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Survival in Living Kidney Donors: An Australian and New Zealand Cohort Study Using Data Linkage

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Background. Living kidney donors are a highly selected healthy population expected to have high survival postdonation, but mortality studies are limited. Our study aimed to compare mortality in living kidney donors with the general population in Australia and New Zealand, hypothesizing that donor survival would exceed average survival. **Methods.** All living kidney donors in Australia, 2004–2013, and New Zealand, 2004–2012, from the Australian and New Zealand Living Kidney Donor Registry were included. We ascertained primary cause of death from data linkage with national death registers. Standardized mortality ratios and relative survival were estimated, matching on age, sex, calendar year, and country. **Results.** Among 3253 living kidney donors, there were 32 deaths over 20331 person-years, with median follow-up 6.2 years [interquartile range: 3.9–8.4]. Only 25 donors had diabetes-fasting blood sugar level predonation, of which 3 had impaired glucose tolerance. At discharge, the median creatinine was 108 $\mu\text{mol/L}$ and estimated glomerular filtration rate was 58 mL/min/1.72 m². Four deaths occurred in the first year: 2 from immediate complications of donation, and 2 from unrelated accidental causes. The leading cause of death was cancer (n = 16). The crude mortality rate was 157 (95% confidence interval [CI], 111–222)/100 000 person-y, and the standardized mortality ratio was 0.33 (95% CI, 0.24–0.47). The 5-year cumulative relative survival was 1.019 (95% CI, 1.014–1.021), confirming that the survival probability in living kidney donors was 2% higher relative to the general population. **Conclusions.** As expected, mortality in living kidney donors was substantially lower than the general population and is reassuring for potential donor counseling. The Living Donor Registry only captured a third of the deaths, highlighting the benefit of data linkage to national death registries in the long-term follow-up of living kidney donors.

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There are approximately 1000 kidney transplants each year in Australia and 200 in New Zealand. In 2017, living kidney donors accounted for 24% and 37% of those, respectively.¹ Clinical guidelines recommend extensive medical

testing when assessing potential living donors to ensure the risks to the donor and recipient are minimized.^{2,3} Though these guidelines vary among countries, in general, assessments exclude occult cardiovascular disease, diabetes and

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cancers, and set a threshold of kidney function above average (or above average for age) under which a donor would be excluded.² Despite this extensive screening process, kidney donation can have lifelong implications for living donors. This includes an increased risk of hypertension, mean occurrence 12–24 months,⁴ end-stage kidney disease, median time of 11–18 years postdonation,^{5,6} and adverse pregnancies.⁷

Evaluating outcomes postdonation in living donors does present challenges. Long-term follow-up is difficult to maintain for several reasons. As living donors are healthy individuals, they may default from regular follow-up and are more geographically mobile.⁸ Other barriers to long-term surveillance include donor inconvenience and associated costs. Therefore, postdonation information is often incomplete or poorly reported and may be nonrepresentative.⁹ The extensive selection process of living donors also means matched studies have relied on convenience cohorts to find suitable controls who have undergone similar screening.¹⁰ Relying on cohort data assembled for other research questions can introduce selection bias that impact comparative results. Using general population data as a comparator is a common epidemiological approach, although the expectation is that living donors will exceed average survival, representing the healthier extreme of the general population.

To date, there have only been 7 studies worldwide that have evaluated survival in living kidney donors, none from Australia and New Zealand.^{11–17} Only 2 studies compared mortality to the general population, with the remaining studies matching to healthy controls. All these studies found survival in living donors was higher than expected in the comparator group, except for 1 matched study in Norway.¹⁵ However, survival estimates did vary between countries which may reflect differences in postdonation care. Further, changes over time in criteria used for assessment and acceptance of living donors may result in greater mortality risks, particularly as the age of both donors and recipients has increased over time. A recent assessment of the risk profile of living donors in Australia found that 9% of donors had at least 1 absolute contradiction according to national guidelines.¹⁸ While we would expect living donors to have higher survival than the average general population, there are no studies to date in Australia or New Zealand. Hence, our study sought to verify that survival postdonation is greater among all living kidney donors compared with the general population in Australia and New Zealand using linked data.

MATERIALS AND METHODS

Study Design and Setting

We performed a population-based cohort study of all adult living kidney donors who donated in Australia and in New Zealand. Australia and New Zealand have broadly comparable population demographics, such as racial make-up and life expectancy.^{19,20} Both countries have universal healthcare. All deaths within both countries are subject to mandatory reporting, with data aggregated in death registers. Medical certificates completed by a medical doctor record the fact of death and the cause of death, detailing both the underlying and contributing causes of death. The underlying cause of death is defined as the disease or condition that began the sequence of events which lead to the death. Contributing or other causes of death are defined as other diseases or conditions which contributed to the death but were not the underlying cause.

Study Populations and Data Sources

Living Donors

The Australian and New Zealand Living Kidney Donor Registry, established in 2004, collects retrospective and prospective data on all living kidney donors in Australia and New Zealand.^{18,21} All transplant units in Australia and New Zealand register all living donors and contribute data prospectively. Data are collected either via web-based or printed survey forms at predonation assessment, at donation, and then annually postdonation. Core data collected include donor demographics (date of birth, sex, racial background, body mass index, and smoking status), comorbidities (hypertension, glucose tolerance and diabetes, and other comorbid conditions), predonation laboratory results (glucose tolerance test, serum creatinine, urea, proteinuria), donation details (date of donation, donation hospital, operation type, and peri- and postdonation adverse events), and death information (date of death and cause of death). The estimated glomerular filtration rate was calculated using the chronic kidney disease epidemiology collaboration formula.²²

Data Linkage

We used data linkage to link the Living Kidney Donor Registry to each of the national death registers to determine the date and underlying and contributing causes of death in living donors. The scope of the linkage was limited by data availability in Living Kidney Donor Registry in each country, where data on all donors before 2004 was not available, January 1, 2004 to December 31, 2013. We were also limited by the available death information in the New Zealand death register which did not have death information at the time of linkage for deaths occurring from January 1, 2013 to December 31, 2013. In Australia, death information in the death register was available until December 31, 2015. Hence, in this analysis, we included all living kidney donors in Australia during 2004–2013 and in New Zealand during 2004–2012.

The Australian Institute of Health and Welfare (AIHW) and New Zealand Ministry of Health performed the data linkage using best-practice privacy-preserving protocols. In Australia, living donors were linked with the National Death Index using probabilistic record linkage, using combinations of identifiers from date of birth, sex, and first and last names. In New Zealand, living donors were linked with the Mortality Collection database, using deterministic record linkage matching on the National Health Index number.

Only deidentified data were made available to researchers for this study, after data linkage was complete. Ethics approval was granted for this study from the University of Sydney (Project No.: 2014/917), AIHW (Reference No.: EO2015/3/181), and the New Zealand Ministry of Health (Reference No.: 14/NTB/171).

Death Ascertainment and Cause of Death

In both countries, information from medical certificates, coroners' reports, and Births, Deaths and Marriages Registry is collated and coded to an international standard, known as the International Classification of Diseases. An Australian modified version was developed by the National Centre for Classification in Health, currently in its Tenth revision, referred to as ICD-10-AM. The underlying cause of death provided by the national death registries was used to determine the cause of death, using the ICD-10-AM diagnosis codes. The main

causes of death were categorized using the AIHW definition of leading causes of death.²³

Reference Population

Our reference population were the national populations from Australia and New Zealand. These data were obtained from the Australian Bureau of Statistics and the New Zealand Ministry of Health, respectively.

Statistical Analyses

As living donors are highly selected, we hypothesized their survival postdonation would exceed the average survival in the general population. Time was measured from the date of donation until the donor died or December 31, 2015 (Australia only) or December 31, 2012 (New Zealand only), whichever came first. A small proportion of incorrect links can occur when using probabilistic record linkage, and donor deaths occurring outside of Australia and New Zealand are not captured by the national death registers. Therefore, donors were censored at the date of death captured in the Living Kidney Donor Registry if they were reported to have died and the national death registers had not captured any death.

We estimated mortality rates and used indirect standardization to estimate standardized mortality ratios (SMRs) which compared living donors with the reference general population, matching on age (5-y bands), sex, and calendar year. The SMR provides a relative measure which compares the observed mortality rate in the study population to expected mortality rate given in the reference population.

We estimated the cumulative relative survival using the life table approach with Ederer II method used to estimate the expected survival.^{24,25} The cumulative relative survival can be interpreted as the proportion of patients alive compared with the expected in the reference population after x years of follow-up. A cumulative relative survival >1.0 indicates a greater proportion of the study population survived than expected from the reference population. We used the same reference general population as used to estimate SMR, matching on country, age, sex, and calendar year.

Data were analyzed using Stata version 15 (Stata Corporation, College Station, TX).

RESULTS

Patient Characteristics

There were a total of 3255 living donors in Australia, 2004–2013, and in New Zealand, 2004–2012. The linkage process is shown in Figure 1. Two donors were excluded as they were likely incorrectly linked, where their date of death in the national death registry was before their donation date. Hence, a total of 3253 living donors were included in our analysis.

In our study population, the median age at donation was 50 years (interquartile range [IQR]: 42–58) and 57% were female (Table 1). The majority were from Australia (85%) and had a European racial background (86%). Fasting glucose at donation was recorded for 83% of donors, of which most (98%) had a normal fasting glucose (≤ 6.0 mmol/L). A 2-hour glucose tolerance test was recorded for half of the donors (53%), of which 96% had a normal glucose tolerance (≤ 7.7 mmol/L). Of the 17 donors with an impaired fasting glucose, 9 had a normal glucose tolerance, 3 had an impaired glucose

tolerance, and 5 did not undergo a 2-hour glucose tolerance test. Of the 25 donors with diabetes-fasting blood sugar level, 9 had a normal glucose tolerance, 3 had an impaired glucose tolerance, 8 did not undergo a 2-hour glucose tolerance test, and 5 had no available data. Overall, the transplant units reported 16 donors with diabetes ($<0.5\%$) and 340 donors with hypertension requiring medication (10%). At donation, over half had either an overweight (42%) or obese (17%) body mass index.

The majority of donors did not experience adverse events at donation (87%) (Table 2). A total of 328 donors did experience at least 1 adverse event, including 1 acute myocardial infarction, 17 hemorrhages, 6 pulmonary emboli, and 304 other adverse events. The most commonly reported other adverse event was gastrointestinal (24%), surgery related (16%), and respiratory (12%). The majority of gastrointestinal “other” adverse events included vomiting/nausea (40%), followed by ileus (22%) and constipation (18%). The serum creatinine concentration was recorded at discharge for 97% of donors. Most donors (92%) had a discharge creatinine concentration <150 $\mu\text{mol/L}$ (<1.7 mg/dL), and the median was 108 $\mu\text{mol/L}$ (1.22 mg/dL) (IQR: 92–127 $\mu\text{mol/L}$; 1.04–1.44 mg/dL). The estimated glomerular filtration rate at discharge was >60 mL/min/1.72 m² for 47% of donors, with a median of 58 mL/min/1.72 m² (IQR: 51–68 mL/min/1.72 m²).

Deaths

There were 33 deaths observed over 20 331 person-years of follow-up, with 32 deaths captured in the national death registers and 1 additional death captured by the Living Kidney Donor Registry only (Figure 1). Of the 32 deaths captured in the national death registers, 10 deaths (31%) were captured in the Living Kidney Donor Registry; 21 of the 22 deaths which were not captured in the Living Kidney Donor Registry occurred over 1.5 years postdonation.

The median follow-up time was 6.2 years (IQR: 3.9–8.4 y). Four deaths occurred in the first year after donation, including 2 within 30 days of donation (Figure 2A; Figure S1, SDC, <http://links.lww.com/TXD/A239>). Both donors who died within 30 days of donation experienced adverse events at the time of donation, one had a postoperative thromboembolic event and the other had a cardiac arrest subsequent to massive hemorrhage (related to technical surgical issue). These 2 deaths were classified as “Other kidney or ureter disorders” in the national death registers (median time to death: 7.5 d) (Table 3). The 2 other deaths during the first year postdonation were due to external causes of morbidity and mortality (1 land transport accident and 1 accidental fall). A further 3 deaths contributed to external causes of death (median time to death: 6.9 y).

Half the deaths were from neoplasms (median time to death: 5.5 y) and nearly 20% were from cardiovascular causes (median time to death: 7.0 y). The earliest cancer death occurred between 1.5 years and 2 years from donation and was due to pancreatic cancer (Figure 2B; Figure S1, SDC, <http://links.lww.com/TXD/A239>). Of the 16 cancer deaths, pancreatic cancer ($n = 3$; time to death range: 1.6–10.0 y) was most common, followed by breast cancer ($n = 2$; time to death range: 3.5–5.6 y), lung cancer ($n = 2$; time to death range: 3.7–7.5 y), mesothelioma ($n = 2$; time to death range: 5.4–7.1 y), and stomach cancer ($n = 2$; time to death range: 7.2–7.4 y). There were also 2 deaths from mental and behavioral disorders (time to death

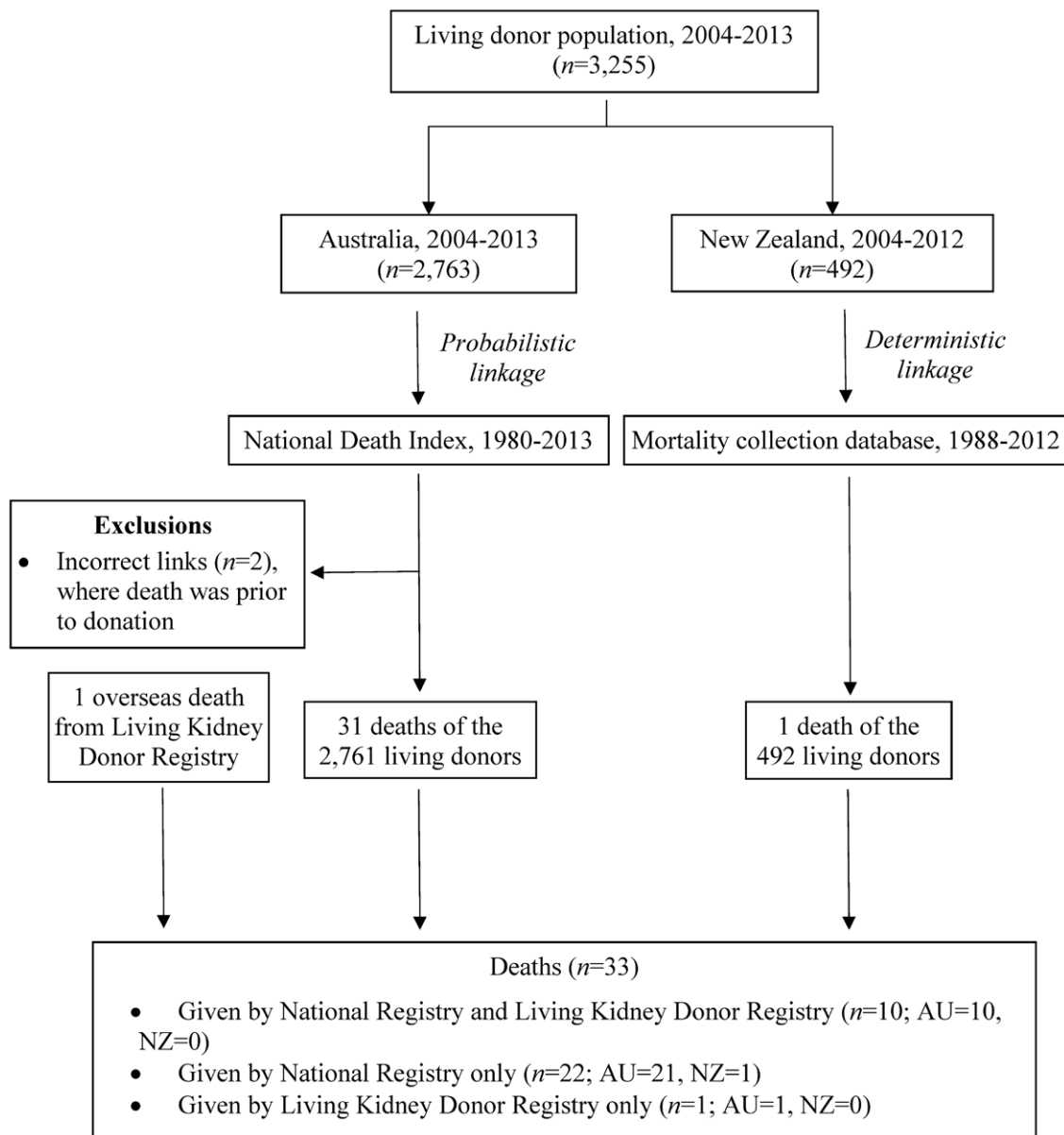


FIGURE 1. Flowchart of living donor linkage and matching of death date. AU, Australia; NZ, New Zealand.

range: 2.4–6.0 y) and 1 death from diseases of the nervous system (time to death: 5.8 y).

Mortality Rates

Overall, the crude mortality rate was 157 (95% confidence interval [CI], 111–222)/100 000 person-years and the SMR was 0.33 (95% CI, 0.24–0.47), indicating that living donor population had only about one-third of the deaths expected in the general population. The SMR has remained relatively stable over time (Figure 3A). Since 2008, living donors have half or less than half the deaths expected from the matched general population. The SMR was also relatively consistent across age and sex (test for interaction: $P > 0.100$) (Figure 3B).

Relative Survival

The observed survival in the living donors exceeded the expected survival for up to 8 years postdonation, with a relative survival exceeding 1.0 for the entire follow-up period

(Figure 4). At 5 years postdonation, the observed survival in living donors was 99.3% and the expected survival was 97.5%; thus, the 5-year survival probability was 2% higher among living donors relative to the general population (cumulative relative survival: 1.019; 95% CI, 1.014–1.021). Hence, an additional 2% of the living donor population were alive compared with the expected proportion alive from the matched general population.

DISCUSSION

Using data linkage, we found 33 deaths among all living kidney donors over a decade in Australia and New Zealand. The living kidney donor population had about one-third of the deaths compared with the general population of the same age, sex, and calendar year. The survival probability of living donors was also comparable or even greater than the general population. Overall, half the deaths in living donors were attributed to cancer.

TABLE 1.
Characteristics of living donors by death status

Characteristics	Dead	Alive	Total
	n (%) ^a	n (%) ^a	n (%) ^a
Total (%)	32 (1) ^b	3221 (99) ^b	3253 (100) ^b
Age at donation (y)			
≤29	1 (3)	170 (5)	171 (5)
30–49	4 (13)	1439 (45)	1443 (44)
50–64	18 (56)	1369 (43)	1387 (43)
65–74	8 (25)	231 (7)	239 (7)
≥75	1 (3)	12 (<0.4)	13 (<0.5)
Median [IQR]	61 [57–66]	50 [42–57]	50 [42–58]
Gender			
Female	15 (47)	1844 (57)	1859 (57)
Male	17 (53)	1377 (43)	1394 (43)
Y of donation			
2004–2009	23 (72)	1625 (50)	1648 (51)
2010–2013	9 (28)	1596 (50)	1605 (49)
Country			
Australia	31 (97)	2730 (85)	2761 (85)
New Zealand	1 (3)	491 (15)	492 (15)
Racial background			
European	32 (100)	2773 (86)	2805 (86)
Indigenous Oceania	0 (–)	111 (3)	111 (3)
Asian	0 (–)	229 (7)	229 (7)
African and Middle Eastern	0 (–)	38 (1)	38 (1)
Other	0 (–)	25 (1)	25 (1)
Not reported	0 (–)	45 (1)	45 (1)
Smoking status			
Current/former	19 (59)	1247 (39)	1266 (39)
Never	13 (41)	1888 (59)	1901 (58)
Unknown	0 (–)	86 (3)	86 (3)
Fasting glucose at donation (mmol/L)			
Normal (≤6.0)	24 (75)	2648 (82)	2672 (82)
Impaired (6.1–6.9)	0 (–)	17 (1)	17 (1)
Diabetes (≥7.0)	1 (3)	24 (1)	25 (1)
Missing	7 (22)	532 (17)	539 (17)
Median [IQR]	5.0 [5.0–5.2]	5.0 [4.9–5.0]	5.0 [4.9–5.0]
2-h glucose tolerance test at donation (mmol/L)			
Normal (≤7.7)	12 (38)	1617 (50)	1629 (50)
Impaired (7.8–11.0)	0 (–)	67 (2)	67 (2)
Diabetes (≥11.1)	0 (–)	3 (<0.1)	3 (<0.1)
Not performed	18 (56)	1036 (32)	1054 (32)
Missing	2 (6)	498 (15)	500 (15)
Median [IQR]	4.5 [4.0–5.6]	5.0 [4.0–6.0]	5.0 [4.0–6.0]
Self-reported comorbidities			
Diabetes	0 (–)	16 (<0.5)	16 (<0.5)
Hypertension	4 (13)	330 (10)	334 (10)
Body mass index (kg/m ²)			
Underweight (≤18.4)	1 (3)	20 (1)	21 (1)
Normal (18.5–24.9)	8 (25)	1106 (34)	1114 (34)
Overweight (25.0–29.9)	16 (50)	1365 (42)	1381 (42)
Obese (≥30.0)	4 (13)	561 (17)	565 (17)
Missing	3 (9)	169 (5)	172 (5)

^aColumn percentages.

^bRow percentages.

IQR, interquartile range.

This is the first study with medium- to long-term follow-up of living kidney donors in Australia and New Zealand. We were able to use data linkage to ascertain deaths and reduce lost to follow-up in our study population. The Living

Kidney Donor Registry only captured 10 of the 33 deaths reported in the National Death Registry. There is no formal system for maintaining follow-up in living donors after donation, which can underestimate deaths among the living

TABLE 2.
Summary of early complications posttransplant

Characteristics	Dead	Alive	Total
	n (%) ^a	n (%) ^a	n (%) ^a
Total (%)	32 (1) ^b	3221 (99) ^b	3253 (100)
Adverse events post-donation			
Acute myocardial infarction	0 (–)	1 (<0.1)	1 (<0.1)
Hemorrhage	2 (6)	15 (<0.5)	17 (1)
Pulmonary Embolus	1 (3)	5 (<0.2)	6 (<0.2)
Other ^c	2 (6)	302 (9)	304 (9)
None	27 (84)	2814 (87)	2841 (87)
Not reported	0 (–)	84 (3)	84 (3)
Serum creatinine at discharge in $\mu\text{mol/L}$ (mg/dL)			
≤ 100 (≤ 1.1)	10 (31)	1250 (39)	1260 (39)
101–150 (1.1–1.7)	18 (56)	1636 (51)	1654 (51)
≥ 151 (≥ 1.7)	3 (9)	234 (7)	237 (7)
Missing	1 (3)	101 (3)	102 (3)
Median ($\mu\text{mol/L}$) [IQR]	119 [91–134]	108 [92–127]	108 [92–127]
Median (mg/dL) [IQR]	1.34 [1.03–1.51]	1.22 [1.04–1.44]	1.22 [1.04–1.44]
Estimated glomerular filtration rate ^d at discharge (mL/min/1.72 m ²)			
≥ 90	1 (3)	90 (3)	91 (3)
60–89	10 (31)	1383 (43)	1393 (43)
30–59	20 (63)	1642 (51)	1662 (51)
≤ 29	0 (–)	4 (<0.2)	4 (<0.2)
Missing	1 (3)	102 (3)	103 (3)
Median [IQR]	53 [49–60]	58 [51–68]	58 [51–68]

^aColumn percentages.

^bRow percentages.

^cOther adverse events included gastrointestinal (n = 72), surgery related (n = 49), respiratory (n = 35), pain (n = 32), renal (n = 24), cardiac (n = 18), other (n = 21), allergic reactions (n = 14), neurological and psychological (n = 9), testicular (n = 9), no details (n = 9), liver related (n = 8), and fever (n = 4).

^dCalculated using the CKD-EPI formula.²⁰

CKD-EPI, chronic kidney disease epidemiology collaboration; IQR, interquartile range.

kidney donor population. Internationally, many living kidney donor registries have had difficulty in maintaining long-term follow-up, with barriers including lack of funding, inconvenience for donor, and unpaid donor time.⁸ For example, the United Network for Organ Sharing extended follow-up of living donors from 12 months to 24 months in 2008; however, data completeness still remains low.²⁶ Further, data linkage to national death registries has not been undertaken due to poor data quality of social security numbers and other demographics. Hence, our study has demonstrated that linkage to national death registries is highly beneficial in the setting of living donors where long-term follow-up is often inadequate.

The living donor population experienced fewer deaths than expected from in the matched general population. Previous studies have shown similar results when comparing mortality in the living donor population to the general population^{11–13} or matched controls.^{14–17} In a Swedish study with 20-year follow-up, there were 33 deaths in living donors and the expected deaths was 46, giving an estimated SMR of 0.72.¹¹ A matched cohort study in Canada found the mortality rate from cardiovascular causes in living donors was about half that of the controls (living donors 1.05/1000 person-y; controls 2.48/1000 person-y).¹⁴ We also found that mortality rates across age and calendar year remained lower in living donors compared with the general population. In contrast, a US study found the mortality rate among older living donors was comparable to matched controls (living donors 4.9/1000 person-y; controls 5.6/1000 person-y).¹⁶ Lower mortality rates among living donors are likely due to them being a highly selected group

that undergo extensive medical and psychosocial assessment. There is also some indication that our older living donors are even more highly selected compared with other countries, with the lowest SMR among those aged 50–64 years. On the other hand, greater survival in Australian living donors may reflect differences in care received postdonation or in mortality rates in the general population. Our findings suggest that undergoing live kidney donation does not place them at a greater risk of mortality compared with people in the general population of the same age and sex.

Our study findings align with previous studies, providing no evidence of decreased survival among living donors compared with the general population. While previous studies comparing to the general population have not presented relative survival, 2 studies have reported the observed and expected survival in living donors using alternate estimation methods.^{11,13} In a Swedish study, the observed survival exceeded the expected survival up to 20 years postdonation, where at 5 years postdonation the observed survival was 4% higher relative to the expected survival.¹¹ In comparison, in our study, we found the observed survival was only 2% higher than the expected survival. This may be due to the Swedish study including living donors from a much earlier era, from 1964 to 1994, where they may have more selective criteria for donation. A more recent study in Japan reported the observed survival in living donors at 98.2% and the expected survival at 97.0% at 5 years postdonation, which was similar to our findings.¹³ In a matched cohort, the survival gain in living donors was less pronounced, where the

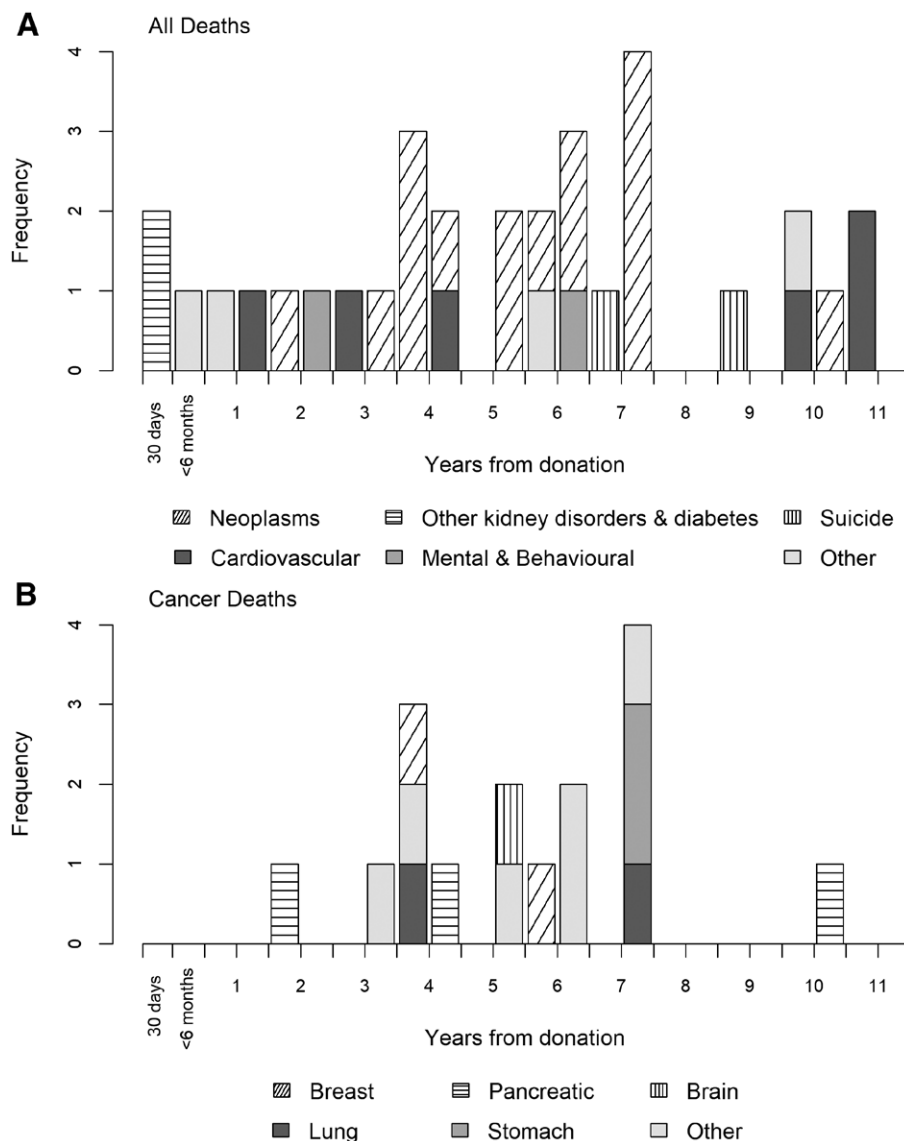


FIGURE 2. Frequency histogram of time from donation to death for: (A) all deaths; (B) cancer deaths. The 2 deaths within 30 days of donation were a result of adverse events at the time of donation. One donor had a postoperative thromboembolic event, and the other had a cardiac arrest subsequent to massive hemorrhage.

survival probability in living donors was 0.5% higher than controls at 5-year follow-up.¹⁷ It is important to note that relative survival is rarely reported to exceed 1, as it is more commonly used to compare a diseased population with a reference population. One study in a healthy cohort of athletes has reported relative survival >1.0, but comparably lower than reported in our living donors.²⁷

Although it might seem that the results from the SMR and relative survival are not compatible, they in fact coincide completely. SMR is a relative measure of observed to expected deaths, while relative survival is a relative measure of observed to expected survival (ie, probability of surviving in those at risk). The observed 32 deaths were only a third of the deaths expected in the matched general population, but this is only a relative measure of the number of deaths. On the other hand, the survival derived in the relative survival considers the proportion alive relative to those remaining at risk during follow-up, using the observed deaths for the observed survival and the expected deaths for the expected survival.

However, both the absolute number of observed and expected deaths are still relatively small considering the sample of 3000 persons. Thus, estimating survival using either the observed or the expected number of deaths results in similar survival probabilities, reflecting a small increase in relative survival (unlike SMR where we see a substantial difference in the relative number of deaths).

Cancer was the leading cause of death among our living kidney donor population, accounting for 50% of deaths. Potential living donors are medically assessed to ensure transmission risks to recipients are minimized, and the longevity of the kidney is maintained. In Australia, a recent history of cancer or active cancer is regarded as an absolute contradiction in guidelines for living donor assessment.²⁸ However, screening is only deemed necessary based on the person's cancer history, family risk, age, and sex.²⁹ Thus, it is unclear if current cancer screening in potential living donors is adequate to detect undiagnosed malignancies. In our cohort, the first cancer death occurred 1.6 years

TABLE 3.
Causes of death for living donors

ICD-10-AM Codes	Description	Freq (%)
(C00–D49)	Neoplasms	16 (50.0)
(C25)	Pancreatic cancer	3 (9.4)
(C50)	Breast cancer	2 (6.3)
(C33–C34)	Lung cancer	2 (6.3)
(C45–C49)	Malignant neoplasms of mesothelial and soft tissue	2 (6.3)
(C16)	Stomach cancer	2 (6.3)
(C71)	Brain cancer	1 (3.1)
(C18–C21)	Colorectal cancer	1 (3.1)
(C61)	Prostate cancer	1 (3.1)
(C90)	Multiple myeloma and malignant plasma cell neoplasms	1 (3.1)
(C26, C39, C76–C80)	Cancer, unknown, ill-defined	1 (3.1)
(I00–I99)	Diseases of the circulatory system	6 (18.8)
(I20–I25)	Coronary heart disease	3 (9.4)
(I60–I69)	Cerebrovascular disease	2 (6.3)
(I71)	Aortic aneurysm and dissection	1 (3.1)
(U50–U73, U90, V00–Y98)	External causes of morbidity and mortality	5 (15.6)
(X60–X84)	Suicide	2 (6.3)
(V01–V89)	Land transport accidents	2 (6.3)
(W00–W19)	Accidental falls	1 (3.1)
(N00–N99)	Diseases of the genitourinary system	2 (6.3)
(N25–N29)	Other kidney or ureter disorders	2 (6.3)
(F00–F99)	Mental and behavioral disorders	2 (6.3)
(F01, F03, G30)	Dementia and Alzheimer disease	1 (3.1)
(F10–F19)	Mental and behavioral disorders due to psychoactive substance use	1 (3.1)
(G00–G99, except G30)	Diseases of the nervous system	1 (3.1)
(G12)	Spinal muscular atrophy and related syndromes	1 (3.1)
	Total	32 (100.0)

ICD-10-AM, International Classification of Diseases, 10th Revision, Australian Modification.

postdonation from pancreatic cancer and the remaining cancer deaths occurred after 3 years postdonation, with a median of 5.5 years postdonation. Further, data on cancer transmission from an organ donor to recipient are limited to case reports and case series. Future studies are needed to assess whether there was any evidence of cancer transmissions from these living donors. On the other hand, our findings may be a result of extensive cardiac screening of potential living donors, including ECG, echo, and stress testing, leading to exclusion of those at increased risk of cardiovascular death.²⁸ Other developed countries have reported similar findings with cancer the most common cause of death among living donors, while cardiovascular disease is the main cause of death among the general population.^{13,30}

As expected, our findings showed that living donors have better survival compared with the general population. However, this is the first study in Australia and New Zealand to evaluate survival in living donors with complete follow-up using data linkage. We used the general population as the reference population as used in other studies.^{11,13} Although the reference population is ideally comparable to living donors except for the exposure, which is donating a kidney, there are limited other available comparison populations from Australia and New Zealand. Living donors are highly selected and screened for medical conditions. A matched cohort would require mortality data on at least 6000–9000 individuals without the screened medical conditions and similar age distribution for appropriate power and

precision.^{31,32} Further, selection bias may occur if selected controls are not representative of those who would be eligible for kidney donation.³³ This may occur if controls are overly screened for medical conditions or if using controls from existing cohorts formed for other research purposes. In addition, overmatching may occur which can reduce study efficiency or bias results.³⁴ Therefore, our results do not suggest that kidney donation has no impact on survival in living donors but rather that, as expected, living donors maintain high survival postdonation compared with the general population.

There are other limitations to our study. First, we used probabilistic linkage in the Australian living donors and deterministic linkage in our New Zealand living donors. Probabilistic linkage may result in incorrectly linked donors. Nonetheless, the estimated false positive rate is relatively low at <5 per 1000 records.³⁵ Second, we included all living donors from 2004 to 2013, with a median follow-up of 6.2 years. While our follow-up is somewhat limited, this is comparable to other survival studies in living donors.^{14,16,17} Further, we were limited to data collected in the Living Kidney Donor Registry, which is not exhaustive of all screening performed or multiple measures pretransplant. For example, it is possible that some donors with diabetes lost weight before donation and subsequently normalized glucose metabolism but we were unable to explore this with the available data. Repeating this study in the future when longer follow-up is available and the collection of further donor assessment data will provide additional insights.

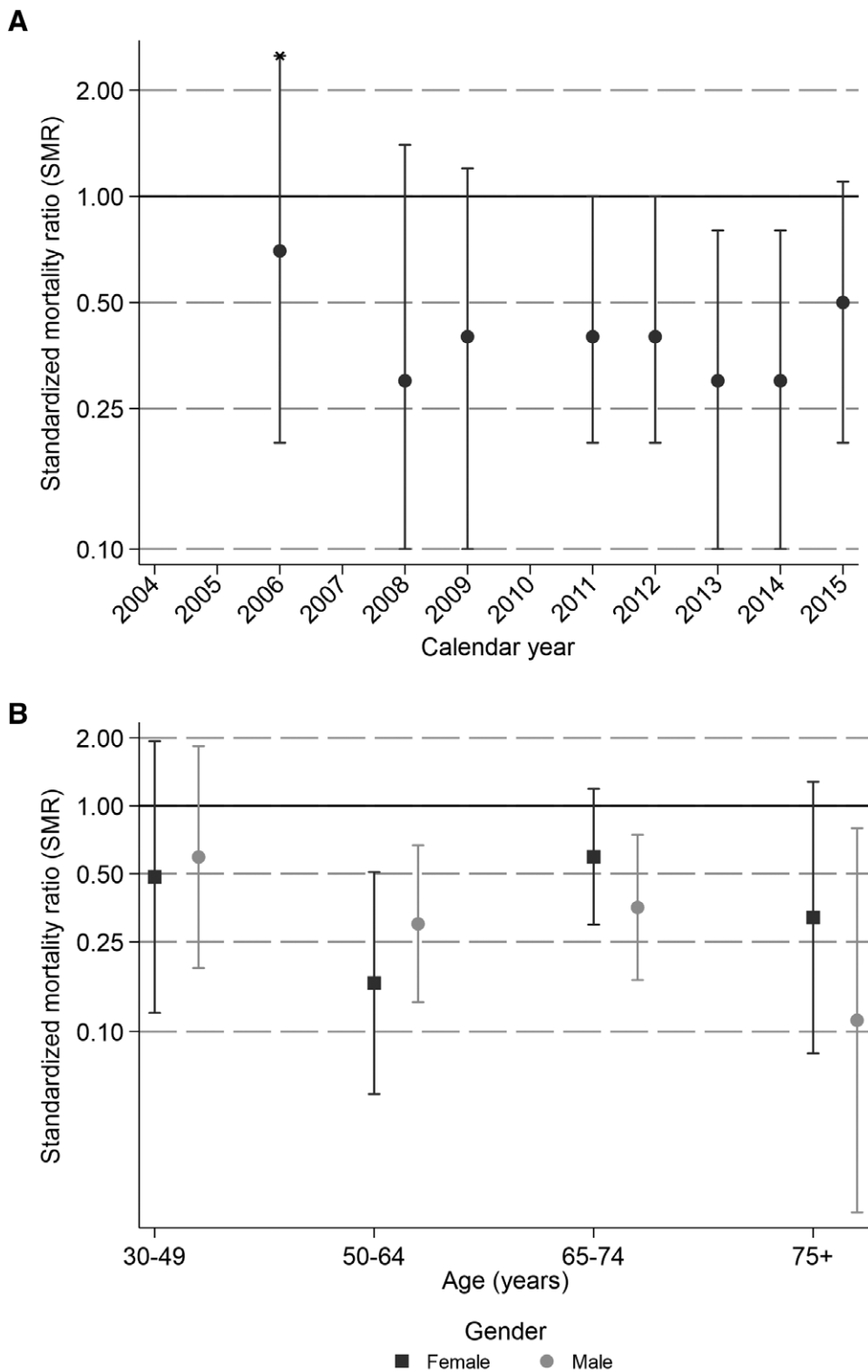


FIGURE 3. The estimated standardized mortality ratios (SMR) with 95% confidence intervals for all-cause deaths by: (A) calendar year of follow-up, and (B) age during follow-up and sex. The standardized mortality ratio (y axis) is displayed on a logarithmic scale.

In conclusion, we found that living kidney donors experienced fewer deaths and higher than expected survival post-donation in Australia and New Zealand. These findings are necessary for informing potential organ donors of the associated mortality risks and help to guide shared decision making. Future studies with longer follow-up are needed to assess whether these survival gains pertain long term.

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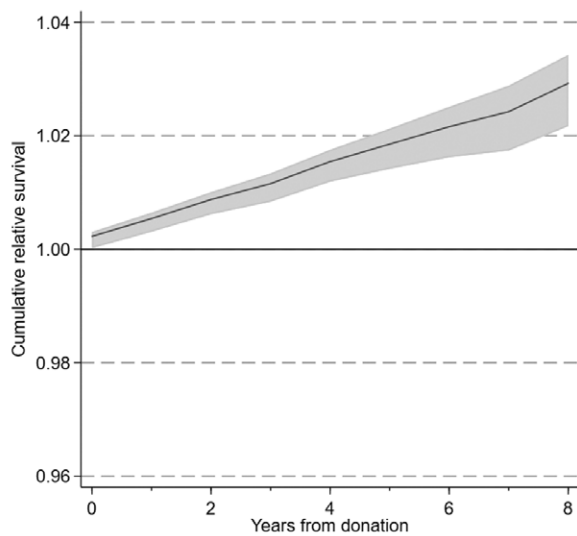


FIGURE 4. Cumulative relative survival of living donor population compared with the general population, matching on age, calendar year, and gender.

process. The interpretation and reporting of these data are the responsibility of the Editors and in no way should be seen as an official policy of interpretation of Australian and New Zealand Dialysis and Transplant (ANZDATA), AIHW, or the New Zealand Ministry of Health.

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