Kidney Medicine

The Kidney Failure Risk Equation Score and CKD Care Delivery Measures: A Cross-sectional Study

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Rationale & Objective: The 4-variable kidney failure risk equation (KFRE) allows for the prediction of chronic kidney disease (CKD) progression using age, sex, estimated glomerular filtration rate, and urine albumin/creatinine ratio. Electronic health records enable KFRE auto-calculation, and registries allow population-level application. We assessed whether 2-year KFRE score categories are associated with CKD care metrics.

Study Design: Cross-sectional cohort.

Setting & Participants: This study included individuals with CKD in March 2020 who were receiving care within the Partners HealthCare system in Massachusetts.

Outcomes: The presence of sufficient data to calculate the KFRE and, among those with a KFRE score, performance on CKD clinical care metrics, including (1) prescription of angiotensin-converting enzyme inhibitor or angiotensin receptor blocker; (2) blood pressure at goal (<140/90 mm Hg) based on clinic measurements; (3) composite metric of hepatitis B virus immunity; (4) composite metric of referral, evaluation, or waitlist status for kidney transplantation; (5) advance directive documentation; (6) yearly influenza vaccination; and (7) pneumonia vaccination.

Analytical Approach: Multivariable logistic regression analysis was used to analyze the association of KFRE score category with CKD care metrics.

Results: Of 61,546 patients, 18,272 (30%) had auto-calculated 2-year KFRE scores; the remaining patients lacked KFRE scores because of absent albuminuria assessment. Individuals with a KFRE score were more likely to have a primary care provider or nephrologist. Among patients with 2-year KFRE scores, high-risk patients had increased odds of completing advance directives (OR, 1.52; 95% CI, 1.07-2.17), while low-risk patients had decreased odds of influenza vaccination (OR, 0.85; 95% CI, 0.75-0.97). Patients with moderate- and high-risk KFRE scores had lower odds of having blood pressure at goal (OR, 0.77; 95% CI, 0.61-0.96 and OR, 0.63; 95% CI, 0.44-0.88, respectively).

Limitations: Albuminuria data may have been assessed outside of the Partners system.

Conclusions: A higher-risk KFRE score is associated with the delivery of some but not all CKD care measures. An opportunity exists to improve albuminuria measurement.

Visual Abstract included

Complete author and article information provided before references.

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Chronic kidney disease (CKD) is a highly morbid, costly, and increasingly common health condition worldwide, and of importance, in some cases is amenable to efforts to slow progression.[1] The progression of CKD to end-stage kidney disease (ESKD) may be delayed and/or prevented through the implementation of evidence-based therapies.[2-6] For those patients who do transition to ESKD, an understanding of the risk of CKD progression can optimize timing of care interventions, such as immunizations, dialysis access placement, and referral and evaluation for kidney transplantation.[7,8] The Tangri kidney failure risk equation (KFRE) can predict the risk of progression from CKD to ESKD using 4 variables—age, sex, estimated glomerular filtration rate (eGFR), and urine albumin/creatinine ratio (UACR)—and has been validated in multiple international cohorts.[9,10]

The KFRE has been studied in the context of risk-based triage for nephrology referrals to optimize the capacity of health care systems, and proposals for primary care adoption of CKD risk stratification have been published.[11-14] Importantly, it has been recognized that albuminuria measurement represents a limitation to risk-based approaches, given the historically low rates of completion of this test.[15] Automated risk calculations based on readily available clinical and laboratory information can facilitate care delivery.[16] The Partners HealthCare System (PHS) CKD registry enables the auto-population of the KFRE score. We sought to understand the association of the KFRE score with CKD care delivery metrics among CKD patients within our health system.

In this study, we examine the distribution of ESKD progression risk, using KFRE scores across the CKD population, and the association of KFRE risk score category with performance on CKD care measures. Care measures included prescription of an angiotensin-converting enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB); blood pressure at a goal of <140/90 mm Hg; documented immunity to hepatitis B virus; referral, evaluation, or waitlist status for kidney transplantation; and completion of advance directive documentation. Given that a large proportion of patients did not have KFRE scores because of the absence of UACR testing, we examined the factors associated with having had UACR testing within the past year to understand how to improve testing and increase KFRE utilization.

PLAIN-LANGUAGE SUMMARY

The Tangri kidney failure risk equation (KFRE) can predict the risk of progression from chronic kidney disease to end-stage kidney disease using 4 variables—age, sex, estimated glomerular filtration rate, and urine albumin/creatinine ratio—and was validated in multiple cohorts. Risk stratification using KFRE has been studied in the hopes of optimizing health care system capacity. This cross-sectional study was conducted to assess the current state of the application of the KFRE in a large integrated health system and opportunities to apply the KFRE broadly for risk-based triage. We found that only one-third of patients had KFRE scores auto-calculated because of missing annual urine albumin/creatinine ratio testing and among those with KFRE scores, there was variable association with care delivery metrics.

METHODS

Setting

PHS includes 2 large academic medical centers and affiliated community primary care and specialty practices in Massachusetts. The study was conducted under PHS institutional review board exemption as meeting the requirements of quality improvement research.

Partners HealthCare Chronic Kidney Disease Registry

The development and validation of the PHS CKD registry have been previously described.[17] Patients are included in the CKD registry based on clinical and billing data from the network-wide electronic health record (EHR) (EPIC systems). Patients are classified as having CKD if they meet one of the following criteria: (1) most recent eGFR <60 mL/min/1.73m^2 and one additional eGFR <60 mL/min/1.73m^2 at least 90 days prior; or (2) at least 2 values of urine total protein or urine albumin >300 mg/g; or (3) ESKD or dialysis on the problem list or as an *International Classification of Diseases, Tenth Revision* code during an encounter. Urine total protein to creatinine values are converted to urine albumin to creatinine as previously described.[10]

Definitions

Race was classified by patient self-identification, based on demographic data in the EHR. The EPIC Partners EHR has classifications for White, Black/African American, Hispanic, Asian, American Indian or Alaska Native, Hawaiian or Pacific Islander, other, not available, or declined. American Indian or Alaska Native persons and Hawaiian or Pacific Islanders were grouped together, and persons with entries that were blank, other, not available, or declined were grouped.

CKD staging was defined by Kidney Disease Improving Global Outcomes guidelines.[12] CKD stage 3 was defined as an eGFR of 30-59 mL/min/1.73 m^2, CKD stage 4 was defined as an eGFR of 16-29 mL/min/1.73 m^2, and CKD stage 5 was defined as an eGFR of ≤15 mL/min/1.73 m^2.

The KFRE score categories were adapted from a suggested framework produced by the original KFRE score investigators.[18] In this framework, patients with a 2-year risk KFRE score of <3%, 3%-9.9%, 10%-39.9%, and ≥40% are categorized as very low, low, moderate, and high risk for progression to ESKD (Fig 1).

Metrics

We examined the association of KFRE score category with 7 CKD care measures chosen to reflect the spectrum of care delivery from early CKD to late CKD: (1) prescription of an ACE-I or ARB; (2) composite metric of hepatitis B virus immunity by titer or by documentation of hepatitis B virus vaccination; (3) composite metric of referral, evaluation, or waitlist status for kidney transplantation; (4) advance directive documentation completion; (5) influenza vaccination within the past year; (6) pneumonia vaccination; and (7) blood pressure management, defined as blood pressure being at a goal of systolic less than 140 mm Hg and diastolic less than 90 mm Hg (Fig 1).

Statistical Analysis

Medians, interquartile ranges, and proportions were assessed for trends in demographic and clinical characteristics among patients in the various KFRE score categories. After the initial selection of care measures, a preliminary review of data revealed an insufficient number of events for the composite metric of either hemodialysis catheter placement or arteriovenous fistula placement. Therefore, no multivariable logistic regression model was performed for this metric.

We conducted univariable logistic regression analysis for the association of individual factors with various care metrics. We analyzed the association of KFRE score category with 5 CKD care measures using multivariable logistic regression analysis. We also fit a separate multivariable logistic regression model for the metric of having had a UACR test performed. Complete case analysis was used in the selection of observations for all multivariable logistic regression models. All statistical analyses were performed using Stata version 15 (StataCorp). All multivariable logistic regression models were found to have an acceptable fit when subjected to the Hosmer-Lemeshow goodness of fit test.

RESULTS

Patient Demographics and Clinical Characteristics, Stratified by KFRE Risk Category

Demographics and clinical characteristics of the patients are shown in Table 1. The median age (interquartile range)

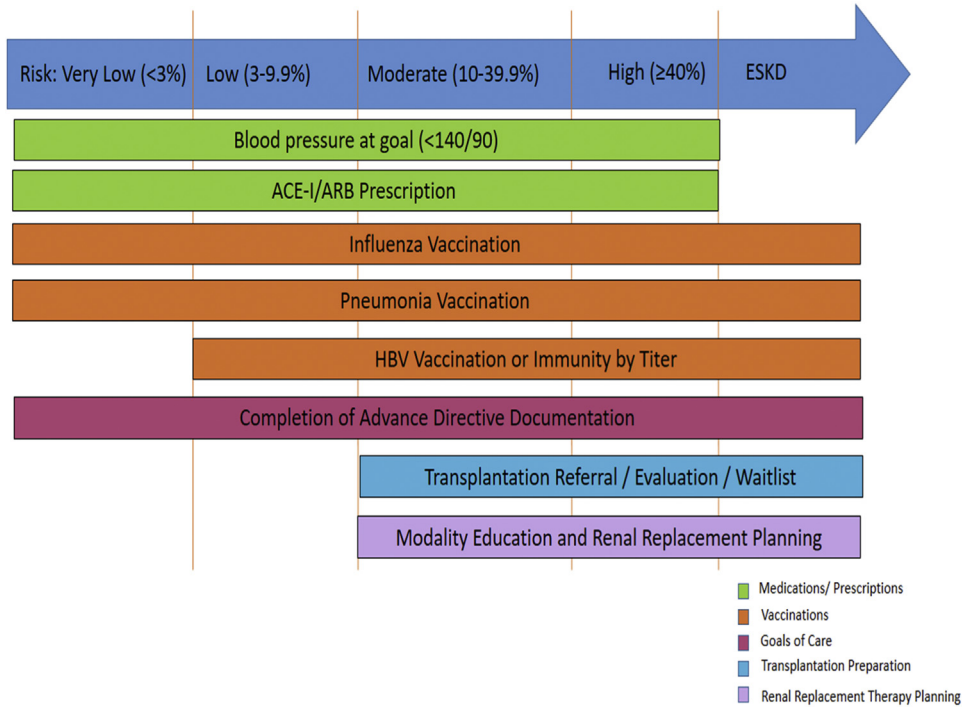

Figure 1. Spectrum of chronic kidney disease care delivery metrics based on 2-year KFRE score category. Association between KFRE score category and renal replacement therapy planning and education was not analyzed in this study because of insufficient sample size for multivariable analysis. Abbreviations: ACE-I/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; ESKD, end-stage kidney disease; HBV, hepatitis B virus.

in years of patients in this study was 77 (70-85); 34,750 (56.5%) were women, 53,384 (86.7%) were White, 2,346 (3.8%) were African American, and 556 (0.9%) were Hispanic. With respect to comorbidities, 48,074 (78.1%) had hypertension, 43,760 (71.1%) were overweight or obese, followed by 18,974 (30.8%) with diabetes, and 14,679 (23.9 %) with coronary artery disease. Patients found to be in moderate- and high-risk categories were younger and more likely to be men. The proportion of non-White patients was highest in the high-risk category at 81 (15.9%). Rates of active smoking also increased in higher-risk categories.

With regard to advanced CKD care metrics, there was a trend toward increased completion of these metrics in higher-risk categories, specifically access placement, referral/evaluation/waitlist status for transplantation, hepatitis B immunization, and completion of advance directive documentation; Massachusetts Order for Life-Sustaining Treatment (MOLST form). As reflected in Table 1, the MOLST completion varied from 10% in the very low-risk category to 12.1% in the moderate-risk category and 14.1% in the high-risk category. However, other metrics like ACE-I/ARB use, influenza vaccination, and pneumonia vaccination had a trend toward reduced rates with increasing risk category. For example, based on our reviews, the ACE-I/ARB use varied from 52.5% in the very low-risk category to 48.6% in the moderate-risk category and 43.4% in the high-risk category.

Association of Care Metrics With KFRE Score

Among the 6 prespecified metrics of interest, only 3 demonstrated an association with KFRE score category after adjustment for other variables in multivariable logistic regression analyses. Patients in the high-risk category were found to have increased odds of completion of the MOLST form, an advance directives document (Table 2; odds ratio [OR], 1.52; 95% CI, 1.07-2.17). Patients in the low-risk category were found to have decreased odds of having received influenza vaccination within the past year (Table 3; OR, 0.85; 95% CI, 0.75-0.97). With regard to blood pressure management, moderate- and high-risk patients had reduced odds of having blood pressure at a prespecified goal of <140/90 mm Hg (Table 4; OR, 0.77; 95% CI, 0.61-0.96; OR, 0.63; 95% CI, 0.44-0.88, respectively).

Although the association of care measures with KFRE score was not commonly found, several other variables demonstrated association with multiple care measures, notably the presence of an in-network care provider, comorbidities, and patient race (Tables S1-S4).

Process Measure of Completed UACR Testing Within the Past Year

Of 61,546 patients, 18,272 (29.7%) had 2-year KFRE scores and the remainder had missing UACR data. Patients with a PHS primary care provider (PCP) or PHS nephrologist had increased odds of completing testing, as did

Table 1. Patient Demographics and Performance on Care Metrics, Stratified by 2-Year KFRE Score Category

Variable	Tangri 2-Year Kidney Failure Risk Equation Category				
	Very Low, <3% (n = 13,925)	Low, 3%-9.9% (n = 2,369)	Moderate, 10%-39.9% (n = 1,469)	High, ≥ 40% (n = 509)	Unknown (n = 43,274)
Demographics					
Median age, y (Q1, Q3)	76 (69-82)	75 (68-83)	74 (65-81)	70 (60-79)	78 (71-86)
Female sex, n (%)	7,220 (51.8%)	1,067 (45.0%)	632 (43.0%)	221 (43.4%)	25,610 (59.2%)
Race, n (%)					
White	11,588 (83.2%)	1,937 (81.8%)	1,156 (78.7%)	374 (73.5%)	38,329 (88.6%)
African American	813 (5.8%)	142 (6.0%)	112 (7.6%)	44 (8.6%)	1,235 (2.9%)
Asian	389 (2.8%)	82 (3.5%)	64 (4.4%)	29 (5.7%)	854 (2.0%)
Hispanic	215 (1.5%)	31 (1.3%)	21 (1.4%)	6 (1.2%)	283 (0.7%)
AIAN-HAPI	23 (0.2%)	5 (0.2%)	2 (0.1%)	2 (0.4%)	53 (0.1%)
Other/declined/unavailable	897 (6.4%)	172 (7.3%)	114 (7.8%)	54 (10.6%)	2,520 (5.8%)
BMI (kg/m^2), n (%)					
Underweight (<18.5)	130 (0.9%)	32 (1.4%)	13 (0.9%)	7 (1.4%)	801 (1.9%)
Normal (18.5-24.9)	2,708 (19.4%)	526 (22.2%)	319 (21.7%)	116 (22.8%)	11,665 (27.0%)
Overweight (25.0-29.9)	4,661 (33.5%)	730 (30.8%)	475 (32.3%)	147 (28.9%)	15,220 (35.2%)
Obese (≥30.0)	6,241 (44.8%)	1,044 (44.1%)	627 (42.7%)	232 (45.6%)	14,392 (33.3%)
Unknown	185 (1.3%)	37 (1.6%)	35 (2.4%)	7 (1.4%)	1,196 (2.8%)
Payor, n (%)					
Commercial	994 (7.1%)	136 (5.7%)	90 (6.1%)	24 (4.7%)	1,898 (4.4%)
Medicaid	186 (1.3%)	37 (1.6%)	39 (2.7%)	14 (2.8%)	212 (0.5%)
Medicare	5,510 (39.6%)	786 (33.2%)	422 (28.7%)	97 (19.1%)	11,909 (27.5%)
Unknown	7,235 (52.0%)	1,410 (59.5%)	918 (62.5%)	374 (73.5%)	29,255 (67.6%)
Comorbidities, n (%)					
Active smoker	675 (4.8%)	152 (6.4%)	100 (6.8%)	46 (9.0%)	1,652 (3.8%)
Former smoker	6,158 (44.2%)	1,058 (44.7%)	623 (42.4%)	179 (35.2%)	16,487 (38.1%)
Diabetes	8,060 (57.9%)	1,353 (57.1%)	861 (58.6%)	300 (58.9%)	8,400 (19.4%)
Hypertension	12,208 (87.7%)	2,120 (89.5%)	1,331 (90.6%)	452 (88.8%)	31,963 (73.9%)
Congestive heart failure	2,637 (18.9%)	758 (32.0%)	491 (33.4%)	170 (33.4%)	7,769 (18.0%)
Coronary artery disease	3,895 (28.0%)	823 (34.7%)	501 (34.1%)	137 (26.9%)	9,323 (21.5%)
ASCVD risk score, n (%)					
Low (<5%)	371 (2.7%)	66 (2.8%)	49 (3.3%)	15 (2.9%)	1,096 (2.5%)
Borderline (5%-7.4%)	243 (1.7%)	45 (1.9%)	18 (1.2%)	8 (1.6%)	771 (1.8%)
Intermediate (7.5%-19.9%)	1,529 (11.0%)	170 (7.2%)	124 (8.4%)	39 (7.7%)	4,079 (9.4%)
High (20% +)	2,964 (21.3%)	420 (17.7%)	241 (16.4%)	81 (15.9%)	4,645 (10.7%)
Unknown	8,818 (63.3%)	1,668 (70.4%)	1,037 (70.6%)	366 (71.9%)	32,683 (75.5%)
Utilization, n (%)					
In-network PCP	10,846 (77.9%)	1,635 (69.0%)	933 (63.5%)	273 (53.6%)	24,488 (56.6%)
In-network nephrologist	5,410 (38.9%)	1,437 (60.7%)	954 (64.9%)	298 (58.5%)	3,077 (7.1%)
CKD stage, n (%)					
Stage 3A	7,811 (56.1%)	97 (4.1%)	21 (1.4%)	0 (0.0%)	26,543 (61.3%)
Stage 3B	5,611 (40.3%)	1,178 (49.7%)	247 (16.8%)	31 (6.1%)	13,205 (30.5%)
Stage 4	502 (3.6%)	1,088 (45.9%)	1,087 (74.0%)	250 (49.1%)	3,047 (7.0%)
Stage 5	1 (0.0%)	6 (0.3%)	114 (7.8%)	228 (44.8%)	479 (1.1%)
Medications, n (%)					
ACE-I/ARB	7,307 (52.5%)	1,148 (48.5%)	714 (48.6%)	221 (43.4%)	11,707 (27.1%)
β-blocker	7,395 (53.1%)	1,447 (61.1%)	935 (63.6%)	330 (64.8%)	19,704 (45.5%)
Calcium channel blocker	5,085 (36.5%)	1,091 (46.1%)	783 (53.3%)	304 (59.7%)	12,319 (28.5%)
Diuretics	6,405 (46.0%)	1,317 (55.6%)	861 (58.6%)	299 (58.7%)	17,555 (40.6%)
Aspirin	5,907 (42.4%)	1,071 (45.2%)	661 (45.0%)	208 (40.9%)	10,546 (24.4%)
Statin	8,689 (62.4%)	1,521 (64.2%)	950 (64.7%)	292 (57.4%)	16,433 (38.0%)
CKD care metrics, n (%)					
Access placement					
Catheter	10 (0.1%)	13 (0.5%)	10 (0.7%)	3 (0.6%)	36 (0.1%)

(Continued)

Table 1 (Cont'd). Patient Demographics and Performance on Care Metrics, Stratified by 2-Year KFRE Score Category

Variable	Tangri 2-Year Kidney Failure Risk Equation Category				
	Very Low, <3% (n = 13,925)	Low, 3%-9.9% (n = 2,369)	Moderate, 10%-39.9% (n = 1,469)	High, ≥ 40% (n = 509)	Unknown (n = 43,274)
Arteriovenous fistula or graft	10 (0.1%)	9 (0.4%)	32 (2.2%)	27 (5.3%)	116 (0.3%)
Kidney transplant status					
Referral	10 (0.1%)	5 (0.2%)	21 (1.4%)	31 (6.1%)	46 (0.1%)
Evaluation	8 (0.1%)	6 (0.3%)	24 (1.6%)	20 (3.9%)	45 (0.1%)
Waitlist	2 (0.0%)	0 (0.0%)	2 (0.1%)	0 (0.0%)	14 (0.0%)
MOLST completed	1,394 (10.0%)	293 (12.4%)	178 (12.1%)	72 (14.1%)	5,189 (12.0%)
Immunizations					
Influenza	7,484 (53.7%)	1,096 (46.3%)	645 (43.9%)	185 (36.3%)	15,146 (35.0%)
Pneumonia	8,883 (63.8%)	1,492 (63.0%)	856 (58.3%)	264 (51.9%)	15,795 (36.5%)
HBV—immune by titers or vaccination	1,320 (9.5%)	259 (10.9%)	211 (14.4%)	81 (15.9%)	2,293 (5.3%)
Prescribed medication potentially contraindicated because of kidney function					
Not applicable (eGFR >30 mL/min/m^2)	13,422 (96.4%)	1,275 (53.8%)	268 (18.2%)	31 (6.1%)	39,748 (91.9%)
No	334 (2.4%)	803 (33.9%)	928 (63.2%)	367 (72.1%)	2,600 (6.0%)
On potentially unsafe medication	103 (0.7%)	189 (8.0%)	212 (14.4%)	91 (17.9%)	645 (1.5%)
On unsafe medication (eGFR ≤30 mL/min/m^2)	66 (0.5%)	102 (4.3%)	61 (4.2%)	20 (3.9%)	281 (0.6%)

Abbreviations: ACE-I, Angiotensin-converting enzyme inhibitor; AIAN-HAPI, Alaska Native, American Indian, Hawaiian, or Pacific Islander; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; eGFR, estimated glomerular filtration rate in mL/min/m^2; HBV, hepatitis B virus; KFRE, kidney failure risk equation; MOLST, Massachusetts Order for Life-Sustaining Treatment; PCP, primary care provider; PHS, Partners HealthCare System; Q1, 25th percentile; Q3, 75th percentile.

patients with concomitant obesity (OR, 1.08; 95% CI, 1.02-1.14), diabetes (OR 6.39; 95% CI 6.09-6.72), or hypertension (OR, 1.45; 95% CI, 1.36-1.54). Asian, African American, and Hispanic patients were at increased odds of having completed testing than White patients (Table S5).

DISCUSSION

In this study, we found that only one-third of the patients had their KFRE risk scores auto-calculated because of missing annual UACR testing in more than 70% of the population. Only 3 care delivery metrics were associated with KFRE risk score categories: (1) advance directive completion, increased odds among high-risk category 2-year KFRE patients; (2) influenza vaccination, decreased odds among low-risk category 2-year KFRE patients; and (3) blood pressure management, decreased odds of having blood pressure at goal among moderate- and high-risk patients. We also found that in-network provider care is associated with increased odds of annual UACR testing as well as other care delivery metrics.

To our knowledge, our study is the first to examine whether the KFRE score is associated with care delivery metrics. Studies to date examining the application of the KFRE have focused on risk-based triage with respect to nephrology care. In one study in Manitoba, Canada, the median number of referrals increased from 68 per month to 94 per month after the application of a KFRE-based cutoff of 3% 5-year risk for triage purposes. Furthermore, the median wait times improved from 230 days to 58 days, illustrating the effectiveness of risk-based triage in improving accessibility to nephrology care.[11]

A study designed to assess the clinical impact of KFRE implementation in a primary care CKD study cohort in the United Kingdom found that the application of a KFRE-based cutoff of greater than 5% 5-year risk expands the eligibility for nephrology referral compared with that in existing guidelines.[12] An ongoing multicenter cluster randomized controlled trial plans to assess the impact of a risk-based care approach on management of CKD, including use of ACE-I/ARBs, sodium-glucose cotransporter 2 inhibitors, hypertension management, and cardiovascular risk mitigation.[14]

Consistent with other studies, we showed that the absence of UACR data impairs the widespread application of the KFRE across an entire population. In our study, UACR testing was associated with having an in-network nephrologist or PCP and diabetes. This is not surprising, given that there is likely increased awareness about the importance of proteinuria measurement in patients with diabetes and that the lack of interoperability between health systems may impact UACR capture.

Table 2. Multivariable Logistic Regression-MOLST Complete

Variable	Odds Ratio	*P* Value	95% CI
KFRE category			
Very low	1.0 (reference)		
Low	1.15	0.12	0.96-1.37
Moderate	1.21	0.11	0.96-1.52
High	1.52	0.02	1.07-2.17
Other Variables			
Age (per y)	1.08	<0.0005	1.07-1.08
Female sex	1.36	<0.0005	1.22-1.51
Has In-network PCP	1.30	<0.0005	1.14-1.49
Has In-network nephrologist	0.70	<0.0005	0.62-0.78
Has diabetes	1.09	0.15	0.97-1.21
Has hypertension	0.91	0.32	0.76-1.09
Has CHF	2.11	<0.0005	1.88-2.37
Has CAD	1.20	0.002	1.07-1.34
eGFR (per mL/min)	0.99	0.003	0.98-1.00
BMI category (kg/m^2)			
Normal (18.5-24.9)	1.0 (reference)		
Underweight (<18.5)	1.46	0.07	0.97-2.20
Overweight (25.0-29.9)	0.79	0.001	0.69-0.90
Obese (≥30.0)	0.69	<0.0005	0.60-0.79
Race category			
White	1.0 (reference)		
AIAN-HAPI	0.83	0.81	0.18-3.77
Asian	0.53	0.001	0.37-0.76
African American	0.83	0.14	0.65-1.06
Hispanic	0.46	0.009	0.26-0.82

Abbreviations: AIAN-HAPI, Alaska Native, American Indian, Hawaiian, or Pacific Islander; BMI, body mass index; CAD, coronary artery disease; CHF, congestive heart failure; eGFR, estimated glomerular filtration rate; KFRE, kidney failure risk equation; MOLST, Massachusetts Order for Life-Sustaining Treatment; PCP, primary care provider.

Table 3. Multivariable Logistic Regression-Influenza Vaccine

Variable	Odds Ratio	*P* Value	95% CI
KFRE category			
Very low	1.0 (reference)		
Low	0.85	0.01	0.75-0.97
Moderate	0.90	0.22	0.77-1.07
High	0.84	0.20	0.64-1.10
Other variables			
Age (per y)	1.01	<0.0005	1.01-1.02
Female sex	1.05	0.18	0.98-1.13
Has in-network PCP	16.10	<0.0005	14.42-17.96
Has in-network nephrologist	1.10	0.01	1.02-1.19
Has diabetes	1.17	<0.0005	1.09-1.26
Has hypertension	1.41	<0.0005	1.26-1.59
Has CHF	1.21	<0.0005	1.11-1.32
Has CAD	1.03	0.52	0.96-1.12
eGFR (per mL/min)	1.00	0.52	1.00-1.01
BMI category (kg/m^2)			
Normal (18.5-24.9)	1.0 (reference)		
Underweight (<18.5)	0.92	0.67	0.64-1.33
Overweight (25.0-29.9)	0.97	0.56	0.88-1.07
Obese (≥30.0)	0.99	0.90	0.90-1.09
Race			
White	1.0 (reference)		
AIAN-HAPI	1.25	0.60	0.55-2.81
Asian	0.90	0.32	0.74-1.10
African American	0.79	0.001	0.69-0.91
Hispanic	1.00	0.98	0.77-1.30

Abbreviations: AIAN-HAPI, Alaska Native, American Indian, Hawaiian, or Pacific Islander; BMI, body mass index; CAD, coronary artery disease; CHF, congestive heart failure; eGFR, estimated glomerular filtration rate; KFRE, kidney failure risk equation; MOLST, Massachusetts Order for Life-Sustaining Treatment; PCP, primary care provider.

In the Veterans Affairs health system, less than 50% of adults with diabetes and less than 30% of adults with hypertension were tested for albuminuria in 2018.[19] Kaiser Permanente Southern California found that only 32% of patients with confirmed CKD, defined as having an eGFR less than 60 mL/min on 2 separate occasions at least 90 days apart, had UACR testing.[20] Another recent study of a large CKD registry in Los Angeles found that only 8.7% and 4.1% of patients had albuminuria and proteinuria assessments, respectively.[21]

In our study, only one-third of the total registry population had UACR testing, enabling KFRE score calculation, complicating the interpretation of the associations found in our study. The findings from our institution and others demonstrate that there is room for improvement in health systems across the nation in assessing the UACR and incorporating it into daily clinical workflows. In an ideal state, complete UACR data would enable the calculation of the KFRE for the entire population of CKD patients within a system and allow system-wide decision making regarding the provision of care.

The widespread use of EHRs now allows for the estimation of risk across populations through automated calculation of risk scores, such as the KFRE. Despite this, there is limited evidence of widespread EHR-based adoption of KFRE calculation. Furthermore, the notable lack of widespread UACR testing in patients with CKD, hypertension, and diabetes limits the ability of health systems to adopt KFRE calculation for a population of patients and apply risk stratification to guide targeted care delivery. Efforts are needed to improve UACR testing. Studies have shown that systematic attempts to improve the completion rate of UACR testing can be successful compared with that of controls.[16,22] Much of the focus in improving UACR

Table 4. Multivariable Logistic Regression- Blood Pressure at Goal

Variable	Odds Ratio	*P* Value	95% CI
KFRE category			
Very low	1.0 (reference)		
Low	0.99	0.93	0.83-1.19
Moderate	0.77	0.02	0.61-0.96
High	0.63	0.008	0.44-0.88
Other variables			
Age (per y)	1.00	1.00	1.00-1.00
Female sex	0.95	0.29	0.86-1.05
Has in-network PCP	2.51	<0.0005	2.25-2.80
Has in-network nephrologist	1.38	<0.0005	1.24-1.54
Has diabetes	1.44	<0.0005	1.30-1.60
Has hypertension	1.09	0.26	0.94-1.27
Has CHF	1.66	<0.0005	1.44-1.92
Has CAD	1.44	<0.0005	1.27-1.63
eGFR (per mL/min)	0.99	0.10	0.99-1.00
BMI category (kg/m^2)			
Normal (18.5-24.9)	1.0 (reference)		
Underweight (<18.5)	1.34	0.26	0.80-2.25
Overweight (25.0-29.9)	1.08	0.25	0.95-1.24
Obese (≥30.0)	1.24	0.002	1.08-1.41
Race			
White	1.0 (reference)		
AIAN-HAPI	1.92	0.38	0.45-8.22
Asian	1.07	0.66	0.80-1.42
African American	0.79	0.02	0.66-0.96
Hispanic	0.72	0.09	0.50-1.05

Abbreviations: AIAN-HAPI, Alaska Native, American Indian, Hawaiian, or Pacific Islander; BMI, body mass index; CAD, coronary artery disease; CHF, Congestive Heart Failure; eGFR, estimated glomerular filtration rate; PCP, primary care provider.

testing has been on PCPs, but as our study highlights, patients seen by nephrologists are also often lacking annual UACR testing.

Once UACR testing rates improve, health care systems should ensure automated calculation of the KFRE to guide PCPs and nephrologists regarding the risk of progression and the need for timely CKD care. This can be performed within the context of an EHR-based registry, similar to that in our institution, or through manual calculation and entry by midlevel providers into initial referral requests to nephrology, as has been done in at least 1 center.[11]

In our study, the KFRE score was associated with metrics in a limited way (advanced directives and influenza vaccination). This overall lack of association between the KFRE score and care delivery most likely reflects that our institution, like many others, has not formally implemented risk-based triage and care of CKD patients using the the KFRE. If the KFRE was being used to guide CKD care delivery, we would expect to see an association between risk score categories and care delivery metrics as outlined in Fig 1. For example, we would see increased odds of hepatitis B immunity and transplantation for patients with a high KFRE score. The substantial missing UACR and KFRE data make the interpretation of the associations found here challenging. In our system, like most others, the paradigm of CKD care delivery is still largely relative to patient-level eGFR trends and cutoffs (ie, a threshold eGFR <20 mL/min/1.73 m^2 is used for transplantation referral). We do acknowledge that some care delivery metrics, such as the prescription of ACE-Is or ARBs may decrease with a rising KFRE at higher stages of CKD.

Static eGFR or trended eGFR have been employed traditionally in determining staging and care delivery decisions. ESKD progression risk scoring is future oriented and likely better than static eGFR based cutoffs as criteria for care delivery decision making at the individual patient and population level.

We propose a multistep effort to improve KFRE calculation and application (Fig 2). First, we advocate for a population-level approach to increasing UACR measurement. This could involve leveraging a CKD registry, established algorithms, and coordinators to identify patients who are missing testing and order UACR testing. Another approach could involve a system-wide educational campaign directed at both PCPs and nephrologists regarding the importance of UACR testing and EHR-based best practice alerts, which alert when a CKD patient is due for testing. Opt-out ordering may be an option for improving testing rates.

Second, auto-calculation of the KFRE is needed and could occur within the context of a CKD registry or as part of eGFR and UACR reporting. Third, a KFRE risk category should be incorporated at the point of care for both PCPs and nephrologists. This can be achieved through best practice alerts, documentation smart phrases, laboratory readouts, and order entry.

Finally, health systems should create best practices or algorithms related to recommended care delivery based on the KFRE score directed to providers. For example, a KFRE risk score of moderate or high would guide PCPs to refer to nephrology. Relatively low thresholds of 3% to 5% at 5 years have been used in other studies.[11,12] Similarly, for nephrologists, a KFRE risk score of high would guide nephrologists to start planning for kidney replacement therapy and transplant evaluation.

Our work has several strengths. The study examines a large cohort of patients with CKD and has data available for important demographic, clinical, laboratory, and care delivery measures. There was a clear definition of clinical metrics relevant to CKD care, which involved iterative review by primary care, nephrology, and transplant providers. Finally, we were able to auto-calculate and integrate the KFRE scores within our CKD registry to compare with

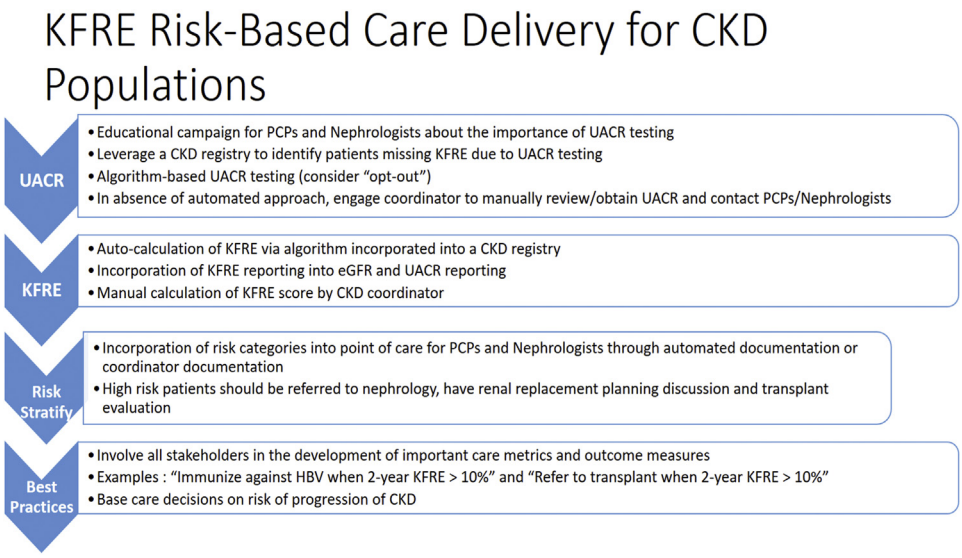

Figure 2. Proposed population-level utilization of risk prediction to improve chronic kidney disease (CKD) care delivery. Abbreviations: eGFR, estimated glomerular filtration rate; HBV, hepatitis B virus; KFRE, kidney failure risk equation; PCPs, primary care providers; UACR, urine albumin/creatinine ratio.

relevant CKD measures. Our registry has incorporated KFRE scores since 2017, enabling providers to use the KFRE and impact care delivery metrics. As a result, our analysis is reflective of a population-based approach to risk prediction to guide treatment.

The major limitation to our study is the lack of widespread UACR testing, which has been noted nationally and internationally, limiting the broad use of the KFRE. In addition, our study includes 1 health care system, which may limit generalizability because practice patterns may vary. Also, some of our data may be incomplete because of the lack of interoperability among EHRs in our geographic area and the possibility of fragmented care. Finally, a relatively small number of events limited the number of predictors that could be incorporated into the analysis of composite metric of kidney transplant referral, evaluation, or waitlist status, and similarly, prevented analysis of dialysis access placement.

A concerted effort to improve the understanding of population-level risk for progression to ESKD will require improved testing for UACR as well as implementation and dissemination of risk-based care delivery strategies at institutional, regional, and potentially national levels. Two key steps that can be taken by health care systems seeking to incorporate the KFRE into CKD care delivery workflow include (1) widespread use of automated calculation of the KFRE in clinical notes, clinic appointment lists, and clinic referral centers and (2) development of best practice algorithms to assist frontline providers in adhering to timely implementation of care measures.

Enhanced UACR testing can enable assessment of the KFRE across a larger proportion of the population, and KFRE risk stratification can guide important care delivery to patients with CKD. By implementing a clear care delivery pathway defined by KFRE risk stratification, risk-based CKD care delivery can be facilitated for the entire population.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1: Multivariable Logistic Regression-Pneumonia Vaccine

Table S2: Multivariable Logistic Regression-HBV Immunity

Table S3: Multivariable Logistic Regression-ACE-I/ARB Use

Table S4: Multivariable Logistic Regression for Composite Outcome of Renal Transplant Referral, Evaluation, or Waitlist Status.

Table S5: Multivariable Logistic Regression-Completed Urine Albumin/Creatinine Ratio (UACR) Testing Past 1 Year

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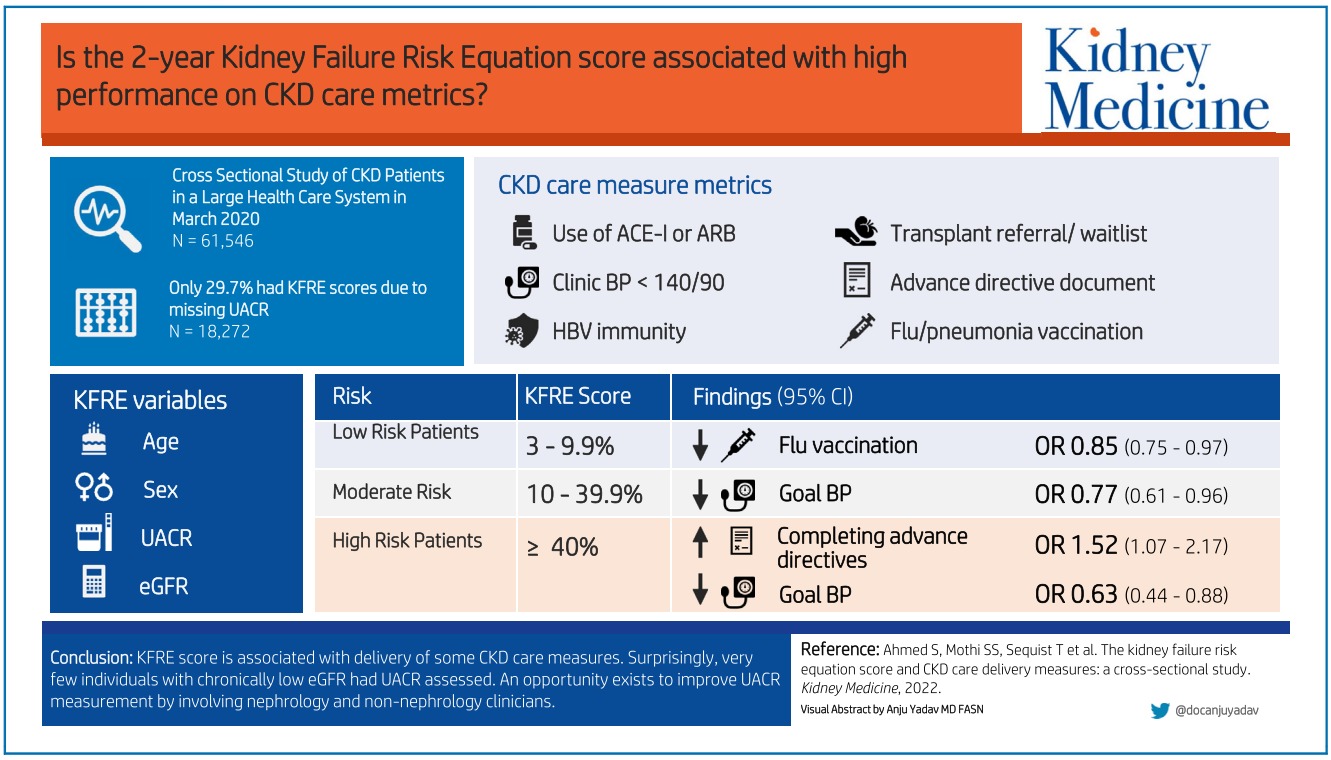
REFERENCES

1. Bikbov B, Purcell CA, Levey AS. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2020;395(10225):709-733.
2. Levey AS, Rocco MV, Anderson S. K/DOQI clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease. *Am J Kidney Dis*. 2004;43(5)(suppl 1):S1-S290.
3. Orth SR. Effects of smoking on systemic and intrarenal hemodynamics: influence on renal function. *J Am Soc Nephrol*. 2004;15(suppl 1):S58-S63.
4. Orth SR, Hallan SI. Smoking: a risk factor for progression of chronic kidney disease and for cardiovascular morbidity and mortality in renal patients—absence of evidence or evidence of absence? *Clin J Am Soc Nephrol*. 2008;3(1):226-236.
5. De Brito-Ashurst I, Varagunam M, Raftery MJ, Yaqoob MM. Bicarbonate supplementation slows progression of CKD and improves nutritional status. *J Am Soc Nephrol*. 2009;20(9):2075-2084.
6. Zelniker TA, Wiviott SD, Raz I, et al. SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials. *Lancet*. 2019;393(10166):31-39.
7. Levin A, Lewis M, Mortiboy P, et al. Multidisciplinary predialysis programs: quantification and limitations of their impact on patient outcomes in two Canadian settings. *Am J Kidney Dis*. 1997;29(4):533-540.
8. Curtis BM, Ravani P, Malberti F, et al. The short- and long-term impact of multi-disciplinary clinics in addition to standard nephrology care on patient outcomes. *Nephrol Dial Transplant*. 2005;20(1):147-154.
9. Tangri N, Stevens LA, Griffith J, et al. A predictive model for progression of chronic kidney disease to kidney failure. *JAMA*. 2011;305(15):1553-1559.
10. Tangri N, Grams ME, Levey AS, et al. Multinational assessment of accuracy of equations for predicting risk of kidney failure: a meta-analysis. *JAMA*. 2016;315(2):164-174.
11. Hingwala J, Wojciechowski P, Hiebert B, et al. Risk-based triage for nephrology referrals using the kidney failure risk equation. *Can J Kidney Health Dis*. 2017;4:2054358117722782.
12. Major RW, Shepherd D, Medcalf JF, Xu G, Gray LJ, Brunskill NJ. The Kidney Failure Risk Equation for prediction of end stage renal disease in UK primary care: an external validation and clinical impact projection cohort study. *PLOS Med*. 2019;16(11):e1002955.
13. Bhachu HK, Cockwell P, Subramanian A, Nirantharakumar K, Kyte D, Calvert M. Cross-sectional observation study to investigate the impact of risk-based stratification on care pathways for patients with chronic kidney disease: protocol paper. *BMJ Open*. 2019;9(6):e027315.
14. Harasemiw O, Drummond N, Singer A, et al. Integrating risk-based care for patients with chronic kidney disease in the community: study protocol for a cluster randomized trial. *Can J Kidney Health Dis*. 2019;6:2054358119841611.
15. Bello AK, Ronksley PE, Tangri N, et al. Quality of chronic kidney disease management in Canadian primary care. *JAMA Netw Open*. 2019;2(9):e1910704.
16. Tuot DS, McCulloch CE, Velasquez A, et al. Impact of a primary care CKD registry in a US public health safety-net health care delivery system: a pragmatic randomized trial. *Am J Kidney Dis*. 2018;72(2):168-177.
17. Mendu ML, Ahmed S, Maron JK, et al. Development of an electronic health record-based chronic kidney disease registry to promote population health management. *BMC Nephrol*. 2019;20(1):72.
18. Tangri N, Ferguson T, Pro KP. Pro: risk scores for chronic kidney disease progression are robust, powerful, and ready for implementation. *Nephrol Dial Transplant*. 2017;32:748-751.
19. Centers for Disease Control and Prevention. Chronic kidney disease surveillance system—United States. Accessed January 22, 2021. http://www.cdc.gov/ckd
20. Sim JJ, Batech M, Danforth KN, Rutkowski MP, Jacobsen SJ, Kanter MH. End-stage renal disease outcomes among the Kaiser Permanente Southern California creatinine safety program (creatinine SureNet): opportunities to reflect and improve. *Perm J*. 2017;21:16-143.
21. Tuttle KR, Alicic RZ, Duru OK, et al. Clinical characteristics of and risk factors for chronic kidney disease among adults and children: an analysis of the CURE-CKD registry. *JAMA Netw Open*. 2019;2(12):e1918169.
22. Mendu ML, Schneider LI, Aizer AA, et al. Implementation of a CKD checklist for primary care providers. *Clin J Am Soc Nephrol*. 2014;9(9):1526-1535.


Is the 2-year Kidney Failure Risk Equation score associated with high performance on CKD care metrics?
Kidney Medicine
Cross Sectional Study of CKD Patients in a Large Health Care System in March 2020
N = 61,546
Only 29.7% had KFRE scores due to missing UACR
N = 18,272
CKD care measure metrics
Use of ACE-I or ARB
Clinic BP < 140/90
HBV immunity
Transplant referral/ waitlist
Advance directive document
Flu/pneumonia vaccination
KFRE variables
Age
Sex
UACR
eGFR
Risk
KFRE Score
Findings (95% CI)
Low Risk Patients
3 - 9.9%
Flu vaccination
OR 0.85 (0.75 - 0.97)
Moderate Risk
10 - 39.9%
Goal BP
OR 0.77 (0.61 - 0.96)
High Risk Patients
≥ 40%
Completing advance directives
OR 1.52 (1.07 - 2.17)
Goal BP
OR 0.63 (0.44 - 0.88)
Conclusion: KFRE score is associated with delivery of some CKD care measures. Surprisingly, very few individuals with chronically low eGFR had UACR assessed. An opportunity exists to improve UACR measurement by involving nephrology and non-nephrology clinicians.
Reference: Ahmed S, Mothi SS, Sequist T et al. The kidney failure risk equation score and CKD care delivery measures: a cross-sectional study. Kidney Medicine, 2022.
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