About 7% of the adult population has non-dialysis-dependent chronic kidney disease (CKD) and many millions of people worldwide are at risk of kidney failure, cardiovascular disease and death attributable to their CKD [1–4]. However, risk is not uniform—for some the presence of CKD will have no appreciable impact on their life, while in others it strongly predicts the development of kidney failure and need for ongoing dialysis. Prediction models have the potential to stratify patients with CKD by their risk for these clinically important outcomes [5–7]. This can then be used to better tailor advice and treatment for an individual CKD patient. Obtaining the expected 5-year incidence of various outcomes can be as simple as typing in up to eight patient characteristics into an online web form and observing the output from the model (http://www.qxmd.com/calculate-online/nephrology/kidney-failure-risk-equation) [8]. However, prediction models need to be internally and externally validated before widespread use.

In this edition of the journal, Peeters et al. externally validated the full and abbreviated forms of the kidney failure risk equation (KFRE) in an independent CKD population. They selected 595 non-transplant patients in the Netherlands enrolled in the MASTERPLAN trial between 2004 and 2005, and in this cohort confirmed the accuracy of the full (eight-variable model) and abbreviated (three- and four-variable model) KFRE. Missing data for one or more variables in the eight-variable model was found in only 6% (36 of 595) of patients. Performance of the full KFRE, as evaluated by the ROC-AUCs (area under the receiver operating characteristic curve), was excellent (>0.8 for all models). The full KFRE also performed well when tested separately in patients with stage 3 and stage 4 CKD. The ROC-AUCs for the 8-, 4- and 3-variable models were 0.84, 0.78 and 0.74 for stage 3 CKD and 0.71, 0.71 and 0.72 for stage 4 CKD, respectively. Compared with the full KFRE, the discrimination for the abbreviated KFRE (4- and 3-variable models) was also good. The full KFRE also showed better calibration than the abbreviated 4- and 3-variable models (−4.1 versus −7.1% and −7.4%, respectively; calibration defined as the discrepancy between observed and predicted quintiles of risk; in other words, how well model predictions agree with actual data [9]). The authors note that the low number of patients in each of the stage 3 and 4 CKD subgroups make any conclusions about differences in model performance between the full and abbreviated KFRE uncertain. They conclude that the full KFRE did not perform better than the simpler models. Overall, despite differences in kidney failure rate, patient population and clinical setting, this study provides evidence that the KFRE can perform well in an independent patient population.

The KFRE in question was derived by Tangri et al. in 2011 in a cohort from Toronto, Canada, and validated in a cohort from Vancouver, Canada [8]. The authors developed multiple models and validated three: the abbreviated KFRE, consisted of three [age, sex and estimated glomerular filtration rate (eGFR)] or four variables (age, sex, eGFR and albumin-to-creatinine ratio), and the full KFRE, which incorporated routine biochemical data (calcium, phosphate, bicarbonate and albumin) into an eight-variable model. Some of the early criticisms of the KFRE centered around missing data in both the derivation and validation cohorts as well as selection of a cohort already under the care of the nephrologist. Further studies testing the external validity of the KFRE were encouraged forming the basis of the study by Peeters et al. [10]. It is well known that models derived in one cohort frequently perform less well in other cohorts.
Factors such as true differences in disease and/or biology in other patient cohorts, demographics, available clinical data and practice setting are all possible explanations for differences in model performance [9]. As an example, the Framingham study equation performs best in the original development cohort, but model coefficients and baseline rates often need to be adjusted in different patient populations [11].

The KFRE is a risk prediction model that utilizes highly accessible and routinely collected demographic and biochemical data. Compared with other existing models for predicting the progression of CKD, the KFRE has now been validated in two independent populations [12]. However, we must be cautious as this external validation was also done in patients already under the care of a nephrologist. The equation is yet to be validated in a primary care setting where the vast majority of patients with CKD are not referred for nephrology care. If the equation proves successful in primary care, it can be used to guide referrals for additional nephrology assessment, treatment and follow-up. Whether the full KFRE is better than the abbreviated KFRE in the primary care setting also remains to be determined.

Ultimately, the best proof for the benefits KFRE will be if clinical practices that use it have better patient outcomes and lower costs than those who do not. Given the available treatment options, will better identification of high-risk patients reduce progressive kidney disease? We certainly hope so, and there is proof that prediction models can be effective when applied to clinical practice [13]. We must also be reminded that kidney failure is not the only important clinical outcome in CKD. The development of additional risk prediction models for cardiovascular outcomes and death attributed to CKD is also needed. In the meantime, the study by Peeters et al. provides evidence of the potential generalization of the KFRE. The equation is on the road to being clinically useful. We await with anticipation studies that test the KFRE in the broader CKD population as well as trials to determine if that model use improves clinical outcomes and costs.

**CONFLICT OF INTEREST STATEMENT**

None declared.

(See related article by Peeters et al. Validation of the kidney failure risk equation in European CKD patients. Nephrol Dial Transplant 2013; 28: 1773–1779.)

**REFERENCES**


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