

**Supplemental Material: Performance of the Kidney Failure Risk Equation by Disease Etiology in Advanced CKD**

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## Supplemental Table 1. TRIPOD checklist for prediction model validation.



TRIPOD Checklist: Prediction Model Development and Validation

Section/Topic	Item	Checklist Item	Page	
<b>Title and abstract</b>				
Title	1	D;V	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	Page 1
Abstract	2	D;V	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	Pages 2-3
<b>Introduction</b>				
Background and objectives	3a	D;V	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	Page 4
	3b	D;V	Specify the objectives, including whether the study describes the development or validation of the model or both.	Page 5
<b>Methods</b>				
Source of data	4a	D;V	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	Pages 6-7
	4b	D;V	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	Pages 6-7
Participants	5a	D;V	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	Pages 6-7
	5b	D;V	Describe eligibility criteria for participants.	Pages 6-7
	5c	D;V	Give details of treatments received, if relevant.	N/A
Outcome	6a	D;V	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	Pages 7-8
	6b	D;V	Report any actions to blind assessment of the outcome to be predicted.	N/A
Predictors	7a	D;V	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	Page 8
	7b	D;V	Report any actions to blind assessment of predictors for the outcome and other predictors.	N/A
Sample size	8	D;V	Explain how the study size was arrived at.	Page 7, Fig 1
Missing data	9	D;V	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	Page 9
Statistical analysis methods	10a	D	Describe how predictors were handled in the analyses.	N/A (validation only)
	10b	D	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	N/A (validation only)
	10c	V	For validation, describe how the predictions were calculated.	Pages 8-9
Risk groups	10d	D;V	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	Pages 9-10
	10e	V	Describe any model updating (e.g., recalibration) arising from the validation, if done.	N/A (validation only)
	11	D;V	Provide details on how risk groups were created, if done.	Pages 9-10
Development vs. validation	12	V	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	N/A (noncomparative validation after sample split) Pages 8-7
<b>Results</b>				
Participants	13a	D;V	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	Figure 1 and Figure 1
	13b	D;V	Describe the characteristics of the participants (basic demographics, clinical features, available predictors). Including the number of participants with missing data for Tables 1 and S2, Pages 11-12	Tables 1-6, pp. 14-16
	13c	V	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	Table S3, pp. 14-15
Model development	14a	D	Specify the number of participants and outcome events in each analysis.	N/A (validation only)
	14b	D	If done, report the unadjusted association between each candidate predictor and outcome.	N/A (validation only)
Model specification	15a	D	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	N/A (validation only)
	15b	D	Explain how to use the prediction model.	N/A (validation only)
Model performance	16	D;V	Report performance measures (with CIs) for the prediction model	Pages 12-14, Fig 2-4/S1-2, Tables 2/S4-6
Model-updating	17	V	If done, report the results from any model updating (i.e., model specification, model performance).	N/A
<b>Discussion</b>				
Limitations	18	D;V	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	Page 16-17
Interpretation	19a	V	For validation, discuss the results with reference to performance in the development data, and any other validation data.	Pages 15-18
	19b	D;V	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	Pages 15-18
Implications	20	D;V	Discuss the potential clinical use of the model and implications for future research.	Pages 17-18
<b>Other information</b>				
Supplementary Information	21	D;V	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	Supplemental material
Funding	22	D;V	Give the source of funding and the role of the funders for the present study.	Page 19

**Supplemental Table 2. Baseline characteristics of 637 patients with advanced CKD referred to the Ottawa Hospital Multi-Care Kidney Clinic from 2010 to 2013.**

	All (N=637)	Diabetic Kidney Disease (N=311)	Hypertensive Nephrosclerosis (N=110)	Glomerulonephritis (N=97)	Polycystic Kidney Disease (N=41)	Other (N=78)
<b>Kidney Disease Etiology</b>						
<b>Demographics</b>						
Age, median (IQR)	68 (57, 77)	67 (59, 76)	77 (72, 84)	59 (48, 74)	58 (52, 67)	66 (51, 76)
Female, N (%)	245 (38)	119 (38)	45 (41)	26 (27)	22 (54)	33 (42)
Race, N (%)						
White	463 (73)	225 (72)	90 (82)	59 (61)	32 (78)	57 (73)
Black	41 (6)	17 (5)	2 (2)	12 (12)	1 (2)	9 (12)
Asian	26 (4)	16 (5)	3 (3)	4 (4)	1 (2)	2 (3)
Other	107 (17)	53 (17)	15 (14)	22 (23)	7 (17)	10 (13)
<b>Baseline Kidney Parameters</b>						
Serum Creatinine mg/dL, median (IQR)	3.6 (2.9, 4.5)	3.4 (2.9, 4.3)	3.5 (2.7, 4.1)	4.1 (3.6, 5.1)	3.9 (3.1, 4.6)	3.7 (3.1, 2.0)
eGFR mL/min/1.73m <sup>2</sup> , median (IQR)	15 (11, 19)	16 (12, 20)	14 (11, 17)	14 (11, 17)	15 (11, 19)	15 (11, 20)
Urine Albumin-to-Creatinine Ratio mg/g, median (IQR)	1167 (281, 2613)	1762 (665, 3628)	260 (100, 919)	2063 (1088, 3211)	242 (106, 391)	542 (100, 1258)
<b>Other Laboratory Data</b>						
Serum Potassium mEq/L, median (IQR)	4.5 (4.1, 4.8)	4.5 (4.1, 4.9)	4.5 (3.9, 4.8)	4.6 (4.2, 5.0)	4.2 (3.9, 4.5)	4.4 (4.0, 4.8)
Serum Calcium mg/dL, median (IQR)	8.9 (8.5, 9.2)	8.8 (8.5, 9.1)	9.0 (8.7, 9.3)	8.7 (8.4, 9.0)	9.1 (8.9, 9.4)	9.0 (8.7, 9.4)
Serum Phosphate mg/dL, median (IQR)	4.1 (3.6, 4.6)	4.2 (3.7, 4.7)	3.9 (3.5, 4.4)	4.1 (3.6, 4.8)	3.8 (3.3, 4.4)	3.9 (3.3, 4.5)
Serum Bicarbonate mEq/L, median (IQR)	24 (22, 26)	24 (22, 26)	24 (22, 28)	23 (21, 25)	25 (23, 27)	24 (21, 26)
Serum Albumin g/dL, median (IQR)	3.5 (3.2, 3.8)	3.5 (3.1, 3.7)	3.6 (3.3, 3.8)	3.5 (3.1, 3.7)	3.8 (3.6, 4.1)	3.5 (3.3, 3.8)
<b>Blood Pressure Data</b>						
Systolic Blood Pressure mmHg, median (IQR)	130 (120, 146)	134 (122, 152)	130 (119, 148)	130 (122, 142)	120 (112, 132)	124 (115, 136)
Diastolic Blood Pressure mmHg, median (IQR)	70 (60, 78)	69 (60, 75)	68 (60, 70)	72 (66, 80)	76 (68, 84)	70 (60, 80)
ACE Inhibitor/ARB Use, N (%)	316 (50)	161 (52)	40 (36)	53 (55)	28 (68)	34 (44)
Diuretic, N (%)	408 (64)	240 (77)	75 (68)	45 (46)	17 (41)	31 (40)
<b>Body Mass Index, kg/m<sup>2</sup>,</b> <b>Median (IQR)</b>	29 (25, 34)	31 (27, 36)	27 (24, 32)	27 (24, 32)	26 (23, 31)	27 (24, 31)
<b>KFRE, %</b>						
2-Year, 4-Variable						
Mean (SD)	48 (28)	52 (28)	32 (25)	65 (25)	37 (22)	43 (28)
Median (IQR)	48 (21, 74)	54 (27, 76)	26 (12, 44)	68 (49, 85)	36 (20, 52)	38 (18, 66)
5-Year, 4-Variable						
Mean (SD)	75 (27)	79 (25)	58 (30)	89 (17)	68 (25)	69 (30)
Median (IQR)	87 (53, 98)	91 (63, 99)	361 (33, 84)	97 (87, 100)	75 (51, 90)	77 (46, 97)

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; CKD, chronic kidney disease; dL, deciliter; eGFR, estimated glomerular filtration rate; g, gram; IQR, interquartile range; KFRE, kidney failure risk equation; kg, kilogram; m, meter; mEq, milliequivalents; mg, milligram; mL, milliliter; mmHg, millimeters of mercury; N, number; SD, standard deviation; yr, year.

**Supplemental Table 3. Comparison of study cohort to the KFRE development cohort.<sup>1</sup>**

	<b>Comparison of Study Validation Cohort to the KFRE Development Cohort</b>	
	2-Year Validation Cohort (N=1293)	Development Cohort (N=3449)
Age, yr, mean (SD)	67 (15)	70 (14)
Female sex, N (%)	501 (39)	1503 (44)
Mean systolic BP, mmHg, mean (SD)	136 (22)	130 (22)
Mean diastolic BP, mmHg, mean (SD)	71 (13)	71 (12)
Baseline eGFR, mL/min/1.73m <sup>2</sup> , mean (SD)	16 (6)	36 (13)
Serum creatinine, mg/dL, mean (SD)	3.8 (1.3)	2.2 (1.3)
Serum calcium, mg/dL, mean (SD)	8.9 (0.6)	9.4 (0.6)
Serum phosphate, mg/dL, mean (SD)	4.2 (0.9)	4.0 (0.9)
Serum albumin, mg/dL, mean (SD)	3.5 (0.5)	4.0 (0.5)
Serum bicarbonate, mEq/L, mean (SD)	24 (3)	26 (4)
Urine albumin-to-creatinine ratio, mg/g, median (IQR)	1277 (2581)	93 (378)
Kidney failure events	541 (42)	386 (11)

Abbreviations: BP, blood pressure; dL, deciliter; g, gram; IQR, interquartile range; KFRE, kidney failure risk equation; m, meter; mEq, milliequivalents; mg, milligram; mL, milliliter; mmHg, millimeters of mercury; min, minute; N, number; SD, standard deviation; yr, year.

**Supplemental Table 4. Kidney failure and death prior to kidney failure by kidney disease etiology.**

<b>Observed Rates of Kidney Failure and Death Prior to Kidney Failure</b>						
	All	Diabetic Kidney Disease	Hypertensive Nephrosclerosis	Glomerulonephritis	Polycystic Kidney Disease	Other
<b><u>2-Year Analysis</u></b>						
Total Population, N	1293	637	213	196	74	173
Kidney Failure, N (%)	541 (42)	273 (43)	56 (26)	123 (63)	31 (42)	58 (34)
Deaths Prior to Kidney Failure, N (%)	144 (11)	65 (10)	43 (20)	11 (6)	0 (0)	25 (14)
<b><u>5-Year Analysis</u></b>						
Total Population, N	637	311	110	97	41	78
Kidney Failure, N (%)	406 (64)	208 (67)	43 (39)	81 (84)	37 (90)	37 (47)
Deaths Prior to Kidney Failure, N (%)	111 (17)	46 (15)	44 (40)	4 (4)	0 (0)	17 (22)

**Supplemental Table 5: Calibration data for 2-year KFRE by kidney disease etiology.**

<b>Predicted vs. Observed 2-Year Rates of Kidney Failure</b>			
<u>Kidney Disease Etiology</u>	<u>2-Year Rates of Kidney Failure</u>		<u>P-Value</u>
	Predicted by KFRE	Observed	(Hosmer-Lemeshow)
All (N=1293)	48%	42% (541/1293)	0.36
Diabetic Kidney Disease (N=637)	53%	43% (273/637)	0.38
Hypertensive Nephrosclerosis (N=213)	31%	26% (56/213)	0.44
Glomerulonephritis (N=196)	63%	63% (123/196)	0.90
Polycystic Kidney Disease (N=74)	36%	42% (31/74)	0.78
Other (N=173)	41%	34% (58/173)	0.70

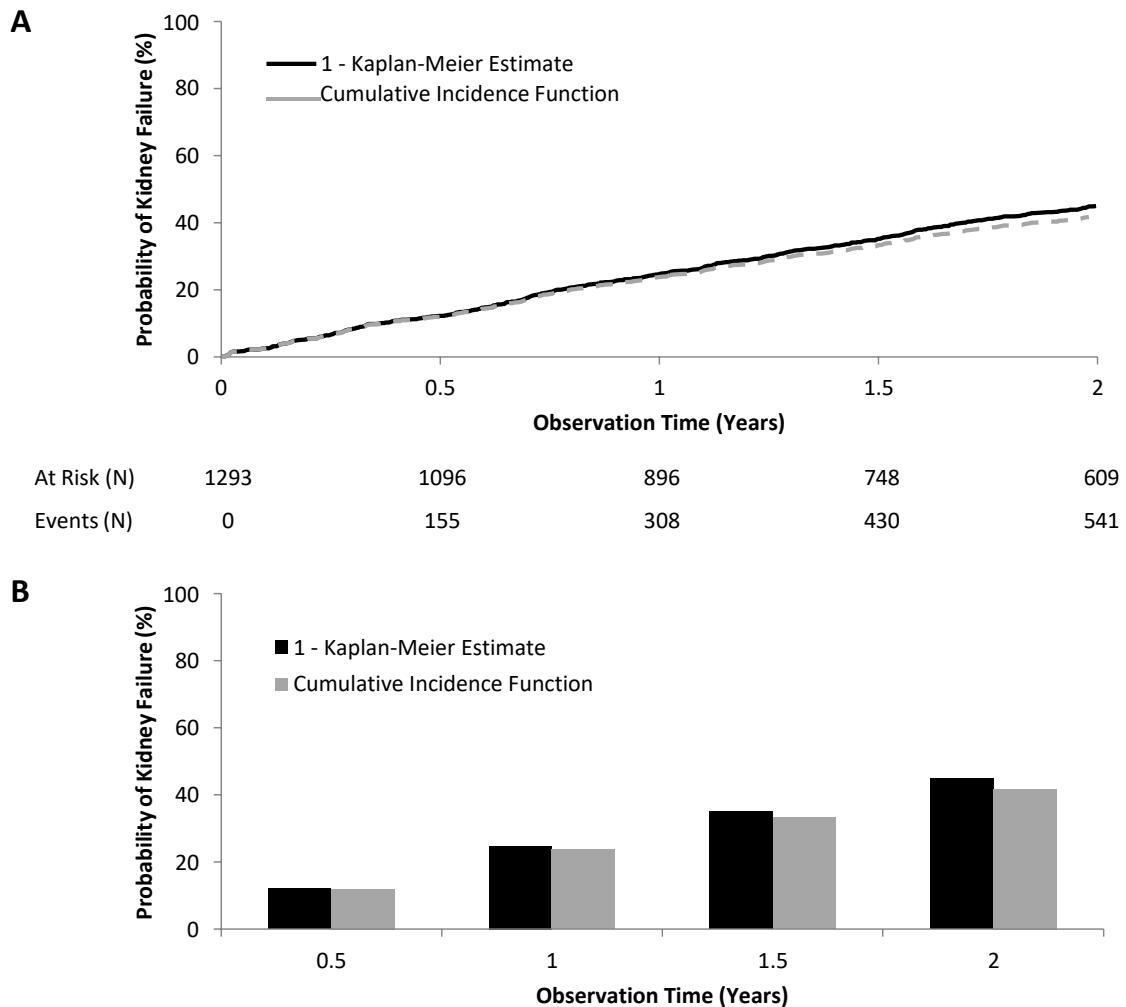
Abbreviations: KFRE, kidney failure risk equation.

**Supplemental Table 6: Calibration data for 5-year KFRE by kidney disease etiology.**

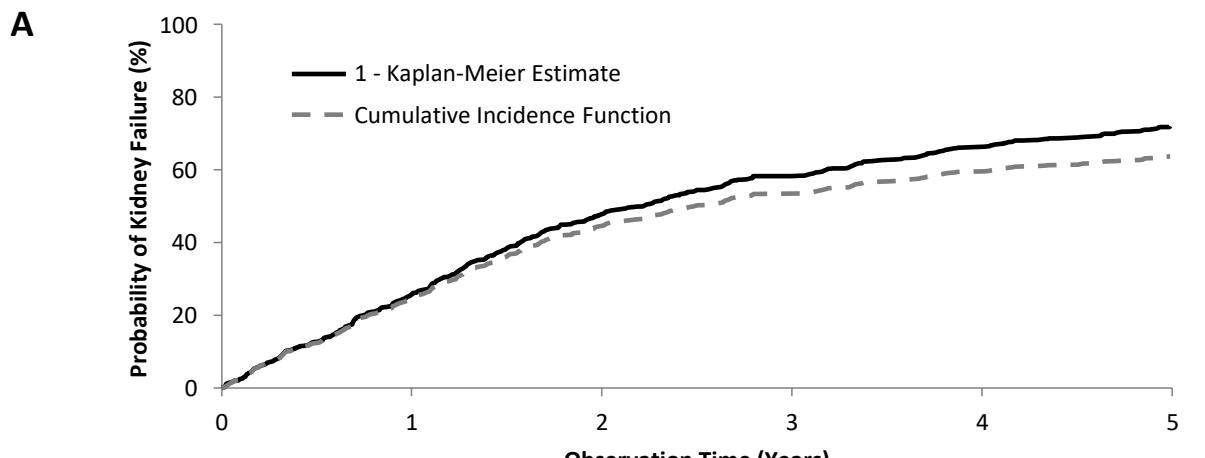
<u>Kidney Disease Etiology</u>	<u>Predicted vs. Observed 5-Year Rates of Kidney Failure</u>		<u>P-Value</u> (Hosmer-Lemeshow)
	<u>5-Year Rates of Kidney Failure</u> Predicted by KFRE	<u>Observed</u>	
All (N=637)	75%	64% (406/637)	0.31
Diabetic Kidney Disease (N=311)	79%	67% (208/311)	0.34
Hypertensive Nephrosclerosis (N=110)	58%	39% (43/110)	0.29
Glomerulonephritis (N=97)	89%	84% (81/97)	0.08
Polycystic Kidney Disease (N=41)	68%	90% (37/41)	0.73
Other (N=78)	69%	47% (37/78)	0.05

Abbreviations: KFRE, kidney failure risk equation.

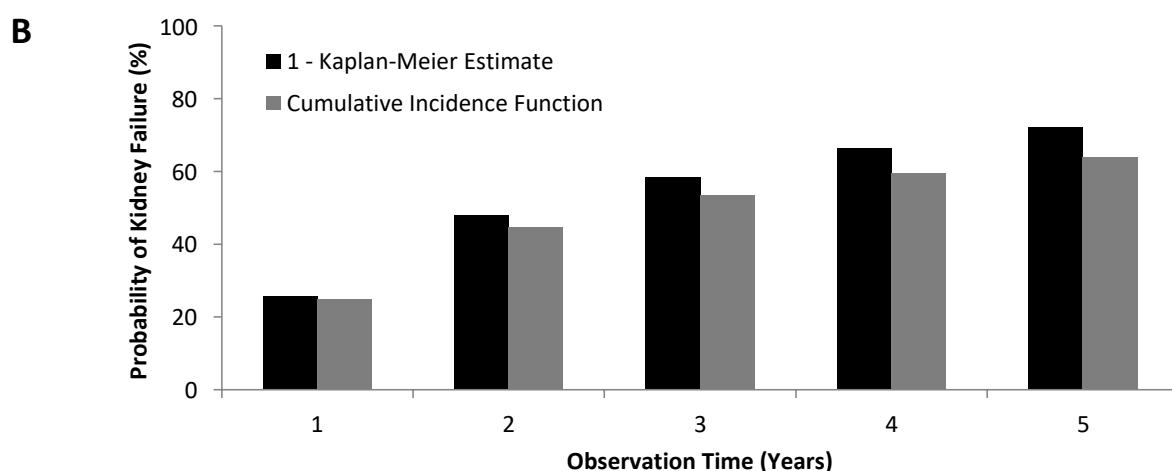
**Supplemental Figure 1. Competing risk analysis for 2-year KFRE.** Comparison of 1 minus the Kaplan-Meier Estimate (observed probability of kidney failure where death prior to kidney failure is censored) and the cumulative incidence function (observed probability of kidney failure where death prior to kidney failure is treated as a competing event).



**Supplemental Figure 2. Competing risk analysis for 5-year KFRE.** Comparison of 1 minus the Kaplan-Meier Estimate (observed probability of kidney failure where death prior to kidney failure is censored) and the cumulative incidence function (observed probability of kidney failure where death prior to kidney failure is treated as a competing event).



At Risk (N)	637	435	289	211	163	120
Events (N)	0	158	284	340	379	406



## **Supplemental References**

1. Tangri N, Stevens LA, Griffith J, Tighiouart H, Djurdjev O, Naimark D, Levin A, Levey AS: A predictive model for progression of chronic kidney disease to kidney failure. *JAMA*, 305: 1553-1559, 2011