Assessing competing risks of death versus renal replacement therapy in CKD

Kidney Failure Risk Equation (KFRE) score was found to be a statistically significant predictor of death as well as the need for renal replacement therapy (RRT), according to this retrospective primary care cohort study published in the *British Journal of General Practice*. The probability of death increased with each category of 5-year KFRE (<5%, 5–20% and >20%) and was significantly greater than the probability of requiring RRT in each category, apart from in the >20% category in people of Asian and Black ethnicities. Overall, 11% of the cohort had a KFRE 5-year risk >5%, and would thus be recommended for nephrology referral according to NICE NG203. The competing probability of death is not formally captured in KFRE, depriving people of this information when considering need for nephrology referral, and primary care teams may thus want to use the KDPredict calculator, which estimates the risk of both need for RRT and death, alongside the KFRE. This study reminds us that urinary albumin:creatinine ratio is still not being consistently measured even in people with chronic kidney disease, despite being important in informing blood pressure targets, monitoring frequency, drug treatments and overall risk.

Pam Brown
GP in Swansea

Chronic kidney disease (CKD) affects six in 100 adults, and a quarter of people over the age of 65 years, in the UK. It increases the risk of cardiovascular disease and renal disease progression, in some cases requiring renal replacement therapy (RRT): dialysis or renal transplant.

Predicting the individual risk of progression to RRT allows us to target treatment, and the NICE (2021) NG203 guideline on CKD recommends use of the Kidney Failure Risk Equation (KFRE) to predict 5-year RRT risk. The KFRE is calculated using the person's age, sex, estimated glomerular filtration rate (eGFR) and urinary albumin:creatinine ratio (uACR), which should all be available in those with CKD. However, it is estimated that 50% of those with diabetes and 70% of those with high blood pressure in the UK do not have uACR checked annually (Healthcare Quality Improvement Partnership, 2017), meaning the calculator cannot be used.

The KFRE UK calculator site can be used in consultations to demonstrate the impact of management options, such as blood pressure control and use of drugs such as ACE inhibitors, ARBs and SGLT2 inhibitors on 5-year risk of needing RRT. The site includes patient education about the roles of the kidneys; signs and symptoms of CKD; and a warning about avoiding NSAIDs, including those bought over the counter. The KFRE does not, however, take into account the important competing risk of death, which is often more likely than progression to RRT in people with CKD.

The study

In this retrospective primary care cohort study published in the *British Journal of General Practice*, Stewart and colleagues used the Greater Manchester Care Record (GMCR) to evaluate the association between KFRE scores and the probability of death versus need for RRT. Since there are currently no population-level data on the number of people with a KFRE risk >5% (who should be considered for referral to nephrology), the study also sought to quantify this. The GMCR contains de-identified data from 2.85 million people across 433 general practices in Greater Manchester.

Adults with CKD stage 3–5, diagnosed by eGFR, were included; those without any eGFR or uACR results and those already on RRT or

Citation: Brown P (2026) Diabetes Distilled: Assessing competing risks of death versus progression to renal replacement therapy in people with CKD. *Diabetes & Primary Care* **28**: [Early view publication]

Table 1. KFRE 5-year risk category and predicted risk of renal replacement therapy or death.

KFRE category	Associated adjusted outcome – RRT	Associated adjusted outcome – Death	Probability of no event
<5%	0.1%	11.9%	87%
5–20%	2%	23%	75%
>20%	14%	29%	57%

KFRE=Kidney Failure Risk Equation.

with previous renal transplant were excluded, as were those with dementia or a palliative care diagnosis, since their risk of death was likely to be substantially increased compared to that in the population with CKD. Four cohorts were created for analysis:

- CKD stage 3–5 cross-sectional cohort, used to describe the overall CKD population (*n*=109 543).
- CKD stage 3–5 cohort with at least one uACR measurement and, therefore, suitable for a KFRE calculation (*n*=65 801; 60.1% of the total cohort).
- CKD stage 3–5 cohort with no uACR during the study period (*n*=43 742; 39.9% of the total cohort).
- CKD with uACR measurements during 2018 or 2019, used in multinomial regression analyses to measure the relative risk of death and RRT across the three KFRE risk categories over the 5–6-year follow-up period (*n*=30 197; 27.6% of the total cohort).
  - ➤ KFRE scores were categorised as <5%, 5–20% and >20%.

All eGFRs were recalculated using the CKD-EPI equation. Most people in each cohort were living with either overweight or obesity, and the majority were White; 6.6% were of Asian ethnicity, 2.7% Black ethnicity and just under 10% other non-White ethnicities. Deprivation was high. The five most prevalent comorbidities present at start of the study were hypertension (63.5%), diabetes (30.1%), depression (29.8%), coronary heart disease (19.8%) and acute kidney injury (14.7%).

Results

uACR measurement rates varied from year to year, from 27.1% in 2020 to 34.7% in 2023. The proportion with a 5-year KFRE risk >5% also varied from year to year, with an average of 11% over the study period.

Using adjusted probabilities from the multinomial regression model, the associated risks for the three KFRE categories are shown in *Table 1*. KFRE score was a statically significant predictor of both death and the need for RRT. The probability of death increased with each category of KFRE and was significantly greater than the probability of requiring RRT in each category.

Risk of RRT

When those with a KFRE of 5–20% were compared to those with a KFRE <5%, their relative risk of RRT was 21-times greater, and this rose to a 200-times greater relative risk in those with KFRE >20%. People of Asian and Black ethnicities had approximately double the relative risk of RRT compared with those of White ethnicity.

Death

People with a KFRE score of 5–20% had double the relative risk of death compared to those with KFRE score <5%, and this rose to a four-times greater risk in those with KFRE score >20%. Those of Asian and Black ethnicity had a significantly lower risk of death (relative risk 0.66 and 0.30, respectively) compared with those of White ethnicity.

Ethnicity and socioeconomic status

When the impact of ethnicity and socioeconomic status was considered:

- White ethnicity: Probability of death was greater than that of RRT regardless of socioeconomic status. Those of White ethnicity had a greater probability of death in each KFRE category than those of Asian and Black ethnicities.
- Asian and Black ethnicities: Probability of death was greater than that of RRT in the KFRE categories of <5% and 5–20%, but in those with KFRE >20% the probability of RRT was greater than that of death.

- Black ethnicities: In those with >20% KFRE, the difference in probability between RRT and death was greater than for people of Asian ethnicity.

Having diabetes, hypertension, osteoporosis, coronary heart disease, heart failure, stroke, transient ischaemic attack, acute kidney injury, schizophrenia or an eating disorder were all associated with a significantly higher relative risk of death. In contrast, glomerulonephritis and kidney stones were associated with a significantly lower relative risk of death.

The proportion of people with CKD stages 3–5 who had a KFRE score >5%, and hence could be considered for referral to nephrology, across the cohort increased from 9.3% (1657 people) in 2018 to 12.6% (1828 people) in 2023, with an average of 11% across the years of the study. The authors believe this is the first time these rates have been estimated in England.

Discussion

The KFRE is useful in quantifying numbers who may be referred to nephrology, but for primary care, the authors conclude that its failure to account for the competing risk of death is a significant limitation, and that we should consider using other risk prediction tools, such as KDpredict, available at: https://kdpredict.com.

The authors suggest the high competing risk of death in this study is likely to reflect high prevalences of cardiovascular disease, multimorbidity and older age in this primary care cohort. The higher risk of RRT in Black and Asian people may be due to faster progression of CKD, higher rates of diabetic nephropathy and a genetic variant in people of Black ethnicity.

Strengths of this study include the large contemporary primary care database, recalculation of eGFRs using CKD-EPI, and the use of regression analyses adjusted for multiple comorbidities and renal diagnoses. Limitations included high rates of missing uACR data and the fact that the multinomial regression did not include the time to an event, potentially limiting how robust the probabilities are. Additionally, end-stage renal disease was defined by diagnostic codes, which may have excluded those who received only conservative management but who may have had a high risk of death, and data were included from the COVID-19 pandemic, when investigations and management were restricted.

Implications for practice

This paper is a useful reminder that, since uACR was removed from the Quality and Outcomes Framework indicators in 2015, we have not been consistently achieving measurement in primary care, even in people known to have CKD. Knowing the uACR is vital to allow decisions on blood pressure targets, frequency of CKD monitoring, and use of ACE inhibitors, ARBs and, in those with type 2 diabetes, finerenone, for reduction of albuminuria. Knowing the uACR may also prompt the use of SGLT2 inhibitors in people without type 2 diabetes (all those with type 2 diabetes should already be receiving an SGLT2 inhibitor, as per new NICE NG28 guidance), and use of once-weekly semaglutide in those with type 2 diabetes (following results of the FLOW study), to slow CKD progression. Likewise, despite NICE recommending use of the KFRE since 2021, it remains underused.

In this study cohort, uACR measurement had improved slightly year on year, apart from in 2020 during the pandemic. It was only possible to calculate KFRE in around 35% of people even during the year of highest measurement rates. This suggests that some people with CKD will remain undiagnosed if their eGFR is above 60 mL/min/1.73 m^2 and their CKD diagnosis is dependent on a uACR of ≥3 mg/mmol. Across the UK, around 40% of those with CKD stage 3–5 are uncoded and, thus, may be unknown to both primary and secondary care (Stewart et al, 2014).

Since NICE does not take into consideration ethnicity and competing risk of death when encouraging us to refer people with a KFRE of 5% or more, we may currently be over-referring older people with White ethnicity to nephrology, while undertreating their cardiovascular disease and other comorbidities contributing to mortality risk, and not prioritising those who may have a higher risk of RRT and thus would benefit from early renal opinion and support.

Read more

Diabetes Distilled: Predicting risk of kidney failure and mortality – a new tool

KDpredict algorithm accurately estimates risk of renal failure and mortality over 1–5 years.

Diabetes & Primary Care **26**: 67–8

Click here to access

Use of the Kidney Failure Risk Equation: A regional retrospective primary care cohort study in England

Read the article in full (open access)

As discussed in *Diabetes Distilled* previously, some primary care teams are still unaware of KFRE or are not using it consistently, despite its also being a useful educational resource to share with patients. Primary care teams may also want to consider using KDpredict, which allows calculation of the risk of both RRT and death over a 5-year timespan, alongside KFRE, to inform shared decision-making about referral and to understand the importance of proactive care for comorbidities. ■

Healthcare Quality Improvement Partnership (2017). *National Chronic Kidney Disease Audit – National Report (Part 1)*. HQIP, London

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

Stewart S, Kalra PA, Blakeman T et al (2024) Chronic kidney disease: Detect, diagnose, disclose – a UK primary care perspective of barriers and enablers to effective kidney care. *BMC Med* **22**: 331

Stewart S, Kalra PA, Kontopantelis E et al (2026) Use of the Kidney Failure Risk Equation: A regional retrospective primary care cohort study in England. *Br J Gen Pract* **76**: e356–65

Practice points

1. Measurement of eGFR and uACR are both vital in all those groups recommended by NICE to identify people with CKD.
2. NICE recommends using the Kidney Failure Risk Equation (KFRE) to assess the risk of needing renal replacement therapy in people with CKD, and referring those with a 5-year risk of ≥5% to nephrology.
3. However, the KFRE does not account for ethnicity or competing risk of death, and thus may lead to over-referral to nephrology and undertreatment of cardiovascular disease and other comorbidities contributing to mortality risk.
4. Primary care teams may want to consider using KDpredict, which allows calculation of the risk of both renal replacement therapy and death over a 5-year timespan, alongside the KFRE.