

LIVER TRANSPLANTATION IN AUSTRALIA

7TH REPORT FROM THE COMBINED REGISTRIES OF THE AUSTRALIAN LIVER TRANSPLANT CENTRES DATA TO 30/06/94

**MARCH 1995
Edited By**

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Table of Contents

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

Figure 15	PATIENT SURVIVAL - FULMINANT DISEASE	30-31
Figure 16	PATIENT SURVIVAL MALIGNANCY vs HEP B vs HEP C vs AUTOIMMUNE vs OTHER DISEASES.	32-33
Figure 17	PATIENT SURVIVAL PAEDIATRIC RECIPIENTS WHOLE LIVER vs REDUCED LIVER.	34-35
Figure 18	PATIENT AND GRAFT SURVIVAL LRD.	36-37
Figure 19	PATIENT SURVIVAL BY AGE AT TRANSPLANT	38-39
Figure 20	PATIENT SURVIVAL BY YEAR OF TRANSPLANT - AUSTRALIA	40-41
Figure 21	PRIMARY GRAFT SURVIVAL DONOR AGE vs SURVIVAL	42-43
Figure 22	CAUSES OF PATIENT DEATH - ALL PATIENTS	44-45
Figure 23	CAUSES OF DEATH AUSTRALIAN, NEW ZEALAND, OTHER	46-47
Figure 24	CAUSES OF GRAFT FAILURE - ALL GRAFTS	48-49
Figure 25	CAUSE OF GRAFT FAILURE AUSTRALIAN, NEW ZEALAND, OTHER	50-51
Figure 26	DONATION BY YEAR	52-53

Foreword

The liver transplant centres in Australia report details of their liver graft recipients to a combined registry so that a National analysis can be done. Established centres are situated in Adelaide, Brisbane, Melbourne, Perth and Sydney.

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 for the sixth and seventh reports. In the seventh report is presented data concerning all liver grafts and recipients since orthotopic liver transplantation began in Australia in 1985 until June 30, 1994. Prior to 1985 there had been only one (auxiliary) liver graft implanted in 1968.

The format of the report presents analysis of outcomes in Australian citizens, New Zealand citizens and those from other countries. This allows 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.

AGR Sheil
GW McCaughan

FIGURE 1. NUMBER OF TRANSPLANTS.

The number of transplants performed in Australia since 1985 is shown in Figure 1. After a steady increase in the numbers of transplants in the early years the totals appear to be plateauing in the 140 - 150 range. The number of operations performed does not equate to the number of recipients of grafts as some patients received secondary grafts. Thirty one 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

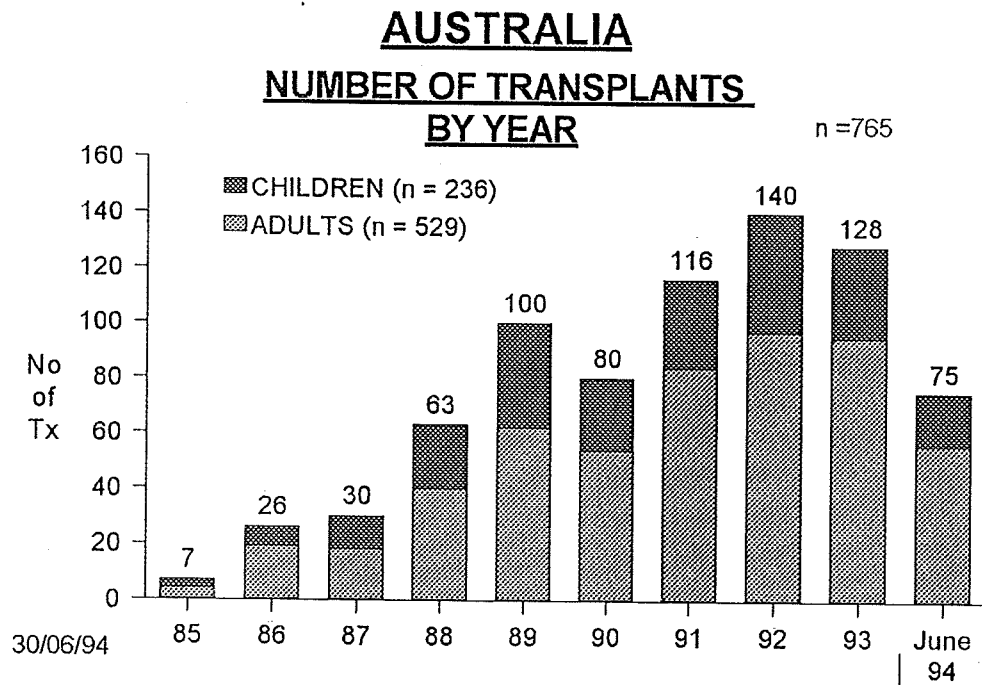


FIGURE 2 NUMBER OF RECIPIENTS BY YEAR

The number of patients who received grafts by year are shown in Figure 2. The total number is 699. Recipients are divided into a) Australian citizens b) New Zealand citizens and c) Others.

Australian Citizens

The number of Australian recipients increased steadily from 1985, and appears to be stabilizing at about 100 per year. The proportion of patients who are children has been consistently around 22%. 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. With around 100 patients receiving grafts and an estimated 12 dying on waiting lists, the demand for 1993 was approximately 6.5 per million of population. The need for liver transplantation is expected to increase as the indications for the procedure are widened and because of those patients with liver grafts who will require retransplantation for a variety of reasons.

New Zealand Citizens

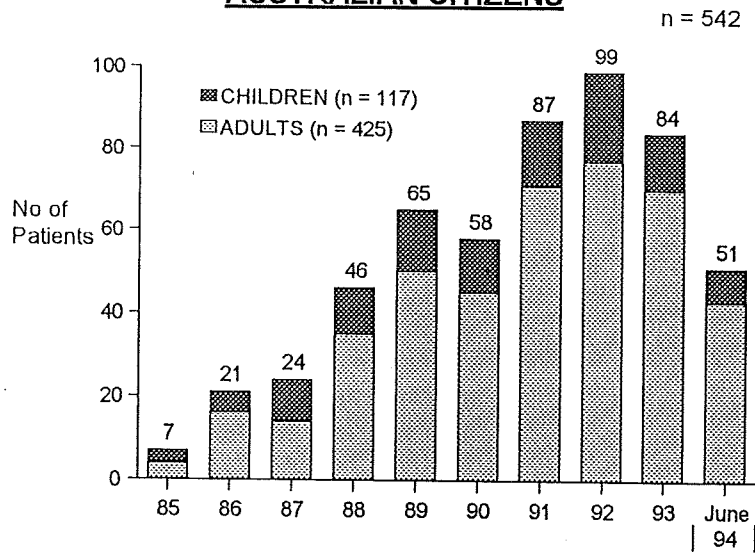
The number of New Zealand patients referred for treatment seems to be levelling off at about 14 per year. Children represent 28% of the total. With the NZ population currently 3.4 million, this represents treatment by transplantation of 4 per million of population per year.

Other Citizens

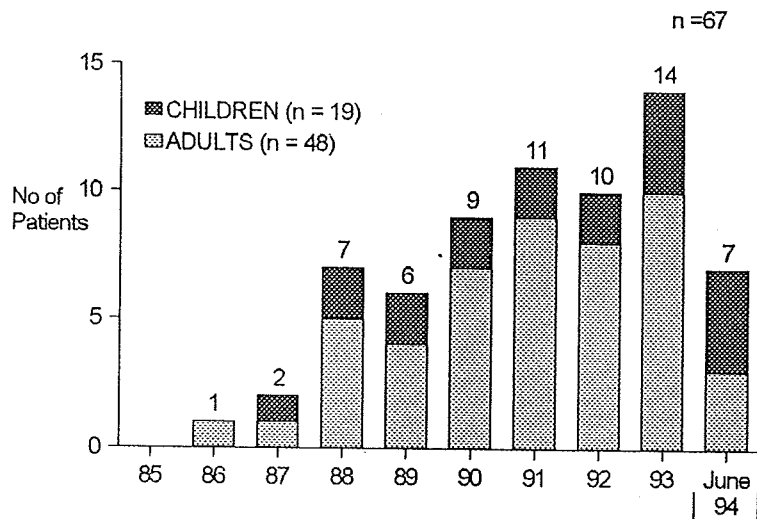
Most Other Citizens have been children (67). Only 23 adults have been referred for transplantation from countries over-seas (apart from New Zealand). In the last 3 years the numbers of adults have gradually increased while the numbers of children have decreased.

FIGURE 2
NUMBER OF RECIPIENTS BY YEAR (n = 699)

AUSTRALIAN CITIZENS



NZ CITIZENS



OTHER CITIZENS

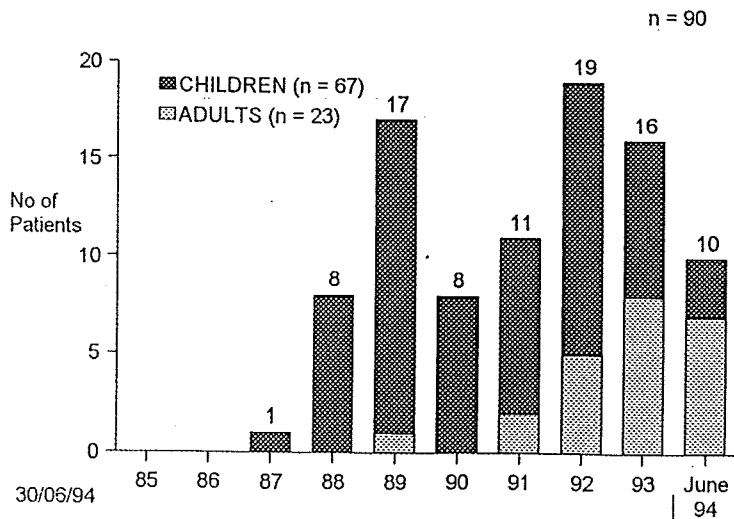


FIGURE 3 NUMBER OF RECIPIENTS BY AGE.

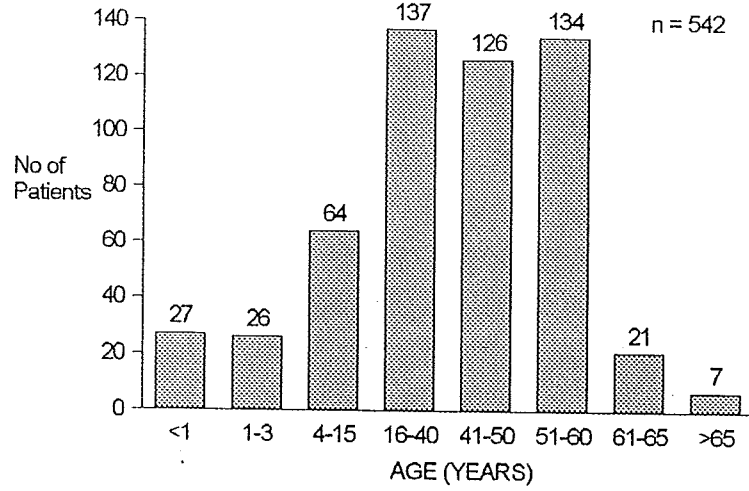
Patients of all ages may require treatment by liver transplantation. The youngest patient, an Australian citizen, was aged 4 months and the oldest, also an Australian citizen was 67 years. The oldest New Zealand patient was almost 61 years and the oldest patient from Other countries, 61 years. While 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 have been treated than older children. In those patients referred from other countries the distribution is heavily skewed towards infants and young children

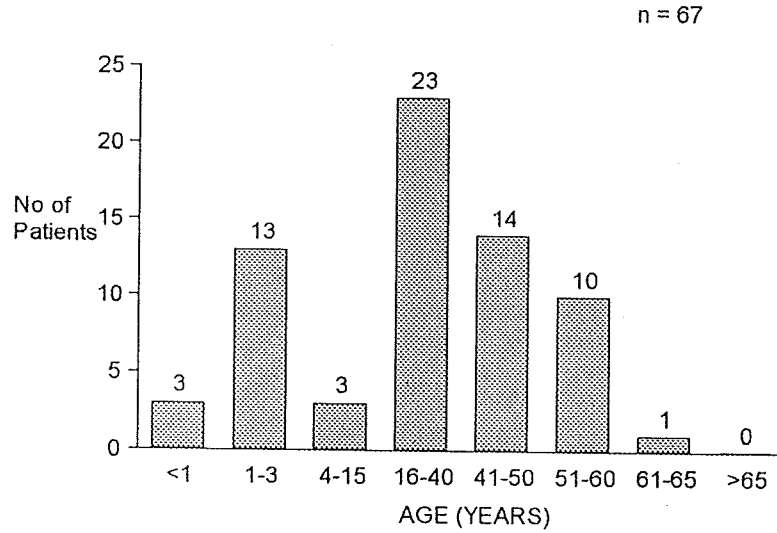
FIGURE 3

NUMBER OF RECIPIENTS BY AGE

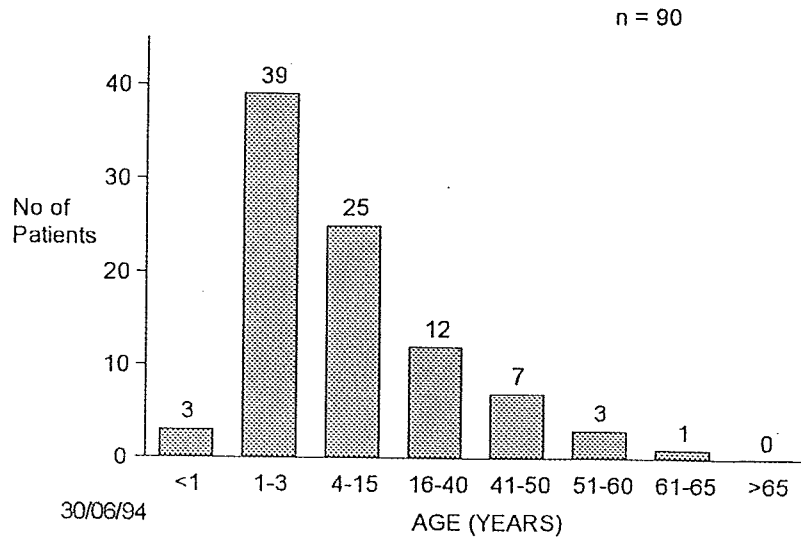
AUSTRALIAN CITIZENS



NZ CITIZENS



OTHER CITIZENS



30/06/94

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. Currently, 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

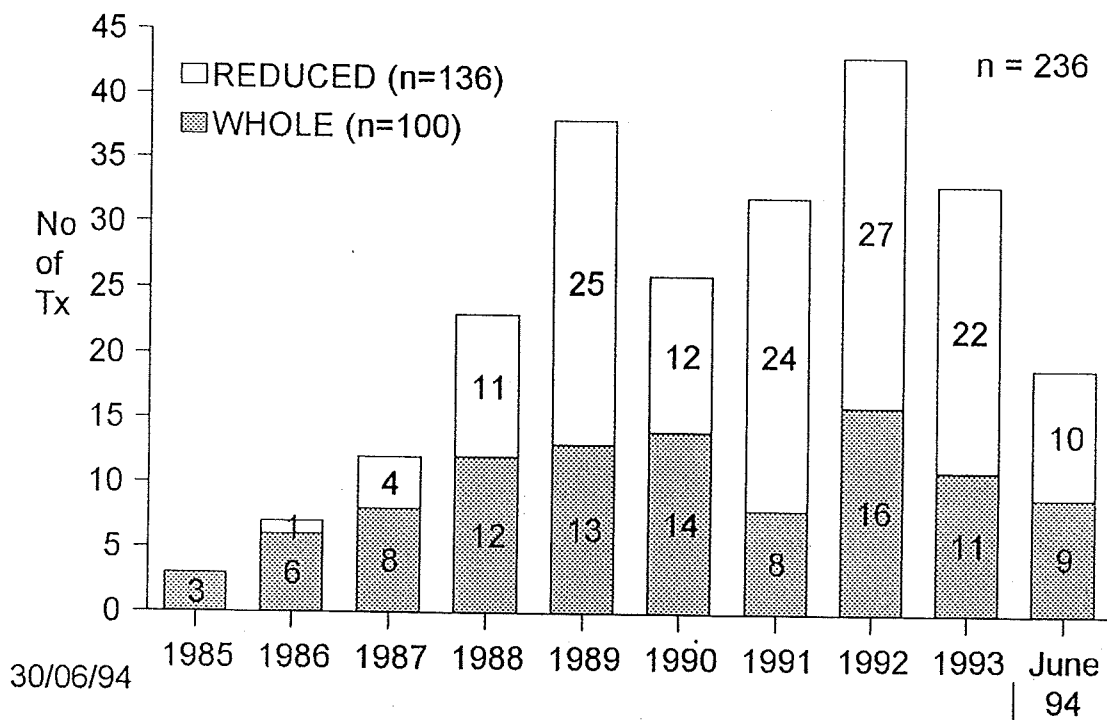
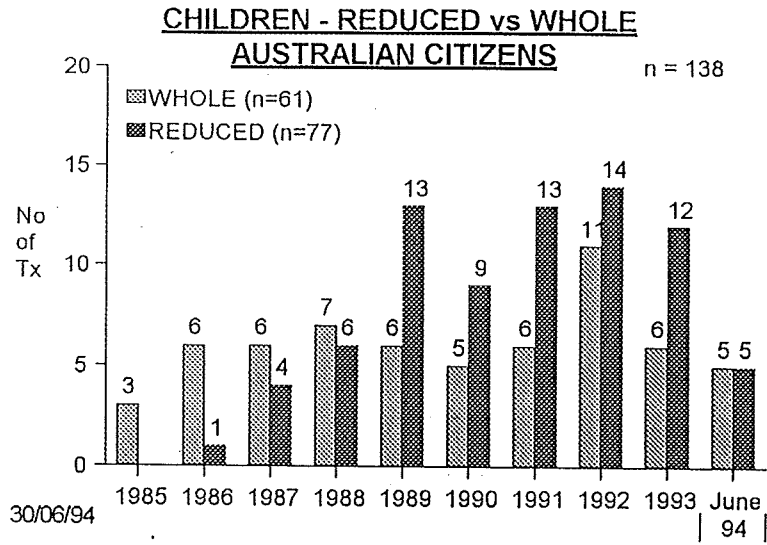


FIGURE 5. NUMBER OF GRAFTS BY YEAR. CHILDREN
REDUCED V WHOLE. AUSTRALIA. NEW ZEALAND.
OTHER.

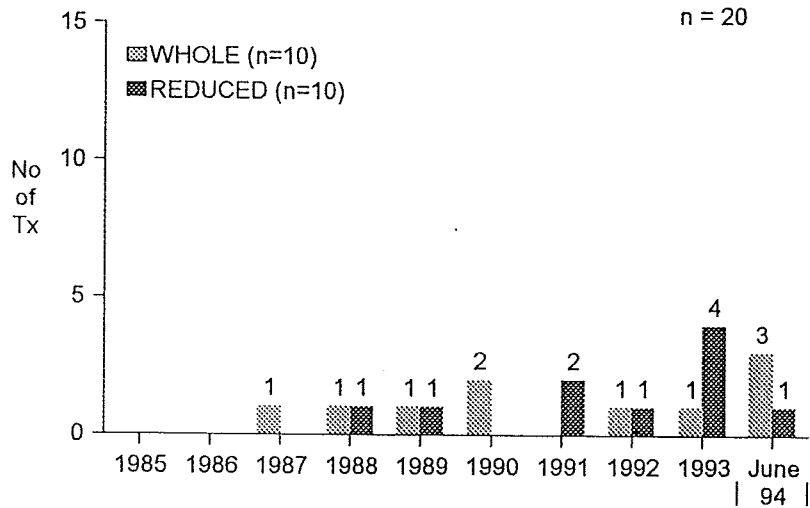
The pattern of increasing proportions of reduced grafts occurs in both Australian and New Zealand children and is particularly marked in those referred from other countries.

FIGURE 5

NUMBERS OF GRAFTS BY YEAR



NZ CITIZENS



OTHER CITIZENS

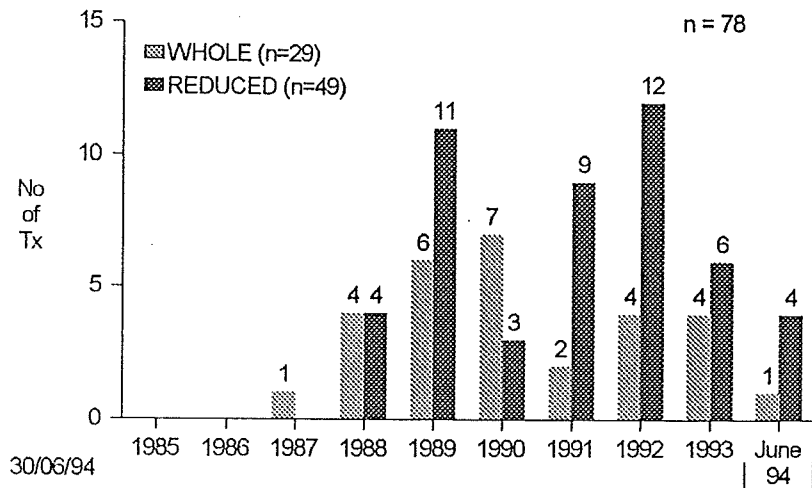


FIGURE 6. PRIMARY DISEASES OF RECIPIENTS.

The primary diseases of recipients are shown in Figure 6 which reveals that many conditions contribute groups of 8 - 13% of the total requiring treatment in Australia. They include autoimmune hepatitis (AH, 8%), chronic viral hepatitis (CVH, 10%), primary sclerosing cholangitis (13%), primary biliary cirrhosis (10%) cryptogenic cirrhosis (8%) and alcoholic cirrhosis (8%). A break-up of the chronic viral hepatitis group is shown in Fig. 7. In children, the major group is biliary atresia which contributes 12% to the total. The metabolic disorders (11%) span both adults and children as does fulminant hepatitis (10%). To date, relatively few patients have received grafts for malignancy (4%).

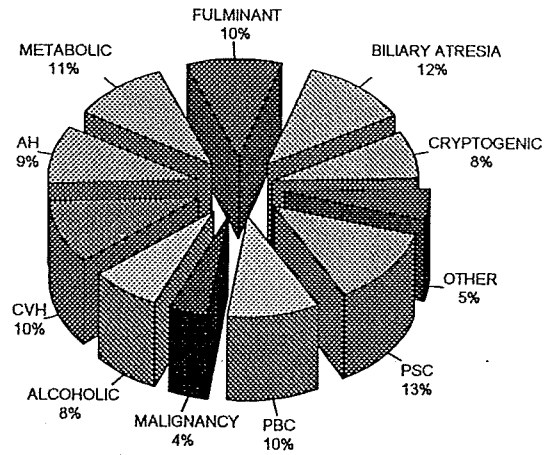
With New Zealand citizens (in comparison to Australians) there are modestly increased proportions of patients with fulminant hepatic failure (21%), biliary atresia (21%) and primary sclerosing cholangitis (18%). Primary biliary cirrhosis (8%) is similar in proportion as is cryptogenic cirrhosis (8%). AH is approximately the same (7%) while CVH (3%) and metabolic disorders (5%) are reduced. The numbers of patients with alcoholic cirrhosis and with malignancy are low (2% and 1% respectively). With Other citizens 72% of patients have biliary atresia. CVH accounts for 8% of patients with other causes of liver failure contributing small percentages only.

FIGURE 6

PRIMARY DISEASES OF RECIPIENTS

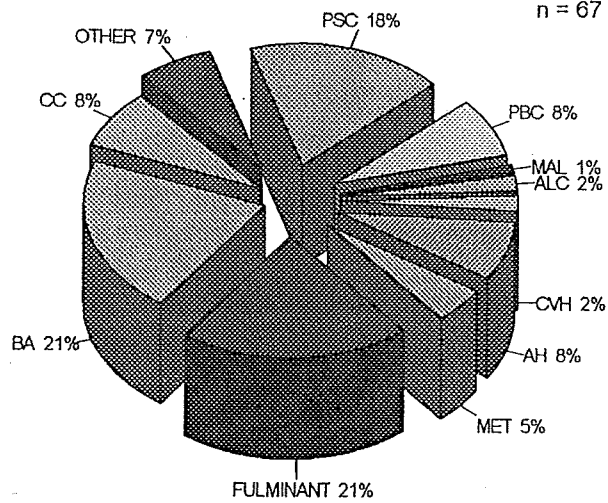
AUSTRALIAN CITIZENS

n = 542



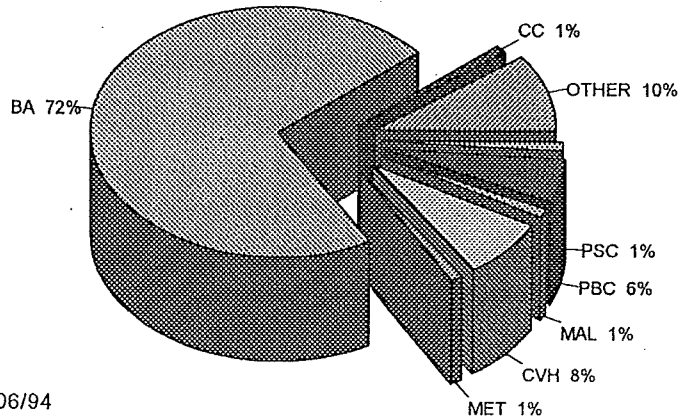
NEW ZEALAND CITIZENS

n = 67



OTHER CITIZENS

n = 90



30/06/94

FIGURE 7. CHRONIC VIRAL HEPATITIS

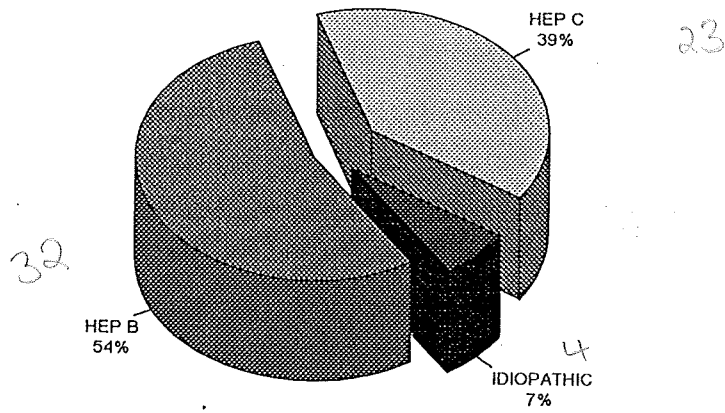
The aetiology of chronic viral hepatitis (CVH) in Australian citizens shows that most (54%) are Hep B. Hep C contributes 39% and idiopathic 7%. In New Zealand citizens only 2 patients with CVH have received grafts. One had Hep B and 1 Hep C. Seven Other citizens received grafts for CVH, 2 (29%) having Hep B and 5 (71%) Hep C.

FIGURE 7

CHRONIC VIRAL HEPATITIS

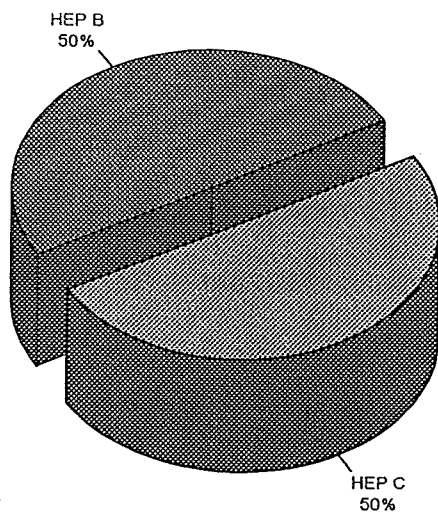
AUSTRALIAN CITIZENS

n = 60



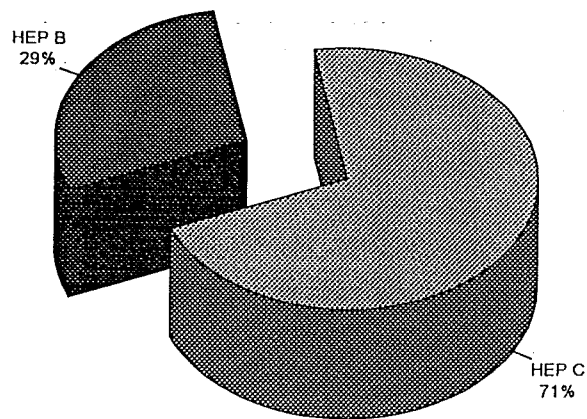
NZ CITIZENS

n = 2



OTHER CITIZENS

n = 7



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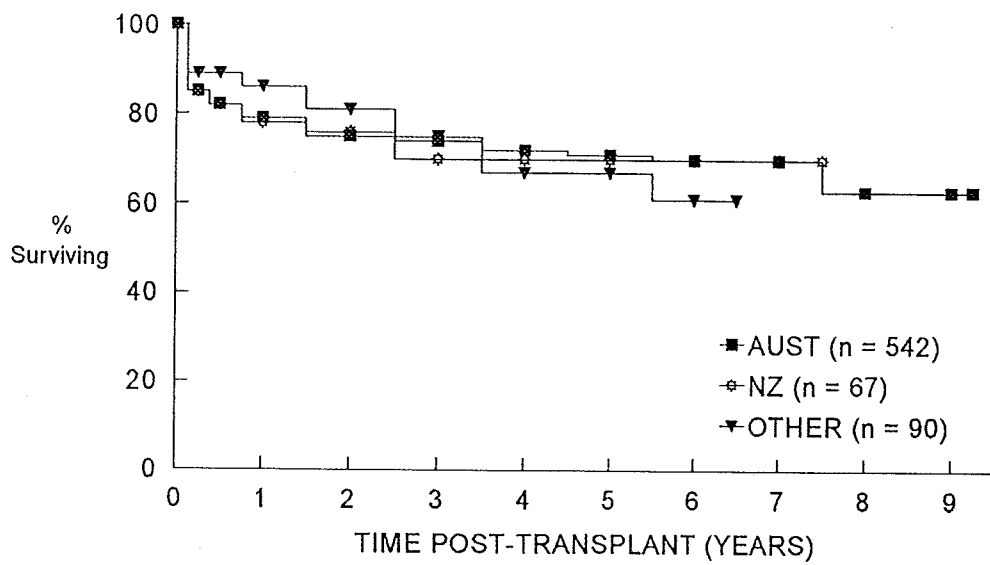
FIGURE 8 *PATIENT SURVIVAL POST Tx.*

Patient survivals for Australian and New Zealand citizens are similar. Survival at 1 year following transplantation is about 80% and at 5 years 70%. Survival for Other Citizens is a little less in the long term at 61%.

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

FIGURE 8

PATIENT SURVIVAL POST Tx



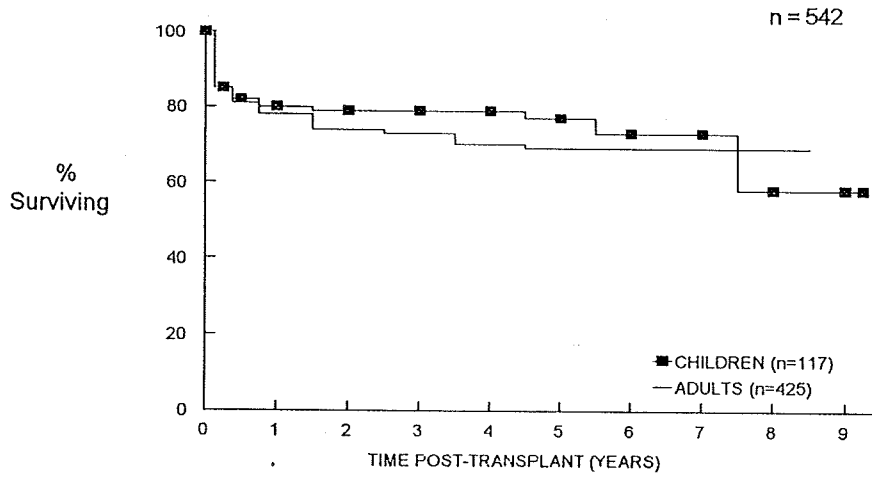
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FIGURE 9. PATIENT SURVIVAL - ADULTS AND CHILDREN.

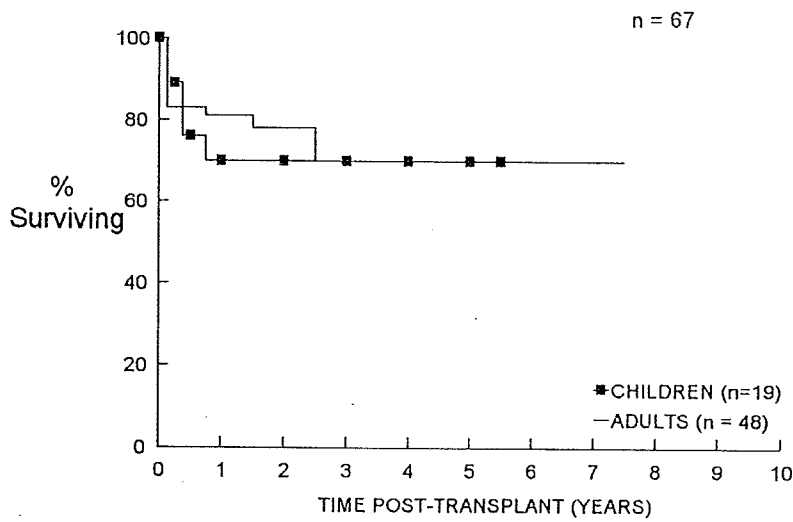
While early survival for Australian children is a little improved on that for Australian adults, there is little difference in the long term (about 70%). An analysis in Australian children and adults excluding the recurrent diseases Hep B and Malignancy, which impact particularly on adults, is shown in Figure 10. There is no difference for child and adult NZ citizens (5 yr survival 70%). Child Other Citizens have a five year survival of (57%).

FIGURE 9

PATIENT SURVIVAL - ADULTS AND CHILDREN
AUSTRALIAN CITIZENS



NZ CITIZENS



OTHER CITIZENS

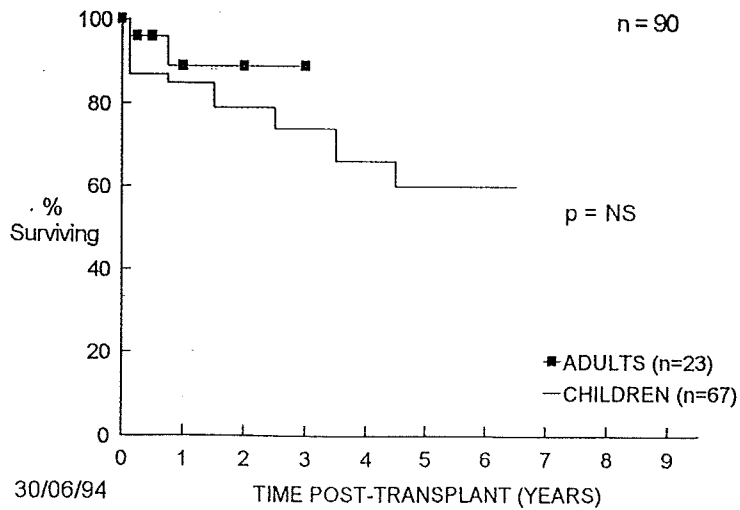
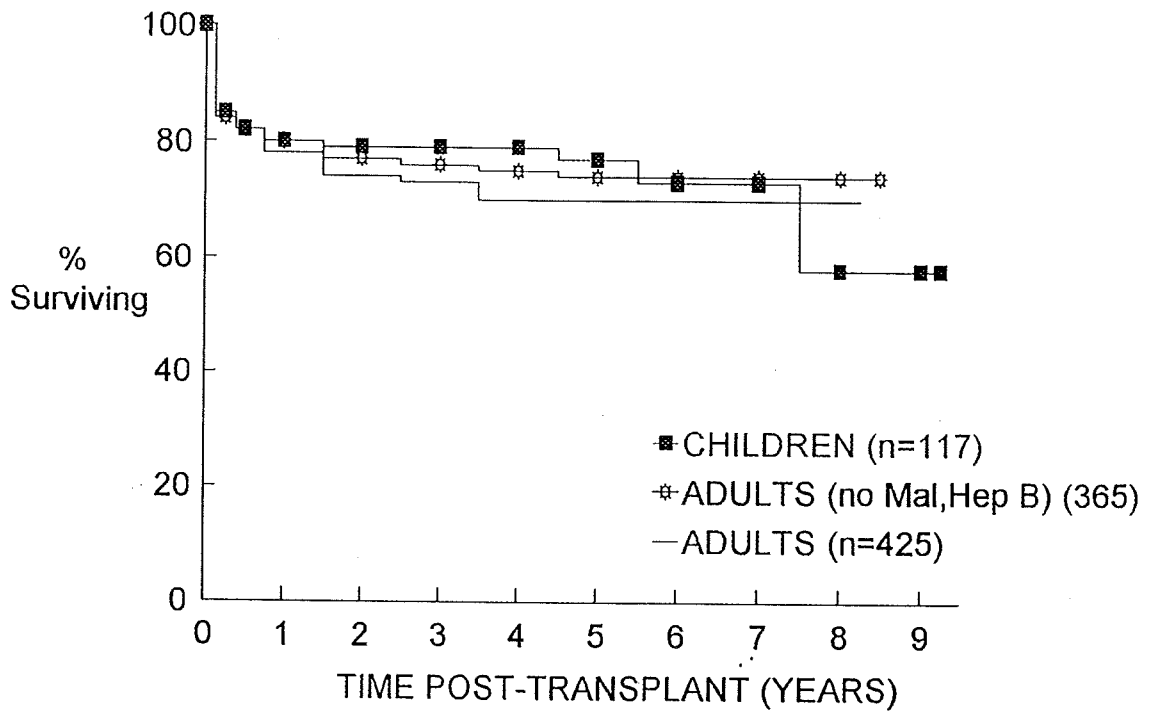


FIGURE 10. PATIENT SURVIVAL, AUSTRALIAN CITIZENS,
CHILDREN, ADULTS AND ADULTS EXCLUDING
MALIGNANCY AND HEPATITIS B.

An analysis of the survival of adults excluding those whose primary liver conditions were 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**



30/06/94

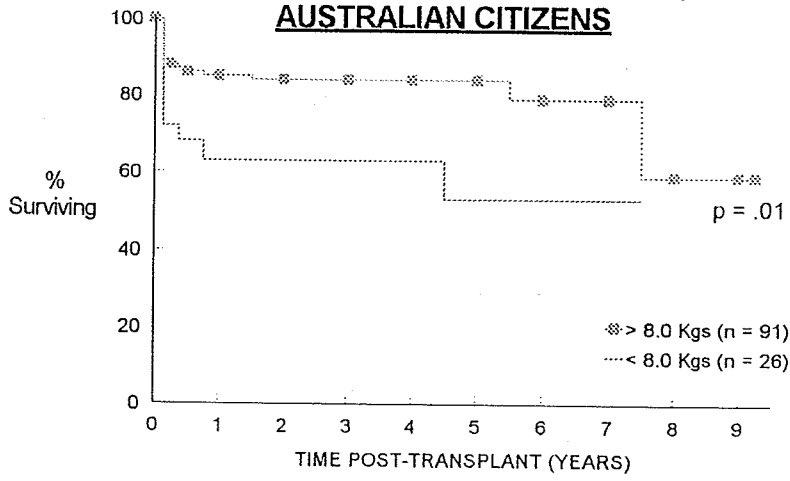
FIGURE 11. CHILDREN > 8.0 KG AND < 8.0 KG.

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 84% at 5 years post transplant compared to 53% for children less than 8.0 kgs. This general pattern occurred also for New Zealand citizens and Other citizens.

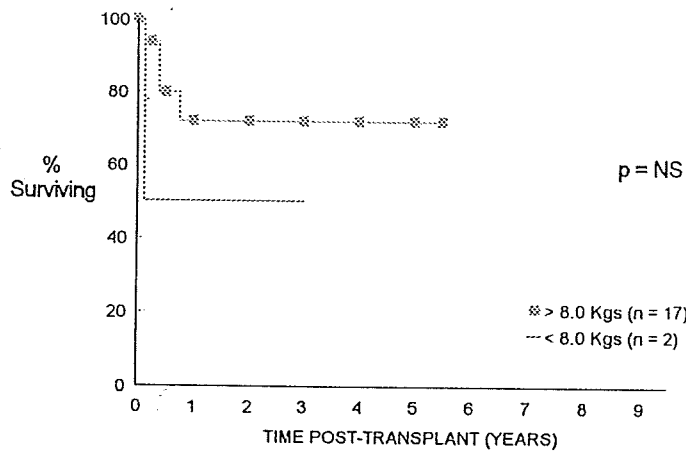
FIGURE 11

PATIENT SURVIVAL

CHILDREN > 8.0 KG AND < 8.0 KG
AUSTRALIAN CITIZENS



NZ CITIZENS



OTHER CITIZENS

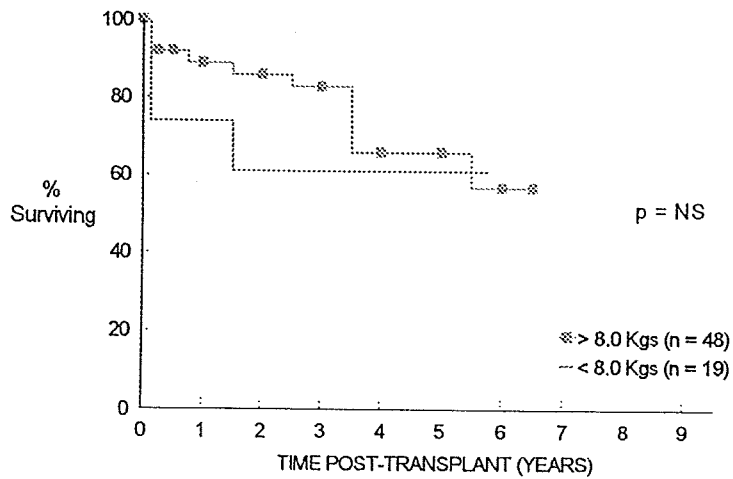


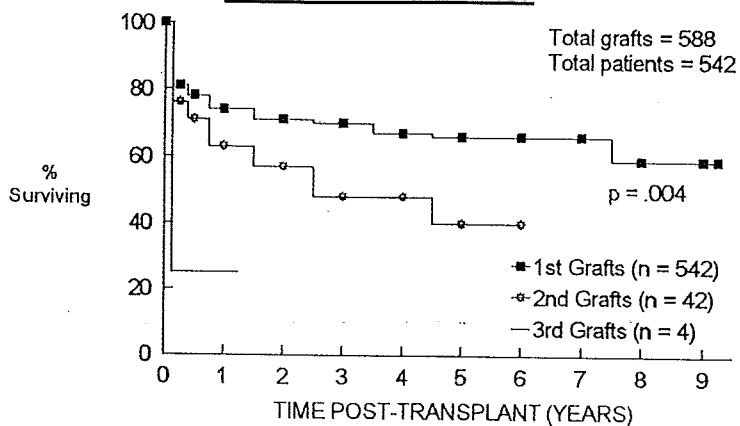
FIGURE 12 GRAFT SURVIVAL - PRIMARY AND SECONDARY

Primary grafts for Australian citizens (n = 542) show a 1 year survival of 74% and 5 year survival of 66%. Second grafts do somewhat worse with 1 year survival of 62% and sustained function of 40%. One of 4 third grafts in the Australian experience remains functional. The pattern for first and secondary grafts for New Zealand citizens and Other citizens are similar. The primary graft survival for New Zealand citizens is 74% at 1 year and 65% long term whilst Other citizens are 83% and 55% respectively. Secondary graft survival for New Zealand citizens is 50% at 1 year, and 35% for Other citizens.

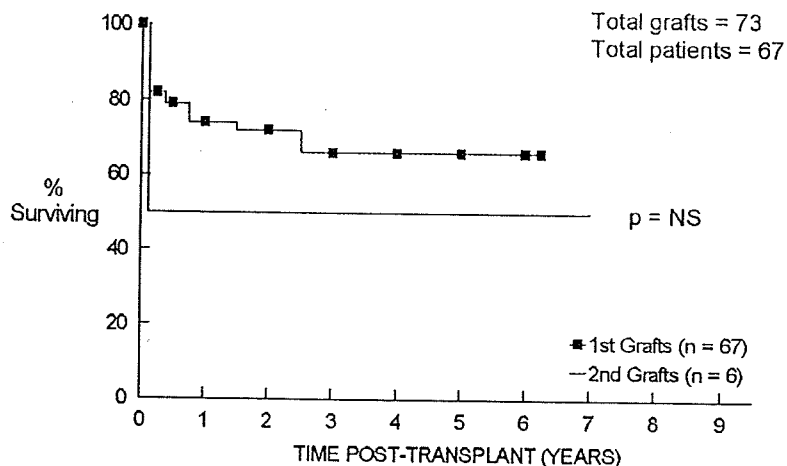
FIGURE 12

GRAFT SURVIVAL - PRIMARY AND SECONDARY

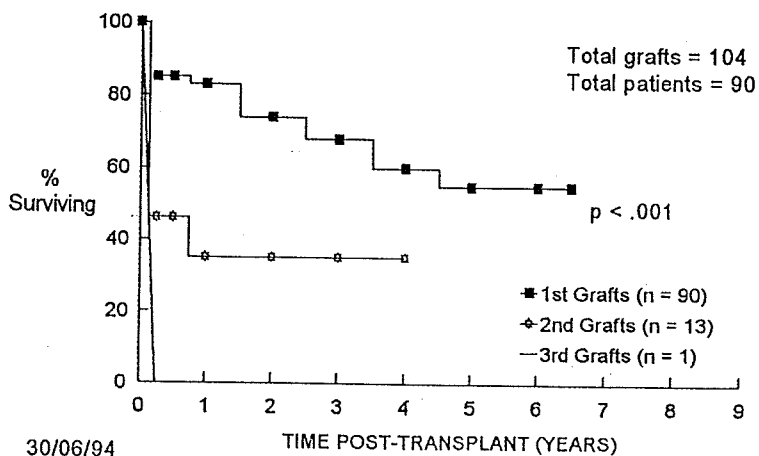
AUSTRALIAN CITIZENS



NZ CITIZENS



OTHER CITIZENS



30/06/94

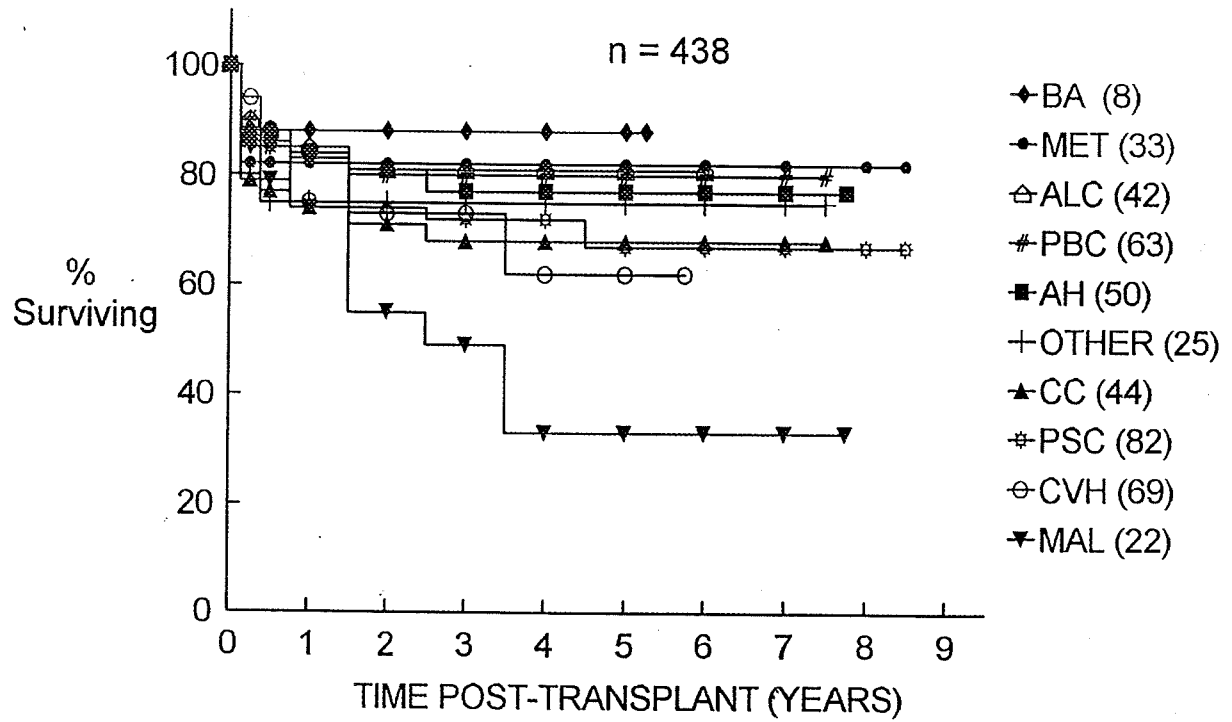
FIGURE 13 *DISEASE AND OUTCOME*
ADULTS.

Survival for adults with metabolic disorders (33), alcoholic liver disease (42), primary biliary cirrhosis (63) and autoimmune hepatitis (50) in the 5 - 7 year follow-up is close to 80%. Few adults (8) received grafts for biliary atresia - 7 of these survive. Survival for those with cryptogenic cirrhosis (44) at 5 years is 68% and for chronic viral hepatitis (CVH, 60) 62%. The results for the sub-groups of CVH (Hep B, Hep C) are shown in Fig. 16. Five year survival for PSC (82) is 67%. For malignancy (22) 33%. The outcome for those with Fulminant Hepatic Failure are shown in Fig. 15.

FIGURE 13

PATIENT SURVIVAL

DISEASE AND OUTCOME - ADULTS



30/06/94

FIGURE 14. PATIENT SURVIVAL
DISEASE AND OUTCOME
CHILDREN.

The major groups for children are biliary atresia (136 pts - 65% 5 year survival) and metabolic disorders (29 - 75% 5-7 year survival). All children with malignancy (3), AH (1) and PBC (1) are surviving (100%) as are 2 of 4 (50%) with cryptogenic cirrhosis. Five year survival for 16 with other conditions is 80%. The outcome for those with Fulminant Hepatic Failure is shown in Fig. 15.

FIGURE 14

PATIENT SURVIVAL DISEASE AND OUTCOME - CHILDREN

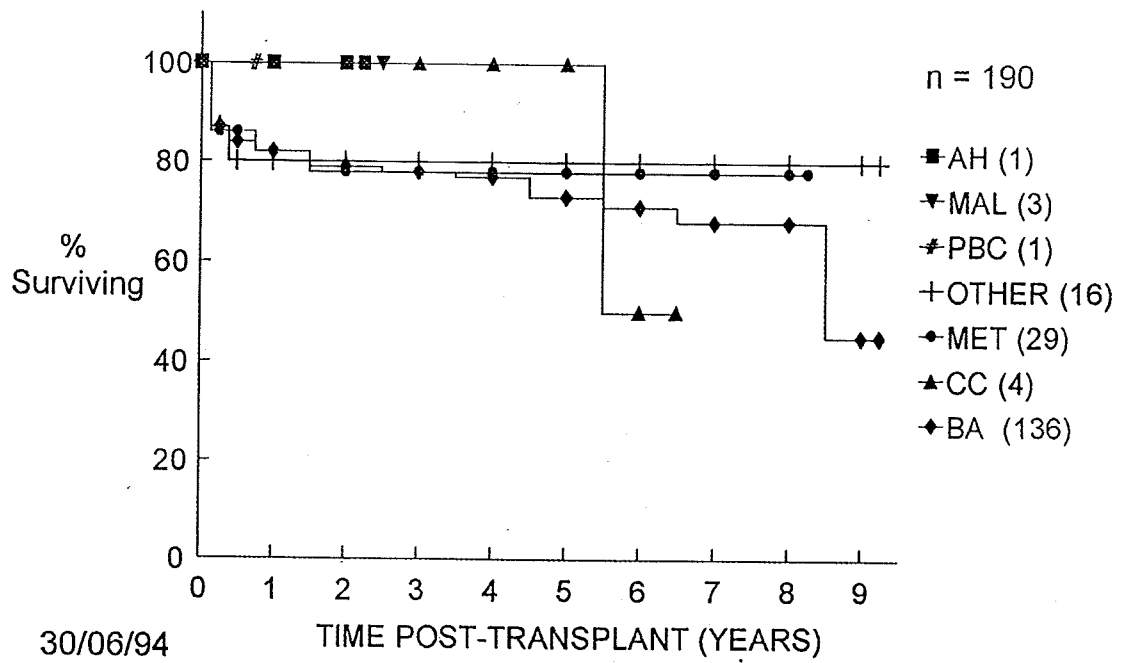


FIGURE 15 PATIENT SURVIVAL - FULMINANT DISEASE.

Fifty eight adults and 13 children with fulminant disease have received grafts. Five year survival for adults is 65% and for children 54%. One child with fulminant disease from New Zealand has received a graft. Thirteen New Zealand adults in fulminant failure received grafts; 3 and 5 year survivals are 77%. The common causes of fulminant hepatitis in adults were idiopathic (53%), Hep B (19%), drugs (16%) and Wilsons disease (7%). Rare causes were Hep C (3%) and autoimmune (2%). Of the 13 children with FHF 8 (62%) were idiopathic, 2 (15%) Wilsons disease, 2 (15%) drug-induced and 1 (8%) α -1-antitrypsin.

FIGURE 15

PATIENT SURVIVAL FULMINANT DISEASE

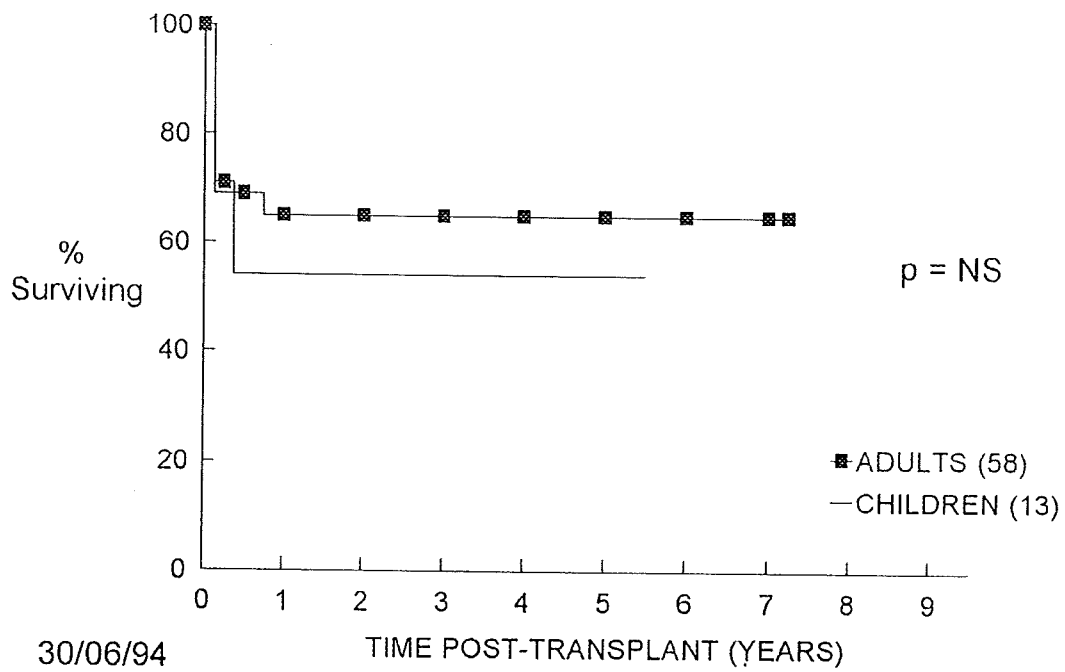


FIGURE 16 ADULT PATIENT SURVIVAL
MALIGNANCY vs HEP B vs HEP C vs AUTOIMMUNE
vs OTHER DISEASES

Survival for patients with Hep C (77% 5 year survival) and autoimmune hepatitis (77% 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 52% at 5 years and with malignancy 33%.

FIGURE 16

ADULT PATIENT SURVIVAL
MALIGNANCY vs HEP B vs HEP C vs
AUTOIMMUNE vs OTHER DISEASES

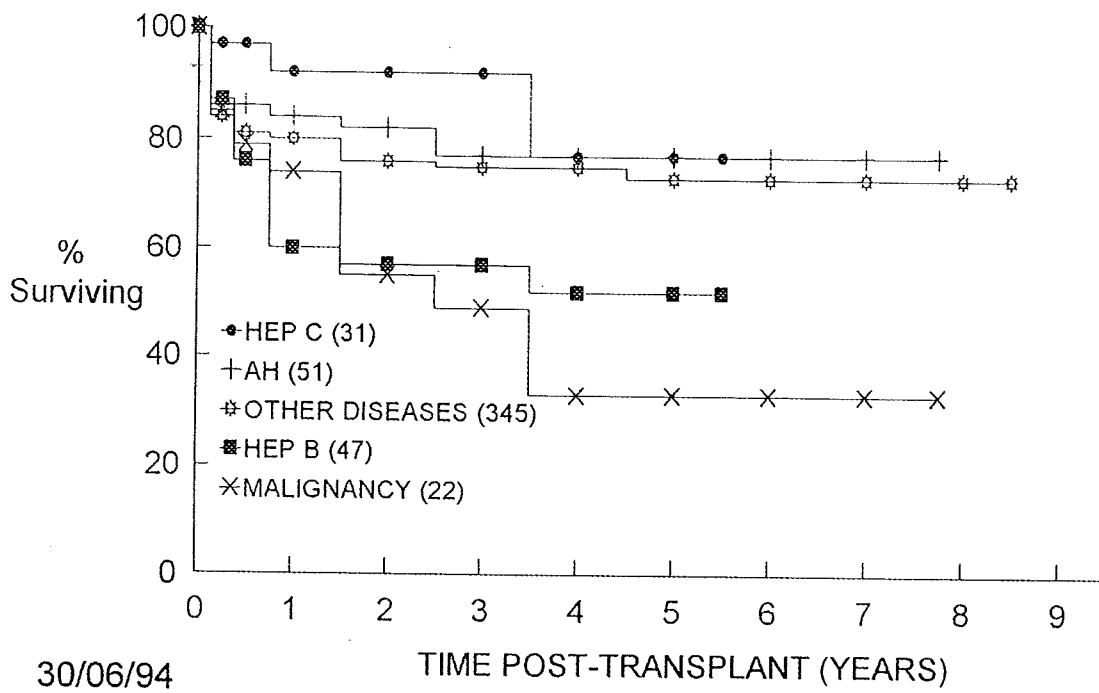


FIGURE 17 PATIENT SURVIVAL
PAEDIATRIC RECIPIENTS
WHOLE LIVER vs REDUCED LIVER.

The survival of children who received whole livers and those who received reduced livers is similar. One year survival for the former is 85% and for the latter 78%. Five - 7 years survival is approximately 80% and 73% respectively.

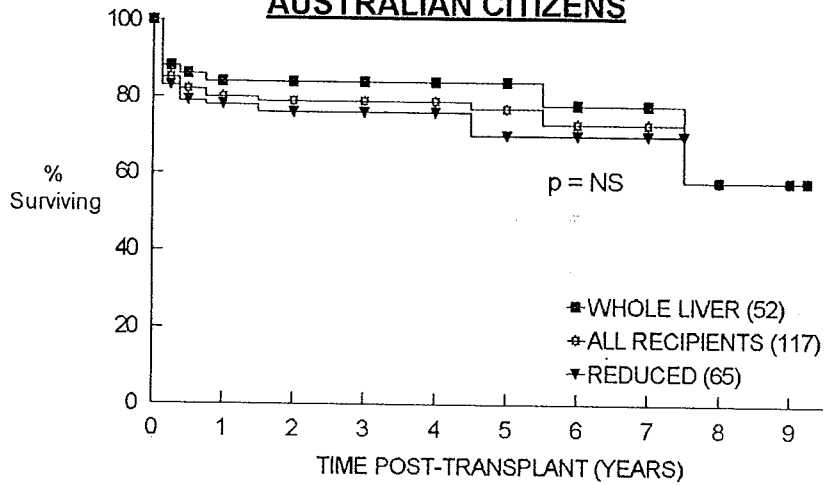
While NZ children who receive whole grafts (n = 10) appear to be doing better than those who receive part grafts (n = 9) the numbers of patients are too few for valid analysis.

With overseas children 1 year survival is improved for whole grafts (93% v 80%) but prolonged survival favours part grafts (52% for whole grafts v 71% for part grafts).

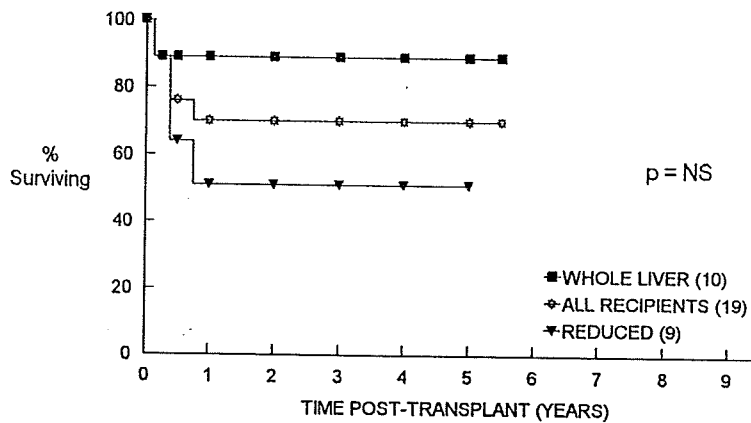
FIGURE 17

PAEDIATRIC PATIENT SURVIVAL

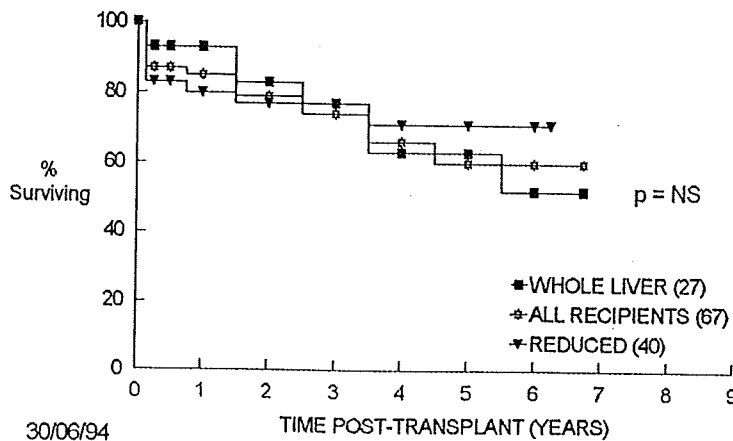
WHOLE LIVER V REDUCED LIVER AUSTRALIAN CITIZENS



NZ CITIZENS



OTHER CITIZENS



30/06/94

FIGURE 18 PATIENT AND GRAFT SURVIVAL
LRD.

Three of 5 patients who received living related donor grafts survive. One patient survives 5 years post initial LRD transplant (which functioned for 9.5 months) with a secondary cadaveric donor graft. Two of 5 LRD grafts currently continue to function at 31 and 24 months post-transplant.

FIGURE 18

AUSTRALIA

PATIENT AND GRAFT SURVIVAL

LRD

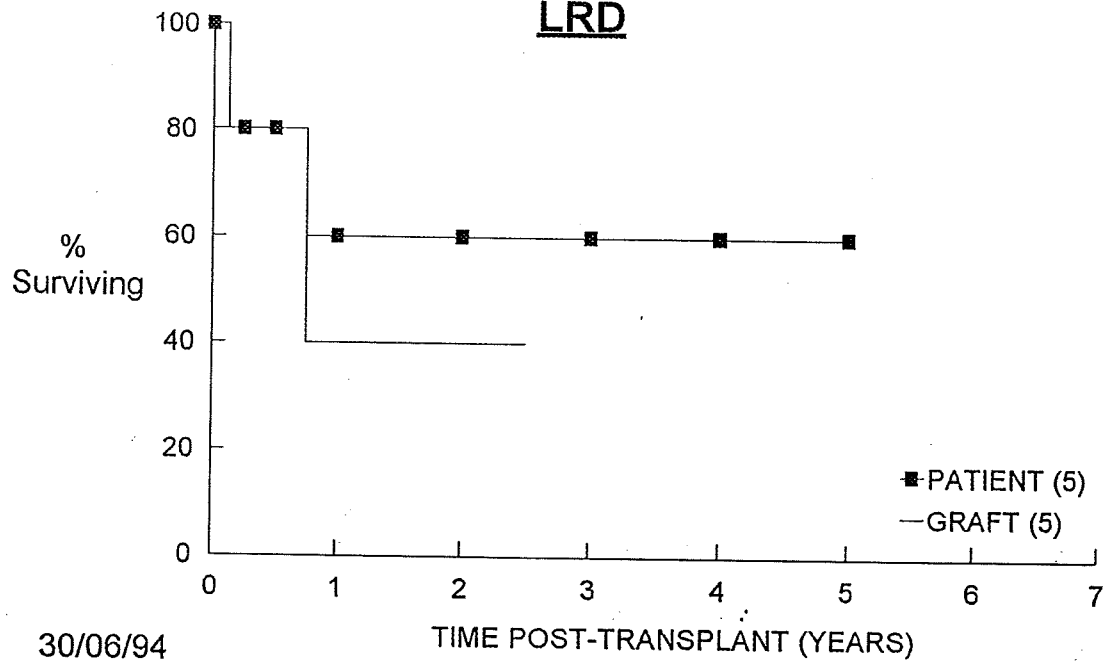


FIGURE 19 PATIENT SURVIVAL BY AGE AT TRANSPLANT.

For Australian patients the groups which survive best are those aged 1-2 (n = 26) and 3 - 14 years (n = 64). 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 (n = 27) is 72% at 1 year and 60% at 5 years. In the Australian experience patients > 60 (n = 28) currently have a 85% 1 year and 60% 3 year survival, while the 15 - 54 (n = 337) and 55 - 60 (n = 60) age groups survived equivalently with prolonged survival of 70%.

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 at 65% compared to Australian patients.

FIGURE 19

PATIENT SURVIVAL BY AGE AT TRANSPLANT

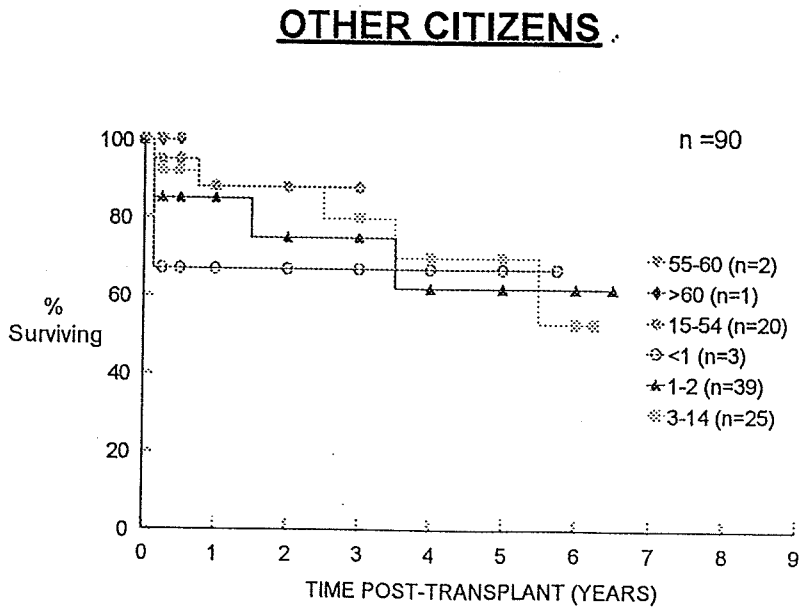
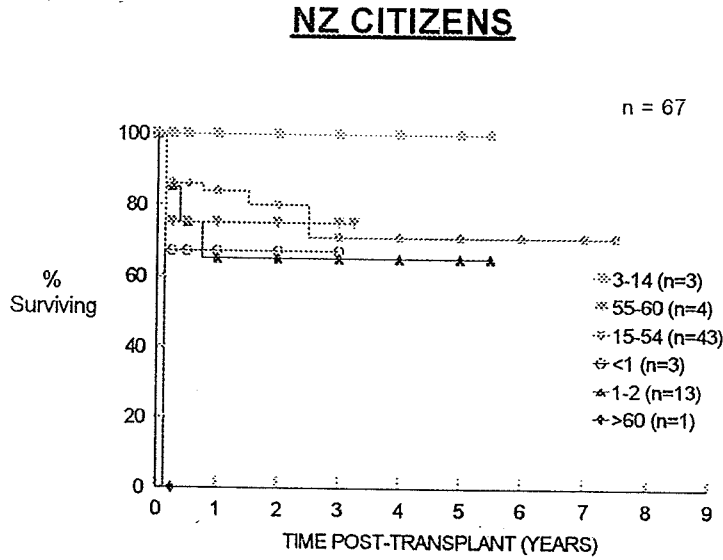
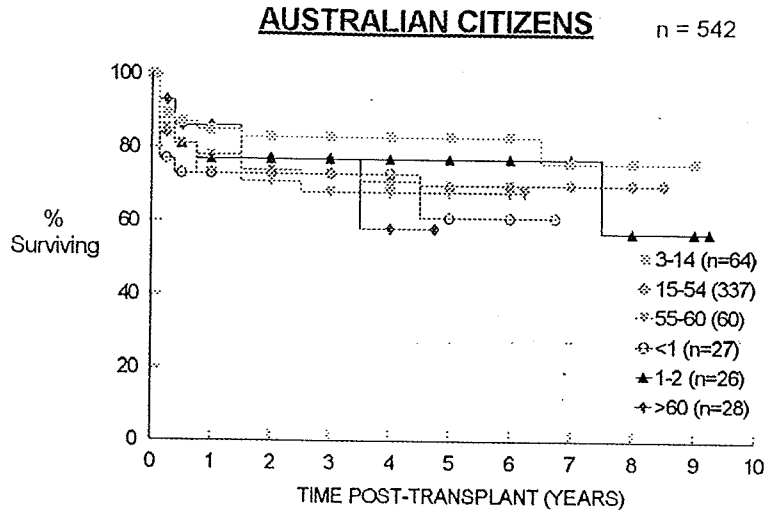


FIGURE 20 PATIENT SURVIVAL BY YEAR OF TRANSPLANT - AUSTRALIA

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)	73	59	55
1987 (n = 27)	70	56	44
1988 (n = 61)	74	71	69
1989 (n = 88)	68	65	61
1990 (n = 75)	81	77	
1991 (n = 109)	89	84	
1992 (n = 128)	82		
1993 (n = 114)	81		

The actuarial six month survival for 68 grafts transplanted in 194 is 88%.

FIGURE 20

PAIENT SURVIVAL - BY YEAR OF Tx
AUSTRALIA

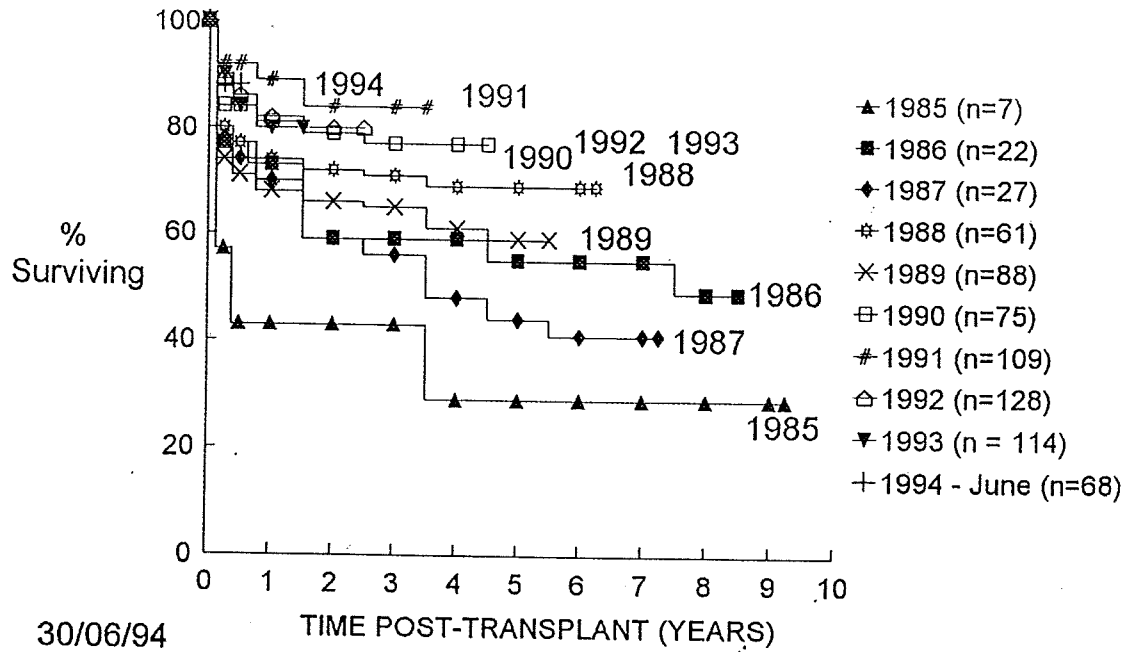


FIGURE 21 PRIMARY GRAFT SURVIVAL
DONOR AGE vs SURVIVAL

Primary grafts from donors in all the age groups from donors aged 0 - 60 survive equivalently between 60 and 70% at 5 years. The numbers of grafts from older donors are too few for analysis though early results are encouraging.

FIGURE 21

PRIMARY GRAFT SURVIVAL
DONOR AGE vs SURVIVAL

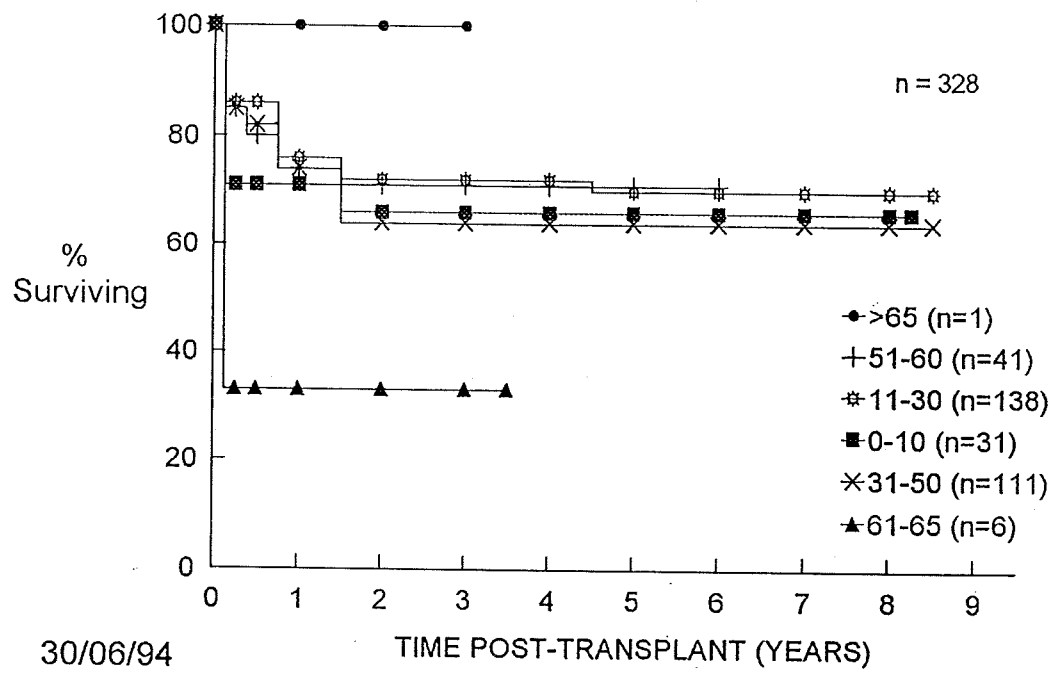


FIGURE. 22 CAUSES OF PATIENT DEATH - ALL PATIENTS

Of the total 699 patients, 174 (25%) have died.

CAUSES OF DEATH

	No	%	
		of deaths	of all patients
Graft Failure	52	30	7
Sepsis	48	28	7
Cerebral catastrophies	27	16	4
Malignancy	20	11	3
Cardiovascular	9	5	1
Operative	6	3	1
Respiratory	6	3	1
Gastrointestinal	1	1	0.1
Miscellaneous	5	3	0.7
TOTALS	174	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

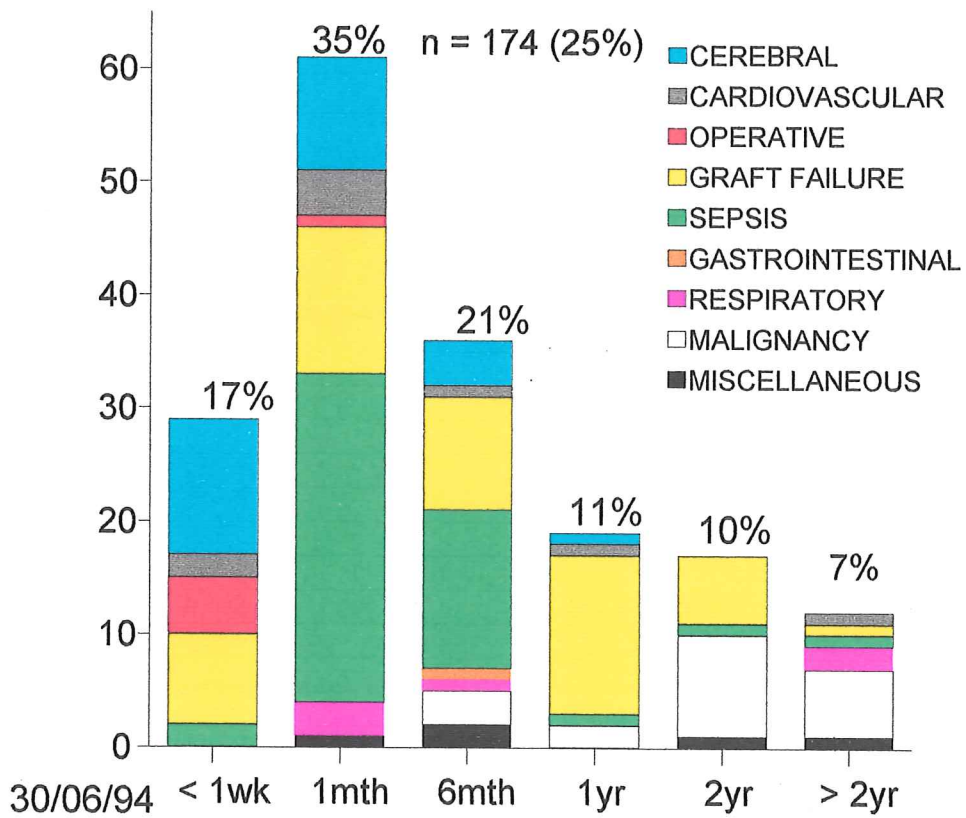


FIGURE 23 CAUSE OF DEATH
AUSTRALIA, NEW ZEALAND, OTHER

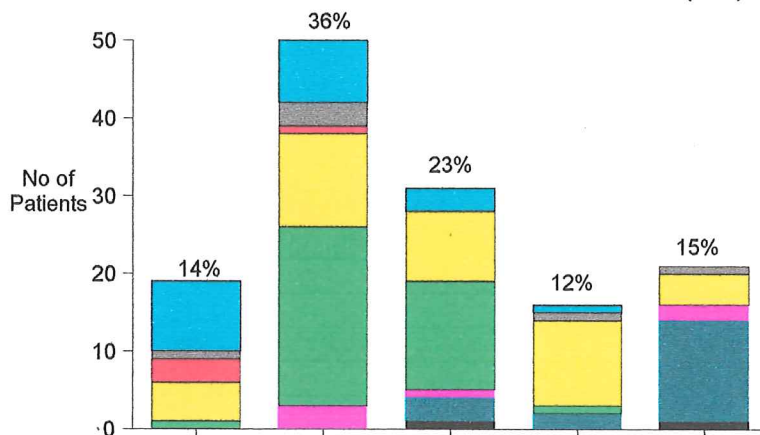
The proportions of patients who have died is the same amongst Australian citizens, New Zealand citizens and Other citizens (about 25%). The numbers of New Zealanders and Other citizens who died are relatively small, making analysis difficult. However, the pattern is generally similar to that for Australia.



FIGURE 23

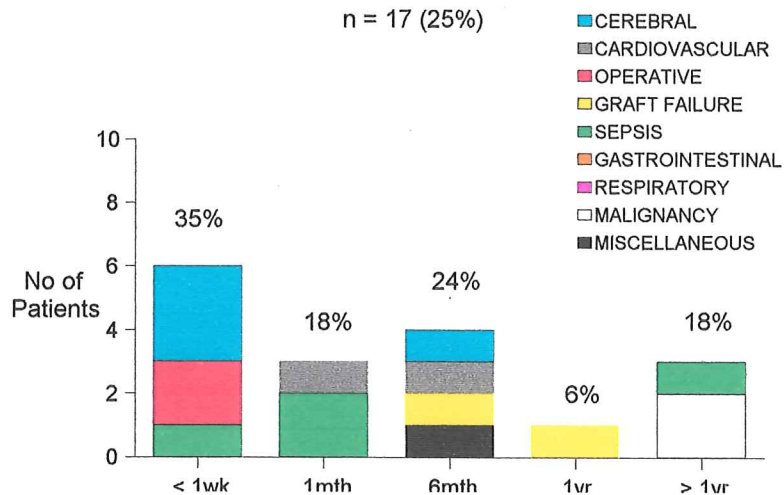
CAUSE OF DEATH
AUSTRALIAN CITIZENS

n = 137 (25%)



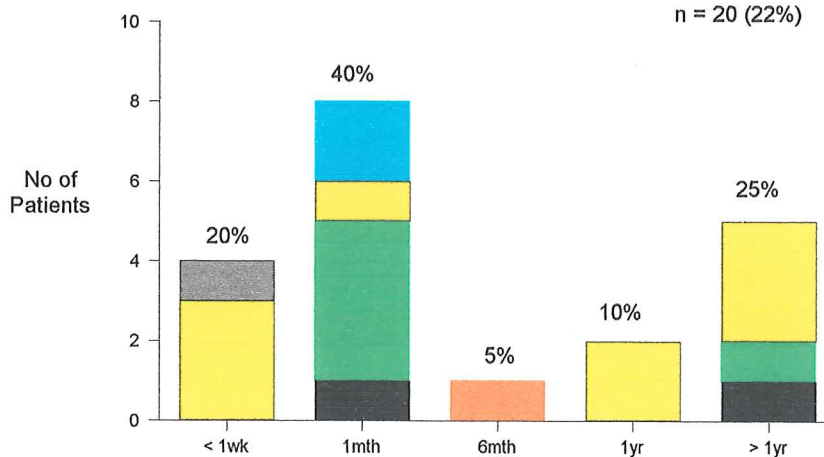
NZ CITIZENS

n = 17 (25%)



OTHER CITIZENS

n = 20 (22%)



30/06/94

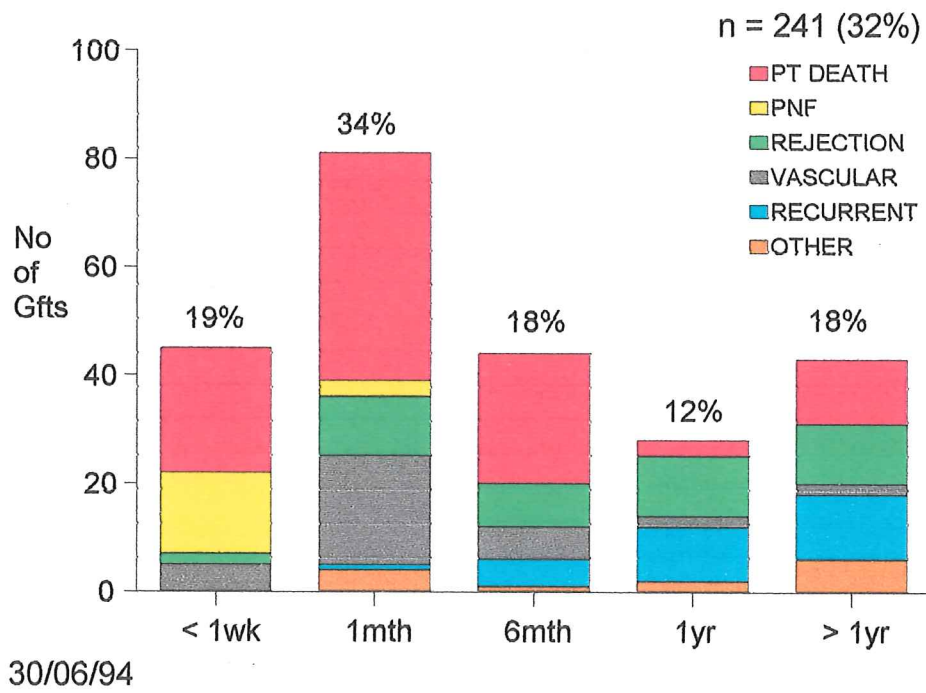
FIGURE 24 CAUSE OF GRAFT FAILURE - ALL GRAFTS

	No	%	
		of graft failures	of all grafts
Patient death	104	43	13
Rejection	43	18	6
Vascular	35	14	5
Primary non function	18	8	2
Recurrent disease	28	12	4
Other	13	5	2
TOTALS	241	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



**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 relatively uncommon 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.

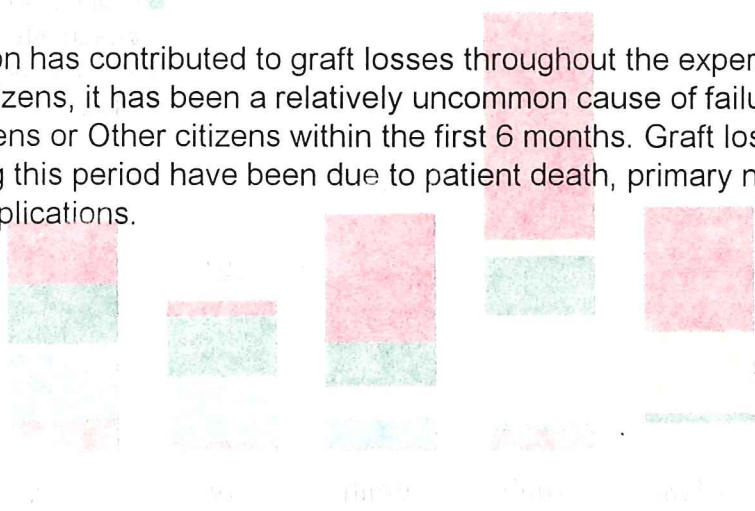
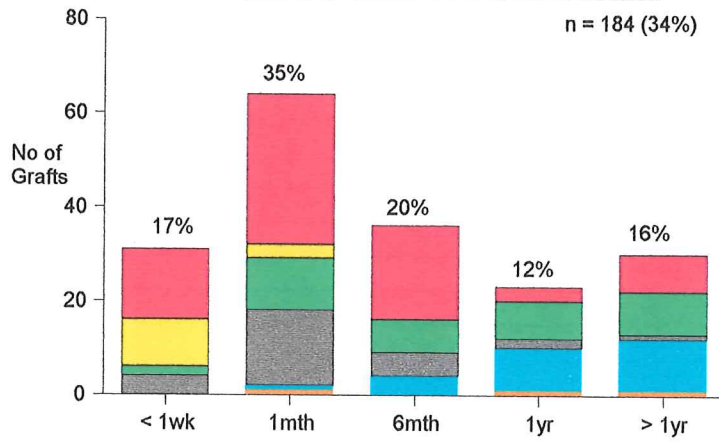


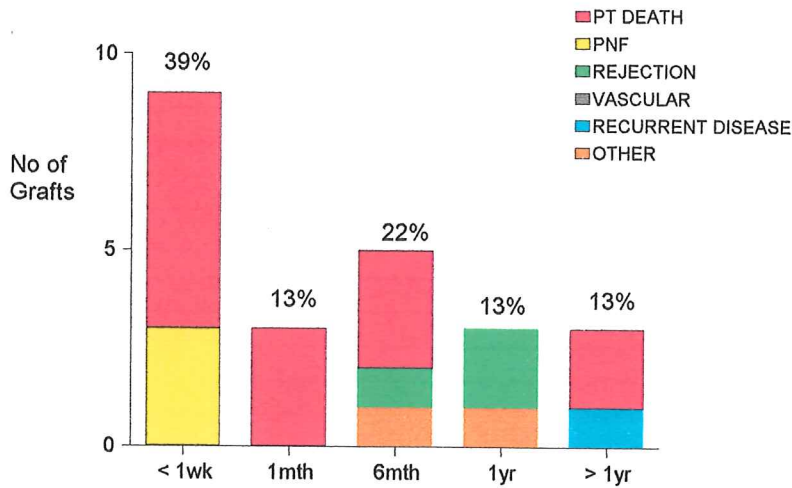
FIGURE 25

**CAUSE OF GRAFT FAILURE
AUSTRALIAN CITIZENS**



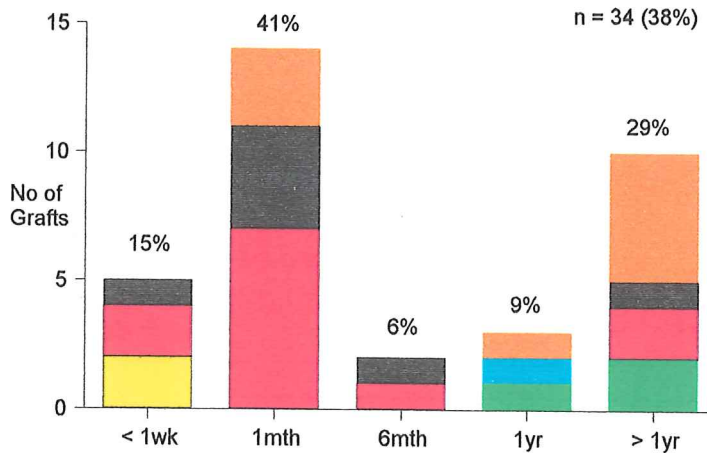
NZ CITIZENS

n = 23 (34%)



OTHER CITIZENS

n = 34 (38%)



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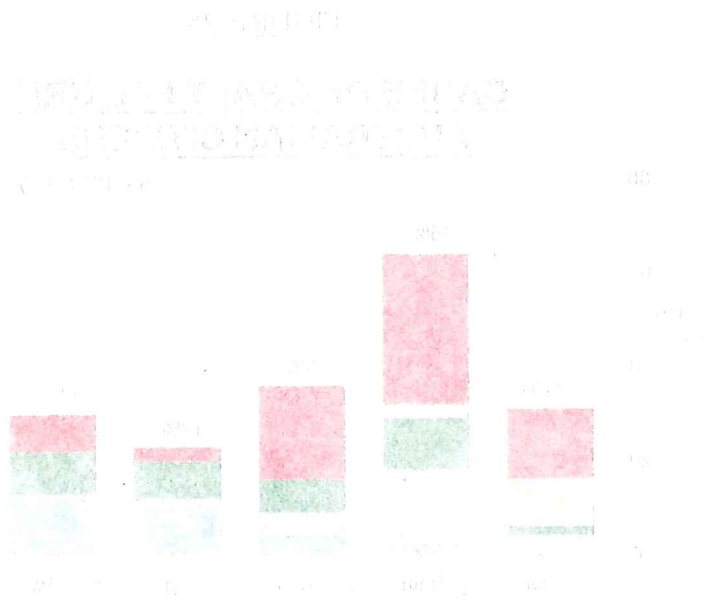


FIGURE 26 DONATION BY YEAR

The information on organ donation was provided by the Australian Transplant Coordinators Association and ANZData.

The total number of liver donors increased steadily between 1990 - 1992, plateaued in 1993 but has increased in the first six months of 1994. There has been a major contribution from New Zealand.



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	38	18	9	8	24	136
1993	26	40	25	13	6	17	128
1994 (June)	15	23	16	5	4	21	84

30/06/94