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### A simple screening score for diabetes for the Korean population

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# What is prediction model?

- A "**prediction**" is a statement or claim that a particular event will occur in the future (or now).
- Response is often binary (event/no-event).
- Mathematical equation can be used to model the probability (or rate) of event.
  - Numeric algorithm can be derived to grade the risk, often by simplifying the mathematical model.
  - Prediction models provide diagnostic or prognostic probabilities

# Why important?

- Prediction models are valuable for medical practice and for research purposes.
- People use it in real world (esp., lay and underserved people)-- used in clinical or community setting, self-use for (pre-)screening or risk assessment/prediction.
  - In public health, models may help target preventive interventions to subjects at relatively high risk of having or developing a disease.

# Why important?

- In clinical practice, prediction models may inform patients and their treating physicians on the probability that a disease is (will be) present and may also assist medical decision making.
  - When the probability is relatively high, treatment is indicated; if the probability is very low, no treatment is indicated.
  - For example, Framingham risk score for CVD

# **Good Modeling**

- If prediction model is not used in the real world, it is not a prediction model. It is a regression model (or academic glory).
- That's why it should perform well statistically. More importantly, it should be clinically relevant/meaningful.

# For good prediction models

- 1. Simple and easy, but not too simple
- 2. Variable selection
- 3. Variable categorization
- 4. Sample size (N) & data/variables
- 5. Population characteristics

# 1. Simple and easy

- User-friendliness and easy use are important!
  - if statisticians or clinicians can not use it easily, how lay persons can use?
- Interactions or nonlinear function may make prediction model/risk score more accurate but complex.

### **Diabetes risk score in UK**

|                               | Risk score | Characteristic                         |
|-------------------------------|------------|--|
| α                             | -6.322     | Constant                               |
| $\beta_1 x_1$                 | -0.879     | Female                                 |
| $\beta_2 X_2$                 | 1.222      | Prescribed antihypertensive medication |
| $\beta_3 X_3$                 | 2.191      | Prescribed steroids                    |
| $\beta_4 x_4$                 | 0.063      | x age in years                         |
| β <sub>5</sub> x <sub>5</sub> | 0          | Body mass index $< 25$                 |
| , , , ,                       | 0.699      | Body mass index $= 25$ to 27.49        |
|                               | 1.970      | Body mass index $= 27.5$ to 29.99      |
|                               | 2.518      | Body mass index $\ge$ 30               |
| $\beta_{6} x_{6}$             | 0          | No first degree relative had diabetes  |
|                               | 0.728      | Parent or sibling had diabetes         |
|                               | 0.753      | Parent and sibling had diabetes        |
| β <sub>7</sub> x <sub>7</sub> | 0          | Non-smoker                             |
|                               | -0.218     | Ex-smoker                              |
|                               | 0.855      | Current smoker                         |

<sup>3</sup>Probability of having Type 2 diabetes =  $\frac{1}{1+e^{-(\alpha+\beta_1x_1+\beta_2x_2\cdots+\beta_nx_n)}}$ 

Diabetes Metab Res Rev 2000; 16: 164±171

# 2. Variable selection

- >10 variables may be too many.
- Not all significant predictors may be included in the final model (statistical vs. clinical significance)
  - difficult and easy variables.
- >1 model may be developed to accommodate different data availabilities, e.g. with or without blood test.

# Risk score for predicting incidence of diabetes in middle-aged Korean

| Table 2. Multivariate Logistic Regression for Type 2 Diabetes |                  |         |                  |                  |                  |                  |  |
|---|------------------|---------|------------------|------------------|------------------|------------------|--|
|   | Basic model      |         | Clinical mo      | Clinical model 1 |                  | Clinical model 2 |  |
|   | OR (95% CI)      | P value | OR (95% CI)      | P value          | OR (95% CI)      | P value          |  |
| Age (years)   | 1.02 (1.01–1.03) | 0.0053  | 1.02 (1.00–1.04) | 0.0007           | 1.01 (1.00–1.03) | 0.0528           |  |
| Parental or sibling history of diabetes                       | 1.90 (1.46–2.49) | <0.0001 | 1.84 (1.38–2.41) | <0.0001          | 1.75 (1.32-2.31) | <0.0001          |  |
| Current smoking   | 1.68 (1.35–2.09) | <0.0001 | 1.35 (1.06–1.66) | 0.0103           | 1.26 (1.00–1.58) | 0.0522           |  |
| BMI(kg/m <sup>2</sup> )                                       |                  |         |                  |                  |                  |                  |  |
| <23   | 1 (reference)    | -       | 1 (reference)    | -                | 1 (reference)    | -                |  |
| 23–24   | 1.50 (1.12–2.01) | 0.0064  | 1.21 (0.89–1.63) | 0.2219           | 1.18 (0.87–1.59) | 0.2987           |  |
| 25–29   | 2.03 (1.56-2.65) | <0.0001 | 1.37 (1.04–1.82) | 0.0267           | 1.27 (0.96–1.69) | 0.0939           |  |
| ≥30   | 3.17 (2.09-4.80) | <0.0001 | 2.07 (1.33-3.21) | 0.0012           | 1.78 (1.15–2.77) | 0.0105           |  |
| Hypertension status   | 1.81 (1.44–2.28) | <0.0001 | 1.49 (1.17–1.89) | 0.0012           | 1.51 (1.19–1.92) | 0.0008           |  |
| FPG (mg/dl)   |                  |         |                  |                  |                  |                  |  |
| <90   |                  |         | 0.38 (0.30-0.48) | <0.0001          | 0.41 (0.32-0.52) | <0.0001          |  |
| 90–99   |                  |         | 1 (reference)    | -                | 1 (reference)    | -                |  |
| 100–125   |                  |         | 3.34 (2.38-4.71) | <0.0001          | 3.19 (2.26-4.50) | <0.0001          |  |
| HDL-C (mg/dl)   |                  |         |                  |                  |                  |                  |  |
| <35   |                  |         | 1.47(1.12–1.93)  | 0.0050           | 1.47 (1.12–1.93) | 0.0056           |  |
| 35–49   |                  |         | 1 (reference)    | -                | 1 (reference)    | -                |  |
| ≥50   |                  |         | 0.83 (0.63–1.10) | 0.1782           | 0.82 (0.62-1.08) | 0.1566           |  |
| TG (mg/dl)  |                  |         |                  |                  |                  |                  |  |
| <120  |                  |         | 1 (reference)    | -                | 1 (reference)    | -                |  |
| 120–149   |                  |         | 1.40 (1.02–1.93) | 0.0385           | 1.37 (1.00–1.89) | 0.0537           |  |
| ≥150  |                  |         | 2.12 (1.63–2.77) | <0.0001          | 2.00 (1.53-2.61) | <0.0001          |  |
| HbA1c (%)   |                  |         |                  |                  |                  |                  |  |
| <5.5 (37 mmol/mol)  |                  |         |                  |                  | 1 (reference)    | -                |  |
| 5.5-6.4 (37-46 mmol/mol)                                      |                  |         |                  |                  | 2.66 (2.02–3.51) | <0.0001          |  |
| AROC  | 0.65 (0.62-0.68) |         | 0.75 (0.72–0.77) |                  | 0.77 (0.74-0.79) |                  |  |
| Hosmer-Lemeshow   | 5.560            | 0.6964  | 2.090            | 0.9781           | 4.893            | 0.7690           |  |

# 3. Variable categorization

- Most statisticians agree with Royston (2005)
   *Dichotomizing continuous predictors in multiple regression: a bad idea.*
- However, filling in continuous information (e.g. blood pressure, BMI, CRP) can be hard for many people.
- 'Continuous models' vs. 'Categorical models' – for computer-based platform vs. pencil & paper.

## 4. Sample size & data/variables

- No absolute consensus on N requirement. As the goal is a stable regression equation, larger is better.
- "*large & representative*" sample from the target population (if not, less reproducible or generalizable)
- We may need to save some N for internal validation.

# 5. Population characteristics

- Universal model may not exist.
- Separate models may be warranted:
  - by sex
  - by race or country (e.g. many countries have their own diabetes score)
  - by age
  - high risk (e.g. clinical setting) vs. general population
  - first vs. recurrent event

### Framingham risk score in Chinese Adults



CMCS indicates Chinese Multi-provincial Cohort Study. Coronary heart disease (CHD) events included coronary death and myocardial infarction.

# Steps in Model development

Step 1: Model Development
Step 2: Model Evaluation
Step 3: Validations - including feasibility and usefulness
Step 4: Refinement or improvement in

model or presentation (if desired)

# Statistical tools for model development

- Regression models linear, logistic, Cox model
   -- explicit mathematical formula and numeric scoring system can be derived (e.g. guided by regression coefficients)
- **Tree-based methods** Classification and Regression Tree, Recursive Partitioning
  - -- can handle complex interactions
  - -- cut-points identified
  - -- can handle numerous candidate variables

# Statistical measures for model evaluation

- Sensitivity & Specificity most popular
- Discrimination (ROC/AUC) most popular
- Predictive values positive, negative
- Likelihood ratio positive, negative
- Accuracy (e.g. Youden index, Brier score)
- Number needed to treat or screen (NNT, NNS)
- Model fit (e.g. AIC, BIC)
- Lack of fit (e.g. Hosmer-Lemeshow test)
- R<sup>2</sup> (coefficient of determination)
- P-value (significance) universally popular

# Prevalent vs. Incident events

### Prevalent/concurrent event

- cross-sectional data is used.
- useful for *asymptomatic* disease for screening undiagnosed cases (e.g. breast cancer, diabetes, kidney disease), not for all diseases.
- simplicity in prediction model/risk score is important.
- Incident/future event
  - prospective study of event-free cohort is needed.
  - simplicity is less important.

# How to disseminate?

- Good models deserves good marketing/PR.
- How to present? Figure, score card or click-click-click?
  - computer (e.g. web-based) vs. paper-pencil method.
  - Smartphone apps
- May work with Public Affair team in your institution.
  - at times, press release/interview follow (esp., for 1<sup>st</sup> study)
  - no one reads/understands your paper as well as you do.
     Deliver the main findings clearly.
- May work with authority and practitioners to implement/distribute your method - preferably after validation.

## Sample risk scores on internet

- Cancer: <u>http://riskfactor.cancer.gov/cancer\_risk\_prediction/</u> <u>http://www.mskcc.org/mskcc/html/5794.cfm</u> <u>http://www4.utsouthwestern.edu/breasthealth/cagene/</u>
- APACHE: http://www.sfar.org/scores2/apache22.html
   http://www.apache-web.com/public/pub\_main.html
- Charlson comorbidity index: <u>http://en.wikipedia.org/wiki/Comorbidity#Charlson\_index</u>
- Framingham score: <u>http://framinghamriskscore.com/</u>
- UK CVD score: <u>http://www.riskscore.org.uk/</u>
- PROCAM score: <u>http://www.chd-taskforce.de/</u>
- Reynolds score: <u>http://www.reynoldsriskscore.org/</u>
- ABCD score: <u>http://www.strokecenter.org/Trials/scales/ABCDScore.pdf</u>
- Diabetes risk score: <u>http://www.diabetes.org/risk-test.jsp</u>
- German diabetes risk score: <u>http://www.dife.de/</u>
- Angina score: <u>http://www.anginarisk.org/</u>
- Pneumonia score: <u>http://www.ahrq.gov/clinic/pneuclin.htm#head1</u>
- SCORED: <u>http://unchealthcare.org/site/newsroom\_OLD/scored.pdf</u>
- Depression: <u>http://www.psycom.net/depression.central.screening.html</u>
- Autism: <a href="http://www.txautism.net/docs/Guide/Evaluation/AutismScreen\_Assess.pdf">http://www.txautism.net/docs/Guide/Evaluation/AutismScreen\_Assess.pdf</a>
- Medical calculator: <u>http://medcalc3000.com/</u>

### PREDICTION MODELS IN DIABETES: DIABETES RISK SCORE



### FINnish Diabetes RIsk SCore

### FINDRISC

Score range 1-24 p

AUC 0.85 Sensitivity 73% Specificity 83%

Lindström et al. Diabetes Care 2003; 26: 725-731



#### **TYPE 2 DIABETES RISK ASSESSMENT FORM**

Circle the right alternative and add up your points.

#### 1. Age

- 0 p. Under 45 years
- 2 p. 45–54 years
- 3 p. 55-64 years
- 4 p. Over 64 years

#### 2. Body-mass index

- (See reverse of form)
- 0 p. Lower than 25 kg/m<sup>2</sup>
- 1 p. 25-30 kg/m<sup>2</sup>
- 3 p. Higher than 30 kg/m<sup>2</sup>

#### 3. Waist circumference measured below the ribs (usually at the level of the nevel)

ribs (usually at the level of the navel) MEN WOMEN 0 p. Less than 94 cm Less than 80 cm

- 3 p. 94–102 cm 80–88 cm
- 4 p. More than 102 cm More than 88 cm



4. Do you usually have daily at least 30 minutes of physical activity at work and/or during leisure time (including normal daily activity)? 0 p. Yes 2 p. No

5. How often do you eat vegetables, fruit or berries? 0 p. Every day

1 p. Not every day

#### 6. Have you ever taken antihypertensive medication regularly?

0p. No 2p. Yes

7. Have you ever been found to have high blood glucose (eg in a health examination, during an illness, during pregnancy)?

0p. No 5p. Yes

8. Have any of the members of your immediate family or other relatives been diagnosed with diabetes (type 1 or type 2)?

#### 0 p. No

- 3 p. Yes: grandparent, aunt, uncle or first cousin (but no own parent, brother, sister or child)
- 5 p. Yes: parent, brother, sister or own child

### Total Risk Score

| The risk of developing             |  |  |
|------------------------------------|--|--|
| type 2 diabetes within 10 years is |  |  |
| :                                  |  |  |
| r than 7 Low: estimated 1 in 100   |  |  |
| will develop disease               |  |  |
| Slightly elevated:                 |  |  |
| estimated 1 in 25                  |  |  |
| will develop disease               |  |  |
| Moderate: estimated 1 in 6         |  |  |
| will develop disease               |  |  |
| High: estimated 1 in 3             |  |  |
| will develop disease               |  |  |
| r Very high:                       |  |  |
| 0 estimated 1 in 2                 |  |  |
| will develop disease               |  |  |
| Please turn over                   |  |  |
|                                    |  |  |

Test decimal hu Deafasese Isakka Tuamilahta. Danastmant of Duklis Lladtk Haiumeritu of Usleinki, and Isana Lindsteim MEC. National Duklis Lladtk Instituta

#### The Australian Type 2 Diabetes Risk Assessment Tool (NUSPERX)

#### 1. Your age group?

| Under 35 years   | 0 points |
|------------------|----------|
| 35 – 44 years    | 2 points |
| 45 – 54 years    | 4 points |
| 55 – 64 years    | 6 points |
| 65 years or over | 8 points |
| 2. Your gender?  |          |
| Female           | 0 points |
| Male             | 3 points |

#### 3. Ethnicity/Country of birth:

| 3a. | Are you of Aboriginal, Torres Strait Islander, |          |
|-----|--|----------|
|     | Pacific Islander or Maori descent?             |          |
|     | No   | 0 points |
|     | Yes  | 2 points |
| 3b. | Where were you born?                           |          |

Asia (including the Indian sub-continent), Middle East, North Africa, Southern Europe 2 points Other 0 points

4. Have either of your parents, or any of your brothers or sisters been diagnosed with diabetes (type 1 or type 2)?

| No  | 0 points |
|-----|----------|
| Yes | 3 points |

 Have you ever been found to have high blood glucose (sugar) (for example, in a health examination, during an illness, during pregnancy)?

 No
 0 points

 Yes
 6 points

6. Are you currently taking medication for high blood pressure?

No 0 points Yes 2 points

 Do you currently smoke cigarettes or any other tobacco products on a daily basis?
 No
 0 points
 Yes
 2 points

- 8. How often do you eat vegetables or fruit? Everyday 0 points Not everyday 1 point
- On average, would you say you do at least 2.5 hours of physical activity per week (for example, 30 minutes a day on 5 or more days a week)?

| Yes | 0 points |
|-----|----------|
| No  | 2 points |
|     |          |

#### 10. Your waist measurement taken below the ribs (usually at the level of the navel)?

#### For those of Asian or Aboriginal or Torres Strait Islander descent:

| Women            |   |
|------------------|---|
| Less than 80 cm  | 0 points  |
| 80 – 90 cm       | 4 points  |
| More than 90 cm  | 7 points  |
|                  |   |
| Women            |   |
| Less than 88 cm  | 0 points  |
| 88 – 100 cm      | 4 points  |
| More than 100 cm | 7 points  |
|                  | Less than 80 cm<br>80 – 90 cm<br>More than 90 cm<br>Women<br>Less than 88 cm<br>88 – 100 cm |

#### Your risk of developing type 2 diabetes within 5 years\*:

Add up your score

Less than 5: Low risk Approximately one person in every 100 will develop diabetes. 6-14: Intermediate risk For scores of 6-8, approximately one person in every 50 will develop diabetes. For scores of 9-14, approximately one person in every 20 will develop diabetes. 15 or more: High risk For scores of 15-19, approximately one person in every seven will develop diabetes. For scores of 20 and above, approximately one person in every three will develop diabetes.

If you scored 15 or more points, it is important that you discuss your score with your doctor.

\*The overall score may overestimate the risk of diabetes in those aged less than 25 years and underestimate the risk of diabetes in people of Aboriginal and Torres Strait Islander descent

The Australian Type 2 Diabetes Firsk Assessment Tool was originally developed by the International Diabetes Institute on behalf of the Australian, State and Territory Governments as part of the COAG Diabetes reducing the risk of type 2 diabetes initiative.

#### **Annals of Internal Medicine**

#### ARTICLE

#### Development and Validation of a Patient Self-assessment Score for Diabetes Risk

Heejung Bang, PhD; Alison M. Edwards, MStat; Andrew S. Bomback, MD, MPH; Christie M. Ballantyne, MD; David Brillon, MD; Mark A. Callahan, MD; Steven M. Teutsch, MD, MPH; Alvin I. Mushlin, MD, ScM; and Lisa M. Kern, MD, MPH

| Risk Factor                | Odds Ratio<br>(95% Cl) | P Value | Log<br>(Odds<br>Ratio) | Score<br>Assigned |
|----------------------------|------------------------|---------|------------------------|-------------------|
| Age                        |                        |         |                        |                   |
| <40 y                      | Reference              | —       | -                      | 0                 |
| 40–49 y                    | 2.6 (1.3-5.0)          | 0.004   | 0.95                   | 1                 |
| 50–59 y                    | 4.8 (2.2–10.6)         | < 0.001 | 1.57                   | 2                 |
| ≥60 y                      | 8.1 (3.9–16.9)         | < 0.001 | 2.09                   | 3                 |
| Sex                        |                        |         |                        |                   |
| Female                     | Reference              | -       | -                      | 0                 |
| Male                       | 2.6 (1.8–3.7)          | < 0.001 | 0.96                   | 1                 |
|                            |                        |         |                        |                   |
| Family history of diabetes |                        |         |                        |                   |
| No                         | Reference              | -       |                        | 0                 |
| Yes                        | 2.0 (1.5–2.6)          | < 0.001 | 0.67                   | 1                 |
|                            |                        |         |                        |                   |
| History of hypertension    |                        |         |                        | -                 |
| No                         | Reference              | -       |                        | 0                 |
| Yes                        | 1.9 (1.2–2.9)          | 0.004   | 0.64                   | 1                 |
| Obsetted                   |                        |         |                        |                   |
| Obesity†                   | D.(                    |         |                        | 0                 |
| Not overweight or obese    | Reference              | -       | - 0.27                 | 0                 |
| Overweight                 | 1.3 (0.6–2.8)          | 0.47    | 0.27                   | 1                 |
| Obese                      | 3.1 (1.6–5.8)          | < 0.001 | 1.12                   | 2                 |
| Extremely obese            | 7.3 (4.0–13.4)         | < 0.001 | 1.99                   | 3                 |
| Physically active          |                        |         |                        |                   |
| No                         | Reference              | -       |                        | 0                 |
| Yes                        | 0.7 (0.5–1.0)          | 0.06    | -0.34                  | -1                |
|                            |                        |         |                        |                   |

- development dataset
  - NHANES 1999 to 2004
  - 5258 participants
  - Undiagnosed diabetes of 2.8%
  - Score: 0-9
  - Cut-off point: 5
  - AUC of 0.79
- Validation dataset
  - NHANES 2005 to 2006
  - Sens. 79% Spec. 67%
  - AUC 0.83

### **ARE YOU AT RISK FOR** TYPE 2 **DIABETES?**

#### TAKE THE TEST. YOU NEED TO KNOW.

American Diabetes Association.

www.diabetes.org 1-800-DIABETES

#### **Diabetes Risk Test**

This simple tool can help you determine your risk for having type 2 diabetes.

|  | Vrite your score<br>in the box. | Height   | ١  | Neight (lbs.  | )   |
|--|---------------------------------|--|--|---|---|
| <40 years (0 points)<br>40—49 years (1 point)                  | -                               | 4' 10"   | 119-142  | 143-190   | 191+  |
| 50—59 years (2 points)   |                                 | 4' 11"   | 124-147  | 148-197   | 198+  |
| 60 years or older (3 points)                                   |                                 | 5' 0"  | 128-152  | 153-203   | 204+  |
| Are you a man or a woman?                                      |                                 | 5' 1"  | 132-157  | 158-210   | 211+  |
| Man (1 point)  |                                 | 5' 2"  | 136-163  | 164-217   | 218+  |
| Woman (0 points)   |                                 | 5' 3"  | 141-168  | 169-224   | 225+  |
| 3 If you are a woman, have                                     |                                 | 5' 4"  | 145-173  | 174-231   | 232+  |
| you ever been diagnosed<br>with gestational diabetes?          |                                 | 5' 5"  | 150-179  | 180-239   | 240+  |
| Yes (1 point)  |                                 | 5' 6"  | 155-185  | 186-246   | 247+  |
| No (0 points)  |                                 | 5' 7"  | 159-190  | 191-254   | 255+  |
| A Do you have a mother,  |                                 | 5' 8"  | 164-196  | 197-261   | 262+  |
| father, sister, or brother                                     |                                 | 5' 9"  | 169-202  | 203-269   | 270+  |
| with diabetes?   |                                 | 5' 10"   | 174-208  | 209-277   | 278+  |
| Yes (1 point)  |                                 | 5' 11"   | 179-214  | 215-285   | 286+  |
| No (0 points)  |                                 | 6' 0"  | 184-220  | 221-293   | 294+  |
| Have you ever been diagnosed<br>with high blood pressure?      |                                 | 6' 1"  | 189-226  | 227-301   | 302+  |
| Yes (1 point)  |                                 | 6' 2"  | 194-232  | 233-310   | 311+  |
| No (0 points)  |                                 | 6' 3"  | 200-239  | 240-318   | 319+  |
| Are you physically active?                                     |                                 | 6' 4"  | 205-245  | 246-327   | 328+  |
| Yes (0 points)   |                                 |  | (1 Point)  | (2 Points)  | (3 Points)  |
| No (1 point)   |                                 |  | (1 Folinty   | (2 Points)  | (3 Politics)  |
| What is your weight status? (see chart at right)               |                                 |  | and the second | less than the<br>e green colur<br>(0 points)                                |   |
| Adapted from Bang et al., Ann intern Med<br>151:775-783, 2009. | Y<br>d<br>if<br>d<br>g          | f you scored 5<br>ou are at increase<br>iabetes. Howeve<br>you do have typ<br>ition that preced<br>lucose levels are<br>octor to see if ac | ed risk for h<br>r, only your<br>ee 2 diabete<br>les type 2 di<br>higher than                                    | aving type 2<br>doctor can t<br>s or prediab<br>abetes in wl<br>normal). Ta | ell for sure<br>etes (a con-<br>hich blood<br>alk to your |



# Qingdao diabetes risk score

| Men              | Score            | Women   | Score |
|------------------|------------------|---------|-------|
| ≤ 2.3            | 1                | ≤ 2.0   | 1     |
| 2.4-2.6          | 4                | 2.1-2.3 | 3     |
| 2.7-2.9          | 8                | 2.4-2.6 | 6     |
| ≥ 3.0            | 12               | ≥ 2.7   | 9     |
| Age (years)      | Score            |         |       |
| ≤ 35             | 1                |         |       |
| 36-45            | 3                |         |       |
| 46-55            | 6                |         |       |
| 56-65            | 9                |         |       |
| ≥ 65             | 12               |         |       |
| Diabetes in pare | nts and/or sibli | ngs     | Score |
| Negative         |                  |         | 1     |
| Positive         |                  |         | 8     |
| Score range      |                  |         | 3-32  |

\*1 Chinese chi  $\approx$  33 cm.

- 2002/2006 survey
   N=1986/4336
- OGTT
- Score: 3-32
- Cut-off point: 14
- Sens. 84.2%
- Spec. 39.8%
- AUC 0.673

Diabetic Med 2010

# Thai diabetes risk score

| Risk factor                              | Coefficient | Diabetes risk score |
|--|-------------|---------------------|
| Age (years)                              |             |                     |
| 34–39                                    |             | 0                   |
| 40-44                                    | -0.07       | 0                   |
| 45-49                                    | 0.27        | 0<br>1<br>2         |
| ≥50                                      | 0.60        | 2                   |
| Sex                                      |             |                     |
| Women                                    |             | 0                   |
| Men                                      | 0.44        | 2                   |
| BMI (kg/m <sup>2</sup> )                 |             |                     |
| <23                                      |             | 0                   |
| ≥23 but <27.5                            | 0.69        | 3                   |
| ≥27.5                                    | 1.24        | 5                   |
| Waist circumference (cm)                 |             |                     |
| <90 in men, <80 women                    |             | 0<br>2              |
| ≥90 in men, ≥80 in women                 | 0.56        | 2                   |
| Hypertension                             |             |                     |
| No                                       |             | 0                   |
| Yes                                      | 0.64        | 2                   |
| History of diabetes in parent or sibling |             |                     |
| No                                       |             | 0                   |
| Yes                                      | 1.08        | 4                   |

- Score: 1-17
  - Cutoff score:

**-6** 

- Sens. 77%; Spec. 60%
- AUC: 0.74

Diabetes Care 29:1872–1877, 2006

### DIABETES SCREENING SCORE FOR KOREAN ADULTS

# Prevalence of diabetes in Korean adults, 30y or older, KNHANES



Diagnosis of diabetes: FPG≥126mg/dl, or physician diagnosis or oral hypoglycemic agents or insulin use

Choi YJ, et al. Diabetes Care 32:2016–2020, 2009 2008 KNHANES reports

## Awareness of Diabetes, by year, KNHANES



Awareness: proportion of known diabetes among total diabetes

(%)

Choi YJ, et al. Diabetes Care 32:2016–2020, 2009 2008 KNHANES reports



Awareness: proportion of known diabetes among total diabetes

Choi YJ, et al. Diabetes Care 32:2016–2020, 2009 2008 KNHANES reports

# Aim of our study

- To develop and validate a self-assessment score for diabetes risk in Korean adults using simple clinical parameters to provide a reliable and easy tool for the layperson without the need for a clinician's input.
- To compare the new algorithm with other existing screening models from different ethnic populations

# **Research design and methods**

- Korea National Health and Nutrition Examination Survey (KNHANES)
  - Population-based, cross-sectional health survey
  - Korea Centers for Disease Control and Prevention (KCDC)
  - To monitor the general health and nutrition status of Koreans
- Development data sets
  - KNHANES 2001 and 2005
- Validation data sets
  - KNHANES 2007-2008
## **Ascertainment of Diabetes**

#### **1** Known diabetes (Known DM)

- previous diagnosis by physician
- Use of insulin or oral anti-diabetic medications

#### ② Undiagnosed diabetes (New DM)

- Fasting glucose ≥ 126 mg/dl
- Non-fasting glucose ≥ 200 mg/dl
- ③ Impaired fasting glucose (IFG)
  - Fasting glucose 100-125 mg/dl

## **Definition of Co-variables**

- **Age**: <35, 35-44, ≥45 years
- Sex: male, female
- **Body mass index (BMI)**: <23, 23-24.9, ≥25 kg/m<sup>2</sup>
- Waist circumferences (WC): <84/77, 84-89.9/77-83.9, ≥90/84cm (M/F) by 50 & 75 percentile
- Family history of DM: no, yes (father, mother, or siblings)
- Hypertension: no, yes (physician diagnosis or medication or ≥140/90 mmHg)
- **Smoking**: never or ex-smoker, current smoker
- **Alcohol**: none or <1, 1-4.99,  $\geq$ 5 of daily intake of soju (drink/day)
- **Physical activity**: sedentary+light, ≥moderate+vigorous

## Statistical analyses

#### Model development

- Multiple logistic regression analysis
- Predictors; continuous variables first,

categorized in the final model

- Backward elimination
- Weighted scoring system, ORs

(e.g. 1 for OR 1.52, 3 for OR 3.19)

- Established screening models
  - ADA diabetes risk questionnaire II, US screening score, Rotterdam model, Qingdao diabetes risk score, Thai risk score,

## Standard validation measures

- Proportion of high-risk individuals
- Sensitivity, Specificity
- Positive predictive value (PPV)
- Negative predictive value (NPV)
- Positive/Negative likelihood ratio
- Youden index
- AUC

# Clinical characteristics of participants in KNHANES 2001-2005 by diabetes status

| Characteristics      | NGT         | IFG         | Undiagnosed DM | Known DM    | р       |
|----------------------|-------------|-------------|----------------|-------------|---------|
| n                    | 7,052       | 2,209       | 341            | 600         |         |
| Age, y               | 42.1 (0.3)  | 48.6 (0.5)  | 51.2 (0.8)     | 59.8 (0.6)  | < 0.001 |
| Men, %               | 44.4        | 50.5        | 51.9           | 49.1        | < 0.001 |
| FH of DM, %          | 14.1        | 14.9        | 22.6           | 28.4        | 0.006   |
| Smoking, Current %   | 25.8        | 27.2        | 36.4           | 28.7        | 0.004   |
| Alcohol, drink/day   | 0.7 (0.0)   | 1.0 (0.1)   | 1.5 (0.2)      | 0.9 (0.1)   | < 0.001 |
| ≥5 drink/day, %      | 3.7         | 6.3         | 10.9           | 6.6         | < 0.001 |
| Physically active, % | 9.4         | 12.6        | 11.3           | 7.5         | 0.001   |
| BMI, kg/m²           | 23.2 (0.1)  | 24.6 (0.1)  | 25.3 (0.2)     | 24.9 (0.2)  | < 0.001 |
| Waist, cm            |             |             |                |             |         |
| Male                 | 82.7 (0.2)  | 86.3 (0.3)  | 88.4 (0.7)     | 87.7 (0.6)  | < 0.001 |
| Female               | 76.8 (0.2)  | 82.0 (0.4)  | 85.6 (0.9)     | 86.7 (0.6)  | < 0.001 |
| FPG, mg/dl           | 87.6 (0.2)  | 107.4 (0.2) | 150.0 (2.2)    | 133.7 (2.2) | < 0.001 |
| Systolic BP, mmHg    | 117.0 (0.4) | 125.9 (0.5) | 131.4 (1.2)    | 131.6 (1.0) | < 0.001 |
| Diastolic BP, mmHg   | 76.0 (0.2)  | 80.1 (0.4)  | 82.5 (0.8)     | 79.6 (0.5)  | < 0.001 |
| HTN, %               | 19.4        | 37.4        | 45.8           | 58.2        | < 0.001 |
| Total Chol., mg/dl   | 182.1 (0.6) | 194.5 (0.9) | 201.7 (2.7)    | 195.9 (1.7) | < 0.001 |
| Triglycerides, mg/dl | 123.1 (1.4) | 156.9 (2.7) | 215.4 (17.9)   | 189.1 (8.7) | < 0.001 |
| HDL Chol., mg/dl     | 46.0 (0.2)  | 44.6 (0.3)  | 42.9 (0.6)     | 41.7 (0.5)  | < 0.001 |

Data are mean (SE) or %. N; by un-weighted number. FPG, fasting plasma glucose. P value; comparison between NGT, IFG and undiagnosed DM group excluding known DM group

# Logistic regression analyses for related factors for undiagnosed diabetes

| Variables                 | β<br>coefficient | Odds ratio<br>(95% Cl) | р       | Score<br>assigned |
|---------------------------|------------------|------------------------|---------|-------------------|
| Intercept                 | -5.608           |                        |         |                   |
| Age, y                    |                  |                        |         |                   |
| < 35                      |                  | Ref                    |         | 0                 |
| 35-44                     | 1.068            | 2.91 (1.74, 4.88)      | <0.0001 | 2                 |
| ≥ 45                      | 1.305            | 3.69 (2.23, 6.11)      | <0.0001 | 3                 |
| Family history of DM      |                  |                        |         |                   |
| No                        |                  | Ref                    |         | 0                 |
| Yes                       | 0.621            | 1.86 (1.29, 2.68)      | 0.0008  | 1                 |
| Hypertension              |                  |                        |         |                   |
| No                        |                  | Ref                    |         | 0                 |
| Yes                       | 0.417            | 1.52 (1.17, 1.97)      | 0.0018  | 1                 |
| Waist circumference, cm   |                  |                        |         |                   |
| < 84/77 (M/F)             |                  | Ref                    |         | 0                 |
| 84-89.9/77-83.9           | 0.779            | 2.18 (1.47, 3.24)      | 0.0001  | 2                 |
| ≥ 90/84                   | 1.161            | 3.19 (2.20, 4.64)      | <0.0001 | 3                 |
| Smoking status            |                  |                        |         |                   |
| Non or ex-smoker          |                  | Ref                    |         | 0                 |
| Current smoker            | 0.386            | 1.47 (1.08, 2.01)      | 0.0155  | 1                 |
| Alcohol intake, drink/day |                  |                        |         |                   |
| Never or <1               |                  | Ref                    |         | 0                 |
| 1-4.9                     | 0.493            | 1.64 (1.16, 2.32)      | 0.0055  | 1                 |
| ≥ 5                       | 0.795            | 2.21 (1.42, 3.45)      | 0.0004  | 2                 |
|                           |                  | $\Delta I I C = 0.730$ | mavim   | al score is 11    |

AUC = 0.730. maximal score is 11.

# Performance of diabetes screening method in development & validation datasets

| Method, by dataset                | High<br>risk,<br>% | Sensiti-<br>vity (%) | Specifi-<br>city (%) | PPV | NPV | Positive<br>LR | Negative<br>LR | Youden<br>index | AUC   |
|-----------------------------------|--------------------|----------------------|----------------------|-----|-----|----------------|----------------|-----------------|-------|
| Development dataset               | KNHA               | NES 200              | 01-2005              |     |     |                |                |                 |       |
| ≥4                                | 60                 | 89                   | 41                   | 5   | 99  | 1.52           | 0.27           | 30              |       |
| ≥5*                               | 47                 | 81                   | 54                   | 6   | 99  | 1.75           | 0.36           | 35              | 0.730 |
| ≥6                                | 34                 | 65                   | 67                   | 7   | 98  | 2.00           | 0.51           | 33              |       |
| Validation dataset                | KNHANES 2007-2008  |                      |                      |     |     |                |                |                 |       |
| After imputation; ≥5 <sup>†</sup> | 48                 | 80                   | 53                   | 4   | 99  | 1.68           | 0.39           | 32              | 0.742 |

\* best cut-point; area Under the ROC curve (AUC) : 0.730 (95% CI: 0.720-0.739), p=0.0001 † after imputing the missing data of family history of diabetes

# Performance of new and existing diabetes screening method in development datasets

| Method, by dataset   | High<br>risk,<br>% | Sensiti-<br>vity (%) | Specifi-<br>city (%) | PPV | NPV | Positive<br>LR | Negative<br>LR | Youden<br>index | AUC   |
|----------------------|--------------------|----------------------|----------------------|-----|-----|----------------|----------------|-----------------|-------|
| Development dataset  | KNHANES 2001-2005  |                      |                      |     |     |                |                |                 |       |
| New Score (≥5)       | 47                 | 81                   | 54                   | 6   | 99  | 1.75           | 0.36           | 35              | 0.730 |
| ADA questionnaire II | 21                 | 41                   | 79                   | 7   | 97  | 2.01           | 0.74           | 21              | 0.604 |
| US screening score   | 14                 | 33                   | 86                   | 8   | 97  | 2.44           | 0.77           | 20              | 0.685 |
| Rotterdam model      | 29                 | 53                   | 72                   | 7   | 98  | 1.89           | 0.65           | 25              | 0.661 |
| Qingdao risk score   | 36                 | 62                   | 65                   | 6   | 98  | 1.77           | 0.59           | 27              | 0.693 |
| Thai risk score      | 46                 | 74                   | 55                   | 6   | 98  | 1.64           | 0.48           | 29              | 0.689 |

\* best cut-point; area Under the ROC curve (AUC) : 0.730 (95% CI: 0.720-0.739), p=0.0001

<sup>†</sup> after imputing the missing data of family history of diabetes

# Prevalence of undiagnosed diabetes according to the risk score



# Self-assessment screening questionnaire for undiagnosed diabetes

| Question   | Answe   | Enter your Score<br>(Enter 0 if you don't know) |  |
|--|---|---|--|
| 1. Your age group?                                 | < 35 y (0 point)                                      |   |  |
|  | 35-44  y (2 points)<br>$\geq 45 \text{ y (3 points)}$ |   |  |
| 2. Have either of your parents or siblings         | No (0 point)  |   |  |
| been diagnosed with diabetes?                      | Yes (1 point)   |   |  |
| 3. Are you currently taking medication             | No (0 point)  |   |  |
| for hypertension or do you have hypertension       | Yes (1 point)   |   |  |
| (i.e.g, blood pressures greater than 140/90 mmHg)? |   |   |  |
| 4. What is your waist circumference                | Men   | Women   |  |
| (taken below the ribs,                             | < 84 cm (33 inch) (0 point)                           | < 77 cm (30 inch) (0 point)                     |  |
| usually at the level of the navel)?                | 84-89.9 cm (33-34.9 inch) (2 points)                  | 77-83.9 cm (30-32.9 inch) (2 points)            |  |
|  | $\geq$ 90 cm (35 inch) (3 points)                     | $\geq$ 84 cm (33 inch) (3 points)               |  |
| 5. Do you currently smoke cigarettes on a daily    | Never or Ex-smoker (0 point)                          |   |  |
| basis?   | Current smoker (1 point)                              |   |  |
| 6. How much alcohol do you drink on a daily        | Never or less than 1 drink / day (0 point             | nt)   |  |
| basis? (regardless of types of alcohols)           | 1-4.9 drinks /day (1 point)                           |   |  |
|  | $\geq$ 5 drinks /day (2 points)                       |   |  |
| TOTAL SCORE (add points from questions 1-6)        |   |   |  |

## 한국인 당뇨병 위험지수



이용호, 김대중, 박석원 등. Diabetes Care 2012

## Summary & Conclusions

- We developed and validated a simple and practical tool to identify high-risk subjects for diabetes in a Korean population.
  - We intended to establish a simple risk score model without using laboratory tests or difficult calculations such as BMI
- The model included age, family history of diabetes, hypertension, waist circumference, smoking status and alcohol intake.

## Summary & Conclusions

- Diabetes risk assessment models developed in white populations tend to poorly predict high-risk subjects for diabetes in Korean populations.
- Our risk model is an alternative approach that easily can be used in communities and clinical settings to screen individuals at high risk for diabetes.

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