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Comparison of Estimated Glomerular Filtration Rates and Albuminuria in Predicting Risk of Coronary Heart Disease in a Population with High Prevalence of Diabetes Mellitus and Renal Disease

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Abstract

Improved accuracy in predicting coronary heart disease (CHD) risk in persons with diabetes and kidney disease is needed. Addition of albuminuria to established methods of CHD risk calculation was reported in the Strong Heart Study (SHS) cohort. In this article, the addition of estimated glomerular filtration rate (eGFR) is evaluated with data from 4,549 American Indian SHS participants, ages 45–74 years. After adjustment for Framingham CHD risk factors, hazard ratios for eGFR as a predictor of CHD were 1.69 (95% confidence interval: 1.34, 2.13) in women and 1.41 (95% confidence interval: 0.94, 2.13) in men. Models including albuminuria, eGFR, or both scored higher in discriminatory power than models using conventional risk factors alone in women; in men the improvement was seen only for albuminuria and the combination of albuminuria and eGFR. Hosmer–Lemeshow assessments showed good calibration for the models using eGFR alone in both genders, followed by models including albuminuria alone in both genders. Adding eGFR improved the NRI in women (0.085, $p=0.0004$) but not in men (0.010, $p=0.1967$). NRI and IDI were improved in both genders using both albuminuria and eGFR (NRI: 0.135, $p<0.0001$; IDI: 0.027, $p<0.0001$ in women; NRI: 0.035, $p<0.0196$; IDI: 0.008 $p<0.0156$ in men). Therefore, a risk calculator including albuminuria enhances CHD prediction compared with one using only standard risk factors in men and women. Including eGFR alone improves risk

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prediction in women, but for men it is preferable to have both eGFR and albuminuria. In conclusion, this enhanced calculator should be useful in estimating CHD risk in populations with high prevalence of diabetes and renal disease.

Keywords

coronary heart disease; diabetes; estimated glomerular filtration rate; risk prediction

INTRODUCTION

In populations with high rates of diabetes mellitus, associated renal disease contributes substantially to coronary heart disease (CHD). Previous studies have addressed the effect of estimated glomerular filtration rate (eGFR) and albuminuria, either synergistically or independently, in predicting cardiovascular disease (CVD) risk; however, those data were based on randomized clinical trials or generated from population-based studies with various disease characteristics.^{1, 2,3,4} A Norwegian study, composed of a population with high prevalence of diabetes and CVD,⁵ suggested that low eGFR and albuminuria were synergistic risk factors in predicting cardiovascular mortality in the elderly. The Strong Heart Study (SHS) is a unique source of information on CHD and renal disease in a population with high prevalence of diabetes mellitus and kidney abnormalities.^{6,7} Lee et al. demonstrated the importance of including albuminuria in a CHD risk calculator, along with age, hypertension, low-density lipoprotein cholesterol (LDL-C), and diabetes, to predict 10-year risk. In the current analysis, longitudinal data from the SHS are used to examine the value of incorporating eGFR as a measure of kidney function in CHD risk prediction, since eGFR is now commonly available and widely used in clinical settings.

METHODS

The SHS was initiated in 1988 to investigate CVD and its risk factors in geographically diverse groups of American Indians. The SHS design, methods, and laboratory techniques have been published.^{8,9} The Indian Health Service, institutional review boards, participating tribes, and the MedStar Health Research Institute approved the study, and informed consent was obtained. This cohort includes 4549 men and women ages 45 to 74. Three examinations took place in 1989–1991, 1993–1995, and 1998–2000. Excluded from the analyses were 182 participants with definite CHD (definite CHD, definite myocardial infarction [MI], or ECG-evident MI) or stroke before the baseline examination.

Baseline and follow-up examinations consisted of a personal interview and physical examination.¹⁰ Weight, height, blood pressure, and waist and hip circumferences were measured.^{8,9} Body mass index (BMI) was calculated using height and weight (kg/m^2). Hypertension was classified into 3 categories, according to JNC-VII (7th Joint National Committee on Hypertension) criteria:¹¹ normal (systolic blood pressure [SBP] <120 mmHg, diastolic blood pressure [DBP] <80 mmHg, and no anti-hypertensive medication); pre-hypertension (SBP 120–139 mmHg or DBP 80–89 mmHg and no anti-hypertensive medication); and hypertension (SBP $\geq$ 140 mmHg or DBP $\geq$ 90 mmHg and/or taking anti-hypertensive medication). Blood was drawn and a urine sample obtained at the baseline examination after a 12-hour fast. Blood measures included plasma cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), LDL-C, and fasting glucose. Serum creatinine was measured via an automated alkaline picrate method; urinary albumin was measured via an automated nephelometric immunochemical procedure.^{8,12,13} Diabetes was defined as fasting plasma glucose [FPG] $\geq$ 126 mg/dL [6.99 mmol/L] or receiving insulin or oral anti-hyperglycemic treatment).¹⁴ Albuminuria was categorized (units milligrams/

gram) as follows: microalbuminuria = albumin/creatinine ≥ 30 to < 300 ; macroalbuminuria = albumin/creatinine ≥ 300 . Estimated GFR was calculated using the abbreviated Modification of Diet in Renal Disease (MDRD) equation:¹⁵

$$eGFR = 186 \times (S_{CR})^{-1.154} \times AGE^{-0.203} \times (0.742 \text{ if Female}) \times (1.210 \text{ if African-American}).$$

Because SHS includes only American Indians, the MDRD term for ethnicity was excluded.

Estimated GFR was dichotomously categorized as either preserved ≥ 60 ml/min/1.73m²) or decreased (< 60 ml/min/1.73m²). Age was used as a continuous variable in the prediction equation. LDL-C was classified into 5 groups according to NCEP ATP III criteria:¹⁶ < 100 , 100–129, 130–159, 160–189, and ≥ 190 mg/dL (< 2.59 , 2.59–3.35, 3.36–4.13, and ≥ 4.14 mmol/L); HDL-C was classified into 3 categories: < 40 , 40–59, and ≥ 60 mg/dL (< 1.04 , 1.04–1.54, and ≥ 1.55 mmol/L). The baseline exam was conducted before lipid lowering therapy was widely used by IHS providers.

CHD events occurring during the follow up were ascertained from the annual surveillance or at the second or third examinations.¹⁷ Medical records were abstracted, and CHD death and events were confirmed by Mortality and Morbidity Review Committees.¹⁷ The data used in these analyses consisted of incident fatal and nonfatal CHD events (definite MI, definite CHD, ECG-evident definite MI, fatal definite MI, definite and possible fatal CHD, and sudden death due to CHD) occurring during the median 15-year follow up from the baseline examination through December 31, 2007; loss to follow-up was $< 1\%$. Time to event was calculated from the date of the baseline examination to the date of the CHD event or last follow-up. Baseline characteristics of the study population were calculated by gender and incident CHD status at the end of 2007. A chi-square test was used to compare categorical risk factors; an independent t-test was used to compare continuous risk factors in those who did and did not develop CHD.

Cox proportional hazards models¹⁸ were used with the basic Framingham risk covariates to develop CHD risk estimates. A number of models were considered in developing the optimal prediction equation, including models with various forms of the significant risk factors (i.e., as continuous and categorical variables). Interaction terms, such as age $\times$ LDL-C, age $\times$ HDL-C, age $\times$ SBP, age $\times$ DBP, and log (albumin/creatinine) $\times$ diabetes also were considered, and none were significant. We sequentially added eGFR and albuminuria to the models to assess the improvement in CHD risk prediction when including measures of kidney function. We considered and compared the following models using SHS data in our analyses: 1) Framingham CHD risk model; 2) Framingham model with adjusted coefficients and SHS data; 3) Model 2 plus data-specific cut-off points; 4) Model 3 plus albuminuria; 5) Model 3 plus eGFR; 6) Model 3 plus albuminuria and eGFR. Model 6 was used to develop the currently used SHS CHD risk calculator.

To assess the ability of the prediction equations to discriminate between participants who would develop CHD and those who would not, we used the c-index (area under the receiver-operating characteristic curve).¹⁹ A c-statistic (also known as area under the curve (AUC) or c-index) value of 0.70 or greater indicates relatively good discrimination.²⁰ The Hosmer-Lemeshow chi-square statistic was calculated to assess model calibration. Values < 20 (p value ≥ 0.01) indicate good calibration.^{21,22}

We used the Hosmer-Lemeshow chi-square statistic to assess each model's calibration and the c-statistic, a widely used measure of discrimination. However, the c-statistic is not sensitive for detecting differences in discrimination ability between models with and without

new markers,^{23,24,25} and may not be optimal for prospective risk prediction.²⁶ Therefore, we further assessed the reclassification ability by using reclassification tables.²⁶ Reclassification tables for participants with and without incident CHD were constructed using estimated CHD risk categories based on ATP III 10-yr CHD risk criteria.²⁷ We computed net reclassification improvement (NRI)²⁸ to assess improvement in CHD prediction obtained by introducing eGFR and/or albuminuria into the models. We also computed the integrated discrimination improvement (IDI), which does not require a specific cut-off point for risk categories, to determine improvement in sensitivity and specificity.²⁸ Tests to determine whether the improvement in NRI and IDI differed significantly from zero were performed.

RESULTS

Among the 4,367 participants without CHD or definite stroke at baseline, 1009 (529 women and 480 men) had developed CHD by the end of 2007. Men and women who developed CHD events were older; had higher LDL-C and SBP, lower HDL-C and eGFR, and higher prevalences of diabetes and albuminuria at baseline (Table 1).

To assess the association of incident CHD with albuminuria and eGFR, hazard ratios were calculated adjusted for Framingham CHD risk factors. Hazard ratios for eGFR were 1.69 (95% confidence interval [CI]: 1.34–2.13) in women and 1.41 (95% CI: 0.94–2.13) in men. Hazard ratios for microalbuminuria and macroalbuminuria were 1.56 (95% CI: 1.24–1.95) and 2.90 (95% CI: 2.26–3.71), respectively, in women and 1.23 (95% CI: 0.96–1.57) and 1.88 (95% CI: 1.39, 2.55), respectively, in men.

The coefficients underlying the CHD prediction equations for men and women were generated from models adding albuminuria (Model 4), eGFR (Model 5), or both (Model 6) (Table 2). With the individual's risk factors ($\mathbf{x} = (x_1, x_2, \dots, x_p)$), estimated coefficients ($b_1, b_2, \dots, b_p$), and Breslow's estimate for $S_0(t)$, the probability of developing CHD ($P(t, \mathbf{x})$) within 10 years for an individual with a given set of risk factor values ($x_1, x_2, \dots, x_p$) could be calculated by the equation of $1 - [S_0(t)]^{\exp(\sum b_i x_i)}$. Further details of the equations are shown in the Appendix. To illustrate the application of Table 2, for a 65-year-old male smoker with diabetes and macroalbuminuria, SBP=120 mmHg, DBP=85mmHg, eGFR=80 ml/min/1.73m², LDL-C=130 mg/dL, and HDL-C=68 mg/dL, and no antihypertensive medication, the estimated probability of developing CHD in 10 years can be calculated as follows:

$$\begin{aligned} \sum b_i x_i = & 0.0444(65) + 0.3200(\text{LDL-C}=130-159) + (-0.0091)(\text{HDL-C} \geq 60) \\ & + 0.3440(\text{pre-hypertension}) + 0.5733(\text{diabetes present}) + 0.3797(\text{current smoker}) + \\ & 0.6348(\text{macroalbuminuria present}) + 0.1721(\text{eGFR} < 60) = 5.3008 \end{aligned}$$

$$\text{Exp}(\sum b_i x_i) = \text{Exp}(5.3008) = 200.497; \text{ thus, } P(t) = 1 - S_0(t)^{200.497} = 1 - 0.2932 = 0.7068.$$

Thus, the estimated probability of developing CHD in 10 years for this participant is 71%.

Prediction models based on the underlying equation and coefficients used, and whether eGFR and albuminuria were included, were compared using the c-index, Hosmer-Lemeshow chi-square statistic, and NRI and IDI measures (Table 3). C-statistics for models using albuminuria, eGFR or both were slightly higher than models using conventional risk factors alone in women; in men the improvement was seen only for albuminuria and the combination. On the other hand, measures of discrimination showed that, without adjustments, the Framingham CHD risk model performed poorly in this population. After adjustments for prevalence of risk factors and incidence of CHD in American Indians (Model 3), CHD prediction was improved significantly. The Hosmer-Lemeshow statistics

yielded by the addition of eGFR alone (Model 5) showed better calibration for men and women than the addition of both eGFR and albuminuria (Model 6).

We evaluated the improvement in Models 4, 5, and 6 using methods proposed by Pencina et al.²⁸ Participants were classified into the 3 risk groups defined by the ATP III. Models 4, 5, and 6 were examined by cross-classifying expected risks and comparing these risks with the observed proportions of CHD events in each group. Table 4 shows the reclassification of risk for participants with and without incident CHD after including eGFR, stratified by gender. While the table shows general agreement between the classifications, the number of participants in predicted risk categories changed significantly with the addition of eGFR in women (NRI=0.085, $p=0.0004$; IDI=0.010, $p=0.0003$), implying improved classification of those with and without incident CHD event(s). In contrast, eGFR alone did not improve classification in men (NRI=0.010, $p=0.1967$; IDI=-0.0005, $p=0.3558$). When eGFR was added to the model that already included albuminuria, the reclassification of persons with and without CHD into appropriate risk categories improved significantly in both women and men.

DISCUSSION

In this article, the contributions of eGFR alone and in combination with albuminuria in CHD prediction have been examined, and a CHD risk prediction algorithm using eGFR has been provided for use with American Indians. We found that adding eGFR (a measure of kidney filtration capacity) or albuminuria (a reflection of renal disease and generalized inflammation) to a risk calculator using established CVD risk factors was beneficial in identifying participants at risk for CHD, but that eGFR contributed less to the model for men than for women. This risk prediction calculator was derived in a population with high prevalence of diabetes and diabetes-associated renal disease, a condition now common in many ethnic groups; thus this calculator probably can be used with other populations with similar risk factors.

Albuminuria has previously been identified as an independent risk factor for CHD in the American Indian population, with macroalbuminuria having a stronger effect than microalbuminuria.²⁹ Other studies have explored the combined contribution of including measures of albuminuria and eGFR in assessing CVD risk and mortality, mostly in randomized clinical trials.^{2,4} However, few population-based studies have addressed the additional contribution of including both measures in the context of CVD risk prediction. The Gubbio Population Study³⁰ of middle-aged white subjects with low prevalence of diabetes reported that the lack of association between albuminuria and eGFR provides complementary information, thus separating different groups at risk and leading to additional, independent information for assessing CVD risk. The HUNT II study³¹ showed that adding albuminuria and eGFR improved traditional risk models and led to better prediction of CVD mortality. Another investigation, using a representative sample of U.S. adults, reported an independent non-synergistic effect of albuminuria and low eGFR on CVD and all-cause mortality.³² A study of a large prospective database in Hong Kong found that, when adjusted for eGFR and albuminuria, the associations between lipid, A1c, BP, duration of diabetes, and CHD were attenuated.³³ Moreover, a population-based study in the Netherlands reported that including both eGFR and albuminuria in risk prediction was associated with improved prediction for vascular events.³⁴ Taken together, this literature suggests that the additional contribution of including measures of albuminuria and/or eGFR may vary depending on the population or outcome of interest.

In the current study, including eGFR or albuminuria provided significant and additive effects as CHD predictors in women; in men either including albuminuria or including both

albuminuria and eGFR improved risk prediction, as shown by the c-statistic. Measures of reclassification of participant risk category indicated significant improvement using albuminuria or the combination in both genders and for eGFR alone in women. Both albuminuria and decreased kidney function are highly correlated with diabetic nephropathy. Albuminuria indicates vascular damage which may or may not be directly related to loss of filtration capacity, while eGFR is a direct measure of kidney dysfunction and could be used when information on urinary albumin excretion is unavailable. In clinical situations where only one measure is available, then either one should be used in women; in men it appears that having both measures is preferable. This risk calculator allows physicians treating populations with high prevalence of diabetes and renal disease to more precisely project the likelihood of a CHD event within 10 years.

When considering the contribution of adding new markers into prediction models, several measures of model fit need consideration. With the use of diagnostic statistics, we found that eGFR is a significant predictor of CHD for women in this population after adjustments for age, LDL-C, HDL-C, blood pressure, diabetes, current smoking, and albuminuria. In women, most measures of predictive power, calibration, and reclassification improved after including eGFR. In men, the prediction did not improve when including eGFR alone in the equation. On the other hand, reclassification indices should be taken into account; when we used the NRI and IDI measures, both showed improvements in reclassification in both genders when albuminuria and eGFR were used together.

In conclusion, a CHD risk calculator including eGFR or albuminuria may enhance care in Indian Health Service facilities and in other settings serving populations with high prevalence of diabetes and kidney disease. In clinical situations where only an albuminuria or eGFR measure is available, then either one should be used to better evaluate patient CHD risk. For men, however, it is preferable to have both measures. We have developed a software tool for this CHD risk calculator that we plan to make easily accessible and downloadable. This calculator could be downloaded into personal computers in facilities caring for populations with high prevalence of diabetes and kidney disease.

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APPENDIX

Methods for Developing the Prediction Equations

Cox proportional hazards models were used to develop the prediction equations. Based on the estimated coefficients, a coronary heart disease (CHD)-event-free distribution function was estimated:³⁵

$$S(t, \mathbf{x}) = [S_0(t)]^{\exp(\sum b_i x_i)} \quad (1)$$

where $S_0(t)$ is the estimated baseline survival (time to CHD event) function, $\mathbf{x} = (x_1, x_2, \dots, x_p)$ are the covariates, and $b_1, b_2, \dots, b_p$ are the estimated coefficients. $S_0(t)$ was estimated according to a method proposed by Breslow.³⁶ Then,

$$P(t, \mathbf{x}) = 1 - S(t, \mathbf{x}) \quad (2)$$

gives the probability of developing CHD at time t . This equation was used to predict the probability of developing CHD in t years for an individual with a given set of covariates, $\mathbf{x}$. SAS³⁷ was used to obtain Breslow's estimates, and consequently $P(t, \mathbf{x})$.

With this term and Breslow's estimate for $S_0(t)$, the probability of developing CHD, that is, $P(t, \mathbf{x})$ in Equation (2) above, in any number of years up to 10 years for any individuals with a given set of risk factor values, $x_1, x_2, \dots, x_p$ could be calculated. For example, the exponent term $\sum b_i x_i$ in equation 1 from model 5 was as follows:

For women:

$$\begin{aligned} \sum b_i x_i = & 0.0210(\text{Age}) + 0.3229 (\text{if LDL-C is } 100-129) + 0.3576 (\text{if LDL-C} = 130-159) + \\ & 0.3892 (\text{if LDL-C} = 160-189) + 1.0253 (\text{if LDL-C} \geq 190) + 0.1675 (\text{if HDL-C} < 40) + \\ & (-0.0066) (\text{if HDL-C} \geq 60) + 0.1381 (\text{if pre-hypertension}) + 0.6142 (\text{if hypertension}) \\ & + 1.1888 (\text{if diabetes present}) + 0.3988 (\text{if current smoker}) + 0.5235 (\text{if eGFR} < 60). \end{aligned}$$

For men:

$$\begin{aligned} \sum b_i x_i = & 0.0434(\text{Age}) + 0.0766 (\text{if LDL-C is } 100-129) + 0.3081 (\text{if LDL-C} = 130-159) + \\ & 0.7928 (\text{if LDL-C} = 160-189) + 0.8438 (\text{if LDL-C} \geq 190) + 0.3076 (\text{if HDL-C} < 40) + \\ & (0.0489) (\text{if HDL-C} \geq 60) + 0.3357 (\text{if pre-hypertension}) + 0.5133 (\text{if hypertension}) \\ & + 0.7146 (\text{if diabetes present}) + 0.3555 (\text{if current smoker}) + 0.3461 (\text{if eGFR} < 60). \end{aligned}$$

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Table 1

Baseline Characteristics by Gender and Coronary Heart Disease Status at the end of 2007

Variable	Without incident CHD	With incident CHD	P*
Women			
Age (years)	56.2±8.0	58.1±8.0	<0.001
Body mass index (kg/m ²)	31.5±6.7	31.7±5.9	.3877
Total cholesterol (mg/dL)	190±39	202±43	<0.001
High-density lipoprotein cholesterol (mg/dL)	49±13	45±12	<0.001
Low-density lipoprotein cholesterol (mg/dL)	114±33	122±36	<0.001
Systolic blood pressure (mmHg)	126±20	134±24	<0.001
Diastolic blood pressure (mmHg)	75±10	76±10	.0979
Estimated glomerular filtration rate (MDRD)	79.7±23.0	76.4±31.1	.0069
Diabetes mellitus (%)	41.6	72.1	<0.001
Microalbuminuria (%)	17.8	26.5	<0.001
Macroalbuminuria (%)	8.0	23.7	<0.001
Current smoker (%)	29.4	30.6	.5756
Men			
Age (years)	54.9±7.8	57.2±8.0	<0.001
Body mass index (kg/m ²)	29.7±6.2	30.2±5.4	.1382
Total cholesterol (mg/dL)	186±40	197±42	<0.001
High-density lipoprotein cholesterol (mg/dL)	44±14	41±12	<0.001
Low-density lipoprotein cholesterol (mg/dL)	115±33	125±35	<0.001
Systolic blood pressure (mmHg)	127±18	131±18	<0.001
Diastolic blood pressure (mmHg)	80±10	80±10	.0798
Estimated glomerular filtration rate (MDRD)	88.0±19.6	85.7±19.5	.0273
Diabetes mellitus (%)	35.7	52.2	<0.001
Microalbuminuria (%)	17.0	20.8	.0708
Macroalbuminuria (%)	8.1	12.6	.0045
Current smoker (%)	40.2	43.5	.2016

Data are mean ±STD or %.

* Student's t tests were used for continuous variables and chi-square tests were used for categorical variables.

Table 2

β -Coefficients Underlying Coronary Heart Disease Prediction Equations

Variable	Model 4		Model 5		Model 6	
	Women	Men	Women	Men	Women	Men
Age, y	0.0303	0.0463	0.0210	0.0434	0.0262	0.0444
Low-density lipoprotein cholesterol (mg/dL)						
<100	Referent	Referent	Referent	Referent	Referent	Referent
100–129	0.3299	0.0847	0.3229	0.0766	0.3145	0.0661
130–159	0.3616	0.3235	0.3576	0.3081	0.3727	0.3200
160–189	0.3471	0.8157	0.3892	0.7928	0.3339	0.8117
≥190	1.0491	0.8264	1.0253	0.8438	0.9747	0.8235
High-density lipoprotein cholesterol (mg/dL)						
<40	0.1464	0.3198	0.1675	0.3076	0.1618	0.3049
40–59	Referent	Referent	Referent	Referent	Referent	Referent
≥60	−0.0266	0.0136	−0.0066	0.0489	−0.0367	−0.0091
Blood pressure						
Normal	Referent	Referent	Referent	Referent	Referent	Referent
Prehypertension	0.0862	0.3396	0.1381	0.3357	0.1056	0.3440
Hypertension	0.4514	0.4857	0.6142	0.5133	0.4301	0.4819
Diabetes mellitus	0.9263	0.5903	1.1888	0.7146	0.9296	0.5733
Current smoker	0.4441	0.3825	0.3988	0.3555	0.4494	0.3797
Albuminuria						
Microalbuminuria	0.4437	0.2049	---	---	0.4284	0.2034
Macroalbuminuria	1.0640	0.6321	---	---	0.9942	0.6348
Estimated glomerular filtration rate (MDRD)						
≥ 60	---	---	Referent	Referent	Referent	Referent
< 60	---	---	0.5235	0.3461	0.3093	0.1721
Baseline survival function at 10 years, S_0 (10 years)	0.9938	0.9946	0.9897	0.9935	0.9924	0.9939

Model 4: Model 3 plus albuminuria.

Model 5: Model 3 plus eGFR.

Table 3

Measures of Discriminatory Predictive Power

	C-statistic	Hosmer-Lemeshow	Net reclassification improvement ^I (P-value)	Integrated Discrimination Improvement (P-value)
<i>Women</i>				
Model 1	0.684	25.6(p=0.0012)	---	---
Model 2	0.711	9.16(p=0.3287)	---	---
Model 3	0.713	7.20(p=0.5152)	Model without albuminuria or eGFR	Model without albuminuria or eGFR
Model 4	0.727	14.6(p=0.0667)	0.129 (<.0001)	0.022(<.0001)
Model 5 (eGFR < 60)	0.718	10.9(p=0.2070)	0.085(0.0004)	0.010(0.0003)
Model 6	0.728	18.5(p=0.0175)	0.135(<.0001)	0.027(<.0001)
<i>Men</i>				
Model 1	0.663	40.7(p<0.0001)	---	---
Model 2	0.697	11.3 (p=0.1879)	---	---
Model 3	0.689	14.6(p=0.0667)	Model without albuminuria or eGFR	Model without albuminuria or eGFR
Model 4	0.699	19.4 (p=0.0130)	0.017(0.1395)	0.008(0.0067)
Model 5 (eGFR < 60)	0.688	14.1(p=0.0781)	0.010(0.1967)	-0.0005 (0.3558)
Model 6	0.696	22.8 (p=0.0036)	0.035 (0.0196)	0.008 (0.0156)

^I using <6, 6–20, >20% 10-year CHD risk categories.

Model 1: Framingham CHD risk model.

Model 2: Framingham model using SHS data and adjusting the coefficients.

Model 3: Model 2 plus data-specific cut-off points.

Model 4: Model 3 plus albuminuria.

Model 5: Model 3 plus eGFR.

Model 6: Model 3 plus albuminuria and eGFR.

Table 4

Reclassification of Risk Among People With and Without a Coronary Heart Disease Event During Follow-Up

Frequency (row percent), women [men]	Model with albuminuria			Model with eGFR			Model with albuminuria and eGFR		
	<10%	10–20%	>20%	<10%	10–20%	>20%	<10%	10–20%	>20%
<i>Participants with a CHD event</i>									
<10%	24(96.0) [14(100)]	1(4.0) [0(0)]	0(0) [0(0)]	25(100) [14(100)]	0(0) [0(0)]	0(0) [0(0)]	24(96.0) [14(100)]	1(4.0) [0(0)]	0(0) [0(0)]
10–20%	56(56.5) [1(1.2)]	61(44.5) [74(85.1)]	26(19.0) [12(13.8)]	40(29.2) [1(1.1)]	91(66.4) [81(92.1)]	6(4.4) [6(6.8)]	51(37.2) [1(1.2)]	58(42.3) [72(82.8)]	28(20.4) [14(16.1)]
>20%	0(0) [0(0)]	29(17.4) [6(2.8)]	138(82.6) [208(97.2)]	0(0) [0(0)]	13(7.7) [5(2.4)]	157(92.4) [204(97.6)]	0(0.0) [0(0)]	28(16.9) [6(2.9)]	138(83.1) [203(97.1)]
<i>Participants without a CHD event</i>									
<10%	623(99.4) [201(93.1)]	4(0.6) [15(6.9)]	0(0) [0(0)]	630(100) [217(99.1)]	0(0) [2(0.9)]	0(0) [0(0)]	622(99.2) [202(93.5)]	5(0.8) [14(6.5)]	0(0) [0(0)]
10–20%	56(51.7) [18(3.1)]	447(40.8) [525(89.6)]	82(7.5) [43(7.3)]	472(43.0) [9(1.5)]	588(53.6) [569(96.4)]	38(3.5) [12(2.0)]	558(51.2) [21(3.6)]	446(40.9) [518(88.9)]	87(8.0) [44(7.6)]
>20%	0(0) [0(0)]	150(31.5) [42(7.8)]	327(68.6) [495(92.2)]	0(0) [0(0)]	65(13.8) [19(3.5)]	407(86.2) [525(96.5)]	0(0) [0(0)]	162(34.5) [54(10.1)]	308(65.5) [482(89.9)]