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# Prediction of the 20-year incidence of diabetes in older Chinese
## Application of the competing risk method in a longitudinal study

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## Abstract

The competing risk method has become more acceptable for time-to-event data analysis because of its advantage over the standard Cox model in accounting for competing events in the risk set. This study aimed to construct a prediction model for diabetes using a subdistribution hazards model.

We prospectively followed 1857 community residents who were aged ≥ 55 years, free of diabetes at baseline examination from August 1992 to December 2012. Diabetes was defined as a self-reported history of diabetes diagnosis, taking antidiabetic medicine, or having fasting plasma glucose (FPG) ≥ 7.0 mmol/L. A questionnaire was used to measure diabetes risk factors, including dietary habits, lifestyle, psychological factors, cognitive function, and physical condition. Gray test and a subdistribution hazards model were used to construct a prediction algorithm for 20-year risk of diabetes. Receiver operating characteristic (ROC) curves, bootstrap cross-validated Wolber concordance index (C-index) statistics, and calibration plots were used to assess model performance.

During the 20-year follow-up period, 144 cases were documented for diabetes incidence with a median follow-up of 10.9 years (interquartile range: 8.0–15.3 years). The cumulative incidence function of 20-year diabetes incidence was 11.60% after adjusting for the competing risk of nondiabetes death. Gray test showed that body mass index, FPG, self-rated heath status, and physical activity were associated with the cumulative incidence function of diabetes after adjusting for age. Finally, 5 standard risk factors (poor self-rated health status [subdistribution hazard ratio (SHR) = 1.73, $P = 0.005$], less physical activity [SHR = 1.39, $P = 0.047$], 55–65 years old [SHR = 4.37, $P < 0.001$], overweight [SHR = 2.15, $P < 0.001$] or obesity [SHR = 1.96, $P = 0.003$], and impaired fasting glucose [IFG] [SHR = 1.99, $P < 0.001$]) were significantly associated with incident diabetes. Model performance was moderate to excellent, as indicated by its bootstrap cross-validated discrimination C-index (0.74, 95% CI: 0.70–0.79) and calibration plot.

Poor self-rated health, physical inactivity, being 55 to 65 years of age, overweight/obesity, and IFG were significant predictors of incident diabetes. Early prevention with a goal of achieving optimal levels of all risk factors should become a key element of diabetes prevention.

**Abbreviations:** 95% CI = 95% confidence interval, BADL = basic activities of daily living, BLSA = Beijing Longitudinal Study of Aging, BMI = body mass index, BP = blood pressure, CES-D = Center for Epidemiological Studies Depression, CIF = cumulative incidence function, C-index = Wolber concordance index, FPG = fasting plasma glucose, HDL-C = high-density lipoprotein cholesterol, IADL = instrumental activities of daily living, ICD = international classification of disease, IFG = impaired fasting glucose, LDL-C = low-density lipoprotein cholesterol, MMSE = mini mental state examination, SHR = subdistribution hazard ratio, SRH = self-rated health, TC = total cholesterol, TG = triglycerides.

**Keywords:** Beijing, competing risk, diabetes, risk prediction, subdistribution hazards model

## 1. Introduction

Diabetes is a well-recognized cause of premature death and disability and is associated with increased risk of cardiovascular disease, kidney failure, blindness, and lower-limb amputation.[1] While the incidence and prevalence of diabetes have been increasing globally, these increases have occurred at particularly accelerated rates in low- and middle-income countries.[2–4] China has the second highest prevalence of and the largest absolute disease burden associated with diabetes in the world.[5] Older adults are one of the fastest growing age groups worldwide, especially in Beijing City.[6] By the end of 2008, the total population of Beijing had reached 12.3 million, with people aged over 60, over 65, and over 80 making up 17.7%, 13.2%, and 2.4% of the total population, respectively.[7]

Researchers have been able to construct multivariable risk prediction models intended to aid clinicians in risk assessment. Within these models, the most commonly identified predictors are demographic characteristics, cardio-metabolic health indicators, and lifestyle behaviors.[3] However, the currently used diabetes risk prediction algorithms were developed for prediction over periods of 10 years or less. Increasing life expectancy and elderly populations suggest the need for longer-term risk prediction tools. Second, few studies have considered emerging psychological factors such as adverse life events and depression.[8,9] Some studies have suggested a potential link between psychological stress and incident diabetes.[10,11] Third, only a small number of studies have assessed the association between cognitive function and diabetes incidence using tools such as the mini mental state examination (MMSE).[12,13] Fourth, the performance of existing diabetes prediction models varies by country and age.[14–17] Despite the large number of risk prediction models being developed, only a very small minority have been designed for middle-aged and older Asian populations, especially Chinese populations.[15,18,19]

Moreover, conventional statistical methods for the analysis of time-to-event data assume the absence of competing risks.[9,10,20] However, competing risk of death should be an important consideration in the study of elderly populations.[21] Ignoring the presence of competing risks can result in estimates of the incidence of the event of interest that are biased upwards, as well as incorrect estimates of the associations between predictors and outcomes.[21–24] In particular, the sum of the incidence estimates for each event type will exceed the estimate of the incidence of the composite outcome, defined as any of the event types.[23] To overcome these problems, the subdistribution hazards model, or Fine–Gray model, was proposed,[25] in which a cumulative incidence function (CIF) is used to estimate the incidence of an event while taking into account the presence of competing events.[23,26] The subdistribution hazards model has been increasingly applied for the prediction of disease.[24,27,28] However, to the best of our knowledge, no algorithm has been proposed to quantify the 20-year risk of diabetes using the subdistribution hazards model.

In this report, we describe the development of a prediction model for estimating the 20-year risk of incident diabetes in Chinese elders free of diabetes at baseline. Our risk estimates allow adjustment for the competing risk of nondiabetes death and consider lifestyle behaviors, psychological factors, cognitive function, and physical condition simultaneously. This tool is based on the Beijing Longitudinal Study on Aging (BLSA), which has contributed to the creation of a 10-year risk score algorithm for coronary artery disease using a subdistribution hazards model,[28] and this tool offers 20 years of rigorous surveillance for diabetes.

## 2. Methods

### 2.1. The BLSA study

Using the 10% population sampling data from Beijing collected during China's fourth census, a 3-stage (i.e., natural living environment, education level, and age) stratification-random-clustering sampling procedure was performed to ensure the representativeness of the Beijing elderly population in general.[29,30] From August 1992 to December 2012, a community-based cohort of 2101 people (1037 men and 1064 women, 55–96 years old) were recruited for the BLSA in Beijing, China. Periodic health examinations, including questionnaire interviews, anthropometric measurements, clinical examinations, and laboratory assessments, were performed in the years 1992, 1994, 1997, 2000, 2004, 2007, 2009, and 2012. We used complete data obtained during the period from 1992 to 2012 in this study. Two hundred forty-four subjects were excluded because they had a baseline fasting plasma glucose (FPG) level greater than or equal to 7.0 mmol/L (126 mg/dl), had a history of diabetes (as informed by a physician), were taking antidiabetic medicine, or had missing blood examination data. Thus, 1857 persons were included in our analyses. Overall, 925 men and 932 women without diabetes at baseline were included in this study.

This study followed the guidelines of the Helsinki Declaration and was approved by the Ethics Committee of Xuanwu Hospital, Capital Medical University. Written informed consent was obtained from all participants.

### 2.2. Assessment of risk factors and outcomes

Demographic characteristics and information about dietary habits, lifestyle, psychological factors, and physical condition were obtained using questionnaires with a high degree of reliability and accuracy that were designed by the Beijing Geriatric Clinical and Research Center and Australia Geriatric Research Center of Flinders University.[29–32]

A food frequency questionnaire was used for dietary assessment.[33] Then, a latent class model was constructed, and the best model was selected according to Bayesian information criterion values. Based on the posterior probability (representing the frequency of food intake), dietary habits were divided into 3 latent groups: overnutrition diet, intermediate-type diet, and meat-based diet. Self-reported smoking, drinking, residential area, health status, sad events, and physical activity frequency were evaluated. Self-rated health (SRH) was used as an expression of social, psychological, and biologic dimensions. In the present study, SRH was based on asking individuals to compare their health status to that of age peers. Experience of a sad event was defined as suffering at least one of the following events in past three years: loss of job, change of living environment, life setbacks in children, seriously ill spouse, seriously ill children, death of spouse, death of children, death of parents, death of good friends, not getting along well with spouse, not getting along well with neighbors, not getting along well with children, financial difficulties, stolen or lost property, and serious natural disasters (i.e., fire, flood, or earthquake).

The Center for Epidemiological Studies Depression (CES-D) scale was used to measure depression level, with a maximum score of 60 and standard cutoff value of 16.[34] A higher score

corresponded to a more severe condition. The MMSE scale was used to differentiate between cognitive levels.[35] The critical threshold values were as follows: illiterate > 17, primary school education > 20, secondary or higher education > 24. Physical limitation was assessed using the instrumental activities of daily living (IADL) and basic activities of daily living (BADL) surveys.[36] The subjects were categorized into complete ability or disability based on these 2 scales, respectively.

Age was categorized into 3 subgroups: 55 to 65 years, 66 to 75 years, and ≥ 76 years. Marital status was divided into 2 categories: married and unmarried. Body mass index (BMI) was calculated according to the equation BMI = weight (kg)/height (m)$^2$ and was classified based on the common Chinese criteria,[37] that is, thin (BMI < 18.5 kg/m$^2$), normal (18.5 ≤ BMI < 24.0 kg/m$^2$), overweight (24.0 ≤ BMI < 28.0 kg/m$^2$), and obese (BMI ≥ 28.0 kg/m$^2$).

Blood pressure (BP) was measured twice on the left arm of seated participants using a mercury sphygmomanometer and an appropriately sized cuff, and the average of the blood pressure measurements was considered the examination blood pressure. Two measurements of BP were taken 5 minutes apart. If the 2 measurements differed by more than 5 mm Hg, then an additional reading was taken, and the final average of the readings was used for analysis purposes. BP was classified into 2 groups: high (systolic blood pressure > 140 mm Hg or diastolic blood pressure > 90 mm Hg) and normal blood pressure.

Blood samples were collected after an overnight fasting period of at least 12 hours. FPG, total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) levels were subsequently determined using standardized enzymatic methods. According to the standards for impaired fasting glucose (IFG) and dyslipidemia, an FPG level of 6.1 to 6.9 mmol/L was considered IFG.[37] A TC level of 5.18 mmol/L or greater, TG level of 1.7 mmol/L or greater, HDL-C level less than 1.03 mmol/L in men or 1.29 mmol/L in women, or an LDL-C level of more than 3.35 mmol/L was considered dyslipidemia.[38]

The outcome of interest was the first incidence of diabetes at follow-up. This incidence was identified as a self-reported history of diabetes diagnosis, taking antidiabetic medicine after the baseline examination, or having a measured FPG level of ≥ 7.0 mmol/L (126 mg/dL) at any of the periodic examinations.[38] The date of diagnosis (incidence) was defined as the examination date at which a new case of diabetes was identified or the diagnosis date if a recent diabetes history was reported by questionnaire, whichever came first. Survival status was determined through interviews with surviving household members or neighbors when surviving household members were unavailable. Information was verified for a subset of participants based on household registration records. Cause of death was determined according to the International Classification of Disease (ICD), ninth revision (ICD-9 or ICD-10). Nondiabetes deaths, including deaths due to cardiovascular diseases, cancers, and other causes, were defined as competing events.

### 2.3. Statistical analysis

Time of follow-up accrued from the return date of the 1992 questionnaire until incidence of diabetes, death, loss to follow-up, or end of follow-up (December 2012), whichever came first. Considering the extensive length of follow-up and potential bias due to the competing risk of nondiabetes mortality, we employed the subdistribution hazards model to adjust risk estimates for the competing risk of nondiabetes mortality.[23] The subdistribution hazards model calculates the cumulative incidence of diabetes in the following manner:

$$\widehat{CIF}(20) = \sum_{t_i < 20} \hat{\lambda}(t_i)\hat{s}(t_{i-1}).$$

The quantities under summation denote the instantaneous hazard of diabetes at event time $t_i$ and survival rate from both diabetes and nondiabetes death past event time $t_{i-1}$.

Subdistribution hazards models were fitted to predict the risk of developing diabetes using the "cmprsk," "crrstep," and "survival" packages in R software (R Foundation for Statistical Computing, Vienna, Austria). For the first step, univariate subdistribution hazards models were used to regress the subdistribution hazard of diabetes incidence on all 19 candidate variables, and variables with estimated regression coefficients having a statistical significance of $P > 0.20$ were removed. Gray test was also performed to compare the cumulative incidence function of diabetes between groups defined by each variable after adjusting for age. Then, all significant variables were included in a multivariate prediction model with backward selection. For the third step, the remaining variables were included to build the final prediction model. For each model, subdistribution hazard ratios (SHRs) and 95% confidence intervals (95% CIs) were calculated to estimate relative risk. All continuous variables were categorized to build the model. We did not examine any interactions between the independent variables.

After the prediction models were developed, it was critical to evaluate their performance. Discrimination of the model was assessed using Wolber concordance index (C-index) with R packages "pec," "rms," and "pROC."[39] The C-index was used to give a quantitative assessment of the model's predictive ability. The calibration of the model was assessed graphically by comparing the predicted probability to the observed probability across 10 deciles of predicted risk.[40] Calibration referred to the agreement between observed outcomes and predictions. The more spread between the 10 deciles, the better discriminating the model. The calibration plot was generated with the R package "pec." Additionally, internal validation was performed to estimate the potential for overfitting and positivity of the models using 1000 times bootstrap resampling with the R package "pROC."

All P-values reported are 2-sided. Independent 2-sample $\chi^2$ tests were performed using SAS software (Version 9.2, SAS Institute Inc., Cary, NC). Subdistribution hazards models, receiver operating characteristic (ROC) curves, C-indexes, calibration plots, and bootstrap internal validations were performed in R software (version 3.3.1).

## 3. Results

### 3.1. Baseline characteristics

Among the 2101 community dwellers aged 55 years or over in 1992, 244 participants were excluded because of taking antidiabetic drugs, reporting a history of diabetes, having FPG ≥ 7.0 mmol/L (126 mg/dl), or missing blood examination data. We followed up 1857 participants without diabetes at baseline for a median period of 9.8 years. The average ages were 69.00 (8.81) years for women and 69.88 (8.55) years for men at baseline. Overall, 144 cases were diagnosed with diabetes incidence at a median follow-up of 10.9 (interquartile range: 8.0–15.3) years. The diabetes incidence density was 7.908/1000
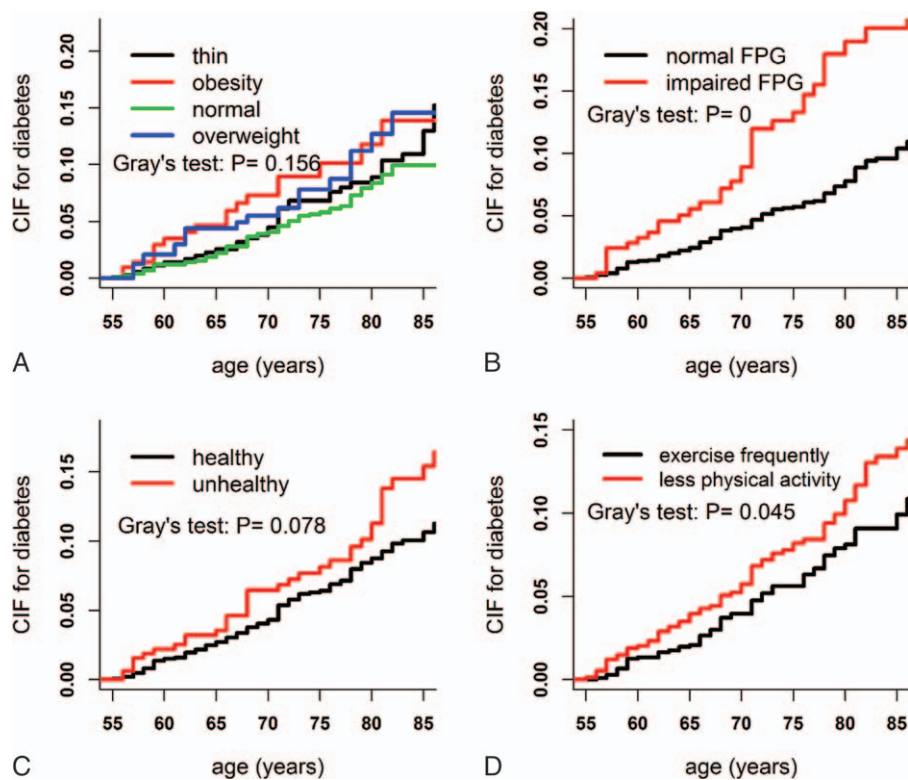
**Figure 1.** The CIFs of diabetes: comparing the different groups after adjusting age. (A) CIFs for body mass index groups; (B) CIFs for the normal FPG group and impaired FPG group; (C) CIFs for the results of self-health assessment; (D) CIFs for the exercise group and exercise infrequently group. CIF = cumulative incidence functions, FPG = fasting plasma glucose.

person-years. After we adjusted for the competing risks of nondiabetes deaths, the CIF of incident diabetes was 11.60%. The result of the Gray test showed that after adjusting for age, BMI, FPG, SRH status, and physical activity were associated with the cumulative incidence function of diabetes (Fig. 1). There were differences between the incident diabetes and nondiabetes groups in the distributions of age, disability, marital status, self-assessment of health, blood lipids, and physical exercise at baseline ($P < 0.05$) (Table 1). By the end of 2012, there had been 144 failure events and 920 deaths from nondiabetic causes. Approximately 4.7% of participants were lost to follow-up (n = 87). Sensitivity analysis showed that there were no significant differences in the distributions of baseline characteristics between those lost to follow-up and those followed.

### 3.2. Results from univariate analyses for the BLSA population

Univariate subdistribution hazards models were used to regress the subdistribution hazard of diabetes incidence on all 19 candidate variables; the estimated regression coefficients, estimated regression subhazard ratios, estimated 95% CI, and statistical significance of the estimated regression coefficients are reported in Table 2. After accounting for competing events in the risk set, the univariate subdistribution hazards model showed that sex, age, BMI, FPG, self-assessment of health, exercise, disability, marital status, blood lipid level, education level, and dietary habits were associated with diabetes incidence.

Women were at higher risk of diabetes than men (SHR = 1.50, 95% CI = 1.08–2.08, P = 0.015). Divorced and single individuals

were at a higher risk of diabetes (SHR = 1.82, 95% CI = 1.22–2.71, P = 0.003) than those who were married. Those individuals with impaired FPG and abnormal blood lipids were at a higher risk of diabetes than those with normal FPG (SHR = 2.12, 95% CI = 1.46–3.08, P < 0.001) and normal blood lipids (SHR = 1.75, 95% CI = 1.24–2.46, P < 0.001). Disability and poor self-assessment of health were associated with higher risk of diabetes than normal ability (SHR = 0.40, 95% CI = 0.19–0.84, P = 0.016) and normal self-health assessment (SHR = 1.57, 95% CI = 1.09–2.29, P = 0.017), respectively.

For multiple categorical variables, the following were associated with a higher risk of diabetes incidence: overweight (SHR = 2.58, 95% CI = 1.73–3.85, P < 0.001), obesity (SHR = 2.35, 95% CI = 1.52–3.63, P < 0.001), and overnutrition diet (SHR = 1.54, 95% CI = 1.08–2.20, P = 0.018). Illiterate individuals were at a lower risk of incident diabetes than those had graduated (SHR = 0.55, 95% CI = 0.30–0.99, P = 0.045). Those aged 55 to 65 and 66 to 75 years had an increased risk of diabetes incidence than those aged > 76 years (SHR = 5.48, 95% CI = 3.01–10.00, P < 0.001; SHR = 2.32, 95% CI = 1.21–4.43, P = 0.011).

### 3.3. Development of prediction models

All significant variables from univariate analyses were included in a multivariate risk prediction model, and 5 variables remained after backward selection (Table 3). In the final Fine–Gray competing risk regression model, the risk of diabetes incidence decreased with increasing age (55–65 age group: SHR = 4.37, 95% CI = 2.36–8.10; 66–75 age group: SHR = 1.98, 95% CI = 1.02–3.83). A greater risk of diabetes incidence was associated

**Table 1**

**Baseline characteristics between participants of incident diabetes and nondiabetes from the BLSA study.**

| Characteristic | Total (n = 1857) | | | Men (n = 925) | | | Women (n = 932) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Diabetes (%) | Nondiabetes (%) | P | Diabetes (%) | Nondiabetes (%) | P | Diabetes (%) | Nondiabetes (%) | P |
| Sex | | | 0.042 | – | – | – | – | – | – |
| Men | 60 (6.49) | 865 (93.51) | | | | | | | |
| Female | 84 (9.01) | 848 (90.99) | | | | | | | |
| Age group | | | <0.001 | | | <0.001 | | | <0.001 |
| 55–65 | 93 (13.92) | 575 (86.08) | | 40 (11.49) | 308 (88.51) | | 53 (16.56) | 267 (83.44) | |
| 66–75 | 39 (5.76) | 638 (94.24) | | 17 (4.90) | 330 (95.10) | | 22 (6.67) | 308 (93.33) | |
| ≥76 | 12 (2.34) | 500 (97.66) | | 3 (1.30) | 227 (98.70) | | 9 (3.19) | 273 (96.81) | |
| Smoke | | | 0.902 | | | 0.121 | | | 0.309 |
| Yes | 44 (7.87) | 515 (92.13) | | 26 (8.23) | 290 (91.77) | | 18 (7.41) | 225 (92.59) | |
| No | 100 (7.70) | 1198 (92.30) | | 34 (5.58) | 575 (94.42) | | 66 (9.58) | 623 (90.42) | |
| Drink | | | 0.680 | | | - | | | 0.458 |
| Yes | 34 (8.23) | 379 (91.77) | | 0 | 0 | | 34 (8.23) | 379 (91.77) | |
| No | 110 (7.62) | 1334 (92.38) | | 60 (6.49) | 865 (93.51) | | 50 (9.63) | 469 (90.37) | |
| Depression | | | 0.507 | | | 0.983 | | | 0.279 |
| Yes | 29 (8.63) | 307 (91.37) | | 12 (6.45) | 174 (93.55) | | 17 (11.33) | 133 (88.67) | |
| No | 115 (7.56) | 1406 (92.44) | | 48 (6.50) | 691 (93.50) | | 67 (8.57) | 715 (91.43) | |
| Sad event | | | 0.942 | | | 0.674 | | | 0.799 |
| Yes | 47 (7.82) | 554 (92.18) | | 21 (6.98) | 280 (93.02) | | 26 (8.67) | 274 (91.33) | |
| No | 97 (7.72) | 1159 (92.28) | | 39 (6.25) | 585 (93.75) | | 58 (9.18) | 574 (90.82) | |
| IADL | | | 0.015 | | | 0.813 | | | 0.003 |
| Disability | 7 (3.45) | 196 (95.55) | | 6 (5.94) | 95 (94.06) | | 1 (0.98) | 101 (99.02) | |
| Normal | 137 (8.28) | 1517 (91.72) | | 54 (6.55) | 770 (93.45) | | 83 (10.00) | 747 (90.00) | |
| ADL | | | 0.025 | | | 0.793 | | | 0.007 |
| Disability | 8 (3.85) | 200 (96.15) | | 6 (5.88) | 96 (94.12) | | 2 (1.89) | 104 (98.11) | |
| Normal | 136 (8.25) | 1513 (91.75) | | 54 (6.56) | 769 (93.44) | | 82 (9.93) | 744 (90.07) | |
| Marital status | | | 0.001 | | | 0.023 | | | 0.015 |
| Mateless | 30 (4.88) | 585 (95.12) | | 11 (3.77) | 281 (96.23) | | 19 (5.88) | 304 (94.12) | |
| Have a spouse | 114 (9.18) | 1128 (90.82) | | 49 (7.74) | 584 (92.26) | | 65 (10.67) | 544 (89.33) | |
| MMSE | | | 0.917 | | | 0.497 | | | 0.631 |
| Abnormal | 28 (7.89) | 327 (92.11) | | 13 (7.65) | 157 (92.35) | | 15 (8.11) | 170 (91.89) | |
| Normal | 116 (7.72) | 1386 (92.28) | | 47 (6.23) | 708 (93.77) | | 69 (9.24) | 678 (90.76) | |
| Self-rated health | | | 0.015 | | | 0.77 | | | 0.002 |
| Not health | 36 (11.04) | 290 (88.96) | | 12 (6.98) | 160 (93.02) | | 24 (15.58) | 130 (84.42) | |
| Health | 108 (7.05) | 1423 (92.95) | | 48 (6.37) | 705 (93.63) | | 60 (7.71) | 718 (92.29) | |
| Fasting plasma glucose | | | <0.001 | | | | | | 0.002 |
| Impaired | 35 (13.62) | 222 (86.38) | | 0 | 0 | | 35 (13.62) | 222 (86.38) | |
| Normal | 109 (6.81) | 1491 (93.19) | | 60 (6.49) | 865 (93.51) | | 49 (7.26) | 626 (92.74) | |
| Blood lipid | | | 0.001 | | | 0.072 | | | 0.009 |
| Abnormal | 49 (11.48) | 378 (88.52) | | 18 (9.33) | 175 (90.67) | | 31 (13.25) | 203 (86.75) | |
| Normal | 95 (6.64) | 1335 (93.36) | | 42 (5.74) | 690 (94.26) | | 53 (7.59) | 645 (92.41) | |
| Blood pressure | | | 0.854 | | | 0.990 | | | 0.869 |
| Abnormal | 70 (7.87) | 819 (92.13) | | 28 (6.50) | 403 (93.50) | | 42 (9.17) | 416 (90.83) | |
| Normal | 74 (7.64) | 894 (92.36) | | 32 (6.48) | 462 (93.52) | | 42 (8.86) | 432 (91.14) | |
| Education level | | | 0.087 | | | 0.089 | | | 0.572 |
| College or above | 66 (6.75) | 912 (93.25) | | 28 (5.29) | 501 (94.71) | | 38 (8.46) | 411 (91.54) | |
| High school or below | 78 (8.87) | 801 (91.13) | | 32 (8.08) | 364 (91.92) | | 46 (9.52) | 437 (90.48) | |
| Body mass index | | | 0.187 | | | 0.988 | | | 0.133 |
| Thin | 37 (10.16) | 327 (89.84) | | 11 (6.92) | 148 (93.08) | | 26 (12.68) | 179 (87.32) | |
| Normal | 69 (6.68) | 964 (93.32) | | 35 (6.31) | 520 (93.69) | | 34 (7.11) | 444 (92.89) | |
| Overweight | 20 (8.13) | 226 (91.87) | | 7 (6.31) | 104 (93.69) | | 13 (9.63) | 122 (90.37) | |
| Obesity | 18 (8.41) | 196 (91.59) | | 7 (7.00) | 93 (93.00) | | 11 (9.65) | 103 (90.35) | |
| Area | | | 0.322 | | | 0.139 | | | 0.631 |
| Mountain | 29 (9.86) | 265 (90.14) | | 20 (9.26) | 196 (90.74) | | 9 (11.54) | 69 (88.46) | |
| Rural | 36 (7.68) | 433 (92.32) | | 18 (6.34) | 266 (93.66) | | 18 (9.73) | 167 (90.27) | |
| Urban | 79 (7.22) | 1015 (92.78) | | 22 (5.18) | 403 (94.82) | | 57 (8.52) | 612 (91.48) | |
| Diet | | | 0.167 | | | | | | 0.463 |
| Overnutrition diet | 55 (8.97) | 558 (91.03) | | 17 (6.88) | 230 (93.12) | 0.248 | 38 (10.38) | 328 (89.62) | |
| Intermediate type | 63 (6.61) | 890 (93.39) | | 26 (5.36) | 459 (94.64) | | 37 (7.91) | 431 (92.09) | |
| Extra serving of meat | 26 (8.93) | 265 (91.07) | | 17 (8.81) | 176 (91.19) | | 9 (9.18) | 89 (90.82) | |
| Physical activity | | | 0.012 | | | 0.114 | | | 0.026 |
| No | 73 (9.63) | 685 (90.37) | | 33 (7.89) | 385 (64.82) | | 40 (11.76) | 300 (88.24) | |
| Yes | 71 (6.46) | 1028 (93.54) | | 27 (5.33) | 480 (35.18) | | 44 (7.43) | 548 (92.58) | |

P values were based on 2-independent-sample χ² tests.
ADL = activities of daily living, BLSA = Beijing Longitudinal Study of Aging, IADL = instrumental activities of daily living, MMSE = mini mental state examination.

## Table 2

**Subdistribution hazard ratios for univariate subdistribution hazards model from the BLSA study.**

| Characteristic | Log-hazard ratio (β) | Subdistribution hazard ratio | 95% CI for hazard ratio | P |
|---|---|---|---|---|
| Sex (men) | | | | |
| Women | 0.41 | 1.50 | (1.08, 2.08) | 0.015 |
| Age group, y | | | | |
| ≥76 | Ref. | Ref. | | – |
| 55–65 | 1.70 | 5.48 | (3.01, 10.00) | <0.001 |
| 66–75 | 0.84 | 2.32 | (1.21, 4.43) | 0.011 |
| Body mass index, kg/m$^2$ | | | | |
| 18.0–23.9 | Ref. | Ref. | | – |
| <18.0 | −0.52 | 0.60 | (0.33, 1.06) | 0.077 |
| 24.0–27.9 | 0.95 | 2.58 | (1.73, 3.85) | <0.001 |
| ≥28.0 | 0.86 | 2.35 | (1.52, 3.63) | <0.001 |
| Fasting glucose (normal) | | | | |
| 6.1–6.9 | 0.75 | 2.12 | (1.46, 3.08) | <0.001 |
| Self-rated health (healthy) | | | | |
| Unhealthy | 0.45 | 1.57 | (1.09, 2.29) | 0.017 |
| Physical activity (yes) | | | | |
| No | 0.31 | 1.36 | (1.00, 1.96) | 0.059 |
| Smoke (no) | | | | |
| Yes | −0.02 | 0.98 | (0.69, 1.40) | 0.919 |
| Drink (no) | | | | |
| Yes | 0.15 | 1.16 | (0.79, 1.70) | 0.459 |
| Depressions (no) | | | | |
| Yes | 0.12 | 1.12 | (0.75, 1.69) | 0.570 |
| Sad event (no) | | | | |
| Experienced | −0.01 | 1.00 | (0.70, 1.41) | 0.978 |
| BADL (abled) | | | | |
| Disabled | −0.52 | 0.60 | (0.09, 3.99) | 0.594 |
| IADL (abled) | | | | |
| Disabled | −0.93 | 0.40 | (0.19, 0.84) | 0.016 |
| Marital status (married) | | | | |
| Divorced or single | 0.60 | 1.82 | (1.22, 2.71) | 0.003 |
| MMSE (normal) | | | | |
| Abnormal | 0.002 | 1.00 | (0.66, 1.51) | 0.993 |
| Blood pressure (mm Hg) | | | | |
| SBP>140 or DBP>90 | 0.05 | 1.05 | (0.76, 1.46) | 0.752 |
| Blood lipid (normal) | | | | |
| High | 0.559 | 1.75 | (1.24, 2.46) | 0.001 |
| Education level (graduate) | | | | |
| High school diploma | −0.54 | 0.58 | (0.21, 1.64) | 0.31 |
| Junior diploma | −0.05 | 0.95 | (0.46, 1.94) | 0.88 |
| Primary school | −0.36 | 0.70 | (0.38, 1.29) | 0.25 |
| Illiterate | −0.61 | 0.55 | (0.30, 0.99) | 0.045 |
| Area (mountain) | | | | |
| Rural | −0.29 | 0.75 | (0.46, 1.21) | 0.241 |
| Urban | −0.05 | 0.95 | (0.62, 1.45) | 0.806 |
| Diet (intermediate level) | | | | |
| Overnutrition diet | 0.43 | 1.54 | (1.08, 2.20) | 0.018 |
| Extra serving of meat | 0.18 | 1.19 | (0.76, 1.87) | 0.44 |

BADL = basic activities of daily living, BLSA = Beijing Longitudinal Study of Aging, DBP = diastolic blood pressure, IADL = instrumental activities of daily living, MMSE = mini mental state examination, SBP = systolic blood pressure.

with impaired FPG (SHR = 1.99, 95% CI = 1.37–2.90), poor self-assessment of health (SHR = 1.73, 95% CI = 1.19–2.51), overweight status (SHR = 2.15, 95% CI = 1.44–3.21), and obese status (SHR = 1.96, 95% CI = 1.27–3.03). Those who did not exercise were at a higher risk of diabetes (SHR = 1.39, 95% CI = 1.04–1.91).

### 3.4. Model prediction performance and bootstrapping cross-validation

The discrimination of the subdistribution hazard model was assessed using the C-index for prediction models with competing risks. The apparent discrimination of the model predicting 20-year diabetes incidence was equal to 0.74 (95% CI: 0.70–0.78) (Fig. 2). The sensitivity, specificity, Youden index, positive predictive value, and negative predictive value of the subdistribution hazards model were 0.81, 0.52, 0.67, 0.13, and 0.97, respectively. The estimated regression coefficients, estimated regression hazard ratios, estimated 95% CI, and statistical significance of the estimated regression coefficients at 20 years were generated using the subdistribution hazards model and bootstrap cross-validation with 1000 bootstrap samples (Table 4). The estimate of the C-index at 20 years using bootstrap cross-validation with 1000 bootstrap samples was 0.74 (95% CI: 0.70–0.79).

**Table 3**

Subdistribution hazard ratios for multivariate subdistribution hazards model from the BLSA study.

| Characteristic | Log-hazard ratio (β) | Subdistribution hazard ratio | 95% CI for hazard ratio | P |
|---|---|---|---|---|
| Age group, y | | | | |
| ≥76 | Ref. | Ref. | Ref. | |
| 55–65 | 1.48 | 4.37 | (2.36, 8.10) | <0.001 |
| 66–75 | 0.68 | 1.98 | (1.02, 3.83) | 0.043 |
| Body mass index, kg/m$^2$ | | | | |
| 18.0–23.9 | Ref. | Ref. | Ref. | |
| <18.0 | −0.44 | 0.64 | (0.36, 1.14) | 0.131 |
| 24.0–27.9 | 0.76 | 2.15 | (1.44, 3.21) | <0.001 |
| ≥28.0 | 0.68 | 1.96 | (1.27, 3.03) | 0.002 |
| Fasting plasma glucose (normal) | Ref. | Ref. | Ref. | |
| IFG | 0.69 | 1.99 | (1.37, 2.90) | <0.001 |
| Self-rated health (healthy) | Ref. | Ref. | | – |
| Unhealthy | 0.55 | 1.73 | (1.19, 2.51) | 0.004 |
| Physical activity (yes) | Ref. | Ref. | Ref. | |
| No | 0.33 | 1.39 | (1.04, 1.91) | 0.047 |
| C-index | | 0.74 (95% CI: 0.70–0.78) | | |

BLSA = Beijing Longitudinal Study of Aging, C-index = Wolber concordance index, IFG = impaired fasting glucose.

The calibration of the model was assessed graphically by comparing the predicted probability of 20-year diabetes incidence to the observed probability of 20-year diabetes incidence across 10 deciles of predicted risk (Fig. 3). Overall, the model displayed moderate-good calibration, with a modest degree of underprediction in subjects in the 6th and 7th deciles of predicted risk. The subdistribution hazards model performed moderately well in terms of discrimination and calibration.

## 4. Discussion

In this report, we describe the construction of a simple prediction model to estimate 20-year risk of diabetes based on factors easily available during epidemiological research. The results are based on over 20 years of rigorous follow-up and ascertainment of diabetes incidence and death. Our prediction model accounts for the competing risk of nondiabetes death.



**Figure 2.** ROC curves for competing-risk-based diabetes prediction model at t = 20-year. 95% CI = 95% confidence intervals, ROC = receiver operating characteristic.

Previously, this community-based retrospective study including a middle-aged and older Chinese population found a relatively low rate of incident diabetes after a 20-year follow-up.[19] Age, BMI, FPG, self-rated health, and physical activity were all significantly associated with incident diabetes during the 20-year follow-up period. In terms of discrimination and calibration, our algorithm performed moderately well in predicting the risk of 20-year incident diabetes. Subdistribution hazards models, which extend the Cox proportional hazards model to competing-risks data by considering the subdistribution hazard,[41–43] do not censor but rather "carry forward" competing event(s) in the risk set with appropriate weighting.[44,45] The present study extended and expanded on the previous general diabetes risk prediction models for middle-aged and older Chinese.

Currently, risk scores such as the Finnish Diabetes Risk Score,[46] Framingham DM Risk Score[15] Cambridge Diabetes Risk Score,[47] and German Diabetes Risk Score[48] are the most widely used for clinical guidelines. In addition, there are a number of other important risk algorithms or functions.[3] However, a prediction model specifically designed to estimate the risk of incident diabetes, especially in the context of competing risks, in Chinese middle-aged and older populations was not previously available. Our risk prediction model provided a feasible tool for identifying individuals who have a high risk of diabetes among middle-aged and older adults in Beijing.

The AUCs of previous diabetes risk scores for older adults ranged from 0.71 to 0.78.[18,19,49] Our prediction model, which was based on a subdistribution hazards model, had a moderately high C-index value of 0.74 (95% CI: 0.70–0.78). Of note, a model providing a C-index value of less than 0.80 for predicting incident diabetes may have limited clinical utility. However, all predictors included in our models are readily available clinical variables. The negative predictive value of the model (0.97) was very high; however, the positive predictive value was low (0.13) primarily because of the low incidence of diabetes in the studied population. Thus, the model is most clinically applicable for use in ruling out the risk of incident diabetes. Based on the prediction model, risk factors may be intervened upon, and health may be placed high on the social, economic, and political agenda of city governments.[50]

**Table 4**

Bootstrap-adjusted subdistribution hazard ratios for multivariate subdistribution hazards model from the BLSA study.

| Characteristic | Log-hazard ratio (β) | Subdistribution hazard ratio | 95% CI for hazard ratio | P |
|---|---|---|---|---|
| Age group, y | | | | |
| ≥76 | Ref. | Ref. | Ref. | |
| 55–65 | 1.48 | 4.37 | (2.28, 8.38) | <0.001 |
| 66–75 | 0.68 | 1.98 | (0.99, 3.96) | 0.054 |
| Body mass index, kg/m² | | | | |
| 18.0–23.9 | Ref. | Ref. | Ref. | |
| <18.0 | −0.44 | 0.64 | (0.34, 1.21) | 0.171 |
| 24.0–27.9 | 0.76 | 2.15 | (1.41, 3.28) | <0.001 |
| ≥28.0 | 0.68 | 1.96 | (1.26, 3.06) | 0.003 |
| Fasting plasma glucose (normal) | Ref. | | Ref. | |
| IFG | 0.69 | 1.99 | (1.36, 2.93) | <0.001 |
| Self-rated health (healthy) | Ref. | | Ref. | |
| Unhealthy | 0.55 | 1.73 | (1.18, 2.53) | 0.005 |
| Physical activity (yes) | Ref. | | Ref. | |
| No | 0.33 | 1.39 | (1.04, 1.91) | 0.047 |
| C-index | | 0.74 (95% CI: 0.70–0.79) | | |

BLSA = Beijing Longitudinal Study of Aging, C-index = Wolber concordance index, IFG = impaired fasting glucose.

In our prediction model, based on the subdistribution hazards model, age was the strongest predictor of incident diabetes. Individuals with an age of 55 to 65 years had the highest risk of developing diabetes in our model, followed by individuals with ages ranging from 66 to 75 years. Similar results were found in the Guangzhou Biobank Cohort Study, which was a 4.1-year population-based follow-up of Chinese persons aged 50 years and above.[18]

BMI was the second strongest predictor in our model and has been included in most published scores used to predict incident diabetes.[18] Obesity, assessed by BMI, might play an important role in developing diabetes, which is similar to results described in previous reports from developing countries.[51] Some policies can be enacted to reduce BMI.[52] Most recent research suggests that sitting time remains a risk factor for diabetes in obese populations.[53] In our model, the FPG variable was the third strongest predictor of incident diabetes. This result is generally consistent with those of previous reports.[49] IFG has been defined as a fasting glucose level from 6.1 to 6.9 mmol/L. It is not surprising that individuals with IFG have a high risk of

developing diabetes. The risk of incident diabetes increased with increased FPG levels.

We are the first to include SRH in a diabetes prediction score. SRH is an expression of health that emphasizes social, psychological, and biologic dimensions[54] and is one of the most widely used yet poorly understood measures of health.[55] In the present study, SRH was assessed by asking individuals to compare their health status to that of similarly aged peers. SRH scores may provide additional valuable information for risk prediction in patients with diabetes[56] and have been recommended as a tool for cardiovascular disease risk assessment.[57] Thus, diabetes guidelines should extend their focus to both the clinical and social aspects of diabetes and include questions on patient SRH.[58]

Physical activity has also been identified as an important predictor of incident diabetes, which is potentially mediated through environmental pathways.[48] Physical inactivity has been suggested to be the greatest public health problem of the 21st century[59] and is thought to be responsible in up to 27% of cases for the development of diabetes.[60] Prospective evidence has accumulated that physical inactivity and sedentary behavior are independent risk factors for diabetes.[61,62] It has been demonstrated that interventions increasing physical activity are able to reduce the incidence of diabetes in high-risk adults.[63–66] It has been recommended that at least 30 minutes of regular, moderate-intensity physical activity on most days are required to reduce the risk of diabetes and cardiovascular disease.[66] In contrast, muscle strengthening and balance training may reduce falls in older adults. The 2010–2012 Korean National Health and Nutrition Examination Survey also demonstrated that high-risk drinking might be associated with a higher risk of diabetes in men.[67] Another reason for this association is that participants who frequently exercised were more likely to be aware of their blood glucose levels than people who never or rarely exercised. Similarly, alcohol drinkers were less likely to be aware of their blood glucose levels than were nondrinkers.[68]

Health promotion is crucial to keep the elderly fit and minimize healthcare costs through increasing the number of active years among elders. Health promotion is also a method to manage the care of the elderly. Health can be influenced by different forces, including social inequalities, the economy,
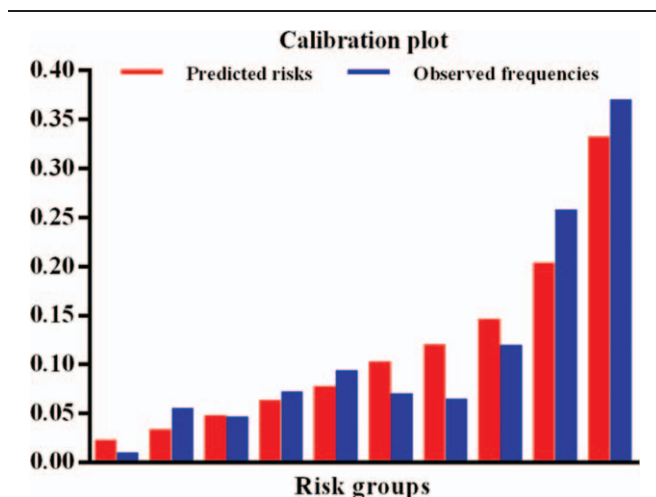


**Figure 3.** Calibration plot by 10 deciles for diabetes prediction models.

setting (healthy cities), empowerment level (education and literacy), mental well-being, medical care and scientific approaches, behavior (physical activity, nutrition, and demographic changes), and politics (national/regional).[69] Thus, there is a need to strengthen the healthcare system to generate awareness and enable early detection and self-management. More importantly, barriers to effective management and health-seeking behaviors should be taken into consideration while planning strategies.[61]

There were some limitations to our study. First, we did not include waist circumference. However, the Guangzhou Biobank Cohort Study showed that using waist circumference or waist-to-hip ratio instead of BMI did not substantially improve model discrimination. Second, due to the long-term follow-up, follow-up bias may have resulted very easily. However, sensitivity analysis showed that there were no significant differences in the distributions of baseline characteristics between those individuals lost to follow-up and those who were followed. In addition, external validation of an independent elderly population in China is needed, and similar studies with larger numbers and other populations should be conducted since the sample size in this study was small.

## 5. Conclusion

In conclusion, our study showed that poor SRH status, physical inactivity, being 55 to 65 years old, overweight or obesity status, and IFG were significant predictors of incident diabetes. We developed a prediction model for diabetes based on a community cohort of elderly Chinese and using a subdistribution hazards model that adjusted for the competing risk of nondiabetes death during the long-term follow-up. This model could be applied to predict the risk of diabetes among Chinese adults over 55 years old. In the future, early prevention with a goal of achieving optimal levels of all risk factors should be a key element of diabetes prevention.

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## References

[1] Levitan EB, Song Y, Ford ES, et al. Is nondiabetic hyperglycemia a risk factor for cardiovascular disease? A meta-analysis of prospective studies. Arch Intern Med 2004;164:2147–55.

[2] World Health Organization. Global status report on noncommunicable diseases 2014. http://www.who.int/nmh/publications/ncd-status-report-2014/en/. Accessed 19 Jan 2015.

[3] Collins GS, Mallett S, Omar O, et al. Developing risk prediction models for type 2 diabetes: a systematic review of methodology and reporting. BMC Med 2011;9:103.

[4] Viswanathan V, Sathyamurthy S. Global increase in the prevalence of diabetes with special reference to the Middle East and Asia. Diabetes Technol Ther 2015;17:676–8.

[5] Chen R, Song Y, Hu Z, et al. Predictors of diabetes in older people in urban China. PLoS One 2012;7:e50957.

[6] Pin S, Spini D. Meeting the Needs of the Growing Very Old Population: Policy Implications for a Global Challenge. J Aging Soc Policy 2016;28:218–31.

[7] Chen Z, Yu J, Song Y, et al. Aging Beijing: challenges and strategies of health care for the elderly. Ageing Res Rev 2010;9(Suppl 1):S2–5.

[8] Chida Y, Hamer M. An association of adverse psychosocial factors with diabetes mellitus: a meta-analytic review of longitudinal cohort studies. Diabetologia 2008;51:2168–78.

[9] Vimalananda VG, Palmer JR, Gerlovin H, et al. Depressive symptoms, antidepressant use, and the incidence of diabetes in the Black Women's Health Study. Diabetes Care 2014;37:2211–7.

[10] Nyberg ST, Fransson EI, Heikkila K, et al. Job strain as a risk factor for type 2 diabetes: a pooled analysis of 124,808 men and women. Diabetes Care 2014;37:2268–75.

[11] Novak M, Bjorck L, Giang KW, et al. Perceived stress and incidence of Type 2 diabetes: a 35-year follow-up study of middle-aged Swedish men. Diabet Med 2013;30:e8–16.

[12] Anstey KJ, Sargent-Cox K, Eramudugolla R, et al. Association of cognitive function with glucose tolerance and trajectories of glucose tolerance over 12 years in the AusDiab study. Alzheimers Res Ther 2015;7:48.

[13] Lehtisalo J, Lindstrom J, Ngandu T, et al. Diabetes, glycaemia, and cognition-a secondary analysis of the Finnish Diabetes Prevention Study. Diabetes Metab Res Rev 2016;32:102–10.

[14] Schmidt MI, Duncan BB, Bang H, et al. Identifying individuals at high risk for diabetes: The Atherosclerosis Risk in Communities study. Diabetes Care 2005;28:2013–8.

[15] Wilson PW, Meigs JB, Sullivan L, et al. Prediction of incident diabetes mellitus in middle-aged adults: the Framingham Offspring Study. Arch Intern Med 2007;167:1068–74.

[16] Stern MP, Williams K, Haffner SM. Identification of persons at high risk for type 2 diabetes mellitus: do we need the oral glucose tolerance test? Ann Intern Med 2002;136:575–81.

[17] Kengne AP, Beulens JW, Peelen LM, et al. Non-invasive risk scores for prediction of type 2 diabetes (EPIC-InterAct): a validation of existing models. Lancet Diabetes Endocrinol 2014;2:19–29.

[18] Xu L, Jiang CQ, Schooling CM, et al. Prediction of 4-year incident diabetes in older Chinese: recalibration of the Framingham diabetes score on Guangzhou Biobank Cohort Study. Prev Med 2014;69:63–8.

[19] Ye X, Zong G, Liu X, et al. Development of a new risk score for incident type 2 diabetes using updated diagnostic criteria in middle-aged and older chinese. PLoS One 2014;9:e97042.

[20] Akter S, Rahman MM, Abe SK, et al. Nationwide survey of prevalence and risk factors for diabetes and prediabetes in Bangladeshi adults. Diabetes Care 2014;37:e9–10.

[21] Lau B, Cole SR, Gange SJ. Competing risk regression models for epidemiologic data. Am J Epidemiol 2009;170:244–56.

[22] Kim HT. Cumulative incidence in competing risks data and competing risks regression analysis. Clin Cancer Res 2007;13(2 Pt 1):559–65.

[23] Austin PC, Lee DS, D'Agostino RB, et al. Developing points-based risk-scoring systems in the presence of competing risks. Stat Med 2016;35:4056–72. doi: 10.1002/sim.6994.

[24] Austin PC, Lee DS, Fine JP. Introduction to the analysis of survival data in the presence of competing risks. Circulation 2016;133:601–9.

[25] Noordzij M, Leffondre K, van Stralen KJ, et al. When do we need competing risks methods for survival analysis in nephrology? Nephrol Dial Transplant 2013;28:2670–7.

[26] Logan BR, Zhang MJ, Klein JP. Regression models for hazard rates versus cumulative incidence probabilities in hematopoietic cell transplantation data. Biol Blood Marrow Transplant 2006;12(1 suppl 1):107–12.

[27] Koller MT, Leening MJ, Wolbers M, et al. Development and validation of a coronary risk prediction model for older U.S. and European persons in the Cardiovascular Health Study and the Rotterdam Study. Ann Intern Med 2012;157:389–97.

[28] Liu L, Tang Z, Li X, et al. A Novel Risk Score to the Prediction of 10-year Risk for Coronary Artery Disease Among the Elderly in Beijing Based on Competing Risk Model. Medicine (Baltimore) 2016;95:e2997.

[29] Tang Z, Wang HX, Meng C, et al. The prevalence of functional disability in activities of daily living and instrumental activities of daily living among elderly Beijing Chinese. Arch Gerontol Geriatr 1999;29:115–25.

[30] Tang Z, Zhou T, Luo YX, et al. Risk factors for cerebrovascular disease mortality among the elderly in Beijing: a competing risk analysis. PLoS One 2014;9:e87884.

[31] Zhou T, Li X, Tang Z, et al. Risk factors of CVD mortality among the elderly in Beijing, 1992-2009: an 18-year cohort study. Int J Environ Res Public Health 2014;11:2193–208.

[32] Grundy SM, Pasternak R, Greenland P, et al. Assessment of cardiovascular risk by use of multiple-risk-factor assessment equations: a statement for healthcare professionals from the American Heart Association and the American College of Cardiology. Circulation 1999;100:1481–92.

[33] Wang W, Tang Z, Li X, et al. Eight-year change in dietary pattern and metabolic status among the elderly people in Beijing. Journal of Capital Medical University (Chinese) 2012;2:218–22.

[34] Radloff LS. The CES-D scale a self-report depression scale for research in the general population. Appl Psychol Meas 1977;1:385–401.

[35] Li X, Wang W, Gao Q, et al. The trajectories and correlation between physical limitation and depression in elderly residents of Beijing, 1992–2009. PLoS One 2012;7:e42999.

[36] Jefferson AL, Byerly LK, Vanderhill S, et al. Characterization of activities of daily living in individuals with mild cognitive impairment. Am J Geriatr Psychiatry 2008;16:375–83.

[37] Chen C, Lu FC. The guidelines for prevention and control of overweight and obesity in Chinese adults. Biomed Environ Sci 2004;17(suppl):1–36.

[38] Catapano AL, Reiner Z, De Backer G, et al. ESC/EAS Guidelines for the management of dyslipidaemias The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). Atherosclerosis 2011;217:3–46.

[39] Wolbers M, Blanche P, Koller MT, et al. Concordance for prognostic models with competing risks. Biostatistics 2014;15:526–39.

[40] Wolbers M, Koller MT, Witteman JC, et al. Prognostic models with competing risks: methods and application to coronary risk prediction. Epidemiology 2009;20:555–61.

[41] Nicolaie MA, van Houwelingen JC, de Witte TM, et al. Dynamic prediction by landmarking in competing risks. Stat Med 2013;32:2031–47.

[42] Pintilie M. An introduction to competing risks analysis. Rev Esp Cardiol 2011;64:599–605.

[43] Novak K, Toren K, Lappas G, et al. Occupational status and incidences of ischemic and hemorrhagic stroke in Swedish men: a population-based 35-year prospective follow-up study. Eur J Epidemiol 2013;28:697–704.

[44] Forsblom C, Harjutsalo V, Thorn LM, et al. Competing-risk analysis of ESRD and death among patients with type 1 diabetes and macro-albuminuria. J Am Soc Nephrol 2011;22:537–44.

[45] Graham SM, Raboud J, McClelland RS, et al. Loss to follow-up as a competing risk in an observational study of HIV-1 incidence. PLoS One 2013;8:e59480.

[46] Lindstrom J, Tuomilehto J. The diabetes risk score: a practical tool to predict type 2 diabetes risk. Diabetes Care 2003;26:725–31.

[47] Rahman M, Simmons RK, Harding AH, et al. A simple risk score identifies individuals at high risk of developing type 2 diabetes: a prospective cohort study. Fam Pract 2008;25:191–6.

[48] Schulze MB, Hoffmann K, Boeing H, et al. An accurate risk score based on anthropometric, dietary, and lifestyle factors to predict the development of type 2 diabetes. Diabetes Care 2007;30:510–5.

[49] Kanaya AM, Wassel Fyr CL, de Rekeneire N, et al. Predicting the development of diabetes in older adults: the derivation and validation of a prediction rule. Diabetes Care 2005;28:404–8.

[50] World Health Organization. Healthy cities. 2016. http://www.euro.who.int/en/health-topics/environment-and-health/urban-health/activities/healthy-cities.

[51] Bernabé-Ortiz A, Carrillo-Larco RM, Gilman RH, et al. Contribution of modifiable risk factors for hypertension and type-2 diabetes in Peruvian resource-limited settings. J Epidemiol Community Health 2016;70:49–55.

[52] Orr MG, Kaplan GA, Galea S. Neighborhood food, physical activity, and educational environments and black/white disparities in obesity: a complex systems simulation analysis. J Epidemiol Community Health 2016;70:862–7.

[53] Petersen CB, Bauman A, Tolstrup JS. Total sitting time and the risk of incident diabetes in Danish adults (the DANHES cohort) over 5 years: a prospective study. Br J Sports Med 2016;doi: 10.1136/bjsports-2015-095648 [Epub ahead of print].

[54] World Health Organization. Ottawa charter for health promotion. 1986. http://www.euro.who.int/de/publications/policy-documents/ottawa-charter-for-health-promotion,-1986. Accessed 12 Dec 2015.

[55] Jylha M. What is self-rated health and why does it predict mortality? Towards a unified conceptual model. Soc Sci Med 2009;69:307–16.

[56] Hayes AJ, Clarke PM, Glasziou PG, et al. Can self-rated health scores be used for risk prediction in patients with type 2 diabetes? Diabetes Care 2008;31:795–7.

[57] May M, Lawlor DA, Brindle P, et al. Cardiovascular disease risk assessment in older women: can we improve on Framingham? British Women's Heart and Health prospective cohort study. Heart 2006;92:1396–401.

[58] Nielsen AB, Jensen P, Gannik D, et al. Change in self-rated general health is associated with perceived illness burden: a 1-year follow up of patients newly diagnosed with type 2 diabetes. BMC Public Health 2015;15:439.

[59] Blair SN. Physical inactivity: the biggest public health problem of the 21st century. Br J Sports Med 2009;43:1–2.

[60] World Health Organization. Global health risks. 2009. http://www.who.int/healthinfo/global_burden_disease/GlobalHealthRisks_report_full.pdf.

[61] Shrivastava U, Misra A, Gupta R, et al. Socioeconomic factors relating to diabetes and its management in India. J Diabetes 2016;8:12–23.

[62] Young DR, Hivert M-F, Alhassan S, et al. Sedentary behavior and cardiovascular morbidity and mortality. A science advisory from the American Heart Association. Circulation 2016;doi: 10.1161/CIR.0000000000000440 [Epub ahead of print].

[63] Orozco LJ, Buchleitner AM, Gimenez-Perez G, et al. Exercise or exercise and diet for preventing type 2 diabetes mellitus. Cochrane Database Syst Rev 2008;16:6.

[64] Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. Diabetes Care 1997;20:537–44.

[65] Leischik R, Foshag P, Strauss M, et al. Physical activity, cardiorespiratory fitness and carotid intima thickness: sedentary occupation as risk factor for atherosclerosis and obesity. Eur Rev Med Pharmacol Sci 2015;19:3157–68.

[66] World Health Organization. Global strategy on diet, physical activity and health. 2004. http://www.who.int/dietphysicalactivity/strategy/eb11344/strategy_english_web.pdf. Accessed 15 Dec 2015.

[67] Hong SW, Linton JA, Shim JY, et al. High-risk drinking is associated with a higher risk of diabetes mellitus in Korean men, based on the 2010-2012 KNHANES. Alcohol 2015;49:275–81.

[68] Wang C, Yu Y, Zhang X, et al. Awareness, treatment, control of diabetes mellitus and the risk factors: survey results from northeast China. PLoS One 2014;9:e103594.

[69] Leischik R, Dworrak B, Strauss M, et al. Plasticity of health. Ger J Med 2016;1:1–7.