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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

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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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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 dipstick. 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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dardized 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 calculated 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

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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 m^2 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 ckdpcrisk.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).

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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 m²*	eGFR <60 mL/min/1.73 m², *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). T4

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 specificity 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**). T5

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

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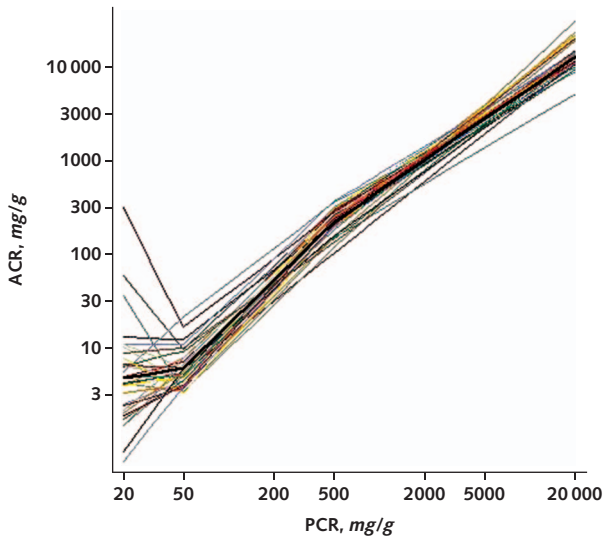
Figure. Relationship between urine PCR and urine ACR values in individual cohorts (*multicolored lines*) and after random-effects meta-analysis (*thick black line*) in the crude model.



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**, available 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 × log (min (PCR/50, 1)) + 1.5793 × log (max(min(PCR/500, 1), 0.1)) + 1.1266 × log (max (PCR/500, 1)))
Predicted error	pErr = sqrt (exp (−2.2996 + 0.1043 × log (min (pACR/30, 1)) − 0.4401 × log (max(min(pACR/300, 1), 0.1)) − 0.3897 × log (max (pACR/300, 1))))
Adjusted	
Predicted ACR	pACR = exp (5.2659 + 0.2934 × log (min (PCR/50, 1)) + 1.5643 × log (max(min(PCR/500, 1), 0.1)) + 1.1109 × log (max (PCR/500, 1)) − 0.0773 × (if female) + 0.0797 × (if diabetic) + 0.1265 × (if hypertensive))
Predicted error	pErr = sqrt (exp (−2.0664 + 0.1658 × log (min (pACR/30, 1)) − 0.4599 × log (max(min(pACR/300, 1), 0.1)) − 0.3084 × log (max (pACR/300, 1)) + 0.0847 × (if female) − 0.2553 × (if diabetic) − 0.2299 × (if hypertensive)))
Dipstick	
Crude	
Predicted ACR	pACR = exp (2.4738 + 0.7539 × (if trace) + 1.7243 × (if +) + 3.3475 × (if ++) + 4.6399 × (if >++))
Predicted error	pErr = sqrt (exp (−1.3710 + 0.6843 × log (min (pACR/30, 1)) − 0.1869 × log (max(min(pACR/300, 1), 0.1)) − 0.9220 × log (max (pACR/300, 1))))
Adjusted	
Predicted ACR	pACR = exp (2.0373 + 0.7270 × (if trace) + 1.6775 × (if +) + 3.2622 × (if ++) + 4.5435 × (if >++) + 0.0822 × (if female) + 0.27249 × (if diabetic) + 0.33627 × (if hypertensive))
Predicted error	pErr = sqrt (exp (−0.4525 + 0.5939 × log (min (pACR/30, 1)) − 0.1292 × log (max(min(pACR/300, 1), 0.1)) − 0.2610 × log (max (pACR/300, 1)) − 0.0772 × (if female) − 0.2093 × (if diabetic) − 0.1624 × (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 ≥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 × pErr), exp (log (pACR) + 1.96 × pErr).

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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.

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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.

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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 intercohort 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.

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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.

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