

Volume 27, No 1, 2024, 70-78

### ORIGINAL ARTICLE

## Sex disparity in the uptake of kidney replacement therapy in South Africa

Kutlo Motlhobogwa<sup>1</sup>, Kathryn Manning<sup>1</sup>, M Razeen Davids<sup>2</sup>, Elmi Muller<sup>3</sup>, Tinus du Toit<sup>1</sup>

<sup>1</sup>Department of Surgery, University of Cape Town, Cape Town, South Africa; <sup>2</sup>Division of Nephrology, Department of Medicine, University of Stellenbosch, Cape Town, South Africa; <sup>3</sup>Faculty of Medicine and Health Sciences, University of Stellenbosch, Cape Town, South Africa.

### ABSTRACT

**Background:** Sex disparity in kidney replacement therapy has been extensively studied globally. However, the situation in Africa, particularly in South Africa, remains poorly understood. This study aims to fill this knowledge gap by recording a comprehensive analysis of prevalent and incident KRT patients in South Africa, shedding light on potential disparities between the sexes.

**Methods:** This retrospective cohort study used data from the national kidney replacement therapy registry, to examine potential sex disparities. We analysed prevalence data on 31 December 2017 and incidence data from 1 January 2013 to 31 December 2017. Specifically, we calculated sex-specific prevalence, annual incidence, and cumulative incidence per million population (pmp), to gain insights into the patterns and trends related to kidney replacement therapy among the sexes.

**Results:** On 31 December 2017, 10 745 patients with a median age of 52.6 years (interquartile range 41.8-62.3 years) years were receiving KRT, of whom 40.4% were women. A significantly lower proportion of women received KRT than men (148.7 vs 229.4 pmp; P = 0.001). On further analysis, the KRT prevalence in men and women was 73.9 and 56.3 pmp in the public sector, and 1 112.0 and 613.5 pmp in the private sector. The proportion of preemptive transplants (8.6% vs 8.2%), overall transplants (17.2% vs 17.7%), treatment discontinuation (8.3% vs 8.9%) and death (53.0% vs 53.3%) were comparable between men and women. There was a clear de-escalating trend in the incidence of KRT over the 5-year study period for both sexes.

**Conclusion:** A sex-specific disparity in KRT prevalence was observed, reflecting higher rates of KRT in male compared to females except transplant. This may suggest socio-cultural or socio-economic bias, but impact of biological factors cannot be excluded.

Keywords: sex disparity; kidney transplant; dialysis; haemodialysis; access to health.

### INTRODUCTION

In keeping with observed global trends, the incidence of chronic kidney disease (CKD) in South Africa has been on the increase [1]. As a leading cause of mortality, accounting for an estimated 1 000 deaths per million people (pmp) annually, CKD is a major public health challenge in South Africa [2]. Local reports have demonstrated a crude prevalence of CKD in a geographical cohort of 17.3% [3], and an age-adjusted prevalence of 6.4% in a cohort of teachers [4]. In addition, a further exponential rise in CKD in sub-Saharan Africa has been projected over the ensuing 10 years due to an escalating dual burden of communicable and non-communicable diseases [5].

Sex disparity in KRT prevalence has been well-documented worldwide, but no large-scale studies of that kind have been performed on the African continent. Globally, the age-standardised prevalence of CKD has been reported to be 1.29 times higher in women than in men [6]. However, the age-standardised incidence of kidney transplantation and dialysis was 1.47 times higher



Received 21 May 2024; accepted 19 September 2024; published 04 November 2024. Correspondence: Kutlo Motlhobogwa, <u>kutlo.gm@gmail.com</u>. © The Author(s) 2024. Published under a <u>Creative Commons Attribution 4.0 International License</u> DOI: https://doi.org/10.21804/27-1-6527 in men than in women [6]. A complex interplay of biological, socio-cultural, and socio-economic factors has been described and may explain, at least in part, sex differences in KRT prevalence.

In two community-based surveys performed on a total of I 691 participants in the Western Cape province of South Africa, the age-adjusted prevalence of CKD (according to the CKD-EPI equation) was higher in women than in men [3,4]. In addition, three single-centre reports from the Western Cape that spanned 27 years and included a total of 4 107 public sector patients with CKD, indicated that marginally more men were being presented for admittance to KRT programmes [7-9]. In two of the three studies, gender was not a predictor of acceptance to KRT [8,9]. However, in one of the reports, women were significantly more likely to be accepted for KRT [7]. With this in mind, we investigated sex differences in both prevalent and incident KRT patients on a national and provincial scale.

### **METHODS**

This was a retrospective, national-registry-based study that explored demographic, geographic, and clinical variables of prevalent KRT patients on 31 December 2017 and incident KRT patients from 1 January 2013 to 31 December 2017. The study was performed according to STROBE guidelines.

#### Aim

Our aim was to investigate sex-specific differences in prevalent and incident patients undergoing KRT and, where appropriate, to present these findings in relation to the general population.

### **Study population**

All incident KRT patients that were entered into the South African Renal Registry (SARR) database from 1 January 2013 to 31 December 2017, as well as prevalent KRT patients on 31 December 2017, were included in the analysis.

### **General population**

During the corresponding period, general population estimates were based on the mid-year estimates of Statistics South Africa, which included the provincial and sex-specific distribution of the population [10-14]. The number of members who were registered with a medical scheme on 31 December 2017 was obtained from the Council for Medical Aid Schemes' annual report for 2016/2017 [15].

### Data collection and definitions

The research protocol was approved by the Faculty of Health Sciences Human Research Ethics Committee of the University of Cape Town (HREC reference number: 626/2019) and included a waiver of informed consent. A successful application was made to the SARR (approved by the Health Research Ethics Committee of the University of Stellenbosch: Project ID 3997; reference number N11/01/028) to extract and supply retrospective, anonymised data for specific variables, as defined by the study protocol. The registry assumed that sex was assessed by self-identification.

Incident patients were captured by completion of a newpatient registration form at the start of chronic dialysis or at the time of a pre-emptive kidney transplant. Prevalent patients were captured by completion of an annual assessment form on 31 December 2017, which included all patients that were receiving chronic dialysis or were living with a functioning kidney transplant. Specific forms and/or sections were completed during patient transfers (from one KRT modality to another) and to record patients who had reached a permanent end to treatment (discontinuation of treatment and/or death).

The registry assumed that a functioning kidney transplant was maintained unless there was evidence of allograft failure or death. Post-transplant patients were considered lost-to-follow-up if no registry entries were made within 365 days after allograft failure was recorded, in the absence of evidence of death. Dialysis patients were considered lost-to-follow-up if no registry entries were made for 365 days in the absence of evidence of death.

Some of the variables that were recorded for incident kidney transplant recipients were incomplete, including data on the provincial distribution (unknown in 103 men and 60 women; 18.8%) and donor type (unknown in 60 men and 38 women; 11.3%; living donor not classified in 2 men and 2 women; 0.5%).

#### **Statistical analysis**

Quantitative data were analysed using Stata/SE version 16.1 (StataCorp, College Station, Texas). Demographic, geographic, and clinical variables for prevalent and incident patients were summarised using descriptive statistics, including frequencies and percentages for categorical variables and median values with an interquartile range (IQR) for numeric data.

#### Prevalence data analysis

Prevalence was calculated for the national KRT cohort on 31 December 2017 and compared for women and men. Additional comparative analysis was performed to analyse sex differences according to provincial distribution, medical insurance status, and KRT modality. Prevalence was expressed per million population (pmp) for each KRT



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cohort (national, provincial, medically insured, and KRT modality) by using the sex-stratified estimated end-of-year population for 2017.

#### Incidence data analysis

Annual incidence rates of KRT (including dialysis and preemptive transplant) were calculated for each study year. The annual incidence rates of kidney transplants that were performed during the study period were calculated and compared for women and men. These were expressed in pmp by using the estimated mid-year population for each study year (2013-2017). Cumulative incidence was calculated and expressed in pmp by determining the proportion of cumulative new cases and the estimated mid-year population over the 5-year study period. The cumulative incidence of treatment discontinuation and mortality was calculated also over the 5-year study period. The number of discontinuations and deaths that were reported was expressed as a percentage of the cumulative estimated annual mid-year prevalence of KRT patients for each study year (2013–2017). The reasons for treatment discontinuation and cause of mortality were expressed as percentages of the total number of discontinuations and of deaths, respectively.

The two-sample proportion test was used to compare women and men as a proportion of the general population in terms of prevalence, cumulative incidence, and incidence rates. The proportions of women and men were also compared in terms of the initial and maintenance KRT modality, discontinuation of treatment, and death. A P value of <0.05 was considered statistically significant.

### RESULTS

### Overall and sex-specific analysis of prevalent KRT cohort

### Demographics and treatment rate

On 31 December 2017, 10 745 patients were receiving KRT, of whom 4 344 (40.4%) were women and 6 401 (59.6%) were men. The overall median age, the median age for women and the median age for men were 52.6 (IQR 41.8–62.3), 51.8 (IQR 40.2–62.6) and 53.1 (IQR 42.7–62.2) years, respectively. The estimated population of South Africa at the end of 2017 was reported by Statistics South Africa to be 57 123 800, of whom 29 223 450 (51.2%) were women and 27 900 350 (48.8%) were men.

Figure I shows the proportion of the population that underwent KRT at the end of 2017 overall, by sex and by province. Overall KRT provision was 181.1 pmp, with a significantly lower proportion of women receiving KRT than men (148.7 vs 229.4 pmp; P 0.001). Treatment rates ranged from 56.7 pmp in Mpumalanga province to 347.3 pmp in the Western Cape. In keeping with the national trend, a consistent disparity in the sex-specific prevalence of KRT could be observed across all nine provinces, with a significantly lower proportion of women undergoing KRT (Figure 1).

According to the Council for Medical Schemes, 8 872 036 South Africans (15.5%) were registered with a medical



Figure I. Overall and sex-specific prevalence of KRT on 31 December 2017, according to province, healthcare sector, and KRT modality.

Abbreviations: GP, Gauteng; KZN, KwaZulu-Natal; WC, Western Cape; EC, Eastern Cape; LP, Limpopo; MP, Mpumalanga; NW, North West; FS, Free State; NC, Northern Cape; HD, Haemodialysis; PD, Peritoneal Dialysis; Tx, Transplant.



scheme on 31 December 2017, translating nationally to 16.1% female and 15% male. Overall, the proportion of the medically insured population (private sector) that received KRT was 857.9 pmp compared to 65 pmp accessing public healthcare facilities (Figure 1). The proportion of women and men that received KRT was 56.3 and 73.9 pmp in the public sector (P = 0.114), and 613.5 and 1 112 pmp in the private sector (P < 0.001) (Figure 1).

Of 10 745 patients, 7 683 (71.5%) received haemodialysis (HD), 1 863 (17.3%) were alive with a functioning kidney transplant, and 1 199 (11.2%) received peritoneal dialysis (PD). A greater proportion of women received maintenance PD (13.1 vs 9.8%; P 0.001), whereas relatively more men accessed HD (72.7 vs 69.7%; P 0.001). Of the 1 863 patients that were living with a functioning kidney transplant, 17.5% were men and 17.2% were women (P = 0.709).

The initial treatment modality was recorded in 10 708 of the 10 745 prevalent patients. Most patients (73.6%) began KRT by HD, followed by PD (18%) and pre-emptive transplantation (8.4%). Women were more likely to be initiated on PD (21.1% vs 15.9%; P 0.001), and men on HD (75.8% vs 70.2%; P < 0.001). The proportion of pre-emptive transplantation in men and women was comparable in this cohort (8.2% vs 8.6%; P = 0.498).

### Overall and sex-specific analysis of incident KRT cohort

### Cumulative incidence, incidence rates and trends over time

From I January 2013 to 31 December 2017, 8 292 new patients were initiated on KRT in the form of chronic dialysis or pre-emptive kidney transplantation. Fewer

women (40.4%) were started on KRT than men (59.6%), with a cumulative incidence of 23.9 pmp and 36.9 pmp, respectively (P = 0.096). The annual KRT incidence rate varied between 25.6 pmp and 33.3 pmp and a de-escalating trend was observed over the 5-year study period overall and in both men and women (Figure 2).

The annual transplant incidence rate was low, ranging between 2.4 pmp and 3.8 pmp transplants per year (Figure 3). Of the 868 transplant recipients, 352 (40.6%) were women and 516 (59.4%) were men, translating to a cumulative transplant incidence of 2.5 pmp and 3.8 pmp, respectively (P = 0.706). On further analysis, a lower cumulative transplant incidence in women was observed across 7 of the 9 provinces, excluding the North West and Free State. Accurate statistical analysis could not be performed in 6 of the 9 provinces due to insufficient numbers, and in the other three provinces the sex-specific differences did not reach statistical significance. Compared to the private healthcare sector (8.5 pmp vs 15.1 pmp; P = 0.221), the difference in cumulative transplant incidence between women and men in the public sector was less pronounced (1.1 pmp vs 1.5 pmp; P = 0.564). The donor type was documented in 766 of the 868 transplants and showed that women were just as likely as men to be transplanted with a deceased donor kidney (60.3% vs 61.0%) and a living donor kidney (39.7% vs 39%). The sex of the donors was not recorded as part of this study.

### Overall and sex-specific analysis of events that resulted in the termination of KRT

### Treatment discontinuation

During the 5-year study period, KRT was discontinued in 926 patients, of whom 359 were women and 567 men





### Figure 3. Overall and sex-specific cumulative incidence of kidney transplants from 1 January 2013 to 31 December 2017, according to province, healthcare sector and donor type.

Abbreviations: GP, Gauteng; KZN, KwaZulu-Natal; WC, Western Cape; EC, Eastern Cape; LP, Limpopo; MP, Mpumalanga; NW, North West; FS, Free State; NC, Northern Cape; DD, deceased donor; LUD, Living related donor; LRD, Living related.

Table 1. Reasons for the discontinuation of treatment in KRT patients during the 5-year study period.					
	Overall, N (%)	Men, N (%)	Women, N (%)	P value	
Total number of patients at risk	48 360 (100)	26 592 (55)	21 748 (45)		
Treatment discontinuation	926 (1.9)	567 (2.1)	359 (1.7)	< 0.00	
Reason for discontinuation of KRT (as a proportion of total number of discontinuations)					
Clinical reason	453 (48.9)	277 (48.9)	176 (49)		
Regained kidney function	294 (31.7)	175 (30.9)	9 (33. )	0.467	
Patient's or family's choice	108 (11.7)	70 (12.3)	38 (10.6)	0.416	
Doctor's recommendation	48 (5.2)	30 (5.3)	18 (5)	0.853	
No dialysis access	3 (0.3)	2 (0.4)	I (0.3)	_	
Economic reason	40 (4.3)	22 (3.9)	18 (5)	0.408	
Lost to follow-up	280 (30.2)	175 (30.9)	105 (29.2)	0.602	
Other	153 (16.5)	93 (16.4)	60 (16.7)	-	

(Table 1). The treatment discontinuation rate was 1.9% overall, with lower rates observed in women compared to men (1.7% versus 2.1%, P = 0.001). Treatment discontinuation was mostly attributed to regained kidney function; however, a large proportion of patients were lost to follow-up. Clinical reasons for discontinuation were comparable for both women and men.

### Mortality

The mortality rate was 11.7% overall and was significantly lower in women than in men (10.6% vs 12.8%; P = 0.001) (Table 2). Cardiovascular disease was the leading cause of death overall, in women and in men (22.2%, 20.8% and 23.1% of all reported deaths). Men were significantly more likely to die of cardiovascular disease (23.1% vs 20.8%; P = 0.001) and women were more likely to die of cerebrovascular disease (2.7% vs 1.8%; P = 0.017) and pulmonary embolism (1.2% vs 0.6%; P = 0.016). The cause of death was recorded as unknown for over one-third of deaths reported (37.2%) (Table 2).

#### DISCUSSION

To our knowledge, this is the first national registry-based report that records sex disparity in KRT from the African continent. In keeping with numerous international reports

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Table 2. Overall and sex-specific causes of mortality in KRT patients during the 5-year study period.					
	Overall, N (%)	Men, N (%)	Women, N (%)	P value	
Total number of patients at risk	48 360 (100)	26 592 (55)	21 748 (45)	_	
Total deaths recorded	5 715 (11.8)	3 412 (12.8)	2 303 (10.6)	<0.001	
Cause of death (as a proportion of total deaths)					
Cardiovascular	I 266 (22.2)	788 (23.1)	478 (20.8)	< 0.00	
Infective	554 (9.7)	310 (9.1)	244 (10.6)	0.059	
Cerebrovascular	22 (2. )	60 (1.8)	62 (2.7)	0.017	
Malignancy	89 (1.6)	53 (1.6)	36 (1.6)	0.977	
Pulmonary embolism	49 (0.9)	21 (0.6)	28 (1.2)	0.016	
Uraemia	42 (0.7)	22 (0.6)	20 (0.9)	0.332	
Other	I 466 (25.7)	853 (25.0)	613 (26.6)	_	
Unknown	2   27 (37.2)	1305 (38.2)	822 (35.7)	_	

on the topic, our study confirms the presence of sex disparity within prevalent and incident KRT patient cohorts across South Africa, with fewer women receiving KRT than men.

In the prevalent cohort, the KRT treatment rate was lower for women on both a provincial and national scale. The disparity in treatment rate could be demonstrated consistently across all nine provinces, irrespective of whether the province's overall treatment rate was at the higher (Western Cape at 347.3 pmp) or lower (Limpopo at 67.5 pmp and Mpumalanga at 56.7 pmp) ends of the spectrum. Without population epidemiological estimates on endstage kidney disease (ESKD), it is a challenge to interpret this finding as either a reflection of a lesser demand for KRT or a lower accessibility of KRT services in women.

Furthermore, it is important to compare KRT access between public and private sectors. South Africa is considered one of most unequal countries in the world, with a Gini coefficient of 0.65 according to expenditure data and 0.69 based on per capita income data [16]. One of the many manifestations of inequality is the marked disparity in healthcare resources between the public and private sectors, which is highlighted in relation to the provision of KRT [17]. As a result, the rationing of KRT services in the public sector has been unavoidable, and acceptance rates to access these services have typically been below 50% for decades [7-9]. In the private healthcare sector, KRT has been recognised as a prescribed minimum benefit, and access to KRT is guaranteed for all who require it, if they are active members of a medical scheme. Therefore, the best estimate of the demand for KRT in South Africa is the proportion of medically insured patients receiving KRT in the private sector. At the end of 2017, the prevalent KRT treatment rate in the medically insured population of 8 872 036 was estimated to be 857.9 pmp. Marginally more women than men were active members of a medical scheme (16.1% vs 15%), yet the KRT treatment rate was much lower in women (613.5 pmp) than in men (1 112 pmp), which may indicate that women develop ESKD less often, have a lower demand for KRT than men or were more likely to decline KRT.

In the public healthcare sector, which serves the remaining 84.5% of the population, rationing of KRT services is implemented according to national guidelines on the provision of KRT [18]. An assessment committee in each province categorises patients into three groups: category | patients are guaranteed KRT, category 2 patients are offered treatment as resources allow, and category 3 patients are palliated. Of the 1 665 patients who were assessed for KRT in two Western Cape centres, an average of 12.4%, 44.4%, and 43.2% were assessed as categories I, 2, and 3, respectively [7,8]. Ultimately, less than half of the patients presented were accepted, which could partly explain the low public sector KRT treatment rate of 65 pmp reported in our study. The proportion of women and men that relied on the public sector for the provision of KRT services was similar (83.9% vs 85%), yet the KRT treatment rate for women in the public sector was lower than for men (56.3 pmp vs 73.9 pmp). However, this sex-specific disparity in treatment rate was much less pronounced than what was observed in the private sector, where access to KRT was essentially unrestricted. Contrary to our findings, the global age-standardised prevalence of CKD has been reported to be 1.29 times higher in women than in men [6,19,20]. Three single-centre reports from the Western Cape province that spanned 27 years and included 4 107 patients with CKD indicated that marginally more men (2 163,



52.7%) than women (1 944, 47.3%) were presented for acceptance to KRT services [7-9]. In two of the three studies, gender was not a predictor of acceptance to KRT [8,9]. Nonetheless, in one of the reports, women were significantly more likely to be accepted into the KRT programme [7]. Even though the participants' baseline characteristics were not representative of other provinces, the findings from these three studies confirmed that the rationing of KRT services was not inadvertently biased against women, at least not in the Western Cape province. This finding may not be applicable to other provinces, especially those employing different selection criteria to access KRT in the public sector.

Despite being based on sound moral, ethical, and legal principles, the categorisation and prioritisation of public sector patients in need of KRT does not necessarily ensure equity of treatment, as highlighted by a previous local report stating that, in their experience, socio-economic factors influence decision-making more profoundly than medical criteria [9]. Patients that required KRT were more likely to be accepted if they were currently employed and were contributing positively to the economy and society at large [7-9]. A general household survey noted that South African women had lower functional literacy rates than men and that they were more likely to leave school prematurely to attend to family commitments such as marriage, pregnancy, and raising children [21]. To control for this, the assessment process for accessing KRT in the public sector will regard women caring for children as equivalent to men who are employed. Even so, income disparity based on gender in South Africa has been reported, with men more likely to receive salaries or wages and women more likely to rely on pensions and social grants [22]. This suggests that there may be a close association between gender and socio-economic status in the South African population and that a KRT assessment process heavily focused on socio-economic factors may unintentionally result in bias against women.

The true prevalence of ESKD in South Africa is not known and KRT rates are likely to be a large underestimate, particularly in the public sector. Two community-based surveys performed on a total of 1 691 participants in the Western Cape province have estimated the age-adjusted prevalence of CKD to be between 6.4% and 17.3%, according to the CKD-EPI equation [3,4]. These rates were considerably higher than those reported by previous population-based studies from sub-Saharan Africa [23,24]. The prevalence of CKD was higher in women than in men, which was in keeping with numerous epidemiological CKD screening studies performed in the United States [19,20]. However, as 73.9% of the 1 691 participants were women and 91.4 % were of mixed ancestry, the participants from these two surveys were not representative of the provincial or national population. Even though CKD seems to be more prevalent in women, many investigators have reported a slower rate of progression to ESKD in women, with more men reaching ESKD [25-27]. Sex-specific differences in glomerular structure, haemodynamic condition, and the effect of sex hormones on kidney cells are some of the factors believed to contribute to gender differences and influence CKD progression [26].

In our study, women were significantly more likely to start KRT by PD and were more likely to be maintained on PD than men. Multiple factors may be responsible for this finding, including patient choice, staff training, access to sanitation and to continuous supply of electricity. Another explanation could be that women may have exhibited more residual kidney function at the time of presentation because of slower disease progression. The fact that more women were being maintained on PD could simply be a consequence of more women being started on PD as their initial modality. In contrast, men were more likely to begin KRT by HD and were more commonly maintained on HD. The same rationale could explain this phenomenon, as men may have demonstrated less residual kidney function at the time of diagnosis. However, this assumption is speculative, as many other factors, including employment status, socioeconomic factors, patient attitude, and body image concerns, may have played a role as well.

A lower cumulative incidence of kidney transplants in women was noted in our study and was consistently observed across donor categories (deceased, living related, or unrelated). The most pronounced disparity was found in the private healthcare sector, where women were being transplanted at a rate of 8.5 pmp and men at 15.1 pmp over the study period. In the public sector, one can estimate the number of women (56.3 pmp) and men (73.9 pmp) that were awaiting transplantation based on the numbers enrolled for dialysis. Considering that women in the public sector were transplanted at a lower rate of I.I pmp and men at a rate of 1.5 pmp, the number of transplants performed relative to those awaiting the operation was equivalent for women and men. In addition, the proportion of women and men who underwent pre-emptive transplantation was comparable.

A previous systematic review that investigated the outcomes of ESKD patients who started dialysis in sub-Saharan Africa concluded that most patients discontinued treatment and died [28]. In contrast, recent KRT survival data from South Africa reported an overall one-year survival of 90.4%



[29], and a one-year survival of 86.4% in elderly patients [30]. Our results are comparable to these findings, as a 1.9% discontinuation rate and a 11.7% mortality rate were observed over the 5-year study period. Men were significantly more likely to discontinue treatment than women, but the reasons for doing so were comparable. A significantly higher mortality rate on KRT was observed in men, with death from cardiovascular disease the most common cause of mortality regardless of sex. Women were more likely to die of cerebrovascular disease and pulmonary embolism than men.

This study has several limitations, including its retrospective nature and reliance on healthcare providers to capture and enter data accurately. A large proportion of patients (30.2%) were lost to follow-up, which would have adversely affected the accuracy of the KRT discontinuation data. The cause of death on KRT was reported as unknown in 37.2% of cases, negatively influencing the accuracy of the data.

### CONCLUSION

A sex-specific disparity in KRT prevalence has been observed but may reflect higher KRT requirements in men. Gender did not affect access to kidney transplantation, irrespective of healthcare sector or donor type. Further studies are required to investigate and quantify the biological, socio-cultural, and socio-economic factors that result in sex disparity in South African KRT patients as well as the epidemiology of end-stage kidney disease.

### Acknowledgements

The authors would like to acknowledge the Department of Surgery, University of Cape Town, for organising and covering the expenses of the research-writing week that provided a unique opportunity for the first author to receive feedback from colleagues and senior consultants during the writing process.

### Funding

None to declare.

### **Conflict of interest**

The authors have no conflicts of interest to declare.

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