BMJ Open

Use of the kidney failure risk equation to inform clinical care of patients with chronic kidney disease: a mixed-methods systematic review

Harjeet Kaur Bhachu,[1,2,3] Anthony Fenton ,[1,2] Paul Cockwell,[1,4] Olalekan Aiyegbusi,[2,3,5,6] Derek Kyte ,[2,3,7] Melanie Calvert [2,3,5,6]

To cite: Bhachu HK, Fenton A, Cockwell P, *et al*. Use of the kidney failure risk equation to inform clinical care of patients with chronic kidney disease: a mixed-methods systematic review. *BMJ Open* 2022;**12**:e055572. doi:10.1136/bmjopen-2021-055572

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2021-055572).

Received 23 August 2021
Accepted 17 December 2021

For numbered affiliations see end of article.

Correspondence to
Dr Anthony Fenton;
a.fenton@bham.ac.uk

ABSTRACT

Rationale and objective The Kidney Failure Risk Equation (KFRE) predicts the risk of end-stage kidney disease in patients with chronic kidney disease (CKD). This study aimed to evaluate the impact of the utility of KFRE in clinical practice.

Study design Systematic review.

Setting and study populations Adult patients with CKD but not receiving renal replacement therapy enrolled in studies where KFRE was used in clinical care pathways.

Selection criteria for studies All studies published from April 2011 to October 2021 identified from Medline, Cumulative Index to Nursing and Allied Health Literature, Embase and reference and citation searches of included studies.

Data extraction Relevant data were extracted, and two reviewers independently assessed study quality using appropriate appraisal tools.

Analytical approach Findings reported as a narrative synthesis due to heterogeneity of the included studies.

Results Of 1635 studies identified, 440 duplicates were removed. The remaining 1195 titles and abstracts were screened. All five studies for full-text review were included in the analysis. Three uses of KFRE were assessed: (1) primary to specialty care interface; (2) general nephrology to multidisciplinary care transition; and (3) treatment planning. Evidence of impact on number of patient referrals into nephrology care was conflicting. However, wait times improved in one study. Although KFRE identified high-risk patients for increased multidisciplinary support, there was concern patients stepped down, no longer meeting eligibility criteria, may lack access to services.

Conclusions This is the first systematic review of studies that have assessed the actual impact of KFRE in clinical practice with five studies of varying quality reported to date. Trials are in progress assessing the impact on clinical outcomes of using KFRE in clinical practice, and KFRE is being incorporated into guidelines for CKD management. Further studies are needed to assess the impact of KFRE on clinical care.

Trial registration number Protocol registered on PROSPERO before initiation of the study (Ref: CRD42020219926).

Strengths and limitations of this study

- ► To the best of our knowledge, this is the first systematic review to examine the evidence for the impact of the use of the Kidney Failure Risk Equation in clinical practice.
- ► A mixed-methods approach was used to allow the inclusion of both quantitative and qualitative evidence.
- ► Study quality ranged widely, and some studies did not provide adequate detail of their population characteristics, such that generalisability was difficult to assess.
- ► Furthermore, the statistical analysis was limited in several studies.

BACKGROUND

The global prevalence of chronic kidney disease (CKD) is estimated to be 9.1%, and CKD was the 12th leading cause of death in 2017.[1] CKD is also associated with an increased risk of progression to end-stage kidney disease (ESKD). Risk stratification in CKD can enable more efficient care, with specialty care targeted to patients at higher risk of ESKD, while sparing those with low risk unnecessary intervention and undue anxiety associated with this.[2 3]

Most guideline criteria for referral of patients to specialist nephrology care use estimated glomerular filtration rate (eGFR), eGFR decline and urine albumin:creatinine ratio (ACR) thresholds rather than a quantified ESKD risk.[4] Such criteria often result in the referral of patients at low risk of ESKD and the non-referral of patients at high risk.[5] Therefore, recent CKD guidelines endorse risk-based thresholds for specialty referral and renal replacement therapy (RRT) planning.[6 7]

The best validated risk prediction model is the Kidney Failure Risk Equation (KFRE),

which predicts the 2-year and 5-year risk of ESKD in patients with stages 3–5 CKD and has undergone extensive validation.[8–10] The equation can easily be embedded into electronic medical records and is also readily available online.[11]

It is uncertain whether the use of the KFRE in clinical practice has a meaningful impact on clinical pathways and health outcomes and how patients and healthcare professionals view the KFRE. We carried out a systematic review of the available evidence of the impact of the use of the KFRE in clinical practice.

METHODS

The study protocol was registered on PROSPERO (Ref: CRD42020219926), and the study is reported as per the 'Preferred Reporting Items for Systematic Review and Meta-Analysis' (PRISMA) checklist.[12]

Data sources and searches

Two reviewers (HKB and AF) independently searched MEDLINE (Ovid), Cumulative Index to Nursing and Allied Health Literature (EBSCO) and Embase (Ovid) for studies between April 2011 to October 2021 that examined the impact of utilising the KFRE in patients with CKD.

The search strategies (online supplemental table S1) were developed with the support of an information specialist and used keywords, index terms and Medical Subject Headings terms tailored and applied to each individual database. No language restrictions were applied. We also hand searched the reference lists of included studies and performed a forward citation review of these studies and the original KFRE development study.[13] All results obtained at each stage of the process were entered into EndNote V.X9.3.3 (Clarivate Analytics, Pennsylvania, USA), and duplicates were removed. Any disagreements regarding study inclusion were resolved by discussion or decided by a third reviewer (PC) where necessary.

Study selection and eligibility criteria

Studies were included if they:

1. Were published from April 2011 (the date of the initial KFRE paper publication) to October 2021.
2. Studied adults with CKD but not receiving renal replacement therapy (dialysis or kidney transplantation).
3. Used the KFRE to estimate the risk of ESKD.
4. Evaluated the actual rather than potential impact of using the KFRE in clinical practice.

Studies were excluded if they were development or validation studies only, narrative reviews, editorials, commentaries or opinions, or letters.

The two reviewers (HKB and AF) independently screened the titles and abstracts against the eligibility criteria. Potentially relevant studies were identified, and final inclusion was based on full-text examination. Reasons for exclusion following full-text review were documented.

Data extraction and quality assessment

The following key data were extracted: (1) study details (author, year of publication, title and location of study), (2) study type, (3) aim, (4) study population characteristics, (5) method, (6) results, (7) key findings, (8) strengths and limitations and (9) author conclusions.

Methodological validity was assessed independently by the two reviewers (HKB and AF) using the Critical Appraisal Skills Programme appraisal tools,[14] Joanna Briggs Institute Critical Appraisal Tools[15] and Centre for Evidence-Based Management Critical Appraisal of a Survey.[16]

Data synthesis and analysis

Due to different study methods and the heterogeneity of study characteristics, individual analysis for quantitative studies and qualitative studies was not conducted. Findings were reported as a narrative synthesis adopting the methods presented by Popay *et al*[17]: (1) theoretical reason for basis of evaluated intervention, that is, using the KFRE, (2) descriptive summary of study characteristics and critical appraisal, (3) exploration of associations within and between studies and (4) assessing the strength of evidence and limitations of the synthesis process.

Patient and public involvement

There was no patient and public involvement in the conduct of this systematic review.

RESULTS

The database search identified 1099 studies, and a further 536 studies were identified from the forward citation search of the KFRE development study.[13] Four hundred and forty duplicates were removed, resulting in 1195 studies taken forward for the title and abstract screening. Five studies fulfilled the criteria for full-text review. No additional studies were identified from reference review and forward citation review of the selected studies. Results of the search are presented in the (PRISMA) flow diagram[12] (figure 1).

Study characteristics

Table 1 presents the details of the included studies. Three studies took place in Canada,[3 18 19] one in Australia[20] and one in the USA.[21] Four studies were quantitative, and one study used a mixed-methods approach, whereby the strengths of both qualitative (interviews) and quantitative (surveys) research elements were combined to gain a broader view of their experience applying the KFRE.[3] The KFRE was used at three transition points: (1) the primary to specialty care interface,[18 20] (2) general nephrology to multidisciplinary care or advanced care kidney clinics[3 19] and (3) to guide treatment planning in a private healthcare setting,[21] including referrals to primary or nephrology care, medication changes and laboratory recommendations. No study stated the baseline risk used (North American or non-North American). Only two

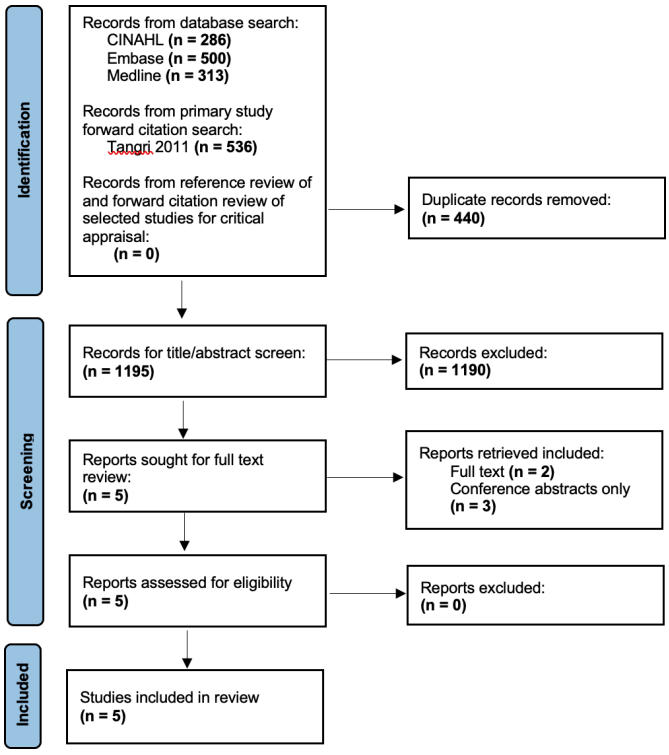

Figure 1 Flow diagram to show the studies identified from searches.

studies stated which version of the KFRE was used, but all studies stated if they calculated 2-year or 5-year ESKD risk.

Hingwala *et al*[18] applied a quasiexperimental (pre–post) study design to patients referred to three renal centres in the Manitoba Renal Program, Manitoba, Canada. Wait times (between referral and nephrology visit) and number of consults were compared from the periods preimplementation and postimplementation of the new triage criteria: significant criteria or 4-variable KFRE 5-year risk >3%. Patients with a 3%–10% risk were booked as non-urgent (<6 months) and those with a >10% risk were booked as urgent (<4 weeks).

A similar pre–post study design was used in the study by Hong *et al*,[20] where they implemented new criteria, using a 5-year KFRE score of >3%, for patients referred to the St George Hospital Renal Department (New South Wales, Canada). Patients referred with a <3% risk were accepted at the discretion of a nephrology consultant. The number of consults pretriage and post-triage periods were compared.

The KFRE was applied within a secondary care setting in two studies. Smekal *et al*[3] used a mixed-methods approach to gauge the views of patients and providers 1 year after implementing the KFRE in 2017 to guide transition into the CKD multidisciplinary clinic. Criteria for transition were KFRE 2-year risk ≥10% or eGFR ≤15 mL/min/1.73 m^2. Postimplementation interviews took place with nine patients discharged from the CKD multidisciplinary clinic, the relative of one patient discharged from the clinic and 17 multidisciplinary CKD healthcare providers. Preimplementation and postimplementation of the new criteria, all patients from the CKD multidisciplinary and general nephrology clinics were invited to complete a paper-based experience survey, and all multidisciplinary CKD healthcare providers were asked to complete an online job satisfaction survey.

Che *et al*[19] retrospectively compared the outcomes of 643 patients from the Multi-Care-Kidney-Clinic, for patients with advanced CKD, before and after the revision of the clinic eligibility criteria, in Ontario, Canada. The new criteria applied included eGFR <15 mL/min/1.73 m^2 and KFRE 2-year risk >10%. If eligibility criteria were not met, patients were discharged from the clinic.

Lastly, Sendek *et al*[21] applied the 4-variable KFRE (2-year risk >15%) to the population in Duke Connected Care, a Medicare Shared Savings Program that manages the healthcare of over 46 000 Medicare patients. Patients alive and with no evidence of ESKD, a prior nephrology visit or acute kidney injury without chronic dysfunction were referred for 'population health rounding' where their electronic health record was reviewed weekly with a multidisciplinary team to decide on changes in management. Number of patients rounded each month, time per case and any actions taken were recorded.

Results are shown in table 2, along with key findings from the critical appraisal. The three themes identified are described further.

Primary care to specialty care interface

Two studies[18 20] reported outcomes following the introduction of a new referral process incorporating a 5-year ESKD risk threshold of >3% to triage patients from primary care to specialty care, although they also incorporated additional referral criteria for eligibility for specialty care review. Both studies measured the number of consults preimplementation and postimplementation of the KFRE: Hingwala *et al* found monthly referrals increased by 45%,[18] whereas Hong *et al* found referrals decreased by 25%–30%.[20]

Hingwala *et al* also showed a significant reduction in the wait-time from referral to review (median 58 vs 230 days) following implementation of the new triage system.[18]

General nephrology to multidisciplinary/advanced kidney care clinic

Patients under nephrology care may be managed in a general nephrology clinic or, for patients with more advanced CKD, a multidisciplinary clinic focused on managing CKD complications and RRT preparation. Two studies examined the use of the KFRE at this interface and introduced similar eligibility criteria for entry into and management in the multidisciplinary clinic: a 2-year ESKD risk >10% or eGFR <15 mL/min/1.73 m^2 (formula used for calculating eGFR not specified in the studies).

Che *et al*[19] found that by applying these criteria to all prevalent patients in the multidisciplinary clinic, 73% remained in the clinic, 5% were stepped down to general nephrology care and 22% were discharged to primary care. Of the latter, 11% required rereferral to nephrology,

Table 1 Characteristics of included studies

Study	Healthcare setting, country	Study design	Population, N	KFRE details	Inclusion/exclusion criteria	Intervention	Control	End-points	Follow-up
Hingwala *et al*[18]*	Primary to nephrology care, Manitoba, Canada	Quasiexperimental	Patients referred to three renal centres in the Manitoba Renal Program, n/a	4-variable KFRE for 5-year risk	12-month period immediately following implementation of triage was observed as a transition period to the new triage system and was excluded from the final analysis. No triage unless all four variables available or other indication provided.	Referral if significant criteria OR KFRE 5-year risk >3%. If no criteria met, then back to referrer with 'low risk letter'. If risk 3%–10% book as non-urgent (<6 months). If risk >10% book as urgent (<4 weeks).	Pretriage: no set criteria. Referrals triaged as urgent, non-urgent or 'do not book' by an individual rotating nephrologist.	Compared between pretriage and post-triage periods: 1. Wait time between referral and nephrology visit (days). 2. Number of consults.	Pretriage 1 January 2011 to 31 December 2011. Post-triage 1 January 2013 to 31 December 2013
Hong *et al*[20]†	Primary to nephrology care, New South Wales, Australia	Pre–post	Patients referred to St George Hospital Renal Department, n/a	KFRE for 5-year risk, unclear on number of variables	n/a	In January 2019 triage consultant and risk-based triage introduced. Referral if KFRE 5-year risk >3%. If <3% risk, referral on consultant discretion.	Pretriage periods in 2018 and 2017.	Number of consults between pretriage and post- triage periods.	2017–2019
Smekal *et al*[9] *	Multidisciplinary to general nephrology care, Alberta, Canada	Mixed-methods	Interviews, 27: Southern Alberta Renal Program, nine patients and one family member; multidisciplinary CKD healthcare providers in Calgary, Alberta: 17. Survey in Calgary, Alberta: patients from CKD clinics: 413; CKD healthcare providers: 73.	KFRE for 2-year risk, unclear on number of variables	Interviews: patients age >18 years with non-dialysis CKD, discharged from multidisciplinary to general nephrology care and multidisciplinary CKD healthcare providers (nephrologists, nurses and allied health professionals). Survey: all patients from CKD multidisciplinary and general nephrology clinics and all multidisciplinary CKD healthcare providers.	Transition to CKD multidisciplinary clinic when KFRE 2-year risk ≥10% or eGFR ≤15 mL/min/1.73 m^2 implemented in 2017. Interviews postimplementation. Surveys postimplementation: patient: paper-based care experience survey and provider: online job satisfaction survey.	Surveys preimplementation: patient: paper-based care experience survey and provider: online job satisfaction survey.	Interview data collection stopped once data saturation reached. Survey responses returned within time period.	Survey distributed to patients November 2016–January 2017 (preimplementation) and January 2018–March 2018 (postimplementation). Survey responses from providers November 2016–January 2017 (preimplementation) and April 2018 (postimplementation).
Che *et al*[19]†	Discharges from multidisciplinary care, Ontario, Canada	Retrospective cohort	Prevalent CKD patients in MCKC in 2013 with available data: 643.	4-variable KFRE for 2-year and 5-year risk	Included CKD patients from MCKC with available data.	Revised eligibility criteria between 2016 and 2018 from eGFR <30 mL/min/1.73 m^2 to eGFR <15 mL/min/1.73 m^2 and KFRE 2-year risk >10%. If not eligible, then discharged from MCKC.	n/a	Number discharged from MCKC, rereferred, commenced RRT and died.	2013–January 2020

Continued

Table 1 Continued

Study	Healthcare setting, country	Study design	Population, N	KFRE details	Inclusion/exclusion criteria	Intervention	Control	End-points	Follow-up
Sendak *et al*[21]†	Private care, North Carolina, USA	Prospective cohort	Duke Connected Care a MSSP 413.	KFRE for 2-year risk, unclear on number of variables	Patients alive and without evidence of ESKD. Excluded if had past nephrology visit and those with AKI without chronic dysfunction.	Patients with a KFRE 2-year risk >15% referred for 'population health rounding' – in-depth EHR weekly review with MDT to decide on changes in management	n/a	Number of patients rounded per month, time per case during rounds, % of patient at rounds that have action taken, incidence of ESKD, RRT modality, number of dialysis crash-starts.	June 2015 for 5 months

*Full text.
†Conference abstract.
AKI, acute kidney injury; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; EHR, electronic health record; ESKD, end-stage kidney disease; KFRE, Kidney Failure Risk Equation; MCKC, Multi-Care-Kidney-Clinic; MDT, multidisciplinary team; MSSP, Medicare Shared Savings ProgramProgramme; N, number; n/a, not available; RRT, renal replacement therapy.

and 6% ultimately required RRT, although the majority in the context of an unforeseen acute illness.

Smekal *et al*[3] evaluated patient and healthcare providers' views and experiences following the implementation of the new KFRE-based criteria for multidisciplinary clinic management. Providers felt using KFRE to target high-risk patients was a key strength, limiting inappropriate referrals and improving the clinic's focus. The caseload was felt to be more 'acute' but overall workload not significantly changed, and there was no significant difference in job satisfaction. Providers also expressed concern that there may be inadequate access to and a lower quality of care for low-risk patients discharged from the multidisciplinary clinic, such as with education and monitoring. Some nurses reported discharged patients were contacting them for test results, and patients reported missing this aspect of their care. Although there was some improvement in patients' experience of access to care, caring staff and safety of care, most patients were satisfied with their care both preimplementation and postimplementation, and there was no difference in patients' overall care experience.

Treatment planning

The study by Sendak *et al*[21] took place in an 'Accountable Care Organisation' within the Medicare Shared Savings Program (Medicare is a health insurance programme mainly for people aged ≥65 years in the USA). A 2-year ESKD risk threshold of >15% was applied to the cohort to identify high-risk CKD patients, not already under nephrology review, for a multidisciplinary review of their electronic healthcare record (EHR). The reviews were able to be performed relatively rapidly (average 2 min 12 s) and led to changes in management in 21.8% of cases, most often a referral for nephrology review.

Critical appraisal

All 5 studies were limited to a single centre or region. No randomised control trials were identified. Two were cohort studies[19 21], one was a mixed-method study[3] and two were quasiexperiment studies.[18 20] All studies stated a clear aim or issue to be addressed. Sample size varied depending on the study method, and two studies did not state it.[18 20] Participant baseline characteristics data were not available in two studies[19 20] and lacking in one study[18] where preintervention information was not available. For the qualitative aspect of the mixed-methods study,[3] the patients selected were English-speaking only. Although this may have allowed for simpler data analysis as there was no requirement for language translation, this selection bias may limit the perspectives obtained of those experiencing the intervention. In this same study, the survey response rate for patients was unclear, and for providers, no data were provided to establish any difference in demographics to non-responders. Although mostly proportions were reported in the data analysis of quantitative studies, there was a lack of reporting of statistical significance, strength of any associations or measures

Table 2 Results and critical appraisal of included studies

Study	Baseline characteristics: Age (years)	Sex (male (%))	eGFR (mL/min/1.73 m^2)	Urine ACR	Results	Key findings	Strengths	Limitations	Additional points from critical appraisal
Hingwala *et al* (2017)*	Pretriage: not presented. Post-triage: 68 (median).	Pretriage: not presented. Post-triage: 50.3.	Pretriage: not presented. Post-triage: 39 (median).	Pretriage: not presented. Post-triage: 9.2 (median).	Pretriage: ▶ Referrals booked for appointment: not presented. ▶ Median monthly referrals: 68/month (range 44–76). ▶ Median wait time: 230 days (range: 126–355). Post-triage: ▶ Referrals booked for appointment: 66%. ▶ Median monthly referrals: 94 /month (range 61–147). ▶ Median wait time 58 days (range: 48–69).	Monthly referral increase of 45%. Median wait times improved (p<0.001).	Low-cost triage system. Triage process allows for clinical judgement, such that 'low-risk' patients according to KFRE are identified for nephrology review where necessary.	Lack of data presented for pretriage period (eg, baseline characteristics and number of booking) to allow for detailed historical comparison (pre-riage). No clinical or economic impact assessment of implementing KFRE triage system. No long-term follow-up on patients triaged as low risk. May not be applicable to teams operating under capacity without wait lists.	Washout period for 1 year when implementing criteria. Additional capacity to see referrals (additional nephrologist hired in September 2013, physician-assistant led clinic from Sept 2012). 'Hawthorne effect'. Three centres. No financial support. Authors declared no competing interests.
Hong *et al* (2020)*	Not presented	Not presented	Not presented	Not presented	Compared with 2018 when KFRE-based triage implemented: ▶ 25% fewer consults in 2019 (30% less than in 2017). ▶ Fewer patients had a low-risk KFRE at triage (46% vs 48%). ▶ Fewer low-risk patients had clinic follow-up (50% vs 52%). More low-risk patients remaining in clinic (86% vs 60%) had alternative reasons for follow-up (ie, eGFR < 30 mL/min, moderate proteinuria, or uncontrolled hypertension).	Implementing the KFRE-based triage system reduced overall and low-risk patient numbers in outpatient clinics.	Triage system allowed for consultant discretion for low-risk patients to be followed up	No baseline characteristics presented for patients either preimplementation or postimplementation of the KFRE-based triage process. Low-risk patients with eGFR <30 or moderate proteinuria still followed up. Inability to calculate KFRE score for referrals at triage (28% in 2018, 36% in 2019) due to missing urine ACR.	Limited data therefore unable to compare if pretriage versus post-triage groups were similar. Single centre. Unclear if results are 'significant'. No comment on what was done for patients with missing ACR.

Continued

Table 2 Continued

Study	Baseline characteristics: Age (years)	Baseline characteristics: Sex (male (%))	Baseline characteristics: eGFR (mL/min/1.73 m^2)	Baseline characteristics: Urine ACR	Results	Key findings	Strengths	Limitations	Additional points from critical appraisal
Smekal *et al* (2019)†‡	Pre-KFRE implementation: Patients: survey 10%<50; 28% 50–64; 22% 65–74; 39% ≥75. Healthcare providers: not presented. Post-KFRE implementation: Patients: ▶ interviews 10% 50–64; 30% 65–74; 60%≥75. ▶ survey 17%<50; 19% 50–64; 27% 65–74; 38%≥75. Healthcare providers: not presented.	Pre-KFRE implementation: ▶ Patients (survey): 60. ▶ Healthcare providers (survey): 28. Post-KFRE implementation: Patients: ▶ Interviews: 50. ▶ Survey: 57. Healthcare providers ▶ Interviews: 29 ▶ Survey: 27.	Not presented	Not presented	Interviews: ▶ 9/23 (39%) patients and 17/75 (23%) providers interviewed. ▶ Five themes were identified among patients and providers and two additional categories identified among providers only. Questionnaire: ▶ Majority of patients satisfied with their care in both periods with no overall differences. However, there were improvements in patients' experience of access to care, caring staff and safety of care. ▶ Of the 75 providers, 40 (53%) and 33 (44%) completed the preimplementation and postimplementation job satisfaction survey, respectively; no differences in providers' job satisfaction.	Patients and healthcare providers reported ▶ Improved the focus of MDT clinics by targeting high-risk patients. ▶ Using KFRE to target care to high-risk patients was a key strength. Enhanced the sustainability of the clinics. Providers expressed concern that there may be inadequate access to and lower quality of care for low-risk patients discharged from multidisciplinary care, although patients did not experience this. No difference in patients' care experience. No difference in healthcare provider job satisfaction.	Includes both patient and provider perspectives. Presents both qualitative and quantitative data.	More healthcare providers than patients in qualitative component; data saturation was achieved in both groups. Most patients interviewed had >5 years in MDT care prior to discharge so may not be representative of general nephrology patients. Patients discharged from MDT clinics within previous 12 months so limited time period following implementation of risk approach. Unable to pair presurvey and post-survey responses or establish response rate. Single centre.	Limited to English-speaking participants. Low response rate. Detailed information on data collection and analysis, questions provided. Mostly female providers. Funder had no role in the project. Authors declared no competing interests.

Continued

Table 2 Continued

Study	Baseline characteristics: Age (years)	Sex (male (%))	eGFR (mL/min/1.73 m^2)	Urine ACR	Results	Key findings	Strengths	Limitations	Additional points from critical appraisal
Che *et al* (2020)§	Not presented	Not presented	<30	Not presented	470 (73%) continued follow-up in MCKC. Of 142 (22%) discharged to primary care: ▶ 52 (37%) died. ▶ 15 (11%) rereferred to nephrology (at median 982 (IQR 560) days). ▶ 8 (6%) initiated RRT (at median 850 (1411)) days; 5 (63%) for unforeseen acute illness). 31 (5%) discharged to general nephrology.	Discharge of a significant number of patients when moving to new criteria, few of whom ultimately required RRT that could have been prevented.	'Low loss to follow-up'.	Completeness of data and follow-up unclear. May not be generalisable as based on one regional renal programme.	Unclear reason for chosen threshold or if this is the ideal level. Limited data. No comparison or control group. No detail on missing data.
Sendak *et al* (2016)§	Not presented	Not presented	Not presented	Not presented	Of 335 patients of 413 eligible: 73 (21.8 %) management changes: ▶ 53 (72.6%) to nephrology. ▶ 8 (11.0%) to primary care. ▶ 7 (9.6%) lab recommendations. ▶ 4 (5.5%) medication recommendations. Average time-per-case per health round 2 min 12 s. Of the remaining 262 (78.2%) patient screening did, however, identify: ▶ 110 (42.0%) seeing a nephrologist. ▶ 35 (13.3%) recently deceased. ▶ 25 (9.5%) on dialysis.	Patients with CKD at high risk of progression to ESKD can be identified using validated algorithms applied to structured data that is readily available. A significant proportion of patients identified in this way require management changes, including patients that require nephrology review. Limited ability to screen out patients using structured data. Health rounds can be performed relatively rapidly.	KFRE easily applicable. Highlights additional patients for review in primary/specialty care.	No data on long-term outcomes. Data from one renal programme, therefore, may not be generalisable.	Elderly patients. Later months more efficient as workflow optimised – not taken into consideration for time per case. Private healthcare setting so not generalisable.

Appraisal tool used for the studies:
*Joanna Briggs Institute Quasiexperimental study checklist.
†CASP Cohort Study Checklist.
‡CASP Qualitative Studies Checklist (interviews).
§Centre for evidence-based management critical appraisal of a survey.
ACR, albumin:creatinine ratio; CASP, Critical Appraisal Skills Programme; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; KFRE, Kidney Failure Risk Equation; MCKC, Multi-Care-Kidney-Clinic; MDT, multidisciplinary team; RRT, renal replacement therapy.

Table 3 Randomised control trials currently in progress

Study	Healthcare setting, country	Study design	Population, N	KFRE details	Inclusion/exclusion criteria	Intervention	Control	End-points	Follow-up
Jhamb *et al* (2019) – The Kidney CHAMP Study[29]	Primary care, Pittsburgh, USA	Cluster RCT	1650 high-risk CKD patients	Not presented	Patients with high-risk CKD (as defined by validated risk prediction models or by current eGFR value or recent decline in eGFR values). Inclusion: age 18–85 years, eGFR <60 mL/min/1.73 m^2. Exclusion: history of renal transplant, on maintenance dialysis, recent (within 12 months) outpatient nephrology visit, baseline eGFR less than 15 mL/min/1.73 m^2, expected survival <6 months, active substance dependence or severe/uncontrolled psychiatric condition.	EHR-based PHM intervention: nephrologist-led E-consults, pharmacist-led medication reviews and nurse-led CKD education.	Usual care	Primary outcome is a composite of 40% reduction in eGFR or ESKD. Secondary outcomes: improved hypertension control, use of RAASi and avoidance of renally contraindicated medications.	42 months
Harasemiw *et al* (2019)[30]	32 primary care clinics, Manitoba and Alberta, Canada	Multicentre cluster RCT	Estimate each clinic to have 185 patients with CKD	Not presented	Inclusion: aged 18 years and older with CKD G3-G5 attending the participating clinics	Active knowledge translation intervention: addition of KFRE and decision aids to clinics' Data Presentation Tool, patient-facing visual aids, a medical detailing visit and sentinel feedback reports.	Usual care: exposed to current guidelines for CKD management, without active dissemination.	Primary outcomes: proportion of patients with measured urine ACR, and proportion of patients appropriately treated with ACEi or ARB. Secondary outcomes: the optimal management of diabetes, hypertension and cardiovascular risk; prescriptions of NSAIDs; and decline in eGFR. Substudy: measure patients' CKD-specific health literacy and trust in physician care via surveys administered in the clinic postvisit; measure provider satisfaction with the risk prediction tools; at the health system level, outcomes including cost of CKD care, and appropriate referrals for patients at high risk of kidney failure.	Primary and secondary outcomes reviewed at 1 year after the intervention implementation. Exception for decline in eGFR, which will be measured 2 years postintervention.

Continued

Table 3 Continued

Study	Healthcare setting, country	Study design	Population, N	KFRE details	Inclusion/exclusion criteria	Intervention	Control	End-points	Follow-up
Green *et al* (2018) – PREPARE NOW Study[31]	Nephrology care, Geisinger Health System kidney specialty clinics, Pennsylvania, USA	Cluster RCT	1572 participants	8-variable KFRE 2-year risk score	Inclusion: patients currently receiving care at Geisinger nephrology practices, aged 18 years and older with advanced kidney disease determined by eGFR or presence of albuminuria.	Implement new electronic health information tools (disease registry and risk prediction tools) to help providers recognise patents in need of Kidney Transitions Care. Implement a Kidney Transitions Specialist who will provide and facilitate integrated delivery of patient support programmes.	Usual care	Primary outcomes: change in % patients feeling in control of their decision making, change in number of hospitalisations and change in % patients with advance directives for kidney care. Secondary outcomes: change in % self-care patients with biomedical care plans, change in % patients with values aligned care, change in % patients with preferences for renal replacement therapy documented, change in % patients with emergency dialysis initiation, change in months to kidney failure and change in % patients with vascular access (eg, fistula) in place at dialysis initiation.	36 months
Hemmelgarn *et al* (2018)[33]	Nephrology multidisciplinary CKD clinics, Alberta, Canada	Pre/post cohort	Not presented	Not presented	Inclusion: adults aged 18 years and older with sustained eGFR <30 mL/min/1.73 m^2, who are followed by a nephrologist. Exclusion: patients receiving dialysis or with a kidney transplant prior to the study period.	Transition to CKD multidisciplinary clinic when KFRE 2-year risk ≥10% or eGFR ≤15 mL/min/1.73 m^2.	Pretriage period	Clinical outcomes (hospitalisation and emergency department visits and death), use of modalities that improve patient experience and outcomes (home dialysis and kidney transplantation), resource use (physician visits and laboratory tests), process-based quality indicators for appropriate CKD care (assessment of albuminuria, use of ACE-I/ARBs in those with albuminuria, and statins), costs and proportion of patients risk stratified and appropriately managed.	Cohort accrual for the preperiod from April 2015 to April 2016. Postperiod, cohort accrual from April 2017 to April 2018, with follow-up to April 2019.

ACEi, ACE inhibitor; ACR, albumin:creatinine ratio; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; EHR, electronic health record; ESKD, end-stage kidney disease; KFRE, Kidney Failure Risk Equation; NSAID, non-steroidal anti-inflammatory drugs; PHM, population health management; RAASi, renin–angiotensin–aldosterone system inhibitors; RCT, randomised control trial.

of precision in most. Three studies[19–21] reported only proportions when applying the intervention. These three studies had not commented on the number of patients, if any, who could not be assessed for risk due to missing data or whether there were any confounding factors.

DISCUSSION

In this systematic review, we identified five studies of varying methodologies evaluating the actual impact of utilising the KFRE in clinical practice for patients with CKD. The equation was used in three main areas: (1) triaging patients between primary and specialty nephrology care, (2) directing patients between general nephrology and multidisciplinary advanced CKD care clinics; and (3) treatment planning where high-risk patients within a healthcare programme were identified for a multidisciplinary EHR review.

Interpretation of the results in the context of other evidence

The findings of previous studies exploring the potential impact of applying the KFRE at the primary care speciality care interface suggest referral numbers could potentialy increase depending on the threshold criteria set.[5 22 23] This is consistent with the findings of Hingwala *et al*,[18] who reported an increase in referrals. However, wait times improved, possibly related to additional capacity to see referrals and a 'Hawthorne effect' (better performance as a result of healthcare professionals' awareness of being observed in a study).[24] In contrast, Hong *et al*,[20] who implemented the same risk threshold, reported a fall in referrals. These contrasting findings likely reflect differences in local practice and case-mix, whereby a higher proportion of low-risk patients (ie, older, higher eGFRs, lower urine ACRs) were managed by nephrology rather than by primary care before implementation of the KFRE criteria, compared with the centre reported by Hingwala *et al*. We were unable to review any population differences pretriage and post-triage or between studies due to a lack of reported data.[18 20]

In specialist nephrology care, many centres have advanced kidney care clinics for those patients who require increased multidisciplinary support to manage CKD complications and prepare for RRT.[25 26] The KFRE has the potential to identify patients at higher risk of ESKD to more efficiently direct increased support and resources for this group. Those identified as low risk can be stepped down, reducing clinic burden and unnecessary interventions. Two studies evaluated this part of the CKD pathway and applied similar eligibility criteria for multidisciplinary clinic management. Che *et al*[19] found many patients could be discharged from the multidisciplinary clinic, the majority back to primary care, with only a small number referred back to nephrology care or ultimately requiring RRT.

The findings of Smekal *et al*[3] suggest some anxiety regarding reduced access to services, education and monitoring when patients are discharged from the multidisciplinary clinic to general nephrology care based on their KFRE-calculated risk. Maintaining patient and provider satisfaction with CKD care when using the KFRE to discharge patients is an important issue that will require the considered configuration of local renal service delivery to ensure accessibility and patient safety. It remains unknown if the application of the KFRE to identify higher risk patients for multidisciplinary care impacts key outcomes such as progression of CKD, commencing RRT, cardiovascular events or mortality.

Sendak *et al*[21] reviewed the impact of using KFRE in a private healthcare setting in a primarily elderly population to identify patients who required input from medical teams (in primary or specialist care), treatment changes or additional lab testing. The results of this study may not be easily generalisable as this is not a widely used provider model in some countries.

Other suggested areas of use have been for planning RRT in an elderly population where competing risk of death is of concern[27] and for creation of vascular access,[28] but no studies have implemented and evaluated this.

Limitations of the evidence included in the review and the review process

The studies varied widely in methodologies used. The benefit of this mixed-methods review is a greater breadth of understanding and evidence around the application of the risk-based KFRE in clinical practice. This can provide a more rounded body of evidence to inform changes in clinical practice and policy decision making. No randomised control trials were identified.

Study quality also ranged widely. Some studies did not provide adequate detail of their population characteristics. As a result, it was difficult to assess if the population was representative or findings could be generalised. Recognising differences between study populations was also limited by the lack of data. Few studies adequately completed statistical analysis and so it was challenging to decipher significant findings. Authors of the identified studies were not approached for additional information, and we recognise this as a limitation.

Implication of the results for practice, policy and future research

While this study has identified the ease of use of the KFRE to triage patients and highlight those who would benefit from changes in management, plus the potential effect on the number of referrals and patients' and providers' experience and perspectives, the impact on health outcomes and economic benefit are still unknown.

More high-quality studies are needed to confidently support the widespread use of KFRE, particularly randomised control trials with a focus on health outcomes and economic impact. Four trials that are in currently progress will assess the outcomes of applying the KFRE (table 3). The Kidney CHAMP study,[29] a cluster randomised controlled trial in Pittsburgh, USA, will review the effectiveness of integrating the KFRE

into EHR to identify patients at high risk of progression who require intervention such as nephrology guidance, medication reviews and targeted CKD education. Outcomes assessed will be a composite of a 40% reduction in eGFR and ESKD. A multicentre cluster randomised control trial in Canada[30] aims to review the risk-based approach in the primary care setting. The intervention, providing patients and providers in primary care with a patient's KFRE score and the risk-based referral criteria, will be reviewed to assess if it improves appropriate patient management, improves a patient's CKD-specific health literacy and affects the cost of care compared with usual care. The PREPARE NOW study,[31] a cluster randomised control trial within a nephrology specialty care setting in Pennsylvania, USA, is applying the KFRE among a suite of digital tools integrated with EHRs to alert the healthcare team of patients at risk of progression and need for intervention. This will be in addition to multiple other components, and patient-reported, biomedical and health system outcomes will be collected. Early findings support the 'ease of use' and 'helpfulness' of the tools.[32] The fourth trial, with details described in the protocol by Hemmelgarn *et al*,[33] is a multiphase mixed-methods study. Following the completion of phase 2, findings have been published by Smekal *et al*,[3] a study that met the criteria for inclusion in this systematic review. The whole trial took on a pre–post design and applied the KFRE to patients in nephrology multidisciplinary CKD clinics in Alberta, Canada. The final phase will aim to evaluate the costs of care and outcomes before and after the introduction of risk-based triage, such as healthcare resource use, frequency of testing, modality choice and death.

Despite the lack of sufficient impact studies, strong evidence to date from validation studies and studies investigating potential impact in clinical practice have been encouraging. As a result, several CKD guidelines have or are in the process of incorporating KFRE risk-based criteria in their pathways.[6 7 34]

CONCLUSION

The KFRE has been extensively validated, but there has been relatively little evaluation of its clinical and economic impact. This is the first study to systematically review studies exploring at the actual impact of using the KFRE in clinical practice. Additional high-quality studies are required, and trials assessing the impact of using KFRE at various stages across the CKD pathway are in progress.

Author affiliations
[1]Department of Renal Medicine, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK
[2]Institute of Applied Health Research, University of Birmingham, Birmingham, UK
[3]Centre for Patient-Reported Outcomes Research (CPROR), Institute of Applied Health Research, University of Birmingham, Birmingham, UK
[4]Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK
[5]NIHR Birmingham Biomedical Research Centre, NIHR Surgical Reconstruction and Microbiology Research Centre and NIHR ARC, Birmingham, UK
[6]Birmingham Health Partners Centre for Regulatory Science and Innovation, University of Birmingham, Birmingham, UK
[7]School of Allied Health and Community, University of Worcester, Worcester, UK

Contributors HKB, PC, MC and DK conceived the study. HKB developed the methodology with guidance from PC, MC, DK, OA and AF. The database, reference and citation searches were completed by HKB and AF. Screening and selection of the included studies was conducted by HKB and AF; PC as the third reviewer was consulted for any disagreements. HKB and AF critically appraised the included studies. HKB drafted the initial manuscript and all authors contributed to revision and approval of the final manuscript. HKB, as guarantor, accepts full overall responsibility for the conduct of this study.

Funding This project received funding from University Hospitals Birmingham Charity (charity register number: 1165716) - Renal Research Fund (no award/grant number).

Competing interests PC reports grants from Kidney Research UK, National Institute for Health Research (NIHR), MRC and EU Horizon 20/20 programme, and personal fees from NAPP Pharmaceuticals outside the submitted work. OA receives funding from the NIHR Birmingham Biomedical Research Centre, NIHR Applied Research Centre (ARC), West Midlands at the University of Birmingham and University Hospitals Birmingham NHS Foundation, Innovate UK (part of UK Research and Innovation), Gilead Sciences Ltd and Janssen Pharmaceuticals, Inc. OLA declares personal fees from Gilead Sciences Ltd, GlaxoSmithKline (GSK) and Merck outside the submitted work. DK reports grants from Macmillan Cancer Support, Innovate UK, the NIHR, NIHR Birmingham Biomedical Research Centre and NIHR SRMRC at the University of Birmingham and University Hospitals Birmingham NHS Foundation Trust, and personal fees from Merck and GSK outside the submitted work. MC is an NIHR Senior Investigator and receives funding from the NIHR Birmingham Biomedical Research Centre, the NIHR Surgical Reconstruction and Microbiology Research Centre and NIHR ARC West Midlands at the University of Birmingham and University Hospitals Birmingham NHS Foundation Trust, Health Data Research UK, Innovate UK (part of UK Research and Innovation), Macmillan Cancer Support, UCB Pharma and GSK. MC has received personal fees from Astellas, Takeda, Merck, Daiichi Sankyo, Glaukos, GSK and the Patient-Centered Outcomes Research Institute outside the submitted work.

Patient consent for publication Not applicable.

Ethics approval This study does not involve human participants.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data sharing not applicable as no datasets generated and/or analysed for this study. Data sharing not applicable for this systematic review.

ORCID iDs
Anthony Fenton http://orcid.org/0000-0003-2665-6924
Derek Kyte http://orcid.org/0000-0002-7679-6741
Melanie Calvert http://orcid.org/0000-0002-1856-837X

REFERENCES

1 Bikbov B, Purcell CA, Levey AS, *et al*. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic

analysis for the global burden of disease study 2017. *Lancet* 2020;395:709–33.
2 Daker-White G, Rogers A, Kennedy A, *et al*. Non-disclosure of chronic kidney disease in primary care and the limits of instrumental rationality in chronic illness self-management. *Soc Sci Med* 2015;131:31–9.
3 Smekal MD, Tam-Tham H, Finlay J, *et al*. Patient and provider experience and perspectives of a risk-based approach to multidisciplinary chronic kidney disease care: a mixed methods study. *BMC Nephrol* 2019;20.
4 National Institute for Health and Care Excellence (UK). *Chronic kidney disease in adults: assessment and management (CG182)*. London: National Institute for Health and Care Excellence (UK), 2014.
5 Bhachu HK, Cockwell P, Subramanian A, *et al*. Impact of using Risk-Based stratification on referral of patients with chronic kidney disease from primary care to specialist care in the United Kingdom. *Kidney Int Rep* 2021;6:2189–99.
6 Kidney disease: improving global outcomes (KDIGO) CKD work group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Inter suppl* 2013;3:1–150.
7 Farrington K, Covic A, Aucella F. Clinical practice guideline on management of older patients with chronic kidney disease stage 3B or higher (eGFR <45 mL/min/1.73 m ^{2}). *Nephrology Dialysis Transplantation* 2016;31:ii1–66.
8 Ramspek CL, de Jong Y, Dekker FW, *et al*. Towards the best kidney failure prediction tool: a systematic review and selection aid. *Nephrol Dial Transplant* 2020;35:1527–38.
9 Tangri N, Grams ME, Levey AS, *et al*. Multinational assessment of accuracy of equations for predicting risk of kidney failure: a meta-analysis. *JAMA* 2016;315:164–74.
10 Ramspek C, de Jong Y, Dekker F, *et al*. FP367PREDICTIVE models for progression of chronic kidney disease to kidney failure: a systematic review. *Nephrology Dialysis Transplantation* 2018;33:i155.
11 The kidney failure risk equation.
12 Liberati A, Altman DG, Tetzlaff J, *et al*. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med* 2009;6:e1000100.
13 Tangri N, Stevens LA, Griffith J, *et al*. A predictive model for progression of chronic kidney disease to kidney failure. *JAMA* 2011;305:1553–9.
14 Critical appraisal skills programme. Available: https://casp-uk.net/ [Accessed 14 Apr 2021].
15 Joanna Briggs Institute critical appraisal tools. Available: https://jbi.global/critical-appraisal-tools [Accessed 14 Apr 2021].
16 Center for Evidence-Based Management (CEBMa). Critical appraisal of a survey. Available: https://www.cebma.org/wp-content/uploads/Critical-Appraisal-Questions-for-a-Survey.pdf [Accessed 14 Apr 2021].
17 Popay J, Roberts H, Sowden A. Guidance on the conduct of narrative synthesis in systematic reviews: a product from the ESRC methods programme 2006.
18 Hingwala J, Wojciechowski P, Hiebert B, *et al*. Risk-Based triage for nephrology referrals using the kidney failure risk equation. *Can J Kidney Health Dis* 2017;4:205435811772278.
19 Che M, Thanabalasingam SJ, Iliescu EA. Patient outcomes following discharge from a CKD clinic. *Journal of the American Society of Nephrology* 2020;31:227.
20 Hong R, Pirabhahar S, Turner K. Triage system for nephrology referrals using the kidney failure risk equation (KFRE) score. *Nephrology* 2020;25:53.
21 Sendak M, Cameron B, Komives E. Developing a data-driven work flow for population health rounding. *Journal of General Internal Medicine* 2016;31:S874–5.
22 Slattery LM. Applying novel kidney failure risk equations applications to new patient referrals: a 6-month retrospective review. *Journal of the American Society of Nephrology* 2019;30:1173.
23 Major RW, Shepherd D, Medcalf JF, *et al*. The kidney failure risk equation for prediction of end stage renal disease in UK primary care: an external validation and clinical impact projection cohort study. *PLoS Med* 2019;16:e1002955.
24 McCambridge J, Witton J, Elbourne DR. Systematic review of the Hawthorne effect: new concepts are needed to study research participation effects. *J Clin Epidemiol* 2014;67:267–77.
25 Nicoll R, Robertson L, Gemmell E, *et al*. Models of care for chronic kidney disease: a systematic review. *Nephrology* 2018;23:389–96.
26 Evans M, Lopau K. The transition clinic in chronic kidney disease care. *Nephrol Dial Transplant* 2020;35:ii4–10.
27 Nastasa A, Apetrii M, Onofriescu M, *et al*. P0184RISK prediction for death and end-stage renal disease does not parallel real-life trajectory of older patients with advanced chronic kidney disease - a romanian center experience. *Nephrology Dialysis Transplantation* 2020;35:iii486.
28 Inston N, Lok CE. Improving precision in prediction: using kidney failure risk equations as a potential adjunct to vascular access planning. *J Vasc Access* 2019;20:95–7.
29 Jhamb M, Yabes J, Fischer G. Electronic health record based population health management for improving CKD care: the kidney-coordinated health management partnership (Champ) study. *JASN* 2019;30:525.
30 Harasemiw O, Drummond N, Singer A, *et al*. Integrating Risk-Based care for patients with chronic kidney disease in the community: study protocol for a cluster randomized trial. *Can J Kidney Health Dis* 2019;6:205435811984161.
31 Green JA, Ephraim PL, Hill-Briggs FF, *et al*. Putting patients at the center of kidney care transitions: prepare now, a cluster randomized controlled trial. *Contemp Clin Trials* 2018;73:98–110.
32 Green JA, Ephraim PL, Hill-Briggs F, *et al*. Integrated digital health system tools to support decision making and treatment preparation in CKD: the prepare now study. *Kidney Med* 2021;3:565–75.
33 Hemmelgarn BR, Smekal MD, Weaver RG, *et al*. Implementation and evaluation of a risk-based approach to guide chronic kidney disease care: protocol for a multiphase mixed-methods study. *Can J Kidney Health Dis* 2018;5:205435811775361.
34 National Institute for Health and Care Excellence (UK). *Chronic kidney disease: assessment and management (NG203)*. London: National Institute for Health and Care Excellence (UK), 2021.