

# Predicting 5-Year Risk of RRT in Stage 3 or 4 CKD: Development and External Validation

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## Abstract

**Background and objectives** Only a minority of patients with CKD progress to renal failure. Despite the potential benefits of risk stratification in the CKD population, risk prediction models are not routinely used. Our objective was to develop and externally validate a clinically useful and pragmatic prediction model for the 5-year risk of progression to RRT in stage 3 or 4 CKD.

**Design, setting, participants, & measurements** We used a retrospective cohort design. The development cohort consisted of 22,460 Kaiser Permanente Northwest members with stage 3 or 4 CKD (baseline 2002–2008). The validation cohort consisted of 16,553 Kaiser Permanente Colorado members with stage 3–4 CKD (baseline 2006–2008). The final model included eight predictors: age, sex, eGFR, hemoglobin, proteinuria/albuminuria, systolic BP, antihypertensive medication use, and diabetes and its complications.

**Results** In the Northwest and Colorado cohorts, there were 737 and 360 events, and observed 5-year Kaplan–Meier risks of 4.72% (95% confidence interval [95% CI], 4.38 to 5.06) and 2.57% (95% CI, 2.30 to 2.83), respectively. Our prediction model performed extremely well in the development cohort, with a c-statistic of 0.96, an R<sup>2</sup> of 79.7%, and good calibration. We had similarly good performance in the external validation cohort, with a c-statistic of 0.95, R<sup>2</sup> of 81.2%, and good calibration. In the external validation cohort, the observed risk was slightly lower than the predicted risk in the highest-risk quintile. Using the top quintile of predicted risk as a cutpoint gave a sensitivity of 92.2%.

**Conclusions** We developed a pragmatic prediction model and risk score for predicting the 5-year RRT risk in stage 3 and 4 CKD. This model uses variables that are typically available in routine primary care settings, and can be used to help guide important decisions such as timing of referral to nephrology and fistula placement.

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## Introduction

CKD is a major public health problem, leading to increased morbidity, mortality, and health care costs (1–4). More than 10% of adults in the United States have CKD (5). Appropriate referral to nephrology care can help with slowing disease progression, timely planning for dialysis and/or kidney transplantation, and optimal access for dialysis initiation (6,7). However, only a minority of individuals with CKD progress to renal failure (4,8–10). Therefore, a clinically useful risk prediction model of the risk of progression to RRT (dialysis or kidney transplantation) could be useful in helping guide decisions concerning the timing of referral to nephrology, timing of fistula placement, and other important interventions such as time of preemptive kidney transplant and predialysis education (6,7,11).

Despite the potential benefits of risk stratification in the CKD population, risk prediction models are not routinely used for this application (7). Ideally, before a risk prediction model is incorporated into clinical practice, it should show good internal and external

validity and be clinically useful (7,12–14). A recent systematic review of risk prediction models to predict the risk of progression to renal failure among individuals with CKD identified only two studies that met the criteria for clinical usefulness (including factors such as effect on clinical decision making and ease of use) (7) – a risk prediction score developed at Kaiser Permanente Northwest (KPNW) (6) and a series of models developed by Tangri *et al.* (4,10,15).

The KPNW model predicts the 5-year risk of progression to RRT among individuals with stage 3 or 4 CKD. It includes six predictors: age, sex, kidney function, hypertension, diabetes, and anemia. It has never been externally validated, relied upon the outdated Modification of Diet in Renal Disease Study GFR-estimating equation (16), and modeled natural history data that predated the National Kidney Foundation's 2002 Clinical Practice Guidelines (17).

The aims of this study were: (1) to improve the KPNW prediction model for the 5-year risk of progression to RRT among individuals with stage 3 or 4 CKD through more flexible specification of the six original predictors,

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addition of other clinically important predictors, and use of more contemporaneous data; and (2) to externally validate the KPNW prediction model using an independent cohort from Kaiser Permanente Colorado (KPCO).

## Materials and Methods

### Study Population

**Development Cohort.** The development cohort was based in KPNW, a health maintenance organization which serves the Portland, Oregon and Vancouver, Washington metropolitan areas. We assembled a retrospective cohort using data available in the electronic health record and other linked databases, such as outpatient pharmacy and outpatient laboratory results. During the study period, KPNW had an annual membership of approximately 480,000.

We identified a cohort of individuals with stage 3 or 4 CKD by requiring two outpatient serum creatinine tests that were used to estimate GFR according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (18). To be eligible, the two eGFRs had to meet the Kidney Disease Outcomes Quality Initiative criteria for stage 3 or 4 CKD (eGFR between 15 ml/min per 1.73 m<sup>2</sup> and 59 ml/min per 1.73 m<sup>2</sup>) and be separated by 90–730 days without any intervening eGFRs <15 ml/min per 1.73 m<sup>2</sup> or ≥60 ml/min per 1.73 m<sup>2</sup>. If individuals had multiple pairs of qualifying eGFRs, we used the most recent pair (nearest to December 31, 2008) that still allowed for 5 years of follow-up. We used the second eGFR in the pair as the individual's index date. Individuals had to meet the following eligibility criteria: (1) be aged 30–89 years at the index date, (2) have continuous membership and prescription drug coverage through the health plan for the year before the index date, and (3) have no known history of dialysis or kidney transplantation preceding the index date. Individuals did not need to have been seen or referred to a nephrologist in order to be eligible. Data on baseline eligibility was collected from January 1, 2002 through December 31, 2008, with follow-up data available through December 31, 2013.

**Validation Cohort.** The independent validation cohort was based in KPCO, which serves the Denver–Boulder, Colorado metropolitan area. During the study period, KPCO and KPNW had similar annual membership. We used the same criteria for cohort eligibility. Data on baseline eligibility was collected from January 1, 2006 through December 31, 2008, with follow-up data available through December 31, 2013.

The study was reviewed and approved by the KPNW Institutional Review Board (IRB). The KPCO IRB ceded oversight to the KPNW IRB.

### Variables

**Dependent Variable.** The outcome was progression to RRT, which was defined as initiation of chronic dialysis or kidney transplantation. We censored individuals at the time of death, discontinuation of health plan coverage, or 5 years after the index date. KPNW maintains a registry that records the date of dialysis initiation and kidney transplantation for individuals who progressed to RRT while they were members of KPNW. Events from Colorado were

determined *via* physician adjudication by chart review (by E.B.S.) of individuals with relevant International Classification of Diseases, Ninth Edition (ICD-9) codes, with the investigator blinded to the individuals' predicted risks.

**Candidate Predictor Variables.** Using information in the electronic health record, we measured characteristics during the 1-year baseline period. We considered the six variables included in the original KPNW prediction model (age, sex, eGFR, hypertension, diabetes, and anemia) (6), as well as additional potential predictors that were suggested by a panel of Kaiser Permanente nephrologists (proteinuria/albuminuria, body mass index (BMI), antihypertensive medication use, and prescription nonsteroidal anti-inflammatory drugs [NSAID] use). In order to allow more flexible modeling, we replaced hypertension with systolic BP, anemia by hemoglobin, and diabetes by the Diabetes Complications Severity Score (19). The Diabetes Complications Severity Index is based on ICD-9 codes, and counts the following complications: retinopathy, nephropathy, neuropathy, cerebrovascular disease, cardiovascular disease, peripheral vascular disease, and metabolic complications such as diabetic ketoacidosis. We excluded nephropathy from our index, because we measured that with laboratory tests; consequently, our adaptation of the index has a potential range of 0–6 complications (19). For laboratory and biometric data, the closest value before and within 365 days of the index date was used. GFR was estimated from serum creatinine using the CKD-EPI estimating equation (18). Proteinuria/albuminuria was defined according to the Kidney Disease Improving Global Outcomes 2012 CKD Clinical Practice Guidelines as present if: spot albumin-to-creatinine ratio (ACR) ≥30 mg/g, spot protein-to-creatinine ratio ≥150 mg/g, or urine dipstick test ≥1+ (20). If there were multiple urine tests on the same day, then the results were used in the following order: ACR, protein-to-creatinine ratio, urine dipstick. Medication use was defined as a prescription medication fill in the 90 days before the index date. For continuous variables, we initially parameterized the variables using restricted cubic splines with five knots to explore nonlinear relations.

### Missing Data

For predictor characteristics with missing values, we applied multiple imputation using chained equations (21,22). The imputation procedure generated ten datasets including all of the predictors in the regression model and the RRT outcome (21,23). We imputed the following predictors: proteinuria/albuminuria, hemoglobin, systolic BP, and BMI. The one exception to multiple imputation was race in the estimation of eGFR. We estimated GFR according to the observed race when it was known, and assumed nonblack race when it was missing because most (approximately 90%) of the members in both health plans were nonblack (24,25).

### Statistical Analyses

**Model Development.** We developed the model using statistical methods described by Harrell and Steyerberg and endorsed by the Prognosis Research Strategy (PROGRESS) Group (26–28) and outlined in the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis Or Diagnosis (TRIPOD) guidelines (29). We identified candidate

predictors of RRT *a priori* and fit a full Cox regression model. To avoid over-fitting the model, we required 20 RRT events per degree of freedom. For continuous predictors modeled using restricted cubic splines, when the shape of the adjusted relation (in the full model) appeared linear, we simplified the parameterization. For hemoglobin and systolic BP, a single linear term was used in the final models. For eGFR, the model would not converge with five knots, and so a restricted cubic spline with three knots was used. We observed too few events to explore statistical interactions between the main effects. The magnitude and statistical significance of the coefficients played no role in determining which predictors to retain. After fitting the full, *a priori* model, we used the Harrell step-down method with linear regression to simplify the model and drop the weakest predictors while retaining 99% of the variation explained by the full model (30). In addition, we used the step-down method to examine the percentage of variation explained by using a four-variable model with age, sex, eGFR, and albuminuria/proteinuria, and a one-variable model containing only eGFR.

We validated the model internally using the Harrell bootstrap resampling method to estimate slope shrinkage (degree of optimism, or overfitting) in the development cohort (26). We calculated the bootstrap-corrected concordance statistic (c-statistic) and the D-statistic to assess discrimination or separation between high- and low-risk individuals (31). We calculated the R<sup>2</sup>-statistic on the basis of the D-statistic to assess combined discrimination and accuracy (32). We assessed discrimination graphically by dividing the cohort into quintiles on the basis of the 5-year predicted risks and then plotting the mean predicted risks along with the Kaplan–Meier observed risks as failure curves (33). The same failure curves also assess the accuracy or calibration of the predictions by comparing the agreement between the predicted and observed risks

throughout the follow-up. We approximated the exact Cox regression equation using a simplified points-based risk scoring system to improve its usability utility for settings requiring manual calculation (34).

**External Validation.** We validated the KPNW Prediction Model externally or clinically using the Colorado cohort according to methods described by Royston and Altman (35). Specifically, we calculated the 5-year predicted risk of RRT for each individual in the Colorado cohort on the basis of the Cox regression model's exact linear predictor on the basis of coefficients derived from the Northwest cohort (24). We imputed missing values before calculating the predicted risks. We updated the baseline hazard function to the Colorado population, but did not recalibrate the Cox regression equation by calculating Colorado-specific regression coefficients. We calculated the c-statistic and D-statistic to assess discrimination, and the R<sup>2</sup>-statistic on the basis of the D-statistic to assess variation explained. We divided the Colorado cohort into quintiles on the basis of the 5-year predicted risk, and assessed calibration graphically by plotting the mean predicted cumulative risk for each quintile together with the Kaplan–Meier observed cumulative risk.

We used SAS Version 9.4 (SAS Institute Inc., Cary, NC) for dataset construction, and Stata Version 13.0 (StataCorp, College Station, TX) and the R (version 3.1.2) open source software (R Foundation for Statistical Computing; www.R-project.org) for the internal and external validation.

## Results

### Model Development in the Northwest Cohort

Among the 22,460 individuals in the Northwest cohort, 737 progressed to RRT. The 5-year Kaplan–Meier risk of progression to RRT was 4.72% (95% confidence interval

**Table 1. Distribution of baseline characteristics of the development and validation cohorts**

Baseline Demographic and Clinical Characteristics	Development Cohort, Northwest, 2002–2008	Validation Cohort, Colorado, 2006–2008
Total, N	22,460	16,553
Mean age (SD), yr	74.6 (10.1)	74.7 (9.0)
Women, n (%)	13,378 (59.6)	10,270 (62.0)
Diabetes, n (%) <sup>a</sup>	7702 (34.3)	4463 (27.0)
Mean Diabetes Complications Severity Index among individuals with diabetes (SD) <sup>a</sup>	3.14 (2.4)	1.57 (1.2)
<b>Mean systolic BP (SD), mmHg</b>	131.2 (20.1)	129.4 (18.6)
Missing values, n (%)	17 (0.1)	46 (0.3)
Antihypertensive medication use, n (%)	19,104 (85.1)	13,563 (81.9)
Mean eGFR (SD), ml/min per 1.73 m <sup>2b</sup>	46.8 (10.1)	47.5 (9.8)
<b>Mean hemoglobin (SD), g/dl</b>	13.0 (1.7)	14.1 (1.8)
Missing values, n (%)	2513 (11.3)	2551 (15.4)
<b>Proteinuria/albuminuria, n (%)</b>	5557 (24.7)	3826 (23.1)
Missing values, n (%)	5869 (26.1)	4409 (26.6)

<sup>a</sup>We identified diabetes using International Classification of Diseases, Ninth Edition (ICD-9) diagnosis codes. The Diabetes Complications Severity Index is based on ICD-9 codes, and counts the following complications: retinopathy, nephropathy, neuropathy, cerebrovascular disease, cardiovascular disease, peripheral vascular disease, and metabolic complications such as diabetic ketoacidosis. We excluded nephropathy from our index, because we measured that with laboratory tests; consequently, our adaptation of the index has a potential range of 0–6 complications (19).

<sup>b</sup>eGFR was estimated using serum creatinine and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

Variable	Hazard Ratio (95% CI)	Points
Sex, men	1.98 (1.90 to 2.30)	10
<b>Age, yr</b>		
30–34	–	41
35–39	–	39
40–44	–	36
45–49	–	33
50–54	–	31
55–59	–	28
60–64	–	25
65–69	–	23
70–74	–	21
74–79	–	16
80–84	–	9
85–89	–	0
<b>eGFR, ml/min per 1.73 m<sup>2</sup></b>		
59–55	–	0
54–50	–	6
49–45	–	13
44–40	–	22
39–35	–	33
34–30	–	46
29–25	–	59
24–20	–	73
19–15	–	86
Proteinuria/albuminuria	1.61 (1.32–1.96)	7
<b>Hemoglobin, g/dl</b>		
≥15.0	Ref	0
14.0–14.9	1.17 (1.11 to 1.23)	2
13.0–13.9	1.37 (1.23 to 1.52)	5
12.0–12.9	1.61 (1.37 to 1.88)	7
11.0–11.9	1.88 (1.52 to 2.32)	10
10.0–10.9	2.20 (1.69 to 2.87)	12
9.0–9.9	2.58 (1.88 to 3.54)	14
8.0–8.9	3.02 (2.09 to 4.38)	17
<8.0	3.54 (2.32 to 5.41)	19
<b>Diabetes</b>		
No diabetes	Ref	0
Diabetes, no complications	1.10 (0.77 to 1.56)	1
Diabetes, one complication	1.54 (1.21 to 1.97)	7
Diabetes, two complications	1.63 (1.30 to 2.04)	7
Diabetes, three or more complications	1.93 (1.60 to 2.33)	10
<b>Systolic BP, mmHg</b>		
<120	Ref	0
120–124	1.09 (1.07 to 1.12)	1
125–129	1.19 (1.14 to 1.25)	3
130–134	1.31 (1.22 to 1.40)	4
134–139	1.43 (1.30 to 1.57)	5
140–144	1.56 (1.39 to 1.76)	7
145–149	1.71 (1.48 to 1.96)	8
150–154	1.86 (1.58 to 2.20)	10
155–159	2.04 (1.69 to 2.46)	11
≥160	2.23 (1.80 to 2.75)	12
Antihypertensive medication	1.50 (1.12 to 2.01)	6

The eight characteristics in the model accounted for 15 degrees of freedom. The prognostic index or linear predictor has a linear relation with the 5-year risk of RRT such that a one-unit increase maps to a constant number of risk score points (on an arbitrary scale). A higher point value on the risk score corresponds to a higher predicted risk of RRT. For an individual patient, providers can add the risk score points presented here to calculate the total risk score points, and then use the cut-points in Supplemental Table 3 to determine the predicted risk. 95% CI, 95% confidence interval; –, age and eGFR were specified using restricted cubic splines, so hazard ratios are not available.

**Table 3. Performance statistics for the Kaiser Permanente Northwest prediction model**

Statistic	Development Cohort, Northwest	Validation Cohort, Colorado
c-statistic (95% CI)	0.96 (0.95, 0.97)	0.95 (0.94, 0.97)
D (95% CI)	4.06 (3.91, 4.20)	4.25 (4.04, 4.45)
R <sup>2</sup> (95% CI)	79.7 (78.6, 80.8)	81.2 (79.6, 82.6)
Bootstrap-corrected c-statistic	0.96	
Slope shrinkage	0.009	

The D-statistic measures a model’s ability to separate the higher- and lower-risk patients. Each individual has a predicted risk on the basis of the Cox model. The D-statistic compares individuals above the median predicted risk to individuals below the median according to their observed risk of the event. When D is exponentiated, it is the hazard ratio comparing the higher- and lower-risk groups. A D-statistic of zero means that the model failed to separate higher- and lower-risk patients. The D-statistic can be used to calculate the R<sup>2</sup>-statistic, a summary measure of a model’s predictive ability that reflects both separation and accuracy (*i.e.*, agreement between an individual’s predicted and observed risk of the event). An R<sup>2</sup> of 0% means the model failed to explain variation in the occurrence of the event. An R<sup>2</sup> of 100% means the model explained all of the variation (31,32). 95% CI, 95% confidence interval.

[95% CI], 4.38 to 5.06). Table 1 describes the baseline characteristics of the final eight predictor variables. There were missing values for systolic BP (0.1%), hemoglobin (11.2%), and proteinuria/albuminuria (26.1%). NSAID use and BMI were not retained in the model, as they contributed the least to the explained variation. Current use of an NSAID had an adjusted hazard ratio of 0.93 (95% CI, 0.55 to 1.55). BMI cannot be summarized meaningfully as a hazard ratio because it was modeled as a restricted cubic spline. However, both were weak predictors, and we were able to drop both of them while still preserving 99.8% of the explained variation in the full model. One predictor, eGFR, explained most of the variation in the full model: 80.9%. A total of four predictors—eGFR, albuminuria/proteinuria, age, and sex—explained 93.7% of the variation in the full model. Because our *a priori* objective was to retain 99% of the variation explained by the full model, we validated the simplified eight-predictor model: age, sex, eGFR, hemoglobin, proteinuria/albuminuria, systolic BP, antihypertensive medication use, and diabetes and its complications (Table 1, Supplemental Table 1).

The hazard ratios and simplified points-based system derived from the Cox model are shown in Table 2, and the full Cox model equation in Supplemental Figure 1. The mean predicted risk of progression to RRT was 4.73%. The slope-shrinkage statistic, which assesses the extent to which the model may be over-fit to the development data,

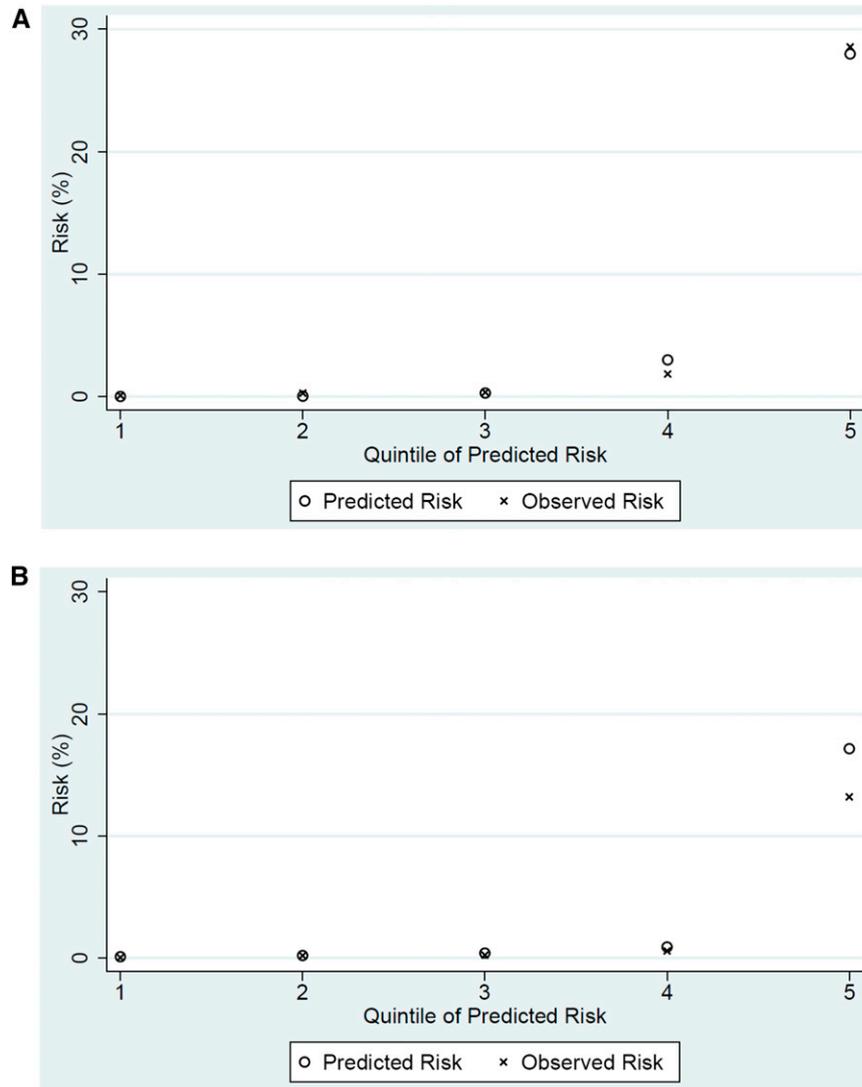
was 0.009 (on a scale from 0 to 1 where 0 indicates no overfitting). Summary statistics from the internal validation of the Cox regression model indicated excellent performance in the Northwest cohort (Table 3). The bootstrap-corrected c-statistic (0.96) indicated excellent discrimination or separation of high- and low-risk individuals (larger values mean better discrimination). The R<sup>2</sup> value indicates that the prediction model explained 79.7% of the variation in risk of progression to RRT. The highest-risk quintile identified 90.8% of the patients who started RRT (*i.e.*, the sensitivity) (Table 4). The positive predictive value, sensitivity, and specificity for different cut points of predicted risk are shown in Supplemental Table 2. Agreement (calibration) was high, with the predicted risk very closely aligned with observed events for all quintiles (Figure 1, Supplemental Figure 2). Truncating the follow-up at 2 years yielded very similar summary statistics, with an R<sup>2</sup> of 77.9% and bootstrap-corrected c-statistic of 0.96.

**External Validation of the KPNW Prediction Model**

In the Colorado cohort, there were 16,553 individuals and 360 events (Table 1). The risk of progression to RRT was lower in the Colorado cohort than the Northwest cohort, with a 5-year Kaplan–Meier risk of 2.57% (95% CI, 2.30 to 2.83). The Colorado and Northwest cohorts were very similar (Table 1). The mean hemoglobin was higher as expected due to the Colorado altitude, and the prevalence of diabetes was

**Table 4. Observed and predicted 5-year risk of RRT by quintile of predicted risk for the Kaiser Permanente Northwest prediction model**

Quintile	Northwest (Development) Cohort				Colorado (External Validation) Cohort			
	N	Events	Kaplan–Meier Observed 5-Yr Risk (%)	Predicted 5-Yr Risk (%)	N	Events	Kaplan–Meier Observed 5-Yr Risk (%)	Predicted 5-Yr Risk (%)
1	4492	3	0.09	0.002	3311	2	0.03	0.10
2	4492	9	0.28	0.03	3311	5	0.19	0.20
3	4492	11	0.34	0.28	3310	6	0.23	0.40
4	4492	45	1.84	2.99	3311	15	0.57	0.90
5	4492	669	28.55	27.98	3310	332	13.20	17.15
Total	22,460	737	4.72	4.73	16,553	360	2.57	3.41



**Figure 1. | Predicted and observed 5-year risk by quintile of predicted risk from the Kaiser Permanente Northwest prediction model. (A) Northwest cohort (development cohort). (B) Colorado cohort (external validation cohort).**

lower (34.3% versus 27.0%). The percentage of individuals with data for all eight predictors was 65.1%.

The KPNW eight-variable prediction model performed extremely well in the Colorado cohort. The mean predicted risk of progression to RRT was 3.41%. Using the highest risk quintile as the cutoff resulted in a sensitivity of 92.2% (332 out of 360). The model had excellent calibration (Figure 1) and discrimination (Table 3). The prediction model explained 81.2% of the variation in risk of progression to RRT, with a c-statistic of 0.95. The observed risk was lower than the predicted risk for the highest-risk quintile.

## Discussion

The KPNW prediction model performed extremely well in both the development and validation cohorts, with excellent discrimination and acceptable calibration. In developing the KPNW model, we attempted to build a pragmatic model that can be applied to CKD stages 3 and 4 and relies upon eight variables typically available in routine clinical practice:

age, sex, eGFR, hemoglobin, proteinuria/albuminuria, systolic BP, antihypertensive medication use, and diabetes and its complications (36).

Although we envision the KPNW prediction model being used in population-based disease management with autoscoring from an electronic health record, it could also be used during an individual physician-patient interaction. Predicted risk can be calculated either using the underlying risk predictor from the Cox model (Supplemental Figure 1) or manually calculated using the points-based system (Supplemental Table 2). By focusing on individuals at high risk, clinicians or health systems may be able to more effectively target interventions. Potential interventions include population management approaches, such as clinical pharmacist outreach to optimize medication use, patient education by nursing staff, additional work-up, and referrals to nephrology. Use by health systems can support “precision delivery,” where information from the electronic health records is used to predict risk, personalize care, and provide

high quality care (37). Accordingly, in developing the KPNW model, we only evaluated candidate predictors with limited missing data to facilitate its use in routine primary care or in a population-based disease management program. The risk score can be used to identify individuals above a certain risk for progression to RRT (e.g.,  $\geq 20\%$ ), or to rank the population at highest risk (e.g., the top quintile of the population). Using the KPNW prediction model to identify the quintile of the population at highest predicted risk has a sensitivity of 92.2%. As an example of a potential use for this prediction model, KPNW currently uses a prediction equation similar to this to target clinical pharmacist outreach and nephrology referrals to individuals with the highest predicted risk.

eGFR is the strongest predictor of progression to RRT; it is responsible for 80.9% of the explanatory value of the full ten-variable model. Furthermore, a four-variable model with age, sex, eGFR, and albuminuria/proteinuria (such as that developed by Tangri *et al.* [10,15]) retains 93.6% of the full ten-variable model. As the model is designed to be used in a population management setting where electronic health data are available, retaining the additional four variables adds little to the complexity and improves its predictive ability. Most importantly, it allows the model to be used in patients who do not have an available measure of albuminuria or proteinuria.

Limitations of our model include the low overall incidence of ESRD and lack of racial diversity in the development and validation cohorts (4). The ESRD rate in the Colorado, Oregon, and Washington ESRD Networks are among the lowest in the United States, and in prediction modeling *c*-statistics tend to be higher in low-risk settings with extreme heterogeneity in the distribution of the predictor characteristics (4). In addition, both cohorts were derived from integrated managed care populations, which could affect generalizability to the extent that practice patterns influence the risk of progression to RRT. Another limitation is that we treated albuminuria/proteinuria as a dichotomous variable to reduce the number of patients with missing data by allowing for the use of a variety of methods of albuminuria/proteinuria ascertainment (urine ACR, protein-to-creatinine ratio, and dipstick protein). This likely led to underestimation of its potential prognostic value. Finally, the mortality rate was high in both of our cohorts. Although we did not conduct a competing risk analysis, our model likely overestimates the risk of RRT, especially for the highest-risk patients.

In conclusion, we have developed a pragmatic prediction model and risk score for predicting the 5-year risk of RRT among individuals with stage 3 and 4 CKD. As this model uses variables that are typically available in routine primary care settings, we feel that it is especially well suited to automated use at a system-wide level where it can be used to help guide decisions concerning clinical pharmacist outreach to optimize medication use, patient education by nursing staff, additional work-up, timing of referral to nephrology, timing of fistula placement, and other important interventions such as timing of preemptive kidney transplant and predialysis education.

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#### Disclosures

None.

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