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A Risk Score for Chronic Kidney Disease in the General Population

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Abstract

Background—Stratification of individuals at risk for chronic kidney disease may allow optimization of preventive measures to reduce disease incidence and complications. We sought to develop a risk score that estimates an individual's absolute risk of incident chronic kidney disease.

Methods—Framingham Heart Study participants free of baseline chronic kidney disease, who attended a baseline examination in 1995–1998 and follow-up in 2005–2008, were included in the analysis (n=2,490). Chronic kidney disease was defined as an estimated glomerular filtration rate <60 ml/min/1.73m² using the Modification of Diet in Renal Disease (MDRD) equation. Participants were assessed for the development of chronic kidney disease at 10 years follow-up. Stepwise logistic regression was used to identify chronic kidney disease risk factors, and these were used to construct a risk score predicting 10-year chronic kidney disease risk. Performance characteristics were assessed using calibration and discrimination measures. The final model was externally validated in the bi-ethnic Atherosclerosis Risk in Communities (ARIC) Study (n=1,777).

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Results—There were 1,171 men and 1,319 women at baseline, and the mean age was 57.1 years. At follow-up, 9.2% (n=229) had developed chronic kidney disease. Age, diabetes, hypertension, baseline estimated glomerular filtration rate and albuminuria were independently associated with incident chronic kidney disease ($p<0.05$), and these covariates were incorporated into a risk function (c-statistic 0.813). In external validation in the ARIC study, the c-statistic was 0.79 in whites (n=1,353) and 0.75 in blacks (n=424).

Conclusion—Risk stratification for chronic kidney disease is achievable using a risk score derived from clinical factors that are readily accessible in primary care. The utility of this score in identifying individuals in the community at high risk of chronic kidney disease warrants further investigation.

Introduction

The international adoption of the Kidney Disease Outcomes Quality Initiative (K/DOQI) classification system for chronic kidney disease (1) by the Kidney Disease: Improving Global Outcomes (KDIGO) initiative(2) has resulted in improved detection of undiagnosed chronic kidney disease. However, despite a disease prevalence of 13.1% in the United States(3), awareness rates remain low(4). Due to the availability of treatments to reduce the risk of these outcomes, the early identification of patients with chronic kidney disease is a public health priority(5–7).

Chronic kidney disease is frequently clinically silent in the early stages resulting in most patients being detected shortly before, or with, the onset of symptomatic disease, when the impact of available therapeutics is markedly reduced(8, 9). Early identification of chronic kidney disease may provide the best opportunity for appropriate patient evaluation and institution of treatments known to slow renal function decline (10, 11). This process requires integrated risk stratification, with defined testing strategies for asymptomatic individuals subsequently identified as being at increased risk(12).

A risk score that identifies those at higher risk for future kidney disease has been proposed as such a prediction and stratification device (13–15). Cardiovascular risk scores, such as the Framingham score(16), have influenced public health policy in the primary prevention of cardiovascular disease(17). The proposed renal risk score would identify individuals at the highest risk for future chronic kidney disease, permitting targeted medical management at a primary care level. Furthermore, it would help in the assessment of new technologies, biomarkers, and genetic data for risk prediction, as well as facilitate enrollment in future primary prevention trials(13–15, 18). Several risk factors for the development of chronic kidney disease have been identified from prospective studies, including age, male gender, ethnicity, diabetes mellitus(19), hypertension, dyslipidemia, obesity and high-normal urinary albumin excretion(13). We hypothesized that chronic kidney disease may be predicted by a risk score containing a subset of clinical variables, and aimed to formulate a prediction algorithm composed of risk factors easily assessed in the primary care setting.

Methods

Participants

Participants were derived from the Framingham Heart Study (FHS) Offspring cohort. Briefly, participants attend a study examination every 4–8 years(20). Each visit incorporates a detailed medical history, physical examination, blood pressure measurements, anthropometry, and laboratory assessment of risk factors. Participants who attended both the sixth (1995–1998) and eighth (2005–2008) exam cycles were included in the present analysis. Of 3532 participants who attended the baseline examination, 80 were excluded

because serum creatinine was not measured, 294 were excluded due to prevalent chronic kidney disease; 275 died and an additional 393 did not return for follow-up, leaving 2490 in the final analysis. Of these, 2149 had a urinary albumin-to-creatinine ratio (UACR) measured at the baseline examination. Participants who did not attend for follow-up were generally older, more likely to smoke, and had higher rates of hypertension, diabetes, and cardiovascular disease. All provided written informed consent, and the institutional review board of the Boston Medical Center, Boston, Massachusetts approved the study.

Outcome definition

The National Kidney Foundation clinical practice guidelines definition of chronic kidney disease was used (estimated glomerular filtration rate (eGFR) $<60\text{mL}/\text{min}/1.73\text{m}^2$)(1). eGFR was calculated using the 4-variable Modification of Diet in Renal Disease (MDRD) equation(21). As a secondary analysis, we also assessed the performance a model with GFR estimated by the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation (22). Serum creatinine was measured by the Jaffé method, and a 2-step calibration process was used, as previously described(19).

Covariate assessment

Two blood pressure measurements were taken using a mercury sphygmomanometer after 5 minutes rest and the average was used in the analyses. Hypertension was defined as systolic blood pressure $\geq 140\text{mmHg}$, diastolic blood pressure $\geq 90\text{mmHg}$, and/or use of antihypertensive medications. Body mass index was defined as weight in kilograms divided by the square of height in meters. Persons reporting having smoked cigarettes during the previous year were classified as current smokers. Fasting levels of HDL-cholesterol and plasma glucose were measured using standardized assays. Diabetes mellitus was defined as a fasting plasma glucose level $\geq 126\text{mg}/\text{dL}$ or use of medication.

Proteinuria was assessed both by dipstick assay (Ames Labstix, Elkhart, Indiana) and by UACR. Spot morning urine samples assessed by urine dipstick were briefly dipped during the clinic visit and read after 1 minute(23). Urine samples were stored at -20°C and then transitioned to -80°C until quantification. Urinary albumin concentration was measured using immunoturbidimetry (<http://www. Roche-Diagnostics.us>). Urinary creatinine was assessed using the modified Jaffé method; the intra-assay coefficient of variation was 1.7% to 3.8%. Albuminuria was defined as a spot UACR of $\geq 30\text{mg}/\text{g}$. The prevalence of albuminuria in the Framingham Heart Study is similar to that in the nationally representative National Health and Nutrition Examination Survey (NHANES) cohort (9.2% in Framingham vs. 9.5% in NHANES).(3)

Prevalent cardiovascular disease was defined as a history of one or more of: non-fatal myocardial infarction, angina pectoris, stroke or transient ischemic attacks, peripheral vascular disease or congestive heart failure.

Statistical analysis

Multivariable logistic regression models were used to assess risk factors for chronic kidney disease, selected from earlier reports(13). Variables were sequentially added in a pre-specified order and incorporated using a $p < 0.05$ threshold for entry and retention in the final model.

Three analysis models were used: Model 1 contained only clinical variables. Candidates for entry in order of inclusion were: age (rounded down to nearest integer), gender, diabetes, hypertension, hypertension treatment, HDL-cholesterol ($<40\text{mg}/\text{dL}$ (men) and $<50\text{mg}/\text{dL}$ (women)), triglycerides ($>150\text{mg}/\text{dL}$ or treatment), obesity (body mass index $\geq 30\text{kg}/\text{m}^2$),

current smoking (yes/no) and cardiovascular disease. Model 2 comprised the basic clinical model plus baseline eGFR by category (60–74mL/min/1.73m², 75–89mL/min/1.73m², 90–120mL/min/1.73m² and >120mL/min/1.73m²). Model 3 comprised Model 2 plus UACR and dipstick hematuria (yes/no). In a secondary analysis, dipstick proteinuria was substituted for quantitative albuminuria in model 3.

Variables were dichotomized to enhance clinical utility. A risk scoring system for chronic kidney disease was developed using previously established methods. In brief, each variable is assigned points proportional to the product of its regression coefficient from the multiple logistic regression model for chronic kidney disease (described above) and the measured value of that variable (16, 24). A more detailed description of the development of Framingham risk score functions has been reported previously(24).

To assess calibration, the agreement between predicted and recorded 10-year event rates in deciles of predicted risk was examined, and a Hosmer- Lemeshow statistic was calculated. Model discrimination was estimated by c-statistic(25). Internal validation of the c-statistics was performed using bootstrapping with 1000 replications of individuals sampled with replacement. Analyses were performed using SAS (version 9.1).

External Validation in the Atherosclerosis Risk in Communities Study

A detailed description of the design of the Atherosclerosis Risk in Communities (ARIC) Study has been published(26). It is a prospective, multicenter study of men and women selected from the general population in four US communities. In total, 15,792 participants aged 45 to 64 years were enrolled between 1987 and 1989, and attended three subsequent visits approximately every 3 years. We selected participants from visit 4 (1996–1998) for the present study, as urine samples were obtained at that visit. All participants provided written informed consent and the institutional review board approved the study protocol.

The ARIC Carotid MRI Study exam was used as the follow-up visit (2004–2005). Participants were selected from the surviving ARIC Study participants using a stratified sampling plan(27). Participants with contrast media allergy, a contraindication to MRI or a prior carotid endarterectomy were excluded. Of 4306 persons invited, 1403 refused, 837 were ineligible, leaving 2066 participants. Of these, 69 were excluded because baseline serum creatinine was not available, 128 due to prevalent chronic kidney disease, 35 because follow-up serum creatinine was not available, and 57 due to missing covariates, leaving 1777 participants for analysis.

Outcome and Covariate Definitions in the ARIC Participants

Participants in the ARIC study underwent blood testing and were assessed for cardiovascular risk factors. HDL-cholesterol and blood glucose were assessed on fasting samples. Diabetes was defined as: fasting blood glucose ≥ 126 mg/dL or ≥ 200 mg/dL if not fasting, use of medication or self-report. Blood pressure recordings were taken using three seated measurements and the average of the second and third readings was recorded. Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or use of medication. Current smoking status was defined by self-report.

As in FHS, serum creatinine was measured using a modified Jaffé method and calibrated(19). Spot urine samples were collected and stored at -70°C . Urinary albumin levels were measured by nephelometry and urinary creatinine levels were measured using the Jaffé method(28).

Statistical Methods

Performance of the risk score was evaluated in the bi-ethnic ARIC Study. Logistic regression was performed using the variables and β -coefficients derived in FHS. Logistic regression functions were calculated in the overall sample and by ethnicity. The performance of the FHS prediction functions was assessed using discrimination and calibration metrics.

Calibration

ARIC participants were divided into deciles according to FHS function of predicted 10-year chronic kidney disease risk. Plots were generated showing predicted and actual event rates for each decile, where the predicted event rate was calculated by summing the FHS predicted risk within decile. A Hosmer-Lemeshow chi-square test (29) was used to compare the differences between predicted and actual event rates, with small values indicating good calibration.

Results

Framingham Heart Study baseline characteristics

Baseline characteristics of the Framingham Heart Study (FHS) cohort are presented in Table 1. The mean age was 57.1 years and 53.0% were women. During 10-years of follow-up, 229 (9.2%) participants developed chronic kidney disease; they tended to be older (64.2 vs. 57.1 years), have higher rates of diabetes (18.3% vs. 7.4%) and hypertension (62.9% vs. 35.3%), and lower baseline eGFR (81 vs. 92 ml/min/1.73m²).

Model 1: clinical model

Age, diabetes and hypertension met criteria for inclusion in this model (Table 2; Model 1). Gender did not meet the p-value <0.05 threshold. Model 1 had a c-statistic of 0.786.

Model 2: clinical model and baseline eGFR

Baseline eGFR category met the significance threshold when added to the model 1 stepwise regression analysis (p<0.001), and inclusion improved the c-statistic to 0.812 (Table 2; Model 2; c-statistic comparison with Model 1 p=0.001).

Model 3: Model 2 plus measure of proteinuria

Baseline UACR met the significance threshold when added to model 2 (Table 2; Model 3; p=0.009). The receiver operating characteristic curve for the final renal risk score in FHS is presented in Figure 1a. Substitution of dipstick proteinuria ($\geq$ trace) for UACR in Model 3 produced similar results (OR 1.62; 95% CI 1.13–2.33; p=0.009; c-statistic 0.813).

Effect estimates for model 3 derived using the CKD-EPI equation were similar to those of the primary analysis (Table 3).

Development of the risk score

The final model included age, hypertension, diabetes, baseline eGFR and albuminuria (Table 2). Predicted 10-year risk deciles were similar to observed risks (Hosmer-Lemeshow (χ^2) 7.27; p=0.60). Internal validation yielded a c-statistic of 0.79. We developed a weighted scoring system of risk factors and related each total score to an absolute risk of chronic kidney disease over 10 years. The 10-year risk of chronic kidney disease according to risk score category is presented in Table 4.

ARIC Baseline Characteristics

Baseline characteristics of the ARIC cohort are presented in Table 1. The final prediction model was applied to the ARIC sample (n=1,777), 337 (19.0%) of which developed chronic kidney disease over a median follow-up of 8.5 years. Approximately a quarter of participants were African-American.

Validation of risk score in ARIC

Using the FHS function, the c-statistic in ARIC was 0.76, with good calibration for deciles of predicted risk (Hosmer-Lemeshow statistic (χ^2) 9.14; p=0.33). The c-statistic was 0.75 for African-Americans (n=424) and 0.79 for whites (n=1,353). The receiver operating curves for the final renal risk score in ARIC, stratified by race, are presented in Figure 1b.

Discussion

We examined predictors of incident chronic kidney disease among individuals in the community and developed a risk score including the predictors: age, hypertension, diabetes, eGFR category and albuminuria. The risk score demonstrates excellent discrimination and calibration, and the model performed well when applied externally to ARIC Study participants. Finally, although derived from an exclusively white population, the risk score performed well in African-Americans.

Improved clinical prediction is a cornerstone of personalized and individualized medicine(30), and prediction tools such as the Framingham cardiovascular risk score(16) have helped shape public health policy in the primary prevention of cardiovascular disease(17). However, despite the identification of several key renal risk factors from prospective studies(13), similarly useful models for kidney disease prediction do not exist. We are aware of two prior published risk prediction scores for incident chronic kidney disease. The first was derived and validated using data from 14,155 middle-aged and older adults in the community(31). The final model included 8 variables: age, gender, anemia, hypertension, diabetes mellitus, cardiovascular disease, history of heart failure, and peripheral vascular disease. This risk score had moderate discriminatory power (c-statistic=0.70) and did not contain data on baseline GFR or proteinuria. The second risk score was compromised by poor discriminatory power (c-statistic=0.67) and short follow-up (median 2.2 years)(32). The present work advances efforts at risk prediction in renal disease, permitting early identification of at-risk individuals with a high degree of accuracy, using a parsimonious set of readily available clinical variables.

There are several potential implications of this work. First, by allowing physicians to determine an individual's estimated risk for chronic kidney disease, the score may inform clinical counseling and decision-making. For example, a higher chronic kidney disease risk score may weigh against a decision to use a potentially nephrotoxic intervention, favor increased intensity and frequency of follow-up testing and, in equivocal cases, assist in the decision to institute renal primary prevention measures. Use of the score may further serve to raise the profile of kidney disease among the general population, a key goal given current awareness rates of less than 10% in people with chronic kidney disease stage 3(4).

Second, the score may prove useful in the evaluation of new biomarkers of renal risk(33). A key challenge involves demonstrating that novel biomarkers offer independent, incremental information beyond what is already known based on traditional risk factors. A sophisticated new biomarker may have good independent predictive ability, but should be evaluated by its ability to improve risk prediction beyond the suggested risk equation, which comprises less expensive, traditional factors.

Finally, it is noteworthy that the power of the risk score is predominantly driven by clinical risk factors, based on the fact that the basic clinical model of age, diabetes and hypertension has considerable discriminatory power of itself (Model 1; c-statistic 0.786). As this model requires no prior laboratory testing to be performed, it could be used for focused renal screening, identifying individuals in whom creatinine measurement would be most cost-effective. A formal cost-effectiveness analysis would be required before introducing the score into the public health arena, one of several potential future research directions emerging from this work. Other avenues for future research include an assessment of performance in predicting advanced chronic kidney disease or end-stage kidney disease, a comparison with a genetic risk score comprising recently identified genetic predictors of chronic kidney disease (34, 35), or an assessment of performance in other ethnic groups, such as Hispanics or Asians.

There are numerous strengths to this study, including the community-based sample with long duration of follow-up, rigorous and detailed assessment of risk factors including measures of baseline renal function and proteinuria, and external validation in the bi-ethnic ARIC Study. The parsimonious list of variables in the final model is also a significant strength, enhancing the score's utility and applicability. Several limitations should also be acknowledged. Baseline and follow-up creatinine were measured on a single occasion; multiple measurements in observational epidemiology are not feasible. Furthermore, GFR was estimated using the MDRD equation(21), which may underestimate GFR in both healthy individuals and those with chronic kidney disease (36). However, a comparison of definitions of incident chronic kidney disease in the setting of epidemiological research demonstrates that the present definition (estimated GFR of $<60\text{ml/min/1.73m}^2$) is the most sensitive(37), which is desirable in view of the potential application of the risk score for population screening. In addition, the target populations were European- and African-Americans; the generalizability is limited in other ethnicities. Nearly 20% of participants did not return for the eighth exam cycle, potentially biasing our results towards the null. Although family history is a risk factor for kidney disease(38), too few participants had complete family history data to construct a risk function. Finally, the risk score should not be used as a substitute for established urinalysis screening intervals in people with diabetes, nor for appropriate and timely nephrology referral in cases where persistent proteinuria exists or where progression is rapid.

In conclusion, we have developed a simple risk prediction algorithm that estimates an individual's 10-year probability of developing chronic kidney disease, permitting risk stratification for chronic kidney disease using clinical factors readily accessible in primary care. The role of this risk score in identifying individuals in the community at high risk of chronic kidney disease warrants further investigation.

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Figure 1.

Receiver operating characteristic curves for the final renal risk score in a) the derivation (FHS) and b) validation datasets (ARIC; stratified by race).

Table 1

Baseline Characteristics of Participants in the FHS and ARIC Studies. Data presented as mean with standard deviation in parenthesis for continuous variables or percentage with number in parenthesis for categorical variables.

	FHS	ARIC
Number of participants	2490	1777
Age, years	57.1 (8.9)	62.4 (5.4)
Female gender, %	53.0 (1319)	50.6 (900)
Ethnicity		
White, %	100 (2490)	76.1 (1353)
Black, %	NA	23.9 (424)
Diabetes, %	7.4 (184)	13.4 (239)
Systolic blood pressure, mm Hg	126 (18)	128 (18)
Hypertension, %	35.3 (878)	46.1 (819)
High density lipoprotein cholesterol, mg/dL	52 (16)	50 (17)
Triglycerides, mg/dL	137 (98)	139 (82)
Obesity (Body mass index ≥ 30 kg/m ²), %	27.1 (673)	31.0 (552)
Current smoking, %	14.3 (355)	14.2 (252)
Cardiovascular Disease, % *	8.3 (206)	7.3 (130)
Estimated glomerular filtration rate, ml/min/1.73m ²	92 (23)	85 (16)
Categorical eGFR, ml/min/1.73m ²		
60–74 ml/min/1.73m ² , %	20.0 (499)	30.9 (549)
75–89 ml/min/1.73m ² , %	35.4 (882)	32.2 (572)
90–119 ml/min/1.73m ² , %	35.0 (238)	34.1 (605)
≥ 120 ml/min/1.73m ² , %	9.6 (871)	2.9 (51)
Dipstick proteinuria **, %	17.1 (422)	NA
Albuminuria [§] , %	9.2 (197)	5.7 (101)

Abbreviation: eGFR = estimated glomerular filtration rate

SI conversion factors: To convert cholesterol level to millimoles per liter, multiply by 0.0259 and triglyceride level to millimoles per liter, multiply by 0.0113.

Data was ≥ 99.7 % complete for all variables except albumin to creatinine ratio, which was 86% complete.

* includes coronary heart disease and congestive heart failure

** defined as trace or above

[§] defined as spot urine albumin to creatinine ratio of ≥ 30 mg/g

Table 2

Renal Risk Score in FHS for the development of chronic kidney disease, defined as eGFR < 60 ml/min/1.73m² at exam 8*

Model	Covariate	Odds Ratio (95% confidence interval)	P value
Model 1 **	Age, per year	1.11 (1.09 – 1.13)	<0.001
	Diabetes mellitus	1.94 (1.29 – 2.90)	0.002
	Hypertension	2.08 (1.53 – 2.80)	<0.001
Model 2 ***	Age	1.09 (1.07 – 1.11)	<0.001
	Diabetes mellitus	2.27 (1.49 – 3.46)	<0.001
	Hypertension	2.09 (1.54 – 2.84)	<0.001
	eGFR category		<0.001
	90–119ml/min/1.73m ²	1.00 (referent)	NA
	60–74ml/min/1.73m ²	3.94 (2.58 – 6.00)	<0.001
	75–89ml/min/1.73m ²	1.78 (1.17 – 2.73)	0.007
Model 3 ****	≥120ml/min/1.73m ²	1.18 (0.58 – 2.43)	0.65
	Age	1.09 (1.07 – 1.12)	<0.001
	Diabetes mellitus	1.73 (1.08 – 2.77)	0.02
	Hypertension	2.10 (1.51 – 2.94)	<0.001
	eGFR category [§]		<0.001
	90–119ml/min/1.73m ²	1.00 (referent)	NA
	60–74ml/min/1.73m ²	3.73 (2.36 – 5.90)	<0.001
	75–89ml/min/1.73m ²	1.66 (1.05 – 2.62)	0.03
	≥120ml/min/1.73m ²	0.95 (0.42 – 2.15)	0.89
	Quantitative albuminuria [£]	1.62 (1.04 – 2.53)	0.035

* Best fitting statistical model shown

** c-statistic for model = 0.786

*** c-statistic for model = 0.812

**** c-statistic for model = 0.813

[§] compared to eGFR 90–119ml/min/1.73m²

[£] defined as urine albumin to creatinine ratio ≥ 30 mg/g. May be substituted with dipstick proteinuria, defined as trace or above.

Table 3

Comparison of odds ratios for chronic kidney disease using MDRD and CKD-EPI equations

	MDRD Odds Ratio [95% CI]	CKD-EPI* Odds Ratio [95% CI]
Age, per year	1.09 [1.07, 1.12]	1.10 [1.08, 1.13]
Diabetes	1.73 [1.08, 2.77]	1.61 [1.02, 2.56]
Hypertension	2.10 [1.51, 2.94]	2.14 [1.56, 2.92]
GFR 60–74 ml/min/1.73m ²	3.73 [2.36, 5.90] [§]	4.75 [3.10, 7.28] ^{§§}
GFR 75–89 ml/min/1.73m ²	1.66 [1.05, 2.62] [§]	2.18 [1.45, 3.29] ^{§§}
Microalbuminuria [£]	1.62 [1.04, 2.53]	1.35 [0.86, 2.11]

[§] compared to eGFR 90–119ml/min/1.73m²^{§§} compared to eGFR > 90ml/min/1.73m², as too few to analyze with GFR > 120ml/min using CKD-EPI equation.[£] defined as urine albumin to creatinine ratio ≥ 30 mg/g.

* C-statistic for the CKD-EPI model 0.836. The improvement in c-statistic compared to the primary analysis (0.813) is due to differential handling of the age variable by the 2 equations (c-statistic for age-only in the MDRD model: 0.77; c-statistic for age-only in the CKD-EPI model: 0.79).

Table 4

Risk of chronic kidney disease at 10 Years in the development (FHS) cohort according to risk category

Risk Factor	Points Awarded	Risk Score	10-year risk of chronic kidney disease
Age (years)		0	0%
30–34	0	1	0%
35–39	1	2	1%
40–44	2	3	1%
45–49	3	4	2%
50–54	4	5	3%
55–59	4	6	5%
60–64	5	7	9%
65–69	6	8	14%
70–74	7	9	20%
75–79	8	10	30%
80–85	9	11	41%
		12	54%
Diabetes (yes)	1	13	66%
		14	76%
Hypertension (yes)	1	15	84%
Dipstick proteinuria (trace or above) **	1		
Estimated Glomerular Filtration Rate			
60 to 74 ml/min/1.73m ²	3		
75 to 89 ml/min/1.73m ²	1		
90 to 119 ml/min/1.73m ²	0		
Above 120 ml/min/1.73m ²	0		

* The risk score is calculated by adding the points for each risk factor from column 2 (points awarded).

** Dipstick proteinuria may be substituted with quantitative albuminuria, defined as urine albumin to creatinine ratio ≥ 30 mg/g.

C statistic for overall score is 0.813.