CHAPTER 10

CANCER REPORT

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CANCER REPORT

This year the cancer report contains results of a new ANZDATA analysis on survival after cancer diagnosis, and also shows how ANZDATA cancer data has been used to inform health economics - this time looking at the implications of screening for cervical cancer in transplant recipients.

Cancer and survival after kidney transplantation

In previous reports we have quantified the increased risk of cancer at most sites after transplantation, and also provided tools to help clinicians estimate the *a priori* potential risk of cancer after transplantation for different patient groups. Previous reports have also estimated patient and graft survival for the transplanted population, but little has been published to estimate how survival is affected for transplant recipients who subsequently develop cancer. This report compares mortality among four groups: those with transplant but no cancer, those with transplant and cancer, those with cancer but no transplant, and those with neither transplant nor cancer (i.e. the general population).

We included all patients registered on ANZDATA between 1988 and 2005, as these date limits corresponded with available data for the comparison populations, i.e. the cancer population and the general population of Australia and New Zealand.

We did not include non-melanocytic skin cancers, as these are not recorded for the general population and so meaningful comparison is not easily achievable. For information on the general population we sourced survival data from the Australian Bureau of Statistics (http://www.abs.gov.au/) and Statistics New Zealand (http://www.stats.govt.nz/default.htm). For information on the general population with cancer we sourced survival data from the National Cancer Statistics Clearing House at the Australian Institute of Health and Welfare (http://www.aihw.gov.au/cancer/inbex.cfm) and the New Zealand Health Information Service (http://www.nzhis.govt.nz/).

Using indirect standardisation by age, sex and calendar year we compared the death rates among the four groups (Figure 10.1). As expected, there are differences in survival for men and for women. It is clear that death rates for people with transplant and no cancer are similar to those with cancer but no transplant, and that these death rates are similar to people 30 years older in the general population with neither transplant nor cancer. After transplantation cancer co-morbidity has devastating consequences; at all ages the mortality rate of people with both transplant and cancer are much higher.

Figure 10.1

Death Rates Indirectly Standardised
by Age, Sex and Calendar Year
Australia and New Zealand 1988 - 2005
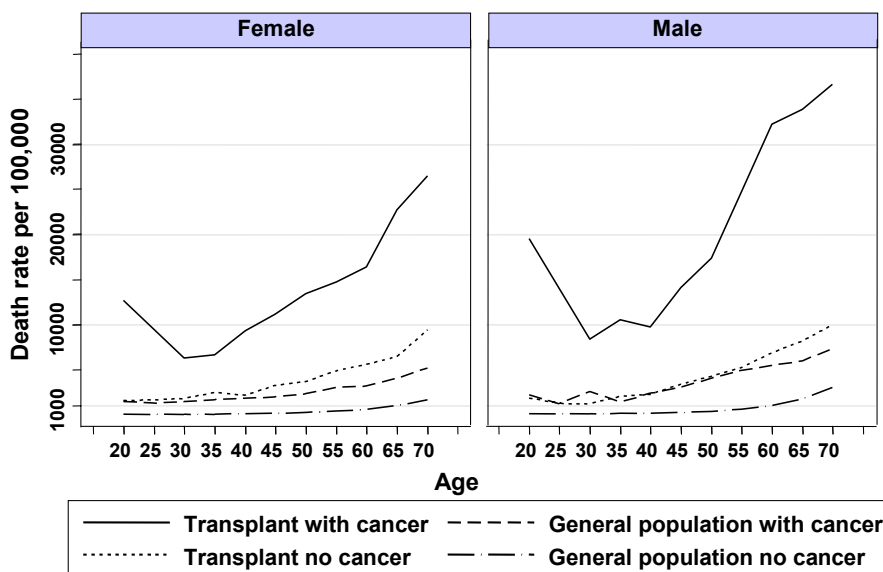
Within the ANZDATA transplant population, we identified risk factors for early death for different recipient groups. Using Cox regression, we calculated Hazard Ratios (HR: 95% CI), and absolute risk of death with and without cancer, again excluding non-melanocytic skin cancer.

Between 1963 and 2006 there were 15,183 transplant recipients, with a mean follow-up 9.0 years, and a total 135,968 years of risk. During follow-up 1642 (10.8%) developed at least one cancer and 6,479 (42.7%) died. Within the transplant population, older age and male sex increased risk of death (transplanted > 55 years versus < 35 years (HR 4.47: 4.15-4.83) male versus female (HR 1.09: 1.04-1.15), as did diabetic ESKD (versus glomerulonephritis, (HR 1.78: 1.61-1.96) and graft failure (HR 3.81: 3.62-4.01), but white racial background was protective (HR 0.79: 0.73-0.85). After allowing for these effects, cancer diagnosis increased risk of early death more than four fold (HR 4.12: 3.84-4.43). These results can be seen in Figure 10.2.

Figure 10.2	
Risk of Death after Transplantation	
Risk Factor	**Hazard Ratio**
Age at transplant	
< 35 years	1.0
35-44 years	1.9
45-54 years	3.1
≥ 55 years	4.5
Men versus women	1.1
Diabetic ESKD versus other causes	1.8
White race versus non-white race	0.8
Graft failure versus continued function	3.8
Cancer versus no cancer	4.1

These results can be used to estimate the effect of cancer diagnosis on risk of death in absolute terms for different clinical scenarios. With continued graft function, risk of death varies: for a young (< 35 years) white woman with GN and no cancer risk is 1:42, but rises to 1:10 with cancer. A non-white man aged 45-55 years with diabetic ESKD and a functioning transplant, can expect a 1:17 risk of death, rising to 1:4 with cancer.

USING ANZDATA TO INFORM ECONOMIC MODELS OF CERVICAL CANCER SCREENING STRATEGIES

In previous reports, we have estimated the costs and benefits of screening for the two most common cancers, colorectal and breast, in the dialysis and transplant populations. After transplantation, the incidence of cervical cancer, a virus-related malignancy, is at least two to three-fold greater than the age and gender matched general population. Despite the significant increase in risk, there is little information about the benefits and harms of screening transplant recipients for cervical cancer. In this report, we have provided cost-effectiveness analyses estimating the costs and outcomes of cervical cancer screening in women with kidney transplants.

Two deterministic Markov models were developed to simulate the natural history of progression of cervical dysplasia and the effects of screening (using conventional and the newer liquid-based cytology (LBC)) in a cohort of women with kidney transplants. We used data from the ANZDATA Registry and information extrapolated from the general population to inform the natural history.

Outcomes of the model included the average costs, in Australian dollars, average benefits, in life years saved (LYS) and the incremental cost-effectiveness ratio of screening using Pap smear compared with no screening, and screening using liquid-based cytology compared with conventional cytology.

The incremental cost-effectiveness (ICER) is calculated using the following formula:

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

where the "new" were screened and the "comparator" were the unscreened populations.

All costs and benefits are also discounted using a recommended discount rate of 5% per annum. A simplified structure of the model is shown in Figure 10.3. 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 10.3

Simplified Structure of the Model for Cervical Cancer Screening
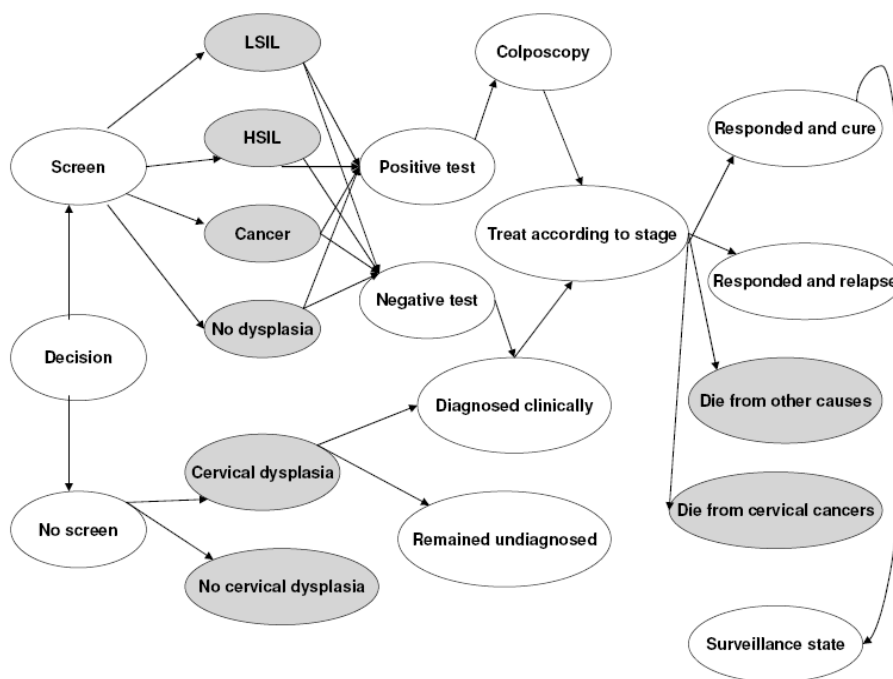
* Ovals in light grey represent data obtained from the ANZDATA Registry (1995-2006)

Ovals in white represent data extrapolated from the general population

Costs and outcomes of current practice (screening using annual conventional cytology)

The total costs for annual conventional Pap screening were $2432 per woman compared to the total costs for no screening of $1824 per woman, giving the incremental costs due to screening of $608. The total benefits of screening per woman were 15.205 LYS compared to 15.55 LYS of no screening, a difference of 0.05 LYS (18.2 days). The ICER of annual conventional Pap screening in transplanted women compared with no screening was $12,160 LYS.

Cost-effectiveness of liquid-based cytology

After a screening period of 50 years, the incremental benefits of screening with LBC compared with conventional cytology were 0.70 days of life saved with the incremental costs of $254, and an ICER of $127,000/LYS.

When a series of one-way sensitivity analyses were performed, the model was most sensitive to the costs of conventional Pap smear, costs of investigating and treating false positive results, discount rate, test specificity of the screening tool, disease prevalence, participation rate and the starting age of screening.

Assuming a cost-effectiveness threshold of $50,000/LYS, annual screening using conventional cytology remained highly-cost-effective despite varying between the best and worse estimates (Figure 10.4).

In the model comparing LBC screening and conventional cytology, despite testing the influential variables between the very best and worst estimates, the ICER remained very high and unfavourable.

The current program of conventional cytological screening in transplanted women compared with no screening appears highly cost-effective, with an ICER of less than $12,000/LYS.

Annual conventional cytological screening using Pap smear should be recommended for women (age ≥ 18) with kidney transplants.

The newer technology (LBC) adds minimal benefits but considerable costs, and should not be recommended as a routine screening tool for transplanted women.

Figure 10.4

One Way Sensitivity Analyses Showing the Influential Variables of the Screen Model

(Using Pap cytology compared with no screening)

ICER ($/LYS)
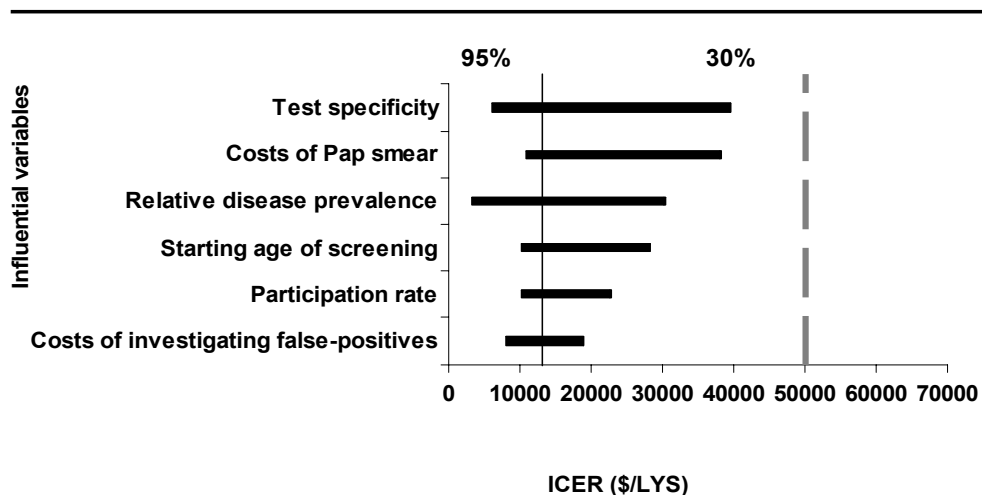
* *Grey dotted line represents the cost-effectiveness threshold of $50,000/LYS*

\# *Black vertical line represents the ICER of Pap screening compared with no screening at base-case analysis ($12,177/LYS)*