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Estimated Albumin Excretion Rate Versus Urine Albumin-Creatinine Ratio for the Assessment of Albuminuria: A Diagnostic Test Study From the Prevention of Renal and Vascular Endstage Disease (PREVEND) Study

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Abstract

Background—The albumin-creatinine ratio (ACR) in spot urine samples is recommended for albuminuria screening instead of measured albumin excretion rate (mAER) in 24-hour urine collections. In those with extremes of muscle mass, differences in spot urine creatinine may lead to under- or over-estimation of mAER by ACR. We hypothesized that calculating estimated AER (eAER) using spot ACR and estimated creatinine excretion rate (eCER) may improve albuminuria assessment.

Study Design—Diagnostic test study.

Setting & Participants—2711 community-living individuals from the general population of the Netherlands participating in the Prevention of Renal and Vascular Endstage Disease (PREVEND) Study.

Index Test—eAER was computed as the product of ACR and eCER. eCER was computed using three previously validated methods (Ix, Ellam, Walser).

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Supplementary Material

Table S1: Demographic characteristics of participants based on age

Table S2: Demographic characteristics of participants based on sex.

Note: The supplementary material accompanying this article (doi: _____) is available at www.ajkd.org

Reference Test—mAER, based on two 24-hour urine collections. Accuracy of the eAER and ACR were defined as the percentage of participants falling within 30% (P_{30}) of mAER.

Results—The mean age was 49 years, 46% were male, mean eGFR was 84 ± 15 ml/min/1.73 m² and median mAER was 7.2 (IQR, 5.4–11.0) mg/d. The mean measured CER was 1381 mg/d, the median ACR was 4.9 mg/g. Using the Ix equation, the median eAER was 6.4 mg/d. In the full cohort, eAER was more accurate and less biased compared to ACR (P_{30} : 48.9% vs. 33.6%; bias, –34.2% vs –14.1%, respectively). In subgroup analysis, improvement was most notable in the middle and highest weight tertiles and in males. Using the other methods for eCER produced similar results.

Limitations—Little ethnic heterogeneity and generally healthy cohort make extension of findings to other races and chronically ill uncertain.

Conclusions—In a large community-dwelling cohort, eAER was more accurate than ACR in assessing albuminuria.

Spot (untimed) urinary protein or albumin-creatinine ratios (ACRs) from first morning void specimens have largely replaced timed urine collections for proteinuria screening in outpatient settings. Several studies suggest that the spot ACR is a reasonably accurate indicator of albuminuria,^{1,2} and KDIGO guidelines now consider the ACR an acceptable first line screening test.³ The ACR uses urine creatinine in the denominator to correct for urine tonicity. However, creatinine excretion is also influenced by muscle mass, suggesting that the ACR may be prone to bias introduced by differences in muscle mass.⁴ Indeed, we and others have shown that older age, female gender, and lower body weight are associated with a higher ACR, independent of measured 24-hour urine albumin excretion, likely reflecting lower muscle mass in these groups, leading to lower urine creatinine, and thus higher ACR.^{5,6}

We have previously developed and validated an equation which incorporates age, gender, race and weight as proxies of muscle mass to calculate 24-hour estimated creatinine excretion rate (eCER).⁷ In the current study, we hypothesize that multiplying first morning void ACR by the eCER to determine the estimated albumin excretion rate (eAER) will attenuate the bias introduced by variable creatinine excretion between individuals, leading to a more accurate estimation of AER compared to spot first morning void ACR alone. To test this hypothesis, we examined the relationship of the eAER and ACR with timed urine collections among 2711 participants in the Prevention of Renal and Vascular Endstage Disease (PREVEND) Study and compared the eAER with the performance of previously developed eCER equations.

Methods

Participants

The PREVEND Study was designed to investigate the relationship of urinary albumin excretion with kidney and cardiovascular disease in a large cohort drawn from the general population of the city of Groningen, the Netherlands. Details of the protocol have been described elsewhere.^{8,9} In brief, all inhabitants of the city of Groningen aged 28–75 years

were sent a questionnaire and a vial to collect a first-morning-void urine sample. Urine albumin and creatinine were measured among the 40,856 (47.8%) who responded (Figure 1). Participants with type 1 diabetes mellitus and pregnant females were excluded. All subjects with a urinary albumin concentration ≥ 10 mg/L ($n = 7,768$) were invited to participate in PREVEND, and 6,000 consented and agreed. A randomly selected sample of subjects with a urinary albumin concentration of <10 mg/L ($n = 3,394$) was also invited, and 2,592 agreed. The PREVEND cohort constitutes therefore 8,952 participants, who were then asked to participate in a clinic visit that involved collecting 2 consecutive-day 24-hour urine samples. The PREVEND Study has been approved by the local ethics committee and was performed in accordance with Declaration of Helsinki guidelines.

For this analysis, all 2592 participants with urine albumin < 10 mg/L on the first morning void specimen were included. In addition, we included a computer-generated random sample of 828 individuals who had urine albumin concentration ≥ 10 mg/L, leading to a total of 3420 participants. This number of individuals was chosen to reconstitute a study sample with urine albumin concentrations representative of the 40,856 total respondents from Groningen. We excluded those participants with missing spot urine albumin or creatinine data ($n=709$). The remaining 2711 participants comprised the study sample for this analysis.

All participants completed a questionnaire regarding health, demographic and family history. Blood pressure measurements, anthropometric data (height, weight) and fasting venous blood samples were collected. Participants were provided with thorough written instructions on collecting two 24-hour urine samples on two consecutive days, and were instructed to store urine in polyethylene containers at 4°C for no more than 4 days prior to study visit, to refrain from urine collection if suffering from an intercurrent illness and to avoid heavy exercise during urine collection.

Measurements and Definitions

Urine albumin was determined in first-morning void and 24-hour specimens by nephelometry (BN II, Dade Behring Diagnostic, Marburg, Germany), with intra-assay and inter-assay coefficients of variation (CVs) $< 4.3\%$ and 4.4% , respectively. There was a median of 85 (interquartile range [IQR], 62–111) days between spot urine testing and 24-hour collections. Urinary creatinine was assessed by Kodak Ektachem dry chemistry (Eastman Kodak, Rochester, NY). Intra-assay and interassay CVs were 0.9% and 2.9% , respectively. ACR was calculated in the first morning-void sample, provided before enrollment. Measured AER (mAER) was calculated as the mean value from the two 24-hour urine collections, and was considered to be the gold standard metric of albuminuria for our analysis. Serum creatinine concentration was measured by Kodak Ektachem dry chemistry, an automatic enzymatic method. Estimated GFR (eGFR) was calculated by the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) creatinine equation.¹⁰ Chronic kidney disease was defined as an eGFR < 60 ml/min/1.73m².³

Measured creatinine excretion rate (mCER; in mg/d) was calculated as the mean of urinary creatinine concentration from two 24-hour urine collections multiplied by the 24-hour urine volume. The eCER (in mg/d) was calculated using the previously validated 4-variable

equation⁷ and is identified as $eCER_{Ix}$ herein. For comparison, we calculated $eCER$ using two other equations and evaluated the accuracy, precision, and bias. The first equation was recently derived by Ellam and colleagues¹¹ and incorporates race, gender, and age, notably without the use of weight. This equation was derived using data from the MDRD (Modification of Diet in Renal Disease) Study cohort and validated in the CRIC (Chronic Renal Insufficiency Cohort) and DCCT (Diabetes Control and Complications Trial) cohorts. We also performed the analysis using a well known creatinine excretion equation derived by Walser¹² using race, gender, age, and weight. These formulae are summarized in Box 1.

Statistical Analysis

Subjects were divided into tertiles based on weight and age, and patient characteristics were compared between groups. Differences across tertiles were compared using ANOVA for continuous variables and the chi square test for categorical variables. Subjects were also compared based on gender, and differences across groups were compared using t-test for normally distributed variables, Mann Whitney U test for skewed variables, or chi square test, as appropriate. Data were expressed as mean $\pm$ standard deviation when normally distributed or as median (IQR) when the distribution was skewed.

We calculated $eAER$ by multiplying the ACR by the $eCER$ computed from the Ix , Ellam, and Walser equations, yielding $eAER_{Ix}$, $eAER_{Ellam}$, and $eAER_{Walser}$, respectively. We compared accuracy by examining the percentage of participants with an $eAER$ falling within 20% (P_{20}) and 30% (P_{30}) of $mAER$. Bias was calculated as the median and percentage difference between the $mAER$ and the ACR , $eAER_{Ix}$, $eAER_{Ellam}$, and $eAER_{Walser}$, with precision calculated as the 95% limits of agreement about the difference. We calculated 95% confidence limits of the median using distribution-free confidence limits. This analysis was performed in the full cohort, among age and weight tertiles, and stratified by gender.

Direct comparison was made between ACR and $eAER$ in order to compare accuracy, despite the different units of measurement. While ACR is expressed in mg/g, $eAER$ and $mAER$ are expressed in mg/d. We considered this comparison valid nonetheless, because in order to utilize ACR , one has to accept the assumption that average creatinine excretion is approximately 1 g/d, and because clinically measured ACR is considered a reliable estimate of $mAER$.

All analyses were conducted using SAS statistical software version 9.3 (SAS Institute Inc). Two sided p-values < 0.05 were considered statistically significant for all analyses.

Results

The mean age of the 2711 person study sample was 49 (range, 28–75) years, and 46% were male. The median $mAER$ was 7.2 (IQR, 5.4–11.0) mg/d, and median ACR was 4.9 mg/g (IQR, 3.6–7.7) mg/g. The mean $eGFR$ was 84 ± 15 ml/min/1.73 m² and 5.6% had an $eGFR < 60$ ml/min/1.73 m². Mean body weight was 77 ± 13 kg, and mean $mCER$ was 1381 ± 403 mg/d.

Baseline characteristics of the participants by weight tertiles are shown in Table 1. Participants with higher weight were older, more frequently male, and had higher mCER, eCER, and mAER. As expected, while the median ACR level was similar across weight tertiles, a graded increase in eAER_{IX} was apparent with increasing weight. A similar comparison of baseline characteristics by age and sex can be found in Tables S1 and S2 (provided as online supplementary material).

The accuracy and bias of the ACR and various AER estimation methods in the full cohort and various subgroups are compared in Tables 2 and 3. For accuracy, we compared the percentage of individuals whose eAER by each method fell within 30% of the mAER. In the full cohort, the eAER calculated by any method improved accuracy at 30% (P_{30} : 33.6%, 48.9%, 48.3%, 48.8%, for ACR, eAER_{IX}, eAER_{Ellam}, and eAER_{Walser}, respectively). Accuracy improved across all age tertiles, among the middle and highest weight tertiles, and in males. Notably, the magnitude of improvement in accuracy was greatest among those with higher weights, younger age, and males. Those in the lowest weight tertile and females did not show an improvement in accuracy.

The ACR underestimated mAER in all subgroups (tables 4 and 5), with the highest degree of underestimation bias among males and the highest weight tertile. The eAER using all methods improved accuracy in most subgroups, although there was little to no improvement again among females and those in the lowest weight tertile.

Discussion

We demonstrate that computing eAER using various methods improved accuracy of assessment of albuminuria in community-living individuals with low-grade albuminuria. This improvement appeared most pronounced in groups with higher average muscle mass (males, younger, higher body weight), suggesting that ACR may systematically underperform in those with higher mCER values. This lends credence to the practice of using age- and gender-adjusted cutoffs for albuminuria, and suggests that future studies should determine if weight-based cutoffs might also improve diagnostic accuracy, although adoption of the proposed methods for computing eCER would render separate cut-offs unnecessary. Our findings provide a proof of concept demonstrating that estimating AER using ACR and simple eCER equations derived only from demographics may improve accuracy of albuminuria assessment using spot specimens.

The PREVEND cohort represents a community-dwelling cohort, and among this group there did not appear to be any substantial differences in the improvement in precision and accuracy among the three eCER equations assessed. When compared among the participants of CRIC,¹¹ eAER_{IX} and eAER_{Ellam} both improved accuracy over ACR alone, although eAER_{Ellam} had less overall bias, suggesting that among participants with kidney disease, eAER_{Ellam} may outperform eAER_{IX}. Despite the absence of the weight term in the Ellam equation, among all weight tertiles in PREVEND, eAER_{Ellam} performed comparably to eAER_{IX}. This may make the Ellam equation more straightforward for estimating AER in clinical practice when weights are not routinely available or easily accessible, and ultimately would aid in the use of automating reporting of eAER values. However, the relative

importance of weight as a variable in CER estimating equations may be greater in populations with greater rates of obesity or malnutrition; this could be tested in other clinical populations.

The presence of albuminuria is a well-established risk factor for adverse cardiovascular and renal events, which supports continued efforts to improve accuracy of estimation. Therefore, improving the estimation of AER may ultimately have clinical and public health implications. Prior work in the PREVEND cohort has demonstrated that participants with an elevated ACR but without elevated mAER do not appear to have the same risk for adverse cardiovascular outcomes as participants with elevated mAER.⁵ We have previously shown that female sex, older age, and lower weight were associated with higher spot ACR at the same level of mAER.⁵ Similarly, Cirillo et al^{13,14} demonstrated that persons with high ACR but without high mAER had a lower prevalence of coronary heart disease. These studies emphasize the impact of low or high CER on albuminuria assessment, and the bias introduced by differences in CER, as well as the potential prognostic implications of this bias.

We had limited power to evaluate persons with overt proteinuria in this cohort. Consequently calculating eAER did not provide a significant change in albuminuria categorization (normal vs microalbuminuria vs macroalbuminuria). However, since albuminuria is becoming increasingly viewed as a continuous marker of disease risk, even small improvements may have prognostic importance. Many prior studies,^{15,16,17} including studies from PREVEND,^{18,19} have established that greater albuminuria, even in a range once considered normal, is associated with increased risk for cardiovascular events and mortality. This is reflected in the latest KDIGO guidelines,³ which no longer endorse use of the term “microalbuminuria.” Consequently, more accurate assessment of albuminuria may be important in studies evaluating large populations and eventually in individual risk prediction. However, we studied a community-living population, most of whom were middle aged and healthy. Future studies are required to determine whether our findings extend to persons at extremes of body weight, and might yield more accurate estimates of cardiovascular risk and renal risk prognostication.

Strengths of this study include the large, well characterized population, the availability of spot morning urine samples followed by two carefully collected 24-hour urine measurements, and the wide range of creatinine excretion. This study also has important limitations. The median mAER was 7.2 mg/d; future studies are needed to elucidate the effect of computing eAER in cohorts with higher mAER values. We evaluated a European cohort, and consequently there was little racial/ethnic heterogeneity. Race is known to influence muscle mass and creatinine excretion, and extension of our findings to other races is uncertain. We evaluated a middle-aged, predominantly healthy community-living population. Whether the findings generalize to hospitalized, institutionalized, and chronically ill patients, who may have more marked differences in muscle mass relative to the general population, is also unknown.

In conclusion, various methods of calculating eAER using eCER equations more accurately reflect mAER than ACR alone among community-living individuals, and may help improve

assessment of albuminuria in research studies and in clinical practice, when only spot specimens are available. The improved accuracy of eAER was consistent among those with higher mCER values. Future studies are required to determine whether eAER improves risk prediction for CVD and kidney disease outcomes relative to the ACR and whether these results generalize to infirm and/or hospitalized patients, where extremes of muscle mass may be more common.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Hutchison AS, O'Reilly DS, MacCuish AC. Albumin excretion rate, albumin concentration, and albumin/creatinine ratio compared for screening diabetics for slight albuminuria. *Clinical Chemistry*. 1988; 34:2019–2021. [PubMed: 3168213]
2. Price CP, Newall RG, Boyd JC. Use of Protein:Creatinine Ratio Measurements on Random Urine Samples for Prediction of Significant Proteinuria: A Systematic Review. *Clinical Chemistry*. 2005; 51:1577–1586. [PubMed: 16020501]
3. Stevens PE, Levin A. Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Guideline Development Work Group Members. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. *Ann. Intern. Med.* 2013; 158:825–830. [PubMed: 23732715]
4. Ellam TJ. Albumin:creatinine ratio--a flawed measure? The merits of estimated albuminuria reporting. *Nephron Clin Pract.* 2011; 118:c324–c330. [PubMed: 21293155]
5. Carter CE, et al. Influence of Urine Creatinine on the Relationship between the Albumin-to-Creatinine Ratio and Cardiovascular Events. *Clinical Journal of the American Society of Nephrology: CJASN*. 2012
6. Mattix HJ, Hsu C, Shaykevich S, Curhan G. Use of the albumin/creatinine ratio to detect microalbuminuria: implications of sex and race. *J. Am. Soc. Nephrol.* 2002; 13:1034–1039. [PubMed: 11912263]
7. Ix JH, et al. Equations to estimate creatinine excretion rate: the CKD epidemiology collaboration. *Clin J Am Soc Nephrol.* 2011; 6:184–191. [PubMed: 20966119]
8. Heerspink HJL, et al. Albuminuria Assessed From First-Morning-Void Urine Samples Versus 24-Hour Urine Collections as a Predictor of Cardiovascular Morbidity and Mortality. *Am. J. Epidemiol.* 2008; 168:897–905. [PubMed: 18775924]
9. Pinto-Sietsma SJ, et al. Urinary albumin excretion is associated with renal functional abnormalities in a nondiabetic population. *J. Am. Soc. Nephrol.* 2000; 11:1882–1888. [PubMed: 11004219]
10. Levey AS, et al. A new equation to estimate glomerular filtration rate. *Ann. Intern. Med.* 2009; 150:604–612. [PubMed: 19414839]
11. Fotheringham J, Campbell M, Ellam T. Estimated Albumin Excretion Rate Versus Urine Albumin-Creatinine Ratio for the Estimation of Measured Albumin Excretion Rate: Derivation and Validation of an Estimated Albumin Excretion Rate Equation. *Am J Kidney Dis.* **In Press**.

12. Walser M. Creatinine excretion as a measure of protein nutrition in adults of varying age. *JPEN J Parenter Enteral Nutr.* 1987; 11:73S–78S. [PubMed: 3312696]
13. Cirillo M, Laurenzi M, Mancini M, Zanchetti A, De Santo NG. Low muscular mass and overestimation of microalbuminuria by urinary albumin/creatinine ratio. *Hypertension.* 2006; 47:56–61. [PubMed: 16344360]
14. Cirillo M, et al. Cohort Profile: The Gubbio Population Study. *Int J Epidemiol.* 2013
15. Arnlöv J, et al. Low-grade albuminuria and incidence of cardiovascular disease events in nonhypertensive and nondiabetic individuals: the Framingham Heart Study. *Circulation.* 2005; 112:969–975. [PubMed: 16087792]
16. Zeeuw D, de, Parving H-H, Henning RH. Microalbuminuria as an Early Marker for Cardiovascular Disease. *JASN.* 2006; 17:2100–2105. [PubMed: 16825327]
17. Knight EL, Curhan GC. Albuminuria: moving beyond traditional microalbuminuria cut-points. *Curr. Opin. Nephrol. Hypertens.* 2003; 12:283–284. [PubMed: 12698066]
18. Hillege HL, et al. Urinary albumin excretion predicts cardiovascular and noncardiovascular mortality in general population. *Circulation.* 2002; 106:1777–1782. [PubMed: 12356629]
19. Hillege HL, et al. Microalbuminuria is common, also in a nondiabetic, nonhypertensive population, and an independent indicator of cardiovascular risk factors and cardiovascular morbidity. *Journal of Internal Medicine.* 2001; 249:519–526. [PubMed: 11422658]

Box 1. Measured and estimated values used in analysis

Measured Creatinine Clearance

$$mCCr \text{ (mL/min)} = \text{Urine Cr (mg/dL)} * 24\text{-h urine volume (dL)} / \text{serum Cr (mg/dL)} * 1440 \text{ (min/d)}$$

Measured Creatinine Excretion Rate

$$mCER \text{ (mg/d)} = \text{Urine Cr (mg/dL)} * 24\text{-h urine volume (mL)} / 100$$

Estimated Albumin Excretion Rate

$$eAER \text{ (mg/d)} = ACR * eCER$$

Ix⁷ Equation for Estimated Creatinine Excretion Rate

$$eCER_{Ix} \text{ (mg/d)} = 879.89 + 12.51 * [\text{weight (kg)} - 6.19] * \text{age} + 34.51 \text{ (if black)} - 379.42 \text{ (if female)}$$

Ellam¹¹ Equation for Estimated Creatinine Excretion Rate

$$eCER_{Ellam} \text{ (mg/d)} =$$

$$\text{Male/Black: } 1413.9 + (23.2 * \text{age}) - (0.3 * \text{age}^2)$$

$$\text{Female/Black: } 1148.6 + (15.6 * \text{age}) - (0.3 * \text{age}^2)$$

$$\text{Male/Nonblack: } 1307.3 + (23.1 * \text{age}) - (0.3 * \text{age}^2)$$

$$\text{Female/Nonblack: } 1051.3 + (5.3 * \text{age}) - (0.1 * \text{age}^2)$$

Walser¹² Equation for Estimated Creatinine Excretion Rate

$$eCER_{Walser} \text{ (mg/d)}$$

$$\text{Male: } (28.2 - 0.172 * \text{age}) * \text{weight (kg)}$$

$$\text{Female: } (21.9 - 0.115 * \text{age}) * \text{weight (kg)}$$

Figure 1.
Participant Selection for the Prevention of Renal and Vascular Endstage Disease (PREVEND) cohort

Table 1

Demographic characteristics of participants overall and by weight tertiles

Characteristic	Overall (N = 2711)	Lowest Weight (<70.6 kg; n = 917)	Middle Weight (70.6–82 kg; n = 910)	Highest Weight (>82 kg; n = 884)	P*
Age (y)	49 ± 12	47 ± 12	50 ± 13	50 ± 12	<0.001
Male sex	45.6	14.0	52.2	71.5	<0.001
Body mass index (kg/m ²)	25.8 ± 3.9	22.8 ± 2.3	25.5 ± 2.5	29.3 ± 3.8	<0.001
Serum creatinine (mg/dl)	0.94 ± 0.16	0.87 ± 0.13	0.95 ± 0.16	0.99 ± 0.16	<0.001
eGFR (ml/min/1.73 m ²)	83.6 ± 15.2	84.5 ± 15.1	83.1 ± 15.7	83.1 ± 14.7	0.08
eGFR < 60 ml/min/1.73 m ²	5.6	4.4	6.6	5.9	0.1
Spot urine creatinine (mg/dl)	125 ± 60	115 ± 58	125 ± 61	136 ± 60	<0.001
Urine volume (ml)	1648 ± 550	1668 ± 600	1640 ± 516	1637 ± 529	0.4
mAER** (mg/d)	7.2(5.4–11.0)	6.5(5.1–9.9)	7.0(5.5–10.6)	8.0(6.0–13.0)	<0.001
Albuminuria					
30–300 mg/d	6	3.8	6	8.4	<0.001
>300 mg/d	0.5	0	0.5	1	0.01
mCER (mg/d)	1381 ± 403	1130 ± 258	1373 ± 346	1651 ± 409	<0.001
eCER (mg/d)	1335 ± 307	1052 ± 170	1347 ± 218	1615 ± 220	<0.001
ACR (mg/g)	4.9(3.6–7.7)	5.1(3.7–7.4)	4.8(3.6–7.8)	4.8(3.5–7.9)	0.1
eAER _{ix} (mg/d)	6.4(4.7–10.2)	5.2(3.9–7.8)	6.5(4.9–10.4)	7.8(5.7–12.7)	<0.001
eAER _{Ellam} (mg/d)	6.4(4.7–10.0)	5.7(4.2–8.7)	6.7(4.8–10.1)	7.2(5.2–11.6)	0.009
eAER _{Waiser} (mg/d)	6.6(4.8–10.6)	5.3(4.0–8.0)	6.6(5.1–10.6)	8.2(6.0–13.2)	0.002

Note: Values for categorical variables are given as percentages; values for continuous variables are given as mean ± standard deviation or median [interquartile range]. Conversion factor for serum creatinine in mg/dL to μmol/L, ×88.4.

eGFR, estimated glomerular filtration rate; mAER, measured albumin excretion rate; mCER = measured creatinine excretion rate; eCER = estimated creatinine excretion rate. ACR = albumin-creatinine ratio. eAER = estimated albumin excretion rate.

* P-value for comparison across weight tertile groups using analysis of variance.

** Determined from average of two 24-hour urine collections.

Table 2
Performance of the creatinine excretion equations in full cohort in terms of accuracy and bias

	P ₂₀ (95% CI)	P ₃₀ (95% CI)	Median Bias (95% CI)*	Median Percent Bias (95% CI)*	95% Limits of Agreement**
ACR	21.2(19.6 to 22.7)	33.6(31.8 to 35.3)	-2.3(-2.5 to -2.2)	-34.2 (-35.7 to -33.2)	5.9 to -20.3
eAER _{ix}	33.0(31.2 to 34.7)	48.9(46.9 to 50.7)	-1.0(-1.1 to -0.8)	-14.1(-15.9 to -12.4)	11.2 to -15.0
eAER _{Ellam}	32.9(31.2 to 34.8)	48.3(46.4 to 50.2)	-0.9(-1.0 to -0.8)	-13.3(-15.3 to -11.6)	11.1 to -15.0
eAER _{Walser}	33.3(31.5 to 35.0)	48.8(46.9 to 50.7)	-0.8(-0.9 to -0.7)	-11.3(-13.3 to -9.6)	11.7 to -15.0

Note. N=2,711. Median bias expressed in mg/g.

Abbreviations and definitions: ACR = albumin-creatinine ratio; CI, confidence interval; eAER = estimated albumin excretion rate; P₂₀ and P₃₀, percentage of participants with eAER falling within 20% and 30%, respectively, of measured albumin excretion rate.

* Of the median,

** Of the median bias.

Table 3

Accuracy of the creatinine excretion equations in subgroups

	Full Cohort (N=2711)	Lowest Weight (<70.6 kg; n = 917)	Middle Weight (70.6–82 kg; n = 910)	Highest Weight (>82 kg; n = 884)	Lowest Age (28–41 y; n = 863)	Middle Age (42–53 y; n = 924)	Highest Age (54–75 y; n = 924)	Male (n=1235)	Female (n=1476)
ACR	33.6(31.8 to 35.3)	41.2(38.0 to 44.4)	33.6(30.6 to 36.7)	25.6(22.7 to 28.4)	30.6(27.5 to 33.7)	31.7(28.7 to 34.7)	38.2(35.1 to 41.3)	24.9(22.5 to 27.4)	40.8(38.3 to 43.3)
eAER _K	48.9(46.9 to 50.7)	44.5(41.2 to 47.8)	50.5(47.3 to 53.9)	51.6(48.2 to 54.9)	51.7(48.3 to 55.1)	47.9(44.7 to 51.2)	47.0(43.8 to 50.4)	52.7(49.8 to 55.5)	45.7(43.1 to 48.3)
eAER _{Elliam}	48.3(46.4 to 50.2)	46.6(43.3 to 50.0)	50.7(47.4 to 53.9)	47.7(44.4 to 51.0)	49.8(46.4 to 53.1)	48.4(45.2 to 51.6)	47.0(43.8 to 50.2)	53.5(50.7 to 56.3)	44.0(41.4 to 46.5)
eAER _{Walser}	48.8(46.9 to 50.7)	45.4(42.1 to 48.7)	50.2(46.9 to 53.5)	50.8(47.5 to 54.1)	51.0(47.6 to 54.4)	48.4(45.1 to 51.7)	47.1(43.8 to 50.4)	50.4(47.5 to 53.2)	47.4(44.9 to 50.0)

Note: Values are given as P30 (95% confidence interval).

Abbreviations and definitions: ACR = albumin-creatinine ratio; eAER = estimated albumin excretion rate; P30, percentage of participants with eAER falling within 30% of measured albumin excretion rate.

Table 4

Median bias using the creatinine excretion equations among subgroups

	Lowest Weight (<70.6 kg; n = 917)	Middle Weight (70.6-82 kg; n = 910)	Highest Weight (>82 kg; n = 884)	Lowest Age (28-41 y; n = 863)	Middle Age (42-53 y; n = 924)	Highest Age (54-75 y; n = 924)	Male (n=1235)	Female (n=1476)
ACR	-1.6(-1.8 to -1.4)	-2.4 (-2.6 to -2.1)	-3.2(-3.4 to -3.0)	-2.4(-2.6 to -2.2)	-2.4(-2.7 to -2.2)	-2.1(-2.3 to -1.8)	-3.2(-3.4 to -3.0)	-1.6(-1.7 to -1.4)
eAER _K	-1.3(-1.5 to -1.2)	-0.7(-1.0 to -0.5)	-0.6(-0.9 to -0.4)	-0.9(-1.2 to -0.7)	-1.0(-1.3 to -0.8)	-0.9(-1.1 to -0.7)	-0.6(-0.8 to -0.4)	-1.2(-1.4 to -1.0)
eAER _{Ellam}	-0.9(-1.1 to -0.7)	-0.7(-0.9 to -0.5)	-1.2(-1.5 to -0.9)	-0.9(-1.1 to -0.6)	-0.9(1.2 to -0.7)	-0.9(-1.2 to -0.7)	-0.3(-0.6 to -0.1)	-1.3(-.5 to -1.1)
eAER _{Wälsér}	-1.3(-1.4 to -1.1)	-0.6(-0.9 to -0.4)	-0.2(-0.5 to -0.1)	-0.5(-0.8 to -0.3)	-0.8(-1.0 to -0.6)	-0.9(-1.2 to -0.7)	-0.6(-0.8 to -0.4)	-0.9(-1.1 to -0.8)

Note: Values are given as median bias (95% confidence interval of the median) in mg/g.

Abbreviations : ACR = albumin-creatinine ratio; eAER = estimated albumin excretion rate.

Table 5

Median percent bias using the creatinine excretion equations among subgroups

	Lowest Weight (<70.6 kg; n= 917)	Middle Weight (70.6-82 kg; n = 910)	Highest Weight (>82 kg; n = 884)	Lowest Age (28-41 y; n = 863)	Middle Age (42-53 y; n = 924)	Highest Age (54-75 y; n = 924)	Male (n=1235)	Females (n=1476)
ACR	-26(-28.2 to -22.5)	-34(-36.4 to -31.7)	-42.7(-44.9 to -40.9)	-37.7(-39.8 to -34.7)	-36.0(-38.6 to -33.7)	-27.8(-30.9 to -24.4)	-42.9(-44.7 to -41.4)	-25.7(-27.6 to -22.7)
eAER _K	-21.4(-24.2 to -18.7)	-11.7(-14.5 to -8.7)	-9.2(-11.9 to -4.9)	-14.5(-17.5 to -11.2)	-15.7(-18.2 to -12.9)	-12.7(-15.3 to -9.4)	-8.9(-11.2 to -6.3)	-19.0(-21.1 to -16.7)
eAER _{Ellam}	-14.5(-17.4 to -11.2)	-10.7(-13.0 to -7.8)	-16.2(-18.1 to -12.2)	-14.0(-16.7 to -10.5)	-13.7(-17.1 to -10.6)	-12.5(-15.9 to -9.4)	-4.4(-7.7 to -1.4)	-20.7(-23.1 to -18.2)
eAER _{Walser}	-20.4(-22.3 to -17.1)	-9.7(-12.3 to -5.7)	-3.1(-6.5 to 0.7)	-8.5(-11.4 to -4.1)	-12.7(-15.4 to -9.3)	-13.4(-16.3 to -10.1)	-7.7(-10.0 to -4.7)	-14.7(-16.6 to -12.1)

Note: Values are given as median percent bias (95% confidence interval of the median).

Abbreviations : ACR = albumin-creatinine ratio; eAER = estimated albumin excretion rate.

Measured Creatinine Clearance

$$mCCr \text{ (mL/min)} = \text{Urine Cr (mg/dl)} * 24\text{-h urine volume (dl)} / \text{serum Cr (mg/dl)} * 1440 \text{ (min/d)}$$

Measured Creatinine Excretion Rate

$$mCER \text{ (mg/d)} = \text{Urine Cr (mg/dl)} * 24\text{-h urine volume (ml)} / 100$$

Estimated Albumin Excretion Rate

$$eAER \text{ (mg/d)} = ACR * eCER$$

Ix⁷ Equation for Estimated Creatinine Excretion Rate

$$eCER_{Ix} \text{ (mg/d)} = 879.89 + 12.51 * [\text{weight (kg)} - 6.19] * \text{age} + 34.51 \text{ (if black)} - 379.42 \text{ (if female)}$$

Ellam¹¹ Equation for Estimated Creatinine Excretion Rate

$$eCER_{Ellam} \text{ (mg/d)} =$$

$$\text{Male/Black: } 1413.9 + (23.2 * \text{age}) - (0.3 * \text{age}^2)$$

$$\text{Female/Black: } 1148.6 + (15.6 * \text{age}) - (0.3 * \text{age}^2)$$

$$\text{Male/Nonblack: } 1307.3 + (23.1 * \text{age}) - (0.3 * \text{age}^2)$$

$$\text{Female/Nonblack: } 1051.3 + (5.3 * \text{age}) - (0.1 * \text{age}^2)$$

Walser¹² Equation for Estimated Creatinine Excretion Rate

$$eCER_{Walser} \text{ (mg/d)}$$

$$\text{Male: } (28.2 - 0.172 * \text{age}) * \text{weight (kg)}$$

$$\text{Female: } (21.9 - 0.115 * \text{age}) * \text{weight (kg)}$$