

Prognostic Performance of the 2-Year Kidney Failure Risk Equation and Kidney Replacement Therpay (KRT) Preparedness in Advanced CKD: Resolving Spectrum Bias in a Malaysian Cohort

Jun Min Em

University Malaya Medical Centre

Shahaznani Lee Mohd Shaharuddin

University of Malaya

Wan Noorhayati Wan Abdullah

University Malaya Medical Centre

Fatimah Hasanah Mohd Radzi

University Malaya Medical Centre

Khai Vern Poon

University of Malaya

Shing Shen Bay

University of Malaya

Soo Ying Yew

University Malaya Medical Centre

Elisya Liyana Abdullah

University of Malaya

Chee Keong Thye

University Malaya Medical Centre

Shok Hoon Ooi

University Malaya Medical Centre

Shian Feng Cheng

University Malaya Medical Centre

Yee Wan Lee

University of Malaya

Chye Chung Gan

University of Malaya

Maisarah Jalalonmuhali

University of Malaya

Chew Ming Wong

University of Malaya

Kok Peng Ng

University of Malaya

Wan Ahmad Hafiz Wan Md Adnan

University of Malaya

Soo Kun Lim

sookunlim@um.edu.my

University of Malaya

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Abstract

Introduction

The Kidney Failure Risk Equation (KFRE) is a validated model utilised to predict the risk of progression to end-stage kidney disease (ESKD) among patients with chronic kidney disease (CKD). Historical clinical pathways frequently rely on estimated glomerular filtration rate (eGFR) thresholds for kidney replacement therapy (KRT) education, which may underestimate temporal progression risk. This study evaluates the prognostic performance of the 2-year KFRE, examines potential spectrum bias across disease stages, and explores its observational association with KRT preparedness in a Malaysian tertiary centre.

Methodology

This retrospective cohort study analysed adults with advanced CKD evaluated by CKD educators. Patient outcomes were tracked until 31 July 2026. The 2-year KFRE was derived utilising the conventional 4-variable equation. Multiple Imputation by Chained Equations (MICE) was utilised to handle missing baseline proteinuria data for 38 patients. The primary endpoint was progression to ESKD, analysed using a Fine-Gray subdistribution hazard model to account for pre-ESKD mortality. Model discrimination was assessed using pooled and stage-stratified Receiver Operating Characteristic (ROC) analyses. Model discrimination was assessed using pooled and stage-stratified Receiver Operating Characteristic (ROC) analyses. Model calibration was assessed visually by plotting the mean predicted 2-year KFRE probabilities against observed Kaplan-Meier ESKD event probabilities across risk quintiles, with formal goodness-of-fit mathematically evaluated using both the standard Hosmer-Lemeshow (HL) test and the survival-adapted Greenwood-Nam-D'Agostino (GND) test.

Results

The imputed cohort comprised 245 patients (mean age 64.3 ± 13.4 years; 54.3% male) with a mean baseline eGFR of 13.8 ± 6.3 ml/min/1.73m². Over the observation period, 157 patients (64.1%) progressed to ESKD. Stratified analysis revealed spectrum bias: in Categories G3-G4, eGFR showed limited discrimination (AUC 0.500; 95% CI 0.393–0.617), whereas the KFRE maintained better prognostic utility (AUC 0.655; 95% CI 0.539–0.773). Goodness-of-fit testing confirmed significant model miscalibration (GND Chi-square 37.26, $P < 0.001$), as the uncalibrated equation systematically overpredicted absolute risk. Adjusted for diabetes and composite atherosclerotic cardiovascular disease (ASCVD), patients in the $\geq 40\%$ KFRE risk tier demonstrated a 3.04-fold increased subdistribution hazard for ESKD (95% CI 2.04–4.53, $P < 0.001$). Among 122 patients initiating KRT, 60.7% commenced via central venous catheters.

Conclusion

The 2-year KFRE is a reliable prognostic tool for ESKD progression, offering clearer risk discrimination than eGFR in earlier CKD stages (G3-G4), though regional baseline recalibration is recommended to correct mathematical overprediction and prevent premature KRT preparation in lower-risk patients. Furthermore, the high incidence of catheter-dependent dialysis initiation in this cohort underscores the ongoing clinical challenge of late referrals, which limits the practical utility of risk-based surgical planning.

INTRODUCTION

Chronic kidney disease (CKD) is a globally recognised health consideration, affecting approximately 10% of the worldwide population [1]. The prevalence of end-stage kidney disease (ESKD) continues to grow in Malaysia, placing increased demand on existing dialysis and transplant services. According to the 32nd Malaysian Dialysis & Transplant Registry (MDTR) report, 55,237 patients were receiving dialysis in Malaysia at the end of 2024, with incident dialysis patients reaching 9,473 in the same year [2]. Globally, the average number of incident ESKD diagnoses worldwide is 144 per million population, underscoring wide international variation in ESKD burden and capacity for care [3].

Structured kidney education programmes empower patients, affording them time to understand their condition, foster adherence to medications, and strategically explore KRT modalities [4]. In Malaysia, kidney education programmes are available in tertiary centres; however, a standard national programme has yet to be established. Patients are often referred to educational sessions late in their disease progression, leaving them unprepared for crucial treatment decisions [5]. Traditional referral pathways have historically relied on strict eGFR thresholds (typically $< 30 \text{ ml/min/1.73m}^2$), which may inadvertently delay comprehensive education [6]. However, eGFR as an isolated metric may occasionally misrepresent the pace of disease progression, potentially delaying referrals for younger patients or prompting premature preparation in older demographics with slower progression rates [5, 6]. Consequently, patients are often referred to educational sessions late in their disease course, leaving limited time for informed decision-making and surgical access preparation.

The 2-year Kidney Failure Risk Equation (KFRE), introduced by Tangri et al. [7], offers a composite, validated approach to estimate short-term ESKD risk, and has recently been integrated into KDIGO 2024 guidelines to facilitate risk-based triage [8, 9]. While international validation is extensive, local studies examining its historical performance in Malaysia are still emerging [10, 11]. This study retrospectively evaluates the prognostic utility of the 2-year KFRE in a Malaysian tertiary cohort, explores the effect of spectrum bias on predictive accuracy across CKD stages, and characterises the relationship between baseline risk and clinical KRT preparedness.

METHODOLOGY

Study Design and Data Collection

This single-centre, retrospective observational cohort study extracted historical data from adults (age ≥ 18 years) with an eGFR < 60 ml/min/1.73m² evaluated by a CKD educator at the University Malaya Medical Centre. Patients diagnosed with acute kidney injury (AKI) or already established on dialysis (CKD Category G5D) prior to counselling were excluded. The observation period concluded on 31 July 2026. Follow-up duration was calculated from the date of the initial referral utilised for the baseline KFRE calculation.

KRT counselling was performed by dedicated nurses who provided education on CKD progression and KRT modalities. Patient-relevant clinical and biochemical data were collected retrospectively from electronic medical records (EMR). The 2-year KFRE score was derived using the conventional, non-calibrated 4-variable pooled equation [7]. This model incorporates age, sex, eGFR, and UACR. When direct UACR data were absent, values were computationally converted from available UPCR utilising Chronic Kidney Disease Prognosis Consortium (CKD-PC) multivariable-adjusted conversion equations [12].

Missing Data Handling

To minimise selection bias associated with missing baseline proteinuria data which was a requirement for KFRE-2 calculation, Multiple Imputation by Chained Equations (MICE) using a Random Forest regressor (100 iterations) was employed to impute missing variables for 38 patients. The imputed dataset (N = 245) served as the primary analytic cohort. Complete-case analysis (N = 207) was performed simultaneously and is detailed in the Supplementary Appendix as a sensitivity analysis.

Endpoint Definitions

The primary composite endpoint was defined as progression to ESKD, encompassing both formal initiation of KRT and, for patients on a conservative palliative pathway, reaching physiological kidney failure defined by standardised clinical indications (including refractory fluid overload, or severe uraemia) alongside a terminal eGFR < 5 ml/min/1.73m².

A secondary, descriptive endpoint focused on KRT preparedness among the subset of patients with documented KRT access modalities. Optimal preparedness was categorised as initiating haemodialysis via a mature arteriovenous fistula (AVF) or commencing peritoneal dialysis (PD), whereas suboptimal preparedness was defined as central venous catheter initiation. Patients pursuing conservative palliative care were exclusively tracked for the ESKD primary endpoint but excluded from the secondary access modality analyses.

Statistical Analyses

Data processing was performed using IBM SPSS version 29.0.2 and Python 3.10. Continuous variables were tested for normality of distribution; parametric data are presented as means $\pm$ standard deviations (SD), and non-parametric data as medians with interquartile ranges (IQR).

Predictive discrimination was mapped using Receiver Operating Characteristics (ROC) curves with 1,000-iteration bootstrapped 95% confidence intervals (CIs). To account for spectrum bias inherent in pooling heterogeneous severity groups, ROC analyses were stratified by early (Categories G3-G4) versus late (Category G5ND) referral statuses. Model calibration was assessed visually by plotting the mean predicted 2-year KFRE probabilities against observed Kaplan-Meier ESKD event probabilities across risk quintiles, and a cohort-specific recalibrated baseline risk was calculated. Furthermore, model calibration was formally evaluated using two mathematical goodness-of-fit tests across risk quintiles: the standard Hosmer-Lemeshow (HL) test (evaluated at 24 months, strictly excluding patients censored prior to 24 months without an event), and the survival-adapted Greenwood-Nam-D'Agostino (GND) test, which appropriately incorporates temporal progression and right-censoring dynamics inherent in survival data.

Survival analysis was conducted using a Fine-Gray subdistribution hazard model to account for the competing risk of pre-ESKD mortality [13]. To avoid collinearity with variables inherently embedded within the KFRE equation, the model evaluated time-to-ESKD by stratifying patients into $< 40\%$ and $\geq 40\%$ tiers. The model was adjusted for diabetes mellitus and composite atherosclerotic cardiovascular disease (ASCVD), encompassing established ischaemic heart disease, heart failure, and cerebrovascular accidents. Temporal progression to ESKD was visualised utilising Kaplan-Meier estimates stratified by KDIGO tiers.

Ethical Considerations

The study protocol was approved by the University of Malaya Medical Centre Medical Research Ethics Committee (Approval No. 2026316-16517). The requirement for informed consent was waived by the ethics committee due to the retrospective nature of the study and the use of de-identified patient data collected during standard clinical care. The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

RESULTS

A total of 344 patients were initially screened. After excluding patients with AKI (N = 47) or established KRT (N = 52), the final imputed cohort comprised 245 cases. (Refer Fig. 1)

Baseline Characteristics

The imputed cohort generally presented with advanced disease (Table 1). The mean age was 64.3 ± 13.4 years, comprising 54.3% males. The mean referral eGFR was 13.8 ± 6.3 ml/min/1.73m². Stratified by KDIGO 2-year KFRE risk tiers, 6.9% of the cohort scored $< 10\%$, 25.7% scored between 10–40%, and the

majority (67.3%) had a risk $\geq 40\%$. The CKD category distribution was predominantly G5ND (61.2%) and G4 (37.1%). During the observation period, 157 patients (64.1%) progressed to the primary endpoint of ESKD.

Table 1
Baseline Characteristics of the Study Population (N = 245)

Characteristics	Value(s)
Demographics	64.3 $\pm$ 13.4
Age, years (Mean $\pm$ SD)	133 (54.3%)
Gender	112 (45.7%)
Male	
Female	
Clinical Parameters at Referral	13.8 $\pm$ 6.3
eGFR, ml/min/1.73m² (Mean $\pm$ SD)	53.4 $\pm$ 27.7%
KFRE at 2-years (Mean $\pm$ SD)	17 (6.9%)
<10%, n(%)	63 (25.7%)
10–40%, n(%)	165 (67.3%)
$\geq 40\%$, n(%)	
CKD Grading	4 (1.6%)
G3A and 3B	91 (37.1%)
G4	150 (61.2%)
G5ND	
Primary Disease of CKD	186 (75.9%)
Diabetes mellitus	44 (18.0%)
Hypertension	10 (4.1%)
Glomerulonephritis	3 (1.2%)
Obstructive uropathy	2 (0.8%)
Autosomal Dominant Polycystic Kidney Disease	
Established Atherosclerotic Cardiovascular Disease (ASCVD)	62 (25.3%)
Ischaemic heart disease	32 (13.1%)
Heart failure	15 (6.1%)
Stroke or Transient Ischaemic Attack	21 (8.6%)

Risk Prediction and Stratification

Conventional pooled ROC curve analysis of the 2-year KFRE for predicting ESKD demonstrated moderate discrimination (AUC 0.746; 95% CI 0.677–0.810), similar to baseline eGFR (AUC 0.737; 95% CI 0.665–0.804) (Refer Fig. 2). However, stratifying the cohort revealed underlying spectrum bias (Table 2). In earlier clinical categories (G3-G4; N = 95), eGFR showed diminished discriminative utility (AUC 0.500; 95% CI 0.393–0.617). In contrast, the KFRE maintained better prognostic utility in this subset (AUC 0.655; 95% CI 0.539–0.773). Within the late-stage G5ND subset (N = 150), discrimination was comparable between the KFRE (AUC 0.646; 95% CI 0.537–0.744) and eGFR (AUC 0.631; 95% CI 0.532–0.728).

Table 2
Subgroup Stratification of ROC Discrimination (Spectrum Bias Analysis)

CKD Category Subset	Total Patients (N)	ESKD Events (N)	2-Year KFRE AUC	Baseline eGFR AUC	P-Value*
Pooled Cohort	245	157	0.746 (0.677–0.810)	0.737 (0.665–0.804)	0.731
Categories G3-G4	95	42	0.655 (0.539–0.773)	0.500 (0.393–0.617)	0.012
Category G5ND	150	115	0.646 (0.537–0.744)	0.631 (0.532–0.728)	0.781
Remarks: Discriminative capacity of the 2-year KFRE compared to baseline eGFR across distinct CKD stages. P-values derived from a 1,000-iteration bootstrapped z-test comparing the empirical Area Under the Curve (AUC) differences between the two models. P-value > 0.05 is highlighted in bold.					

Visual calibration curve analysis (Fig. 3) indicated that the uncalibrated pooled equation generally overpredicted absolute 2-year ESKD risk in the lower and intermediate risk quintiles. Temporal survival analysis of this imputed cohort yielded an observed 2-year ESKD probability, establishing a cohort-specific recalibrated baseline risk of 38.9%. Formal goodness-of-fit testing corroborated this visual miscalibration; both the standard HL test (Chi-square = 57.70, P < 0.001) and the survival-adapted GND test (Chi-square = 37.26, P < 0.001) firmly rejected the null hypothesis of a perfect fit, mathematically confirming significant systematic overprediction across the cohort's quintiles (Table 3).

Table 3
Goodness-of-Fit Assessment of the 2-Year KFRE (Calibration Across Quintiles)

Risk Quintile	Total Patients (N)	Mean Predicted Probability	Observed 24-Month KM Probability
Quintile 1	49	13.2%	7.1%
Quintile 2	49	36.1%	43.4%
Quintile 3	49	55.0%	34.5%
Quintile 4	49	72.0%	43.5%
Quintile 5	49	90.7%	66.1%
Remarks: Calibration was formally evaluated using the survival-adapted Greenwood-Nam-D'Agostino (GND) test (Chi-square = 37.26, $P < 0.001$) and the standard Hosmer-Lemeshow binary test (Chi-square = 57.70, $P < 0.001$, evaluated among patients uncensored at 24 months). Both tests indicated a significant deviation from perfect fit, statistically confirming systematic overprediction by the uncalibrated equation.			

Time-to-Event and Survival Outcomes

Utilising an adjusted Fine-Gray subdistribution hazard model to account for competing pre-ESKD mortality, patients in the high-risk $\geq 40\%$ tier were evaluated against the lower-risk $< 40\%$ baseline (Table 4). Adjusting for baseline diabetes and composite ASCVD, patients in the $\geq 40\%$ KFRE tier exhibited a 3.04-fold increased subdistribution hazard for progression to ESKD (95% CI 2.04–4.53, $P < 0.001$). (Fig. 4)

Table 4
Fine-Gray Subdistribution Hazard Model in Complete Cases

Predictor	Subdistribution Hazard Ratio (sHR)	95% Confidence Interval (CI)	p-value
2-year KFRE $\geq 40\%$	3.04	2.04–4.53	< 0.001
Diabetes Mellitus	0.99	0.68–1.45	0.959
Composite ASCVD	0.84	0.57–1.23	0.365
Note: Model explicitly excludes age and gender to prevent collinearity with KFRE inherent variables. Pre-ESKD mortality is handled as a competing risk.			

KRT Modalities upon Initiation

Within the 157 patients progressing to ESKD, 35 patients (22.3%) opted for conservative management under palliative care. The remaining 122 patients initiated KRT. As detailed in Table 5, 60.7% initiated haemodialysis using a suboptimal central venous catheter, while 24.6% initiated optimally via a mature

AVF, and 15.6% commenced peritoneal dialysis. Consequently, of the 104 total patients who initiated haemodialysis, the mature AVF utilisation rate was only 28.8% within that specific modality.

Table 5
Modalities of KRT Initiation among KRT-Initiating Subgroup (N = 122)

Modality	Number of Patients	Percentage (%)
Haemodialysis (Catheter)	74	60.7%
Haemodialysis (AVF)	30	24.6%
Peritoneal Dialysis (PD)	19	15.6%
Note: The 35 patients pursuing conservative palliative care were exclusively tracked for the ESKD primary endpoint and excluded from the KRT initiation modality access analyses.		

DISCUSSION

This retrospective cohort study evaluated the prognostic value of the 2-year KFRE in an advanced CKD population and observed its correlation with clinical KRT preparedness. Following MICE imputation to preserve sample size and exclusion of misclassified pre-dialysis cases, patients exceeding the $\geq 40\%$ risk threshold demonstrated a 3.04-fold increased adjusted subdistribution hazard for ESKD progression, independent of composite ASCVD and diabetic status. The application of this competing risk framework is particularly vital in our specific demographic; given the high prevalence of diabetes (75.9%) and composite ASCVD, traditional Cox proportional hazards models would likely overestimate the absolute risk of ESKD by failing to account for patients who die prior to reaching kidney failure.

Stage-stratified analysis highlighted the presence of spectrum bias in pooled ROC outcomes. While eGFR performed similarly to the KFRE in the combined data and the late-stage G5ND subset, its predictive utility was notably reduced in the earlier G3-G4 categories (AUC 0.500). In these earlier stages, the KFRE offered more reliable discrimination (AUC 0.655). While an absolute AUC of 0.655 denotes relatively weak clinical discrimination, this attenuation is likely multifactorial, driven by the smaller subgroup sample size (N = 95), a lower absolute event rate (37 ESKD events), and the inherent unpredictability of temporal progression in earlier-stage disease. This aligns with the premise that while eGFR is a practical indicator of imminent failure in advanced disease, composite tools like the KFRE may offer clearer prognostic stratification earlier in the disease course when there is more flexibility for multidisciplinary intervention.

Furthermore, calibration analysis and comprehensive goodness-of-fit testing (GND Chi-square 37.26, $P < 0.001$) demonstrated that the original North American-derived equation systematically overpredicted risk in lower and intermediate quintiles within this cohort. Our survival analysis established an observed local 2-year ESKD baseline risk of 38.9%, reinforcing the established necessity of mathematically recalibrating the equation's intercept to match regional progression and competing mortality rates prior to widespread

clinical implementation [14], typically achieved by updating the baseline survival function while retaining the original model coefficients.

Regarding clinical preparedness, a substantial portion of the cohort relied on temporary dialysis access, with 60.7% of KRT initiators commencing via central venous catheters. Rather than reflecting the prognostic accuracy of the KFRE, these outcomes likely illustrate the broader clinical challenges associated with late nephrology referrals [15]. In this cohort, 61.2% of patients were already at CKD Category G5ND upon referral for kidney education. According to the National Kidney Foundation's KDOQI clinical practice guidelines, achieving a mature, usable AVF frequently requires extensive surgical planning, vessel mapping, and prolonged post-operative maturation times ranging from several weeks to months [16]. By referring patients at such an advanced physiological state, clinical pathways actively negate the surgical maturation window the KFRE is expressly designed to create. This contrasts heavily with international benchmarks, such as in Japan, where early referral and distinct healthcare policies drive AVF utilisation rates well beyond 72% [17, 18]. When patients are referred at an advanced physiological stage, the practical window for risk-based access planning is considerably narrowed. To mitigate this late-referral bottleneck, automated KFRE reporting integrated directly into electronic medical records (EMR) could serve as an objective, system-wide trigger for timely vascular access referrals, bridging the gap between prognostic risk and surgical preparedness.

Strengths and Limitations

A primary strength of this study is its utilisation of MICE which the selection bias often present in retrospective analyses with missing proteinuria data [12], and the Fine-Gray competing risk regression appropriately isolated ESKD risk from pre-dialysis mortality [13].

However, the findings must be interpreted within the context of the study's limitations. First, as a single-centre retrospective study with a cohort predominantly in advanced CKD stages (G4-G5ND), the results may not be fully generalisable to earlier-stage primary care settings. Given that most patients in this cohort already met standard clinical criteria for KRT preparation based on KDIGO guidelines [8], this dataset is less suited to evaluate the effectiveness of the KFRE $\geq 40\%$ threshold as an early referral trigger in the wider community. Furthermore, explicit granular data on surgical referral for vascular access creation, and exact fistula maturation durations relative to KRT commencement were unavailable.

CONCLUSION

The 2-year KFRE is a valuable prognostic tool for predicting progression to ESKD, offering improved risk discrimination over isolated eGFR in earlier CKD stages (Categories G3-G4). For optimal accuracy, regional recalibration adapting to local baseline risks is recommended to rectify mathematical overprediction observed in goodness-of-fit analyses. However, the observed reliance on catheter-dependent dialysis initiation within this cohort highlights the ongoing clinical challenge of late patient

referral. To fully realise the benefits of risk-based KRT preparation and vascular access planning, prognostic tools like the KFRE may need to be integrated earlier in the primary care pathway to ensure adequate lead time for multidisciplinary intervention.

Declarations

Conflicts of Interest:

The authors declare no known competing financial interests or personal relationships that could have appeared to influence the work.

Funding:

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data Availability:

De-identified participant data and analytic code will be made available upon reasonable request to the corresponding author, subject to institutional approval and journal policy.

Ethics Approval & Consent:

The study protocol was approved by the Medical Research Ethics Committee (MREC), University of Malaya Medical Centre. The requirement for informed consent was waived due to the retrospective nature of the study and the use of de-identified patient data.

Generative Artificial Intelligence (AI):

We declare that generative AI (Gemini 3.1) was utilised to assist with grammatical error correction and manuscript structure. The authors have checked the manuscript for accuracy and take full responsibility for all content.

References

1. Kovesdy CP. Epidemiology of chronic kidney disease: An update 2022. *Kidney Int Supplements*. 2022;12(1):7–11. <https://doi.org/10.1016/j.kisu.2021.11.003>.
2. Hooi LS, Ong LM, Sunita B, Loh CL, Thong KM, Philip NJ, Choo CL. 32nd report of the Malaysian dialysis & transplant registry. *Malaysian Society of Nephrology*; 2025.
3. Bello AK, Okpechi IG, Levin A, Ye F, Saad S, Zaidi D, Johnson DW. ISN–Global kidney health atlas. *International Society of Nephrology*; 2023.

4. Faldu CT, Knicely DH. Advanced chronic kidney disease and patient education. *Kidney Dialysis*. 2025;5(3):32. <https://doi.org/10.3390/kidneydial5030032>.
5. Koch-Weser S, Porteny T, Rifkin DE, Agarwal A, Weiner DE, Ladin K, Wofford S. Patient education for kidney failure treatment: A mixed-methods study. *Am J Kidney Dis*. 2021;78(5):690–9. <https://doi.org/10.1053/j.ajkd.2021.02.334>.
6. Oliva-Damaso N, Delanaye P, Oliva-Damaso E, Payan J, Glasscock RJ. Risk-based versus GFR threshold criteria for nephrology referral in chronic kidney disease. *Clin Kidney J*. 2022;15(11):1996–2005. <https://doi.org/10.1093/ckj/sfac104>.
7. Tangri N, Stevens LA, Griffith J, Tighiouart H, Djurdjev O, Naimark D, Levey AS. A predictive model for progression of chronic kidney disease to kidney failure. *JAMA*. 2011;305(15):1553–9. <https://doi.org/10.1001/jama.2011.451>.
8. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int*. 2024;105(4S):S117–314.
9. Major RW, Shepherd D, Medcalf JF, Xu G, Gray LJ, Brunskill NJ. (2019). The Kidney Failure Risk Equation for prediction of end stage renal disease in UK primary care. *PLoS Med*, 16(11), e1002955.
10. Ooi YG, Sarvanandan T, Hee NKY, Lim QH, Beh HC, Rozi NR, Lim LL. Clinical utility of kidney failure risk equation in diabetes and chronic kidney disease. *J ASEAN Federation Endocr Soc*. 2024;39(S1):3536. <https://doi.org/10.15605/jafes.039.S1.055>.
11. Rozi NR, Selvaraj CS, Tan JK, Lim ZF, Nordin NW, Mazhar NH, Lim LL. Kidney failure risk equation (KFRE), a risk-based triage for nephrology referrals: A mixed-methods study at pre-implementation phase among healthcare providers. *Prim Care Diabetes*. 2025;19(6):636–45. <https://doi.org/10.1016/j.pcd.2025.08.001>.
12. Sumida K, Nadkarni GN, Grams ME, Sang Y, Ballew SH, Coresh J, CKD Prognosis Consortium. Conversion of urine protein-creatinine ratio or urine dipstick protein to urine albumin-creatinine ratio for use in chronic kidney disease screening and prognosis. *Ann Intern Med*. 2020;173(6):426–35.
13. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. *J Am Stat Assoc*. 1999;94(446):496–509.
14. Tangri N, Grams ME, Levey AS, Coresh J, Appel LJ, Astor BC, CKD Prognosis Consortium. Multinational assessment of accuracy of equations for predicting risk of kidney failure: A meta-analysis. *JAMA*. 2016;315(2):164–74. <https://doi.org/10.1001/jama.2015.18202>.
15. Smart NA, Titus TT. Outcomes of early versus late nephrology referral in chronic kidney disease: A systematic review. *Am J Med*. 2011;124(11):1073–80. <https://doi.org/10.1016/j.amjmed.2011.04.026>.
16. Lok CE, Huber TS, Lee T, Shenoy S, Yevzlin AS, Abreo K, National Kidney Foundation. KDOQI clinical practice guideline for vascular access: 2019 update. *Am J Kidney Dis*. 2020;75(4):S1–164. <https://doi.org/10.1053/j.ajkd.2019.12.001>.

17. Nitta K, Goto S, Masakane I, Hanafusa N, Taniguchi M, Hasegawa T, Nakamoto H. incidence, prevalence, and mortality. Ren Replace Therapy. 2020;6:41. <https://doi.org/10.1186/s41100-020-00286-9>. Annual dialysis data report for 2018, JSDT Renal Data Registry: survey methods, facility data,.
18. Ozeki T, Shimizu H, Fujita Y, Inaguma D, Maruyama S, Ohyama Y, Tagaya T. The type of vascular access and the incidence of mortality in Japanese dialysis patients. Intern Med. 2017;56(5):481–5. <https://doi.org/10.2169/internalmedicine.56.7563>.

Figures

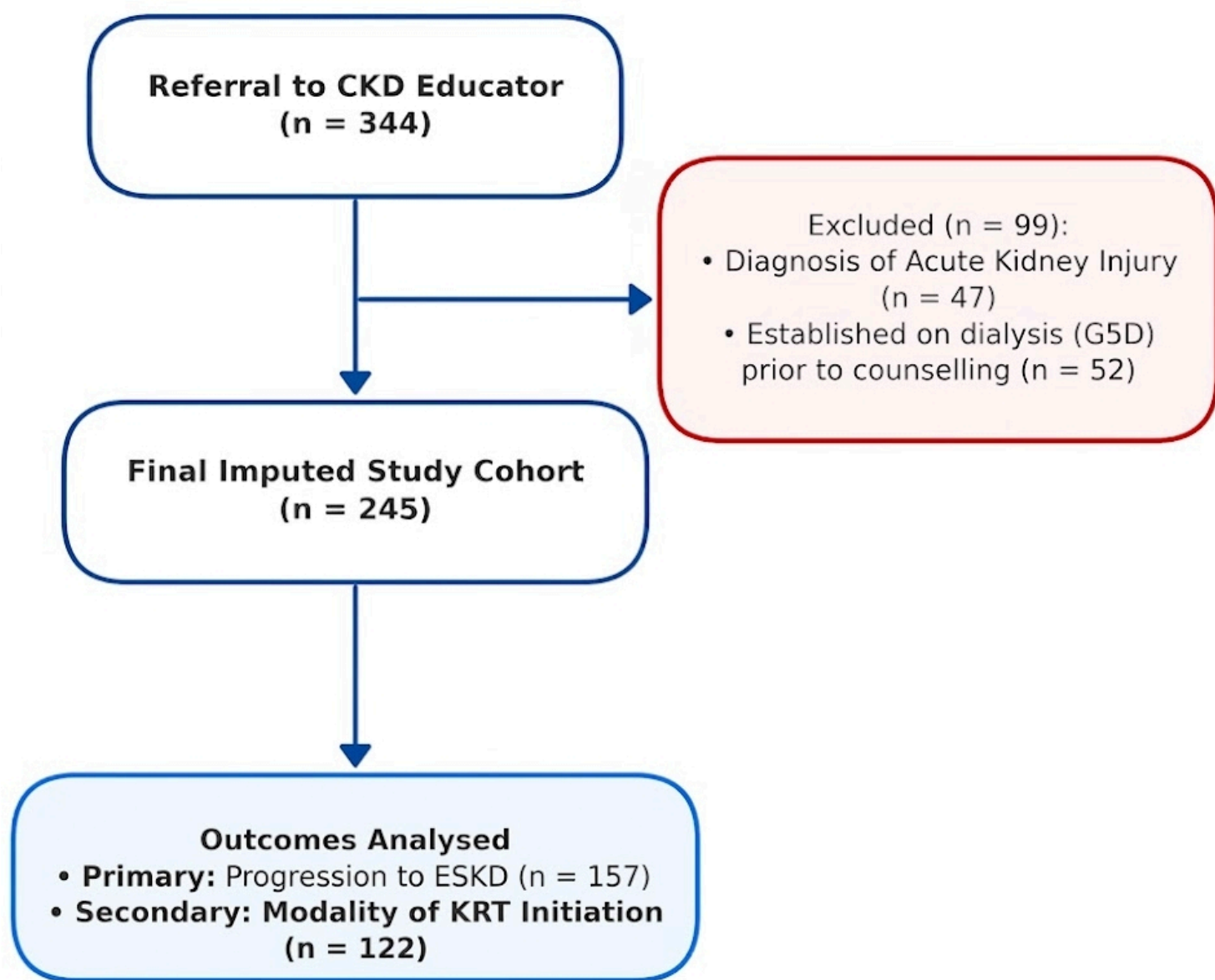


Figure 1

Flow Diagram of Screening and Study Cohort

The initial screening included 344 patients referred to the CKD educator. After excluding patients with acute kidney injury (N=47) and those already established on dialysis prior to counselling (N=52), the final study cohort comprised 245 patients following Multiple Imputation by Chained Equations (MICE) for missing baseline KFRE-2 components. Outcomes Analysed: Primary Progression to ESKD (n = 157) and Secondary Modality of KRT Initiation (n = 122).

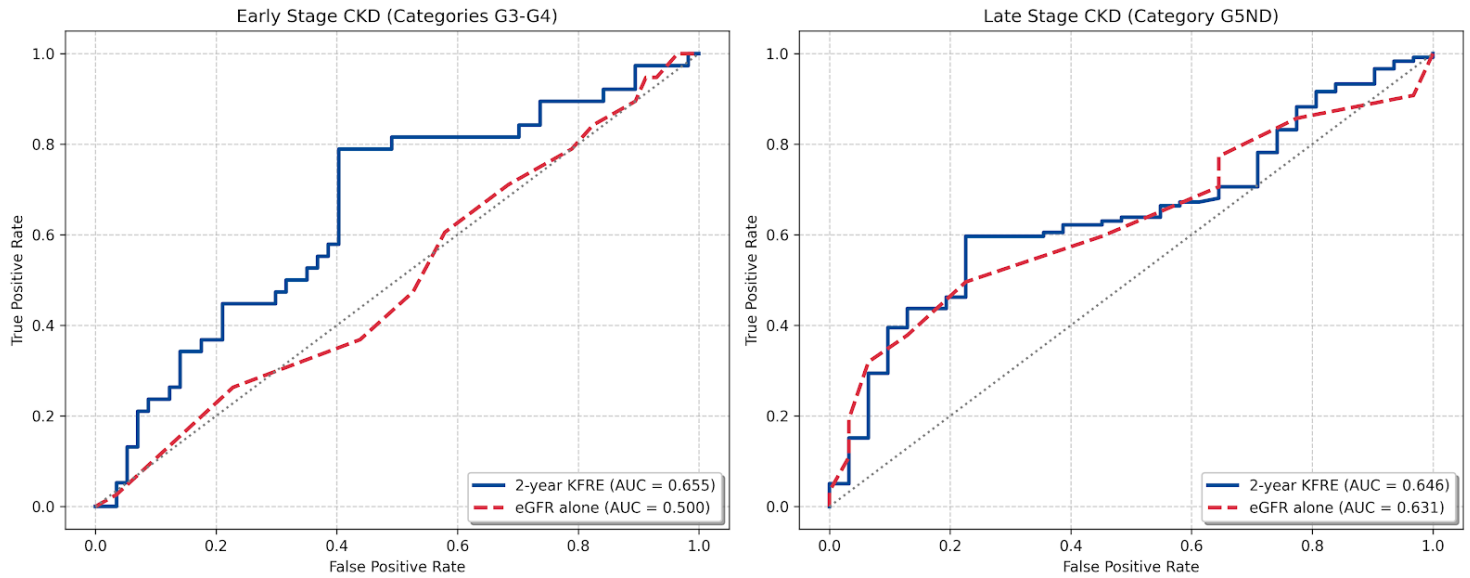


Figure 2

Stratified Receiver Operating Characteristic (ROC) analysis comparing the discriminative utility of the 2-year KFRE and baseline eGFR for predicting progression to ESKD

Remarks: The cohort was stratified by clinical stage to resolve underlying spectrum bias. The analysis highlights significantly diminished eGFR discrimination in early-stage CKD (Categories G3-G4; AUC 0.500) compared to the composite KFRE (AUC 0.655, $P = 0.012$), whereas both prognostic metrics demonstrated comparable capacity in late-stage Category G5ND.

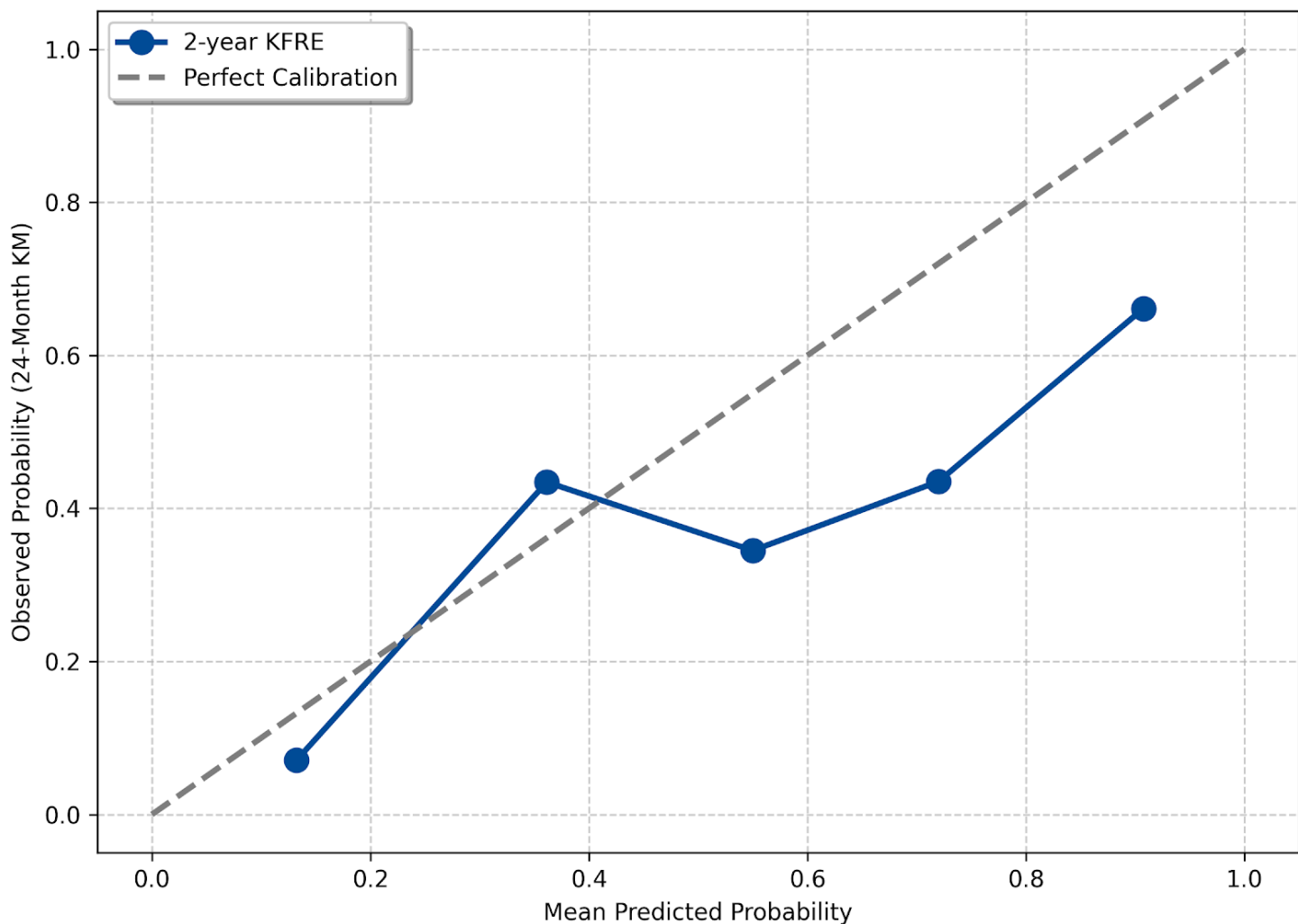


Figure 3

Calibration Plot of the 2-Year KFRE for Predicting ESKD within the Imputed Cohort.

Remarks: The graph plots the mean predicted 2-year ESKD probability against the observed 24-month Kaplan-Meier event probability across computed risk quintiles. The dashed grey line represents perfect calibration. The uncalibrated original equation demonstrates systematic overprediction, a miscalibration statistically confirmed by both the GND test ($p < 0.001$) and standard HL test ($p < 0.001$).

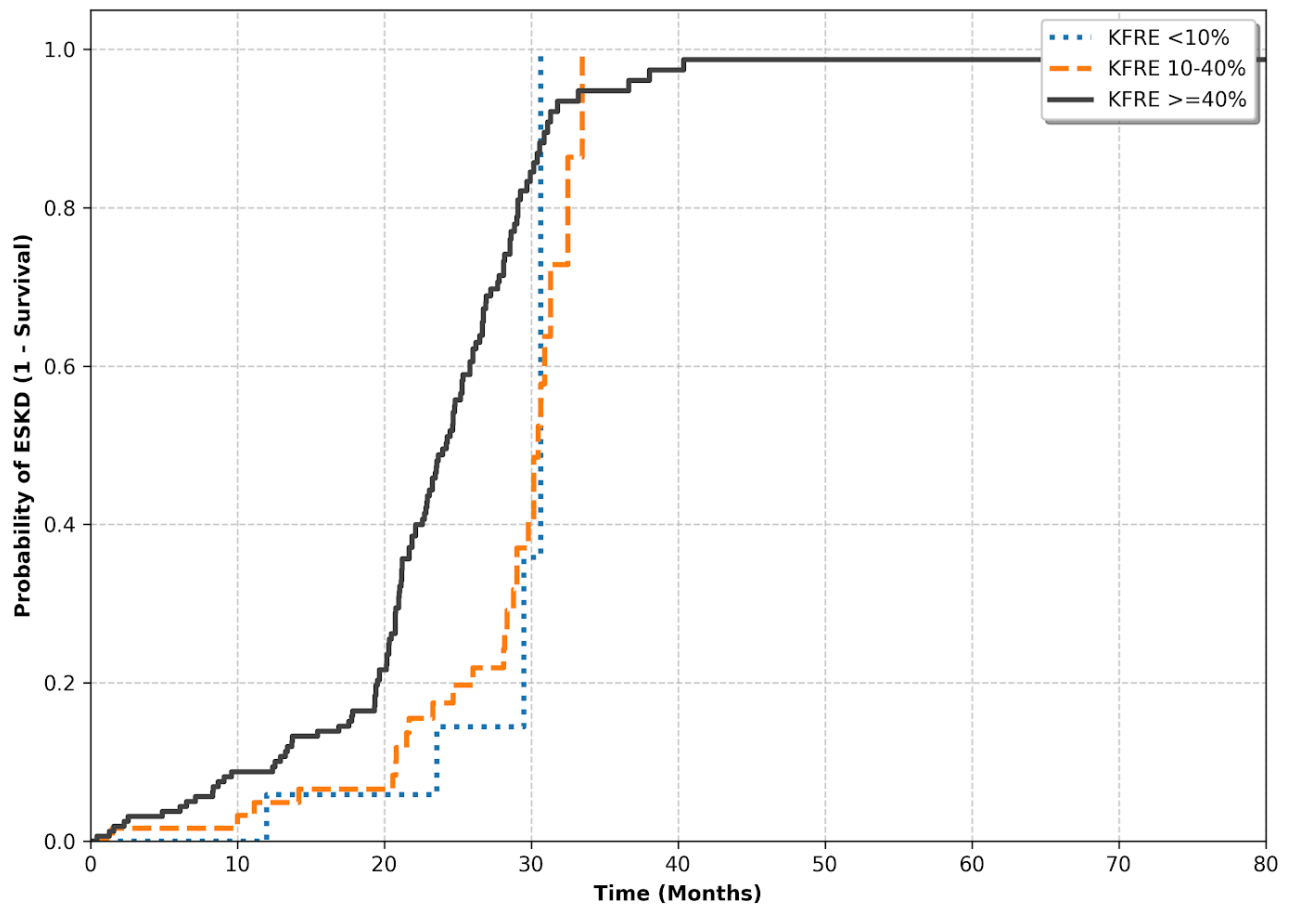


Figure 4

Kaplan-Meier Estimates of Temporal Progression to ESKD, stratified by KDIGO KFRE Risk Tiers.

Remarks: The step plot illustrates the probability of physiological progression to ESKD (calculated as 1 minus survival probability) over time. Patients are stratified into KDIGO 2-year KFRE risk tiers: <10% (dotted line), 10-40% (dashed line), and ≥40% (solid line). The corresponding number of patients at risk in each tier at 20-month intervals is detailed in the table directly below the x-axis.