

AUSTRALIA & NEW ZEALAND



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LIVER TRANSPLANT REGISTRY



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

DATA TO 31-12-2011

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STATISTICAL METHODS

Kaplan-Meier survival curves have been produced using SPSS® for Windows™ Release 19.0, SPSS Inc.

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The Cancer Registry is maintained at Transplantation Services, Royal Prince Alfred Hospital, Sydney. Report prepared by Pamela Dilworth, Marie Mulhearn and Dr Deborah Verran.

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Preface

We are pleased to present the 23rd Report of the Australia and New Zealand Liver Transplant Registry (ANZLTR). This report contains data to the 31st December 2011 and analyses the cumulative data since the establishment of the first liver transplantation unit in Australia or New Zealand in 1985.

The Australia and New Zealand Liver Transplant Registry (ANZLTR) is a collaborative effort of the liver transplantation centres in Australia (Adelaide, Brisbane, Melbourne, Perth, Sydney) and New Zealand (Auckland). The Registry is supervised by the Management Committee which is involved in the ongoing supervision of the development of the Registry. The members of the Management Committee are listed on the front page.

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 contribute their data by direct entry into the ANZLTR database. A full list of the Units and their contact information can be found in Appendix I. In particular we are grateful to the efforts of Pamela Dilworth, Program Manager and Marie Mulhearn for their 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, prepare the Cancer Report.

The registry has financial support and we are grateful to the Australian Government, through the Australian Organ and Tissue Authority, for their financial contribution.

Some additional funds are received from Janssen-Cilag Pty Ltd and Novartis Pharmaceuticals Australia Pty Ltd on an ad hoc basis.

Comments are always welcome and should be forwarded to the Coordinating Centre at the contact information listed on the front page as should requests for further copies of this Report. The report is now also available on the ANZLTR public web site www.anzltr.org from where the report can be downloaded. Slides are available on request from the Coordinating Centre.

Stephen Lynch
Glenda Balderson





Summary

Page

5. Between January 1985 and 31st December 2011, 4034 orthotopic liver transplants (OLT) were performed in Australia and New Zealand on 3735 patients, 3065 adult patients [82%] and 670 children (< 16 years) [18%]. The median age of all recipients was 47 years. The ages ranged from 24 days to 73.1 years. There is a significant difference in gender distribution between children (M=46%) and adults (M=64%)
6. Two hundred and twenty-five new patients were transplanted in 2011 compared with 233 in 2010.
7. The trend to increasing age of adult recipients in recent years continued and the overall adult median age is now 50.2 years. The median age of new adult recipients in 2010/2011 was 54.2 years.
- 8-9. In 2011, 5 more transplants were performed than in 2010 [253 vs 248]. Split grafts continue to make a significant contribution to the total number of paediatric transplants performed providing 14 of 35 [40%] grafts in 2011 and 176 of 766 [23%] overall. In children, other reduced size grafts have been used in 350 [46%] cases including 56 living donor grafts. One child has been treated with liver cell implantation. Of adult patients, 223 have received reduced size grafts - 182 split liver grafts (including 1 as auxiliary graft), 28 other reduced size grafts (1 as auxiliary graft) and 13 living donor grafts. 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 hepatitis C [CVH : HCV] is the primary disease in 22% of recipients and chronic hepatitis B [CVH : HBV] in 7 %. Full details of specific diagnoses categories by age group are listed in the Appendices for - Metabolic disorders (Appendix II), Other diseases (Appendix III), Fulminant Hepatic Failure (Appendix IV).
- 12-15. The number of patients transplanted for non alcoholic fatty liver disease [NAFLD/NASH] continued to increase with 11 new patients transplanted in 2011 bringing the total to 69. While the proportion of adult patients transplanted with a primary diagnosis of chronic viral Hepatitis B, C or B/C/D fell slightly in 2011 compared with the previous era, the number with a primary diagnosis of hepatocellular carcinoma [HCC] is higher at 13% with the majority of these patients having a secondary diagnosis of CVH. When patients with either primary or secondary diagnosis of Hepatitis B, C or both are included, the overall incidence of CVH in new adult patients in 2011 was 45%.
16. Overall 1 year patient survival of all patients is 88% at 1 year, 81% at 5 years and 72% at 10 years. Children have a significantly better survival rate than adults with an actuarial survival of 72% at 25 years post-transplant.
17. Whilst older children had superior early survival than infants and babies, long term survival is similar. Older adult recipients (60-65 and >65 years) had poorer longer term outcomes.
- 18-19. Patient survival in 2000-04 cohort shows continued improvement in outcome for the first 10 years compared with earlier cohorts. This is seen in both children and adults. One year patient survival in 2010-11 cohort was 91% for all patients [96% for children, 90% for adults].



Summary

20. The type of primary deceased donor graft, (whole, reduced or split liver), had no significant effect on patient survival in children or adults. Reduced grafts in adults had worse early outcomes than whole or split-liver grafts.
21. Smaller children and babies weighing < 8 kg at the time of transplant had inferior early survival compared to heavier children but similar long term results.
22. Adult patients transplanted for biliary atresia or hepatitis virus co-infections had the best longer term survival while those whose primary disease was malignancy had a significantly lower survival rate. Longer term survival for patients transplanted for Hepatitis C was also lower.
23. In children, patient survival was similar for all disease groups though lower in patients whose primary disease was malignancy. There were no differences in survival between adults and children transplanted for fulminant hepatic failure [acute and sub-acute] with overall 5 year survival of 77%.
24. Recent cohorts of adult patients with a primary diagnosis of hepatitis B continue to show a significantly improved survival which is not seen in adult patients with hepatitis C as primary disease. Patients transplanted for malignancy continue to have a poor outcome but some improvement in longer term outcome is seen in patients transplanted since 2000.
- 25-26. Overall graft survival was 75% at 5 years. Survival was significantly worse in second and third grafts in both children and adults.
27. Overall split liver grafts have similar graft survival to whole liver grafts. Reduced grafts have lower survival in the early post-transplant years in both children and adults.
- 28-29. Vascular complications and rejection were the commonest indications for retransplantation. Eleven percent of retransplants were due to poor early graft function. Retransplantation for recurrent disease was most prevalent in adults [10% PSC, PBC, AIH and 9% HBV, HCV].
- 30-33. Sepsis is the most frequent cause of death in both adults and children. Full details of Miscellaneous and Other Graft Failure deaths are listed in Appendix V. Thirty-four percent of all deaths occurred within 6 months of transplant. Early graft failure was due to poor or no early graft function. By 1 year malignancy and graft failure from recurrent disease or chronic rejection cause most deaths. Deaths due to de novo malignancy and chronic rejection are increasing with longer survival time.
34. There was an increase in the number of cadaveric donors in 2011 with 243 grafts transplanted from deceased donors. The number of livers split to produce two transplantable grafts was 14 in 2011. Thirteen liver grafts donated after cardiac death were transplanted. The number of people on the waiting list at 31 December 2011 was slightly lower than the number on the waiting list at 31 December 2010.
35. Donor age has increased significantly in recent years. Long term graft survival trends lower in several older donor age groups.



Summary

36. Seventy patients [56 children, 13 adults] have now received a living donor graft with 10 performed in 2011. Sixty-five were transplanted as a primary graft, 4 as second and 1 as a third graft. The median age of the donors was 34.2 years with a range of 20.1 to 54.5 years. One adult graft was a domino whole liver graft.
37. The number of patients listed for transplantation continued to increase in 2011 with 186 remaining on the waiting list at 31 December 2011. Patient delistings due to death, becoming too ill or tumour [HCC] progression accounted for 8% of all delistings while 253 [48%] were transplanted. Forty three patients were listed as urgent in 2011 [15 with initial listing as Category 1 and 28 Category 2]. Twelve [80%] of Category 1 and 24 [86%] of Category 2 patients had a positive outcome.
- 38-39. Median waiting times tended to be higher in 2011 in some blood groups. Blood group B patients had the longest waiting times.
40. Cancer in liver transplant recipients was analysed from two perspectives. Firstly, those who had a liver cancer diagnosis at the time of transplantation (as primary, secondary or incidental) and secondly those who developed a cancer post transplantation (de novo skin and de novo non skin cancer). Overall 701 (19%) patients were transplanted who had a liver malignancy-271 (7%) as a primary diagnosis and 430 (12%) as a secondary diagnosis or incidental tumour, with Hepatocellular carcinoma being the most common. Post transplant 102 (15%) of these patients developed a recurrent cancer whilst in 90 (13%) of these patients' death was related to their initial cancer.
- 41-43. There continues to be an increase in the number of patients being transplanted for primary malignancy evident in the most recent patient cohort of 2008-2011.
- 43-45. Four hundred and thirty patients [12%] had liver cancer as a secondary or incidental diagnosis with hepatocellular carcinoma the most common. Of these 46 (11%) died from their malignancy. Those with cholangiocarcinoma had significantly poorer survival.
46. Patient survival was significantly worse in the 701 (19%) patients with pre transplant liver malignancy compared with patients with other forms of liver disease.
- 47-48. Two hundred and seventy five de novo non-skin other types of cancers developed in 257 patients (7%). Sixteen patients developed more than one de novo cancer. Forty patients had a pretransplant liver cancer. One hundred and two (40%) patients died from these types of cancer. The three most common categories of de novo non-skin cancer were - Cancers of the alimentary tract (98), lymphoma (74) and genitourinary (36).
- 49-50. The incidence of de novo non-skin cancers appears to now be related to the type of pre transplant underlying liver disease. Most notable is the incidence of de novo non-skin malignancy in patients with underlying Primary Sclerosing Cholangitis and HCV, both being statistically significant ($p < 0.0001$).
51. Six hundred and seventeen patients (18%) developed 3508 skin cancers with 237 patients having multiple skin cancer types and 26 developed melanoma.

The cumulative risk of diagnosis of any cancer post transplant is approaching 40% by 20 years.

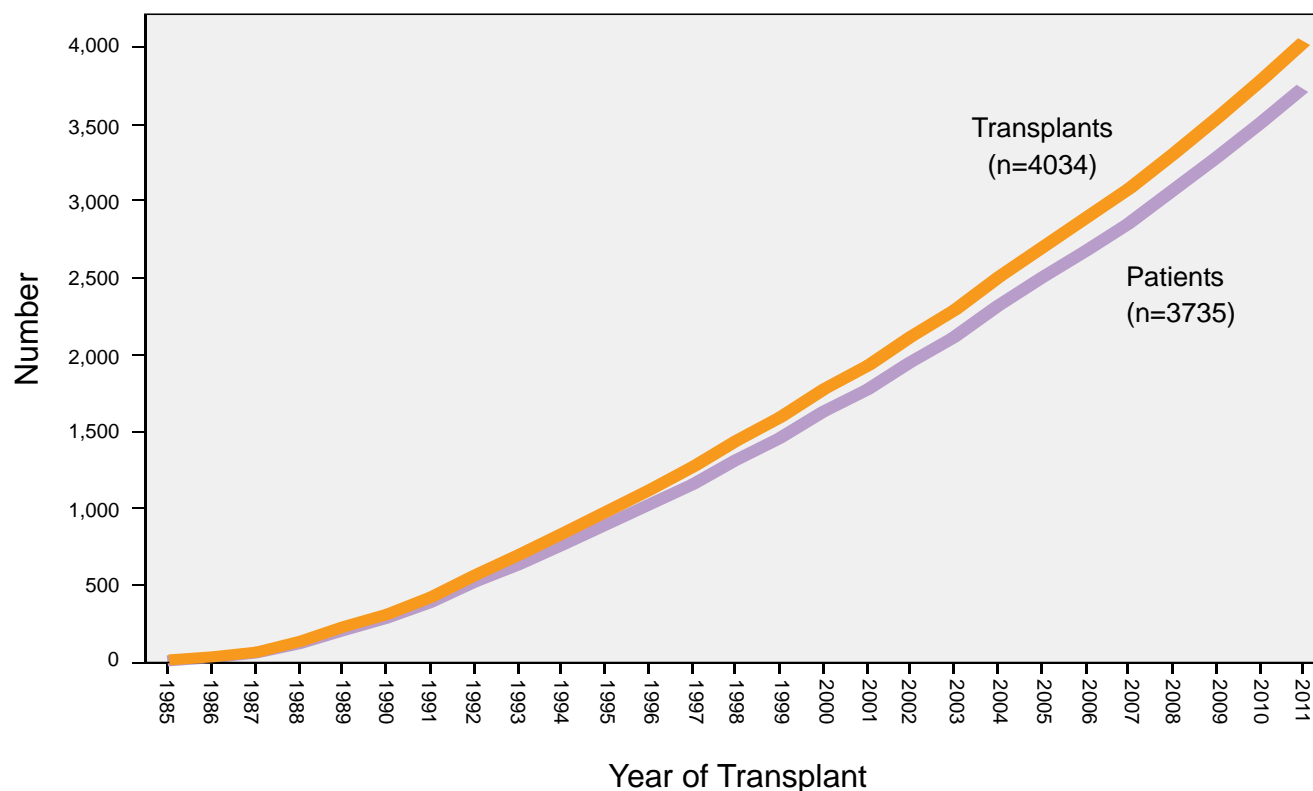




Section 1

Demographic Data

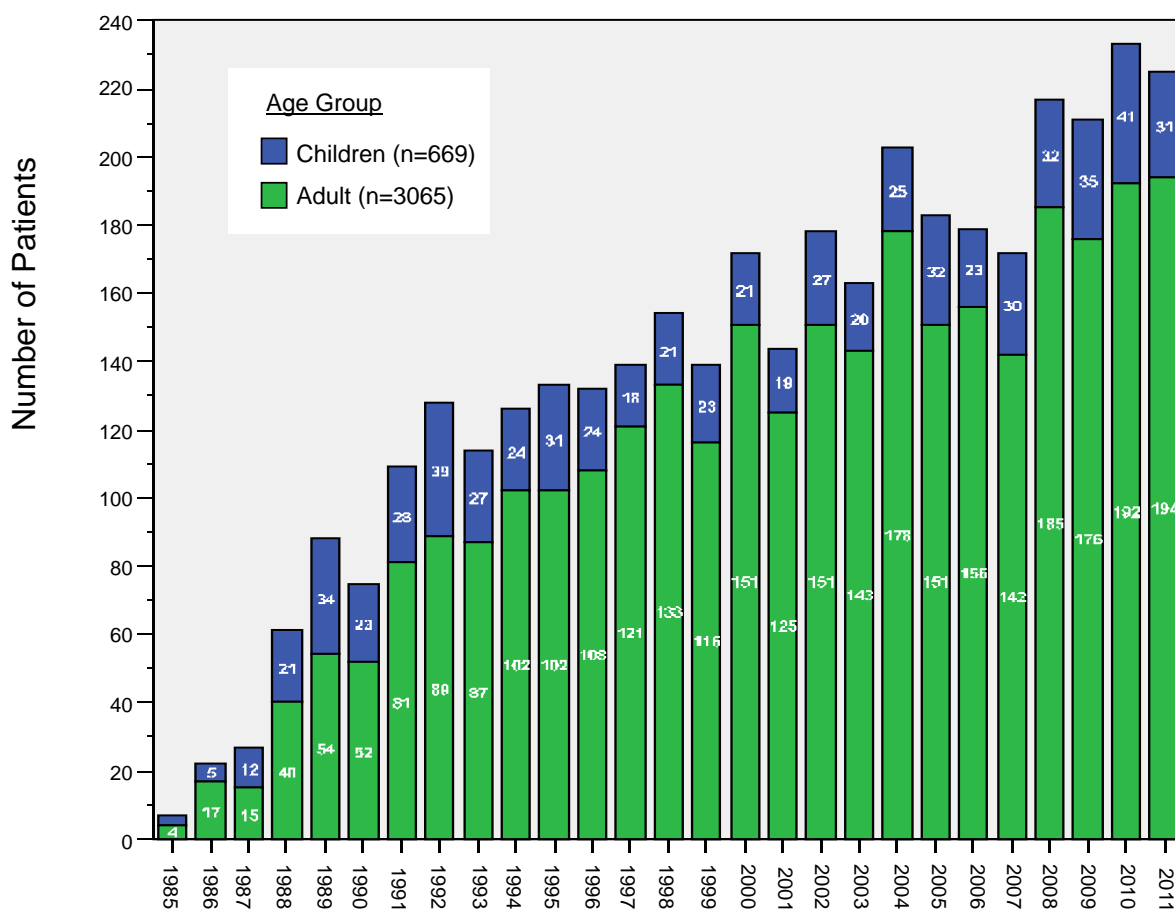




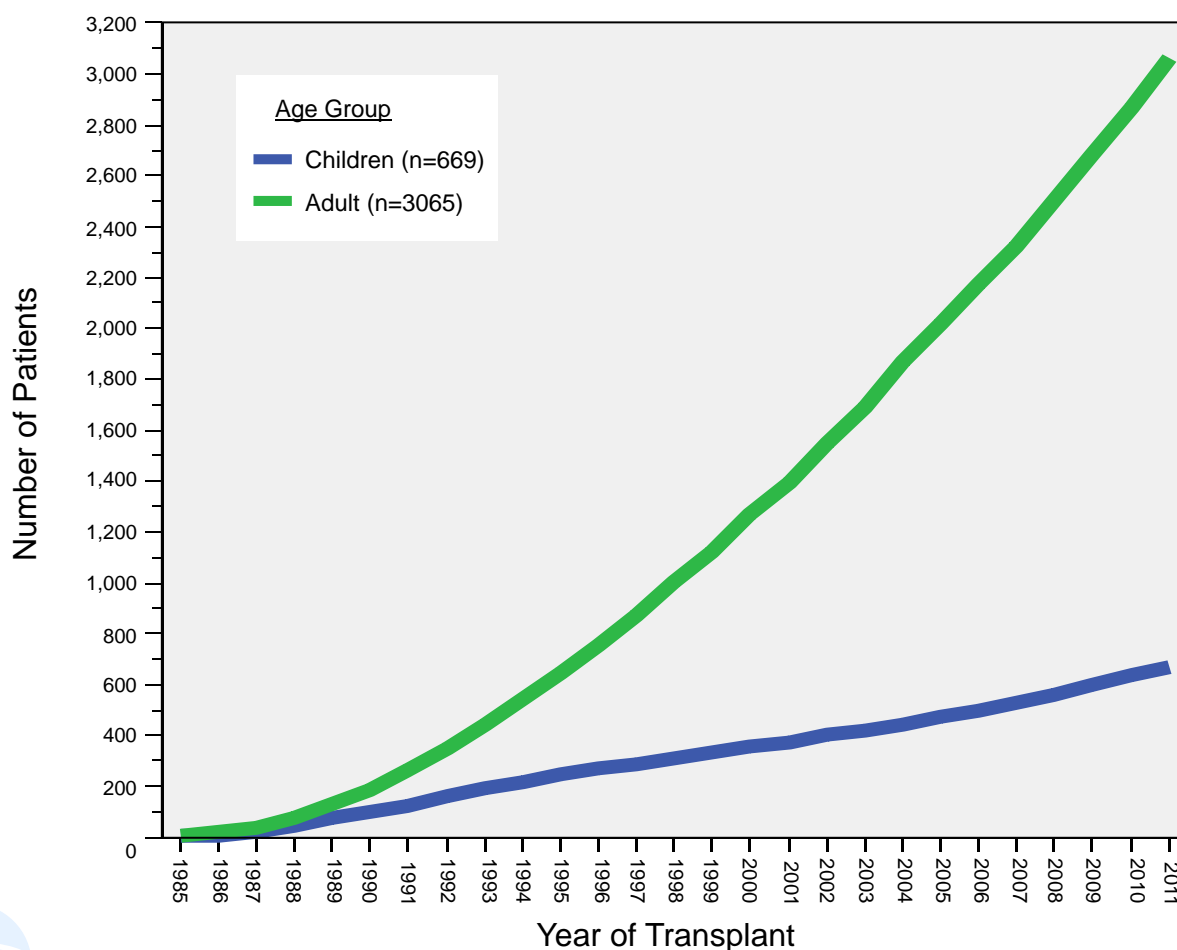
Summary Statistics - Age and Gender

ALL PATIENTS TRANSPLANTED

	Children [<16y]	Adults	Total
Patients	670	3065	3735
Age			
<i>Mean ± SD</i>	4.5 ± 4.5y	48.3 ± 11.6y	40.5 ± 19.9y
<i>Median</i>	2.4y	50.2y	47.4y
<i>Range</i>	24d - 15.9y	16.0 - 73.1y	24d - 73.1y
Gender			
<i>Female</i>	360 (54%)	1087 (35.5%)	1447 (39%)
<i>Male</i>	310 (46%)	1978 (64.5%)	2288 (61%)
Surviving	536 (80%)	2193 (72%)	2729 (73%)

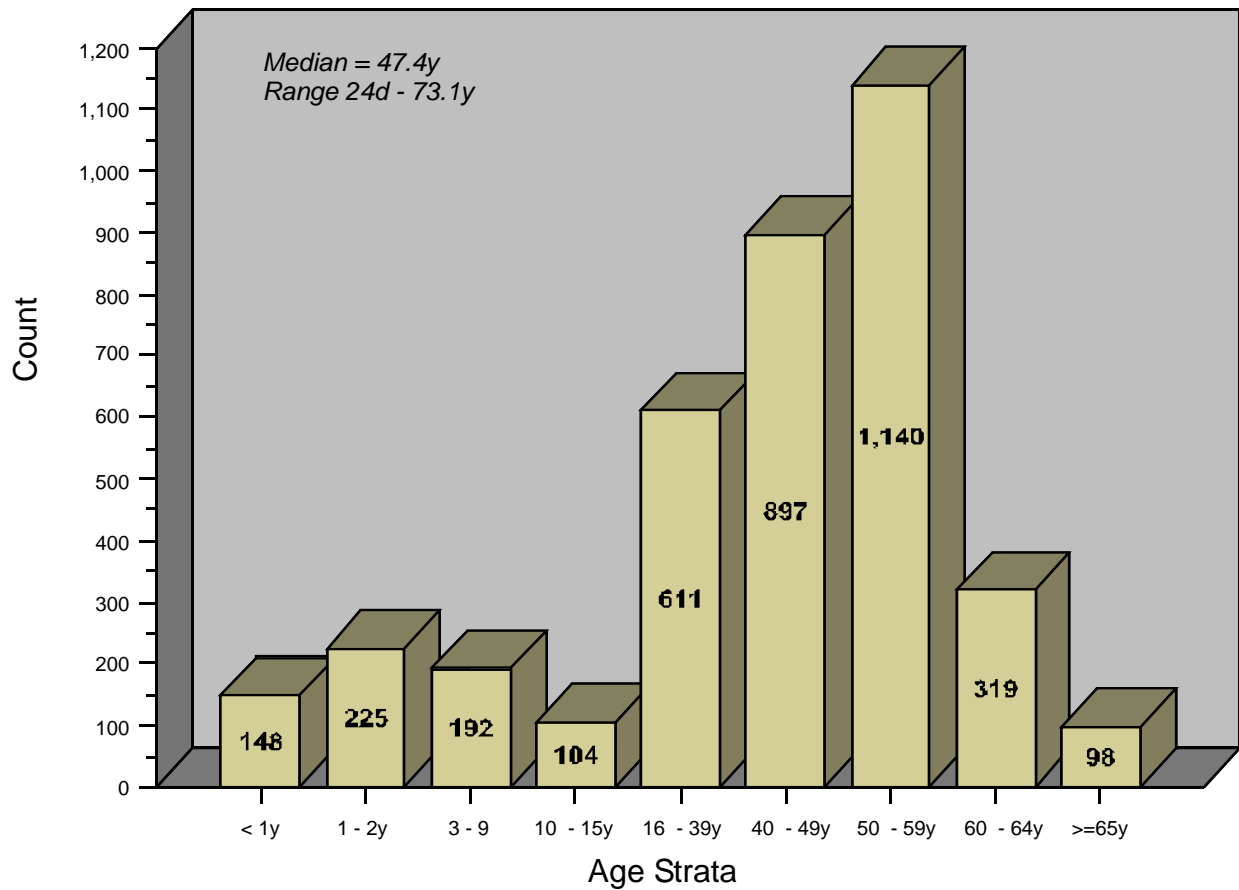


Cumulative Number of New Patients Transplanted

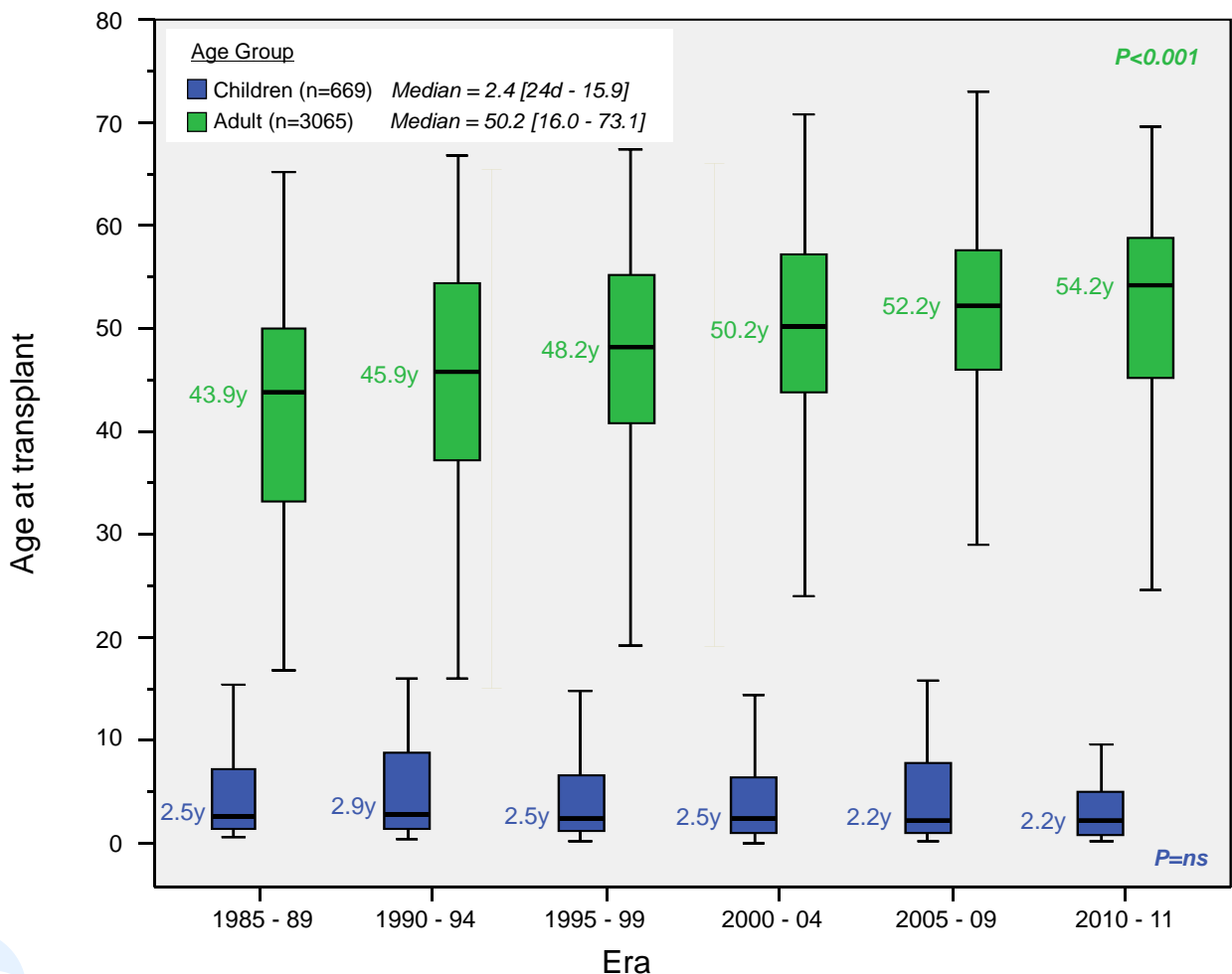


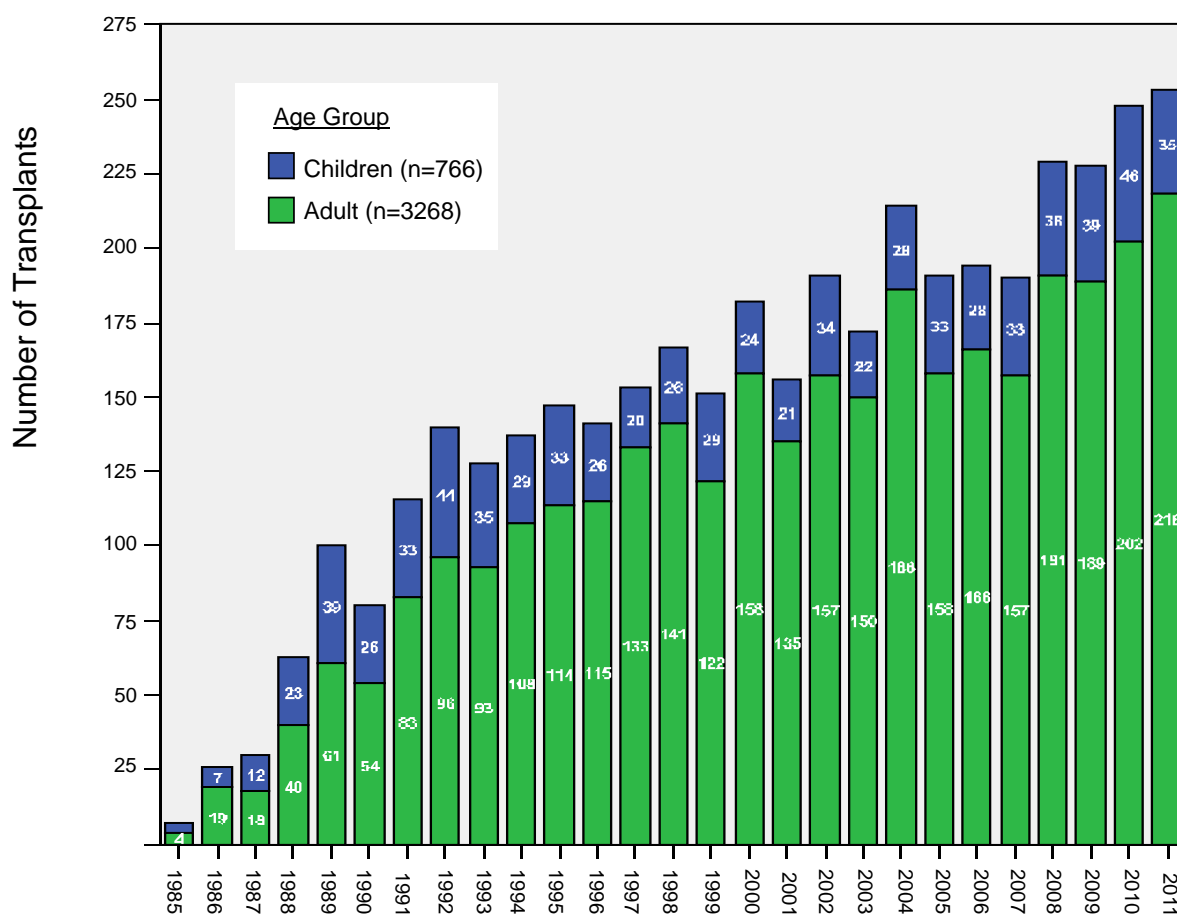
Number of Recipients By Age at Primary Transplant

N=3735

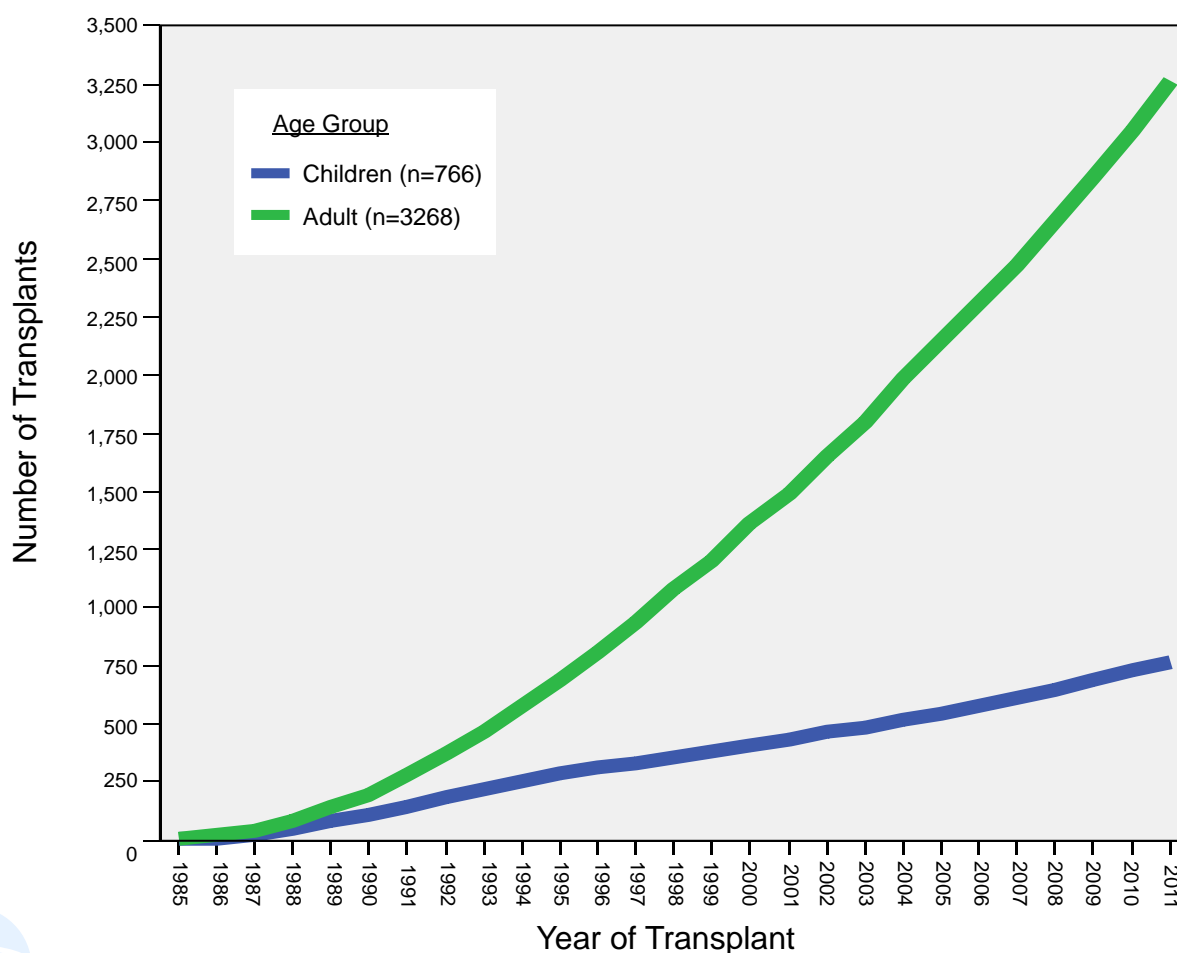


Age at Primary Transplant by Era





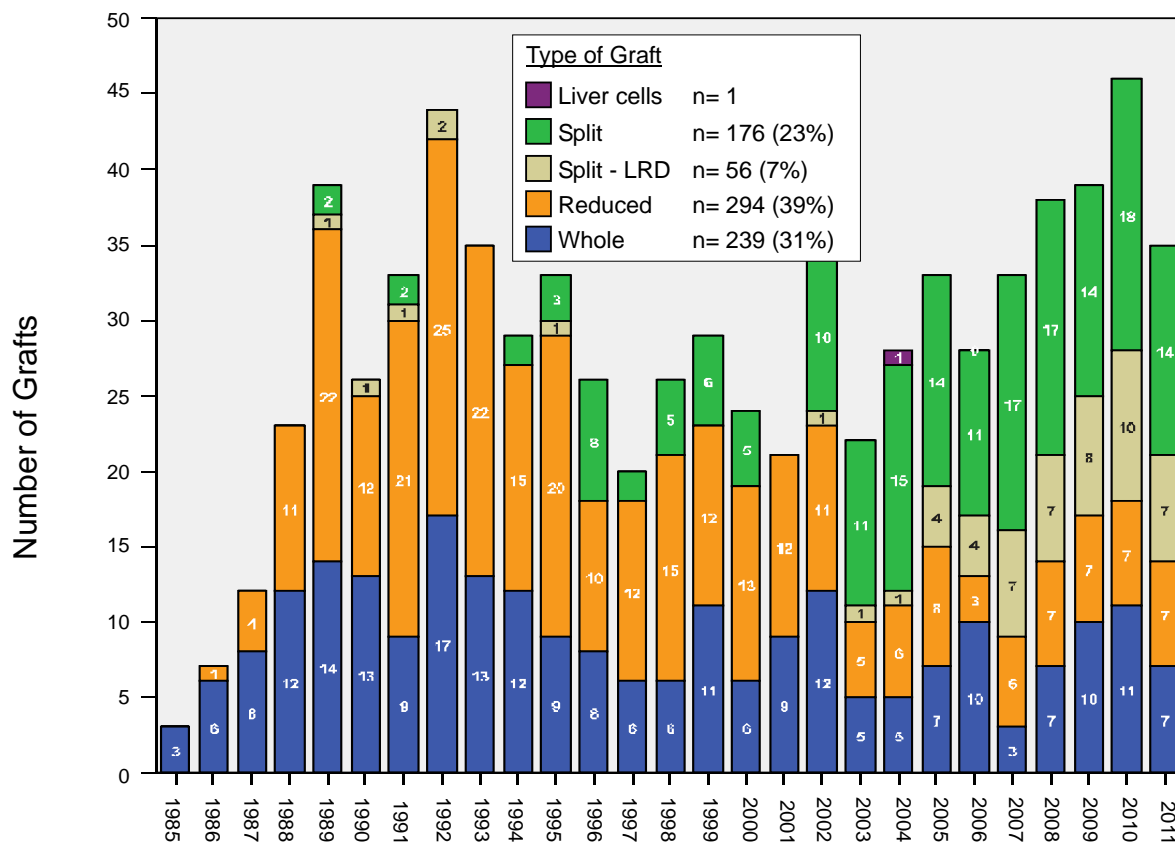
Cumulative Number of Transplants



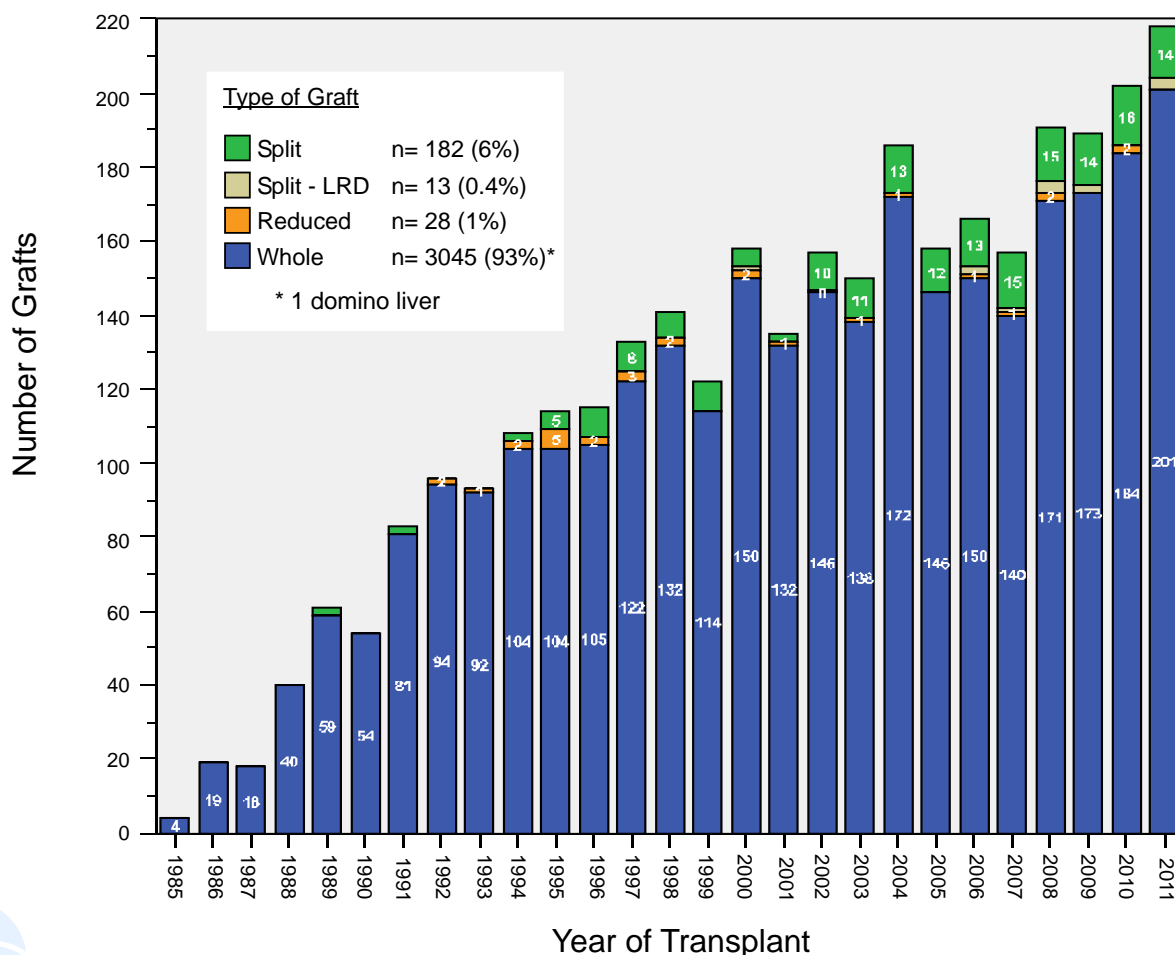
Type of Graft by Year Split vs Reduced vs Whole



Children (n = 766)



Adults (n = 3268)

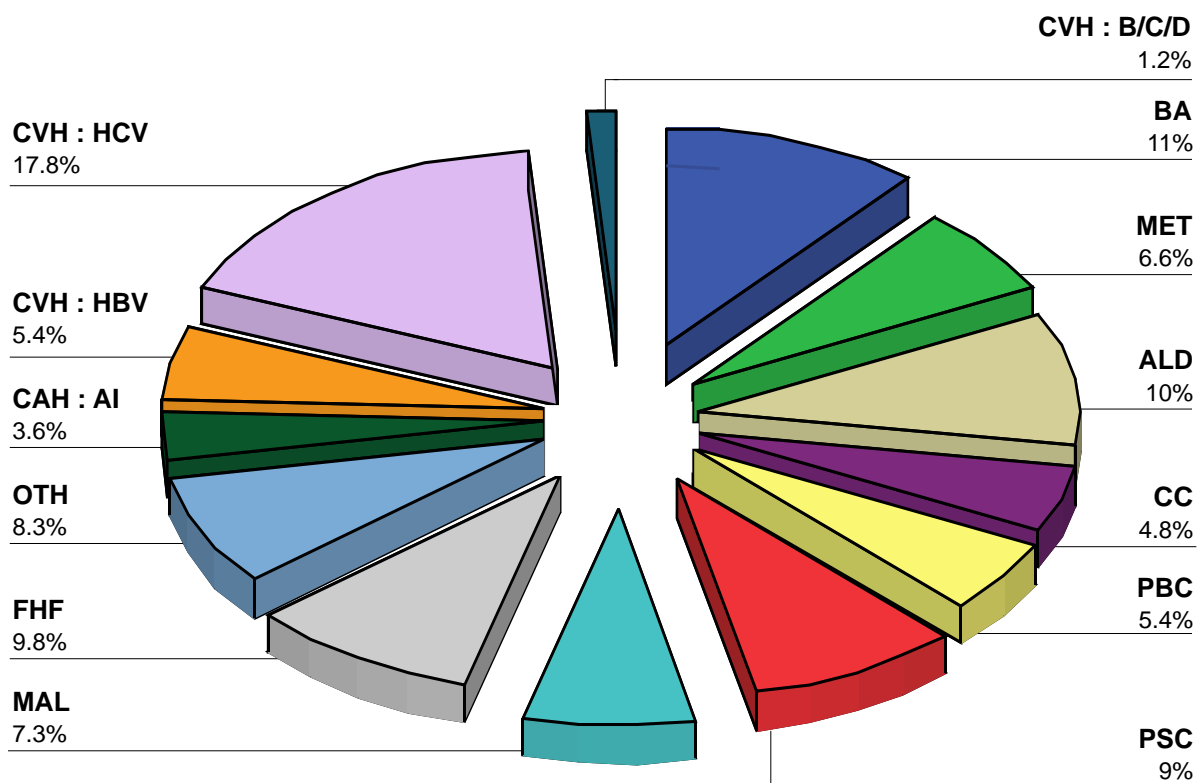




Section 2

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 : HBV	- Chronic viral hepatitis B
CVH : HCV	- Chronic viral hepatitis C
CVH : B/C/D	- Chronic viral hepatitis B / C / D

* See Appendices for details

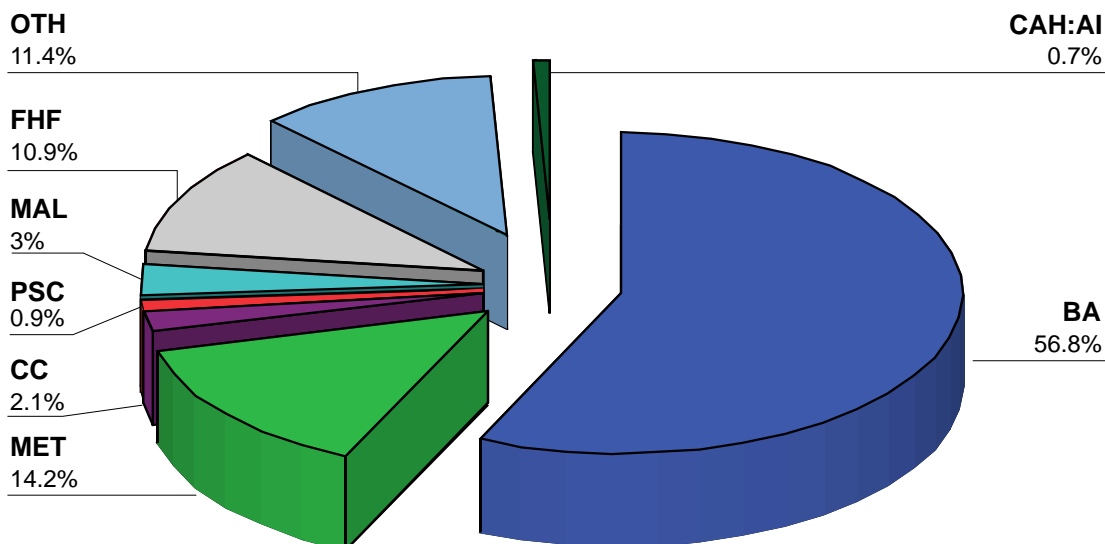
Primary Diseases of Children

n = 669

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REPORT

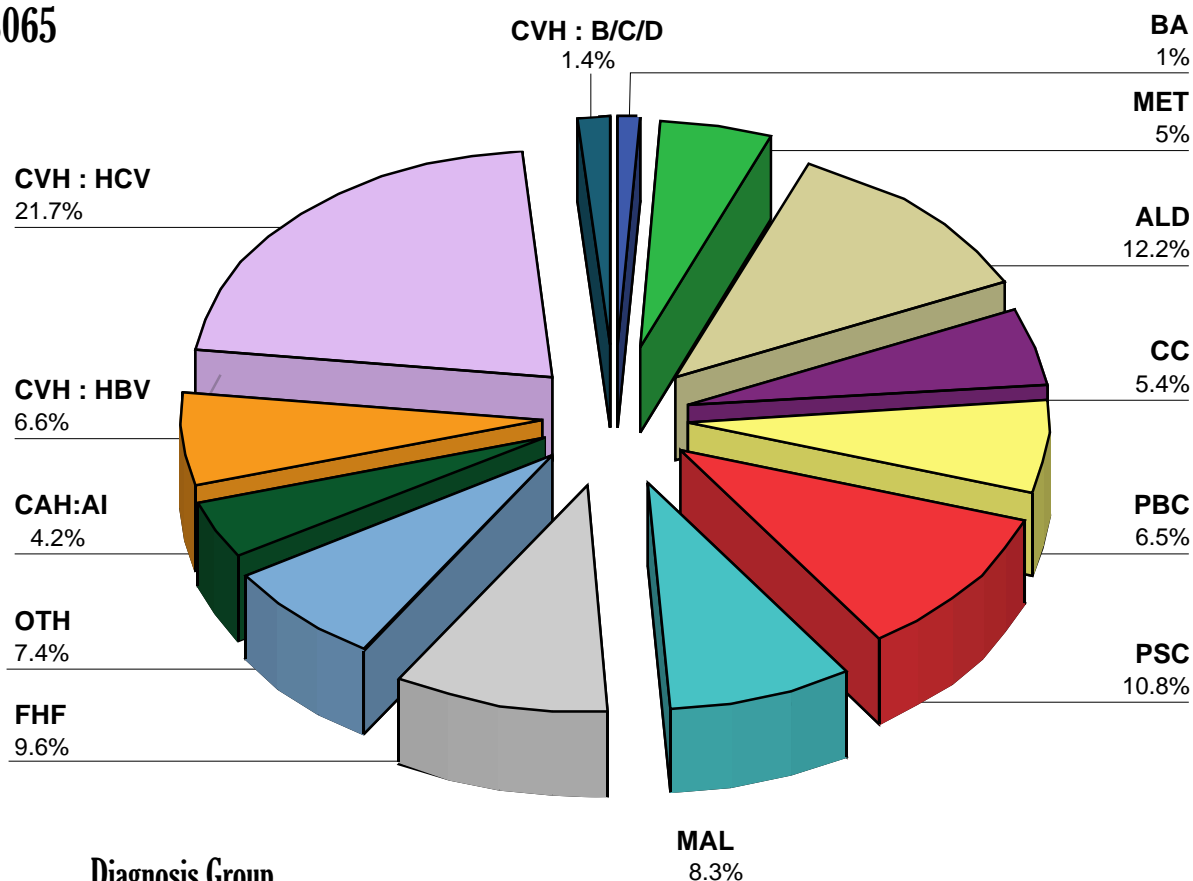


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Primary Diseases of Adult Recipients

n = 3065

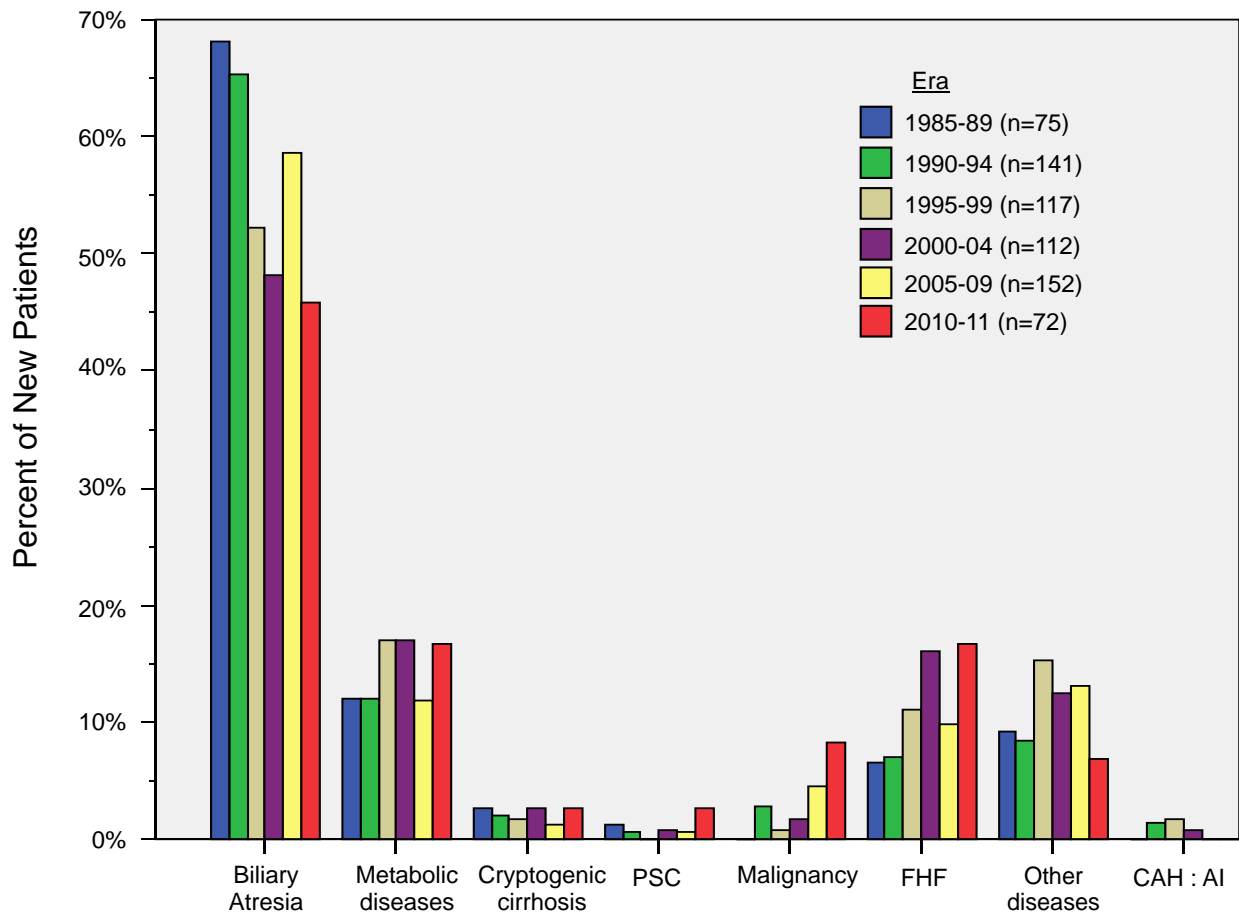


Diagnosis Group

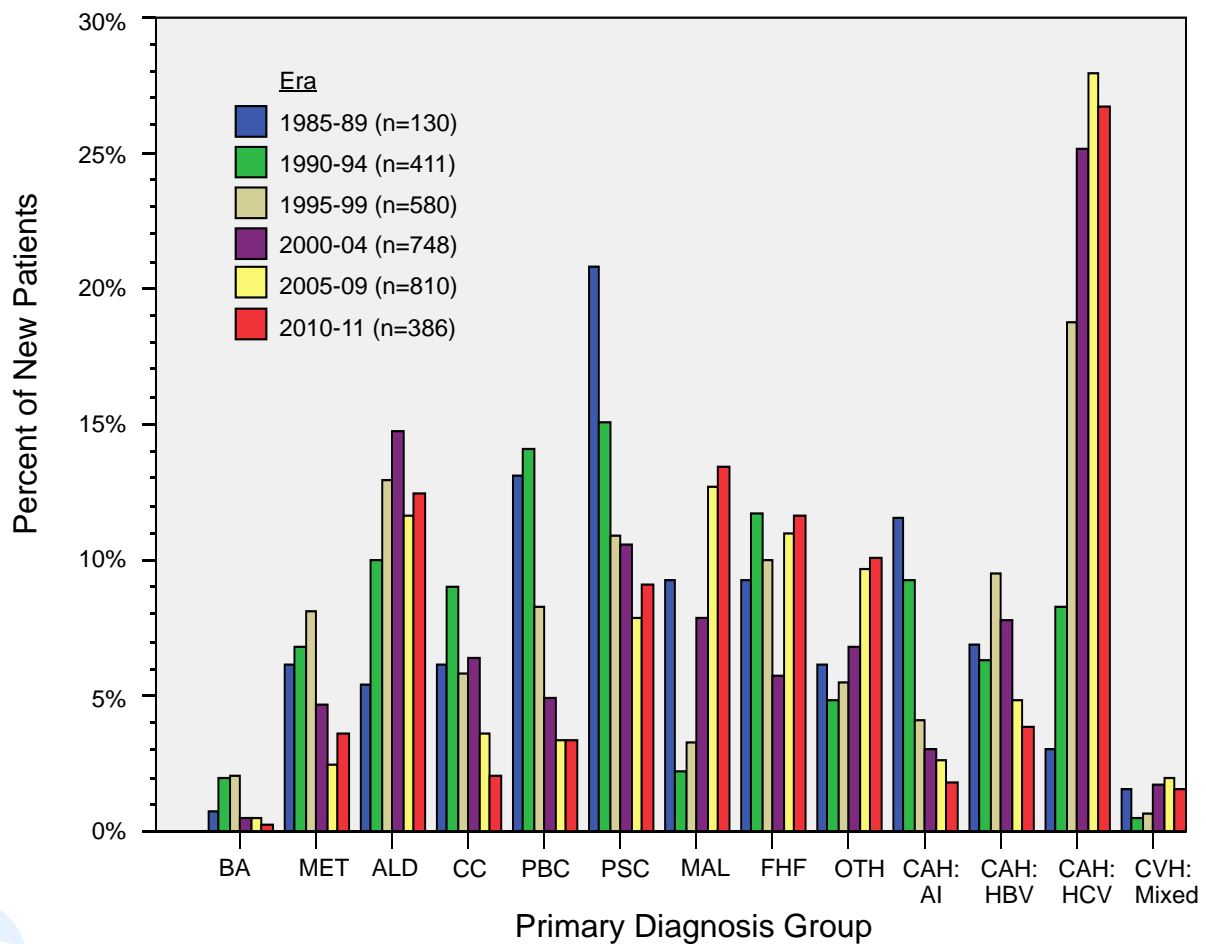
BA	- Biliary atresia	MAL	- Malignancy
MET	- Metabolic diseases	FHF	- Fulminant hepatic failure
ALD	- Alcoholic cirrhosis	OTH	- Other diseases
CC	- Cryptogenic cirrhosis	CAH : AI	- Chronic active hepatitis [autoimmune]
PBC	- Primary biliary cirrhosis	CVH : HBV	- Chronic viral hepatitis B
PSC	- Primary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

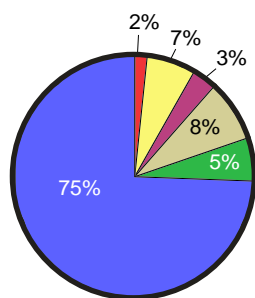


Children (n=669)

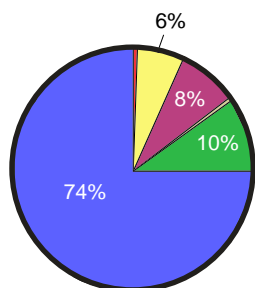


Adults (n = 3065)

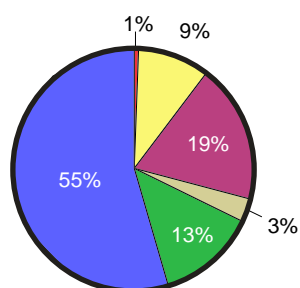




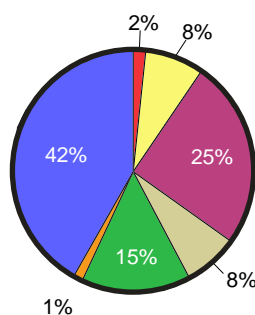
— 1985 - 89
(n=130)



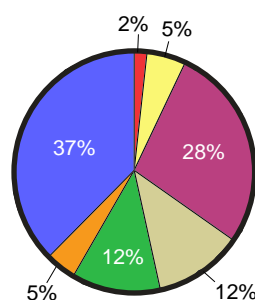
— 1990 - 94
(n=411)



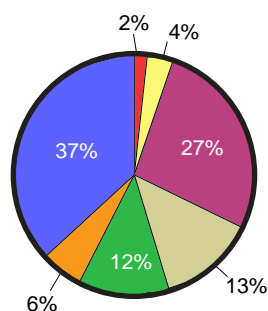
— 1995 - 99
(n=580)



— 2000 - 04
(n=748)

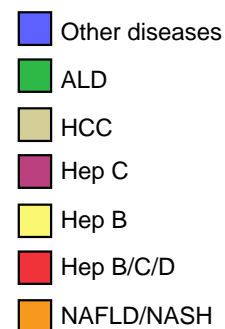


— 2005 - 09
(n=810)

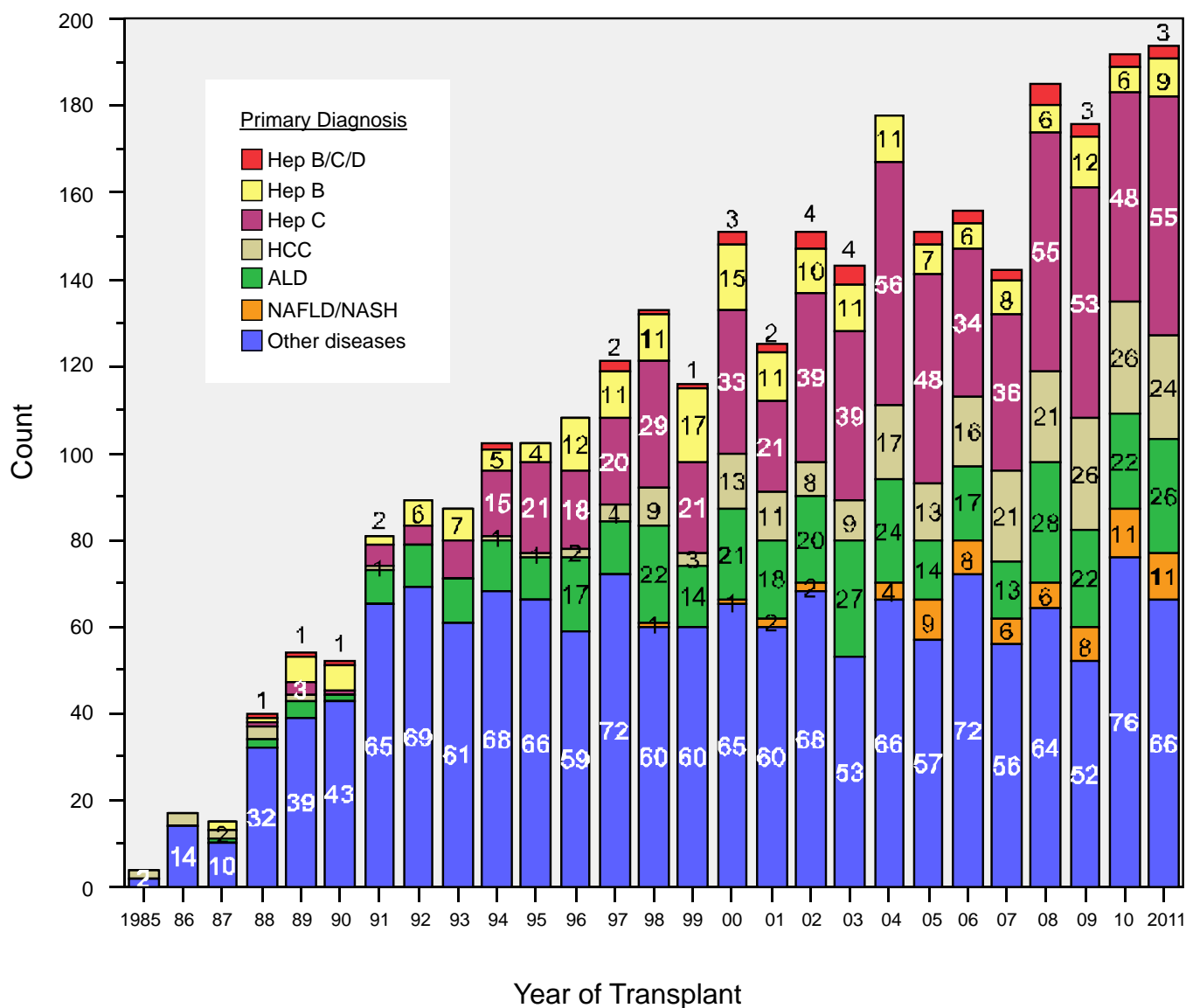


— 2010 - 11
(n=386)

Adult Diagnosis



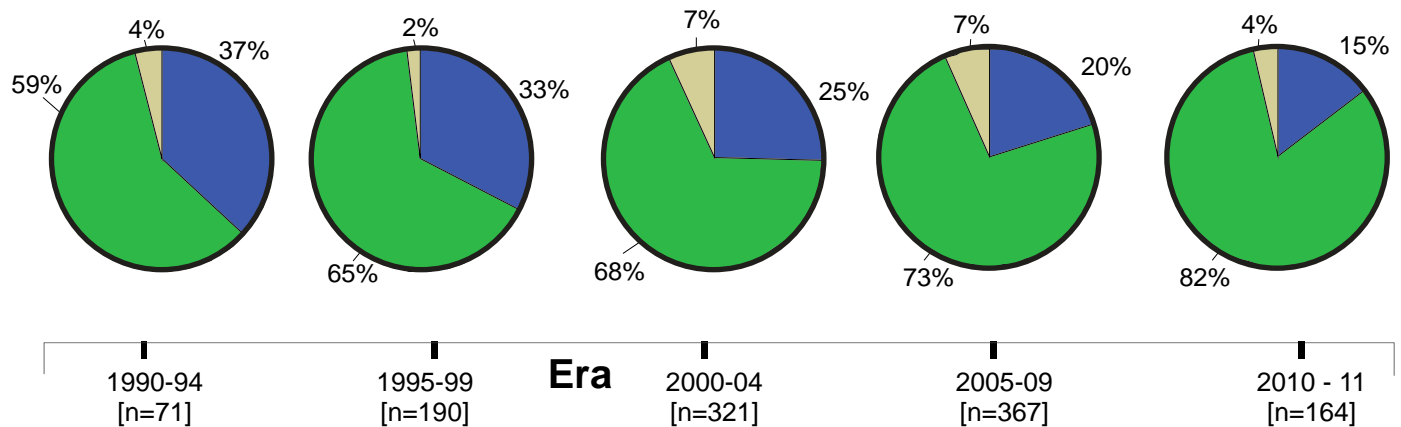
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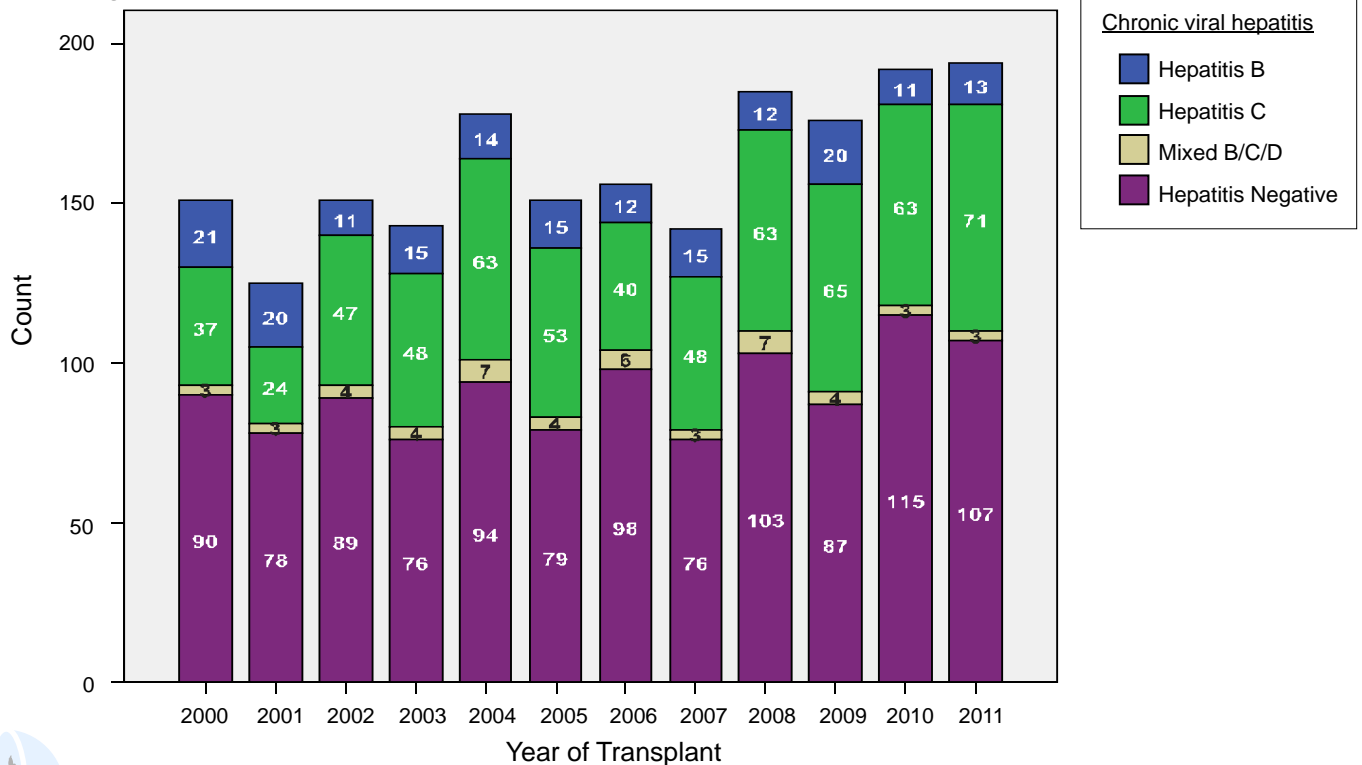


			Secondary / Tertiary diagnosis					
Primary Diagnosis		n =	Hepatitis C	Hepatitis B	Hepatitis B,C	HCC	NAFLD	ALD
	Hepatitis C	664		8		163	2	165
	Hepatitis B	203	4			71		4
	Hepatitis BD/BC/BCD	42				5		7
	HCC + cirrhosis	237	107	71	5		5	34
	ALD	375	13	3		45	5	
	NAFLD	69		2		11		1
	Other	1475	15	7		45	3	22
	TOTAL	3065						

Type of Chronic Viral Hepatitis in Adult Patients



Hepatitis diagnosis

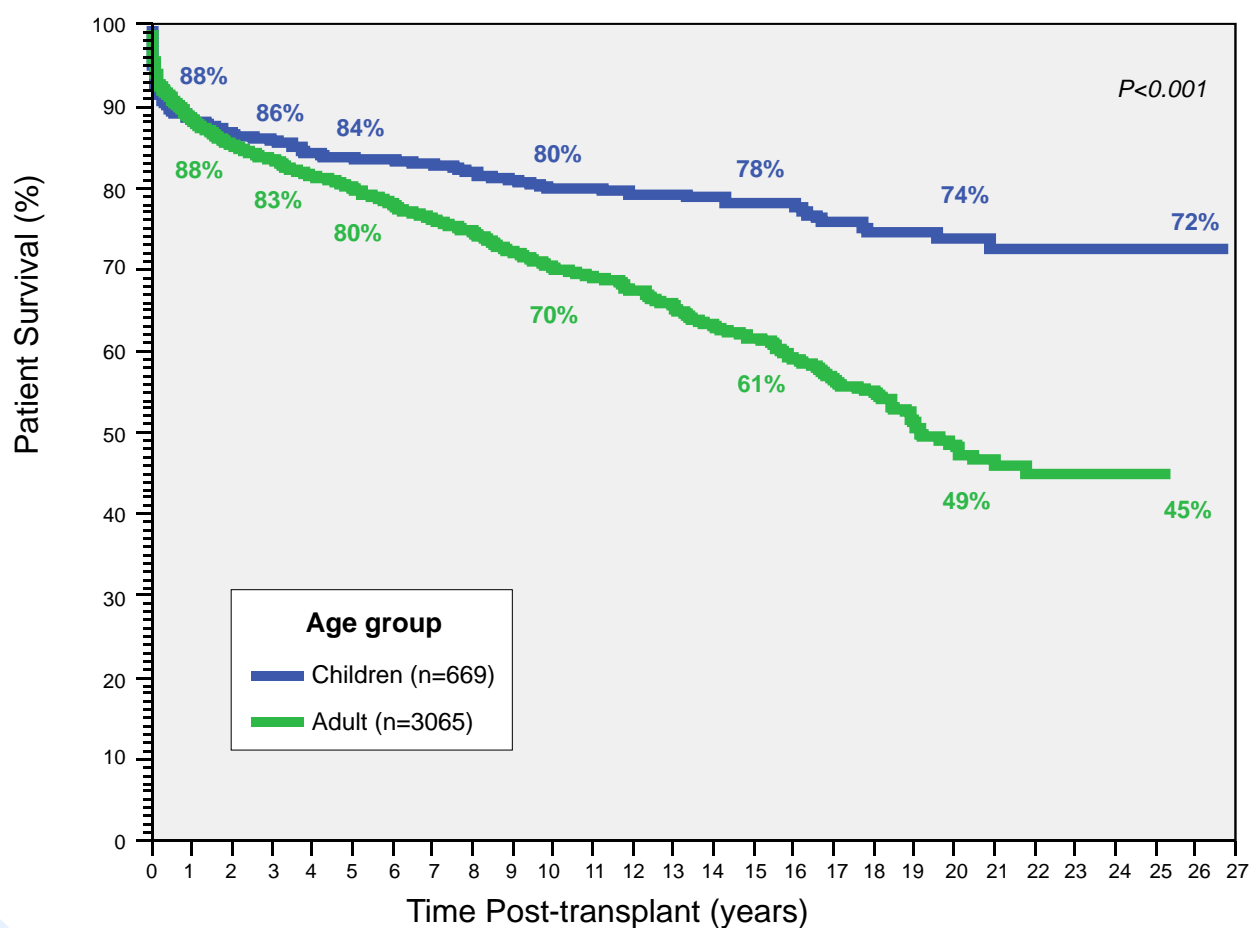
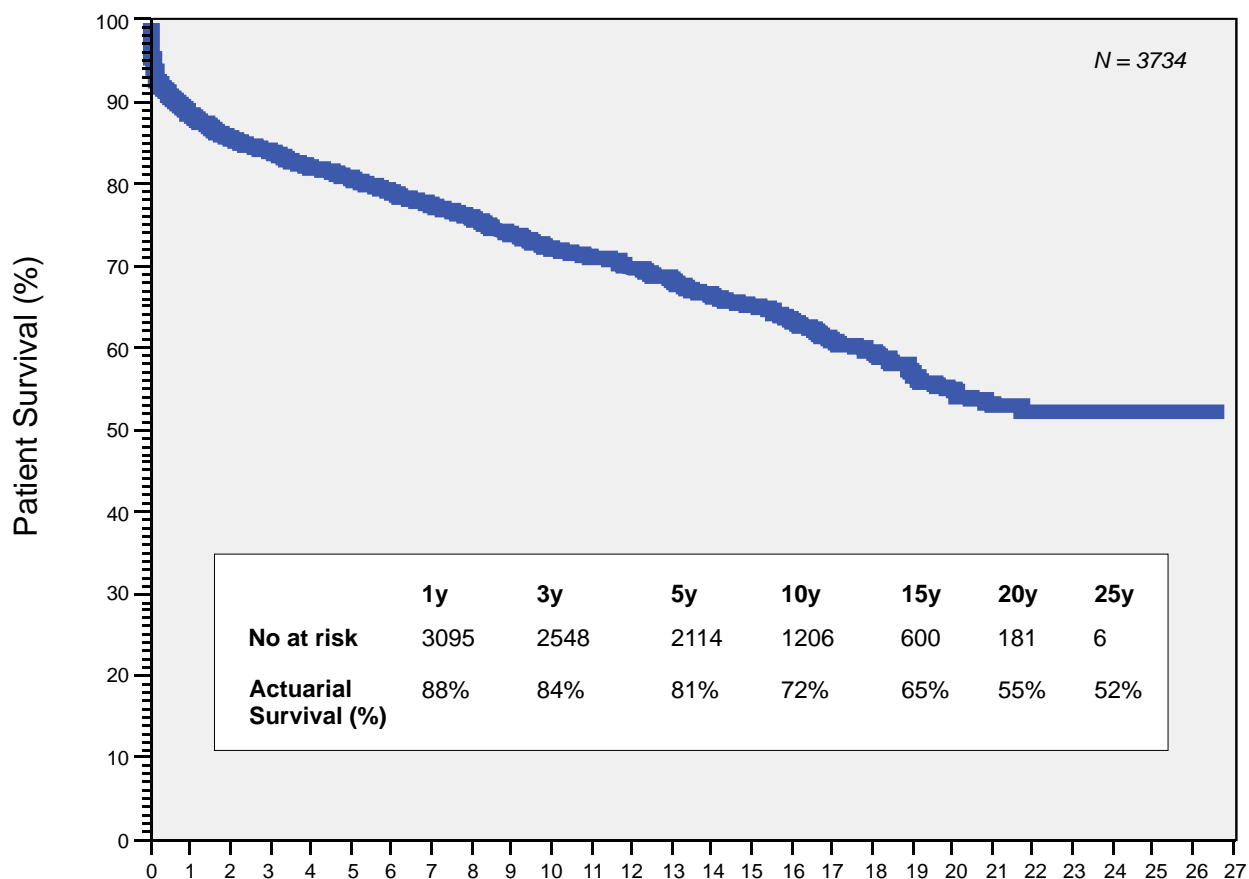




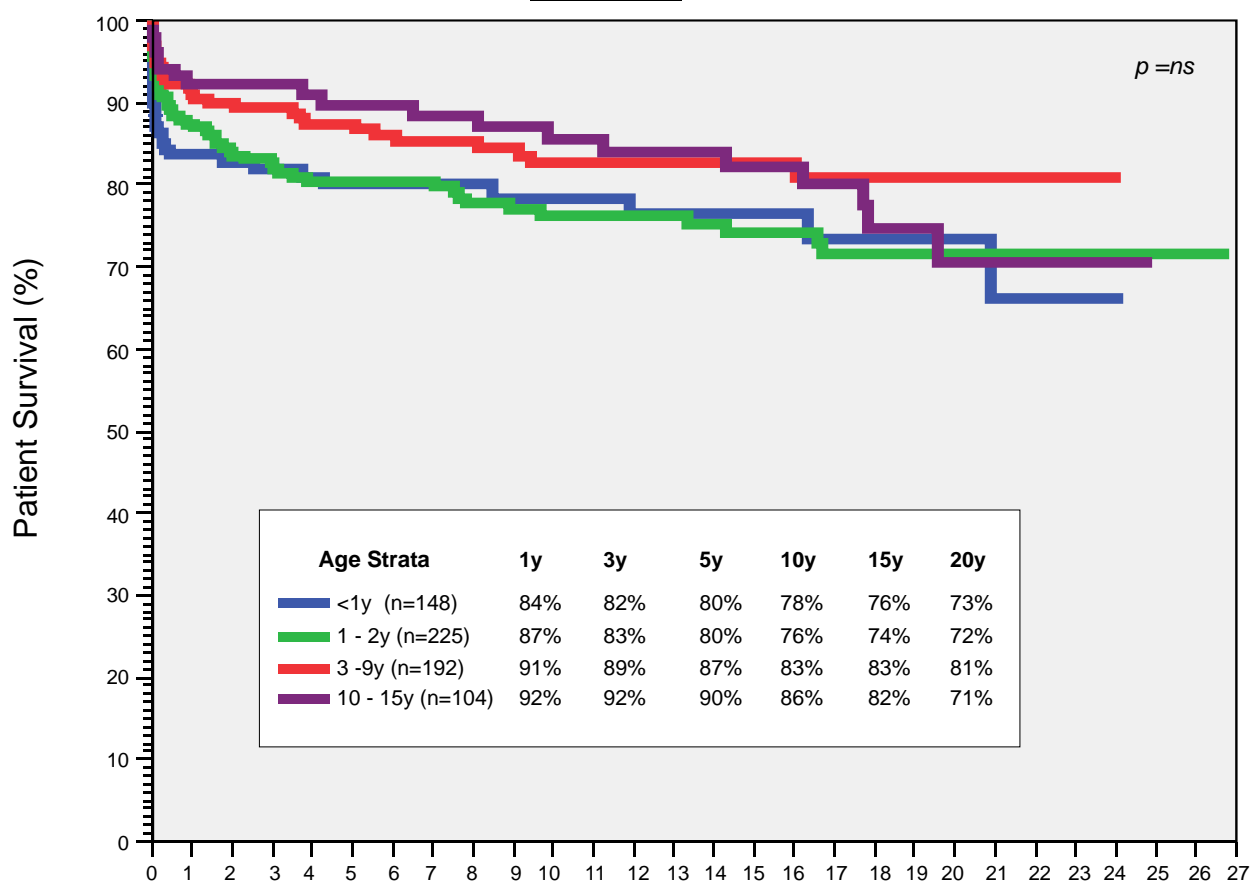
Section 3

Patient Survival

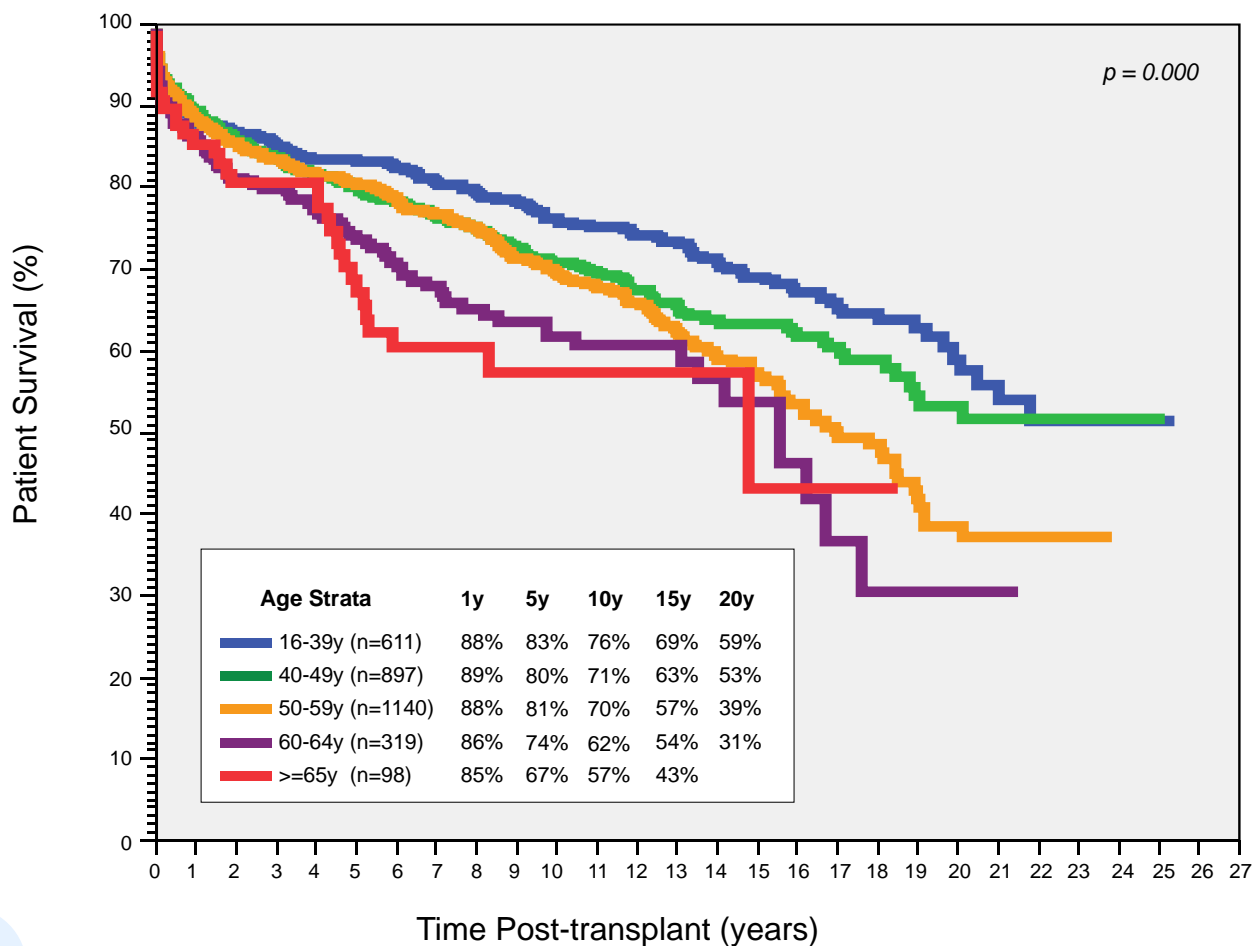


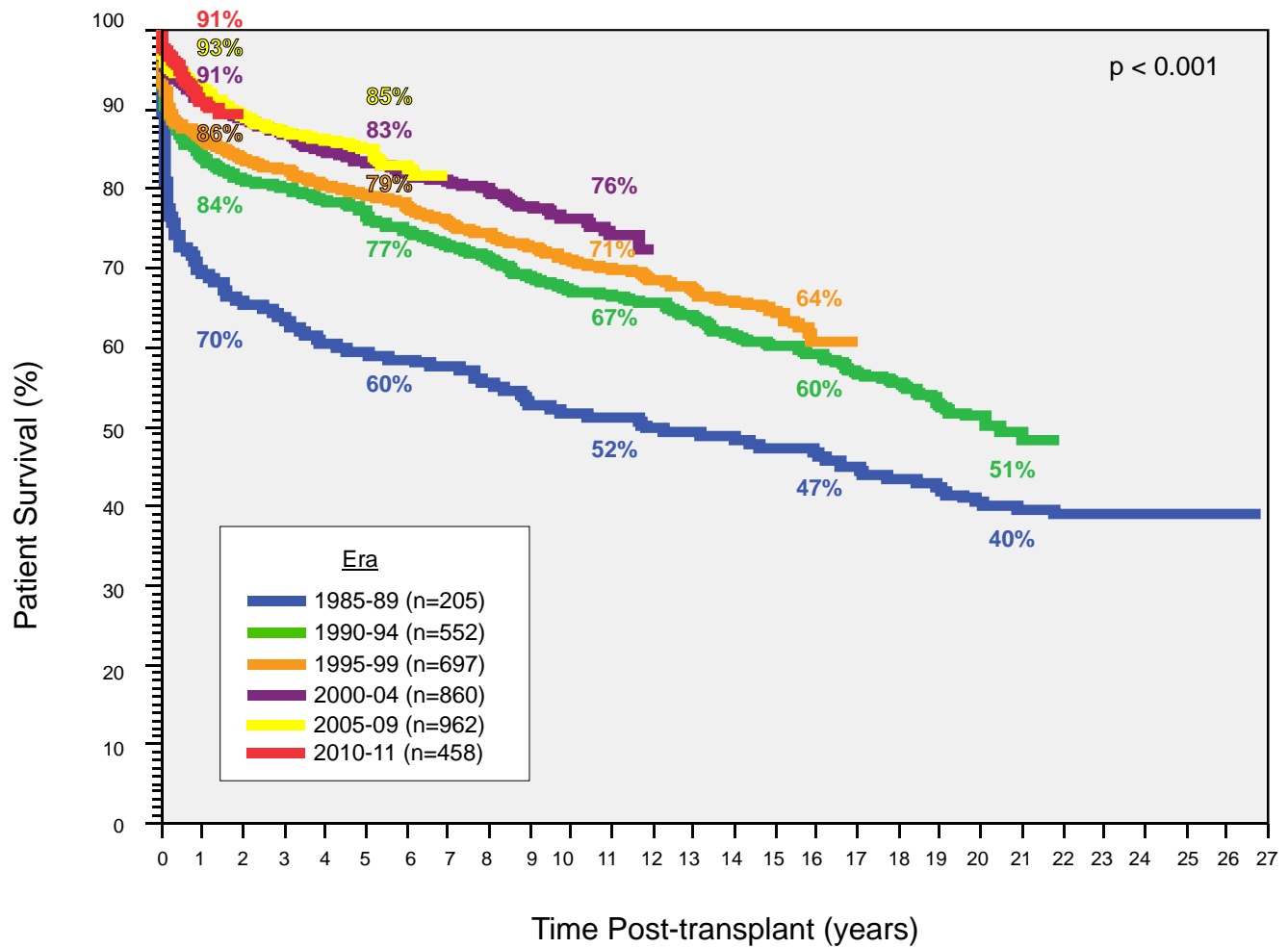


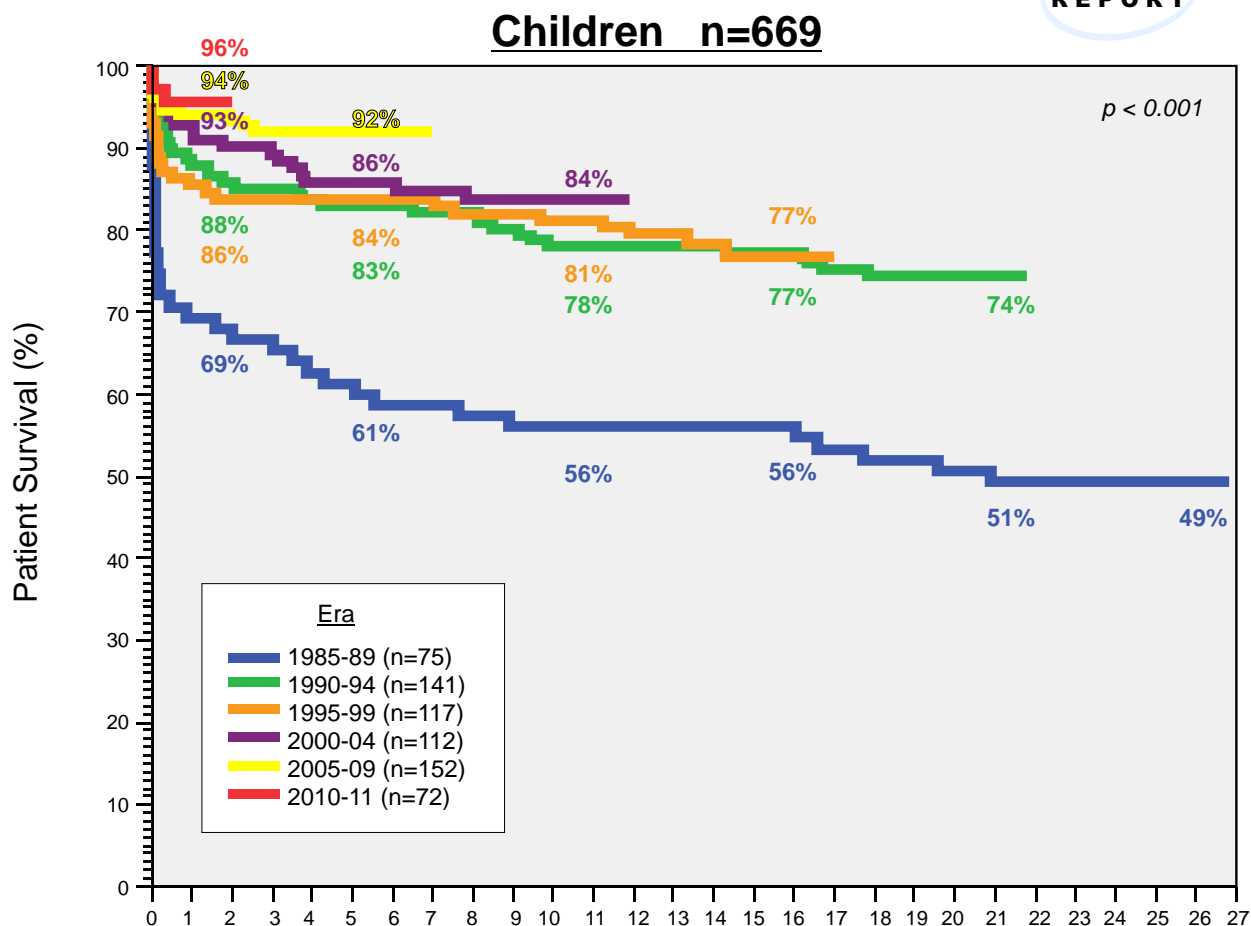
Children n = 669



Adults n = 3065

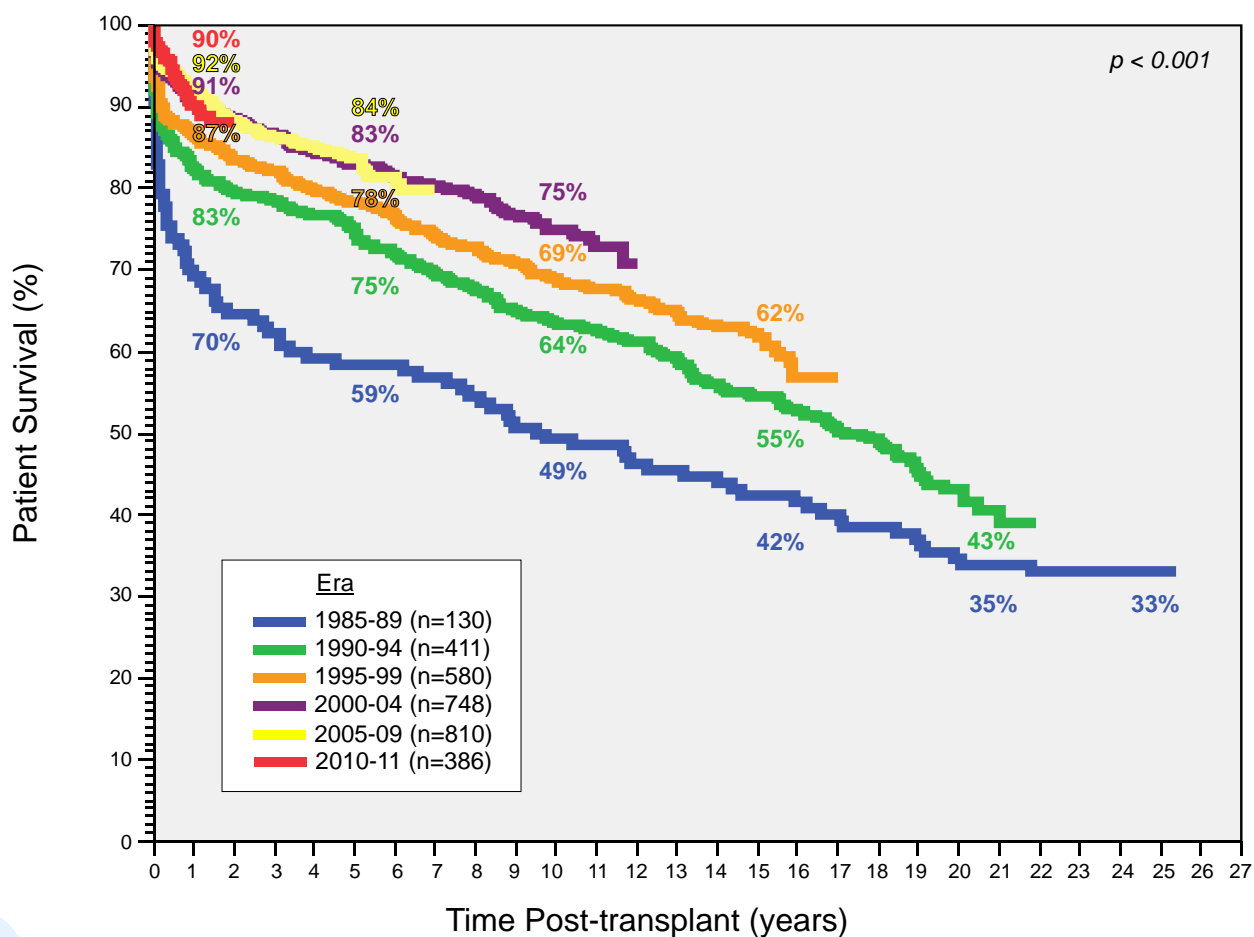






Patient Survival - Adults

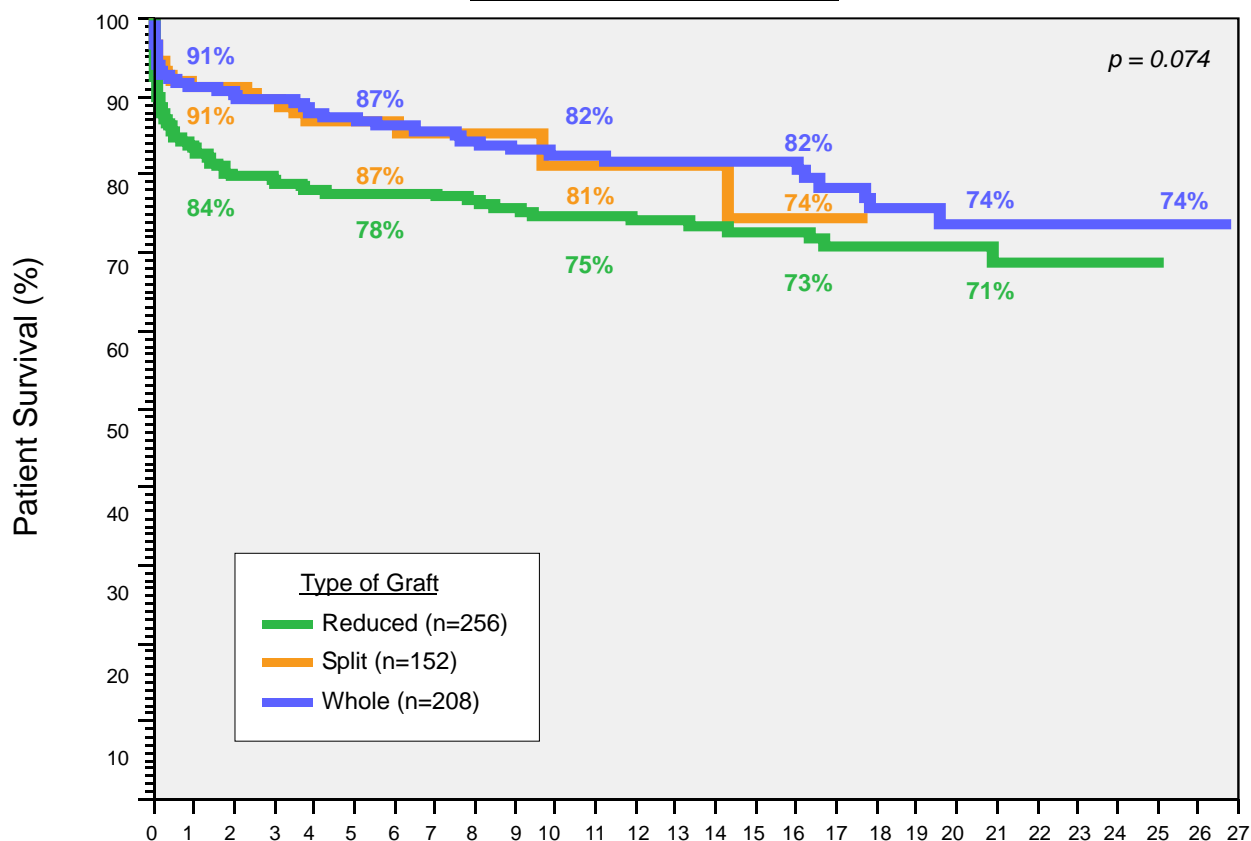
Adults n = 3065



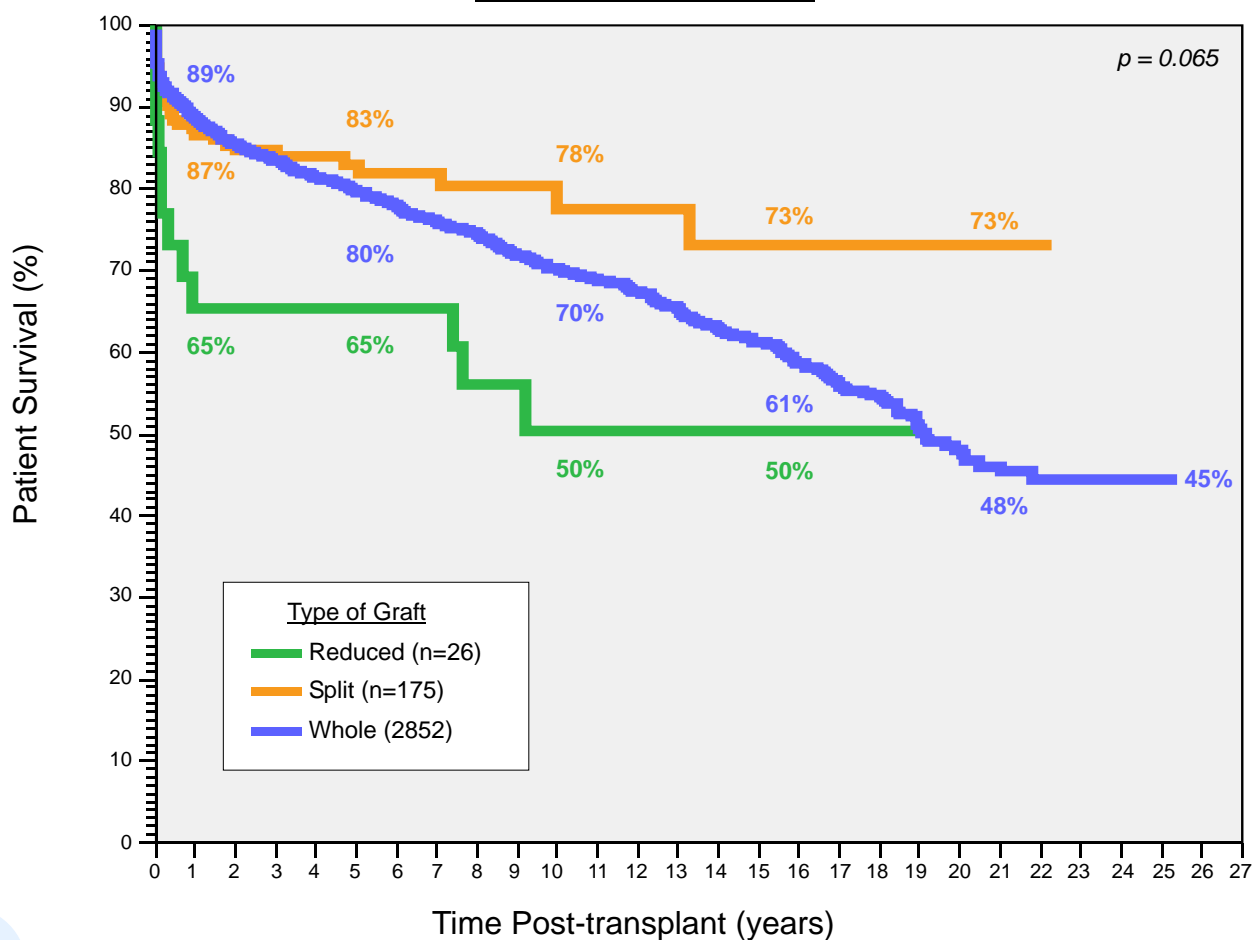
Patient Survival by Type of Primary Graft [Deceased donors]

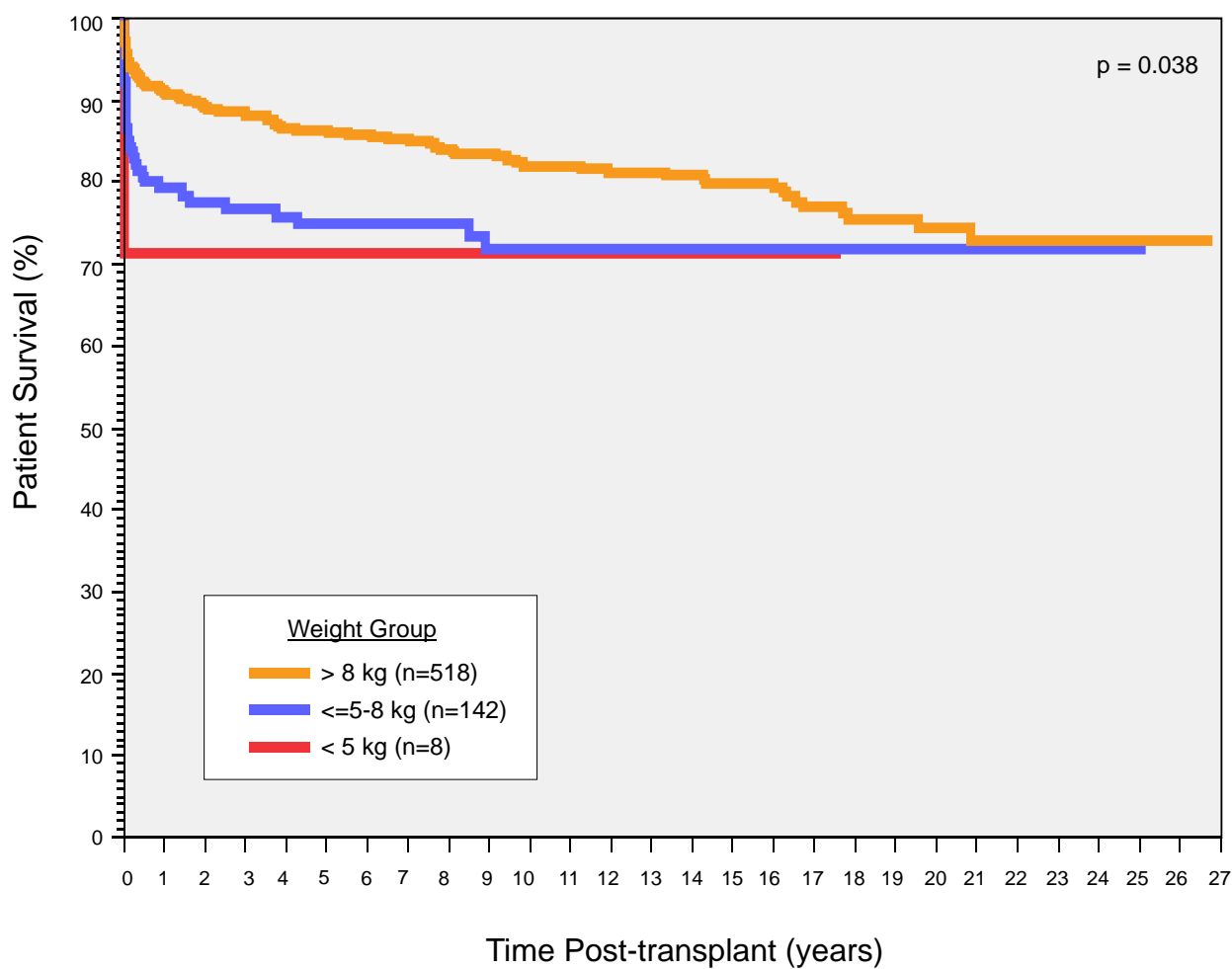


Children - n = 616



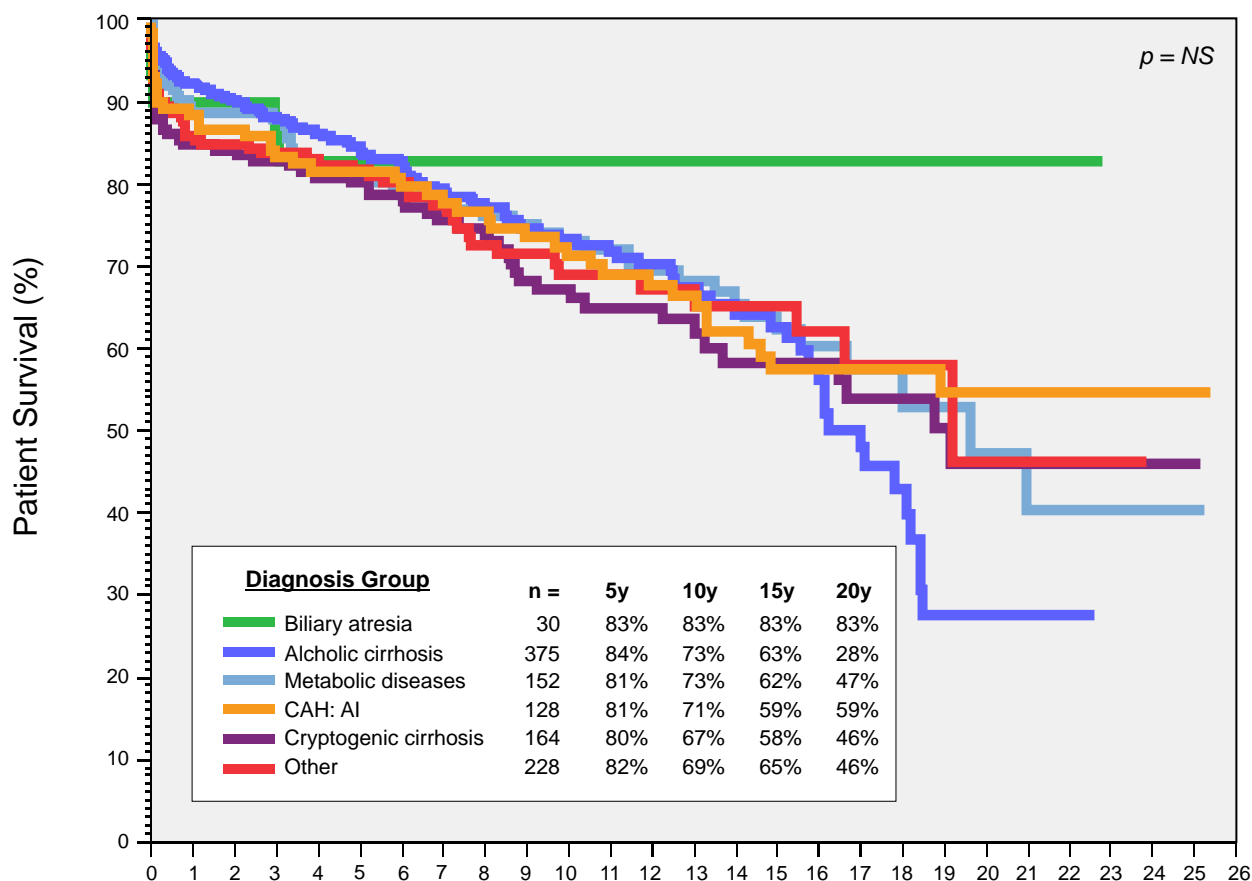
Adults - n = 3053



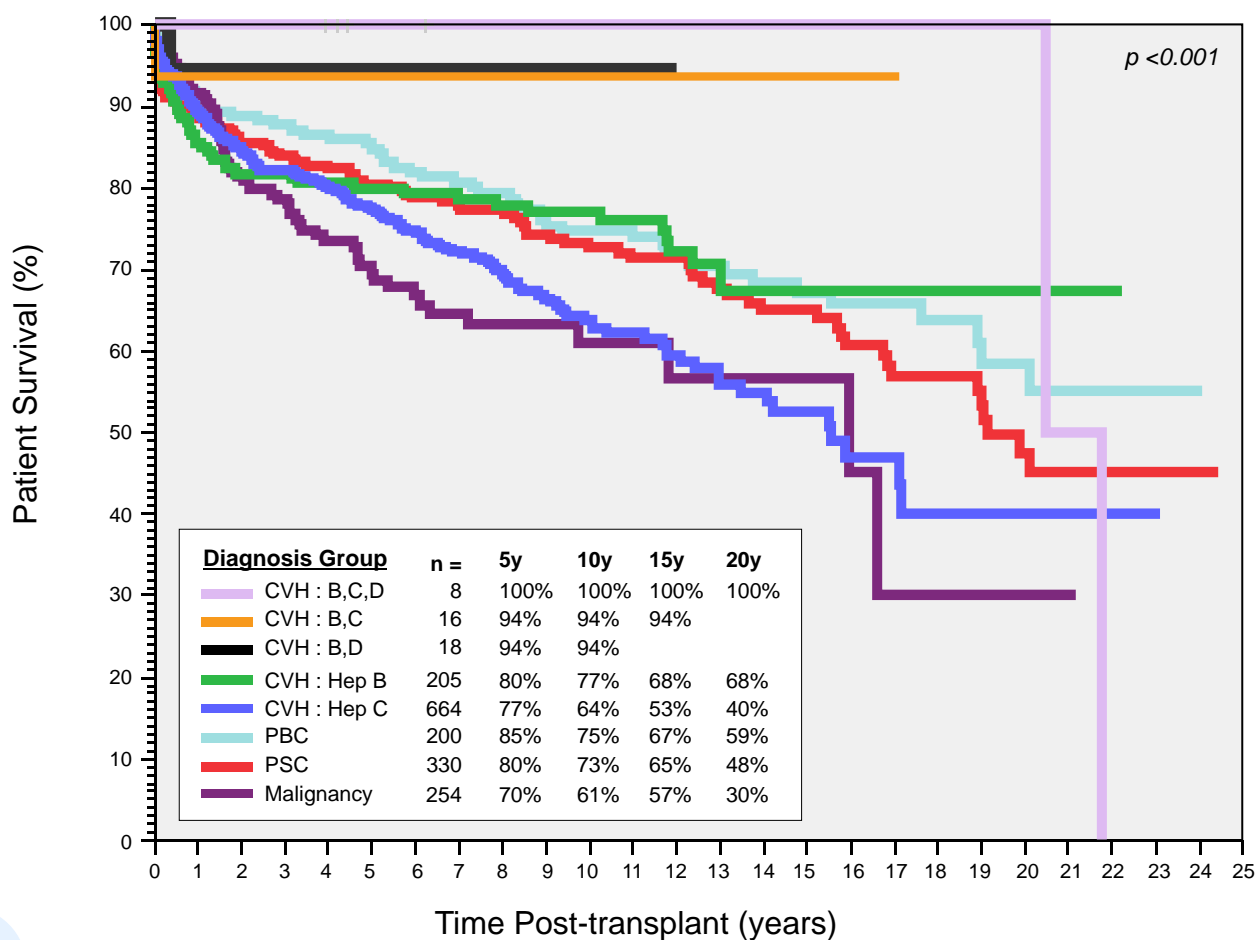




(1) Adults [excluding FHF] - n=1077

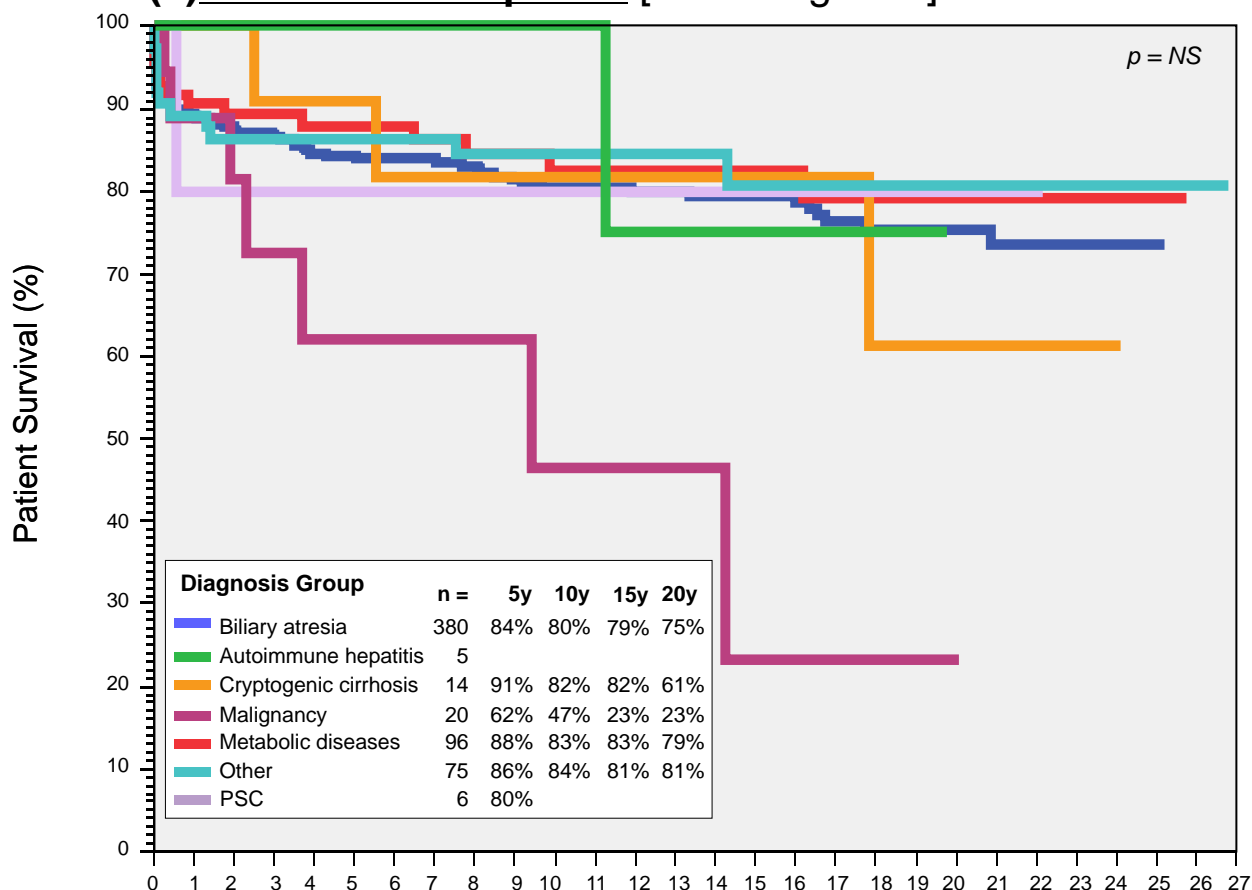


(2) Adults [excluding FHF] - n=1693

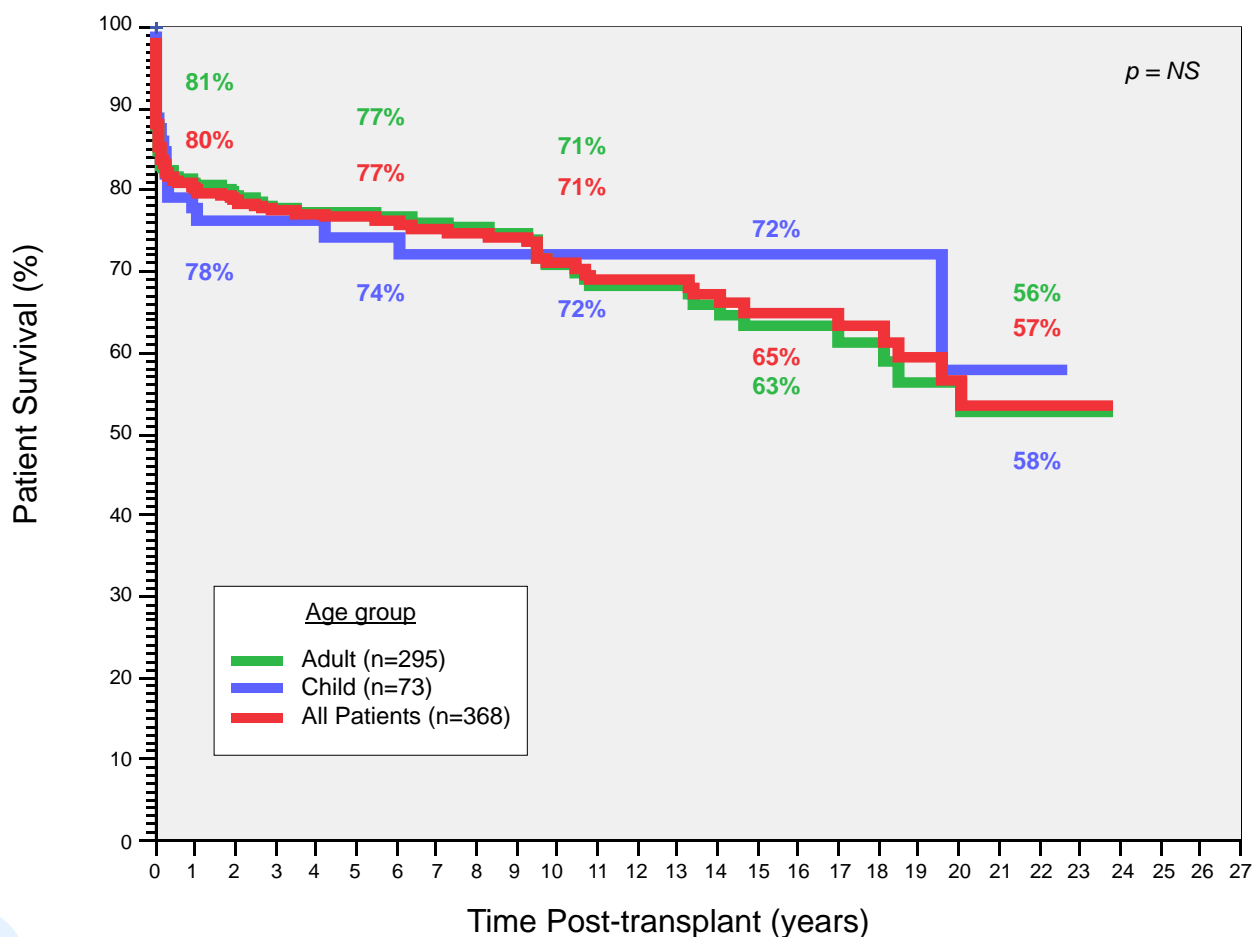


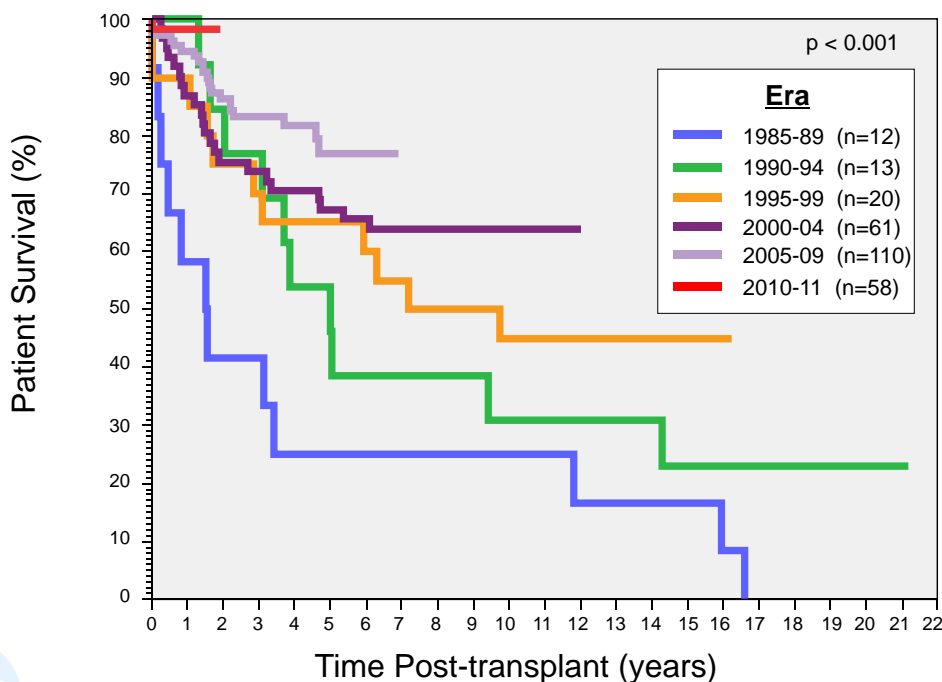
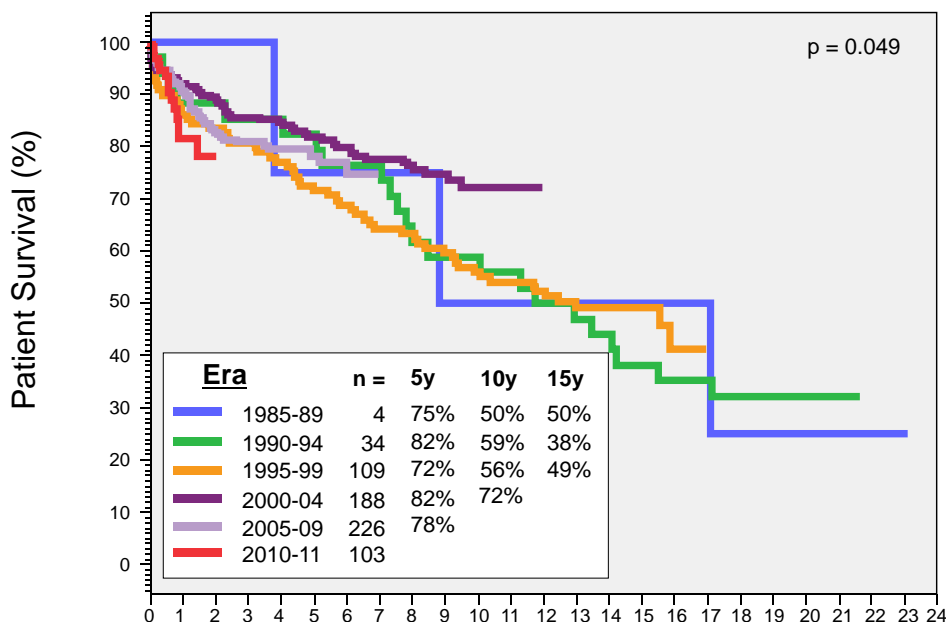
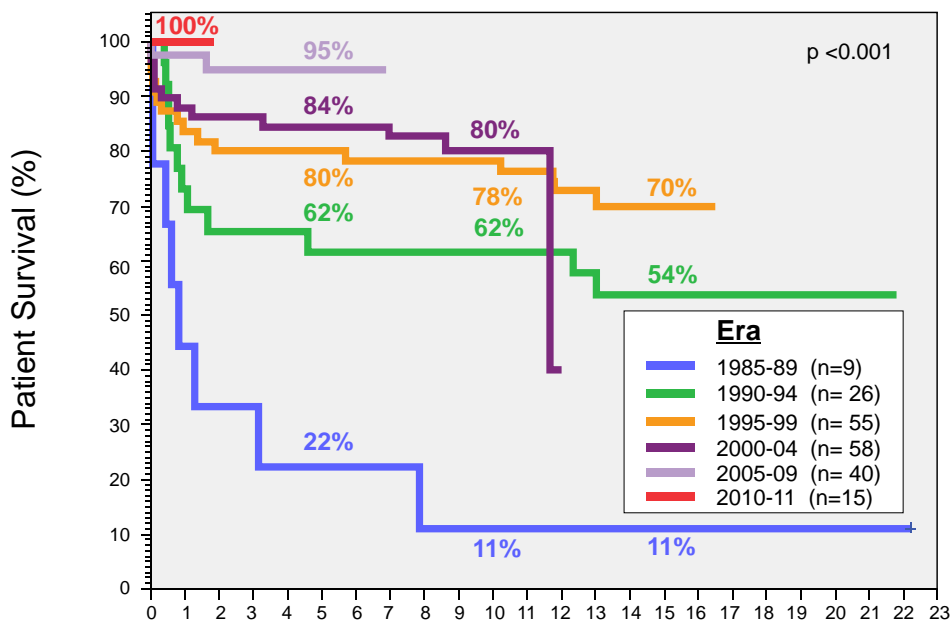


(3) Paediatric recipients [excluding FHF] - n=596



(4) Fulminant hepatic failure n=368



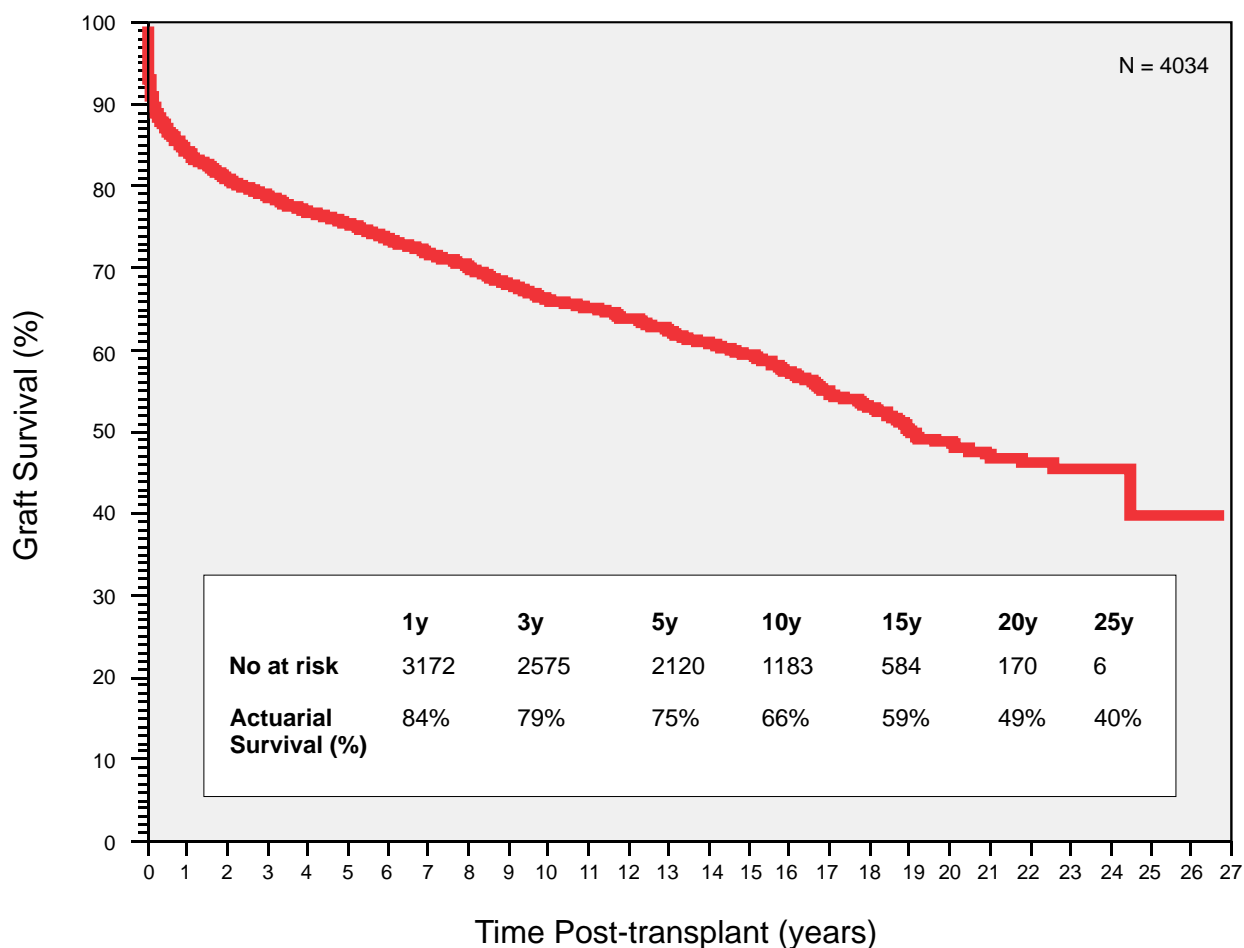




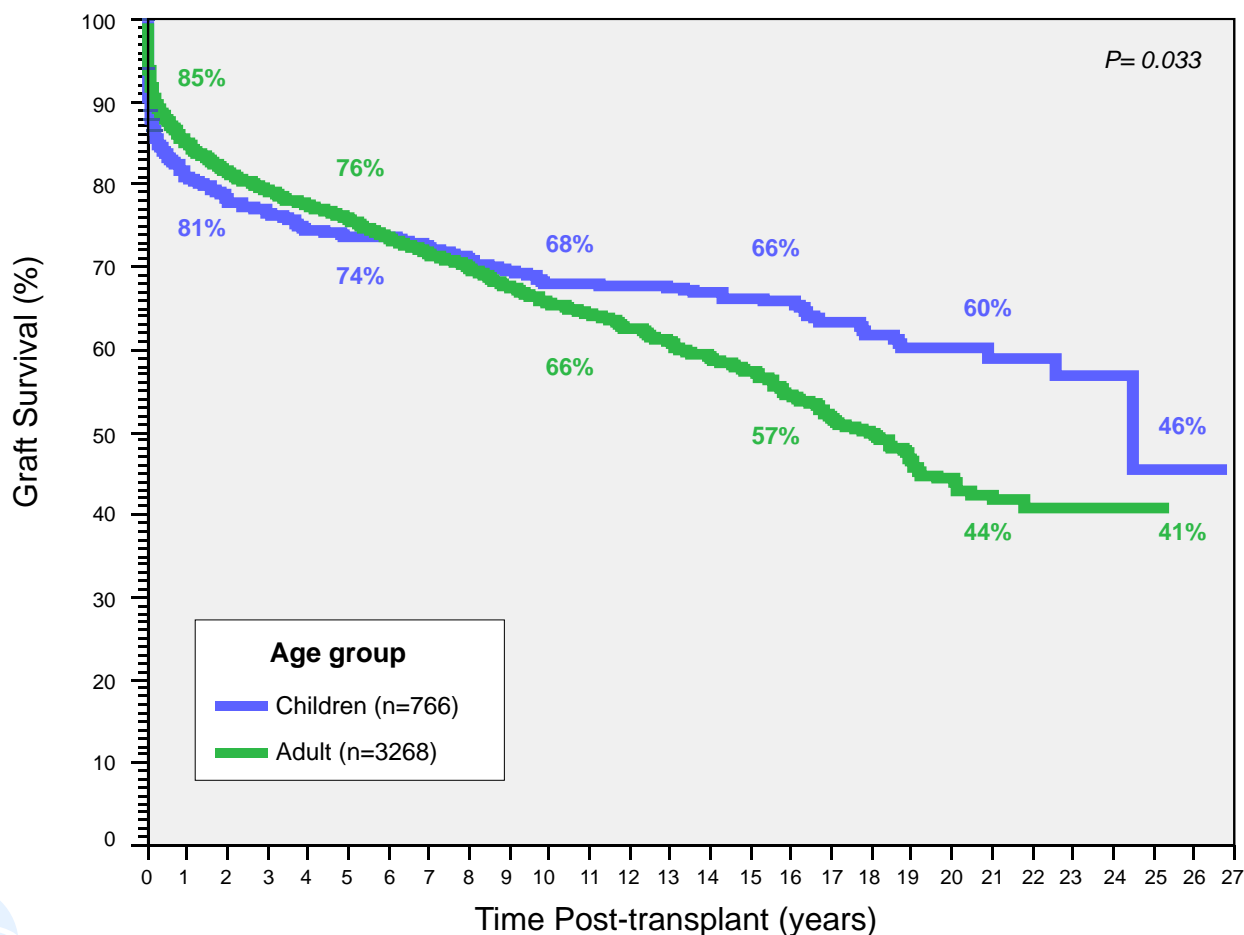
Section 4

Graft Outcome



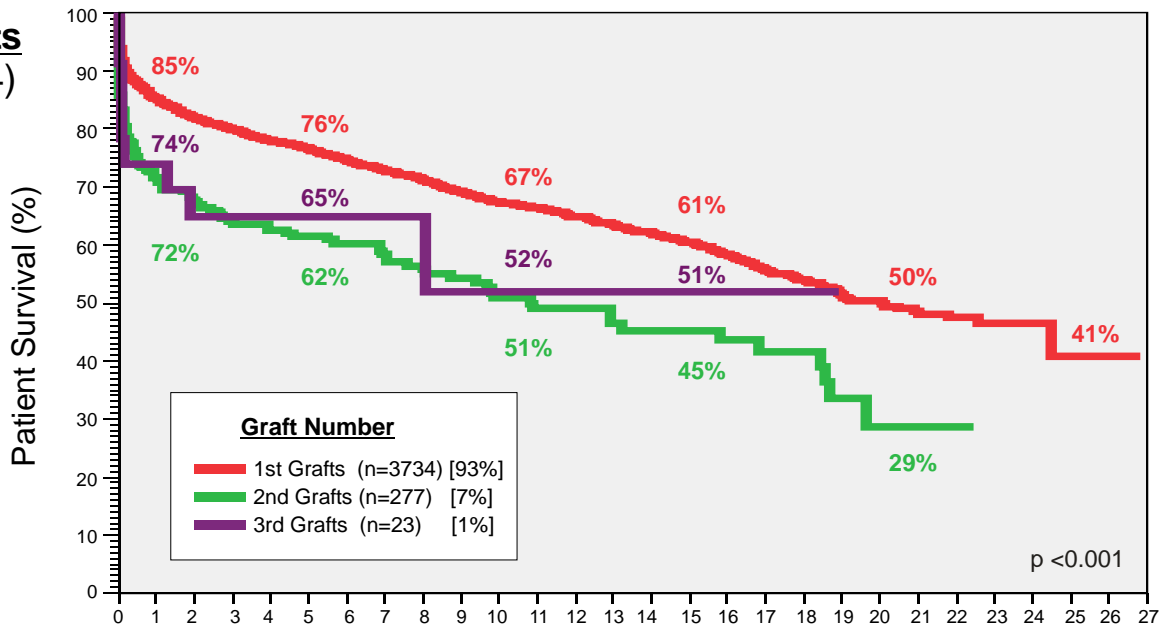


Graft Survival by Age Group

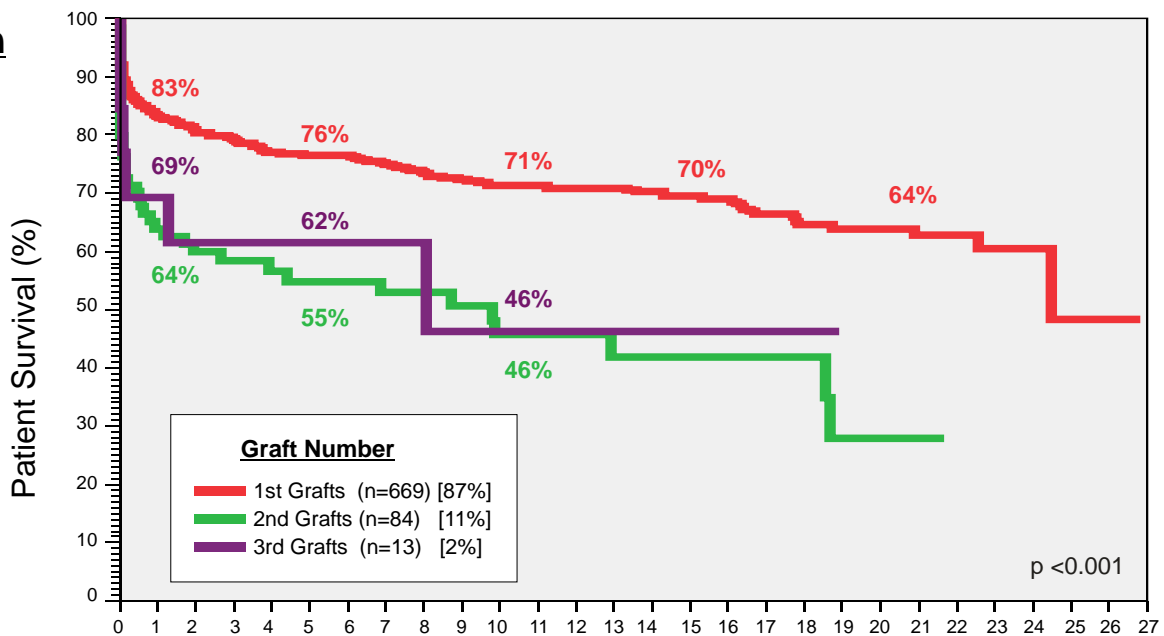




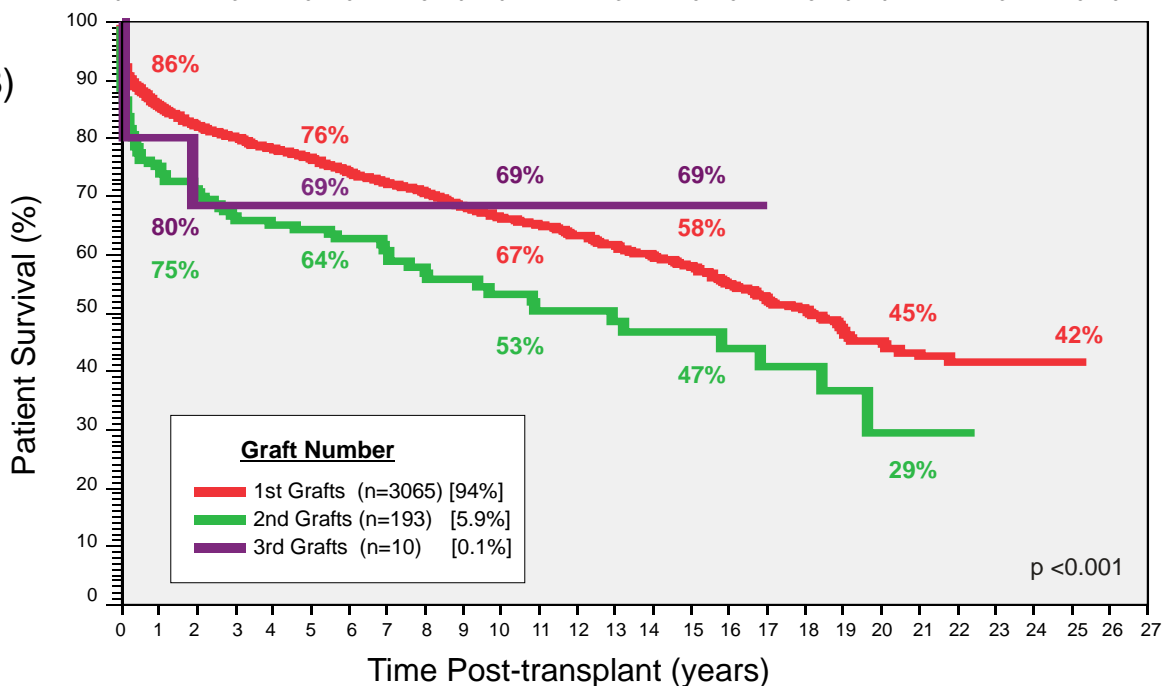
All Grafts (n= 4034)



Children (n= 766)

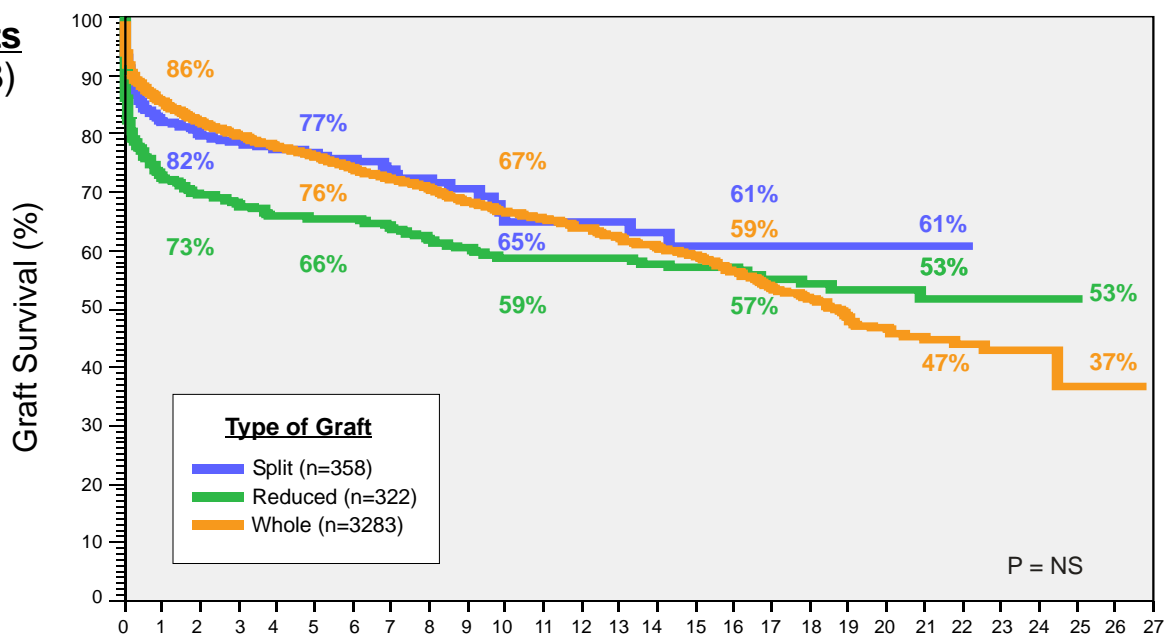


Adult (n= 3268)

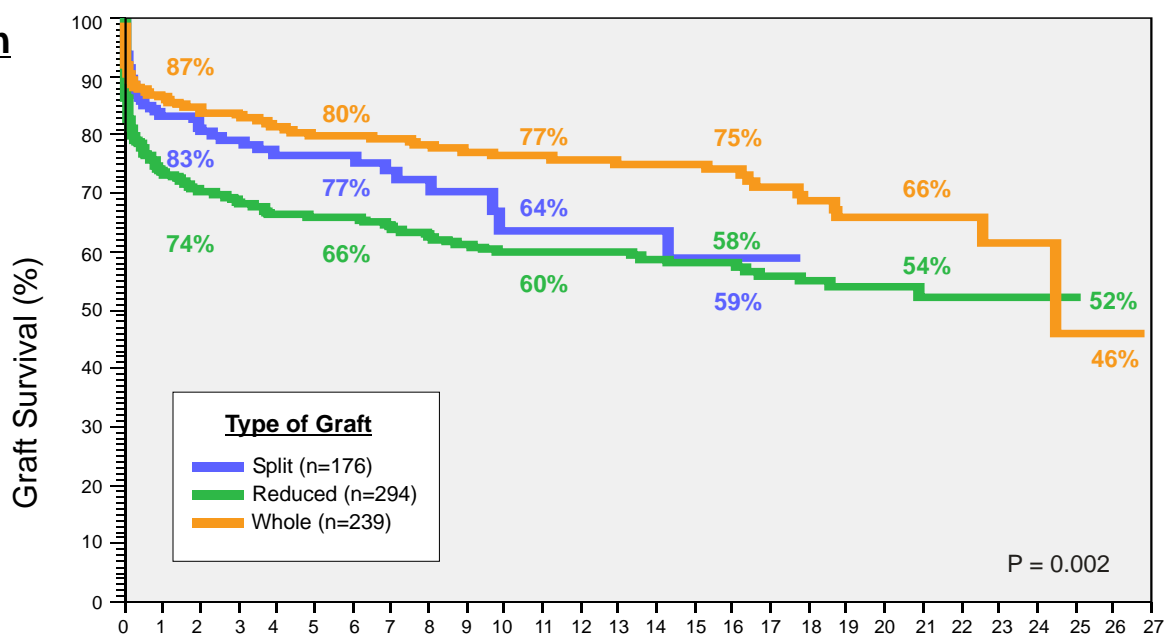




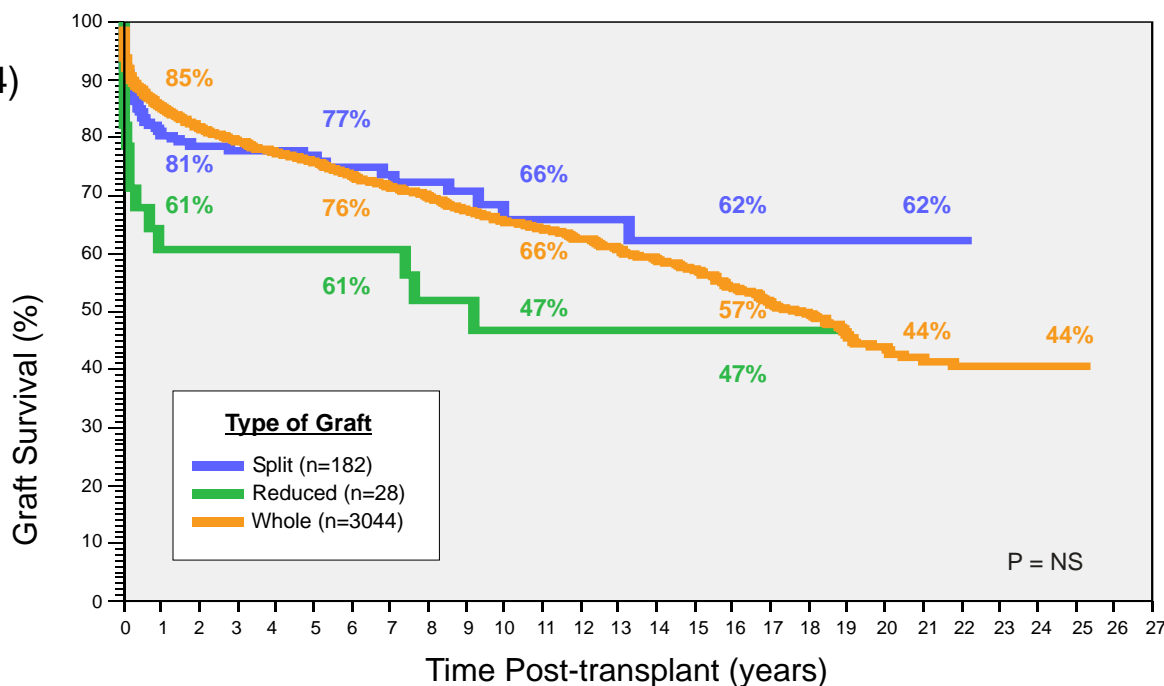
All Grafts (n= 3963)



Children (n= 709)

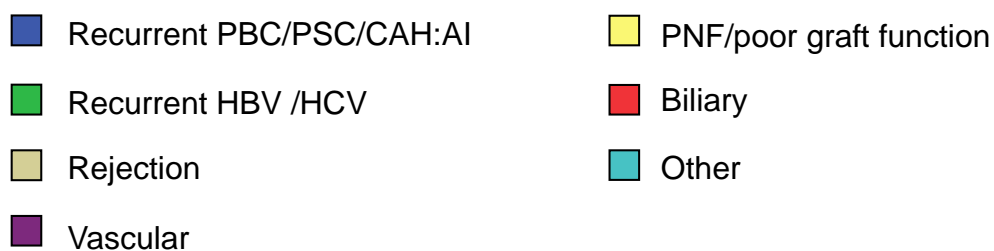
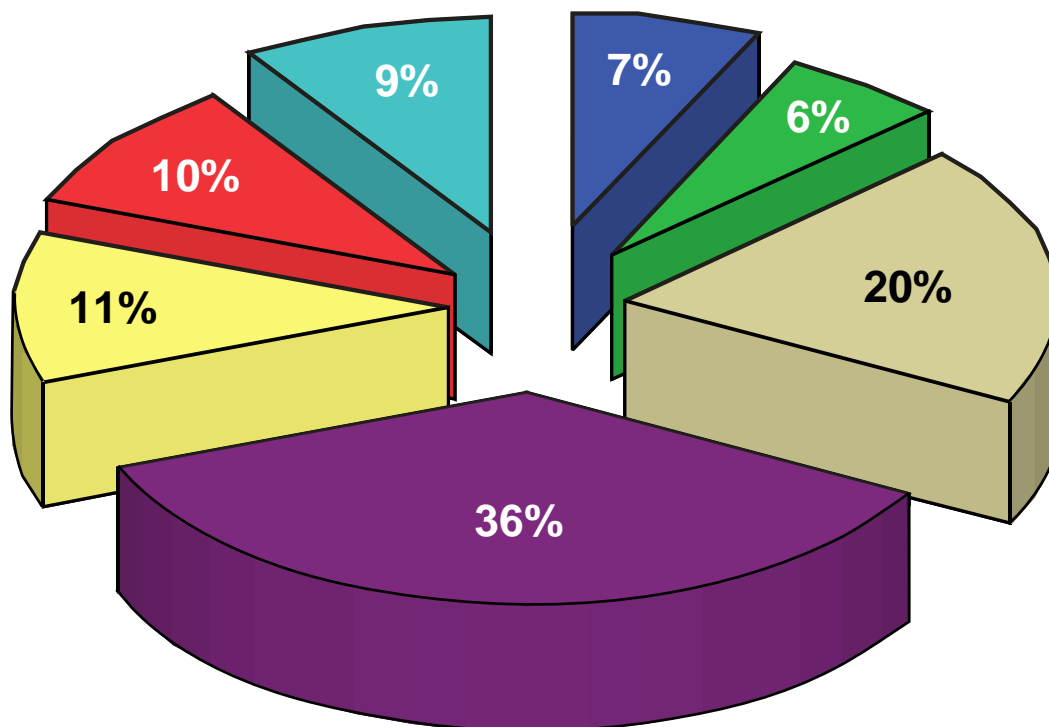


Adult (n= 3254)



Indication for Retransplantation

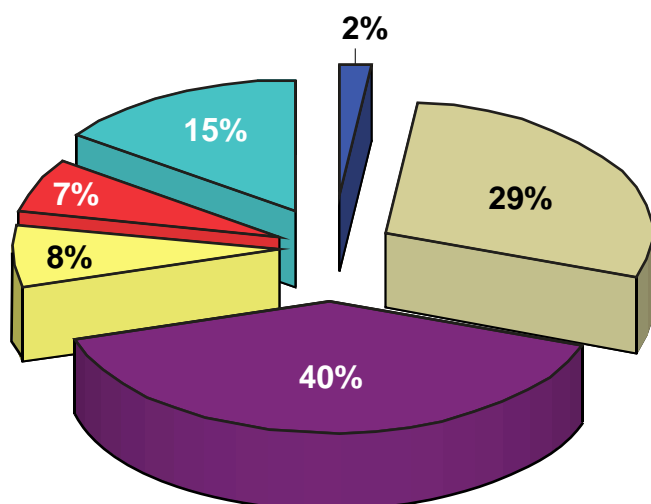
n = 299 (276 2nd grafts, 23 3rd grafts)



Age Group

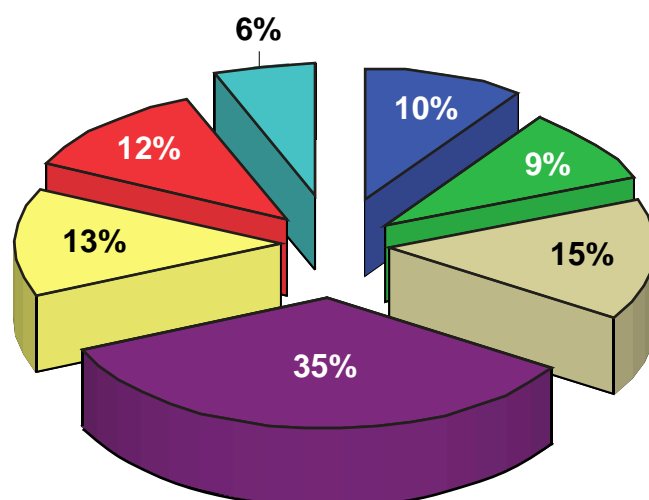
Children

(n= 105)



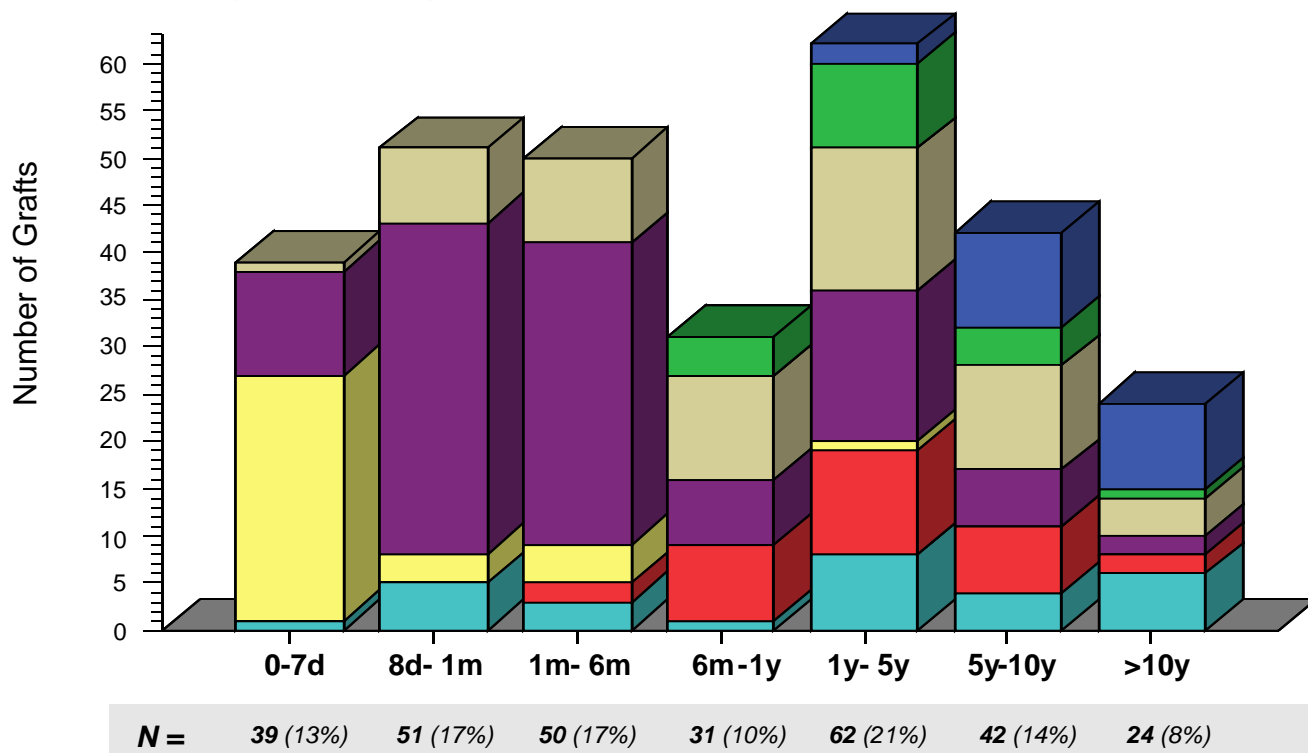
Adults

(n= 194)

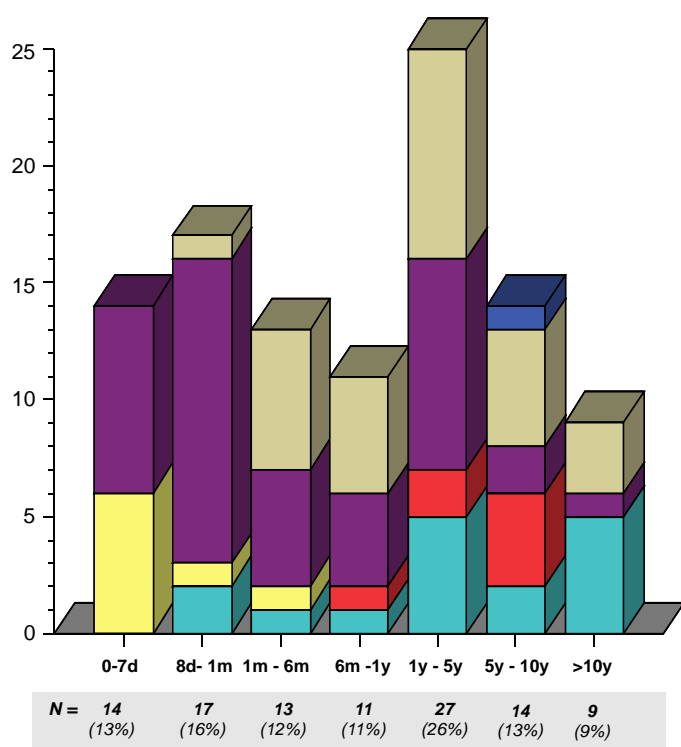


Indication for Retransplantation

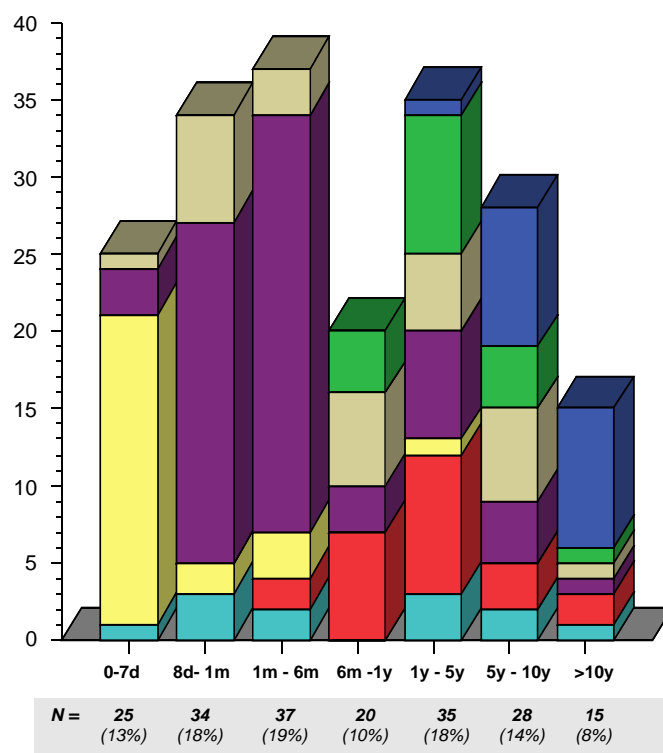
n = 299 (276 2nd grafts, 23 3rd grafts)



Children (n=105)



Adults (n=194)





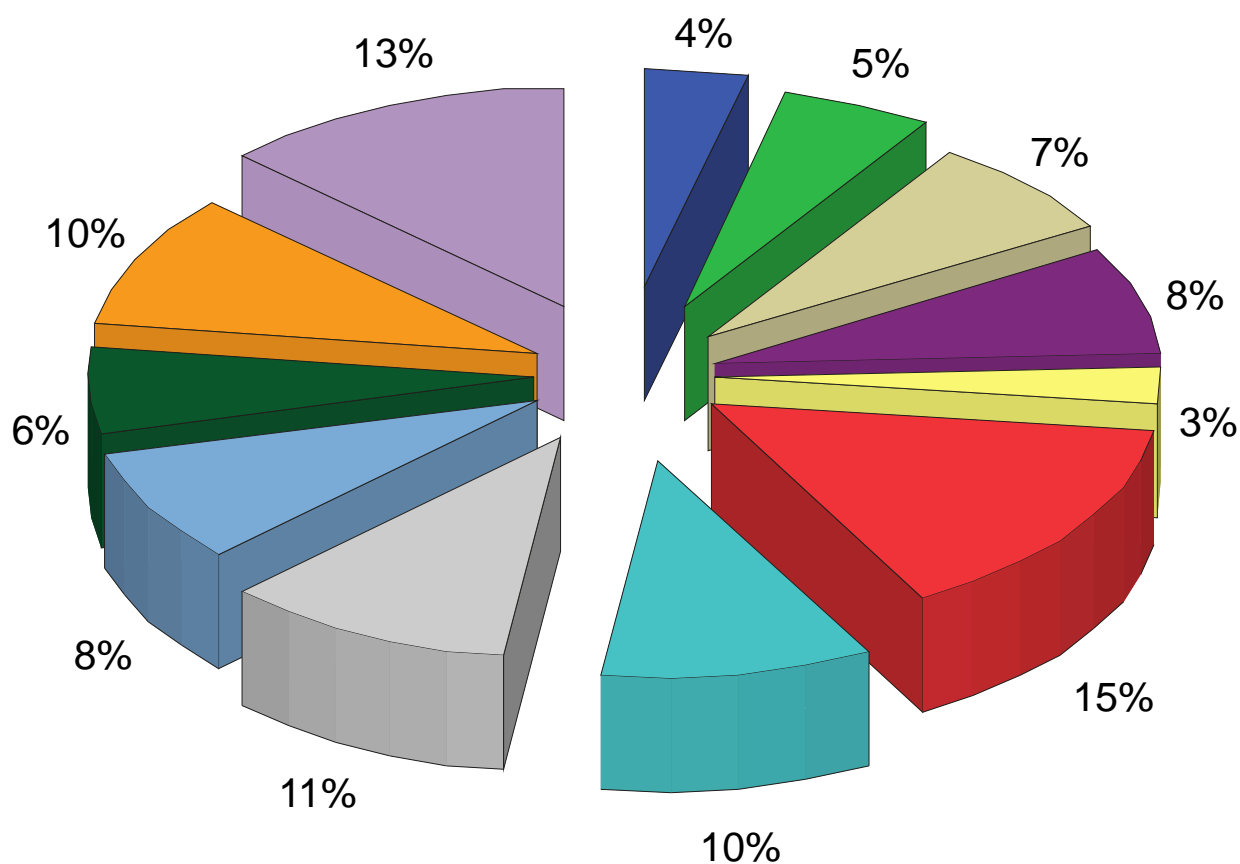
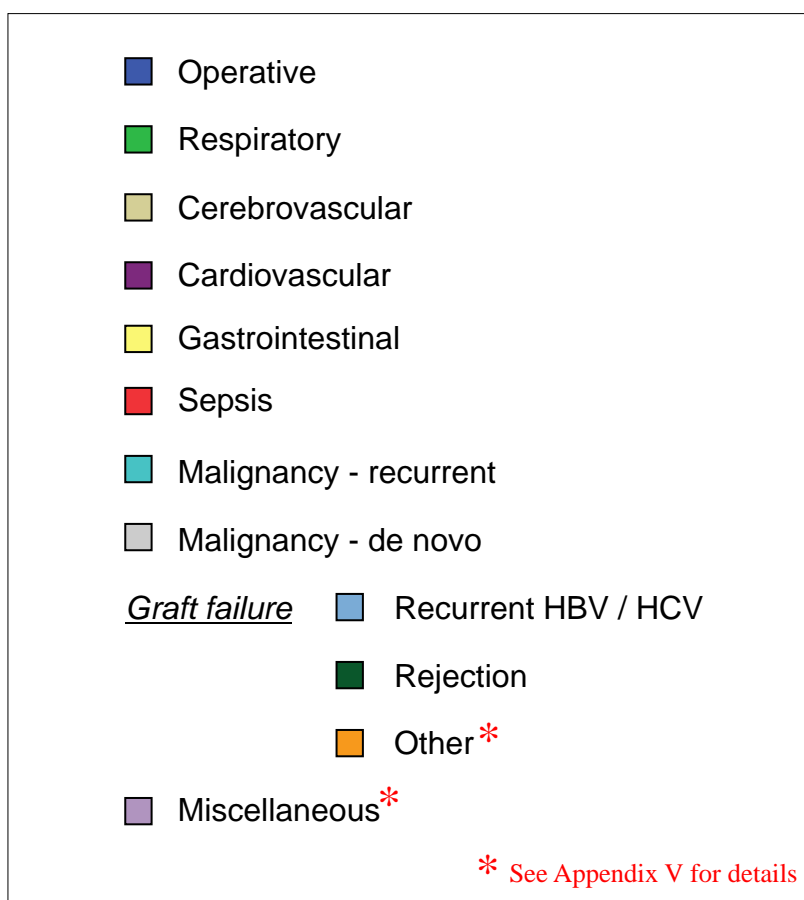
Section 5

Cause of Patient Death

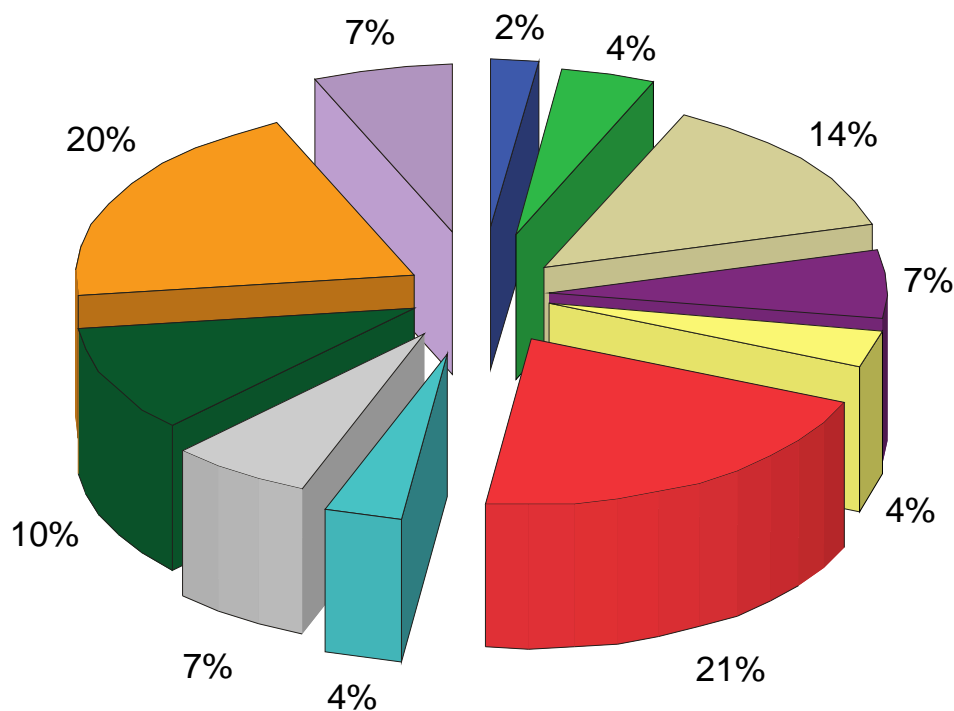




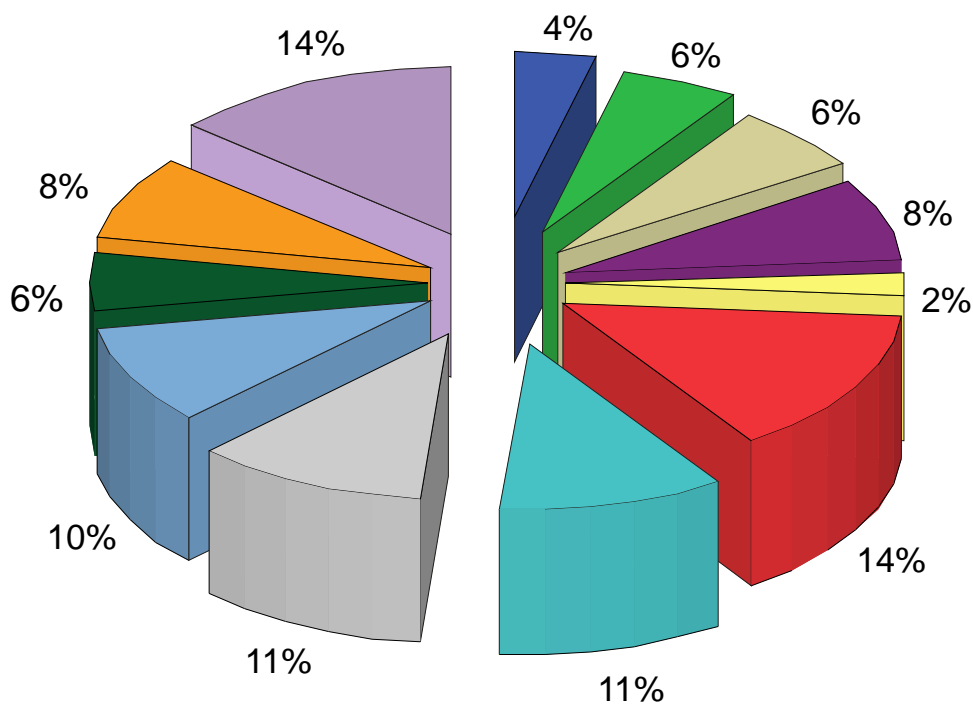
All Patients n = 1006



Causes of Death in Children n = 134

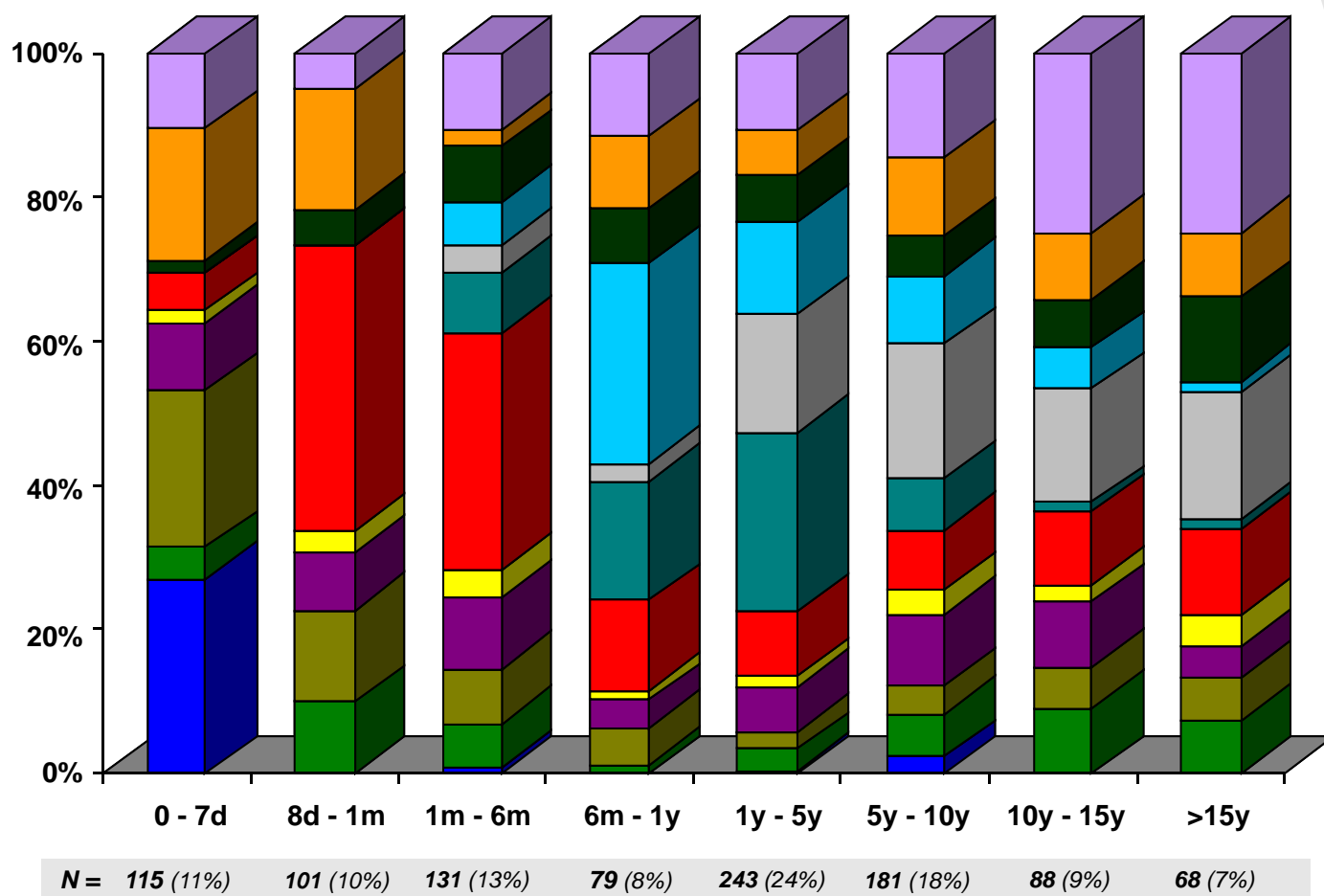


Causes of Death in Adult n = 872



- | | | | |
|-----------------|------------------------|----------------------|---------------------|
| Operative | Gastrointestinal | <u>Graft failure</u> | Recurrent HBV / HCV |
| Respiratory | Sepsis | | Rejection |
| Cerebrovascular | Malignancy - recurrent | | Other* |
| Cardiovascular | Malignancy - de novo | Miscellaneous* | |

* See Appendix V for details



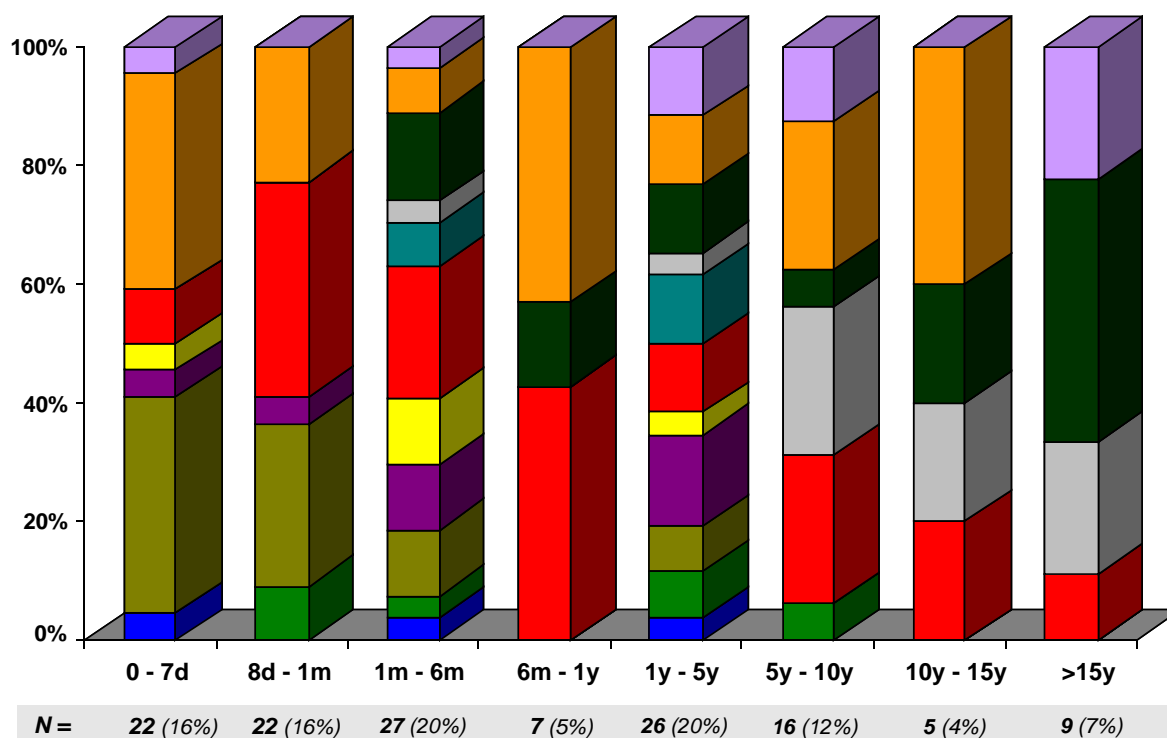
* See Appendix V for details

Cause of Death by Time Post Transplant Children (n=134)

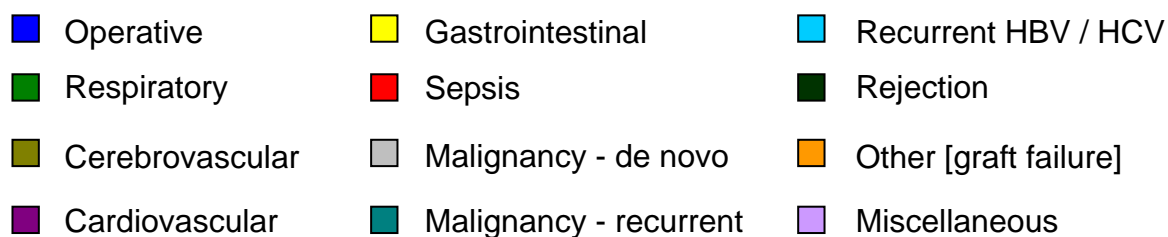
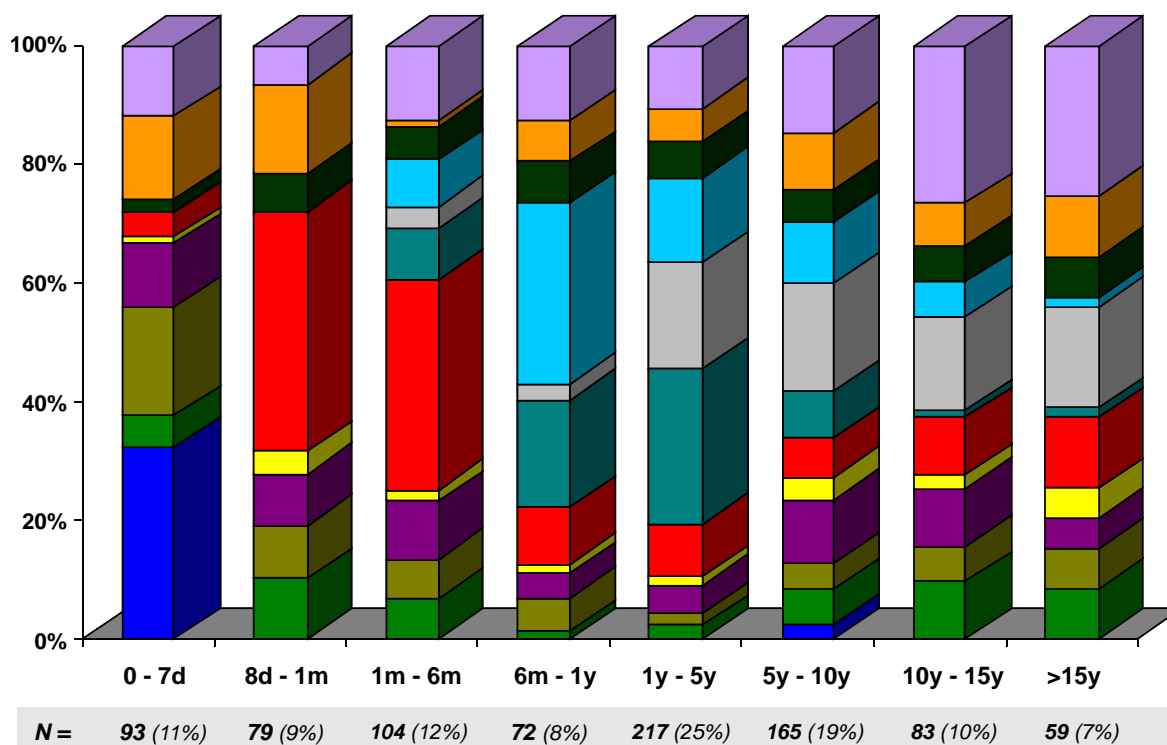
23RD ANZLT REGISTRY
REPORT



CLICK HERE
to go to Contents page



Cause of Death by Time Post Transplant Adult (n=872)





Section 6

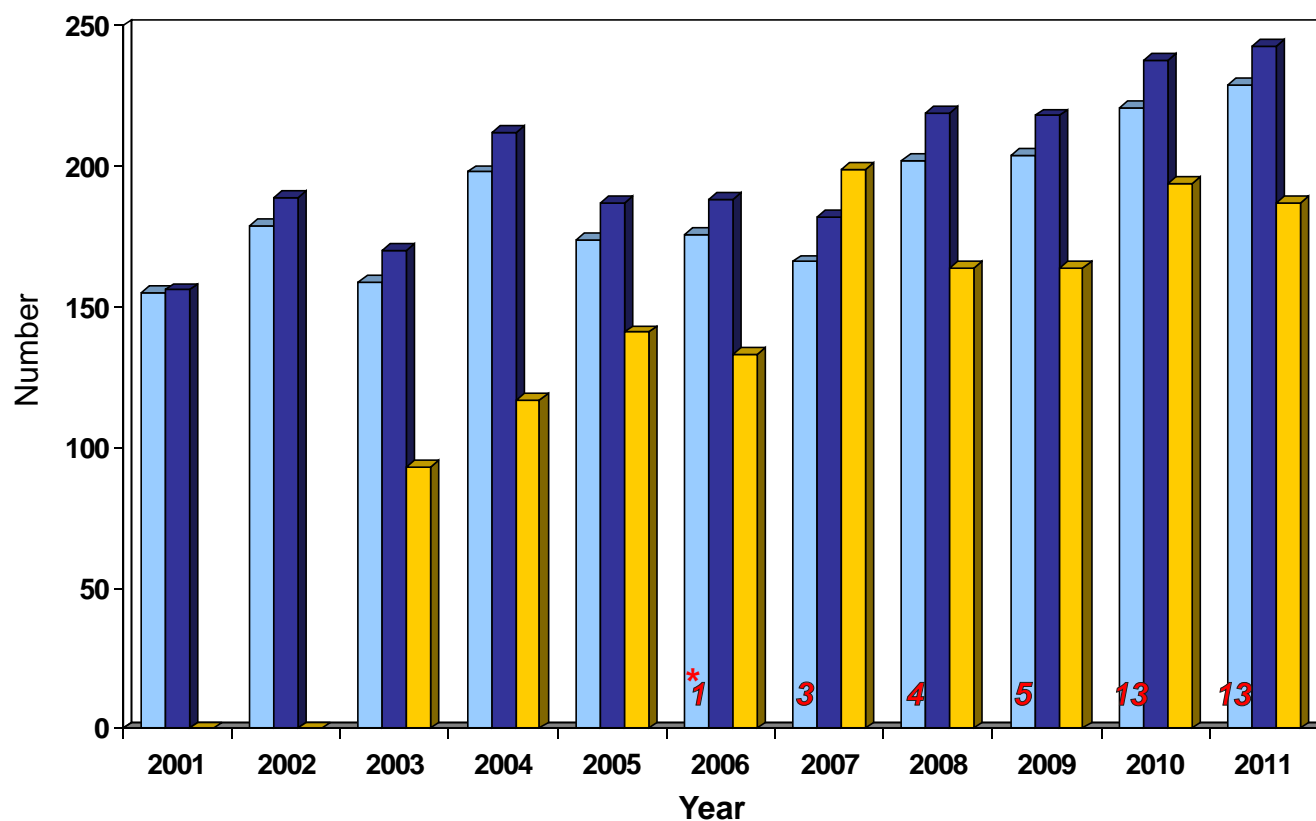
Deceased Donor Information



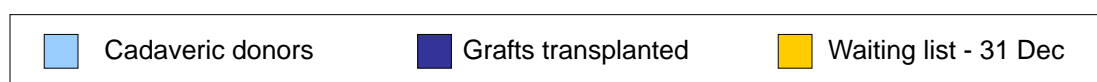


	QLD	NSW/ACT	VIC/TAS	SA/NT	WA	NZ	TOTAL
2001	37	40	26	14	9	29	155
2002	34	42	38	24	11	30	179
2003	34	32/3	29/2	13	15	31	159
2004	30	49/4	35/1	26/1	17	35	198
2005	24	36/8	38/2	17/3	25	21	174
2006	28	34/3	39/6	25	17	24	176
2007	25	36/1	36	19/2	15	32	166
2008	33	40/3	41/5	31/1	25	23	203
2009	35	46/4	36/5	28/2	15	33	204
2010	30	55/8	53/6	18/2	17	32	221
2011	44	52/7	49/3	22/2	20	30	229

Grafts from deceased donors

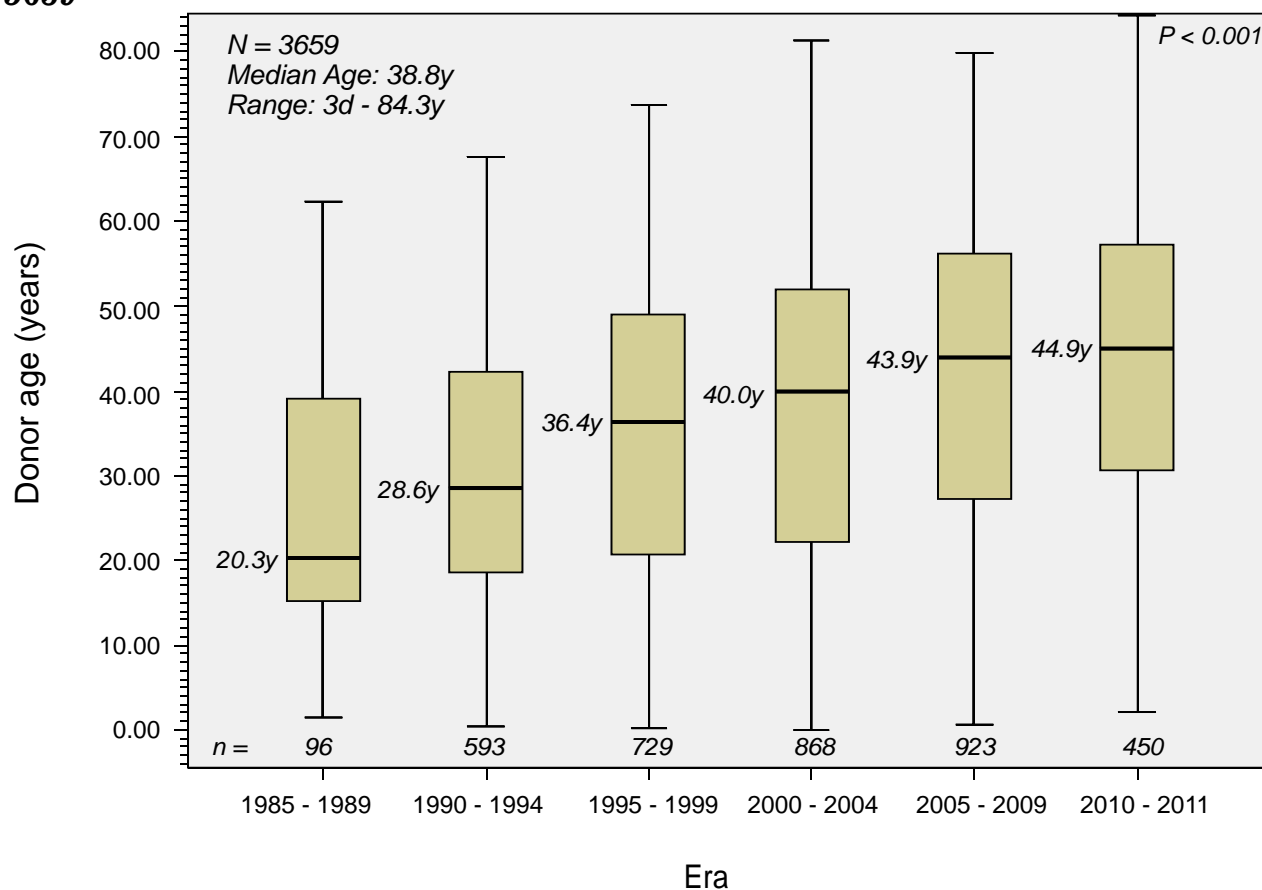


DCD donors*



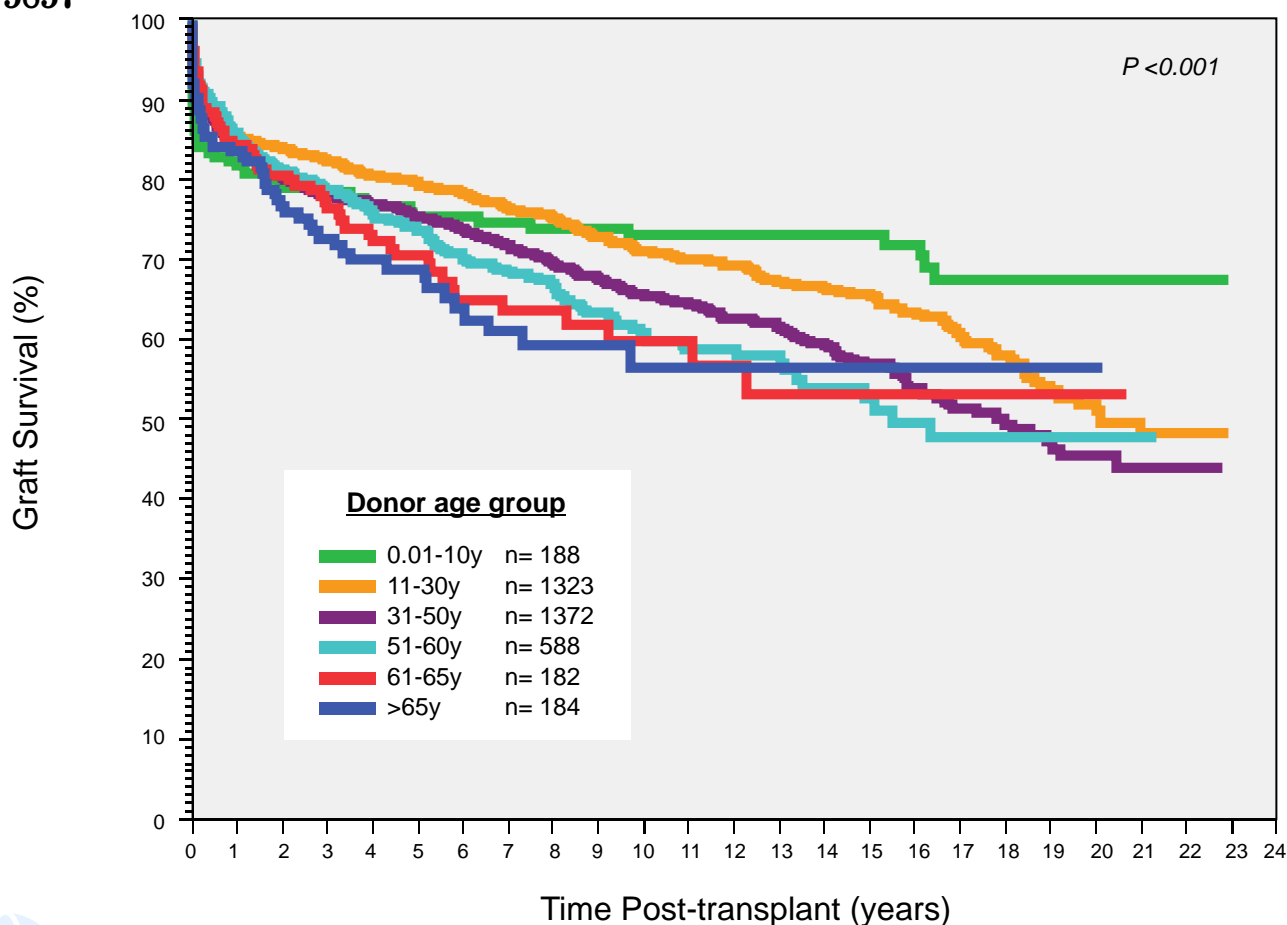
Donor Age by Era

N = 3659



Graft Survival by Donor Age

N = 3837





Section 7

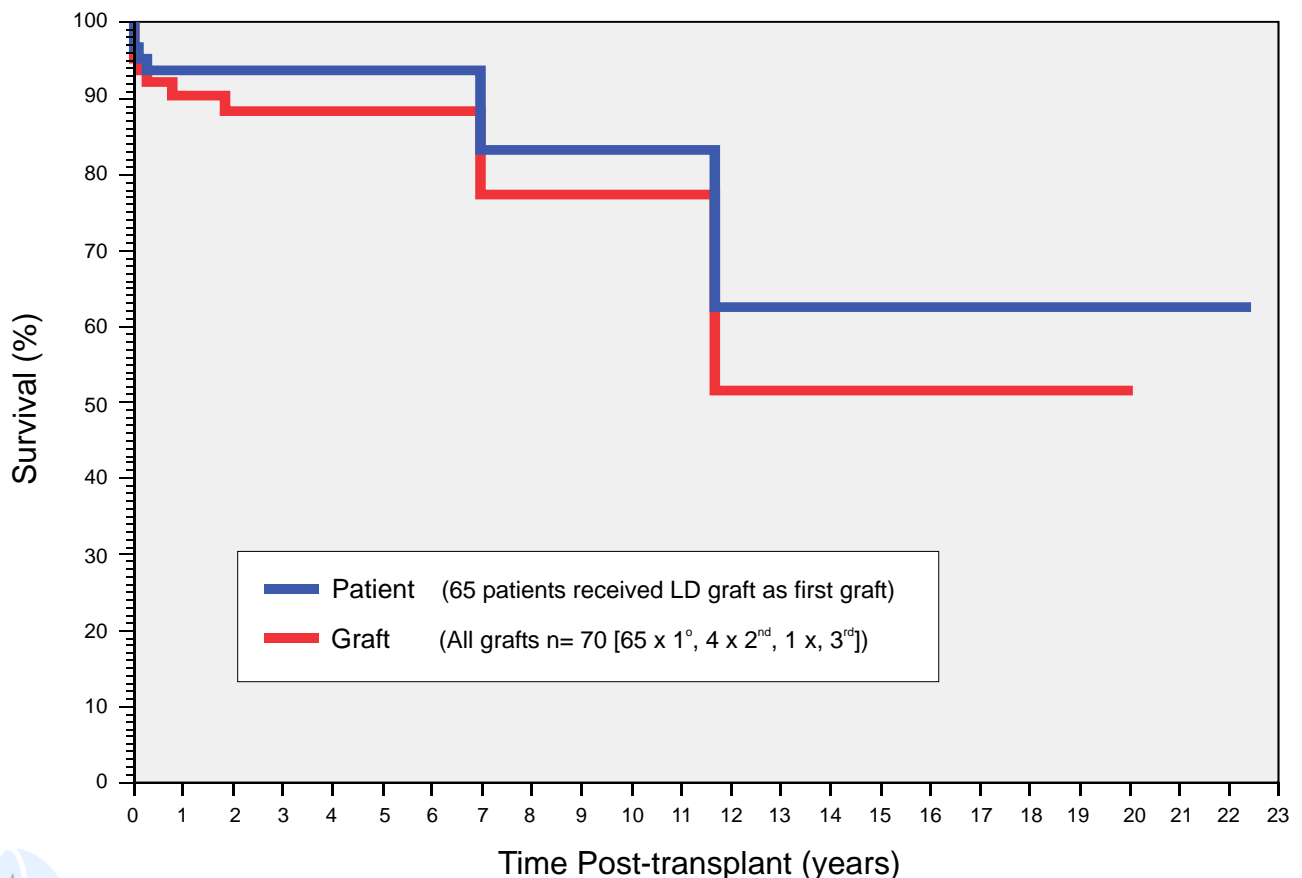
Living Donor Transplantation





	Recipient Age Group		
	Child [n=56]	Adult [n=14] [*]	All [n=70]
Donor gender	-	-	-
Male	34	9	43
Female	22	5	27
Donor age	-	-	-
Median	35.3y	30.3y	34.1y
Range	20.1 - 54.5y	22.8 - 44.2y	20.1 - 54.5y
Donor relationship	-	-	-
Mother	14	-	14
Father	28	-	28
Son	-	4	4
Daughter	-	1	1
Grandmother	1	-	1
Grandfather	1	-	1
Sister	-	3	3
Brother	1	3	4
Aunt	5	-	5
Family friend	4	1	5
Cousin	2	-	2
Spouse	-	1	1

* 1 x whole liver domino transplant





Section 8

Waiting List



Waiting List Activity

[Data 1/1/05 - 31/12/11]



Activity	2005	2006	2007	2008	2009	2010	2011		
Listed at 1 January	117	145	133	199	169	175	200	-	TOTAL 2011
New listings	292	259	338	290	335	335	-	324	
TOTAL	409	404	471	489	504	510	200	324	524
OUTCOME					OUTCOME				
Transplant	191 [47%]	194 [48%]	190 [40%]	229 [47%]	228 [46%]	248 [49%]	118	135	253 [48%]
Delisted	72 [18%]	77 [19%]	86 [18%]	96 [20%]	101 [20%]	68 [13%]	36	50	85 [16%]
Died on list	26	18	35	48	32	12	6	11	17
Too sick	9	13	13	14	17	12	2	15	17
Tumour progression	9	8	11	7	8	12	10	10	20
Improved	15	16	17	15	18	16	5	7	12
Other	13	22	10*	11	26	12*	12	7	19*
Still listed at 31 Dec	146 [35%]	133 [33%]	199 [43%]	169 [34%]	175 [34%]	194 [38%]	47	139	186 (35%)

[* Alcohol/drug use, Alternate Treatment, Temporary Suspension, Infection]

Outcome of Initial Urgent Listing

OUTCOME	CATEGORY 1						
	2005 (n=14)	2006 (n=16)	2007 (n=18)	2008 (n=13)	2009 (n=17)	2010 (n=19)	2011 (n=15)
TRANSPLANTED	4 } 64%	12 } 88%	10 } 67%	3 } 46%	9 } 65%	13 } 74%	12 } 80%
IMPROVED	5 }	2 }	2 }	3 }	2 }	1 }	- }
DIED / TOO SICK	5	2	6	7	6	5	3
OTHER TREATMENT	-	-	-	-	-	-	-

OUTCOME	CATEGORY 2						
	2005 (n=31)	2006 (n=26)	2007 (n=32)	2008 (n=24)	2009 (n=21)	2010 (n=30)	2011 (n=28)
TRANSPLANTED	20 } 68%	21 } 88%	24 } 88%	20 } 83%	18 } 90%	23 } 93%	22 } 86%
IMPROVED	1 }	2 }	4 }	1 }	1 }	5 }	2 }
DIED / TOO SICK	10	2	2	3	2	1 / 1	3
OTHER TREATMENT	-	1	-	-	-	-	1 active 31/12/11

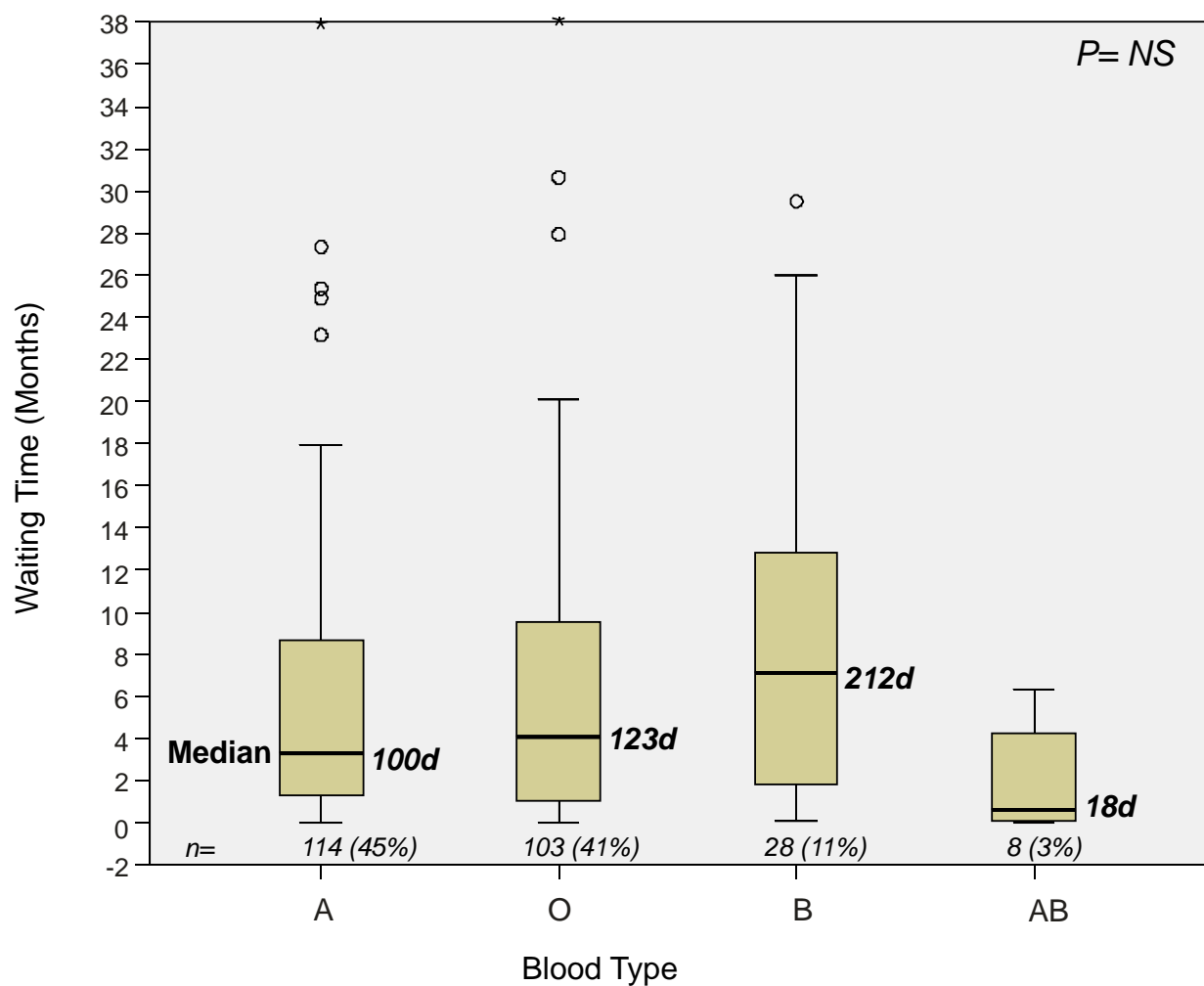


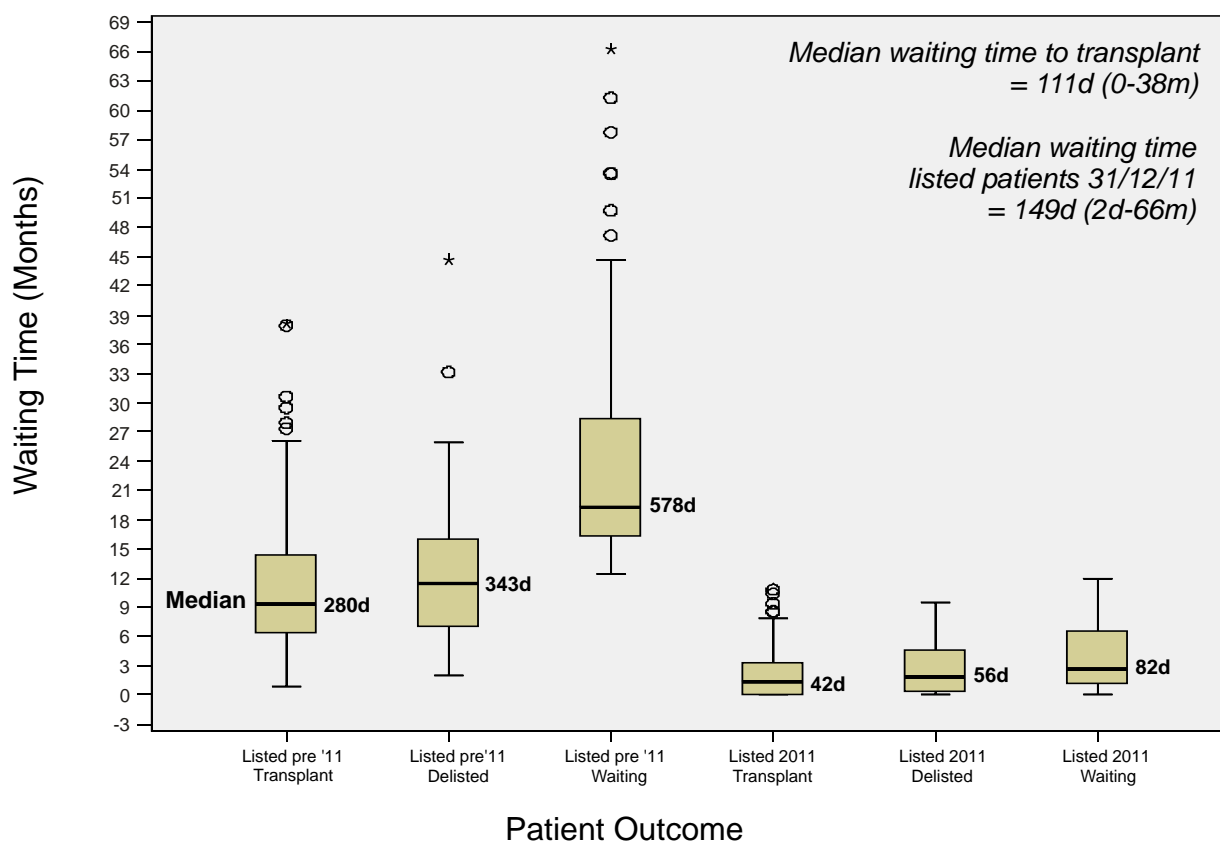
	Blood Group				
	A	O	B	AB	TOTAL
n=	210 (40%)*	224 (43%)	71 (13%)	19 (4%)	524
Not transplanted	96	121	43	11	271
Transplanted	114 (54%)**	103 (46%)	28 (39%)	8 (42%)	253

* % of total number listed

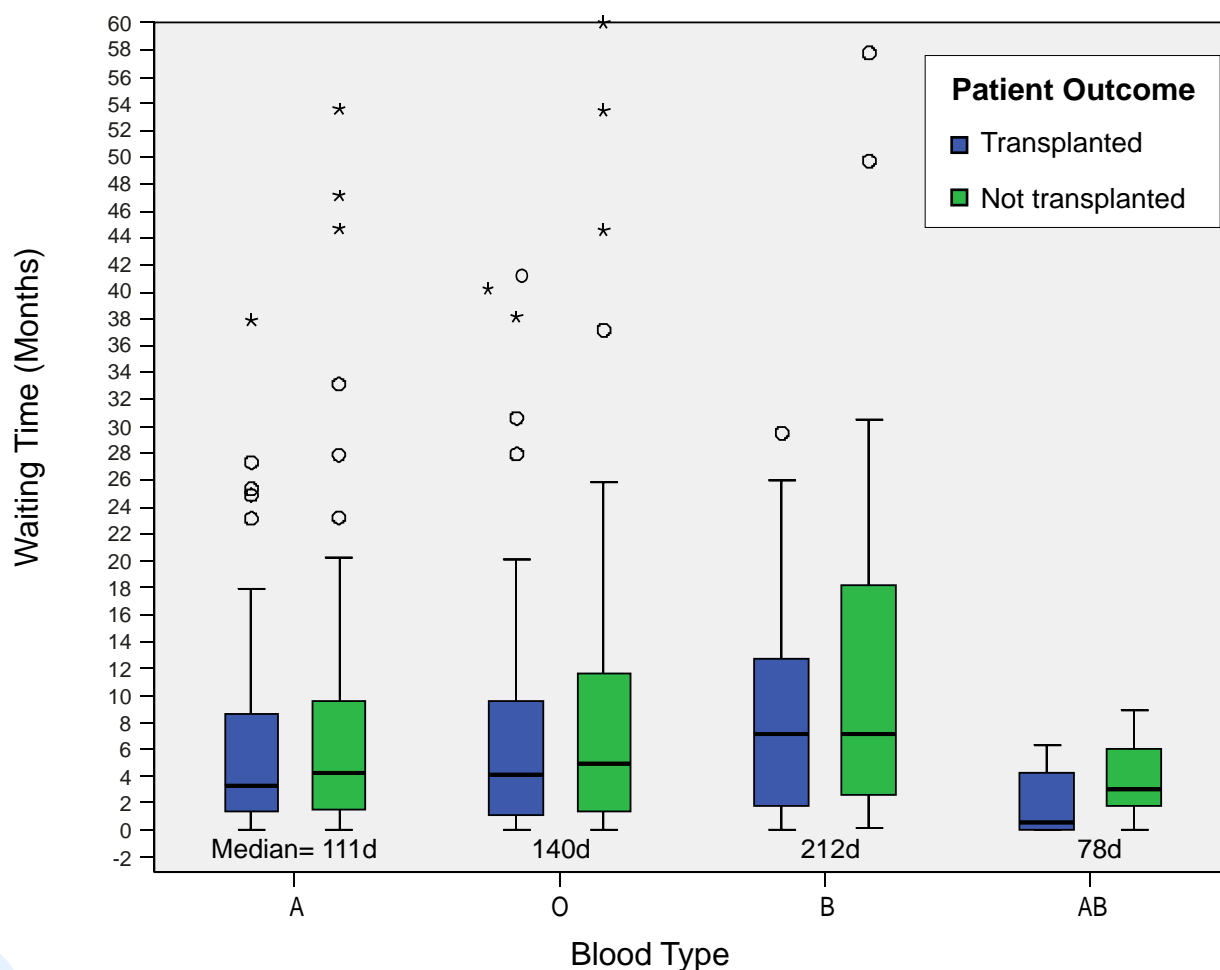
** % of blood group

Waiting Time to Transplant 2011





Waiting Time by Outcome & Blood Group





Section 9

Liver Transplantation and Cancer



Cancer in Liver Transplant Recipients

N = 3734



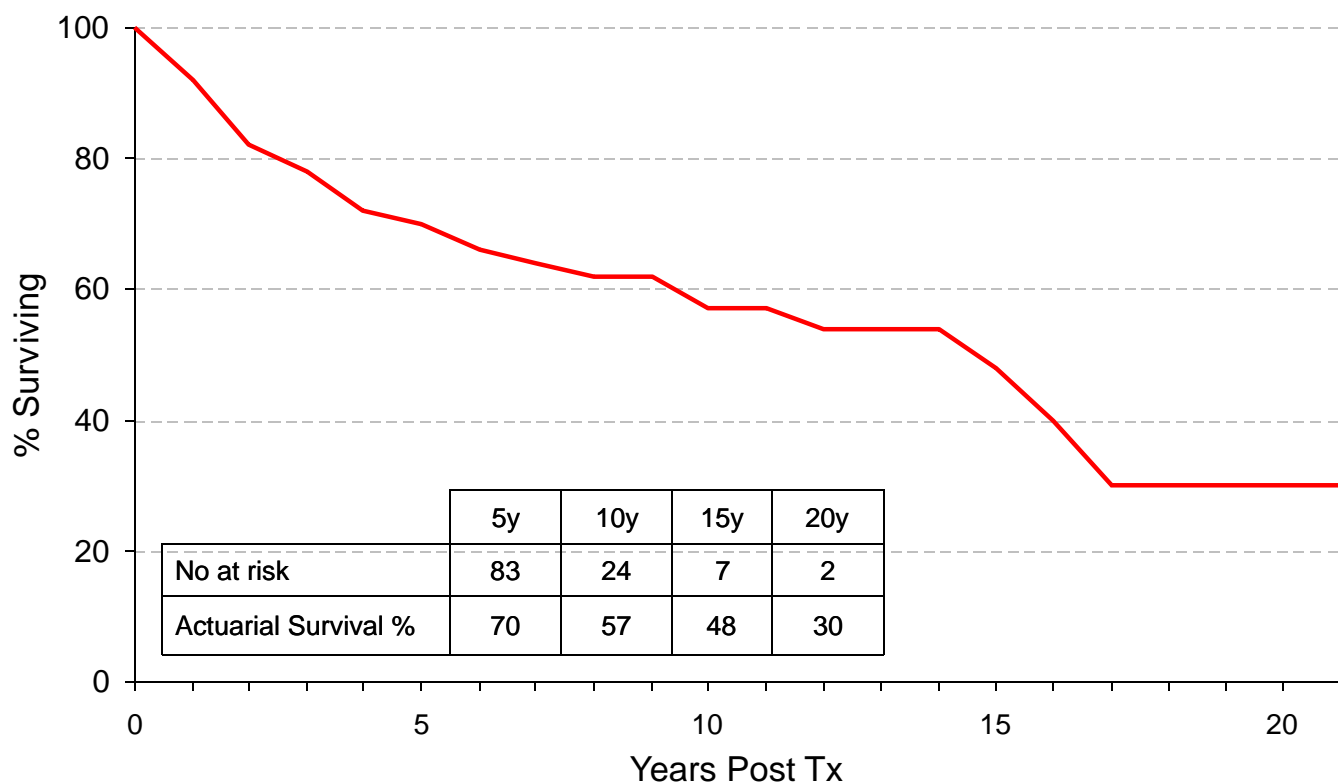
At Tx	
Transplant for Liver Cancer	271 (7%)
Liver Ca as a Secondary Diagnosis	430 (12%) 432 Ca
Total	701 (19%)
Post Tx	
Recurrent Liver Ca	102 (15% of pts with Ca at Tx)
De Novo Ca	257 (7%) 275 Ca
Skin Ca	514 (14%) 3508 Ca
Total	875 (23%)
Multiple Ca	237
Pre-Tx cancer developed de novo cancer	15 (3% of pts with Ca at Tx)
Transferred from Donor	2
Developed non skin Ca < 90days	9

Liver Cancer as Primary Diagnosis

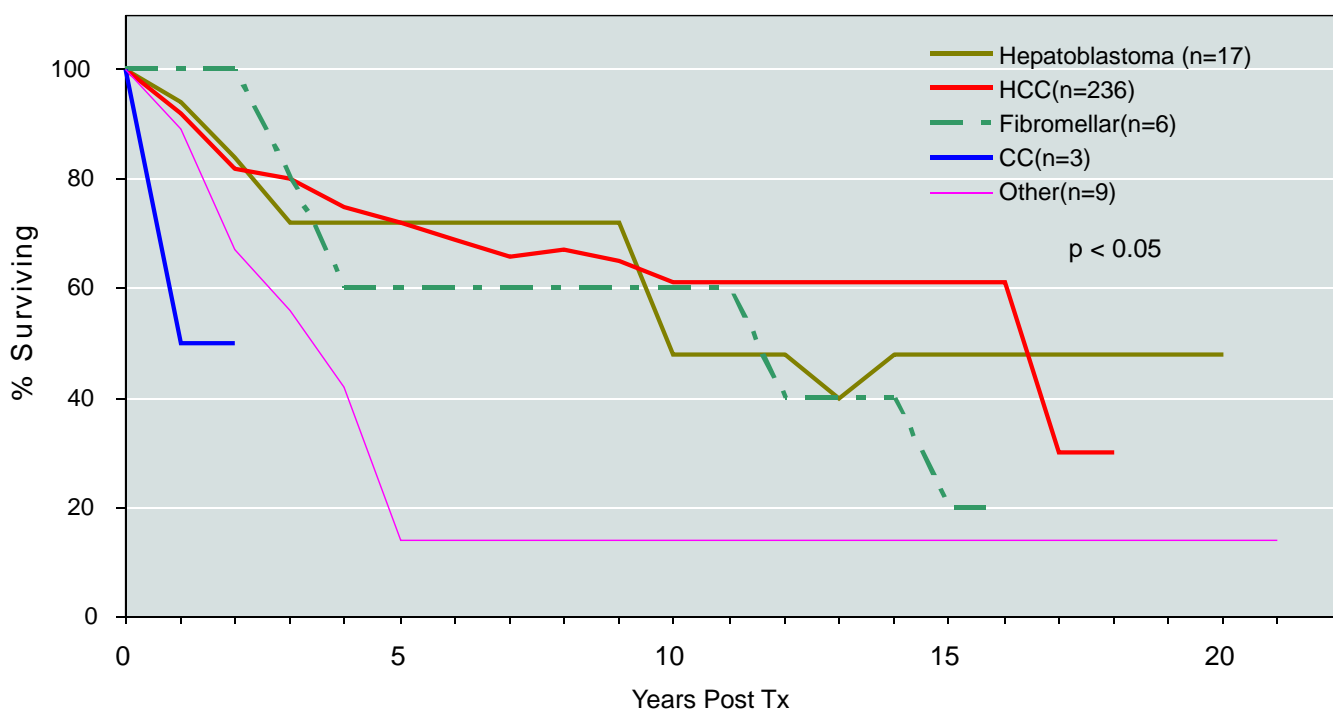
N= 3734

TYPE OF CA	No	DIED	DIED OF THIS CA
HEPATOCELLULAR CA	236	56	56 (24%)
HEPATOBLASTOMA	17	4	4 (22%)
FIBROLAMELLAR	6	5	5 (83%)
CARCINOID	4	4	4 (100%)
CHOLANGIOCARCINOMA	3	1	1 (50%)
ANGIOSARCOMA	1	1	1 (100%)
EPITHELOID HAEMANGIOENDOTHELIOMA	2	0	0
GASTRINOMA	1	1	1 (100%)
PANCREATIC ISLET CELL	1	1	1 (100%)
TOTALS	271 (7% of pts)	73 (29% of those with PCa)	43 (57% of those with PCa)

Overall Survival
Primary Liver Cancer
N = 271 (7% of patients transplanted)



Overall Survival
Primary Liver Cancer
N = 271/3734(7%)



Primary Liver Cancer

Actuarial Survival Summary

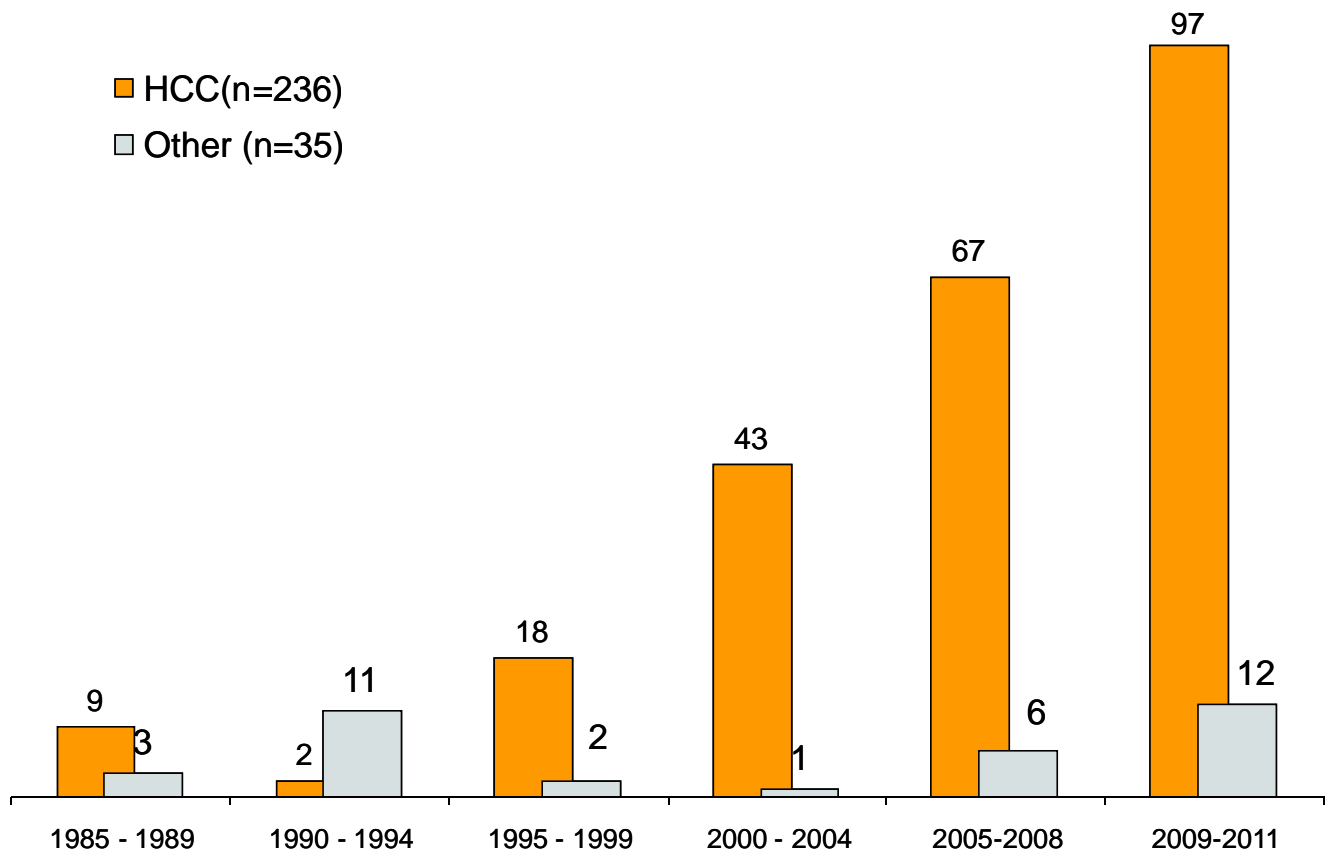
n = 3734

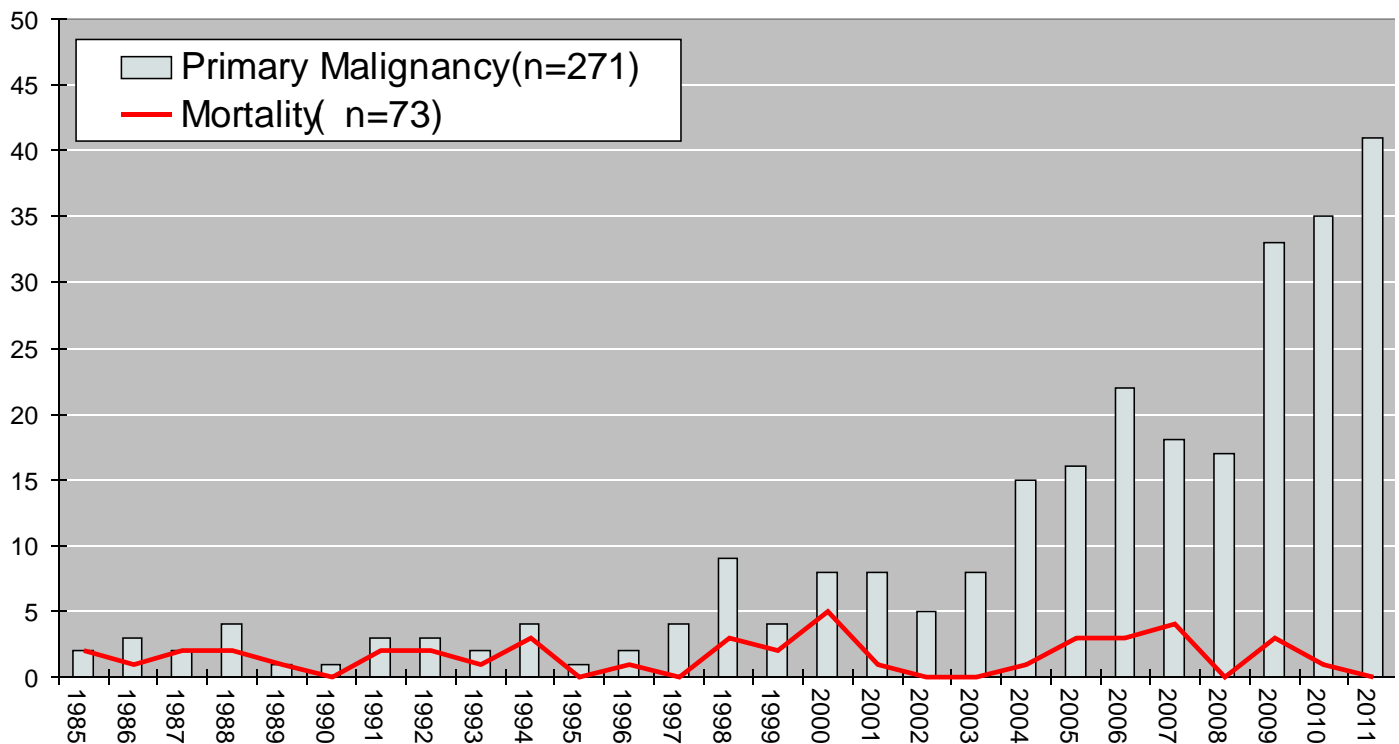


		1y	5y	10y	15y	20y
HCC (n=236)	nr	181	73	18	4	
	% surviving	77	30	25	2	
Hepatoblastoma (n=17)	nr	17	5	3	2	1
	% surviving	100	29	18	12	48
Other (n=9)	nr	9	4	2	1	1
	% surviving	100	44	22	11	14
Fibrolamellar (n=6)	nr	6	4	4	2	
	% surviving	100	60	60	20	
CC (n=3)	nr	3				
	% surviving	100				

Liver Cancer as Primary Diagnosis

n = 271



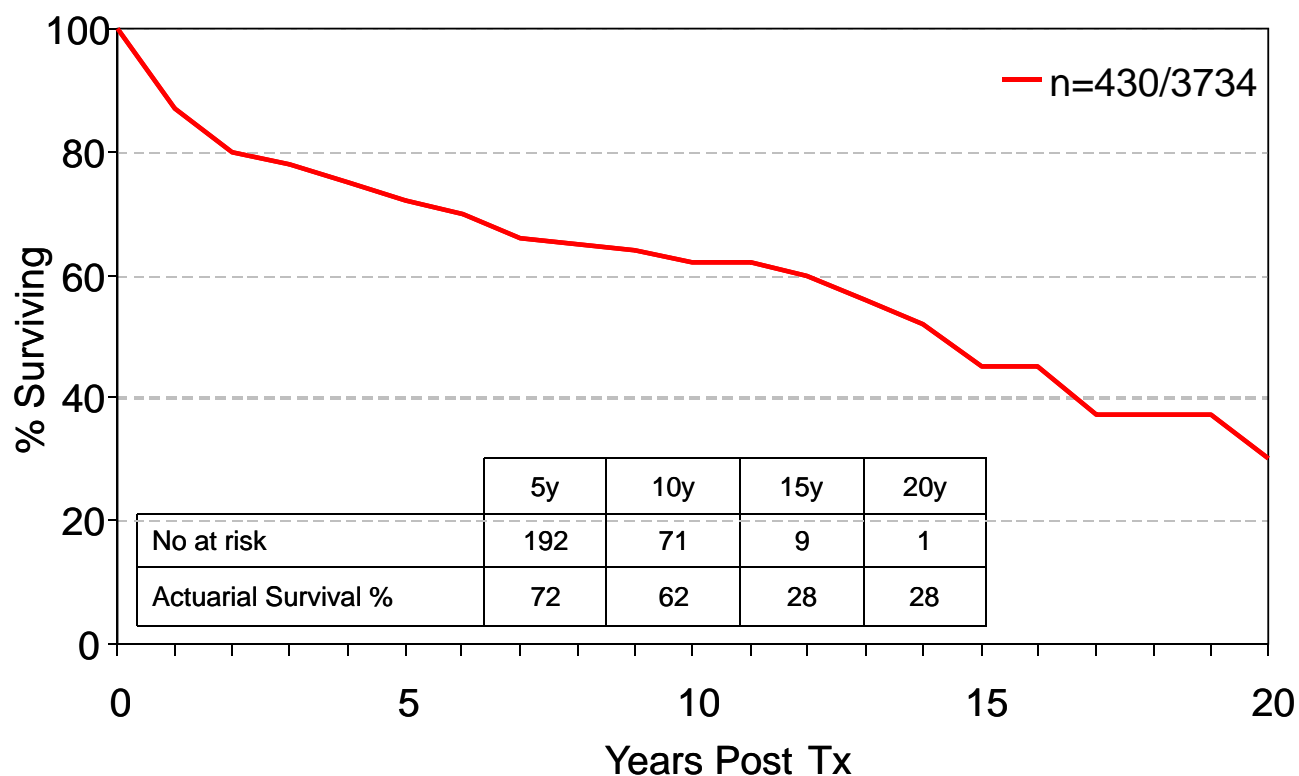


Liver Cancer as a Secondary Diagnosis n = 3734

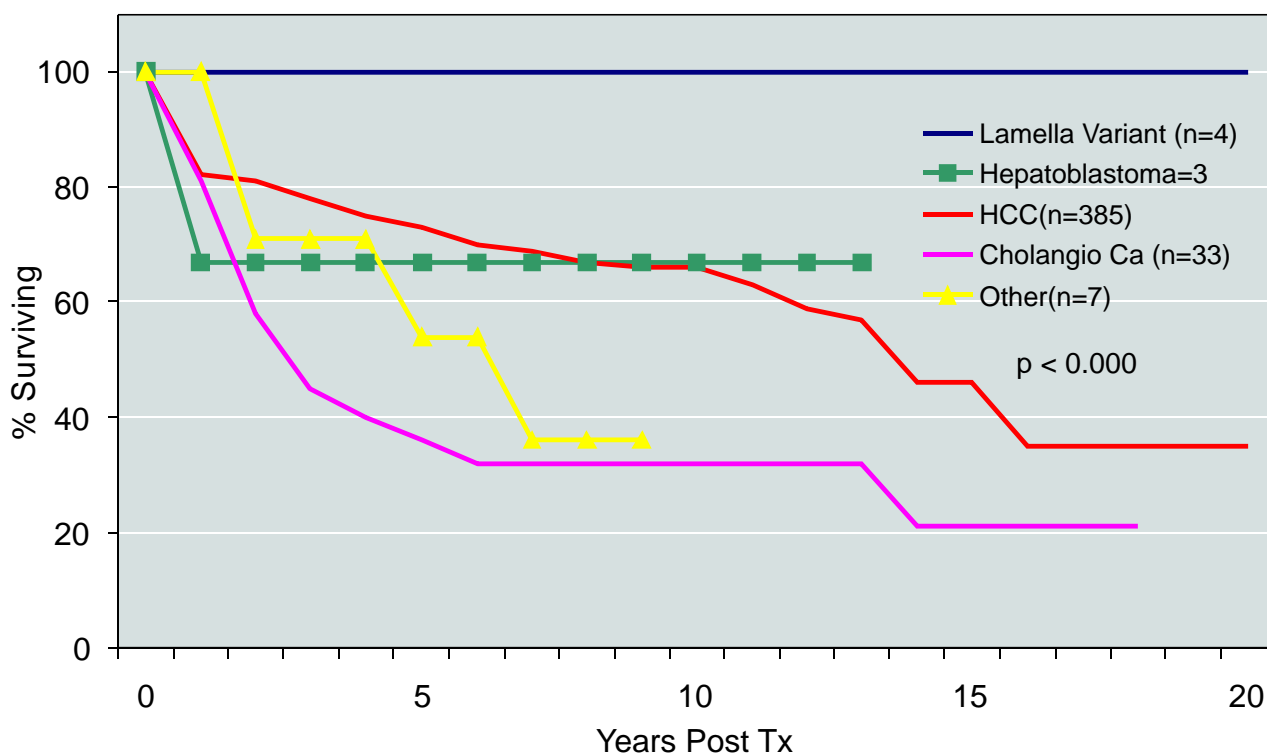
	No	Died	Died of This Cancer
HEPATOCELLULAR CA*	385	114	30 (8%)
CHOLANGIO CA	33	22	14(42%)
HEPATOBLASTOMA*	3	1	0
LAMELLAR VARIANT	4	0	0
OTHER	7	5	2 (29%)
Total	432* in 430pts (12%)	142(33% of pts with SCa)	46 (11% of pts with SCa)

* 2 patients had 2 secondary/incidental cancers

Overall Survival Liver Cancer as a Secondary Diagnosis



Liver Cancer as a Secondary Diagnosis n = 3734

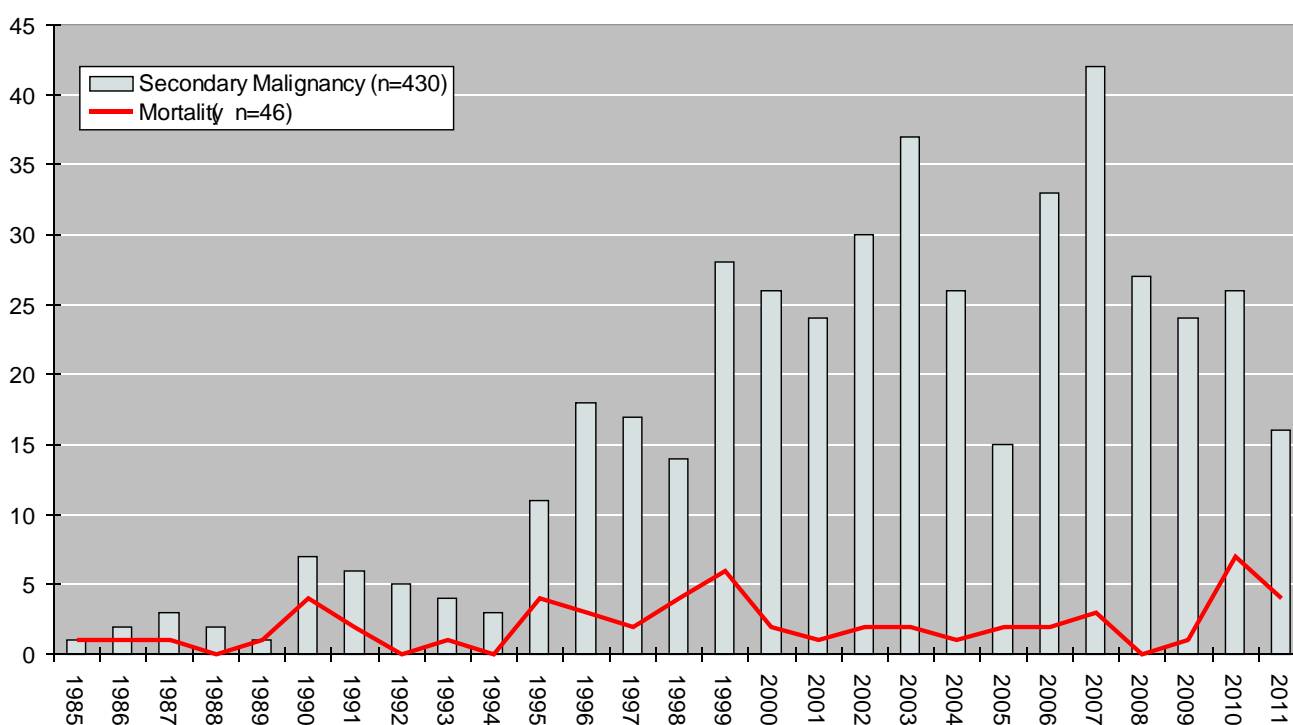


Secondary Liver Cancer Actuarial Survival Summary n = 430/ 3734(12%)



		1y	5y	10y	15y	20y
HCC (n=385)	nr	305	178	65	7	1
	% surviving	87	75	66	46	35
Cholangio Ca (n=33)	nr	27	10	5	2	
	% surviving	81	36	32	21	
Hepatoblastoma (n=3)	nr	3	2	2	1	
	% surviving	100	67	67	67	
Lamella Variant (n=4)	nr	4	4	2	2	1
	% surviving	100	100	100	100	100
Other (n=7)	nr	7	4			
	% surviving	100	54			

Liver Cancer as a Secondary Diagnosis Incidence and Mortality n = 430/3734 (12%)



Liver Cancer (Primary or Secondary Diagnosis)

n = 3734

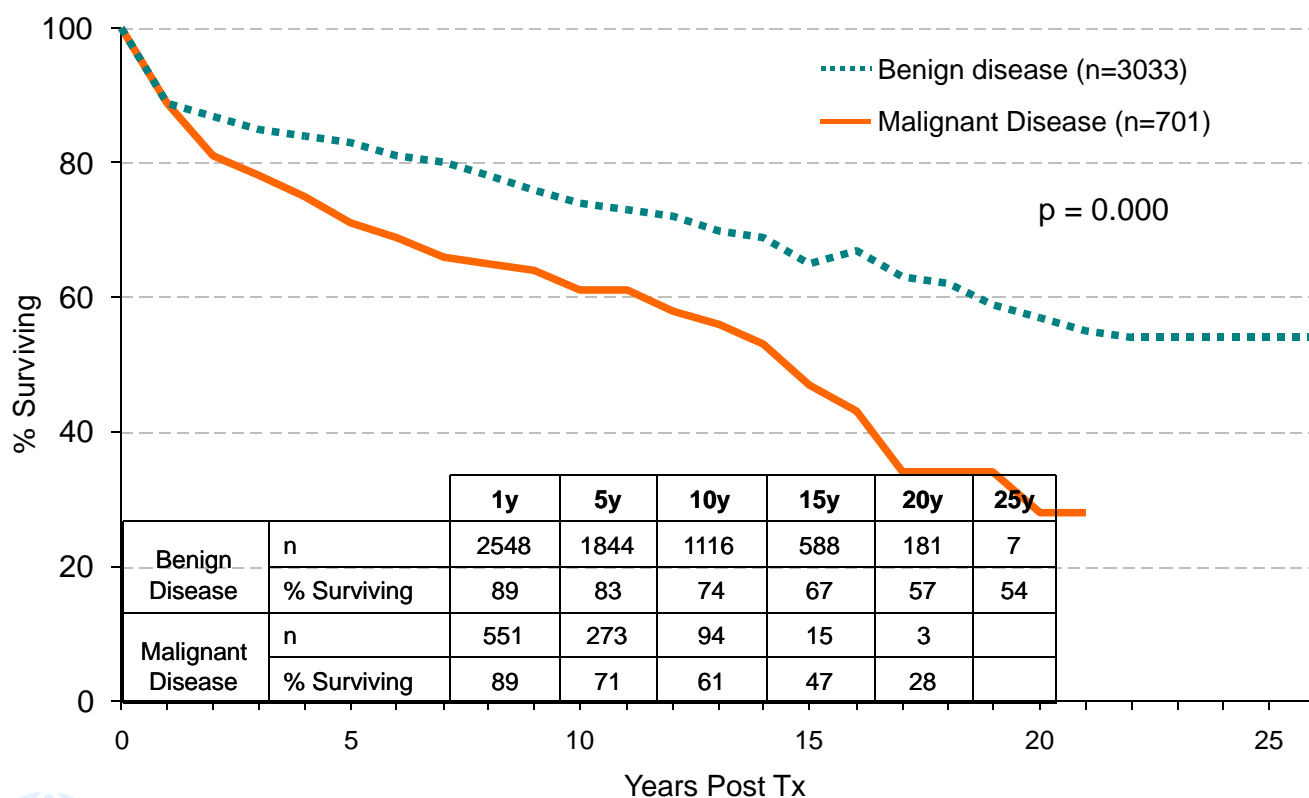


TYPE OF CA	NO	DIED	DIED OF THIS CA
HEPATOCELLULAR CA*	620	171	60 (10%)
CHOLANGIOCARCINOMA	36	23	15 (42%)
HEPATOBLASTOMA*	20	5	3 (15%)
LAMELLAR VARIANT	10	5	2 (10%)
ADENOCARCINOMA	5	4	1 (20%)
CARCINOID	4	4	4 (100%)
EPITHELOID HAEMANGIOENDOTHELIOMA	3	0	0
ANGIOSARCOMA	2	2	2 (100%)
GASTRINOMA	1	1	1 (100%)
PANCREATIC ISLET CELL	1	1	1 (100%)
TOTALS	701* (19% of pts)	216 (31% of those with Ca)	89 (13% of those with Ca at Tx)

* 1 pt had a primary and incidental cancer, 2 pts had 2 secondary cancers

Patient Actuarial Survival Benign Disease vs Pre Transplant Liver Malignancy

n = 3734



De Novo Non Skin Cancer

No at Risk = 3734



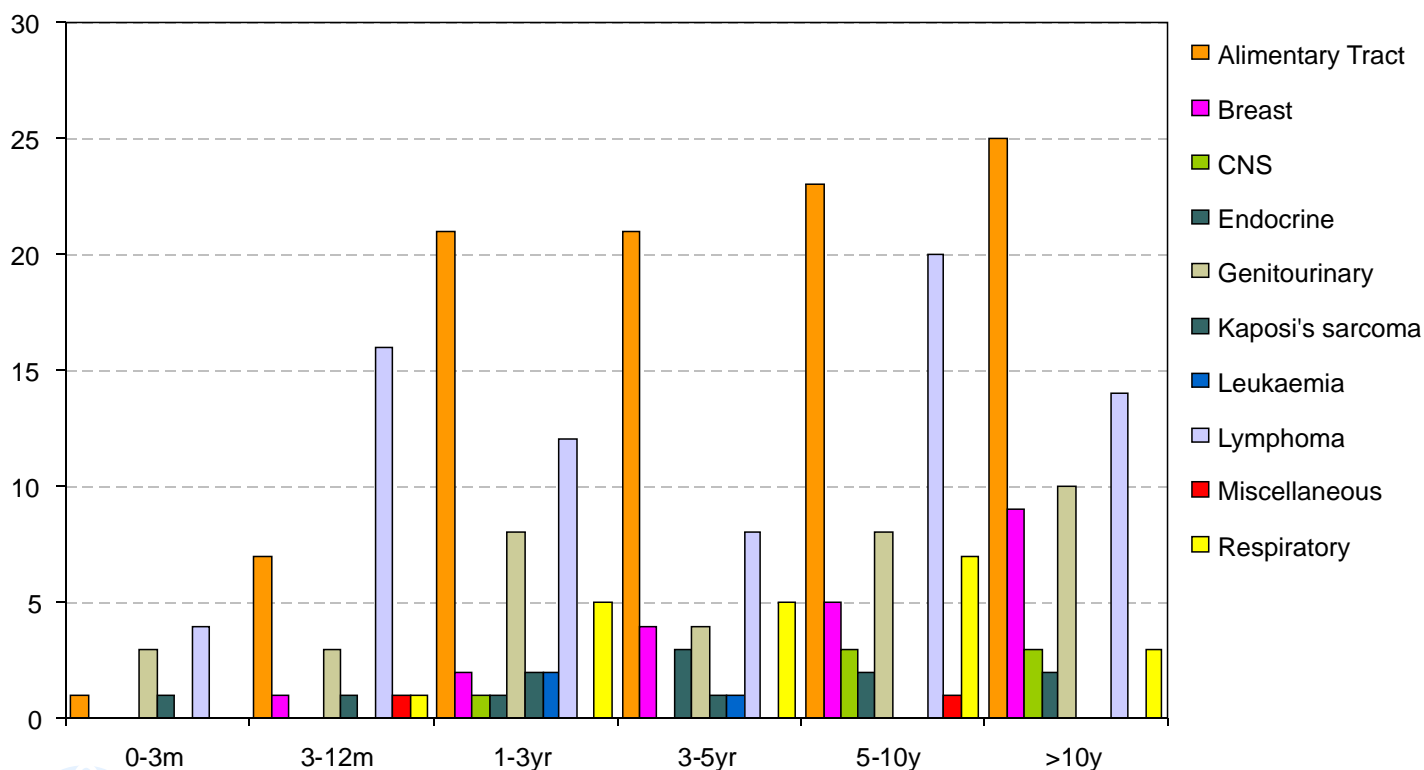
	No	Male	Female	Age of pts (yrs) m=median	Mths to diagnosis m =median	Died of This Cancer
Alimentary*	98	74	24	12.6 – 78 (m 57)	3 – 218 (m 797)	42 (43%)
Lymphoma*	74	46	28	1– 70 (m 41)	1 – 214 (m 64)	26 (35%)
Genitourinary*	36	23	13	21 – 75 (m 59)	2 – 231 (m 87)	4 (11%)
Breast	21	-	21	30 – 74 (m 53)	11 –241(m 112)	7 (33%)
Respiratory	21	17	4	29 – 74(m 57)	7 – 212(m70)	15 (71%)
Kaposi's	5	4	1	32 – 65 (m 51)	2 – 48 (m 21)	0
Endocrine	8	3	5	36 – 70 (m 54)	35 – 213 (m89)	2 (25%)
CNS	7	5	2	16.5 – 75 (m 57)	14 –211(m118)	5 (86%)
Leukaemia	3	1	2	2.9.– 49 (m 30)	16 – 44 (m 30)	0
Miscellaneous	2	0	2	65 – 67 (m 66)	6 – 60 (m 75)	0
Total	*275ca/ 256 pts	173	102	1 – 78 (m 53)	1 – 231 (m 72)	102 (40% of pts with Ca)

Forty patients also had a liver cancer at Tx; * 16 patients had more than 1 de novo malignancy

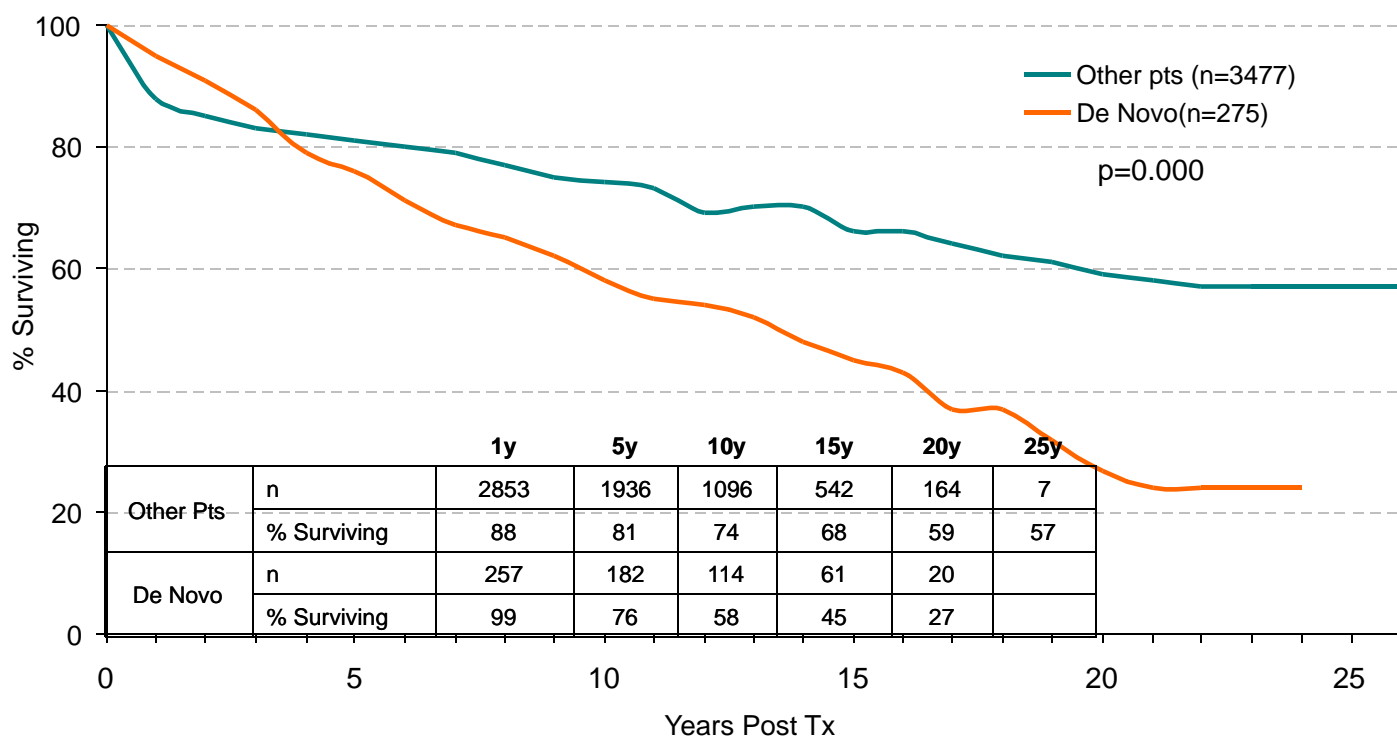
Time to 1st De Novo Non Skin Cancer

n = 3734

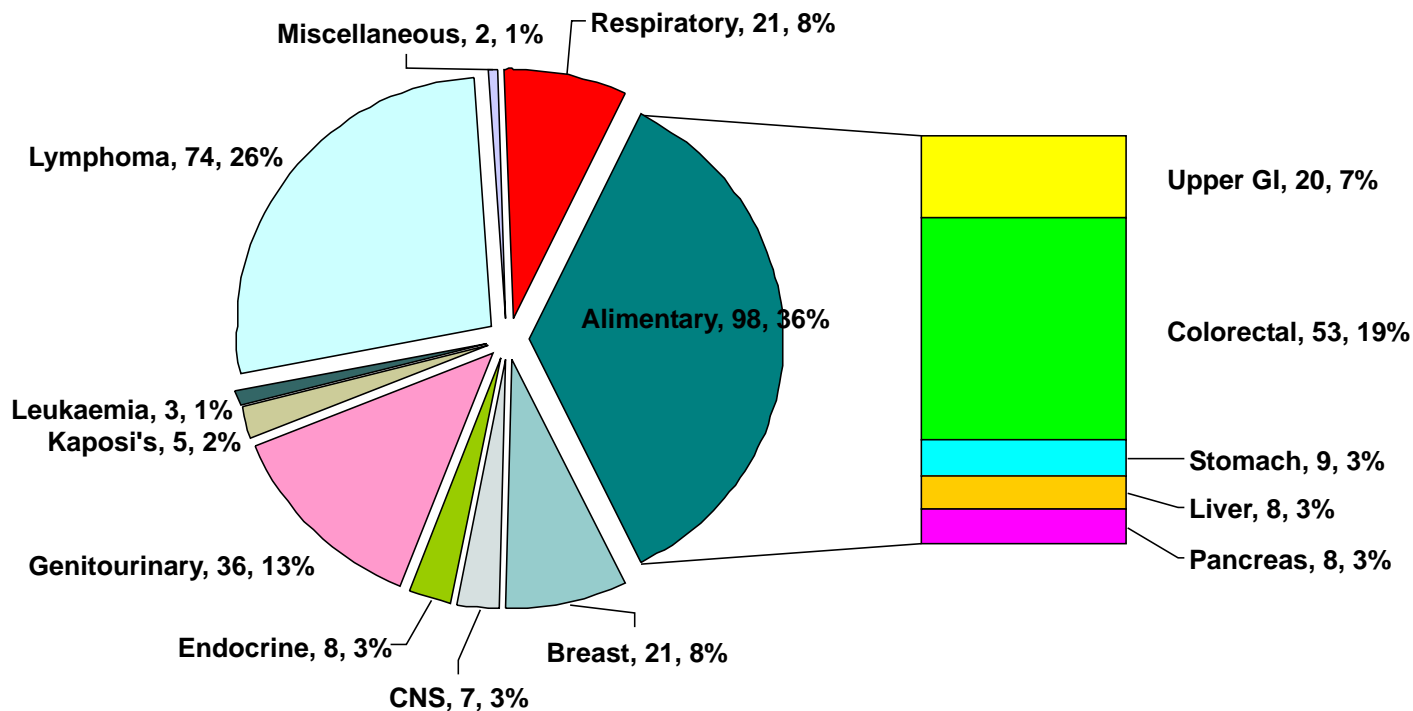
275 cancers in 256 pts (7% of all pts)



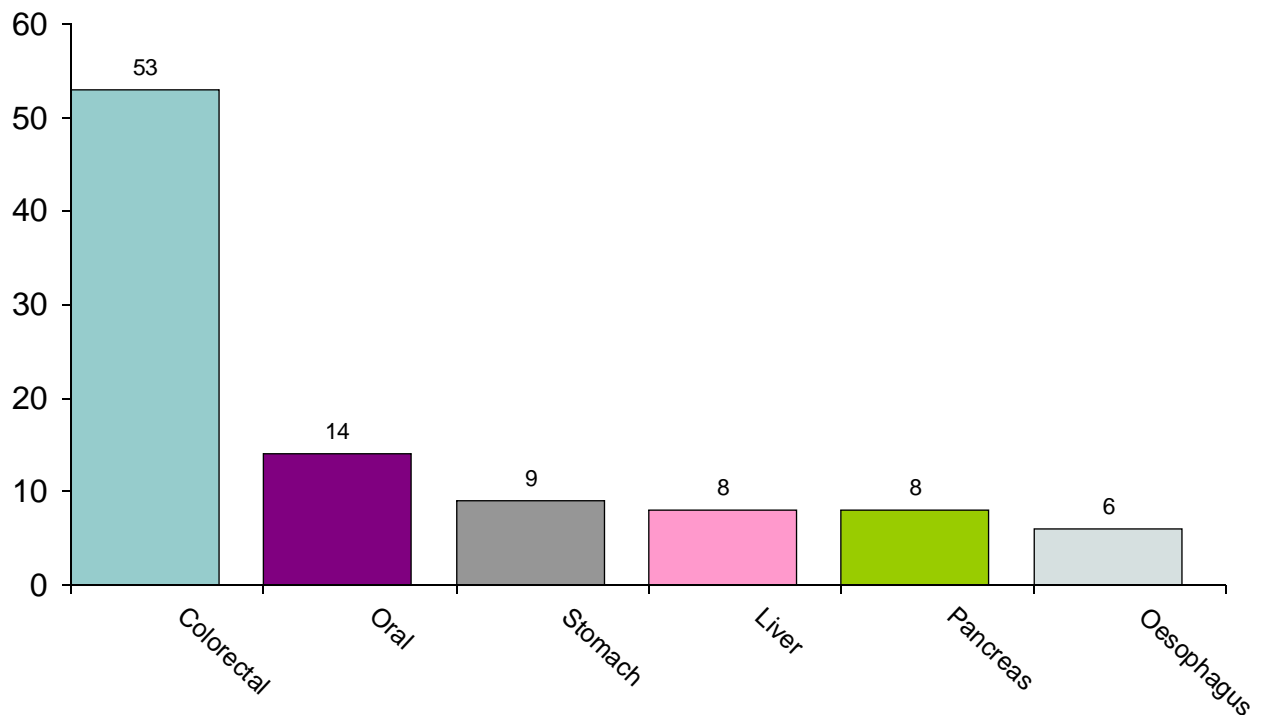
De Novo Non Skin Cancer vs All Patients n = 3734



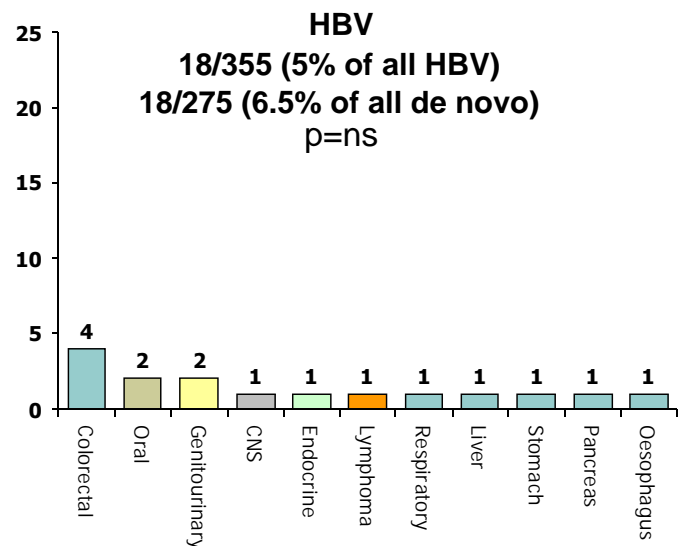
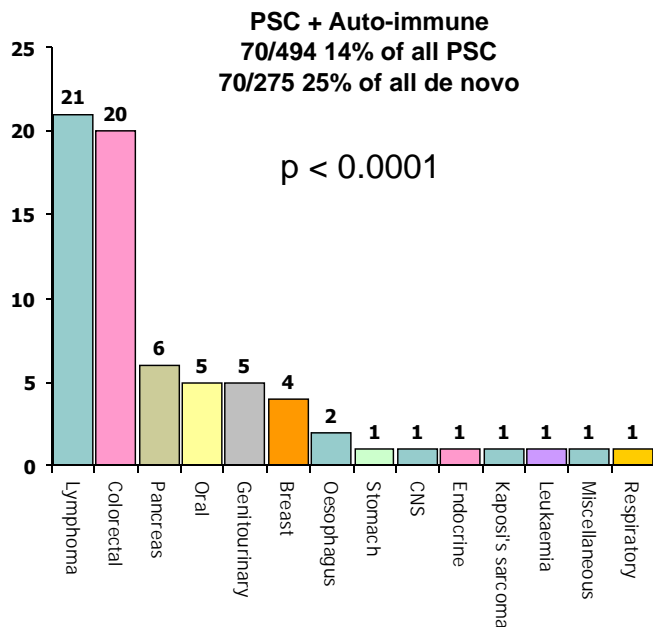
De Novo Non Skin Cancer n = 275/3734 (7%)



De Novo Non Skin Cancer Alimentary Tract Incidence n = 98/275 de novo cancers (36%)

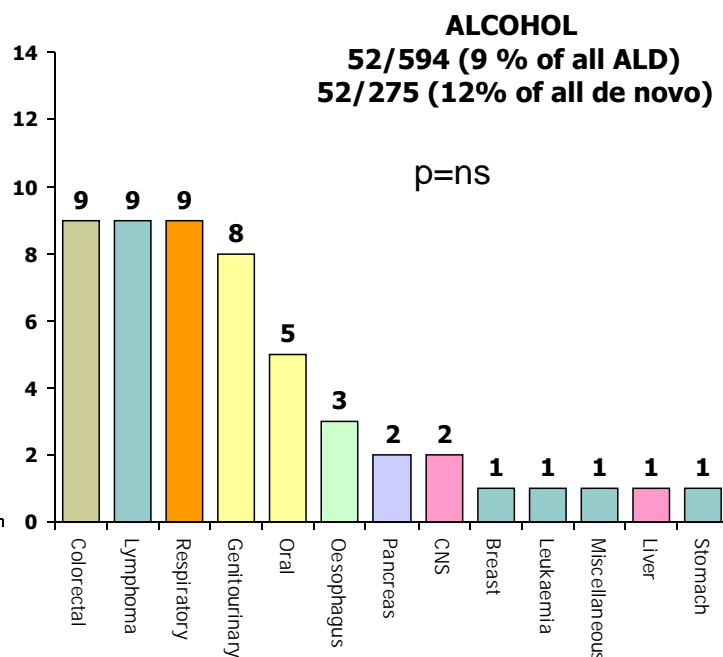
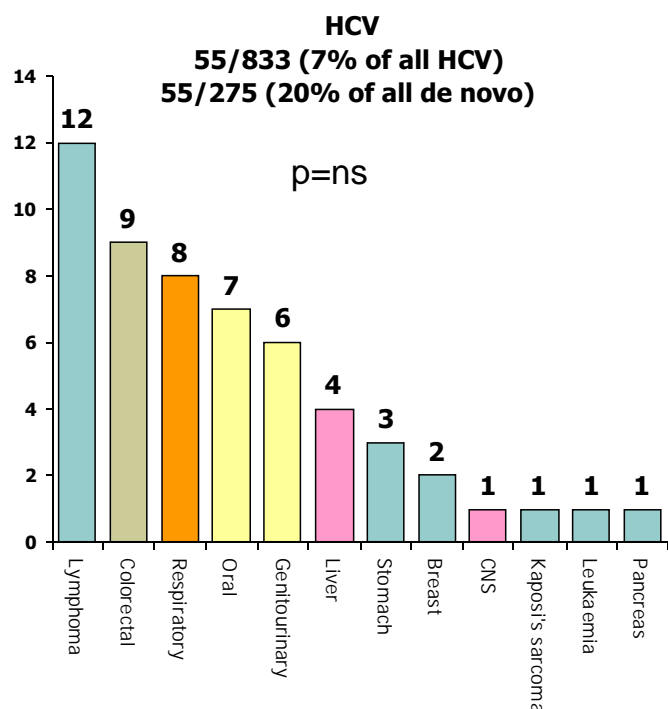


Pre Transplant Liver Disease and De Novo Non Skin Cancer n = 275/3734 (7%)



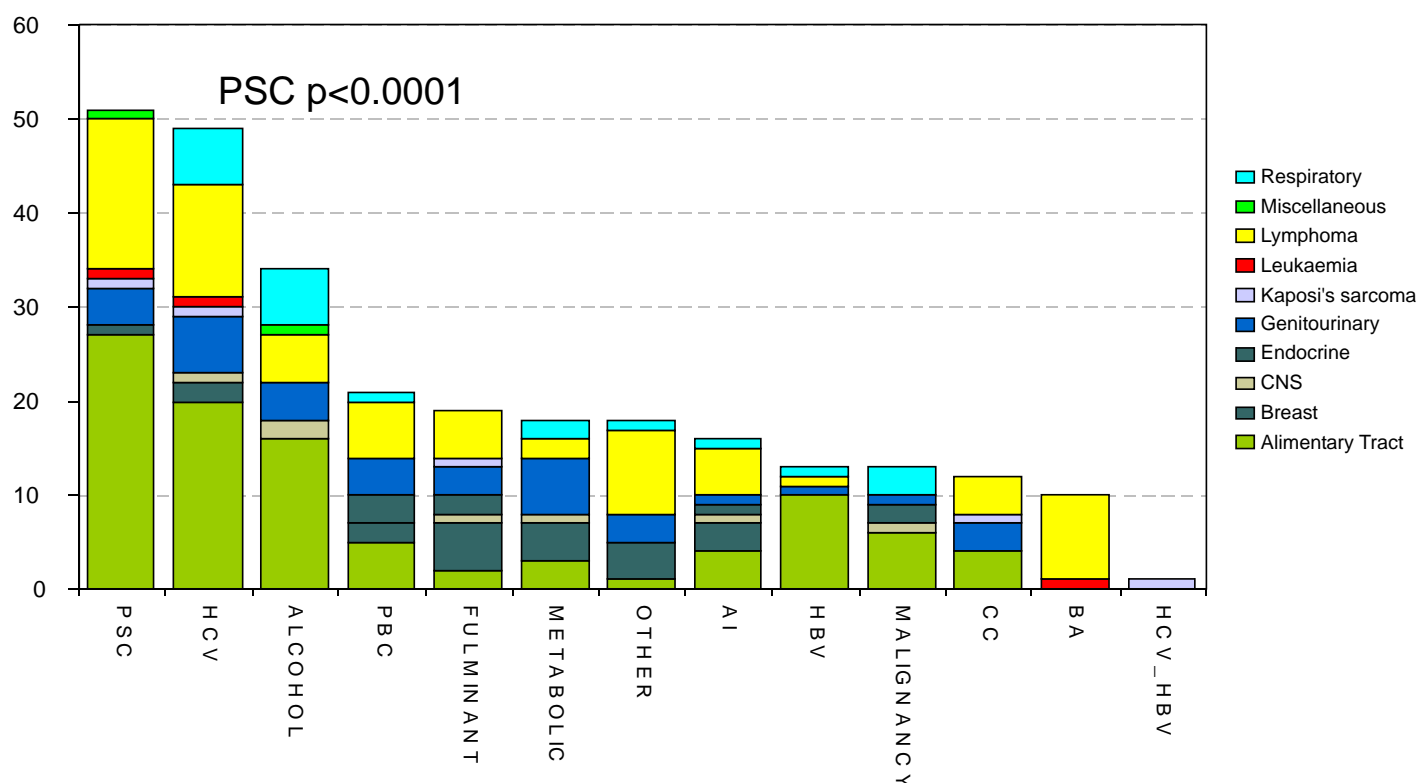
Pre Transplant Liver Disease and De Novo Non Skin Cancer

n = 275/3734(7%)



Primary Liver Disease and De Novo Non Skin Cancer

n = 275/3734 (7%)





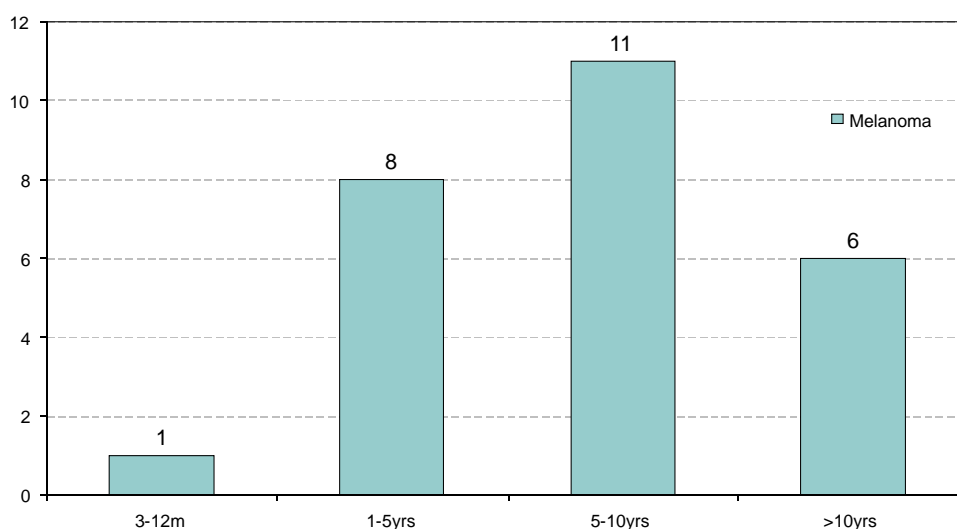
Type of Skin Cancer	Pts	Cancers
BCC	309	971
SCC	336	1388
Melanoma	26	26
Total	514 (15% of all pts)**	3508

****237 pts had multiple skin cancer types**

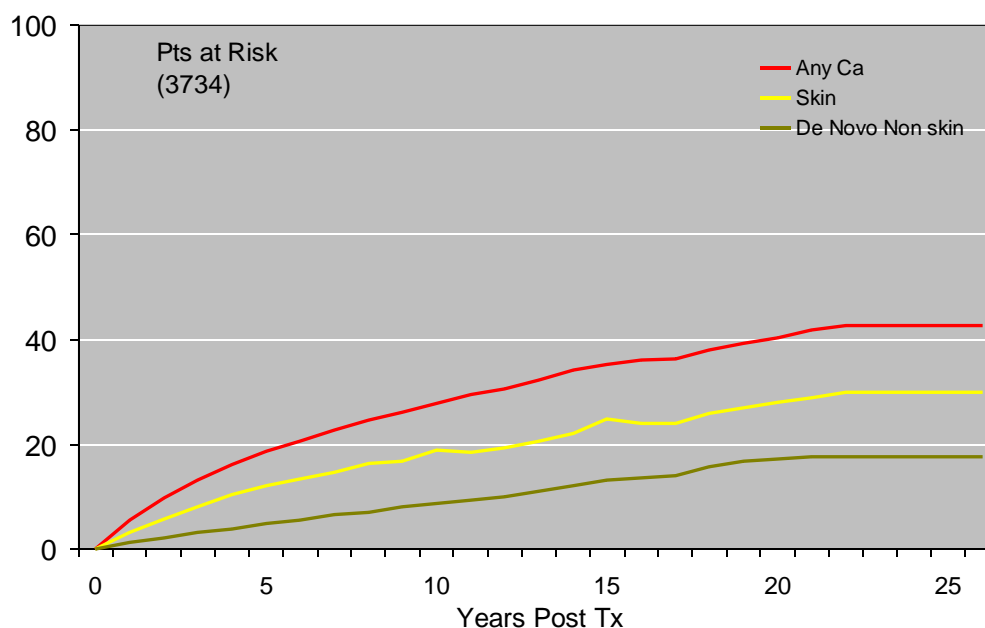
Time to Melanoma Skin Cancer Development

n = 3734

26 (0.7% of all pts)



Cumulative Risk of Diagnosis of Cancer Following Liver Tx. 1985-2011





Appendix I

Liver Transplant Units of Australia and New Zealand

Australian National Liver Transplant Unit

Royal Prince Alfred Hospital

Missenden Road

CAMPERDOWN NSW 2050

Email: pamela.dilworth@sswahs.nsw.gov.au

<http://www.sswahs.nsw.gov.au/Gastro/LiverTransplant/default.htm>

and

The Children's Hospital at Westmead

Hawkesbury Road

WESTMEAD NSW 2145

Victorian Liver Transplantation Unit

The Austin Hospital

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HEIDELBERG VIC 3084

<http://www.austin.org.au/Content.aspx?topicID=397>

and

The Royal Children's Hospital

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PARKVILLE VIC 3052

Queensland Liver Transplant Service

Princess Alexandra Hospital

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and

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HERSTON QLD 4029

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/

WA Liver Transplantation Service

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Verdun Street

NEDLANDS WA 6009

New Zealand Liver Transplant Unit

Auckland City 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	34	47	81
Crigler-Najjar	7	1	8
Familial amyloid polyneuropathy	0	30	30
Glycogen storage disease	0	3	3
Haemochromatosis	3	26	29
Homozygous Hypercholesterolemia	5	2	7
Idiopathic copper toxicosis	1	0	1
Indian childhood cirrhosis	1	0	1
Other*	9	5	14
Primary hyperoxaluria	7	6	13
Tyrosinemia	4	0	4
Urea cycle disorders**	17	4	21
Wilsonts disease	8	28	36
Total	96	152	248

* *Bile acid synthesis disorder*
Protein C deficiency
Methylmalonic acidemia
Familial immunodeficiency
Mitochondrial disease
Amyloidosis
Maple syrup urine disease
Porphyria
Propionic acidemia

** *OTC deficiency 12*
Citrullinemia 4
Argininosuccinic aciduria 3
Carbamyl phosphate synthetase deficiency



Appendix III

ANZLTR PRIMARY Diagnosis - Other by Age Group

Primary Diagnosis	Age group		Total
	Child	Adult	
Alagille syndrome	24	5	29
Alagille non-syndromic	2	0	2
Benign liver tumour - Adenomatosis	0	2	2
Benign liver tumour - Hemangioma	0	2	2
Caroli's disease / congenital hepatic fibrosis	3	17	20
Choledocal cyst	1	2	3
Cholestatic disease-Other	1	7	8
Chronic Budd Chiari	1	29	30
Congenital biliary fibrosis	0	2	2
Ductopenia	1	3	4
Granulomatous hepatitis / sarcoidosis	0	4	4
Histiocytosis X	4	0	4
Liver Trauma	0	1	1
Neonatal hepatitis	4	0	4
Nodular regenerative hyperplasia	0	6	6
Non alcoholic fatty liver (NAFLD or NASH)	0	69	69
Polycystic Liver disease	0	16	16
Polycystic liver and kidney disease	0	7	7
Progressive familial intrahepatic cholestasis(PFIC)	18	5	23
Secondary biliary cirrhosis	2	12	14
Secondary biliary cirrhosis - Hepatolithiasis	0	4	4
Secondary biliary cirrhosis - Cystic fibrosis	11	15	26
Other - specify [#]	3	22	25
Total	75	230	305

Vanishing bile duct syndrome
Haemangioteliectasia
Veno-occlusive disease
Chronic Active Hepatitis A
Non-cirrhotic portal hypertension
Kassabach-Merritt syndrome
Arterial-venous malformation
Hereditary haemorrhagic telangiectasia / OWRD
Oriental cholangio hepatitis

Coach syndrome
Biliary sclerosis



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	7	16	23
Acute - -1 -AAT	2	0	2
Acute Autoimmune hepatitis	0	6	6
Acute Unknown / unspecified	43	86	129
Acute - Paracetamol	2	13	15
Acute - Other drugs	3	20	23
Acute Herbs / mushrooms	0	6	6
Acute - Hepatitis A	0	3	3
Acute - Hepatitis B	0	52	52
Acute - NonA-NonB	6	13	19
Acute - Hepatitis E	0	1	1
Acute - Post liver resection	1	1	2
Subacute - Budd Chiari	1	2	3
Subacute - Wilson's	2	4	6
Subacute Autoimmune hepatitis	1	12	13
Subacute - Drug / Herbs	1	9	10
Subacute - Unknown / unspecified	4	30	34
Subacute - Hepatitis A	0	2	2
Subacute - Hepatitis B	0	16	16
Subacute - NonA - NonB	0	1	1
Total	73	295	368



Appendix V

ANZLTR Causes of Patient death

<u>Graft failure - other</u>	Age group		Total
	Children	Adult	
Vascular thrombosis	7	14	21
<i>Hepatic artery</i>	4	8	12
<i>Portal vein</i>	2	6	8
<i>Hepatic vein</i>	1	-	1
Non thrombotic infarction	2	-	2
Primary non function	4	16	20
Massive haemorrhagic necrosis	4	0	4
Recurrent disease (<i>ALD, PSC, CAH:AI</i>)	-	17	17
De novo Hep C	-	3	3
Biliary Complications	3	11	14
Other (<i>PNC, immune hepatitis, outflow obstruction</i>)	7	8	15
TOTAL	27	69	96

<u>Miscellaneous</u>	Children	Adult	
Multiorgan failure	5	45	50
Renal Failure	1	27	28
Graft vs Host disease	-	6	6
Social (<i>accident, suicide, non-compliance, Rx withdrawn</i>)	1	12	13
Sudden death (<i>cause unknown</i>)	1	22	23
Other (<i>Hyperkalaemia, motor neurone disease, diabetes complications, drug reaction, progression FAP, essential thrombocythemia</i>)	1	13	14
TOTAL	9	125	134