

Conversion of Urine Protein–Creatinine Ratio or Urine Dipstick to Urine Albumin–Creatinine Ratio for Use in Chronic Kidney Disease Screening and Prognosis

An Individual Participant–Based Meta-analysis

Keiichi Sumida, MD, MPH, PhD*; Girish N. Nadkarni, MD, MPH*; Morgan E. Grams, MD, PhD; Yingying Sang, MSc; Shoshana H. Ballew, PhD; Josef Coresh, MD, PhD; Kunihiro Matsushita, MD, PhD; Aditya Surapaneni, PhD; Nigel Brunskill, MD, PhD; Steve J. Chadban, MD, PhD; Alex R. Chang, MD, MS; Massimo Cirillo, MD; Kenn B. Daratha, PhD; Ron T. Gansevoort, MD, PhD; Amit X. Garg, MD, PhD; Licia Iacoviello, MD, PhD; Takamasa Kayama, MD, PhD; Tsuneo Konda, MD, PhD; Csaba P. Kovcsdy, MD; James Lash, MD; Brian J. Lee, MD; Rupert Major, MD, PhD; Marie Metzger, PhD; Katsuyuki Miura, MD, PhD; David M.J. Naimark, MD, MSc; Robert G. Nelson, MD, PhD; Simon Sawhney, MD, PhD; Nikita Stempniewicz, MSc; Mila Tang, MSc; Raymond R. Townsend, MD; Jamie P. Traynor, MD; José M. Valdivielso, PhD; Jack Wetzels, MD, PhD; Kevan R. Polkinghorne, MBChB, PhD†; and Hiddo J.L. Heerspink, PhD‡; for the Chronic Kidney Disease Prognosis Consortium‡

Background: Although measuring albuminuria is the preferred method for defining and staging chronic kidney disease (CKD), total urine protein or dipstick protein is often measured instead.

Objective: To develop equations for converting urine protein-creatinine ratio (PCR) and dipstick protein to urine albumin-creatinine ratio (ACR) and to test their diagnostic accuracy in CKD screening and staging.

Design: Individual participant-based meta-analysis.

Setting: 12 research and 21 clinical cohorts.

Participants: 919 383 adults with same-day measures of ACR and PCR or dipstick protein.

Measurements: Equations to convert urine PCR and dipstick protein to ACR were developed and tested for purposes of CKD screening (ACR, ≥ 30 mg/g) and staging (stage A2: ACR, 30 to 299 mg/g; stage A3: ACR, ≥ 300 mg/g).

Results: Median ACR was 14 mg/g (25th to 75th percentile of cohorts, 5 to 25 mg/g). The association between PCR and ACR was inconsistent for PCR values less than 50 mg/g. For higher PCR values, the PCR conversion equations demonstrated moderate sensitivity (91%, 75%, and 87%) and specificity (87%, 89%, and 98%) for screening (ACR, >30 mg/g) and classification into stages A2 and A3, respectively. Urine dipstick categories of trace

or greater, trace to +, and ++ for screening for ACR values greater than 30 mg/g and classification into stages A2 and A3, respectively, had moderate sensitivity (62%, 36%, and 78%) and high specificity (88%, 88%, and 98%). For individual risk prediction, the estimated 2-year 4-variable kidney failure risk equation using predicted ACR from PCR had discrimination similar to that of using observed ACR.

Limitation: Diverse methods of ACR and PCR quantification were used; measurements were not always performed in the same urine sample.

Conclusion: Urine ACR is the preferred measure of albuminuria; however, if ACR is not available, predicted ACR from PCR or urine dipstick protein may help in CKD screening, staging, and prognosis.

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 * Drs. Sumida and Nadkarni share first authorship.
 † Drs. Polkinghorne and Heerspink share last authorship.
 ‡ For members of the Chronic Kidney Disease Prognosis Consortium, see the Appendix (available at Annals.org).

Increased urinary protein levels predict adverse kidney and cardiovascular outcomes in various populations and settings (1–5). Albumin is the most abundant protein in the urine in most types of proteinuric kidney disease, and its laboratory assay was recently standardized (6, 7). Thus, measurement of albuminuria is considered the gold standard for quantifying urinary protein. Clinical practice guidelines recommend screening for and monitoring of albuminuria and incorporate increased levels of albuminuria into the definition and staging of chronic kidney disease (CKD) (8–12). In addition, several tools for assessing absolute risk for end-stage kidney disease, cardiovascular disease, and death require albuminuria as an input (13–16).

Rather than measuring albuminuria, many providers and research studies quantify urinary protein by using a total protein assay or semiquantitative urine dip-

stick. These methods may be used because of lower cost, tradition, or other considerations; however, they are probably less precise than those that measure urine albumin directly. Total protein assays are not standardized, and their sensitivity for different protein components may vary (17). Dipstick protein measures provide only a gross categorization of urine protein levels (17). Furthermore, whereas urine protein and urine albumin tests typically quantify a 24-hour collection, or are stan-

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standardized to urine creatinine to estimate 24-hour excretion, dipstick protein measures are obtained at a single time point and do not correct for dilution.

The Kidney Disease Improving Global Outcomes (KDIGO) guideline notes that if albuminuria measurement is not available, urine reagent strip results may be substituted, with dipstick protein values of “trace to +” and “+ or greater” assigned to albuminuria categories of 30 to 299 mg/g and 300 mg/g and higher, respectively (12). Likewise, protein-creatinine ratio (PCR) values of 150 to 500 mg/g and greater than 500 mg/g may be assigned to the respective albuminuria categories (12). Single studies have examined the relationship between PCR or urine dipstick protein categories and urine albumin-creatinine ratio (ACR) (12, 18–28). However, the diagnostic performance of these thresholds and the consistency of relationships across several cohorts and health systems have not been established. The aim of this study was to develop equations to convert urine PCR and dipstick protein to ACR and to evaluate their performance for use in efforts to screen for, categorize, and risk stratify patients with CKD.

METHODS

Participating Cohorts

The Chronic Kidney Disease Prognosis Consortium (CKD-PC) includes study cohorts from around the world containing information on kidney measures. The CKD-PC's design was described previously (29); in brief, cohorts were initially identified in 2009 through a literature search using key search terms. The consortium continues to grow and remains open (criteria for joining are available at www.ckdpc.org). The selection of cohorts for this report is described in **Supplemental Appendix 1** (available at Annals.org). For this article, cohorts are categorized by whether they contain participant information primarily from data collected from structured research cohort visits or as part of clinical care (**Supplemental Appendix 1**) (29). For the current study, cohorts were included if they contained at least 200 participants with measures of ACR and PCR or dipstick protein on the same day, and if they contained a full range of ACR values (both <300 mg/g and ≥300 mg/g). The type of cohort was not restricted; thus, included cohorts could be prospective studies, clinical trials, or administrative health care data sets. Likewise, there was no restriction on type of laboratory assay. All analyses in the present study were restricted to participants aged 18 years or older. This study was approved for use of deidentified data and the need for informed consent was waived by the institutional review board at Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland.

Procedures

Methods of collecting urine to assess ACR, PCR, and urine dipstick varied by eligible cohort and included collections of morning spot urine, random spot urine, and 24-hour urine (**Supplemental Appendix 1**). Estimated glomerular filtration rate (eGFR) was calcu-

lated by using the Chronic Kidney Disease Epidemiology Collaboration creatinine equation (30). For cohorts in which the creatinine measurement was not standardized to isotope dilution mass spectrometry, values were multiplied by 0.95 before eGFR was calculated (31). We defined diabetes as a fasting glucose level of 7.0 mmol/L or greater (≥126 mg/dL), a nonfasting glucose level of 11.1 mmol/L or greater (≥200 mg/dL), a hemoglobin A_{1c} value of 6.5% or greater, use of glucose-lowering drugs, or self-reported diabetes. Hypertension was defined as blood pressure above 140/90 mm Hg or the use of antihypertensive medications. Participants with a history of myocardial infarction, coronary revascularization, heart failure, or stroke were considered to have a history of cardiovascular disease.

Statistical Analysis

Model Development

Within each cohort, the relationships between ACR and PCR were modeled by using multivariable-adjusted linear regression models (**Supplemental Appendix 1**). After models were fit in each cohort, relationships were visually depicted to demonstrate intercohort variation. Because of low heterogeneity, a multivariate random-effects meta-analysis using the restricted maximum likelihood for estimation and inputs of point estimates and variances for each cohort was performed by using the Stata (StataCorp) command *mvmeta* (32). A similar procedure was followed for urine dipstick protein, which was categorized as negative, trace, +, ++, or greater than ++. In sensitivity analyses, we also evaluated the associations between measures from urine samples collected within 90 days of each other.

Model Testing

Predicted levels of ACR and the prediction interval (5th to 95th percentile) were calculated on the basis of the crude and adjusted models for all combinations of sex, diabetes, and hypertension (**Supplemental Appendix 1**). To assess the real-world utility of the prediction equations, we evaluated the sensitivity, specificity, and positive and negative predictive values of PCR thresholds for screening for CKD (ACR, ≥30 mg/g) and categorizing it as stage A2 (ACR, 30 to 299 mg/g) or stage A3 (ACR, ≥300 mg/g). For the crude model, we used a single threshold for all participants; for the adjusted model, we varied the threshold to be the PCR level corresponding to the predicted ACR of 30 mg/g and 300 mg/g for each combination of sex, diabetes, and hypertension. For urine dipstick protein, we evaluated the trace and greater, trace to +, and ++ categories for CKD screening and staging, respectively. Sensitivity, specificity, and positive and negative predictive values were summarized across cohorts by using the intercohort median and interquartile range. Sensitivity and specificity were meta-analyzed by using the Stata command *metandi*, fitting a 2-level mixed logistic regression model with independent binomial distributions for the true-positives and true-negatives conditional on the sensitivity and specificity in each study and a bivariate normal model with the logit transforms of sensitivity

and specificity across studies (33). Analyses were also performed in subgroups of sex, eGFR, diabetes, and hypertension.

Among participants with an eGFR below 60 mL/min/1.73 m² in cohorts that supplied data on serum creatinine and same-day PCR and ACR, we plotted the 2-year 4-variable kidney failure risk equation (KFRE) using the predicted ACR versus the equation using the observed ACR (13, 34). We evaluated sensitivity, specificity, and positive and negative predictive values for the clinical thresholds of 20% and 40% 2-year risk for kidney failure separately in cohorts sending data to the Data Coordinating Center and in the 12 OptumLabs Data Warehouse (OLDW) cohorts. Finally, we compared the discrimination of the KFRE using predicted ACR to that using observed ACR in the cohorts with data on end-stage kidney disease outcomes.

All analyses were performed in Stata 15. Statistical significance was determined by using a 2-sided test with a threshold *P* value of less than 0.050.

Role of the Funding Source

The funders had no role in the study design, data collection, analysis, data interpretation, or writing of the report.

RESULTS

Participant Characteristics

The study included 919 383 participants in 33 cohorts, including 12 research (*n* = 36 592) and 21 clinical cohorts (*n* = 882 791), with data collected between 1982 and 2019 (Table 1). Overall, mean age was 61 years (SD, 15); 50% of the participants were female, 4.8% were black, 56% had diabetes, and 72% had hypertension. Among the 919 383 participants, 147 066 pairs of ACR and PCR tests and 1 903 359 pairs of ACR and urine dipstick tests were performed. Median ACR was 14 mg/g (25th to 75th percentile of cohorts, 5 to 25 mg/g); median PCR was 197 mg/g (25th to 75th percentile of cohorts, 89 to 682 mg/g); and 7.0% of urine dipstick tests indicated the presence of trace proteins, 3.9% of +, 1.8% of ++, and 2.2% of greater than ++ (Table 1 and Supplement Table 1, available at Annals.org).

Relationship Between PCR and ACR and Between Urine Dipstick Category and ACR

For PCR values above 50 mg/g, the relationship between PCR and ACR was nearly linear on the log scale, with a shallower slope for values greater than 500 mg/g than for those from 50 to 500 mg/g and relative consistency across cohorts (Figure, Supplement Figure 1 [available at Annals.org], and Supplement Table 2 [available at Annals.org]). Below a PCR of 50 mg/g, little consistency in association was seen across cohorts. The crude model showed a 2.99-fold increase in predicted ACR for each doubling of PCR in the range of 50 to 500 mg/g, and a 2.18-fold increase in predicted ACR for each doubling of PCR over 500 mg/g. In the adjusted model, the respective increase in predicted ACR for changes in PCR was similar (2.96-fold and 2.16-fold)

and the effects of sex, diabetes, and hypertension on the relationship were relatively small (Supplement Table 3, available at Annals.org). The relationship between PCR and ACR remained highly similar across all combinations of sex, diabetes, and hypertension status (Supplement Figure 2, available at Annals.org). The meta-analyzed associations between PCR and ACR were also similar when values measured within 90 days were used (Supplement Table 4, available at Annals.org).

A graded relationship was observed between urine dipstick protein categories and ACR, with some heterogeneity across cohorts (Supplement Figure 3 and Supplement Table 5, A, available at Annals.org). The relationship between dipstick category and ACR remained largely similar in the adjusted model, with relatively small effects of sex, diabetes, and hypertension (Supplement Table 5, B, available at Annals.org). The relationship between dipstick category and ACR was also similar when all values measured within 90 days were used (Supplement Table 6, available at Annals.org).

Prediction Model Performance

Table 2 shows the prediction equations for converting PCR to ACR and urine dipstick protein categories to ACR on the basis of meta-analyzed associations of same-day measures, as well as the equations for predicted error. Scatter plots of observed versus predicted ACR showed closer approximation in the higher than lower levels in most cohorts (Supplement Figure 4, available at Annals.org). Predicted ACR values and their 95% prediction intervals (incorporating both SE and predicted error, interpreted as the interval in which a 95% chance existed that a concomitantly measured ACR would fall into that interval) for various levels of PCR and dipstick categories are shown in Table 3 and Supplement Table 7 (available at Annals.org), respectively. The predicted ACR levels corresponding to PCRs of 150 mg/g and 500 mg/g were 33 mg/g (95% prediction interval, 12 to 90 mg/g) and 220 mg/g (prediction interval, 113 to 427 mg/g), respectively, in the crude model. Thresholds of the PCR levels corresponding to predicted ACRs of 30 mg/g and 300 mg/g used to test performance were 142 mg/g and 660 mg/g, respectively. The predicted values of ACR for trace, +, ++, and greater than ++ dipstick protein categories were 25 mg/g (prediction interval, 8 to 80 mg/g), 67 mg/g (prediction interval, 21 to 207 mg/g), 337 mg/g (prediction interval, 132 to 860 mg/g), and 1229 mg/g (prediction interval, 734 to 2057 mg/g), respectively. A tool for converting PCR or dipstick values to ACR is available at ckdpcrsk.org/pcr2acr.

Diagnostic Test Accuracy

Screening for CKD

The sensitivity, specificity, and positive and negative predictive values of the predicted ACR by using the PCR conversion equation for detecting an ACR of 30 mg/g or greater (that is, CKD screening) varied by cohort but were similar between the crude and adjusted models (Supplement Table 8, available at Annals.org).

Table 1. Baseline Characteristics in Participants With Urine PCR or Dipstick Measurements on the Same Day as the ACR Measure*

Study†	Participants, n	Cohort Type‡	Mean Age (SD), y	Median ACR (25th-75th percentile of cohorts), mg/g	Mean eGFR (SD), mL/min/1.73 m ²	eGFR < 60 mL/min/1.73 m ² , n (%)	Female, %	DM, %	HTN, %
AusDiab	11 204	Research	55 (15)	5 (4-9)	84 (17)	944 (8)	55	9.7	36
CanPREDDICT	2648	Research	68 (13)	141 (27-769)	27 (10)	2236 (100)	37	49	97
CRIC	3772	Research	58 (11)	51 (8-449)	45 (15)	3200 (85)	45	48	88
IDNT	1706	Research	60 (8)	1380 (586-2682)	50 (19)	1166 (72)	34	100	100
MASTERPLAN	516	Research	61 (12)	77 (16-344)	36 (16)	479 (93)	31	44	95
NIPPON DATA2010	2796	Research	59 (16)	6 (3-18)	97 (17)	77 (3)	57	13	36
Nefrona	274	Research	59 (13)	184 (34-659)	33 (17)	241 (90)	39	30	98
NephroTest	1677	Research	60 (15)	83 (14-451)	43 (22)	1341 (80)	33	30	92
Pima	6081	Research	38 (15)	13 (7-38)	115 (21)	192 (3)	58	37	28
RENAAL	722	Research	61 (7)	1013 (375-2287)	42 (14)	617 (88)	38	100	100
SUN-Macro	896	Research	63 (9)	1405 (663-2516)	33 (11)	840 (99)	23	100	100
Takahata	4300	Research	64 (10)	9 (6-18)	97 (13)	65 (2)	55	9.3	62
CURE-CKD	429	Clinical	61 (18)	51 (11-223)	59 (32)	226 (58)	48	26	52
Geisinger	3128	Clinical	67 (15)	35 (9-221)	51 (25)	2195 (73)	52	67	95
ICES-KDT	589 989	Clinical	60 (16)	14 (5-25)	83 (23)	97 253 (17)	50	54	71
LCC	7384	Clinical	77 (10)	10 (4-35)	50 (13)	5821 (79)	59	51	96
Mt_Sinai_BioMe	1679	Clinical	61 (15)	61 (11-524)	49 (26)	1123 (70)	48	49	79
OLDW									
Cohort 1	16 341	Clinical	62 (14)	16 (7-41)	75 (24)	4140 (27)	52	75	82
Cohort 2	16 396	Clinical	64 (14)	16 (7-52)	74 (26)	4906 (31)	50	84	85
Cohort 3	30 940	Clinical	60 (15)	9 (5-27)	81 (23)	5571 (18)	52	47	64
Cohort 4	57 673	Clinical	63 (14)	16 (7-49)	75 (25)	15 407 (28)	52	69	74
Cohort 5	27 204	Clinical	59 (15)	21 (7-45)	80 (28)	6596 (25)	53	76	82
Cohort 6	2318	Clinical	62 (15)	16 (7-63)	71 (27)	774 (35)	53	73	85
Cohort 7	12 226	Clinical	66 (13)	12 (6-35)	72 (23)	3803 (31)	50	74	82
Cohort 8	8083	Clinical	62 (15)	15 (6-60)	75 (25)	2230 (29)	51	71	80
Cohort 9	3971	Clinical	58 (14)	13 (6-31)	82 (25)	753 (20)	48	57	71
Cohort 10	26 396	Clinical	61 (15)	11 (5-35)	80 (24)	5098 (20)	51	58	69
Cohort 11	53 960	Clinical	61 (14)	12 (5-45)	76 (25)	13 925 (27)	46	53	70
Cohort 12	7942	Clinical	60 (15)	11 (5-45)	79 (27)	1853 (24)	53	65	75
PSP-CKD	1253	Clinical	76 (10)	18 (6-53)	50 (16)	503 (73)	52	45	83
RCAV	9361	Clinical	66 (11)	13 (6-56)	72 (20)	2436 (28)	3.6	81	92
Sunnybrook	2043	Clinical	58 (18)	82 (16-391)	59 (32)	1135 (56)	49	40	67
West of Scotland	4075	Clinical	67 (14)	19 (4-95)	33 (19)	3766 (92)	46	35	42
Total	919 383	-	61 (15)	14 (5-25)	80 (25)	190 912 (21)	50	56	72

ACR = albumin-creatinine ratio; AusDiab = Australian Diabetes, Obesity, and Lifestyle Study; CanPREDDICT = Canadian Study of Prediction of Death, Dialysis and Interim Cardiovascular Events; CRIC = Chronic Renal Insufficiency Cohort; CURE-CKD = Center for Kidney Disease Research, Education, and Hope; DM = diabetes mellitus; eGFR = estimated glomerular filtration rate; HTN = hypertension; ICES-KDT = Institute for Clinical Evaluation Science, Kidney, Dialysis, and Transplant Program; IDNT = Irbesartan Type II Diabetic Nephropathy Trial; LCC = The Leicester City and County Chronic Kidney Disease Cohort; MASTERPLAN = Multifactorial Approach and Superior Treatment Efficacy in Renal Patients With the Aid of a Nurse Practitioner; NIPPON DATA2010 = National Integrated Project for Prospective Observation of Non-communicable Disease and Its Trends in the Aged 2010; OLDW = OptumLabs Data Warehouse; PCR = protein-creatinine ratio; PSP-CKD = Primary-Secondary Care Partnership to Prevent Adverse Outcomes in Chronic Kidney Disease; RCAV = Racial and Cardiovascular Risk Anomalies in CKD Cohort; RENAAL = Reduction of Endpoints in Non-insulin Dependent Diabetes Mellitus With the Angiotensin II Antagonist Losartan; SUN-Macro = Sulodexide Macro-albuminuria trial.

* If several measurements were done per person, a random visit was selected.

† For more details about the studies, including references, see Supplemental Appendix 2 (available at Annals.org).

‡ Cohort type indicates whether the data were collected as part of structured research cohort visits or as part of clinical care.

In the crude model, meta-analyzed sensitivity and specificity of the PCR-based equation for detecting an ACR of 30 mg/g or above were 91.2% (95% CI, 87.3% to 93.9%) and 86.5% (CI, 81.4% to 90.3%), respectively, and pooled median positive and negative predictive values were 91.1% (25th to 75th percentile of cohorts, 87.5% to 94.5%) and 84.5% (25th to 75th percentile of cohorts, 77.6% to 89.4%), respectively (Table 4 and Supplement Table 8, available at Annals.org).

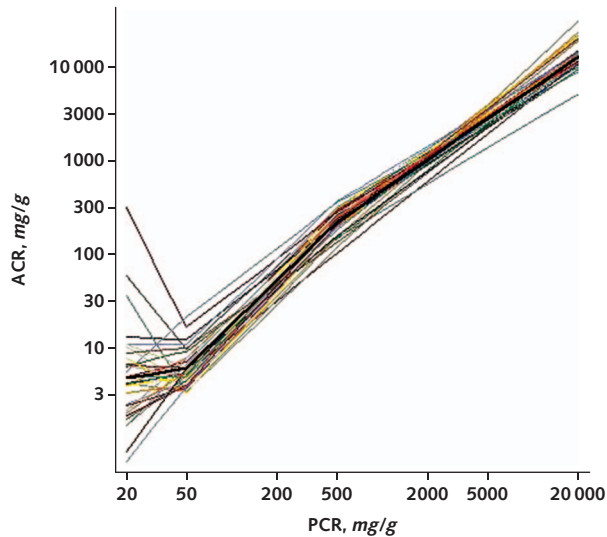
The sensitivity, specificity, and positive and negative predictive values for urine dipstick categories of trace and greater for ACRs of 30 mg/g and above varied across cohorts (Supplement Table 9, available at Annals.org). The meta-analyzed sensitivity and specific-

ity of the urine dipstick categories of trace and greater for detecting ACRs of 30 mg/g and above were 62.0% (CI, 50.9% to 72.0%) and 87.8% (CI, 83.3% to 91.2%), respectively, and pooled median positive and negative predictive values were 70.8% (25th to 75th percentile of cohorts, 65.8% to 73.6%) and 81.7% (25th to 75th percentile of cohorts, 77.6% to 85.2%), respectively (Table 5 and Supplement Table 9).

CKD Staging

The sensitivity and specificity of the crude PCR conversion equation for identifying CKD stage A2 (ACR, 30 to 299 mg/g) were 74.9% (CI, 70.8% to 78.7%) and

Figure. Relationship between urine PCR and urine ACR values in individual cohorts (multicolored lines) and after random-effects meta-analysis (thick black line) in the crude model.



Associations were estimated by using log-transformed urine ACR and urine PCR, with the latter modeled by using linear splines with knots at 50 mg/g and 500 mg/g. ACR = albumin-creatinine ratio; PCR = protein-creatinine ratio.

88.7% (CI, 86.3% to 90.7%), respectively, and the positive and negative predictive values were 72.5% (25th to 75th percentile of cohorts, 69.2% to 75.6%) and 88.7% (25th to 75th percentile of cohorts, 86.0% to 91.1%), respectively (Table 4 and Supplement Table 10, avail-

able at Annals.org). The equations had slightly higher sensitivity and higher specificity for detecting CKD stage A3 (ACR, ≥ 300 mg/g), with meta-analyzed sensitivity and specificity of 86.6% (CI, 83.5% to 89.2%) and 97.5% (CI, 96.2% to 98.3%), respectively, and pooled median positive and negative predictive values of 90.4% (25th to 75th percentile of cohorts, 88.3% to 94.8%) and 95.1% (25th to 75th percentile of cohorts, 91.5% to 97.5%). Performance was similar when the adjusted equation was used (Table 4 and Supplement Table 10 and Table 11, available at Annals.org).

Dipstick values of trace to + had lower sensitivity and specificity for CKD stage A2 (Table 5 and Supplement Table 12, available at Annals.org). Dipstick values of ++ had meta-analyzed sensitivity and specificity of 77.6% (CI, 71.7% to 82.6%) and 97.5% (CI, 95.5% to 98.6%), respectively, for CKD stage A3 (Table 5 and Supplement Table 13, available at Annals.org). Diagnostic performance was highly similar among subgroups based on sex, diabetes, hypertension, and CKD G (glomerular filtration rate) stage (Table 5).

CKD Prognosis

The kidney failure risk estimates calculated by the 2-year 4-variable KFRE using predicted ACR versus the KFRE using observed ACR showed agreement, particularly in the OLDW cohorts (Supplement Figure 5, available at Annals.org). In the crude model, the sensitivity and specificity for the 2-year 40% kidney failure risk threshold were 80.5% and 99.6%, respectively, in cohorts that sent data to the Data Coordinating Center and 95.6% and 99.4%, respectively, in the OLDW cohorts. The median c-statistic for the 2-year KFRE across cohorts was 0.879 (25th to 75th percentile of cohorts,

Table 2. Equations for Converting Urine PCR to Urine ACR and Urine Dipstick Protein to Urine ACR From the Crude and Adjusted Models*

Model	Equation†‡
PCR	
Crude	
Predicted ACR	$pACR = \exp(5.3920 + 0.3072 \times \log(\min(PCR/50, 1)) + 1.5793 \times \log(\max(\min(PCR/500, 1), 0.1)) + 1.1266 \times \log(\max(PCR/500, 1)))$
Predicted error	$pErr = \sqrt{\exp(-2.2996 + 0.1043 \times \log(\min(pACR/30, 1)) - 0.4401 \times \log(\max(\min(pACR/300, 1), 0.1)) - 0.3897 \times \log(\max(pACR/300, 1)))}$
Adjusted	
Predicted ACR	$pACR = \exp(5.2659 + 0.2934 \times \log(\min(PCR/50, 1)) + 1.5643 \times \log(\max(\min(PCR/500, 1), 0.1)) + 1.1109 \times \log(\max(PCR/500, 1)) - 0.0773 \times (\text{if female}) + 0.0797 \times (\text{if diabetic}) + 0.1265 \times (\text{if hypertensive}))$
Predicted error	$pErr = \sqrt{\exp(-2.0664 + 0.1658 \times \log(\min(pACR/30, 1)) - 0.4599 \times \log(\max(\min(pACR/300, 1), 0.1)) - 0.3084 \times \log(\max(pACR/300, 1)) + 0.0847 \times (\text{if female}) - 0.2553 \times (\text{if diabetic}) - 0.2299 \times (\text{if hypertensive}))}$
Dipstick	
Crude	
Predicted ACR	$pACR = \exp(2.4738 + 0.7539 \times (\text{if trace}) + 1.7243 \times (\text{if +}) + 3.3475 \times (\text{if ++}) + 4.6399 \times (\text{if +++}))$
Predicted error	$pErr = \sqrt{\exp(-1.3710 + 0.6843 \times \log(\min(pACR/30, 1)) - 0.1869 \times \log(\max(\min(pACR/300, 1), 0.1)) - 0.9220 \times \log(\max(pACR/300, 1)))}$
Adjusted	
Predicted ACR	$pACR = \exp(2.0373 + 0.7270 \times (\text{if trace}) + 1.6775 \times (\text{if +}) + 3.2622 \times (\text{if ++}) + 4.5435 \times (\text{if +++}) + 0.0822 \times (\text{if female}) + 0.27249 \times (\text{if diabetic}) + 0.33627 \times (\text{if hypertensive}))$
Predicted error	$pErr = \sqrt{\exp(-0.4525 + 0.5939 \times \log(\min(pACR/30, 1)) - 0.1292 \times \log(\max(\min(pACR/300, 1), 0.1)) - 0.2610 \times \log(\max(pACR/300, 1)) - 0.0772 \times (\text{if female}) - 0.2093 \times (\text{if diabetic}) - 0.1624 \times (\text{if hypertensive}))}$

ACR = albumin-creatinine ratio; PCR = protein-creatinine ratio.

* In milligrams per gram.

† Diabetic is defined as a fasting glucose level ≥ 7.0 mmol/L (126 mg/dL), a nonfasting glucose level ≥ 11.1 mmol/L (200 mg/dL), a hemoglobin A_{1c} value $\geq 6.5\%$, use of glucose-lowering drugs, or self-reported diabetes. Hypertensive is defined as blood pressure $>140/90$ mm Hg or the use of antihypertensive medications. Log refers to the natural log-transformation (ln).

‡ Prediction interval: $\exp(\log(pACR) - 1.96 \times pErr)$, $\exp(\log(pACR) + 1.96 \times pErr)$.

Table 3. Predicted Urine ACR Values and Their Prediction Intervals for Various Urine PCR Levels From the Crude and Adjusted Equations*†

PCR	ACR								
	Crude Model				Adjusted Model				
	Male				Female				
	No HTN		HTN		No HTN		HTN		
No DM	DM	No DM	DM	No DM	DM	No DM	DM		
50	6 (2-15)	5 (2-15)	6 (2-14)	6 (2-15)	6 (3-15)	5 (2-14)	5 (2-14)	6 (2-14)	6 (3-14)
150	33 (12-90)	29 (9-96)	32 (11-89)	33 (12-94)	36 (15-88)	27 (8-93)	30 (10-87)	31 (10-92)	33 (13-86)
500	220 (113-427)	194 (90-419)	210 (108-408)	220 (113-428)	238 (134-424)	179 (79-407)	194 (96-394)	203 (100-413)	220 (119-407)
700	321 (174-592)	281 (139-571)	305 (165-562)	319 (172-591)	346 (202-591)	260 (123-552)	282 (147-540)	296 (154-567)	320 (182-563)
1000	480 (272-845)	418 (216-811)	453 (255-806)	475 (266-847)	514 (311-850)	387 (192-779)	419 (228-770)	439 (238-810)	476 (280-810)
2000	1047 (644-1703)	903 (501-1627)	978 (586-1632)	1025 (613-1714)	1110 (710-1736)	836 (449-1556)	905 (528-1554)	949 (551-1633)	1027 (641-1648)
3000	1653 (1059-2580)	1417 (818-2454)	1535 (952-2474)	1608 (995-2599)	1742 (1147-2643)	1312 (735-2342)	1421 (858-2351)	1488 (897-2471)	1612 (1038-2504)
5000	2940 (1975-4376)	2499 (1511-4133)	2707 (1748-4192)	2836 (1827-4403)	3072 (2096-4502)	2314 (1360-3935)	2506 (1579-3976)	2625 (1650-4177)	2843 (1899-4257)

ACR = albumin-creatinine ratio; DM = diabetes mellitus; HTN = hypertension; PCR = protein-creatinine ratio.

* All values are milligrams per gram; to convert to milligrams per millimole, divide by 8.84 mmol/g.

† The prediction interval was estimated as the predicted level of ACR ± 1.96 times the square root of the addend of the squared SE term and the squared predicted error.

0.842 to 0.907) when observed ACR was used, 0.883 (25th to 75th percentile of cohorts, 0.844 to 0.909) for ACR predicted with the crude equation, and 0.883 (25th to 75th percentile of cohorts, 0.845 to 0.909) for ACR predicted with the adjusted equation. The c-statistic for the use of predicted rather than observed ACR was statistically worse in only 2 of 25 cohorts (Supplement Table 14, available at Annals.org).

DISCUSSION

In this international collaborative meta-analysis of 919 383 participants from 33 cohorts, we found an overall consistent relationship between PCR and ACR for PCR values greater than 50 mg/g and between urine dipstick protein categories and ACR across a wide range of cohorts. We developed equations for converting PCR or urine dipstick protein categories to ACR and evaluated them for potential use in individual screening and classification efforts and risk prediction. For efforts to categorize patients into CKD stages A2 and A3, the PCR conversion equations demonstrated

moderate sensitivity and specificity (>74%) for detecting ACRs of 30 to 299 mg/g and 300 mg/g and greater; the urine dipstick categories of trace to + and ++ had high specificity (>88%) but lower sensitivity (<78%) for identifying ACRs of 30 to 299 mg/g and 300 mg/g and greater, respectively. For individual risk prediction, the estimated 2-year 4-variable KFRE using predicted ACR was very similar to the one using observed ACR.

Our empirically developed equation for converting PCR to ACR corresponded well with threshold estimates in the current KDIGO guideline on CKD staging (12). The guideline recommends use of ACR for defining and staging CKD, with ACR values of 30 mg/g and 300 mg/g defining albuminuria categories A2 and A3, respectively. Our crude equation suggests that a "trace" value on urine dipstick corresponds to an ACR of 25 mg/g, "+" corresponds to an ACR of 67 mg/g, and "++" corresponds to an ACR of 337 mg/g. Likewise, we estimate in the crude PCR equation that a PCR value of 150 mg/g corresponds to an ACR of 33 mg/g, albeit with a prediction interval of 12 to 90 mg/g, and

Table 4. Crude Model Sensitivity and Specificity for Detecting Different Urine ACR Levels From Equivalent Urine PCR Levels, Overall and by Subgroup

Group	Participants, n	ACR ≥30 mg/g, PCR ≥142 mg/g		ACR 30-299 mg/g, PCR 142-660 mg/g		ACR ≥300 mg/g	
		Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Overall	147 066	0.912 (0.873-0.939)	0.865 (0.814-0.903)	0.749 (0.708-0.787)	0.887 (0.863-0.907)	0.866 (0.835-0.892)	0.975 (0.962-0.983)
Male	87 621	0.914 (0.875-0.941)	0.880 (0.831-0.916)	0.755 (0.710-0.794)	0.891 (0.867-0.911)	0.858 (0.827-0.885)	0.977 (0.964-0.985)
Female	59 445	0.910 (0.871-0.939)	0.851 (0.798-0.892)	0.739 (0.699-0.775)	0.886 (0.858-0.909)	0.881 (0.847-0.908)	0.975 (0.962-0.983)
No diabetes	71 124	0.871 (0.828-0.904)	0.889 (0.849-0.920)	0.711 (0.667-0.751)	0.878 (0.848-0.902)	0.826 (0.791-0.856)	0.981 (0.969-0.988)
Diabetes	74 757	0.929 (0.900-0.950)	0.852 (0.795-0.895)	0.775 (0.742-0.804)	0.884 (0.863-0.902)	0.882 (0.853-0.906)	0.970 (0.957-0.979)
No hypertension	37 030	0.856 (0.806-0.895)	0.909 (0.872-0.936)	0.678 (0.626-0.727)	0.896 (0.865-0.920)	0.932 (0.785-0.871)	0.980 (0.966-0.989)
Hypertension	108 656	0.919 (0.884-0.944)	0.856 (0.803-0.897)	0.759 (0.719-0.795)	0.882 (0.859-0.902)	0.870 (0.839-0.896)	0.974 (0.961-0.982)
CKD							
Stage G1-G2	61 299	0.863 (0.819-0.898)	0.911 (0.878-0.936)	0.733 (0.685-0.775)	0.889 (0.863-0.910)	0.818 (0.778-0.853)	0.987 (0.979-0.992)
Stage G3	44 032	0.918 (0.876-0.947)	0.826 (0.740-0.888)	0.752 (0.714-0.787)	0.876 (0.851-0.898)	0.860 (0.820-0.892)	0.974 (0.960-0.983)
Stage G4-G5	28 174	0.960 (0.943-0.971)	0.728 (0.637-0.803)	0.755 (0.717-0.790)	0.881 (0.853-0.905)	0.924 (0.900-0.942)	0.916 (0.873-0.945)

ACR = albumin-creatinine ratio; CKD = chronic kidney disease; PCR = protein-creatinine ratio.

that a PCR value of 500 mg/g corresponds to an ACR of 220 mg/g (prediction interval, 113 to 427 mg/g). These conversions are quite similar to those suggested by KDIGO, in which dipstick protein values of "trace to +" and "+ or greater" and PCR values of 150 to 500 mg/g and greater than 500 mg/g are assigned to albuminuria categories 30 to 299 mg/g and 300 mg/g or greater, respectively (12). In contrast, our results were slightly different from the suggested value of nephrotic-range proteinuria, noted as a PCR value of 3000 mg/g or an ACR value of 2220 mg/g in the guideline (12). On the basis of our crude model, a 3000-mg/g PCR corresponded to a 1603-mg/g ACR (prediction interval, 1015 to 2532 mg/g).

Despite widespread awareness of the importance of using ACR measurements as the gold standard to assess and monitor CKD, inconsistencies still exist in the measurement of ACR versus PCR in clinical practice and in research studies across the world (22). Because the costs of measuring total protein may be lower than those for measuring albumin, financial considerations may affect the implementation of ACR measurement (12). Clinical reasons also may exist for practitioners to use PCR instead of ACR to quantify and monitor clinically significant levels of proteinuria (such as in cases of glomerulonephritis or perhaps nephrotic-range proteinuria). In this context, our PCR conversion equations may have public health, clinical, and research implications from a practical and cost-effective perspective, facilitating the use of PCR as a screening, staging, and prognostic tool for CKD.

Previous studies (based on an English-language MEDLINE search through March 2020) investigating the relationship between PCR and ACR reported inconsistent results, with some showing strong correlation (18–20, 22) and others not (21). In a recent study from a population-based cohort of 47 714 adults in Canada, Weaver and colleagues (35) derived equations to estimate ACR from PCR, taking into account nonlinearity and modification by several clinical characteristics. At higher PCR levels, an approximately linear relationship was seen between PCR and ACR, but the relationship

was less correlated at lower levels, with nearly no relationship at PCR values below 50 mg/g (35). Our results were generally consistent with these observations but further increased the generalizability to a large and diverse international population, confirming good concordance of our PCR conversion equations with the current KDIGO estimates (12). Of importance, these equations might allow implementation of risk prediction models in which ACR has been incorporated (13, 15, 16, 36), leading to increased opportunities for practitioners who measure only PCR to use these tools for better decision making and patient management. Our results demonstrated similar estimates for the KFRE when predicted (vs. observed) ACR was used, supporting the potential utility of predicted ACR in risk prediction. Our PCR conversion equations also might facilitate data integration across research studies in a broad range of populations. Although the adjusted equation incorporated sex, hypertension, and diabetes, the coefficient values were small. Given that the crude model is simpler and performs nearly the same as the adjusted model, the crude equation may be preferable for ease of implementation.

The urine dipstick test has been widely used as an initial screening tool for evaluating proteinuria primarily because of its low cost, simplicity, and ability to provide rapid point-of-care information to both clinicians and patients (24). However, commonly used reagent strip devices for total protein measurement do not adjust for urinary concentration and provide only semiquantitative results. Studies have consistently shown that urine dipstick testing has low sensitivity for CKD screening (ACR, ≥ 30 mg/g) despite its high specificity (23–27). Indeed, in our study, the dipstick category of trace and greater had low sensitivity (62.0%) but high specificity (87.8%) for detecting ACRs of 30 mg/g or greater. However, if detecting CKD stage A3 (ACR, ≥ 300 mg/g) were the goal, the sensitivity of the ++ category was 77.6%, with a specificity of 97.5%. In many settings, access to laboratory services is limited, and low-cost diagnostic tools, such as urine dipstick tests, are essential (24, 25). The performance of these tools should be evaluated

Table 5. Crude Model Sensitivity and Specificity for Detecting Different Urine ACR Levels From Equivalent Dipstick Categories, Overall and by Subgroup

Group	Participants, n	ACR ≥ 30 mg/g, by Dipstick Trace or Greater		ACR 30–299 mg/g, by Dipstick Trace or +		ACR ≥ 300 mg/g, by Dipstick ++ or Greater	
		Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Overall	1 903 359	0.620 (0.509–0.720)	0.878 (0.833–0.912)	0.356 (0.296–0.421)	0.882 (0.843–0.913)	0.776 (0.717–0.826)	0.975 (0.955–0.986)
Male	974 381	0.663 (0.559–0.753)	0.875 (0.831–0.909)	0.385 (0.319–0.456)	0.881 (0.842–0.911)	0.803 (0.745–0.851)	0.971 (0.948–0.984)
Female	928 978	0.569 (0.453–0.678)	0.880 (0.834–0.915)	0.328 (0.272–0.390)	0.883 (0.843–0.914)	0.742 (0.682–0.794)	0.974 (0.958–0.984)
No diabetes	689 075	0.611 (0.490–0.720)	0.873 (0.826–0.909)	0.353 (0.283–0.429)	0.881 (0.837–0.914)	0.775 (0.719–0.823)	0.979 (0.961–0.989)
Diabetes	1 213 978	0.631 (0.524–0.726)	0.876 (0.833–0.910)	0.359 (0.301–0.421)	0.880 (0.845–0.909)	0.783 (0.723–0.832)	0.970 (0.948–0.983)
No hypertension	449 679	0.583 (0.460–0.698)	0.873 (0.822–0.911)	0.356 (0.297–0.420)	0.881 (0.838–0.914)	0.758 (0.696–0.811)	0.983 (0.965–0.992)
Hypertension	1 453 584	0.628 (0.523–0.723)	0.877 (0.833–0.911)	0.360 (0.299–0.426)	0.881 (0.843–0.911)	0.785 (0.727–0.834)	0.971 (0.947–0.984)
CKD							
Stage G1–G2	1 431 248	0.578 (0.469–0.680)	0.881 (0.838–0.914)	0.366 (0.310–0.425)	0.884 (0.946–0.913)	0.720 (0.693–0.746)	0.983 (0.972–0.990)
Stage G3	346 405	0.656 (0.550–0.748)	0.869 (0.826–0.902)	0.377 (0.312–0.478)	0.873 (0.836–0.902)	0.799 (0.746–0.844)	0.967 (0.944–0.981)
Stage G4–G5	80 529	0.800 (0.716–0.864)	0.840 (0.784–0.884)	0.389 (0.306–0.480)	0.870 (0.825–0.904)	0.852 (0.809–0.887)	0.940 (0.900–0.964)

ACR = albumin-creatinine ratio; CKD = chronic kidney disease.

within the local context of test availability, cost, and objectives in considering strategies for CKD screening and staging.

The study results must be interpreted in light of some limitations. We used pairs of PCR and ACR or urine dipstick protein and ACR tested on the same day, but not necessarily in the same urine sample. Thus, we may have overestimated the error in conversion, because albuminuria is subject to intraindividual biological variability, even on the same day, due to various pathologic and nonpathologic factors (such as posture, exercise, and fever). Across cohorts, ACR, PCR, and urine dipstick protein were tested in different clinical settings by using different laboratory assays, which may also explain some of the observed intra- and inter-cohort variation. Substantial between-laboratory variation has been reported in current assays to measure total urine protein, mostly by using either turbidimetry or colorimetry (17, 37). The main reason for this is a variable mixture of protein in the urine, which makes it difficult to define a standardized reference material for measuring total urine protein (17). Nevertheless, our results show a fairly consistent relationship between PCR and ACR across diverse cohorts, at least at PCR levels of 50 mg/g and greater, allowing for the development of ACR equations by combining meta-analyzed β -coefficients with little heterogeneity. For PCRs less than 50 mg/g, we found no consistent association; however, it is fair to say that most corresponding ACR values are below 30 mg/g. Finally, caution is warranted in cases of non-albumin-predominant proteinuria (such as α_1 -microglobulin, immunoglobulins, and monoclonal heavy or light chains), which may also have diagnostic or prognostic value (38).

In conclusion, we developed equations for converting PCR or urine dipstick protein categories to ACR by using random-effects meta-analysis in 33 multinational cohorts. Our PCR conversion equations demonstrated relatively high specificity and sensitivity for detecting CKD stage A2 and higher, and the 2-year KFRE using predicted ACR performed similarly to that using observed ACR. Although further testing is required to establish the robustness and utility of these equations, our results suggest that if ACR is not available, predicted ACR may be useful and informative for harmonization across research studies, CKD screening and classification efforts, and use in risk prediction equations.

From University of Tennessee Health Science Center, Memphis, Tennessee (K.S.); Icahn School of Medicine at Mount Sinai, New York, New York (G.N.N.); Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland (M.E.G., Y.S., S.H.B., J.C., K.M., A.S.); Leicester General Hospital, University Hospitals of Leicester NHS Trust, and University of Leicester, Leicester, United Kingdom (N.B., R.M.); Royal Prince Alfred Hospital and Kidney Node, University of Sydney, Sydney, New South Wales, Australia (S.J.C.); Geisinger Health, Danville, Pennsylvania (A.R.C.); University of Naples "Federico II," Naples, Italy (M.C.); Providence Sacred Heart Medical Center and Gonzaga University School of Anesthesia, Spokane, Washington (K.B.D.); University Medical Center Groningen,

University of Groningen, Groningen, the Netherlands (R.T.G.); ICES and Western University, London, Ontario, Canada (A.X.G.); IRCCS Neuromed, Pozzilli, Italy, and University of Insubria, Varese, Italy (L.I.); Yamagata University, Yamagata, Japan (T.K., T.K.); Memphis Veterans Affairs Medical Center and University of Tennessee Health Science Center, Memphis, Tennessee (C.P.K.); University of Illinois at Chicago, Chicago, Illinois (J.L.); Kaiser Permanente, Hawaii Region, and Moanalua Medical Center, Honolulu, Hawaii (B.J.L.); Paris Saclay University, Paris-Sud University, UVSQ, CESP, INSERM U1018, Villejuif, France (M.M.); Shiga University of Medical Science Seta-Tsukinowa-cho, Shiga, Japan (K.M.); Sunnybrook Hospital, University of Toronto, Toronto, Ontario, Canada (D.M.N.); National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Phoenix, Arizona (R.G.N.); University of Aberdeen, Aberdeen, Scotland (S.S.); American Medical Group Association, Alexandria, Virginia (N.S.); University of British Columbia, Vancouver, British Columbia, Canada (M.T.); Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania (R.R.T.); Queen Elizabeth University Hospital, Glasgow, Scotland (J.P.T.); Institute of Biomedical Research of Lleida and Spanish Research Network for Renal Diseases, Lleida, Spain (J.M.V.); Radboud University Medical Center, Nijmegen, the Netherlands (J.W.); Monash University, Clayton, Victoria, Australia (K.R.P.); and University of Groningen, University Medical Center, Groningen, the Netherlands, and The George Institute for Global Health, Sydney, New South Wales, Australia (H.J.H.).

Note: Drs. Grams and Coresh had full access to all analyses, and all authors had final responsibility for the decision to submit for publication, informed by discussions with collaborators.

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Reproducible Research Statement: *Study protocol and statistical code:* Available from CKD-PC (e-mail, ckdpc@jhmi.edu). *Data set:* Under agreement with the participating cohorts, CKD-PC cannot share individual data with third parties.

Corresponding Authors: Josef Coresh, MD, PhD, and Morgan E. Grams, MD, PhD, Chronic Kidney Disease Prognosis Consortium, 2024 East Monument Street, Baltimore, MD 21287; e-mail, ckdpc@jhmi.edu.

Current author addresses and author contributions are available at [Annals.org](https://annals.org).

References

- Hemmelgarn BR, Manns BJ, Lloyd A, et al; Alberta Kidney Disease Network. Relation between kidney function, proteinuria, and adverse outcomes. *JAMA*. 2010;303:423-9. [PMID: 20124537] doi:10.1001/jama.2010.39
- Lea J, Greene T, Hebert L, et al. The relationship between magnitude of proteinuria reduction and risk of end-stage renal disease: results of the African American study of kidney disease and hypertension. *Arch Intern Med*. 2005;165:947-53. [PMID: 15851648]
- Matsushita K, van der Velde M, Astor BC, et al; Chronic Kidney Disease Prognosis Consortium. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet*. 2010;375:2073-81. [PMID: 20483451] doi:10.1016/S0140-6736(10)60674-5
- Astor BC, Matsushita K, Gansevoort RT, et al; Chronic Kidney Disease Prognosis Consortium. Lower estimated glomerular filtration rate and higher albuminuria are associated with mortality and end-stage renal disease. A collaborative meta-analysis of kidney disease population cohorts. *Kidney Int*. 2011;79:1331-40. [PMID: 21289598] doi:10.1038/ki.2010.550
- van der Velde M, Matsushita K, Coresh J, et al; Chronic Kidney Disease Prognosis Consortium. Lower estimated glomerular filtration rate and higher albuminuria are associated with all-cause and cardiovascular mortality. A collaborative meta-analysis of high-risk population cohorts. *Kidney Int*. 2011;79:1341-52. [PMID: 21307840] doi:10.1038/ki.2010.536
- Seegmiller JC, Miller WG, Bachmann LM. Moving toward standardization of urine albumin measurements. *EJIFCC*. 2017;28:258-267. [PMID: 29333145]
- Miller WG, Bachmann LM, Fleming JK, et al; Laboratory Working Group of the National Kidney Disease Education Program and the IFCC Working Group for Standardization of Albumin in Urine. Recommendations for reporting low and high values for urine albumin and total protein [Letter]. *Clin Chem*. 2019;65:349-350. [PMID: 30459169] doi:10.1373/clinchem.2018.297861
- Johnson DW, Jones GR, Mathew TH, et al; Australasian Proteinuria Consensus Working Group. Chronic kidney disease and measurement of albuminuria or proteinuria: a position statement. *Med J Aust*. 2012;197:224-5. [PMID: 22900872]
- Montañés Bermúdez R, Gràcia García S, Pérez Surribas D, et al; Sociedad Española de Bioquímica Clínica y Patología Molecular. Consensus document. Recommendations on assessing proteinuria during the diagnosis and follow-up of chronic kidney disease. *Nefrología*. 2011;31:331-45. [PMID: 21780317] doi:10.3265/Nefrología.pre2011.Jan.10807
- Japanese Society of Nephrology. Evidence-based practice guideline for the treatment of CKD. *Clin Exp Nephrol*. 2009;13:537-66. [PMID: 19960305] doi:10.1007/s10157-009-0237-8
- Li PK, Chow KM, Matsuo S, et al; Asian Forum for Chronic Kidney Disease Initiatives. Asian chronic kidney disease best practice recommendations: positional statements for early detection of chronic kidney disease from Asian Forum for Chronic Kidney Disease Initiatives (AFCKDI). *Nephrology (Carlton)*. 2011;16:633-41. [PMID: 21771177] doi:10.1111/j.1440-1797.2011.01503.x
- Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2013;3:1-150.
- Tangri N, Stevens LA, Griffith J, et al. A predictive model for progression of chronic kidney disease to kidney failure. *JAMA*. 2011;305:1553-9. [PMID: 21482743] doi:10.1001/jama.2011.451
- Matsushita K, Coresh J, Sang Y, et al; CKD Prognosis Consortium. Estimated glomerular filtration rate and albuminuria for predic-

- tion of cardiovascular outcomes: a collaborative meta-analysis of individual participant data. *Lancet Diabetes Endocrinol*. 2015;3:514-25. [PMID: 26028594] doi:10.1016/S2213-8587(15)00040-6
- Grams ME, Sang Y, Levey AS, et al; Chronic Kidney Disease Prognosis Consortium. Kidney-failure risk projection for the living kidney-donor candidate. *N Engl J Med*. 2016;374:411-21. [PMID: 26544982] doi:10.1056/NEJMoa1510491
- Grams ME, Sang Y, Ballew SH, et al. Predicting timing of clinical outcomes in patients with chronic kidney disease and severely decreased glomerular filtration rate. *Kidney Int*. 2018;93:1442-1451. [PMID: 29605094] doi:10.1016/j.kint.2018.01.009
- Lamb EJ, MacKenzie F, Stevens PE. How should proteinuria be detected and measured? *Ann Clin Biochem*. 2009;46:205-17. [PMID: 19389884] doi:10.1258/acb.2009.009007
- Atkins RC, Briganti EM, Zimmet PZ, et al. Association between albuminuria and proteinuria in the general population: the AusDiab Study. *Nephrol Dial Transplant*. 2003;18:2170-4. [PMID: 13679498]
- Wu MT, Lam KK, Lee WC, et al. Albuminuria, proteinuria, and urinary albumin to protein ratio in chronic kidney disease. *J Clin Lab Anal*. 2012;26:82-92. [PMID: 22467323] doi:10.1002/jcla.21487
- Guy M, Borzomato JK, Newall RG, et al. Protein and albumin-to-creatinine ratios in random urines accurately predict 24 h protein and albumin loss in patients with kidney disease. *Ann Clin Biochem*. 2009;46:468-76. [PMID: 19729498] doi:10.1258/acb.2009.009001
- Methven S, MacGregor MS, Traynor JP, et al. Assessing proteinuria in chronic kidney disease: protein-creatinine ratio versus albumin-creatinine ratio. *Nephrol Dial Transplant*. 2010;25:2991-6. [PMID: 20237054] doi:10.1093/ndt/gfq140
- Fisher H, Hsu CY, Vittinghoff E, et al. Comparison of associations of urine protein-creatinine ratio versus albumin-creatinine ratio with complications of CKD: a cross-sectional analysis. *Am J Kidney Dis*. 2013;62:1102-8. [PMID: 24041612] doi:10.1053/j.ajkd.2013.07.013
- Konta T, Hao Z, Takasaki S, et al. Clinical utility of trace proteinuria for microalbuminuria screening in the general population. *Clin Exp Nephrol*. 2007;11:51-5. [PMID: 17384998]
- White SL, Yu R, Craig JC, et al. Diagnostic accuracy of urine dipsticks for detection of albuminuria in the general community. *Am J Kidney Dis*. 2011;58:19-28. [PMID: 21411199] doi:10.1053/j.ajkd.2010.12.026
- McTaggart MP, Price CP, Pinnock RG, et al. The diagnostic accuracy of a urine albumin-creatinine ratio point-of-care test for detection of albuminuria in primary care. *Am J Kidney Dis*. 2012;60:787-94. [PMID: 22721931] doi:10.1053/j.ajkd.2012.05.009
- Lim D, Lee DY, Cho SH, et al. Diagnostic accuracy of urine dipstick for proteinuria in older outpatients. *Kidney Res Clin Pract*. 2014;33:199-203. [PMID: 26885477] doi:10.1016/j.krcp.2014.10.003
- Park JI, Baek H, Kim BR, et al. Comparison of urine dipstick and albumin:creatinine ratio for chronic kidney disease screening: a population-based study. *PLoS One*. 2017;12:e0171106. [PMID: 28151999] doi:10.1371/journal.pone.0171106
- Lambers Heerspink HJ, Gansevoort RT, Brenner BM, et al. Comparison of different measures of urinary protein excretion for prediction of renal events. *J Am Soc Nephrol*. 2010;21:1355-60. [PMID: 20634296] doi:10.1681/ASN.2010010063
- Matsushita K, Ballew SH, Astor BC, et al; Chronic Kidney Disease Prognosis Consortium. Cohort profile: the chronic kidney disease prognosis consortium. *Int J Epidemiol*. 2013;42:1660-8. [PMID: 23243116] doi:10.1093/ije/dys173
- Levey AS, Stevens LA, Schmid CH, et al; CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150:604-12. [PMID: 19414839]
- Levey AS, Coresh J, Greene T, et al; Chronic Kidney Disease Epidemiology Collaboration. Expressing the Modification of Diet in Renal Disease Study equation for estimating glomerular filtration rate with standardized serum creatinine values. *Clin Chem*. 2007;53:766-72. [PMID: 17332152]
- DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7:177-88. [PMID: 3802833]

33. Reitsma JB, Glas AS, Rutjes AW, et al. Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. *J Clin Epidemiol.* 2005;58:982-90. [PMID: 16168343]
34. Tangri N, Grams ME, Levey AS, et al; CKD Prognosis Consortium. Multinational assessment of accuracy of equations for predicting risk of kidney failure: a meta-analysis. *JAMA.* 2016;315:164-74. [PMID: 26757465] doi:10.1001/jama.2015.18202
35. Weaver RG, James MT, Ravani P, et al. Estimating urine albumin-to-creatinine ratio from protein-to-creatinine ratio: development of equations using same-day measurements. *J Am Soc Nephrol.* 2020;31:591-601. [PMID: 32024663] doi:10.1681/ASN.2019060605
36. Nelson RG, Grams ME, Ballew SH, et al; CKD Prognosis Consortium. Development of risk prediction equations for incident chronic kidney disease. *JAMA.* 2019. [PMID: 31703124] doi:10.1001/jama.2019.17379
37. Marshall T, Williams KM. Total protein determination in urine: elimination of a differential response between the coomassie blue and pyrogallol red protein dye-binding assays. *Clin Chem.* 2000;46:392-8. [PMID: 10702527]
38. Schrader J, Lüders S, Kulschewski A, et al; MARPLE Study Group. Microalbuminuria and tubular proteinuria as risk predictors of cardiovascular morbidity and mortality in essential hypertension: final results of a prospective long-term study (MARPLE Study)*. *J Hypertens.* 2006;24:541-8. [PMID: 16467658]

Current Author Addresses: Dr. Sumida: Division of Nephrology, Department of Medicine, University of Tennessee Health Science Center, 956 Court Avenue, Suite A220, Memphis, TN, 38163.

Dr. Nadkarni: One Gustave L. Levy Place, Box 1243, New York, NY 10029.

Drs. Grams, Ballew, Coresh, Ballew, Matsushita, and Surapaneni, and Ms. Sang: Chronic Kidney Disease Prognosis Consortium, 2024 East Monument Street, Baltimore, MD 21287.

Dr. Brunskill: Department of Nephrology, Leicester General Hospital, Gwendolen Road, Leicester, LE5 4PW, United Kingdom.

Dr. Chadban: Kidney Centre RPA, Level 2, Professor Marie Bashir Centre, Royal Prince Alfred Hospital, Missendon Road, Camperdown, New South Wales 2050, Australia.

Dr. Chang: 100 North Academy Ave, Danville, PA 17822.

Dr. Cirillo: Department of Public Health, Azienda Ospedaliera Universitaria Federico II, via Sergio Pansini 5, 80131 Naples, Italy.

Dr. Daratha: Providence Sacred Heart Medical Center and Gonzaga University School of Anesthesia, Providence Sacred Heart Doctor's Building, 105 West 8th Avenue, Suite 6050W, Spokane, WA 99204.

Dr. Gansevoort: Department of Nephrology, University Medical Center Groningen, P.O. Box 30.001, 9700 RB Groningen, The Netherlands.

Dr. Garg: Department of Medicine, Epidemiology and Biostatistics, Western University, 800 Commissioners Road E, ELL-101, Victoria Hospital, P.O. Box 5010, London, ON N6A 5W9, Canada.

Dr. Iacoviello: IRCCS Neuromed, Via dell'Elettronica, 86077 Pozzilli (IS), Italy.

Dr. Kayama: Global Center of Excellence Program Study Group, Yamagata University School of Medicine, 2-2-2 Iida-Nishi, Yamagata 990-9585, Japan.

Dr. Konta: Department of Public Health and Hygiene, Yamagata University Graduate School of Medical Science, 2-2-2 Iida-Nishi, Yamagata 990-9585, Japan.

Dr. Kovesdy: Division of Nephrology, University of Tennessee Health Science Center, 956 Court Avenue, Room B222, Memphis TN, 38163.

Dr. Lash: Division of Nephrology, Department of Medicine, University of Illinois at Chicago, 840 South Wood Street (M/C 793), Chicago, IL 60612.

Dr. Lee: Moanalua Medical Center, 3288 Moanalua Road, Honolulu, HI 96819.

Dr. Major: Department of Health Sciences, George Davies Centre, University of Leicester, 15 Lancaster Road, Leicester, LE1 7HA, United Kingdom.

Dr. Metzger: CESP INSERM U1018, Hôpital Paul Brousse, Bat 15/16, 16 avenue Paul Vaillant Couturier, Villejuif 94807, France.

Dr. Miura: Department of Public Health Director, Center for Epidemiologic Research in Asia, Shiga University of Medical Science Seta-Tsukinowa-cho, Otsu, Shiga, 520-2192, Japan.

Dr. Naimark: Rm. 386, 1929 Bayview Ave., Toronto, ON M4G 3E8, Canada.

Dr. Nelson: National Institutes of Health, 1550 East Indian School Road, Phoenix, AZ 85014.

Dr. Sawhney: Aberdeen Centre for Health Data Science, University of Aberdeen, Foresterhill Campus, Aberdeen, AB25 2AN, United Kingdom.

Mr. Stempniewicz: One Prince Street, Alexandria, VA 22314.

Ms. Tang: University of British Columbia, 4/F Howe Site, 1081 Burrard Street, Vancouver, BC V6Z1Y6, Canada.

Dr. Townsend: University of Pennsylvania, Renal Division, 3400 Spruce Street, 122 Founders Building, Philadelphia, PA 19104.

Dr. Traynor: Glasgow Renal and Transplant Unit, Renal 1st Floor, Zone 3 OZ 1-3, Office Block, Queen Elizabeth University Hospital, 1345 Govan Road, Glasgow, G51 4TF, United Kingdom.

Dr. Valdivielso: Vascular and Renal Translational Research Group, Biomedical Research Institute of Lleida, Av. Alcalde Rovira Roure, 80, 25198 Lleida, Spain.

Dr. Wetzels: Department of Nephrology 464, Radboud University Medical Center, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands.

Dr. Polkinghorne: Monash Medical Centre, 246 Clayton Road, Clayton, Melbourne, Victoria 3168, Australia.

Dr. Heerspink: Department of Clinical Pharmacy and Pharmacology, De Brug 50C-1-011; EB70, University Medical Center Groningen, P.O. Box 30001, 9700 AD Groningen, The Netherlands.

Author Contributions: Conception and design: G.N. Nadkarni, M.E. Grams, N. Brunskill, S.J. Chadban, M. Cirillo, K.R. Polkinghorne.

Analysis and interpretation of the data: K. Sumida, M.E. Grams, Y. Sang, S.H. Ballew, K. Matsushita, A. Surapaneni, N. Brunskill, A.R. Chang, M. Cirillo, K.B. Daratha, C.P. Kovesdy, R. Major, K. Miura, D.M.J. Naimark, S. Sawhney, N. Stempniewicz, R.R. Townsend, K.R. Polkinghorne, H.J.L. Heerspink.

Drafting of the article: K. Sumida, G.N. Nadkarni, M.E. Grams, Y. Sang, S.H. Ballew, A.R. Chang, M. Cirillo, K.B. Daratha, J. Lash, D.M.J. Naimark, J.P. Traynor, J.M. Valdivielso, J. Wetzels, K.R. Polkinghorne, H.J.L. Heerspink.

Critical revision for important intellectual content: K. Sumida, G.N. Nadkarni, M.E. Grams, Y. Sang, S.H. Ballew, J. Coresh, K. Matsushita, N. Brunskill, S.J. Chadban, A.R. Chang, M. Cirillo, R.T. Gansevoort, T. Kayama, T. Konta, C.P. Kovesdy, M. Metzger, K. Miura, D.M.J. Naimark, R.G. Nelson, S. Sawhney, N. Stempniewicz, K.R. Polkinghorne.

Final approval of the article: K. Sumida, G.N. Nadkarni, M.E. Grams, Y. Sang, S.H. Ballew, J. Coresh, K. Matsushita, A. Surapaneni, N. Brunskill, S.J. Chadban, A.R. Chang, M. Cirillo, K.B. Daratha, R.T. Gansevoort, A.X. Garg, L. Iacoviello, T. Kayama, T. Konta, C.P. Kovesdy, J. Lash, B.J. Lee, R. Major, M. Metzger, K. Miura, D.M.J. Naimark, R.G. Nelson, S. Sawhney, N. Stempniewicz, M. Tang, R.R. Townsend, J.P. Traynor, J.M. Valdivielso, J. Wetzels, K.R. Polkinghorne, H.J.L. Heerspink.

Provision of study materials or patients: N. Brunskill, R.T. Gansevoort, L. Iacoviello, C.P. Kovesdy, R. Major, R.G. Nelson, S. Sawhney, R.R. Townsend, J. Wetzels, K.R. Polkinghorne.

Statistical expertise: Y. Sang, J. Coresh.

Obtaining of funding: G.N. Nadkarni, M.E. Grams, J. Coresh, C.P. Kovesdy, J. Lash, K. Miura, R.R. Townsend.

Administrative, technical, or logistic support: M.E. Grams, S.H. Ballew, J. Coresh, R.T. Gansevoort, C.P. Kovesdy, M. Tang.

Collection and assembly of data: M.E. Grams, S.H. Ballew, J. Coresh, K. Matsushita, N. Brunskill, S.J. Chadban, M. Cirillo, K.B. Daratha, R.T. Gansevoort, A.X. Garg, L. Iacoviello, T. Konta, C.P. Kovesdy, B.J. Lee, R. Major, K. Miura, R.G. Nelson, S. Sawhney, N. Stempniewicz, M. Tang, R.R. Townsend, J.P. Traynor, J.M. Valdivielso, J. Wetzels, K.R. Polkinghorne, H.J.L. Heerspink.

APPENDIX: MEMBERS OF THE CKD-PC

CKD-PC Investigators and Collaborators

AusDiab (Australian Diabetes, Obesity, and Lifestyle Study)

Kevan R. Polkinghorne*, Steven J. Chadban*, Robert Atkins†

CanPREDDICT (Canadian Study of Prediction of Death, Dialysis and Interim Cardiovascular Events)

Adeera Levint†, Ognjenka Djurdjevt†, Mila Tang*

CRIC (Chronic Renal Insufficiency Cohort)

Hernan Rincon Choles†, Edward Horwitz†, Farsad Afshinnia†, Raymond R. Townsend*

CURE-CKD (Center for Kidney Disease Research, Education, and Hope)

Katherine Tuttle†, Kenn B. Daratha*, Radica Alicic†, Cami R. Jones†

Geisinger Health System

Alex R. Chang*, Gurmukteshwar Singht†, Jamie Greent†, H. Lester Kirchnert†

GLOMMS 2 (Grampian Laboratory Outcomes, Morbidity and Mortality Studies–2)

Simon Sawhney*, Corri Black†, Angharad Markst†, Lynn Robertson†

ICES-KDT (Institute for Clinical Evaluation Science, Kidney, Dialysis, and Transplant Program)

Amit X. Garg*

IDNT (Irbesartan Type II Diabetic Nephropathy Trial)

Hiddo J.L. Heerspink*

Kaiser Permanente Hawaii

Brian J. Lee*

LCC (The Leicester City and County Chronic Kidney Disease Cohort)

Nigel Brunskill*, Rupert Major*, David Shepherd†, James Medcalf†

MASTERPLAN (Multifactorial Approach and Superior Treatment Efficacy in Renal Patients With the Aid of a Nurse Practitioner)

Jack Wetzels*, Peter Blankestijnt†, Arjan van Zuilent†, Jan van de Brand†

Moli-sani

Massimo Cirillo*, Licia Iacoviello*

Mount Sinai BioMe Biobank Platform

Girish N. Nadkarni*, Erwin P. Bottingert†, Ruth J.F. Loost†, Stephen B. Ellist†

Nefrona

José M. Valdivielso*, Marcelino Bermúdez-López†, Milica Bozic†, Serafi Cambray†

NephroTest Study

Benedicte Stengel†, Marie Metzger*, Martin Flammant†, Pascal Houillier†, Jean-Philippe Haymann†

NIPPON DATA2010 (National Integrated Project for Prospective Observation of Non-communicable Disease and Its Trends in the Aged 2010)

Katsuyuki Miura*, Akira Okayama†, Aya Kadota†, Sachiko Tanaka†

OLDW (OptumLabs Data Warehouse)

Nikita Stempniewicz*, John Cuddeback†, Elizabeth Cieminst†, Emily Carbonara†, Stephan Dunning†

Pima Indian Study

Robert G. Nelson*, William C. Knowlert†, Helen C. Lookert†

PSP-CKD (Primary–Secondary Care Partnership to Prevent Adverse Outcomes in Chronic Kidney Disease)

Nigel Brunskill*, Rupert Major*, David Shepherd†, James Medcalf†

RCAV (Racial and Cardiovascular Risk Anomalies in CKD Cohort)

Csaba P. Kovcsdy*, Keiichi Sumida*, Miklos Molnart†, Praveen Potukuchit†

RENAAL (Reduction of Endpoints in Non-insulin Dependent Diabetes Mellitus With the Angiotensin II Antagonist Losartan)

Hiddo J.L. Heerspink*, Michelle Pena†, Dick de Zeeuw†

SUN-Macro (Sulodexide Macro-albuminuria Trial)

Hiddo J.L. Heerspink*

Sunnybrook Cohort

David M.J. Naimark*, Navdeep Tangrit†

Takahata Study

Takamasa Kayama*, Tsuneo Konta*

West of Scotland Study

Patrick B. Mark*, Jamie P. Traynor*, Peter C. Thomson†, Colin C. Geddes†

CKD-PC Steering Committee

Josef Coresh (Chair)*, Shoshana H. Ballew*, Alex R. Chang*, Ron T. Gansevoort*, Morgan E. Grams*, Orlando Gutierrez†, Tsuneo Konda*, Anna Köttgen†, Andrew S. Levey†, Kunihiro Matsushita*, Kevan R. Polkinghorne*, Elke Schäffner†, Mark Woodward†, Luxia Zhang†

CKD-PC Data Coordinating Center

Shoshana H. Ballew (Assistant Project Director)*, Jingsha Chen (Programmer)†, Josef Coresh (Principal Investigator)*, Morgan E. Grams (Director of Nephrology Initiatives)*, Kunihiro Matsushita (Director)*, Yingying Sang (Lead Programmer)*, Aditya Surapeneni (Programmer)*, Mark Woodward (Senior Statistician)†

* Members of the CKD-PC who authored this work.

† Members of the CKD-PC who contributed to this work but did not author it.