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Impact of routine reporting of estimated glomerular filtration rate using the European Kidney Function Consortium and Chronic Kidney Disease Epidemiology Collaboration equations in a Western Australian community population

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Abstract

Aim: In 2020, the European Kidney Function Consortium (EKFC) published a new creatinine-based equation to estimate glomerular filtration rate (eGFR) to overcome known limitations in existing equations. The aim of this study is to model the potential impact on service referral and health expenditure of routine reporting of eGFR using the EKFC equation as compared to the CKD-EPI equation in a Western Australian population.

Methods: eGFR was calculated for 760 614 patients with 2 368 234 creatinine results using the CKD-EPI and EKFC formulas. Patients were grouped into a CKD cohort if they had at least two eGFR results of <60 ml/min/1.73 m^2 from tests at least 90 days apart. The impact of each equation on the reclassification of CKD stages, CKD cohort classification, the rate of change in eGFR and direct health costs were assessed.

Results: About 90.66% of patients had a lower eGFR when calculated using the EKFC equation. About 12.6% of individuals were classified into a different CKD stage using the EKFC equation with 97.43% of these patients classified into a higher (more advanced) stage. There was a 25.9% increase in the number of patients identified as having CKD when calculated using the EKFC equation. Direct health costs also increased with the use of EKFC reporting.

Conclusion: Use of the EKFC equation will increase population prevalence of CKD and will result in a shift to higher stages of CKD. This has implications for monitoring and referral of patients within specialist services and has the potential to increase the need for multidisciplinary care.

KEYWORDS
chronic, glomerular filtration rate, renal insufficiency

Summary at a glance

This study considers the application of the recently published European Kidney Function Consortium (EKFC) equation in 2020 to estimate the glomerular filtration rate. It compares the impact when shifting from the use of the CKD-EPI equation to the EKFC equation, by modelling potential differences on service referral and health expenditure on a Western Australian community population.

1 | INTRODUCTION

The estimated glomerular filtration rate (eGFR) is used clinically as a marker for kidney disease, and is derived from creatinine-based mathematical equations.[1] To date, several different approaches have been used to calculate eGFR. These equations were developed using population data and have had limited utility in younger and older patients due to physiological differences.[2,3] This leads to poor estimation of eGFR in these demographic groups. With the evolution of computational methods for large population data analytics, research has continued to refine the eGFR to improve management and to better understand the burden of chronic kidney disease (CKD) for a given population.[4]

Equations that have been widely adopted for reporting of eGFR include the Modification of Diet in Renal Disease (MDRD) Study equation[5] and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)[6] equation for use in adults, the Chronic Kidney Disease in Children Study (CkiD)[7] equation for children, and the full age spectrum (FAS)[2] equation. Currently, the CKD-EPI and CkiD equations are recommended for eGFR reporting by the Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines.[8]

Recently, the European Kidney Function Consortium (EKFC) equation was developed to combine design features of the FAS and CKD-EPI equations in order to overcome known limitations with the FAS and CKD-EPI formulas.[9] Specifically, the design of the EKFC equation corrects the overestimation of eGFR in young adults experienced with the CKD-EPI equation as they transition from the CkiD equation used for children, and demonstrates improved performance for the age groups of 18–40 and ≥65 years.[9,10] However, it has faced some criticism due to its development and validation on a Caucasian population of European descent, decreasing its potential applicability in many regions with more ethnically diverse populations.[9,10] This also raised the issue regarding the reliability of eGFR estimates for ethnic groups such as the Aboriginal Australian population.[11,12]

Since the publication of the EKFC equation in late 2020,[9] there has been several published comparisons on the impact of changing from the CKD-EPI to the EKFC equation for routine reporting of eGFR, demonstrating a shift to decreased values of eGFR that primarily affects the classification of younger and older patients with good kidney function at the lower (less advanced) stages of CKD.[13,14] Results from two studies comparing a range of creatinine based equations with measured GFR on selected populations of elderly Chinese patients[15] and white patients and self-reported black ethnicity patients in the United Kingdom[16] also demonstrated that the EKFC equation was less likely to overestimate GFR compared to the CKD-EPI equation in these populations. As increased screening and referral to tertiary services is recommended for patients with CKD stages 3a or higher (i.e., more advanced CKD stages), reclassification of patients to higher CKD stages may result in significant implications on health care expenditure.

The effect of the use of the MDRD and CKD-EPI equations to model the prevalence of CKD in an Australian population and its economic impact was reported by Mitchell et al.[17] The study noted that the introduction of CKD-EPI to replace the MDRD reporting reduced the population prevalence of CKD and better identified patients at risk of further decline in renal function, which could reduce unnecessary costs related to surveillance and referral. Given the recent development of the EKFC equation, we will use the same Australian population to model the potential impact of routine reporting of eGFR using the EKFC equation in place of the currently used CKD-EPI equation.

2 | METHODS

2.1 | Study population and cohorts

We performed a retrospective cross-sectional study using serum creatinine results processed by a single pathology provider that operates in the Northern Territory and Western Australia. The pathology provider operator has collection centres across the state and services a representative cross-section of the population, however most collection centres are largely community based and does not service hospital or tertiary centres. The raw de-identified dataset contained 999 393 unique patients for a 10-year period from February 2002 to August 2012, with serum creatinine, age and sex recorded but excluded ethnicity. Tests that resulted in an eGFR greater than 150 ml/min/1.73 m^2 calculated by the CKD-EPI equation were excluded, as were those missing dates of birth, sex, or serum creatinine values. Test results with a patient postcode from a state other than Western Australia were also excluded. Patients with more than one test with at least 1 year of follow up from their first test were defined as the general baseline cohort.

The general cohort included 760 614 patients from Western Australia with 2 368 234 creatinine test results who were over the

age of 18 years for all pathology tests. About 52.73% of the general cohort patients had more than one creatinine test, and 44.9% of patients had more than one test with at least 1 year of follow up from their first test (the trend cohort). The trend cohort consisted of 341 470 patients with 1 857 702 creatinine test results.

The median age of the general cohort at their first baseline test was 50 years (range 18–106; mean 50; SD 17) and 54.2% were female. The median number of tests per person was 2 (range 1–364; mean 3.1) and the median time between the first and last test for the trend cohort was 4.4 years (range 1–10.6; mean 4.8 years).

The eGFR was calculated using both the CKD-EPI (Appendix A) and EKFC (Appendix B) equations for the general cohort's first baseline test, resulting in a median eGFR calculated by the CKD-EPI equation of 90.76 ml/min/1.73 m^2 (range 1.3–150; mean 89.3, SD 21.2), compared to a median of 88.7 ml/min/1.73 m^2 when calculated using the EKFC equation (range 1.5–146, mean 84.6, SD 19.8).

The eGFR was also calculated by both the CKD-EPI and EKFC equations for all tests for all patients in the general cohort. Patients were then grouped into a CKD cohort if they had at least two eGFR results of <60 ml/min/1.73 m^2 from tests at least 90 days apart. 57 483 patients with 535 102 creatinine tests were identified as having CKD when calculated by the CKD-EPI equation, while 72 381 patients with 633 216 creatinine tests were identified as having CKD when calculated by the EKFC equation, an increase of 14 898 patients (25.9%).

Data preparation, processing and analysis was performed using python version 3.8.3.[18] Normality of the distributions of the difference in calculated eGFR for the two equations for each sex for CKD-EPI stage and age groups and for the distribution of calculated eGFR for the two equations for the general cohort not classified into the EKFC cohort was assessed with D'Agostino and Pearson test, while the homogeneity of variances for non-paired data was assessed using Levene's test. Non-parametric data for patients grouped by CKD-EPI stage and age groups were analysed using Kruskal-Wallis or Chi-square tests where applicable. Additional data such as albuminuria was unavailable for this study to confirm kidney damage, and is discussed as a limitation of this study. The differences in eGFR (eGFR calculated by the EKFC equation minus the eGFR calculated by the CKD-EPI equation) were assessed for males and females grouped by CKD-EPI stage and age categories using a Kruskal-Wallis test followed by Dunn's test with Bonferroni correction for multiple comparisons to determine statistical significance. Differences in age in years were assessed for males and females grouped by reclassification stage using a Kruskal-Wallis test followed by Dunn's test with Bonferroni correction for multiple comparisons to determine statistical significance. Differences in the proportions of males and females grouped into different reclassification stages by EKFC reporting were assessed using Chi-square contingency tests with Bonferroni correction for multiple comparisons to determine statistical significance. Non-parametric paired data for the calculated eGFR for both equations for the general cohort not classified into the EKFC CKD cohort were assessed for each sex by age groups by the Wilcoxon signed-rank test.

Direct health costs for each CKD stage for the year 2011 (the last calendar year with complete data) were estimated for the CKD-EPI and EKFC cohorts using previously published costing information taken modelled by Wyld and colleagues.[19] This model is from a NSW health setting, with annual costs per patient of $2719 for CKD stages 1 and 2, $3489 for CKD stages 3a and 3b, and $14 545 for CKD stages 4 and 5. Each patient was assigned to a single CKD stage for the year, based on their average eGFR for creatinine tests performed in the year 2011.

3 | RESULTS

3.1 | Differences in eGFR values

Using the eGFR values calculated from both the CKD-EPI and EKFC equations for the general cohort's baseline test results ($n = 760\,614$) led to 90.66% of patients having a lower eGFR value when eGFR was estimated using the EKFC equation compared to the CKD-EPI equation (Figure S1).

The biggest differences between eGFR calculated from the two equations (eGFR calculated from EKFC – eGFR calculated from CKD-EPI) was observed in younger and older patients with well-preserved kidney function (Figure 1), where the median differences for both males and females are significantly greater than patients with worse kidney function of all ages ($p < .001$ for all groups [Dunn's test with Bonferroni correction]). For example, patients with CKD-EPI eGFR results >90 ml/min/1.73 m^2 (CKD staging of 1, noting that no other data was available to confirm kidney damage) and aged between 18–29 and above 70 years as well as patients aged >90 years with CKD-EPI eGFR results between 60 and 89 ml/min/1.73 m^2 (CKD staging of 2) had the biggest median differences, ranging from −17.5 to 10 ml/min/1.73 m^2. In comparison, patients with CKD-EPI eGFR results below 30 ml/min/1.73 m^2 (resulting in a CKD staging of 4 or 5) in all age groups had much smaller differences, with median differences ranging from −2 to 2 ml/min/1.73 m^2. Listed below are detailed median differences for patients with CKD-EPI eGFR results >90 ml/min/1.73 m^2 for the following age groups:

1. Ages 18–29: −12 and −10 ml/min/1.73 m^2 for females and males, respectively.
2. Ages 70–79: −10 ml/min/1.73 m^2 for both females and males.
3. Ages 80–89: −12 and −14 ml/min/1.73 m^2 for females and males, respectively.
4. Ages >90: −15 and −17.5 ml/min/1.73 m^2 for females and males, respectively.

Patients with CKD-EPI eGFR results between 60 and 89 ml/min/1.73 m^2 aged >90 years median differences: −11 and −9 ml/min/1.73 m^2 for females and males, respectively. For patients with CKD-EPI eGFR results below 30 ml/min/1.73 m^2 median differences ranged from −2 to 2 ml/min/1.73 m^2 for females and males of all age groups.

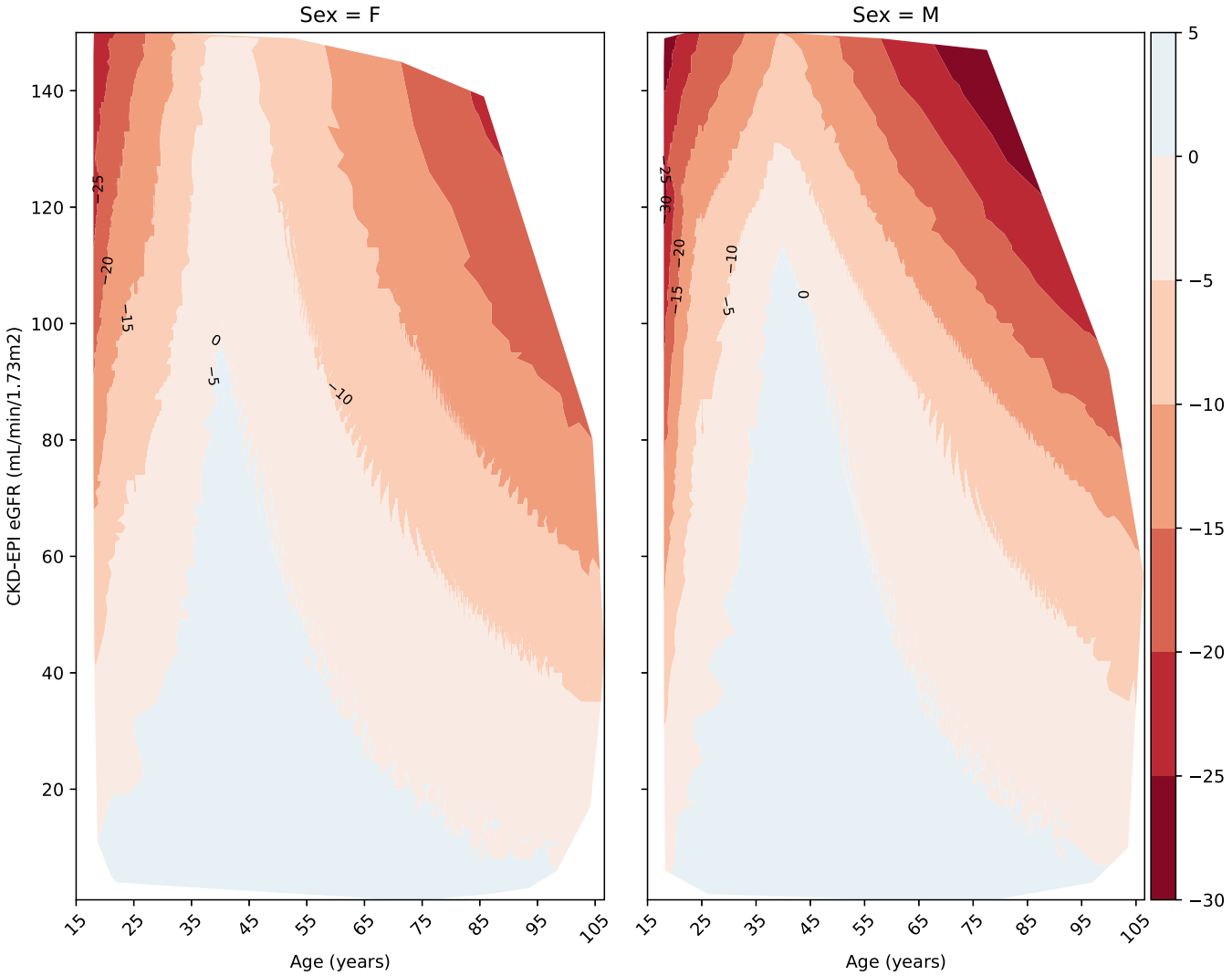

FIGURE 1 Contour plots with the difference between eGFR calculated via EKFC minus the eGFR calculated by the CKD-EPI equation for baseline serum creatinine results for 760 614 patients. Females are on the left, males on the right. Contour lines representing the differences are plotted every 5 ml/min/1.73 m^2 with the eGFR calculated by the CKD-EPI equation on the *y*-axis and age in years on the *x*-axis. Negative differences (the eGFR calculated by EKFC reporting is lower than the eGFR calculated by CKD-EPI reporting) are represented by red shading, and positive differences are indicated by blue shading

3.2 | Reclassification of CKD stages

More patients (51.49%, $n = 391\,661$) were classified as CKD stage 1 for CKD-EPI reporting, compared to EKFC reporting (45.33%, $n = 328\,762$) for Table 1. 95 818 patients (12.6%) were reclassified to a different CKD stage from CKD-EPI to EKFC reporting (Table 1). Of the reclassified patients, 97.43% were reclassified to a higher (worse) CKD stage from the CKD-EPI to EKFC reporting (Table 1). The prevalence of more advanced renal impairment, indicated by a CKD staging of 3a–5, increased from 8.85% to 11.45% with EKFC reporting.

Reclassification rates were highest in CKD stages 1 and 3a for CKD-EPI to EKFC reporting (Table 1 and Figure 2). The biggest differences in numbers of patients being reclassified from CKD-EPI reporting was seen in CKD stage 1 (to CKD stage 2 for EKFC reporting, 67.71% of all reclassified patients) and CKD stage 2 (to CKD stage 3a for EKFC reporting, 20.91% of all reclassified patients, Table 1).

The impact of reclassification from CKD-EPI to EKFC reporting was highest in patients with normal kidney function (25.35% of all reclassified patients were aged 60–69 and reclassified from CKD stage 1 to 2, the next highest group were patients aged 18–29, also reclassified from CKD stage 1 to 2 [16.35% of all reclassified patients, Figure 3]).

Guidelines recommend that patients with CKD stage 3 or higher should undergo more intense clinical evaluation and surveillance, such as cardiac risk testing and regular albuminuria in parallel with their creatinine assessment.[20] As CKD stage 3a defines the group of patients where more intensive screening is recommended, we assessed the differences in sex and age for patients who were reclassified from stage

TABLE 1 eGFR reclassification with EKFC reporting by CKD stage for the CKD-EPI and EKFC equations.

	EKFC stage						
CKD-EPI stage	1	2	3a	3b	4	5	Total
1	326 782 (83.4%)	64 879 (16.6%)					391 661
2	1980 (0.7%)	279 632 (92.7%)	20 033 (6.6%)				301 645
3a		287 (0.7%)	35 210 (83%)	6924 (16.3%)			42 421
3b			90 (0.5%)	15 868 (91.1%)	1461 (8.4%)		17 419
4				56 (0.9%)	5891 (98.1%)	59 (1%)	6006
5					49 (3.4%)	1413 (96.6%)	1462
Total	328 762	344 798	55 333	22 848	7401	1472	760 614

Note: Reclassification rates for each CKD-EPI stage are in brackets. Reclassification to a lower CKD stage is represented by blue shading (i.e., kidney function is better), reclassification to a higher stage is represented by red shading (i.e., kidney function is worse). No shading indicates no reclassification (i.e., stayed in the same stage).

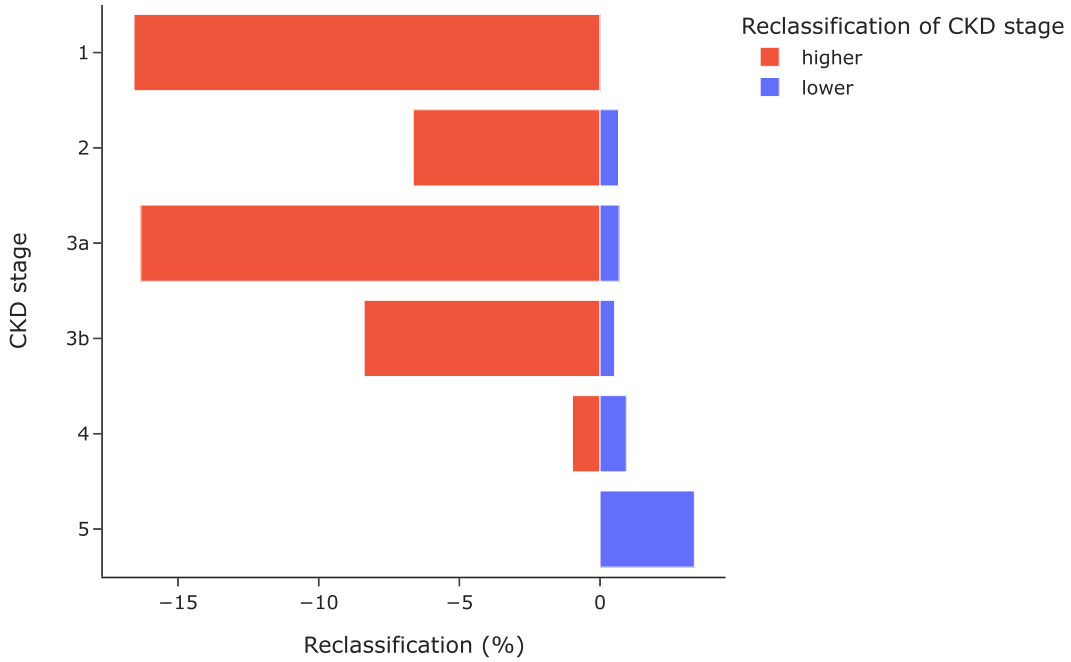

FIGURE 2 Reclassification rates of baseline CKD stages with each equation for 760 614 patients. Negative reclassification rates in red indicate reclassification to a higher CKD stage (i.e., kidney function is worse). Positive reclassification rates in blue indicate reclassification to a lower CKD stage (i.e., kidney function is better)

2 to 3a or 3a to 2 with EKFC reporting. Patients reclassified to CKD stage 3a (n = 20 033) tended to be older (median 75.91 vs. 57.31 years, $p < .0001$ [Dunn's test with Bonferroni correction]) and female (62.81% vs. 49.42%, $p < .0001$, $\chi^2 = 1339.67$) compared to those remaining in CKD stage 2 ($n = 279\,632$).

Patients reclassified to CKD stage 2 from CKD stage 3a ($n = 287$) tended to be male (76.65% vs. 46%, $p < .0001$, $\chi^2 = 106.34$) and younger (median 44.7 vs. 73.39 years $p < .0001$ [Dunn's test with Bonferroni correction]), compared to those remaining in CKD stage 3a ($n = 352\,410$), while patients reclassified from CKD stage 3a to 3b ($n = 6924$) tended to be female (31.18% male, $p < .0001$, $\chi^2 = 516.65$) and older (median 82.34 years, $p < .0001$ [Dunn's test with Bonferroni correction], Figure 4).

4 | IMPACT OF RECLASSIFICATION ON RATES OF CHANGE IN EGFR

A potential negative impact of reclassification is if patients are disadvantaged via a reclassification to a lower CKD stage (i.e., missing out on appropriate opportunities for surveillance and intervention), if their rates of loss of eGFR over time are similar to the higher CKD stage designated via CKD-EPI reporting.[17] We therefore calculated the annual rates of change of eGFR calculated by the EKFC equation for patients who were originally classed as CKD stage 2 or 3a via the CKD-EPI equation and had at least 1 year of follow-up, and compared the median annual rate of change of eGFR between those who were reclassified with EKFC reporting and those who remained at the same stage.

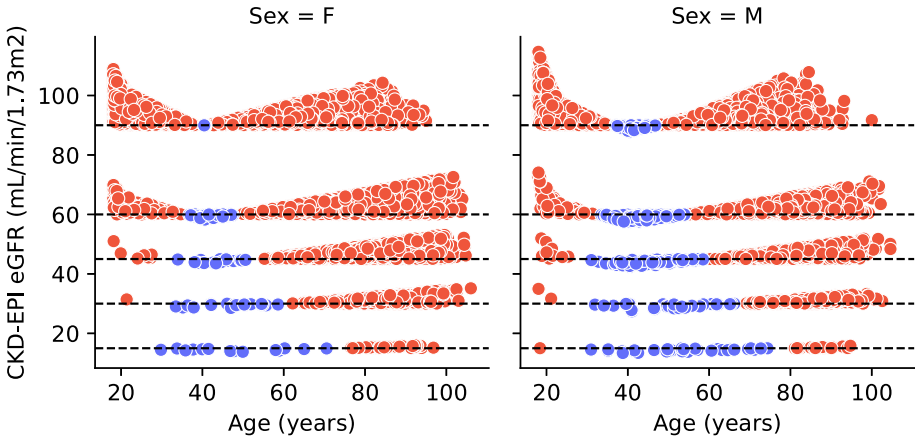

FIGURE 3 CKD stage when reported for females (left, 56 410 patients) and males (right, 39 408 patients) for the CKD-EPI to EKFC reporting. Reclassification to a lower CKD stage is represented by blue markers (i.e., kidney function is better), reclassification to a higher stage is represented by red markers (i.e., kidney function is worse)

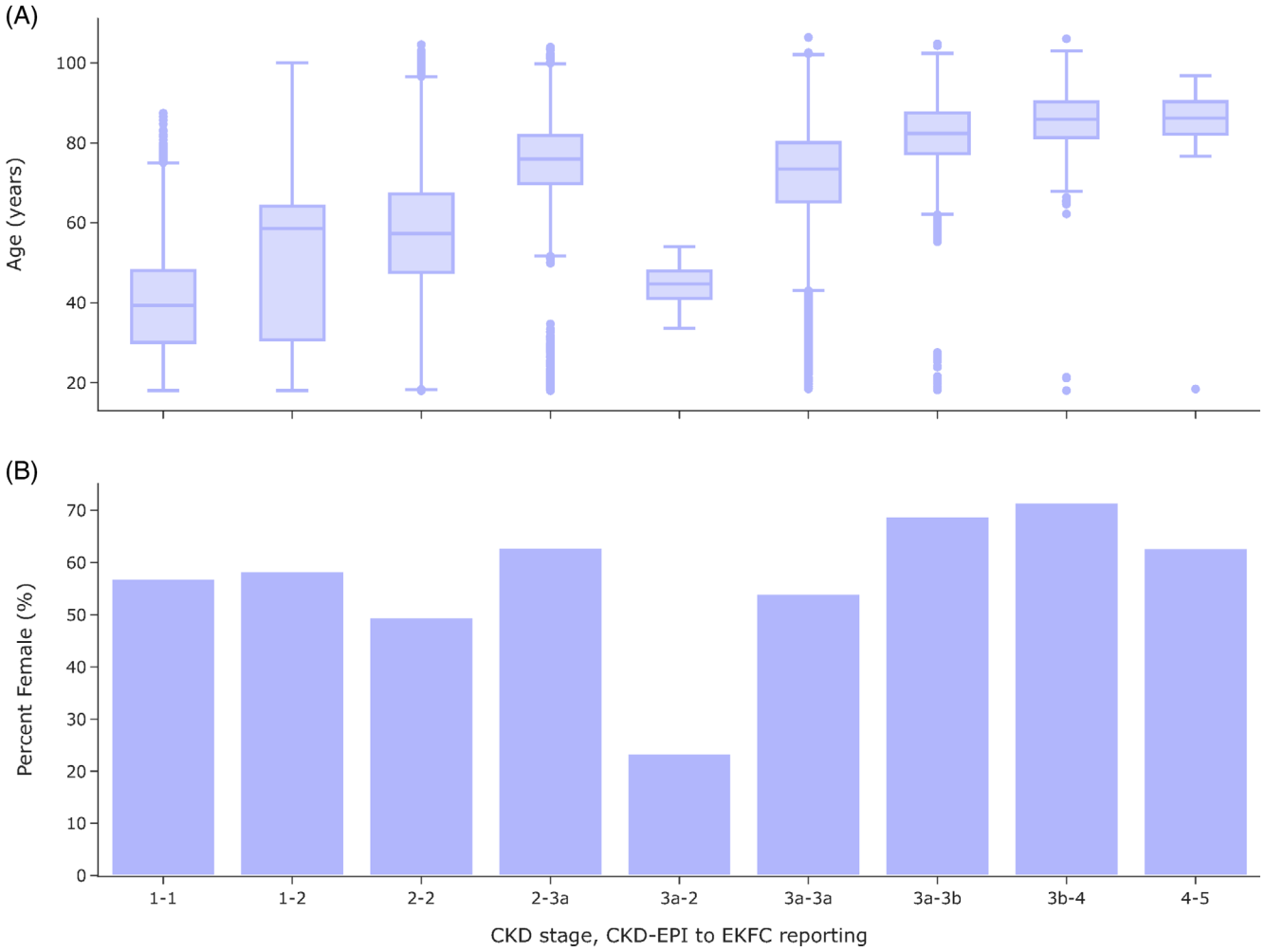

FIGURE 4 (A) Box plots by age for comparison of select cohorts for CKD stages from CKD-EPI to EKFC reporting. (B) Proportion of female patients in select cohorts for CKD stages from CKD-EPI to EKFC reporting

154 044 patients were originally classed as CKD stage 2 via the CKD-EPI equation and had at least 1 year of follow-up, with a median baseline CKD-EPI eGFR of 78.43 and median inclusion time of 4.64 years. 7.38% of these patients ($n = 11\,375$) were reclassified into stage 3a with EKFC reporting, while the rest remained classified at CKD stage 2.

23 536 patients were originally classed as CKD stage 3a via the CKD-EPI equation and had at least 1 year of follow-up, with a median baseline CKD-EPI eGFR of 54.33 and median inclusion time of 4.63 years. 15.06% and 0.5% of these patients ($n = 3545$, $n = 118$) were reclassified into stage 3b and stage 2, respectively

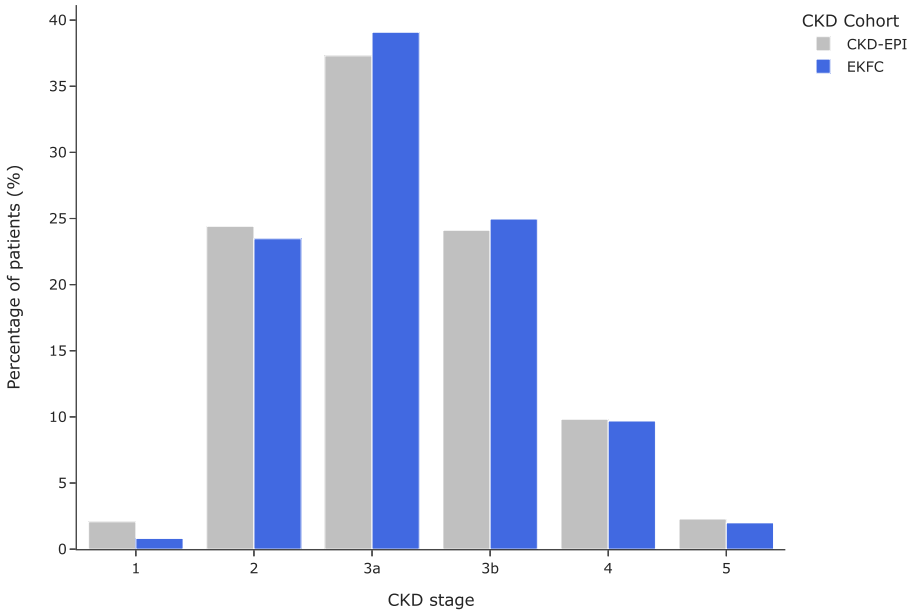

FIGURE 5 Percentage of patients in each CKD stage for CKD cohorts classified by each equation (CKD-EPI cohort indicated by grey bars, EKFC cohort by blue bars)

TABLE 2 Direct health cost in AUD for the various CKD stages for the year 2011

CKD stage	Number of patients	Direct health cost (AUD$)
CKD-EPI reporting		
1	43	116 917
2	4635	12 602 565
3a	11 070	38 623 230
3b	5763	20 107 107
4	1936	28 159 120
5	337	4 901 665
Total		104 510 604
EKFC reporting		
1	16	43 504
2	4980	13 540 620
3a	14 715	51 340 635
3b	7640	26 655 960
4	2432	35 373 440
5	340	4 945 300
Total		131 899 459
Increase with EKFC reporting		AUD$27 388 855

with EKFC reporting, while the rest remained classified at CKD stage 3a.

For patients reclassified to a higher CKD stage (from CKD stage 2 to 3a and 3a to 3b), the median annual rates of change from the initial to last test results were similar (−0.68 and −0.65 ml/min/1.73 m^2 per year, $p = 1$ [Dunn's test with Bonferroni correction]), and were significantly lower ($p < .001$ [Dunn's test with Bonferroni correction]) than the rates of change for patients remaining in CKD stages 2 and 3a (−0.48 and −0.43 ml/min/1.73 m^2 per year, $p = 1$) and for patients reclassified from CKD stage 3a to 2 (0.86 ml/min/1.73 m^2 per year, $p < .001$ [Dunn's test with Bonferroni correction]). This suggests that the introduction of EKFC reporting would not reclassify patients to a lower CKD stage (i.e., better kidney function) who were actually at increased risk of progressive renal impairment (according to the median annual rate of change of eGFR).

5 | IMPACT ON CLASSIFICATION OF CKD

Use of EKFC resulted in a 25.9% increase in the number of patients being classified with CKD compared to CKD-EPI reporting. When serial eGFR results of these cohorts are assessed (each patient is counted once in each CKD stage they have a result for, with a range of 1–6 unique CKD stages [stage 3 divided into 3a and 3b] and median of 2 unique CKD stages), proportionally more patients are categorized into CKD stages 3a and 3b for the EKFC reporting compared to the CKD-EPI equation (Figure 5).

Proportionally more female patients are classified with CKD with the use of EKFC reporting (56.7% vs. 55.5% for CKD-EPI reporting), as well as an increased proportion of patients aged in the 60–69 and 70–79 age groups (baseline age) at their first CKD stage 3a result in the EKFC CKD cohort compared to the CKD-EPI cohort.

The increase in the number of patients classified with CKD would also result in an overall increase in the direct health cost. Using 2011 as an example, the overall cost increases by $27 388 855 when using EKFC reporting compared to CKD-EPI reporting; as shown in Table 2.

6 | EFFECT OF AGE ON EGFR

Kidney function declines with aging, with a decrease in GFR usually beginning around 30–40 years which tends to accelerate after the age of 50–60.[21] Both the CKD-EPI and EKFC equations model the age

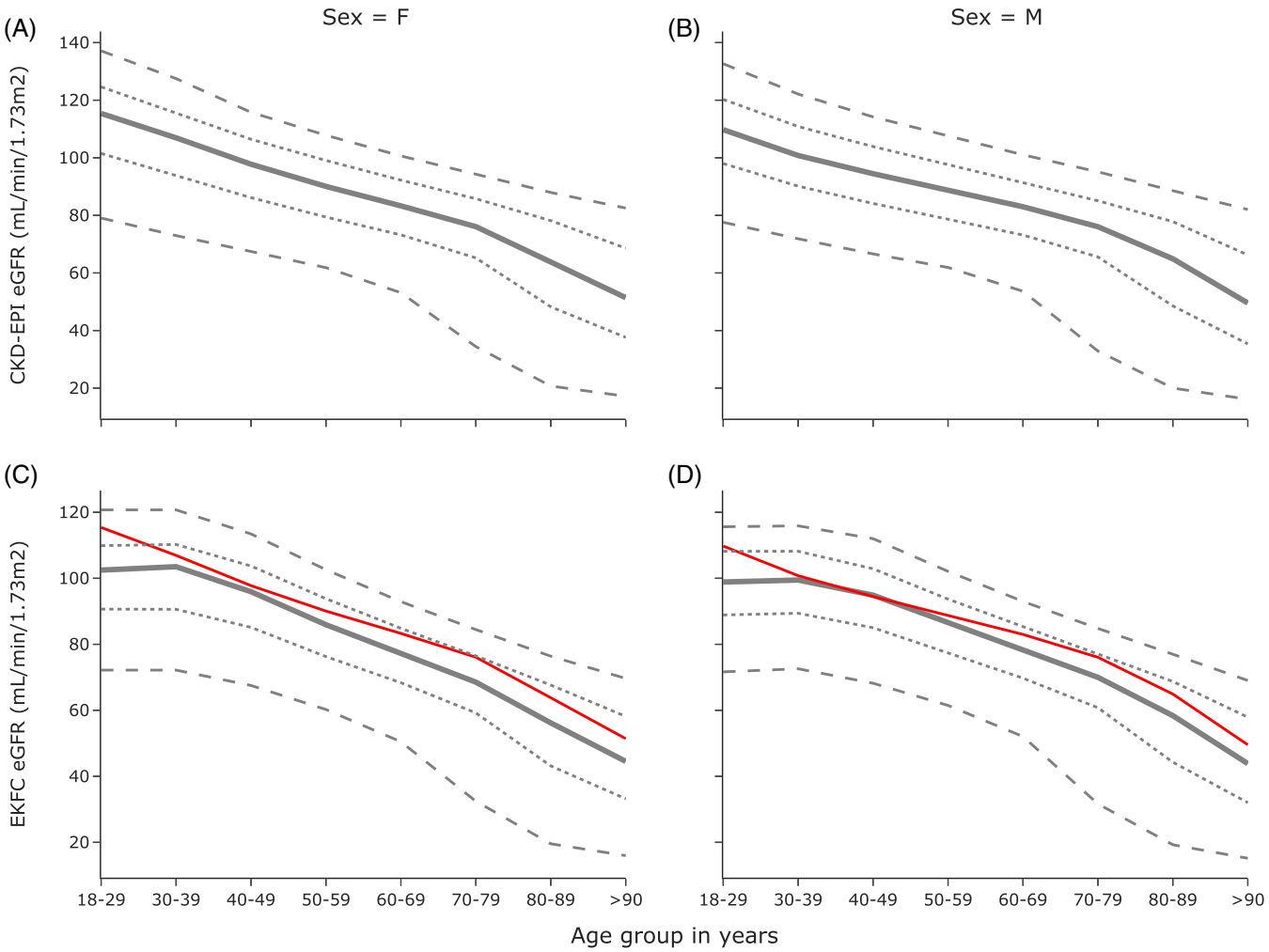

FIGURE 6 Percentile plots for baseline eGFR values for patients in the general cohort not classified into the CKD cohort for each Equation (2.5% and 97.5% [dash], 25% and 75% [dot], median [solid]). The red line for (C and D) is the median for the CKD-EPI equation presented in (A and B). (A) Baseline eGFR results for females from the general cohort not classified into the CKD cohort when applying the CKD-EPI equation ($n = 380\,432$). (B) baseline eGFR results for males from the general cohort not classified into the CKD cohort when applying the CKD-EPI equation ($n = 322\,699$). (C) Baseline eGFR results for females from the general cohort not classified into the CKD cohort when applying the EKFC equation ($n = 371\,266$). (D) Baseline eGFR results for males from the general cohort not classified into the CKD cohort when applying the EKFC equation ($n = 316\,967$).

dependency of GFR, but in slightly different ways. GFR estimated by the EKFC equation is fairly constant from the ages of 25 to 40, with the threshold for the age parameter introduced after the age of 40. Conversely, age is included as a parameter for all adults in the CKD-EPI equation, resulting in an overestimation of GFR in adults below the age of 40 compared to the EKFC equation results.[6]

To assess the effect of age on GFR in the general population as estimated by both equations, we produced percentile plots for the baseline eGFR values for patients in the general cohort who were not identified as part of the CKD cohort using the EKFC equation (Figure 6, $n = 688\,233$).

For both males and females, the largest differences in median eGFR between the two equations was for the 18–29 age group (female median eGFR of 115.39 and 102.47 ml/min/1.73 m^2 and male median eGFR 109.76 and 98.87 ml/min/1.73 m^2 for CKD-EPI and EKFC reporting, respectively). The median eGFR was significantly higher for CKD-EPI reporting for both sexes in all age groups ($p < .001$ [Wilcoxon signed-rank test]), with the exception of males in the age group of 40–49 where the median eGFR was significantly higher for EKFC reporting (<0.001 [Wilcoxon signed-rank test]), although the differences were smallest for the age groups 30–39, 40–49 and 50–59 in both sexes, with males demonstrating smaller differences between the equations compared to females (Figure 6c,d).

7 | DISCUSSION

The estimation of GFR has been used widely as an indicator of kidney function. The multiple common approaches to calculating eGFR are all inherently limited in their applicability to individual patients. In particular,

the eGFR determined by the CKD-EPI equation that has been most recently adopted has limited applicability in younger and older patients. Due to its wide-spread use, this has significant implications for individuals at-risk of, or diagnosed with CKD. The EKFC equation was developed to overcome the limitations of the CKD-EPI equation and to provide a better estimation for younger people transitioning into adulthood. Our study aimed to assess the changes in eGFR between the CKD-EPI and EKFC equations using a population of 760 614 Australians with recorded measures of serum creatinine over a 10-year period.

The results show that 90.66% of patients had a lower eGFR when calculated using the EKFC equation compared to the CKD-EPI equation, with the biggest difference occurring in younger and older people with good kidney function (Figure 1). This resulted in an overall increase in the number of individuals classified as having CKD based on current staging guidelines for eGFR. In our limited dataset respective values on albuminuria were not available. Given that it is recommended to consider proteinuria in diagnosis of CKD in the early stages 1–2, the validity of reclassification in these stages is unclear.

In total 12.6% of individuals were classified into a different CKD stage using the EKFC equation compared to CKD-EPI. Of these, the vast majority (97.43%) were classified into a higher (or worse) stage. Of particular interest was the increase in prevalence of more advanced renal impairment (CKD stages 3a–5) from 8.85% with CKD-EPI compared to 11.45% with EKFC reporting. Given the shift into higher risk categories for cardiovascular morbidity and death in the higher stages of CKD, this increase in prevalence has implications for monitoring and referral of patients within specialist services and a potential increase in the need for multidisciplinary care.

The implementation of routine eGFR reporting in Australia[22] and adoption of clinical guidelines by Kidney Health Australia, has helped with interpretation of creatinine levels and facilitate staging of CKD.[20] These guidelines recommend that appropriate referral to a nephrologist should occur when an individual is within CKD stage 3b.[20] Although this study shows that the percentage of reclassification is small, this shift in a small population percentage would overwhelm renal services especially of those reclassified from stage 3a to 3b.

While reclassification of patients into a higher CKD stage would increase the burden on the health system, reclassification into a lower CKD stage may have significant implications for an individual at risk of disease progression. We show that patients in stages 2–3a that are reclassified into a higher stage of disease using EKFC eGFR had significantly faster rate of deterioration (based on eGFR) compared to patients that remained in the same stage or were reclassified into a better stage of CKD. This implies that reclassification using EKFC in these early stages of disease is appropriate for identifying patients at risk of disease progression. While this assumption is limited by a lack of more comprehensive clinical and pathological information and long-term outcomes, the value of EKFC in identifying at-risk patients for early intervention should be considered.

Based on the most recently available cost data for each respective CKD stage, there was a total cost increase of over AUD$27 m for the year 2011 based on the stage of CKD implied by EKFC equation (Table 2). Given that patient costs are usually associated with treatment of presenting symptoms and associated procedures, irrespective of disease classification, this may not reflect a realistic change. However, there may be impact on public health services where there is an increase in referral to tertiary services as a result of more patients reaching the criteria for early-stage disease.

There are several limitations of our study. Data on ethnicity was not included as a variable in the CKD-EPI equation as it was not provided by the pathology provider. In addition, there were also no other data that was available for this study to confirm kidney damage apart from eGFR. This also meant that albuminuria was unavailable to enable assignment of albuminuria categories, which have been demonstrated to have prognostic significance.[8] Although the EKFC equation was not developed on a diverse population, and the impact of different ethnic backgrounds on performance is unclear, the estimated prevalence of African-Australian people is very low (≈≤1.6%),[23,24] and the inclusion of Indigenous patients (estimated prevalence of 3.9% in WA) is unlikely to have biased outcomes.[11] Furthermore there is now a move away from ethnicity-based corrections in algorithms for the prediction of CKD[16,25,26] since they may potentiate structural racism and health disparities. Additionally, our cohort was extracted from a single pathology provider that services a higher proportion of primary care referrals than specialist or tertiary care referrals, and as such there is a limited representation of higher stage CKD cases that are seen in the hospital setting. The impact of a change in eGFR calculation from lower creatinine values remains a target for further investigation. The study would also be strengthened by validation against direct measurement of GFR using both equations.

8 | CONCLUSION

The need for accurate and easy assessment of kidney function remains a priority so that at risk individuals can be detected and appropriate opportunities for intervention and referral identified. Accurate classification is also important for prescribing and predicting healthcare utilization and costs. The evolution of outpatient renal function analysis from consideration of creatinine levels and reciprocal creatinine plots through to staging of renal function based on eGFR measurements has been essential in achieving this. Whilst further validation in the Australian population is required, use of the EKFC equation warrants further clinical investigation for its potential value in suitable populations.

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CONFLICT OF INTEREST

The authors declare no conflict of interest in the subject matter or information discussed in this manuscript.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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APPENDIX A

CKD-EPI equation to estimate GFR (ml/min/1.73 m^2). SCr is serum creatinine in mg/dl, κ is 0.7 for females and 0.9 for males, α is −0.329 for females and −0.411 for males, min indicates the minimum of SCr/κ or 1, and max indicates the maximum of SCr/κ or 1. Note, as ethnicity was not recorded, we were unable to make any adjustments when calculating the eGFR.

$$\text{eGFR} = 141 \times \min\left(\frac{\text{SCr}}{\kappa}, 1\right)^{\alpha} \times \max\left(\frac{\text{SCr}}{\kappa}, 1\right)^{-1.209} \times 0.993^{\text{Age}} \times 1.018[\text{if female}]$$

APPENDIX B

EKFC equation to estimate GFR (ml/min/1.73 m^2). SCr is serum creatinine in μmol/L. To convert to mg/dl, divide by 88.4.

Age	SCr/Q	Equation
2–40 years	<1	$\text{eGFR} = 107.3 \times \left(\frac{\text{SCr}}{Q}\right)^{-0.322}$
	≥1	$\text{eGFR} = 107.3 \times \left(\frac{\text{SCr}}{Q}\right)^{-1.132}$
>40 years	<1	$\text{eGFR} = 107.3 \times \left(\frac{\text{SCr}}{Q}\right)^{-0.322} \times 0.990^{(\text{Age}-40)}$
	≥1	$\text{eGFR} = 107.3 \times \left(\frac{\text{SCr}}{Q}\right)^{-1.32} \times 0.990^{(\text{Age}-40)}$

Q values

Sex	Age	Equation
Female	2–25 years	$\ln(Q) = 3.080 + 0.177 \times \text{Age} - 0.223 \times \ln(\text{Age}) - 0.00596 \times \text{Age}^2 + 0.0000686 \times \text{Age}^3$
Male	2–25 years	$\ln(Q) = 3.200 + 0.259 \times \text{Age} - 0.543 \times \ln(\text{Age}) - 0.00763 \times \text{Age}^2 + 0.0000790 \times \text{Age}^3$
Female	>25 years	$Q = 62\,\mu\text{mol/L}$
Male	>25 years	$Q = 80\,\mu\text{mol/L}$