Predicting risk of kidney failure and mortality – a new tool

KDpredict, a new kidney failure prediction tool which also estimates mortality risk over 1–5 years, demonstrated improved predictive accuracy for end-stage renal disease development compared with the current Kidney Failure Risk Equation in this study published in the *BMJ*. KDpredict was developed using innovative machine learning algorithms to predict the competing endpoints in a large population of Canadian people aged 77–80 years developing stage G3b or G4 chronic kidney disease (CKD), who were then followed up for 5–6 years. Cohorts from Denmark and Scotland were used to demonstrate applicability to other countries, potentially making it usable in the UK population. CKD affects greater numbers of older people, many of whom will have higher risk of mortality than of developing end-stage renal disease; hence, the estimation of the competing mortality risk with KDpredict may be helpful in discussions and decision making. However, NICE currently recommends use of the Kidney Failure Risk Equation and consideration of specialist referral in those with a 5-year risk of 5% or greater, so this new tool should be used alongside this rather than as a replacement. Both tools can aid our consultations with people with CKD, and hopefully they will help motivate people to consider lifestyle and drug changes to reduce their risk.



Pam Brown GP in Swansea

linical prediction models can be used to estimate whether a condition is present (diagnostic models) or will occur in the future (prognostic models) (Kengne et al, 2024). The NICE (2021) NG203 guideline recommends the use of the Kidney Failure Risk Equation (KFRE) in people with chronic kidney disease (CKD; defined as persisting eGFR <60 mL/min/1.73 m² or ACR \ge 3 mg/ mmol for 90 days), which uses age, sex, eGFR and ACR to predict the 1-year and 5-year likelihood of developing end-stage renal disease (ESRD). People with a 5-year risk of 5% or greater are recommended to be referred for specialist assessment, along with other groups, in the NG203 guideline.

The KFRE calculator is interactive and allows users to explore the impact on risk progression of tight blood pressure control or addition of an ACE inhibitor/ARB, SGLT2 inhibitor or, if type 2 diabetes is also present, addition of finerenone. Most clinicians find the tool useful, although it is not fully integrated into all electronic record systems.

The KDpredict tool

In the present study, Liu and colleagues developed the KDpredict tool (available at https://kdpredict.com) using artificial intelligence and a "super learner" algorithm to identify the best algorithm and model for predicting progression to ESRD and mortality. Compared with KFRE, the KDpredict algorithm used data from an older age group (median 77-80 years compared with 69-70 years) with lower eGFRs (<45 vs <59 mL/min/1.73 m²) at the point of their initial diagnosis with CKD of at least stage 3b. KDpredict was then evaluated for use in cohorts in Denmark and Scotland, where it was compared with KFRE for predictive accuracy. Although both calculators use the same four core risk factors (age, sex, eGFR and ACR), KDpredict can also include diabetes and cardiovascular disease as predictors (Figure 1).

In the Scottish study, conducted in nearly 8000 people with stage G3b–G4 CKD and a median age of 77–80 years, KDpredict consistently outperformed KFRE in predicting kidney failure risk at 1–5 years, as well as estimating

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Figure 1. Predicted risk outcomes from the KDpredict algorithm. Image captured from <u>https://kdpredict.com</u>

all-cause mortality. CKD risk predictions differed significantly between the two tools, with KFRE providing higher risk estimates as it does not take into account the competing risk of mortality. Faced with values above and below the specialist referral threshold of 5% over 5 years, clinicians would need reassurance that the value predicted by KDpredict should be used, thus avoiding uncertainty about the most appropriate management. It is suggested the mortality risk data would be used alongside the ESRD risk to aid person-centred decision making and discussions regarding the competing risks, so that an informed choice can be made about whether specialist referral is appropriate. The authors conclude that this tool could be incorporated into electronic medical record systems and could be adapted to different health systems.

Practice implications

CKD affects up to 10% of adults in general, and up to 30% of those with type 2 diabetes. Large numbers of people with CKD, with and without diabetes, remain undiagnosed. Furthermore, diagnosis is often inaccurately coded and many people remain unaware of their diagnosis despite our best efforts to share this at point of measurement. People with CKD are at high risk of cardiovascular disease and this is the main cause of death, so managing this risk and minimising progression to ESRD remain the priorities. Usually these aims require similar management: smoking cessation;

good blood pressure control, including use of ACE inhibitors/ARBs; lipid control with statins and newer therapies; glycaemic control with drugs that reduce risk of cardiovascular events and CKD progression, such as SGLT2 inhibitors and GLP-1 receptor agonists; and addition of finerenone if appropriate.

It is not clear whether this tool's ability to predict mortality risk will alter management significantly, and this will need to be sensitively handled if we choose to share it to aid decision making. The KDpredict tool is designed to be used once – at the time of diagnosis of at least CKD3b – whereas KFRE can be used repeatedly.

As clinicians, it is useful for us to understand the benefits and limitations of the prediction tools we currently use, and how AI can be harnessed to develop better tools to help us optimise care delivery. This paper, and its accompanying editorial and *Fast Facts* article explaining risk prediction models (Kengne et al, 2024; Gerd and Ravani, 2024), will help us better understand this in relation to CKD. However, right now, we still need to optimise our screening for CKD, code accurately, and ensure we help people reduce their risks of cardiovascular disease and CKD progression as much as possible using lifestyle changes and the drugs available.

NICE (2021) continues to recommend use of the KFRE and a 5% 5-year threshold as one criterion for consideration of referral, so we should continue to follow this recommendation, even if we use KDpredict to inform our discussions with older people with CKD.

Click here to read the study in full

Gerds TA, Ravani P (2024) Predicting the risks of kidney failure and death in adults with moderate to severe chronic kidney disease. BMJ 385: q721

Kengne AP, George C, Ameh OI (2024) Predicting the outcomes of chronic kidney disease in older adults. *BMJ* **385**: q749

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NICE (2021) Chronic kidney disease: assessment and management [NG203]. Available at: <u>www.nice.org.uk/guidance/ng203</u>