BMC Nephrology
https://doi.org/10.1186/s12882-026-04878-1
Article in Press

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Received: 10 June 2025
Accepted: 26 February 2026
Published online: 19 March 2026

Cite this article as: Hoy W.E., Diwan V., Wang Z. *et al.* Profiles and outcomes of indigenous patients with chronic kidney disease in renal speciality clinics in the public health system in Queensland, Australia. *BMC Nephrol* (2026). https://doi.org/10.1186/s12882-026-04878-1

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Manuscript ID: cd33d9d7-8dce-4b72-9aaa-ad000c112701 v3.0

Profiles and Outcomes of Indigenous Patients with chronic kidney disease in renal speciality clinics in the public health system in Queensland, Australia.

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Abstract

Background: High rates of chronic kidney disease (CKD) are well recognised in Australia's Indigenous people, but kidney replacement therapy (KRT) registrations give an incomplete view of disease burden and outcomes. We describe profiles and outcomes of Indigenous people with preterminal CKD in the renal specialty practices of the public health system in the state of Queensland, through a prospective cohort study.

Methods: Adults patients with non-dialysis CKD from twelve public renal speciality services in Queensland were recruited to the CKD QLD Registry and followed until the start of KRT, renal death without KRT, or nonrenal death, or until censored in June 2020. Demographic and clinical information, hospital admissions and outcomes were compiled from clinical and administrative data collected by Queensland Health.

Results: 7,595 CKD patients were enrolled. 641 (8.4%) were Indigenous, more than twice their proportion in Queensland's population They lived more remotely than non-Indigenous patients, were more disadvantaged, younger, more often female and more often had diabetes and had 35.3% greater hospital costs. They were 50% more likely to develop ESKF, and when they did, more than twice as likely to start KRT, a function of their younger age. Notably, however, half of the Indigenous and 72% of the non-Indigenous patients with endpoints did not start KRT. Their estimated 4.7-fold increase in incident KRT aligns well with official statistics.

Conclusions: Routinely collected service data reveal a more expansive view of CKD and its outcomes in Indigenous patients under renal specialty care in Queensland. Such surveillance can inform health services planning for CKD patients beyond expectations of KRT needs and can underpin ongoing evaluations.

Key Learning Points

What was known:

- High rates of kidney replacement therapy (KRT) are recognised in Australian Aboriginal people, but, without a systematic surveillance system for CKD before end stage is reached, the scope of the underlying problem is incompletely understood. Comprehensive CKD management plans must not be based exclusively on profiles of the highly selected group who receive KRT.
- In this prospective cohort study, Indigenous and non-Indigenous adult patients with preterminal CKD in public renal practices in Queensland were characterised and followed until an “endpoint” of end stage kidney failure (ESKF), whether or not it resulted in KRT, or a nonrenal death, or a censor date in June 2020.
- Using Queensland Health datasets, we linked individual demographic and administrative information to clinical and biochemical data from routine visits and data on hospital admissions, KRT procedures and deaths. The study captured 12 of the 13 major renal practice sites in Queensland and >80% of estimated prevalent patients in those sites.

This study adds:

- The proportion of Indigenous people in the CKD cohort was more than twice their population representation. Indigenous patients were almost 10 years younger than non-Indigenous patients at recruitment and at endpoints, and lived more remotely, were more profoundly disadvantaged, more frequently diabetic, and had longer, more costly hospital admissions.

- Over follow up, about 37% of patents reached endpoints, which involved ESKF in 82% of Indigenous and 67% of non-Indigenous persons. ESKF incidence was 50% higher in Indigenous patients, and constituted all the significant difference in endpoints between the two groups
- Among those who developed ESFK, 62% of Indigenous and 41% of non-Indigenous persons received KRT, compatible with the younger age of indigenous patients. Those who received KRT represented 51% vs 27% of all endpoints in their respective cohorts, with an adjusted relative risk for Indigenous patients of 2.24.

Potential impact:

- Cohort studies within registries using routine clinical and administrative data can illuminate the broad spectrum of patients with preterminal CKD, their clinical course, the scope of outcomes beyond KRT and distinguish features of different risk groups. Such systems should inform predictions, policy and planning and underpin ongoing evaluations.
- The apparent achievement of equity of provision of KRT to Indigenous Queenslanders with ESKF in the context of age is remarkable considering major challenges of socioeconomic disadvantage and remoteness, but very significant barriers remain to provision of accessible KRT for all Indigenous people who need it.
- Like many populations in epidemiologic transition**,** prevention and mitigation of the excessive burden of CKD in Queensland's

Indigenous people depend on vast improvements in socioeconomic status plus an intense focus on obesity, the metabolic syndrome and diabetes. Newer medications, largely introduced since this study, are probably already conferring additional benefit.

Keywords:

Chronic kidney disease, CKD burden, CKD monitoring, CKD QLD registry, Indigenous Australians

Introduction

High rates of chronic kidney disease (CKD) are well recognised in Australia's Indigenous people. Australia aspires towards equitable access to government funded kidney replacement therapy (KRT) and has an excellent registry of those who start that treatment [1], although there are many challenges to its provision in remote areas. However, monitoring kidney disease burden through kidney replacement therapy (KRT) registrations precludes a view of preterminal CKD, where all the opportunities lie to modify CKD expression and progression; furthermore, exclusive monitoring of KRT ignores ESKF deaths where KRT is not applied as well deaths of "nonrenal" causes in persons whose CKD is not yet terminal. Renal service provision must accommodate these broader perspectives.

We define the characteristics, outcomes and hospital admissions utilization in adult Indigenous persons with chronic kidney disease (CKD) attending public renal specialty practices in the Australian state of Queensland (QLD) who agreed to participate in a registry, called

CKD.QLD. Information was compiled from routine clinical and administrative data sets generated by Queensland Health.

Queensland has a vast area of 1,852,642 sq km, with a diverse range of regions, terrain and climates. Its 2016 population was about 4.7 million. Of these, 186,482 (3.97%) were self-designated as Indigenous Australians: 81.5% were mainland Aboriginal people, 9.2% were Torres Strait Islanders, and 9.3% had Aboriginal and Torres Strait ancestry[2]

Service provision to sparse populations over more remote areas is a major logistic challenge and expense. For health care, paucity of local clinics and regional hospitals and great distances from specialty services and tertiary hospitals are the reality. Many Indigenous people live hundreds of kilometres from any health services, and transport, time and costs of travel by road or air are considerable.

Two scores describing circumstances of Australia's people are the ARIA score (Accessibility/Remoteness Index of Australia categories)[3] and the IRSD score (Index for Relative Socio-economic Disadvantage [4]. The ARIA score is computed from distance by road of residence from "a wide range of goods, services and opportunities for social interaction". One version employs five categories of "major cities", "inner regional", "outer regional", "remote" and "very remote". In 2016, the proportions of Indigenous Australians living in those ARIA categories were 37.4%, 24%, 19.7%, 6.2% and 12.2%, compared with proportions for non-Indigenous Australians of 72.7%, 17.8%, 8.0% ,1.0% and 0.5% respectively [5]. The IRSD score [6] is derived from a range of social and economic conditions based on information from the five-yearly census and is often expressed in quintiles of 1 (the most disadvantaged) through 5, (the most advantaged) of the values for the general Australian population. IRSD scores for non-Indigenous Australians predictably fall in equal fifths, but the distribution is 47%, 21%, 15%, 10% and 5% respectively for quintiles 1 through 5 for Indigenous Australians, reflecting more heterogeneous distribution and much greater overall disadvantage. By this measure Indigenous people are the most disadvantaged people in Australia. Although most Indigenous people in remote areas are very disadvantaged, so too are many Indigenous people who live in major cities and inner regional areas.

Indigenous Australians have lower life expectancies, higher rates of chronic diseases, worse self-reported health, and more hospitalisations than non-Indigenous people. They have much higher rates of kidney disease and its complications [7]. In 2017-2021 the crude rate of starting kidney replacement therapy (KRT) among Indigenous Queenslanders was about 419 per million, compared with the overall Queensland rate of about 106 per million [1].

The Australian New Zealand Dialysis and Transplant Registry (ANZDATA) has continuously documented patients who receive KRT since 1977. However, there are no government supported registries of persons with preterminal CKD, although most of the potential to reduce the kidney failure, kidney deaths and need for KRT lies in the better understanding and management of CKD before it progresses to kidney failure [8,9].

In 2011 we established a registry named CKD.QLD for patients with preterminal CKD who attended the public renal specialty practices in Queensland [10]. We have already published the first overview of patients in that registry[11]. Here we report the profiles, hospitalisations, and outcomes of Indigenous persons in that registry and consider implications for management and future planning.

Methods

Study subjects were drawn from CKD patients in renal specialty practices in Queensland's public health system (Queensland Health). They had been referred to, triaged and accepted into those practices from outpatient clinics (usually general or family practices or other specialty services), or after hospital admissions or emergency department visits, due to a diagnosis of established or problematic CKD, staged according to Kidney Health Australia's CARI guidelines[12]. These renal clinics are staffed by nephrologists and renal nurses, who provide advice on diagnoses or management and endstage planning, as needed: they also participate in preparation for, and elective introduction of KRT in all persons with advancing CKD, if that treatment is chosen.

In 2009, all the public renal specialty practices of Queensland Health were invited to participate in the newly emerging CKD.QLD Registry and gave estimates of their prevalent non-dialysis CKD patient populations, which totalled about 11,000 patients. Between June 2011 and June 30th 2018, during their normal clinical visits, patients aged ≥18 years with an established diagnosis of CKD who were not on KRT were invited by clinical staff, as time allowed, to join the registry, with written informed consent.

Clinical and demographic data were supplied by practice sites and additional data extracted as needed from their Queensland Health clinical records and administrative datasets. Indigenous status assignment was by self-report. Patients were followed from individual date of consent until the endpoints of end stage kidney failure (ESKF), reflected in the start of KRT or in renal death without KRT, or until nonrenal death, or until the censor date of 30th June 2020. For patients who received an interim period of dialysis before a transplant could be performed, the endpoint of the follow-up period was the first date of ESKF. All hospital admissions, length of stay and total costs were documented.

CKD patients already on KRT were not enrolled in the CKD.QLD Registry: in Australia all persons enrolled in maintenance KRT programs are followed through the ANZDATA registry [1,14]. If CKD registry patients started KRT during follow-up they were documented as developing a KRT endpoint when KRT began and were then censored from further participation in this study. Patients with a history of acute kidney injury were only included in the CKD.QLD Registry if, and when, they subsequently developed CKD.

Queensland Health assigns and maintains a unique identification number for everyone who encounters its services, and a longitudinal record is maintained for individuals potentially over the life course. Queensland Health’s Statistical Analysis and Linkage Unit (SALU), linked the individual CKD.QLD registry to the following collections: Queensland Hospital Admitted Patient Data Collection (QHAPDC), Queensland Activity Based Funding (ABF) Model Output Data, Death Registrations from the (Qld) Registry of Births, Deaths and Marriages and Cause of Death Unit Record File from the Australian Coordinating Registry, informing on hospital admissions, and institution of KRT and deaths. We have previously published these data linkage processing methods[15]. QHAPDC data included the date of admission, length of hospital stays and primary and associated reasons for hospital admissions. Each admission was generally assigned a single principal diagnosis (ICD-10-AM code), with options for multiple associated diagnoses. We grouped the principal causes of admissions into 6 categories according to apparent clinical disciplines and disorders. A combination of those 6 categories and 11 specific ICD-10AM chapters was used to compile 17 final "operational" categories that we called the "CKD.QLD grouping", as described previously [16].

Hospital coders assign principal (underlying) and associated causes of deaths based on ICD-10 vol K36 specifications. We defined ESKF as the start of KRT, documented in QHAPDC data, that was sustained for at least three months, or a renal death with diagnoses compatible with terminal renal failure without sustained chronic dialysis. Nonrenal deaths were those to which nonrenal principal causes of death had been assigned (usually other chronic diseases, often cardiovascular, malignancies, ageing, frailty and dementia[17 18)] and the accompanying CKD was potentially an associated diagnosis.

ARIA scores were derived from Sydney University's Psycho-oncology Co-operative Research Group's ARIA Look Up Tool, (https://www.pocog.org.au/aria/default.aspx), employing the five categories previously noted, with the highest category chosen if there were multiple ARIA scores for one postcode. For IRSDs we used Excel data download sheets where ABS had assigned a SEIFA score, decile and IRSD quintile for all suburbs of Australia in 2016 [5].

Stata 16.2 (Stata Corp. Stata Statistical Software: Release 16.0, College Station. TX: Stata Corp LP, 2016) was used for analyses. Hospital admission parameters and incidence rates for “endpoints” were expressed as events per 100 person years (95%CI) to account for the variable follow-up periods, and incidence rates were compared by Indigenous status using Incidence Rate Ratios (IRRs).

Original registry ethics approval was granted in 2010 by the Queensland Health Central Human Research Ethics Committee (HREC/10/QHC/41) and The University of Queensland (No. 20110000290). In 2015, ethics committee oversight was transferred to the Royal Brisbane and Women's Hospital Committee (HREC/15/QRBW/294). A further Public Health Act approval (QCOS/029817/RD006802) was granted in 2017 to release care data of the QH Statistical Analysis and Linkage Unit.

Results

All 13 major renal practice sites originally agreed to participate in the registry. Few individual patients declined (maximum 7, fewer than1 per

1,000). One metropolitan practice site withdrew in mid-2018, after a data-related dispute. The final CKD.QLD cohort, and those included in this analysis, consisted of 7,595 people from 12 of the 13 major public renal practice hubs in the state. These represent about 84% of the estimated CKD patients in those sites.

In the final cohort, 641 patients were Indigenous and 6,964 were not Indigenous. **Table 1** summarises their characteristics by Indigenous status at recruitment into the CKD registry.

Table 1: Characteristics of CKD patients at consent by Indigenous status

	Indigenous N (%)	Non-Indigenous N (%)	P values
Gender			
Males	308 (48.1)	3,785 (54.4)	0.0022
Females	333 (52.0)	3,169 (45.6)	0.0019
Age on enrolment, years			
median (95%CI)	61.1 (51.5-69.7)	69.3 (57.9-77.4)	<0.001
<45 yr	95 (14.8)	759 (10.9)	0.0028

≥45 to <55 yr	108 (16.9)	697 (10.0)	< 0.0001
≥55 to <65 yr	197 (30.7)	1,199 (17.2)	< 0.0001
≥65 to <75 yr	153 (23.9)	2,069 (29.8)	0.0017
≥75 yr	88 (13.7)	2,230 (32.1)	< 0.0001
ARIA Categories*			
Major city	71 (11.2)	2,647 (38.1)	<0.0001
Inner regional	63 (9.9)	1,787 (25.7)	<0.0001
Outer regional	331 (52.0)	1,836 (26.4)	<0.0001
Remote & very remote	171 (26.9)	673 (9.7)	<0.0001
IRSD Quintiles#			
Q1 Highest	7 (1.1)	532 (7.7)	<0.0001
Q2 High	112 (17.6)	1,903 (27.4)	<0.0001
Q3 Middle	96 (15.1)	1,471 (21.2)	0.0003
Q4 Low	202 (31.7)	1.747 (25.2)	0.003
Q5. Lowest	221 (34.6)	1,283 (18.5)	<0.0001
Obese (BMI>30)*	159 (67.7)	2169 (50.9)	<0.0001
Diabetes**	413 (64.6)	3,151 (45.6)	<0.0001
Primary renal disease			
Diabetic nephropathy	262 (40.9)	1,611 (23.2)	< 0.0001
Glomerulonephritis	72 (11.2)	831 (12.0)	0.55
Genetic renal disease	18 (2.8)	384 (5.5)	0.0034
Other	81 (12.6)	1,176 (16.9)	0.0051
Renal vascular disease	136 (21.2)	2,136 (30.7)	< 0.0001
Uncertain	72 (11.2)	816 (11.7)	0.7059
CKD stages at recruitment			
1. eGFR ≥90	63 (9.8)	472 (6.8)	0.0045
2. eGFR 60-<90	89 (13.9)	764 (11.0)	0.0262
3A. eGFR 45-<60	98 (15.3)	1,311 (18.9)	0.025
3B. eGFR 30-<45	169 (26.4)	2,174 (31.3)	0.0102
4. eGFR 15-<30	158 (24.7)	1,744 (25.1)	0.8231
5. eGFR <15	64 (10.0)	489 (7.0)	0.0051
Albuminuria/proteinuria***			
Normal	75 (17.5)	1,746 (29.1)	< 0.0001
Microalbuminuria	95 (22.1)	1,900 (31.7)	< 0.0001
Macroalbuminuria	259 (60.4)	2,358 (39.3)	

Table 1A. *BMI available in 235 Indigenous and 4,263 non-Indigenous persons. **Diabetes available for 639 Indigenous and 6,913 non-Indigenous. *** Albuminuria/proteinuria available in 429 Indigenous and 6004 non-Indigenous persons. #IRSD for 638 Indigenous and 6,935 non-Indigenous.

Among Indigenous patients, there were relatively more females. They were substantially younger at recruitment. In each group, most (63% and 63.4%) had more advanced CKD (stage 3B, 4 and 5). Those with earlier stage disease (stages 1, 2 and 3A, who constituted 36.8% of the cohort, (39% of the Indigenous patients and 36.6% of the nonindigenous patients, p=0.233)) were younger than those with more advanced disease 58.5 (SD16.3) vs 69.8 (SD13) years, p<0.0001) but had the same gender representation (53.1 vs 54.3% male, p=0.233). They had usually been referred for diagnostic or therapeutic advice or had familial or genetic renal diseases. Indigenous patients referred in those earlier stages were also enriched for diagnoses of GN and disease of unknown cause, and nonindigenous patients with earlier stage referrals had higher proportions of GN, GRD and disease of unknown cause than later stage referrals. Indigenous patients were more often obese than non-Indigenous patients, although BMI recording was deficient, mostly due to absent recording of height. Indigenous patients had higher proportions of diabetes and diabetic nephropathy and higher rates of macroalbuminuria/proteinuria.

Figure 1A illustrates the more remote residence of Indigenous than non-Indigenous persons in the general Queensland population, and, for each, a relatively greater degrees of remoteness for those in their CKD.QLD populations.

Figure 1A. ARIA codes in the Queensland population and in CKD.QLD by Indigenous status

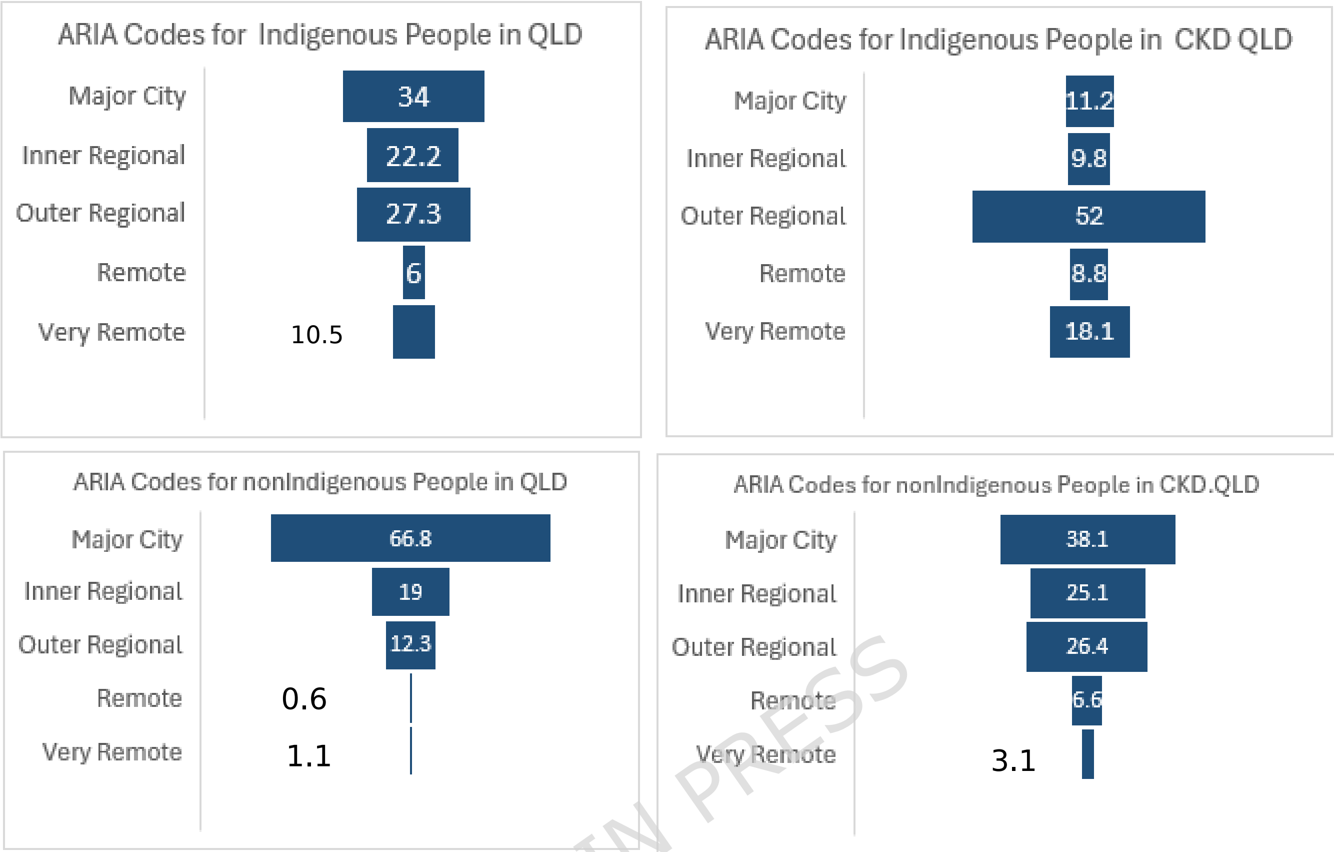


Figure 1B. IRSD Codes in Queensland's population and CKD.QLD patients by Indigenous status.

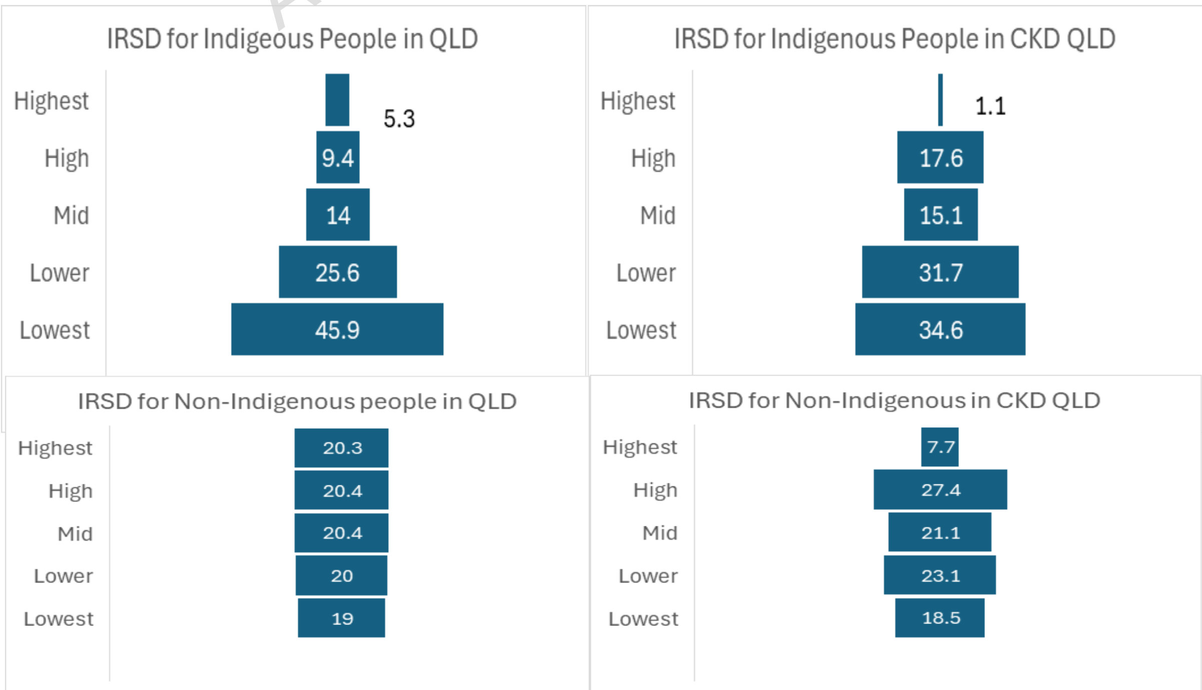


Figure 2A shows a gradation, in both Indigenous and nonindigenous patients, in median ages on enrolment into the registry, according to the recorded primary renal disease. These ages ranged from GRD and GN (the lowest) to renal vascular disease (the highest). However, in every category, Indigenous patients were younger than non-Indigenous patients. Figure 2B shows similar differentials in ages at endpoints among those who reached endpoints during the observation . Figure 2A shows that younger age at recruitment was reflected in every category of primary renal disease.

Figure 2A. Age at consent of CKD.QLD patients, by primary renal disease and Indigenous status

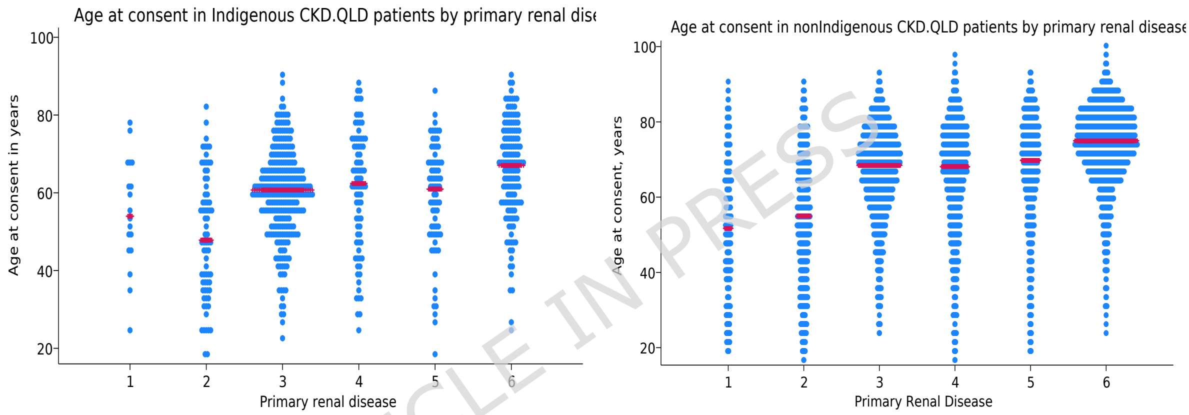
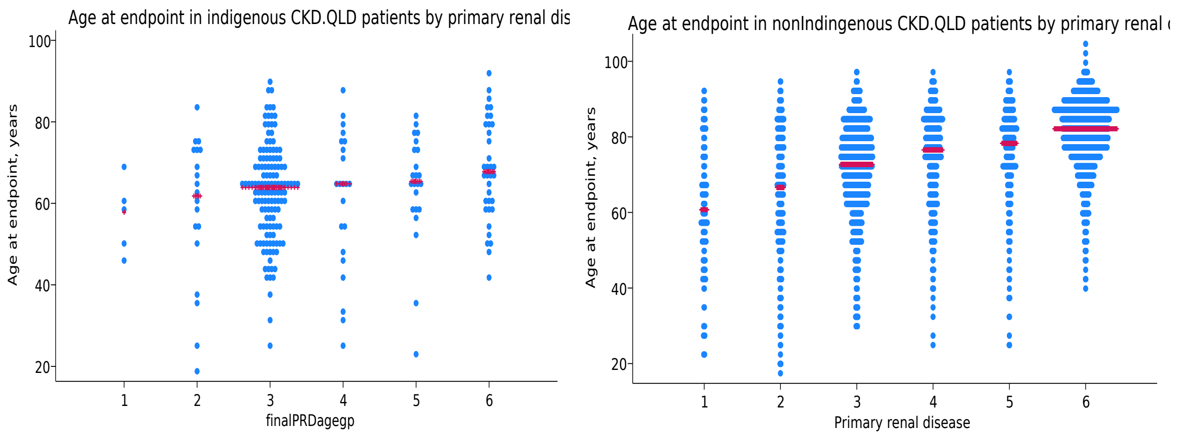


Figure 2B. Age at endpoint of CKD.QLD patients by primary renal disease and Indigenous status



Primary Renal Disease: 1=genetic renal disease1; 2=glomerulonephritis; 3=diabetic nephropathy; 4=other; 5=uncertain; 6=renal vascular disease.

Endpoints by June 2020.

Patients were followed from their individual dates of enrolment into the Registry until the dates of individual endpoints or until the censor date, whichever occurred first. Follow up intervals ranged up to 9.43 years, with means and medians of 4.72 years and 3.36 years respectively. Average follow up was shorter for Indigenous than non-Indigenous patients, shown in Table 2A, due to later enrolments in some hard-to-reach settings, and the faster progression of Indigenous CKD patients to endpoints, described below.

Table 2A also shows that ESKF (KRT and renal death without KRT) comprised 82.4% and 66.5% of endpoints in Indigenous and nonindigenous CKD patients respectively, with an estimated incidence rate 39% higher in Indigenous patients. Conversely, 17.6% and 33.4% of these groups respectively reached nonrenal endpoints (died primarily of nonrenal causes). Among people who developed ESKF, as shown in Table 2B, a much greater proportion of Indigenous than non-Indigenous patients started KRT (62% vs 41%). The higher ESKF incidence rate and great proportion of those with ESKF who started KRT resulted in a KRT incidence rate in Indigenous patients 2.24 times that of nonindigenous patients.

Table 2A. Endpoints during follow up period

	Indigenous 641 enrolees	**Non-Indigenous 6,954 enrolees**
FU person years: total	2,424.3	33,518.3
FU person years, mean (95%CI)	3,776 (3.6-4.0)	4.80 (4.7-4.9) 3.73 (3.7-3.8)

FU person years, gmean (95%CI)	2,747 (2.6-2.9)		
All ESKF, n, % endpoints	192 (82.4%)	1,766 (66.5%)	
Incidence rate	7.93 (6.9-9.1)	5.3 (5.0-5.5)	IRR 1.39, p<0.000
Nonrenal death n, % endpoints	41 (17.6%)	887 (33.4%)	
Incidence rate	1.73 (1.3-2.3)	2.66 (2.4 2.8)	IRR 0.65, p<0.006
Any endpoint, n	234	2,653	
Incidence rate	9.7 (8.5-11.0)	7.9 (7.7-8.3)	IRR 1.22, p<0.000

Incidence rates- per 100 person years (95%CI); gmean-geometric mean; IRR-Incidence rate ratio.

Table 2B. Types of ESKF endpoints

	Indigenous	**Non-Indigenous**	
KRT, n	119	725	
% of all endpoints	50.9%	27.3%	
% of ESKF endpoints	61.9%	41.1%	
Incidence rate	4.9 (4.1-5.9)	2.2 (2.0-2.3)	IRR 2.24, p<0.001
Renal death, no KRT, n	73	1,041	
% of all endpoints	38.2%	39.1%	
` **% of ESKF endpoints**	31.2%	58.9%	
Incidence rate	3.0 (2.4-3.8)	3.1 (2.9-3.3)	IRR 0.957, p=0.78

Incidence rates-per 100 person years (95%CI), IRR-Incidence Rate Ratio

Table 3 shows the eGFR at consent and the ages at consent and at endpoints in patients who had reached endpoints by the censor date.

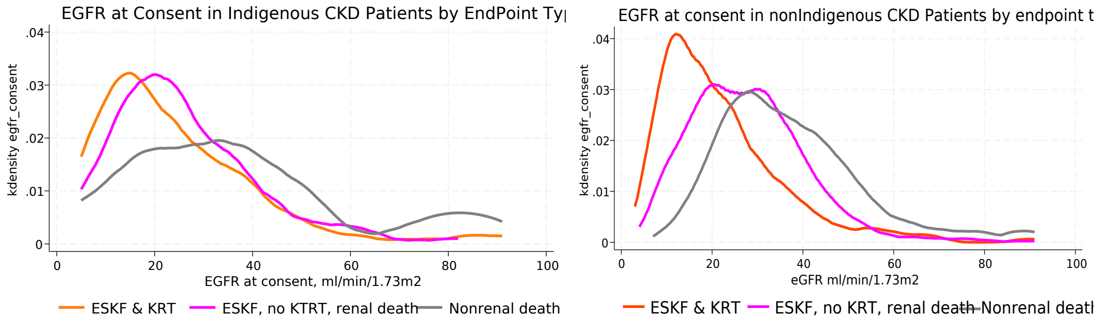
Table 3. eGFR at consent and age at consent and at endpoint by type of endpoint type in CKD patients, by Indigenous status.

Indigenous patients	KRT N=119	Renal death, no KRT N=73	Nonrenal death N=42
eGFR at consent*	20.0 (17.0-22.5)	22.0 (19.0-25.3)	29.2 (24.0-37.1)
Age at consent, yr	52.9 (50.1-52.8)	67.2 (64.3-70.1)	63.8 (60.5-67.2)
Age at endpoint, yr	55.0 (52.4-57.6)	69.7 (66.8-72.7)	66.6 (63.2-70.1
Non-Indigenous patients	KRT n=725	Renal death, no KRT n=1,041	Nonrenal death N=887
eGFR at consent*	18.8 (17.7-19.3)	24.9 (24.2-25.7)	36.1 (35.6 (36.5)
Age at consent	56.2 (55.1-57.3)	75.7 (75-76.3)	74.4 (73.7-75.2)
Age at endpoint	58.9 (57.8-60.1)	77.9 (70.1-78.7)	77.9 (77.1-78.7)

*eGFR: in ml/min/1.73m^2 ; age is median (95%CI)

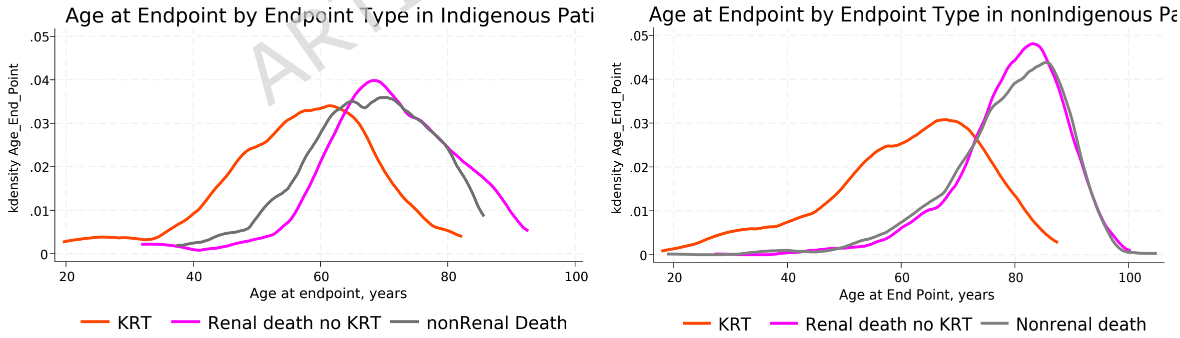
In both Indigenous and nonindigenous patients, eGFR at consent was lower in those who ultimately developed KRT or died a renal death without KRT than in those who ultimately died a nonrenal death, as also shown in more detail in Figure 3.

Figure 3. eGFR on enrolment into the CKD.QLD registry according by type of endpoint reached, by Indigenous status



Ages at endpoints. Ages at endpoints were strikingly associated with the types of endpoints, as summarised in Table 3 and further elaborated in Figure 4A. In both Indigenous and nonindigenous CKD.QLD populations, it was clear those who started KRT were younger when they developed their endpoints than those who died of renal failure without KRT than those who died a nonrenal death.

Figure 4A. Distributions of ages at endpoint-by-endpoint type in Indigenous and nonindigenous CKD.QLD patients.



In addition, among persons who developed endpoints, Indigenous patients were younger than non-Indigenous patients for every type of endpoint. For easier discernment, direct comparisons are shown in Figure 4B. Indigenous patients were on average about 4 years younger than nonindigenous patients when they started KRT, 8 years younger if they died of renal failure without KRT and 12 years younger when they died a nonrenal death.

Figure 4B. **Age at endpoints by endpoint type and Indigenous status.**

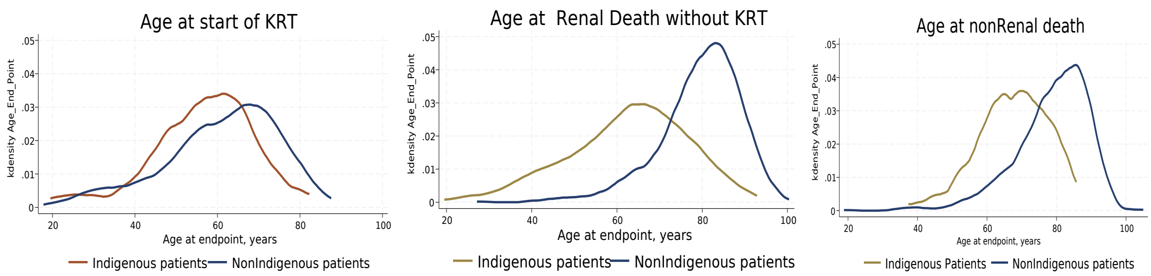
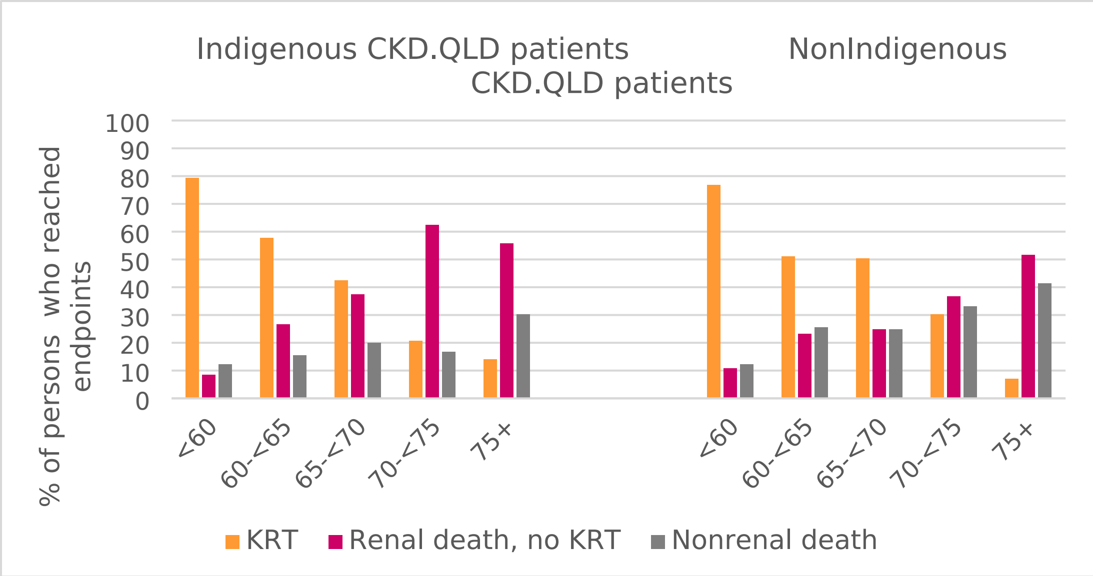


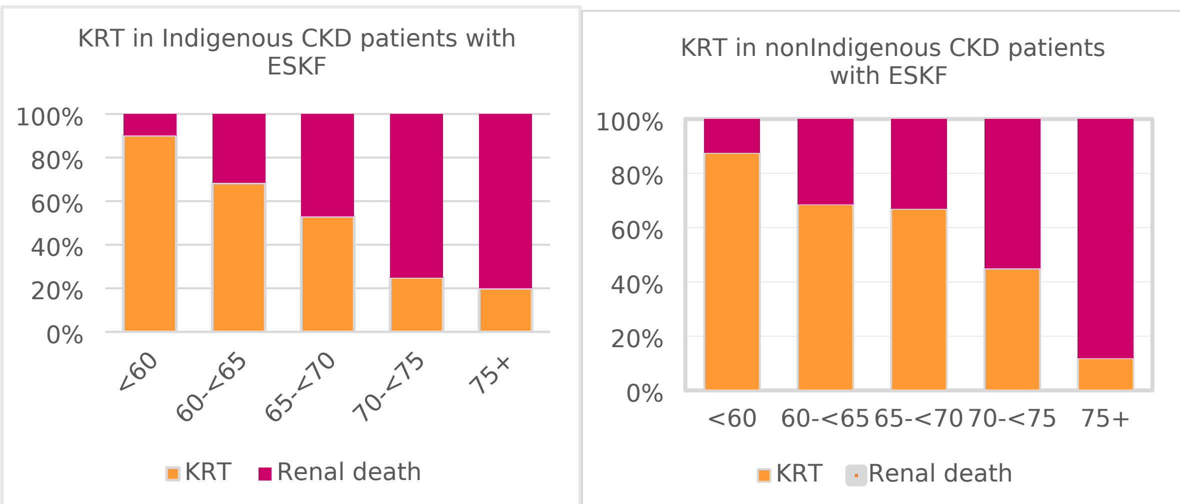
Figure 5A shows the proportions of the three endpoint types experienced by patients who reached an endpoint before the censor date by Indigenous status. In both groups there was a steady decrease in the proportions who started KRT at progressively higher ages, along with generally higher proportions who died renal deaths without KRT or who died nonrenal deaths.

Figure 5A. Changing proportions of endpoint types by age groups at endpoint in CKD.QLD patients by Indigenous status.



With a focus exclusively on ESKF outcomes, Figure 5B shows the progressively lower adoption of KRT as an intervention for ESKF at progressively higher ages, and with no significant difference by Indigenous status.

Figure 5B. Proportions of CKD.QLD patients who developed ESKF and went onto KRT by age group at endpoint and Indigenous status.



Baseline CKD stage and prediction of endpoints.

The rate of development of ESKF was strongly correlated with CKD stage at enrolment in Indigenous and nonindigenous persons. However, for CKD stages 3B, 4 and 5 at recruitment, the cumulative loss of persons to ESKF was perceptibly greater in indigenous than non-Indigenous CKD patients, as show in Figure 6A. Nonrenal deaths, (as assigned by hospital coders) however, were not strongly correlated with baseline CKD stage, as shown in Figure 6B, and were more prominent among Indigenous than nonindigenous patients only for persons who already had advanced CKD (stage 5) at time of enrolment.

Figure 6A. Survival from ESKF of Indigenous and non-Indigenous CKD.QLD patients by CKD stage at consent.

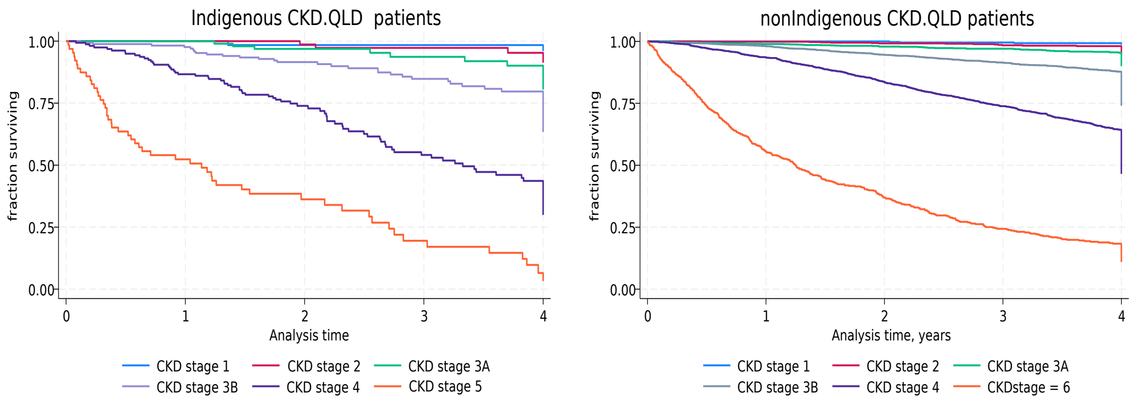


Figure 6B. Survival from nonrenal death of Indigenous and non-Indigenous CKD.QLD patients by CKD stage at consent.

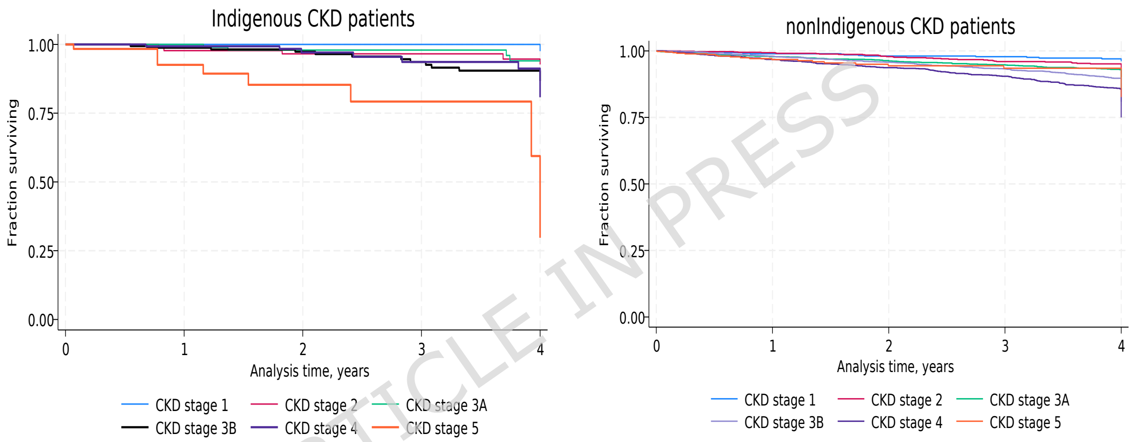


Table 4 shows that the incidence rates of ESKF on follow-up were higher in Indigenous than nonindigenous patients for every stage of CKD at enrolment, although the differences for those enrolled at stages 1&2 and stage 5 were not significant. For all recruitment stages combined, the hazard ratio (CI) of Indigenous relative to nonindigenous patients for ESKF without adjustments was 1.48 (1.28-1.72), p<0.001, adjusted for eGFR at consent it was 1.57 (1.35-1.82), p<0.001 and adjusted for eGFR at consent, age at consent, gender, diabetes and albuminuria/proteinuria at consent it was 1.51 (1.27-78), p<0.001.

Table 4. Incidence rates of ESKF per 100 person years in CKD.QLD patients by Indigenous status and CKD stages at consent.

CKD stage at consent	Incidence rate Indigenous	Incidence rate non-Indigenous		Hazard ratio (95% CI)	
Stages 1&2	0.92	0.53	P=0.218	1.79 (0.8-4.0)	P=0.57
Stage 3A	2.71	1.43	P=0.051	1.96 (1.08-3.51)	P=0.026
Stage 3B	6.15	4.06	P=0.142	1.61 (1.17-2.21)	P=0003
Stage 4	17.8	10.8	p<0.0001	1.76 (1.39-2.21)	P<0.001
Stage 5	58.9	43.2	P=0.041	1.24 (0.92-1.66)	P=0.145

Incidence rates- persons who developed ESKF pr 100 person years:
HR (CI): hazard ratio (95% confidence intervals)
Adjusted for age at consent, gender, diabetes, proteinuria/albuminuria and eGFR at consent.

Hospital admissions.

Among the Indigenous CKD patients, there were 4,398 hospital admissions, a total Length of Stay (LOS) of 18,069 days and total costs of AUD 30.5 million. Among non-Indigenous CKD patients, there were 55,396 admissions, 211,322 days LOS and total costs of AUD $311 million. The annualised rates of admissions, hospital days and hospital costs in Indigenous patients of 182, 747 and $1,260,000 respectively were 9.5%, 18% and 35.2% higher than for in non-Indigenous CKD patients (166, 633, and $931,648 respectively).

For Indigenous CKD patients, the leading five drivers of hospital costs by principal diagnosis were CVD diseases, kidney and related conditions, respiratory system, injuries/fractures/

poisonings, and diabetes and related. For non-Indigenous CKD patients, the leading five causes were CVD diseases, injuries/fractures/poisonings, kidney and related, neoplasm and cancers and respiratory system disorders.

Among Indigenous CKD patients, diabetes-related admissions and costs were dramatically higher with greater remoteness, while total admissions, total hospital costs, multiple day admissions, diabetes associated admissions and emergency department admissions were all strongly correlated with greater socioeconomic disadvantage, shown in Table 5

Table 5. Admissions and costs per 100 person years by IRSD Quintiles for Indigenous Patients with CKD.

	All admissions		>1-day admissions		Emergency admissions		Diabetes-related Admissions	
IRSD Quintiles	**Admissions**	**Costs $**	**Admissions**	**Costs $**	**Admissions**	**Costs $**	**Admissions**	**Costs $**
Highest	221.1	6,181	45.6	389,048	70.2	313,909	3.5	41,403
High	180.5	11,037	71.4	905,324	86.1	583,057	4.9	45,276
Middle	190.9	13,320	89.6	1,155,188	88.9	671,995	4.3	30,198
Low	166.0	11,942	75.5	1,037,457	81.5	728,426	7.5	140,485
Lowest	188.5	13,808	96.8	1,201,971	100.0	723,271	11.1	119,303

Discussion

This cohort study employed a unique registry constituted from practice-based data to define the profiles and outcomes of patients with preterminal (non-dialysis) CKD recruited from public renal practices in a one large Australian state. That view should inform the service needs of persons with established/advancing CKD, beyond the usual narrow focus on patients who seem destined for, or elect, KRT. “Terminal” outcomes assessed included all those who developed ESKF, whether or not they started KRT, as well as those whose principal cause of death had a nonrenal assignment.

With an estimated >80% patient participation, the findings are robust, and consistency with published government KRT incidence rates suggest that the data are of good quality. Similar ongoing surveillance systems are easily constructed where clinical and administrative data are captured electronically.

This is the first description of Indigenous persons with well-established and preterminal CKD in public renal specialty practices in any Australian state, their comparison with contemporaneous non-Indigenous CKD patients in the same practices and their progression to death or kidney failure. It is also the first analysis of hospital admissions of Indigenous people with well-established but preterminal CKD. The description of ARIA and IRSD status in CKD.QLD registry patients is also new information.

Indigenous people were represented in the CKD.QLD registry with double the relative frequency of non-Indigenous people in Queensland. They were strikingly concentrated in more remote areas and had much greater socioeconomic disadvantage. They were younger than non-Indigenous CKD patients, more often female and more often had diabetes and diabetic nephropathy. They had 9.5% more hospital admissions, 18% greater LOS and 35.3% higher annualised hospital costs. They were 50% more likely to develop ESKD than non-Indigenous CKD patients, and almost twice as likely to start KRT than non-Indigenous ESKD patients.

Application of the doubled prevalence of Indigenous people in the registry relative to the background Indigenous population to their 2.24-increase in risk for KRT relative to non-Indigenous CKD patients produces an estimated 4.48 risk exacerbation for KRT in Indigenous vs non-Indigenous people in Queensland. This aligns well with the >4-fold risk exacerbation documented through the ANZDATA Registry. This supports the integrity of the registry's data and mechanisms.

The composite endpoint of ESKF encompasses terminal renal failure independent of the institution of KRT. Given the great variation in the application of KRT among CKD patients who develop renal failure, ESKF is the appropriate yardstick for measurement and comparisons of renal failure burden within and across populations, regions and countries. It is also the more inclusive endpoint for modelling risk for renal failure risk, as we have done here.

The poor socioeconomic status (SES) of Indigenous Queenslanders is well known. This study shows that Indigenous CKD patients were even more disadvantaged than the background Indigenous population and were remarkably more disadvantaged than non-Indigenous CKD registry patients. Furthermore, among Indigenous CKD patients, greater socioeconomic disadvantage was strongly correlated with more hospital admissions and costs, especially multiple-day hospital admissions, diabetes-related admissions, and admissions through the emergency department. The higher rates and proportions of multiday admissions in Indigenous patients probably reflect more advanced CKD and coexisting illness, especially diabetes, which increases with remoteness, as well as extended lengths of stay when readmission is anticipated, and in patients who live far from certain services. Emergency visits are more frequent if elective visits are more restricted.

Studies in various populations support the association of CKD with poverty and disadvantage [20, 21, 22, 23, 24, 25]. Cass et al pioneered this perspective in Australia generally and Indigenous people in particular using ANZDATA registrations of KRT patients as the marker [22,23]. Ritte et al, in a study of 575 Aboriginal adults from >20 sites in urban, regional and remote settings in Northern, Western and Central Australia, using individual level ascertainment of socioeconomic status, showed that reduced kidney function (<60% of "normal") was associated with 3.24-fold likelihood of living in the most remote areas and with the lowest socioeconomic status relative to Aboriginal people who lived in major cities and/or with least deprivation [24].

The complex web of factors contributing to high risk for chronic disease and their complications in low socioeconomic environments is discussed elsewhere.[20,21.] For Indigenous people, chronic distress associated with disruption of their traditional social, and cultural world view and their often-forcible displacement is very real. In our demonstration of the multideterminant nature of CKD in the Indigenous community[26], CKD's association with markers of higher body weight or adiposity was particularly strong. Such changes in body habitus[27] attest to their participation in "The Global Nutritional Transition", as coined by Popkin et al [28]. The broader literature now confirms that overweight and obesity are prominent risk factors for CKD [29], as well as for other common chronic diseases, so that their containment must be central to any preventative strategy.

Beyond disease risk, impaired access/utilisation of quality health services is a major consideration. In remote areas, obvious challenges include sparse facilities, limited supply and rapid turnover of health care personnel, long travel distances, formidable transportation costs, lack of mobile phones and phone credit, as well as language barriers. But a myriad of impediments can also apply in more densely populated areas and metropolitan setting, and include lack of vehicles and fuel, difficulties with public transport, work or childcare commitments, reluctance to miss work, mandatory payments or copayments for visits, medicines and supplies, lower general literacy, poor health literacy, communication problems, (e.g. where English is not the first language), and fear and mistrust of the health system.

Although these considerations apply to health conditions more broadly, CKD attracts especial attention due to the complexity and costs of delivery of KRT for those assessed suitable for that treatment. Furthermore, it is increasingly appreciated that rates of CKD mark "the force of all-cause mortality" within populations [27]. In a recent US National Health Survey[28], self-reported kidney disease was associated with 27 out of 54 specific causes of the 9,564 deaths recorded. Reductions in overall mortality, which is already occurring in Australian Indigenous people [29], will almost certainly flag progressively better kidney health, and vice versa. It is hoped that early interventions, flowing from protocols of chronic disease screening in primary care, might accelerate that trend [30].

The CKD.QLD Registry is a good platform for designing and evaluating new policies and practices. Better outcomes are expected with the recently expanded availability of newer agents within Queensland public health services (SGLT2 inhibitors, DPP-4 inhibitors, GLP-1 inhibitors, and newer mineralocorticoid inhibitors)· which are supplementing current regimens of renin angiotensin blockade, blood pressure and metabolic management and cardiovascular protection [8]. The registry also allows comparisons with other CKD populations, nationally and globally, in which the composite outcome of ESKF will generally be of broader relevance than the subcategory of KRT.

Limitations of this study include omission from the CKD.QKD registry of CKD patients who attended private renal practices for most of their course, and loss to follow up of CKD.QLD recruits through migration out of the state of Queensland. However, these will have little effect on profiles of Indigenous CKD patients, as they infrequently receive care exclusively in the private system, and their migration out of state is minimal [31]. Moreover, there is scant information on renal transplants recipients in this study. The literature on renal transplantation in Indigenous Australians is growing [32,33], but is not further developed here. Persons destined to receive a transplant are, or course, included in the CKD.QLD study cohort, but their endpoint date within the follow-up period is the development of ESKF, which usually occurs months or years before transplantation, except for occasions of pre-emptive living donor transplantation, which has been vanishingly rare in Indigenous CKD patients here.

Health care providers express the need for more KRT facilities for Indigenous people in Queensland, most especially in more remote areas. There are many formidable challenges in providing equitable access to KRT, and, for patients and families, to enduring long term KRT in remote and disadvantaged settings. However, our data suggest that amongst persons who develop ESKF, the proportions who receive KRT are similar for Indigenous and non-Indigenous persons when matched for age group. This alone is a remarkable achievement. Meanwhile efforts continue to delay or prevent ESKF, to expand treatment options and to supply equitable access to KRT [34], despite sometimes daunting challenges.

Acknowledgements

Many thanks to Chris Banney, Leanne Brown, Katrina Duff, Stella Green, Murthy Divi, Stamatina Katsanevas, Erica Lennan, Valli Manickam, Chetana Naresh, Andrea Pollock, Vikas Srivastava, Ada Stevenson, John Killen, Lois Burlund, Andrea Rolfe, Rebecca Barton, Joise Skewes, Michele Harvey, Rachael Brown, Balaji Hiremagalur, Lorraine Bubblitz, Bernadette Taylor, Janine Hale, Sonny Huynh, Anitha Dinesh, Robyn Moyle, Cassandra Stone, Anne Dunne, Andrew Winn, Anne Graham, Peter

Miach, Barbara Harvie, and Mandy Zweedyk, and all the other staff in the renal practices who participated in CKD.QLD. It is a major feat to fit the extra functions and responsibilities of sparsely funded studies into the activities of desperately busy renal clinics which serve patients of complex needs. Those Queensland Health staff helped launch the project and keep it afloat, the quality of their work was impeccable and their support for the patients was unwavering. We are immensely grateful to all the patients who participated in the CKD.QLD Registry and proud of the >99% consent rate to join the registry.

We thank the following teams from Queensland Health for the pertinent datasets and data linkage: the Statistical Analysis and Linkage Unit team, Queensland Hospital Admitted Patient Data Collection team, Queensland Activity Based Funding Model Output Data team, and Registry of Births, Deaths and Marriages and Cause of Death Unit Record team. We have learned that the integrity of their data and processes is second to none.

Declarations

Competing or Financial Interests

The authors have no competing interests as defined by BMC, or other interests that might be perceived to influence the results and/or discussion reported in this paper.

Consent for publication

Not applicable

Data Availability

The datasets analysed during the current study are not publicly available. They belong to QLD Health, the public health service provider, who made them available to this study under conditions of privacy and confidentiality that do not allow such sharing. The dataset is enormous, with multiple data points on more than 7600 people. It contains sensitive information about their health status and healthcare-seeking behaviours. QLD Health feels that, even when specific individual identifiers are used, information about demographic features, Indigenous status, and place of residence can result in identification of specific individuals, particularly of Indigenous people who live in remote areas. This matter could be taken up further with the Information and Statistical branch of QLD Health if deemed absolutely necessary.

Funding Statement

Establishment and operational funding of CKD.QLD was provided by the NHMRC’s Australian Fellowship award to Hoy (“Chronic disease in high-risk populations”, NHMRC 511081), the NHMRC’s Centres of Research Excellence program through the NHMRC CKD.CRE

(APP1079502), by the Colonial Foundation (Melbourne, Australia), by AMGEN Australia and by Queensland Health. None of these funding bodies had any role in the design of the study and collection, analysis, nor in interpretation of data or writing the manuscript.

Conflict of interest disclosure and declaration

The authors have nothing to disclose. This manuscript has not been published previously in whole or part, except as an abstract.

Ethics Statement

Original registry ethics approval was granted in 2010 by the Queensland Health Central Human Research Ethics Committee (HREC/10/QHC/41) and The University of Queensland (No. 20110000290). In 2015, ethics committee oversight was transferred to the Royal Brisbane and Women's Hospital Committee (HREC/15/QRBW/294). A further Public Health Act approval (QCOS/029817/RD006802) was granted in 2017 to release care data of the QH Statistical Analysis and Linkage Unit.

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