# Comparison of Risk Prediction Using the CKD-EPI Equation and the MDRD Study Equation for Estimated Glomerular Filtration Rate

Kunihiro Matsushita, MD, PhD
Bakhtawar K. Mahmoodi, MD, PhD
Mark Woodward, PhD
Jonathan R. Emberson, PhD
Tazeen H. Jafar, MD, MPH
Sun Ha Jee, PhD, MHS
Kevan R. Polkinghorne, FRACP, PhD
Anoop Shankar, MD, MPH, PhD
David H. Smith, RPh, PhD
Marcello Tonelli, MD, SM
David G. Warnock, MD
Chi-Pang Wen, MD, DrPH
Josef Coresh, MD, PhD
Ron T. Gansevoort, MD, PhD
Brenda R. Hemmelgarn, MD, PhD
Andrew S. Levey, MD
for the Chronic Kidney Disease Prognosis Consortium

**Context** The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation more accurately estimates glomerular filtration rate (GFR) than the Modification of Diet in Renal Disease (MDRD) Study equation using the same variables, especially at higher GFR, but definitive evidence of its risk implications in diverse settings is lacking.

**Objective** To evaluate risk implications of estimated GFR using the CKD-EPI equation compared with the MDRD Study equation in populations with a broad range of demographic and clinical characteristics.

**Design, Setting, and Participants** A meta-analysis of data from 1.1 million adults (aged ≥18 years) from 25 general population cohorts, 7 high-risk cohorts (of vascular disease), and 13 CKD cohorts. Data transfer and analyses were conducted between March 2011 and March 2012.

**Main Outcome Measures** All-cause mortality (84 482 deaths from 40 cohorts), cardiovascular mortality (22 176 events from 28 cohorts), and end-stage renal disease (ESRD) (7644 events from 21 cohorts) during 9.4 million person-years of follow-up; the median of mean follow-up time across cohorts was 7.4 years (interquartile range, 4.2-10.5 years).

**Results** Estimated GFR was classified into 6 categories (≥90, 60-89, 45-59, 30-44, 15-29, and <15 mL/min/1.73 m$^2$) by both equations. Compared with the MDRD Study equation, 24.4% and 0.6% of participants from general population cohorts were reclassified to a higher and lower estimated GFR category, respectively, by the CKD-EPI equation, and the prevalence of CKD stages 3 to 5 (estimated GFR <60 mL/min/1.73 m$^2$) was reduced from 8.7% to 6.3%. In estimated GFR of 45 to 59 mL/min/1.73 m$^2$ by the MDRD Study equation, 34.7% of participants were reclassified to estimated GFR of 60 to 89 mL/min/1.73 m$^2$ by the CKD-EPI equation and had lower incidence rates (per 1000 person-years) for the outcomes of interest (9.9 vs 34.5 for all-cause mortality, 2.7 vs 13.0 for cardiovascular mortality, and 0.5 vs 0.8 for ESRD) compared with those not reclassified. The corresponding adjusted hazard ratios were 0.80 (95% CI, 0.74-0.86) for all-cause mortality, 0.73 (95% CI, 0.65-0.82) for cardiovascular mortality, and 0.49 (95% CI, 0.27-0.88) for ESRD. Similar findings were observed in other estimated GFR categories by the MDRD Study equation. Net reclassification improvement based on estimated GFR categories was significantly positive for all outcomes (range, 0.06-0.13; all $P<.001$). Net reclassification improvement was similarly positive in most subgroups defined by age (<65 years and ≥65 years), sex, race/ethnicity (white, Asian, and black), and presence or absence of diabetes and hypertension. The results in the high-risk and CKD cohorts were largely consistent with the general population cohorts.

**Conclusion** The CKD-EPI equation classified fewer individuals as having CKD and more accurately categorized the risk for mortality and ESRD than did the MDRD Study equation across a broad range of populations.

*JAMA. 2012;307(18):1941-1951* www.jama.com

GLOMERULAR FILTRATION RATE (GFR) is used in the diagnosis of chronic kidney disease (CKD)[1,2] and is an independent predictor of all-cause and cardiovascular mortality and kidney failure in a wide range of populations.[3-6] Clinical guidelines recommend reporting estimated GFR when serum creatinine level is measured[1,2]; 84% of US laboratories report estimated GFR.[7] Although the Modification of Diet in Renal Disease (MDRD) Study equation is recommended for estimating GFR,[1,2,8,9] the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) has recently proposed an alternative equation, which applies different coefficients to the same 4 variables used in the MDRD Study equation (age, sex, race, and serum creatinine level).[10] The new CKD-EPI equation estimates measured GFR more accurately than the MDRD Study equation in most,[10-18] but

**For editorial comment see p 1976.**

**Author Affiliations and a list of the investigators and collaborators for the Chronic Kidney Disease Prognosis Consortium** appear at the end of this article.
**Corresponding Author:** Josef Coresh, MD, PhD, Chronic Kidney Disease Prognosis Consortium Data Coordinating Center, 615 N Wolfe St, Baltimore, MD 21205 (ckdpc@jhmi.edu).

©2012 American Medical Association. All rights reserved.



Downloaded From: http://jamanetwork.com/ on 05/21/2013

not all[19,20] studies. However; only 4% of US laboratories reporting estimated GFR used the CKD-EPI equation in June 2011; 92% of laboratories still used the MDRD Study equation and 4% used other equations.[7]

A few studies suggest that the better estimation of GFR by the CKD-EPI equation is reflected in better clinical risk prediction than by the MDRD Study equation.[21-24] However, these studies include predominantly white populations with higher levels of kidney function. In addition, the implications of use of the CKD-EPI equation in the elderly have yet to be elucidated.[25,26] The objective of this collaborative study was to comprehensively evaluate whether estimated GFR computed by the CKD-EPI equation predicts risk for adverse outcomes more accurately than the MDRD Study equation in a broad range of populations. Such information will help clinicians, laboratories, and policy makers decide whether estimated GFR reporting should be based on the MDRD Study equation or the CKD-EPI equation.

## METHODS

Details of the Chronic Kidney Disease Prognosis Consortium (CKD-PC) were described previously.[3-6] To be included in the consortium, a study had to have at least 1000 participants (not applied to studies predominantly enrolling patients with CKD[6]), information at baseline on estimated GFR and urine albumin levels, and a minimum of 50 events for any of the outcomes of interest. As recommended,[1,2] we preferentially selected ratio of urine albumin to creatinine as the measure of albuminuria. However, we also accepted urine albumin excretion and ratio of urine protein to creatinine as well as a qualitative measurement using dipstick.[1] This analysis consists of data from 45 cohorts (25 general population cohorts, 7 high-risk cohorts with participants selected for cardiovascular or kidney disease risk factors, and 13 CKD cohorts). Data transfer (from collaborating cohorts to the CKD-PC Data Coordinating Center) and analyses for the present study were conducted between March 2011 and March 2012. This study is based on secondary data analysis of a preexisting, deidentified, and unlinked data set, and was approved by the institutional review board at the Johns Hopkins Bloomberg School of Public Health. Information about ethical review of individual studies is available in the publications of the constituent cohorts.[21,24,27-69]

We calculated estimated GFR from serum creatinine standardized to isotope dilution mass spectrometry using the MDRD Study equation[9] and the CKD-EPI equation.[10] For studies in which creatinine measurement was not standardized to isotope dilution mass spectrometry, we reduced the creatinine levels by 5%, which is the calibration factor used to adjust nonstandardized MDRD samples to this type of spectrometry.[70]

Diabetes mellitus was defined as fasting glucose level of 7.0 mmol/L or greater, nonfasting glucose level of 11.1 mmol/L or greater, hemoglobin $A_{1c}$ of 6.5% or greater, use of glucose-lowering drugs, or self-reported diabetes (to convert glucose to mg/dL, divide by 0.0555; hemoglobin $A_{1c}$ to a proportion, multiply by 0.01). Hypertension was defined as systolic blood pressure of 140 mm Hg or greater, diastolic blood pressure of 90 mm Hg or greater, or use of any antihypertensive medication. Hypercholesterolemia was defined as total cholesterol level of 6.0 mmol/L or greater ($\geq$5.0 mmol/L in people with prior cardiovascular disease) or use of lipid-lowering drugs (to convert cholesterol to mg/dL, divide by 0.0259). Cardiovascular disease history was defined as a history of myocardial infarction, coronary revascularization, heart failure, or stroke. Smoking was dichotomized as current vs former smokers or nonsmokers. Race/ethnicity was categorized as white, Asian, black, Hispanic, and other.

The outcomes of interest were all-cause mortality, cardiovascular mortality, and end-stage renal disease (ESRD). Cardiovascular mortality was defined as death due to myocardial infarction, heart failure, sudden cardiac death, or stroke. End-stage renal disease was defined as the start of renal replacement therapy or death due to kidney disease other than acute kidney injury.

Statistics were first obtained within each study and then a meta-analysis was performed across studies using a random-effects model. Analyses were restricted to individuals aged 18 years or older. Any individual with missing values for estimated GFR or albuminuria at baseline was excluded. Missing values for all other covariates were estimated by mean imputation. The analysis overview and analytic notes for individual studies are described in the eAppendix 1 at http://www.jama.com). Heterogeneity was quantified using the $\chi^2$ test and the $I^2$ statistic. We conducted a meta-regression analysis with a random-effects model to explore sources of heterogeneity. A meta-analysis was performed separately on the general population, high-risk, and CKD cohorts.

We evaluated the distribution and risk relationship for estimated GFR separately for both equations. Cox proportional hazards models were fitted with estimated GFR linear splines (knots at 30, 45, 60, 75, 90, and 105 mL/min/1.73 $m^2$ [the 105 mL/min/1.73 $m^2$ knot was not applied to CKD cohorts]). All Cox models were adjusted for age, sex, race/ethnicity (blacks vs nonblacks), smoking (current vs former or nonsmokers), history of cardiovascular disease, systolic blood pressure (continuous), diabetes, serum total cholesterol concentration (continuous), body mass index (continuous), and albuminuria (log-transformed ratio of urine albumin to creatinine, log-transformed ratio of urine protein to creatinine as continuous variables, or dipstick as a categorical variable [negative, trace, 1 +, 2 +, and 3 +]). From these models, hazard ratio (HR) was computed for each 1 mL/min/1.73 $m^2$ of estimated GFR from 15 to 120 mL/min/1.73 $m^2$ with a reference point at 95 mL/min/1.73 $m^2$

 ©2012 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/ on 05/21/2013

(50 mL/min/1.73 $m^2$ for CKD cohorts). Model discrimination was assessed using the *c* statistic, which allows for censoring.[71]

We cross-tabulated estimated GFR using clinically relevant categories (≥90, 60-89, 45-59, 30-44, 15-29, <15 mL/min/1.73$m^2$)[1,2] and evaluated the proportion of participants in each category of estimated GFR by the MDRD Study equation that was reclassified by the CKD-EPI equation. To evaluate factors associated with reclassification, baseline characteristics of participants in each study were compared according to the reclassification status by the CKD-EPI equation (reclassified upward to a higher estimated GFR category, not reclassified, or reclassified downward to a lower estimated GFR category). Because there were few participants with an estimated GFR of less than 15 mL/min/1.73 $m^2$ in the general population cohorts (<0.1%) and in high-risk cohorts (0.2%), we only reported results for this estimated GFR category in the CKD cohorts.

Given that GFR category is a central measure for defining, staging, and managing CKD (including indications for referral),[1,2] we designated a priori the effect of reclassification in estimated GFR categories as the primary analysis.[21-23] We assessed risk of clinical outcomes among participants who were reclassified for estimated GFR compared with those who were not reclassified. Overall improvement in reclassification based on estimated GFR was assessed by applying net reclassification improvement (NRI).[21,72] To assess generalizability, we calculated NRI in subgroups according to age (<65 years and ≥65 years), sex, race/ethnicity (white, Asian, and black), and presence or absence of diabetes and hypertension. Due to sparse data, we could not reliably investigate Hispanics and other racial/ethnic groups. The NRI also was estimated in subgroups according to albuminuria levels. All analyses were conducted using Stata version 11.2 (StataCorp). A *P* value of less than .05 was considered statistically significant.

## RESULTS

Participants from 45 cohorts were from 40 countries or regions of Asia, Europe, North America and South America, the Middle East, and Oceania. Baseline characteristics of each cohort are shown in eTable 1 at http://www.jama.com. Overall, 1.1 million adults (940 366 from general population, 151 494 from high-risk, and 38 612 from CKD cohorts) were followed up for 9.4 million person-years (the median of mean follow-up time across collaborating cohorts was 7.4 years [interquartile range, 4.2-10.5 years]). Forty cohorts reported on 84 482 deaths (61 770 from general population, 13 693 from high-risk, and 9019 from CKD cohorts); 28 cohorts reported on 22 176 cardiovascular disease deaths (17 009 from general population, 4271 from high-risk, and 896 from CKD cohorts); and 21 cohorts reported on 7644 ESRD events (730 from general population, 954 from high-risk, and 5960 from CKD cohorts).

Mean estimated GFR was higher when computed by the CKD-EPI equation than by the MDRD Study equation in the general population cohorts (88.9 vs 81.5 mL/min/1.73 $m^2$, respectively; FIGURE 1A) and in the high-risk cohorts (84.6 vs 80.6 mL/min/1.73 $m^2$; eFigure 1A) but was comparable in the CKD cohorts (41.4 vs 40.6 mL/min/1.73 $m^2$) (eFigure 2A). The shift of distribution toward higher estimated GFR by the CKD-EPI equation was more evident in younger people (<65 years), females, and nonblacks (eFigures 3-5). Accordingly, the prevalence of CKD stages 3 to 5 (<60 mL/min/1.73 $m^2$) was lower by the CKD-EPI equation than by the MDRD Study equation in the general population cohorts (6.3% vs 8.7%, respectively) and in the high-risk cohorts (14.6% vs 17.7%). The lower prevalence of CKD stages 3 to 5 by the CKD-EPI equation was observed in most of the individual cohorts; there was a small increase in only 2 cohorts of elderly participants[30,39](eFigure 6).

The pattern of the estimated GFR risk relationship was similar for both equations in the general population cohorts after adjusting for potential confounders (Figure 1B-D). However, the adjusted HR of lower estimated GFR compared with estimated GFR of 95 mL/min/1.73 $m^2$ became significant at a higher level by the CKD-EPI equation than by the MDRD Study equation, particularly for cardiovascular mortality (77 vs 68 mL/min/1.73 $m^2$, respectively) and ESRD (82 vs 70 mL/min/1.73 $m^2$). Within the range of estimated GFR of less than 45 mL/min/1.73 $m^2$, the HRs were largely comparable between both equations for the mortality outcomes. The steeper risk gradient along with low estimated GFR was more evident in the unadjusted analysis for mortality (eFigure 7). The higher risk of all-cause and cardiovascular mortality in the higher estimated GFR range (105-120 mL/min/1.73 $m^2$) was more pronounced for the CKD-EPI equation than the MDRD Study equation. This effect was not observed in the unadjusted analysis. Similar estimated GFR risk relationships were observed in the high-risk and CKD cohorts (eFigure 1B-D and eFigure 2B-D), but the higher risk at higher levels of estimated GFR was not evident. Using these models with estimated GFR splines, traditional risk factors, and albuminuria, the *c* statistic, which focuses on ranking alone and ignores absolute levels and categories,[73] produced results that were almost identical for the CKD-EPI and MDRD Study equations in the general population cohorts for all-cause mortality (0.783 [95% CI, 0.758-0.807] vs 0.783 [95% CI, 0.759-0.808], respectively), for cardiovascular mortality (0.835 [95% CI, 0.800-0.869] vs 0.835 [95% CI, 0.801-0.869]) and for ESRD (0.920 [95% CI, 0.888-0.953] vs 0.919 [95% CI, 0.885-0.952]). Similar findings were observed in the high-risk and CKD cohorts (eTable 2).

In the general population cohorts, 25.0% of participants were reclassified by the CKD-EPI equation (24.4% to a higher estimated GFR category and 0.6% to a lower estimated GFR category) (FIGURE 2). Most reclassifica-

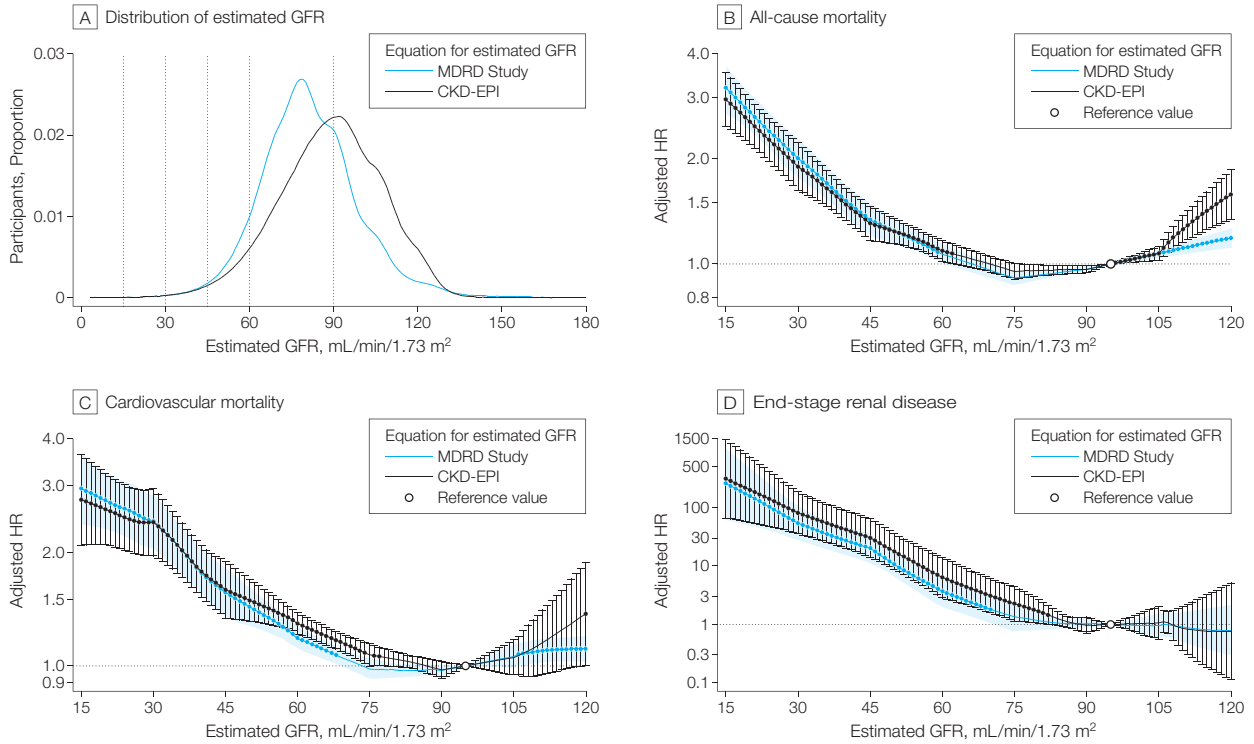
©2012 American Medical Association. All rights reserved.



Downloaded From: http://jamanetwork.com/ on 05/21/2013

tion occurred among participants with estimated GFR between 45 and 89 mL/min/1.73 m$^2$ by the MDRD Study equation. A similar reclassification pattern was observed in the high-risk cohorts, although there was less reclassification (15.4% upward and 1.2% downward; eFigure 8). In the CKD cohorts, we observed much less upward reclas-

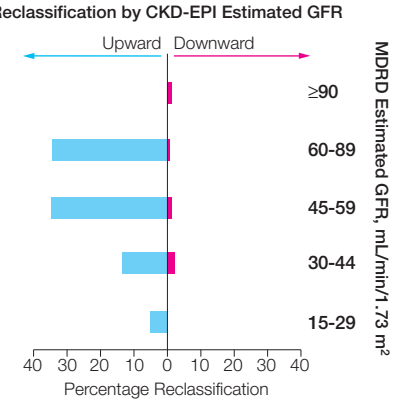
**Figure 1.** Distribution in General Population Cohorts for Estimated GFR and Adjusted Hazard Ratios (HRs) of All-Cause Mortality, Cardiovascular Mortality, and End-Stage Renal Disease




A, Distribution based on kernel density estimation (proportion is for each integer estimated glomerular filtration rate [GFR]). Dotted vertical lines define GFR categories used for chronic kidney disease staging.[1,2] B-D, Error bars indicate 95% confidence intervals for estimated GFR by the CKD-EPI equation. Tinted bands indicate 95% confidence intervals for estimated GFR by the MDRD Study equation. Reference (open circle) is estimated GFR of 95 mL/min/1.73 m$^2$. The filled circles (black and blue dots) represent statistical significance ($P<.05$). Adjustments were made for age, sex, race/ethnicity, smoking, history of cardiovascular disease, systolic blood pressure, diabetes, serum total cholesterol concentration, body mass index, and albuminuria. CKD-EPI indicates Chronic Kidney Disease Epidemiology Collaboration; MDRD, Modification of Diet in Renal Disease.

**Figure 2.** Reclassification Across Estimated GFR Categories by the CKD-EPI Equation From Estimated GFR Categories Based on the MDRD Study Equation

| MDRD Estimated GFR, mL/min/1.73 m$^2$ | CKD-EPI Estimated GFR Category, mL/min/1.73 m$^2$ ≥90 | 60-89 | 45-59 | 30-44 | 15-29 | Total |
|---|---|---|---|---|---|---|
| ≥90 | 259 906 | 3239 (1.2) | | | | 263 145 |
| 60-89 | 204 187 (34.3) | 389 845 | 964 (0.2) | | | 594 996 |
| 45-59 | | 23 908 (34.7) | 44 161 | 804 (1.2) | | 68 873 |
| 30-44 | | | 1476 (13.7) | 9100 | 231 (2.1) | 10 807 |
| 15-29 | | | | 89 (4.8) | 1772 | 1861 |
| Total | 464 093 | 416 992 | 46 601 | 9993 | 2003 | |




Reclassification by the CKD-EPI equation in the general population cohorts. The blue and red bars indicate upward reclassification to a higher estimated GFR category and downward reclassification to a lower estimated GFR category, respectively. Data in pink and blue type are the number (percentage) of participants who were reclassified.

 ©2012 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/ on 05/21/2013

sification (6.6%) but slightly more downward reclassification (3.2%) by the CKD-EPI equation (eFigure 9).

Participants who were reclassified upward to a higher estimated GFR category by the CKD-EPI equation were more likely to be younger, female, and nonblack, and thus have fewer comorbid conditions such as hypertension, diabetes, and clinically significant albuminuria compared with individuals who remained in the same estimated GFR category (TABLE 1, TABLE 2, and eTable 3). In contrast, the participants reclassified downward to a lower estimated GFR category by the CKD-EPI equation were much older than those who were not reclassified in most studies (mean age in general population cohorts, 77 years vs 49 years, respectively). Blacks tended to be reclassified less frequently (in either direction) in the general population cohorts but were reclassified downward more frequently at a lower GFR range (CKD cohorts) compared with nonblacks.

Participants in general population cohorts who were reclassified upward and downward by the CKD-EPI equation had consistently lower and higher incidence rates for all outcomes, respectively, than those who remained in the same estimated GFR category (TABLE 3). This association remained the same even after adjustment for potential confounders, with only a few exceptions (none of which were significant). When we focused on clinically important upward reclassification from CKD stage 3a (estimated GFR 45 to 59 mL/min/1.73 $m^2$) to mildly reduced estimated GFR (60 to 89 mL/min/1.73 $m^2$), this reclassification was associated with lower incidence rates compared with no reclassification (incidence rate per 1000 person-years, 9.9 vs 34.5 [difference, –24.6] for all-cause mortality, 2.7 vs 13.0 [–10.3] for cardiovascular mortality, and 0.5 vs 0.8 [–0.3] for ESRD). Of note, this reclassification was associated with a 20% to 51% lower risk of these outcomes even after the adjustment for traditional risk factors and albuminuria. We obtained similar results for the groups either younger or older than 65 years of age (eTable 4 and eTable 5). Among the statistically significant reclassifications

**Table 1.** Characteristics of Participants in General Population Cohorts According to Reclassification Status by CKD-EPI Equation Compared With MDRD Study Equation for Estimated GFR

| | | Moved Upward to Higher GFR Category | | | No Reclassification | | | Moved Downward to Lower GFR Category | | |
|---|---|---|---|---|---|---|---|---|---|---|
| General Population Cohorts[a] | Total No. | Overall, % | Mean Age, y | Females; Blacks; Albuminuria, %[b] | Overall, % | Mean Age, y | Females; Blacks; Albuminuria, %[b] | Overall, % | Mean Age, y | Females; Blacks; Albuminuria, %[b] |
| Aichi[27] | 4731 | 19 | 48 | 20; 0; 3 | 81 | 48 | 20; 0; 2 | 0 | NA | NA; NA; NA |
| ARIC[21,c] | 11 441 | 8 | 59 | 58; 15; 7 | 90 | 63 | 56; 23; 8 | 2 | 71 | 21; 6; 12 |
| AusDiab[24,c] | 11 179 | 25 | 45 | 60; 0; 4 | 74 | 54 | 54; 0; 7 | 1 | 77 | 27; 0; 23 |
| Beaver Dam CKD[28] | 4857 | 16 | 54 | 64; 0; 2 | 81 | 63 | 55; 0.03; 5 | 2 | 77 | 40; 0; 5 |
| Beijing[29,c] | 1559 | 17 | 54 | 65; 0; 8 | 83 | 61 | 48; 0; 5 | 1 | 74 | 20; 0; 23 |
| CHS[30,c] | 2988 | 0.3 | 73 | 89; 0; 33 | 88 | 78 | 60; 17; 21 | 11 | 81 | 46; 14; 20 |
| CIRCS[31] | 11 871 | 21 | 52 | 69; 0; 3 | 79 | 54 | 59; 0; 3 | 0 | NA | NA; NA; NA |
| COBRA[32,c] | 2872 | 9 | 52 | 49; 0; 12 | 89 | 51 | 53; 0; 9 | 2 | 81 | 40; 0; 15 |
| ESTHER[33] | 9641 | 14 | 59 | 67; 0; 9 | 85 | 62 | 53; 0; 12 | 1 | 72 | 33; 0; 12 |
| Framingham[34,c] | 2956 | 17 | 55 | 58; 0; 9 | 82 | 59 | 52; 0; 13 | 1 | 75 | 25; 0; 21 |
| Gubbio[35,c] | 1681 | 23 | 53 | 52; 0; 3 | 77 | 55 | 56; 0; 4 | 0 | NA | NA; NA; NA |
| HUNT[36,c] | 9659 | 12 | 53 | 64; 0; 6 | 84 | 63 | 54; 0; 13 | 4 | 77 | 45; 0; 19 |
| IPHS[37] | 95 451 | 18 | 53 | 77; 0; 2 | 81 | 60 | 64; 0; 3 | 0.3 | 76 | 12; 0; 4 |
| MESA[38,c] | 6733 | 12 | 56 | 61; 13; 7 | 86 | 63 | 52; 29; 10 | 2 | 78 | 32; 44; 25 |
| MRC[39] | 12 371 | 1 | 77 | 100; 0; 5 | 91 | 81 | 62; 0; 8 | 8 | 84 | 42; 0; 8 |
| NHANES III[40,c] | 15 563 | 13 | 44 | 55; 16; 8 | 86 | 46 | 53; 29; 12 | 2 | 81 | 35; 19; 27 |
| Ohasama[41] | 1956 | 14 | 58 | 80; 0; 7 | 85 | 64 | 62; 0; 8 | 1 | 83 | 22; 0; 39 |
| Okinawa 1983[42] | 9599 | 22 | 43 | 61; 0; 17 | 78 | 54 | 59; 0; 22 | 0.4 | 83 | 52; 0; 32 |
| Okinawa 1993[43] | 93 216 | 21 | 46 | 60; 0; 3 | 79 | 57 | 57; 0; 4 | 1 | 81 | 36; 0; 6 |
| PREVEND[44,c] | 8385 | 27 | 44 | 58; 0.4; 8 | 73 | 51 | 47; 1; 12 | 0.2 | 72 | 15; 0; 30 |
| RanchoBernardo[45,c] | 1474 | 10 | 58 | 66; 0; 8 | 83 | 71 | 59; 0.1; 15 | 7 | 84 | 56; 0; 18 |
| REGARDS[46,c] | 27 306 | 11 | 59 | 68; 18; 8 | 85 | 65 | 53; 43; 16 | 4 | 77 | 36; 30; 21 |
| Severance[47] | 76 201 | 29 | 42 | 53; 0; 5 | 71 | 47 | 48; 0; 5 | 0.1 | 77 | 20; 0; 16 |
| Taiwan[48] | 515 573 | 29 | 37 | 52; 0; 1 | 71 | 43 | 50; 0; 2 | 0.1 | 80 | 22; 0; 9 |
| ULSAM[49,c] | 1103 | 1 | 71 | 0; 0; 11 | 93 | 71 | 0; 0; 16 | 6 | 71 | 0; 0; 19 |
| **Total** | **940 366** | 24 | 43 | 57; 1; 3 | 75 | 49 | 52; 2; 4 | 1 | 77 | 24; 2; 10 |

Abbreviations: CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; GFR, glomerular filtration rate; MDRD, Modification of Diet in Renal Disease; NA, data not applicable.
[a] The study acronyms and abbreviations are listed in eAppendix 2 at http://www.jama.com.
[b] For albuminuria, this is the proportion of participants with ratio of urine albumin to creatinine of 30 mg/g or greater, ratio of protein to creatinine of 50 mg/g or greater, or dipstick protein level of 1 or greater.
[c] This study included ratio of urine albumin to creatinine.

©2012 American Medical Association. All rights reserved.


Downloaded From: http://jamanetwork.com/ on 05/21/2013

in Table 3, heterogeneity across studies was minimal to moderate ($I^2$=0% to 52.5%; $P$ values ranged from 0.82 to 0.006). Similar findings were observed in the high-risk (eTable 6) and CKD cohorts (eTable 7). For ESRD, analysis with mortality as a competing risk provided similar findings (eTable 8).

In the general population cohorts, NRI was significantly positive (favoring the CKD-EPI equation) for all outcomes (0.11 [95% CI, 0.09-0.13] for all-cause mortality, 0.13 [95% CI, 0.09-0.16] for cardiovascular mortality, and 0.06 [95% CI, 0.02-0.10] for ESRD) (FIGURE 3). There was high heterogeneity between individual cohorts for overall NRI ($I^2$=71%-97%; all $P<.01$). However, this heterogeneity reflected quantitative rather than qualitative differences because the CKD-EPI equation was favored in almost all general population cohorts (eFigures 10-12). We conducted a meta-regression analysis with the covariates (eTable 9). Studies with higher mean age and prevalence of diabetes tended to have lower NRI for cardiovascular mortality (eFigure 13 and eFigure 14). The NRI for other associations did not vary significantly across studies.

The NRI was positive in most of the subgroups according to age, sex, race/ethnicity, and presence or absence of diabetes and hypertension (Figure 3). The NRI was comparable between females and males and between those younger than 65 years and those aged 65 years or older except for a lower NRI in those aged 65 years or older for ESRD. The NRI was positive even in the age category of 75 years or older for all-cause mortality (0.03 [95% CI, 0.02 to 0.05]) and cardiovascular mortality (0.02 [95% CI, 0.01 to 0.03]). The NRI was negative but not significant for ESRD (–0.04 [95% CI, –0.10 to 0.02], $P$=.15). The NRI for mortality outcomes was lower in blacks compared with whites and Asians but still significantly favored the CKD-EPI equation. With further stratification by the combination of these demographic variables, the NRI was positive (favoring the

**Table 2.** Characteristics of Participants in High-Risk and Chronic Kidney Disease (CKD) Cohorts According to Reclassification Status by CKD-EPI Equation Compared With MDRD Study Equation for Estimated GFR

| | | Moved Upward to Higher GFR Category | | | No Reclassification | | | Moved Downward to Lower GFR Category | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Cohort[a] | Total No. | Overall, % | Mean Age, y | Females; Blacks; Albuminuria, %[b] | Overall, % | Mean Age, y | Females; Blacks; Albuminuria, %[b] | Overall, % | Mean Age, y | Females; Blacks; Albuminuria, %[b] |
| High-risk | | | | | | | | | | |
| ADVANCE[50,c] | 10 595 | 10 | 62 | 57; 0.4; 31 | 88 | 66 | 41; 0.3; 31 | 2 | 74 | 25; 1; 26 |
| CARE[51] | 4098 | 17 | 54 | 17; 2; 12 | 83 | 60 | 13; 4; 14 | 0.2 | 73 | 0; 0; 57 |
| KEEP[52] | 77 902 | 15 | 48 | 72; 21; 10 | 84 | 55 | 68; 33; 13 | 1 | 79 | 51; 36; 21 |
| KP Hawaii[53,d] | 39 884 | 15 | 51 | 54; 0; 29 | 84 | 60 | 50; 0; 34 | 2 | 82 | 38; 0; 45 |
| MRFIT[54] | 12 854 | 28 | 44 | 0; 3; 4 | 72 | 47 | 0; 9; 4 | 0 | NA | NA; NA; NA |
| Pima[55,c] | 5066 | 4 | 46 | 68; 0; 37 | 96 | 32 | 56; 0; 19 | 0.2 | 76 | 50; 0;t50 |
| ZODIAC[56,c] | 1095 | 10 | 58 | 56; 0; 25 | 88 | 69 | 58; 0; 41 | 2 | 79 | 27; 0; 46 |
| Subtotal | 151 494 | 15 | 49 | 59; 11; 17 | 83 | 56 | 53; 18; 19 | 1 | 72 | 40; 18; 28 |
| CKD | | | | | | | | | | |
| AASK[57,d] | 1094 | 6 | 46 | 66; 100; 63 | 92 | 55 | 37; 100; 62 | 2 | 66 | 21; 100; 54 |
| BC CKD[58,c] | 17 426 | 6 | 52 | 56; 0.1; 76 | 90 | 70 | 45; 0.4; 75 | 4 | 82 | 34; 1; 74 |
| CRIB[59,c] | 308 | 3 | 49 | 38; 0; 63 | 95 | 62 | 34; 6; 87 | 2 | 77 | 17; 17; 100 |
| Geisinger[60] | | | | | | | | | | |
| ACR[c] | 3361 | 3 | 59 | 63; 3; 50 | 96 | 71 | 54; 2; 43 | 1 | 79 | 6; 0; 56 |
| Dipstick | 4509 | 3 | 57 | 80; 6; 32 | 96 | 72 | 62; 1; 25 | 2 | 81 | 27; 3; 27 |
| GLOMMS-1[61] | | | | | | | | | | |
| ACR[c] | 537 | 2 | 54 | 33; 0; 67 | 93 | 73 | 52; 0; 51 | 4 | 80 | 42; 0; 38 |
| PCR[d] | 470 | 4 | 41 | 47; 0; 88 | 91 | 70 | 48; 0; 95 | 5 | 83 | 43; 0; 100 |
| KPNW[62] | 1627 | 10 | 62 | 72; 1; 25 | 86 | 72 | 54; 3; 32 | 4 | 82 | 53; 3; 31 |
| MASTERPLAN[63,c] | 636 | 11 | 49 | 47; 3; 78 | 88 | 62 | 29; 3; 86 | 1 | 72 | 50 0; 75 |
| MDRD[64,d] | 1730 | 14 | 45 | 50; 5; 80 | 86 | 52 | 38; 13; 83 | 1 | 67 | 29; 64; 86 |
| MMKD[65,d] | 202 | 17 | 39 | 41; 0; 94 | 83 | 48 | 33; 0; 95 | 0 | NA | NA; NA; NA |
| NephroTest[66,c] | 928 | 9 | 48 | 33; 8; 51 | 89 | 61 | 31; 10; 65 | 2 | 75 | 0; 13; 73 |
| RENAAL[67,c] | 1513 | 9 | 55 | 34; 8; 100 | 90 | 61 | 37; 15; 100 | 1 | 68 | 0; 67; 100 |
| STENO[68,c] | 886 | 26 | 42 | 48; 0; 46 | 74 | 44 | 42; 0; 50 | 0.1 | 74 | 0; 0; 0 |
| Sunnybrook[69,c] | 3385 | 6 | 52 | 52; 0; 83 | 89 | 71 | 44; 0; 84 | 5 | 82 | 26; 0; 86 |
| Subtotal | 38 612 | 7 | 53 | 58; 5; 67 | 90 | 68 | 47; 5; 66 | 3 | 79 | 28; 10; 65 |

Abbreviations: CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; GFR, glomerular filtration rate; MDRD, Modification of Diet in Renal Disease; NA, data not applicable.
[a] The study acronyms and abbreviations are listed in eAppendix 2 at http://www.jama.com.
[b] For albuminuria, this is the proportion of participants with ratio of urine albumin to creatinine (ACR) of 30 mg/g or greater, ratio of protein to creatinine (PCR) of 50 mg/g or greater, or dipstick protein level of 1 or greater.
[c] This study included ACR.
[d] This study included PCR.

 ©2012 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/ on 05/21/2013

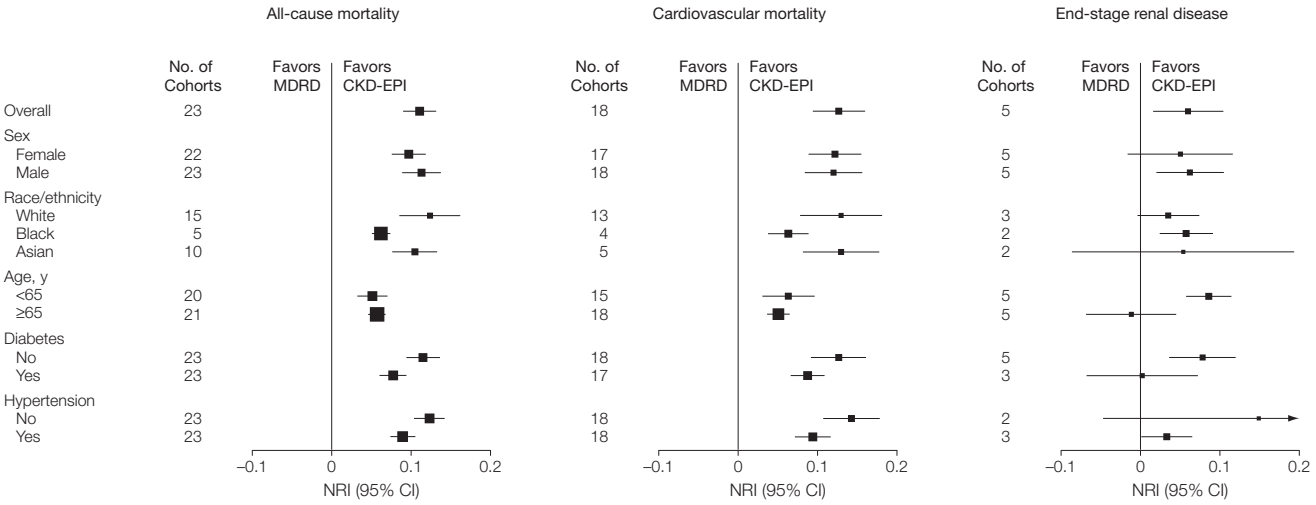
CKD-EPI equation) in 33 of 36 comparisons and was statistically significant in 17 comparisons (eTable 10). None of 3 negative NRIs (favoring the MDRD Study equation) were significant. Similarly, the NRI was positive in most subgroups in the high-risk and CKD cohorts (eFigure 15, eFigure 16, eTable 11, and eTable 12). The NRI also was positive in most subgroups defined according to albuminuria level (eTable 13).

**Table 3.** Clinical Outcomes for the General Population Cohorts According to Reclassification Status by CKD-EPI Equation Compared With MDRD Study Equation for Estimated GFR

| MDRD Estimated GFR Category, mL/min/1.73 m$^2$ | All-Cause Mortality (n = 61 426 Events) by CKD-EPI GFR Reclassification | | | Cardiovascular Mortality (n = 16 923 Events) by CKD-EPI GFR Reclassification | | | End-Stage Renal Disease (n = 666 Events) by CKD-EPI GFR Reclassification | | |
|---|---|---|---|---|---|---|---|---|---|
| | Upward (n = 5586 Events) | None (n = 53 601 Events) | Downward (n = 2239 Events) | Upward (n = 1113 Events) | None (n = 14 979 Events) | Downward (n = 831 Events) | Upward (n = 60 Events) | None (n = 588 Events) | Downward (n = 18 Events) |
| ≥90 | | | | | | | | | |
| CIR[a] | NA[b] | 3.8 | 52.9 | NA[b] | 0.8 | 22.3 | NA[b] | 0.3 | 0.4 |
| AHR[c] | NA[b] | 1 [Reference] | 1.02 (0.89-1.18) | NA[b] | 1 [Reference] | 1.24 (1.01-1.53) | NA[b] | 1 [Reference] | 1.54 (0.50-4.78) |
| 60-89 | | | | | | | | | |
| CIR[a] | 2.2 | 10.2 | 95.1 | 0.4 | 3.0 | 46.0 | 0.1 | 0.2 | 2.3 |
| AHR[c] | 1.03 (0.98-1.08) | 1 [Reference] | 0.98 (0.85-1.14) | 0.93 (0.85-1.02) | 1 [Reference] | 1.21 (1.01-1.43) | 0.47 (0.24-0.93) | 1 [Reference] | 4.44 (1.52-13.00) |
| 45-59 | | | | | | | | | |
| CIR[a] | 9.9 | 34.5 | 111.6 | 2.7 | 13.0 | 52.3 | 0.5 | 0.8 | 1.6 |
| AHR[c] | 0.80 (0.74-0.86) | 1 [Reference] | 1.15 (1.03-1.27) | 0.73 (0.65-0.82) | 1 [Reference] | 1.25 (1.07-1.48) | 0.49 (0.27-0.88) | 1 [Reference] | 2.67 (0.73-9.72) |
| 30-44 | | | | | | | | | |
| CIR[a] | 18.2 | 66.4 | 134.5 | 6.0 | 27.3 | 56.4 | 4.6 | 7.0 | 13.7 |
| AHR[c] | 0.74 (0.61-0.88) | 1 [Reference] | 1.11 (0.79-1.55) | 0.75 (0.54-1.05) | 1 [Reference] | 1.25 (0.68-2.31) | 0.95 (0.43-2.07) | 1 [Reference] | 1.35 (0.51-3.56) |
| 15-29 | | | | | | | | | |
| CIR[a] | 33.4 | 88.1 | NA[d] | 15.7 | 33.6 | NA[d] | 59.5 | 59.7 | NA[d] |
| AHR[c] | 1.04 (0.51-2.15) | 1 [Reference] | NA[d] | 1.66 (0.44-6.30) | 1 [Reference] | NA[d] | 1.13 (0.36-3.54) | 1 [Reference] | NA[d] |

Abbreviations: AHR, adjusted hazard ratio; CIR, crude incidence rate; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; GFR, glomerular filtration rate; MDRD, Modification of Diet in Renal Disease.
[a] Per 1000 person-years.
[b] NA indicates inapplicable.
[c] Adjusted for age, sex, race/ethnicity, smoking, systolic blood pressure, total cholesterol, diabetes, history of cardiovascular disease, body mass index, and albuminuria.
[d] NA indicates unreliable due to the small number of participants.

**Figure 3.** Meta-analyses of Net Reclassification Improvements (NRIs) for All-Cause Mortality, Cardiovascular Mortality, and End-Stage Renal Disease




The sizes of the data markers are proportional to the inverse of the variance of the NRIs.

©2012 American Medical Association. All rights reserved.



Downloaded From: http://jamanetwork.com/ on 05/21/2013

## COMMENT

In our data from more than 1 million participants residing in 40 countries or regions, approximately one-fourth of participants were reclassified to a higher estimated GFR category by the CKD-EPI equation compared with the MDRD Study equation (24.4% in the general population cohorts, 15.4% in the high-risk cohorts, and 6.6% in the CKD cohorts), lowering the prevalence of CKD in all cohorts except for the elderly. Participants who were reclassified upward had lower risks of mortality and ESRD compared with those not reclassified even after adjusting for age, sex, race/ethnicity, and other potential confounders. Individuals who were reclassified downward (0.7%) had higher risk than those who were not reclassified. Positive NRIs also support better overall reclassification by the CKD-EPI equation. Although we observed quantitative heterogeneity in some analyses, most of the studies were in agreement with the pooled results (eFigures 10-12). Importantly, a better risk categorization by the CKD-EPI equation compared with the MDRD Study equation was consistent in almost all subgroups defined by age, sex, race/ethnicity, and clinical characteristics.

Our results confirm and extend results from previous literature.[21-24] First, we observed that the CKD-EPI equation is a better predictor of risk than the MDRD Study equation in CKD cohorts as well as in cohorts with higher estimated GFR. Improved or similar performance across the range of estimated GFR is important for clinical implementation. Second, although the elderly were less often reclassified by the CKD-EPI equation compared with younger people, their future risk also was more correctly classified. Third, we found that the CKD-EPI equation predicts clinical risk more accurately than the MDRD Study equation in Asians. Although there is debate about which estimated GFR equation to use in Asia,[74,75] our results suggest that the CKD-EPI equation would be a better option for risk prediction than the MDRD Study equation. Fourth, we showed that the CKD-EPI equation categorizes risk slightly more accurately than or at least as well as the MDRD Study equation in blacks, even though reclassification is less common in blacks than in whites and Asians. Fifth, we showed that the CKD-EPI equation provides more accurate risk categorization than the MDRD Study equation even after considering albuminuria, a measure of kidney damage. Recent reports suggest using albuminuria in addition to GFR for CKD staging and risk classification.[76,77] Our findings suggest the CKD-EPI equation will be more useful than the MDRD Study equation for this application. Finally, we showed improved risk prediction for ESRD, in addition to mortality and cardiovascular disease shown in most of the previous studies.[21-24]

The CKD-EPI and MDRD Study equations estimate the same physiological function (GFR) using identical variables, thus the comparison of outcome prediction by 2 equations differs from the more common comparison of 2 models with and without a new biomarker. Because the same variables appear in both equations in our study, the difference in predicted risk between the 2 equations should not be expected to be as large as would be sought when adding a new biomarker. Consequently, we did not anticipate improvements in less sensitive statistics (such as the *c* statistic), which ignore absolute levels and categories and focus on ranking alone.[73] This is particularly the case when age, sex, and race/ethnicity are included in the prediction model because coefficients for these variables can compensate for worse prediction by estimated GFR by the MDRD Study equation compared with the CKD-EPI equation.[21]

From another perspective, the use of the identical variables in the CKD-EPI equation requires no additional laboratory costs and enables relatively easy implementation with computerized algorithms. Therefore, a significant overall improvement in risk categorization by the CKD-EPI equation, even if small, would support its clinical use in place of the MDRD Study equation. At this time, only a small proportion of clinical laboratories in the United States have switched to the CKD-EPI equation for estimated GFR reporting.[7] In this context, clinically important reclassification crossing the threshold for CKD definition from CKD stage 3a to mildly reduced estimated GFR (60 to 89 mL/min/1.73m$^2$) was observed in our study in one-third of individuals with estimated GFR by the MDRD Study equation between 45 and 59 mL/min/1.73m$^2$. In the general population cohorts, these individuals had lower risk of mortality and ESRD compared with those who were not reclassified (crude incidence rate difference of −24.6 to −0.3 per 1000 person-years and 20% to 51% lower adjusted HR). Given both lower CKD prevalence estimates and better risk categorization, the use of the CKD-EPI equation would contribute to a more appropriate allocation of health care resources and more targeted prevention and management of CKD complications.

The paradoxically increased mortality risk at higher estimated GFR is noted in several studies and may be due to confounding by muscle wasting secondary to ill health.[21] With the CKD-EPI equation, this risk was not evident in the unadjusted analysis but was evident after age adjustment, suggesting the CKD-EPI equation does not fully overcome this limitation inherent to creatinine-based estimated GFR equations. Other filtration markers not related to muscle mass such as serum cystatin C[78,79] might help to resolve this issue.

Some limitations to our study should be mentioned. Measurements of creatinine were not standardized in all studies; however, we observed similar results when we limited our analysis to studies with serum creatinine measurements standardized to isotope dilution mass spectrometry (data not shown). Most of the participants recorded as blacks were from studies in the United States. Although there are various ethnic groups within Asia (eg,

 ©2012 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/ on 05/21/2013

South Asian and Eastern Asian), we analyzed these groups together. Further analyses will be required for racial/ethnic groups not tested in this study.

Overall, the CKD-EPI creatinine-based equation more accurately classified individuals with respect to risk of mortality and ESRD compared with the MDRD Study equation. Given more accurate GFR estimation,[10] lower CKD prevalence estimates, and better risk categorization by the CKD-EPI equation without additional laboratory costs, its implementation for estimated GFR reporting could contribute to more efficient and targeted prevention and management of CKD-related outcomes.

**Author Affiliations:** Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland (Drs Matsushita, Mahmoodi, Woodward, and Coresh); George Institute, University of Sydney, Sydney, Australia (Dr Woodward); Clinical Trial Service Unit and Epidemiological Studies Unit, Oxford University, Oxford, England (Dr Emberson); Department of Medicine, Aga Khan University, Karachi, Pakistan (Dr Jafar); Department of Epidemiology and Health Promotion, Institute for Health Promotion, Graduate School of Public Health, Yonsei University, Seoul, Korea (Dr Jee); Department of Nephrology, Monash Medical Centre, Victoria, Australia (Dr Polkinghorne); Department of Medicine, Monash University, Victoria, Australia (Dr Polkinghorne); Department of Community Medicine, School of Medicine, West Virginia University, Morgantown (Dr Shankar); Center for Health Research, Kaiser Permanente Northwest, Portland, Oregon (Dr Smith); Department of Medicine, University of Alberta, Edmonton, Canada (Dr Tonelli); Department of Medicine, University of Alabama, Birmingham (Dr Warnock); China Medical University Hospital, Taichung, Taiwan (Dr Wen); Institute of Population Health Science, National Health Research Institutes, Zhunan, Taiwan (Dr Wen); Department of Nephrology, University Medical Center Groningen, Groningen, the Netherlands (Drs Mahmoodi and Gansevoort); Department of Medicine, University of Calgary, Calgary, Alberta, Canada (Dr Hemmelgarn); and Division of Nephrology, Tufts Medical Center, Boston, Massachusetts (Dr Levey).

**Author Contributions:** Dr Coresh had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
*Study concept and design:* Matsushita, Woodward, Wen, Coresh, Gansevoort, Hemmelgarn, Levey.
*Acquisition of data:* Matsushita, Coresh and the Chronic Kidney Disease Prognosis Consortium (CKD-PC) investigators and collaborators.
*Analysis and interpretation of data:* Matsushita, Mahmoodi, Woodward, Emberson, Jafar, Jee, Polkinghorne, Shankar, Smith, Tonelli, Warnock, Wen, Coresh, Gansevoort, Hemmelgarn, Levey.
*Drafting of the manuscript:* Matsushita, Coresh, Levey.
*Critical revision of the manuscript for important intellectual content:* Matsushita, Mahmoodi, Woodward, Emberson, Jafar, Jee, Polkinghorne, Shankar, Smith, Tonelli, Warnock, Wen, Coresh, Gansevoort, Hemmelgarn, Levey.
*Statistical analysis:* Matsushita, Woodward, Coresh and the CKD-PC data coordinating center.
*Obtained funding:* Matsushita, Coresh for the CKD-PC (support for each cohort is listed in eAppendix 3 at http://www.jama.com).
*Administrative, technical, or material support:* Matsushita, Mahmoodi, Coresh with the CKD-PC data coordinating center.
*Study supervision:* Matsushita, Coresh, Levey centrally, and collaborators for each cohort.
**Conflict of Interest Disclosures:** The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Mahmoodi reported receiving grant support from the Netherlands Organization for Scientific Research and the Dutch Kidney Foundation. Dr Shankar reported receiving grant support from the National Institutes of Health. Dr Warnock reported serving as a consultant to Genzyme, Reata, Allocure, and Prion; receiving grant support from Genzyme; serving on speakers bureaus for Abbott; and owning stock options in Reata, Relypsa, Allocure, and Prion. Dr Coresh reported serving as a consultant to Amgen and Merck; and having grants pending with the National Institutes of Health and the National Kidney Foundation. Dr Levey reported being the editor in chief of the *American Journal of Kidney Diseases*; and having grants pending with the National Institute of Diabetes and Digestive and Kidney Diseases and the National Kidney Foundation.
**Funding/Support:** The Chronic Kidney Disease Prognosis Consortium (CKD-PC) Data Coordinating Center is underpinned by a program grant from the US National Kidney Foundation (National Kidney Foundation funding sources include Abbott and Amgen). A variety of sources have supported enrollment and data collection including laboratory measurements and follow-up in the collaborating cohorts of the CKD-PC. These funding sources of the collaborating cohorts are listed in eAppendix 3 at http://www.jama.com.
**Role of the Sponsor:** The sponsors had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript.

**CKD-PC Investigators and Collaborators** (the study acronyms are listed in eAppendix 2):
*AASK:* Jackson Wright, MD, PhD, Case Western Reserve University; Lawrence J. Appel, MD, MPH, Johns Hopkins University; Tom Greene, PhD, University of Utah; and Brad C. Astor, PhD, MPH, University of Wisconsin (all universities in the United States). *ADVANCE:* John Chalmers, MD, PhD, Stephen MacMahon, DSc, PhD, and Mark Woodward, PhD, George Institute, Australia. *Aichi:* Hiroshi Yatsuya, MD, PhD, Kentaro Yamashita, MD, Hideaki Toyoshima, MD, PhD, and Koji Tamakoshi, MD, PhD, Nagoya University, Japan. *ARIC:* Josef Coresh, MD, PhD, Kunihiro Matsushita, MD, PhD, and Yingying Sang, MS, Johns Hopkins University; and Brad C. Astor, PhD, MPH, University of Wisconsin (both universities in the United States). *AusDiab:* Robert C. Atkins, FRACP, DSc, and Kevan R. Polkinghorne, FRACP, MClinEpi, PhD, Monash University; and Steven Chadban, FRACP, PhD, University of Sydney (both universities in Australia). *Beaver Dam CKD:* Anoop Shankar, MD, PhD, West Virginia University; and Ronald Klein, MD, MPH, Barbara E. K. Klein, MD, MPH, and Kristine E. Lee, MS, University of Wisconsin (both universities in the United States). *Beijing Cohort:* Haiyan Wang, MD, Fang Wang, MD, Luxia Zhang, MD, MPH, and Li Zuo, MD, Peking University First Hospital, China. *British Columbia CKD:* Adeera Levin, MD, FRCPC, BC Provincial Renal Agency and University of British Columbia, Canada; and Ognjenka Djurdjev, MSc, BC Provincial Renal Agency and Provincial Health Services Authority, Canada. *CARE:* Marcello Tonelli, MD, SM, University of Alberta, Canada; Frank M. Sacks, MD, Harvard School of Public Health, United States; and Gary C. Curhan, MD, ScD, Harvard School of Medicine, United States. *CHS:* Michael Shlipak, MD, MPH, and Carmen Peralta, MD, MAS, University of California and San Francisco VA Medical Center; Ronit Katz, DPhil, University of Washington; and Linda F. Fried, MD, MPH, VA Pittsburgh Healthcare System (all institutions in the United States). *CIRCS:* Hiroyasu Iso, MD, PhD, MPH, and Tetsuya Ohira, MD, PhD, Osaka University; Akihiko Kitamura, MD, PhD, Osaka Medical Center; and Kazumasa Yamagishi, MD, PhD, University of Tsukuba (all institutions in Japan). *COBRA:* Tazeen H. Jafar, MD, MPH, Muhammad Islam, MSc, and Juanita Hatcher, PhD, Aga Khan University, Pakistan; and Neil Poulter, MSc, FRCP, and Nish Chaturvedi, MD, MRCP, Imperial College London, United Kingdom. *CRIB:* Martin J. Landray, PhD, FRCP, and Jonathan R. Emberson, PhD, University of Oxford; John N. Townend, MD, FRCP, Queen Elizabeth Hospital Birmingham; and David C. Wheeler, MD, FRCP, University College London (all institutions in the United Kingdom). *ESTHER:* Dietrich Rothenbacher, MD, MPH, Hermann Brenner, MD, MPH, Heiko Müller, PhD, Ben Schöttker, PhD, German Cancer Research Center; and Dietrich Rothenbacher, MD, MPH, University of Ulm (both institutions in Germany). *Framingham:* Caroline S. Fox, MD, MPH, and Shih-Jen Hwang, PhD, National Heart, Lung, and Blood Institute; and James B. Meigs, MD, MPH, Massachusetts General Hospital (both institutions in the United States). *Geisinger:* Robert M. Perkins, MD, Geisinger Medical Center, United States. *GLOMMS-1 Study:* Nick Fluck, BSc, MBBC, DPhil, FRCP, Laura E. Clark, MBChB, MRCP, MD, Gordon J. Prescott, BSc, MSc, PhD, CStat, Angharad Marks, MBBCh, MRCP, MSc, and Corri Black, MBChB, MRCP, MSc, MFPH, FFPH, University of Aberdeen, United Kingdom. *Gubbio:* Massimo Cirillo, MD, University of Salerno, Italy. *HUNT:* Stein Hallan, MD, PhD, Knut Aasarød, MD, PhD, Cecilia M. Øien, MD, PhD, and Maria Radtke, MD, PhD, Norwegian University of Science and Technology and St Olavs University Hospital, Norway. *IPHS:* Fujiko Irie, MD, PhD, Ibaraki Prefectural Office; Hiroyasu Iso, MD, PhD, MPH, Osaka University; Toshimi Sairenchi, PhD, Dokkyo Medical University School of Medicine; and Kazumasa Yamagishi, MD, PhD, University of Tsukuba (all institutions in Japan). *Kaiser Permanente NW:* David H. Smith, RPh, PhD, Eric S. Johnson, PhD, and Micah L. Thorp, DO, MPH, Kaiser Permanente Northwest; and Jessica W. Weiss, MD, Oregon Health and Science University (both institutions in the United States). *KEEP:* Allan J. Collins, MD, Suying Li, PhD, and Shu-Cheng Chen, MS, Minneapolis Medical Research Foundation; and Joseph A. Vassalotti, MD, National Kidney Foundation (both institutions in the United States). *KP Hawaii:* Brian J. Lee, MD, Kaiser Permanente Hawaii Region, United States. *MASTERPLAN:* Jack F. Wetzels, MD, PhD, Radboud University Nijmegen Medical Centre; and Peter J. Blankestijn, MD, PhD, and Arjan D. van Zuilen, MD, University Medical Center Utrecht (both institutions in the Netherlands). *MDRD:* Mark Sarnak, MD, MS, Andrew S. Levey, MD, and Vandana Menon, MD, PhD, Tufts Medical Center, United States. *MESA:* Michael Shlipak, MD, MPH, and Carmen Peralta, MD, MAS, University of California and San Francisco VA Medical Center; Mark Sarnak, MD, MS, Tufts Medical Center; Ronit Katz, DPhil, and Ian H. de Boer, MD, MS, University of Washington; and Holly J. Kramer, MD, MPH, Loyola University Medical Center (all institutions in the United States). *MMKD:* Florian Kronenberg, MD, and Barbara Kollerits, PhD, MPH, Innsbruck Medical University, Austria; and Eberhard Ritz, MD, Heidelberg Nierenzentrum, Germany. *MRC Older People:* Paul Roderick, MD, University of Southampton; Dorothea Nitsch, MD, MSc, and Astrid Fletcher, PhD, London School of Hygiene & Tropical Medicine; and Christopher Bulpitt, MD, Imperial College Hammersmith Campus (all institutions in the United Kingdom). *MRFIT:* Areef Ishani, MD, MS, Minneapolis VA Health Care System; and James D. Neaton, PhD,

©2012 American Medical Association. All rights reserved.



Downloaded From: http://jamanetwork.com/ on 05/21/2013

University of Minnesota (both institutions in the United States). *NephroTest:* Marc Froissart, MD, PhD, Paris Descartes University; Benedicte Stengel, MD, PhD, and Marie Metzger, PhD, Centre for Research in Epidemiology and Population Health and University of Paris Sud-11; Jean-Philippe Haymann, MD, PhD, Pascal Houillier, MD, PhD, and Martin Flamant, MD, PhD, Assistance Publique-Hôpitaux de Paris (all institutions in France). *NHANES III:* Brad C. Astor, PhD, MPH, University of Wisconsin; and Josef Coresh, MD, PhD, and Kunihiro Matsushita, MD, PhD, Johns Hopkins University (both universities in the United States). *Ohasama:* Takayoshi Ohkubo, MD, PhD, Shiga University of Medical Science; Masaaki Nakayama, MD, PhD, Fukushima Medical University; and Hirohito Metoki, PhD, MD, Masahiro Kikuya, MD, PhD, and Yutaka Imai, MD, PhD, Tohoku University (all institutions in Japan). *Okinawa 83/93:* Kunitoshi Iseki, MD, University Hospital of the Ryukyus, Japan. *Pima Indian:* Robert G. Nelson, MD, PhD, and William C. Knowler MD, DrPH, National Institute of Diabetes and Digestive and Kidney Diseases, United States. *PREVEND:* Ron T. Gansevoort, MD, PhD, Paul E. de Jong, MD, PhD, Bakhtawar K. Mahmoodi, MD, PhD, Stephan J. L. Bakker, MD, PhD, University Medical Center Groningen, the Netherlands. *Rancho Bernardo:* Simerjot Kaur Jassal, MD, University of California San Diego and VA San Diego Healthcare; and Elizabeth Barrett-Connor, MD, and Jaclyn Bergstrom, MS, University of California San Diego (all institutions in the United States). *RENAAL:* Hiddo J. Lambers Heerspink, PharmD, PhD, and Dick de Zeeuw, MD, PhD, University Medical Center Groningen, the Netherlands; and Barry E. Brenner, MD, PhD, Brigham and Women's Hospital and Harvard School of Medicine, United States. *Renal REGARDS:* David G. Warnock, MD, Paul Muntner, PhD, and Suzanne Judd, PhD, University of Alabama at Birmingham; and William McClellan, MD, MPH, Emory University (both universities in the United States). *Severance:* Sun Ha Jee, PhD, Heejin Kimm, MD, PhD, Jaeseong Jo, BS, Yejin Mok, and Eunmi Choi, Yonsei University, Republic of Korea. *STENO:* Peter Rossing, MD, DMSC, Steno Diabetes Center; and Hans-Henrik Parving, MD, DMSC, University Hospital of Copenhagen (both institutions in Denmark). *Sunnybrook:* Navdeep Tangri, MD, PhD (C), FRCPC, University of Manitoba; and David Naimark, FRCPC, University of Toronto (both universities in Canada). *Taiwan GP:* Chi-Pang Wen, MD, DrPH, China Medical University Hospital, Taiwan; Sung-Feng Wen, MD, University of Wisconsin, United States; Chwen-Keng Tsao, BS, MJ Health Management Institution, Taiwan; and Min-Kuang Tsai, MS, National Health Research Institutes, Taiwan. *ULSAM:* Johan Ärnlöv, MD, PhD, and Anders Larsson, MD, PhD, Uppsala University; and Lars Lannfelt, MD, PhD, Uppsala University Hospital (both institutions in Sweden). *ZODIAC:* Henk J. Bilo, MD, PhD, Nanno Kleefstra, MD, PhD, Klaas H. Groenier, PhD, and Iefke Drion, MD, Isala Clinics; and Hanneke Joosten, MD, University Medical Center Groningen (both institutions in the Netherlands).

**CKD-PC Steering Committee:** Brad C. Astor, PhD, MPH, University of Wisconsin; Josef Coresh, MD, PhD (chair), Johns Hopkins University; Ron T. Gansevoort, MD, PhD, University Medical Center Groningen; Brenda R. Hemmelgarn, MD, PhD, University of Calgary; Paul E. de Jong, MD, PhD, University Medical Center Groningen; Andrew S. Levey, MD, Tufts Medical Center; Adeera Levin, MD, FRCPC, BC Provincial Renal Agency and University of British Columbia; Kunihiro Matsushita, MD, PhD, Johns Hopkins University; Chi-Pang Wen, MD, DrPH, China Medical University Hospital; and Mark Woodward, PhD, George Institute.

**CKD-PC Data Coordinating Center:** Shoshana H. Ballew, PhD (coordinator), Josef Coresh, MD, PhD (principal investigator), Morgan Grams, MD, MHS, Bakhtawar K. Mahmoodi, MD, PhD, Kunihiro Matsushita, MD, PhD (director), Yingying Sang, MS (lead programmer), Mark Woodward, PhD (senior statistician), and administrative support: Laura Camarata, BA, Xuan Hui, BMed, Jennifer Seltzer, BS, and Heather Winegrad (all with Johns Hopkins University, United States).

**Online-Only Material:** 3 eAppendices, 13 eTables, 16 eFigures, and eReferences are available at http://www.jama.com.

## REFERENCES

**1.** National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease. *Am J Kidney Dis*. 2002;39(2)(suppl 1):S1-S266.

**2.** Crowe E, Halpin D, Stevens P, et al. Early identification and management of chronic kidney disease. *BMJ*. 2008;337:a1530.

**3.** Matsushita K, van der Velde M, Astor BC, et al. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts. *Lancet*. 2010; 375(9731):2073-2081.

**4.** van der Velde M, Matsushita K, Coresh J, et al. Lower estimated glomerular filtration rate and higher albuminuria are associated with all-cause and cardiovascular mortality. *Kidney Int*. 2011;79(12):1341-1352.

**5.** Gansevoort RT, Matsushita K, van der Velde M, et al. Lower estimated GFR and higher albuminuria are associated with adverse kidney outcomes. *Kidney Int*. 2011;80(1):93-104.

**6.** Astor BC, Matsushita K, Gansevoort RT, et al. Lower estimated glomerular filtration rate and higher albuminuria are associated with mortality and end-stage renal disease. *Kidney Int*. 2011;79(12):1331-1340.

**7.** The College of American Pathologists. Current status of reporting estimated glomerular filtration rate (eGFR) for adults. http://www.cap.org/apps/docs/committees/chemistry/current_status_of_reporting_eGFR_2011.pdf. Accessed March 6, 2012.

**8.** Miller WG. Estimating glomerular filtration rate. *Clin Chem Lab Med*. 2009;47(9):1017-1019.

**9.** Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Intern Med*. 2006; 145(4):247-254.

**10.** Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150(9):604-612.

**11.** Tent H, Rook M, Stevens LA, et al. Renal function equations before and after living kidney donation. *Clin J Am Soc Nephrol*. 2010;5(11):1960-1968.

**12.** Jones GR. Use of the CKD-EPI equation for estimation of GFR in an Australian cohort. *Pathology*. 2010;42(5):487-488.

**13.** White CA, Akbari A, Doucette S, et al. Estimating glomerular filtration rate in kidney transplantation. *Clin Chem*. 2010;56(3):474-477.

**14.** Cirillo M, Lombardi C, Luciano MG, et al. Estimation of GFR. *Am J Kidney Dis*. 2010;56(4):802-804.

**15.** Eriksen BO, Mathisen UD, Melsom T, et al. Cystatin C is not a better estimator of GFR than plasma creatinine in the general population. *Kidney Int*. 2010; 78(12):1305-1311.

**16.** Lane BR, Demirjian S, Weight CJ, et al. Performance of the chronic kidney disease-epidemiology study equations for estimating glomerular filtration rate before and after nephrectomy. *J Urol*. 2010;183 (3):896-901.

**17.** Michels WM, Grootendorst DC, Verduijn M, et al. Performance of the Cockcroft-Gault, MDRD, and new CKD-EPI formulas in relation to GFR, age, and body size. *Clin J Am Soc Nephrol*. 2010;5(6):1003-1009.

**18.** Murata K, Baumann NA, Saenger AK, et al. Relative performance of the MDRD and CKD-EPI equations for estimating glomerular filtration rate among patients with varied clinical presentations. *Clin J Am Soc Nephrol*. 2011;6(8):1963-1972.

**19.** Kukla A, El-Shahawi Y, Leister E, et al. GFR-estimating models in kidney transplant recipients on a steroid-free regimen. *Nephrol Dial Transplant*. 2010; 25(5):1653-1661.

**20.** Rognant N, Lemoine S, Laville M, et al. Performance of the chronic kidney disease epidemiology collaboration equation to estimate glomerular filtration rate in diabetic patients. *Diabetes Care*. 2011;34 (6):1320-1322.

**21.** Matsushita K, Selvin E, Bash LD, et al. Risk implications of the new CKD Epidemiology Collaboration (CKD-EPI) equation compared with the MDRD Study equation for estimated GFR. *Am J Kidney Dis*. 2010;55(4):648-659.

**22.** Stevens LA, Li S, Kurella Tamura M, et al. Comparison of the CKD Epidemiology Collaboration (CKD-EPI) and Modification of Diet in Renal Disease (MDRD) study equations. *Am J Kidney Dis*. 2011;57(3) (suppl 2):S9-S16.

**23.** Skali H, Uno H, Levey AS, et al. Prognostic assessment of estimated glomerular filtration rate by the new Chronic Kidney Disease Epidemiology Collaboration equation in comparison with the Modification of Diet in Renal Disease Study equation. *Am Heart J*. 2011;162(3):548-554.

**24.** White SL, Polkinghorne KR, Atkins RC, Chadban SJ. Comparison of the prevalence and mortality risk of CKD in Australia using the CKD Epidemiology Collaboration (CKD-EPI) and Modification of Diet in Renal Disease (MDRD) Study GFR estimating equations. *Am J Kidney Dis*. 2010;55(4):660-670.

**25.** Carter JL, Stevens PE, Irving JE, Lamb EJ. Estimating glomerular filtration rate. *QJM*. 2011;104(10): 839-847.

**26.** van den Brand JAJG, van Boekel GAJ, Willems HL, et al. Introduction of the CKD-EPI equation to estimate glomerular filtration rate in a Caucasian population. *Nephrol Dial Transplant*. 2011;26 (10):3176-3181.

**27.** Mitsuhashi H, Yatsuya H, Matsushita K, et al. Uric acid and left ventricular hypertrophy in Japanese men. *Circ J*. 2009;73(4):667-672.

**28.** Shankar A, Klein R, Klein BE. The association among smoking, heavy drinking, and chronic kidney disease. *Am J Epidemiol*. 2006;164(3):263-271.

**29.** Zhang L, Zuo L, Xu G, et al. Community-based screening for chronic kidney disease among populations older than 40 years in Beijing. *Nephrol Dial Transplant*. 2007;22(4):1093-1099.

**30.** Shlipak MG, Katz R, Kestenbaum B, et al. Rate of kidney function decline in older adults. *Am J Nephrol*. 2009;30(3):171-178.

**31.** Shimizu Y, Maeda K, Imano H, et al. Chronic kidney disease and drinking status in relation to risks of stroke and its subtypes. *Stroke*. 2011;42(9):2531-2537.

**32.** Jafar TH, Qadri Z, Hashmi S. Prevalence of microalbuminuria and associated electrocardiographic abnormalities in an Indo-Asian population. *Nephrol Dial Transplant*. 2009;24(7):2111-2116.

**33.** Zhang QL, Koenig W, Raum E, et al. Epidemiology of chronic kidney disease. *Prev Med*. 2009; 48(2):122-127.

**34.** Parikh NI, Hwang S-J, Larson MG, et al. Chronic kidney disease as a predictor of cardiovascular disease (from the Framingham Heart Study). *Am J Cardiol*. 2008;102(1):47-53.

**35.** Cirillo M, Lanti MP, Menotti A, et al. Definition of kidney dysfunction as a cardiovascular risk factor. *Arch Intern Med*. 2008;168(6):617-624.

**36.** Hallan SI, Coresh J, Astor BC, et al. International comparison of the relationship of chronic kidney disease prevalence and ESRD risk. *J Am Soc Nephrol*. 2006;17(8):2275-2284.



**©2012 American Medical Association. All rights reserved.**

Downloaded From: http://jamanetwork.com/ on 05/21/2013

**37.** Noda H, Iso H, Irie F, et al. Low-density lipoprotein cholesterol concentrations and death due to intraparenchymal hemorrhage. *Circulation*. 2009; 119(16):2136-2145.
**38.** Bui AL, Katz R, Kestenbaum B, et al. Cystatin C and carotid intima-media thickness in asymptomatic adults. *Am J Kidney Dis*. 2009;53(3):389-398.
**39.** Roderick PJ, Atkins RJ, Smeeth L, et al. CKD and mortality risk in older people. *Am J Kidney Dis*. 2009; 53(6):950-960.
**40.** Astor BC, Hallan SI, Miller ER III, et al. Glomerular filtration rate, albuminuria, and risk of cardiovascular and all-cause mortality in the US population. *Am J Epidemiol*. 2008;167(10):1226-1234.
**41.** Nakayama M, Metoki H, Terawaki H, et al. Kidney dysfunction as a risk factor for first symptomatic stroke events in a general Japanese population—the Ohasama study. *Nephrol Dial Transplant*. 2007; 22(7):1910-1915.
**42.** Iseki K, Ikemiya Y, Iseki C, Takishita S. Proteinuria and the risk of developing end-stage renal disease. *Kidney Int*. 2003;63(4):1468-1474.
**43.** Iseki K, Kohagura K, Sakima A, et al. Changes in the demographics and prevalence of chronic kidney disease in Okinawa, Japan (1993 to 2003). *Hypertens Res*. 2007;30(1):55-62.
**44.** Hillege HL, Fidler V, Diercks GF, et al. Urinary albumin excretion predicts cardiovascular and noncardiovascular mortality in general population. *Circulation*. 2002;106(14):1777-1782.
**45.** Jassal SK, Kritz-Silverstein D, Barrett-Connor E. A prospective study of albuminuria and cognitive function in older adults. *Am J Epidemiol*. 2010;171 (3):277-286.
**46.** Howard VJ, Cushman M, Pulley L, et al. The reasons for geographic and racial differences in stroke study. *Neuroepidemiology*. 2005;25(3):135-143.
**47.** Kimm H, Yun JE, Jo J, Jee SH. Low serum bilirubin level as an independent predictor of stroke incidence. *Stroke*. 2009;40(11):3422-3427.
**48.** Wen CP, Cheng TY, Tsai MK, et al. All-cause mortality attributable to chronic kidney disease. *Lancet*. 2008;371(9631):2173-2182.
**49.** Ingelsson E, Sundström J, Lind L, et al. Low-grade albuminuria and the incidence of heart failure in a community-based cohort of elderly men. *Eur Heart J*. 2007;28(14):1739-1745.
**50.** Patel A, MacMahon S, Chalmers J, et al. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial). *Lancet*. 2007;370(9590):829-840.
**51.** Tonelli M, Jose P, Curhan G, et al. Proteinuria, impaired kidney function, and adverse outcomes in people with coronary disease. *BMJ*. 2006;332(7555):1426.
**52.** Jurkovitz CT, Qiu Y, Wang C, et al. The Kidney Early Evaluation Program (KEEP): program design and demographic characteristics of the population. *Am J Kidney Dis*. 2008;51(4)(suppl 2):S3-S12.
**53.** Lee BJ, Forbes K. The role of specialists in managing the health of populations with chronic illness. *BMJ*. 2009;339:b2395.
**54.** Ishani A, Grandits GA, Grimm RH, et al. Association of single measurements of dipstick proteinuria, estimated glomerular filtration rate, and hematocrit with 25-year incidence of end-stage renal disease in the multiple risk factor intervention trial. *J Am Soc Nephrol*. 2006;17(5):1444-1452.
**55.** Pavkov ME, Knowler WC, Hanson RL, et al. Predictive power of sequential measures of albuminuria for progression to ESRD or death in Pima Indians with type 2 diabetes. *Am J Kidney Dis*. 2008;51(5): 759-766.
**56.** Bilo HJ, Logtenberg SJ, Joosten H, et al. Modification of diet in renal disease and Cockcroft-Gault formulas do not predict mortality (ZODIAC-6). *Diabet Med*. 2009;26(5):478-482.
**57.** Wright JT Jr, Bakris G, Greene T, et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease. *JAMA*. 2002;288(19):2421-2431.
**58.** Levin A, Djurdjev O, Beaulieu M, Er L. Variability and risk factors for kidney disease progression and death following attainment of stage 4 CKD in a referred cohort. *Am J Kidney Dis*. 2008;52(4):661-671.
**59.** Landray MJ, Thambyrajah J, McGlynn FJ, et al. Epidemiological evaluation of known and suspected cardiovascular risk factors in chronic renal impairment. *Am J Kidney Dis*. 2001;38(3):537-546.
**60.** Perkins RM, Bucaloiu ID, Kirchner HL, et al. GFR decline and mortality risk among patients with chronic kidney disease. *Clin J Am Soc Nephrol*. 2011;6 (8):1879-1886.
**61.** Marks A, Fluck N, Prescott G, et al. Chronic diseases: studying and understanding outcome using routine data: chronic kidney disease (CKD), an example. *J Epidemiol Community Health*. doi:10.1136/jech .2011.142976j.8.
**62.** Keith DS, Nichols GA, Gullion CM, et al. Longitudinal follow-up and outcomes among a population with chronic kidney disease in a large managed care organization. *Arch Intern Med*. 2004;164(6):659-663.
**63.** Van Zuilen AD, Wetzels JF, Bots ML, et al. MASTERPLAN. *J Nephrol*. 2008;21(3):261-267.
**64.** Klahr S, Levey AS, Beck GJ, et al. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. *N Engl J Med*. 1994;330(13):877-884.
**65.** Kronenberg F, Kuen E, Ritz E, et al. Lipoprotein (a) serum concentrations and apolipoprotein(a) phenotypes in mild and moderate renal failure. *J Am Soc Nephrol*. 2000;11(1):105-115.
**66.** Moranne O, Froissart M, Rossert J, et al. Timing of onset of CKD-related metabolic complications. *J Am Soc Nephrol*. 2009;20(1):164-171.
**67.** Brenner BM, Cooper ME, de Zeeuw D, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *N Engl J Med*. 2001;345(12):861-869.
**68.** Jorsal A, Tarnow L, Frystyk J, et al. Serum adiponectin predicts all-cause mortality and end stage renal disease in patients with type I diabetes and diabetic nephropathy. *Kidney Int*. 2008;74(5):649-654.
**69.** Tangri N, Stevens LA, Griffith J, et al. A predictive model for progression of chronic kidney disease to kidney failure. *JAMA*. 2011;305(15):1553-1559.
**70.** Levey AS, Coresh J, Greene T, et al. Expressing the Modification of Diet in Renal Disease Study equation for estimating glomerular filtration rate with standardized serum creatinine values. *Clin Chem*. 2007; 53(4):766-772.
**71.** Pencina MJ, D'Agostino RB. Overall C as a measure of discrimination in survival analysis: model specific population value and confidence interval estimation. *Stat Med*. 2004;23(13):2109-2123.
**72.** Pencina MJ, D'Agostino RB Sr, D'Agostino RB Jr, Vasan RS. Evaluating the added predictive ability of a new marker. *Stat Med*. 2008;27(2):157-172.
**73.** Cook NR. Use and misuse of the receiver operating characteristic curve in risk prediction. *Circulation*. 2007;115(7):928-935.
**74.** Stevens LA, Claybon MA, Schmid CH, et al. Evaluation of the Chronic Kidney Disease Epidemiology Collaboration equation for estimating the glomerular filtration rate in multiple ethnicities. *Kidney Int*. 2011; 79(5):555-562.
**75.** Teo BW, Xu H, Wang D, et al. GFR estimating equations in a multiethnic Asian population. *Am J Kidney Dis*. 2011;58(1):56-63.
**76.** Levey AS, de Jong PE, Coresh J, et al. The definition, classification, and prognosis of chronic kidney disease. *Kidney Int*. 2011;80(1):17-28.
**77.** Tonelli M, Muntner P, Lloyd A, et al. Using proteinuria and estimated glomerular filtration rate to classify risk in patients with chronic kidney disease. *Ann Intern Med*. 2011;154(1):12-21.
**78.** Shlipak MG, Praught ML, Sarnak MJ. Update on cystatin C. *Curr Opin Nephrol Hypertens*. 2006; 15(3):270-275.
**79.** Astor BC, Levey AS, Stevens LA, et al. Method of glomerular filtration rate estimation affects prediction of mortality risk. *J Am Soc Nephrol*. 2009; 20(10):2214-2222.

**©2012 American Medical Association. All rights reserved.**



**Downloaded From: http://jamanetwork.com/ on 05/21/2013**