Estimated GFR in the Korean and US Asian Populations Using the 2021 Creatinine-Based GFR Estimating Equation Without Race

Jimin Hwang,* Kwanghyun Kim,* Josef Coresh, Lesley A. Inker, Morgan E. Grams, and Jung-Im Shin

Rationale & Objective: In 2021, the new Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) updated the creatinine-based estimated glomerular filtration rate (eGFR) equation and removed the coefficient for race. The development and validation of this equation involved binarizing race into African American and non-African American, involving few Asian participants. This study aimed to examine the difference between the 2021 equation and the previous 2009 equation on CKD prevalence estimates in 2 Asian populations.

Study Design: Observational study using 2 national surveys.

Setting & Participants: Participants from the 2019 Korea National Health and Nutrition Survey and participants self-reported as Asian from the 2011-2020 US National Health and Nutrition Survey.

Exposure: eGFR using 2009 and 2021 CKD-EPI creatinine equation.

Outcomes: Prevalence of CKD (eGFR <60 mL/min/1.73 m^2 or urine albumin-creatinine ratio ≥30 mg/g).

Analytical Approach: Sampling-weighted prevalence estimated using the 2009 and 2021 equations as well as the percentage of individuals with CKD G3+ using the 2009 equation being reclassified as not having CKD G3+ using the 2021 equation.

Results: The prevalence of CKD estimated using the 2021 equation was 9.75% (95% confidence intervals [CI], 8.80-10.80%) in Koreans and 11.60% (95% CI, 10.23-13.13%) in US Asians. The prevalence of CKD estimated using the 2021 equation was slightly lower than that using the 2009 equation in both Korean and US Asian populations by 0.63% (95% CI, 0.44-0.90%) and 0.84% (95% CI, 0.52-1.34%), respectively. Furthermore, 32.8% and 30.2% of Koreans and US Asians with CKD G3-5, respectively, estimated using the 2009 equation were reclassified as not having CKD G3-5 when the eGFR was calculated using the 2021 equation.

Limitations: Measured GFR was not available.

Conclusions: Use of the 2021 CKD-EPI creatinine equation leads to a small decrease in CKD prevalence in both Korean and US Asian populations, and of similar magnitude, resulting in significant reclassification among those originally classified as having CKD G3+.

Complete author and article information provided before references.

Correspondence to J.-I. Shin (jshin19@jhmi.edu)

**J.H. and K.K. contributed equally to this work.*

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Chronic kidney disease (CKD) is a leading cause of morbidity and mortality worldwide.[1] CKD-related deaths have steeply increased from 0.60 million in 1990 to 1.43 million in 2019 according to the Global Burden of Disease study,[2] and CKD is projected to be the fifth highest cause of years of life lost worldwide by 2040.[3] CKD is diagnosed by 2 measures: glomerular filtration rate (GFR), a marker of kidney function, and urine albumin-creatinine ratio (UACR), a marker of kidney damage. GFR can be measured directly from urinary or plasma clearance of exogenous filtration, but it is typically estimated from serum filtration markers such as creatinine or cystatin C in clinical practice.[4]

Multiple equations to estimate GFR have been developed, such as the Modified Diet in Renal Disease equation,[5] the 2009 CKD-Epidemiology Collaboration (CKD-EPI) creatinine equation,[6] the 2012 CKD-EPI creatinine-cystatin C equation,[7] and the European Kidney Function Consortium creatinine equation.[8] These equations, which use serum creatinine levels, included a race coefficient to account for a higher average serum creatinine level in African American individuals than non-African American individuals, increasing the estimated GFR (eGFR) level in African American individuals for the same level of serum creatinine level.[5,6,9] As race is a social construct rather than a purely biologic variable, considering there is more variation within than between racial and ethnic groups and clear variation in the magnitude of the variable for African American race across studies (8%-21%), many voiced concerns about using race for clinical decision making.[10-12] As a response, a new equation to calculate eGFR without race, the 2021 CKD-EPI creatinine equation, was developed,[4] which slightly underestimated GFR in African American individuals and overestimated GFR in non-African American individuals. The National Kidney Foundation-American Society of Nephrology Task Force recommended implementation of this new equation in clinical settings and urged conducting future studies to examine the effects of this new GFR estimating equation on all race and ethnic groups.[13]

The prevalence of CKD in Asian nations, as well as the etiologies of CKD, widely varies by region.[14,15] Within the United States, Asian Americans are reported to have a

PLAIN-LANGUAGE SUMMARY

The 2009 serum creatinine-based kidney function estimating equation used demographic information including race. Because race is a social construct, race was eliminated in the new equation developed in 2021. As race was categorized into African American and non-African American during its development, this study examined the impact of the 2021 equation in 2 distinct Asian populations (Koreans and US Asians) using 2 national datasets. We found that the prevalence of chronic kidney disease (CKD) estimated using the 2021 equation was slightly lower that estimated using the 2009 equation in both Koreans and US Asians. Approximately one-third of people with CKD estimated using the 2009 equation were reclassified as not having CKD estimated using the 2021 equation.

higher prevalence of elevated albuminuria and lower probability of reduction in eGFR compared to the White population,[16] possibly blunting the effects of changes in GFR estimating algorithms.

In this study, we used 2 nationally representative datasets to examine the effect of the new 2021 CKD-EPI creatinine equation on CKD prevalence estimates in 2 Asian populations, Koreans living in Korea and Asians living in the United States, and to compare the prevalence of CKD in these 2 populations.

METHODS

Data Source and Study Participants

We used 2 nationally representative datasets: the Korea National Health and Nutrition Survey (KNHANES) for Koreans residing in Korea, and the US National Health and Nutrition Survey (NHANES) for Asians residing in the United States. The KNHANES program, initiated in 1998, is a nationwide cross-sectional survey administered by the Korean Centers for Disease Control and Prevention to assess the health status and nutritional status of Koreans.[17] For our study population, we used the 2019 cycle of the KNHANES study. Among 8,110 total participants in the KNHANES 2019 study cycle, we excluded participants who were aged <20 years, missing serum creatinine measurements, or missing urinary albumin or urine creatinine measurements such that UACR could not be calculated. Finally, 5,735 participants were included as the Korean population in this study (Fig S1A).

NHANES is a nationally representative, population-level survey performed to collect information on health and nutrition in the United States using in-depth interviews, physical examinations, and laboratory test results. NHANES has been oversampling Asians since 2011 to obtain stable population estimates on this subgroup, in addition to the traditionally oversampled Hispanic and non-Hispanic African American populations.[18] In this study, we combined 4 cycles (2011-2013, 2013-2015, 2015-2017, and 2017-2020 pre-pandemic) that oversampled Asians and selected 5,036 participants who self-identified as non-Hispanic Asian in the demographics questionnaire. Applying the same exclusion criteria used for the Korean population, 2,801 Asians aged ≥20 year and without missing values for serum creatinine and UACR were included in the study as the US Asian population (Fig S1B).

Definition of CKD

CKD was defined in accordance with Kidney Disease Improving Global Outcomes (KDIGO) guidelines as eGFR <60 mL/minute/1.73 m^2 or albuminuria defined as UACR ≥30 mg/g.[19] GFR was estimated based on serum creatinine levels measured as part of the standard biochemistry laboratory data in both the KHANES and NHANES datasets. We used 2 different equations to calculate eGFR based on serum creatinine: the 2021 CKD-EPI creatinine-based equation using only age and sex and the 2009 CKD-EPI creatinine-based equation using age, sex, and race.[4,6] In NHANES, UACR was measured from the first collection of random urine by the Mobile Examination Center, using a ratio of urine albumin measured by a fluorescent immunoassay and urine creatinine measured by an enzymatic method. KNHANES provided urine albumin and urine creatinine values measured from a random urine sample.

Definition of Other Demographic and Clinical Information

Information on participants' characteristics including age, sex, waist circumference, body mass index (BMI), smoking, and comorbid conditions (hypertension, diabetes or prediabetes status, stroke, and coronary heart disease) were obtained. Overweight and obesity were defined by Asian-specific BMI cutoffs of 23 and 25 kg/m^2, respectively, as recommended by the World Health Organization in 2000 and the Korean Society for the Study of Obesity.[20,21] Using a single (KNHANES) or an average of 2 blood pressure measurements (NHANES), hypertension was defined as systolic blood pressure >130 mm Hg, diastolic blood pressure ≥80 mm Hg, or self-reported antihypertensive medication use. Diabetes was defined as fasting plasma glucose ≥126 mg/dL, hemoglobin A1c ≥6.5%, self-reported physician diagnosis of diabetes, or use of glucose-lowering agents. Prediabetes was defined as fasting plasma glucose 100-125 mg/dL or hemoglobin A1c 5.7%-6.4%. Smoking status was classified as never smoker (had never smoked or smoked <100 cigarettes during their lifetime), prior smoker (no current smoking and had smoked >100 cigarettes during their lifetime), and current smokers. Stroke and coronary heart disease were self-reported.

Statistical Analysis

Baseline characteristics of the Korean and US Asian populations, overall and by sex, are shown. Continuous variables are presented as means and 95% confidence intervals (CIs), and categorical variables are expressed as weighted proportions with 95% CIs. Weighted survey analyses were used for population estimates. We used recommended KNHANES and NHANES methods for survey weights and variance estimation for each population, respectively.[22,23]

Using the 2 different GFR estimating equations, we estimated the prevalence of CKD, CKD stages for GFR (G3, G4, G5 for eGFR 45-60, 30-45, and <30 mL/min/1.73 m^2, respectively),[19,24] and albuminuria (UACR ≥30 mg/g) in the Korean and US Asian populations, with standard errors. Differences in prevalence according to eGFR estimating equation are presented as percentages, with the 2009 CKD-EPI creatinine equation as the reference. The total number of individuals with CKD or in eGFR category was determined by applying prevalence estimates to the Korean census estimate of 44,902,975 adults aged ≥20 years according to the 2022 Korean Statistical Information Service and the US Census estimate of 14,179,916 Asians using the American Community Survey 2018. Reclassification analyses were performed across age groups (<65 and ≥65 years) to assess the proportion of patients originally classified as CKD G3-5 (defined as eGFR <60 mL/min/1.73 m^2) using the 2009 equation that was reclassified to the group without CKD G3-5 using the 2021 equation.

Using the 2021 CKD-EPI creatinine equation, we compared age (20-39, 40-64, and 65+) and sex-specific prevalence of CKD, CKD G3-5, and albuminuria between the Korean and US Asian populations. We examined the associations between participant characteristics (age, sex, BMI, smoking, hypertension, and diabetes/prediabetes status) and CKD, CKD G3-5, and albuminuria in the Korean and US Asian populations separately using multivariable logistic regression. All statistical analyses were performed with R version 4.0.2 (R Core Team).

RESULTS

Characteristics of the Participants

There were 5,735 participants from the KNHANES study and 2,801 Asian participants from the NHANES study. Overall, US Asians were younger, heavier, less likely to smoke, and less likely to have hypertension and prediabetes but more likely to have diabetes. The prevalence of stroke and coronary heart disease were similar between the 2 populations. In both Koreans and US Asians, men had higher prevalence of obesity, smoking, hypertension, diabetes, and coronary heart disease (Table 1).

Estimated Prevalence of CKD by 2 Different GFR Estimating Equations

There was a slight increase in mean eGFR using the 2021 equation, by 4 mL/min/1.73 m^2 (101 with CKD-EPI 2021, 97 with CKD-EPI 2009) in the Korean population, and by 4 mL/min/1.73 m^2 (104 with CKD-EPI 2021, 100 with CKD-EPI 2009) in the US Asian population.

The estimated prevalence of CKD using the 2021 CKD-EPI creatinine equation was 9.75 % (95% CI, 8.80-10.80) in the Korean population and 11.60% (95% CI, 10.23-13.13) in the US Asian population. The prevalence of CKD estimated using the 2021 CKD-EPI creatinine equation was slightly lower than the prevalence estimated using the 2009 CKD-EPI creatinine equation in both Korean and US Asian populations, by 0.63% (95% CI, 0.44-0.90) and 0.84% (95% CI, 0.52-1.34), respectively. The trend was consistent across GFR stages: the prevalence of CKD G3 through G5 estimated using the 2021 CKD-EPI creatinine equation was lower than the prevalence estimated using the 2009 CKD-EPI creatinine equation, with smaller absolute differences for more advanced GFR stages (Table 2). Decrease in estimated prevalence was most prominent in participants aged ≥65 years, whereas the effect of using the 2021 CKD-EPI creatinine equation were minimal in younger participants (Fig 1, Fig S2).

Reclassification of CKD G Stages Estimated Using the 2021 CKD-EPI Creatinine Equation From Those Using the 2009 Equation

Overall, 32.8% of those originally classified as CKD G3-5 using the 2009 CKD-EPI creatinine equation (31.8% in older adults and 36.1% in young adults) in the Korean population and 30.1% in the US Asian population (31.5% in older adults and 25.5% in young adults) were reclassified as not having CKD G3-5 with the 2021 equation. An additional 0.7% and 1.9% of those with CKD G3-5 determined using the 2009 equation were reclassified into a higher (less severe) GFR category with the 2021 equation in the Korean and US Asian populations, respectively (Tables S1-S3). Notably, 77.8% of Korean and 79.7% of US Asian adults who were reclassified from having CKD G3-5 to not having CKD G3-5 were aged ≥65. In both populations, no individuals were reclassified into a lower (more severe) GFR category or moved across the eGFR threshold of 60 mL/min/1.73 m^2 from not having to having CKD G3-5 when the CKD-EPI 2021 equation was used rather than the 2009 equation.

Comparison of CKD Prevalence Between the Korean and US Asian Populations

The prevalence of CKD and eGFR <60 mL/min/1.73 m^2 estimated using both the 2009 and 2021 CKD-EPI creatinine equations as well as albuminuria were consistently higher in the US Asian population than the Korean population (Table 2). Stratified by age and sex, the prevalence difference between Koreans and US Asians was most marked in older men (aged ≥65), with prevalence of CKD 25.6% and 34.6% in Koreans and US Asians, respectively (Fig 2). In contrast, for older women, the prevalence of CKD was similar at 24.0% in Koreans and 24.5% in US Asians. The difference in older men between Koreans and

Table 1. Demographic and Clinical Characteristics of the Korean and US Asian Populations

	Korean Population[a] (KNHANES 2019)			US Asian Population[b] (NHANES 2011-2020 Pre-Pandemic)		
	Total (N = 5,735)	Men (N = 2,596)	Women (N = 3,139)	Total (N = 2,801)	Men (N = 1,343)	Women (N = 1,458)
Characteristic	Weighted Mean or Proportion (95% CI)			Weighted Mean or Proportion (95% CI)		
Age, y	48.3 (47.4, 49.2)	47.1 (46.1, 48.1)	49.5 (48.6, 50.5)	45.1 (44.1, 46.2)	44.6 (43.3, 45.8)	45.7 (44.4, 46.9)
Waist circumference, cm	84.1 (83.7, 84.5)	87.8 (87.33, 88.3)	80.2 (79.7, 80.7)	88.8 (88.2, 89.3)	92.1 (91.4, 92.7)	85.9 (85.2, 86.5)
BMI, kg/m^2	24.0 (23.9, 24.1)	24.7 (24.49, 24.8)	23.3 (23.2, 23.5)	25.2 (25.0, 25.4)	25.8 (25.5, 26.0)	24.7 (24.4, 25.0)
BMI category						
Normal to underweight (BMI <23)	41.8 (40.1, 43.5)	31.6 (29.3, 33.9)	52.3 (49.8, 54.8)	33.6 (31.2, 36.0)	23.7 (20.3, 27.1)	42.0 (38.9, 45.1)
Overweight (23 ≤ BMI <25)	23.2 (21.9, 24.6)	26.4 (24.3, 28.5)	20.0 (18.4, 21.6)	21.1 (19.3, 22.9)	23.8 (20.8, 26.7)	18.8 (16.3, 21.4)
Obese (BMI ≥25)	35.0 (33.5, 36.5)	42.0 (39.8, 44.3)	27.7 (25.7, 29.7)	45.3 (43.1, 47.6)	52.5 (49.6, 55.5)	39.1 (36.2, 42.1)
Smoking						
Never	57.9 (56.3, 59.4)	28.1 (25.8, 30.4)	88.7 (87.3, 90.2)	85.0 (83.2, 86.8)	73.2 (70.0, 76.5)	94.0 (92.7, 95.4)
Past	22.0 (20.8, 23.3)	38.0 (35.6, 40.4)	5.5 (4.7, 6.4)	6.0 (4.9, 7.1)	10.5 (8.6, 12.5)	2.5 (1.5, 3.4)
Current	20.1 (18.7, 21.5)	34.0 (31.8, 36.2)	5.8 (4.6, 7.0)	9.1 (7.6, 10.5)	16.2 (13.4, 19.1)	3.5 (2.6, 4.4)
Hypertension	49.2 (47.2, 51.2)	55.1 (52.4, 57.7)	43.1 (40.7, 45.5)	41.5 (39.0, 44.0)	47.1 (44.2, 50.0)	36.6 (33.4, 39.7)
Prediabetes	40.5 (38.8, 42.2)	42.0 (39.57, 44.5)	38.9 (37.0, 40.9)	26.7 (24.4, 29.1)	27.2 (24.2, 30.3)	26.3 (23.6, 29.0)
Diabetes	12.2 (11.1, 13.4)	13.6 (12.0, 15.2)	10.8 (9.6, 12.1)	15.7 (14.0, 17.3)	18.1 (16.3, 19.9)	13.6 (11.4, 15.8)
Stroke	1.8 (1.4, 2.2)	2.3 (1.6, 2.9)	1.4 (1.0, 1.9)	1.4 (0.9, 1.8)	1.2 (0.7, 1.7)	1.5 (0.8, 2.2)
Coronary heart disease	2.5 (2.0, 2.9)	3.1 (2.4, 3.8)	1.8 (1.3, 2.3)	2.0 (1.4, 2.5)	2.9 (2.0, 3.8)	1.1 (0.5, 1.8)

Proportions are calculated after excluding those with missing values for that variable.
Abbreviations: BMI, body mass index; CI, confidence interval; KNHANES, Korean National Health and Nutrition Survey; NHANES, National Health and Nutrition Survey.
[a]Korean population: Missing entries in waist circumference (25, 0.4%), BMI (26, 0.5%), hypertension (18, 0.3%), diabetes mellitus (204, 3.7%), smoking (58, 1.0%), stroke (256, 4.5%), coronary heart disease (254, 4.4%).
[b]US Asian population: Missing entries in waist circumference (140, 5.0%), BMI (25, 0.9%), hypertension (207, 7.4%), diabetes mellitus (1, 0.03%), smoking (249, 8.9%), stroke (2, 0.1%), coronary heart disease (4, 0.1%).

Table 2. Prevalence of CKD, GFR Stages, and Albuminuria in Korean and US Asian Populations[a] Using Different GFR Estimating Equations

	Korean Population (KNHANES 2019)			US Asian Population (NHANES 2011-2020 Pre-Pandemic)		
Equation	**Number in Thousands[b]**	**Weighted Percent[b]**	**Change From eGFRcr(ASR), Percent[b]**	**Number in Thousands[b]**	**Weighted Percent[b]**	**Change From eGFRcr(ASR), Percent[b]**
Chronic kidney disease						
CKD-EPI 2009 (ASR)[a]	4,662 (4,212, 5,155)	10.38 (9.38, 11.48)	Ref	1,763 (1,551, 2,000)	12.44 (10.94, 14.10)	Ref
CKD-EPI 2021 (AS)[c]	4,379 (3,949, 4,851)	9.75 (8.80, 10.80)	−0.63 (−0.90, −0.44)	1,645 (1,451, 1,861)	11.60 (10.23, 13.13)	−0.84 (−1.34, −0.52)
eGFR <60 mL/min/1.73 m^2						
CKD-EPI 2009 (ASR)	1,288 (1,081, 1,532)	2.87 (2.41, 3.41)	Ref	523 (383, 712)	3.69 (2.70, 5.02)	Ref
CKD-EPI 2021 (AS)	867 (710, 1,057)	1.93 (1.58, 2.35)	−0.94 (−1.27, −0.69)	365 (259, 513)	2.58 (1.83, 3.62)	−1.11 (−1.6, −0.73)
eGFR <45 mL/min/1.73 m^2						
CKD-EPI 2009 (ASR)	360 (273, 475)	0.80 (0.61, 1.06)	Ref	147 (88.6, 244)	1.04 (0.63, 1.72)	Ref
CKD-EPI 2021 (AS)	278 (201, 383)	0.62 (0.45, 0.85)	−0.18 (−0.30, −0.11)	115 (62.9, 209)	0.81 (0.44, 1.47)	−0.23 (−0.45, −0.12)
eGFR <30 mL/min/1.73 m^2						
CKD-EPI 2009 (ASR)	94.4 (48.8, 182)	0.21 (0.11, 0.41)	Ref	50.8 (18.7, 137)	0.36 (0.13, 0.97)	Ref
CKD-EPI 2021 (AS)	83.4 (41.5, 168)	0.19 (0.09, 0.37)	−0.02 (−0.18, 0.00)	48.1 (16.8, 137)	0.34 (0.12, 0.97)	−0.02 (−0.14, 0.00)
Albuminuria						
UACR ≥30 mg/g	3,871 (3,471, 4,313)	8.62 (7.73, 9.61)	N/A	149 (131, 168)	10.48 (9.26, 11.84)	N/A

Plus–minus values are means ± standard errors.
Abbreviations: AS, age, sex; ASR, age, sex, race; CKD, chronic kidney disease; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; eGFRcr, estimated glomerular filtration rate based on creatinine; GFR, glomerular filtration rate; KNHANES, Korean National Health and Nutrition Survey; N/A, xxx; NHANES, National Health and Nutrition Survey; Ref, reference; UACR, urinary albumin-creatinine ratio.
[a]CKD-EPI 2009 (ASR): estimates using the 2009 CKD-EPI creatinine equation using age, sex, and race.
[b]Values reported with 95% confidence intervals.
[c]CKD-EPI 2021 (AS): estimates using the 2021 CKD-EPI creatinine equation using age and sex.

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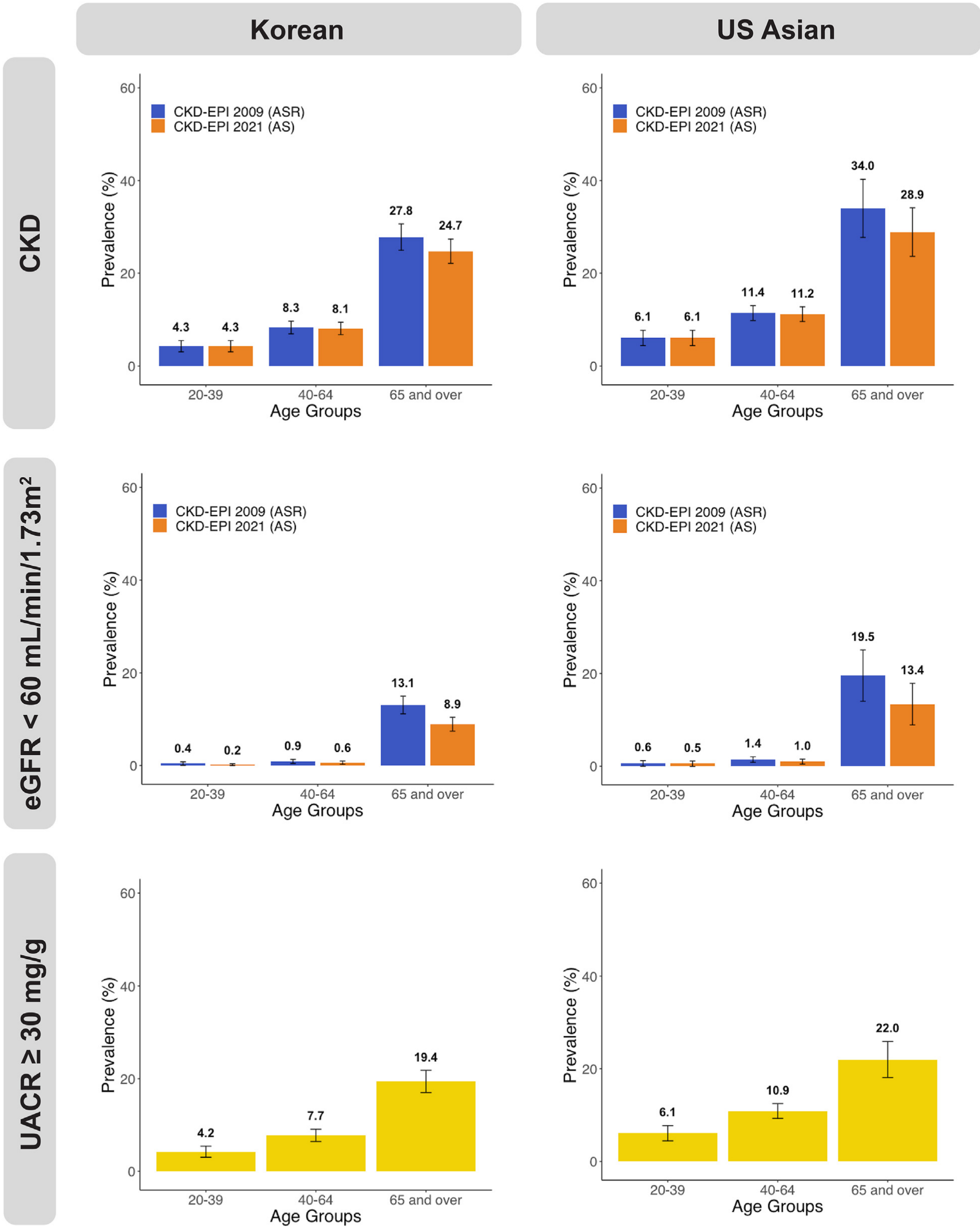

Figure 1. Prevalence of CKD by age using the 2009 and 2021 CKD-EPI creatinine equations in Koreans and US Asians. AS, age, sex; ASR, age, sex, race; CKD, chronic kidney disease; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; UACR, urinary albumin-creatinine ratio.

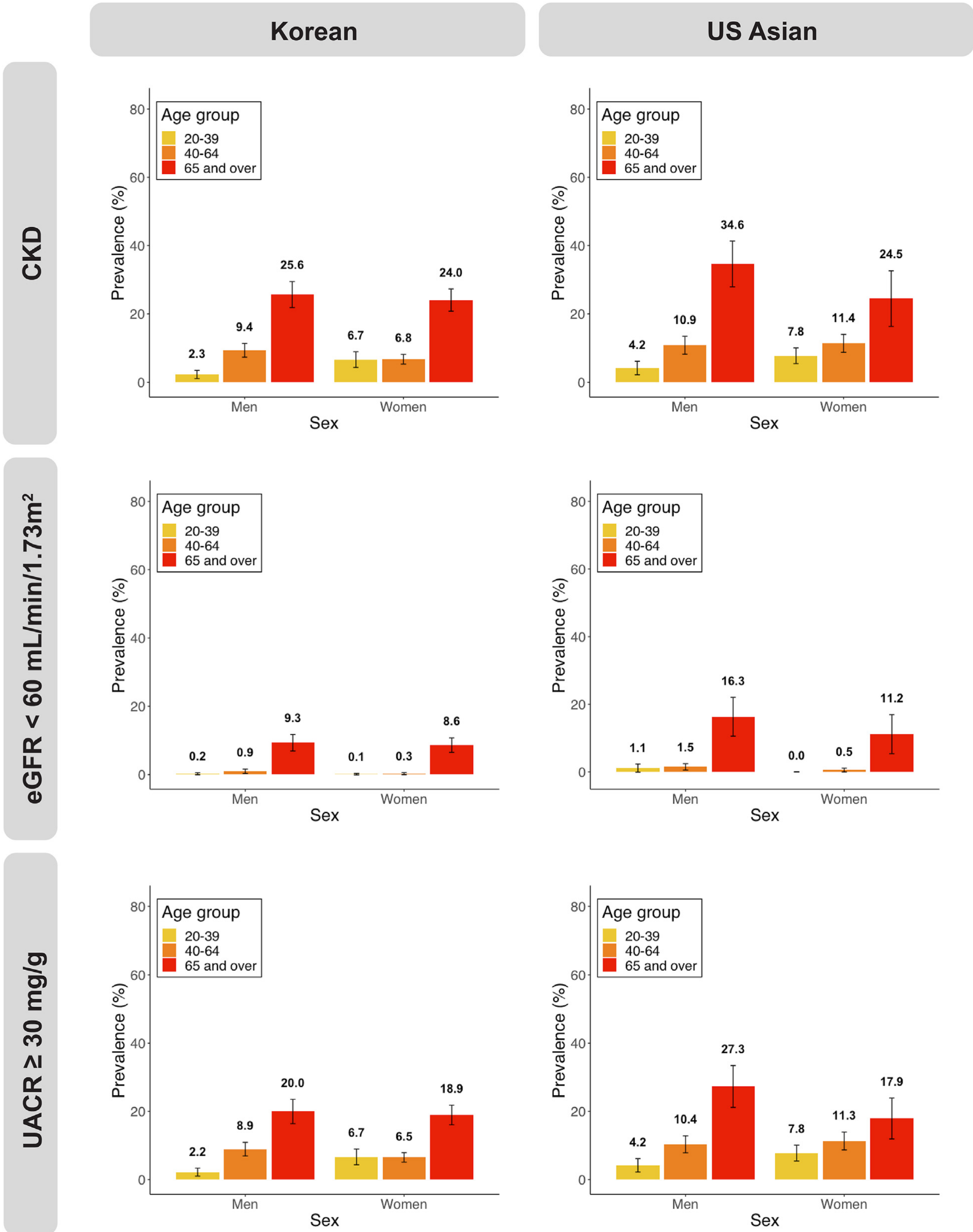

Figure 2. Prevalence of eGFR <60 mL/min/1.73 m^2, albuminuria, and CKD by age and sex in Koreans and US Asians using the 2021 CKD-EPI equation. CKD, chronic kidney disease; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; UACR, urinary albumin-creatinine ratio.

US Asians was driven by both eGFR <60 mL/min/1.73 m^2 and albuminuria; the prevalence of eGFR <60 mL/min/1.73 m^2 and albuminuria were approximately 2- and 1.5-fold higher, respectively, in US Asians compared with Koreans.

Risk Factors of CKD in the Korean and US Asian Populations

In both the Korean and US Asian populations, age was one of the most potent risk factors of CKD. Participants aged ≥65 had higher odds of CKD than participants aged 20-39 years (Korean: fully adjusted odds ratio [OR], 2.67; 95% CI, 1.78-4.02; US Asian: OR, 2.20; 95% CI, 1.35-3.58; Table 3). Women had higher odds of CKD than men in both populations, although the results were not statistically significant in the US Asian population. Hypertension, prediabetes, and diabetes were significant risk factors of CKD, whereas smoking history was not associated with CKD. Interestingly, while higher BMI was associated with higher odds of CKD in the Korean population in the fully adjusted model, there was no significant association between BMI and CKD in the US Asian population after adjustment for other risk factors such as hypertension and diabetes.

Similar trends in association were observed with eGFR <60 mL/min/1.73 m^2 (Table S4) and albuminuria (Table S5). The association with age was stronger with eGFR <60 mL/min/1.73 m^2 than with albuminuria in both populations. In the Korean population, obesity was positively associated with both eGFR <60 mL/min/1.73 m^2 and albuminuria in the fully adjusted model. In the US Asian population, BMI was associated with neither of the outcomes after adjustment.

DISCUSSION

There is scant evidence validating the 2021 CKD-EPI creatinine equation in other non-African American minority populations or populations outside the United States. The distribution of GFRs and prevalence of CKD vary in different Asian countries, possibly due to national and regional differences and genetic heterogeneity, necessitating accumulation of further evidence in this population.[14,15] In this study, we analyzed the effect of using the 2021 CKD-EPI creatinine equation on the prevalence of CKD in Korean and US Asian populations. The prevalence of CKD estimated with the 2021 CKD-EPI creatinine equation was 9.8% in Koreans and 11.6% in US Asians. We detected a small decrease in estimated prevalence in CKD when using the 2021 CKD-EPI creatinine equation compared with the 2009 CKD-EPI creatinine equation, similar to what was seen in the non-African American population used in the original development and validation of the new equation.[4] Furthermore, nearly one-third of participants originally classified as having CKD G3-5 using the 2009 CKD-EPI creatinine equation was reclassified into not having CKD G3-5 using the 2021 CKD-EPI creatinine equation (32.8% in Korean and 30.2% in US Asian populations). Subgroup analysis showed that the effect of using the 2021 CKD-EPI equation on estimated CKD G3-5 prevalence was largest in older populations, whereas the effect in younger adults was minimal.

Our results showed that application of the 2021 CKD-EPI creatinine equation leads to a slightly lower estimate of CKD prevalence than use of the 2009 CKD-EPI creatinine equation in 2 Asian populations. The 2021 CKD-EPI creatinine equation has yielded higher eGFR values and lower CKD prevalence than the 2009 equation in different Asian populations including Chinese, Thai, and Asian Indian populations, consistent with our study.[25-31] We found that the decrease in estimated CKD prevalence is of similar magnitude in both Korean and US Asian populations, implying that lower estimates of CKD prevalence using the 2021 equation is common throughout different locations and subethnicities of the Asian race.

Notably, we saw the largest absolute decrease in estimated CKD prevalence in the elderly population. At an individual level, we found 31.8% and 31.5% of older individuals with CKD G3-5 in the Korean and US Asian populations, respectively, were reclassified as not having CKD G3-5. This result indicates that introduction of the 2021 equation may affect the elderly population the most, who are at highest risk of developing advanced stage CKD and at the highest risk of polypharmacy and comorbid cardiovascular disease, which are closely intertwined with CKD complications. Previous studies that examined the introduction of the CKD-EPI 2021 equation also noted possibly significant systemic overestimation and poorer prediction accuracy in patients with advanced age.[12,26,29] Studies also found significant reclassification in patients with more severe GFR categories toward lower (less severe) CKD categories in non-African American and Asian populations.[12,26,29] The European Renal Association has also expressed concerns regarding decreased accuracy in GFR estimation using the 2021 equation, particularly overestimation of GFR, in the larger part of the European population, and the lack of improvement in predictive value of CKD complications.[32] Likewise, if this equation does lead to higher bias, the use of the 2021 equation could potentially lead to underdiagnosis and undertreatment in Asian populations and ultimately the exacerbation of current disparities.[33] Therefore, there is a need for more robust data evaluating the estimation bias and diagnostic accuracy of the new equation in Asian older adults.

The prevalence of CKD is lower in Asian Americans than in Americans with other ethnicities.[16,34] In this study, we found that the estimated CKD prevalence was higher in the US Asian population than in the Korean population. The Global Burden of Disease study 2017 also reported that the age-standardized prevalence of CKD is higher in the United States (8.14%; 95% CI, 7.61-8.78) than in South Korea (7.10%; 95% CI, 6.56-7.65).[35] Whether the difference in CKD prevalence is due to the higher prevalence of risk

Table 3. Demographic and Clinical Factors and Their Associations With CKD in the Korean and US Asian Populations

	Korean Population (KNHANES 2019)			US Asian Population (2013-2020 Pre-Pandemic)		
CKD	**Prevalence (95% CI), %**	**Age-Sex Adjusted OR (95% CI)**	**Fully Adjusted OR (95% CI)**	**Prevalence (95% CI), %**	**Age-Sex Adjusted OR (95% CI)**	**Fully Adjusted OR (95% CI)**
Age (categorical), y						
20-39	4.3 (3.1, 5.5)	Ref (1.00)	Ref (1.00)	6.1 (4.4, 7.7)	Ref (1.00)	Ref (1.00)
40-64	8.1 (6.8, 9.4)	1.97 (1.38, 2.82)	1.01 (0.68, 1.50)	11.2 (9.6, 12.8)	1.94 (1.39, 2.70)	1.12 (0.72, 1.75)
65+	24.7 (22.1, 27.4)	7.35 (5.28, 10.23)	2.67 (1.78, 4.02)	28.9 (23.6, 34.1)	6.26 (4.36, 9.00)	2.20 (1.35, 3.58)
Sex						
Men	9.3 (7.9, 10.7)	Ref (1.00)	Ref (1.00)	11.2 (9.4, 13.1)	Ref (1.00)	Ref (1.00)
Women	10.2 (9.0, 11.4)	0.99 (0.80, 1.21)	1.35 (1.02, 1.80)	11.9 (10.2, 13.7)	1.03 (0.82, 1.29)	1.30 (0.96, 1.77)
BMI category						
Normal to underweight (BMI <23)	6.3 (5.2, 7.4)	Ref (1.00)	Ref (1.00)	9.3 (7.3, 11.4)	Ref (1.00)	Ref (1.00)
Overweight (23 ≤ BMI <25)	9.4 (7.5, 11.2)	1.35 (1.04, 1.77)	1.1 (0.84, 1.45)	11.7 (8.7, 14.8)	1.15 (0.77, 1.73)	1.03 (0.65, 1.63)
Obese (BMI ≥25)	14.0 (12.1, 16.0)	2.41 (1.88, 3.08)	1.59 (1.23, 2.05)	13.1 (11.0, 15.3)	1.37 (1.05, 1.79)	0.97 (0.70, 1.36)
Hypertension						
No hypertension	4.1 (3.3, 5.0)	Ref (1.00)	Ref (1.00)	5.3 (4.1, 6.5)	Ref (1.00)	Ref (1.00)
Hypertension	15.6 (13.9, 17.4)	3.13 (2.43, 4.03)	2.58 (1.96, 3.4)	20.0 (17.1, 22.8)	3.05 (2.16, 4.29)	2.70 (1.86, 3.93)
Diabetes						
No prediabetes/diabetes	4.4 (3.4, 5.3)	Ref (1.00)	Ref (1.00)	7.0 (5.6, 8.3)	Ref (1.00)	Ref (1.00)
Prediabetes	9.8 (8.4, 11.1)	1.82 (1.36, 2.45)	1.49 (1.10, 2.02)	11.2 (9.4, 13.0)	1.38 (1.03, 1.84)	1.40 (0.98, 1.99)
Diabetes	28.0 (24.3, 31.7)	5.47 (3.95, 7.58)	3.97 (2.84, 5.55)	29.2 (24.4, 34.0)	3.54 (2.73, 4.59)	3.14 (2.19, 4.50)
Smoking						
Never	9.3 (8.2, 10.5)	Ref (1.00)	Ref (1.00)	11.1 (9.6, 12.5)	Ref (1.00)	Ref (1.00)
Past	11.6 (9.4, 13.8)	1.27 (0.92, 1.73)	1.23 (0.90, 1.69)	19.7 (11.1, 28.3)	1.54 (0.89, 2.68)	1.38 (0.78, 2.46)
Current	8.8 (6.8, 10.8)	1.29 (0.93, 1.78)	1.14 (0.81, 1.59)	8.7 (5.4, 12.0)	0.90 (0.54, 1.50)	0.96 (0.54, 1.70)

Abbreviations: AS, age, sex; ASR, age, sex, race; BMI, body mass index; CI, confidence interval; CKD, chronic kidney disease; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; KNHANES, Korean National Health and Nutrition Survey; OR, odds ratio; Ref, reference.

factors such as diabetes, or inclusion of multiple Asian subethnicities in the US Asian cohort, remains to be elucidated. Interestingly, the observed association of obesity with CKD was not consistent between the Korean and US Asian populations in this study. Obesity had a significant independent association with CKD in the Korean population even after adjusting for hypertension and diabetes, but no significant association was observed after adjustment in the US Asian population. Our findings regarding the Korean population are generally consistent with those of previous studies. According to a meta-analysis of 5 million individuals enrolled in the Chronic Kidney Disease Prognosis Consortium, the association between obesity and GFR decline was reduced but still significant after adjustment for comorbid conditions including hypertension and diabetes.[36] Studies on Korean populations have also suggested a positive association between BMI and CKD independent of comorbid conditions.[37,38] The East Asian population is known to be more vulnerable to metabolic dysfunction and visceral adiposity at a given BMI.[39,40] A potential explanation for a more significant association in the Korean population than the US Asian population (encompassing all Asian subethnicities) may include presence of certain genetic or epigenetic factors that increase the susceptibility to kidney dysfunction with increasing BMI at lower thresholds in the Korean population. Further studies are needed to elucidate how obesity contributes to CKD development in diverse populations.

Our study has several limitations. First, as both the KNHANES and NHANES studies are cross-sectional in nature, we used a one-time measurement of serum creatinine to calculate eGFR. Additionally, there were no measured GFRs provided in the databases, preventing us from conducting bias analysis to test the accuracy of the equations. The risk factor analysis was also limited in inferring causality due to the cross-sectional study design. Also, due to the limited number of Asians in the NHANES data, we pooled data from 2011 to 2020 pre-pandemic cycles of the NHANES, whereas for Koreans, the data collection and measurement was performed only in 2019. However, we confirmed that there was no significant trend in CKD prevalence between 2011 and 2020 before pooling the data. Finally, incorporation of all self-reported Asian ethnicities, not just East Asians or Koreans, could lead to population heterogeneity, which may affect the comparability of the US Asian population with the Korean population. Future studies within distinct Asian populations are needed to tease out characteristics and differences within this group. Despite these limitations, our study is one of the few studies that has assessed the effect of the 2021 CKD-EPI equation without race in Asian populations, using 2 nationally representative databases.

In conclusion, the introduction of the 2021 equation resulted in decreased CKD prevalence in Korean and US Asian populations, with a larger decrease in the older population. Almost one-third of individuals with CKD G3-5 deterined using the 2009 equation were reclassified as not having CKD G3-5 with the 2021 equation, and the majority of them were individuals aged ≥65. Further studies for bias assessment and accuracy are needed to better understand the effect of the new equation.

SUPPLEMENTARY MATERIALS

Supplementary File (PDF)

Figure S1: Study population.

Figure S2: Prevalence of eGFR stages by age using the 2009 and 2021 CKD-EPI creatinine equations in Koreans and US Asians.

Table S1: Reclassification Analysis with Different GFR Estimating Equations.

Table S2: Reclassification Analysis with Different GFR Estimating Equations in Adults, Age at or Above 65.

Table S3: Reclassification Analysis with Different GFR Estimating Equations in Adults, Age Below 65.

Table S4: Demographic and Clinical Factors and Their Associations with eGFR <60 mL/min/1.73 m^2 in Korean and US Asian Populations.

Table S5: Demographic and Clinical Factors and Their Associations with Albuminuria in the Korean and US Asian Populations.

ARTICLE INFORMATION

Authors' Full Names and Academic Degrees: Jimin Hwang, MD, MPH, Kwanghyun Kim, MD, PhD, Josef Coresh MD, PhD, Lesley A. Inker, MD, MS, Morgan E. Grams, MD, PhD, and Jung-Im Shin, MD, PhD

Authors' Affiliations: Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, TX (JH); Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD (JH, JC, MEG, J-IS); Department of Preventive Medicine, Yonsei University College of Medicine, Seoul, Korea (KK); Department of Public Health, Graduate School, Yonsei University, Seoul, Korea (KK); Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD (KK); Center for Humanitarian Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD (KK); Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins University, Baltimore, MD (JC, MEG, J-IS); Division of Nephrology, Department of Internal Medicine, Tufts Medical Center, Boston, MA (LAI); and Division of Precision Medicine, Department of Medicine, New York University Grossman School of Medicine, New York City, NY (MEG).

Address for Correspondence: Jung-Im Shin, MD, PhD, Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins University, 2024 E Monument St, Baltimore, MD 21205. Email: jshin19@jhmi.edu

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