



# Derivation and validation of a simple nomogram prediction model for all-cause mortality among middle-aged and elderly general population

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**Background:** A simple clinical model that can predict all-cause mortality in the middle-aged and older adults in general population based on demographics and physical measurement indicators. The aim of this study was to develop a simple nomogram prediction model for all-cause mortality in middle-aged and elderly general population based on demographics and physical measurement indicators.

**Methods:** This was a prospective cohort study. We used data from the 1999–2006 National Health and Nutrition Examination Survey (NHANES), which included adults aged  $\geq 40$  years with mortality status updated through 31 December 2015. Cox proportional hazards regression, nomogram and least absolute shrinkage and selection operator (LASSO) binomial regression model were performed to evaluate the prediction model in the derivation and validation cohort.

**Results:** A total of 13,026 participants (6,414 men, mean age was  $61.59 \pm 13.80$  years) were included, of which 6,671 (3,263 men) and 6,355 (3,151 men) were included in the derivation cohort and validation cohort, respectively. During an average follow-up period of  $129.23 \pm 9.62$  months, 4,321 died. We developed a 9-item nomogram mode included age, gender, smoking, alcohol intake, diabetes, hypertension, marriage status, education and poverty to income ratio (PIR). The area under the curve (AUC) was 0.842 and had good calibration. Internal validation showed good discrimination of the nomogram model with AUC of 0.849 and good calibration. Application of the LASSO regression model in the validation cohort also revealed good discrimination (AUC = 0.854) and good calibration. A time-dependent and optimism-corrected AUC value for the model showed no significant relationship with the change of follow-up time.

**Conclusions:** A simple nomogram model, including age, gender, smoking, alcohol intake, diabetes, hypertension, marriage, education and PIR, could predict all-cause mortality well in middle-aged and elderly general population.

**Keywords:** Derivation; validation; model; all-cause mortality; general population

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## Introduction

Multiple studies have shown that living environment (1), economic status (2,3) and anthropometric indicators (4) were all closely related to mortality. Studies have also demonstrated that obesity (5), elevated blood pressure (6), and diabetes (7) were significantly associated with the risk of all-cause mortality. In addition, meta-analyses suggested that some simple demographic information, such as marital status and education levels were both important factors to predict all-cause mortality (8,9). Meanwhile, many high-quality studies and meta-analyses also indicated that smoking (10) and alcohol consumption (11) were strong risk factors for all-cause mortality.

The aforementioned variables have received attention for being the key components of risk stratification, because these variables were easily measurable, accessible and can be routinely collected. At the moment, there are limited clinical models that use those simple and accessible indicators to predict all-cause mortality among general population.

We present the following article in accordance with the TRIPOD reporting checklist (available at <http://dx.doi.org/10.21037/apm-20-580>).

## Methods

### *Study design and study population*

The study conforms to the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement. All participants were recruited from the 1999–2006 National Health and Nutrition Examination Surveys (NHANES). The NHANES is a nationally representative survey which was designed by the National Center for Health Statistics, Centers for Disease Control and Prevention (NCHS, CDC) to assess the health and nutritional status of non-institutionalized, community-dwelling adults and children in the United States (12). There were 41,474 subjects included in the 1999–2006 NHANES. In the present study, we excluded people aged <40 years (n=28,448). Our final analytical cohort included 13,026 adults as shown in *Figure 1*. The survey protocol was approved by the Institutional Review Board of the Centers for Disease Control and Prevention (Protocol #98-12, Protocol #2005-06, Continuation of Protocol #2005-06). The study conformed to the provisions of the Declaration of Helsinki (as revised in 2013). All participants gave written informed consent.

### *Derivation and validation cohorts*

The derivation and Validation models were developed using data from the NHANES cohort. Participants come from the 1999–2002 surveys were designed as the derivation cohort, while participants from 2003–2006 surveys were used as the validation cohort. Finally, a total of 6,671 and 6,355 subjects were included in the derivation and validation cohort, respectively.

### *Candidate predictor variables*

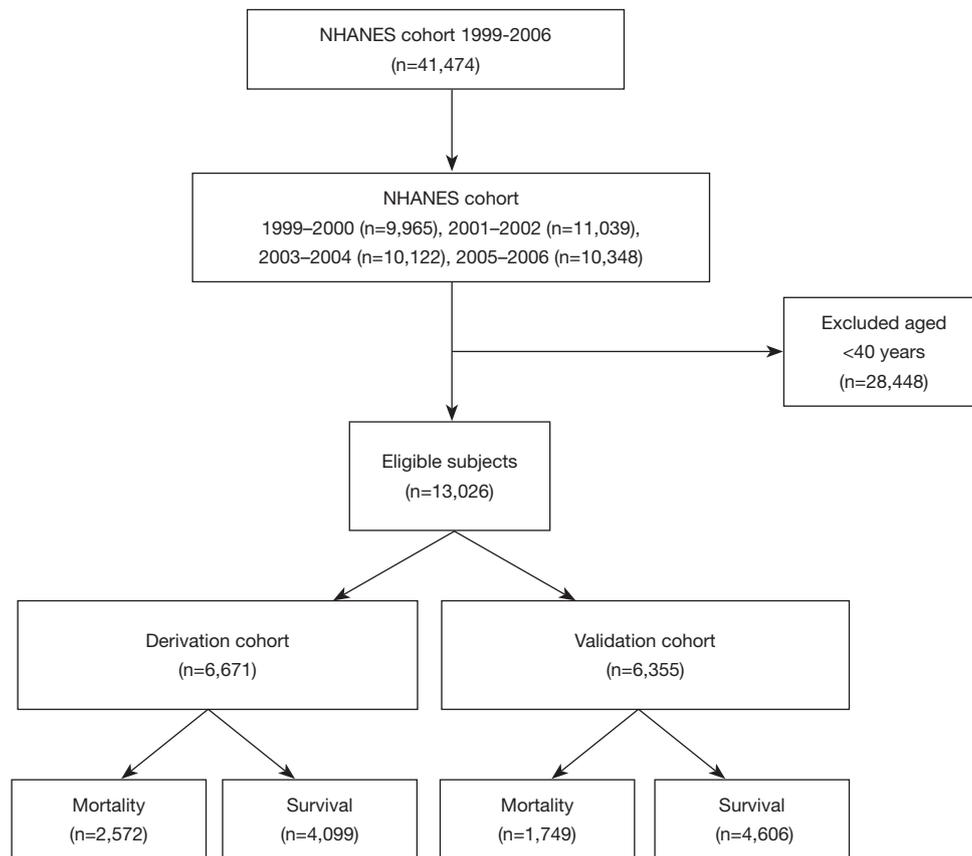
Demographic characteristics of participants were acquired via self-reported questionnaire, including age, gender (female and male), race (non-Hispanic White, Mexican American, Black, other Hispanic, and other), smoking status (current, former, never), alcohol intake in gram (assessed by a 1-day food record), marriage status (married, single, never married), income, education (less than high school, high school diploma and more than high school) and previous diseases (such as diabetes, hypertension). In addition, anthropometric and blood pressure (BP) measurement was performed by standardized procedures. Weight was determined with an electronic digital scale (kilograms), and height (meters) was determined by a stadiometer after deep inhalation. Body Mass Index (BMI) was calculated as weight (kilograms) divided by height squared (meters squared). Poverty to income ratio (PIR) was calculated by dividing family income by the poverty guidelines, specific to family size, as well as the appropriate year and state. Diabetes was defined as fasting blood glucose  $\geq 126$  mg/dL or self-report (13) and hypertension was defined as BP  $\geq 140/90$  mmHg or self-report (14).

### *Mortality*

All-cause mortality data were abstracted from the 1999–2006 NHANES public-use linked mortality files, which captured the vital status and cause of death of survey participants from survey participation (1999–2006) to 31 December 2015. We examined all-cause mortality by using the International Classification of Diseases-10th Revision codes. Detailed mortality variables for participants can be found on the website (<https://www.cdc.gov/nchs/data-linkage/mortality-public.htm>).

### *Statistical analysis*

All the continuous variables were presented as mean  $\pm$



**Figure 1** Flow chart outlining patient selection and grouping process of the study.

standard deviation, and categorical variables were presented in frequency or as a percentage. The Kruskal-Wallis Rank Sum Test, Fisher test, Student's *t*-test and chi-square tests were performed to detect subgroup differences by baseline characteristics. We used univariate and multivariate Cox proportional hazards regression to estimate the risks of all-cause mortality. Hazard ratios (HRs) and 95% CIs were presented as effect estimates. Subgroup analysis was performed according to age (<50, 50–60, 60–70, >70 years), PIR (<1, 1–3, >3) and BMI (<25, ≥25 kg/m<sup>2</sup>). To develop a clinical prediction model, the candidate variables were: age, gender (0= male, 1= female), BMI, SBP, smoking (0= non-smoker, 1= ex-smoker, 2= current smoker), alcohol intake, marriage status (1= married, 2= single, 3= never married), education (0= less than high school, 1= high school diploma, 2= more than high school), PIR, diabetes (0= no, 1= yes) and hypertension (0= no, 1= yes). This study used three methods to establish a predictive model and to verify internal validation. First, a full model including age, gender, BMI, SBP, smoking, alcohol intake, diabetes, hypertension,

marriage, education and PIR were fitted in the derivation model. Second, we established a simplified model by stepwise regression analysis of screening variables. Step Akaike information criterion was used to screen variables into the simplified model. Prediction nomogram was built in the derivation cohort based on multivariate regression analysis. Third, for further checking, a least absolute shrinkage and selection operator (LASSO) binomial regression model was applied to determine the ideal coefficient for each variables and estimate the likelihood deviance. For assessing the discriminative performance of the nomogram, the area under the curve (AUC) in receiver operating characteristic (ROC) analysis was measured to evaluate predictive accuracy. The performance of the model in terms of establishing, discrimination and calibration were evaluated in the validation cohort by using the same methods described above. All analysis was conducted by SPSS 22.0 (SPSS Inc., Chicago, IL, USA) and the R software version 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria). Two tailed *P*<0.05 indicated

statistical significance.

## Results

### *Baseline characteristics of the cohorts*

The final study sample included 13,026 participants (6,414 men, mean age was 61.59±13.80 years). There were 6,671 and 6,355 participants in the derivation cohort and validation cohort, respectively. During the mean follow-up period of 129.23±9.62 months, 4,321 participants have died. As shown in *Table 1*, there were significant differences in SBP, DBP, alcohol use, PIR, marriage, education, race and hypertension between the derivation cohort and validation cohort.

### *The association of candidate predictor variables with all-cause mortality*

As shown in *Table 2*, univariate Cox proportional hazards regression demonstrated that female (HR: 0.79, 95% CI: 0.75–0.84,  $P<0.001$ ), SBP (HR: 1.01, 95% CI: 1.01–1.01,  $P<0.001$ ), DBP (HR: 0.97, 95% CI: 0.97–0.98,  $P<0.001$ ), alcohol intake (HR: 1.00, 95% CI: 1.00–1.00,  $P<0.001$ ), diabetes (HR: 1.83, 95% CI: 1.71–1.97,  $P<0.001$ ) and hypertension (HR: 1.73, 95% CI: 1.63–1.84,  $P<0.001$ ) were associated with all-cause mortality. In addition, current smoker, people who had less than high school education, with age  $\geq 70$  years and PIR  $<1\%$  had the highest risk for all-cause mortality. Further multivariate Cox proportional hazards regression revealed that current smoker (HR: 1.89, 95% CI: 1.63–2.19,  $P<0.001$ ), people who never married (HR: 1.57, 95% CI: 1.25–1.97,  $P<0.001$ ), people aged  $\geq 70$  years (HR: 9.95, 95% CI: 8.18–12.11,  $P<0.001$ ) have a higher risk for all-cause mortality. However, BMI, PIR, DBP and education were inversely associated with all-cause mortality (*Table 2*).

### *Prediction of all-cause mortality in the derivation and validation cohort*

There were 2,572 participants (38.59%) and 1,749 (27.55%) died in derivation and validation cohort, respectively. First, eleven independent predictors for all-cause mortality were enrolled in this full model. Each of these variables was assigned a score on the point scale. After calculating the total score and locating it on the total point scale, we drew a vertical line down to get the predicted probability of all-cause mortality. The higher score of total points reflected

a higher probability of all-cause mortality (*Figure 2A*). Second, in order to optimize the model, step Akaike information criterion was used to screen the optimal variables into the simplified model. As shown in *Figure 2B*, a simple nomogram model, including age, gender, smoking, alcohol intake, diabetes, hypertension, marriage status, education and PIR could predict all-cause mortality among middle-aged and elderly general population. The same analytical method was used for the full and simplified model for making the nomogram, ROC curve and calibration plots. The area under the ROC curve of the full and simplified model was both 0.842 (*Figure 3A*). The analysis method of full model, optimized and simplified model, LAASSO model in the validation cohort were all similar to derivation cohort. In order to validate the training optimized and simplified model, the C statistic of this models were both 0.849 (*Figure 3B*), and nearly the same as the full model in the derivation cohort. The decision curve analysis for the nomogram was demonstrated in *Figure 4*, using the nomogram in the present study to predict all-cause mortality successfully. The decision curve analysis for the nomogram of derivation (*Figure 4A*) and validation (*Figure 4B*) cohort indicated that these models could predict all-cause mortality successfully with good sensitivity and specificity (*Table 3*). What is more, as shown in *Figure 5A*, the optimism-corrected AUC values at different follow-up time, the model had all AUC values more than 0.80. It demonstrated that this model was very stable, and the predictive value of the model has no significant relationship with the follow-up time. Similarly, the model had all AUC values greater than 0.80 at different follow-up time, suggesting no significant change in area under the ROC curve with the change of follow-up time for predicting all-cause mortality in the validation cohort (*Figure 5B*).

In addition, to confirm the predictors of the simplified model, LASSO binomial regression was also performed with  $\lambda$  of 0.0143 and nine predictors were selected into this model. Tuning parameter (lambda) selection in the LASSO model used 10-fold cross-validation. As shown in *Figure 6A,B*, a cross-validated error plot of the LASSO regression model and a coefficient profile plot were produced, respectively. To consolidate and verify the stability of the simplified model, a LASSO cox regression model was performed by using the same variables of the simplified model, and with  $\lambda$  of 0.0108. The path of the coefficients included in this model, with varying log-transformed lambda values, 9 potential predictors, including age, gender, smoking, alcohol intake, diabetes, hypertension, marriage, education

**Table 1** Clinical and demographic data for derivation and validation cohort

	All	Derivation	Validation	P value
Number	13,026	6,671	6,355	
Age (years)	61.59±13.80	61.67±13.80	61.50±13.81	0.479
BMI (kg/m <sup>2</sup> )	28.76±6.21	28.63±6.08	28.89±6.34	0.022
DBP (mmHg)	71.59±13.71	72.72±13.82	70.47±13.51	<0.001
SBP (mmHg)	123.38±16.43	124.03±16.76	122.75±16.08	<0.001
Alcohol intake (gm)	8.18±25.71	8.54±29.35	7.81±21.38	0.128
PIR (%)	2.69±1.61	2.68±1.63	2.71±1.58	0.278
Follow-up time (m)	129.23±49.61	143.68±55.13	114.06±37.50	<0.001
Gender (n, %)				0.445
Male	6,414 (49.24)	3,263 (48.91)	3,151 (49.58)	
Female	6,612 (50.76)	3,408 (51.09)	3,204 (50.42)	
Smoking (n, %)				0.120
Non-smoker	6,135 (47.22)	3,179 (47.83)	2,956 (46.57)	
Ex-smoker	4,359 (33.55)	2,233 (33.60)	2,126 (33.50)	
Current smoker	2,499 (19.23)	1,234 (18.57)	1,265 (19.93)	
Education level (n, %)				<0.001
Less than high school	4,545 (35.06)	2,565 (38.68)	1,980 (31.26)	
High school diploma	3,032 (23.39)	1,465 (22.09)	1,567 (24.74)	
More than high school	5,388 (41.56)	2,602 (39.23)	2,786 (43.99)	
Diabetes (n, %)				0.060
No	10,658 (82.85)	5,501 (83.46)	5,157 (82.21)	
Yes	2,206 (17.15)	1,090 (16.54)	1,116 (17.79)	
Hypertension (n, %)				<0.001
No	7,102 (54.74)	3,794 (57.17)	3,308 (52.18)	
Yes	5,873 (45.26)	2,842 (42.83)	3,031 (47.82)	
Marriage (n, %)				0.133
Married	7,431 (60.68)	3,779 (61.53)	3,652 (59.83)	
Single	4,009 (32.74)	1,975 (32.16)	2,034 (33.32)	
Never married	806 (6.58)	388 (6.32)	418 (6.85)	
Race (n, %)				<0.001
Black	2,533 (19.45)	1,236 (18.53)	1,297 (20.41)	
Mexican American	2,538 (19.48)	1,422 (21.32)	1,116 (17.56)	
Other Hispanic	454 (3.49)	308 (4.62)	146 (2.30)	
Other race	429 (3.29)	196 (2.94)	233 (3.67)	
Non-Hispanic White	7,072 (54.29)	3,509 (52.60)	3,563 (56.07)	

Table 1 (continued)

Table 1 (continued)

	All	Derivation	Validation	P value
Age (years) (n, %)				0.744
<50	3,319 (25.48)	1,688 (25.30)	1,631 (25.66)	
≥50, <60	2,530 (19.42)	1,277 (19.14)	1,253 (19.72)	
≥60, <70	3,019 (23.18)	1,558 (23.35)	1,461 (22.99)	
≥70	4,158 (31.92)	2,148 (32.20)	2,010 (31.63)	
BMI (kg/m <sup>2</sup> ) (n, %)				0.428
<25	3,252 (27.99)	1,627 (28.32)	1,625 (27.66)	
≥25	8,368 (72.01)	4,118 (71.68)	4,250 (72.34)	
PIR (n, %)				0.026
<1	1,902 (16.12)	993 (17.04)	909 (15.23)	
≥1, <3	5,079 (43.05)	2,473 (42.43)	2,606 (43.66)	
≥3	4,816 (40.82)	2,362 (40.53)	2,454 (41.11)	
Mortality (n, %)				<0.001
No	8,692 (66.79)	4,093 (61.41)	4,599 (72.45)	
Yes	4,321 (33.21)	2,572 (38.59)	1,749 (27.55)	

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; PIR, poverty to income ratio.

and PIR were shown in *Figure 6C,D*.

The calibration plots fit a prediction and observation data well in the derivation cohort (*Figure S1A*). The calibration of predictions from the full model demonstrated an excellent correlation between observed and predicted all-cause mortality (*Figure S1B*). As shown in *Figure S2A*, the area under the ROC curve for the derivation sample model was 0.865, suggesting that the simplified clinical tool has a high predictive power to all-cause mortality. The LASSO model showed a great prediction of prognostic capacity for all-cause mortality in middle-aged and elderly general population with an area under the curve (AUC) of 0.854 in the validation cohort (*Figure S2B*). Compared with the full model, simplified model and LASSO model between derivation and validation cohort, we found that these three models have almost the same area under the curve, indicating that the simplified model has a good predictive performance and stability for all-cause mortality among middle-aged and elderly general population.

## Discussion

In the present study, we developed and validated a simple

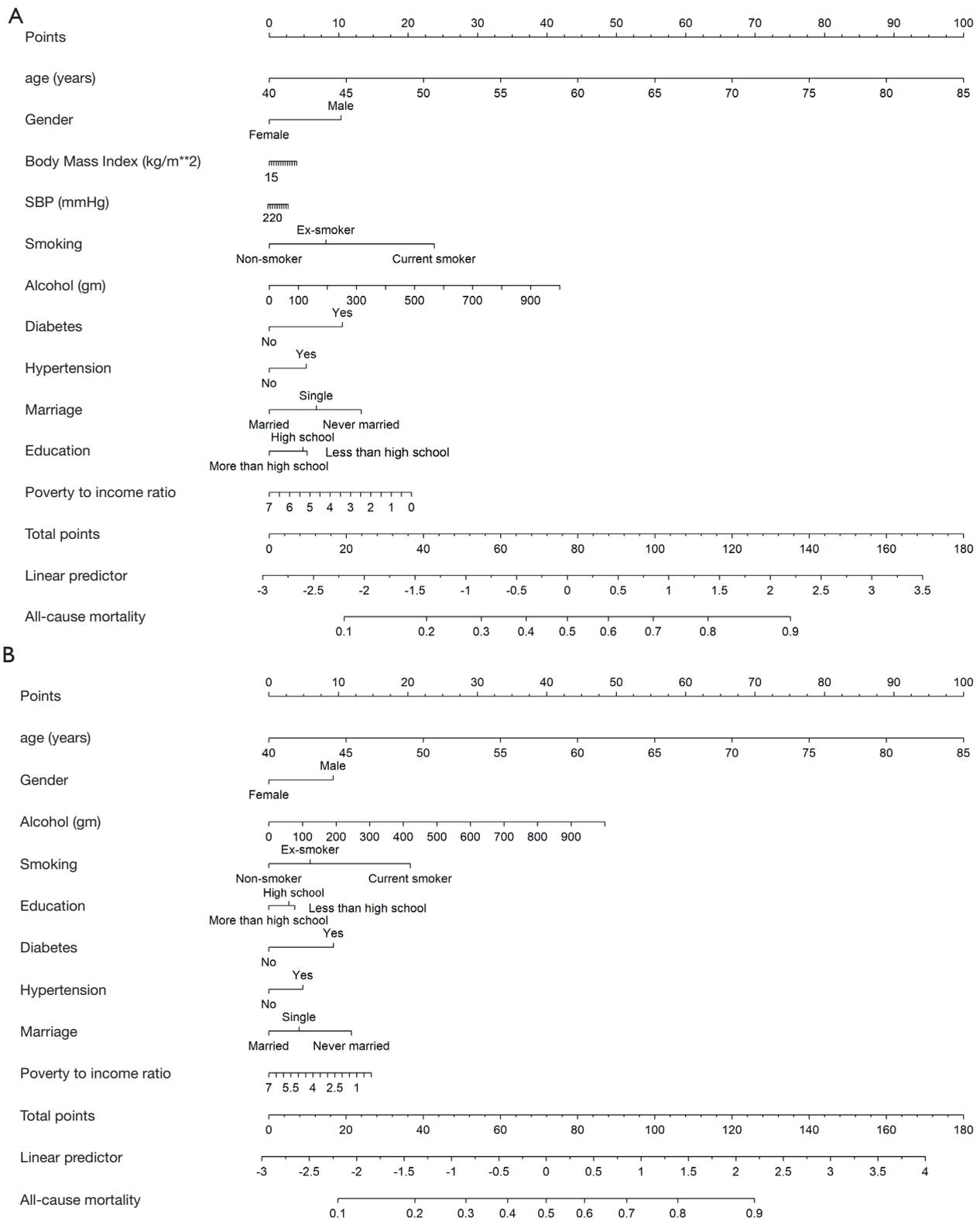
and accurate nomogram model to predict all-cause mortality in the nationally representative cohort. The nomogram model included nine items: age, gender, smoking, alcohol intake, diabetes, hypertension, marriage, education and PIR. To the best of our knowledge, this is the first study to develop a predictive model to predict all-cause mortality among middle-aged and elderly general population. The nomogram model demonstrated good accuracy and discrimination through different model analytical methods.

In the multivariate Cox regression analysis, we found that SBP (15), smoking (16), diabetes (17), hypertension, age and marriage status (18) were significantly associated with all-cause mortality. Our results agreed with previous studies. However, we also showed that DBP, education level, BMI and PIR were inversely associated with all-cause mortality. The J-curve phenomenon of DBP with adverse cardiovascular events has been reported, especially in post-hoc analysis and observational studies. A previous study demonstrated that DBP of less than 70 mm Hg was associated with adverse cardiovascular outcomes, including mortality, supporting the existence of a J-curve relationship (19). The magnitude of relationship between BMI and all-cause mortality is still controversial. A meta-analysis of 239

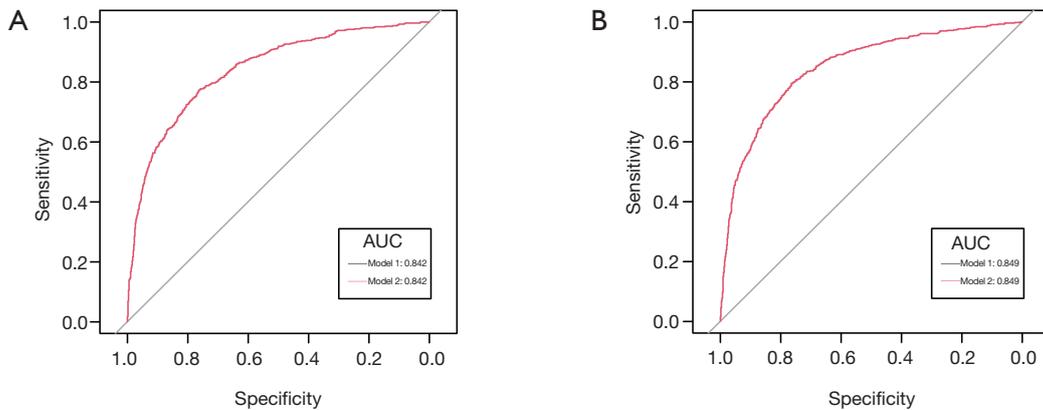
**Table 2** Univariate and multivariate Cox regression analysis of predictors for all-cause mortality

Variable	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value
Gender				
Male	1.0		1.0	
Female	0.79 (0.75, 0.84)	<0.0001	0.63 (0.57, 0.71)	<0.0001
DBP	0.97 (0.97, 0.98)	<0.0001	0.99 (0.99, 1.00)	<0.0001
SBP	1.01 (1.01, 1.01)	<0.0001	1.01 (1.00, 1.01)	0.0004
Alcohol intake	1.00 (1.00, 1.00)	0.0006	1.00 (1.00, 1.00)	0.1490
Smoking				
Non-smoker	1.0		1.0	
Ex-smoker	1.45 (1.35, 1.55)	<0.0001	1.36 (1.20, 1.53)	<0.0001
Current smoker	1.14 (1.05, 1.24)	0.0016	1.89 (1.63, 2.19)	<0.0001
Education level				
Less than high school	1.0		1.0	
High school diploma	0.78 (0.72, 0.84)	<0.0001	0.91 (0.80, 1.04)	0.1705
More than high school	0.53 (0.50, 0.57)	<0.0001	0.85 (0.75, 0.97)	0.0140
Diabetes				
No	1.0		1.0	
Yes	1.83 (1.71, 1.97)	<0.0001	1.46 (1.30, 1.65)	<0.0001
Hypertension				
No	1.0		1.0	
Yes	1.73 (1.63, 1.84)	<0.0001	1.25 (1.12, 1.40)	<0.0001
Marriage				
Married	1.0		1.0	
Single	2.00 (1.88, 2.13)	<0.0001	1.56 (1.39, 1.75)	<0.0001
Never married	0.95 (0.83, 1.10)	0.4957	1.57 (1.25, 1.97)	0.0001
Age				
<50	1.0		1.0	
≥50, <60	1.78 (1.52, 2.09)	<0.0001	1.64 (1.32, 2.05)	<0.0001
≥60, <70	4.06 (3.54, 4.66)	<0.0001	3.50 (2.87, 4.27)	<0.0001
≥70	13.96 (12.31, 15.84)	<0.0001	9.95 (8.18, 12.11)	<0.0001
BMI				
<25	1.0		1.0	
≥25	0.74 (0.68, 0.79)	<0.0001	0.87 (0.78, 0.98)	0.0198
PIR				
<1	1.0		1.0	
≥1, <3	1.05 (0.96, 1.14)	0.3054	1.00 (0.86, 1.15)	0.9453
≥3	0.49 (0.44, 0.54)	<0.0001	0.71 (0.60, 0.84)	<0.0001

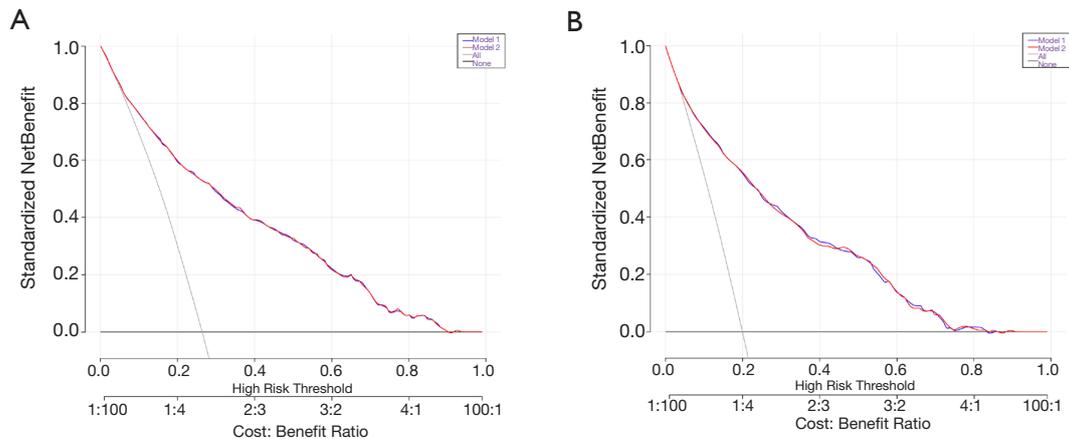
BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; PIR, poverty to income ratio; CI, confidence interval; HR, hazard ratio.



**Figure 2** Nomogram predicting the probability of all-cause mortality in the derivation cohort (A) full model, (B) simplified model.



**Figure 3** Receiver operating characteristic curve analyses of predictors for all-cause mortality: (A) derivation cohort, (B) validation cohort. AUC, area under the curve; model 1, full model; model 2, simplified model.



**Figure 4** Decision curve analysis for the prediction models in both cohorts: (A) derivation cohort, (B) validation cohort. Model 1, full model; model 2, simplified model.

prospective studies in four continents demonstrated that the associations of both overweight and obesity with higher all-cause mortality were broadly consistent in four continents (20). However, a dose-response meta-analysis of prospective cohort studies found a U-shaped association between BMI and all-cause mortality (21).

Therefore, we established a full model including age, gender, smoking, alcohol intake, diabetes, hypertension, marriage status, education levels, SBP, BMI and PIR. Although the full model has good predictive value, the nomogram revealed that the range of SBP and BMI scores vary narrowly, suggesting the utility of SBP and BMI were affected in this full model. In order to optimize the model, step Akaike information criterion was used to screen the

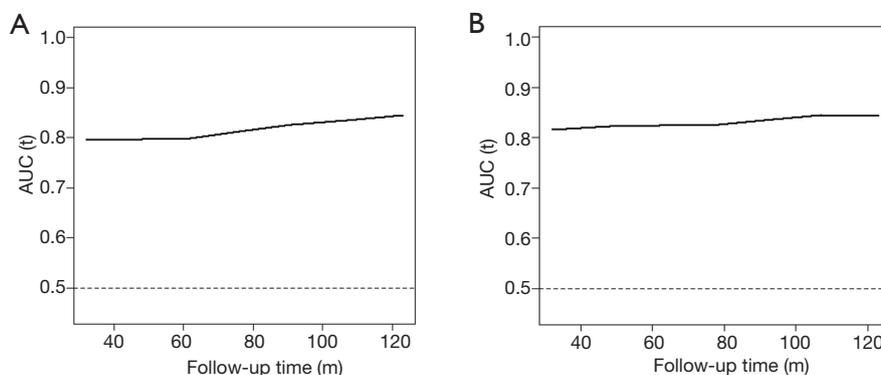
optimal variables into the simplified model. Interestingly, the simplified model has a same AUC in the derivation and validation cohort, but with higher accuracy and specificity compared to the full model in the validation cohort.

Further, LASSO model including the same items of the simplified model were performed by validating the predictive value for all-cause mortality. LASSO model discriminated all-cause mortality best with an AUC of 0.865 and 0.854 in the derivation and validation cohort, suggesting were similar to simplified model with an AUC of 0.842 and 0.849, respectively. In addition, decision curve analysis for the prediction model and time-dependent AUC values of the model in the derivation and validation cohort showed that the simplified model has good stability and

**Table 3** Detective characteristics of the derivation and validation cohort

Test	Full model	Simplified model	P (compare)	Full model	Simplified model	P (compare)
	Derivation	Derivation		Validation	Validation	
ROC area (AUC)	0.842	0.842	0.830	0.849	0.849	0.798
95% CI low	0.826	0.826		0.833	0.833	
95% CI up	0.858	0.858		0.866	0.865	
Specificity	0.781	0.781		0.750	0.788	
Sensitivity	0.757	0.758		0.812	0.774	
Accuracy	0.775	0.775		0.762	0.785	
Positive-likelihood ratio	3.456	3.468		3.241	3.647	
Negative-likelihood ratio	0.311	0.310		0.251	0.287	
Positive-predictive value	0.553	0.554		0.445	0.474	
Negative-predictive value	0.900	0.900		0.941	0.934	

ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval.



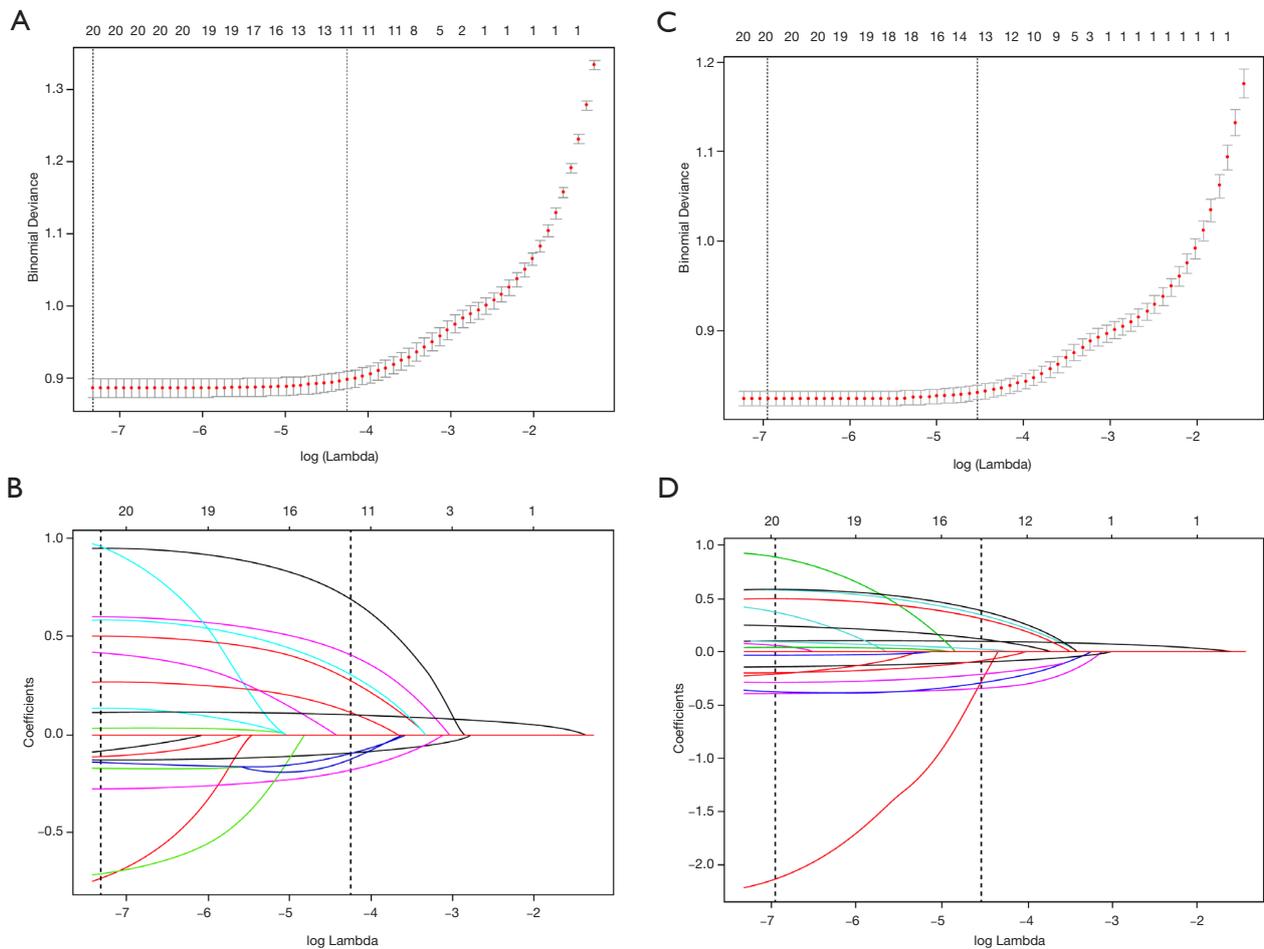
**Figure 5** Time-dependent and optimism-corrected AUC values of the simplified model in both cohorts: (A) derivation cohort, (B) validation cohort. AUC, area under the curve.

accuracy. These results indicated that the model could be easily implemented into clinical practice with convenient, practical and accurate.

In a recent previous study demonstrated that regression models that used age, sex, and indicator variables for the Johns Hopkins' Aggregated Diagnosis Groups (ADGs) categories have accurately predicted one-year all-cause mortality in population-based cohorts of subjects (22). Moreover, there was also research indicated that the Mortality Risk Score (MRS) collapses age, sex, and the ADGs to a single summary score could predict the annual risk of all-cause death in adults very well (23). The ADGs including 32 diagnosis clusters based on the International Classification of Disease (ICD) codes (-9 version, -9-

CM version, or -10 version) (23). Although MRS and ADGs accurately predicted one-year mortality in a general population cohort, these two models included too many variables, which might be difficult to promote in clinical practice. In the present study, our model included fewer variables and has similar discriminating power for all-cause mortality in general adults. It means that our model may be useful for risk assessment and warning in primary care health services.

However, our study has some limitations. On the one hand, our current study did not include blood biomarkers, and we did not adjust some confounding factors of mortality. On the other hand, the simplified model is established in the American population and might not be



**Figure 6** Factors selection using the LASSO logistic regression model in both cohorts. (A) LASSO coefficients of 9 candidate variables in the derivation cohort, (B) identification of the optimal penalization coefficient ( $\lambda=0.0143$ ) in the LASSO model was achieved by 10-fold cross-derivation and the minimum criterion; (C) LASSO coefficients of 9 candidate variables in the derivation cohort, (D) identification of the optimal penalization coefficient ( $\lambda=0.0108$ ) in the LASSO model was achieved by 10-fold cross-validation and the minimum criterion. The left vertical line represents the minimum error, and the right vertical line represents the cross derived/validated error within 1 standard error of the minimum. LASSO, least absolute shrinkage and selection operator.

directly applied to other population.

In conclusion, the present study developed and validated a prediction nomogram that can be conveniently used to predict all-cause mortality among middle-aged and elderly general population. Our model included easy-to-use parameters with good accuracy, which might have important implications for clinical practice.

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### Footnote

**Reporting Checklist:** Available at <http://dx.doi.org/10.21037/apm-20-580>

**Data Sharing Statement:** Available at <http://dx.doi.org/10.21037/apm-20-580>

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/apm-20-580>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The survey protocol was approved by the Institutional Review Board of the Centers for Disease Control and Prevention (Protocol #98-12, Protocol #2005-06, Continuation of Protocol #2005-06). The study conformed to the provisions of the Declaration of Helsinki (as revised in 2013). All participants gave written informed consent.

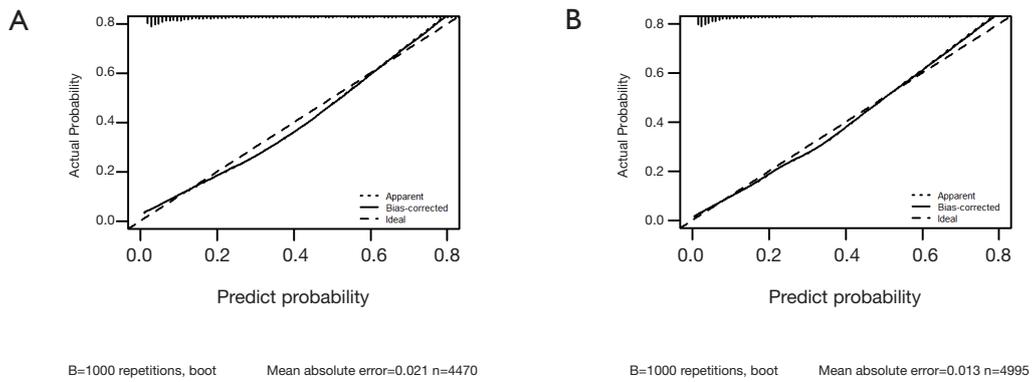
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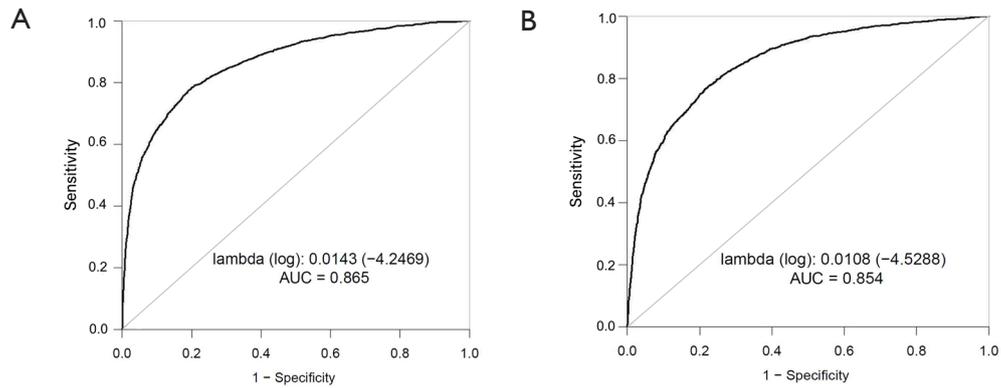
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**Figure S1** Calibration curves for the simplified model in both cohorts: (A) derivation cohort, (B) validation cohort.



**Figure S2** Receiver operating characteristic curve analyses of LASSO model for all-cause mortality in both cohorts: (A) derivation cohort, (B) validation cohort. AUC, area under the curve; LASSO, least absolute shrinkage and selection operator.