Cardiovascular Risk Among Adults With Chronic Kidney Disease, With or Without Prior Myocardial Infarction

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OBJECTIVES
This study sought to determine whether chronic kidney disease (CKD) should be considered a coronary heart disease (CHD) risk equivalent for cholesterol treatment.

BACKGROUND
It is unclear whether patients with CKD have a risk of CHD events or cardiovascular disease (CVD) mortality equivalent to patients with a prior myocardial infarction (MI).

METHODS
Using data from the ARIC (Atherosclerosis Risk in Communities) study, we categorized nondiabetic participants based on their average level of kidney function (estimated glomerular filtration rate ≥60 or 30 to 59 ml/min/1.73 m², which defines stage 3 CKD) and on prior MI (yes or no). Rates and relative risks (RR) of CHD (MI or fatal CHD) events (n = 653) and CVD mortality (n = 209) that occurred over 10 years were compared across these populations.

RESULTS
Among 12,243 middle-age participants, 271 had stage 3 CKD. After adjustment for age, gender, race, and center, CHD incidence and CVD mortality rates per 1,000 person-years by presence of CKD and MI were 4.1 and 1.0 in the presence of neither condition, 8.0 and 3.4 in CKD only, 18.8 and 7.0 in MI only, and 30.8 and 18.0 in CKD and MI. After further adjustment for CVD risk factors, RR of CHD and CVD mortality were statistically significantly lower in subjects with CKD and no prior MI (RR = 0.44 [95% confidence interval (CI) 0.28 to 0.72] for CHD and RR = 0.46 [95% CI 0.24 to 0.90] for CVD mortality) than for subjects with no CKD and a prior MI.

CONCLUSIONS
Stage 3 CKD confers CHD risk that is lower and not equivalent to a prior MI in this middle-aged, general, nondiabetic population.

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It is well established that chronic kidney disease (CKD) increases the risks of cardiovascular morbidity and mortality. These increased risks may be explained by: 1) excess comorbidities or cardiovascular disease (CVD) risk factors in patients with CKD; 2) therapeutic nihilism; 3) lack of benefit or excess toxicities from conventional CKD therapies; and 4) unique pathophysiology in the CKD population.

As a result, the National Kidney Foundation Task Force on Cardiovascular Disease in Chronic Renal Disease (2) and other groups (3,4) have placed patients with CKD in the highest-risk group and recommended that the thresholds for risk factor intervention (e.g., drug therapy to lower low-density lipoprotein [LDL] cholesterol) in CKD patients be lower than in the general population. The National Cholesterol Education Program Adult Treatment Panel-III (NCEP ATP-III) guidelines (5) recommend that diabetes be considered a "risk equivalent" to coronary heart disease (CHD) and that patients with diabetes be treated with lipid-lowering therapies in a similar fashion as their counterparts with a prior myocardial infarction (MI). Chronic kidney disease might also be a CHD risk equivalent, but no study has directly assessed whether the risk of CHD, defined as MI or fatal CHD, and CVD mortality in patients with CKD is as high as in those with clinical CHD. Determining the equivalency in risk for CKD and CHD of future CVD events will assist in the future modification of treatment guidelines.

Therefore, we investigated in a nonreferral, community-derived population whether the rates of CHD and CVD mortality are equivalent in nondiabetic patients with: 1) stage 3 CKD (estimated glomerular filtration rate [eGFR] between 30 and 59 ml/min/1.73 m²) and no history of prior MI; and 2) no CKD (eGFR ≥60 ml/min/1.73 m²) and a history of prior MI.

METHODS

Study population. The ARIC (Atherosclerosis Risk in Communities) study (6) is a prospective investigation of the etiology and natural history of atherosclerosis. The study cohort comprised 15,792 white and black men and women ages 45 to 64 years at baseline in 1987 to 1989, recruited from four U.S. communities. The cohort underwent re-examination visits at roughly 3-year intervals.
Measurement of baseline risk factors. After informed consent, the ARIC participants underwent a standardized medical history and examination that included interviews, a fasting venipuncture, and carotid intima-media thickness (IMT). Participants were classified as never, former, or current smokers. Physical activity in sports was assessed using the Baecke physical activity questionnaire, with scores ranging from 1 (low) to 5 (high), and participants were categorized as low (<2) moderate (2 to 4), or high (≥4) (7). Participants were asked to bring all current medications to their ARIC study visit. Medication use was recorded, including cholesterol-lowering medications, beta-blockers, and angiotensin-converting enzyme inhibitors. Body mass index was calculated as weight in kilograms divided by the square of height in meters.

All participants had a standard 12-lead electrocardiogram at baseline. A prior MI was defined as a self-reported history of physician-diagnosed MI or a history of MI identified on the baseline electrocardiogram, which was characterized by the presence of a major Q-wave or a minor Q-wave with ischemic ST-T changes. Prevalent hypertension was defined as seated diastolic blood pressure ≥90 mm Hg, systolic blood pressure ≥140 mm Hg, or use of antihypertensive medications within the past 2 weeks. Prevalent diabetes mellitus was defined as a fasting serum glucose level ≥7.0 mmol/l (126 mg/dl), nonfasting glucose level ≥11.1 mmol/l (200 mg/l), participant report of a physician diagnosis of diabetes, or current use of any diabetes medication.

Fasting blood samples were drawn from an antecubital vein for measurement of total cholesterol, triglycerides, high-density lipoprotein cholesterol, and fibrinogen (8). The LDL cholesterol was calculated using the Friedewald equation. B-mode carotid ultrasound (Biosound 2000 II SA; Biosound Inc., Indianapolis, Indiana) evaluations were completed on bilateral segments of the extracranial carotid arteries using a standardized protocol (9,10). Mean far wall IMT was used for this analysis.

Ascertainment of the level of kidney function. To ensure that CKD was chronic and to decrease the effect of day-to-day variation in serum creatinine, we included only participants who had both visit 1 and visit 2 serum creatinine measured and calculated the average GFR estimate of the 2 visits. The coefficient of variation of serum creatinine on repeated measurement in a reliability substudy was 4.3%, and the reliability coefficient was 0.68 (11). Serum creatinine was measured using the modified kinetic Jaffe method. The level of kidney function was ascertained by eGFR calculated using the formula developed and validated in the MDRD (Modification of Diet in Renal Disease) study (12,13):

\[
GFR = 186.3 \times (\text{serum creatinine}^{-1.154}) \times (\text{age}^{-0.203}) \\
\times 1.212 \times (\text{if female}) \times 0.742 \times (\text{if female}).
\]

To use this formula, serum creatinine was calibrated by subtraction of 0.24 (14). We assigned participants with a physiologically implausible high eGFR (n = 3) to a maximum of 200 ml/min/1.73 m².

Ascertainment of incident events. The ARIC study ascertained CHD events and mortality from CVD after baseline by identifying all hospitalizations and deaths. For patients hospitalized with potential MI, trained abstractors recorded the presenting signs and symptoms, including chest pain, cardiac enzymes, and related clinical information. Out-of-hospital fatal CHD events were investigated by an interview with one or more next of kin and a questionnaire completed by the patient’s physician. The CHD events were validated by a committee of physicians using standardized criteria (15).

A CHD event was defined as a definite or probable hospitalized MI or definite fatal CHD. The CVD mortality was based only on the death certificate and included any underlying cause of death using International Classification of Diseases-9th Revision codes 390 to 459.

Statistical analysis. Of the 15,792 ARIC study participants, we included 13,980 participants who had serum creatinine measured at both visit 1 and visit 2 and who did not have CHD events or CVD death during this interval. Of these, we excluded 192 participants with missing information or prior MI, 85 of race other than black or white, 4 with stage 4 CKD (eGFR of 15 to 29 ml/min/1.73 m²), and 8 with kidney failure (eGFR <15 ml/min/1.73 m²). Because diabetes is already considered a CHD risk equivalent, we excluded 1,448 participants with prevalent diabetes, leaving a total of 12,243 participants for analysis.

We followed up all participants through the year 2001. For the CHD event analysis, follow-up time was calculated from the visit 2 date to the time of diagnosis of a first CHD event for those with no history of a prior MI and to the time of diagnosis of a recurrent CHD event for those with a history of prior MI. For participants who did not have a CHD event, follow-up ended on the date of last known contact or December 31, 2001. For the CVD mortality analysis, follow-up time was calculated from the visit 2 date to the date of death, date of last known contact, or December 31, 2001.

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CKD as a CHD Risk Equivalent
We categorized participants based on whether they had stage 3 CKD (hereafter referred to as CKD) or not and a baseline history of a prior MI or not. The categories were as follows: 1) no CKD and no prior MI as group 1; 2) no CKD and prior MI as group 2; 3) CKD and no prior MI as group 3; and 4) CKD and prior MI as group 4. These categories were coded with group 2 serving as the reference group for all analyses. Next, we compared participant characteristics across the four categories with differences assessed using analysis of variance, adjusted for age, gender, race, and ARIC study field center. Adjusted for age, sex, race, and ARIC field center.

Among the 12,243 participants, the mean visit 1 eGFR was 92.5 (SD = 19.5) ml/min/1.73 m² and visit 2 eGFR was 86.6 (SD = 18.1) ml/min/1.73 m². The average eGFR of the 2 visits was 89.6 (SD = 17.2) ml/min/1.73 m². The mean age was 54 years. Among 271 participants with CKD, 220 (81.2%) had eGFR between 50 and 60 ml/min/1.73 m², 41 (15.1%) had eGFR between 40 and 49 ml/min/1.73 m², and 10 (3.7%) had eGFR between 30 and 39 ml/min/1.73 m². The mean eGFR was 54.1 (SD = 5.8) ml/min/1.73 m². As Table 1 shows, at baseline patients in group 1 had the most favorable CVD risk factor profile, and those in group 4 had the worst CVD risk factor profile. Compared with patients in group 2, patients in group 3 were more likely to be female, white, and older, and had a lower prevalence of current smoking as well as lower mean values of LDL cholesterol and carotid IMT.

During a mean follow-up of 10 years (123,213 person-years), we identified 653 CHD events and 209 deaths from CVD. The Kaplan-Meier analysis showed a greater probability of CHD (p < 0.0001) and CVD mortality (p = 0.001) for patients in group 2 than for those in group 3 (Figs. 1 and 2).

As Table 2 shows, after adjustment for age, gender, race, and ARIC study field center, the CHD event rate for patients in group 1 was 4.1 per 1,000 person-years, which was about 50% lower than that of those in group 3 (8.0 per 1,000 person-years). The CHD event rate was 18.8 per 1,000 person-years for those in group 2 and 30.8 for those in group 4. Compared with patients in group 2, those in group 1 had a lower multivariable adjusted RR of CHD (RR = 0.29, 95% CI 0.23 to 0.37). The analogous multivariable adjusted RR for patients in group 3, compared with

### Table 1. Baseline Characteristics of Men and Women Across Chronic Kidney Disease (CKD) Categories Based on Estimated Glomerular Filtration Rate (eGFR) and Categories of Prior History of Myocardial Infarction (MI): the ARIC Study

<table>
<thead>
<tr>
<th>Baseline</th>
<th>No CKD, No Prior MI (Group 1)</th>
<th>No CKD, Prior MI (Group 2)</th>
<th>Stage 3 CKD, No Prior MI (Group 3)</th>
<th>Stage 3 CKD, Prior MI (Group 4)</th>
<th>p Value for Contrast Comparing Group 2 vs. Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>11,606</td>
<td>366</td>
<td>250</td>
<td>21</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male, %</td>
<td>43.5</td>
<td>77.9</td>
<td>37.2</td>
<td>71.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age, yrs</td>
<td>54</td>
<td>57</td>
<td>58</td>
<td>60</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>White participants, %</td>
<td>77.7</td>
<td>82.2</td>
<td>89.6</td>
<td>81.0</td>
<td>0.01</td>
</tr>
<tr>
<td>Median eGFR, ml/min/1.73 m²</td>
<td>88</td>
<td>86</td>
<td>56</td>
<td>55</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Prevalence,* (%):</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>29.1</td>
<td>43.2</td>
<td>50.2</td>
<td>68.9</td>
<td>0.054</td>
</tr>
<tr>
<td>Current smoking</td>
<td>24.7</td>
<td>28.1</td>
<td>17.8</td>
<td>20.7</td>
<td>0.004</td>
</tr>
<tr>
<td>Mean levels*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical activity score</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
<td>2.1</td>
<td>0.74</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.1</td>
<td>27.6</td>
<td>28.2</td>
<td>29.7</td>
<td>0.13</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>120</td>
<td>118</td>
<td>123</td>
<td>121</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total cholesterol, mg/dl</td>
<td>214</td>
<td>223</td>
<td>217</td>
<td>213</td>
<td>0.08</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dl</td>
<td>137</td>
<td>146</td>
<td>140</td>
<td>137</td>
<td>0.04</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dl</td>
<td>52.9</td>
<td>48.6</td>
<td>49.3</td>
<td>43.3</td>
<td>0.57</td>
</tr>
<tr>
<td>Fibrinogen, mg/dl</td>
<td>297</td>
<td>316</td>
<td>313</td>
<td>299</td>
<td>0.58</td>
</tr>
<tr>
<td>Carotid intima-media thickness, mm</td>
<td>0.71</td>
<td>0.78</td>
<td>0.73</td>
<td>0.82</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Medication use, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of beta-blockers at baseline</td>
<td>8.9</td>
<td>39.8</td>
<td>23.7</td>
<td>50.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Use of ACE inhibitors at baseline</td>
<td>2.8</td>
<td>5.6</td>
<td>9.7</td>
<td>30.0</td>
<td>0.07</td>
</tr>
<tr>
<td>Use of cholesterol medication</td>
<td>2.3</td>
<td>7.7</td>
<td>3.9</td>
<td>19.1</td>
<td>0.06</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, race, and ARIC field center.

ACE = angiotensin-converting enzyme; HDL = high-density lipoprotein; LDL = low-density lipoprotein.
patients in group 2, was 0.44 (95% CI 0.28 to 0.72). Although not statistically significant, patients in group 4 had the highest risk of CHD, with a multivariable adjusted RR of 1.64 (95% CI 0.79 to 3.42) compared with the reference group.

The lowest CVD mortality rate was found in those in group 1 (1.0 per 1,000 person-years), and the highest rate was found in those in group 4 (18.0 per 1,000 person-years). Patients in group 3 had a CVD mortality rate about half that of those in group 2 (3.4 vs. 7.0 per 1,000 person years). Compared with patients in group 2, the multivariable-adjusted RR of CVD mortality in patients in group 1 was 0.18 (95% CI 0.12 to 0.26) and was 0.46 (95% CI 0.24 to 0.90) in patients in group 3. Patients in group 4 again had the highest RR of CVD mortality, with an almost two-fold greater risk than the reference group (RR = 1.87, 95% CI 0.76 to 4.60).

When the multivariable analyses were repeated using time-dependent covariates for use of cholesterol and anti-hypertensive medications, the adjusted RRs of CHD and CVD mortality were comparable with the results using baseline (i.e., fixed) covariates (data not shown).

**DISCUSSION**

To determine whether CKD confers the same excess risk as clinical CHD, we characterized the rates of CHD events and CVD mortality in nondiabetic patients with stage 3 CKD and in patients without CKD, with or without prior MI. Among patients with a prior MI in this study, those with stage 3 CKD had increased rates of CHD events and CVD mortality compared with those with no CKD. Our findings support previous reports showing that CKD increases the risk of CHD events and mortality in high-risk subjects with known vascular disease or diabetes (16), baseline hypertension (17), or baseline CHD (18–20). The major new finding of this study is that in a community-derived sample, nondiabetic patients with stage 3 CKD and
no prior MI had a CHD event rate 60% lower and a CVD mortality rate nearly 50% lower than did those with no CKD and a prior MI.

Whether CKD is a “CHD risk equivalent,” using NCEP ATP-III terminology (5), is not well established. Data have consistently shown that CKD patients have a higher risk of and poorer survival from CVD events than does the general population (21). In response to these findings, numerous working groups have recommended that CKD should be classified as a CHD risk equivalent (2–4), justifying the uniform consideration of pharmacologic cholesterol-lowering therapy (e.g., with statins) at lower LDL cholesterol levels. On the other hand, recent NCEP ATP-III (5) and European (22) guidelines have not recognized CKD as a CHD risk equivalent. In the current study, middle-age, nondiabetic patients with stage 3 CKD and no prior MI did not have a rate of CHD events as high as those with no CKD and a prior MI. Nondiabetic patients with stage 3 CKD and no prior MI had a 10-year rate of CHD events of 8.0%, whereas those with no CKD and a prior MI had 18.8% risk of having a CHD (i.e., 18.8 of 100 subjects will develop an incident CHD event within 10 years). These data suggest that stage 3 CKD is not a CHD risk equivalent. Because the 10-year CHD event rate in middle-age, nondiabetic patients with stage 3 CKD was 10% or less (5) (Table 2), aggressive statin therapy of LDL cholesterol in these patients is likely to be less cost effective than in those with a history of prior MI. Hence, this study suggests that it may be more appropriate or cost-effective to tailor lipid management for patients with stage 3 CKD based on each individual patient’s global CHD risk assessment (5).

Decreased kidney function is increasingly recognized as a risk factor for CVD mortality and all-cause mortality in the general population (23–26). For example, one study, which pooled data from four large community-based studies, showed that patients with stage 3 to 4 CKD had RRs of 1.36 (95% CI 1.21 to 1.53) for all-cause mortality and 1.19 (95% CI 1.07 to 1.32) for a composite outcome (MI, fatal CHD, stroke, and all-cause mortality) compared with those with eGFR ≥60 ml/min/1.73 m² (26). To our knowledge, our study is the first to report that the rate of CVD mortality in nondiabetic patients with stage 3 CKD and no prior MI is lower than in patients with no CKD and a prior MI.

Also considered for statin therapy might be those with stage 4 CKD. Such patients were rare in our population-based sample (n = 4), but a recent large study by Go et al. (27) reported age-standardized CVD event rates of 37, 113, 218, and 366 per 1,000 person-years for eGFR levels of 45 to 59, 30 to 44, 15 to 29, and <15 ml/min/1.73 m², respectively. In the same study, the age-standardized death rates were 10.8, 48, 114, and 141 per 1,000 person-years for eGFR levels of 45 to 59, 30 to 44, 15 to 29, and <15 ml/min/1.73 m², respectively. Although approximately 20% of patients with CKD in that study already had CHD (27), the high rates of CVD and mortality at an eGFR <30 ml/min/1.73 m² suggest stage 4 CKD (eGFR of 15 to 29 ml/min/1.73 m²), and kidney failure might warrant CHD risk equivalent status.

Many previous studies that evaluated the association of the level of kidney function with CVD morbidity and mortality have focused on selected high-risk groups (19,28–30). In this study, we included middle-age, nondiabetic men and women from 4 U.S. community-based samples and aged eGFR from 2 ARIC visits to define stage 3 CKD. The distribution of eGFR observed in this study should be representative of that of patients with stage 3 CKD, and our results, therefore, are generalizable to the population 45 to 64 years of age with stage 3 CKD. We nevertheless acknowledge a series of limitations. First, there are potential sources of misclassification. The eGFR from serum creatinine using the MDRD formula may not be as accurate as a direct measurement from iothalamate or creatinine clearance using a 24-h urine collection. These measurements, however, are not feasible in a large epidemiologic study and are generally not performed in clinical practice. Our methods conform to current recommendations for estimation of kidney function using creatinine-based equations. If better estimation of kidney function is possible, the consequent

### Table 2. Relative Risks of Coronary Heart Disease and Mortality From Cardiovascular Disease in Persons With Chronic Kidney Disease (CKD) and Without CKD, With or Without History of Myocardial Infarction (MI): the ARIC Study, 1987–2001

<table>
<thead>
<tr>
<th></th>
<th>No CKD, No Prior MI (Group 1)</th>
<th>No CKD, Prior MI (Group 2)</th>
<th>Stage 3 CKD, No Prior MI (Group 3)</th>
<th>Stage 3 CKD, Prior MI (Group 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>11,606</td>
<td>366</td>
<td>250</td>
<td>21</td>
</tr>
<tr>
<td>Fatal coronary heart disease or MI (n = 653)</td>
<td>529</td>
<td>94</td>
<td>22</td>
<td>8</td>
</tr>
<tr>
<td>Event rate per 1,000 person-years*</td>
<td>4.1</td>
<td>18.8</td>
<td>8.0</td>
<td>30.8</td>
</tr>
<tr>
<td>RR (95% CI)*</td>
<td>0.21 (0.17–0.27)</td>
<td>1.0 ref.</td>
<td>0.39 (0.24–0.62)</td>
<td>1.68 (0.82–3.46)</td>
</tr>
<tr>
<td>Multivariable RR (95% CI)†</td>
<td>0.29 (0.23–0.37)</td>
<td>1.0 ref.</td>
<td>0.44 (0.28–0.72)</td>
<td>1.64 (0.79–3.42)</td>
</tr>
<tr>
<td>Cardiovascular disease mortality (n = 209)</td>
<td>146</td>
<td>45</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>Death rate per 1,000 person-years*</td>
<td>1.0</td>
<td>7.0</td>
<td>3.4</td>
<td>18.0</td>
</tr>
<tr>
<td>RR (95% CI)*</td>
<td>0.14 (0.10–0.20)</td>
<td>1.0 ref.</td>
<td>0.46 (0.24–0.87)</td>
<td>2.42 (1.03–5.69)</td>
</tr>
<tr>
<td>Multivariable RR (95% CI)†</td>
<td>0.18 (0.12–0.26)</td>
<td>1.0 ref.</td>
<td>0.46 (0.24–0.90)</td>
<td>1.87 (0.76–4.60)</td>
</tr>
</tbody>
</table>

*Adjusted for age, gender, race, and ARIC field center. †Adjusted for age, gender, race, ARIC field center, cigarette smoking, systolic blood pressure, physical activity, low-density lipoprotein and high-density lipoprotein cholesterol, fibrinogen, carotid intima-media thickness, cholesterol medication and antihypertensive medication (including beta-blockers and angiotensin-converting enzyme inhibitors) use. The p values of all covariates in the adjusted model were <0.05, except for center and race.

CI = confidence interval; RR = relative risk.
CHD and CVD risk associated with CKD may be higher, as seen in recent articles reporting using cystatin C as an estimate of decreased kidney function (31,32). Having a prior MI at baseline was not validated, but relied on a self-reported history and electrocardiogram, creating another potential source of misclassification. Nevertheless, the validity of self-report assessment was confirmed by medical records in 75.5% of men and 60.6% of women in the Cardiovascular Health Study (33). Data on markers of kidney damage, such as microalbuminuria, were not available in the full ARIC study cohort. As such, patients with eGFR ≥60 ml/min/1.73 m² and microalbuminuria (i.e., stage 1 and 2 CKD) were included into the “no CKD” grouping. This misclassification is likely to have biased the observed association away from the null. Second, the definition of CKD included a broad range of GFR. Our sample size did not allow us to separately estimate the rate of CHD events in relation to stage 4 CKD and no prior MI. Third, other nontraditional CVD risk factors such as homocysteine and C-reactive protein were not measured in the ARIC study, and these risk factors have recently been identified to play a role in the development of CVD mortality in patients with CKD (34,35). Fourth, the ARIC study reported serum creatinine values to ARIC study participants and their physicians. It is possible that awareness of serum creatinine might have changed the treatment plan for some participants with CKD. Lastly, the ARIC study did not have information at baseline on time since prior MI or onset of CKD, or on severity of prior MI. Differences in these among various groups compared could have impacted the event rate and RR estimates.

Although CKD was associated with increased rates of CHD and CVD mortality, nondiabetic participants in the ARIC study with stage 3 CKD did not have the same rate of CHD and CVD mortality as their counterparts with a history of MI in this population of middle-age adults. As such, CKD does not seem to carry the same burden of CHD risk and CVD mortality as having a prior MI.

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