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CLINICAL RESEARCH STUDY

Kidney Disease, Framingham Risk Scores, and Cardiac and Mortality Outcomes

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ABSTRACT

BACKGROUND: The Framingham equations were developed to predict incident coronary heart disease. It remains unknown how the presence of chronic kidney disease affects their performance.

METHODS: Individuals without preexisting cardiovascular disease aged 45 to 74 years from the Atherosclerosis Risk in Communities and Cardiovascular Health Studies were analyzed. Using sex- and race-specific Cox models, we evaluated the 5-year risk of coronary heart disease and mortality events associated with both chronic kidney disease and Framingham risk score, the absolute risk of events caused by kidney disease, and model discrimination.

RESULTS: Among 15,717 subjects, 756 (4.8%) had kidney disease. The Framingham risk score independently predicted cardiac and mortality events in all subgroups, whereas kidney disease predicted events in all subgroups except cardiac events in white women. After adjustment for traditional risk factors, the increase in cardiac and mortality events per 1000 person-years attributable to kidney disease was 4.3 and 13.7 for white men, 16.1 and 40.5 for African American men, 1.2 and 5.8 for white women, and 13.6 and 14.2 for African American women, respectively. This represented an additional 17,000 and 12,000 cardiac events and 63,000 and 19,000 deaths per year among whites and African Americans, respectively. Mortality rates attributable to kidney disease, diabetes, and smoking were comparable. Accounting for kidney disease improved discrimination for only mortality outcomes in white men and African American women.

CONCLUSIONS: Chronic kidney disease in a community-based population is an important predictor of cardiac and mortality events, particularly in African Americans, but it does not improve discrimination of Framingham equations. © 2007 Elsevier Inc. All rights reserved.

KEYWORDS: Cardiovascular disease; Chronic kidney disease; Coronary heart disease; Framingham Risk Score; Renal insufficiency

The Framingham Coronary Heart Disease Risk Score allows clinicians to estimate the individual patient risk of coronary disease by accounting for traditional cardiac risk factors, including sex, age, blood pressure, cholesterol, diabetes, and smoking.[1,2] The Framingham Risk Score (FRS) instrument has been validated in racially diverse populations, including the Atherosclerosis Risk in Communities (ARIC) and Cardiovascular Health Studies (CHS). Although there was reasonable agreement between predicted and actual event rates in these population-based cohorts, making recalibration of the equations unnecessary, the ability of the FRS to discriminate between subjects who did and did not develop coronary disease seemed worse in minority cohorts.[3]

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Other risk factors for coronary disease include chronic kidney disease.[4-6] However, the impact of chronic kidney disease at a public health level remains uncertain. Therefore, we investigated the importance of chronic kidney disease by assessing sex- and race-specific risk associated with kidney disease after adjusting for Framingham risk, determining absolute risk associated with kidney disease in excess of and in comparison with traditional cardiac risk factors, and evaluating the impact of kidney disease on the discriminative ability of the Framingham equations in a biracial, community-based cohort.

CLINICAL SIGNIFICANCE

- Kidney disease has a major population impact, particularly in African Americans. Among whites and African Americans, respectively, kidney disease accounts for 17,000 and 12,000 coronary heart disease events and 63,000 and 19,000 deaths per year after adjusting for Framingham risk.
- For mortality outcomes, the impact of kidney disease is similar to the impact of diabetes and smoking.
- Accounting for the presence of chronic kidney disease generally does not improve Framingham risk score discrimination.

METHODS

Study Design

We used 2 limited-access databases that evaluate cardiovascular disease in community-based populations: ARIC and CHS. Pooling these studies allowed for evaluation of individuals in the Framingham study age range while increasing the number of African Americans. From 1987 to 1989, ARIC enrolled 15,792 participants aged 45 to 64 years from 4 communities. The Mississippi center is entirely African American and comprises 80% of the African Americans in ARIC.[7] CHS is a population-based study of 5201 subjects aged 65 years or more who were selected from Medicare eligibility files in 4 communities from 1989 to 1990. An additional 687 African Americans were recruited from 1992 to 1993.[8] We excluded subjects aged more than 74 years to match the Framingham population.

Glomerular filtration rate was estimated with the 4-variable Modification of Diet in Renal Disease study equation.[9-11] We calibrated the ARIC and CHS laboratories indirectly using National Health and Nutrition Examination Survey (NHANES) III data.[6,12-14] We defined chronic kidney disease as an estimated glomerular filtration rate less than 60 mL/min/1.73 m^2.[15] Subjects with a glomerular filtration rate less than 15 mL/min/1.73 m^2 were excluded to avoid including individuals for whom dialysis was likely imminent.

Baseline characteristics included demographics (age, sex, race); medical history (cardiovascular disease, diabetes, smoking); systolic and diastolic blood pressure; and laboratory variables (total cholesterol, high-density lipoprotein cholesterol, creatinine).

Race was defined as white or African American. Cigarette smoking was dichotomized by current use. Diabetes was defined by the use of insulin, oral hypoglycemic medications, or a fasting glucose level of 140 mg/dL or greater to match the original Framingham definition.[16]

Baseline cardiovascular disease included a history of both recognized and silent myocardial infarction, angina, coronary angioplasty and bypass procedures, stroke, transient ischemic attack, and intermittent claudication as defined by consensus committees for the studies. Baseline cardiovascular disease included heart failure in CHS but was not evaluated in ARIC.[7,8]

The final cohort included 15,717 individuals after the following exclusions: 402 subjects missing data on age, race, sex, or creatinine, or of non-white/non-African American race; 32 subjects with a glomerular filtration rate less than 15 mL/min/1.73 m^2; 1915 subjects aged more than 74 years; 556 subjects missing baseline cardiovascular disease data; 2922 subjects with baseline cardiovascular disease; 125 subjects missing baseline blood pressure, cholesterol, diabetes, or smoking data; and 11 subjects without follow-up data.

Outcomes

The primary cardiac outcome included myocardial infarction and fatal coronary heart disease. Consensus committees within ARIC and CHS had identical diagnostic criteria. Myocardial infarction includes both clinically recognized and silent infarctions, diagnosed by electrocardiogram changes, abnormal cardiac enzymes, and symptoms. Fatal coronary disease required chest pain within 72 hours of death and/or known ischemic heart disease in the absence of another potential noncardiac cause of death.[7,8] The secondary outcome was all-cause mortality, because kidney disease may be an important risk factor for other forms of cardiovascular disease.[17,18]

STATISTICAL ANALYSIS

Framingham Scores

We reproduced the 5-year survival function for cardiac outcomes by using individual patient data from the limited-access Framingham (11th visit) and Framingham Offspring (baseline visit) datasets, replicating Framingham techniques and definitions.[2,16,19] With published sex-specific Framingham risk functions for predicting "hard coronary heart disease" outcomes and the values for traditional coronary risk factors (blood pressure and lipid categories, age, diabetes, and smoking) from our study population, we used Cox proportional hazards regression models with coefficients developed by the Framingham investigators to calculate the FRS.[2,3]

Next, sex- and race-specific Cox proportional hazards models were derived from the pooled cohort using the same variables as in the Framingham predictive instrument. These "best Cox" models yielded different coefficients for these risk factors than the original FRS models.

All analyses were sex- and race-specific. Proportions of subjects with chronic kidney disease were stratified by 5-year Framingham probability of coronary heart disease, and these groups were compared using the Cochran-Armitage test for trend. The effects of FRS and kidney disease on time to cardiac and mortality outcomes, were analyzed using Cox regression.

Absolute Risk

Adjusted absolute risk of cardiac and mortality outcomes directly attributable to chronic kidney disease was determined to estimate the event reduction if the exposure, namely, kidney disease, were eliminated. Absolute risk was defined as $Event\ Rate*(HR_{kidney\ disease}-1)$, where the hazard ratio for chronic kidney disease is derived from a Cox model that includes terms for FRS and kidney disease, and the event rate is for individuals without kidney disease.[13]

Comparison with Other Risk Factors

The absolute risk associated with chronic kidney disease was compared with other dichotomous Framingham risk factors (diabetes and smoking). We did not evaluate modifiable nondichotomous risk factors (hypertension and dyslipidemia) because these analyses would require dropping multiple terms from the FRS, making interpretation difficult. We derived an adjusted "best Cox" model

Table 1 Baseline Characteristics and Frequency of Outcomes Among the Pooled Cohort

	Men		Women	
	White (n = 5282)	Black (n = 1513)	White (n = 6548)	Black (n = 2374)
Age (mean ± SD)	57.2 ± 8.0	55.3 ± 7.6	57.7 ± 8.5	55.0 ± 7.6
History of diabetes (%)†	6.3	13.4	5.2	15.7
Current smoker (%)	21.5	36.5	22.2	23.4
Blood pressure categories (mm Hg)				
Optimal (SBP < 120, DBP < 80)	45.2	25.8	51.5	31.6
Normal (SBP < 130, DBP < 85)	22.1	20.5	18.4	21.1
High normal (SBP < 140, DBP < 90)	15.8	18.9	13.3	17.1
Stage I (SBP < 160, DBP < 100)	12.7	22.5	13.0	19.8
Stage II-IV (SBP ≥ 160, DBP ≥ 100)	4.3	12.3	3.9	10.4
Total cholesterol categories (mg/dL)				
<160	9.0	9.5	5.4	8.1
160-199	33.8	34.6	27.6	29.6
200-239	38.4	34.2	39.3	34.3
240-279	15.1	15.0	20.2	19.6
≥280	3.7	6.7	7.5	8.3
HDL cholesterol categories (mg/dL)				
<35	23.3	12.2	4.9	3.9
35-44	35.4	27.4	16.5	17.0
45-49	14.6	13.9	11.6	12.3
50-59	16.8	24.4	25.9	26.1
≥60	9.8	22.1	41.0	40.7
Framingham 5-y probability (%)	3.6% ± 2.9%	3.8% ± 3.2%	1.1% ± 1.5%	1.3% ± 1.8%
Framingham 10-y probability (%)	8.5% ± 6.6%	8.9% ± 7.1%	2.8% ± 3.8%	3.3% ± 4.4%
Kidney function				
Creatinine (mg/dL)	1.0 ± 0.2	1.0 ± 0.2	0.8 ± 0.1	0.8 ± 0.2
Estimated GFR (mL/min/1.73 m^2)	87.5 ± 17.6	99.8 ± 21.7	88.3 ± 19.2	101.9 ± 23.4
CKD (%)	4.6	2.4	6.1	3.2
Study of origin				
ARIC	4346	1353	4981	2112
CHS	936	160	1567	262
Cardiac events	231	60	91	54
Mortality events	211	110	144	89

SBP = systolic blood pressure; DBP = diastolic blood pressure; HDL = high-density lipoprotein; CKD = chronic kidney disease; GFR = glomerular filtration rate; SD = standard deviation.

Continuous variables are presented as mean ± SD. For creatinine, to convert milligrams per deciliter to millimolar quantities, multiply values by 88.4. For HDL and total cholesterol, to convert milligrams per deciliter to millimolar quantities, multiply values by 0.0259.

†To duplicate the original FRS criteria, the history of diabetes was defined as the use of insulin or other diabetes medications or fasting glucose ≥ 140 mg/dL (7.8 mmol/L).

with terms for kidney disease and individual Framingham covariates to obtain the adjusted hazard ratio for diabetes. Then we determined the absolute risk of cardiac and mortality outcomes directly attributable to diabetes. This estimated the event reduction if diabetes were eliminated as an exposure, but kidney disease remained incorporated in risk models. Identical analyses were performed for smoking.

Population Significance

Population data were obtained on white and African American individuals, aged 18 years and older, from US Census Bureau Data (2000), and prevalence data were obtained for individuals with stage 3 and 4 chronic kidney disease, aged 20 years and older, from publications of NHANES 1999 to 2000 data.[20,21] We determined the prevalence of kidney disease based on these estimates and, in conjunction with race-specific absolute risk from models using Framingham coefficients, calculated the number of yearly events attributable to chronic kidney disease.

Discrimination

Discrimination is the ability of a prediction model to separate those who had events from those who did not have events and may be quantified by the *c*-statistic.[3] We examined the change in discrimination between models with and without terms for kidney disease. For each demographic group, we computed 4 *c*-statistics. The first applied the Framingham function to the cohort. The second applied the Framingham function to the cohort and added a kidney disease term. The third used the "best Cox" model. The fourth used the "best Cox" model and added a kidney disease term. Models evaluating discrimination are censored at 5 years. *C*-statistics are compared using a nonparametric approach.[22] To conceptualize the magnitude of changes in *c*-statistics, we removed variables one at a time from the Framingham predictive instrument, calculated *c*-statistics, and compared them with full models. Data were analyzed using SAS Version 9.1 (SAS Institute Inc, Cary, NC).

RESULTS

Among 15,717 individuals without prior cardiovascular disease, 756 had chronic kidney disease, including 242 white men, 36 African American men, 401 white women, and 77 African American women. More than 80% of individuals are from ARIC. Individuals with chronic kidney disease comprised between 2.4% and 6.1% of the study population, with kidney disease more prevalent in whites than African Americans (Table 1).

Framingham Scores

There was a significant association between the 5-year Framingham probability of coronary heart disease and the presence of kidney disease (P_{trend} <.001) for all groups (Figure 1). Individuals with kidney disease had higher event rates, particularly for cardiac events in African Americans, and mortality in all subgroups (Figure 2). In multivariable analyses, increasing FRS posed a highly significant risk for all outcomes, whereas kidney disease was a statistically significant risk factor for all outcomes except cardiac events in white women (Table 2).

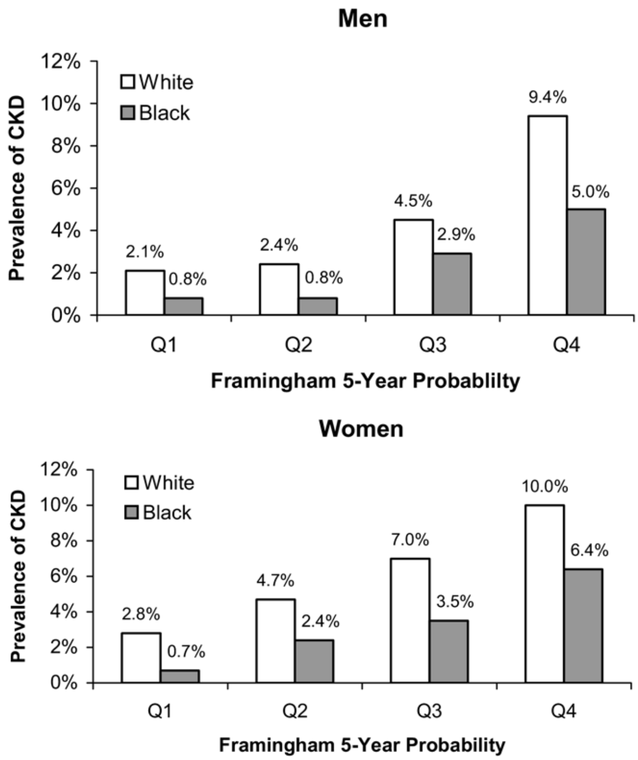

Figure 1 Frequency of chronic kidney disease by calculated Framingham probability of developing coronary heart disease within 5 years, stratified by demographic group. Probability is stratified by sex-specific quartiles. The *P* value for trend within each demographic group is less than .001. CKD = chronic kidney disease.

Absolute Risk

Rates of cardiac and mortality events attributable to reduced kidney function are presented in Figure 3. For white men and women, the increase in cardiac events caused by kidney disease was small (4.3 and 1.2 events per 1000 person-years). The increase in cardiac events in African American men and women was more prominent (16.1 and 13.6 events per 1000 person-years), as was the increase in the mortality events in all subgroups (13.7, 40.5, 5.8 and 14.2 deaths per 1000 person-years for white and African American men and white and African American women, respectively). Analyses including a term for study of origin revealed similar absolute risk (data not shown).

Comparison with Other Risk Factors

Diabetic persons and current smokers had significantly higher cardiac and mortality event rates than nondiabetic

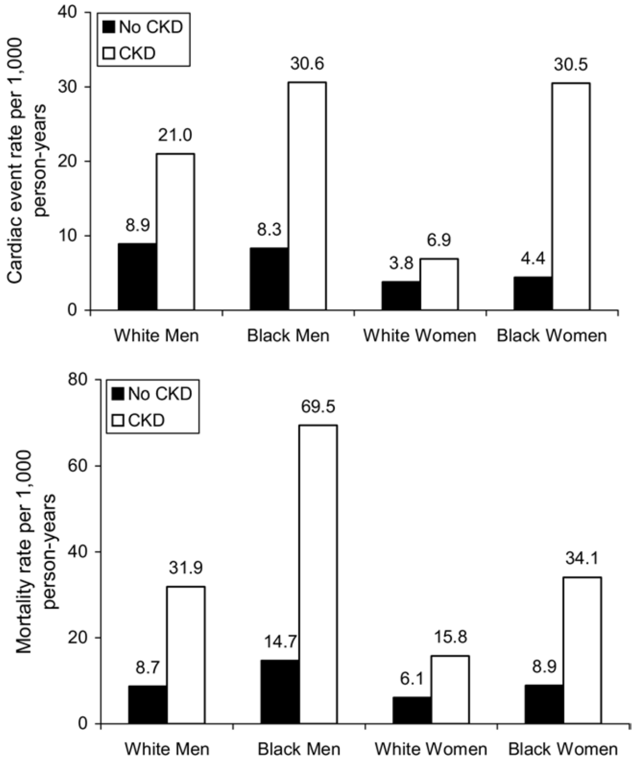

Figure 2 Rates of cardiac and mortality events per 1000 person-years stratified by race, sex, and chronic kidney disease status. CKD = chronic kidney disease.

persons and nonsmokers. Although diabetes and smoking had greater impact than kidney disease on cardiac events in whites, kidney disease in African Americans accounted for a marked increase in cardiac events compared with diabetes and smoking (Figure 4).

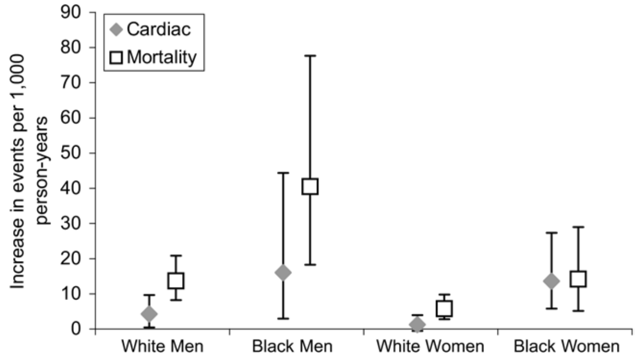

Figure 3 The absolute risk of outcomes because of the presence of chronic kidney disease after accounting for the FRS.

Population Significance

In this predominantly stage 3 chronic kidney disease cohort, 2.6 additional cardiac events per 1000 person-years in whites and 14.6 in African Americans were attributable to kidney disease after accounting for traditional risk factors comprising the FRS. For mortality outcomes, approximately 9.3 additional deaths per 1000 person-years in whites and 24.4 additional deaths in African Americans were attributable to kidney disease. When extrapolated to the US adult population, this represents more than 17,000 additional annual cardiac events among whites and approximately 12,000 additional annual cardiac events among African Americans, and more than 63,000 additional annual deaths among whites and 19,000 additional annual deaths among African Americans.

Discrimination

The addition of kidney disease to predictive models that included FRS did not improve model discrimination for

Table 2 Results of Univariate Proportional Hazards Models and Multivariable Cox Regression Models for Cardiac and Mortality Outcomes (Hazard Ratio [95% Confidence Interval])

	Men		Women	
	White	Black	White	Black
Univariate Models				
Cardiac outcomes				
FRS	2.08 (1.89-2.29)	1.77 (1.45-2.15)	2.76 (2.41-3.16)	2.50 (2.05-3.05)
CKD	2.35 (1.68-3.28)	3.78 (1.76-8.15)*	1.86 (1.21-2.86)*	7.32 (4.22-12.69)
Mortality outcomes				
FRS	1.92 (1.74-2.10)	1.74 (1.50-2.01)	2.22 (2.01-2.46)	1.94 (1.69-2.23)
CKD	3.75 (2.86-4.91)	4.81 (2.88-8.02)	2.57 (1.92-3.43)	4.12 (2.53-6.69)
Multivariable models				
Cardiac outcomes				
FRS	2.04 (1.85-2.25)	1.74 (1.43-2.12)	2.74 (2.40-3.14)	2.32 (1.90-2.84)
CKD	1.48 (1.06-2.08)†	2.93 (1.36-6.35)*	1.33 (0.86-2.04)‡	4.10 (2.32-7.23)
Mortality outcomes				
FRS	1.82 (1.65-2.00)	1.70 (1.47-1.97)	2.19 (1.98-2.42)	1.87 (1.62-2.15)
CKD	2.56 (1.94-3.38)	3.76 (2.24-6.29)	1.94 (1.45-2.60)	2.60 (1.58-4.27)

CKD = chronic kidney disease; FRS = Framingham Risk Score.

CKD is defined as eGFR < 60 mL/min/1.73 m^2. Hazard ratio for FRS presents risk associated with each 1 SD increase. Multivariable models only include terms for FRS and CKD. The SD for FRS for men was 0.8 for both white and African American men and 1.1 for both white and African American women. All *P* values were <.001, except **P* <.01, †*P* <.05, and ‡nonsignificant.

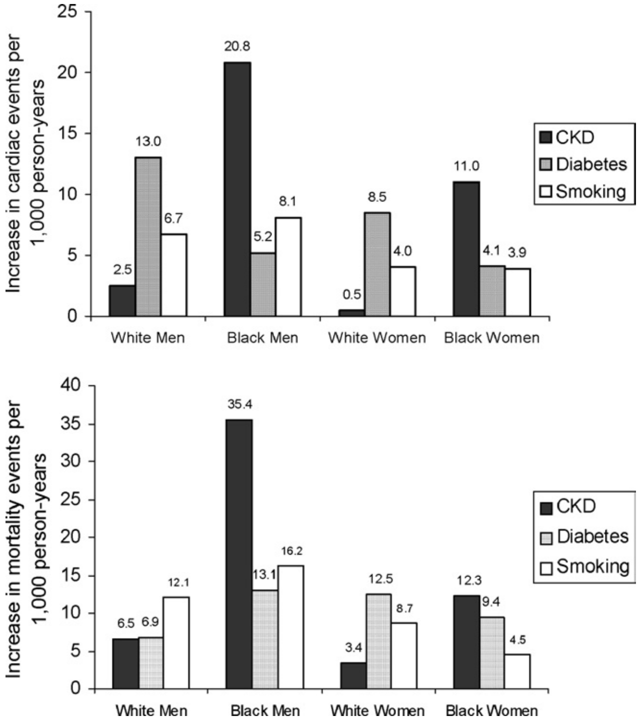

Figure 4 The increase in the rate per 1000 person-years of cardiac and mortality events because of the presence of chronic kidney disease, diabetes, and smoking derived from adjusted "best Cox" models. CKD = chronic kidney disease.

cardiac outcomes, although it improved discrimination for mortality in all subgroups except white women (Table 3). Discrimination was consistently worse in African Americans, regardless of kidney disease status. Removing individual elements of the FRS did not markedly change the *c*-statistic in "best Cox" models. Results were similar for removing other risk factors, demonstrating that discrimination based on multivariable models is relatively robust with the removal of a single term (data not shown).

DISCUSSION

In the current study, we use a biracial, community-based cohort to assess sex- and race-specific risk of coronary heart disease and mortality associated with chronic kidney disease after adjusting for FRS; determine the excess coronary heart disease and mortality risk attributable to kidney disease and compare this with the risk associated with composite elements of the FRS; and evaluate the impact of accounting for kidney disease on the discriminative ability of the Framingham risk equations. We found that both kidney disease and FRS independently predict cardiac and mortality events, and that kidney disease was particularly important in African Americans. Although the presence of chronic kidney disease had a clinically important impact on absolute risk of cardiac and mortality events, particularly in African Americans, adding a term for kidney disease to other traditional risk factors did not improve model discrimination for cardiac outcomes.

The Framingham predictive instrument helps identify individuals at risk for cardiac outcomes, and its external validity has been demonstrated in US populations.[3,16,23,24] In chronic kidney disease, nontraditional factors are prevalent and may increase cardiac risk.[5] In addition, traditional cardiac risk factors are highly prevalent in kidney disease but may be associated with a different magnitude of risk in individuals with kidney disease than in the general population.[25] Given this uncertainty, our goal was to assess the additional impact of chronic kidney disease on adverse events beyond that accounted for by traditional Framingham risk factors.

Our results confirm that chronic kidney disease is an important risk factor for cardiac and mortality outcomes.[4,6,26] After accounting for FRS, there was a 30% to 50% increased risk of coronary heart disease and a 100% increased risk of death among whites with kidney disease, and an approximately 150% to 300% increased risk of coronary disease and a 150% to 300% increased risk of death among African Americans with kidney disease. The mechanism by which kidney disease

Table 3 Discrimination as Presented by the C-Index (Standard Error) for Study Outcomes Stratified by Demographic Characteristics

	FRS	FRS + CKD	Best Cox	Best Cox + CKD
Cardiac events				
White men	0.738 (0.015)	0.740 (0.015)	0.750 (0.015)	0.751 (0.015)
African American men	0.644 (0.032)	0.642 (0.033)	0.675 (0.033)	0.670 (0.033)
White women	0.783 (0.022)	0.784 (0.022)	0.803 (0.021)	0.804 (0.021)
African American women	0.750 (0.033)	0.754 (0.034)	0.792 (0.028)	0.790 (0.029)
Mortality events				
White men	0.650 (0.019)‡	0.666 (0.019)	0.733 (0.016)*	0.737 (0.016)
African American men	0.641 (0.024)	0.648 (0.025)	0.732 (0.020)*	0.741 (0.020)
White women	0.707 (0.021)	0.712 (0.021)	0.743 (0.020)	0.745 (0.020)
African American women	0.689 (0.028)†	0.706 (0.029)	0.716 (0.029)†	0.730 (0.029)

FRS = Framingham Risk Score.

"Best Cox" is a fitted Cox regression model using the same covariates as the FRS models but with coefficients generated for best fit. "+ CKD" indicates models that include a term for CKD. Comparisons are between *c*-scores for "FRS" and "FRS + CKD" and between "Best Cox" and "Best Cox + CKD." *$P < .20$, †$P < .10$, and ‡$P < .05$.

is an independent risk factor for cardiovascular disease outcomes is likely multifactorial. Chronic kidney disease may identify individuals with a longer duration or greater severity of cardiovascular disease risk factors such as hypertension and diabetes. In addition, factors related to kidney disease, including anemia, left ventricular hypertrophy, and inflammation, may increase cardiac risk.[27-30]

Approximately 8 million individuals in the United States have chronic kidney disease defined by an estimated glomerular filtration rate less than 60 mL/min/1.73 m^2.[31] On the basis of our results, adverse outcomes of chronic kidney disease represent a sizable public health issue, particularly in African Americans, in whom 12,000 cardiac events and 19,000 deaths per year are associated with kidney disease after accounting for Framingham risk factors. Chronic kidney disease was comparable to both diabetes and smoking when evaluating cardiac events in African Americans and mortality events in African American men and women and white men.

Adding chronic kidney disease to analyses that already accounted for the FRS only minimally improved discrimination, indicating that there was little change in our ability to determine who will and will not have an event. This finding was expected because our analyses also showed only minimal change in the *c*-statistic after removing individual risk factors, including diabetes, from prediction models. The relatively low prevalence of kidney disease in this cohort likely influences the overall lack of significant impact on discrimination.

Although the Framingham equations examined only cardiac outcomes, it is also important to investigate mortality. Mortality is not subject to misclassification bias, and, because individuals with chronic kidney disease have numerous competing outcomes, one method to account for this is to examine mortality.[32-35] Finally, mortality outcomes will capture deaths that, although not considered "hard coronary heart disease" events, are influenced by the role of kidney disease on cardiac risk factors, including heart failure and systemic vascular disease.

A major finding of the current study was the marked increased risk of adverse outcomes associated with kidney disease in African Americans. This adds to earlier findings by specifying absolute risk beyond traditional risk factors and evaluating our ability to determine the risk of cardiac and mortality outcomes using prediction equations.[6] The profound risk associated with kidney disease in African Americans may be attributable to differences in socioeconomic status or may represent geographic variability, because the majority of African Americans in this study were from the Mississippi cohort of ARIC. Other possibilities include greater severity, longer duration, or worse control of traditional risk factors that cannot be accounted for in regression models. Suggestive evidence for this comes from analysis of NHANES data in which African American race was an independent risk factor for failure to achieve blood pressure goals in individuals with reduced kidney function, perhaps secondary to decreased awareness of chronic kidney disease.[36,37]

Our study has several limitations. Because most participants with kidney disease had an estimated glomerular filtration rate greater than 40 mL/min/1.73 m^2, we cannot comment on the utility of Framingham equations in more advanced disease. We do not have data on microalbuminuria, a component of kidney disease that independently predicts cardiovascular disease.[15,38] Framingham risk equations were derived to calculate cardiac risk, not mortality. However, given the marked degree of competing events between coronary heart disease outcomes and mortality, we elected to analyze predictive ability on both cardiac and mortality outcomes as other studies have done.[35] Finally, findings in this article are based on the supposition that much of the risk unaccounted for by the Framingham equations is attributable to chronic kidney disease. Although we acknowledge that some risk may not be directly caused by kidney disease, adding kidney disease to statistical models captures important information.

Our study has several strengths. We have a large and diverse population with thorough event ascertainment. Although there may be inherent differences between CHS and ARIC, pooling these studies provides a more generalizable age range and power to stratify analyses on race. These populations have been pooled in several other studies, and prior work by our group demonstrated no statistically significant difference by study of origin on incident cardiac and mortality outcomes after risk factor adjustment.[6,39,40]

CONCLUSION

Chronic kidney disease is an important risk factor in individual patients, identifying those at increased risk of cardiac and mortality outcomes. In terms of absolute risk, the magnitude is similar to that seen for diabetes mellitus. The risk associated with chronic kidney disease is particularly notable in African Americans.

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