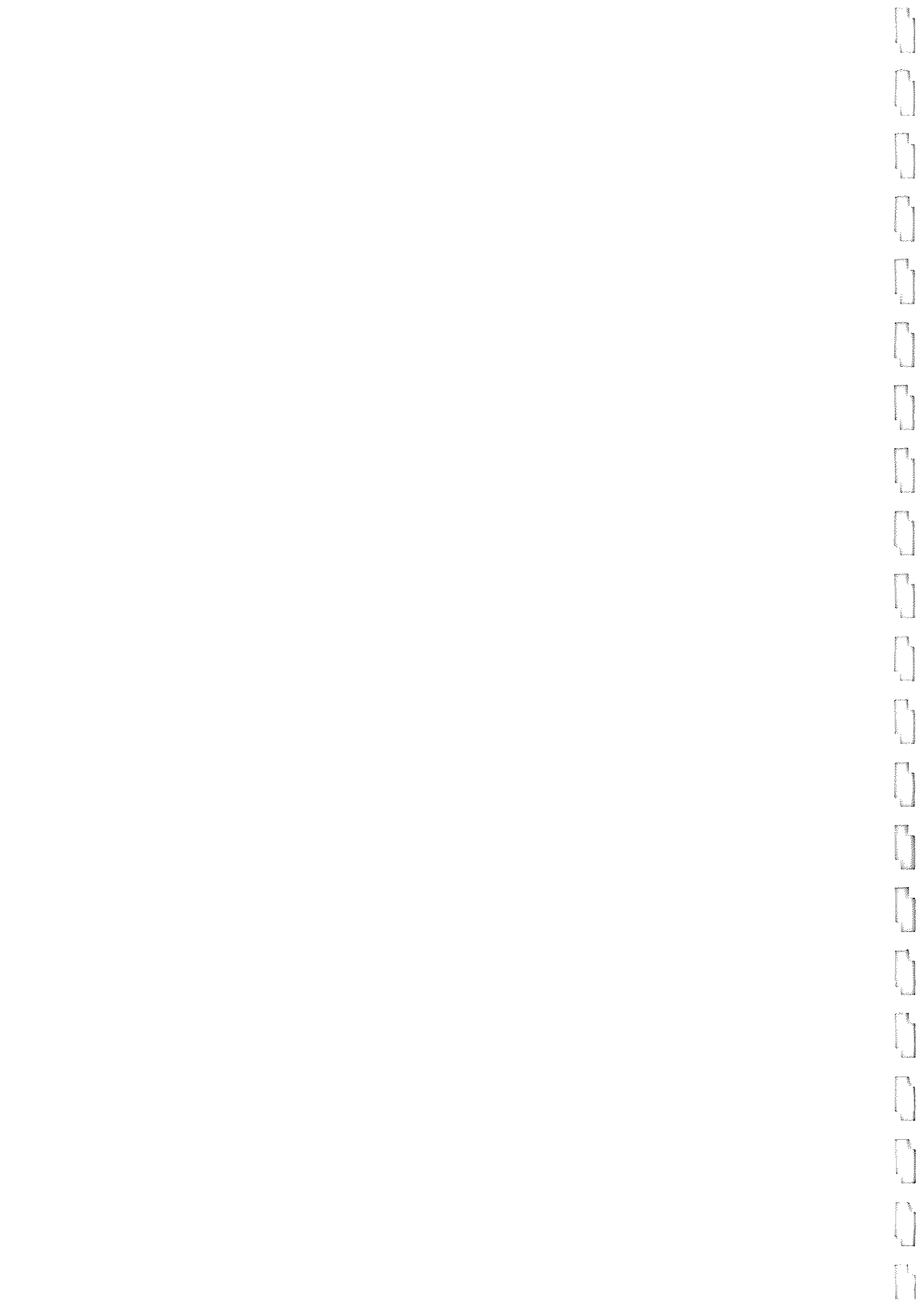


**LIVER TRANSPLANTATION IN  
AUSTRALIA**

**6TH REPORT  
FROM  
THE COMBINED REGISTRIES  
OF  
THE AUSTRALIAN LIVER TRANSPLANT CENTRES  
DATA TO 30/06/93**

**FEBRUARY 1994  
Edited By**

**AGR Sheil  
GW McCaughan**



# Table of Contents

FOREWORD		1
<i>Figure 1</i>	NUMBER OF TRANSPLANTS.	2-3
<i>Figure 2</i>	NUMBER OF RECIPIENTS BY YEAR	4-5
<i>Figure 3</i>	NUMBER OF RECIPIENTS BY AGE.	6-7
<i>Figure 4</i>	NUMBER OF GRAFTS BY YEAR. CHILDREN, REDUCED V WHOLE. AUSTRALIA.	8-9
<i>Figure 5</i>	NUMBER OF GRAFTS BY YEAR.CHILDREN, REDUCED v WHOLE. AUSTRALIA. NEW ZEALAND. OTHER.	10-11
<i>Figure 6</i>	PRIMARY DISEASES OF RECIPIENTS.	12-13
<i>Figure 7</i>	CHRONIC ACTIVE HEPATITIS	14-15
<i>Figure 8</i>	PATIENT SURVIVAL POST Tx.	16-17
<i>Figure 9</i>	PATIENT SURVIVAL - ADULTS AND CHILDREN.	18-19
<i>Figure 10</i>	PATIENT SURVIVAL CHILDREN, ADULTS AND ADULTS EXCLUDING MALIGNANCY AND HEPATITIS. AUSTRALIAN CITIZENS.	20-21
<i>Figure 11</i>	CHILDREN > 8.0 KG AND < 8.0 KG.	22-23
<i>Figure 12</i>	GRAFT SURVIVAL - PRIMARY AND SECONDARY	24-25
<i>Figure 13</i>	DISEASE AND OUTCOME ADULTS.	26-27
<i>Figure 14</i>	PATIENT SURVIVAL DISEASE AND OUTCOME CHILDREN.	28-29
<i>Figure 15</i>	PATIENT SURVIVAL - FULMINANT DISEASE.	30-31

<i>Figure 16</i>	PATIENT SURVIVAL MALIGNANCY vs HEP B vs HEP C vs HEP (AUTOIMMUNE) vs OTHER DISEASES	32-33
<i>Figure 17</i>	PATIENT SURVIVAL PAEDIATRIC RECIPIENTS WHOLE LIVER vs REDUCED LIVER.	34-35
<i>Figure 18</i>	PATIENT AND GRAFT SURVIVAL LRD.	36-37
<i>Figure 19</i>	PATIENT SURVIVAL BY AGE AT TRANSPLANT.	38-39
<i>Figure 20</i>	PATIENT SURVIVAL BY YEAR OF TRANSPLANT - AUSTRALIA	40-41
<i>Figure 21</i>	PRIMARY GRAFT SURVIVAL DONOR AGE VS SURVIVAL	42-43
<i>Figure. 22</i>	CAUSES OF PATIENT DEATH - ALL PATIENTS	44-45
<i>Figure 23</i>	CAUSE OF DEATH AUSTRALIA, NEW ZEALAND, OTHER	46-47
<i>Figure 24</i>	CAUSE OF GRAFT FAILURE - ALL GRAFTS	48-49
<i>Figure 25</i>	CAUSE OF GRAFT FAILURE AUSTRALIA, NEW ZEALAND, OTHER	50-51
<i>Figure 26</i>	DONATION BY YEAR	52-53

## Foreword

The liver transplant centres in Australia report details of their patients who receive liver grafts so that a combined analysis can be done. Established centres are situated in Brisbane, Melbourne and Sydney. New centres are opening in Perth and Adelaide.

The first and second reports from the combined groups came from Sydney. The third and fourth reports were produced in Brisbane. On July 1st 1993 the registry transferred to Sydney from where comes this sixth report. In it are presented data concerning all liver grafts and recipients since orthotopic liver transplantation began in Australia in 1985 until June 30, 1993. Prior to 1985 there had been only one (auxiliary) liver graft implanted in 1968.

The editors have changed the format of the report, presenting analysis of Australian citizens, New Zealand citizens and those from other countries. This allows a more precise evaluation of the needs for and practice of liver transplantation in Australia and New Zealand (no liver transplant unit has been established in New Zealand to date) and reveals what part we are playing in the treatment of individuals from other countries.

We have also joined with the Australian Transplant Coordinators Association and the Transplant Coordinator for New Zealand, Ms Joanna Innes Walker, to include details of liver organ donation. We express gratitude for this and also to ANZDATA and to the editors of the Annual Report, Ms Karen Herbutt and Dr Alex Disney.

The editors thank Ms Pamela Dilworth for data management and presentation of this report. They also thank the Liver Transplant Units for contributing information on their patients.

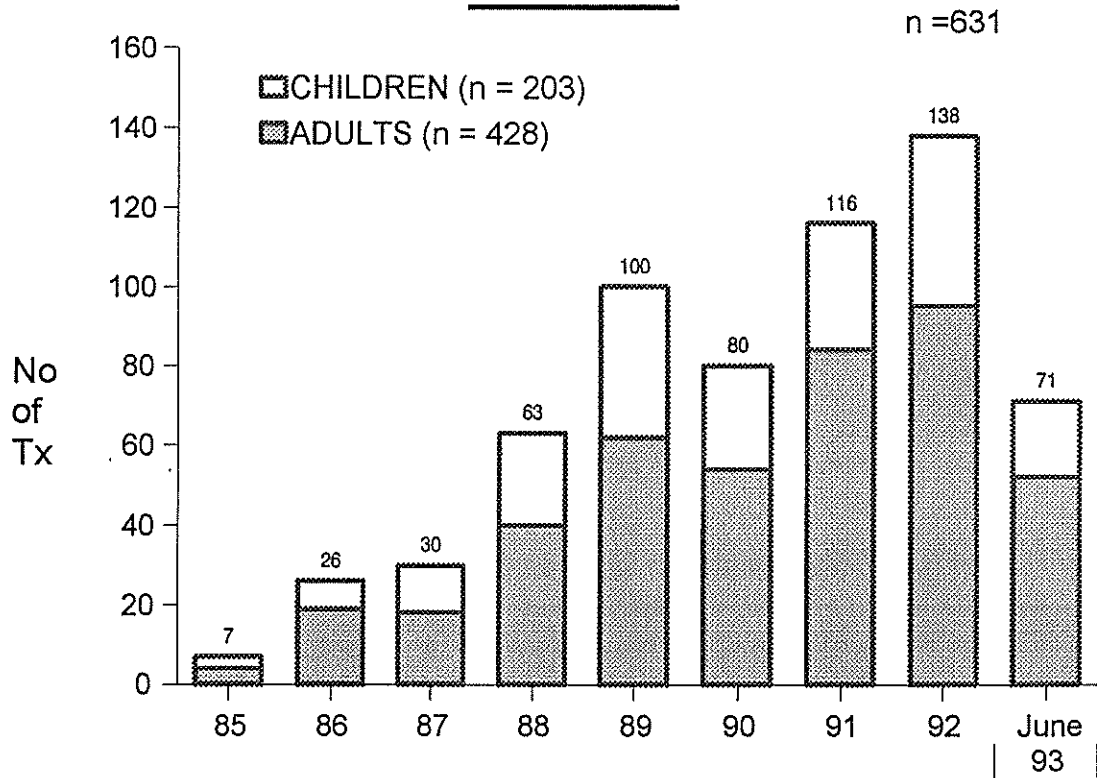
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GW McCaughan

FIGURE 1. NUMBER OF TRANSPLANTS.

The number of transplants performed in Australia since 1985 is shown in Figure 1. Apart from a brief fall in 1990, there has been a steady increase in the yearly numbers. The number of operations performed does not equate to the number of recipients of grafts as some patients received secondary grafts. Thirty two per cent of grafts were in children. This proportion does not reflect the need in Australian or New Zealand citizens which is addressed in Figure 2.

FIGURE 1

**AUSTRALIA**  
**NUMBER OF TRANSPLANTS**  
**BY YEAR**



30/06/93

## FIGURE 2      NUMBER OF RECIPIENTS BY YEAR

The number of patients who received grafts by year are shown in Figure 2. The total number is 576. Recipients are divided into a) Australian citizens b) New Zealand citizens and c) Others.

### Australian Citizens

The number of Australian recipients has increased steadily since 1985, again with the exception of the 1990 year. Ninety seven patients received grafts in 1992. The proportion of patients who are children has been consistently around 23%. By taking into consideration the number of patients treated, and those who died while waiting for a liver transplant, the demand for this form of treatment can be established. Currently, with 97 patients receiving grafts and an estimated 7 dying on waiting lists, the demand for 1992 was approximately 6 per million of population. As the numbers of patients being treated is still increasing, it is apparent that the demand has not yet been answered. The need for liver transplantation will also increase as the indications for the procedure are widened and because some patients with liver grafts will require retransplantation for a variety of reasons.

### New Zealand Citizens

The number of New Zealand patients referred for treatment has also climbed steadily, reaching 11 and 10 in each of 1991 and 1992 respectively and 12 in the first 6 months of 1993. Again, children represent about one quarter of the total. With the NZ population currently 3.4 million, this represents treatment by transplantation of 3 per million of population per year (until the current year). If the sudden increase in numbers treated in 1993 is sustained, the need for liver transplantation in New Zealand will be met.

### Other Citizens

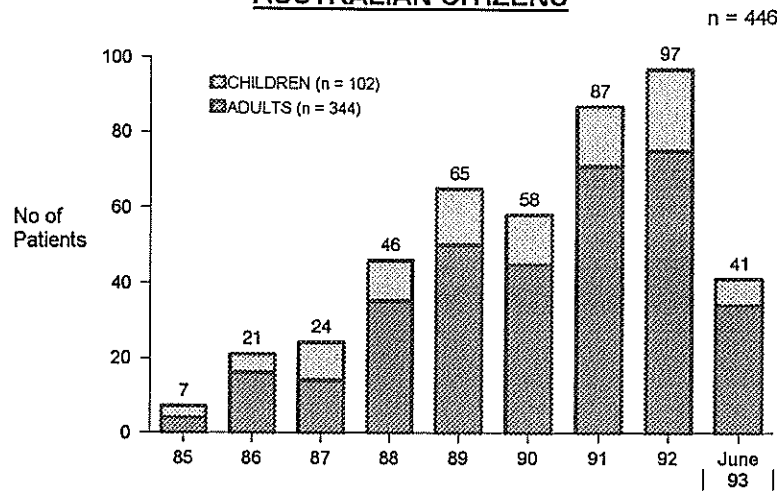
Most Other Citizens have been children (60). Only 12 adults have been referred for transplantation from countries over-seas (apart from New Zealand). In 1992 this number was 5. At the same time 14 children were treated.



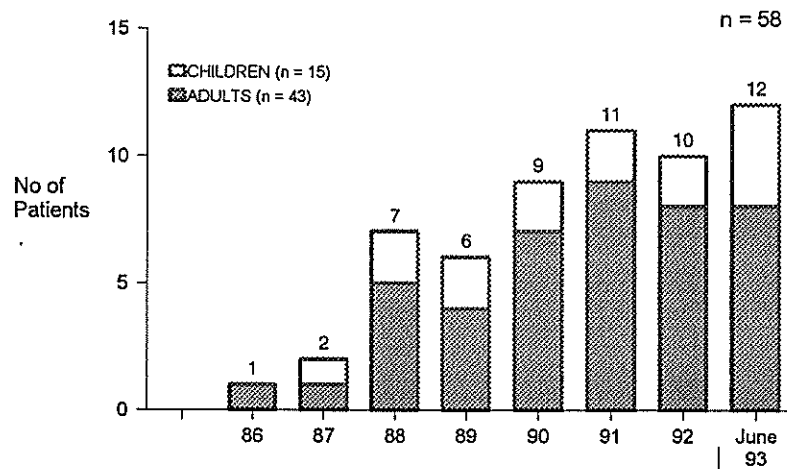
FIGURE 2

**NUMBER OF RECIPIENTS BY YEAR (n = 576)**

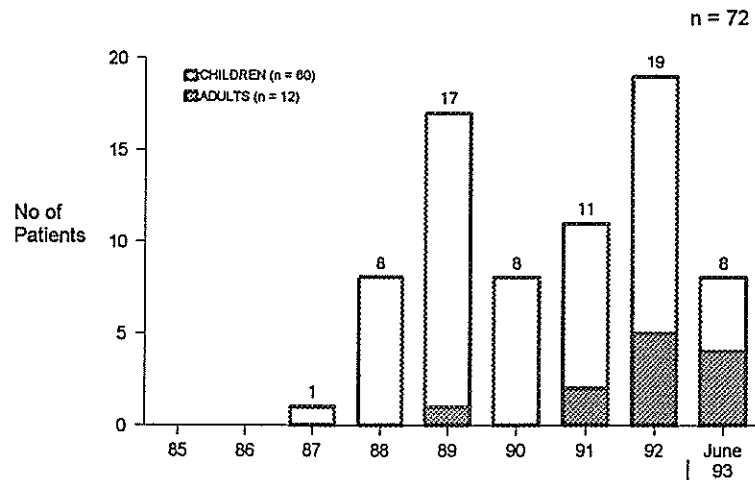
**AUSTRALIAN CITIZENS**



**NEW ZEALAND CITIZENS**



**OTHER CITIZENS**



30/06/93

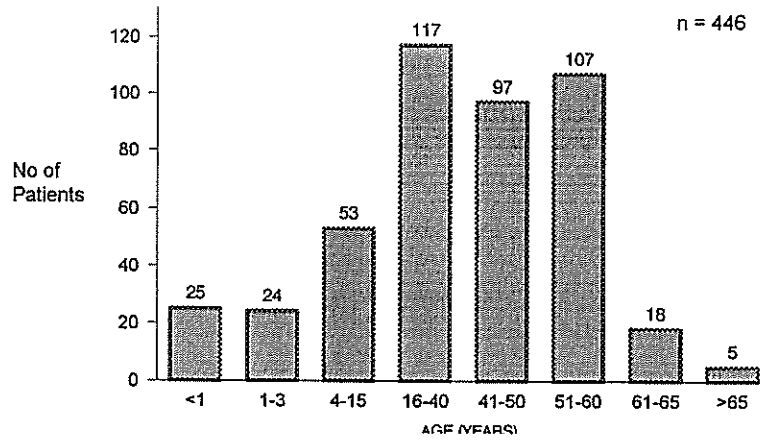
FIGURE 3      NUMBER OF RECIPIENTS BY AGE.

Patients of all ages may require treatment by liver transplantation. The youngest patient, an Australian citizen was aged 4 months and the oldest, also an Australian citizen was 66 years. The oldest New Zealand patient was almost 61 years and the oldest patient from Other countries, 50 years. While significant numbers of babies are treated, the predominant age groups are children aged 4 - 15 years and adults ages aged 16 - 60 years.

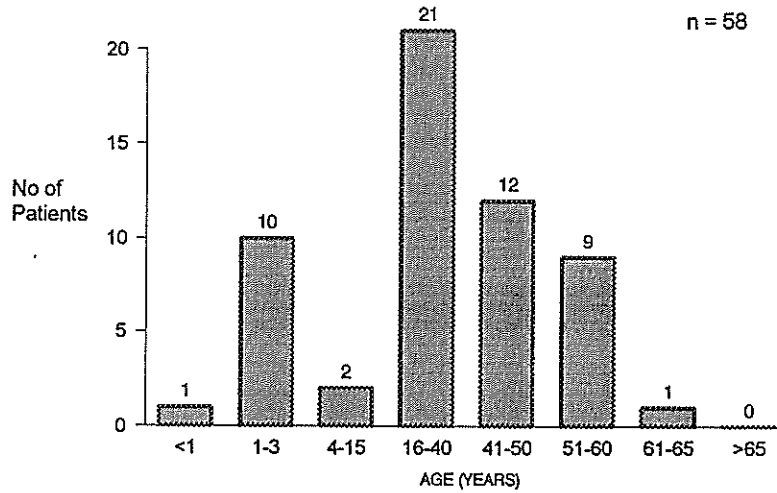
The distribution of recipients in the various age brackets for New Zealand citizens is similar to that of Australians though more young children (11%) have been treated than older children (2%). In those patients referred from other countries the distribution is heavily skewed towards infants and young children

FIGURE 3

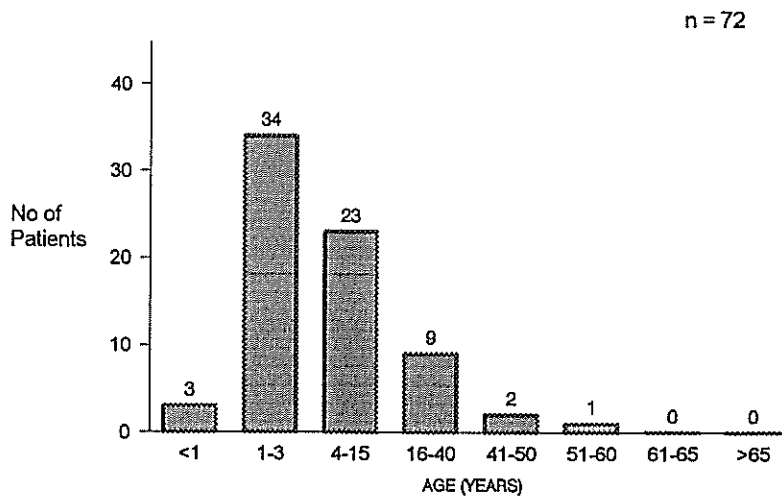
**NUMBER OF RECIPIENTS BY AGE**  
**AUSTRALIAN CITIZENS**



**NZ CITIZENS**



**OTHER CITIZENS**



30/06/93

FIGURE 4. NUMBER OF GRAFTS BY YEAR. AUSTRALIA  
CHILDREN, REDUCED V WHOLE.

Since the first reduced graft was performed in 1986, this form of transplant has increased steadily to become the most frequent type of procedure performed in children. In 1991 and 1992 whole grafts constituted only approximately one third of the total performed. The number of whole and reduced grafts for Australian citizens, New Zealand citizens and Others are shown in Figure 5.

FIGURE 4

**NUMBER OF GRAFTS BY YEAR**  
**AUSTRALIA**  
**CHILDREN - REDUCED vs WHOLE**

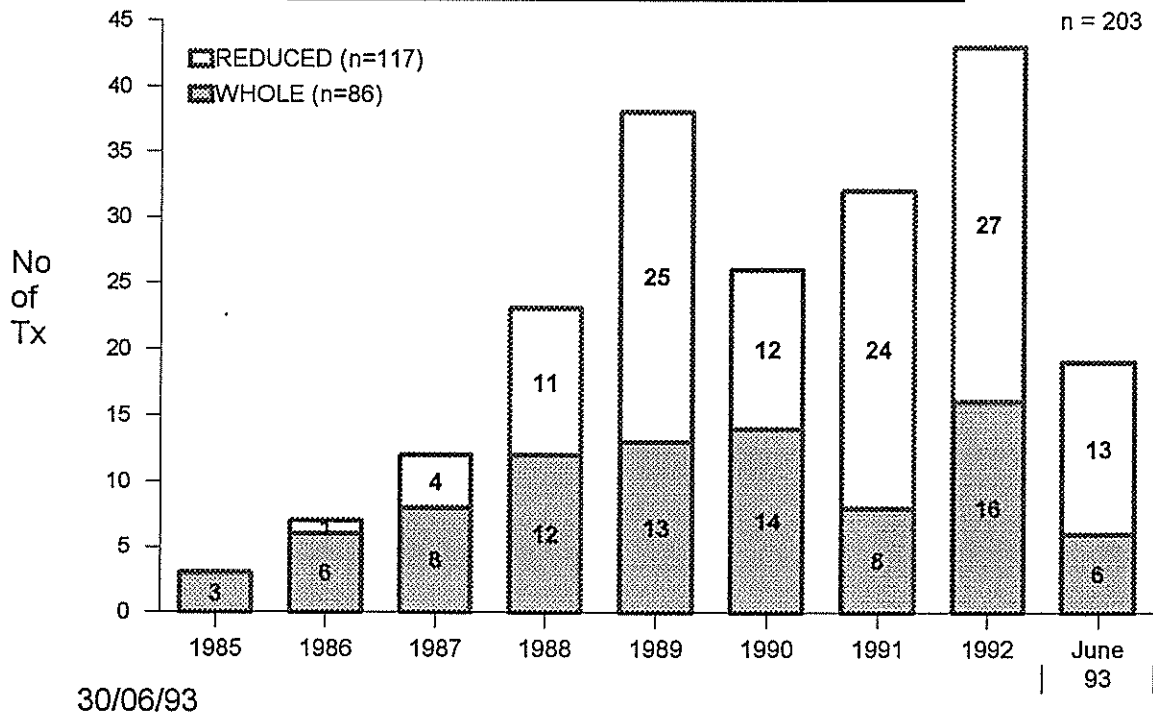
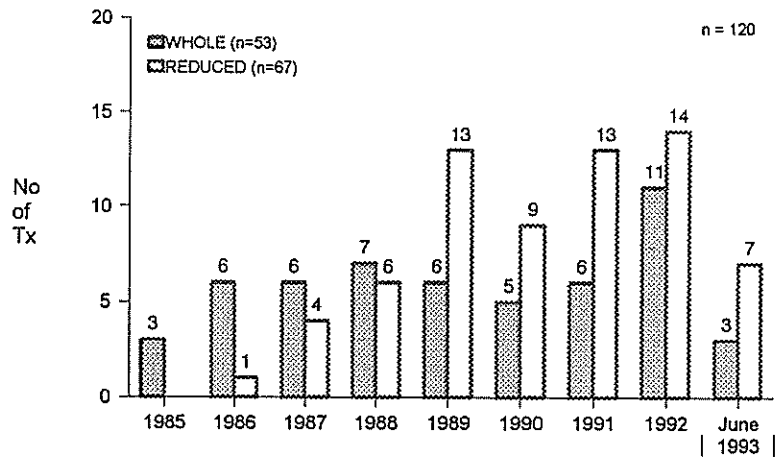


FIGURE 5. NUMBER OF GRAFTS BY YEAR.  
CHILDREN. REDUCED V WHOLE. AUSTRALIA. NEW ZEALAND.  
OTHER.

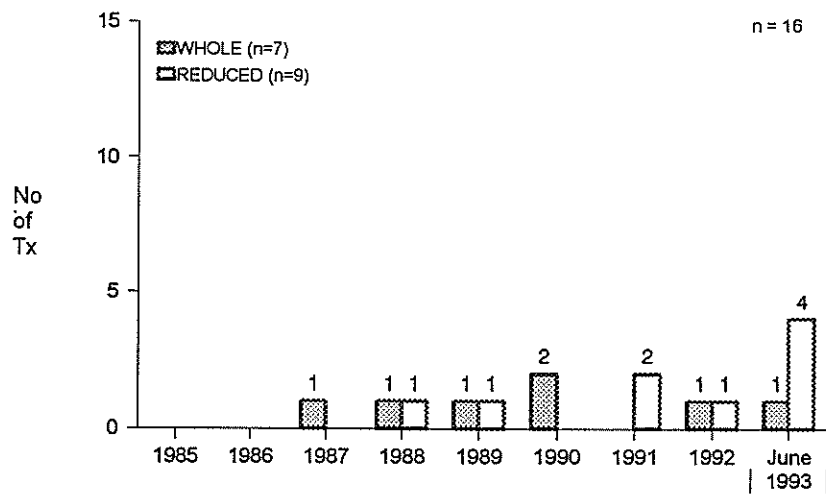
The pattern of increasing proportions of reduced grafts occurs in both Australian and New Zealand children and is particularly marked in those referred from other countries. In 1992 whole grafts constituted 44% of Australian Citizen grafts, 50% of NZ Citizens and 25% of Other Citizens.

FIGURE 5

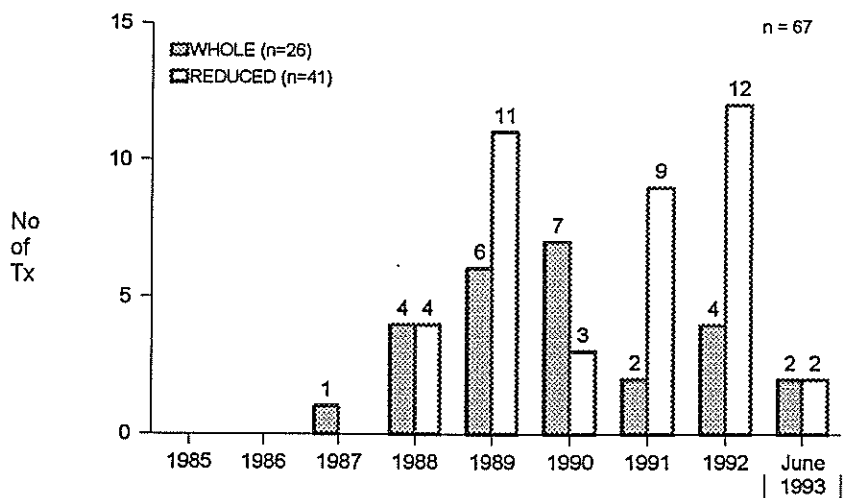
**NUMBERS OF GRAFTS BY YEAR  
CHILDREN - REDUCED vs WHOLE  
AUSTRALIAN CITIZENS**



**NZ CITIZENS**



**OTHER CITIZENS**



30/06/93

FIGURE 6. PRIMARY DISEASES OF RECIPIENTS.

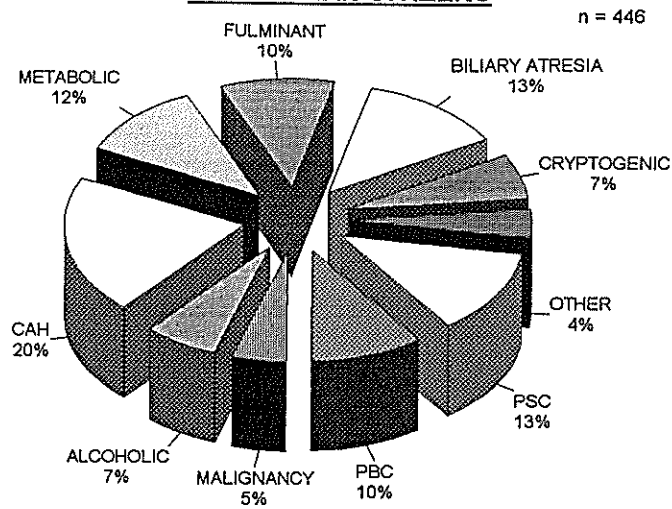
The primary diseases of recipients shown in Figure 6 reveals that the large groups requiring treatment in Australia are patients with chronic active hepatitis (including hepatitis B and C) (20%), those with primary sclerosing cholangitis (13%) and those with primary biliary cirrhosis (10%). A break-up of the chronic active hepatitis group is shown in Fig. 7. In children, the major group is biliary atresia which contributes 13% to the total. The metabolic disorders (12%) span both adults and children as does fulminant hepatitis (10%). To date, relatively few patients have received grafts for cryptogenic cirrhosis (7%), alcoholic cirrhosis (7%) and malignancy (5%).

With New Zealand citizens, in comparison to Australians, there are modestly increased proportions of patients with fulminant hepatic failure (22%), biliary atresia (19%), primary sclerosing cholangitis (17%) . Primary biliary cirrhosis (9%) is similar in proportion as is cryptogenic cirrhosis (7%). Chronic active hepatitis is much reduced (10%) as are metabolic disorders (5%). Again, the numbers of patients with alcoholic cirrhosis and with malignancy are low (both 2%). With Other citizens 78% of patients have biliary atresia. Chronic active hepatitis accounts for 5% of patients with other causes of liver failure contributing small percentages only. No overseas patient has yet received a graft for malignancy.

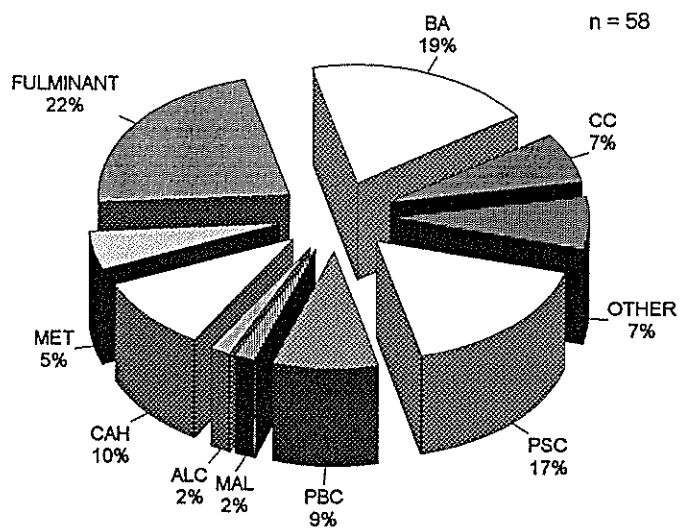


FIGURE 6

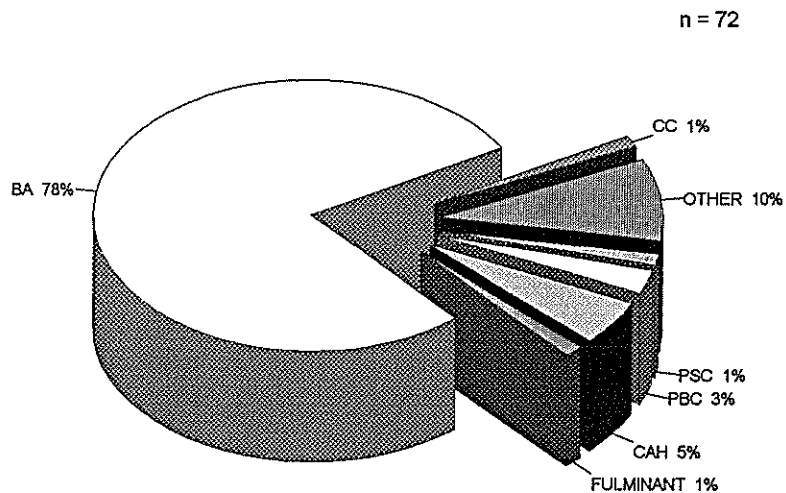
**PRIMARY DISEASES OF RECIPIENTS  
AUSTRALIAN CITIZENS**



**NEW ZEALAND CITIZENS**



**OTHER CITIZENS**



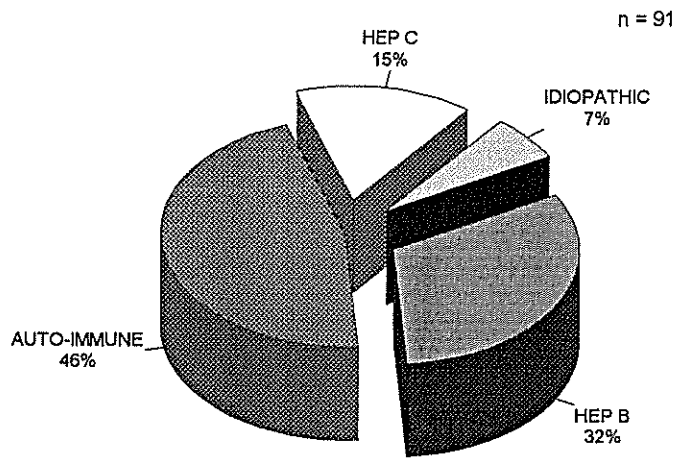
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FIGURE 7.      CHRONIC ACTIVE HEPATITIS

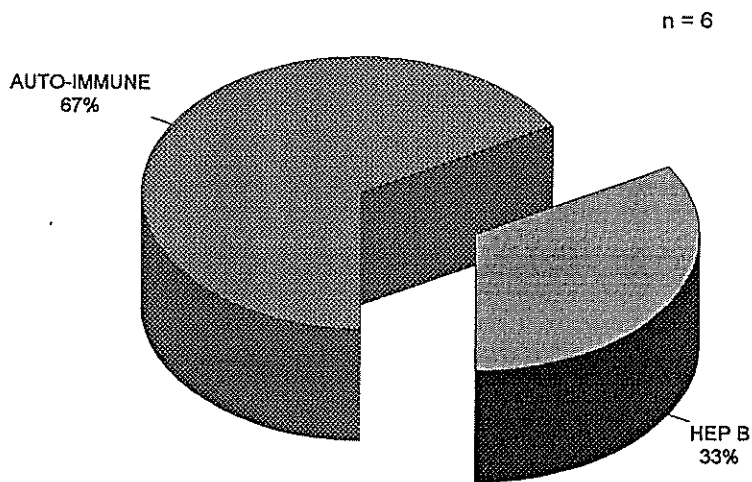
The break-up of chronic active hepatitis in Australian citizens shows that most (46%) are auto-immune while 32% are Hep B. Hep C contributes 15% and idiopathic 7%. In New Zealand citizens there have been no recipients with liver failure due to Hepatitis C, or idiopathic, most being auto-immune (67%), the rest being Hepatitis B (33%). Only 4 Other citizens have received grafts for chronic active hepatitis.

FIGURE 7

**CHRONIC ACTIVE HEPATITIS**  
**AUSTRALIAN CITIZENS**



**NZ CITIZENS**



**OTHER CITIZENS**

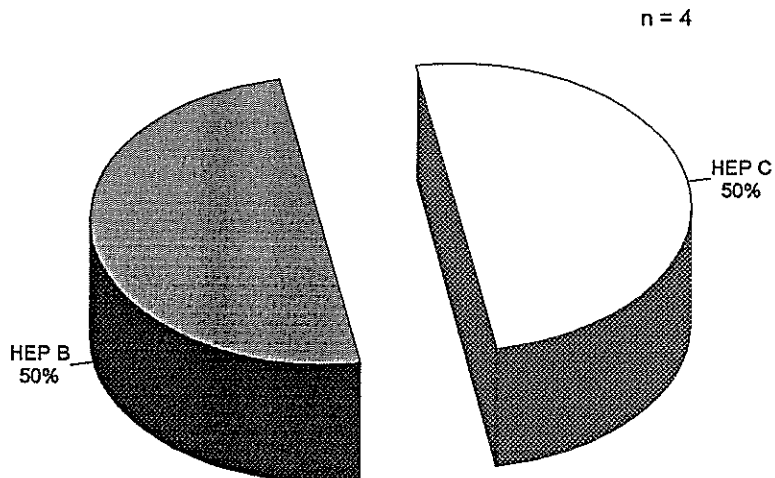


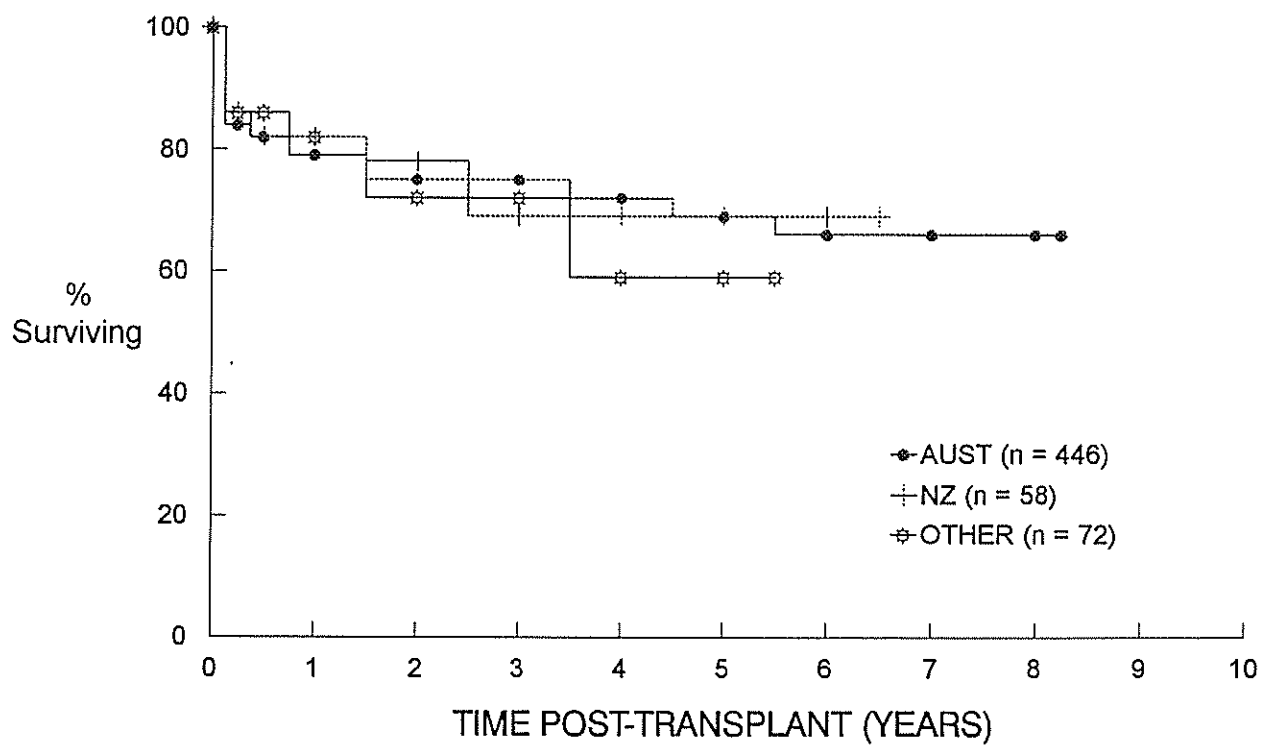
FIGURE 8      PATIENT SURVIVAL POST Tx.

Patient survivals for Australian and New Zealand citizens are similar. Survival from 5 - 7 years following transplantation occurs in approximately 69% of patients. Survival for Other Citizens is a little less in the long term at 59%.

The causes of patient deaths for the various time periods are shown in Figures 22 and 23.

FIGURE 8

### PATIENT SURVIVAL POST Tx



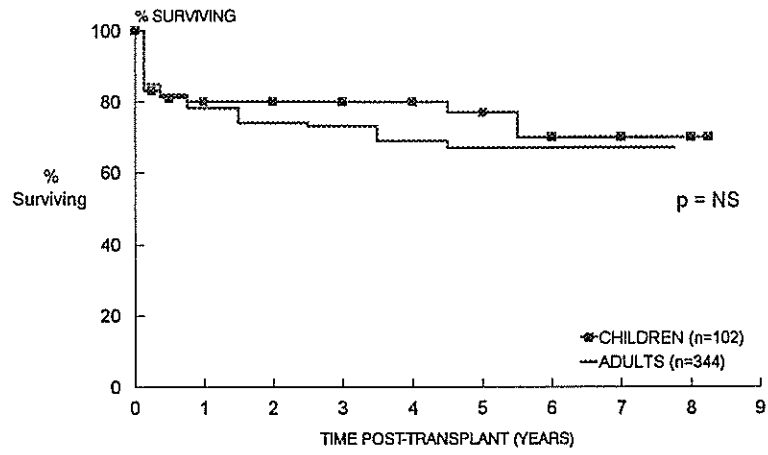
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FIGURE 9. PATIENT SURVIVAL - ADULTS AND CHILDREN.

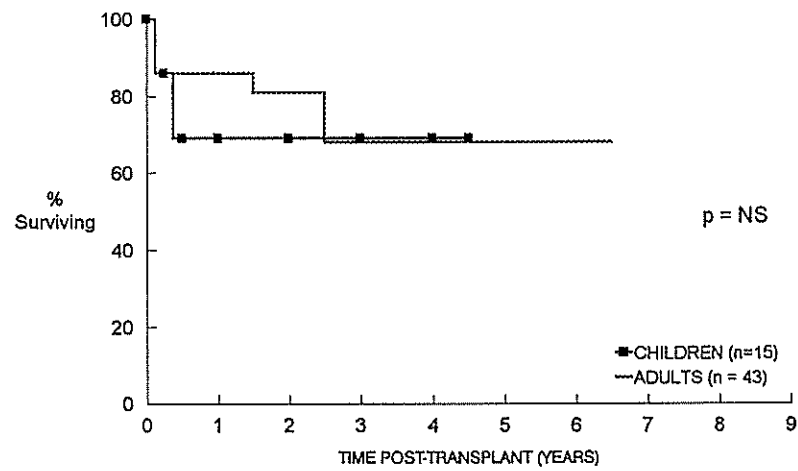
The tendency for improved survival for children (77% survival at 5 years post-transplant) as opposed to adults (67%) is seen in the Australian citizens charts while the number of patients for New Zealand and for Other citizens is too small for valid analysis. The major reasons for the difference in child and adult survival appears to be the occurrence of recurrent disease (hepatitis and malignancy) in adults whereas these causes of primary liver diseases in children are uncommon. The effects of hepatitis and malignancy are revealed in Fig. 10 where, if these causes of primary liver disease are excluded, adults and children survive equivalently.

FIGURE 9

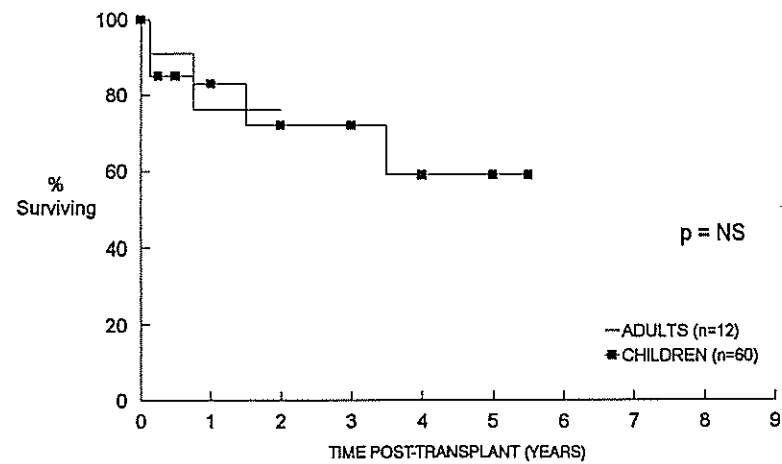
**PATIENT SURVIVAL - ADULTS AND CHILDREN  
AUSTRALIAN CITIZENS**



**NZ CITIZENS**



**OTHER CITIZENS**



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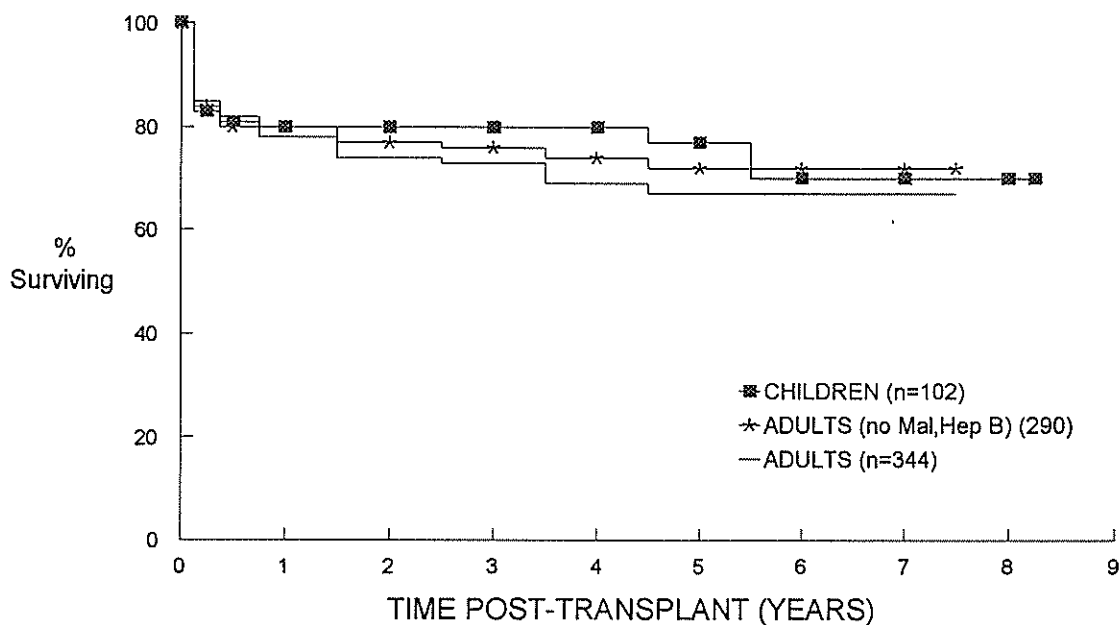
FIGURE 10. PATIENT SURVIVAL  
CHILDREN, ADULTS AND ADULTS EXCLUDING  
MALIGNANCY AND HEPATITIS B. AUSTRALIAN CITIZENS.

An analysis of the survival of adults excluding those whose primary liver conditions was malignancy or hepatitis B reveals that survival for adults without those conditions is similar to that of children.



FIGURE 10

**PATIENT - SURVIVAL - CHILDREN, ADULTS, AND  
ADULTS EXCLUDING MALIGNANCY AND HEPATITIS B  
AUSTRALIAN CITIZENS**



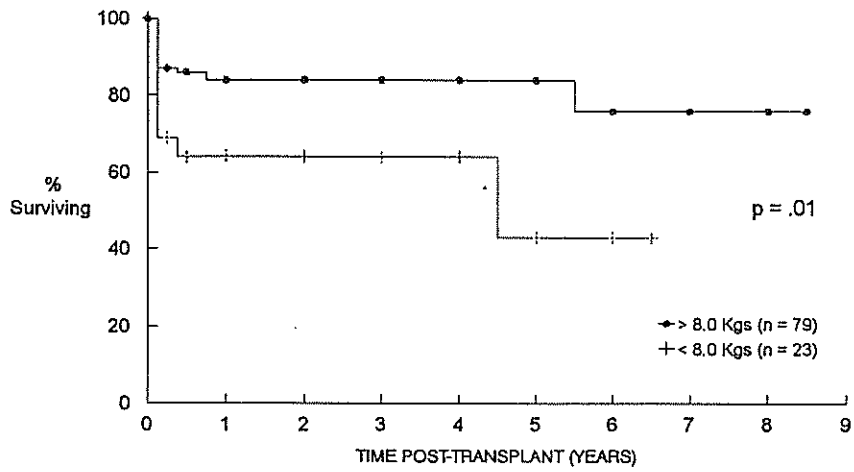
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FIGURE 11. CHILDREN > 8.0 KG AND < 8.0 KG.

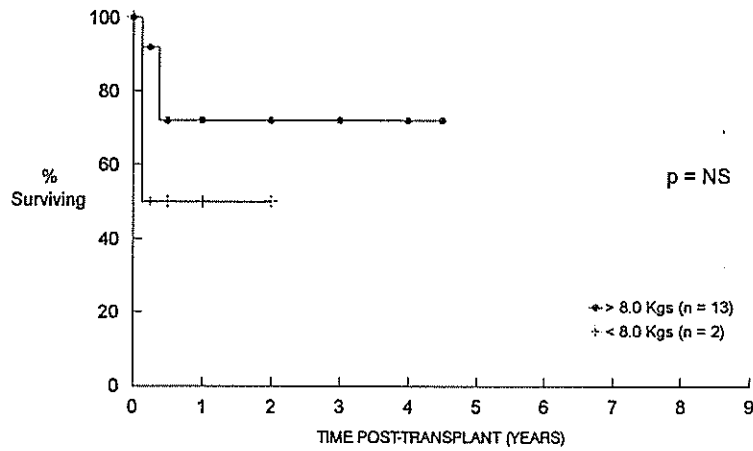
The survival of paediatric patients for Australian citizens weighing greater than 8.0 kgs at the time of transplantation compared to those weighing less than 8.0 kgs shows a marked difference in survival. The larger children have a survival of 86% at 5 years post-transplant compared to 42% for children less than 8.0 kgs. One year survival for the two groups is 88% versus 63%. This general pattern occurred also for New Zealand citizens and Other citizens.

FIGURE 11

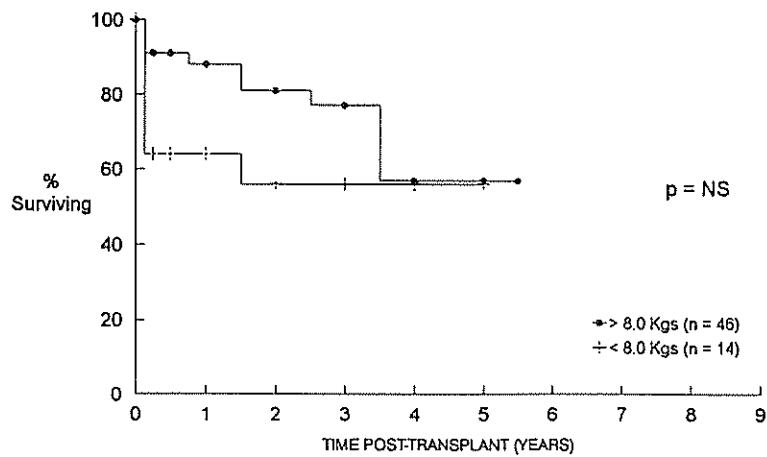
**PATIENT SURVIVAL**  
**CHILDREN > 8.0 KG AND < 8.0 KG**  
**AUSTRALIAN CITIZENS**



**NZ CITIZENS**



**OTHER CITIZENS**



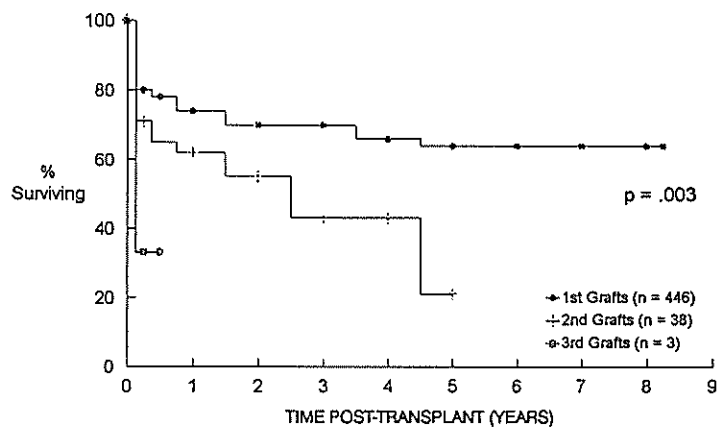
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FIGURE 12      GRAFT SURVIVAL - PRIMARY AND SECONDARY

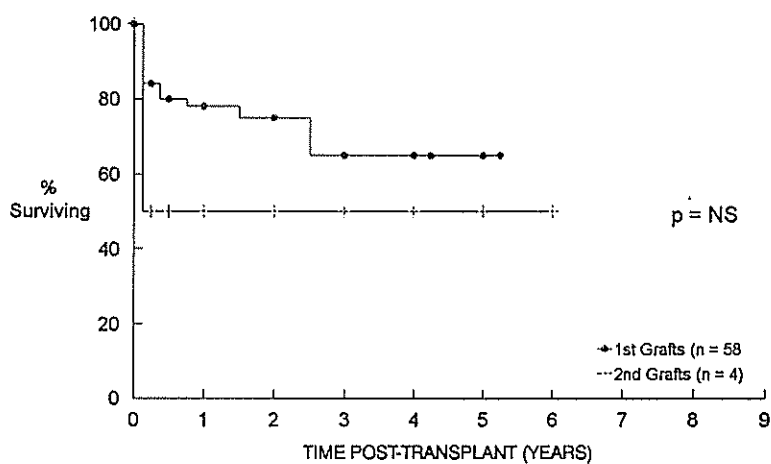
Primary grafts for Australian citizens (n = 446) show a 1 year survival of 74% and 5 - 7 year survival of 64%. Second grafts do somewhat worse with 1 year survival of 62% and sustained function of 44%. One of three third grafts in the Australian experience remains functional. The pattern for first and second grafts for New Zealand citizens and Other citizens are similar. The primary graft survival for New Zealand citizens is 78% at 1 year and 65% long term whilst Other citizens are 78% and 55% respectively. Secondary graft survival for New Zealand citizens is 50% at 1 year (1 of only 2 secondary grafts), and 20% for Other citizens (from a total of 10 secondary grafts).

FIGURE 12

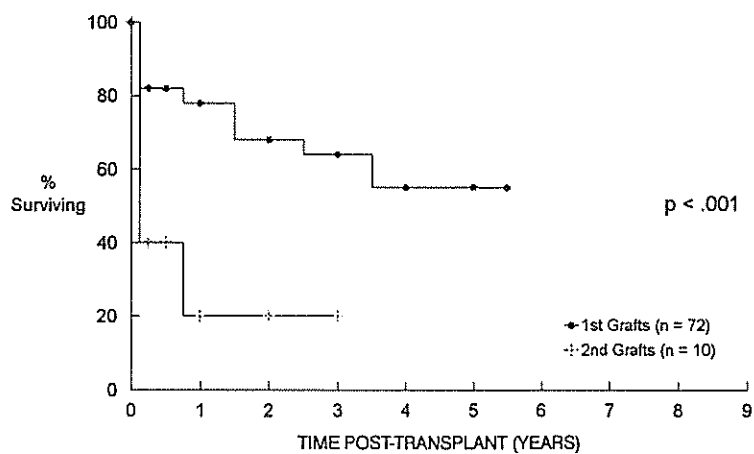
**GRAFT SURVIVAL - PRIMARY AND SECONDARY  
AUSTRALIAN CITIZENS**



**NZ CITIZENS**



**OTHER CITIZENS**



30/06/93

FIGURE 13     DISEASE AND OUTCOME  
ADULTS.

Survival for adults with metabolic disorders (28), alcoholic liver disease (31) and primary biliary cirrhosis (52) in the 5 - 7 year follow-up is close to 80%. Few adults (4) received grafts for biliary atresia - 3 of these survive. Survival for those with cryptogenic cirrhosis (32) at 5 years is 68% and for CAH (100) 65%. The results for the sub-groups of CAH (Auto-immune, Hep B, Hep C and idiopathic) are shown in Fig. 16. Five year survival for PSC (67) is 60%. For malignancy (20) 33%. The outcome for those with Fulminant Hepatic Failure are shown in Fig. 15.

FIGURE 13

### PATIENT SURVIVAL DISEASE AND OUTCOME - ADULTS

n = 352

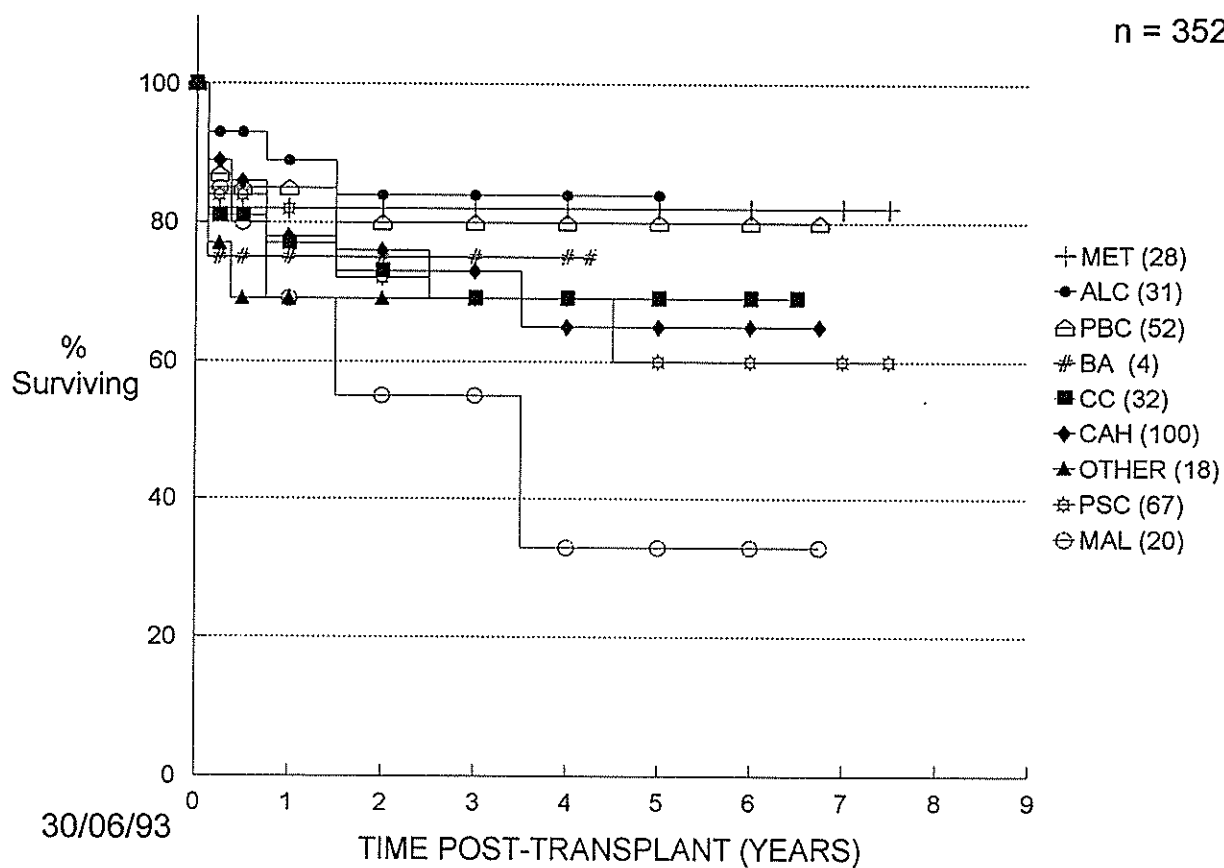


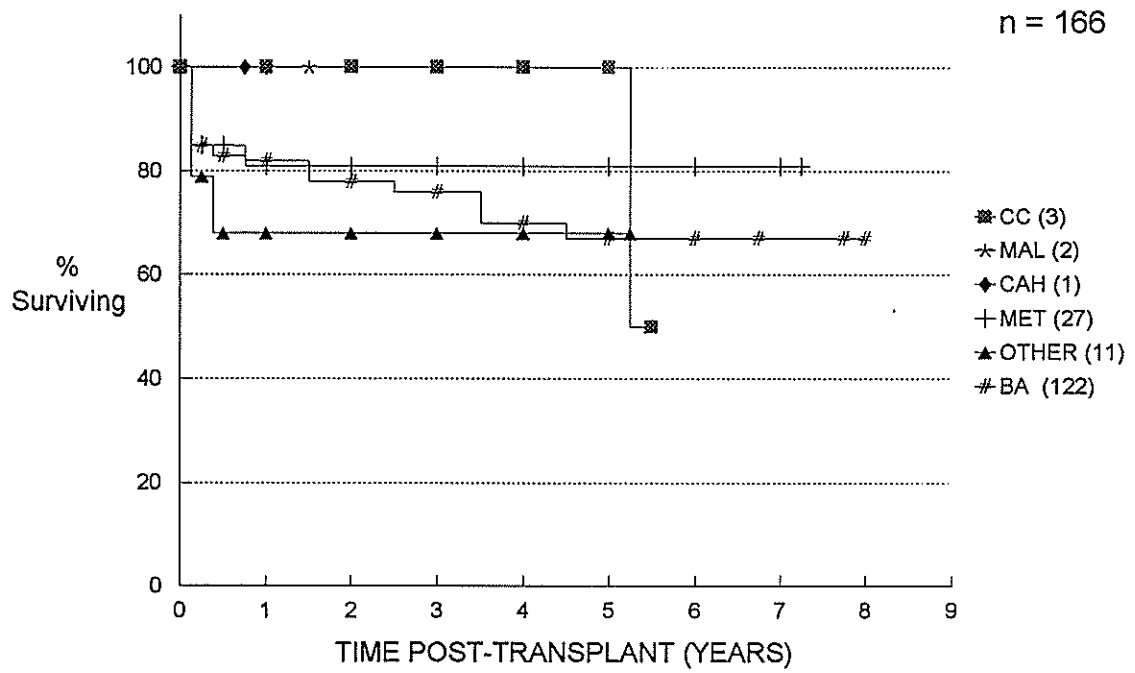
FIGURE 14. PATIENT SURVIVAL  
DISEASE AND OUTCOME  
CHILDREN.

The major groups for children are biliary atresia (122 pts - 67% 5-7 year survival) and metabolic disorders (27 - 82% 5-7 year survival). All children with malignancy (2) and CAH (1) are surviving (100%) as are 2 of 3 (66%) with cryptogenic cirrhosis. Five year survival for those with other conditions is 68%. The outcome for those with Fulminant Hepatic Failure are shown in Fig. 15.



FIGURE 14

**PATIENT SURVIVAL**  
**DISEASE AND OUTCOME - CHILDREN**



30/06/93

FIGURE 15      PATIENT SURVIVAL - FULMINANT DISEASE.

Forty seven adults and 11 children with fulminant disease have received grafts. Five year survival for adults is 72% and for children 61%. No children with fulminant disease from New Zealand or Other countries have received grafts. Eight New Zealand adults in fulminant failure received grafts; 3 and 5 year survivals are 88% and 64% respectively. A single Other overseas citizen with fulminant failure who received a graft survives 2 years post operatively. The common causes of fulminant hepatitis in adults were idiopathic (60%), Hep B (19%), drugs (16%) and Wilsons disease (7%). Rare causes were Hep C (2%) and autoimmune CAH (2%). Of the 11 children with FHF 7 (64%) were idiopathic, 2 (18%) Wilsons disease, 1 (9%) drug-induced and 1  $\alpha$ -1-antitrypsin (9%).

FIGURE 15

**PATIENT SURVIVAL**  
**FULMINANT DISEASE**

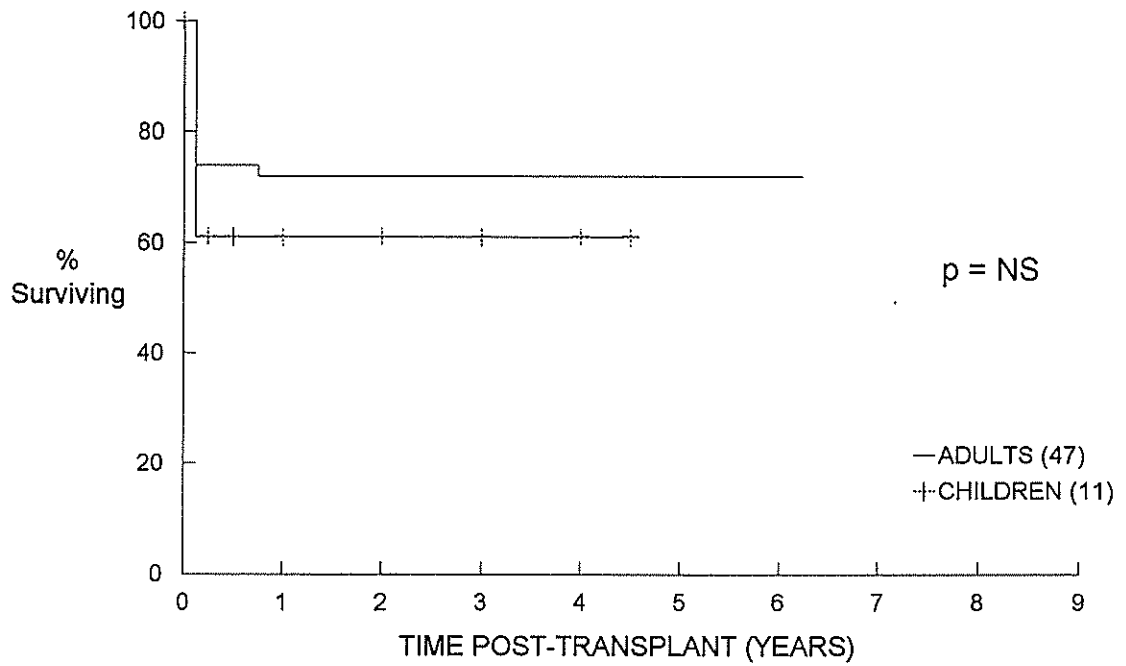


FIGURE 16    PATIENT SURVIVAL  
MALIGNANCY vs HEP B vs HEP C vs HEP (AUTOIMMUNE)  
vs OTHER DISEASES

Survival for patients with Hep C (86% 5 year survival) and autoimmune CAH (79% 5 year survival) are similar to survival of patients with primary liver diseases other than hepatitis or malignancy. However, survival following transplant for those with Hepatitis B is 48% at 5 years and with malignancy 33%.

FIGURE 16

**ADULT PATIENT SURVIVAL**  
**MALIGNANCY vs HEP B vs HEP C vs**  
**CAH (AUTOIMMUNE) vs OTHER DISEASES**

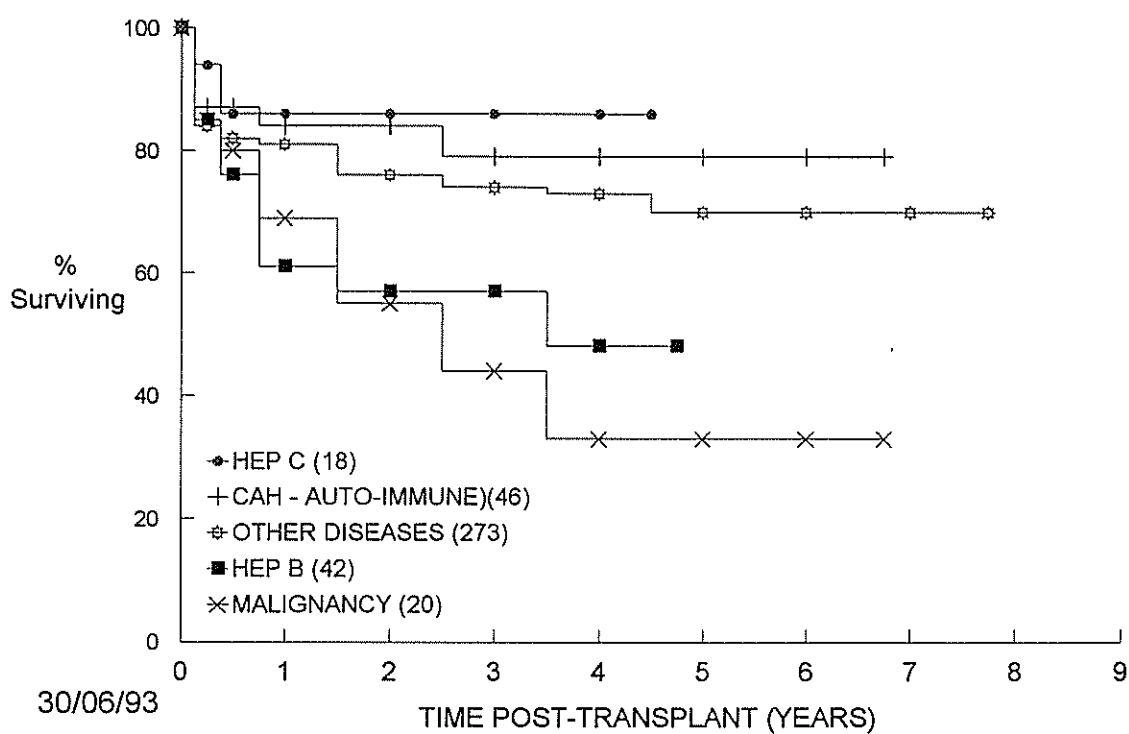


FIGURE 17     PATIENT SURVIVAL  
PAEDIATRIC RECIPIENTS  
WHOLE LIVER vs REDUCED LIVER.

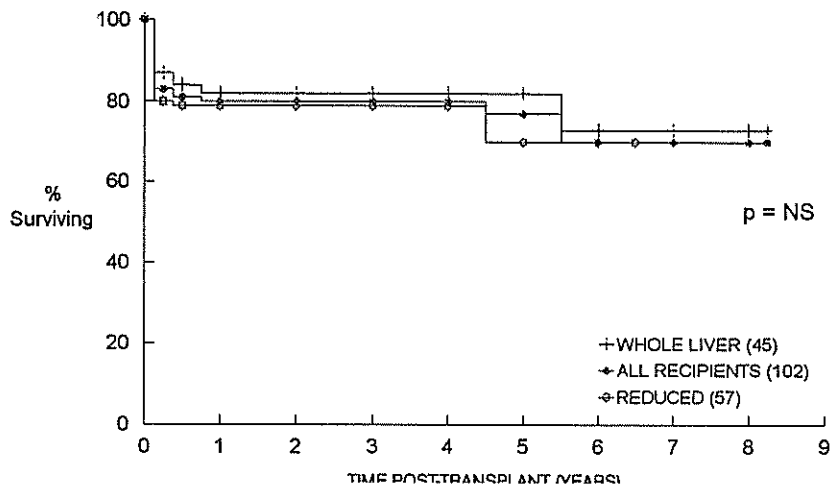
The survival of children who received whole livers and those who received reduced livers is similar. One year survival for the former is 82% and for the latter 79%. Five - 7 years survival for both is approximately 70%.

While NZ children who receive whole grafts (n = 7) appear to be doing better than those who receive part grafts (n = 8) the numbers of patients are too few for valid analysis.

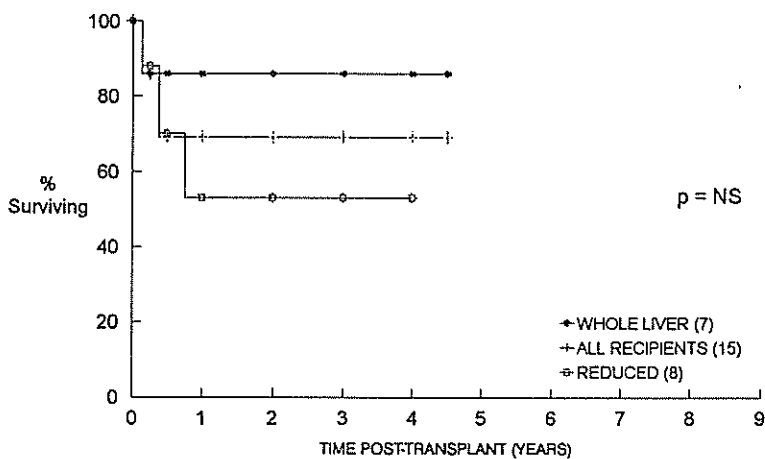
With overseas children 1 year survival is improved for whole grafts (92% v 77%) but prolonged survival is similar (56% for whole grafts v 64% for part grafts).

FIGURE 17

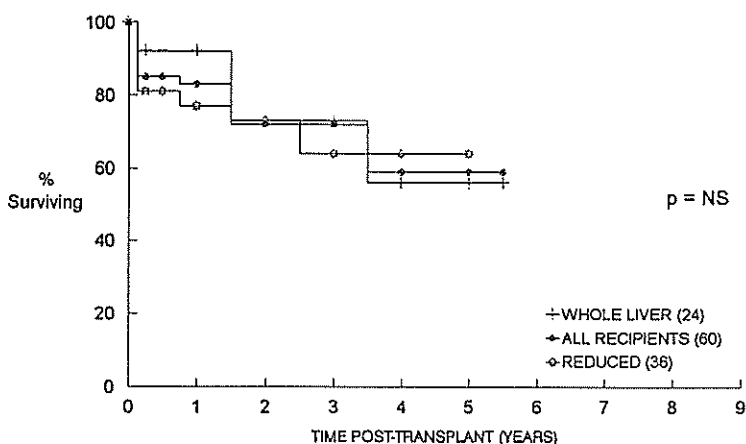
**PAEDIATRIC PATIENT SURVIVAL**  
**WHOLE LIVER V REDUCED LIVER**  
**AUSTRALIAN CITIZENS**



**NZ CITIZENS**



**OTHER CITIZENS**



30/06/93

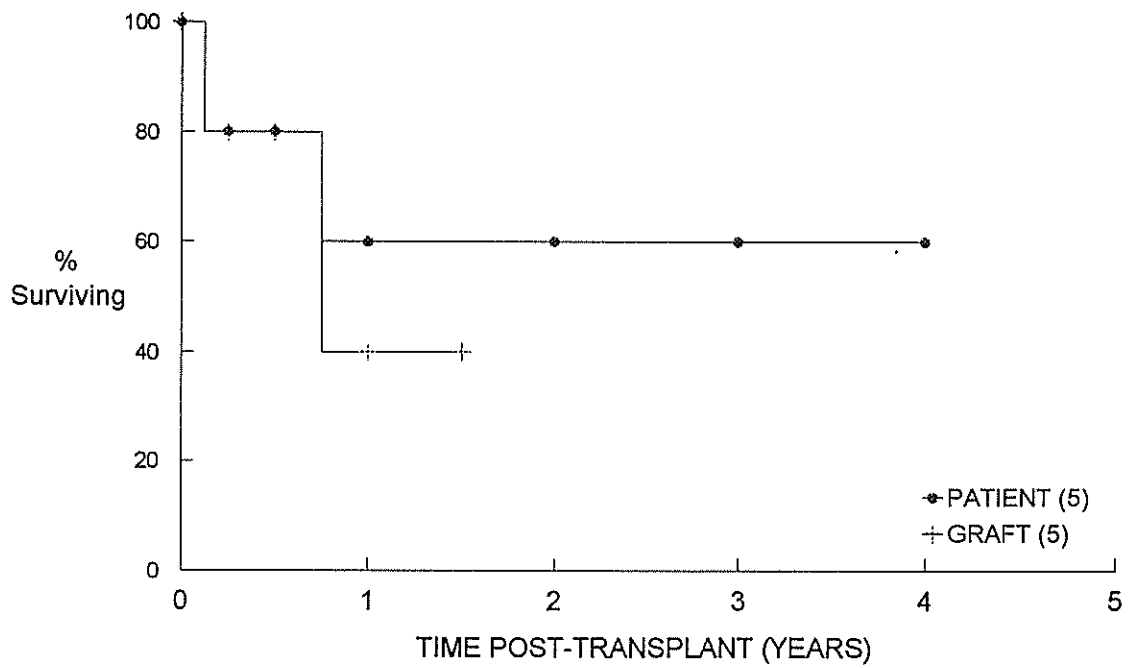
FIGURE 18      PATIENT AND GRAFT SURVIVAL  
LRD.

Three of 5 patients who received living related donor grafts survive. One patient survives with a secondary cadaveric donor graft. Two of 5 LRD grafts currently continue to function at 12 and 18 months post-transplant.



FIGURE 18

**AUSTRALIA**  
**PATIENT AND GRAFT SURVIVAL**  
**LRD**



30/06/93

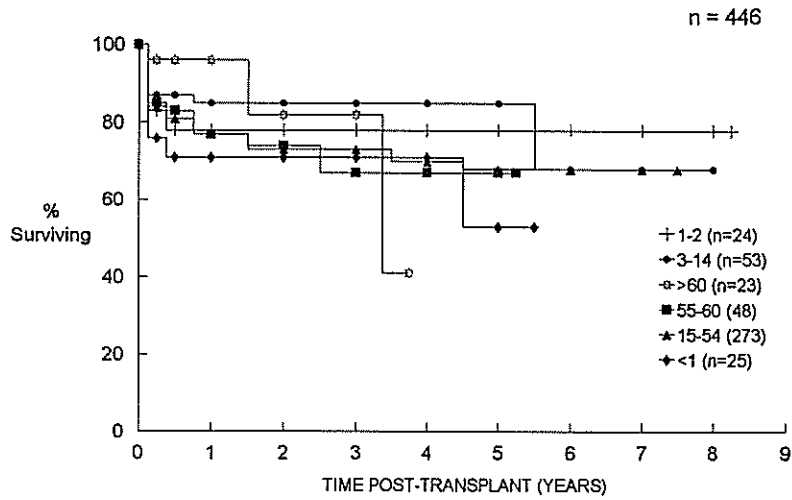
FIGURE 19      PATIENT SURVIVAL BY AGE AT TRANSPLANT.

For Australian patients the groups which survive best are those aged 1-2 (n = 24) and 3 - 14 years (n = 53). Five year survival occurs in approximately 80% of these patients. Again, this reflects that few of these patients receive grafts for malignancy or hepatitis. Survival for those aged < 1yr is 71% at 1 year and 53% at 5 years. In the Australian experience patients > 60 currently have a 82% 3 year survival, while the 15 - 54 and 55 - 60 age groups survived equivalently with prolonged survival of 68%.

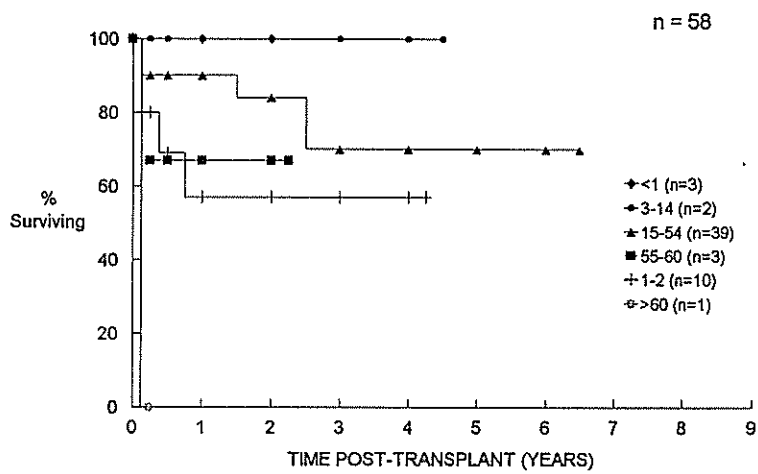
The general pattern for New Zealand citizens and Other citizens, where there are sufficient patients in the groups for analysis, are similar, with the exception that in these patients survival in patients aged 1 - 2 was reduced compared to Australian patients at 57%.

FIGURE 19

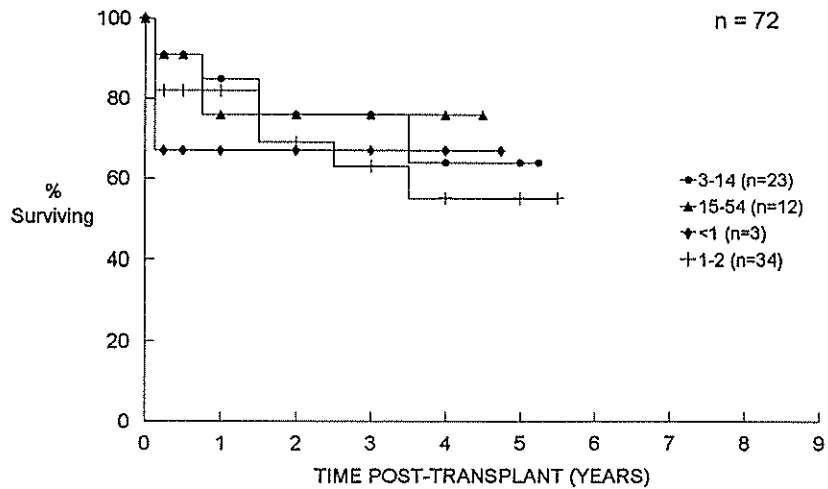
**PATIENT SURVIVAL BY AGE AT TRANSPLANT**  
**AUSTRALIAN CITIZENS**



**NZ CITIZENS**



**OTHER CITIZENS**



30/06/93

FIGURE 20     PATIENT SURVIVAL BY YEAR OF TRANSPLANT - AUSTRALIA

The one, three and five year survivals for patients who received grafts are as follows:

	<u>1 yr</u>	<u>3 yr</u>	<u>5 yr</u>
1985 (n = 7)	43	29	29
1986 (n = 22)	68	59	55
1987 (n = 27)	70	56	44
1988 (n = 61)	74	69	69
1989 (n = 88)	68	65	60
1990 (n = 75)	81	77	
1991 (n = 109)	88		
1992 (n = 126)	83		

The actuarial six month survival for 61 grafts transplanted in 1993 is 84%.

FIGURE 20

PAIENT SURVIVAL - BY YEAR OF Tx  
AUSTRALIA

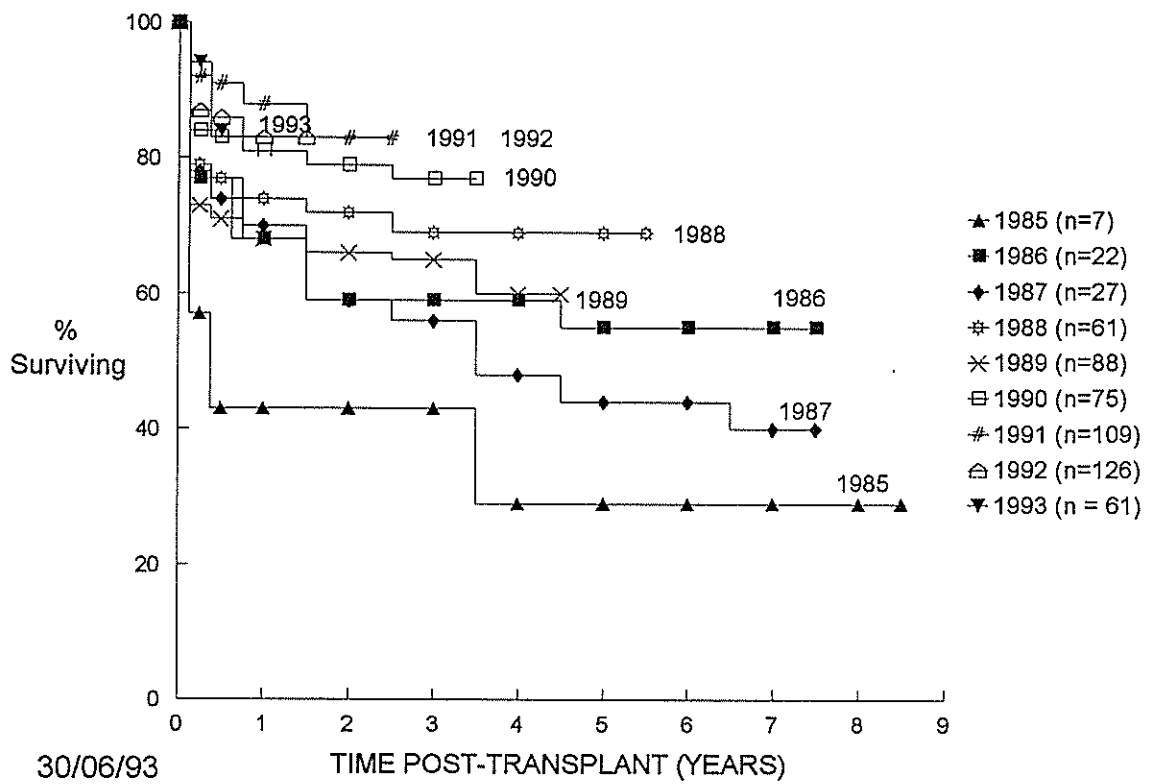
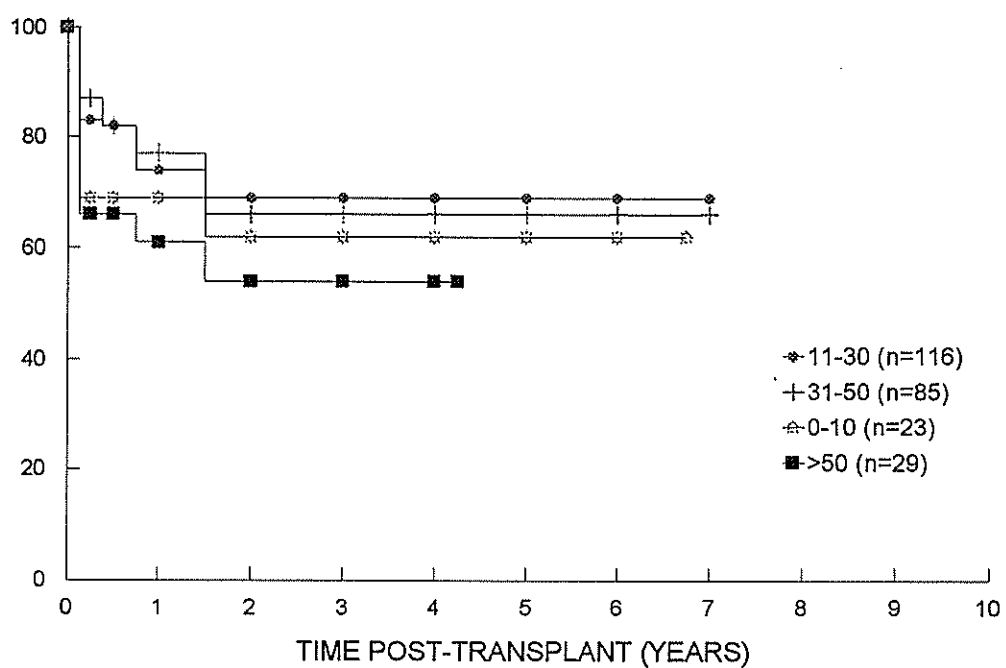


FIGURE 21      PRIMARY GRAFT SURVIVAL  
DONOR AGE vs SURVIVAL

Primary grafts from donors in the age groups up to 50 all survive equivalently between 62 and 69% at 5 years. Grafts from donors aged more than 50 survive less well, sustained function occurring in 55% of cases. Currently this difference is non-significant.

FIGURE 21

**PRIMARY GRAFT SURVIVAL**  
**DONOR AGE vs SURVIVAL**



31/12/92

FIGURE. 22 CAUSES OF PATIENT DEATH - ALL PATIENTS

Of the total 576 patients, 142 (25%) have died.

CAUSES OF DEATH

	No	%	
		of deaths	of all patients
Graft Failure	44	31	8
Sepsis	43	30	7
Cerebral catastrophies	21	15	4
Malignancy	16	11	3
Cardiovascular	7	5	1
Operative	5	3	1
Respiratory	3	2	1
Gastrointestinal	1	1	0.2
Miscellaneous	2	1	0.3
TOTALS	142	100	25

Fig 22 reveals that graft failure is a prominent cause of death throughout the time periods. Other analysis shows that the causes of graft failure change from primary non function, technical failures and those due to acute rejection in the early post-operative weeks to recurrent disease (hepatitis, malignancy) and chronic rejection thereafter (Figure 24). Cerebral catastrophes figure prominently within the first month. Sepsis is the major cause of death in the time periods beyond 1 week up to 6 months post-operation. Beyond 1 year graft failure and malignancy are the major causes.



FIGURE 22

**CAUSE OF DEATH  
ALL PATIENTS**

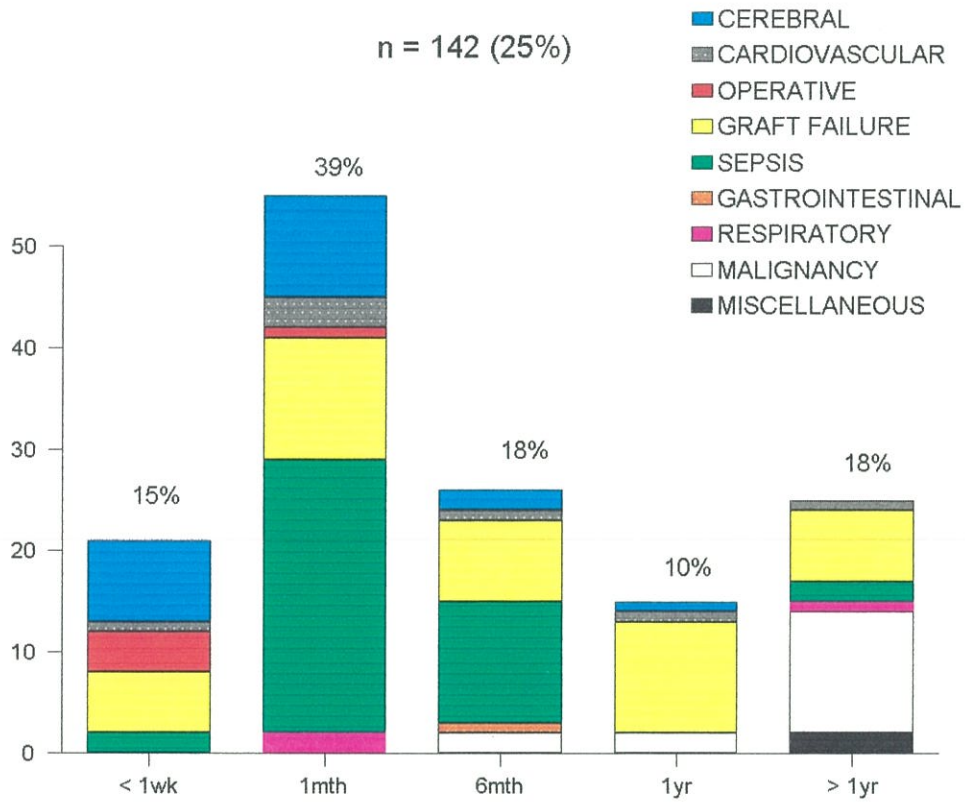
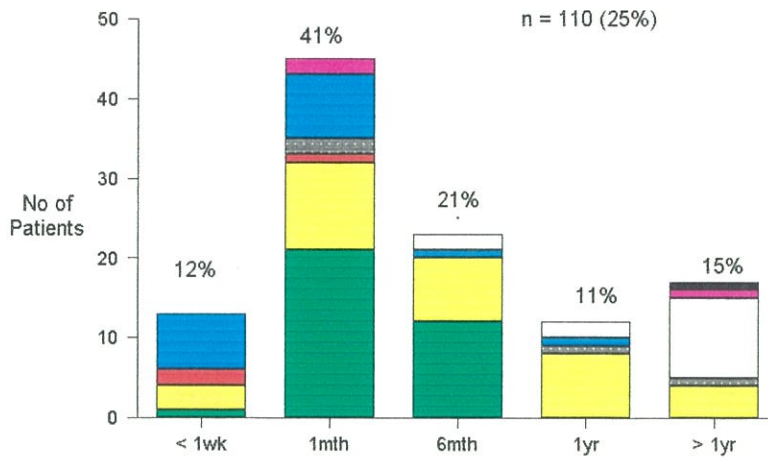


FIGURE 23      CAUSE OF DEATH  
AUSTRALIA, NEW ZEALAND, OTHER

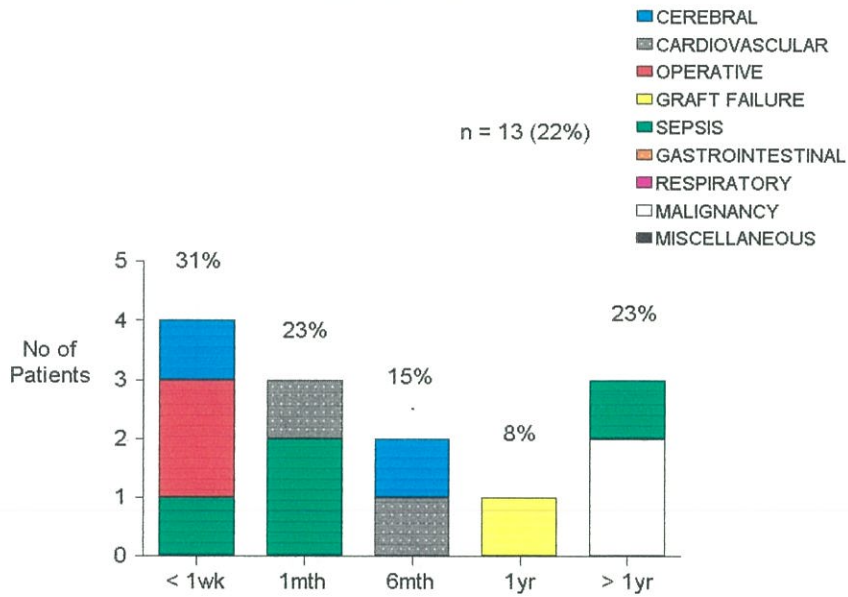
The proportions of patients who have died is the same amongst Australian citizens, New Zealand citizens and Other citizens (about 25%). The numbers of New Zealanders and Other citizens who died are relatively small, making analysis difficult. However, the pattern is generally similar to that for Australia, though for Other citizens later failure was due to graft failure and sepsis there being no contribution by malignancy.

FIGURE 23

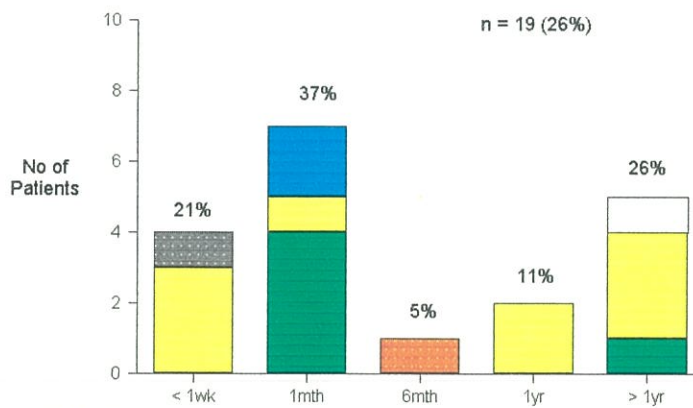
**CAUSE OF DEATH  
AUSTRALIAN CITIZENS**



**NZ CITIZENS**



**OTHER CITIZENS**



30/06/93

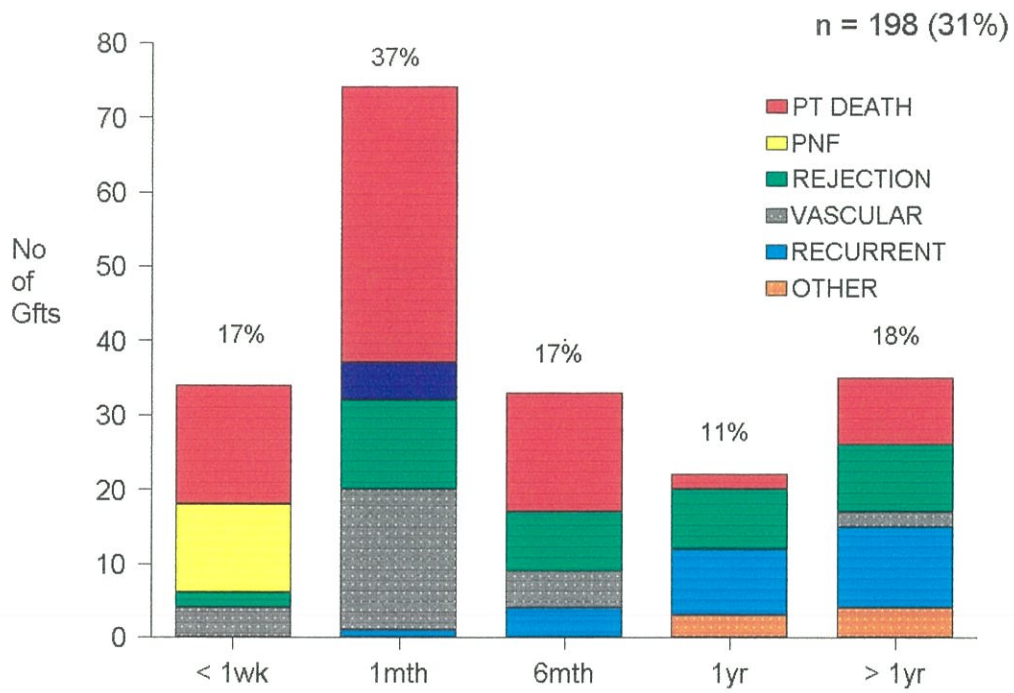
FIGURE 24 CAUSE OF GRAFT FAILURE - ALL GRAFTS

	No	%	
		of graft failures	of all grafts
Patient death	80	40	13
Rejection	39	20	6
Vascular	30	15	5
Primary non function	17	9	3
Recurrent disease	25	13	4
Other	7	4	1
TOTALS	198	100	32

Within the 1st month the major causes of graft loss are patient deaths, primary non function, rejection and vascular complications. After this time patient deaths continue to contribute significantly as does rejection and recurrent disease, mostly hepatitis and malignancy.

FIGURE 24

**CAUSE OF GRAFT FAILURE**  
**ALL GRAFTS**



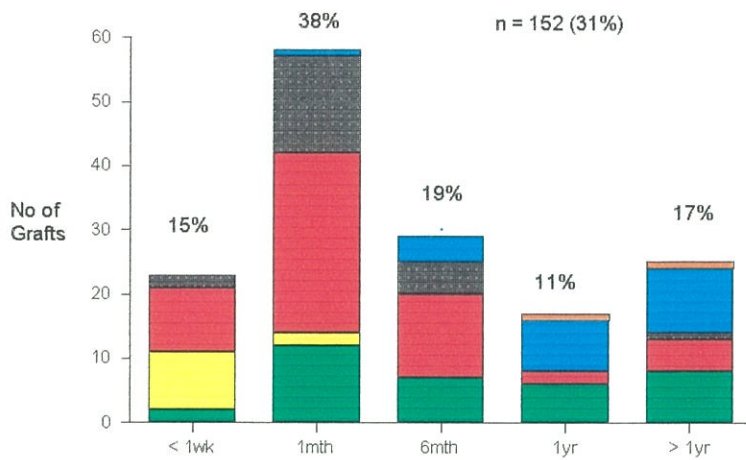
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FIGURE 25      CAUSE OF GRAFT FAILURE  
AUSTRALIA, NEW ZEALAND, OTHER

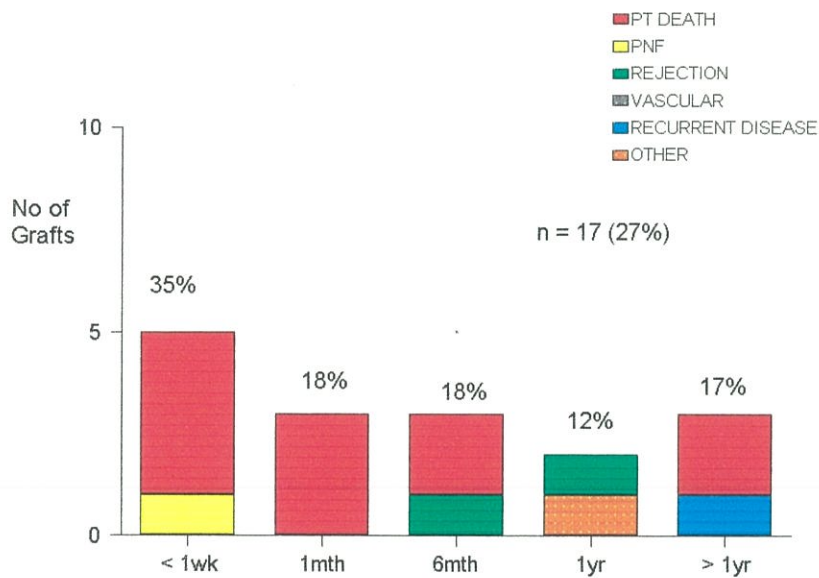
While rejection has contributed to graft losses throughout the experience with Australian citizens, it has been a rare cause of failure amongst New Zealand citizens or Other citizens within the first 6 months. Graft losses in the last 2 groups during this period have been due to patient death, primary non function and vascular complications. Also, graft losses to recurrent disease have been limited to a single Other citizen in these 2 groups.

FIGURE 25

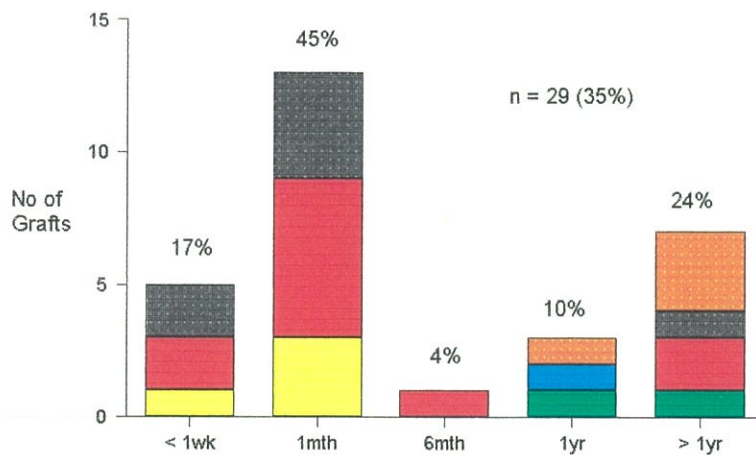
**CAUSE OF GRAFT FAILURE  
AUSTRALIAN CITIZENS**



**NZ CITIZENS**



**OTHER CITIZENS**



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FIGURE 26    DONATION BY YEAR

The information on organ donation was provided by the Australian Transplant Coordinators Association, ANZData and Ms Joanna Innes Walker (NZ).

The total number of liver donors increased steadily between 1990 - 1992 but plateaued in 1993.



FIGURE 26

**DONATION BY YEAR**

	QLD	NSW	VIC/ TAS	SA/ NT	WA	NZ	TOTAL
1990	22	27	17	6	-	7	79
1991	27	38	22	6	9	11	113
1992	41	34	21	8	8	24	136
1993	27	41	24	13	6	17	128

30/06/93

