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Original Investigation

Estimating the Total Incidence of Kidney Failure in Australia Including Individuals Who Are Not Treated by Dialysis or Transplantation

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Claire Sparke, Grad Dipl Clin Epidemiol,[1] Lynelle Moon, PhD,[1] Frances Green, B Human Movement Sci,[1] Tim Mathew, FRACP,[2] Alan Cass, PhD,[3] Steve Chadban, PhD,[4,5] Jeremy Chapman, FRCP,[6] Wendy Hoy, FRACP,[7] and Stephen McDonald, PhD[8,9,10]

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Background: To date, incidence data for kidney failure in Australia have been available for only those who start renal replacement therapy (RRT). Information about the total incidence of kidney failure, including non–RRT-treated cases, is important to help understand the burden of kidney failure in the community and the characteristics of patients who die without receiving treatment.

Study Design: Data linkage study of national observational data sets.

Setting & Participants: All incident treated cases recorded in the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) probabilistically linked to incident untreated kidney failure cases derived from national death registration data for 2003-2007.

Predictor: Age, sex, and year.

Outcomes: Kidney failure, a combination of incident RRT or death attributed to kidney failure (without RRT).

Measurements: Total incidence of kidney failure (treated and untreated) and treatment rates.

Results: There were 21,370 incident cases of kidney failure in 2003-2007. The incidence rate was 20.9/100,000 population (95% CI, 18.3-24.0) and was significantly higher among older people and males (26.1/100,000 population; 95% CI, 22.5-30.0) compared with females (17.0/100,000 population; 95% CI, 14.9-19.2). There were similars number of treated (10,949) and untreated (10,421) cases, but treatment rates were influenced highly by age. More than 90% of cases in all age groups between 5 and 60 years were treated, but this percentage decreased sharply for older people; only 4% of cases in persons 85 years or older were treated (ORs for no treatment of 115 [95% CI, 118-204] for men ≥80 years and 400 [95% CI, 301-531] for women ≥80 years compared with those of the same sex who were <50 years).

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Limitations: Cross-sectional design, reliance on accurate coding of kidney failure in death registration data.

Conclusions: Almost all Australians who develop kidney failure at younger than 60 years receive RRT, but treatment rates decrease substantially above that age.

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Chronic kidney disease (CKD), particularly kidney failure, imposes a substantial health burden in the Australian community. It is estimated that 1 in 9 Australian adults older than 25 years have some degree of CKD.[1] CKD contributed to ~10% of all deaths in 2007[2] and 15% of all hospitalizations in 2009-2010,[3] most of which were for maintenance dialysis. Treatment of CKD accounts for almost 2% of allocated direct health care expenditures, and these costs are increasing in magnitude and as a proportion of total spending.[4]

To date, incidence data for kidney failure in Australia and most other countries have been available for only those who start renal replacement therapy (RRT), referred to here as "treated" kidney failure. Outcomes for all patients receiving RRT for whom kidney function is not anticipated to recover and the intention to treat is long term are captured by the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA).[5] Information about the total incidence of kidney failure, which includes those who die of kidney failure without long-term commencement of RRT (referred

From the [1]Australian Institute of Health and Welfare, Canberra; [2]Kidney Health Australia, Hackney; [3]George Institute for Global Health, University of Sydney; [4]Royal Prince Alfred; [5]University of Sydney, Royal Prince Alfred Hospital, Camperdown; [6]Centre for Transplant and Renal Research, Westmead Hospital, University of Sydney, Westmead; [7]Centre for Chronic Disease at the University of Queensland, Royal Brisbane & Women's Hospital, Herston; [8]ANZDATA; [9]Central Northern Adelaide Renal and Transplantation Service; and [10]Discipline of Medicine, Faculty of Health Sciences, University of Adelaide, Adelaide, Australia.

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Address correspondence to Claire Sparke, Grad Dipl Clin Epidemiol, Australian Institute of Health and Welfare, AIHW GPO Box 570, Canberra, ACT 2601, Australia. E-mail: claire.sparke@aihw.gov.au

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to here as untreated kidney failure), is important to help understand the full burden, as well as the characteristics, of patients who die without receiving treatment, whether by choice or lack of access. Such information also might help better understand differences[6] in the incidence of RRT between countries.

This study expands on results previously published in an Australian government report titled *End-Stage Kidney Disease in Australia: Total Incidence 2003-2007*.[7] It builds on a method used elsewhere to determine kidney failure end points in cohort studies.[8-10] These studies used data linkage to estimate the number of people with kidney failure (or CKD more generally) who did not receive RRT. However, each of these followed up a particular cohort (eg, the National Health and Nutrition Examination Survey [NHANES] in the United States) rather than directly determining the national incidence.

The aim of this study was to estimate the total incidence of kidney failure in Australia for 2003-2007. This was done by linking 2 nationwide data collections—ANZDATA and national mortality data, thereby capturing and allowing analysis of all cases of kidney failure regardless of whether managed with RRT.

METHODS

Data Set Sources and Definitions

Kidney failure cases were identified from 2 different data sources. The first was ANZDATA. The second was the Australian Institute of Health and Welfare National Mortality Database, which includes cause of death and demographic information for all deaths registered in Australia starting in 1965. A third data source, the National Death Index, was used in the linkage process to determine the overlap between the 2 main data sources, described later.

An incident case was defined as a case newly registered on ANZDATA in 2003-2007 (treated kidney failure) or a death registered in 2003-2007 with kidney failure recorded as a cause, but which was not recorded in ANZDATA (untreated kidney failure).

Kidney failure in mortality data was defined as chronic renal failure (*International Classification of Diseases, Tenth Revision* [*ICD-10*] codes N18.0, N18.8, and N18.9), hypertensive renal failure (*ICD-10* codes I12.0, I13.1, and I13.2), or unspecified renal failure (*ICD-10* code N19) as an underlying cause of death, or chronic renal failure, end-stage (*ICD-10* code N18.0), as an associated cause of death. The underlying cause of death refers to the condition that started the course of events leading directly to a person's death. The associated cause of death refers to any other condition thought to have contributed to the death. Mortality data were used to estimate the incidence of untreated cases because by definition, people with kidney failure show signs or symptoms of kidney failure to the extent that they require RRT,[11] and survival for those who do not receive RRT is likely to be short.[12-14] Thus, year of death can be used as a proxy for incidence year.

To avoid double counting, ANZDATA was linked to the National Death Index using probabilistic linkage based on identifying information, including date of birth, name, sex, date of death, and postal code of residence. ANZDATA cases used in the linkage process were all patients receiving treatment in Australia between 2003 and 2007 (regardless of when treatment began), as well as any cases of patients lost to follow-up, to make certain that cases of kidney failure in the mortality data were not mistakenly assigned to the untreated group. These data then were linked to National Mortality Database data (which can be linked to National Death Index data through a unique identifier). If cases were present in both ANZDATA and National Mortality Database data, they were counted only once as treated cases. Approval for the data linkage and analysis was obtained through the Australian Institute of Health and Welfare Ethics Committee.

Statistical Analysis

Total incidence rates were analyzed using Poisson regression, with year, age (in 5-year groupings), and sex as covariates. Interaction between age group and sex and between age group and year also were tested for significance using type III analysis.[15] Denominator population data came from the Estimated Resident Population series produced by the Australian Bureau of Statistics.[16]

Logistic regression analysis was used to examine treatment rates with RRT. For this, the relationship between year, age group, and sex and the probability of no treatment was assessed. Because of the small number of cases in persons younger than 50 years, age groups were set as those younger than 50 years and then 5-year age groups up to 80 years or older. The interaction between age group and sex also was taken into consideration in the model. Hosmer-Lemeshow test and C statistic were used to assess goodness of fit. $P < 0.05$ was considered statistically significant for main effects and interactions. All analyses were done using SAS Enterprise Guide, version 4.3 (SAS Institute Inc).

RESULTS

Total Incidence

There were 21,370 incident cases of kidney failure in 2003-2007, comprising 10,949 treated cases and 10,421 untreated cases. The overall incidence rate was 20.9/100,000 population (95% confidence interval [CI], 18.3-24.0). The incidence rate increased substantially with age, particularly among those older than 70 years, with 63% of all new cases being individuals 70 years or older. The age-adjusted total incidence was higher for males than females (26.1/100,000 population [95% CI, 22.5-30.0] vs 17.0/100,000 population [95% CI, 14.9-19.2]); however, this sex difference was not apparent at younger than 40 years (Table 1). T1

Treatment Rates

Overall, there were similar numbers of treated and untreated cases. However, this varied greatly with age. A very high proportion of cases in younger people were treated: >90% in all age groups between 5 and 60 years. The percentage treated decreased sharply in older people, with only 4% of new cases of persons 85 years or older treated (Figs 1-3). F1-3,AQ: 6

Logistic regression confirmed that treatment rates were influenced highly by age. The odds of not receiving treatment increased sharply with age (Table 2). Sex also was associated with different treatment T2 proportions among older age groups, in which men (aged ≥75 years) were more likely to be receiving

Table 1. Total Incidence of Kidney Failure in Australia, 2003-2007

Age Group (y)	Incident Cases	Population[a]	Incidence Rate/100,000 Population (95% CI)	
			Males	Females
0-4	36	6,484,292	0.8 (0.5-1.1)	0.3 (0.2-0.6)
5-9	46	6,698,649	0.8 (0.5-1.1)	0.6 (0.4-1.0)
10-14	45	6,982,321	0.5 (0.3-0.8)	0.8 (0.5-1.1)
15-19	103	7,024,408	1.6 (1.3-2.1)	1.3 (1.0-1.7)
20-24	156	6,955,491	2.7 (2.2-3.3)	1.8 (1.4-2.3)
25-29	251	7,182,535	4.0 (3.4-4.7)	3.0 (2.5-3.6)
30-34	330	7,527,028	4.8 (4.1-5.6)	4.0 (3.4-4.7)
35-39	461	7,505,170	7.4 (6.5-8.3)	5.0 (4.3-5.7)
40-44	660	7,674,235	10.4 (9.4-11.5)	6.8 (6.0-7.7)
45-49	819	7,326,397	13.7 (12.5-15.0)	8.7 (7.8-9.8)
50-54	980	6,717,716	18.5 (17.0-20.1)	10.8 (9.7-12.0)
55-59	1,224	6,131,134	23.6 (21.9-25.5)	16.3 (14.8-17.8)
60-64	1,274	4,770,305	32.1 (29.8-34.7)	21.2 (19.4-23.3)
65-69	1,586	3,808,303	49.8 (46.4-53.4)	33.7 (31.1-36.6)
70-74	2,046	3,159,318	80.6 (75.8-85.8)	50.1 (46.6-53.9)
75-79	2,716	2,735,712	127.5 (120.6-134.9)	75.8 (71.1-80.8)
80-84	3,095	1,965,117	216.1 (204.7-228.1)	117.5 (110.8-124.7)
≥85	5,542	1,539,790	447.3 (425.7-470.0)	318.7 (305.3-332.8)
Total	21,370	102,187,921	26.1 (22.5-30.0)	17.0 (14.9-19.2)

Note: Total rates are adjusted for age.
Abbreviation: CI, confidence interval.
[a]Five-year population at risk.

treatment than their female counterparts. For the 5-year period used in this study, year did not affect treatment rates and was removed from the final model to derive parameter estimates.

Sensitivity Analyses

Total numbers were recalculated excluding untreated cases for which chronic renal failure, end-stage (*ICD-10* code N18.0), was recorded as an associated cause of death. The total number of cases decreased by 4.5% to 20,408 when these cases were excluded, which equated 9,459 untreated and 10,949 treated.

DISCUSSION

In this study, we found that in 2003-2007, the number of incident cases of kidney failure in Australia was twice as many as those recorded as receiving treatment. Total incidence was higher for older people and men. Most untreated cases were people older than 60 years, and women older than 75 years were less likely to receive treatment than men.

The most striking implication from this study is the substantial number of people older than 60 years who died with kidney failure, but were not treated with

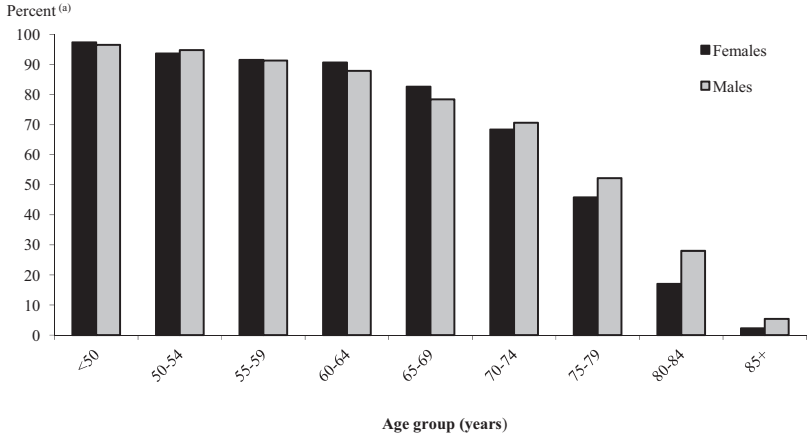

Figure 1. Age-specific renal replacement therapy treatment rates, 2003-2007. [a]Rates are predicted. Adapted and reproduced from Australian Institute of Health and Welfare (AIHW)[7] with permission of the AIHW.

Figure 2. Number of treated and untreated cases, by age group at kidney failure onset, 2003-2007. Adapted and reproduced from Australian Institute of Health and Welfare (AIHW)[7] with permission of the AIHW.

RRT. This is similar to trends reported by others.[9,17] There also was a small number of patients (n = 250) younger than 60 years who were not treated with RRT.

The data available in this analysis do not provide sufficient information about the whole patient profile to provide answers about why some people do not receive RRT. However, there could be a number of reasons. Known factors that could be operating in these older cohorts include late referral, medical comorbid conditions, overall quality of life, and total functional capacity.[18-20] In the Caring for Australasians With Renal Impairment guidelines,[21] it is recommended that patients with an estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2 (CKD stage 4) be referred to a nephrology service to give adequate time to prepare for RRT or supportive management and palliative care.[22] A retrospective study of patients with CKD stages 3 and 4 in the United States referred to a nephrology service compared with those who were stage 4 CKD and not referred found that elderly and female patients were less likely to be referred.[23] In addition, for elderly patients, greater comorbidity was a predictor of nonreferral. In a single-center study of patients 80 years or older, patients not offered dialysis were more likely to be referred late, be socially isolated, have diabetes, and have greater functional impairment.[14]

A recent study from Canada assessed rates of treated and untreated kidney failure in older versus younger adults.[17] In a cohort of more than 1.8 million adults who had a baseline eGFR recorded in outpatient data between 2002 and 2008, they found results similar to those in our study: rates of untreated kidney failure were significantly higher in older adults compared with younger adults. Unlike our study, which defines untreated kidney failure as death attributed to kidney failure in death certificates, that group defined kidney failure as eGFR <15 mL/min/1.73 m^2. There is likely to be a considerable lag in many cases between people achieving eGFR <15 mL/min/1.73 m^2 and death. It

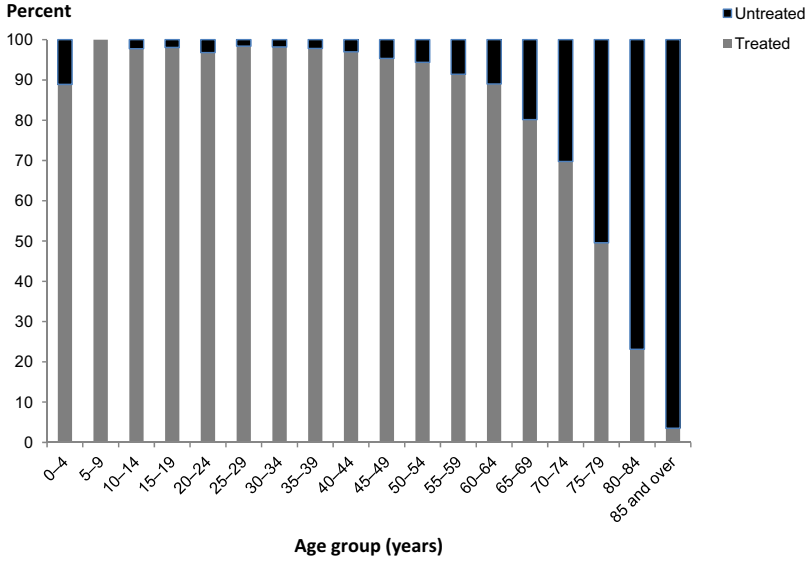

Figure 3. Proportion of all cases that are treated, by age group at kidney failure onset and sex, 2003-2007.

Table 2. Probability of No Treatment

	Females		Males	
Age Group (y)	OR (95% CI)	*P*	OR (95% CI)	*P*
<50	1.0 (reference)		0.8 (0.5-1.2)	0.2
50-54	1.9 (1.2-3.1)	0.01	1.5 (1.0-2.4)	0.06
55-59	2.6 (1.7-3.9)	<0.001	2.7 (1.8-3.8)	<0.001
60-64	2.9 (1.9-4.3)	<0.001	3.9 (2.8-5.4)	<0.001
65-69	5.9 (4.3-8.2)	<0.001	7.7 (5.7-10.5)	<0.001
70-74	13.0 (9.6-17.5)	<0.001	11.7 (8.8-15.6)	<0.001
75-79	33.2 (25.0-44.2)	<0.001	25.7 (19.5-33.9)	<0.001
≥80	399.9 (301.0-531.3)	<0.001	155.5 (118.2-204.4)	<0.001

Note: $\chi^2 = 633.7429$ ($P < 0.001$).
Abbreviations: CI, confidence interval; OR, odds ratio.

also is probable that a proportion of these people will not have died of kidney failure, suggesting that the Canadian study is likely to count more untreated cases than our study.

There could be a number of potential explanations of why women from age 75 years were less likely to be treated than men. These include reasons related to social support and the caring role often played by spouses. In Australia, more women than men 65 years and older are living alone, influenced by a longer life expectancy in women and a higher number of widows than widowers.[24]

The decision to undertake dialysis or transplantation treatment or rely on symptom control and palliation is one taken by an individual in consultation with his or her family and medical advisors. In Australia, there are no regulations governing entitlement to (or denial of) dialysis treatment. This judgment likely will depend on a number of factors evaluated by the individual and his or her medical advisor. There is a lack of research regarding this decision-making process; however, factors may include perceptions of the efficacy of dialysis treatment and the burden that treatment imposes on quality of life, as well as the relative outcomes of dialysis versus no dialysis. Our finding of a large number of untreated cases suggests there is a need to understand whether this decision-making process is undertaken appropriately in all cases and whether there are barriers to accessing treatment, such as for people not living close to available dialysis services.

The large number of untreated cases also indicates a potential group that may be interested in receiving treatment, if services were available and acceptable. There have been many changes in medical care for older patients during the last 5-10 years. For this reason, it is not surprising that more older patients are now receiving active therapy than was the case previously.[25] It is possible that if dialysis outcomes improve or attitudes change in the future, the proportion and number of patients seeking treatment may continue to increase. It is important for planning of RRT services that these trends are monitored, understood, and predicted.

There are known differences in total incidence rates among population groups, including by indigenous status, remoteness areas, and socioeconomic groups.[7] However, due to limitations in data quality, these variables could not be included in the modeling in this study.

International comparisons of the incidence of RRT show a large variation in rates among comparable countries.[6,26,27] Australian incident RRT rates are substantially lower than those of white US citizens and modestly lower than those of most European countries.[27] Higher rates of treated RRT, such as in the United States, might be explained by a greater propensity to provide RRT to older people or higher rates of risk factors such as diabetes.[26] Comparisons of age-specific incident RRT rates show that for people 75 years and older, the rate of treated kidney failure in the United States is 4 times the Australian rate.[5,27] This decreases to approximately 3.4 times the rate when including only US whites. In comparison, the United Kingdom and Australia have similar overall RRT rates,[26] but there are differences between 55 and 79 years of age, with Australian RRT rates being ~20% higher.[5,28] Given the standard use of *ICD* coding on death certifications throughout the world, the methodology used here could be replicated in countries with national renal registries and the ability to link these to death records. This could help examine the extent to which incidence rates are influenced by the propensity to treat older patients.

To our knowledge, this is the first study to estimate the total incidence of kidney failure for a country. Others have used a similar method of data linkage to establish the number of people with kidney failure

who are not given RRT,[8-10,29] but in the context of a cohort follow-up instead of directly determining the total incidence in a country. The *ICD* codes for cause of death used here also differ somewhat from those used in the other studies, with the present study including only kidney failure rather than earlier stages of CKD.

There is some evidence that the choice of codes for cause of death in this study may be conservative and underestimate the number of untreated cases of kidney failure because not all people dying with treated kidney failure had it recorded on their death certificates. For the individuals in this study who started treatment between 2003 and 2007 and died during that period, only 44% had kidney failure (as defined in this study) recorded on their death certificate.[7] A further 44% had other CKD codes recorded on their death certificates, with the remaining 12% having no record of CKD contributing to their death. If the same trend applied to the untreated cases, there would be many more cases than we currently count.

It also is possible that our method may include some untreated cases of persons who had reduced kidney function, but not yet to the degree that necessitated the initiation of dialysis therapy or transplantation. However, this probably pertains to only the fairly small proportion of cases included because they had an associated cause of death of chronic renal failure, end-stage (*ICD-10* code N18.0), and were not treated with RRT. Removing these cases reduced the total incidence estimates by 4.5%. In the remaining untreated cases, renal failure was the underlying cause of death, so they were included. For these cases, it is sensible to suppose that because the disease was severe enough to start the course of events that led directly to the death, it was severe enough be classified as kidney failure.

Counting the untreated cases relies on kidney failure having been recorded correctly in national mortality data and in such a way that CKD is distinguished from it more broadly. There are standard definitions and rules used to record and code causes of death in Australia[30] that promote consistency. However, there may still be a level of inaccuracy. Two studies have compared the cause of death of patients with kidney failure on death certificates with another source of data about deaths, one from Australia and one from the United States.[31,32] Both of these showed wide disparity in agreement between the data sources being compared, depending on the cause of death, although neither compared death certificate data with clinical records, which would be the preferred approach. The Australian study compared ANZDATA with the National Mortality Database in terms of causes of death; agreement ranged from poor (genitourinary diseases) to good (cancer). A wide variety of factors may complicate the comparison between the 2 data sources,[33] including the ANZDATA cause of death data not being based on *ICD-10* coding, and thus comparability is limited.

Further development of the method used to count the untreated cases is key. One approach is to link the current data set with national hospital data. This would identify untreated cases in which the individual is still living. Furthermore, it would give useful information about how the coding in hospitals and deaths databases compare, which could give information to improve the accuracy of the incidence estimates. Another option that may help refine the current measure is a validation study of the mortality data, covering both the accuracy of the death certificate and the coding of that information using the *ICD*.

The creation of the data set described in this analysis, which includes both treated and untreated cases, has greatly heightened our understanding of the total incidence of kidney failure, the divide between treated and untreated cases, and differing patterns by age and sex. This new method of counting will be developed and investigated further in the future.

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