

# AUSTRALIA & NEW ZEALAND

## LIVER TRANSPLANT REGISTRY



From the Combined Registries  
of the Australian and New Zealand  
Liver Transplant Centres

DATA TO 30-06-2004

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Editors : S.V. Lynch, G.A. Balderson

## STATISTICAL METHODS

Kaplan-Meier survival curves have been produced using SPSS® for Windows™ Release 12.0.1 , SPSS Inc.

## ACKNOWLEDGMENT

The Cancer Registry is maintained at Royal Prince Alfred Hospital, Sydney. Report prepared by Pamela Dilworth, Dr Deborah Verran, Dr Graham Stewart.

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# Preface

We are pleased to present the 16<sup>th</sup> Report of the Australia and New Zealand Liver Transplant Registry (ANZLTR). This report contains data to 30<sup>th</sup> June 2004 and analyses cumulative data since the establishment of the first liver transplantation units in Australia or New Zealand in 1985.

The Registry is a collaborative effort of the liver transplant centres in Australia (Adelaide, Brisbane, Melbourne, Perth, Sydney) and New Zealand (Auckland). The Management Committee has decided that the data from all units be combined and analysed in toto to provide an accurate picture of the outcome of liver transplantation in Australia and New Zealand. With the dramatic decline in the numbers of overseas patients being transplanted in Australia and New Zealand, analysis on the basis of country of origin is not included in this Report.

Donor data have been supplied by the Australia and New Zealand Organ Donor Registry and we thank them for their collaboration.

The Editors would also like to thank the staff of all the Liver Transplant Units who now contribute their data by direct entry into the ANZLTR database. A full list of the Units and their contact information can be found in the appendix. In particular we are grateful to the efforts of Pamela Dilworth, Program Manager for her continuing contribution to the maintenance of the Cancer Registry which is based at the Royal Prince Alfred Hospital, Sydney and who together with Dr Deborah Verran and Dr Graham Stewart prepare the Cancer Report.

The registry now has some financial support and we are grateful to the Commonwealth Department of Health and Aging for their financial contribution.

The Registry is supervised by the Management Committee who are involved in the ongoing supervision of the development of the Registry. The members are listed on the inside cover together with contact information of the Coordinating Centre for comments or requests for further copies of this Report.

*Stephen Lynch  
Glenda Balderson*

# Summary

## Page

5. Between January 1985 and 30<sup>th</sup> June 2004 , 2399 orthotopic liver transplants (OLT) were performed in Australia and New Zealand on 2219 patients, 1794 adult patients (> 15 years) [81%] and 425 children [19%]. The median age of all recipients was 45 years. The ages ranged from 24 days to 70.9 years. There is a significant difference in gender distribution between children (M=45%) and adults (M=61%).
6. There was a decrease in the total number of new patients in 2003 compared with 2000 and 2002 for both children and adults.
7. There has been at trend to increasing age in adult recipients in recent years as reflected by the median age compared with the overall adult median age of 46.6 years.
- 8-9. The contribution of split grafts to the total number of transplants in 2003 was similar to the previous year but in total fewer grafts were transplanted in 2003. In children, reduced size grafts have been used in 312 [66%] of 490 cases 256 reduced grafts (including 9 living donor grafts) and 66 split liver grafts. Of adult patients, 24 have received reduced size grafts (including 1 as auxiliary graft and 2 living donor grafts) and 80 [4%] split liver grafts (including 1 as auxiliary graft). One domino transplant of a whole liver has been performed.
- 10-11. Overall chronic viral hepatitis (CVH) is the most common primary indication for liver transplantation. In children, biliary atresia (BA) is the most common primary disease. In adults chronic viral hepatitis is the primary disease in 27% of recipients. Full details of specific diagnoses categories by age group are listed in the Appendices - Metabolic disorders (Appendix II), Other diseases (Appendix III), Fulminant Hepatic Failure (Appendix IV).
- 12-14. The predicted increase in the proportion of adult patients requiring transplantation for CVH is evident in recent data. In the era 2000-04, 36% of adult patients had a primary diagnosis of CVH, 24% with Hepatitis C, 10% Hepatitis B and 1% both Hepatitis B and C. In 2003 38.5% of new adult patients had a diagnosis of CVH. When patients with either primary or a secondary diagnosis of Hepatitis B ,C or both are included, the overall incidence of CVH in new adult patients in 2003 was 47%.
15. Current 1 year patient survival of all patients is 86%, 78% at 5 years and 69% at 10 years. Children had a significantly better survival rate than adults.
16. Whilst older children had superior survival than babies (< 1 year), older adult recipients (60-65 and >65 years) had poorer outcomes.
- 17-18. Patient survival in 2000-03 cohort shows continued improvement in outcome for the first 3 years compared with earlier cohorts. This is seen in both children and adults.
19. The type of primary graft,(whole , reduced or split liver), had no effect on patient survival in either children or adults.
20. Children weighing < 8 kg at the time of transplant had inferior early survival compared to heavier patients.
21. Adult patients transplanted for biliary atresia had the best long term survival while those whose primary disease was malignancy had a significantly lower survival rate.
22. In children, patient survival was similar for all disease groups. There were no differences in survival between adults and children transplanted for fulminant hepatic failure with 5 year survival of 72%.

# Summary

## Page

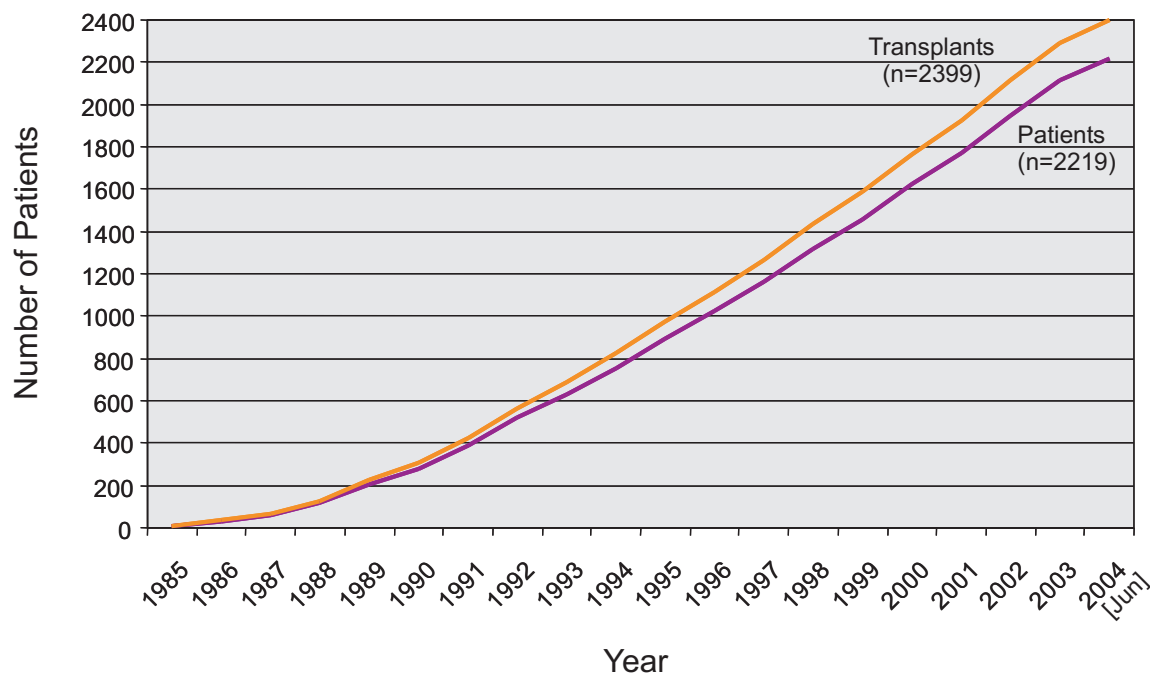
23. Recent cohorts of adult patients with a primary diagnosis of hepatitis B show a significantly improved survival which is not seen in adult patients with hepatitis C as primary disease. Patient transplanted for malignancy continue to have a poor outcome.
24. Twelve patients have received a living related donor graft, 8 children and 3 adults as a primary graft and one child as a second graft.
25. Graft survival was significantly worse in second and third grafts.
26. Both split and other reduced grafts had lower graft survival in the early post-transplant years in both children and adults but with an improving longer term outcome particularly for split grafts.
27. Vascular complications and rejection are the commonest indications for retransplantation.
- 28-29. Overall, sepsis is the most frequent cause of death. Forty-eight percent of all deaths occurred within 6 months of transplant. Early graft failure is due to poor or no early graft function. After 1 year malignancy and graft failure from recurrent disease or chronic rejection cause most deaths. After 5 years cardiovascular disease and de novo malignancy are the most frequent causes.
30. There was a decline in number of cadaveric donors in 2003 resulting in fewer transplants than 2002. Eleven cadaveric grafts were split in 2003.
31. Donor age has significantly increased in recent years. Long term graft survival was significantly lower in grafts from donors aged 61-65y but not those aged over 65y.
32. Preliminary data on waiting list numbers for the first 6 months of collection were available. Ninety-four patients were listed for transplant in Australia and New Zealand at 1/1/04. Ten patients have been delisted and 64 (68%) transplanted by 30/06/04. Since 1/1/04, 113 patients have been listed with 6 subsequently delisted and 48 transplanted. Seventy-nine patients were actively listed at 30/06/04.
- 33-34. Four hundred and nine patients (18%) have had a pre- or post-transplant cancer. Eighty-two (4%) of patients were transplanted for primary malignancy and the type of primary tumour had no influence on survival.
- 35-36. Hepatocellular carcinoma was the most common incidental liver cancer but those with cholangiocarcinoma had significantly poorer survival.
- 37-38. De novo non skin cancers (104) have developed in 101 (5%) patients and 37 have died from this cancer. Cancers of the alimentary tract predominated in adults particularly those aged 45-64y and Non Hodgkins lymphoma was the most common de novo cancer in children.
39. Two hundred and thirty-four (11%) patients have developed 1337 skin cancers; 74 patients had multiple skin cancer types. The cumulative risk of diagnosis on any cancer post transplant is greater than 30% by 15 years.
40. Patients with primary or incidental malignancy had a significantly worse survival than other recipients

# Section 1

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## Demographic Data



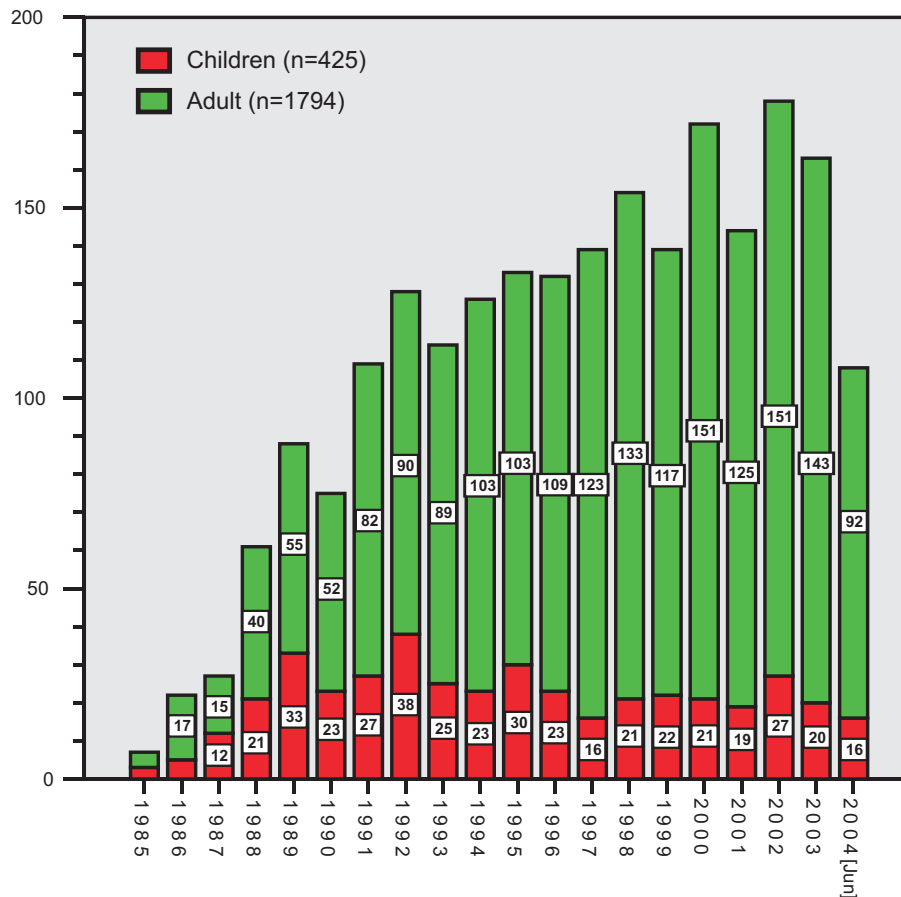


## Summary Statistics - Age and Gender

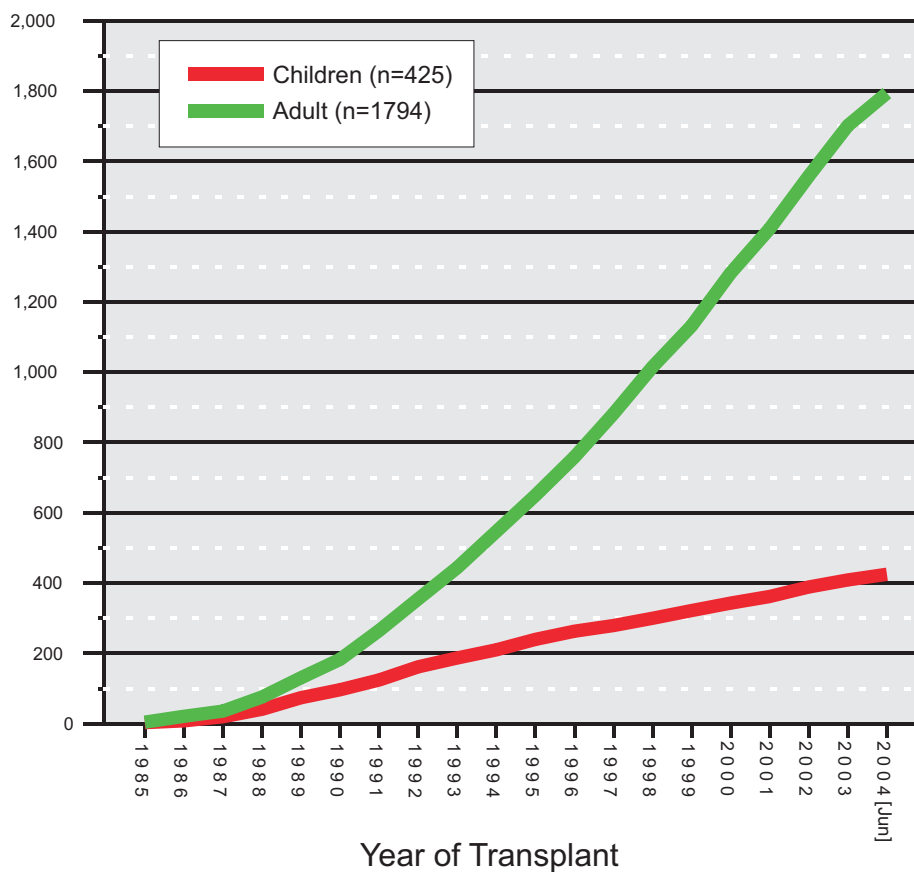
### ALL PATIENTS

	Children	Adults	Total
<b>Patients</b>	425	1794	2219
<b>Age</b>			
<i>Mean ± SD</i>	4.4 ± 4.2	46.6 ± 11.9	38.5 ± 19.8
<i>Median</i>	2.5y	48.3y	45y
<i>Range</i>	24d -14.9y	15.0 - 70.9y	24d - 70.9y
<b>Gender</b>			
<i>Female</i>	233 (55%)	694 (39%)	927 (42%)
<i>Male</i>	192 (45%)	1100 (61%)	1292 (58%)
<b>Surviving</b>	333 (78%)	1339 (75%)	1672 (75%)



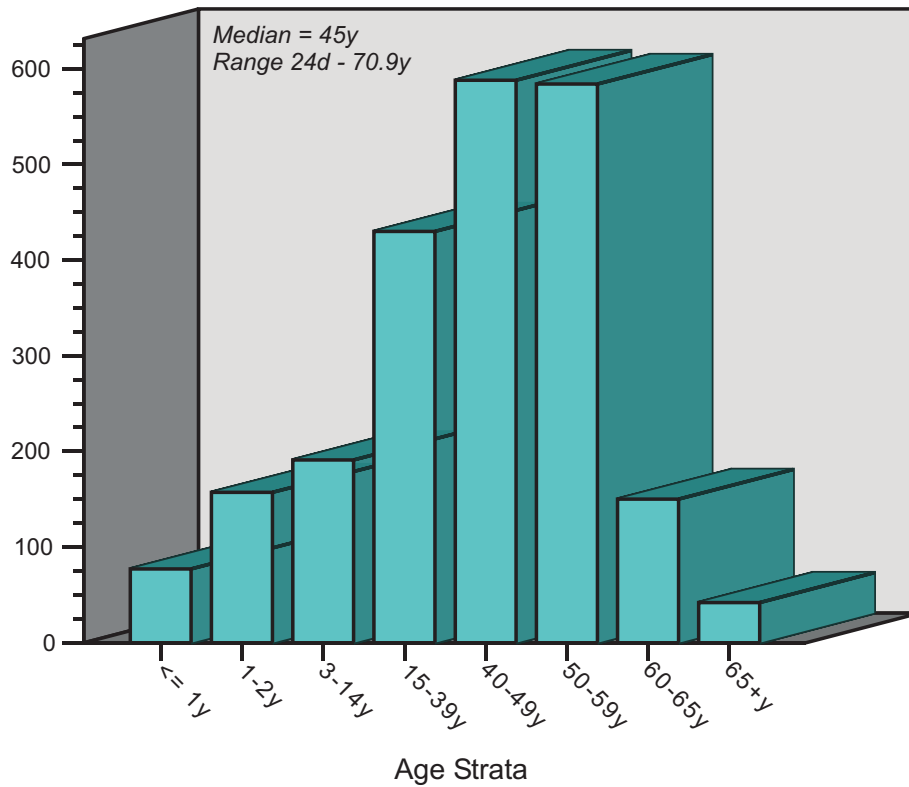


## Cumulative Number of New Patients

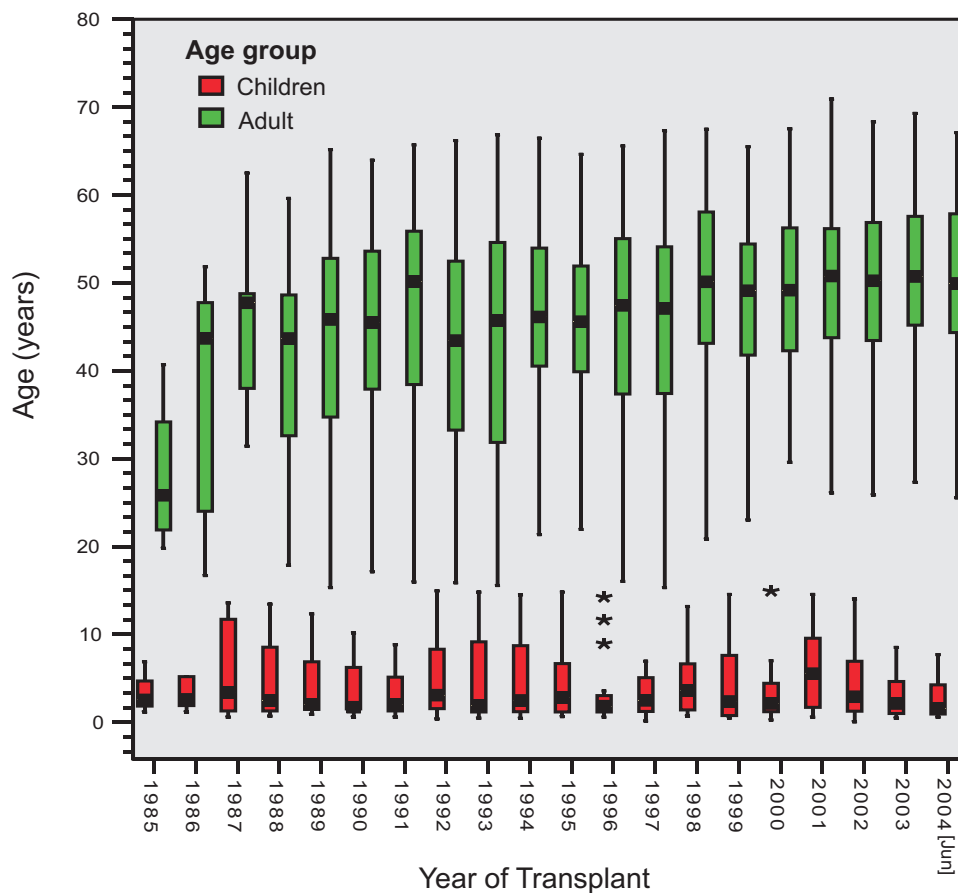


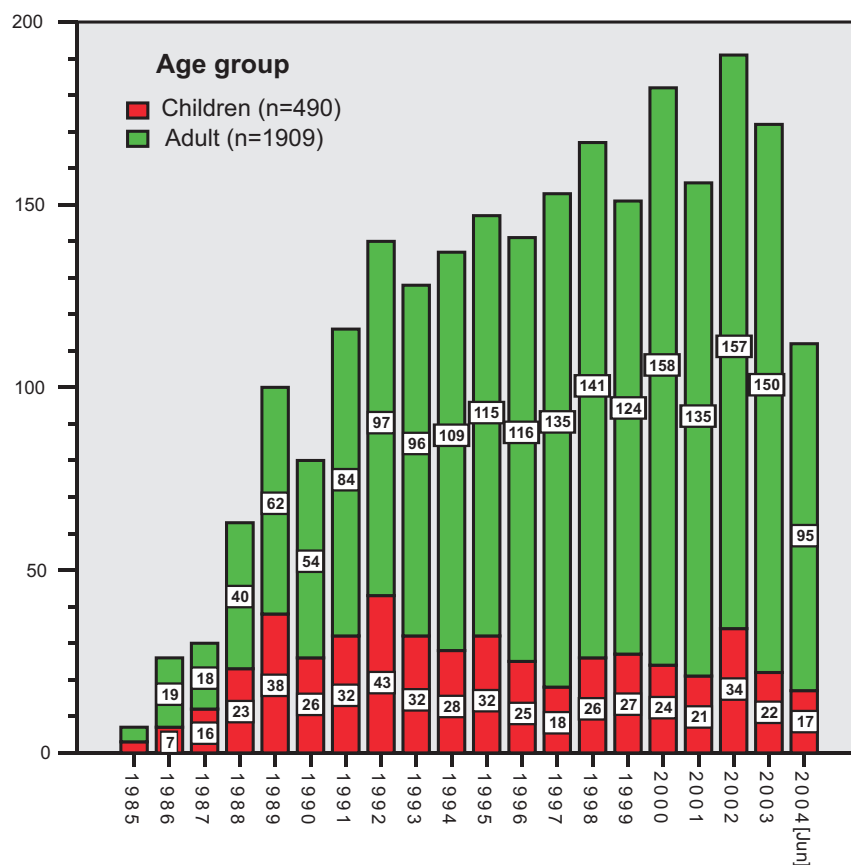
# Number of Recipients By Age at Primary Transplant

N=2219

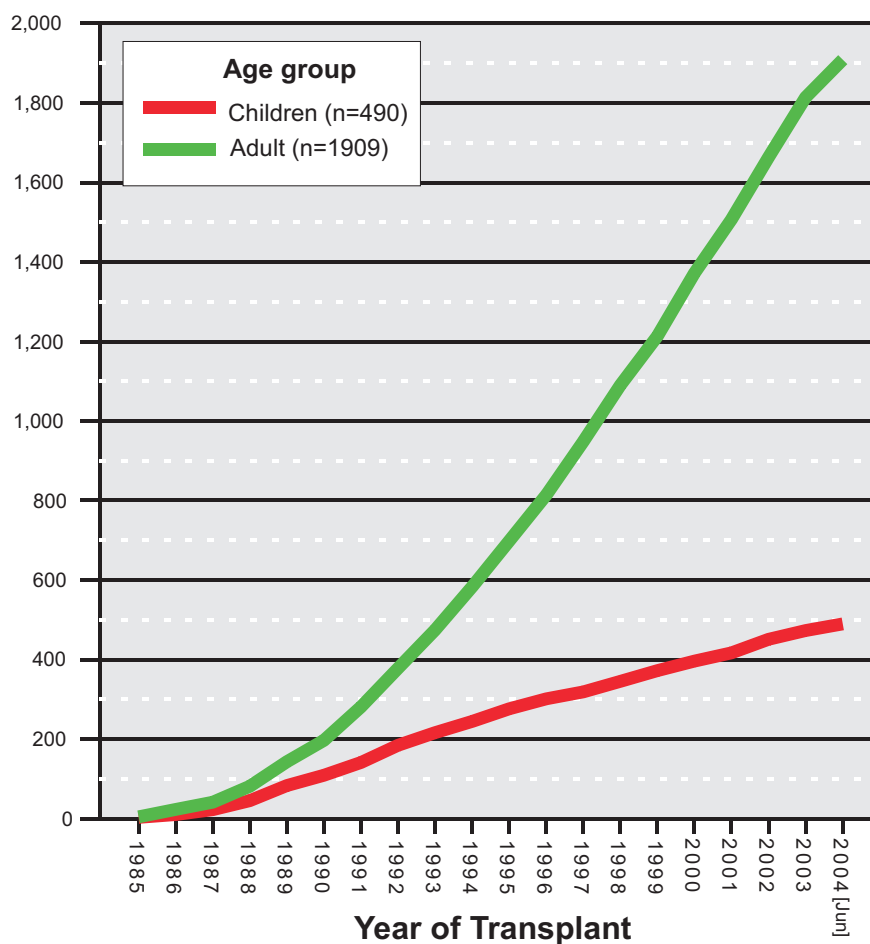


## Age at Primary Transplant by Year

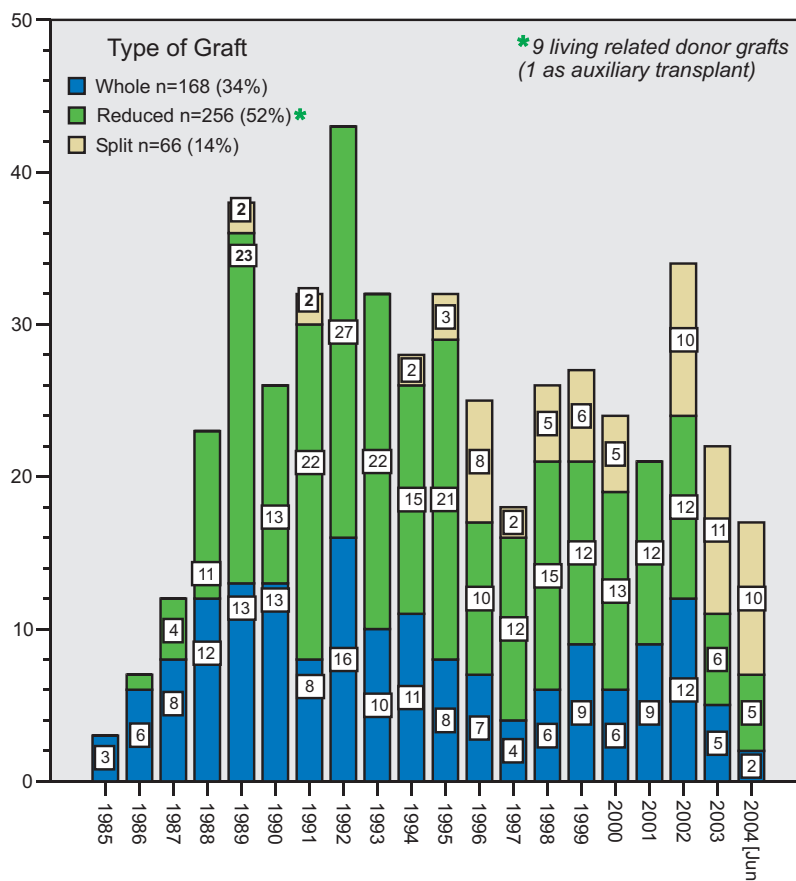




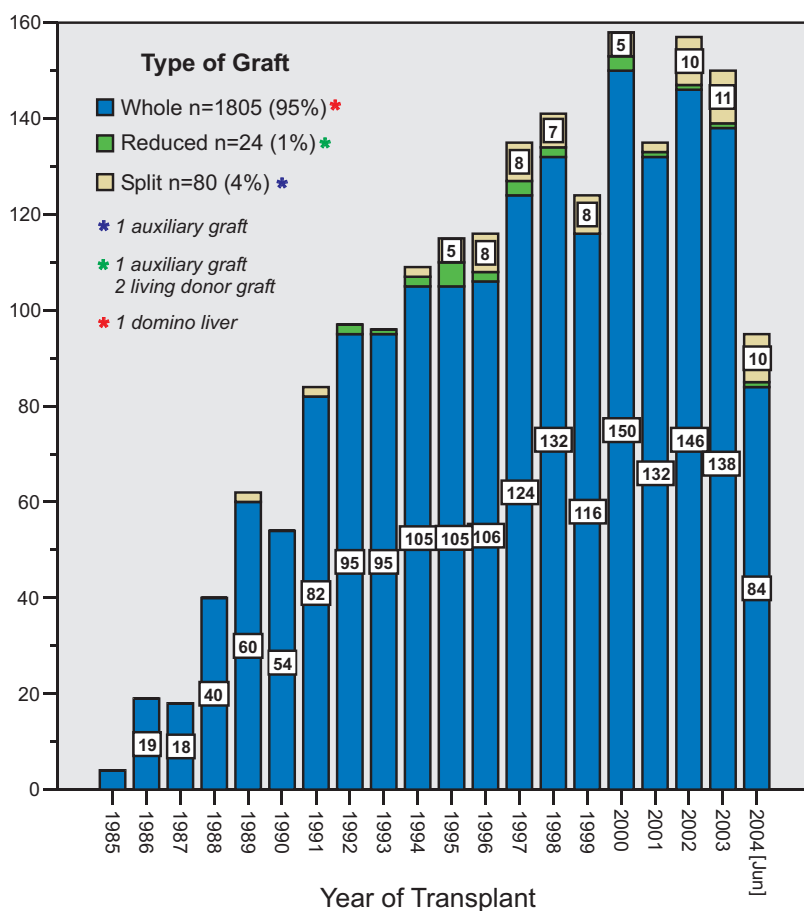
## Cumulative Number of Transplants



# Type of Graft by Year Split vs Reduced vs Whole



**Children (n = 490 )**



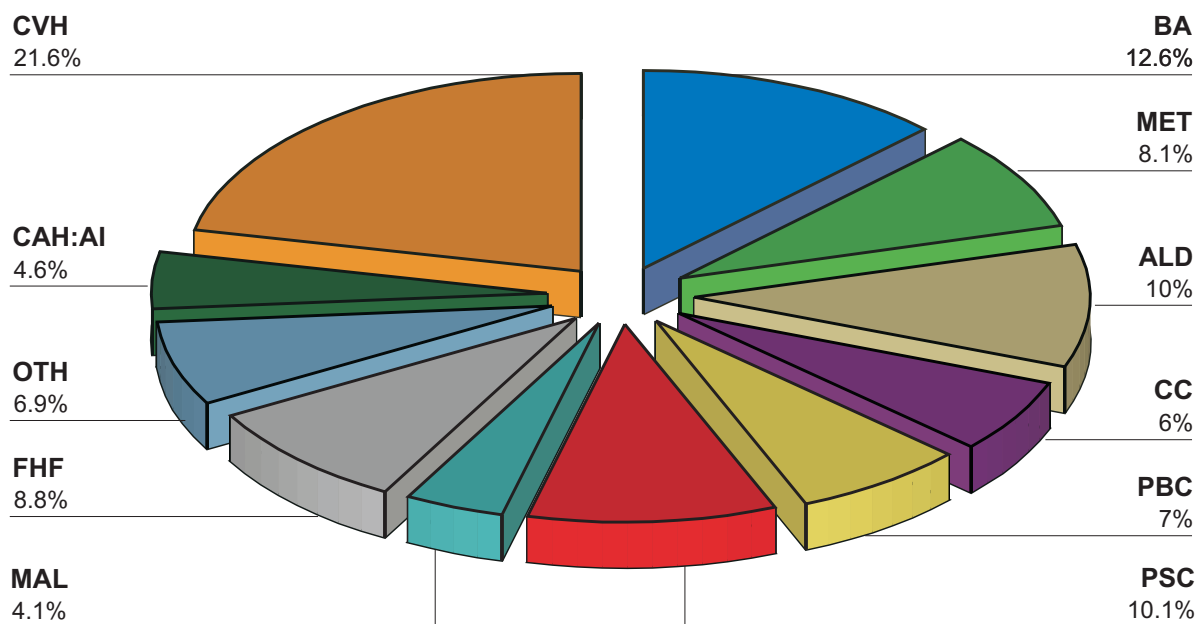
**Adults (n = 1909)**

# Section 2

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## Primary Diagnosis



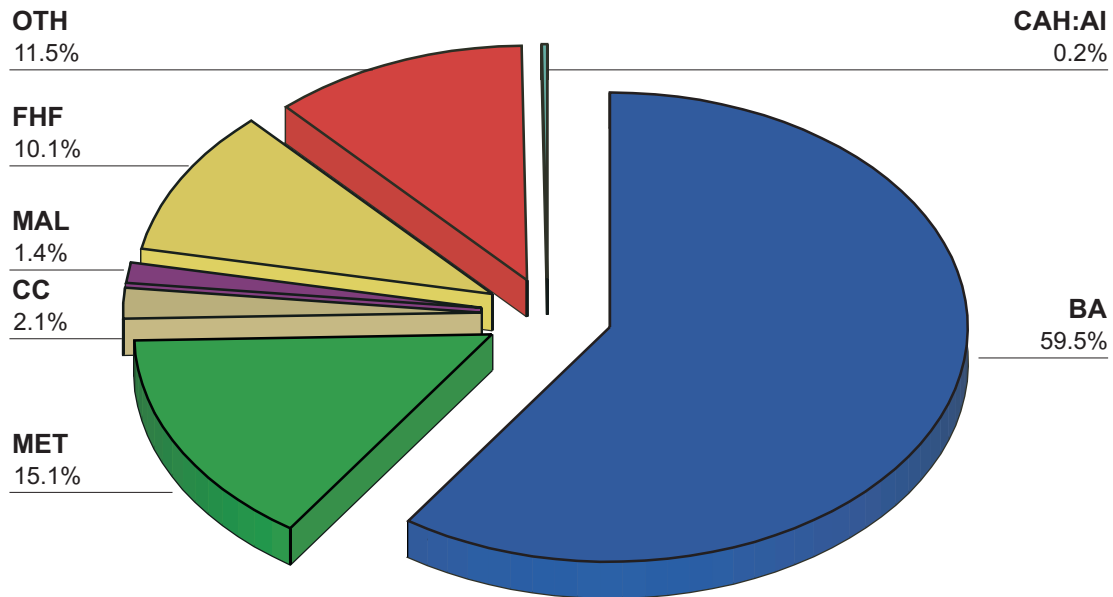


## Diagnosis Group

BA	- Biliary atresia
MET	- Metabolic diseases
ALD	- Alcoholic cirrhosis
CC	- Cryptogenic cirrhosis
PBC	- Primary biliary cirrhosis
PSC	- Primary sclerosing cholangitis
MAL	- Malignancy
FHF	- Fulminant hepatic failure
OTH	- Other diseases
CAH : AI	- Chronic active hepatitis [autoimmune]
CVH	- Chronic viral hepatitis

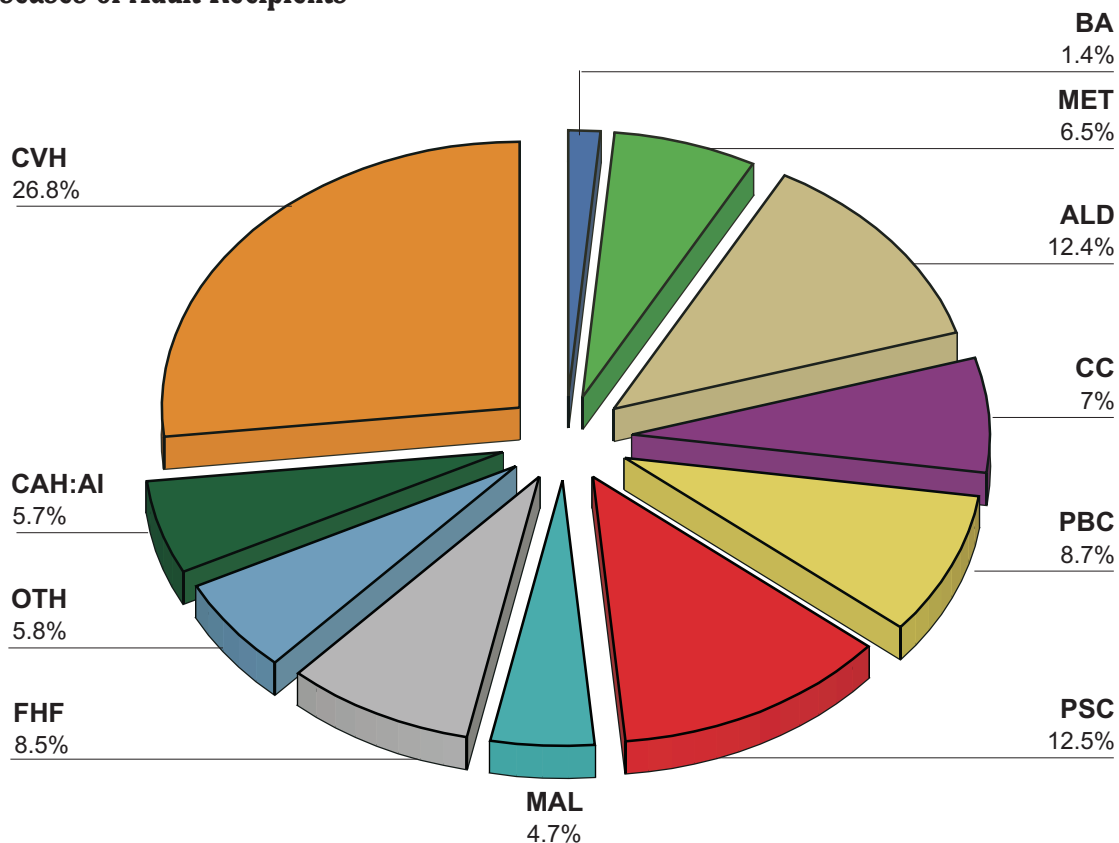
## Primary Diseases of Children

n = 425

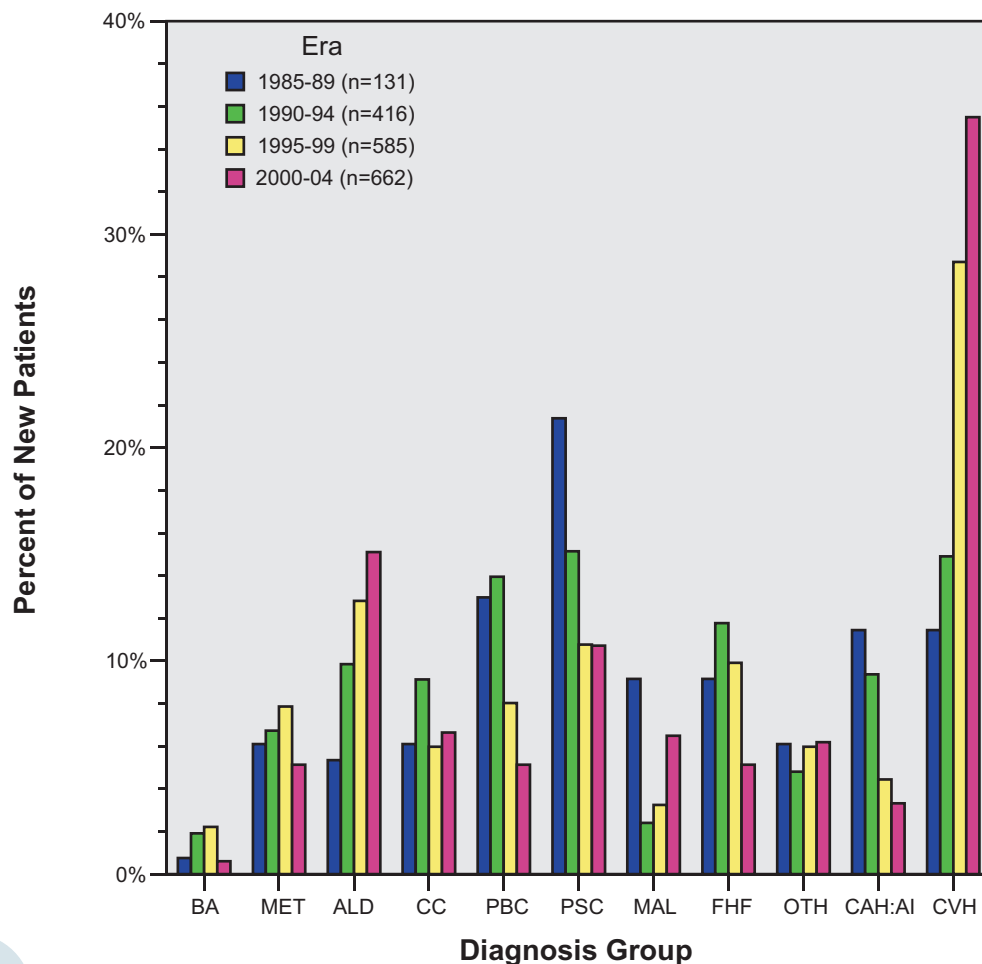
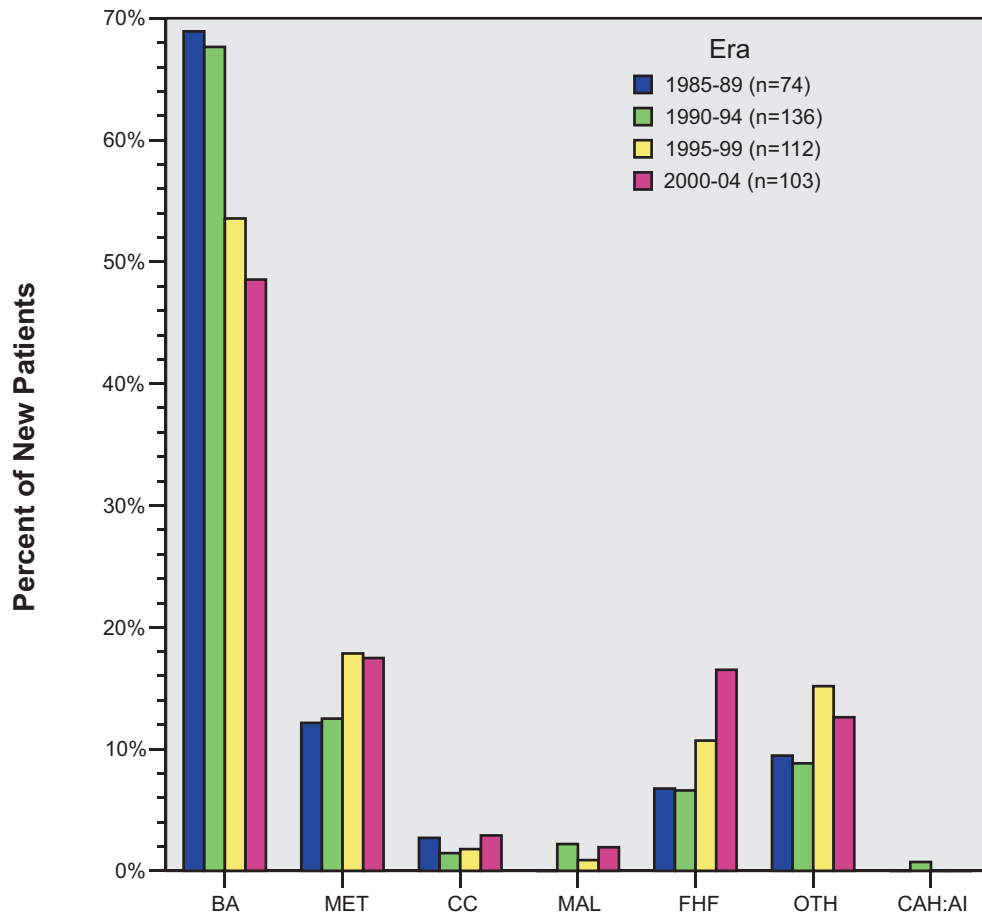


## Primary Diseases of Adult Recipients

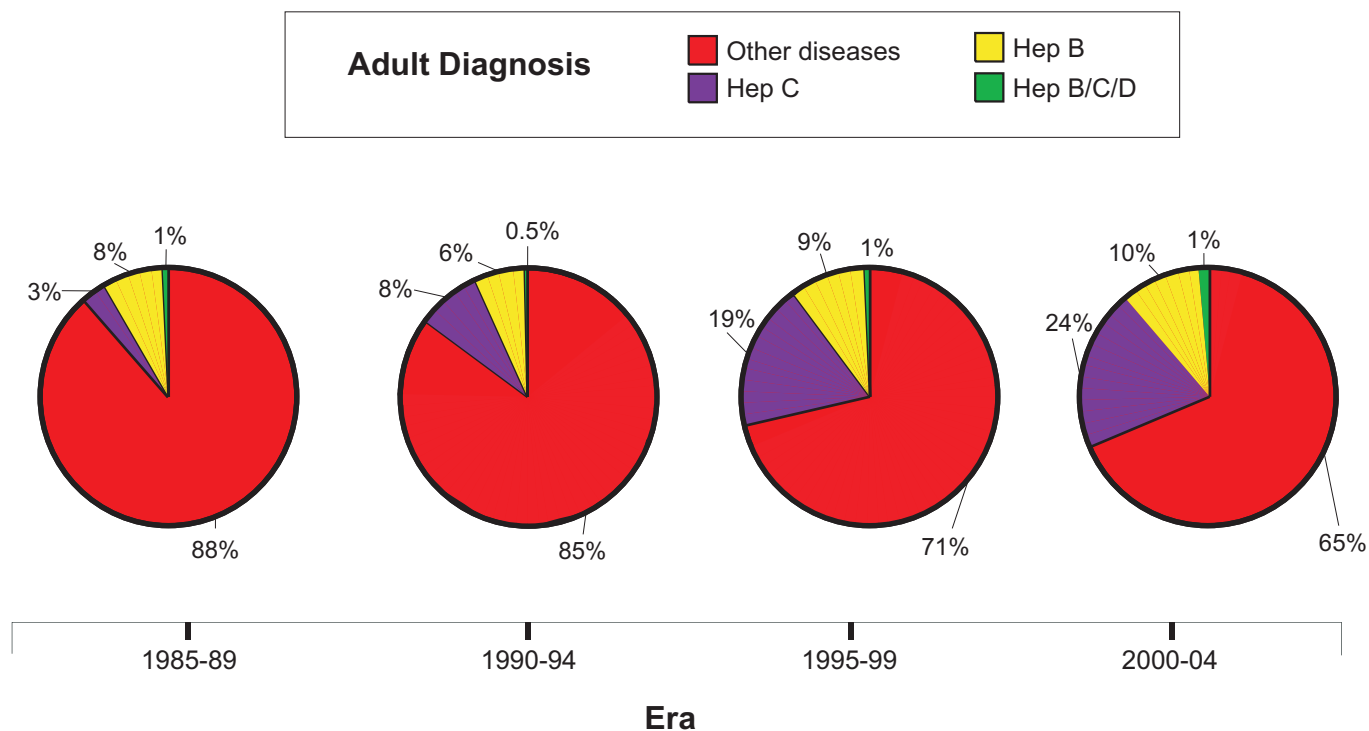
n = 1794



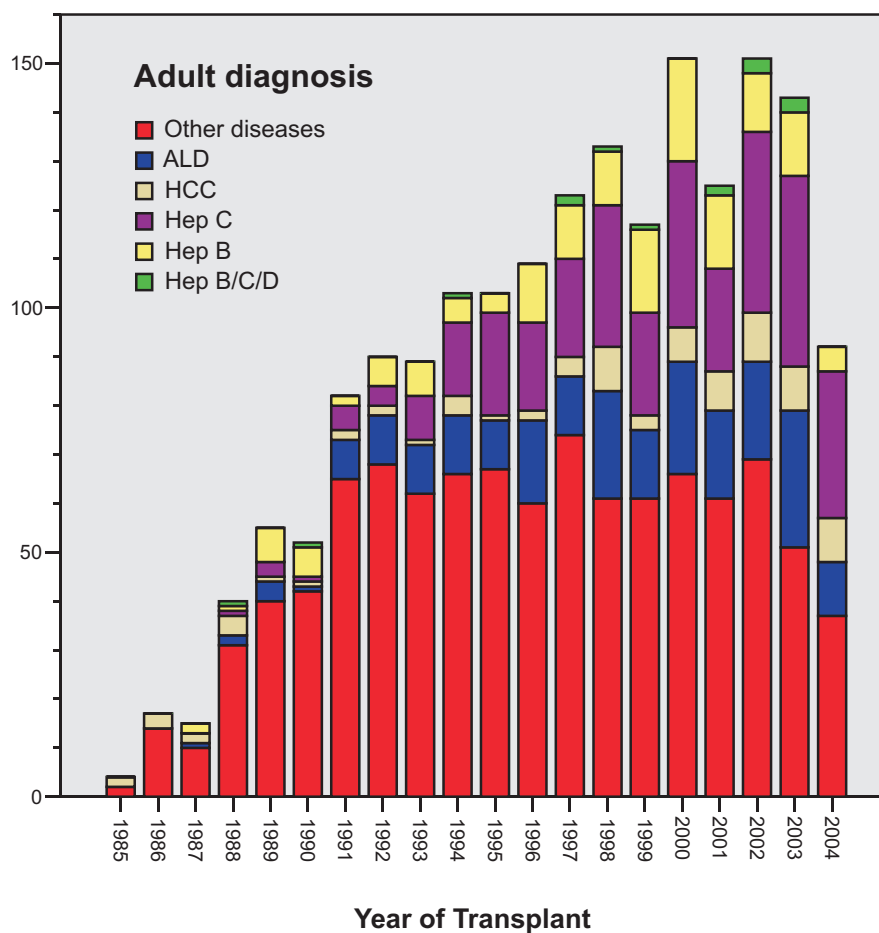
Diagnosis Group			
BA	- Biliary atresia	PSC	- Primary sclerosing cholangitis
MET	- Metabolic diseases	MAL	- Malignancy
ALD	- Alcoholic cirrhosis	FHF	- Fulminant hepatic failure
CC	- Cryptogenic cirrhosis	OTH	- Other diseases
PBC	- Primary biliary cirrhosis	CAH : AI	- Chronic active hepatitis [autoimmune]
		CVH	- Chronic viral hepatitis





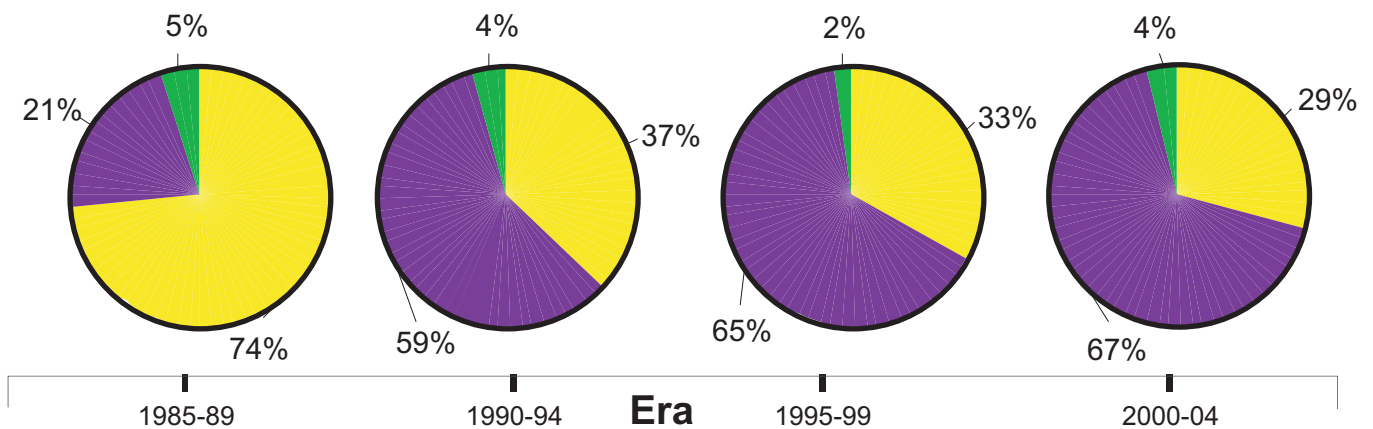


## Adult Primary Diagnosis by Year

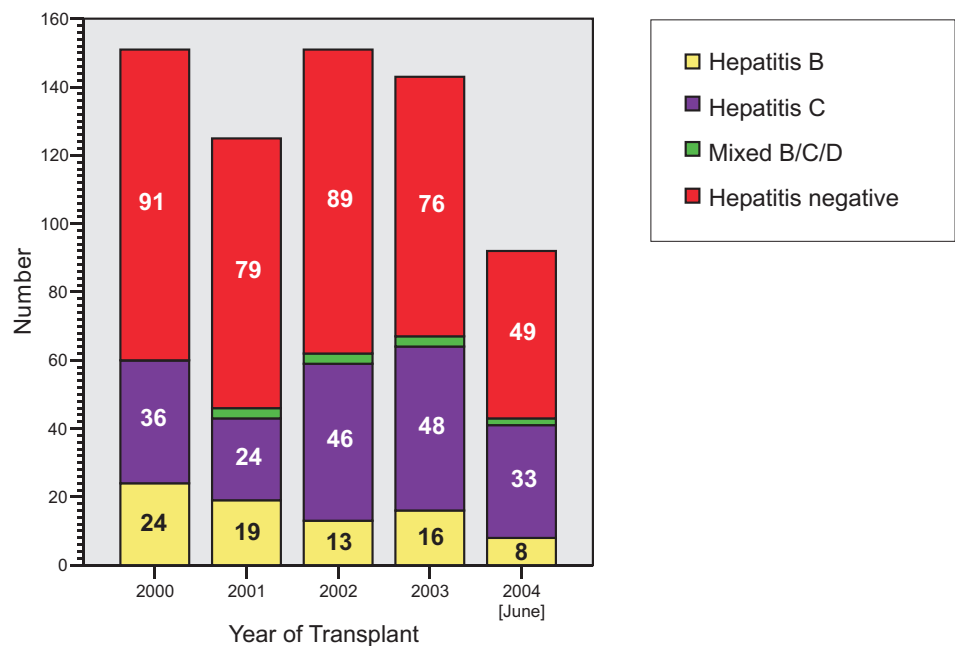


		n =	Secondary / Tertiary diagnosis				
			Hepatitis C	Hepatitis B	Hepatitis B,C	HCC	ALD
Primary Diagnosis	Hepatitis C	308		1		56	62
	Hepatitis B	153				45	4
	Hepatitis BD/BC/BCD	19				2	2
	HCC + cirrhosis	71	34	25	2		3
	ALD	223	9			23	
	Other	1020	10	1		24	12
	<b>TOTAL</b>	<b>1794</b>					

## Type of Chronic Viral Hepatitis in Adult Patients



## Hepatitis diagnosis

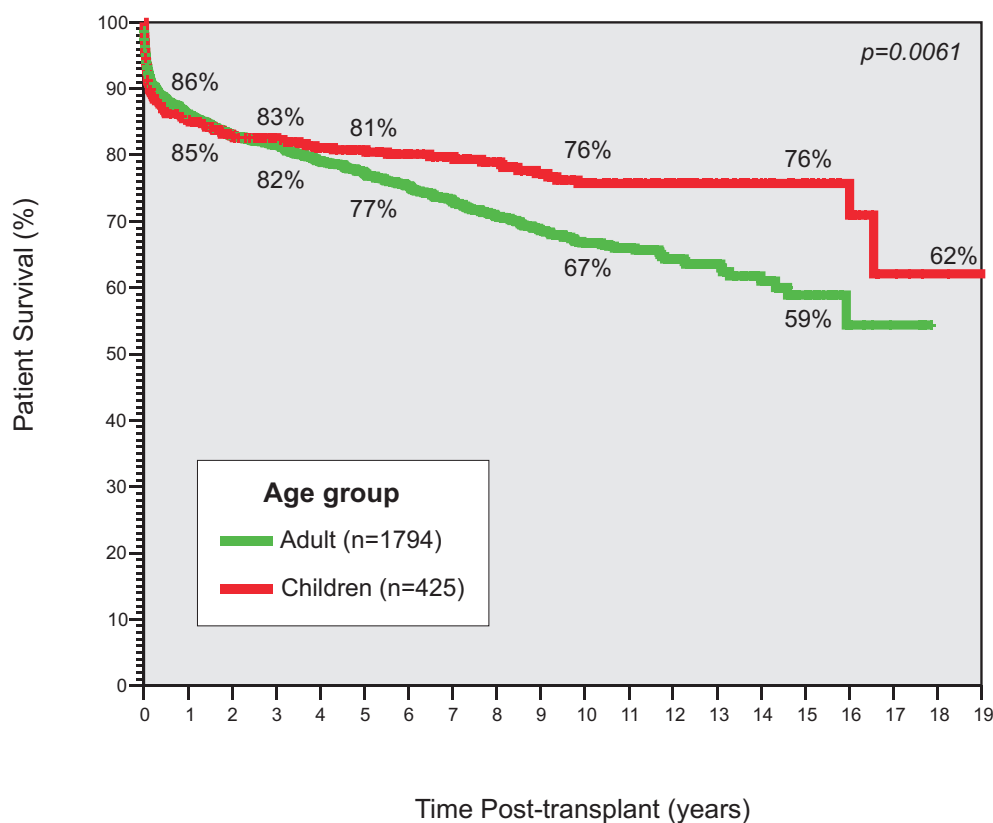
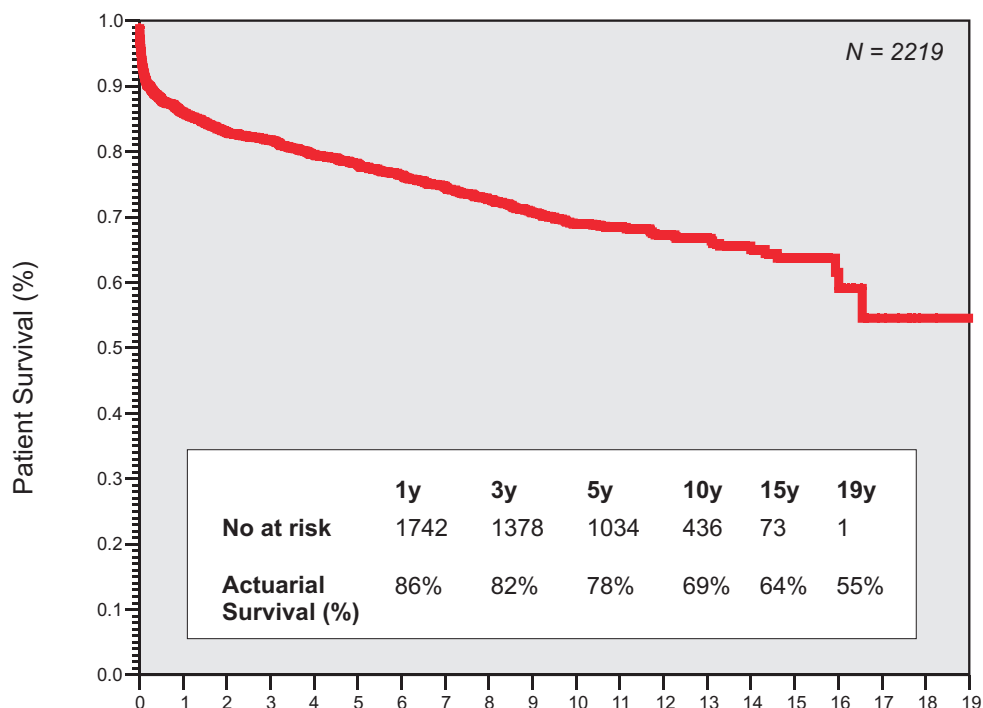


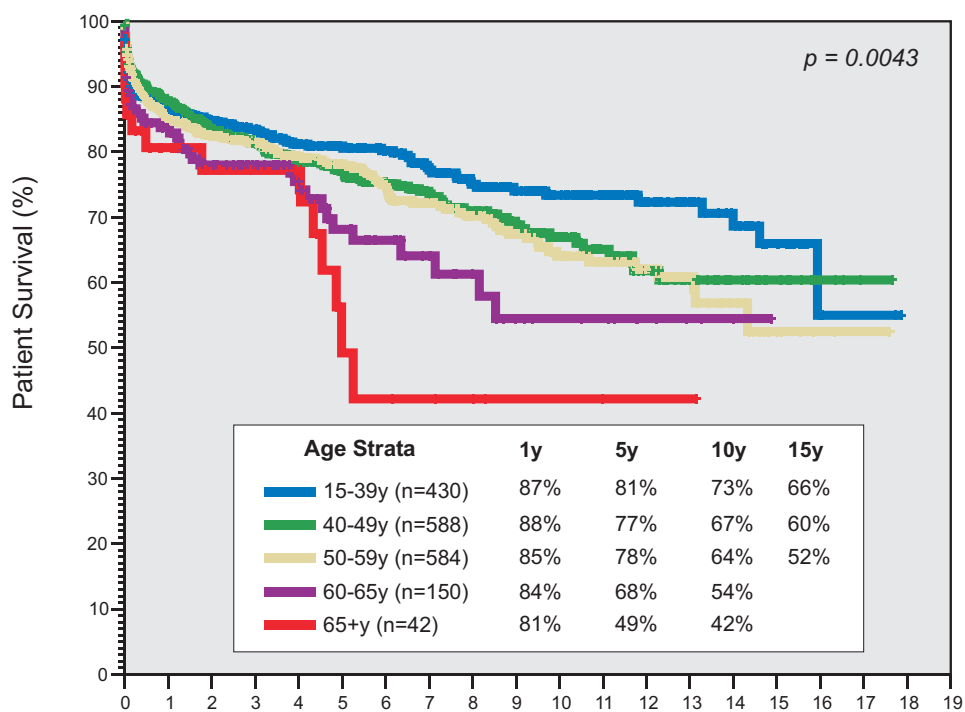
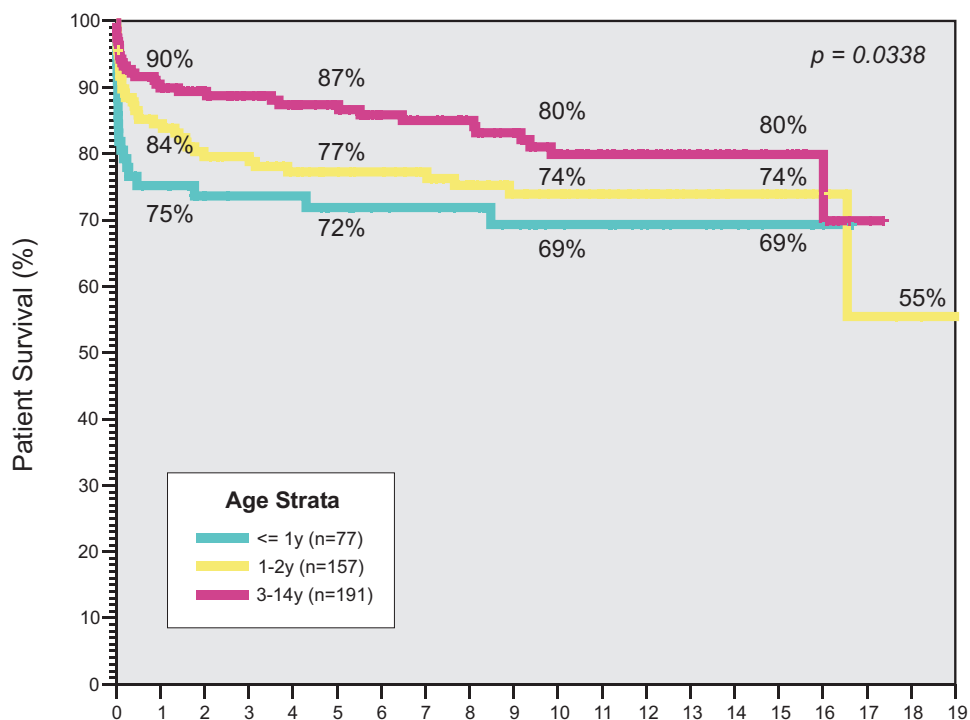
# Section 3

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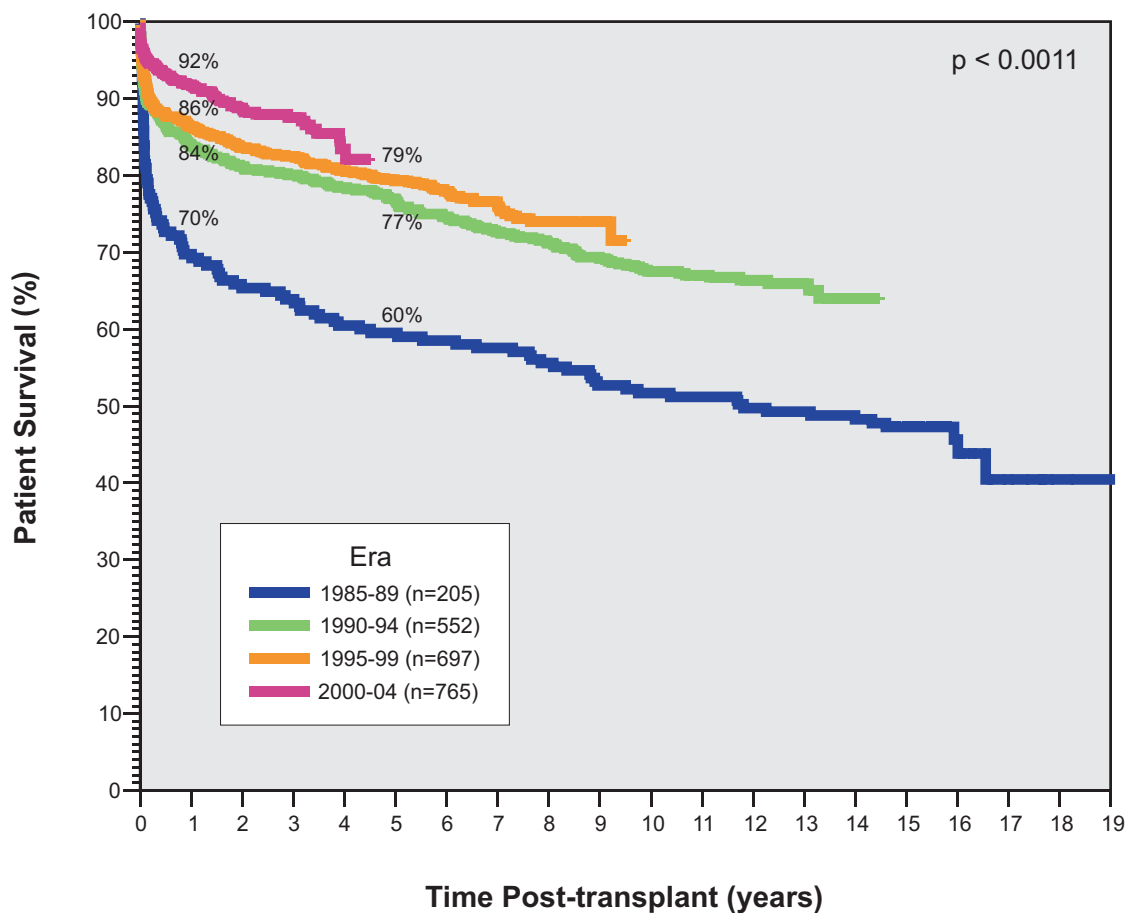
## Patient Survival

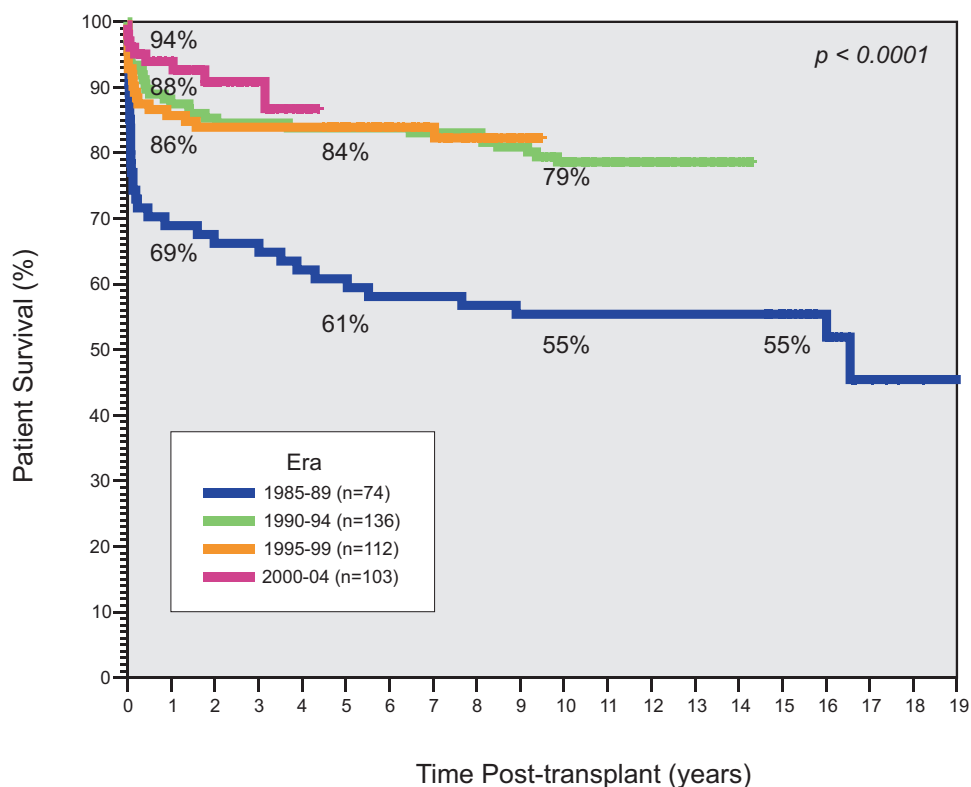




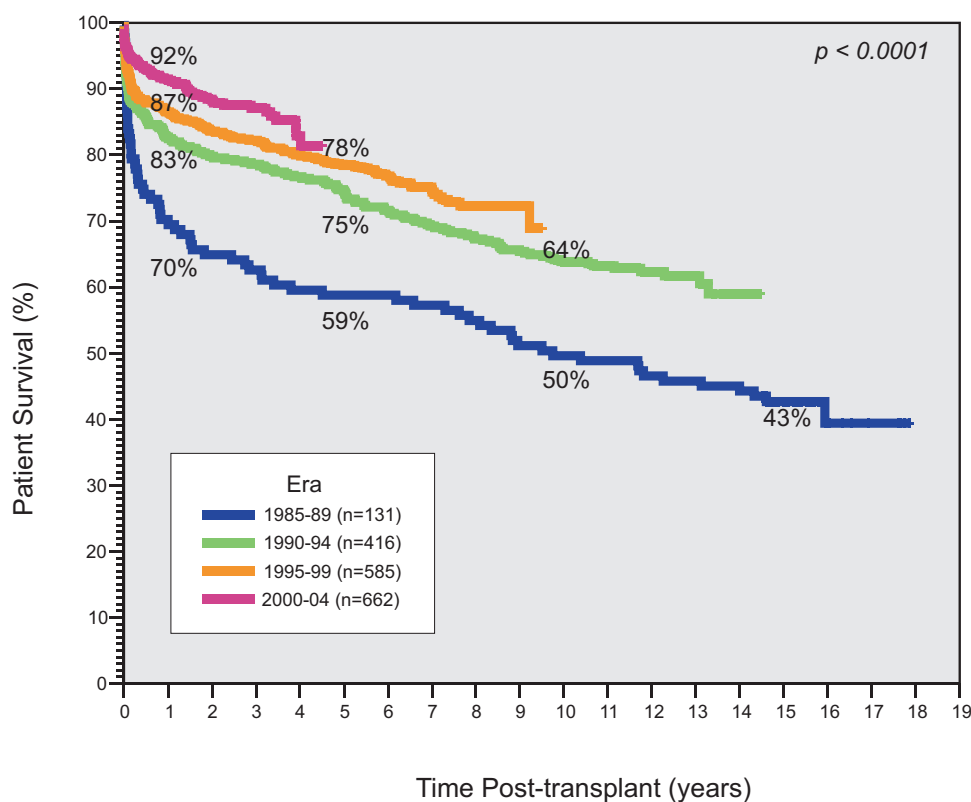


Time Post-transplant (years)

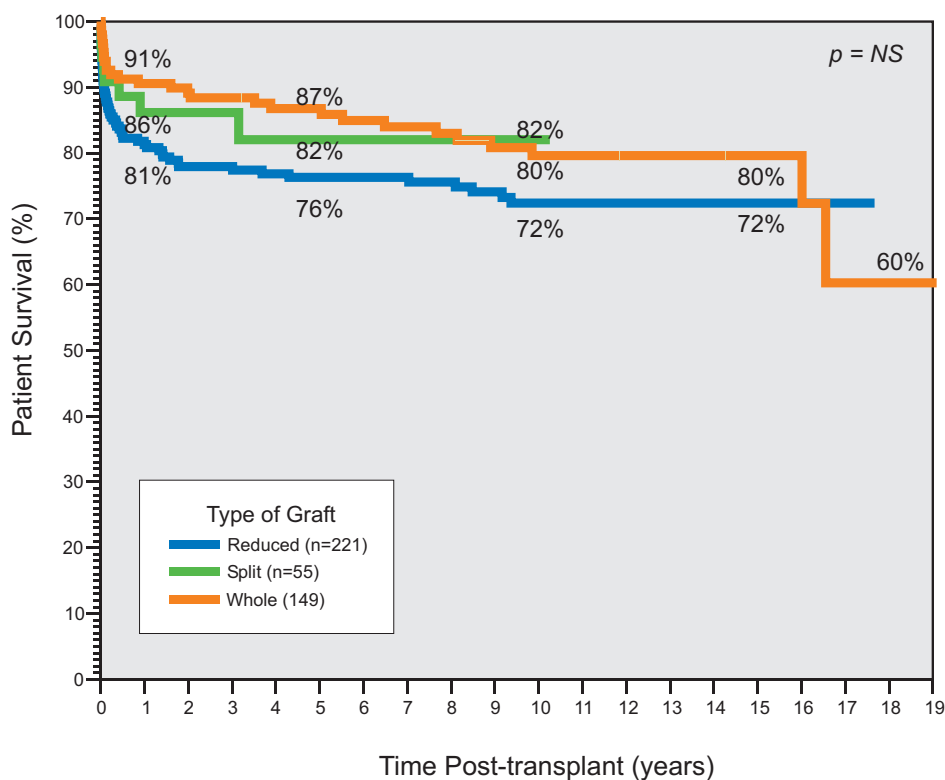




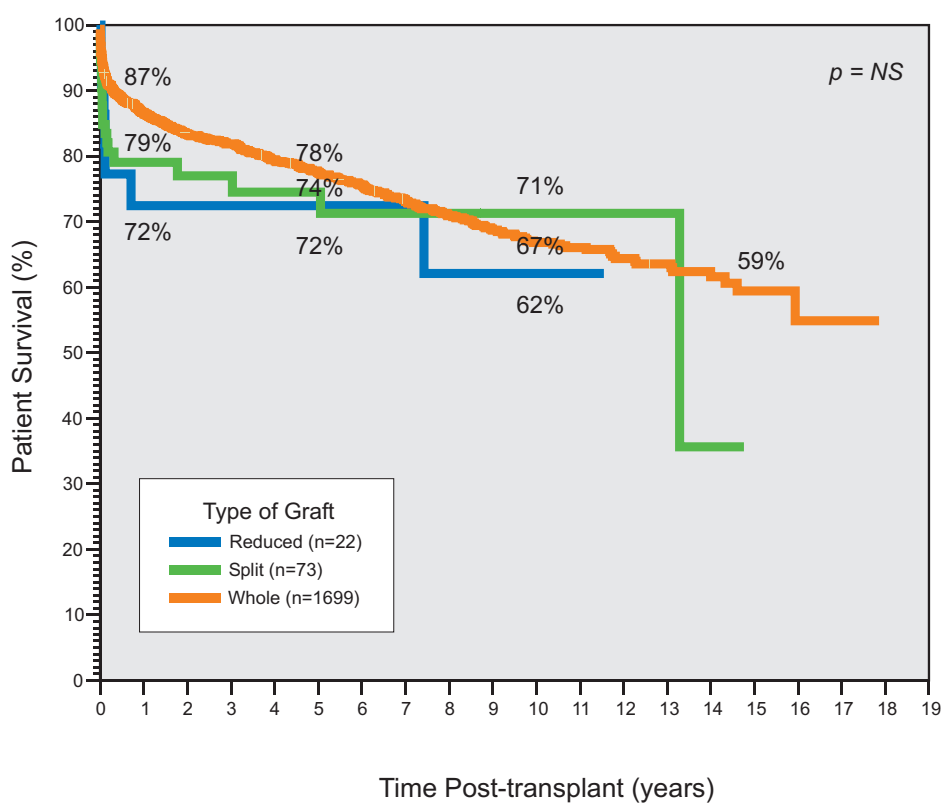
## Patient Survival - Adults



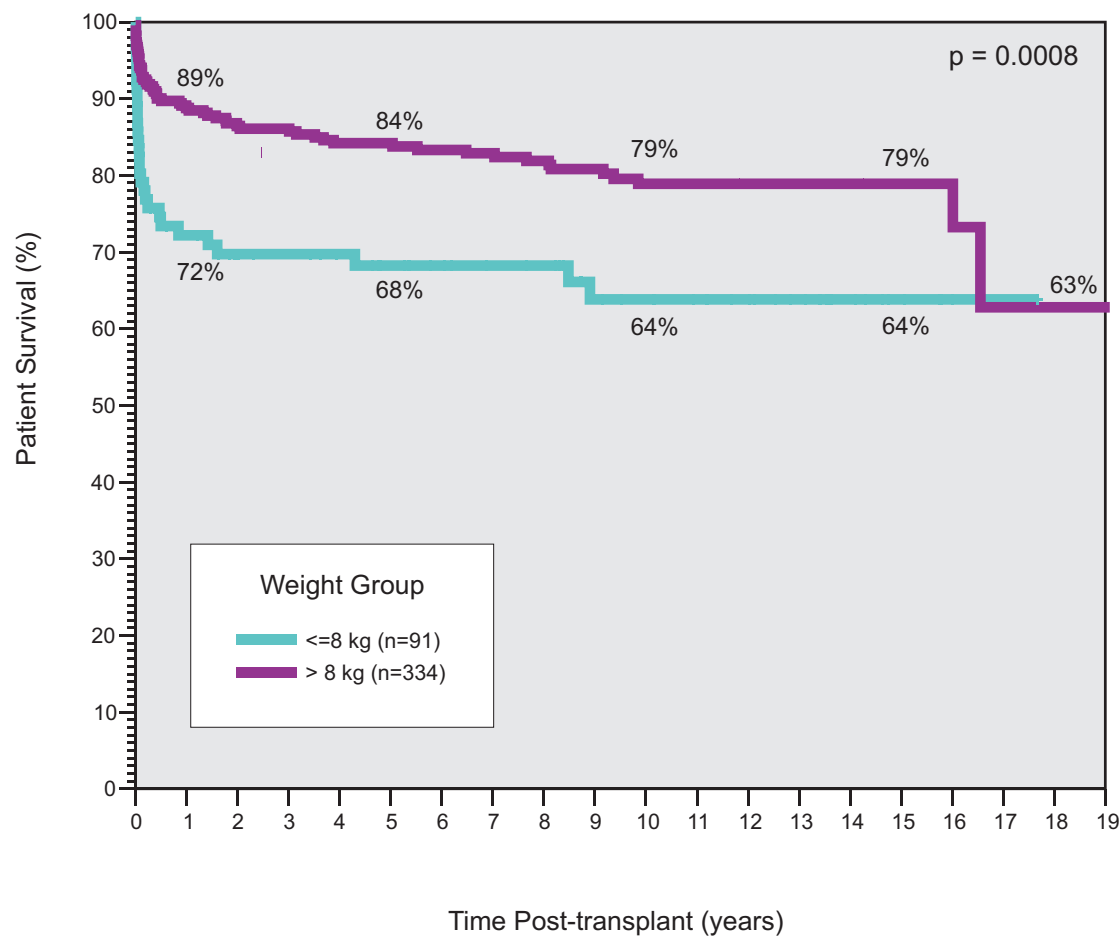
## Children - n = 425



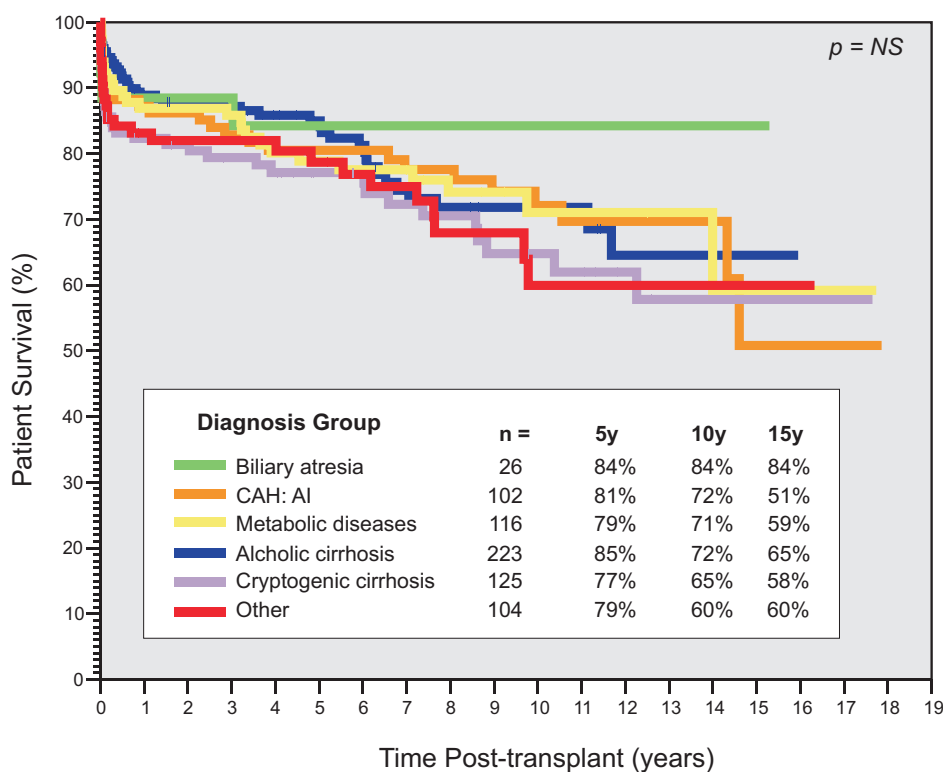
## Adults - n = 1794



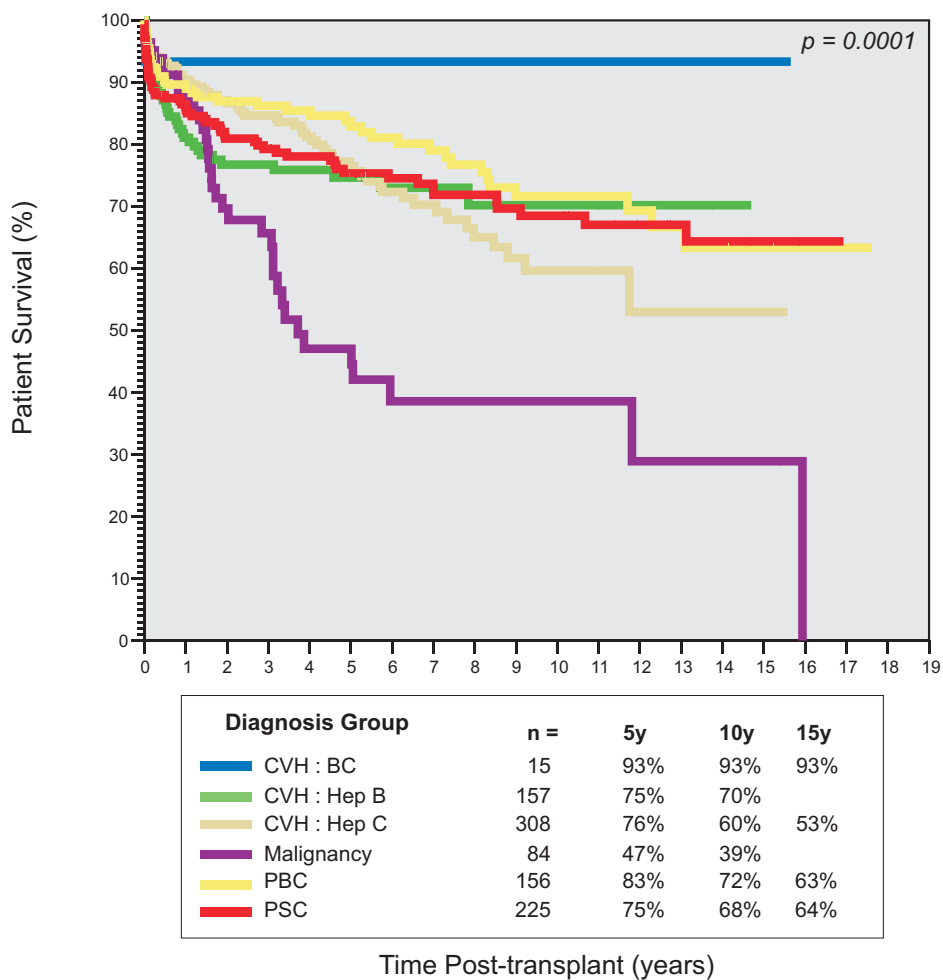




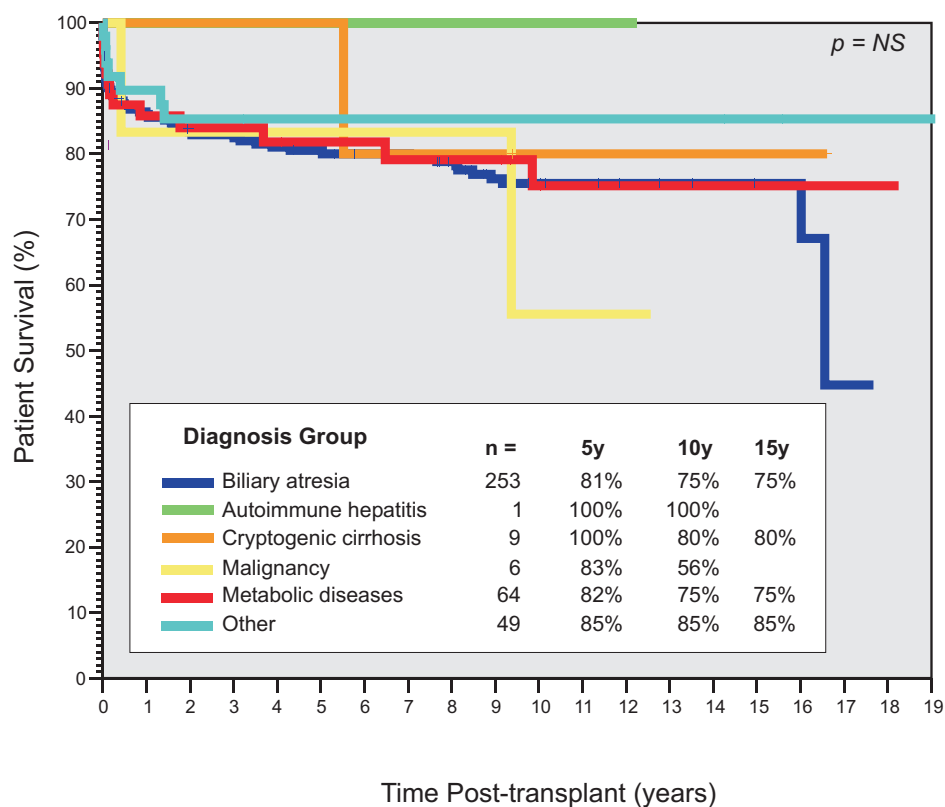
## (1) Adults [excluding FHF] - n=696



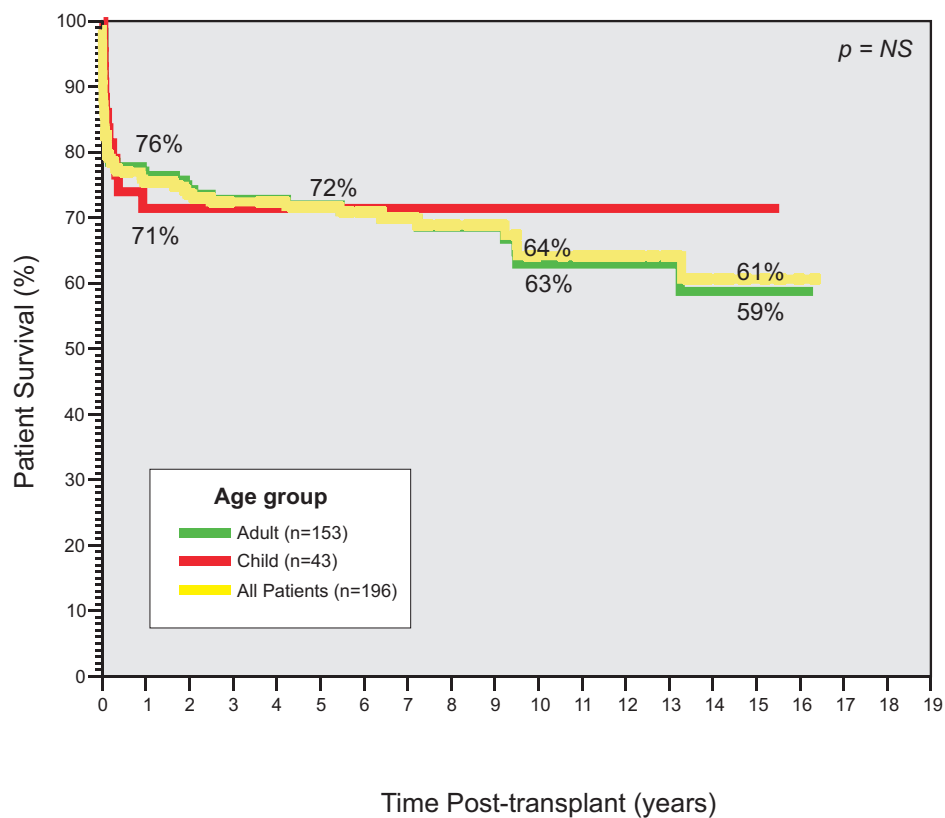
## (2) Adults [excluding FHF] - n=945

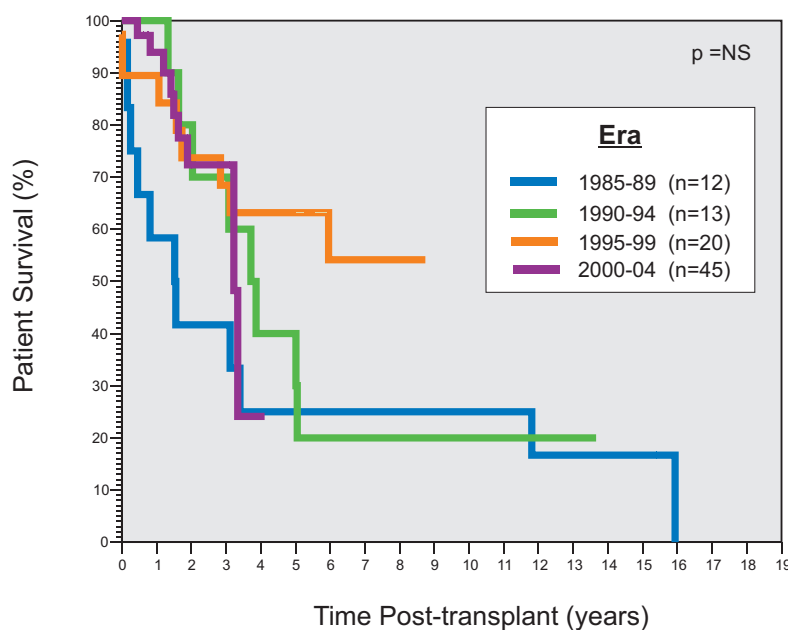
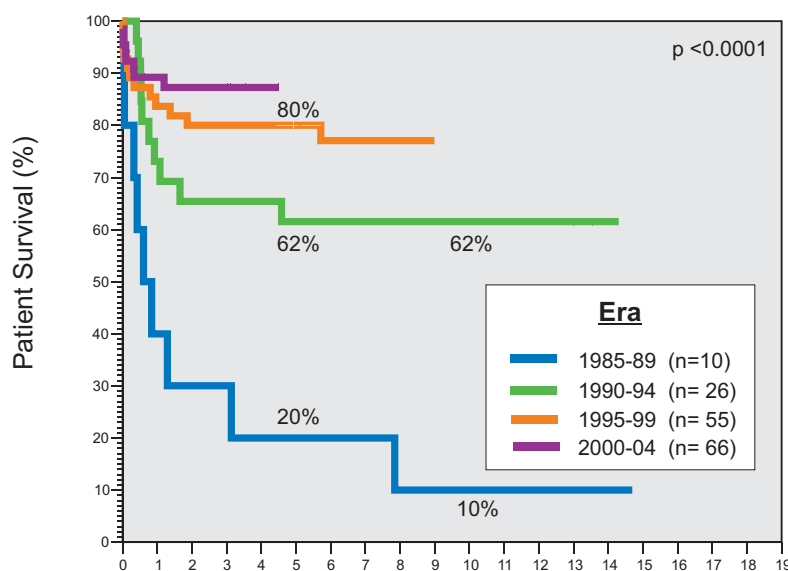
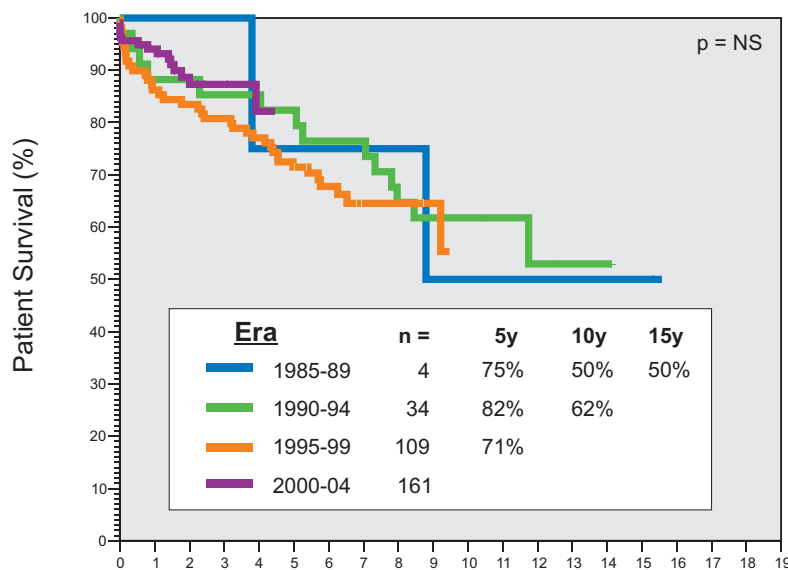


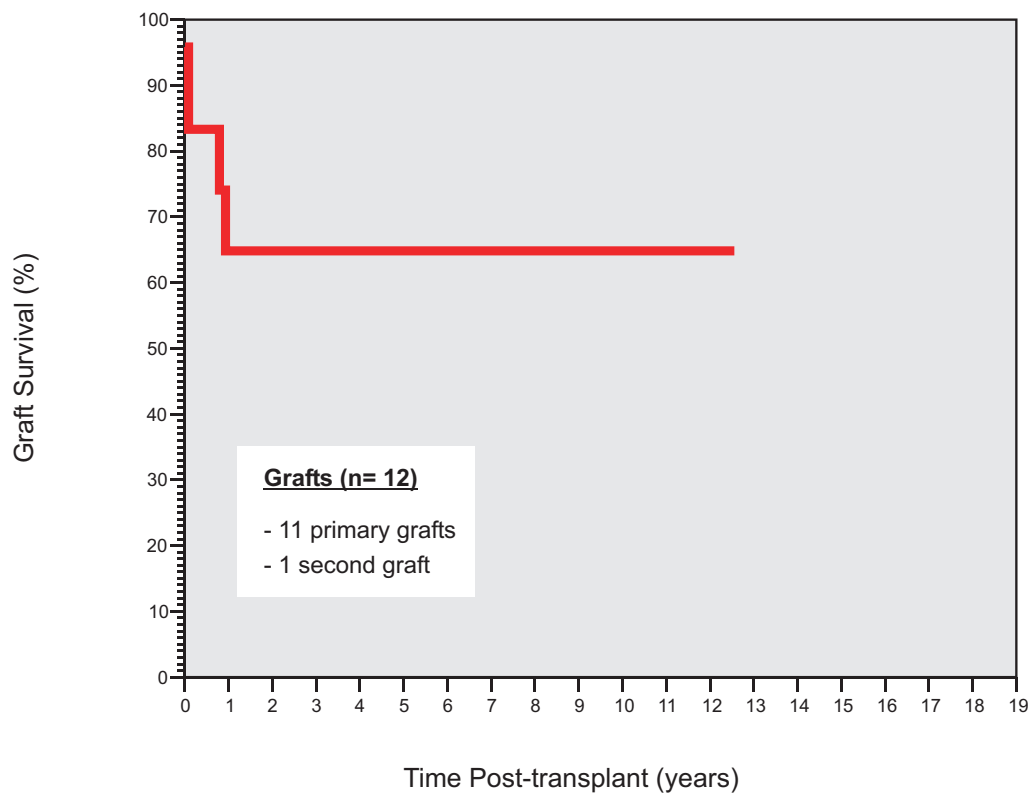
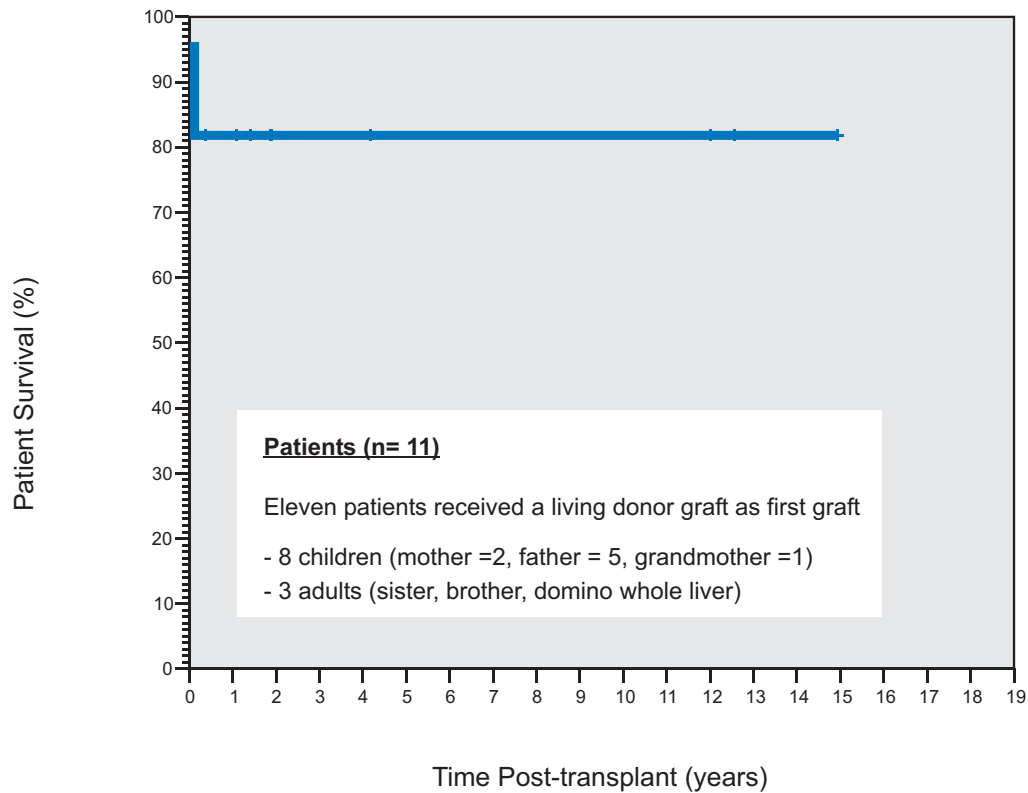
## (3) Paediatric recipients [excluding FHF] - n=382



## (4) Fulminant hepatic failure (n=196)





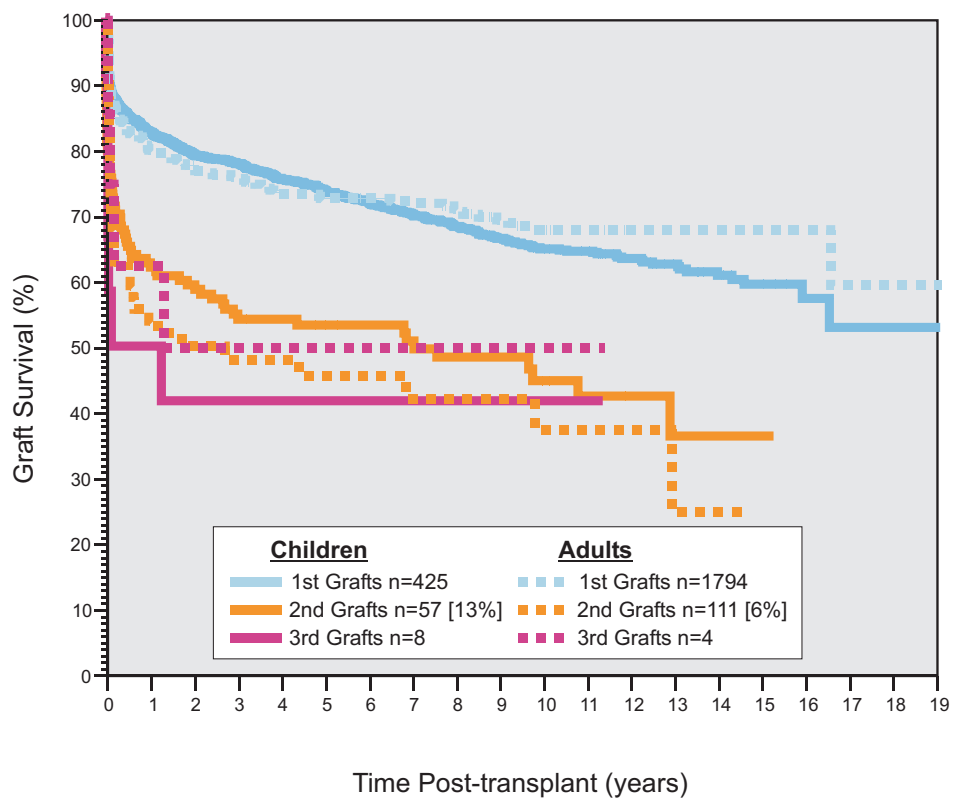
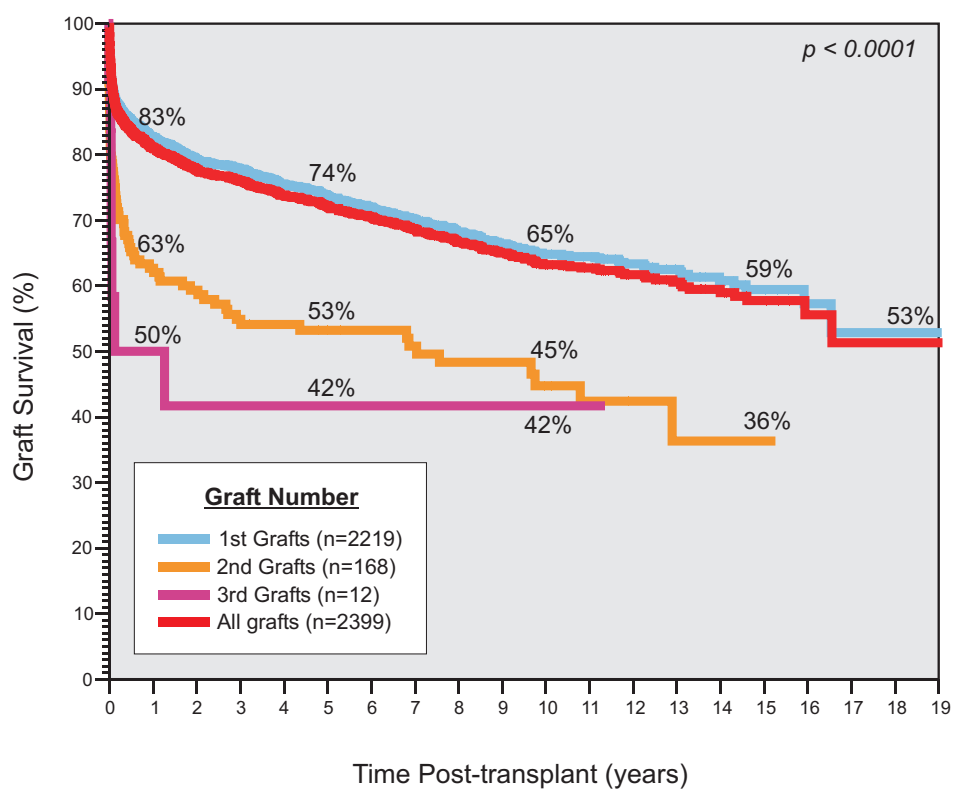


# Section 4

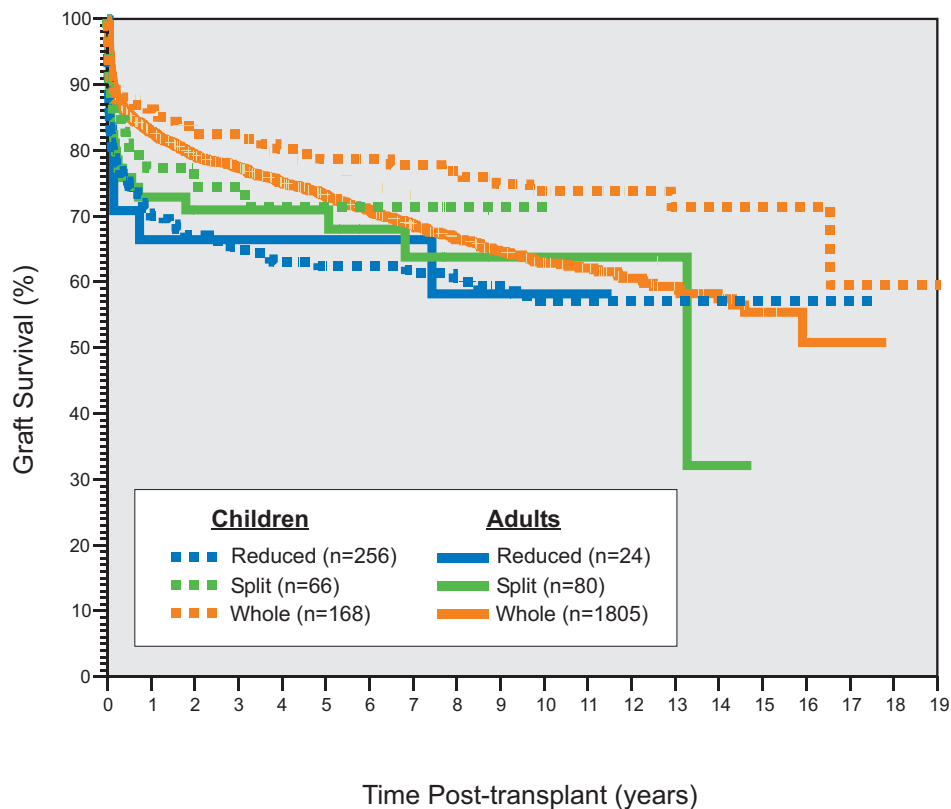
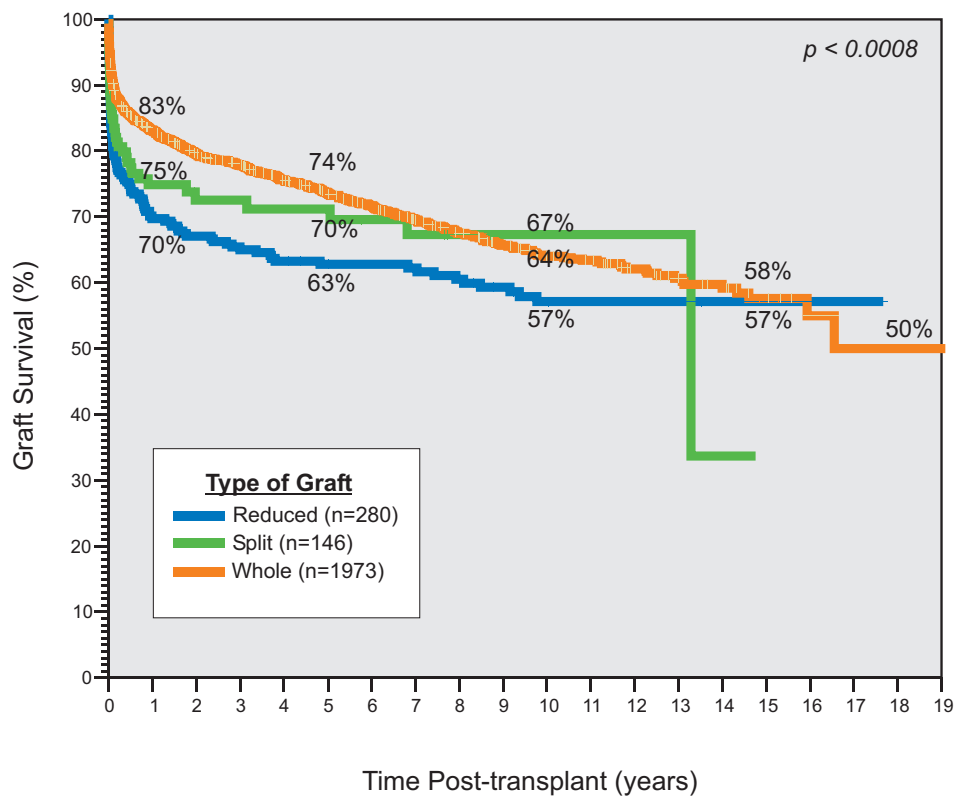
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## Graft Outcome





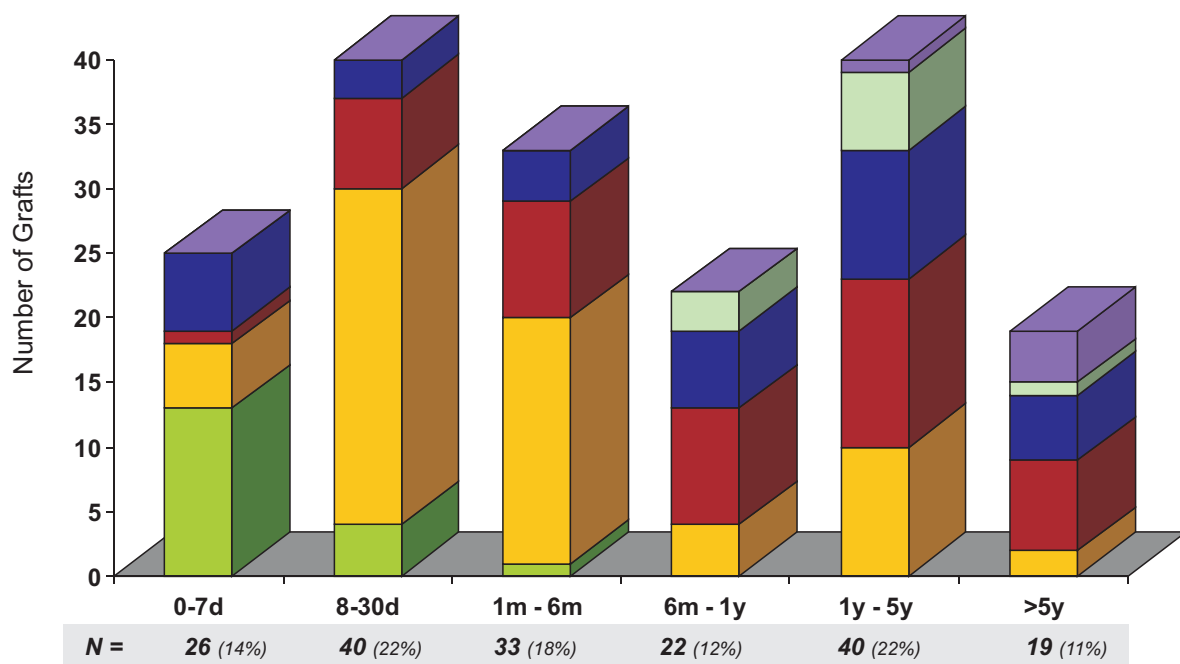
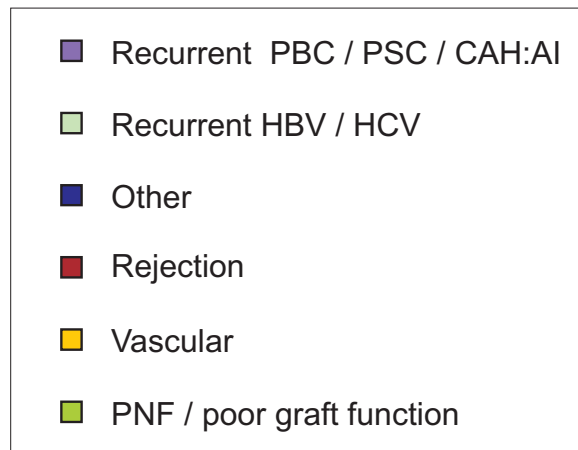
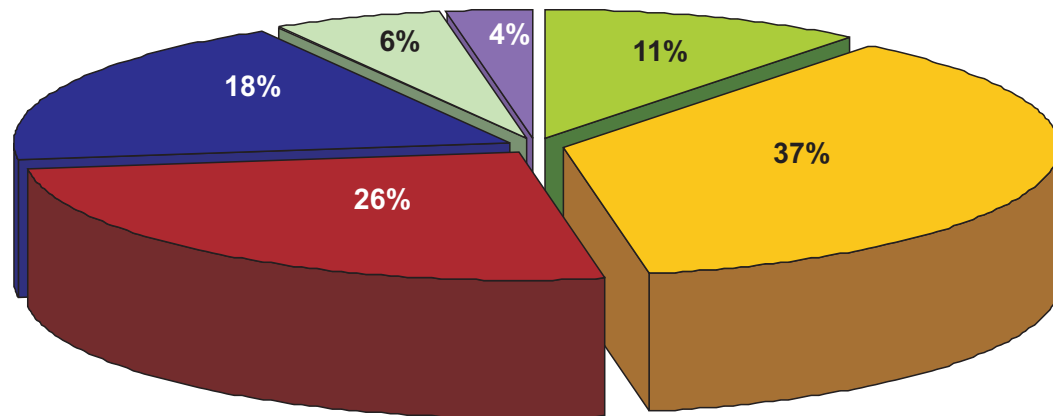
**All grafts (n = 2399)**





## Indication for Retransplantation

n = 180 (168 2nd grafts, 12 3rd grafts)



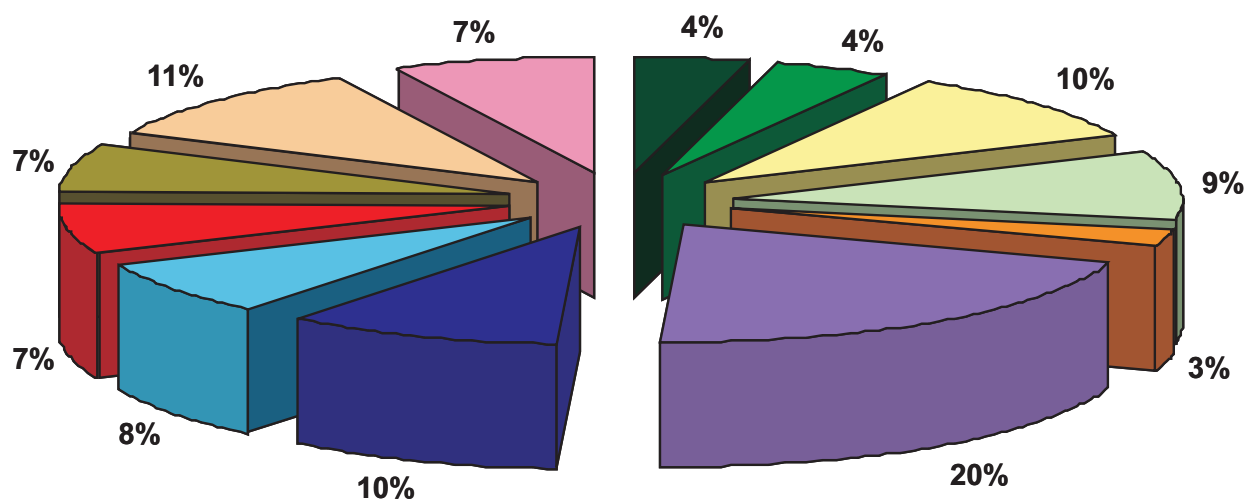
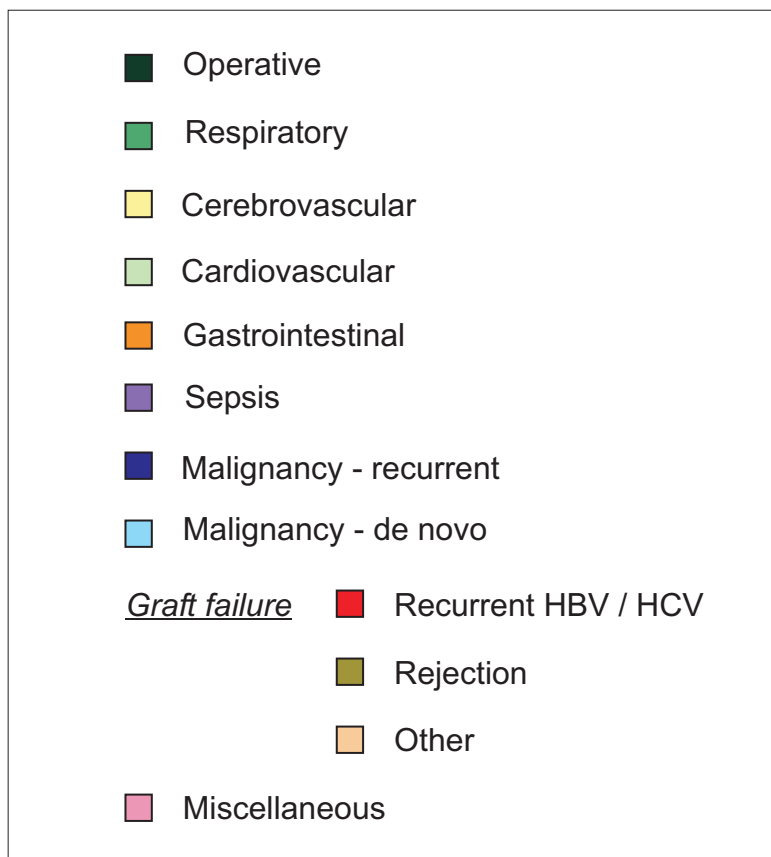
# Section 5

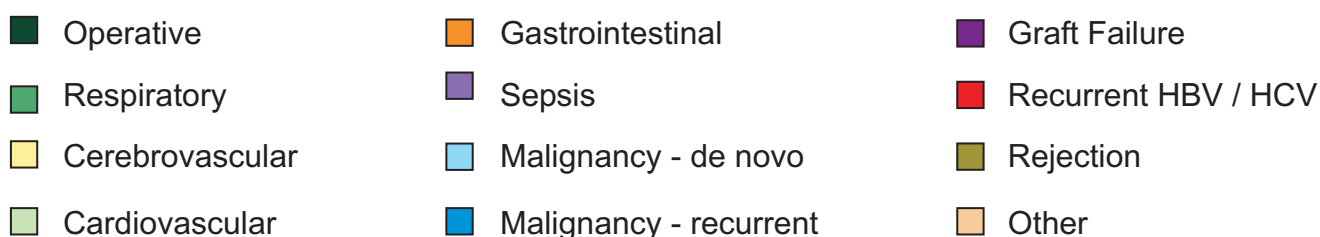
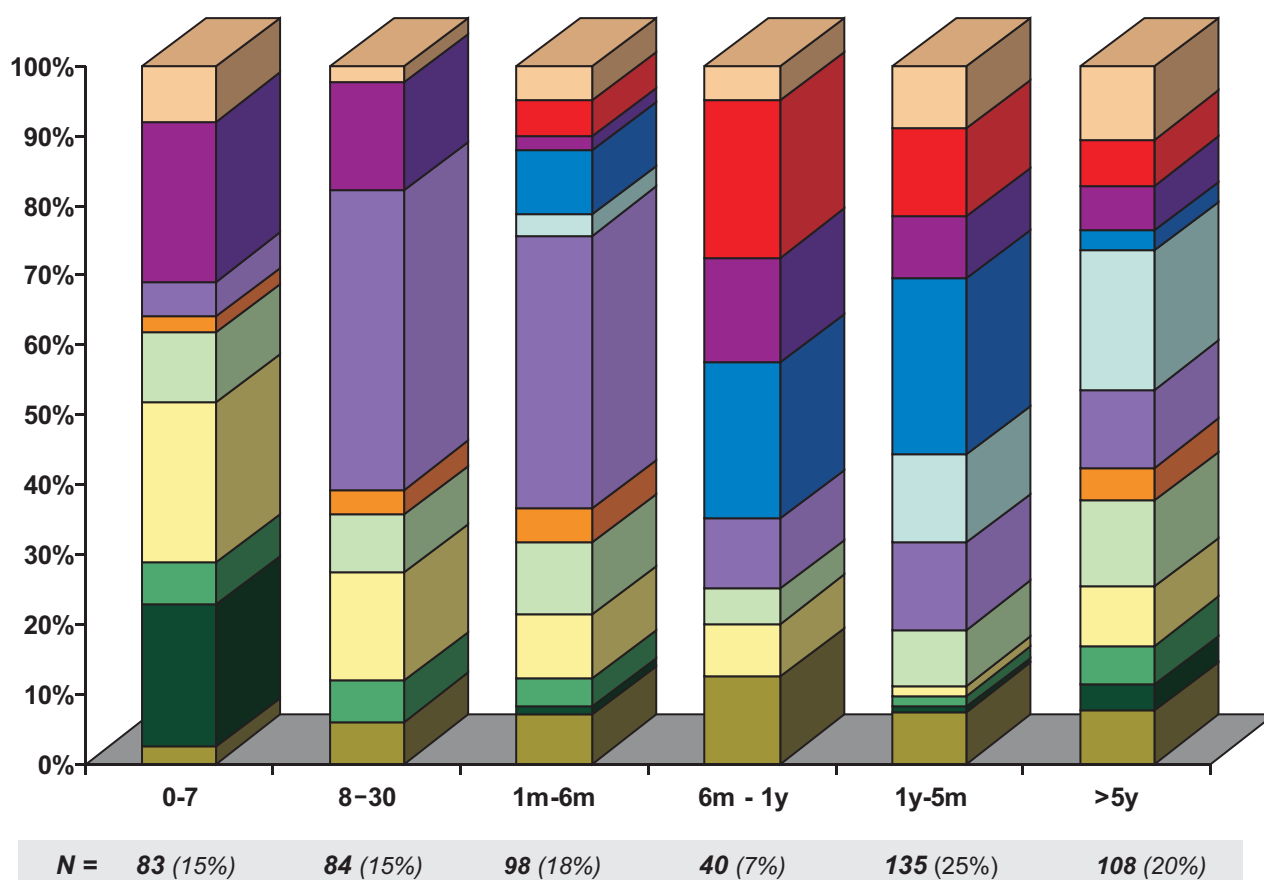
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## Cause of Patient Death



## All Patients n = 547





# Section 6

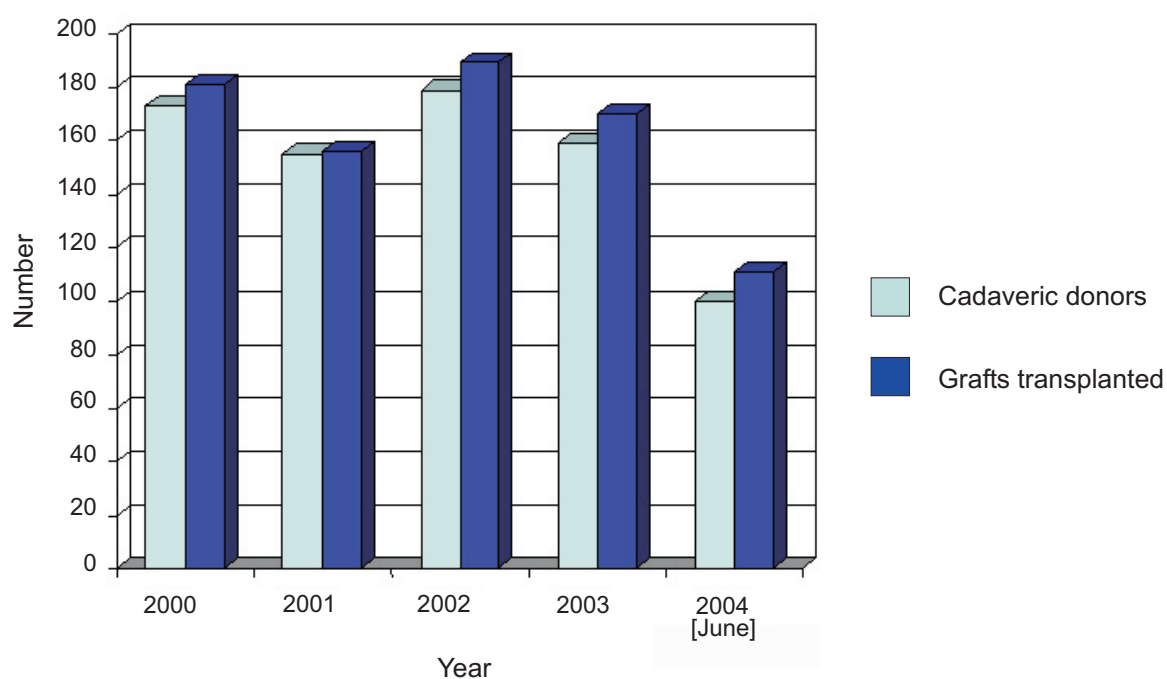
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## Donor Information



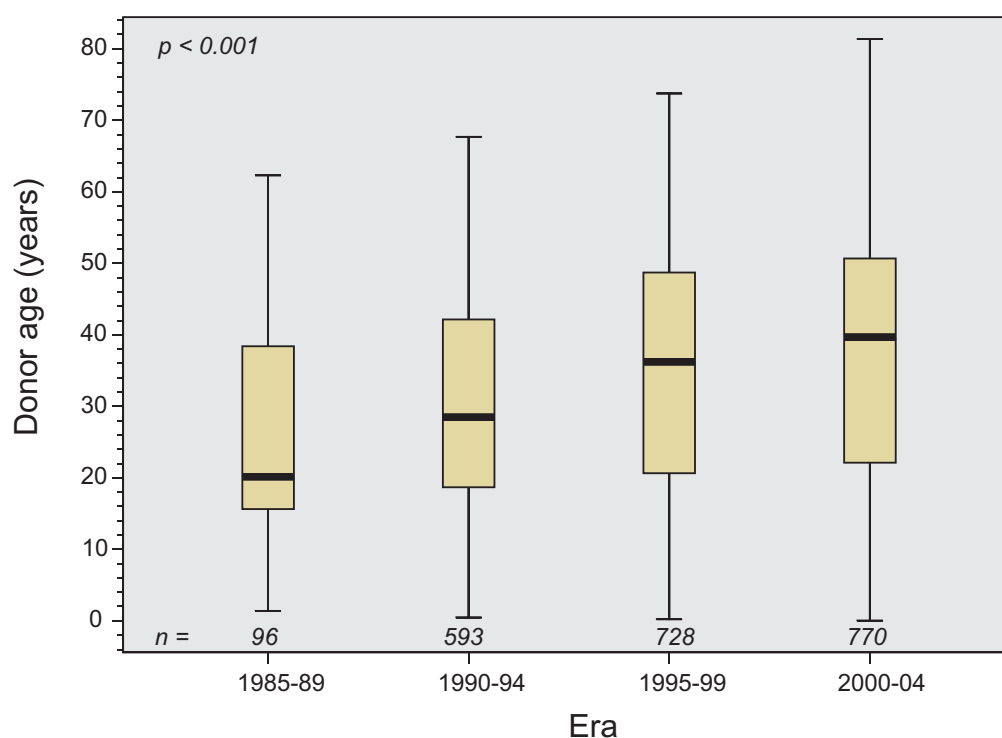
	QLD	NSW/ACT	VIC/TAS	SA/NT	WA	NZ	TOTAL
1990	22	27	16	5		7	77
1991	29	35	20	6	8	11	109
1992	43	32	18	9	8	24	134
1993	28	40	25	12	6	16	127
1994	29	39	23	12	10	21	134
1995	29	44	24	17	8	21	143
1996	26	37	19	17	10	24	133
1997	31	49	19	19	8	22	148
1998	29	44	27	22	13	27	162
1999	15	31	31	29	11	27	144
2000	26	51	26	24	12	34	173
2001	37	40	26	14	9	29	155
2002	34	42	38	24	11	30	179
2003	34	32/3	29/2	13	15	31	159
2004 [June]	18	27/2	15/1	13	9	15	100

## Grafts from cadaver donors



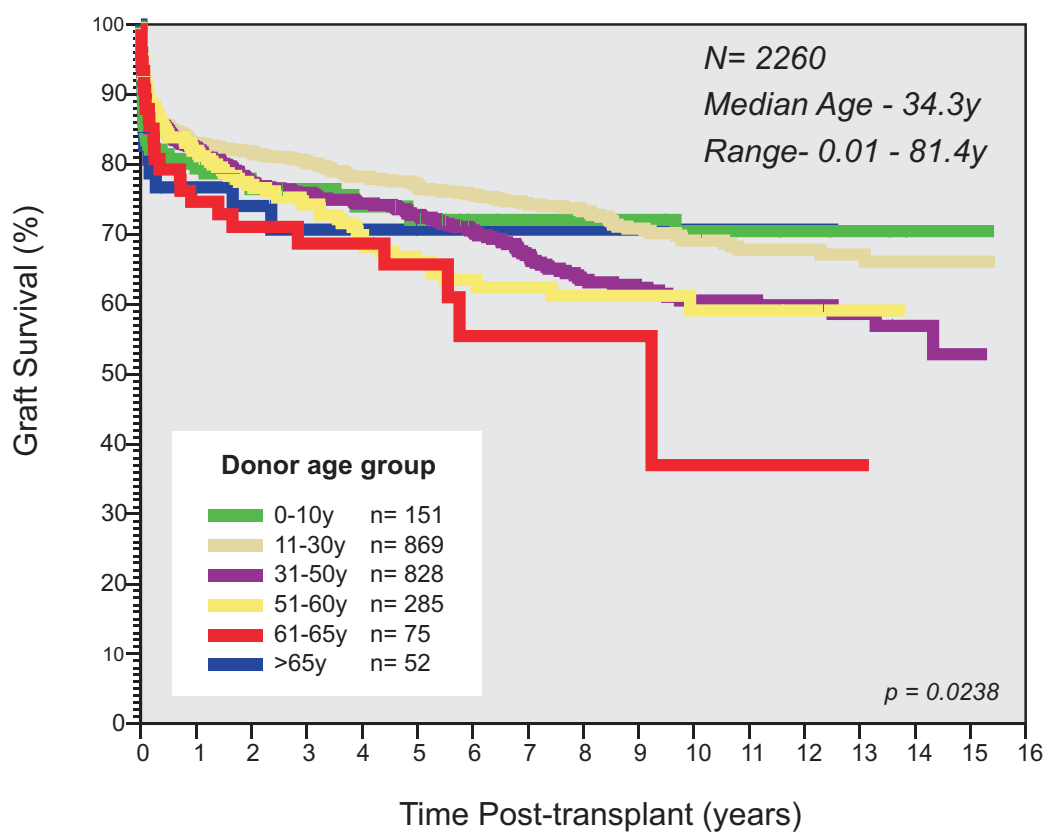
## Donor Age by ERA

N = 2187



## Graft Survival by Donor Age

N = 2260



# Section 7

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## Waiting List





# Waiting List Outcome by Recipient Blood Group

## [ Data 1/1/04 - 30/6/04 ]

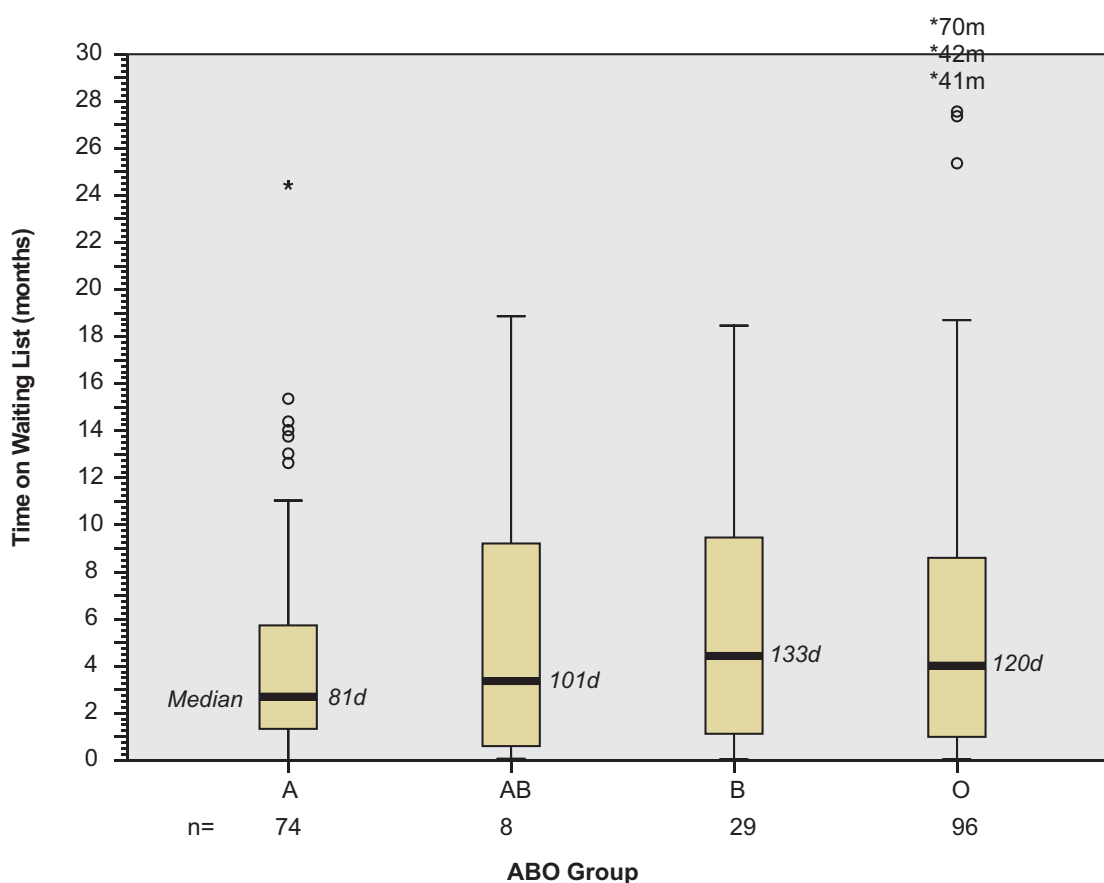
Outcome		Recipient Blood Group				
		A*	O	B	AB	TOTAL
Listed at 1/1/04 n=94	Not transplanted	7 [9.5%] *	19 [20%]	4 [14.%]	0	30 #
	Transplanted	26 [35%]	24 [25%]	9 [31%]	5 [62.5%]	64 (68%)
Listed after 1/1/04 n=113	Not transplanted	17 [23%]	35 [35%]	13 [45%]	1 [12.5%]	65##
	Transplanted	24 [32.5%]	19 [20%]	3 [10%]	2 [25%]	48
TOTAL n=207	Not transplanted	24 [32.5%]	53 [55%]	17 [57%]	1	95
	Transplanted	50 [67.5%]	43 [45%]	12 [43%]	7 [87.5%]	112
		74 [36%]**	96 [46%]	29 [14%]	8 [4%]	207
Listed at 30/06/01		20 [25%]***	45 [57%]	13 [17%]	1 [1%]	79

\* [%] = % of blood group \*\* [%] = % of patients \*\*\* [%] = % listed patients

# 10 patients delisted [too sick, died on list 1 recovered]

## 6 patients delisted [too sick, died on list, tumour progression]

## Waiting Time by Blood Group



# Section 8

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## Liver Transplantation and Cancer



## Types of Cancer in Liver Transplant Recipients N = 2219

<b><u>AT Tx</u></b>		
PRIMARY LIVER CA	82	(4%)
INCIDENTAL CA	192	(9%) 193 Ca
<b>TOTAL</b>	<b>274</b>	<b>(12%)</b>
<b><u>POST Tx</u></b>		
RECURRENT CA	74	(3% of all pts , 27% of pts with Ca at Tx)
DE NOVO CA	101	(5%) 104 Ca
SKIN CA	234	(11%) 1337 Ca
<b>TOTAL</b>	<b>409</b>	<b>(18%)</b>
<b><u>MULTIPLE CA</u></b>	<b>47</b>	

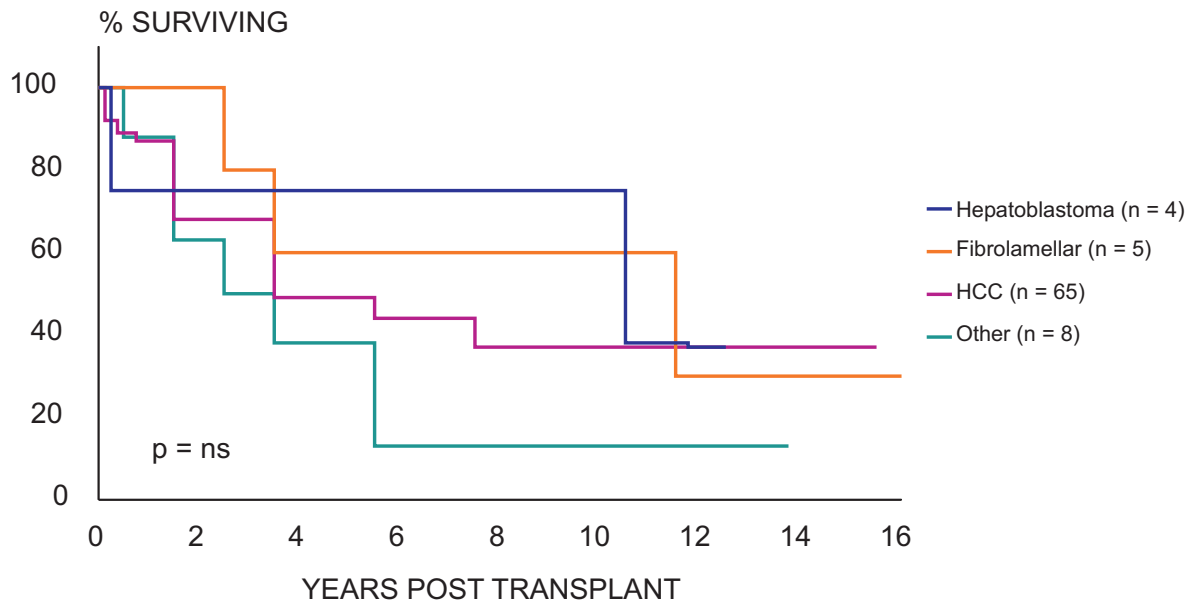
## Primary Liver Malignancy N = 2219 n = 82 (4%) with cancer

TYPE OF CA	No	DIED	DIED OF CA
HEPATOCELLULAR CA	65	25	15 (23%)
LAMELLAR VARIANT	5	4	2 (40%)
CARCINOID	4	4	4 (100%)
ENDOCRINE	2	2	2 (100%)
HEPATOBLASTOMA	4	2	1 (25%)
ANGIOSARCOMA	1	1	1 (100%)
EPITHELOID HAEMANGIOMA	1	0	0
<b>TOTALS</b>	<b>82 (4% of pts)</b>	<b>38 (46% of those with PCa)</b>	<b>25 (30% of those with PCa)</b>

## Primary Liver Cancer

N = 2219

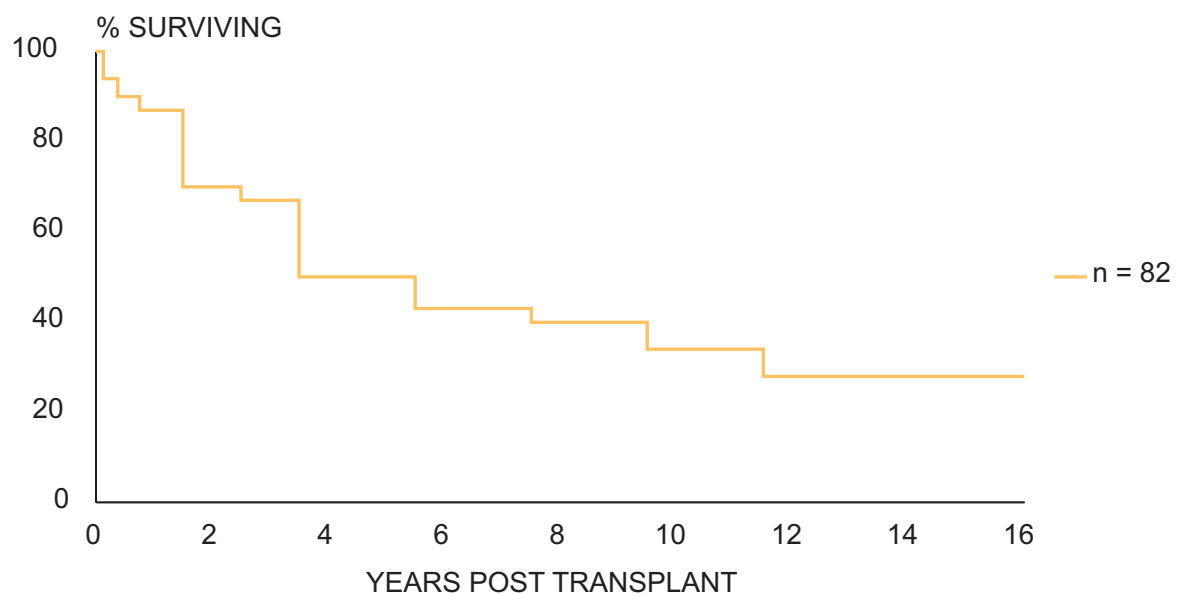
n = 82 (4%) with cancer



## Primary Liver Cancer All Patients

N = 2219

n = 82 (4%) with cancer



## Incidental Liver Cancer

N = 2219

n = 192 (9%)

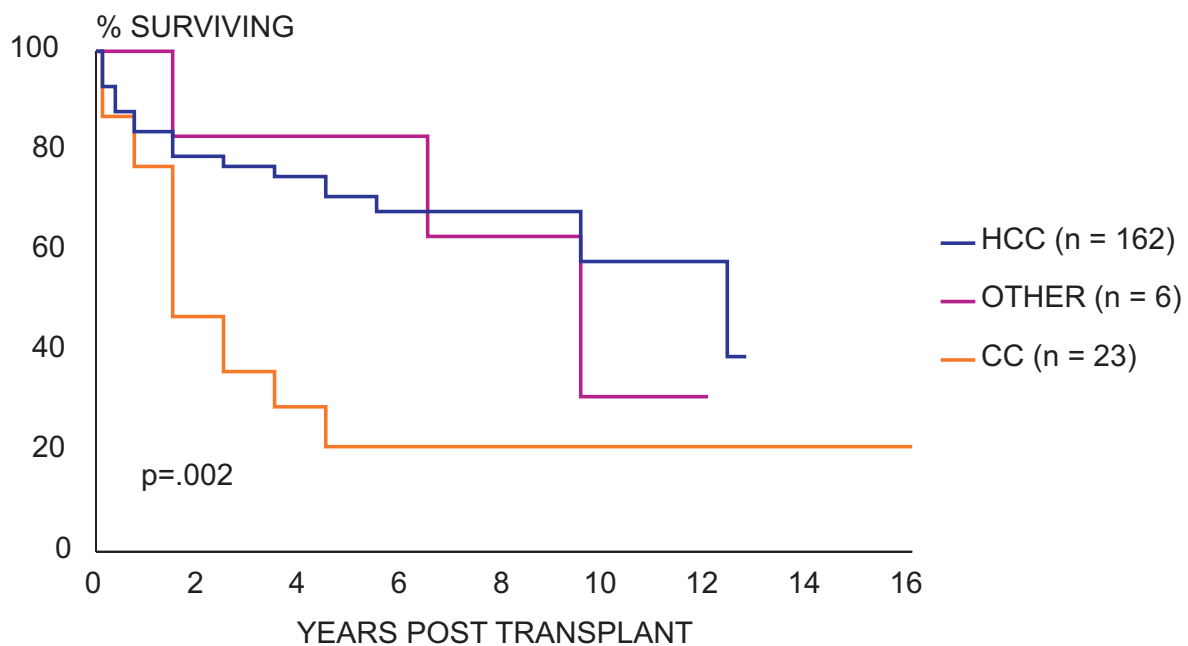
	NO	DIED	DIED OF CA
HEPATOCELLULAR CA*	162	41	15 (9%)
CHOLANGIO CA	23	15	12 (52%)
ANGIOSARCOMA	1	1	1 (100%)
ADENOCARCINOMA	3	2	0
HEPATOBLASTOMA*	2	1	0
FIBROLAMELLAR	1	0	0
FIBROLAMELLAR	1	0	0
TOTALS	193* in 192 (9% of pts)	60 (31%)	28 (15%)

\* 1 patient had 2 different incidental Ca

## Incidental Liver Cancer

N = 2219

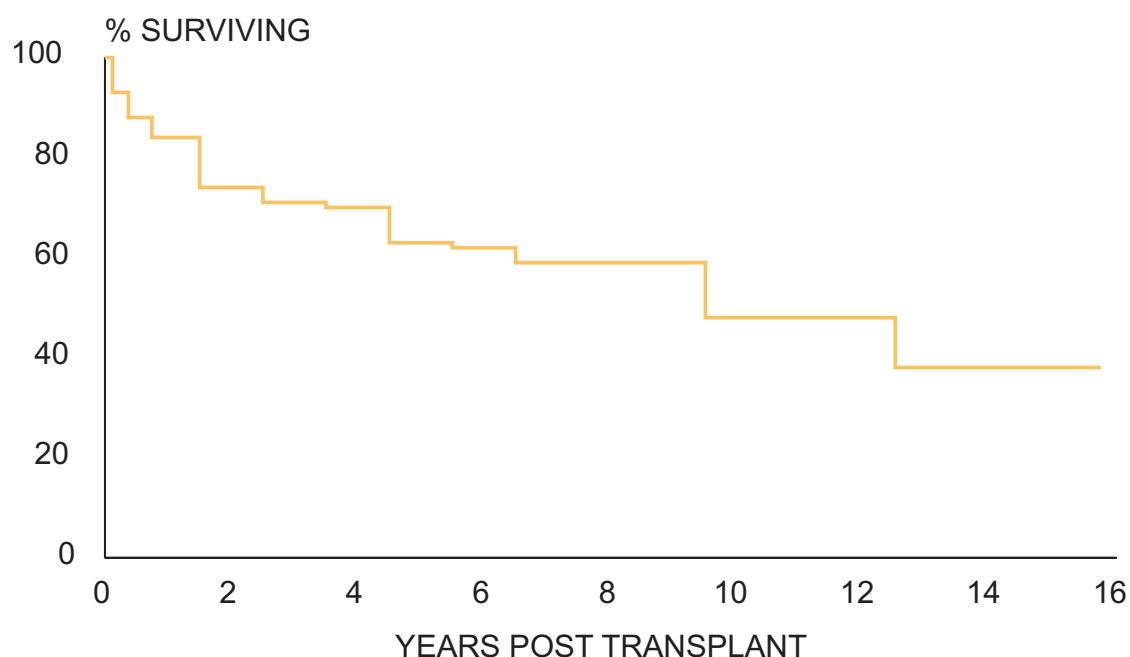
n = 192 (9%)



## Incidental Liver Cancer All Patients

**N = 2219**

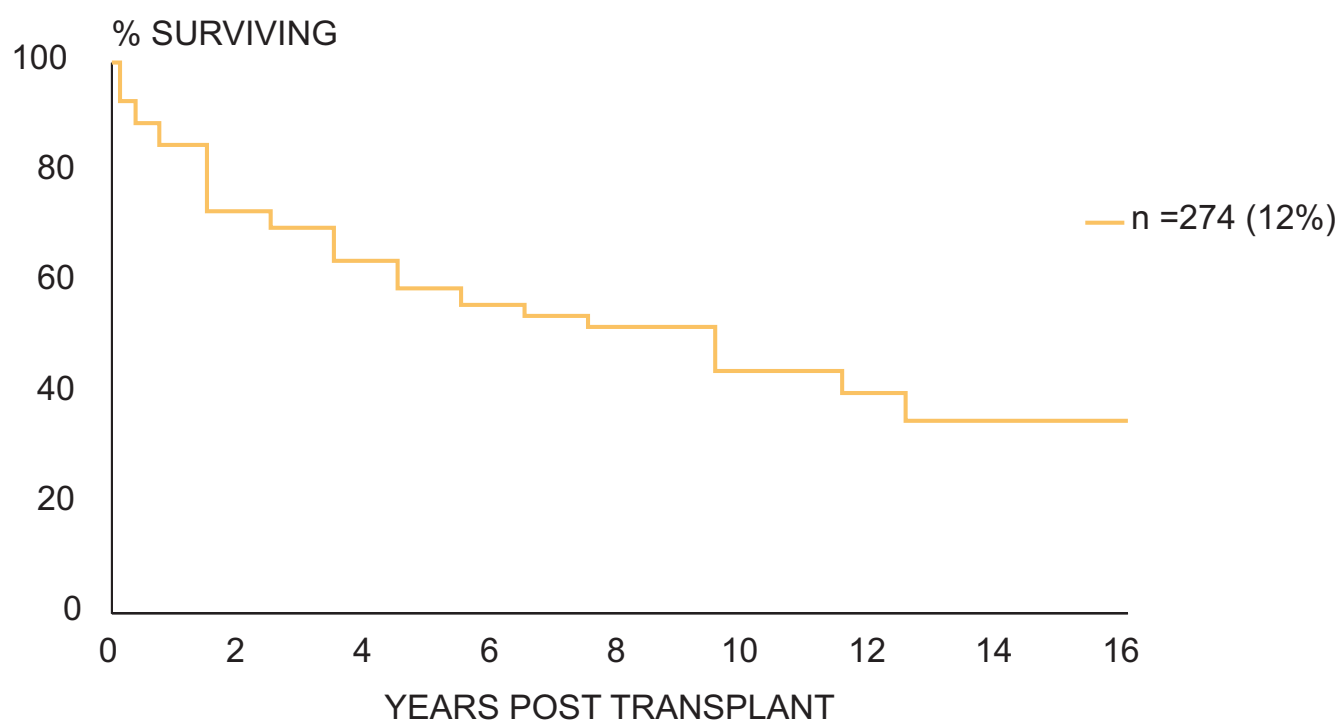
**n = 192 (9%)**



## Pre-Transplant Liver Cancer (Primary and Incidental Disease)

**N = 2219**

**n = 274 (12%)**



## De Novo Non Skin Cancer Post Transplant

N = 2219

n = 101 (5%)

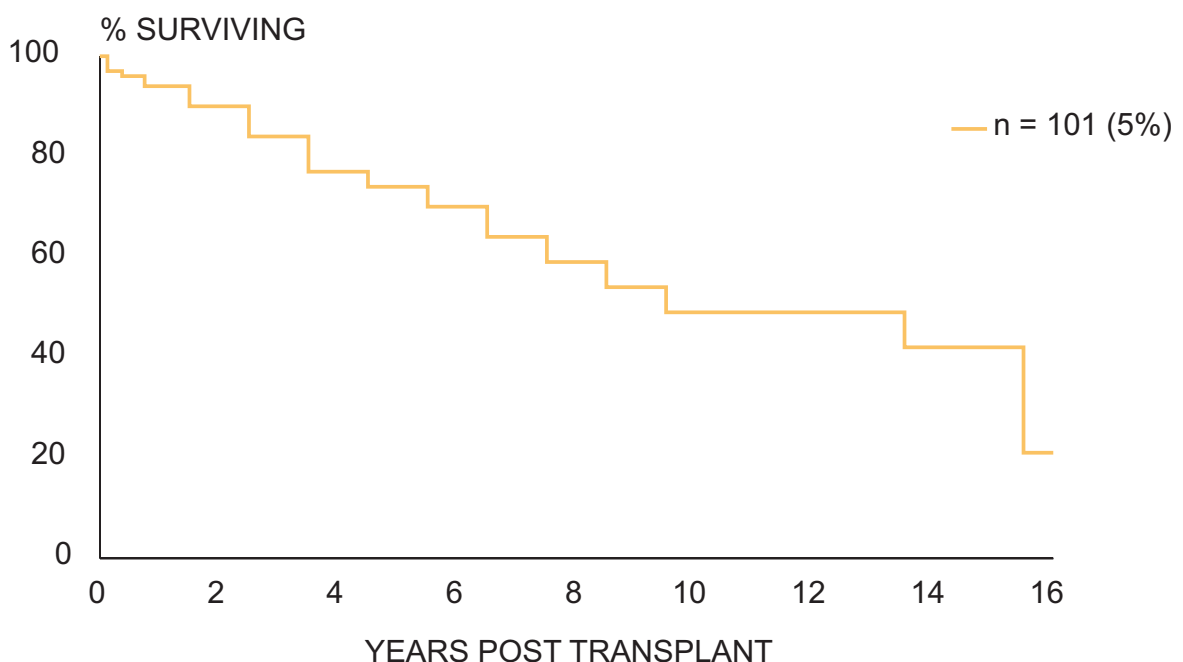
TYPE of CANCER	NO	DIED	DIED THIS CA
NON HODGKINS LYMPHOMA	30	19	15
KAPOSI SARCOMA	5	2	0
ALIMENTARY TRACT	33	15	13
GLOTTIS	1	0	0
STOMACH	7	5	3
COLON	11	5	4
APPENDIX	1	0	0
PANCREAS	3	2	2
GENITO-URINARY	13	6	2
BLADDER	2	2	1
TESTIS	1	0	0
KIDNEY	2	1	0
PROSTATE	2	0	0
RESPIRATORY	5	3	3
LEUKAEMIA	3	1	0
BREAST	8	1	1
ENDOCRINE	4	2	1
CERVIX	3	1	0
CEREBRAL	2	1	1
<b>TOTALS</b>	<b>104 in 101 (5%) pts</b>	<b>52 (50% of pts with Ca)</b>	<b>37 (36% of pts with Ca)</b>

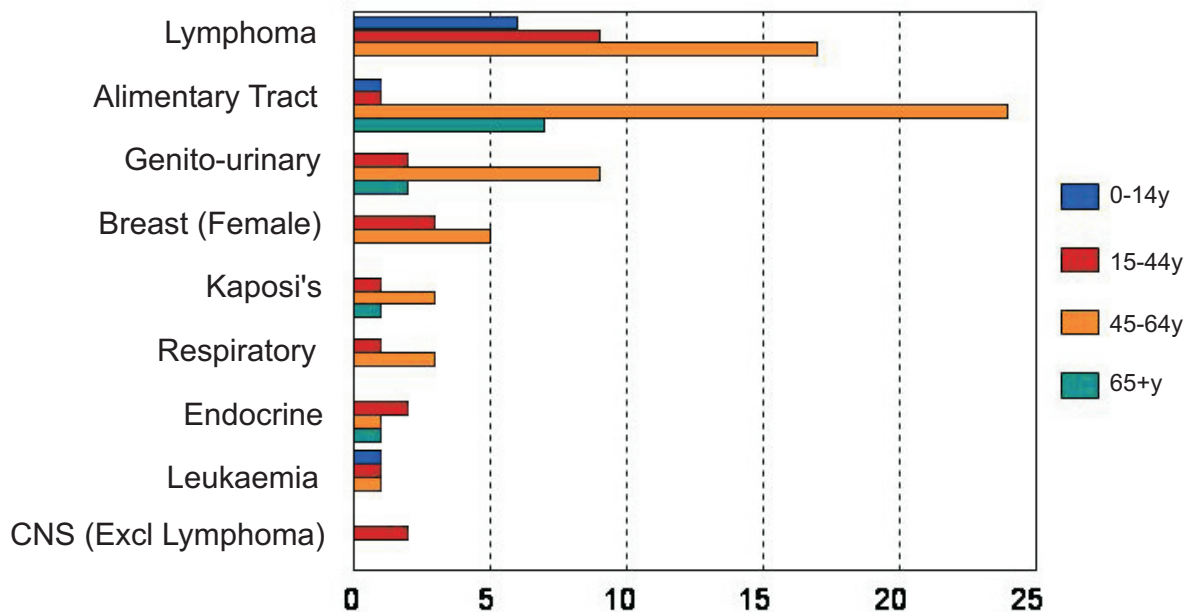
Seven patients also had incidental malignancy; two patients had two de novo malignancies

## De Novo Non Skin Cancer

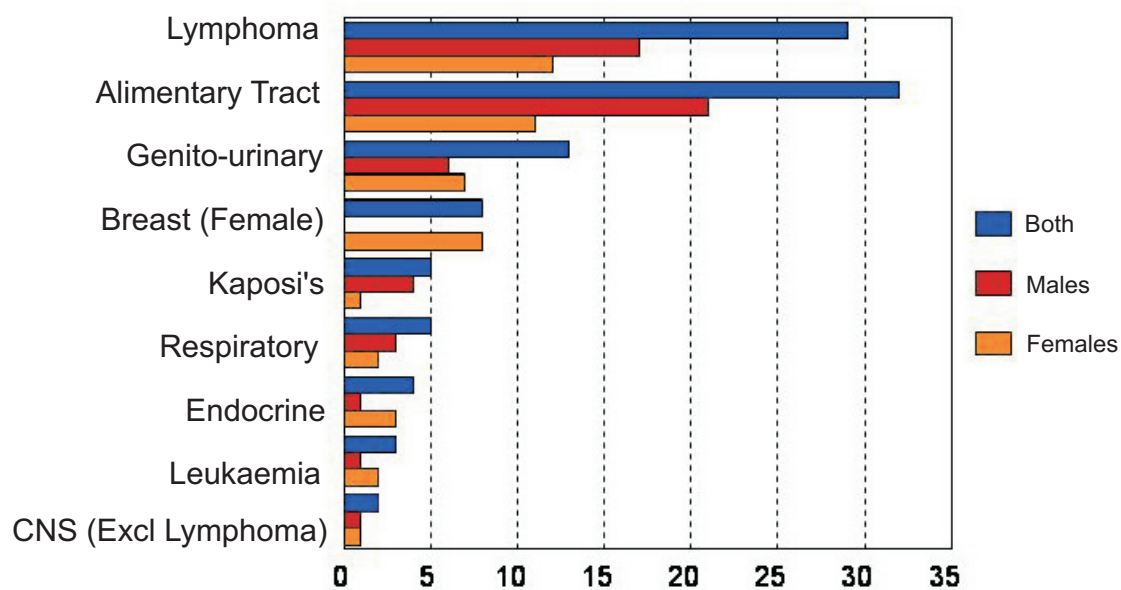
N = 2219

n = 101 (5%)





## De Novo Incidence by Gender

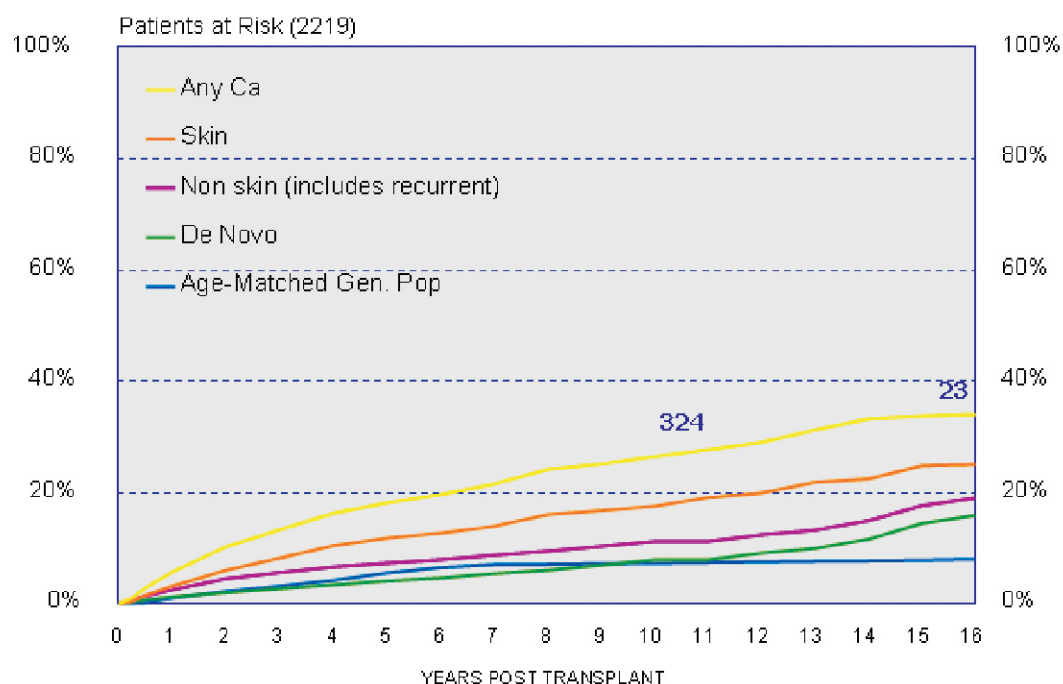




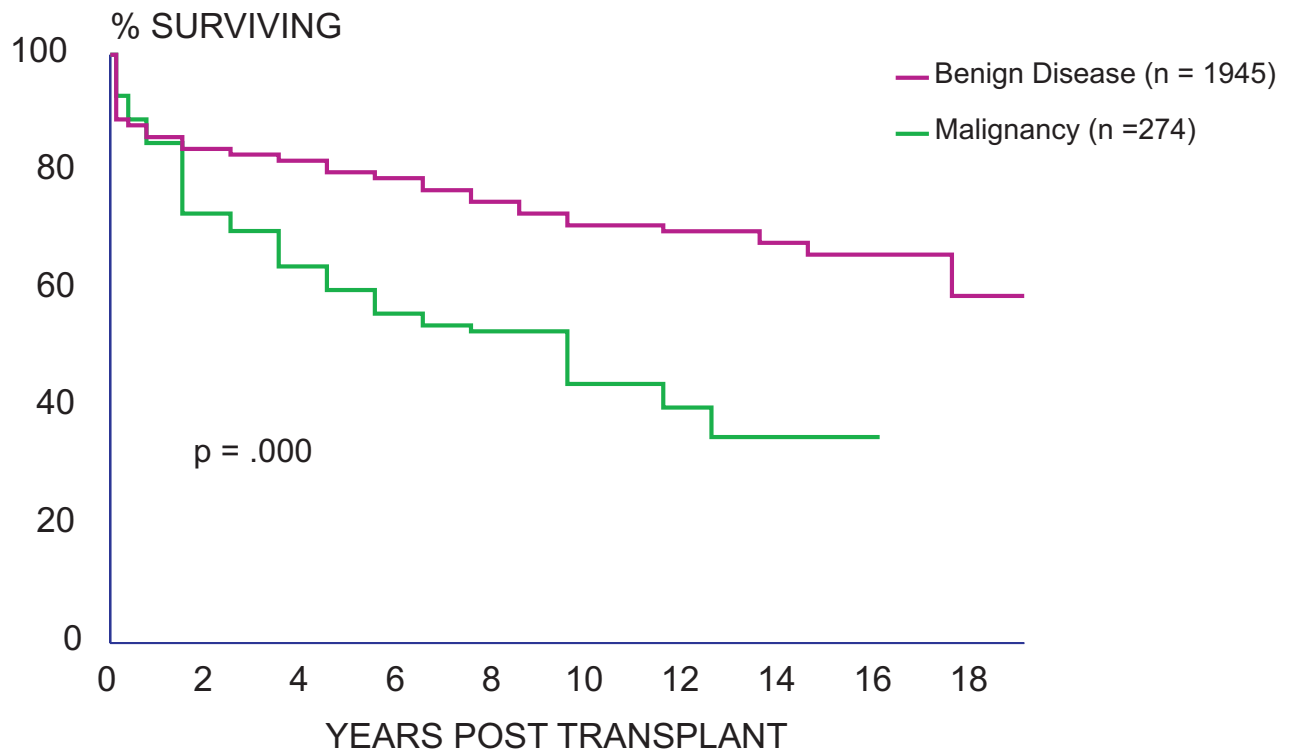
TYPE	CANCERS	PATIENTS
BCC	378	138
SCC	499	148
MELANOMA	8	8
TOTALS	1337	234 ** (11%)

\*\* 74 pts had multiple skin cancer types

## Cumulative Risk of Diagnosis of Cancer Following Liver Tx. 1986 - June 2004 N =2219



## Benign Disease vs Primary or Incidental Malignancy



# Appendix I

## Liver Transplant Units of Australia and New Zealand

<p>Australian National Liver Transplant Unit          Royal Prince Alfred Hospital          Missenden Road          CAMPERDOWN NSW 2050          Email: <a href="mailto:anltu@cs.nsw.gov.au">anltu@cs.nsw.gov.au</a>  <a href="http://www.cs.nsw.gov.au/Gastro/LiverTransplant/default.htm">http://www.cs.nsw.gov.au/Gastro/LiverTransplant/default.htm</a></p>	<i>and</i>	<p>The New Children's Hospital          Hawkesbury Road          WESTMEAD NSW 2145</p>
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<p>Liver Transplant Unit          The Austin          Studley Road          HEIDELBERG VIC 3084</p>	<i>and</i>	<p>Royal Children's Hospital          Flemington Road          PARKVILLE VIC 3052</p>
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<p>Queensland Liver Transplant Service          Princess Alexandra Hospital          Ipswich Road          WOOLLOONGABBA QLD 4102</p>	<i>and</i>	<p>Royal Children's Hospital          Bowen Bridge Road          HERSTON QLD 4029</p>
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South Australian Liver Transplant Unit  
 Flinders Medical Centre  
 Flinders Drive  
 BEDFORD PARK SA 5042  
[http://www.flinders.sa.gov.au/flinders\\_centre\\_for\\_digestive\\_health/](http://www.flinders.sa.gov.au/flinders_centre_for_digestive_health/)

WA Liver Transplantation Service  
 Sir Charles Gardiner Hospital  
 Verdun Street  
 NEDLANDS WA 6009

New Zealand Liver Transplant Unit  
 Auckland Public Hospital  
 Park Road  
 Auckland  
 New Zealand  
[Http://www.nzliver.org/](http://www.nzliver.org/)

# Appendix II

## ANZLTR PRIMARY Diagnosis Metabolic disorders by Age Group

Primary Diagnosis	Age group		Total
	Child	Adult	
-1 Antitrypsin deficiency	28	34	62
Crigler-Najjar	3	1	4
Familial amyloid polyneuropathy	0	25	25
Glycogen storage disease	0	1	1
Haemochromatosis	1	21	22
Homozygous Hypercholesterolemia	3	1	4
Indian childhood cirrhosis	1	0	1
Other *	7	1	8
Primary hyperoxaluria	5	6	11
Tyrosinemia	4	0	4
Urea cycle disorders **	6	2	8
Wilsos disease	6	24	30
Total	64	116	180

\* Bile acid synthesis disorder, Protein C deficiency, methylmalonic acidemia, familial immunodeficiency, mitochondrial disease

\*\* OTC deficiency 6; citrullinemia 2

# Appendix III

## ANZLTR PRIMARY Diagnosis - Other by Age Group

Primary Diagnosis	Age group		Total
	Child	Adult	
Alagille syndrome	21	1	22
Alagille non-syndromic	2	0	2
Benign liver tumour -Adenomatosis	0	1	1
Benign liver tumour-Hemangioma	0	2	2
Caroli's disease	1	10	11
Choledocal cyst	1	1	2
Cholestatic disease-Other	1	2	3
Chronic Budd Chiari	1	22	23
Congenital biliary fibrosis	0	1	1
Ductopenia	0	2	2
Granulomatous hepatitis / sarcoidosis	0	2	2
Histiocytosis X	3	0	3
Liver Trauma	0	1	1
Neonatal hepatitis	3	0	3
Nodular regenerative hyperplasia	0	4	4
Non alcoholic fatty liver (NAFLD or NASH)	0	9	9
Polycystic Liver disease	0	7	7
Polycystic liver and kidney disease	0	4	4
Progressive familial intrahepatic cholestasis(PFIC)	9	4	13
Secondary biliary cirrhosis	1	9	10
Secondary biliary cirrhosis - Hepatolithiasis	0	4	4
Secondary biliary cirrhosis - Cystic fibrosis	5	8	13
Other -specify	1	11	12
Total	49	105	154

# Vanishing bile duct syndrome  
Haemangiotelangiectasia  
Veno-occlusive disease  
Chronic Active Hepatitis A  
Non-cirrhotic portal hypertension  
Kassabach-Merritt syndrome  
Arterial-venous malformation  
Hereditary haemorrhagic telangiectasia

# Appendix IV

## ANZLTR PRIMARY Diagnosis Fulminant Hepatic Failure by Age Group

Primary Diagnosis	Age group		Total
	Children	Adult	
Acute - Budd Chiari	0	2	2
Acute - Wilson's	4	9	13
Acute - -1 -AAT	2	0	2
Acute Autoimmune hepatitis	0	4	4
Acute Unknown / unspecified	30	52	82
Acute -Paracetamol	0	6	6
Acute -Other drugs	2	10	12
Acute Herbs	0	2	2
Acute - Hepatitis A	0	2	2
Acute - Hepatitis B	0	19	19
Acute - NonA-NonB	2	9	11
Acute - Hepatitis E	0	1	1
Acute - Post liver resection	1	0	1
Subacute - Wilson's	0	2	2
Subacute Autoimmune hepatitis	0	4	4
Subacute - Dug	0	2	2
Subacute - Unknown / unspecified	2	22	24
Subacute - Hepatitis A	0	1	1
Subacute - Hepatitis B	0	6	6
Total	43	153	196