesity. Considering that there is no interaction between overweight/obesity and central obesity (p = 0.584, data not shown), and the model with both obesity variables had better discrimination than those with only one obesity variable (AUC: 0.654 vs. overweight/obesity: 0.650, central obesity: 0.644, p < 0.001), we selected the model with both obesity variables. In the exploratory and the validation groups, the AUCs of the model were 0.654 (95% CI 0.637–0.670) and 0.669 (95% CI 0.653–0.686); and HL χ^2 statistics of the model were 17.76 (p = 0.023) and 5.80 (p = 0.670). The two HL χ^2 statistics indicated that diabetes discriminative ability of the model was the same in the two groups. The score point of 6 was the optimal cut-point to predict undiagnosed diabetes with the largest Youden's index (the sensitivity and specificity of the score for detecting undiagnosed diabetes were 64.3% and 58.7% in the exploratory group, 65.5% and 58.7% in the validation group).

We compared the discrimination of the Shanghai Nicheng diabetes screening score with other published models for Chinese in the validation group (Table 3). Our screening score had similar AUC with the New Chinese Diabetes Risk Score (AUC: 0.669 vs. 0.662, p = 0.187), but had significantly higher discriminative ability than other screening

Table 1
Socio-demographic, lifestyle, clinical and biological characteristics of participants with and without undiagnosed diabetes in the cross-sectional survey.

Variables	Without diabetes 12,965 (84.7)	Undiagnosed diabetes[e] 2344 (15.3)	Age- and sex-adjusted OR[b]	95% CI[b]
Sex				
Men	5878 (45.3)	1069 (45.6)	1.00[c]	
Women	7087 (54.7)	1275 (54.4)	1.00[c]	(0.91–1.09)[c]
Age group, years				
45–49	2621 (20.2)	295 (12.6)	1.00[d]	
50–54	3136 (24.2)	483 (20.6)	1.37[d]	(1.17–1.60)[d]
55–59	3095 (23.9)	597 (25.5)	1.71[d]	(1.48–1.99)[d]
60–70	4113 (31.7)	969 (41.3)	2.09[d]	(1.82–2.41)[d]
Education levels				
Low	6154 (47.5)	1273 (54.3)	1.00	
High	6660 (51.4)	1041 (44.4)	0.93	(0.84–1.03)
Physical activity				
< 30 min/day	12,244 (94.4)	2218 (94.6)	1.00	
≥30 min/day	721 (5.6)	126 (5.4)	0.94	(0.77–1.14)
Current drinker				
No	10,958 (84.5)	1934 (82.5)	1.00	
Yes	2007 (15.5)	410 (17.5)	1.20	(1.05–1.38)
Current smoker				
No	9794 (75.5)	1843 (78.6)	1.00	
Yes	3171 (24.5)	501 (21.4)	0.79	(0.69–0.90)
History of CVD				
No	12,492 (96.4)	2257 (96.3)	1.00	
Yes	440 (3.4)	85 (3.6)	0.94	(0.74–1.19)
Hypertension				
No	7175 (55.3)	847 (36.1)	1.00	
Yes	5790 (44.7)	1497 (63.9)	2.05	(1.87–2.25)
TG, mmol/L				
< 1.7	9091 (70.1)	1219 (52.0)	1.00	
≥1.7	3874 (29.9)	1125 (48.0)	2.21	(2.02–2.41)
HDL-C, mmol/L				
≥1.0/1.3 (men/women)	8614 (66.4)	1408 (60.1)	1.00	
< 1.0/1.3 (men/women)	4351 (33.6)	936 (39.9)	1.39	(1.26–1.52)
Dyslipidemia				
No	6960 (53.7)	913 (39.0)	1.00	
Yes	6005 (46.3)	1431 (61.0)	1.91	(1.74–2.09)
Family history of diabetes				
No	11,369 (87.7)	1867 (79.7)	1.00	
Yes	1596 (12.3)	477 (20.3)	1.96	(1.75–2.20)
BMI				
Normal	7505 (57.9)	963 (41.1)	1.00	
Overweight	4857 (37.5)	1136 (48.5)	1.82	(1.65–1.99)
Obesity	603 (4.7)	245 (10.5)	3.13	(2.66–3.69)
Central obesity				
No	8335 (64.3)	1145 (48.8)	1.00	
Yes	4630 (35.7)	1199 (51.2)	1.83	(1.67–2.00)
FPG, mmol/L[a]	5.7 (0.5)	7.3 (1.8)	17.54[f]	(15.63–19.68)[f]
2-h PG, mmol/L[a]	7.1 (1.7)	13.1 (4.1)	29.75[f]	(25.96–34.09)[f]
HbAlc, %[a]	5.5 (0.4)	6.5 (1.5)	14.03[f]	(12.51–15.74)[f]

OR, odds ratio; CI, confidence interval; CVD, cardiovascular disease; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; BMI, body mass index; FPG, fasting plasma glucose; 2-h PG, 2-hour plasma glucose; HbAlc, glycosylated hemoglobin.
Participants are residents of Shanghai aged 45–70 years who were surveyed between April 2013 and August 2014.
Data are presented as frequency (percentage), except [a]Mean (standard deviation).
[b]Odds ratios (95% CI) were adjusted for age and sex by binary logistic regression, except [c]Odds ratio (95% CI) was adjusted only for age and [d] odds ratio (95% CI) was adjusted only for sex.
[e]Undiagnosed diabetes: FPG ≥ 7.0 mmol/L and/or 2-h PG ≥ 11.1 mmol/L, and/or HbAlc ≥ 6.5% but with no previous diagnosis of diabetes.
[f]Odds ratio (95% CI) per standard deviation.

scores (AUC: 0.669 vs. 0.635–0.644, $p < 0.001$).

Fig. 2 shows the performance of the Shanghai Nicheng diabetes screening score and each of the following blood glucose indexes: FPG, 2-h PG, and HbAlc for detecting undiagnosed diabetes. The AUC of the Shanghai Nicheng diabetes screening score was significantly smaller than those of FPG, 2-h PG, and HbAlc (AUC: 0.669 (0.653–0.686) vs. 0.881 (0.868–0.894), 0.934 (0.923–0.944), and 0.834 (0.819–0.848), all $p < 0.001$).

Supplemental Table S1 shows the characteristics of the exploratory group and the validation group.

Sensitivity analysis: (1) Performance of the assessment tool separately for men and women is presented in Supplemental Table S2. The AUCs for men and women were 0.654 (95% CI 0.629–0.680) and 0.684 (95% CI 0.662–0.705), respectively. (2) When the undiagnosed diabetes was diagnosed according to the OGTT criteria, the Shanghai Nicheng diabetes screening score (according to OGTT) was developed and its performance was assessed (shown in Supplemental Tables S3–S5 and Supplemental Fig. S1). Supplemental Table S3 presents the characteristics of participants with prevalent undiagnosed diabetes and without diabetes. Supplemental Table S4 shows the logistic regression

Table 2
Logistic regression coefficients and score points for undiagnosed diabetes.

Variables	OR	95% CI	Logistic regression coefficient	Score point
Age group, years				
45–49	1.00		–	0
50–54	1.19	(0.96–1.47)	0.170	1
55–59	1.40	(1.14–1.73)	0.339	2
60–70	1.55	(1.27–1.88)	0.437	3
Family history of diabetes				
No	1.00		–	0
Yes	1.83	(1.55–2.16)	0.604	4
BMI				
Normal	1.00		–	0
Overweight	1.41	(1.21–1.65)	0.347	2
Obesity	2.04	(1.56–2.66)	0.711	4
Central obesity				
No	1.00		–	0
Yes	1.25	(1.07–1.46)	0.225	1
Hypertension				
No	1.00		–	0
Yes	1.74	(1.52–1.99)	0.555	3

OR, odds ratio; CI, confidence interval; BMI, body mass index.

coefficients and score points of the final model. Supplemental Table S5 shows comparisons of discrimination of the Shanghai Nicheng diabetes screening score (according to OGTT) with other models for Chinese in the validation group. Supplemental Fig. S1 shows comparisons of performance of the Shanghai Nicheng diabetes screening score (according to OGTT) with the three blood glucose indexes for detecting undiagnosed diabetes. The Shanghai Nicheng diabetes screening score model developed using OGTT comprised the same risk factors and had a similar AUC (0.668, 95% CI 0.651–0.685) as that developed according to the 2010 ADA criteria (0.669, 95% CI 0.653–0.686) in the validation group.

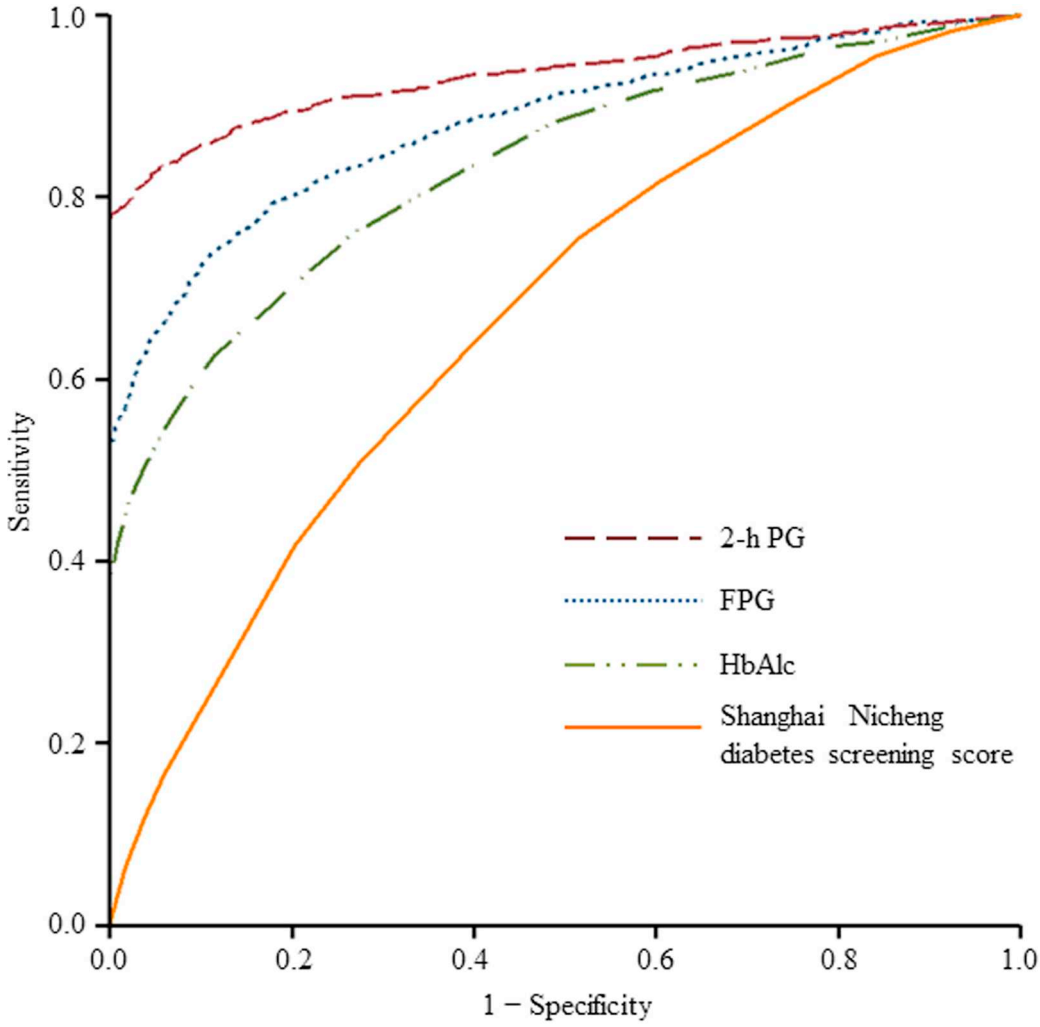
4. Discussion

As the main non-modifiable risk factors of diabetes (Bang et al., 2009; Lindstrom and Tuomilehto, 2003; Zhou et al., 2013), the two variables of age and family history of diabetes were included in most of the diabetes screening score models, as well as in the Shanghai Nicheng diabetes screening score. Glucose tolerance progressively declines with age, and prevalence of type 2 diabetes significantly increased with ageing (Chang and Halter, 2003). Family history of diabetes reflects not only genetic predisposition (Rich, 1990), but also common living environment. The risk of diabetes significantly increased in those with family history of diabetes than in those without, and further increased in those with more first-degree relatives with diabetes (Zhang et al., 2015). Among modifiable risk factors, obesity is an established and important risk factor for type 2 diabetes (Pan et al., 1997). Some researchers argued that Asian populations are more prone to be abdominally obese (Deurenberg et al., 2002). Waist circumference, reflecting central obesity, is a useful indicator of risk of type 2 diabetes for Asians (Chan et al., 2009). Meanwhile, we also found that waist circumference and BMI were independent predictors of undiagnosed diabetes, and that there is no interaction between each other. The final model included the two obesity indices, which reflect general obesity and central obesity, respectively. Our model also showed that hypertension is associated with the prevalence of diabetes. In our study, lifestyle factors such as physical activity, smoking, and drinking were excluded because of statistical insignificance. We used categorical variables instead of continuous variables to develop a simple model for use in the general population. Our non-invasive self-assessment tool was composed of age group, first-degree family history of diabetes, hypertension, overweight/obesity, and central obesity. Compared with the New Chinese

Table 3
Performance of the Shanghai Nicheng diabetes screening score and other published scores for screening diabetes in the Chinese population.

Screening score model	Factors in the model	AUC (95% CI)	Cut-off value	Sensitivity (95% CI)	Specificity (95% CI)	Likelihood ratio (+)	Likelihood ratio (−)	Youden's index
Shanghai Nicheng diabetes screening score	Age, family history of diabetes, BMI, central obesity, hypertension	0.669 (0.653–0.686)	6	65.5 (62.7–68.3)	58.7 (57.5–59.9)	1.59 (1.5–1.7)	0.59 (0.5–0.6)	0.242
New Chinese Diabetes Risk Score (Zhou et al., 2013)	Age, sex, history of diabetes in parent, sibling, or children, BMI, waist circumference, systolic blood pressure	0.662 (0.646–0.679)	30	70.5 (67.7–73.1)	53.0 (51.8–54.2)	1.50 (1.4–1.6)	0.56 (0.5–0.6)	0.235
Qingdao diabetes risk score (Gao et al., 2010)	Age, history of diabetes in parent or sibling, waist circumference	0.635 (0.618–0.652)	16	68.6 (65.9–71.3)	51.0 (49.8–52.2)	1.40 (1.3–1.5)	0.62 (0.6–0.7)	0.196
RuralDiab risk score (Zhou et al., 2017)	Age, sex, family history of diabetes, history of dyslipidemia, physical activity, BMI, waist circumference, diastolic blood pressure	0.644 (0.627–0.661)	18	56.7 (53.7–59.6)	64.3 (63.1–65.5)	1.59 (1.5–1.7)	0.67 (0.6–0.7)	0.210

AUC, area under the receiver-operating characteristic curve; CI, confidence interval; BMI, body mass index.



	2-h PG	FPG	HbAlc	Shanghai Nicheng diabetes screening score
AUC (95% CI)	0.934 (0.923–0.944)	0.881 (0.868–0.894)	0.834 (0.819–0.848)	0.669 (0.653–0.686)

Fig. 2. The performance of FPG, 2-h PG, HbAlc and the Shanghai Nicheng diabetes screening score for detecting undiagnosed diabetes in the validation population. Red line, 2-h PG (AUC 0.934); blue line, FPG (AUC 0.881); green line, HbA1c (AUC 0.834); yellow line, the Shanghai Nicheng diabetes screening score (AUC 0.669). 2-h PG, 2-hour plasma glucose; FPG, fasting plasma glucose; HbAlc, glycosylated hemoglobin; AUC, area under the receiver-operating characteristic curve; CI, confidence interval. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Diabetes Risk Score, the Shanghai Nicheng diabetes screening score performed similarly in discriminating diabetes (AUC: 0.669 vs. 0.662, $p = 0.187$) with fewer variables included and simpler categories of variables, which also has been defined as presence of disease, for example, central obesity (yes/no) vs. six categories of waist circumference.

In our study population, aged ≥45 years old and with > 15% prevalence of undiagnosed diabetes, the AUC of our assessment tool was significantly lower than that of FPG, 2-h PG, and HbA1c (AUC: 0.669 (0.653–0.686) vs. 0.881 (0.868–0.894), 0.934 (0.923–0.944), and 0.834 (0.819–0.848), $p < 0.001$). The American Diabetes Association recommends people be screened for the development of diabetes every three years beginning at age 45 (American Diabetes Association, 2017). Our study showed that aside from non-invasive screening scores, regularly screening for diabetes using plasma glucose is also necessary in the middle-aged and the elderly. In accordance with the hyperglycemic characteristics of the population with undiagnosed diabetes (among the total population, 77.5% with elevated 2-h PG, 52.8% with elevated FPG, and 38.6% with elevated HbA1c), our results showed that the AUC of 2-h PG for discriminating diabetes was the largest. This highlighted the importance of testing 2-h PG in the Chinese population.

The individuals at higher risk of diabetes were identified when their total screening score points exceeded the optimal cut-off value (Aekplakorn et al., 2006; Balkau et al., 2008; Bang et al., 2009; Gao et al., 2010; Hippisley-Cox et al., 2009). When designing detection plans and risk thresholds, AUC, sensitivity, and specificity should not be the only matters taken into consideration; screening goals, medical costs, and feasibility of the prevention plan are also important to consider. Given the lack of health resources per capita and the massive population of China, the development of a non-invasive self-assessment

tool is essential. Additionally, generalizing the screening score to the general population could increase awareness of diabetes in the general public and alert the high-risk population.

Our study had the following three advantages: (1) It was a population-based study, and the large size of the statistical sample (N = 15,039) allowed for random selection of two subsamples for development and validation of the tool within the population it is intended to be used; (2) Diabetes was diagnosed by OGTT and HbAlc criteria; (3) Considering the difficulty of doing OGTT or HbAlc test in the general population, it is valuable to use a simple model to notify people at high risk of prevalent undiagnosed diabetes.

However, there were still some limitations. First, this was a cross-sectional study which does not allow us to estimate diabetes risk and identify predictive factors; for this purpose, cohort-design is needed. Second, the screening score was based on middle-aged and elderly residents in one suburb of Shanghai, which made it unsuitable to directly apply to other populations. Third, the discriminant capacity of the model was not ideal.

5. Conclusion

In conclusion, developing non-invasive convenient simple self-assessment models for the target population is a good first step to identify individuals with an increased likelihood of having prevalent undiagnosed diabetes, but regularly testing for diabetes using blood glucose, especially 2-h PG, is still recommended in middle-aged and elderly Chinese.

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Conflict of interest

None declared.

Author contributions

WJ, XH, JW, and YB made substantial contributions to the conception and design of the study. WJ, XH, JW, LC, PC, LW, and FJ assisted in the acquisition and interpretation of data. JW and XH analysed the data. WJ, JW, XH, and LC drafted the manuscript. All the authors contributed to the critical revision of the manuscript for important intellectual content and approved the final version.

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