RESEARCH COMMUNICATION

Epidemiology of Cancers of the Kidney in an Australian Population

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Abstract

Background. Kidney cancer has a high incidence in Australia by world standards but has attracted little public health attention because of its low ranking among other cancers as a cause of death. Incidence, mortality and survival trends were investigated in this study for an Australian population and cancer control opportunities considered. Design. Age-standardized incidence and mortality rates were analyzed by broad age category using data from an Australian cancer registry. Disease-specific survivals were analyzed using the Kaplan-Meier product limit estimate and multivariable Cox proportional hazards regression. Results. Incidence rates approximately doubled during 1980-2008, with large increases affecting both sexes. Increases were more evident for renal cell and other histology types occurring predominantly in adulthood than childhood nephroblastomas. The male to female incidence ratio approximated 2:1 but decreased over time and was lower in younger than older age groups. The increase in mortality rate was smaller (at 25%) and higher in males (at 36%) than females (at 7%). Mortality increases were restricted to the age range of 70 years and over. Five-year survivals increased from 47% for 1980-84 to 66% for 2000-08 and multivariate predictors of high case fatality were older age at diagnosis and less recent diagnostic period. Country cases had lower survivals than metropolitan cases, although the difference was small. Conclusions. Increases in mortality were smaller than incidence increases, evidently due to offsetting increases in case survival, and did not affect the younger age groups. Further reductions in tobacco smoking and reducing the prevalence of obesity will be important to prevent renal cell carcinomas. Molecular research is advocated to develop targeted therapies and potentially, an effective screening technology. Cancer registries need to routinely publish their data by histology type to enable more detailed global trend analyses. Population registries also need to record stage of cancer at diagnosis to facilitate interpretation of changes in survival.

Keywords: Kidney cancer - incidence - mortality - prevention - control - Australia

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Introduction

Primary cancers of the kidney are the 15th leading cause of cancer death in Australia, accounting for about 2% of all cancer deaths (AIHW, 2010). Kidney cancers have not attracted the same level of public health attention as cancers of the lung, prostate, female breast, large bowel and other more common causes of cancer death in Australia, nor as much attention as more prevalent cancers such as cancers of the skin (AIHW, 2010). Nonetheless kidney cancer has an age-standardized rate in Australia that is high by world standards, with an incidence approximately twice the world average and a mortality rate almost two thirds higher than the corresponding world figure (Ferlay et al., 2010). In general, Australian rates of cancer of the kidney, renal pelvis and ureter are similar to rates for Europe and those estimated by the International Agency for Research on Cancer for the more economically developed countries (Ferlay et al., 2010).

The risk of kidney cancer varies socio-demographically. In Australia there is a steep age gradient, leading to an incidence about 23 times higher in people over 70 years than in those under 50 years of age (AIHW, 2010). Also there is an excess in males with an approximate 2:1 male to female incidence ratio (AIHW, 2010). In general, the Australian born tend to have an incidence about 10% higher than Australian residents born in other countries (CCSA, 2003) (NSW Health, 2010), and residents of postcode areas in the lowest socio-economic quintile have an incidence about 15% higher than for areas in the highest socio-economic quintile (CCSA, 2003) (NSW Health, 2010). While the accuracy of incidence data for Aboriginal and Torres Strait Islander residents is uncertain, this population group appears to have an age-standardized incidence about 20% lower than other residents (Zhang et al., 2011).

Increasing attention is being given to kidney cancer in Australia following an increase in age-standardized

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incidence of about 85% in the 15 years to 2007 although mortality rates have remained relatively stable, with some evidence of a decline since the mid-1990s (AIHW, 2010). Similar incidence increases have been reported in North America (Horner et al., 2009). Between 1980 and 1992, mortality rates for cancers of the kidney and renal pelvis increased by about 1.3% per annum in North America, but this increase was followed by a reduction of about 0.6% per annum during 1992-2006 (Horner et al., 2009). Increases in mortality were also reported in Northern Europe prior to the mid-1990s, followed by declines (Corgna et al., 2007; Levi et al., 2008; Weikert & Ljungberg, 2010; Ondrusova et al., 2011).

In this study Australian cancer registry data are used to investigate time trends in incidence and mortality rates for kidney cancer by age, sex and histology type, and survival outcomes are investigated by diagnostic period, socio-demographic characteristics and histology type. The implications of results for cancer control, research and cancer data collection are indicated.

Materials and Methods

Data collection

The South Australian Cancer Registry was employed as the data source. The Registry has received statutory notifications of invasive kidney cancers with reliable histology information since 1980. The Registry covers all regions of South Australia (one of eight Australian states and territories) and invasive cancers of all types except non-melanoma skin cancers. Its procedures have been described previously (SACR, 2000). Death data are collected through routine notifications, electronic searches of official State death records and the National Death Index at the Australian Institute of Health and Welfare, and from interstate registries. Under-ascertainment has been checked through active follow-up, and with deaths reported independently, and found to be minimal (Bonett et al., 1988; SACR, 2000).

The present study included 4,121 invasive cancers of the kidney (ICD-O-3: C64) diagnosed between 1980 and 2008 (Fritz et al., 2000). They comprised 3,885 renal cell carcinomas (SNOMED 81403, 82603, 82703-83123), 75 nephroblastomas (SNOMED 89603, 89613), 47 other specified histology types (mostly sarcomas), and 114 invasive cancers of non-specified histological type.

Socio-demographic descriptors included age at diagnosis; sex; region of residence, classified as metropolitan or non-metropolitan and as 20 statistical sub-divisions (SACR, 2000); country of birth (World Health Organization criteria) (Ferlay et al., 2010); Aboriginal and Torres Strait Islander status; and relative socio-economic disadvantage, as inferred from residential postcode characteristics using the SEIFA index of relative socio-economic disadvantage (ABS, 1998).

Statistical analyses

A de-identified file was extracted and analysed in-house under provisions of the South Australian Health Care Act 2008, employing STATA 9.2 software (StataCorp, 2005).

Mean annual incidence and mortality rates were calculated by age and sex for six periods, i.e., 1980-84, 1985-89, 1990-94, 1995-99, 2000-04 and 2005-08. Rates were directly standardized by five-year age group (with an open-ended category from 85 years) to the 2001 Australian reference population (Armitage & Berry, 1987; StataCorp, 2005). Ninety-five per cent confidence limits were calculated assuming a Poisson distribution, as described previously (Dobson et al., 1991). Rates were obtained for all ages combined and by broad age category (i.e., under 50, 50-69 and 70 years or more) to investigate time trends.

Differences in socio-demographic descriptors were investigated by histology type. Initially descriptors were analysed as univariate predictors, using the Pearson chi-square test for nominal variables (substituting the Fisher Exact Test when cell sizes were small) and the Kruskal-Wallis ANOVA for ordinal variables (Armitage and Berry, 1987; StataCorp, 2005).

Kaplan-Meier product-limit estimates of disease-specific survival were calculated, using one-day intervals and treating dates of death from other causes prior to the end of 2008, and for people still alive still alive, December 31st, 2008, as censoring dates (Armitage and Berry, 1987; StataCorp, 2005). Multivariable Cox proportional hazards regression was also undertaken to assess socio-demographic and histological predictors of survival from renal cancer. Parallel analyses were undertaken by histology type. The regression analysis employed the same censoring criteria as for the Kaplan-Meier analyses. All predictor variables were entered into the analysis, with backwards elimination of candidate predictors where the fit of the model did not reduce as a consequence ($p>0.05$). Assumptions underlying the analysis, including proportionality and an absence of co-linearity, were found to be satisfied (Armitage & Berry, 1987; StataCorp, 2005).

Disease-specific survival was employed, not relative survival, because the life tables needed to undertake relative survival analyses were not available for many population sub-groups. Analyses have shown very similar survival estimates in South Australia, irrespective of use of disease-specific or relative survival method (SACR, 1997; SACR, 2000), such that the disease-specific survivals presented here are regarded as a good proxy for relative survivals. For example, 10-year relative survival was found to be 49.2% in a study of kidney cancers diagnosed in 1977-2003, which was similar to the 50.8% 5-year disease-specific survival calculated for that same period (SACR, 2007).

Results

Trends in incidence and mortality

Kidney cancers comprised 2.2% of all invasive cancers recorded on the Registry for 1980-2008, 2.6% of those in males and 1.7% of those in females. The proportion increased from 1.8% in 1980-84 to 2.6% in 2005-08. Almost two thirds (65.0%) occurred in males. The great majority were renal cell carcinomas (94.3%) but there was a small number of nephroblastomas (1.8%), other histology types (mostly sarcomas) (1.1%) and other cancers of non-specified histology type (2.8%).

Table 1. Annual Incidence (95% Confidence Limits) of Invasive Cancer of the Kidney per 100,000 Population by Calendar Year and Sex*

	Age (yrs)	1980-84	1985-89	1990-94	1995-99	2000-04	2005-08	Total 1980-2008
Males	< 50	[n=37]	[n=37]	[n=57]	[n=80]	[n=83]	[n=72]	[n=366]
		1.80	1.72	2.29	3.04	3.10	3.34	2.52
		(1.27,2.48)	(1.21,2.37)	(1.73,2.97)	(2.41,3.78)	(2.47,3.84)	(2.61,4.21)	(2.27,2.79)
	50 - 69	[n=123]	[n=176]	[n=174]	[n=249]	[n=294]	[n=286]	[n=1302]
		18.89	26.09	24.75	34.21	36.87	40.44	29.86
		(15.7,22.5)	(22.4,30.2)	(21.2,28.7)	(30.1,38.7)	(32.8,41.3)	(35.9,45.4)	(28.3,31.5)
	70+	[n=73]	[n=97]	[n=138]	[n=201]	[n=274]	[n=228]	[n=1011]
		39.37	43.06	55.72	66.17	79.72	77.23	59.62
		(30.9,49.5)	(34.9,52.5)	(46.8,65.8)	(57.3,76.0)	(70.6,89.7)	(67.5,87.9)	(56.0,63.4)
	Total	[n=233]	[n=310]	[n=369]	[n=530]	[n=651]	[n=586]	[n=2679]
		8.57	10.26	11.55	14.89	16.69	17.34	13.07
		(7.50,9.74)	(9.15,11.5)	(10.4,12.8)	(13.7,16.2)	(15.4,18.0)	(16.0,18.8)	(12.6,13.6)
Females	< 50	[n=27]	[n=23]	[n=35]	[n=54]	[n=45]	[n=33]	[n=217]
		1.30	1.04	1.41	2.05	1.68	1.48	1.49
		(0.86,1.89)	(0.66,1.56)	(0.98,1.96)	(1.54,2.67)	(1.23,2.25)	(1.02,2.08)	(1.30,1.70)
	50 - 69	[n=79]	[n=60]	[n=104]	[n=98]	[n=125]	[n=139]	[n=605]
		11.74	8.46	13.76	13.24	15.25	18.81	13.36
		(9.29,14.6)	(6.45,10.9)	(11.2,16.7)	(10.8,16.1)	(12.7,18.2)	(15.8,22.2)	(12.3,14.5)
	70+	[n=41]	[n=52]	[n=100]	[n=122]	[n=150]	[n=155]	[n=620]
		14.72	15.84	26.36	28.03	30.89	37.62	25.16
		(10.6,20.0)	(11.8,20.8)	(21.5,32.1)	(23.3,33.5)	(26.1,36.3)	(31.9,44.0)	(23.2,27.2)
	Total	[n=147]	[n=135]	[n=239]	[n=274]	[n=320]	[n=327]	[n=1442]
		4.57	3.84	6.10	6.60	6.99	8.17	5.97
		(3.86,5.37)	(3.22,4.55)	(5.35,6.92)	(5.84,7.43)	(6.24,7.80)	(7.31,9.11)	(5.67,6.29)
Persons	<50	[n=64]	[n=60]	[n=92]	[n=134]	[n=128]	[n=105]	[n=583]
		1.54	1.37	1.83	2.53	2.37	2.40	1.99
		(1.19,1.97)	(1.05,1.76)	(1.48,2.24)	(2.12,3.00)	(1.98,2.82)	(1.96,2.91)	(1.83,2.16)
	50 - 69	[n=202]	[n=236]	[n=278]	[n=347]	[n=419]	[n=425]	[n=1907]
		15.07	17.07	19.11	23.49	25.77	29.28	21.38
		(13.1,17.3)	(15.0,19.5)	(16.9,21.5)	(21.1,26.1)	(23.4,28.4)	(26.6,32.2)	(20.43,22.36)
	70+	[n=114]	[n=149]	[n=238]	[n=323]	[n=424]	[n=383]	[n=1631]
		24.55	26.96	37.75	43.86	51.81	55.23	39.53
		(20.3,29.5)	(22.8,31.7)	(33.1,42.9)	(39.2,48.9)	(47.0,57.0)	(49.8,61.1)	(37.63,41.50)
	Total	[n=380]	[n=445]	[n=608]	[n=804]	[n=971]	[n=913]	[n=4121]
		6.29	6.78	8.49	10.40	11.46	12.48	9.21
		(5.97,6.96)	(6.16,7.44)	(7.83,9.19)	(9.69,11.14)	(10.8,12.2)	(11.7,13.3)	(8.93,9.50)

*Directly standardized by age to the Australian population 2001; Data source: South Australian Cancer Registry

Renal cancers accounted for 2.0% of cancer deaths recorded on the Registry for 1980-2008, comprising 2.3% of cancer deaths in males and 1.6% of those in females. The proportion ranged from 1.8% in 1980-84 to 2.3% in 2005-08. Almost two thirds (64.9%) occurred in males. The histology types responsible for these deaths were renal cell carcinomas (91.8%), nephroblastomas (1.2%), other histology types (1.6%) and cancers of non-specified histology type (5.5%).

The mean annual age-standardized incidence (95% confidence limits) per 100,000 for kidney cancer increased by 98.4% from 6.3 (5.7, 7.0) in 1980-84 to 12.5 (11.7, 13.3) in 2005-08, with pronounced increases occurring in both sexes (Table 1). A secular increase was evident in each age group, which increased in magnitude with age from 55.8% for ages under 50 years to 125.0% in the age range of 70 years and older. Increases varied by histology type ($p<0.001$) with a smaller increase applying to nephroblastomas. The proportion of nephroblastomas diagnosed in 2000-08 (25.3%) was smaller than the proportions of other cancers diagnosed in 2000-08 (i.e., 46.4% for renal cell carcinomas; 59.6% for cancers of other histology type; and 31.6% for cancers of non-specified histology type).

The male to female age-standardized incidence ratio was 2.2:1 for 1980-2008, which increased with age from 1.7:1 in people under 50 years to 2.4:1 in people aged 70 years or more (Table 1). There was a markedly higher incidence in the older ages , such that the mean annual incidence per 100,000 in 1980-2008 was 2.0 (1.8, 2.2) for 0-49 years and 21.4 (20.4, 22.4) for 50-69 years, increasing to 39.5 (37.6, 41.5) for 70 years and over.

Univariate analyses by histology type showed a difference by age at diagnosis ($p<0.001$), with 94.7% of nephroblastomas being diagnosed in children under 15 years of age, but conversely most other histology types being diagnosed in the age range of 60 years and older (i.e., 67.4% of renal cell carcinomas; 61.6% of other specified histology type; and 87.8% of non-specified histology types). There was also a difference by sex ($p=0.015$)

Table 2. Annual Mortality Rate (95% Confidence Limits) of Invasive Cancer of the Kidney per 100,000 Population by Calendar Year and Sex*

	Age (yrs)	1980-84	1985-89	1990-94	1995-99	2000-04	2005-08	Total 1980-2008
Males	< 50	[n=13]	[n=13]	[n=14]	[n=13]	[n=17]	[n=12]	[n=82]
		0.59	0.65	0.57	0.50	0.64	0.56	0.59
		(0.31,1.01)	(0.35,1.11)	(0.31,0.96)	(0.27,0.86)	(0.37,1.02)	(0.29,0.98)	(0.47,0.73)
	50 - 69	[n=61]	[n=76]	[n=64]	[n=84]	[n=83]	[n=66]	[n=434]
		9.58	11.41	8.95	11.42	10.45	9.26	10.21
		(7.33,12.3)	(8.99,14.3)	(6.89,11.4)	(9.11,14.1)	(8.32,13.0)	(7.16,11.8)	(9.27,11.22)
	70+	[n=50]	[n=64]	[n=74]	[n=94]	[n=126]	[n=139]	[n=547]
		27.62	29.16	30.67	32.01	37.64	47.52	33.64
		(20.5,36.4)	(22.5,37.2)	(24.1,38.5)	(25.9,39.2)	(31.4,44.8)	(40.0,56.1)	(30.9,36.6)
	Total	[n=124]	[n=153]	[n=152]	[n=191]	[n=226]	[n=217]	[n=1063]
		4.81	5.35	4.95	5.51	5.93	6.54	5.48
		(4.00,5.74)	(4.54,6.27)	(4.19,5.80)	(4.76,6.35)	(5.18,6.76)	(5.70,7.47)	(5.16,5.82)
Females	<50	[n=9]	[n=5]	[n=6]	[n=8]	[n=9]	[n=5]	[n=42]
		0.42	0.21	0.24	0.30	0.34	0.22	0.29
		(0.19,0.80)	(0.07,0.49)	(0.09,0.52)	(0.13,0.59)	(0.16,0.65)	(0.07,0.51)	(0.21,0.39)
	50 - 69	[n=36]	[n=28]	[n=34]	[n=28]	[n=28]	[n=25]	[n=179]
		5.56	3.83	4.54	3.51	3.39	3.33	4.05
		(3.89,7.70)	(2.54,5.54)	(3.14,6.34)	(2.33,5.07)	(2.25,4.90)	(2.15,4.92)	(3.48,4.69)
	70+	[n=30]	[n=38]	[n=70]	[n=68]	[n=67]	[n=81]	[n=354]
		10.68	11.51	18.53	15.42	13.55	18.86	14.62
		(7.21,15.3)	(8.14,15.8)	(14.5,23.4)	(12.0,19.6)	(10.5,17.2)	(15.0,23.4)	(13.1,16.2)
	Total	[n=75]	[n=71]	[n=110]	[n=104]	[n=104]	[n=111]	[n=575]
		2.36	1.95	2.75	2.31	2.14	2.53	2.33
		(1.86,2.96)	(1.52,2.46)	(2.26,3.31)	(1.89,2.80)	(1.75,2.59)	(2.08,3.05)	(2.14,2.53)
Persons	< 50	[n=22]	[n=18]	[n=20]	[n=21]	[n=26]	[n=17]	[n=124]
		0.50	0.43	0.40	0.39	0.49	0.39	0.44
		(0.31,0.76)	(0.25,0.68)	(0.24,0.62)	(0.24,0.60)	(0.32,0.72)	(0.23,0.62)	(0.37,0.52)
	50 - 69	[n=97]	[n=104]	[n=98]	[n=112]	[n=111]	[n=91]	[n=613]
		7.46	7.51	6.67	7.28	6.82	6.19	7.00
		(6.05,9.10)	(6.14,9.10)	(3.41,8.13)	(5.99,8.76)	(5.61,8.21)	(4.98,7.60)	(6.46,7.58)
	70+	[n=80]	[n=102]	[n=144]	[n=162]	[n=193]	[n=220]	[n=901]
		17.26	18.53	23.18	22.38	23.26	30.29	22.21
		(13.7,21.5)	(15.1,22.5)	(193.6,27.3)	(19.1,26.1)	(20.1,26.8)	(26.4,34.6)	(20.8,23.7)
	Total	[n=199]	[n=224]	[n=262]	[n=295]	[n=330]	[n=328]	[n=1638]
		3.39	3.46	3.70	3.74	3.80	4.24	3.70
		(2.94,3.90)	(3.02,3.94)	(3.27,4.18)	(3.33,4.19)	(3.40,4.23)	(3.79,4.72)	(3.51,3.88)

*Directly standardized by age to Australian population 2001; Data source, South Australian Cancer Registry

with a relatively low male to female ratio applying to nephroblastomas (1.0:1) compared with the 2.2:1 applying for renal cancers in general. Histology type also varied by country of birth (p<0.001), with 2.6% of kidney cancers in the Australian born being nephroblastomas compared with a corresponding 0.3% in other patients. This was due to age differences, however. Logistic regression indicated that after adjusting for age at diagnosis, nephroblastomas were not more common among kidney cancers in the Australian born than in sub-groups born in other countries (p>0.150). A difference in histology type was not evident between metropolitan and country residents (p=0.309), or between statistical regions (p=0.150), socio-economically defined groups (p=0.286) or between Aboriginal and Torres Strait Islander and other people (p=0.778) (note however that the number of cancers reported in Aboriginal and Torres Strait Islander patients was small (n=18) and the statistical power available to detect differences by Aboriginal and Torres Strait Islander status was low).

Mortality rates showed less pronounced increases over time than incidence data. The mean annual age-standardized mortality rate per 100,000 increased by 25.1% from 3.4 (2.9, 3.9) in 1980-84 to 4.2 (3.8, 4.7) in 2005-08, with a larger increase of 36.0% applying to males than the 7.2% for females (Table 2). Increases were not indicated in the age range under 70 years, but the mean annual rate in people aged 70 years or more increased by 75.5% from 17.3 (13.7, 21.5) in 1980-84 to 30.3 (26.4, 34.6) in 2005-08, with marked percentage increases affecting both sexes.

Survivals

Survivals from renal cancer were 61.7% at five years, 54.7% at 10 years and 49.7% at 15 years from diagnosis (Table 3). Lower survivals occurred with increasing age at diagnosis (p<0.001) and potentially in country than metropolitan residential areas (p=0.045). Statistically significant differences were not apparent by sex (p=0.999), socio-economic status of residential area (p=0.087), statistical sub-divisions of residential area within

Table 3. Percentage Survival from Invasive Cancer of the Kidney in an Australian population by Socio-demographic and Cancer Characteristics and Years from Diagnosis*

Characteristic	Total	5	10	15	P value**
All cases (n=4,121)	100	61.7	54.7	49.7	-
Age at diagnosis (yrs):					
Under 15 (n=76)	100	79.7	79.7	79.7	
15-39 (n=137)	100	74.0	68.0	68.0	
40-49 (n=370)	100	76.1	71.8	69.4	
50-59 (n=793)	100	68.8	61.2	57.8	p<0.001
60-69 (n=1,114)	100	63.0	55.2	45.9	
70-79 (n=1,093)	100	56.7	48.2	40.6	
80+ (n=538)	100	39.4	30.1	27.6	
Sex:					
Male (n=2,679)	100	61.3	54.2	49.1	p=0.999
Female (n=1,442)	100	62.4	55.7	50.9	
SES (SEIFA):					
Low (n=1,364)	100	60.9	53.2	47.8	
Mid low (n=989)	100	59.6	51.1	47.0	p=0.087
Mid high (n=778)	100	61.0	55.8	53.3	
High (n=990)	100	65.7	59.8	52.6	
Residence:					
City (n=3,054)	100	63.0	56.1	51.0	p=0.045
Country (n=1,067)	100	58.1	50.6	46.3	
Country of birth:***					
Australia (n=2,701)	100	60.4	52.6	47.9	
UK/Ireland (n=544)	100	61.5	54.9	47.8	
South Eur (n=248)	100	62.7	59.2	55.5	p=0.439
West Eur (n=182)	100	59.8	56.8	49.4	
East Eur (n=123)	100	59.7	58.0	52.8	
Other (n=156)	100	53.1	39.3	36.8	
Histology type:					
Renal cell (n=3,885)	100	62.9	55.4	50.1	
Nephroblast. (n=75)	100	76.9	76.9	76.9	p<0.001
Other (n=47)	100	46.7	46.7	46.7	
Unknown (n=114)	100	15.0	12.5	-	
Diagnostic period (yrs):					
1980-84 (n=380)	100	46.7	40.0	35.9	
1985-89 (n=445)	100	51.0	43.5	40.1	
1990-94 (n=608)	100	57.4	59.8	47.2	p<0.001
1995-99 (n=804)	100	66.8	61.3	-	
2000-08 (n=1,884)	100	66.3	-	-	-

*Kaplan-Meier product limit estimate; disease specific survival; Date of censoring of live cases of December 31st, 2008; ** derived using Cox proportional hazards regression

country and metropolitan areas (p>0.100), or country of birth (p=0.439). A difference applied by histology type (p<0.001), however, with higher survivals applying to nephroblastomas than other histology types. Marked increases in survival applied in the more recent diagnostic periods (p<0.001) for all renal cancers combined, with the five-year survival increasing from 46.7% for 1980-84 to 66.3% for 2000-08. The five-year survival was similar for Aboriginal and Torres Strait Islander cases at 58.8% compared with 61.7% for other cases (p=0.794).

Multivariable Cox proportional hazards regression confirmed that risk of case fatality from renal cancers was higher in older patients and country residents, and that case fatality decreased markedly in more recent diagnostic periods (Table 4). Differences were not found by sex, socio-economic status, statistical sub-division, or country of birth (p>0.150), after adjusting for age,

Table 4. Relative Risk of Death (95% Confidence limits) from Invasive Cancer of the Kidney: South Australia, 1980–2008 Diagnoses*

Predictors	Relative risk
Age at diagnosis (yrs):	
Under 50 (reference) (n=583)	1.00
50-59 (n=793)	1.54 (1.34, 1.76)
60-69 (n=1,114)	1.82 (1.50, 2.21)
70-79 (n=1, 093)	2.37 (1.95, 2.88)
80+ (n=538)	4.43 (3.58, 5.49)
Histology type:	
Renal cell (reference) (n=3,885)	1.00
Nephroblastoma (n=75)	0.64 (0.38, 1.07)
Other (n=47)	1.89 (1.24, 2.88)
Unknown (n=114)	3.39 (2.71, 4.25)
Place of residence:	
Metropolitan (reference) (n=3,054)	1.00
Country (n=1,067)	1.23 (1.10, 1.37)
Period of diagnosis:	
1980-84 (reference) (n=380)	1.00
1985-89 (n=445)	0.86 (0.71, 1.03)
1990-94 (n=608)	0.68 (0.57, 0.81)
1995-99 (n=804)	0.48 (0.40, 0.58)
2000-08 (n=1,884)	0.44 (0.37, 0.52)

*Derived from Cox proportional hazards model. Date of censoring of live cases of December 31st, 2008

histology type, and diagnostic period. After adjusting for age and other variables included in the model, renal cell carcinomas tended to have a higher case fatality than nephroblastomas, although statistical significance was not achieved (p=0.091). By comparison, renal cell carcinomas had a lower case fatality than other histology types (Table 4).

Multivariable models also showed that for each histology category, case fatality increased with increasing age at diagnosis but decreased for more recently diagnosed cases. Compared with the 1980-84 diagnostic period, the relative risk for 2000-08 was 0.66 (0.60, 0.71) for renal cell carcinomas, 0.45 (0.21, 0.998) for nephroblastomas, 0.52 (0.27, 0.99) for other specified histology types, and 0.62 (0.45, 0.84) for cancers of non-specified histology type.

Discussion

Renal cancers have a much higher age-standardized incidence in Australia than the world average (Ferlay et al., 2010). Additionally an approximate two-fold increase in incidence was observed in this study between 1980-84 and 2005-08. Similar increases have been reported in North America (Horner et al., 2009). The increase observed in the present study affected both males and females and all age groups, although it was more pronounced in age groups over 70 years.

It is probable that advances in diagnostic imaging have led to increased detection, artificially increasing measured incidence (Weikert & Ljungberg, 2010), leading to earlier cancer stage at diagnosis, but staging data are not reported by the SA Cancer Registry (or most other population-based registries worldwide), so this expectation could not be confirmed. In addition, the increased use of surveillance

imaging is thought to have led to greater detection rates (Volpe, 2007). It seems likely however that earlier detection would have affected all age groups and would not explain the larger secular increases in incidence seen in the older age range.

Tobacco smoking is an established cause of renal carcinomas (Pascual & Borque, 2008; Weikert & Ljungberg, 2010) and would have contributed to the higher incidence in males and the higher male to female sex ratio in the older age groups. The 1:1 male to female sex ratio for nephroblastomas, as compared with the approximate 2:1 ratio for all renal cancers, likely reflects the absence of a smoking contribution in the aetiology of nephroblastoma (Pascual & Borque, 2008; Weikert & Ljungberg, 2010).

While a contribution of tobacco smoking to time trends in renal cancer would be expected, smoking trends have varied by sex (ABS, 2000) in contrast with the increases in incidence in both sexes observed in this study. It seems likely therefore that incidence increases also would have been influenced by other non-smoking factors to which both males and females were exposed, such as increases in obesity, potentially exposures to carcinogenic medications or environmental chemicals (Pascual & Borque, 2008; Weikert & Ljungberg, 2010), and artificial lead-time increases through earlier detection. While the proportion of Australians having haemodialysis for end-stage chronic renal disease has risen, which likely would have increased the risk of renal carcinoma (Pascual & Borque, 2008; Weikert & Ljungberg, 2010; KDA, 2010), the numbers of people so affected are thought to have been too small in proportional terms to explain the large increases in incidence observed in this study (KDA, 2010).

Aboriginal and Torres Strait Islander residents have an excess in many risk factors for renal cancers, including an elevated smoking prevalence, a higher prevalence of obesity, and raised levels of chronic end-stage renal disease (O'Dea et al., 1988; Smith et al., 1992; Hoy, 1996; Hoy et al., 1997). The indication in the literature of a lower incidence of renal cancer in this sub-population than for other Australians, albeit not statistically significant, is unexpected in this context, but may have been due to random error from small numbers or poor recording in cancer registries of Aboriginal and Torres Strait Islander status (Zhang et al., 2011).

In contrast to the two-fold increase in incidence, the age-standardized mortality rate increased by only around 25% between 1980-84 and 2005-08. The scale of increase probably was reduced by offsetting increases in survivals (note: five-year survivals increased from about 47% in 1980-84 to 66% in 2000-08). Survival increases potentially reflected gains in earlier detection and surgical technique, plus improvements from immunotherapy and advances in other systemic treatments (including gains from more aggressive chemotherapy for nephroblastomas). While new targeted therapies may also be improving clinical outcomes for metastatic renal carcinoma, these therapies were introduced too recently to explain the increases in survivals observed in this study (Hutson, 2007).

While there is no indication to date of a decrease in mortality, in contrast to suggested decreases since the mid1990s in North America (Horner et al., 2009), Northern Europe (Corgna et al., 2007; Levi et al., 2008; Weikert & Ljungberg, 2010; Ondrusova et al., 2011) and some other areas of Australia (AIHW, 2010), it is reassuring that mortality increases were not observed in the age range under 70 years despite incidence increases. This may reflect more complete and effective therapies in younger fitter patients and a greater opportunity for survival gains to fully compensate for the smaller incidence increases occurring in these age groups. Hopefully the lack of an increase in mortality in ages less than 70 years will prove to be a cohort effect that will affect the whole population as these younger cohorts move through the older age range.

The lower survivals seen in older patients may also reflect diagnoses at a more advanced stage when prospects for survival are lower, but staging data were not available from the registry to confirm this possibility. Also the lower survivals in country than metropolitan residents may reflect less ready access to the specialist diagnostic and treatment services located in major urban centres. Again, potential differences in stage could not be investigated by place of residence with the data available. Australia has sparsely populated remote areas where attempts are made to optimize access to services and specialist support for local clinicians through telemedicine and other telecommunication technologies, but eliminating access inequalities entirely would not be a realistic prospect at this time.

Gains in survival occurred for all histology sub-types. Although nephroblastomas had higher survivals than other histology types, these cancers mostly affect children. After adjusting for age, nephroblastomas still tended to have higher survivals than renal cell carcinomas, although statistical significance was not achieved (p=0.091). Difficulty was encountered fully adjusting for age, however, due to co-linearity, so it was difficult to determine how much of the higher survivals for nephroblastomas were due to the cancer type and how much was a function of age.

The present study included all renal cancers irrespective of histology type, as presented routinely in national and international population-based reports (Horner et al., 2009; AIHW, 2010; Ferlay et al., 2010). In view of differences in aetiology, biological behaviour, prognosis and treatment by histology, we recommend that population-based registries routinely present their data by histology to facilitate analyses of global trends at this level. International standards of histology groupings have already been specified by the International Agency for Research on Cancer and should be used for this purpose (Parkin et al., 1998).

As molecular science leads to further categorization of cancers by biomarkers, it will also be important for cancer registries to collect data at that level. Opportunities exist for registry experts to work with pathologists in the development of structured pathology reporting and means of transferring data from these reports to registries (RCPA, 2010). Before uniform data can be collected through this means worldwide, internationally agreed protocols for pathology reporting will be needed that include agreed biomarker and staging data (CA, 2008).

In conclusion, incidence rates for renal cancers have

increased in Australia but less so in younger than older age groups. Meanwhile increases in mortality have been smaller apparently due to offsetting increases in case survival. Mortality increases were not evident in this study in the younger age ranges. Emphasis on further reducing tobacco smoking prevalence and levels of obesity will be important to prevent renal carcinoma. Molecular research into renal cancer biomarkers will be important for developing targeted therapies and potentially effective screening methodologies. Cancer registries need to routinely report histology and staging data to facilitate a better interpretation of global trends in incidence and survival.

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