

Title: Validation of the Kidney Failure Risk Equation in an International Consortium

Navdeep Tangri, MD, Andrew S. Levey, MD, M. Grams, MD, Josef Coresh, MD, PhD, FASN, Brad C. Astor, PhD, Allan J. Collins, MD, Ognjenka Djurdjev, Carolyn Raina Elley, MD, PhD, Stein I. Hallan, MD, PhD, Lesley Inker, MD, Csaba P. Kovesdy, MD, Florian Kronenberg, MD, Hidde Jan Lambers Heerspink, PhD, Angharad Marks, MBChB, Sankar D. Navaneethan, MD, FASN, Robert G. Nelson, MD, PhD, Mark J. Sarnak, MD, FASN, Benedicte Stengel, MD, PhD, Mark Woodward, PhD, Kunitoshi Iseki, MD. CKD Prognosis Consortium.

Background: Predicting the progression of CKD can enable early and appropriate nephrology care. We previously developed and validated laboratory based kidney failure risk equations (KFREs) for the progression of CKD to kidney failure in patients referred for nephrology care in Canada. Evaluation in other countries and in non-referred CKD populations is needed.

Methods: We meta-analyzed individual level data from 34,569 patients with CKD Stages 3-5 from 12 cohorts spanning 7 countries. We assessed models containing 3 (age, sex, estimated glomerular filtration rate [GFR]), 4 (+albuminuria) and 8 (+serum albumin, calcium, phosphorous, and bicarbonate) variables from the original publication. We compared hazard ratios for constituent predictors, discrimination, calibration, net reclassification index (NRI), and integrated discrimination index (IDI) for all models.

Results: The original 4- and 8-variable KFREs obtained similar hazard ratios for constituent predictors and achieved excellent discrimination (C statistic >0.84 – Table). Calibration of the original KFREs was adequate at 5 years, and improvements in NRI and IDI were observed in comparison with a 3-variable model (NRI 18%, IDI 5% for the 4-variable, and 25% and 6% for the 8-variable model). Performance in subgroups by age, race and diabetes status was similar.

Conclusions: The previously developed KFREs accurately predict the progression of CKD Stages 3-5 to kidney failure across a wide range of studies. The abbreviated 4-variable equation is simple and highly accurate. Integration in routine clinical practice should be evaluated.

Model	Difference of C Statistic	NRI with risk categories of 0-1%, 1-2%, 2%+	IDI
1 year			
4-var vs. 3-var	0.000 (-0.021, 0.022)	0.183 (0.123, 0.243)	0.048 (0.021, 0.074)
8-var vs. 3-var	0.001 (-0.020, 0.023)	0.253 (0.198, 0.309)	0.060 (0.001, 0.118)
8-var vs. 4-var	0.001 (-0.005, 0.007)	0.093 (0.075, 0.112)	0.011 (-0.033, 0.055)
5 year			
4-var vs. 3-var	0.008 (-0.025, 0.041)	0.168 (0.130, 0.206)	0.037 (-0.007, 0.080)
8-var vs. 3-var	0.016 (-0.009, 0.041)	0.194 (0.163, 0.225)	0.031 (-0.026, 0.088)
8-var vs. 4-var	0.008 (-0.005, 0.020)	0.039 (0.017, 0.062)	-0.004 (-0.024, 0.016)

C-statistic for 3-variable model: 1y = 0.923 (0.889, 0.956); 5y = 0.843 (0.817, 0.868)

C-statistic for 4-variable model: 1y = 0.914 (0.865, 0.963); 5y = 0.851 (0.818, 0.883)

Bold indicates significance compared to 3- or 4-variable model