The HKU Scholars Hub The University of Hong Kong 香港大學學術庫



Title	Simple Non-laboratory- and Laboratory-based Risk Assessment Algorithms and Nomogram for Detecting Undiagnosed Diabetes Mellitus
Author(s)	Wong, CKH; Siu, SC; Wan, EYF; Jiao, FF; Yu, EYT; Fung, CSC; Wong, KW; Leung, AYM; Lam, CLK
Citation	Journal of Diabetes, 2016, v. 8 n. 3, p. 414-421
Issued Date	2016
URL	http://hdl.handle.net/10722/209798
Rights	This is the accepted version of the following article: Journal of Diabetes, 2016, v. 8 n. 3, p. 414-421, which has been published in final form athttp://onlinelibrary.wiley.com/doi/10.1111/1753- 0407.12310/abstract; This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Recto running head: Undiagnosed diabetes algorithms and nomogram Verso running head: C.K.H. WONG et al.

Correspondence

Carlos KH Wong, Department of Family Medicine & Primary Care, The University of Hong Kong, 3/F, Ap Lei Chau Clinic, 161 Ap Lei Chau Main Street, Ap Lei Chau, Hong Kong. Tel.: +852 2518 5688 Fax: +852 2814 7475 Email: carlosho@hku.hk Received: 5 November 2014; revised 26 March 2015; accepted 5 May 2015 © 2015 Wiley Publishing Asia Pty Ltd and Ruijin Hospital, Shanghai Jiaotong University Sch ool of Medicine

Original Article

Simple non-laboratory- and laboratory-based risk assessment algorithms and nomogra m for detecting undiagnosed diabetes mellitus

Carlos K.H. WONG,¹ Shing-Chung SIU,³ Eric Y.F. WAN,¹ Fang-Fang JIAO,¹ Esther Y.T. YU, ¹ Colman S.C. FUNG,¹ Ka-Wai WONG,³ Angela Y.M. LEUNG,² and Cindy L.K. LAM¹ ¹Department of Family Medicine and Primary Care, ²School of Nursing, The University of Ho ng Kong, and ³Department of Medicine and Rehabilitation, Tung Wah Eastern Hospital, Hong Kong

Abstract

Background: The aim of the present study was to develop a simple nomogram that can be u sed to predict the risk of diabetes mellitus (DM) in the asymptomatic non-diabetic subjects ba sed on non-laboratory- and laboratory-based risk algorithms.

Methods: Anthropometric data, plasma fasting glucose, full lipid profile, exercise habits, an d family history of DM were collected from Chinese non-diabetic subjects aged 18–70 years. Logistic regression analysis was performed on a random sample of 2518 subjects to construct non-laboratory- and laboratory-based risk assessment algorithms for detection of undiagnosed DM; both algorithms were validated on data of the remaining sample (n = 839). The Hosme r–Lemeshow test and area under the receiver operating characteristic (ROC) curve (AUC) wer e used to assess the calibration and discrimination of the DM risk algorithms.

Results: Of 3357 subjects recruited, 271 (8.1%) had undiagnosed DM defined by fasting gl ucose \geq 7.0 mmol/L or 2-h post-load plasma glucose \geq 11.1 mmol/L after an oral glucose tolera nce test. The non-laboratory-based risk algorithm, with scores ranging from 0 to 33, included age, body mass index, family history of DM, regular exercise, and uncontrolled blood pressur e; the laboratory-based risk algorithm, with scores ranging from 0 to 37, added triglyceride le vel to the risk factors. Both algorithms demonstrated acceptable calibration (Hosmer–Lemesh ow test: P = 0.229 and P = 0.483) and discrimination (AUC 0.709 and 0.711) for detection of undiagnosed DM.

Conclusion: A simple-to-use nomogram for detecting undiagnosed DM has been developed using validated non-laboratory-based and laboratory-based risk algorithms.

- Significant findings of the study: Validated non-laboratory- and laboratory-based risk assessment algorithms were developed for the prediction of undiagnosed DM in a Chi nese population. The optimal cut-off point on the ROC curve was 18 for the detection of undiagnosed DM in both algorithms.
- What this study adds: The simple and user-friendly nomogram was constructed to ena ble clinicians to estimate an individual's risk of DM and thus to promote targeted scree ning for DM among high-risk individuals in the primary care and community settings.

Key words: calibration, discrimination, nomogram, risk algorithm, undiagnosed diabetes, vali dation.

<A>Introduction

Diabetes mellitus (DM) is highly prevalent and has become one of the major disease burdens worldwide.¹ In particular, undiagnosed DM is associated with a higher risk of diabetes-related complications² and mortality³ compared with normal glucose tolerance because of the lack of awareness of high blood glucose levels and delayed disease management. Early detection of DM through periodic screening has been recommended⁴ for high-risk individuals using 75-g o ral glucose tolerance tests (OGTT), fasting plasma glucose (FPG) tests or HbA1c levels. In a r ecent cost-effectiveness analysis, screening for DM and prediabetes was found to be cost-savi ng among patients at risk compared with no screening.⁵ Nevertheless, a targeted screening app roach based on risk assessment and stratification of high-risk subjects should be undertaken to optimize resource allocation and utilization.⁶

In order to stratify high-risk subjects for DM screening, risk algorithms for the detection of undiagnosed DM have been developed and validated in different populations and healthcar e settings.^{6–9} However, these risk score algorithms are population specific; the combination of risk factors in each algorithm varies across countries, ethnicities, and levels of income based o n the population in which these algorithms were developed. For the Chinese population,^{10–13} most of the risk algorithms^{11–13} were derived from results of laboratory tests, in addition to so ciodemographic and anthropometric data. Interestingly, the majority of these Chinese DM risk algorithms were developed and validated in low income settings.^{10–12} Little is known about th eir performance, calibration, and discrimination in the detection of undiagnosed DM among C hinese populations in non-low income settings. Furthermore, no nomograms for the identificat ion of undiagnosed DM have been developed, which would be an ideal, simple-to-use graphic al tool to facilitate DM risk assessment and stratification in clinical practice and the communit y setting.

The aims of this study were to present and validate a non-laboratory- and laboratory-bas ed risk assessment algorithm for detecting undiagnosed DM among the Chinese population in a non-low income setting. In addition, a simple and user-friendly nomogram was constructed t o enable clinicians to estimate individual DM risk based on non-laboratory and laboratory risk assessment algorithms. Both tools could inform clinical decision making and enable identific ation of individuals at high risk for DM to undergo further screening tests, thus promoting the early detection of DM in the clinical and community settings. In addition, the study provides i nformation on modifiable risk factors to be targeted by health intervention programs for the re duction of individual DM risk.

<A>Methods

Subjects for the development of risk assessment algorithms

This study was part of a Hong Kong professional driver community project to promote health awareness and literacy regarding DM. Details regarding subject recruitment, eligibility criteri a, and interviews have been reported previously.^{14–16}

Subjects were excluded if they self-reported to have clinician-diagnosed DM. For each e ligible subject, we retrieved DM risk factor data, including sociodemographic characteristics, lifestyle, past medical history and family history, which were surveyed through structured inte rview questionnaires. Sociodemographic data included the age, gender, and marital status of t he subjects. For lifestyle factors, we considered self-reported drinking status, smoking status, and exercise frequency. For past medical history, gestational DM was defined by self-reported high blood glucose levels during pregnancy in women without a known diagnosis of DM. A s elf-reported history of hypertension was recorded. A positive family history of DM was define d as either first-degree (parents or siblings) or second-degree (grandparents) relatives having DM.

In addition, anthropometric and laboratory assessments were performed on each subject at baseline. For anthropometric assessment, we measured body mass index (BMI), systolic bl ood pressure (SBP), diastolic blood pressure (DBP), and waist circumference. Blood samples were taken for the measurement of FPG and 2-h post-load plasma glucose in the 75-g OGTT t o determine glycemic status, as well as to determine the full lipid profile, including triglycerid es (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-densit y lipoprotein cholesterol (LDL-C), to assess DM risk. Plasma glucose, TG, TC, and HDL-C w ere measured using the Abbott Architect c16000 chemistry analyzer, whereas LDL-C was deri ved from the Friedewald formula.

Undiagnosed DM was defined as subjects with FPG \geq 7.0 mmol/L or 2-h post-load plas ma glucose \geq 11.1 mmol/L in the 75-g OGTT.

Development and validation of risk assessment algorithms

In all, 3357 subjects completed the questionnaire survey and underwent anthropometric and la boratory assessment during the study period. Simple random sampling was performed to selec t 2518 subjects from the total number of subjects (75% of the total sample) as the developmen t sample. The remaining 25% formed the validation sample.

Data from the development sample (n = 2518) on the following DM risk factors were us ed to develop the risk assessment model: (i) sociodemographic and lifestyle risk factors, inclu ding age (<45, \geq 45–<50, \geq 50–<55, \geq 55–<60, and \geq 60 years), gender, smoking status (active s moker), and exercise frequency; (ii) non-laboratory clinical risk factors, including family hist ory of DM, history of hypertension, obesity (BMI \geq 25 kg/m²), central obesity (waist circumfe rence \geq 80 cm for women and \geq 90 cm for men), and uncontrolled blood pressure (SBP \geq 140 m mHg or DBP \geq 90 mmHg); and (iii) laboratory risk factors, including TG, TC, HDL-C, and LD L-C. Sociodemographic and non-laboratory clinical risk factors were used for the developmen t of the non-laboratory-based risk assessment algorithm. Laboratory risk factors were added to sociodemographic and non-laboratory clinical risk factors for the development of the laborato ry-based risk assessment algorithm.

Based on undiagnosed DM as the outcome, significant risk factors with P < 0.05 in a ste pwise binary logistic regression model were retained in the final risk assessment model. Each risk factor was assigned a weighting in the risk score using respective β -coefficients multipli ed by 10 and rounded to the nearest integer. The risk score for each subject would be the sum of risk score contributed by each risk factor identified by the final risk assessment model.

Non-laboratory- and laboratory-based risk assessment algorithms were validated externa lly using data for the remaining 839 subjects in the validation sample; these subjects had not b een used for algorithm development. The accuracy, calibration, and discrimination of the risk algorithms to detect undiagnosed DM were compared against six previously published DM ris k assessment algorithms,^{10,12,13, 17–19} of which three were developed in Chinese populations (N ew Chinese Diabetes Risk Score,¹⁰ Qingdao Diabetes Risk Score,¹² and Southern Chinese Risk K Score¹³).

Design of a nomogram

Both risk assessment algorithms were then converted into a nomogram (Fig. 1). With regard t o the design of the nomogram, the score for each characteristic for each subject was mapped d irectly on the nomogram using the rule located at the top of the nomogram (Fig. 1). The score s obtained for each characteristic are summed to compute the total DM risk score based on the risk assessment algorithm. Total DM risk scores are mapped in the lower part of the nomogram m to predict the prevalence of undiagnosed DM.

Data analysis

Descriptive statistics of baseline characteristics between development and validation samples were compared using independent *t*-tests for continuous variables and Chi-squared tests for ca tegorical variables.

Risk algorithms were developed and modeled using a stepwise binary logistic regressio n model. The goodness-of-fit of the two models was assessed by Akaike information criterion (AIC) and Bayesian information criterion (BIC) statistics, with the lower values indicating bet ter fit. For each risk algorithm, Youden's index was used to determine the optimal cut-off valu e for detecting undiagnosed DM.²⁰ Accuracy in terms of sensitivity and specificity of the use of risk algorithms at optimal cut-off values for detecting undiagnosed DM were compared wit h diagnosis confirmed by FPG or OGTT as the diagnostic standard. The Hosmer–Lemeshow χ^2 statistic and area under the receiver operating characteristic (ROC) curve (AUC) were use d to assess the calibration and discrimination of these risk algorithms.

All analyses were conducted using SPSS version 20.0 for Windows (IBM Inc., Chicago, IL, USA) and STATA version 13 (STATA Corporation, College Station, TX, USA). Two-side d P < 0.05 was considered significant.

<A>Results

Descriptive characteristics of the 3357 study subjects overall and by analysis samples are pres ented in Table 1. Of 3357 subjects without a prior history of DM, 271 (8.1%) had undiagnose d DM. The prevalence of undiagnosed DM between the development and validation samples did not differ significantly (8.3% vs 7.3%; P = 0.325). The mean (± SD) age of subjects was 5 0.9 ± 7.6 years. Most subjects were male (92.7%) and non-smokers (80.5%). In terms of non-1 aboratory-based clinical characteristics, 31.4% of subjects had a family history of DM, 51.2% had general obesity, 48.1% had central obesity, and 32.2% had uncontrolled blood pressure w ith either SBP >140 mmHg or DBP >90 mmHg; 12.8% of subjects had history of hypertensio n and the subjects in the validation sample were more likely to have hypertension than those i n the development sample. There were no significant differences in laboratory-based clinical c haracteristics between the development and validation samples. For model development based on stepwise binary logistic regression (non-laboratory- vs laboratory-based), there was a significant association between undiagnosed DM and increasin g age for each 5-year stratum from 45 to 60 years (β -coefficient 0.49–1.10 vs 0.19–1.12), ge neral obesity (β -coefficient 0.45 vs 0.35), a positive family history of DM in a first- or secon d-degree relative (β -coefficient 0.72 vs 0.70), exercising regularly (β -coefficient 0.60 vs 0.57), and uncontrolled blood pressure (β -coefficient 0.54 vs 0.0.52). Abnormal TG was signific antly associated with undiagnosed DM in the regression analysis for the laboratory-based risk assessment algorithm. Significant risk factors were used to assign weighted scores, and the tot al risk score for each subject was the sum of all risk scores allocated to each individual risk fa ctor. The scores for non-laboratory- and laboratory-based risk assessment algorithms ranged fr om 0 to 33 and from 0 to 37, respectively. Youden's index suggesting the optimal cut-off valu e for undiagnosed DM was 18 for both risk assessment algorithms. At the optimal cut-off valu e ≥ 18 , the sensitivity and specificity were 57.9% and 68.9%, respectively, for the non-laboratory-based algorithm.

For the external validation of models, the AUC for the non-laboratory- and laboratory-b ased algorithms was 0.709 and 0.711, respectively, supporting model discrimination. The Hos mer–Lemeshow test with P > 0.05 (0.229 and 0.483, respectively) indicated adequate calibrati on of the non-laboratory- and laboratory-based algorithms. Using the validation sample, the se nsitivity and specificity at the optimal cut-off value ≥ 18 for the non-laboratory-based risk algorithm were 63.9% and 67.7%, respectively, whereas those of the laboratory-based risk algorithm mere 72.1% and 57.8%, respectively.

Compared with existing risk algorithms, the risk algorithms developed in the present stu dy exhibited adequate accuracy, discrimination, and calibration. Figure 1 shows the nomogra m that graphically calculated the non-laboratory- and laboratory-based risk scores. The lower part of the nomogram shows the predicted probability of the individual having undiagnosed D M in both routine clinical practice and the community setting. From the nomogram, the predic ted prevalence of undiagnosed DM increases gradually from 1% at a total risk score of 0 to 34 % at a total risk score of 33.

<A>Discussion

The present study developed and validated simple non-laboratory- and laboratory-based risk a ssessment algorithms for predicting undiagnosed DM in the general Chinese population. Base d on the risk assessment algorithms, we developed a simple-to-use nomogram (Fig. 1) for pri mary care clinicians to facilitate risk sharing in such a way that high-risk subjects are identifie d to promote the uptake of DM screening. In addition to risk information sharing, this risk ass essment facilitates the health service provider prioritizing DM prevention strategies and launc hing DM screening in the primary care setting when resources for glycemic testing are limited. Moreover, risk stratification identified high-risk subjects, who were then encouraged to under go DM screening using the most appropriate screening test. Screened subjects were empower ed to increase their awareness of DM and to make lifestyle modifications.

Risk scores with cut-off values ≥ 18 had the best combination of sensitivity and specifici ty for detecting undiagnosed DM. Therefore, subjects with risk scores ≥ 18 were considered to be high-risk subjects recommended to undergo DM screening. Visualization of the nomogra m has important implications for clinicians and subjects. For example, the predicted probabilit y of undiagnosed DM is approximately 15% if subjects score 23 on the non-laboratory-based risk assessment algorithm.

The National Prevalence Health Survey of 46 239 adults in 14 provinces in China found that the prevalence of undiagnosed DM was 6.3%,²¹ and a survey conducted in a nationally re presentative sample of 98 658 Chinese adults reported a prevalence of 8.1% in 2010.²² The pr evalence of undiagnosed DM found in the development (8.3%) and validation (7.3%) samples in the present study is comparable to that in the Chinese population. Thus, the prevalence of undiagnosed DM in the present study was comparable to the Hong Kong prevalence of 9.51%,

as estimated by the International Diabetes Federation.²³

The non-laboratory-based risk assessment algorithm was constructed on the basis of fiv e widely recognized risk factors: age, BMI, family history of DM, exercise frequency, and blo od pressure. This is in line with recent systematic reviews^{7,8} of newly developed risk assessme nt algorithms reporting that the frequently included risk factors are age and BMI, representing measures of body mass. Age group was a main contributor to the risk score for the detection of undiagnosed DM, because we observed a trend for increasing risk score with increasing ag e. Interestingly, there were two modifiable risk factors recognized in our algorithms: BMI and exercise frequency. This implies that health intervention programs, such as body weight moni toring and control and lifestyle interventions, are useful in reducing DM risk in asymptomatic subjects in the Chinese population.

Although the risk factors identified in our algorithms are mostly found in existing algori thms summarized by systematic reviews,^{7,8} there are no existing risk algorithms using the sam e pool of risk factors. Risk factors may be presented in other forms and using alternative defin itions. It should be highlighted that there is no universal consensus regarding the combination of risk factors to be used for the detection of undiagnosed diabetes. Notably, the risk algorith ms developed in one country may not be transferable to other counties, reflected by the poor a bility to calibrate and discriminate the external dataset. For example, two risk algorithms^{12,13} d eveloped using the Chinese population did not have satisfactory performance, with an AUC of ≥ 0.7 in our dataset upon external validation; this could be due, in part, to differences in inco me levels. However, recent studies^{24,25} have not found any clear indication that the addition of ethnicity improves the performance of risk algorithms for predicting diabetes. Therefore, furt her research is required to improve the performance through the additional effects of alternati ve key information, such as spousal history of diabetes.²⁶

A high degree of model discrimination does not necessarily imply identification of true positive diabetes cases. Upon external validation of existing algorithms developed using Cauc

asian populations, the AUC of the algorithm of Bang et al. was <0.7.¹⁷ Even though the discri mination of another two algorithms^{18,19} was greater than that of our algorithms, those algorith ms did not achieve a good trade-off between sensitivity and specificity at predefined optimal c ut-off values. For both algorithms,^{18,19} the specificities were unacceptably low although the se nsitivities were at least 90%. Hence, a high degree of discrimination does not necessarily lead to reasonable performance at recommended cut-off values. In such cases, when an algorithm h as a high degree of discrimination upon external validation, new recommended cut-off values may help balance sensitivity and specificity.

The laboratory-based risk assessment algorithm increased the number of risk factors by including factors such as TG; however, this algorithm may not be able to stratify risks of asy mptomatic subjects without prior laboratory testing. Nevertheless, such an algorithm is likely to be used when identifying high-risk subjects in the routine clinical setting, where blood sam ples are routinely collected for lipid profile assessment.

Limitations

Several limitations of present study should be noted. First, our risk algorithms were developed and validated using Chinese data, so they may not be generalizable to non-Chinese populatio ns. However, only two previous studies^{27,28} included ethnicity in their algorithms, indicating t hat ethnicity is not a common predictive factor for the prediction of diabetes. Second, there w as a high proportion (92.7%) of male professional drivers in our development and validation s amples.

Conclusions

In summary, validated risk assessment algorithms were developed for the prediction of undiag nosed DM in a Chinese population. A corresponding simple-to-use nomogram was constructe d to facilitate risk information sharing and to promote targeted screening for DM among high-

risk individuals in the primary care and community settings. Future studies on the evaluation of our risk algorithms and nomogram to examine the feasibility and validity of their use in tar geted community-based screening for DM are warranted.

<A>Acknowledgements

The authors thank Harriet HY Chung and Kelvin Wong for subject recruitment and data collec tion. Special thanks are extended to Anca Chan for plotting and editing the nomogram.

<A>Disclosure

None declared.

<A>References

- Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. Global estimates of diabetes prevalence for 2013 and projections for 2035. *Diabetes Research and Clinical Practice*. 2014; 103: 137–49.
- 2. Plantinga LC, Crews DC, Coresh J, et al. Prevalence of chronic kidney disease in US adults with undiagnosed diabetes or prediabetes. *Clinical Journal of the American Soc iety of Nephrology*. 2010; 5: 673–82.
- Wild SH, Smith FB, Lee AJ, Fowkes FGR. Criteria for previously undiagnosed diabet es and risk of mortality: 15-year follow-up of the Edinburgh Artery Study cohort. *Dia betic Medicine*. 2005; 22: 490–6.
- American Diabetes Association. Standards of medical care in diabetes–2014. *Diabetes Care*. 2014; 37: S14–S80.
- 5. Chatterjee R, Narayan KMV, Lipscomb J, et al. Screening for diabetes and prediabetes should be cost-saving in patients at high risk. *Diabetes Care*. 2013; 36: 1981–7.
- 6. Buijsse B, Simmons RK, Griffin SJ, Schulze MB. Risk assessment tools for identifyin

g individuals at risk of developing type 2 diabetes. *Epidemiologic Reviews*. 2011; 33: 46–62.

- Brown N, Critchley J, Bogowicz P, Mayige M, Unwin N. Risk scores based on self-re ported or available clinical data to detect undiagnosed type 2 diabetes: A systematic re view. *Diabetes Research and Clinical Practice*. 2012; 98: 369–85.
- Collins GS, Mallett S, Omar O, Yu LM. Developing risk prediction models for type 2 diabetes: A systematic review of methodology and reporting. *BMC Medicine*. 2011; 9: 103.
- Thoopputra T, Newby D, Schneider J, Li SC. Survey of diabetes risk assessment tools: concepts, structure and performance. *Diabetes/Metabolism Research and Reviews*. 20 12; 28: 485–98.
- Zhou X, Qiao Q, Ji L, et al. Nonlaboratory-based risk assessment algorithm for undiag nosed type 2 diabetes developed on a nation-wide diabetes survey. *Diabetes Care*. 201 3; 36: 3944–52.
- Liu M, Pan C, Jin M. A Chinese diabetes risk score for screening of undiagnosed diab etes and abnormal glucose tolerance. *Diabetes technology & therapeutics*. 2011; 13: 5 01–7.
- 12. Gao WG, Dong YH, Pang ZC, et al. A simple Chinese risk score for undiagnosed diab etes. *Diabetic Medicine*. 2010; 27: 274–81.
- Ko G, So W, Tong P, et al. A simple risk score to identify southern Chinese at high risk for diabetes. *Diabetic Medicine*. 2010; 27: 644–9.
- Siu SC, Wong KW, Lee KF, et al. Prevalence of undiagnosed diabetes mellitus and car diovascular risk factors in Hong Kong professional drivers. *Diabetes Research and Cl inical Practice*. 2012; 96: 60–7.
- 15. Wong CKH, Fung CSC, Siu SC, et al. The impact of work nature, lifestyle, and obesit y on health-related quality of life in chinese professional drivers. *Journal of Occupati*

onal and Environmental Medicine. 2012; 54: 989-94.

- Wong CKH, Fung CSC, Siu SC, et al. A short message service (SMS) intervention to prevent diabetes in Chinese professional drivers with pre-diabetes: A pilot single-blind ed randomized controlled trial. *Diabetes Research and Clinical Practice* 2013; 102: 1 58–66.
- 17. Bang H, Edwards AM, Bomback AS, et al. Development and validation of a patient se lf-assessment score for diabetes risk. *Annals of Internal Medicine*. 2009; 151: 775–83.
- Cabrera de León A, Coello SD, Rodríguez Pérez MdC, et al. A simple clinical score fo r type 2 diabetes mellitus screening in the Canary Islands. *Diabetes research and clini cal practice*. 2008; 80: 128–33.
- Heianza Y, Arase Y, Saito K, et al. Development of a screening score for undiagnosed diabetes and its application in estimating absolute risk of future type 2 diabetes in Japa n: Toranomon Hospital Health Management Center Study 10 (TOPICS 10). *The Journ al of Clinical Endocrinology & Metabolism*. 2013; 98: 1051–60.
- 20. Youden WJ. Index for rating diagnostic tests. *Cancer*. 1950; 3: 32–5.
- Yang W, Lu J, Weng J, et al. Prevalence of diabetes among men and women in China. New England Journal of Medicine. 2010; 362: 1090–101.
- Xu Y, Wang L, He J, et al. Prevalence and control of diabetes in chinese adults. *JAMA*. 2013; 310: 948–59.
- 23. Beagley J, Guariguata L, Weil C, Motala AA. Global estimates of undiagnosed diabete s in adults. *Diabetes Research and Clinical Practice*. 2014; 103: 150–60.
- 24. Rosella LC, Mustard CA, Stukel TA, et al. The role of ethnicity in predicting diabetes risk at the population level. *Ethnicity & Health*. 2012; 17: 419–37.
- 25. Tanamas SK, Magliano DJ, Balkau B, et al. The performance of diabetes risk predicti on models in new populations: The role of ethnicity of the development cohort. *Acta Diabetol*. 2015; 52: 91–101.

- 26. Leong A, Rahme E, Dasgupta K. Spousal diabetes as a diabetes risk factor: A systemat ic review and meta-analysis. *BMC Medicine*. 2014; 12: 12.
- 27. Heikes KE, Eddy DM, Arondekar B, Schlessinger L. Diabetes risk calculator: A simpl e tool for detecting undiagnosed diabetes and pre-diabetes. *Diabetes Care*. 2008; 31: 1 040–5.
- 28. Bindraban N, van Valkengoed I, Mairuhu G, et al. Prevalence of diabetes mellitus and the performance of a risk score among Hindustani Surinamese, African Surinamese an d ethnic Dutch: A cross-sectional population-based study. *BMC Public Health*. 2008; 8: 271.

Figure 1 Nomogram to predict the probability of undiagnosed diabetes based on non-labora tory- and laboratory-based risk algorithms. The patient's score for each parameter is plotted o n the appropriate scale and vertical lines are drawn to the line of points to obtain the corresponding scores. All scores are summed to obtain a total points score. The total points score is plotted on the total points line and a vertical line is drawn down to the bottom line. The corresponding value shows the predicted probability of undiagnosed diabetes.

	Total (n = 3357)	Model development sar	P-value	
		ple (n = 2518)	mple (n = 839)	
Sociodemographic characteristics				
Age (years)				0.113
<45	637 (19.0%)	501 (19.9%)	136 (16.2%)	
\geq 45 and \leq 50	767 (22.8%)	571 (22.7%)	196 (23.4%)	
\geq 50 and <55	789 (23.5%)	595 (23.6%)	194 (23.1%)	
\geq 55 and <60	747 (22.3%)	541 (21.5%)	206 (24.6%)	
≥60	417 (12.4%)	310 (12.3%)	107 (12.8%)	
Gender				0.816
Female	246 (7.3%)	183 (7.3%)	63 (7.5%)	

Table 1Sociodemographic and clinical characteristics of subjects without a known history of diabetes in the model development and validation samples

Male	3111 (92.7%)	2335 (92.7%)	776 (92.5%)	
Exercise regularly	1480 (44.1%)	1089 (43.3%)	391 (46.6%)	0.092
Smoking	653 (19.5%)	485 (19.3%)	168 (20.0%)	0.629
Clinical characteristics				
Undiagnosed diabetes	271 (8.1%)	210 (8.3%)	61 (7.3%)	0.325
Family history of diabetes	1053 (31.4%)	778 (30.9%)	275 (32.8%)	0.310
Gestational diabetes ^A	19 (7.7%)	17 (9.3%)	2 (3.2%)	0.117
Hypertension	429 (12.8%)	305 (12.1%)	124 (14.8%)	0.045*
WC (cm)	89.1 ± 8.2	89.0 ± 8.3	89.5 ± 8.2	0.105
Central obesity (WC \geq 90 cm men;	1616 (48.1%)	1196 (47.5%)	420 (50.1%)	0.198
\geq 80 cm women)				
BMI (kg/m ²)	25.4 ± 3.4	25.3 ± 3.4	25.6 ± 3.4	0.094
General obesity (BMI \geq 25 kg/m ²)	1719 (51.2%)	1270 (50.4%)	449 (53.5%)	0.122
SBP (mmHg)	132.4 ± 15.9	132.2 ± 15.9	133.0 ± 16.1	0.242
DBP (mmHg)	80.3 ± 10.7	80.1 ± 10.7	80.8 ± 10.7	0.113
Suboptimal BP (SBP >140 or DBP	1082 (32.2%)	810 (32.2%)	272 (32.4%)	0.893
>90 mmHg)				
FPG (mmol/L)	5.4 ± 1.4	5.4 ± 1.5	5.3 ± 1.2	0.160
TG (mmol/L)	1.7 ± 1.3	1.7 ± 1.3	1.7 ± 1.1	0.997
TC (mmol/L)	5.4 ± 1.0	5.4 ± 1.0	5.4 ± 0.9	0.470
HDL-C (mmol/L)	1.2 ± 0.3	1.2 ± 0.3	1.2 ± 0.3	0.652
LDL-C (mmol/L)	3.5 ± 0.9	3.5 ± 0.9	3.5 ± 0.8	0.477

Data are given as the mean \pm SD or as the number of subjects with percentages in parentheses . Asterisks indicate a significant difference (P < 0.05) between the development and validatio n samples (independent *t*-test or Chi-squared test, as appropriate).

^AOnly for women (n = 246).

BMI, body mass index; BP, blood pressure; SBP, systolic BP; DBP, diastolic BP; TC, total ch olesterol; TG, triglycerides; FPG, fasting plasma glucose; WC, waist circumference.

Table 2 Risk factors and their respective risk scores for non-laboratory- and laboratory	ry-base
--	---------

d risk assessment algorithms based on the development sample

Factors	Non laboratory based algorithm I aboratory based algorithm									
Factors	INOII-18	luora	iory-based at	gonum		Lau	nator	y-based algo	01101111	
	β-Coefficient	OR	95% (CI)	P-value	Score	β -Coefficient	OR	95% (CI)	P-value	Score
Age (years)										
<45	-	1	_	-	0	-	1	_	-	0
$\geq\!45$ and ${<}50$	0.49	1.63	(0.98, 2.73)	0.061	5	0.49	1.63	(0.98, 2.73)	0.062	5
$\geq\!50$ and $<\!\!55$	0.58	1.79	(1.08, 2.97)	0.024*	6	0.59	1.80	(1.09, 2.99)	0.022*	6

\geq 55 and <60	0.83	2.30 (1.39, 3.80) 0.001*	8	0.84	2.31 (1.39, 3.83) 0.001*	8
$\geq\!60$	1.10	3.02 (1.74, 5.23) <0.001*	11	1.12	3.06 (1.76, 5.30) < 0.001*	11
BMI (kg/m ²)						
<25	_	1 – –	0	_	1 – –	0
\geq 25	0.45	1.56 (1.16, 2.11) 0.003*	4	0.35	1.43 (1.05, 1.94) 0.024*	4
Family history of diabe	etes					
No	_	1 – –	0	_	1 – –	0
Yes	0.72	2.05 (1.53, 2.75) <0.001*	7	0.70	2.02 (1.51, 2.71) <0.001*	7
Exercise regularly						
Yes	_	1 – –	0	_	1 – –	0
No	0.60	1.82 (1.34, 2.48) <0.001*	6	0.57	1.76 (1.29, 2.41) <0.001*	6
Suboptimal blood pres	sure					
No	_	1 – –	0	_	1 – –	0
Yes	0.54	1.71 (1.28, 2.30) <0.001*	5	0.52	1.69 (1.25, 2.27) 0.001*	5
Triglyceride (mmol/L)						
<1.7		Not considered		_	1 – –	0
≥1.7				0.43	1.53 (1.14, 2.07) 0.005*	4
Goodness-of-fit						
AIC		1, 381			1, 375	
BIC		1, 433			1,433	

AIC, Akaike information criterion; BIC, Bayesian information criterion; BMI, body mass ind ex; CI, confidence interval; OR, odds ratio.

Table 3	Accuracy, discrimination and calibration of the risk algorithms developed in the present study and existing risk algorithms	using the de
velopmen	t (internal validation) and validation (external validation) samples	

Risk algorithm	Optimal cut-off value (ra	AUC (95% CI)	Sensitivity (%) at cut-off v	Specificity (%) at cutoff	Hosmer-Lemeshow te
	nge)		alue (95% CI)	value (95% CI)	st
Present study					
Internal validation ($n = 2518$)					
Non-laboratory-based algorithm	18 (0–33)	0.686 (0.650, 0.722)	57.9 (51.8, 63.9)	68.9 (67.3, 70.6)	0.159
Laboratory-based algorithm	18 (0–37)	0.696 (0.661, 0.731)	66.2 (59.4, 72.6)	60.2 (58.2, 62.2)	0.053
External validation $(n = 839)$					
Non-laboratory-based algorithm	18 (0–33)	0.709 (0.646, 0.773)	63.9 (50.6, 75.8)	67.7 (64.3, 71.0)	0.229
Laboratory-based algorithm	18 (0–37)	0.711 (0.648, 0.774)	72.1 (59.2, 82.9)	57.8 (54.3, 61.3)	0.483
Existing algorithms					
New Chinese Diabetes risk score [10]	25 (0-51)	0.708 (0.644, 0.772)	98.4 (91.2, 100.0)	15.0 (12.6, 17.7)	0.730
Qingdao Diabetes risk Score [12]	Men 17 (3-32)	0.672 (0.602, 0.742)	75.4 (62.7, 85.5)	53.1 (49.5, 56.6)	0.383
	Women 14 (3-32)				
Southern Chinese Risk score [13]	16 (0–30)	0.664 (0.595, 0.734)	49.2 (36.1, 62.3)	75.2 (72.0, 78.2)	0.208
Spanish Diabetes Risk score [18]	100 (unspecified)	0.728 (0.669, 0.788)	100.0 (94.1, 100.0)	0.1 (0.0, 0.7)	0.935
Patient Self-Assessment score [17]	5 (-1–9)	0.675 (0.607, 0.743)	37.7 (25.6, 51.0)	82.5 (79.7, 85.1)	0.986
TOPICS Diabetes Screening score [19]	8 (0–16)	0.723 (0.663, 0.784)	91.8 (81.9, 97.3)	33.2 (29.9, 36.6)	0.320

NA, not applicable; AUC, area under the receiver operating characteristic curve; TOPICS, Toranomon Hospital Health Management Center Stud

y; CI, confidence interval.