The Development and Validation of a Diabetes Risk Score for High-Risk Thai Adults

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Objective: *To develop a simple risk score to identify high-risk individuals for diabetes screening in Thailand.*
Material and Method: *The authors analyzed data from 75-g oral glucose tolerance tests performed in 159 males and 270 females, aged 48.4 $\pm$ 10.9 years.*
Results: *The independent variables associated with diabetes included age ($p < 0.001$), BMI ($p < 0.01$) and known history of hypertension (HHT) ($p < 0.01$). The risk equation was Y = 3age + 5BMI +50HHT. At the cut-off Y value of 240, the sensitivity and specificity for having diabetes were 96.8% and 24.0%, respectively. The positive predictive value was 17.8% and the negative predictive value was 97.8%. Using the equation in a validation group comprising 1617 subjects, it was found that 560 (34.6%) diabetes screenings could be saved while 28 subjects (12.8%) with diabetes would be missed.*
Conclusion: *The authors have developed a simple risk scoring method that should be helpful in decreasing the number of unnecessary screening and optimizing the costs associated with diabetes screening.*

Keywords: *Diabetes screening, Risk score*

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The prevalence of diabetes, a growing global health problem, is increasing rapidly worldwide. It is projected that the number of adults with diabetes in the world will rise from 135 million in 1995 to 300 million in the year 2025[1]. Patients with type 2 diabetes are at increased risk for both microvascular and macrovascular diseases. Microvascular disease contributes to blindness[2], end-stage renal disease[3], and lower extremity amputations[4,5]. Diabetes also accounts for a 2 to 4-fold increased risk for heart disease and stroke[6,7]. Early treatment of diabetes and the associated cardiovascular risk factors such as hypertension, obesity and dyslipidemia can reduce the occurrence of these complications[8].

In Thailand, the estimated national prevalence of diabetes in adults was 9.6%, which included 4.8% previously diagnosed and 4.8% newly diagnosed diabetes. The prevalence of impaired fasting glucose was 5.4%[9]. This suggests that diabetes is common in Thailand but one-half of all cases are undiagnosed. Universal screening for diabetes in the general population may not be cost-effective and therefore not recommended. The ADA Expert Committee recommended screening for diabetes in subjects at high risk for development of diabetes[10]. A number of investigators have developed screening tools based on risk scores in various populations. However, the ability to generalize such scores across populations can be limited due to differences in the prevalence of risk factors and their strengths of association to diabetes. It was, therefore, the purpose of the present study to develop a simple risk score to identify high-risk Thai adults for diabetes screening.

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Material and Method

Subjects

The risk score was derived from 429 Thai adults (derivation group) without a previous history of diabetes at the outpatient clinic of the Department of

Family Medicine, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand. All subjects had at least one risk factor for diabetes, i.e., family history of diabetes, history of gestational diabetes (GDM), obesity, known hypertension or dyslipidemia. All participants gave written consent before taking part in the present study. The protocols were approved by the Ethical Committee of the Faculty of Medicine, Ramathibodi Hospital, Mahidol University.

Methods

Every subject was ambulatory and had a non-restricted diet for at least 3 days. They were not taking any drug known to affect glucose metabolism. Blood pressure was measured in the sitting position using a mercury sphygmomanometer after resting for 5 minutes. Repeated measurements of blood pressure were performed after at least 1 week if the initial blood pressure was $\geq$ 140 mmHg (systolic) and/or $\geq$ 90 mmHg (diastolic). Serum total cholesterol, triglyceride, and HDL-cholesterol were measured by enzymatic methods in venous blood sample taken after 12 h of an over night fasting. A 75-gram oral glucose tolerance test was carried out as outlined by the WHO Diabetes Study Group[11]. Venous plasma glucose was measured by a glucose oxidase method using a Beckman glucose analyzer. Categorization of the study subjects based on fasting plasma glucose (FPG) and a full OGTT were carried out according to 1997/1998 WHO consultation criteria[10,12].

Development of the risk score

Independent risk factors associated with diabetes as defined by OGTT and the risk equation were determined by a stepwise multiple logistic regression analysis. Receiver operating characteristics (ROC) analysis was used to determine the cut-off value for the risk equation.

Validating of the risk score

Validation of the risk score was performed in a separate population comprising 1617 adults with at least one risk factor for diabetes (validation group). The performance of the risk score was determined with respect to the area under the ROC curve (AUC), sensitivity, specificity, positive predictive value, and negative predictive values.

Statistical analysis

Data were presented as means $\pm$ SD and range. Differences between variables were assessed by unpaired Student's t-test. Associations between variables were tested by linear regression analysis and correlation coefficients were calculated. Statistical significance was set at $p < 0.05$. Sensitivity, specificity, positive and negative predictive values were calculated using standard formulas[13].

Results

Clinical characteristic of the derivation and validation group are summarized in Table 1. There were 270 women (62.9%) and 159 men (37.1%), aged 18-81 years (mean $\pm$ SD = 48.4 $\pm$ 10.9 years). Body mass index (BMI) ranged from 16.6 to 38.2 kg/m^2 with a mean value of 24.7 $\pm$ 3.8 kg/m^2. Risk factors among the studied subjects and validation group are shown in Table 2. In the derivation group, risk factors included dyslipidemia (82.8%) as defined by total cholesterol $\geq$ 200 mg/dl and/or HDL cholesterol < 35 mg/dl for male or < 45 mg/dl for female, a family history of diabetes in first degree relatives (45.5%), obesity with BMI $\geq$ 25 mg/m^2 (41%), hypertension with blood pressure $\geq$ 140/90 mmHg (29.6%) and a history of GDM in 0.2%.

Table 3 shows the independent risk factors associated with diabetes from the stepwise multiple logistic regression analysis. Age, BMI and history of hypertension were significantly associated with diabetes. GDM and a family history of diabetes were not significant risk factors in the present study. The risk equation calculated from parameters derived from the logistic regression analysis was 0.059 age + 0.104 BMI + 1.023 HHT where the presence or absence of HHT was coded 1 and 0, respectively. The formula was then simplified to 3 age + 5 BMI + 50 HHT by multiplying 50 to the original equation.

The performance of the risk score in the derivation group was shown in the ROC curve (Fig. 1). The area under the ROC curve was 0.74 with the p-value < 0.001. Because of the screening purpose of the risk score, the cut-off value was determined by giving higher priority to sensitivity compared to specificity. The derived cut-off value of $\geq$ 240 yielded a sensitivity of 96.8%, specificity 24.0%, positive predictive value 17.8% and negative predictive value 97.8%.

The performance of the risk score in the validation group is shown in Fig. 2. The area under the curve was 0.71 with the p-value < 0.001. Comparison to the performance in the derivation group is shown in Table 3. The sensitivity decreased from 96.8% to 87.1%, the specificity increased from 24.0% to 38.0%, the positive predictive value and the negative predictive value comparable to those in the derivation group

Table 1. Clinical characteristics of derivation and validation group

Parameter	Derivation group (n = 429)		Validation group (n = 1623)	
	Mean ± SD	Range	Mean ± SD	Range
Sex (M:F)	159 : 270		350 : 1273	
Age (y)	48.4 ± 10.9	18-81	42.7 ± 11.5	16-80
BMI (kg/m^2)	24.7 ± 3.4	16.63-38.16	26.0 ± 5.1	16.30-57.14
WHR	0.87 ± 0.07	0.69-1.07	0.87 ± 0.09	0.70-1.44
Fasting glucose (mg/dl)	94.1 ± 15.7	64-207	95.7 ± 25.5	43-412
2h-glucose (mg/dl)	145.0 ± 56.7	64-413	140.5 ± 61.4	35-522
Total Cholesterol (mg/dl)	231.5 ± 42.4	127-372	220.9 ± 54.5	94-685
HDL-Cholesterol (mg/dl)	53.3 ± 14.6	18-115	51.9 ± 14.9	12-182
LDL-Cholesterol (mg/dl)	147.9 ± 40.7	49-284	139.3 ± 46.3	11.2-500
Triglyceride (mg/dl)	157.0 ± 125.9	27-1311	154.3 ± 139.8	24-2745
SBP (mmHg)	123.8 ± 15.5	90-200	123.9 ± 21.3	90-230
DBP (mm/Hg)	79.5 ± 8.9	60-110	78.4 ± 12.1	50-130

BMI: body mass index; WHR: waist hip ratio; SBP: systolic blood pressure; DBP: diastolic blood pressure

Table 2. Risk factors of Derivation group and Validation group

Parameters	Derivation group (n = 429)		Validation group (n = 1623)	
	N	%	N	%
Family history of DM	195	45.5	773	47.6
Obesity (BMI ≥ 25kg/m^2)	176	41.0	836	51.5
Dylipidemia	355	82.8	1228	76.0
History of hypertension	52	12.1	224	13.8
Hypertension	127	29.6	447	28.4
GDM	1	0.2	225	13.9
Atherosclaerosis	0	0.0	6	0.4

Dylipidemia: Total cholesterol ≥ 200 and/or Triglyceride ≥ 200 and/or HDL < 35 for man, < 45 for woman

Table 3. Independent risk factors associated with diabetes

Risk factor	Odds ratio	95%CI
Age	1.061	1.032-1.091
BMI	1.109	1.030-1.194
History of hypertension	2.780	1.398-5.528
GDM	-	-
Family history of diabetes	-	-

BMI: body mass index ; GDM : gestational diabetes mellitus

(Table 4). As shown in Table 5, the prevalence of diabetes in the validation group was 13.5%. Most of the screening effort in this group of high risk subjects would be non-productive. When applying the risk score, 560 (34.6%) of the screening can be avoided. However, 28 out of 218 (12.8%) of the diabetic subjects would be missed.

Discussion

A number of studies have attempted to develop risk functions for diabetes screening in various populations. The functions derived can be helpful in clinical decision making and enhance a more cost-effective approach by identifying subjects at risk in whom screening will be more productive. However, generalization of risk functions across populations with different ethnic and geographical background can be invalid[14]. The sensitivities, specificities and predictive values of various risk functions are usually substantially lower when applied in different populations. The factors underlying such differences are likely to be the differences in relationship between clinical risk factors, genetic background and the risk of diabetes across populations. For examples, the degrees of adiposity as predicted by body mass index are different between Caucasians and Asians. At the same body mass index, the degree of adiposity in Asians is usually higher. In the present study, the authors have developed a simple risk score to be used in the screening for type 2 diabetes in high-risk Thai adults. The final model included information on age, BMI, and

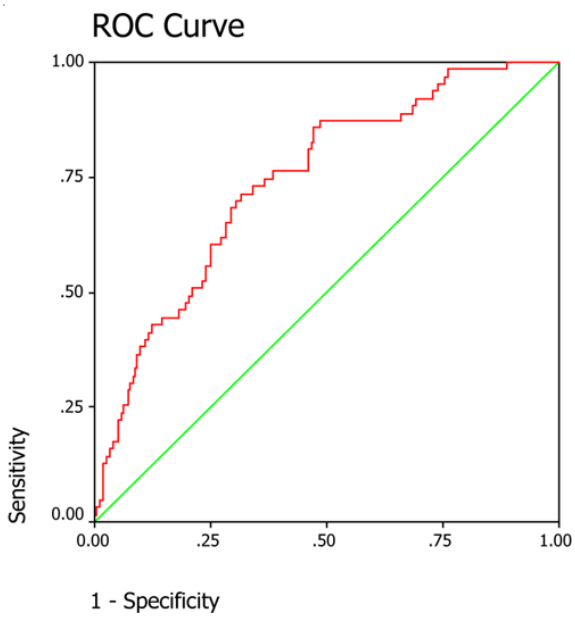

Fig. 1 ROC curve analysis of the performance of the risk score in the derivation group (area under the curve = 0.74, $p < 0.001$)

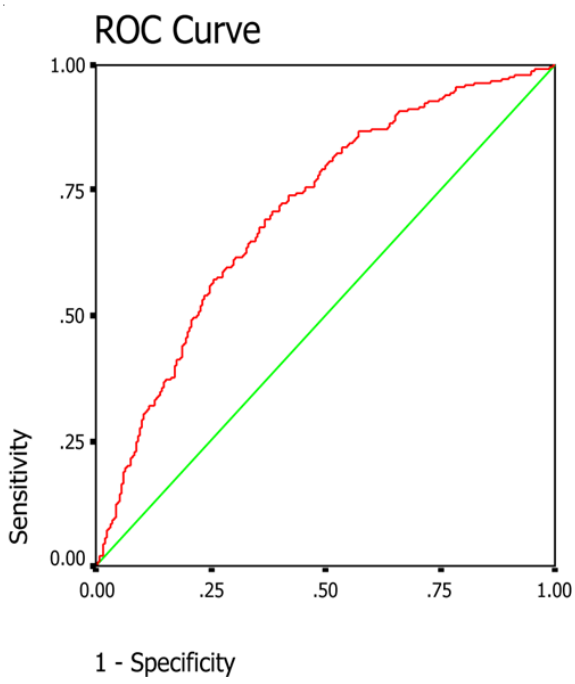

Fig. 2 ROC curve analysis of validation group (area under the curve = 0.71, $p < 0.001$)

Table 4. The performance of risk score equation in derivation and validation group

	Derivation group	Validation group
Sensitivity	96.8%	87.1%
Specificity	24.0%	38.0%
Positive predictive value	17.8%	18.0%
Negative predictive value	97.8%	95.0%

Table 5. The performance of the risk score in the validation group

	Score ≥ 240	Score < 240	Total
DM	190	28	218 (13.5%)
Non-DM	867	532	1398 (87.0%)
Total	1057	560	1617 (100%)

known hypertension. The risk score identifies individuals with previously undiagnosed type 2 diabetes with the sensitivity of 96.8%, specificity 24.0%, positive predictive value 17.8% and negative predictive value 97.8% in the derivation group with a similar result when validated in a separate group of subjects. The cut-off value diabetes was chosen in order for the risk function to achieve high sensitivity albeit low specificity for screening purpose. However, the most appropriate cut-off point should balance the benefit obtained from the correct identification of diabetic subjects with the undesired consequences when patients with diabetes are missed. Health economic modeling will be helpful in this regard and the results are dependent on the risk of long-term complications, modalities utilized for intervention and the extent of consumed resources.

Factors found to be significantly associated with diabetes in the present study included age, BMI and history of hypertension. It is of note that family history and previous gestational diabetes were not found to be significant risk factors. Although a family history of diabetes has been found to be an important risk factor in a number of studies[8,15], it has not been included in other risk scores[16]. The reason of the variation in the significance of diabetes in family members in risk assessment may be related to the difficulty in obtaining accurate information. Diabetes can still be undiagnosed in family members or the information

may be too remote than it cannot be validly recalled. GDM is another well-established risk factor for future diabetes. However, the prevalence of GDM in the present study is relatively low and may be accountable for the statistical exclusion of the variable from the risk equation. Despite the exclusion of some of the previously reported risk factors, the performance of the present risk score is comparable to that of other previously reported scores such as the Inter99 study that included BMI, age and known hypertension. The present study is unique in that it represents the first study to develop a risk score particularly for a Thai population and the performance of the scoring system has been well validated in a separate population. It is now well established that type 2 diabetes can be prevented through weight loss and lifestyle modification[17]. Using the risk score in the risk assessment should render a more cost-effective approach to diabetes screening. It should also be pointed out that the risk score developed is for subjects who are already at high risk of having diabetes, i.e. those with a family history of diabetes, history of gestational diabetes, obesity, known hypertension or dyslipidemia. This raises the pretest probability of diabetes and should render the positive predictive value higher than when applying the score to the general population with lower risk. The application and generalization of the risk score in clinical practice should also take these characteristics of the studied population into account.

Conclusion

The authors have developed a simple risk score to be used in the screening for type 2 diabetes in high-risk Thai adults. The final model included information on age, BMI and known hypertension. The risk scores should be helpful in decreasing the number of unnecessary screening and optimizing the costs associated with diabetes screening.

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References

1. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. Diabetes Care 1998; 21: 1414-31.
2. Moss SE, Klein R, Klein BE. The incidence of vision loss in a diabetic population. Ophthalmology 1988; 95: 1340-8.
3. Humphrey LL, Ballard DJ, Frohnert PP, Chu CP, O'Fallon WM, Palumbo PJ. Chronic renal failure in non-insulin-dependent diabetes mellitus. A population-based study in Rochester, Minnesota. Ann Intern Med 1989; 111: 788-96.
4. Resnick HE, Valsania P, Phillips CL. Diabetes mellitus and nontraumatic lower extremity amputation in black and white Americans: the National Health and Nutrition Examination Survey Epidemiologic Follow-up Study, 1971-1992. Arch Intern Med 1999; 159: 2470-5.
5. Humphrey LL, Palumbo PJ, Butters MA, Hallett JW Jr, Chu CP, O'Fallon WM, et al. The contribution of non-insulin-dependent diabetes to lower-extremity amputation in the community. Arch Intern Med 1994; 154: 885-92.
6. Harris RP, Lux LJ, Bunton AJ, Sutton SF, Lohr KN, Donahue KP, et al. Screening for type 2 diabetes mellitus. Systematic Evidence Review Number 19. Rockville, MD: Agency for Healthcare Research and Quality; 2003. Available at: http://www.ahrq.gov/clinic/serfiles.htm
7. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998; 352: 837-53.
8. Baan CA, Ruige JB, Stolk RP, Witteman JC, Dekker JM, Heine RJ, et al. Performance of a predictive model to identify undiagnosed diabetes in a health care setting. Diabetes Care 1999; 22: 213-9.
9. Aekplakorn W, Stolk RP, Neal B, Suriyawongpaisal P, Chongsuvivatwong V, Cheepudomwit S, et al. The prevalence and management of diabetes in Thai adults: the international collaborative study of cardiovascular disease in Asia. Diabetes Care 2003; 26: 2758-63.
10. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 1997; 20: 1183-97.
11. Diabetes mellitus. Report of a WHO Study Group. World Health Organ Tech Rep Ser 1985; 727: 1-113.
12. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO

consultation. Diabet Med 1998; 15: 539-53.
13. Fletcher RH, Fletcher SW, Wagner EH. Clinical epidemiology: the essentials. Baltimore, MA: Williams & Wilkinss; 1982: 41-58.
14. Glumer C, Vistisen D, Borch-Johnsen K, Colagiuri S. Risk scores for type 2 diabetes can be applied in some populations but not all. Diabetes Care 2006; 29: 410-4.
15. Ruige JB, de Neeling JN, Kostense PJ, Bouter LM, Heine RJ. Performance of an NIDDM screening questionnaire based on symptoms and risk factors. Diabetes Care 1997; 20: 491-6.
16. Lindstrom J, Tuomilehto J. The diabetes risk score: a practical tool to predict type 2 diabetes risk. Diabetes Care 2003; 26: 725-31.
17. Knowler WC. Screening for NIDDM. Opportunities for detection, treatment, and prevention. Diabetes Care 1994; 17: 445-50.

การพัฒนาและการทดสอบความถูกต้องคะแนนความเสี่ยงของการเกิดโรคเบาหวานในคนไทยที่มีความเสี่ยงสูง

ประสิทธิ์ กี่สุขพันธ์, สุวรรณี ชั้นประเสริฐโยธิน, บุญส่ง องค์พิพัฒนกุล, กอบชัย พัววิไล

วัตถุประสงค์*: เพื่อการพัฒนาคะแนนความเสี่ยงของการเกิดโรคเบาหวานในคนไทยที่มีความเสี่ยงสูง*
วัสดุและวิธีการ*: ได้ทำการศึกษาในผู้ชาย 159 คน และหญิง 270 คน อายุเฉลี่ย 48.4 $\pm$ 10.9 ปี ซึ่งทั้งหมดได้รับการทดสอบการทนต่อน้ำตาล (75 gram oral glucose tolerance test)*
ผลการศึกษา*: พบว่าตัวแปรที่มีผลต่อการเกิดโรคเบาหวานคือ อายุ ($p < 0.001$), ดัชนีมวลกาย (BMI, $p < 0.001$), และประวัติความดันโลหิตสูง ($p < 0.01$) สำหรับสมการที่ได้คือ Y (คะแนนความเสี่ยง) = 3 เท่าของอายุ + 5 เท่าของดัชนีมวลกาย + 50 เท่าของประวัติโรคความดันโลหิตสูง ที่ Y (คะแนนความเสี่ยง) = 240 พบว่าค่า sensitivity = 96.8%, specificity = 24.0%, positive predictive value = 17.8%, negative predictive value = 97.8% เมื่อใช้สมการนี้ทดสอบในกลุ่มอาสาสมัครอีกกลุ่มหนึ่ง (validation group) พบว่าสามารถประหยัดค่าใช้จ่ายโดยไม่จำเป็นในการทดสอบการทนต่อน้ำตาลได้ 560 ราย (34.6 %) โดยที่ผู้เป็นเบาหวาน 28 ราย (12.8 %) อาจจะพลาดการวินิจฉัย*
สรุป*: ผู้วิจัยได้พัฒนาคะแนนความเสี่ยงของการเกิดโรคเบาหวานเพื่อใช้ทดสอบในคนไทยที่มีความเสี่ยงสูง ซึ่งจะมีประโยชน์ในการลดการทดสอบผู้ป่วยเบาหวานที่ไม่จำเป็น และสามารถประหยัดค่าใช้จ่ายในการทดสอบเบาหวานในประชากรทั่วไป*