CHAPTER 10

CANCER REPORT

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CANCER REPORT

This year the cancer report has three components. Firstly, we revise the site-specific cancer risk for people undergoing dialysis or after their first kidney transplant. Secondly we examine survival for people with a kidney transplant who are diagnosed with either colorectal or breast cancer and thirdly we use ANZDATA data to inform an economic model of screening for renal cancer in kidney transplant recipients.

SITE SPECIFIC CANCER RISK IN RENAL REPLACEMENT THERAPY

To compare the risk of a cancer at different sites we compared the observed number of incident cancer diagnoses notified to ANZDATA with the expected number of cancer diagnoses in the general population. We used indirect standardisation, standardising for differences in age, sex and calendar year for years 1982 to 2005, to calculate standardised incidence ratios (SIR) with their 95% confidence intervals. SIR can be interpreted as relative risk, where an SIR value of one is risk equal to that of the general population of similar age and sex, living in equivalent time periods, in the same country, and an SIR of two is double the risk. For the general population cancer incidence data we used the Australian Cancer Database (ACD), formerly the National Cancer Statistics Clearing House to compare with Australian ANZDATA registrants.

We examined cancer risk for people treated with dialysis and for after first kidney transplant separately. Once people had received a transplant, all subsequent cancers were counted in the post transplant group even if there was transplant failure and subsequent return to dialysis. Cancer site-specific risk for dialysis patients is summarised in Figure 10.1. Overall data 33,772 people were included in the analysis, with 90,504 person-years of follow up during dialysis treatment and 120,121 person-years of follow up after first transplant.

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When considering cancer risk by cancer site, pattern of increased risk is varied. For many cancers there is a slight increase in risk among dialysis patients with a greater increase post transplantation. Examples of this include common cancer such as lung and colon. For several cancers, the risk increase after transplantation is more marked. The cancers with a more marked risk increase after transplantation are those known or postulated to have viral aetiology - for example cervical cancer, lymphoma, Kaposi's sarcoma.

Caution should always be used when interpreting analyses from observational data. One potential limitation is that cancers collected by ANZDATA and those collected by cancer registries have used different notification systems. A previous report (ANZDATA report 2005) examined possible implications of any misclassification by either notification system, and concluded that although differences did exist, they did not result in important differences to SIR calculations. Other limitations are that we have not used New Zealand general population data in this analysis, and have not been able to adjust for indigenous race, as population cancer statistics are not widely available for indigenous Australians. We hope to be able to address these issues in subsequent analyses.

Figure 10.1

Relative Risk of Diagnosis of Cancer Whilst Undergoing Dialysis and After Kidney Transplantation in Australia and New Zealand

ICD Code	Cancer Site	Number (Dialysis)	SIR (Dialysis)	Number (Post Transplant)	SIR (Post Transplant)
C01-C14	Head and Neck	26	1.25 [0.82-1.83]	66	4.45 [3.44-5.66]
C15	Oesophagus	22	1.61 [1.01-2.44]	28	4.29 [2.85-6.20]
C16	Stomach	34	1.20 [0.83-1.68]	16	1.24 [0.72-2.01]
C17	Small Intestine	8	2.99 [1.29-5.9]	4	2.56 [0.70-6.56]
C18-20	Colorectal	169	1.16 [0.99-1.34]	127	1.72 [1.43-2.04]
C21	Anus	4	1.70 [0.46-4.36]	18	12.4 [7.4-19.7]
C22	Liver	23	2.85 [1.91-4.27]	19	4.43 [2.67-6.91]
C23-24	Gall Bladder	9	1.21 [0.55-2.29]	8	2.35 [1.02-4.63]
C25	Pancreas	22	0.95 [0.60-1.44]	15	1.44 [0.81-2.37]
C30-31	Nasal Cavity, Middle Ear and Sinuses	4	2.5 [0.68-6.40]	7	7.09 [2.85-14.6]
C32	Larynx	8	0.86 [0.37-1.68]	12	2.07 [1.07-3.62]
C33-34	Trachea, Bronchus and Lung	201	1.63 [1.41-1.87]	115	1.96 [1.62-2.35]
C37-38	Other Thoracic Organs	13	17.7 [9.42 - 30.3]	8	15.2 [6.57-30.0]
C40-41	Bone and Articular Cartilage	3	2.64 [0.55-7.73]	5	4.90 [1.59-11.4]
C43	Melanoma of the Skin	107	1.41 [1.16-1.71]	180	3.11 [2.67-3.60]
C45	Mesothelioma	11	1.71 [0.86-3.07]	3	0.98 [0.20-2.86]
C46	Kaposi Sarcoma	8	10.99 [4.75-21.7]	23	25.5 [16.2-38.3]
C47-49	Other Connective and Soft Tissue	3	0.67 [0.14-1.97]	9	2.91 [1.33-5.53]
C50	Breast (Females Only)	116	2.57 [2.13-3.08]	81	2.35 [1.89-2.92]
C51-58	Gynaecological	183	10.0 [8.63-11.6]	231	18.0 [15.7-20.4]
C60	Penis	1	2.47 [0.06-13.7]	9	37.4 [17.1-71.0]
C61	Prostate	100	1.30 [1.05-1.57]	54	1.72 [1.30-2.25]
C62	Testis	1	1.03 [0.03-5.72]	4	1.96 [0.54-5.03]
C63	Other Male Genital Organs	1	8.23 [0.20-45.9]	1	14.7 [0.37-82.1]
C64	Kidney	173	8.30 [7.11-9.63]	122	9.76 [8.10-11.7]
C65-66, C68	Other Urinary Organs	33	6.38 [4.39-8.95]	46	19.6 [14.3-26.1]
C67	Bladder	135	3.77 [3.16-4.46]	93	6.19 [5.00-7.58]
C69	Eye	0	0 [0-1.53]	6	3.80 [1.39-8.36]
C71	Brain	21	1.69 [1.05-2.59]	12	1.33 [0.69-2.32]
C70, C72	Other Central Nervous System	1	1.96 [0.05-10.9]	4	9.06 [2.47-23.2]
C73	Thyroid Gland	35	5.89 [4.10-8.19]	30	4.82 [3.25-6.89]
C74-75	Other Endocrine Glands	5	10.1 [3.29-23.7]	4	9.38 [2.56-24.0]
C76-C80, C26, C39	Unknown Primary Site	67	1.67 [1.29-2.12]	59	3.32 [2.53-4.28]
C81-C85, C96	All Lymphomas	58	1.56 [1.18-2.02]	266	11.4 [10.1-12.9]
C90	Multiple Myeloma	96	7.60 [6.15-9.28]	15	2.48 [1.39-4.09]
C91-95	Leukaemias	23	0.88 [0.56-1.32]	32	2.39 [1.63-3.37]

IMPACT OF BREAST AND COLORECTAL CANCER ON SURVIVAL AFTER KIDNEY TRANSPLANTATION

Transplantation improves expected survival for most people with ESKD compared with remaining on dialysis, however, life expectancy for a transplant recipient is still reduced compared to someone of a similar age and sex without ESKD. People in the general population who are diagnosed with cancer also have a reduced life expectancy compared with those who do not have cancer. We do not know how the life expectancy of someone having both a transplant and a cancer diagnosis is altered. In this work we describe expected survival for transplant patients with breast or colorectal cancer compared to transplant recipients without cancer, and with people in the general population diagnosed with breast or colorectal cancer. Using relative survival techniques, we compared survival in these groups after allowing for the background mortality expected in the general population. The preliminary results of this work were presented at the Transplant Society of Australia and New Zealand 27th Annual Scientific Meeting in Canberra in June 2009.

Relative survival was calculated as the ratio of observed compared to expected survival in the general population of Australia and New Zealand of the same age and sex, over the same time period. A ratio of 1 indicates survival equivalent to the general population, ratios <1 lower survival (higher mortality) compared to the general population. For general population mortality data we used data from the Australian Bureau of Statistics and Statistics New Zealand. The mortality data for people in the general population diagnosed with colorectal or breast cancer was provided by the Australian Cancer Database (ACD), (formerly the National Cancer Statistics Clearing House) and the New Zealand Health Information Service. We used data from ANZDATA for mortality data for both the transplant population, and the transplant population with colorectal or breast cancer.

Data were available for calendar years 1988-2004 from all the data sources, so analysis was limited to this time period. The relative survival analysis standardised for any differences in mortality attributable to age, sex, calendar year and country (Australia or New Zealand) among the populations.

Between 1988-2004 there were 8,958 prevalent kidney transplant recipients in Australia and New Zealand, representing 58,966 years at risk. During this time a total of 72 (0.8%) women were diagnosed with breast cancer and 117 (1.3%) men and women with colorectal cancer.

Relative survival for people with breast cancer is shown in Figure 10.3. The effect of comorbidity with a kidney transplant and breast cancer was pronounced overall and for all age subgroups, with poorer relative survival compared with the transplant alone and the breast cancer alone groups. This is reported in Figure 10.2. For example, a woman aged 50-59 with breast cancer experiences a 14% excess mortality compared with expected background mortality in the general population, a woman of the same age with a transplant experiences 16% excess mortality, and a woman with both a transplant and a breast cancer experiences 48% excess mortality.

Relative survival for people with colorectal cancer is shown in Figure 10.4. Survival differed by age and sex (shown in Figure 10.2). For males > 55 years, the five year relative survival was 0.79 with transplant alone, 0.57 with colorectal cancer alone, but 0.27 with transplant plus colorectal cancer (73% excess mortality compared to general population expectations). Women with both transplant and colorectal cancer had a marked excess mortality compared to men, and to women with cancer alone or transplant alone.

Figure 10.2

Five Year Relative Survival for Transplant Recipients
With or Without Breast or Colorectal Cancer
and People Without Transplants with Breast or Colorectal Cancer

	Colorectal				Breast		
Age Group	**< 55**		**≥ 55**		**< 50**	**50-59**	**≥ 60**
Gender	**Male**	**Female**	**Male**	**Female**	**Female**		
Cancer Alone	0.61	0.63	0.57	0.57	0.83	0.86	0.81
Transplant Alone	0.92	0.91	0.79	0.81	0.91	0.84	0.81
Transplant and Cancer	0.55	0.30	0.27	0.21	0.72	0.52	0.62

For both cancers, relative survival was poorer with transplant plus cancer compared to cancer or transplant alone for these two common cancers, showing that co-morbidity has an adverse effect on outcomes after cancer diagnosis. It is unclear whether cancer treatment is less effective, more toxic, or the underlying cancer more aggressive in people with transplants. Transplant recipients have increased mortality when diagnosed with cancer compared to the cancer and general populations, which is likely to have implications for the benefits and harms of cancer screening programs.

Figure 10.3

Relative Survival for Female Transplant Recipients
With and Without Breast Cancer
and Women with Breast Cancer Alone

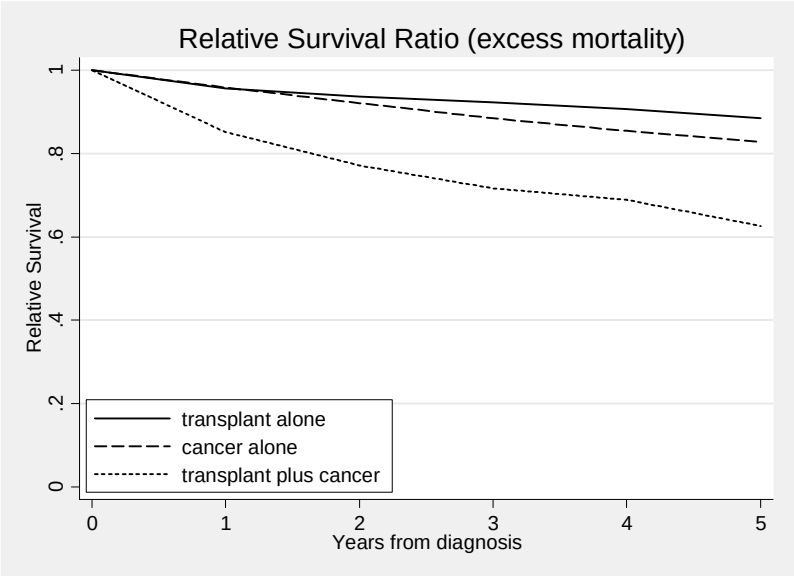
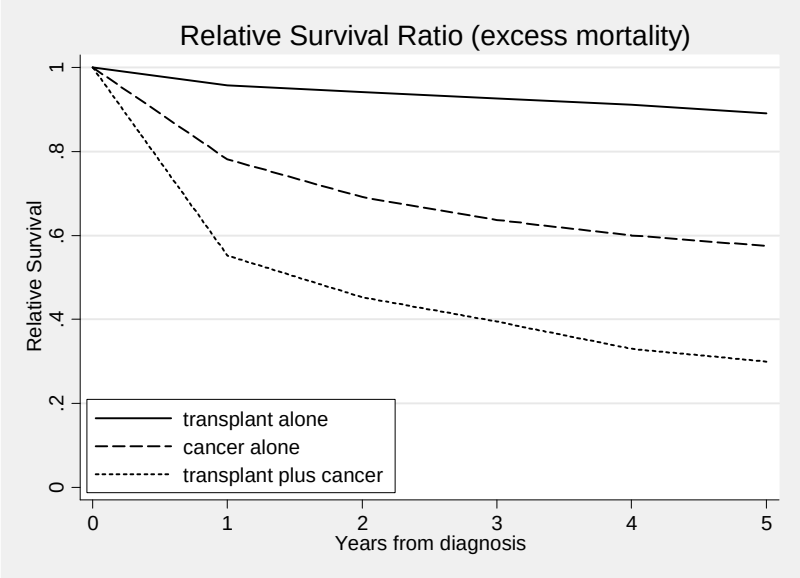


Figure 10.4

Relative Survival for Transplant Recipients
With and Without Colorectal Cancer
and People with Colorectal Cancer Alone



USING ANZDATA DATA TO INFORM AN ECONOMIC MODEL OF SCREENING STRATEGIES FOR RENAL CANCER IN THE KIDNEY TRANSPLANT POPULATION

Earlier in this chapter we showed that cancer risk is increased at most sites in the transplant population compared to the age and sex matched general population. Malignancy is also the second most common cause of death among recipients of kidney transplants. Evidence based strategies to improve cancer-specific prognoses are limited in the transplant population. Screening, which detects early stage disease, may provide plausible means to prevent the development of advanced stage cancer, by allowing earlier intervention before cancer becomes symptomatic. In previous ANZDATA cancer reports, we estimated the overall health benefits and costs of routine screening for breast, colorectal and cervical cancers in the ESKD population. In this report, we have provided the cost-effectiveness analyses of screening kidney transplant recipients for renal cancer.

A decision analytical model was developed to estimate the total and incremental health care costs and benefits of annual and biennial screening for renal cancer in the recipients' native kidneys. We used data from the ANZDATA Registry and the general population to inform the model about the natural history of the disease. Model outcomes included the average costs (in Australian dollars) and health benefits (in life years saved) of annual and biennial screening, and the incremental benefits (in life years saved) and costs (in Australian dollars) of annual and biennial screening compared with no screening.

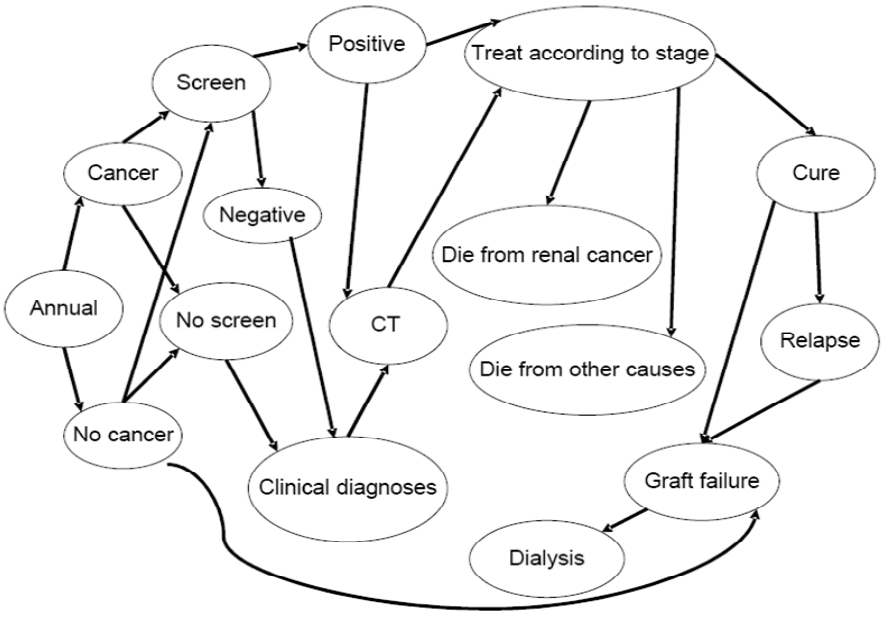
The incremental cost-effectiveness ratio was calculated using the following formula:

$$ICER = \frac{Cost_{New} - Cost_{Comparator}}{Effectiveness_{New} - Effectiveness_{Comparator}}$$

where the new were "screened" and the comparator were "unscreened" transplant recipients. Future costs and outcomes were discounted at 5% per annum. The simplified structure of the decision tree is outlined in Figure 10.5. To assess the robustness of the results we also tested the extent to which this model's assumptions were sensitive to the uncertainties within the variables using one-way sensitivity analyses.

Figure 10.5

Simplified Structure of the Model



Cost and Outcome of Annual and Biennial Screening for Renal Cancer Using Ultrasonography

Assuming a screening participation rate of 70%, the total costs in the annual screening arm were $303,000, compared to $302,600 in the biennial screening arm and $301,700 in the no screening arm per 1000 transplant recipients. The total benefits of annual screening were 13.646 life years, compared to13.645 life years for screening biennially and 13.642 life years for no screening. The incremental benefits of annual screening compared with no screening were 0.004 life-years saved (LYS), and the incremental benefits of biennial screening compared with no screening were 0.003 LYS. The incremental costs of annual screening compared with no screening were $1300 per 1000 transplant recipients. The incremental costs of biennial screening compared with no screening were $900 per 1000 transplant recipients. The incremental cost-effectiveness ration (ICER) of annual screening compared with no screening was $320,988/LYS, and the ICER of biennial screening compared with no screening was $252,100/LYS.

Over the entire screening period, there were six deaths per 1000 transplant recipients from renal cancer in the annual screening arm, compared with seven and eight deaths per 1000 transplant recipients from renal cancer in the biennial screening and the no screening arms. Compared with no screening, the relative risk reduction of death from renal cancer for annual screening was 25%, and 12.5% for biennial screening, with an absolute risk reduction of 0.2% for annual screening and 0.1% for biennial screening.

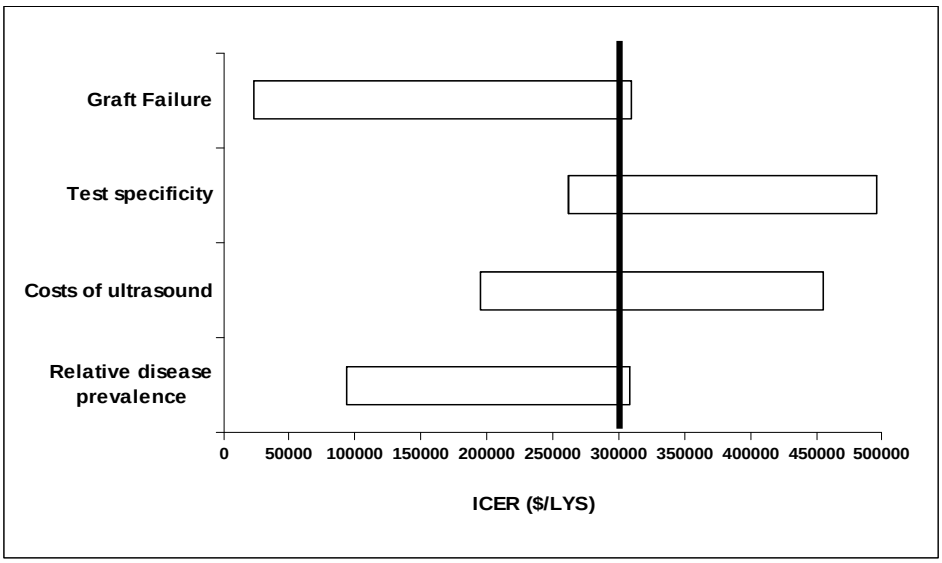
Sensitivity Analysis

When a series of sensitivity analyses were performed, the model was most sensitive to changes in the prevalence of renal cancer, the probability of graft failure and return to dialysis, the cost of ultrasound and the test specificity of ultrasonography to detect a renal cancer. Figure 10.7 shows the change in the ICER over the plausible range of estimates tested in the sensitivity analyses for annual screening compared with no screening. The black vertical line represents the ICER for annual screening compared with no screening at the base-case analysis, $320,988/LYS. There are substantial uncertainties surrounding each of these variables on the overall ICER. If a willingness-to-screen (or the cost-effectiveness) threshold is set at the recommended ratio of $100,000/LYS, annual screening for renal cancer does not appear to be good value for money, unless the annual probability of renal graft failure is less than 2% and the renal cancer prevalence is at least five times greater than the expected prevalence in the transplant population.

Despite the increased risk of renal cancer and the improved life expectancy after transplantation, routine screening (annual and biennial) using ultrasonography in this population does not appear good value for money using current data. Annual and biennial screening for renal cancer achieved very small mortality gains of less than two days of life saved, and at relatively high cost. At best, compared with no screening, the absolute gain in survival is to avoid two deaths from renal cancer per 1000 recipients if screened annually and one death from renal cancer avoided per 1000 recipients if screened biennially, with an ICER at the order of over $300,000/LYS and $200,000/ LYS for screening annually and biennially.

Figure 10.6

One-Way Sensitivity Analysis of Annual Screening for Renal Cancer Using Ultrasonography



#The black vertical line represents the incremental cost-effectiveness ratio of annual screening for renal cancer compared with no screening at base-case analysis ($320,988/LYS)

Influential variables	**Annual screening compared with no screening** Point estimates (plausible range)
Probability of graft failure	0.031 (between 0.02 and 0.04)
Test specificity of ultrasound	0.90 (between 1.0 and 0.5)
Costs of ultrasound	$120 (between $60 and $200)
Relative disease prevalence	1.0 (between 0.8 and 5.0)

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