

AUSTRALIA & NEW ZEALAND

LIVER TRANSPLANT REGISTRY



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

DATA TO 31-12-2012

CD Included
INSIDE BACK COVER



Report PowerPoint
SLIDES

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FUNDING

ANZLTR receives majority funding from the Australian Organ and Tissue Authority supplemented by funds from Janssen-Cilag Pty Ltd.

CITATION

The suggested citation for this report is as follows : ANZLT Registry Report 2012
Australia and New Zealand Liver Transplant Registry
Brisbane, QLD, AUSTRALIA
Editors: S.V. Lynch, G.A. Balderson

STATISTICAL METHODS

Kaplan-Meier survival curves have been produced using IBM SPSS® for Windows™ Release 21.0.

ACKNOWLEDGMENT

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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Contents

Preface	1
Summary	2-4
Section 1	<u>Demographic Data</u>
Summary Statistics	5
Number of New Patients	6
Age of Recipients	7
Number of Transplants and Type of Graft by Year	8-9
Section 2	<u>Primary Diagnosis</u>
Primary Diseases of Recipients	10-11
Primary Diagnosis by Era	12-13
Chronic Viral Hepatitis - Adults Recipients	14-15
Section 3	<u>Patient Survival</u>
Patient Survival	16
Patient Survival by Age at Primary Transplant and Era of Transplant	17-19
Patient Survival by Type of Primary Graft	20
Patient Survival by Weight at Transplant - Children	21
Patient Survival by Primary Disease	22-24
Section 4	<u>Graft Outcome</u>
Graft Survival	25-27
Indication for Retransplantation	28-29
Section 5	<u>Causes of Death</u>
Causes of Patient Death	30-33
Section 6	<u>Deceased Donor Information</u>
Deceased Donors by Year	34
Donor Age and graft outcome	35
Section 7	<u>Living Donor Transplantation</u>
Living Donor Transplantation	36
Section 8	<u>Waiting List</u>
Waiting List Activity and Outcome	37-38
Waiting Time by Blood Group and Outcome	39
Section 9	<u>Liver Transplantation and Cancer</u>
Summary and Type of Primary Liver Cancer	40
Primary Liver Malignancy - Survival, Incidence and Mortality	41-43
Liver Cancer as Secondary Diagnosis - Type and Outcome	43-46
De Novo Non Skin Cancers	47-50
Skin Cancers Post Transplant	51
Cumulative Rate of Cancer Development	51
Appendix I - Transplant Units Australia and New Zealand	52
Appendix II - Metabolic Disorders	53
Appendix III - Other Diseases	54
Appendix IV - Fulminant Hepatic Failure	55
Appendix V - Causes of Patient Death	56



Preface

We are pleased to present the 24th Report of the Australia and New Zealand Liver Transplant Registry (ANZLTR). This report contains data to the 31st December 2012 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 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 2012, 4302 orthotopic liver transplants (OLT) were performed in Australia and New Zealand on 3980 patients, 3266 adult patients [82%] and 714 children (< 16 years) [18%]. The median age of all recipients was 47.6 years. The ages ranged from 24 days to 73.1 years. There is a significant difference in gender distribution between children (M=47%) and adults (M=65%)
6. Two hundred and forty-six new patients were transplanted in 2012 compared with 225 in 2011.
7. The trend to increasing age of adult recipients in recent years continued and the overall adult median age is now 50.4 years. The median age of new adult recipients in 2010-12 was 54.0 years.
- 8-9. In 2015, 15 more transplants were performed than in 2011 [268 vs 253]. Split grafts continue to make a significant contribution to the total number of paediatric transplants performed providing 21 of 46 [46%] grafts in 2012 and 197 of 812 [24%] overall. In children, other reduced size grafts have been used in 367 [45%] cases including 63 living donor grafts. One child has been treated with liver cell implantation. Of adult patients, 245 have received reduced size grafts - 203 split liver grafts (including 1 as auxiliary graft), 29 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 22.4% of recipients and chronic hepatitis B [CVH : HBV] in 6.2 %. 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 12 new patients transplanted in 2011 bringing the total to 81. While the proportion of adult patients transplanted with a primary diagnosis of chronic viral Hepatitis B, C or B/C/D has fallen slightly in era 2010-12 compared with the previous eras, 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 2012 was 45%.
16. Overall 1 year patient survival of all patients is 89% 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 71% 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 2010-12 cohort was 92% for all patients [94% for children, 92% for adults].
20. In both children and adults, there are worse early outcomes in patients receiving a deceased donor reduced size graft as their primary graft compared with split liver graft or whole liver grafts. Split liver grafts and whole livers have similar early outcomes in both children and adults.

Summary

Page

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 or Hepatitis C have significantly lower survival rates.
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 76% at 5 years with significantly better graft survival longer term in children. 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 graft survival in the early post-transplant years in both children and adults.
- 28-29. Vascular complications and rejection were the commonest indications for re-transplantation. Twelve percent of retransplants were due to poor early graft function. Re-transplantation for recurrent disease was most prevalent in adults [9% 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-two 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 2012 with 261 grafts transplanted from deceased donors. The number of livers split to produce two transplantable grafts was 21 in 2012. Seventeen liver grafts donated after cardiac death were transplanted. The number of people on the waiting list at 31 December 2012 was similar to the number on the waiting list at 31 December 2011.
35. Donor age has increased significantly in recent years. Long term graft survival trends lower in several older donor age groups.
36. Seventy-seven patients [63 children, 14 adults] have now received a living donor graft with 7 performed in 2012. Seventy-one were transplanted as a primary graft, 5 as a second and 1 as a third graft. The median age of the donors was 33.8 years with a range of 20.1 to 54.5 years. One adult graft was a domino whole liver graft.
37. This data has been expanded to include a breakdown of total waiting list activity for 2012 by age group. The number of patients listed for transplantation continued to increase in 2012 with 182 remaining on the waiting list at 31 December 2012. Patient delistings due to death, becoming too ill or tumour [HCC] progression accounted for 10% of all delistings while 268 [50%] were transplanted. Thirty five patients were listed as urgent in 2012 [16 with initial listing as Category 1 and 19 Category 2]. Thirteen [81%] of Category 1 and 17 [89%] of Category 2 patients had a positive outcome.



Summary

Page

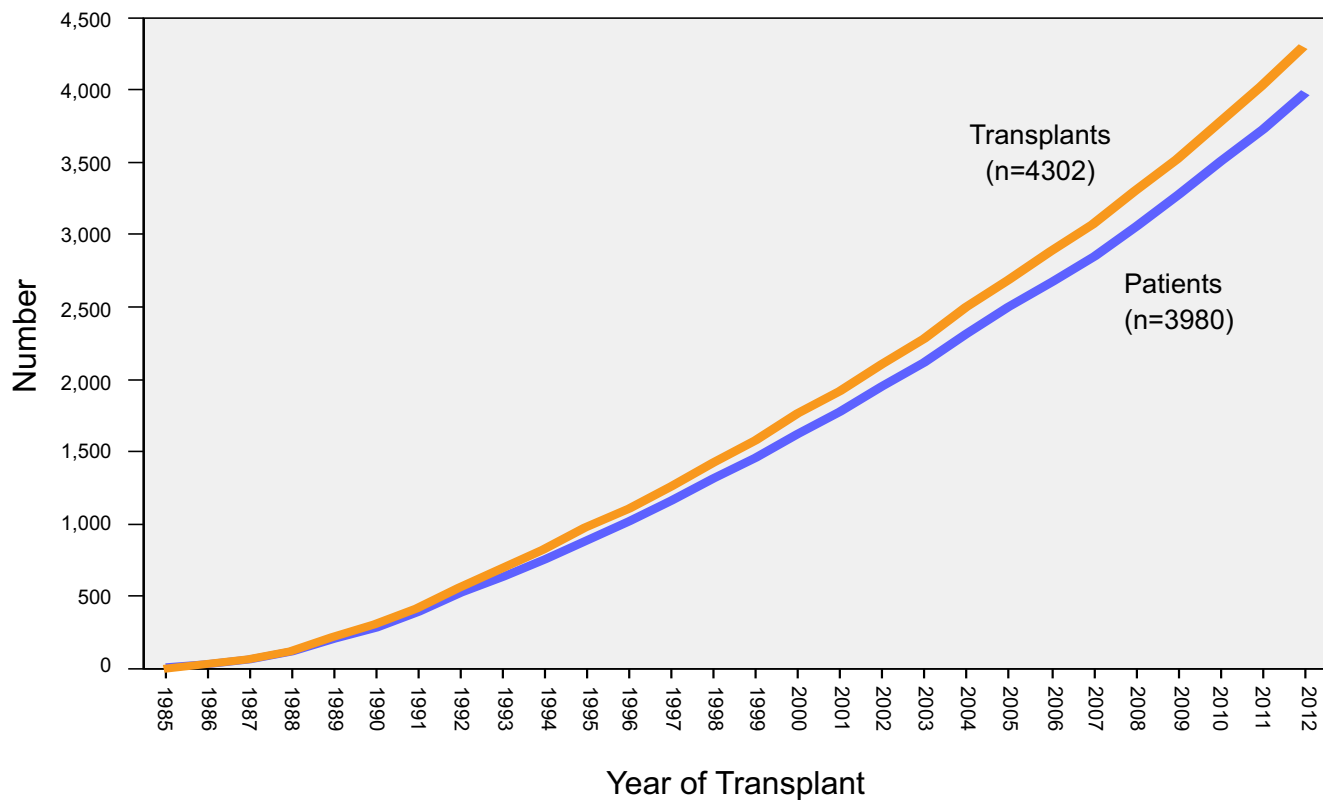
- 38-39. Median waiting times tended to be higher in 2012 in some blood groups. Blood group O patients had the longest waiting times.
40. Cancer in liver transplant recipients was analysed from two perspectives. Firstly, those who had a liver cancer diagnosis at the time of transplantation (as primary, secondary or incidental) and secondly those who developed a cancer post transplantation (de novo skin and de novo non skin cancer). Overall 766 (18%) patients were transplanted who had a liver malignancy - 295 (7%) as a primary diagnosis and 471 (12%) as a secondary diagnosis or incidental tumour, with Hepatocellular carcinoma being the most common. Post transplant 113 (16%) of these patients developed a recurrent cancer whilst 97 patients' death was related to this initial type of tumour.
- 41-43. The longer term survival of patients with liver cancer is significantly poorer for the subgroup of patients with Hepatoblastoma. There also continues to be an increase in the number of patients being transplanted for primary malignancy in the patient cohort for the time period of 2009-2012 with Hepatocellular Carcinoma being the most common underlying cause.
- 43-45. Four hundred and seventy one [12%] had liver cancer as a secondary or incidental diagnosis with hepatocellular carcinoma the most common. Of these 48 (10%) died from their malignancy. Those with cholangiocarcinoma had significantly poorer survival.
46. Patient survival was significantly worse in the 768 (19%) patients with pre transplant liver malignancy compared with patients with other forms of liver disease.
- 47-48. Three hundred and nine de novo non-skin cancers developed in 295 patients (7%). Eleven patients developed more than one type of de novo cancer. One hundred and twenty-two (41%) patients died from their de novo cancer. Cancers of the alimentary tract (114) and lymphoma (79) are the two most common types of de novo cancer.
- 49-50. For the alimentary tract cancers the colon was the predominate site (59). The incidence of de novo non-skin cancers appears to vary according to the diagnosed pre-transplant liver disease, with the incidence of de-novo non-skin malignancy in patients with Primary Sclerosing Cholangitis being statistically significantly higher than for the other underlying liver diseases ($p < 0.0001$).
51. Nine hundred and forty eight patients (25%) developed 3809 skin cancers with 555 patients having multiple skin cancer types and 29 developed melanoma.

Of note, the cumulative risk of diagnosis of any cancer post transplant is approaching 40% by 20 years.

Section 1

Demographic Data

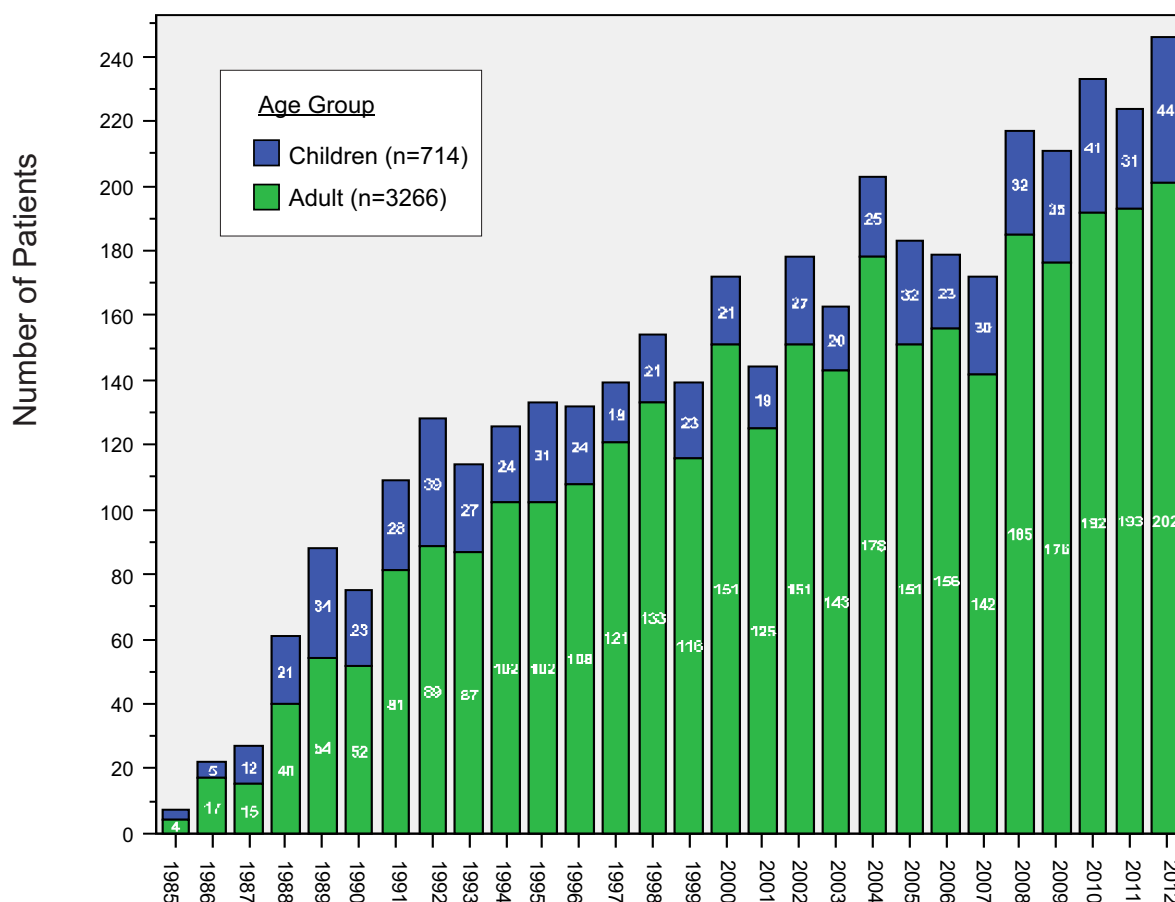




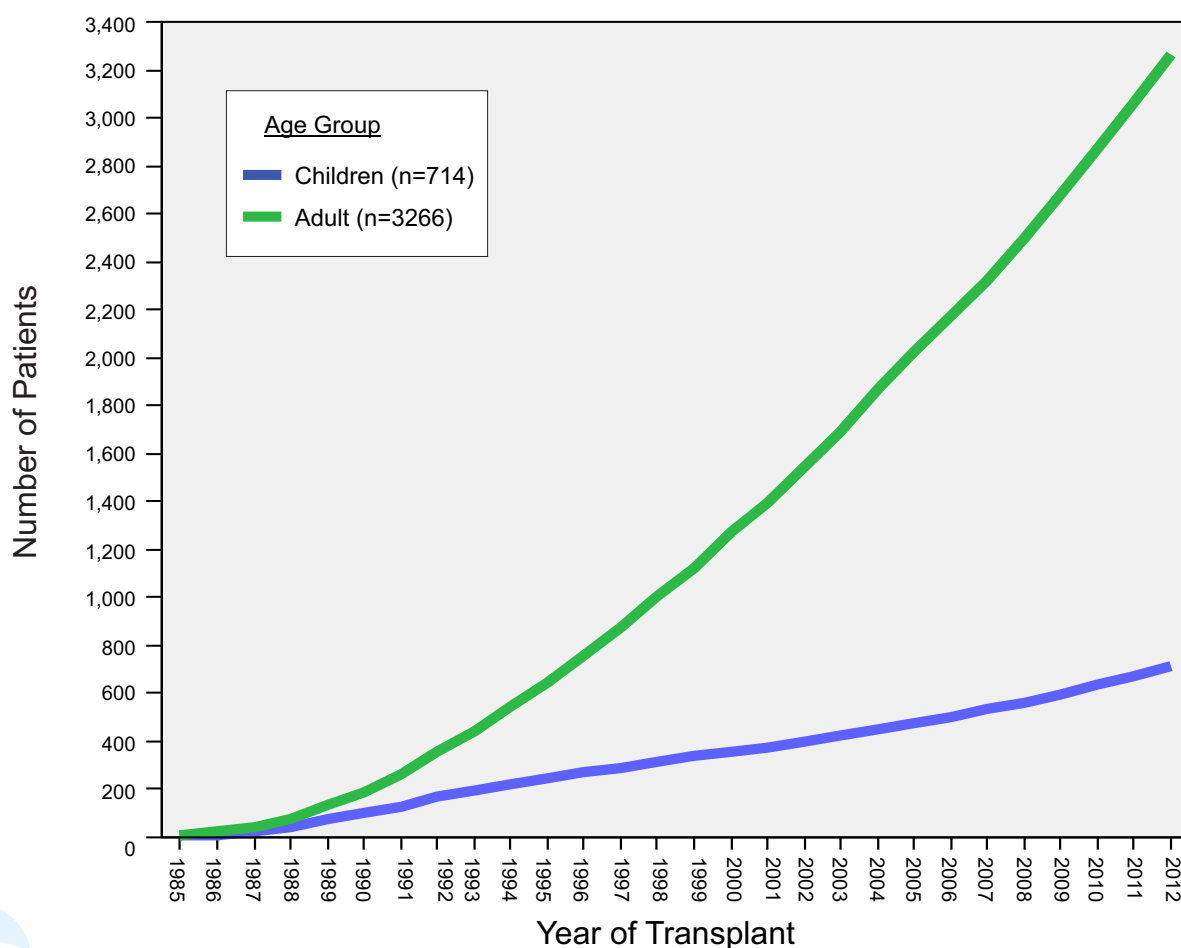
Summary Statistics - Age and Gender

ALL PATIENTS TRANSPLANTED

	Children [<16y]	Adults	Total
<i>Patients</i>	714	3266	3980
Age			
<i>Mean ± SD</i>	4.5 ± 4.5y	48.5 ± 11.6y	40.6 ± 20.0y
<i>Median</i>	2.4y	50.4y	47.6y
<i>Range</i>	24d -15.9y	16.0 - 73.1y	24d - 73.1y
Gender			
<i>Female</i>	381 (53%)	1146 (35%)	1527 (38%)
<i>Male</i>	333 (47%)	2120 (65%)	2453 (62%)
Surviving	573 (80%)	2314 (71%)	2887 (73%)



Cumulative Number of New Patients Transplanted

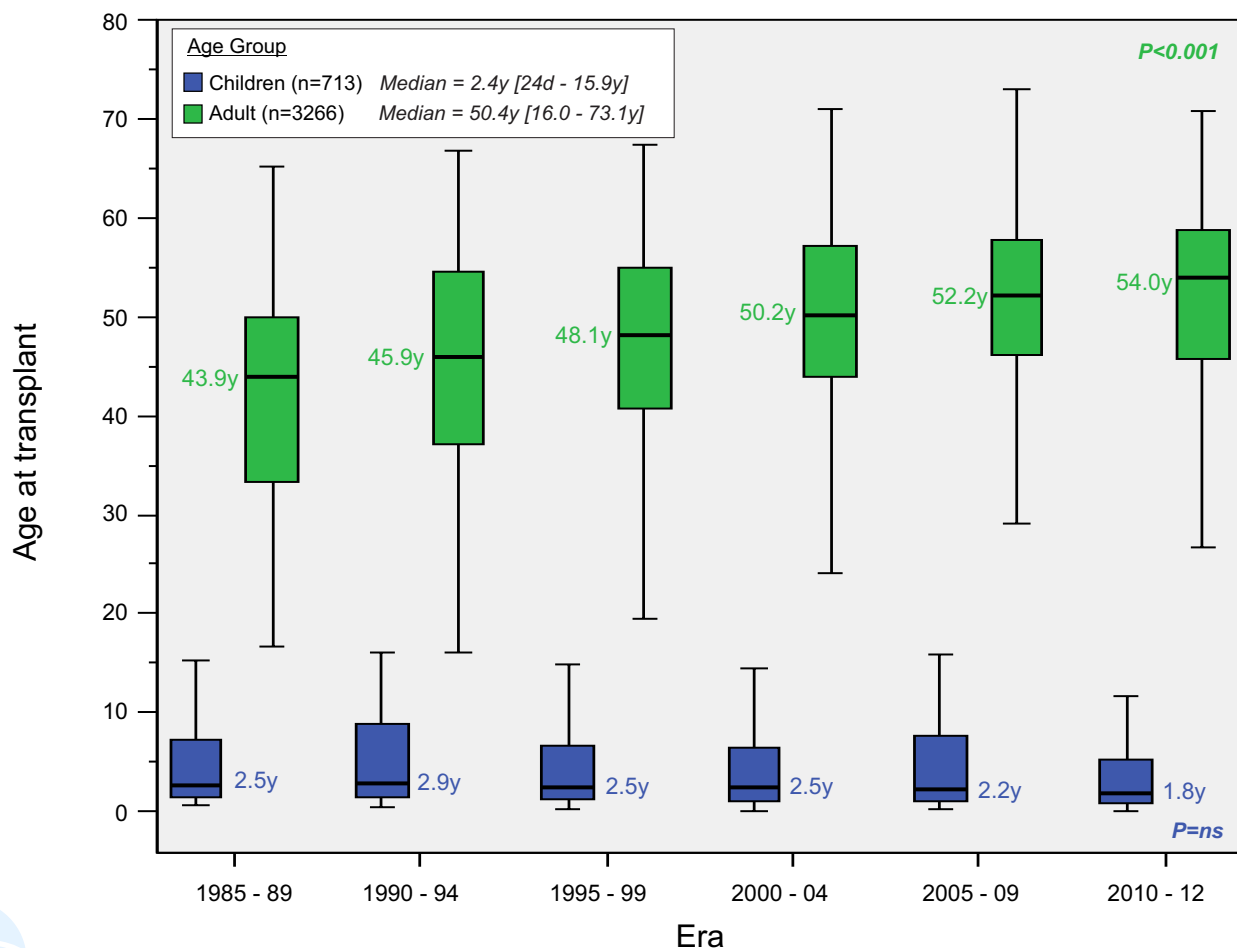


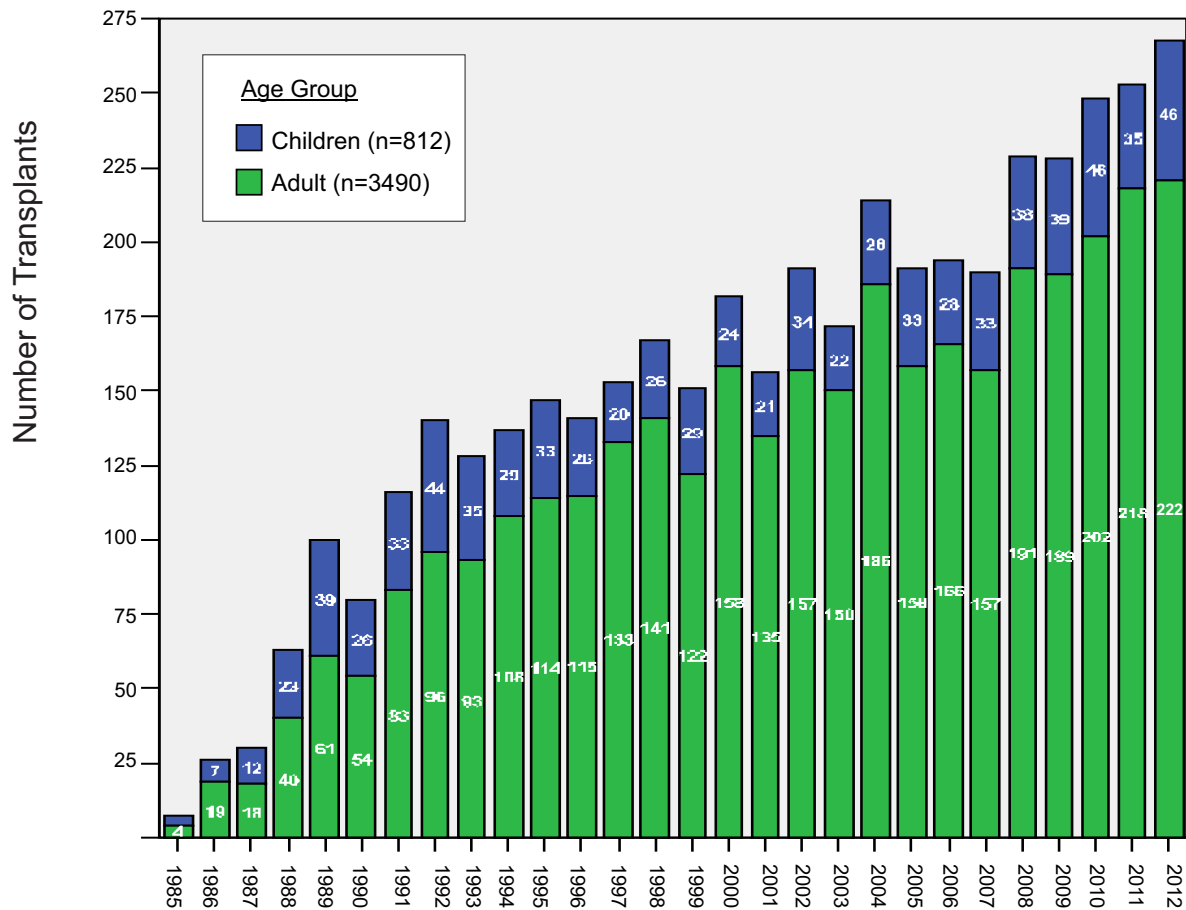
Number of Recipients By Age at Primary Transplant

N=3980

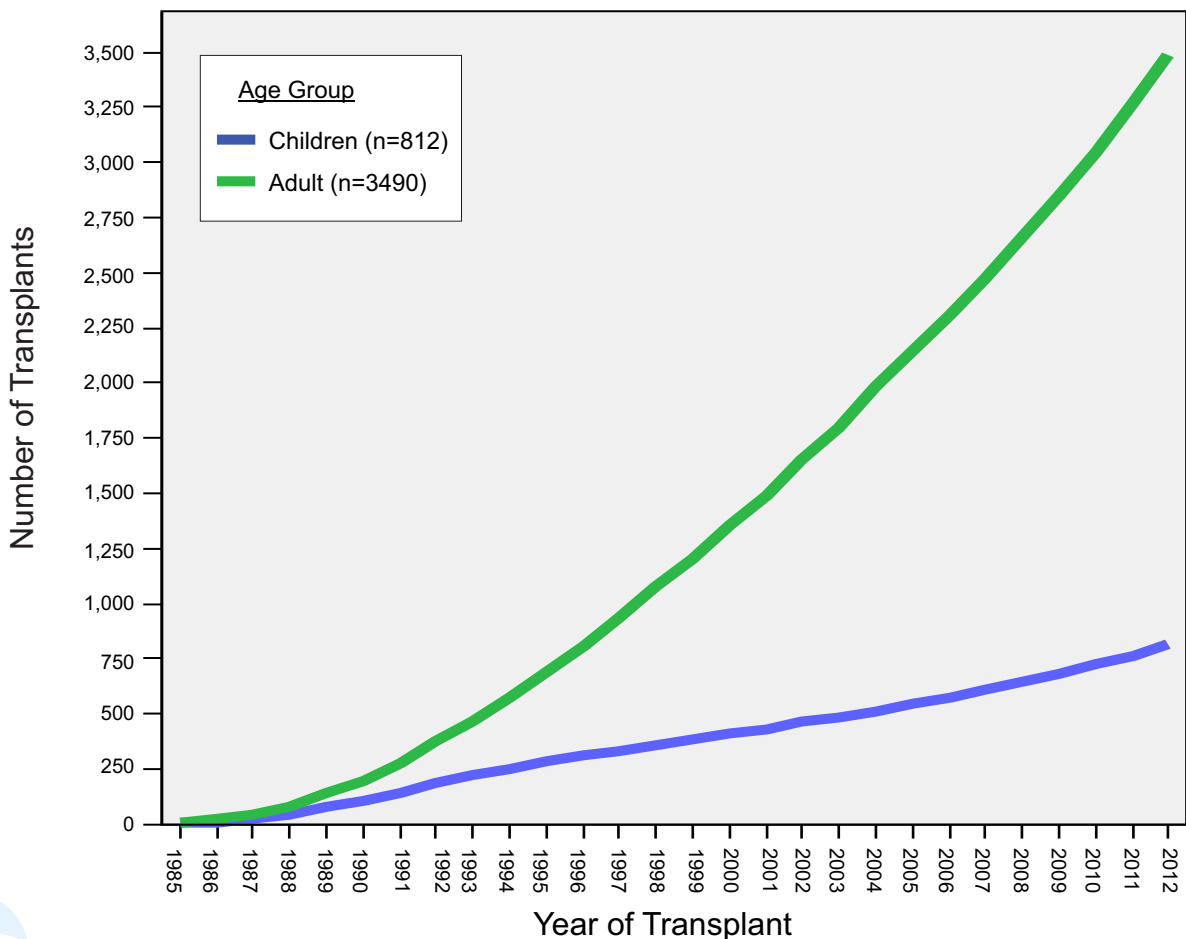


Age at Primary Transplant by Era





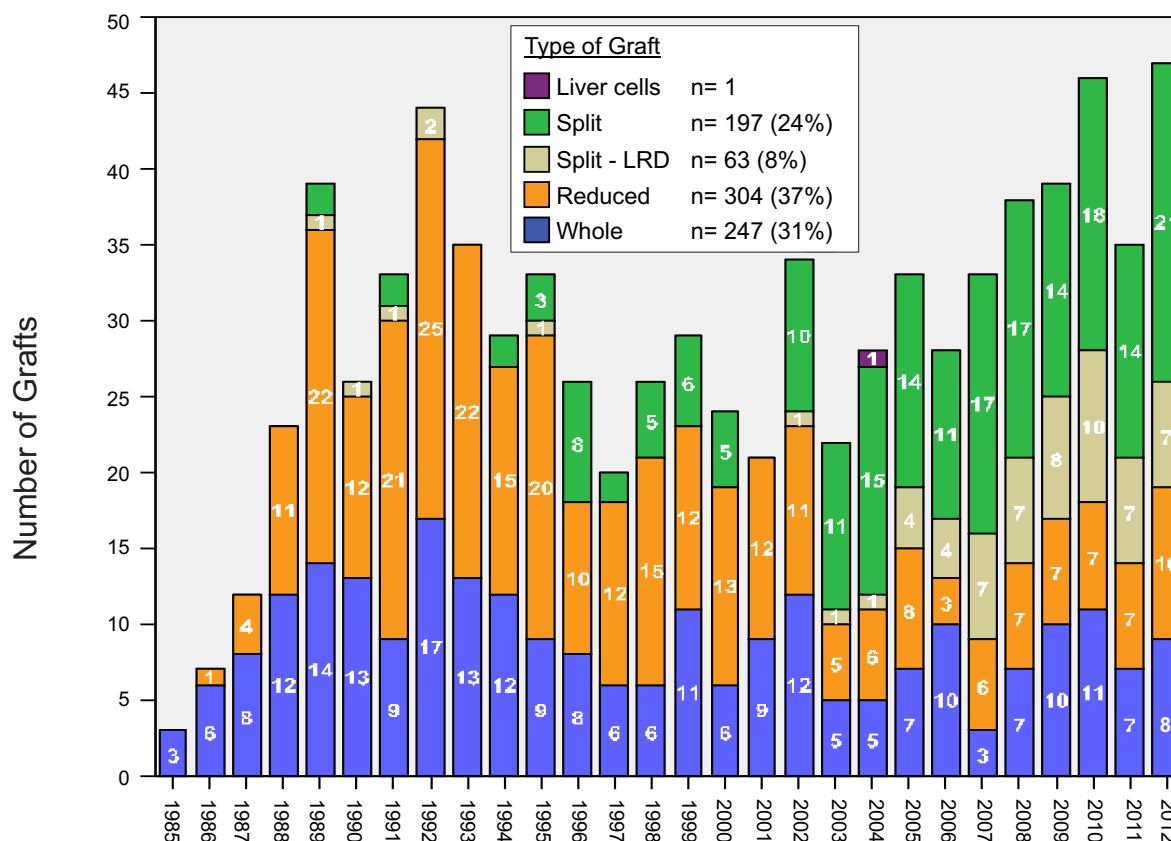
Cumulative Number of Transplants



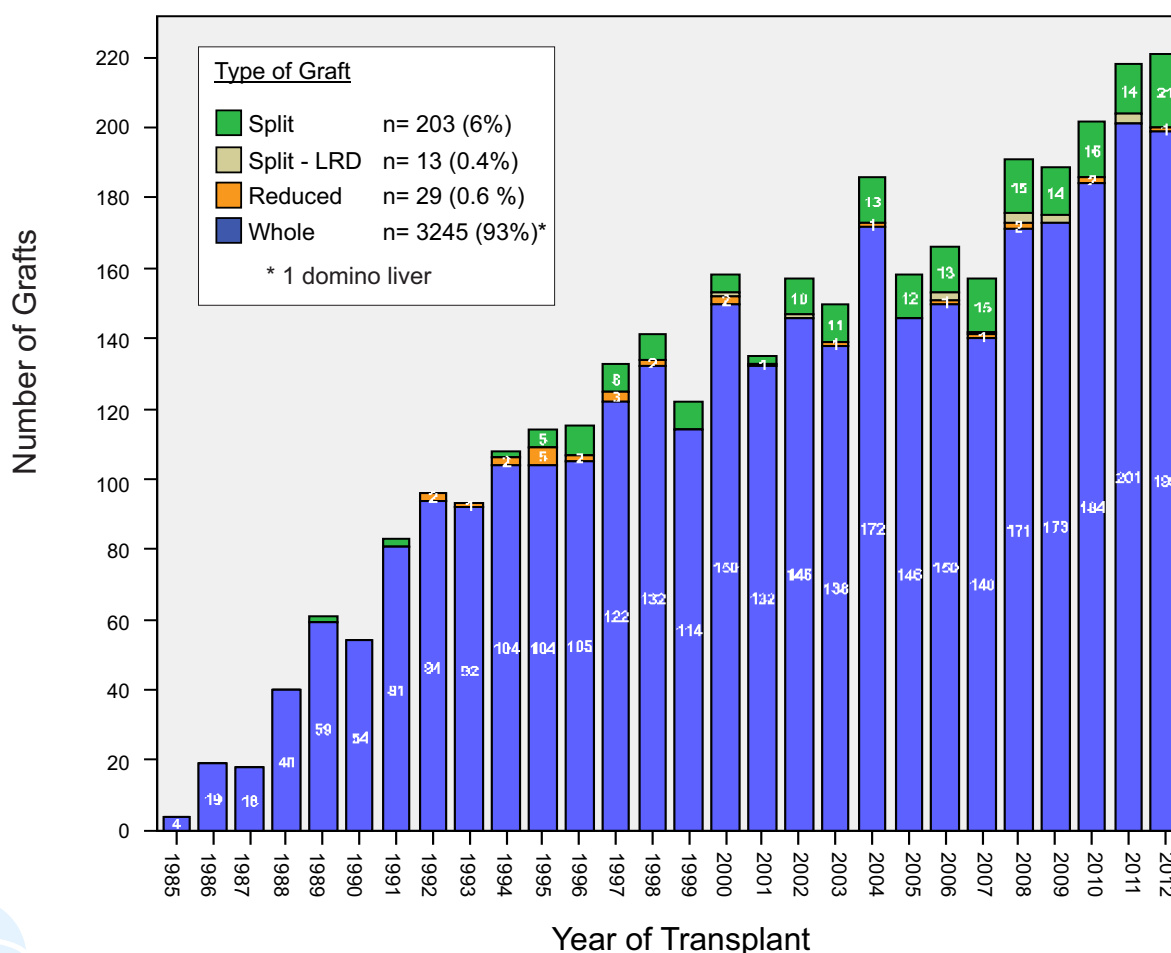
Type of Graft by Year

Split vs Reduced vs Whole

Children (n = 812)



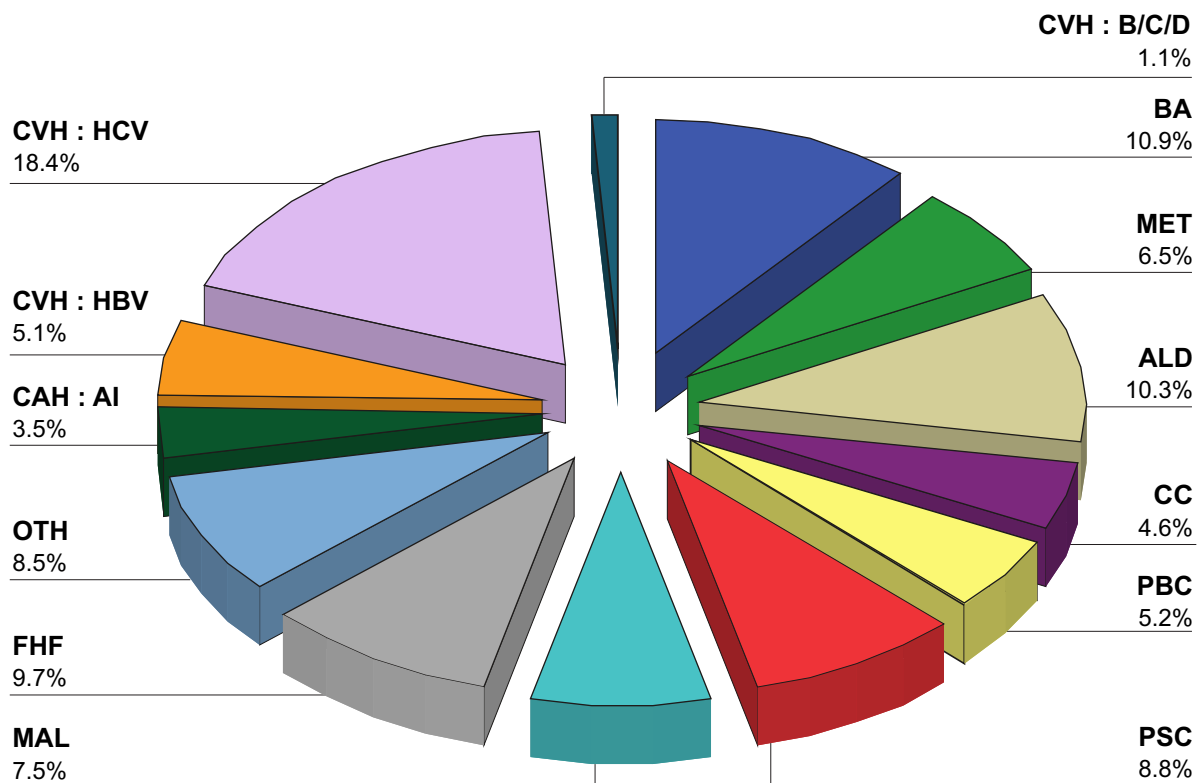
Adults (n = 3490)



Section 2

Primary Diagnosis





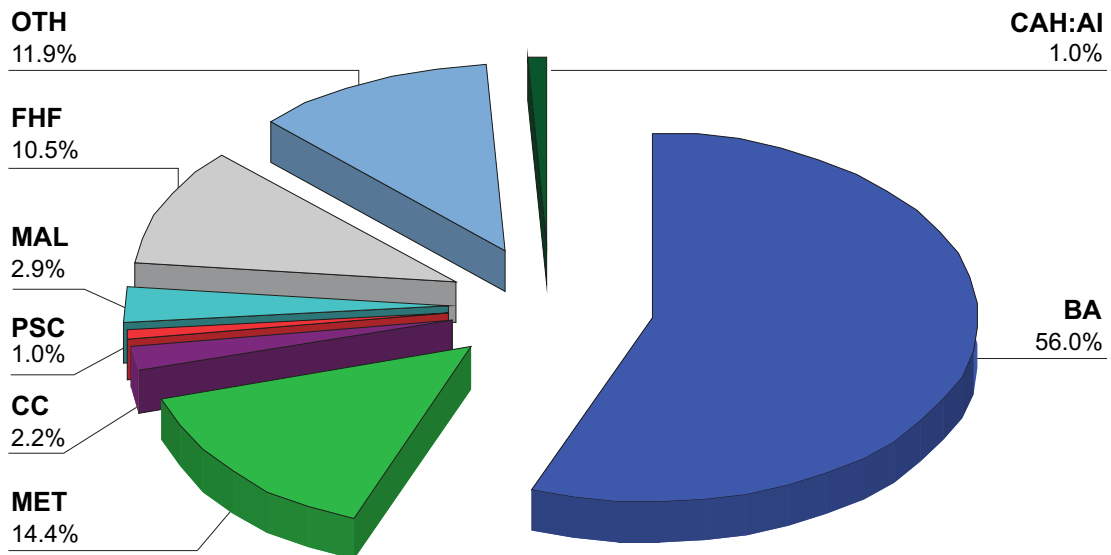
Diagnosis Group

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

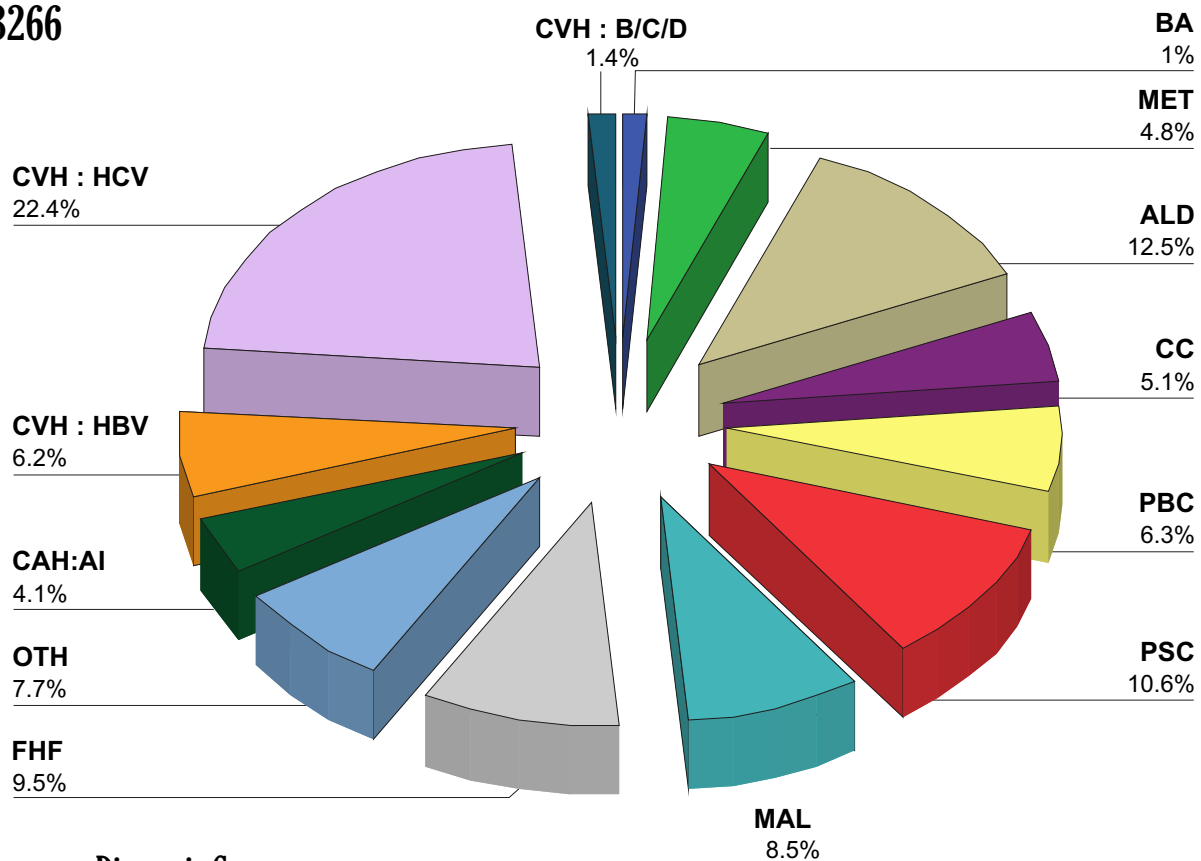
Primary Diseases of Children

n = 714



Primary Diseases of Adult Recipients

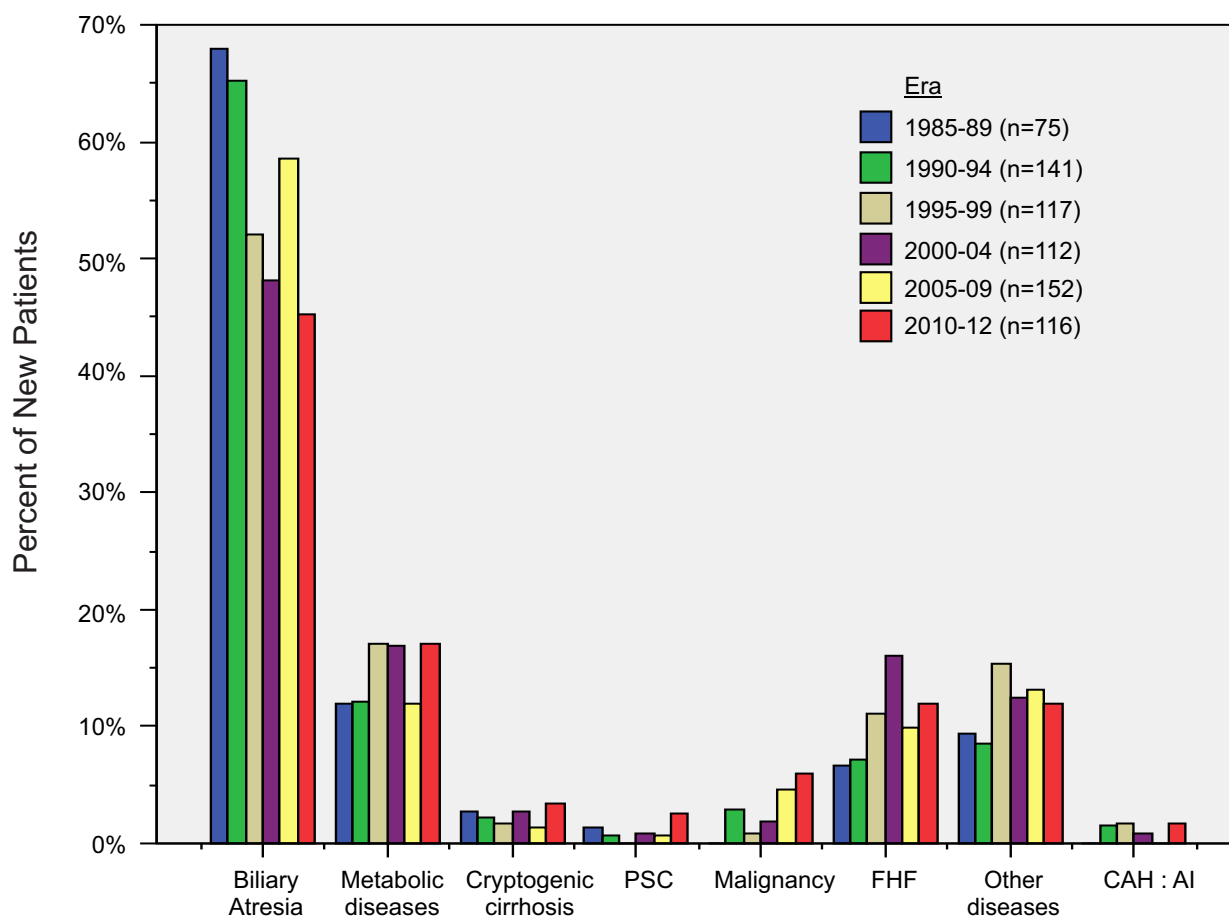
n = 3266



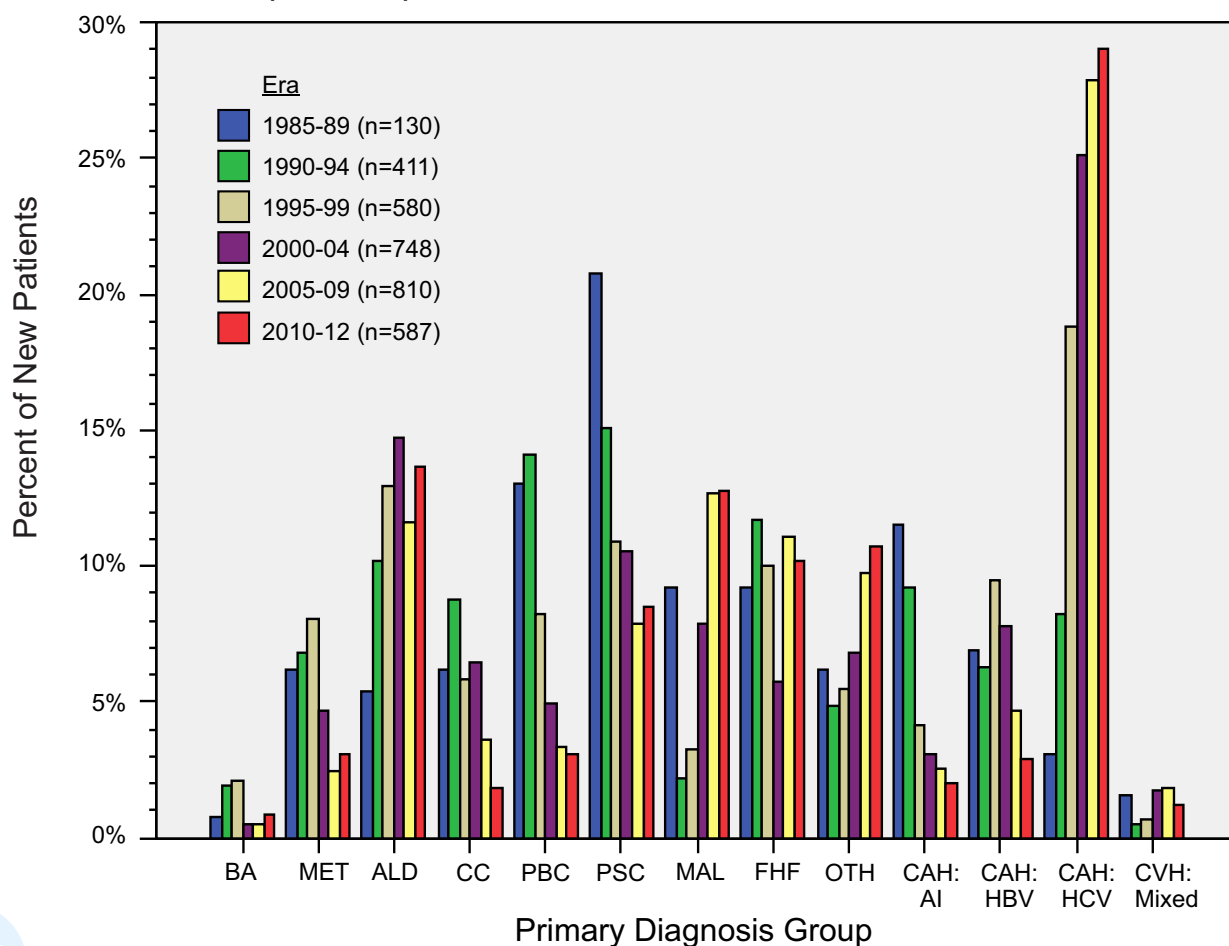
Diagnosis Group

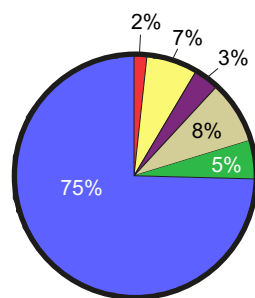
BA	- Biliary atresia	MAL	- Malignancy
MET	- Metabolic diseases	FHF	- Fulminant hepatic failure
ALD	- Alcoholic cirrhosis	OTH	- Other diseases
CC	- Cryptogenic cirrhosis	CAH : AI	- Chronic active hepatitis [autoimmune]
PBC	- Primary biliary cirrhosis	CVH : HBV	- Chronic viral hepatitis B
PSC	- Primary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

Children (n=713)

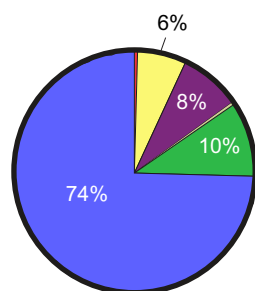


Adults (n = 3266)

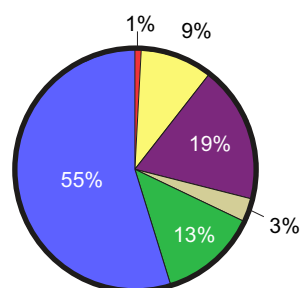




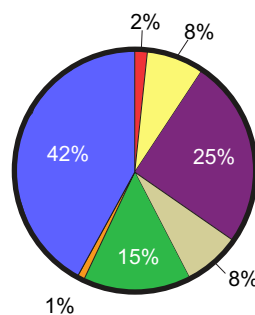
— 1985 - 89
(n=130)



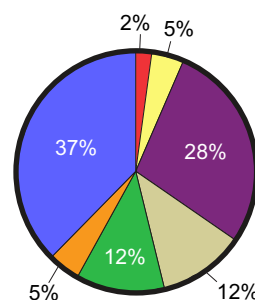
— 1990 - 94
(n=411)



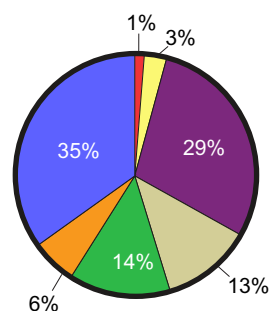
— 1995 - 99
(n=580)



— 2000 - 04
(n=748)

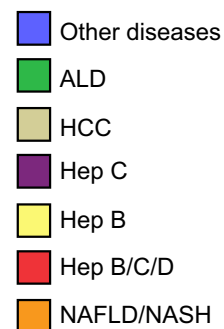


— 2005 - 09
(n=810)

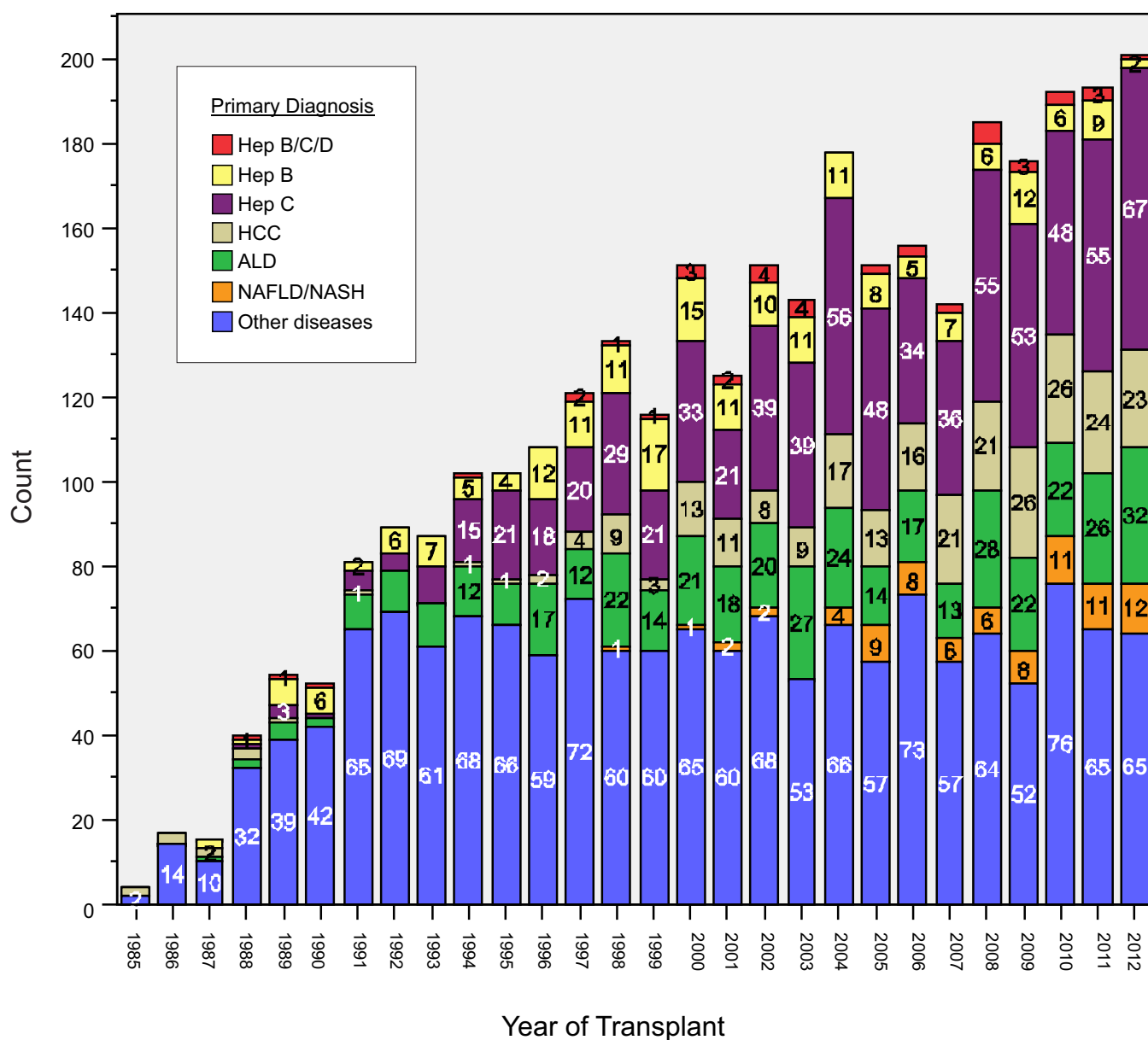


— 2010 - 12
(n=587)

Adult Diagnosis

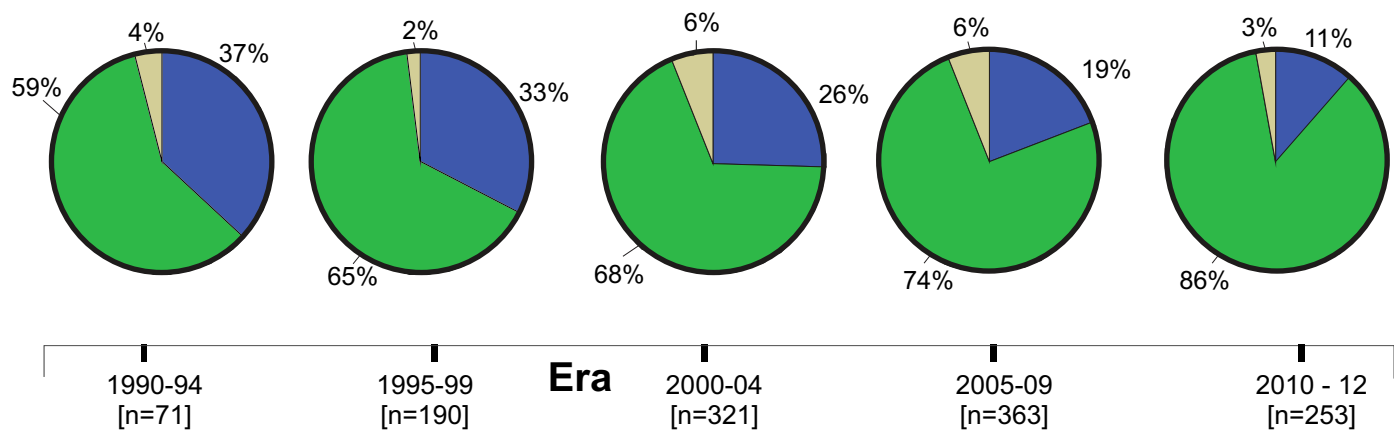


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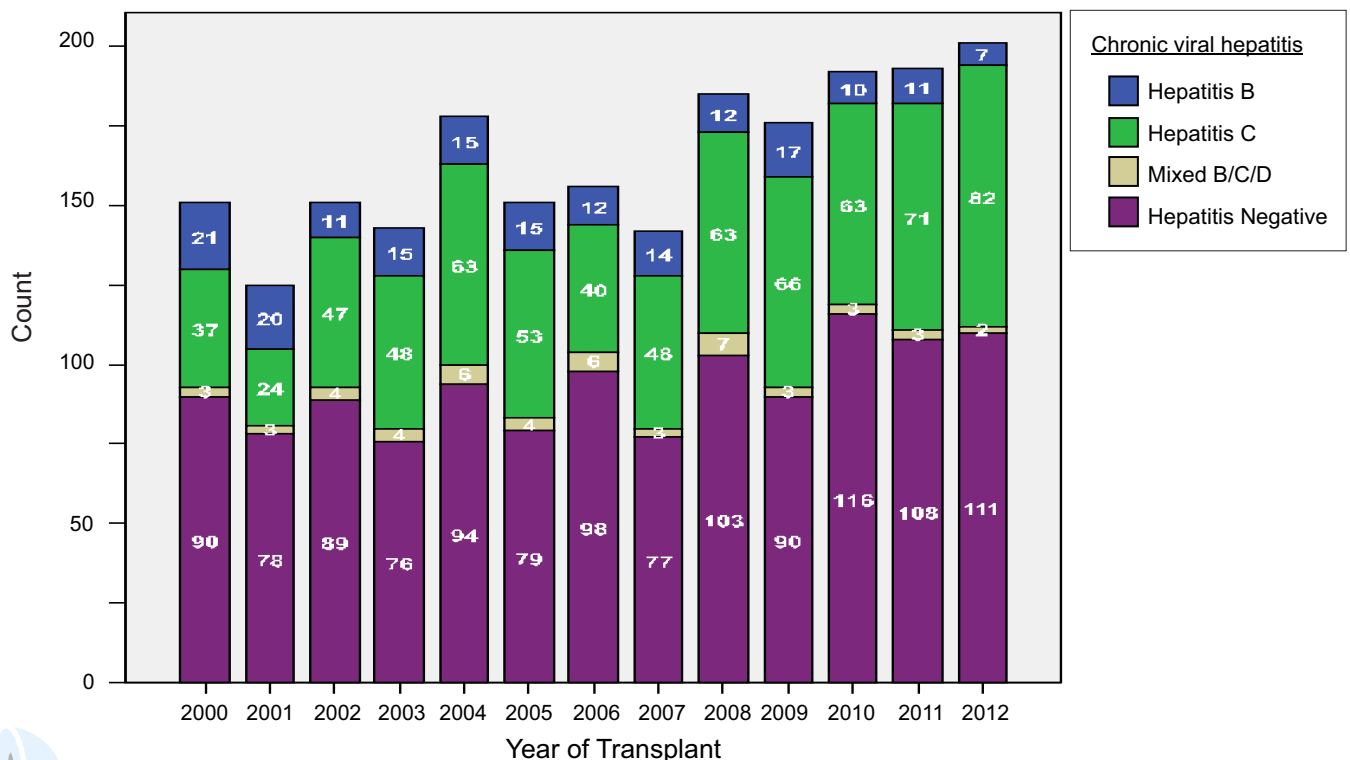


			Secondary / Tertiary diagnosis					
Primary Diagnosis		n =	Hepatitis C	Hepatitis B	Hepatitis B,C	HCC	NAFLD	ALD
	Hepatitis C	731		7		186	3	188
	Hepatitis B	203	3			73		5
	Hepatitis BD/BC/BCD	43				5		7
	HCC + cirrhosis	260	120	68	6		5	42
	ALD	408	18	3		49	6	
	NAFLD	81		2		13		3
	Other	1539	15	8		49	3	22
	TOTAL	3266						

Type of Chronic Viral Hepatitis in Adult Patients



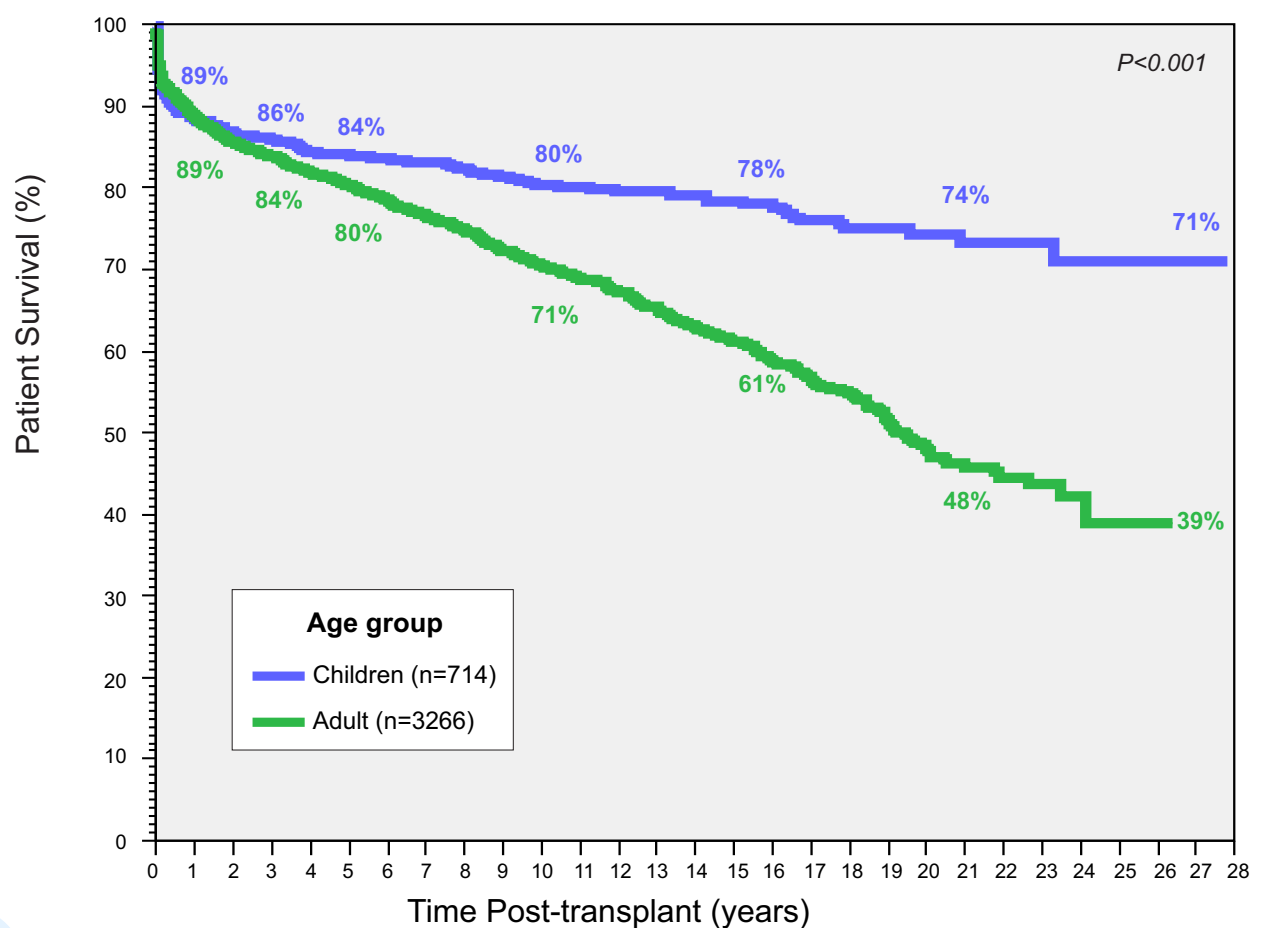
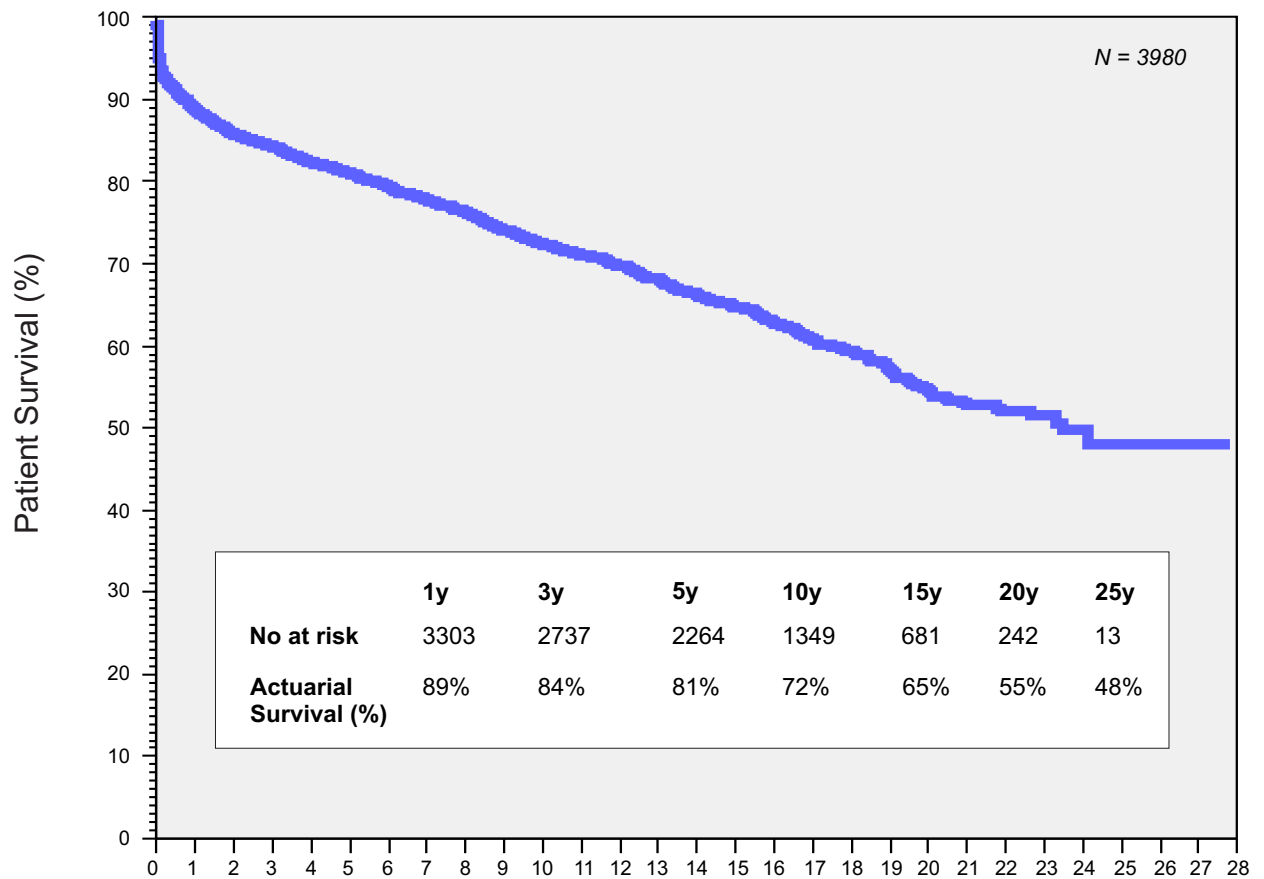
Hepatitis diagnosis



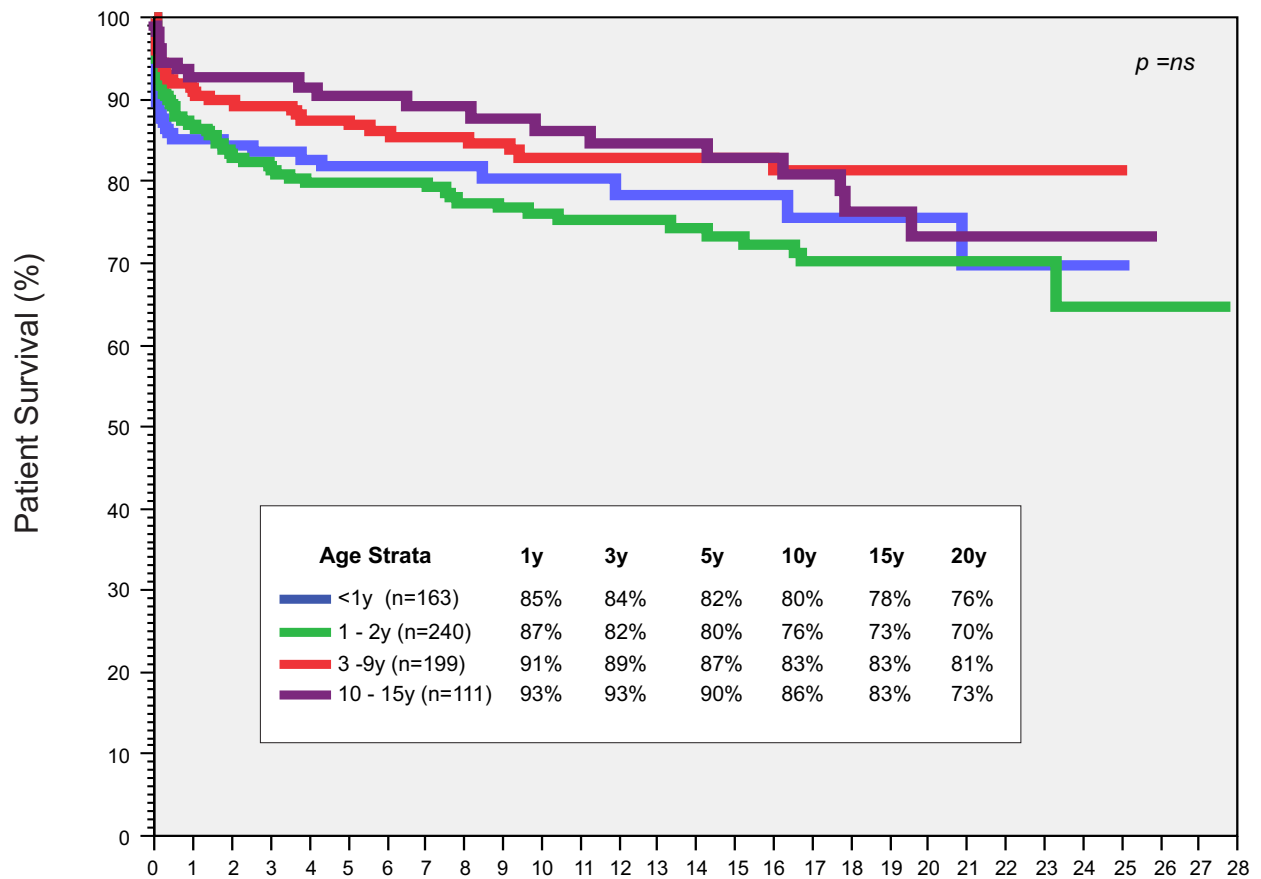
Section 3

Patient Survival

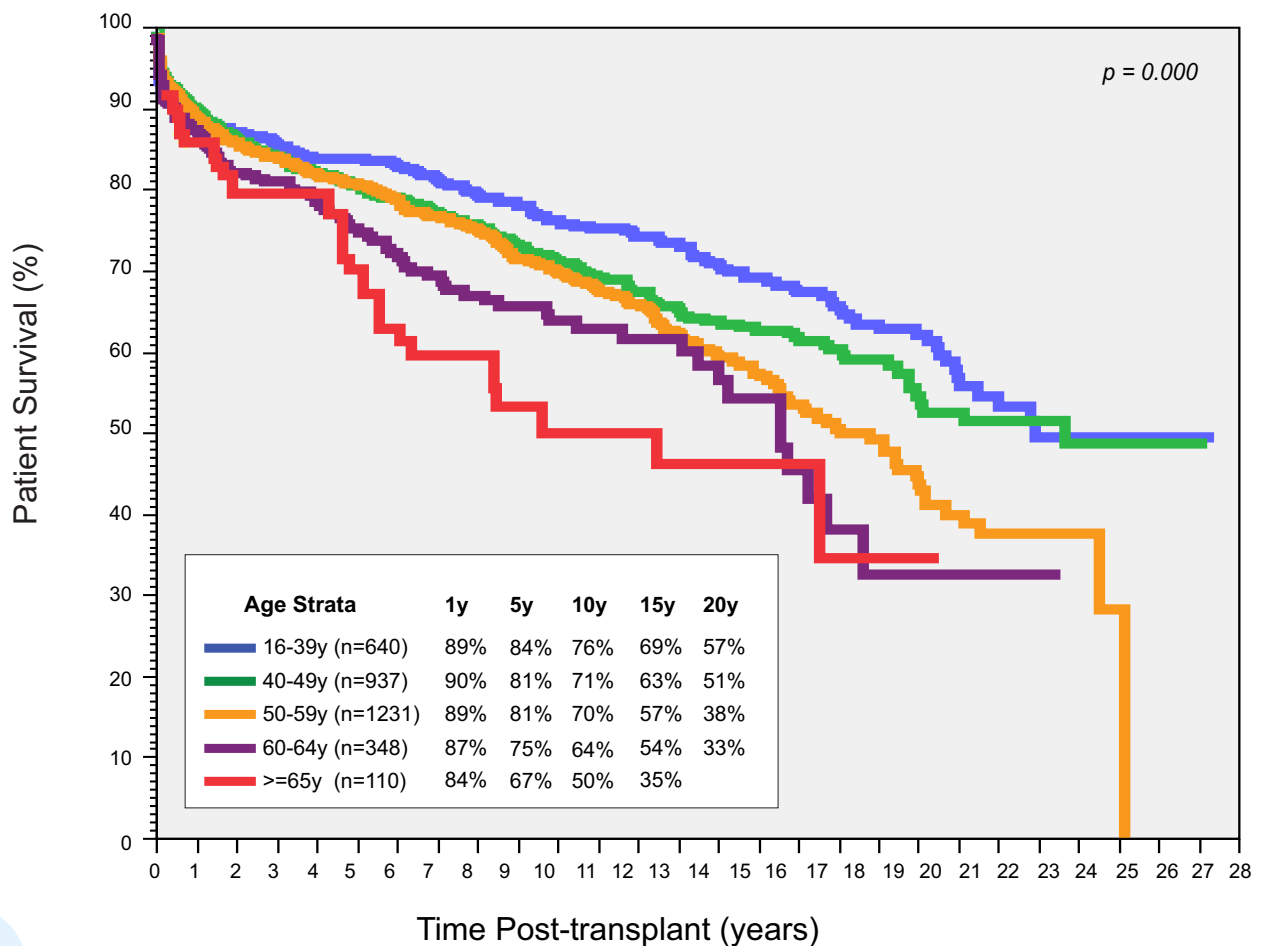


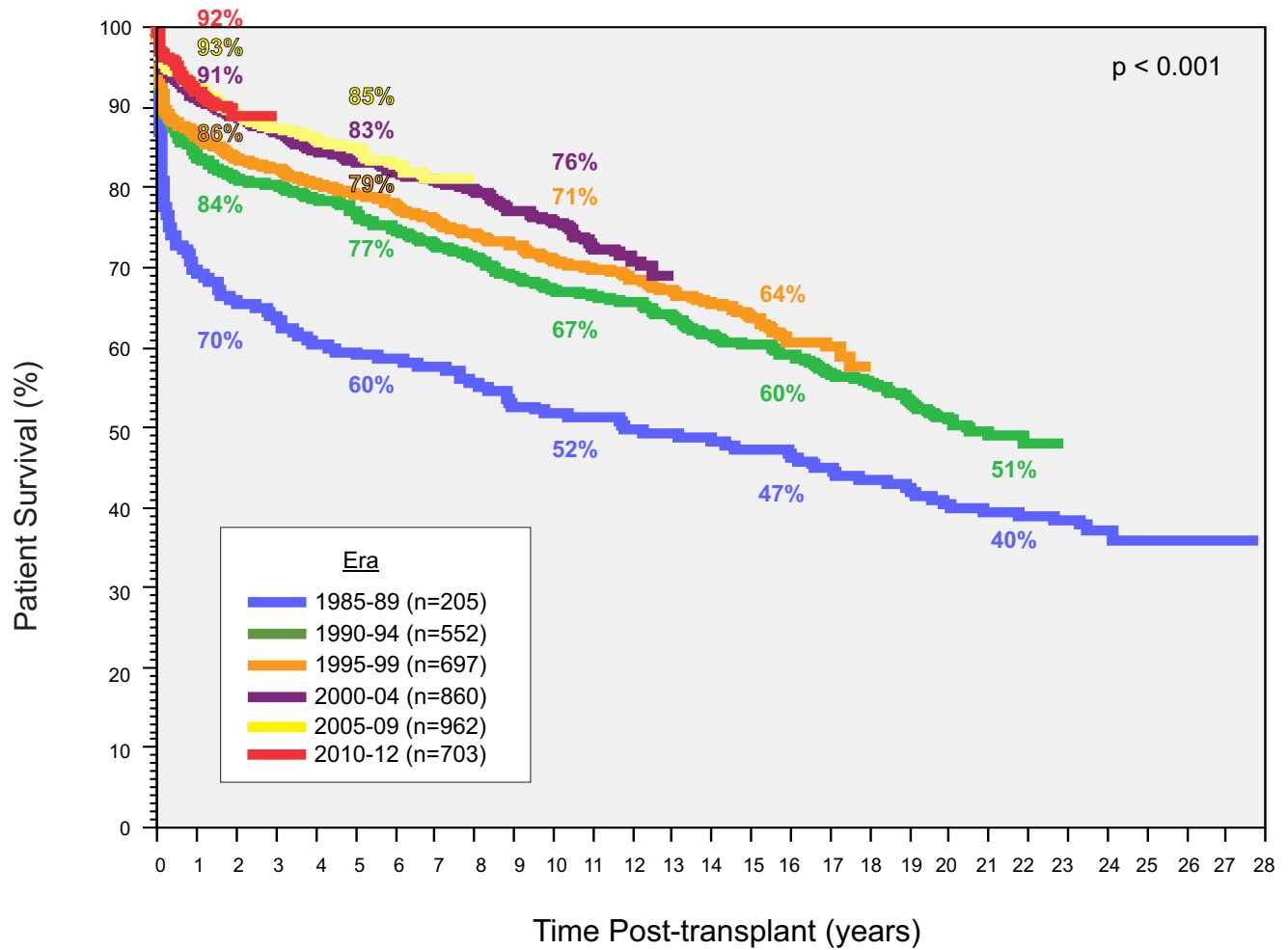


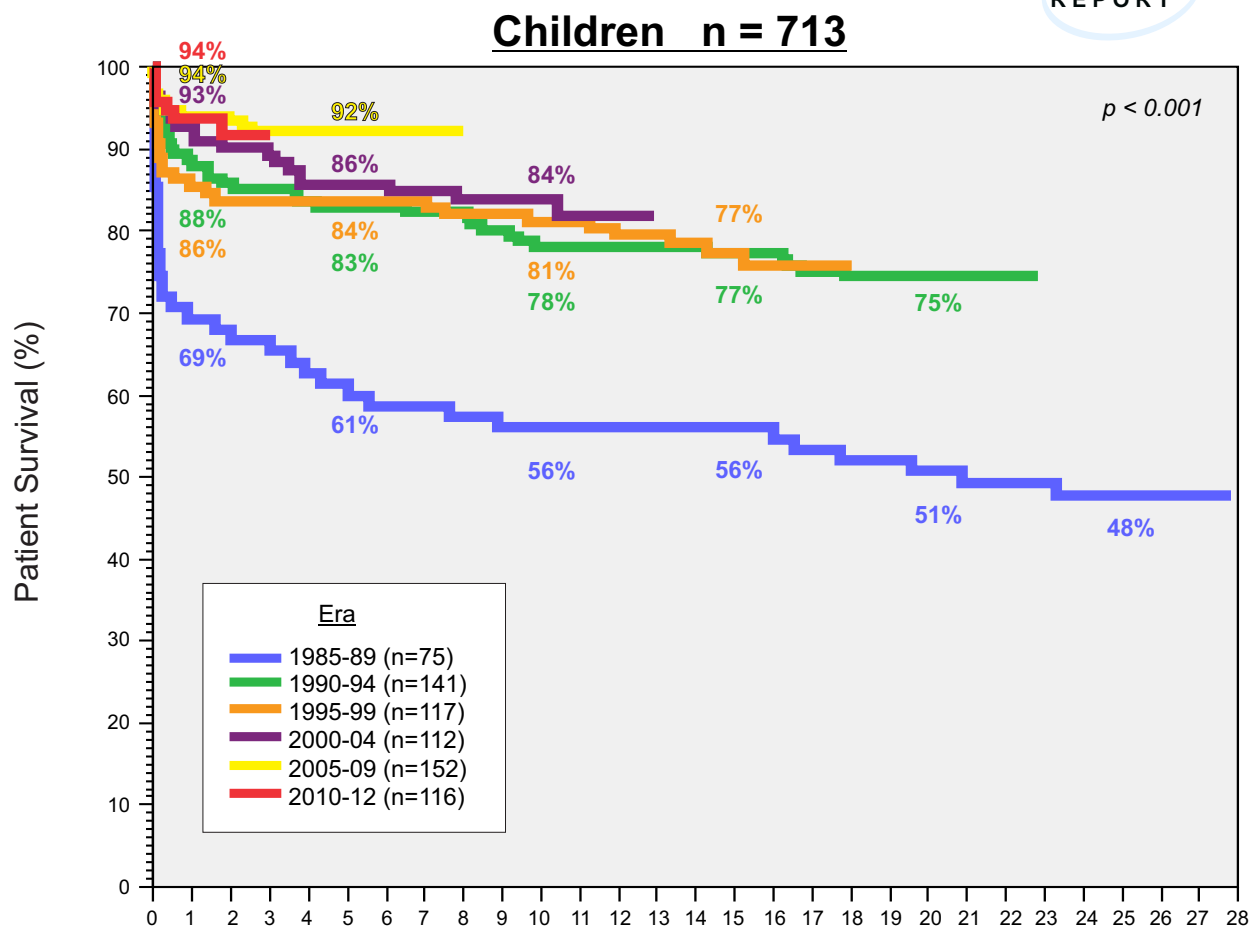
Children n = 713



Adults n = 3266

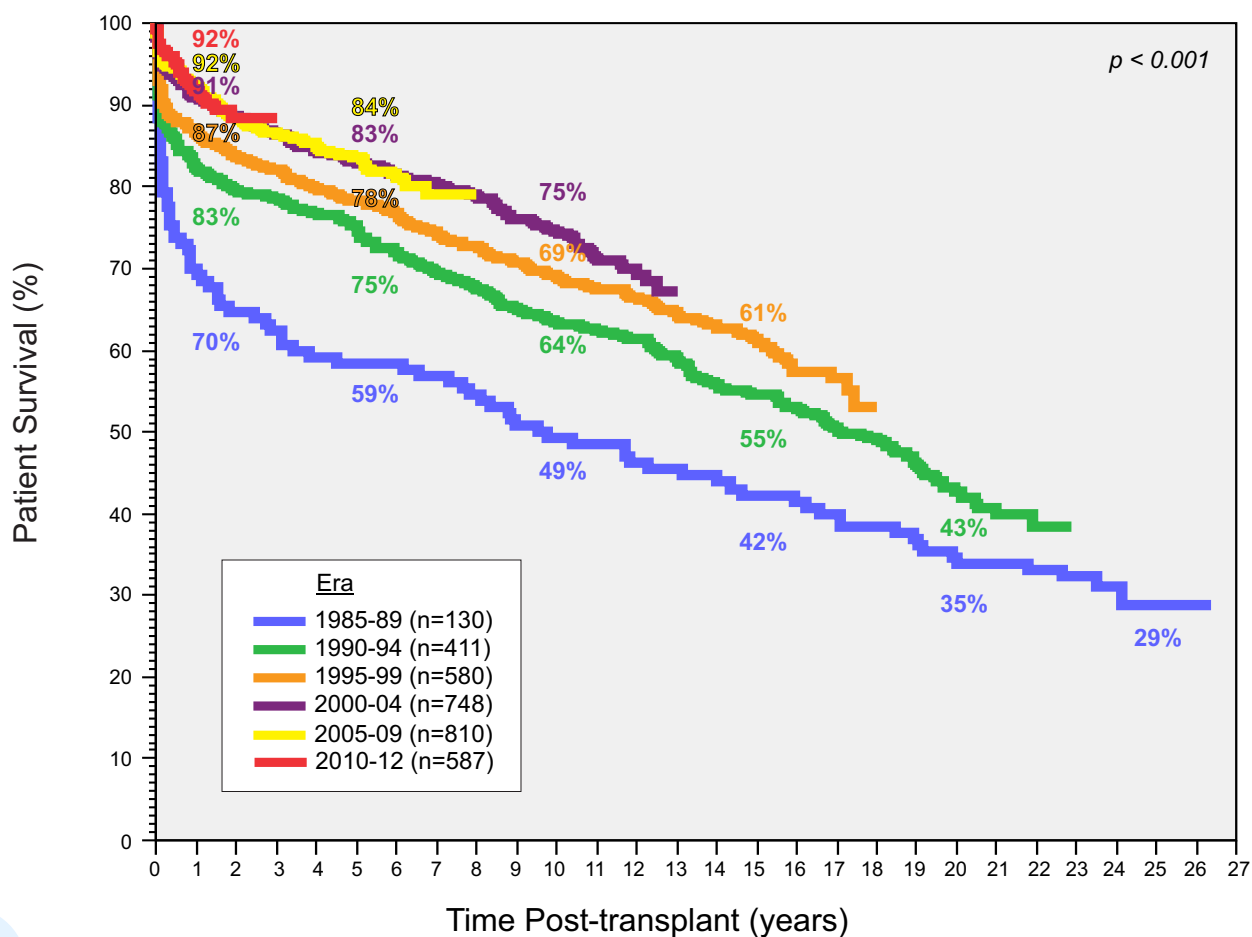






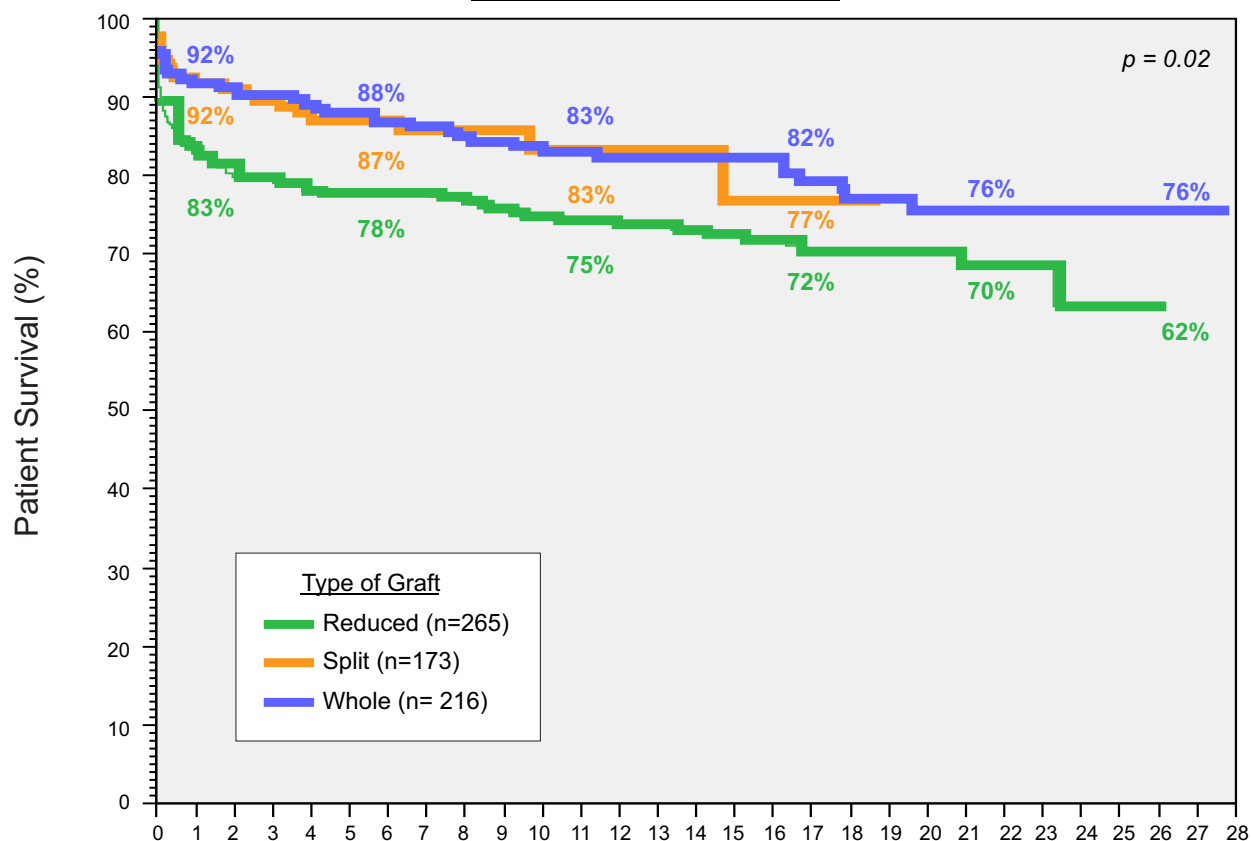
Patient Survival - Adults

Adults n = 3266

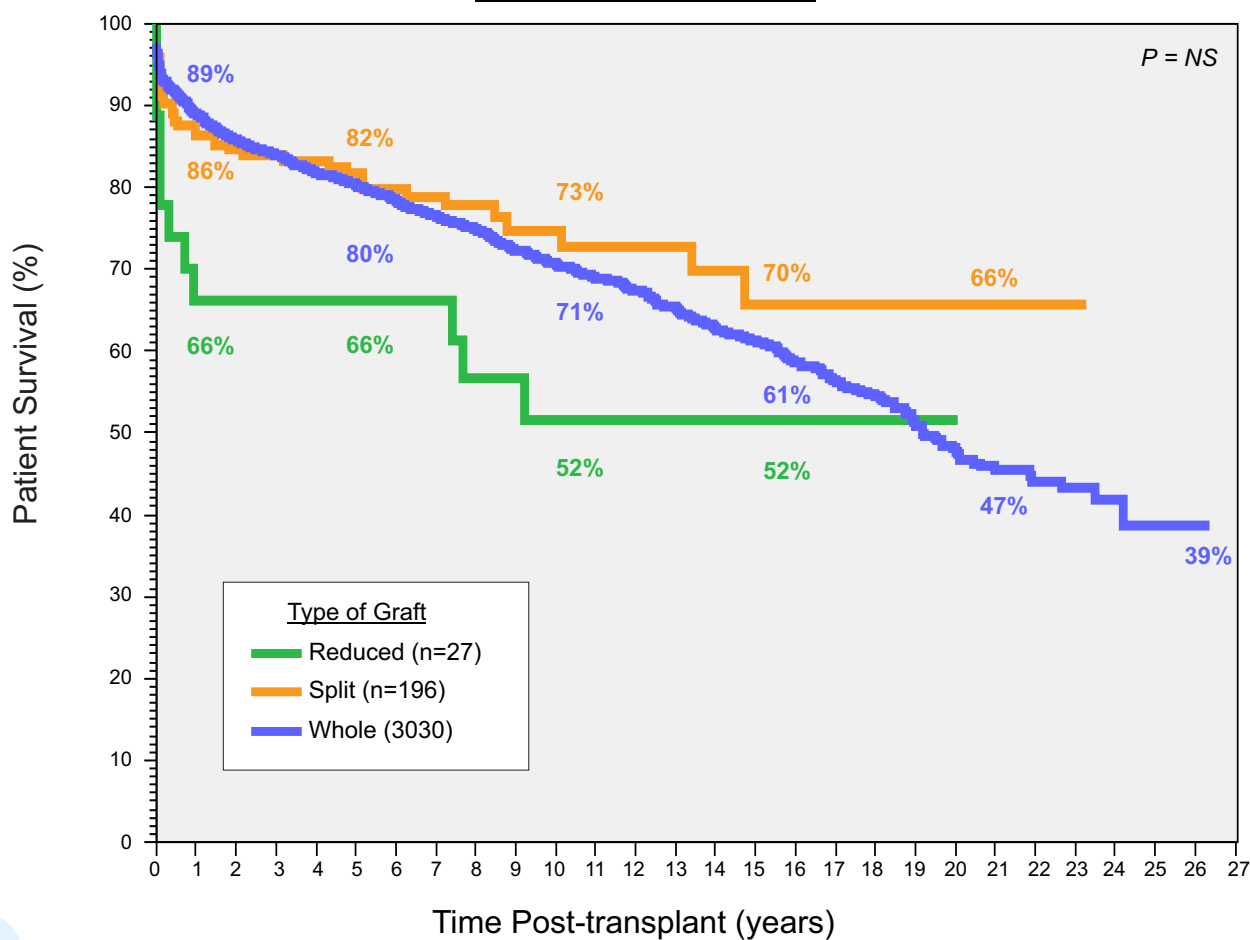


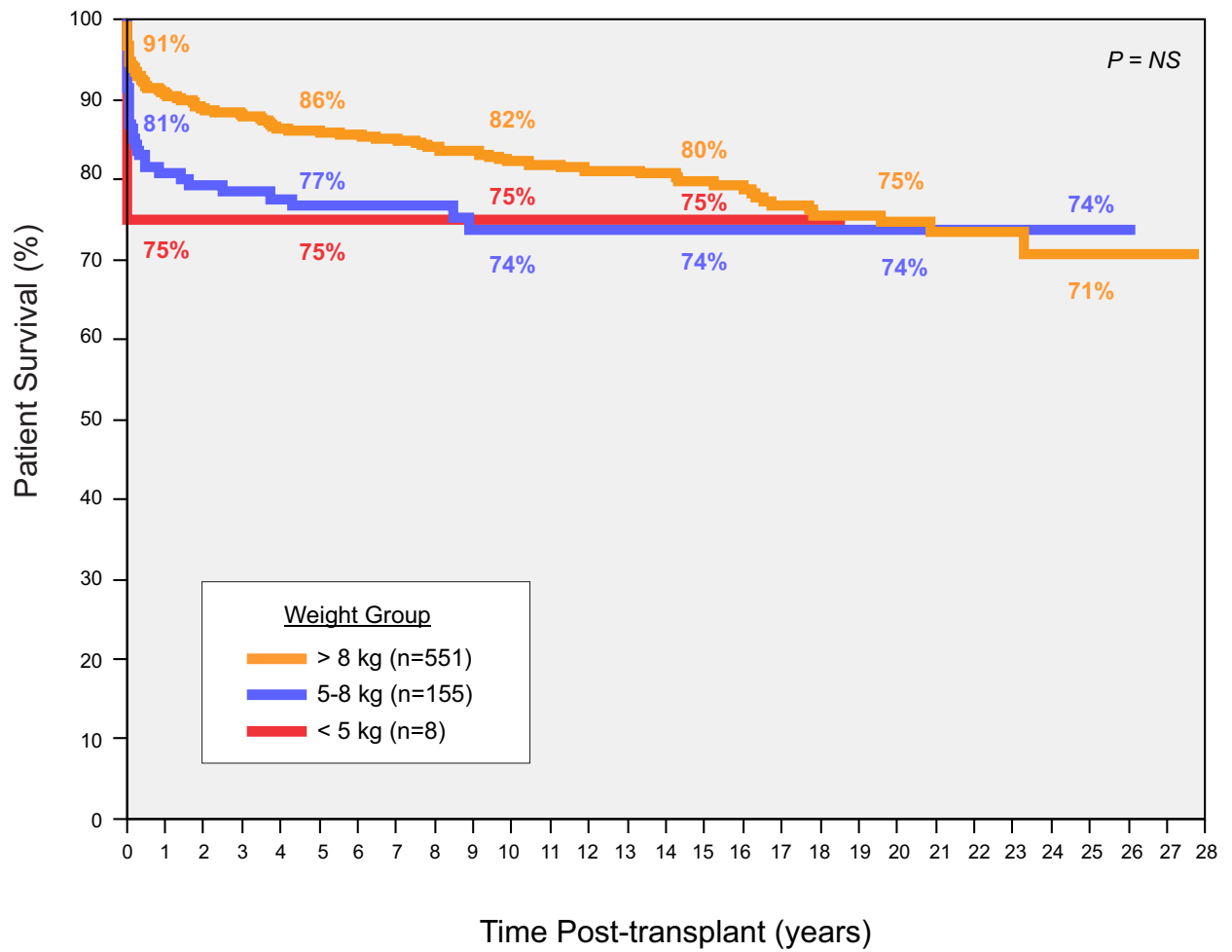
Patient Survival by Type of Primary Graft [Deceased donors]

Children - n = 655

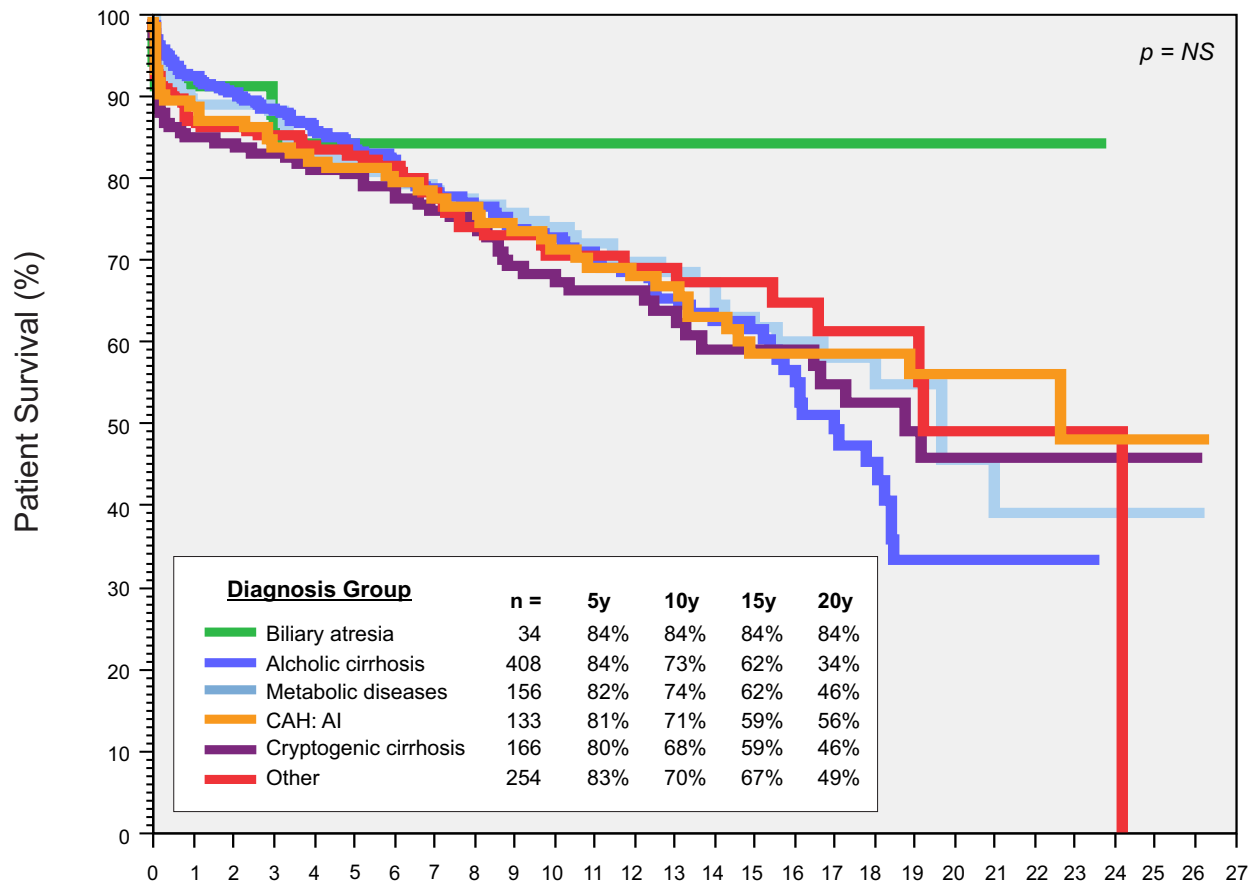


Adults - n = 3253

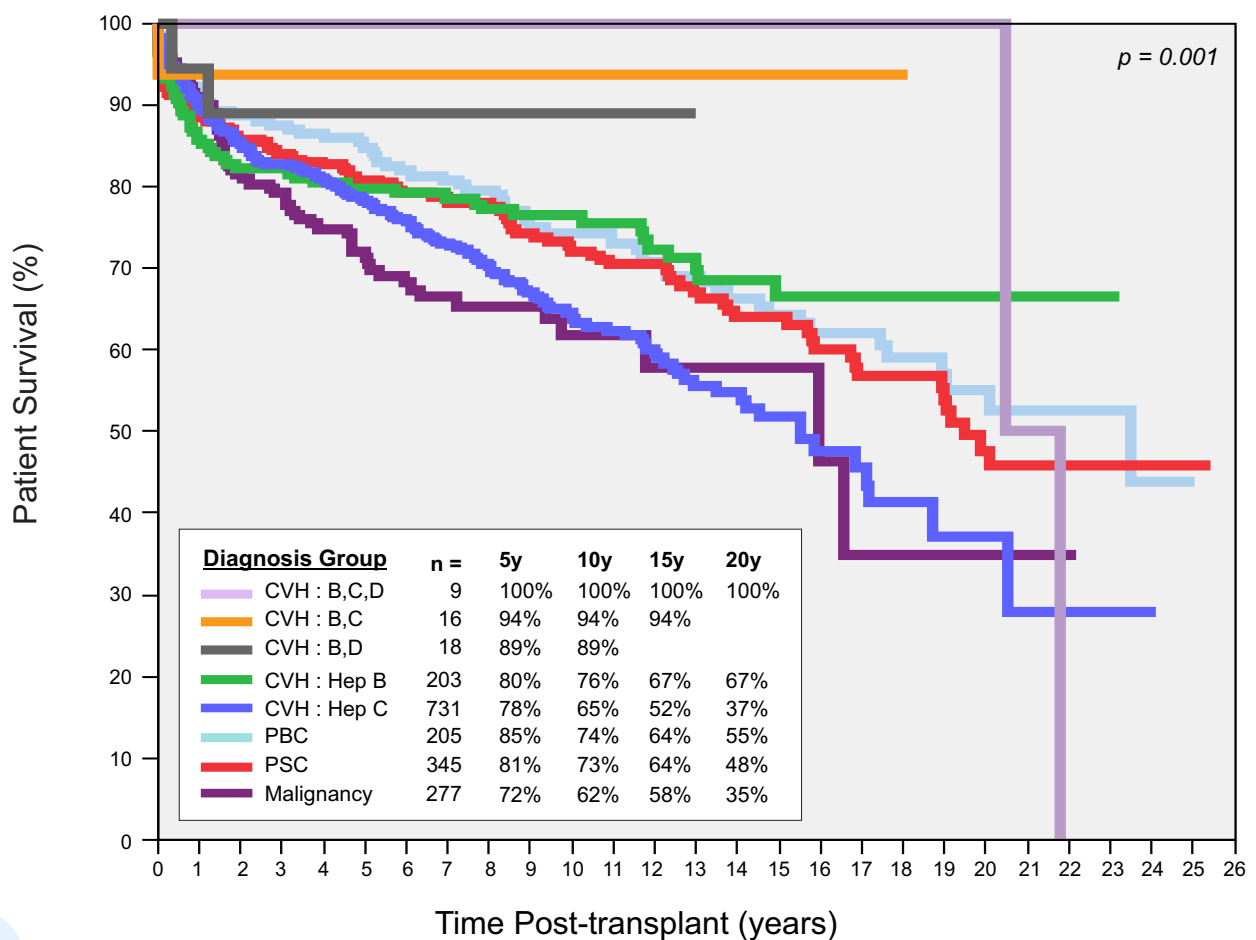




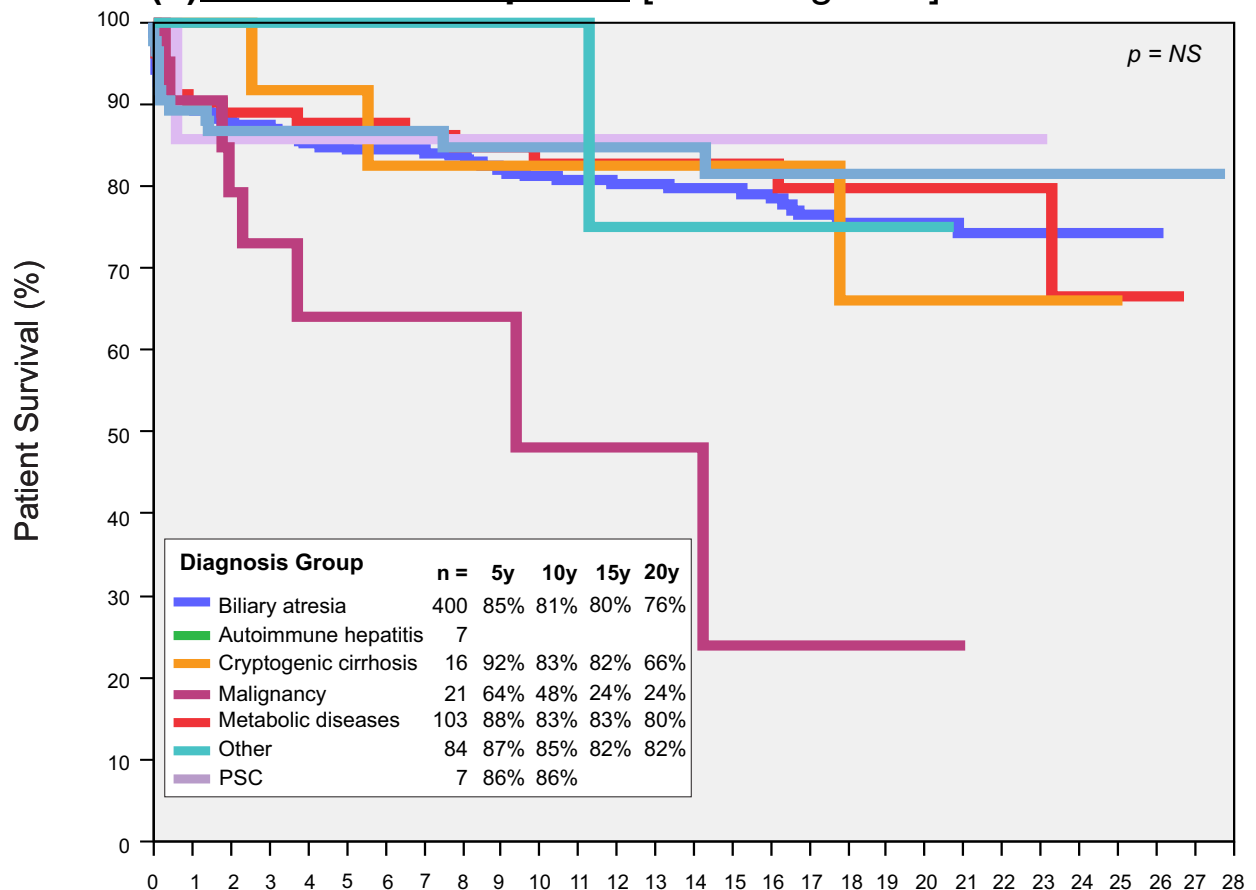
(1) Adults [excluding FHF] - n=1151



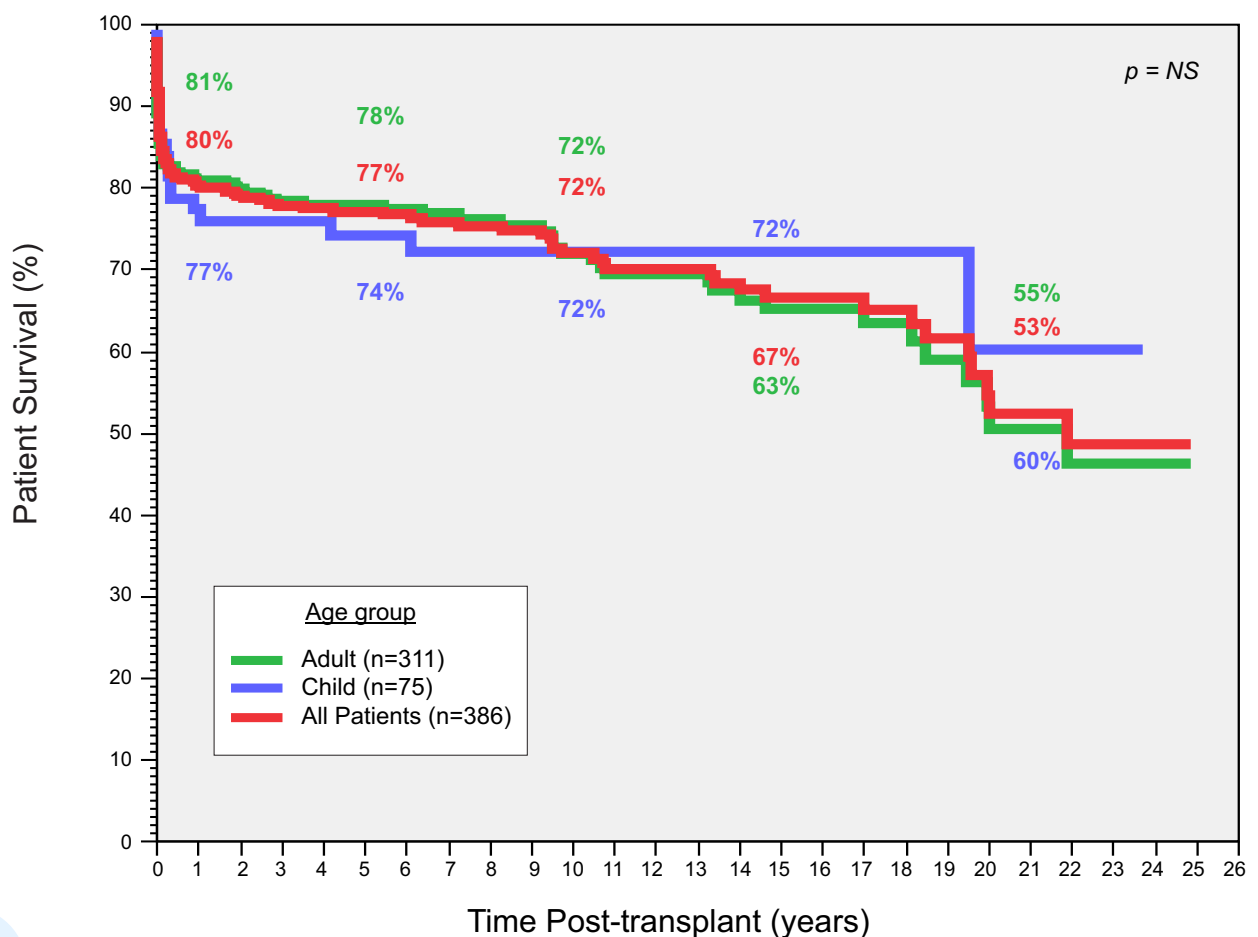
(2) Adults [excluding FHF] - n = 1804

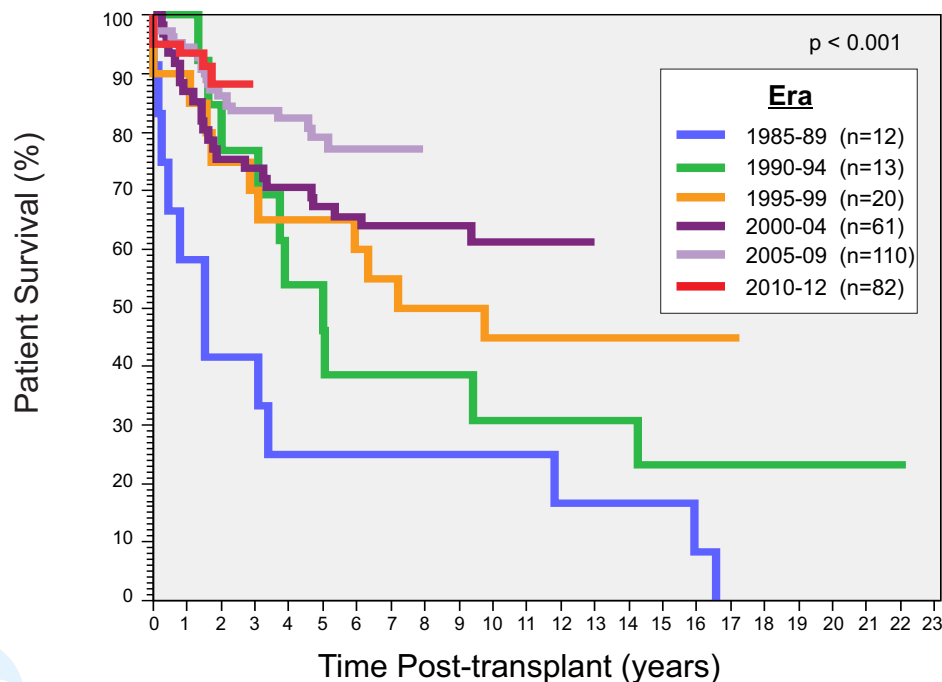
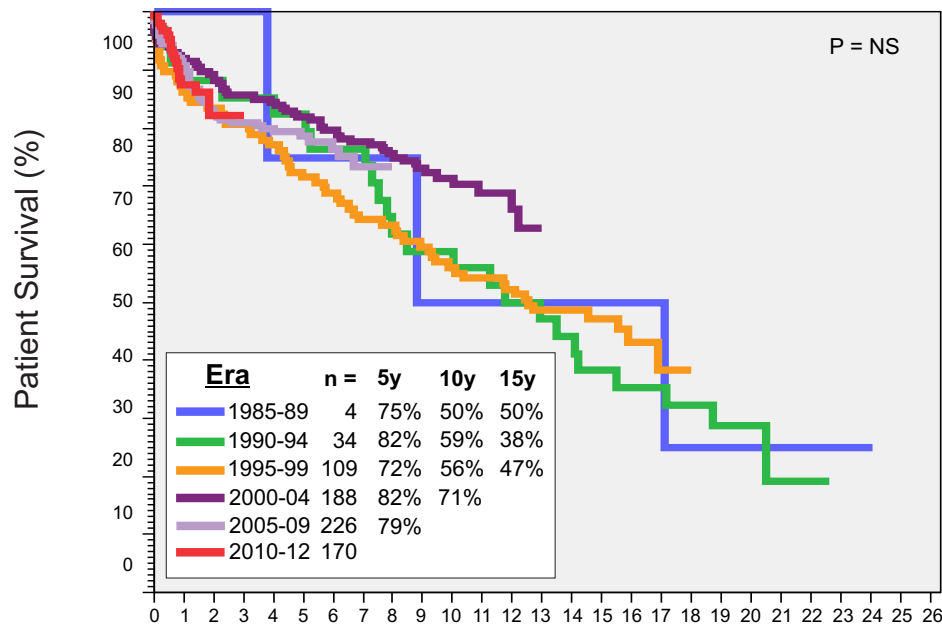
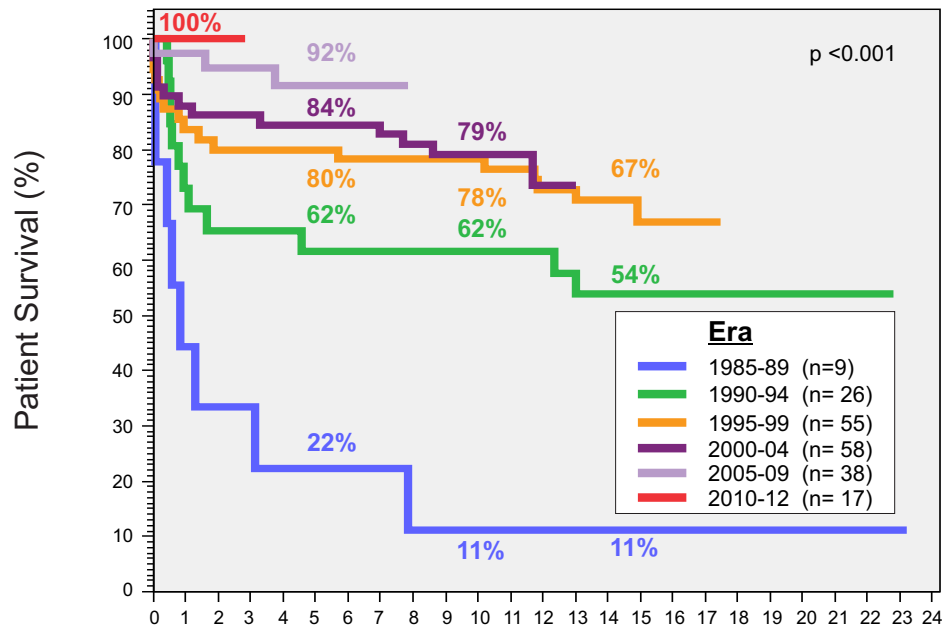


(3) Paediatric recipients [excluding FHF] - n= 638



(4) Fulminant hepatic failure n = 386

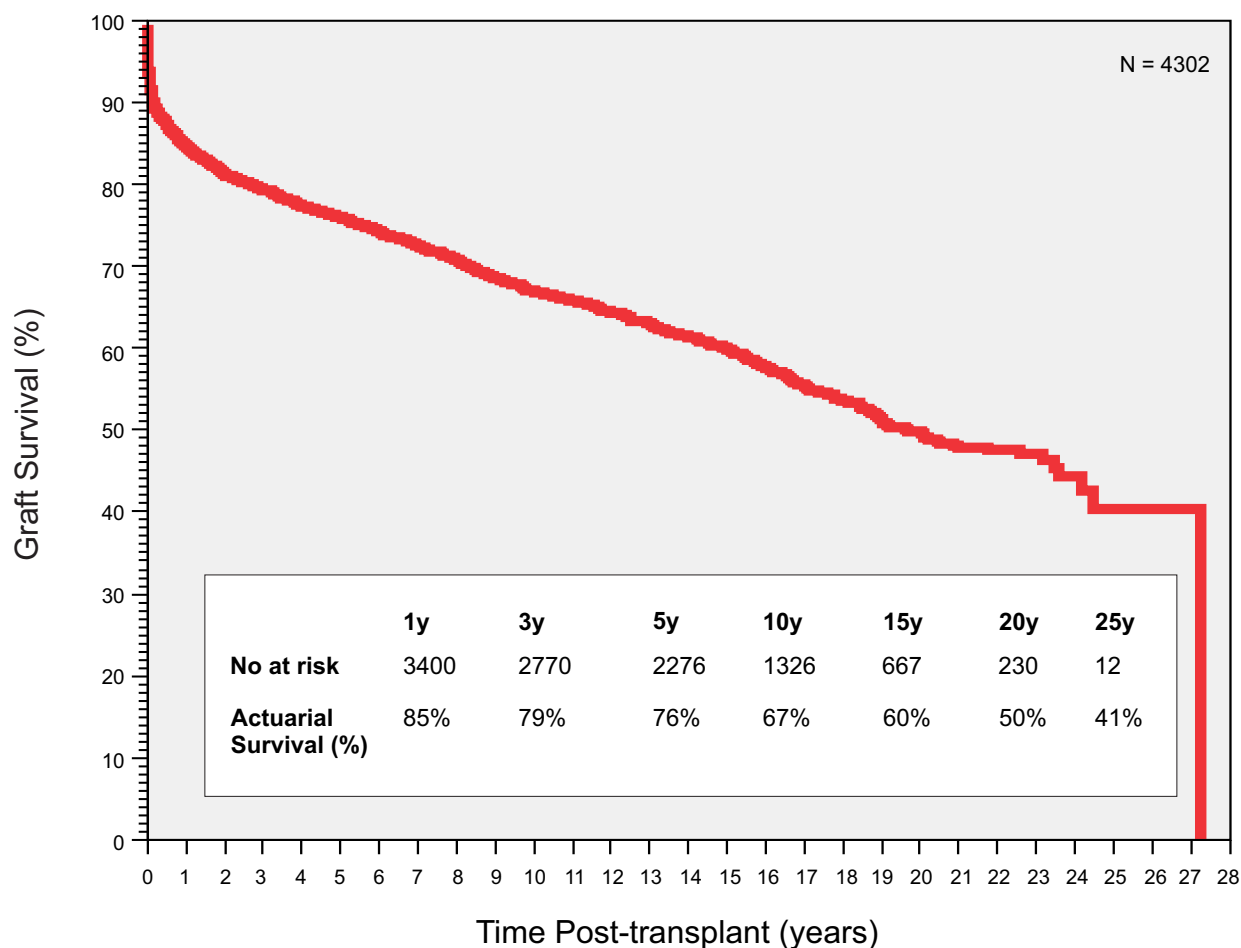




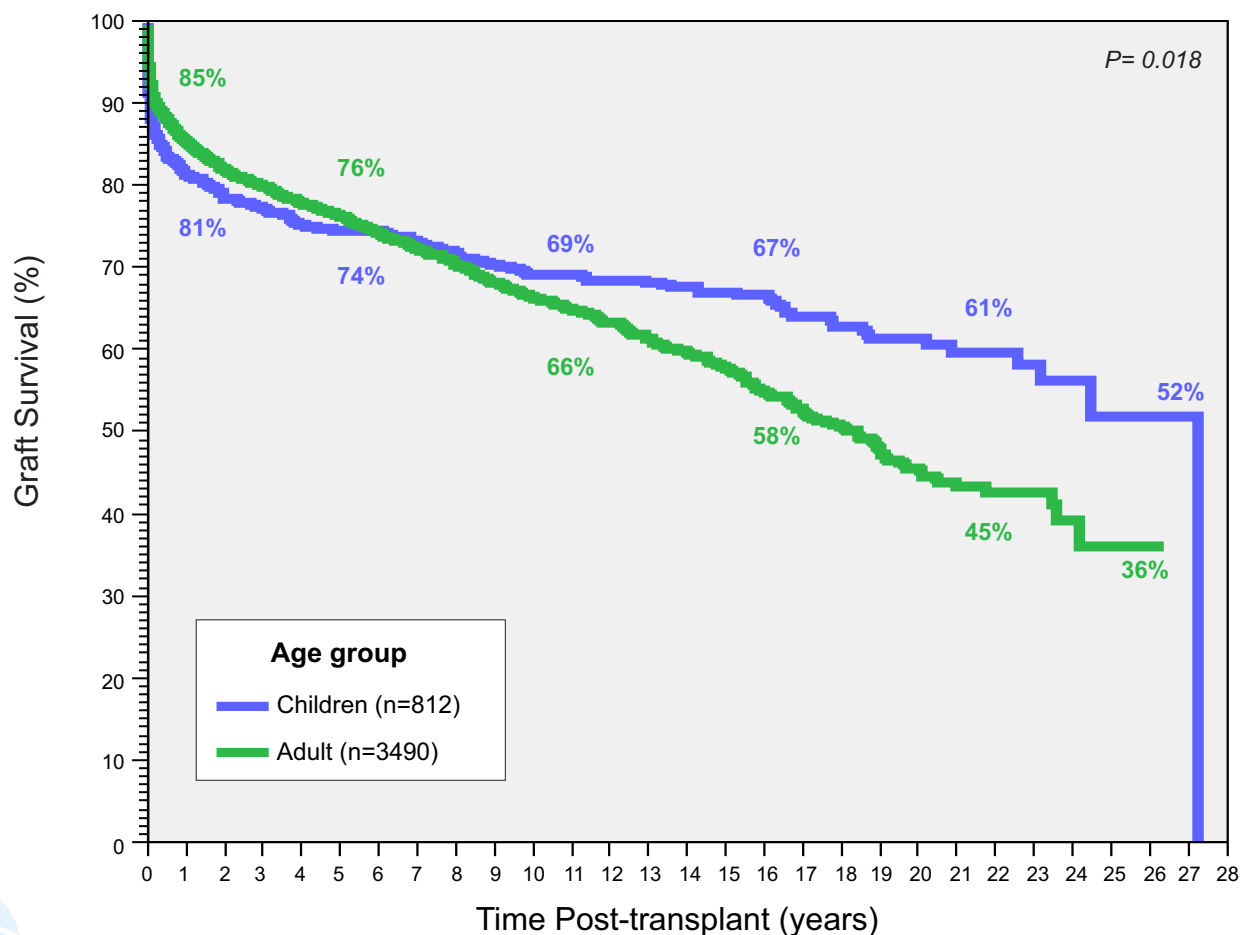
Section 4

Graft Outcome

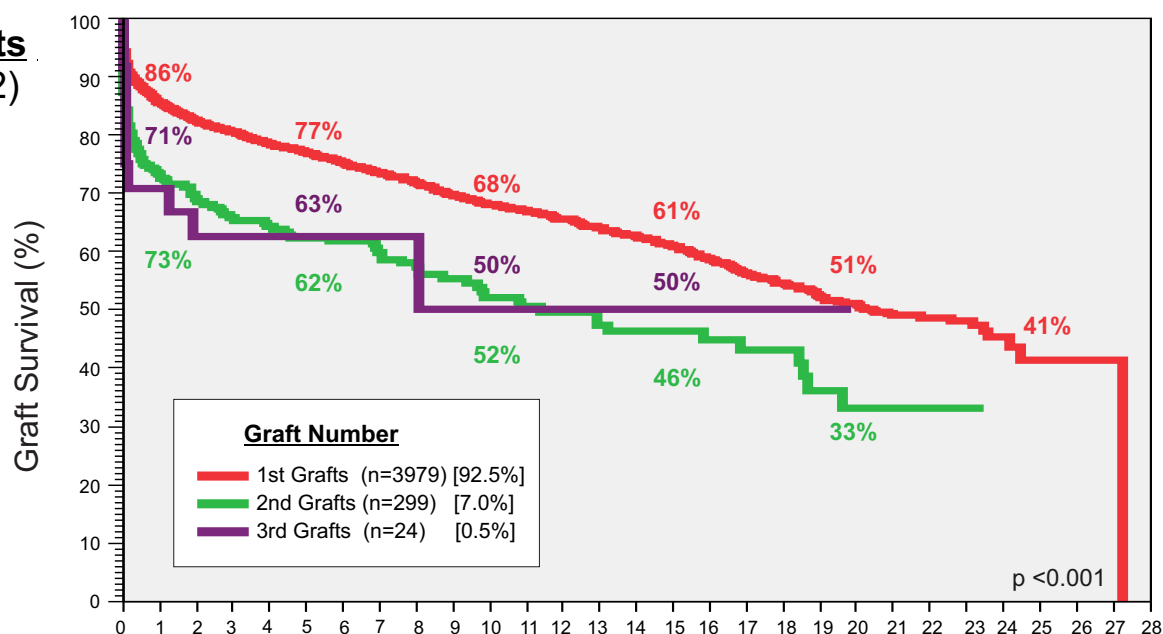




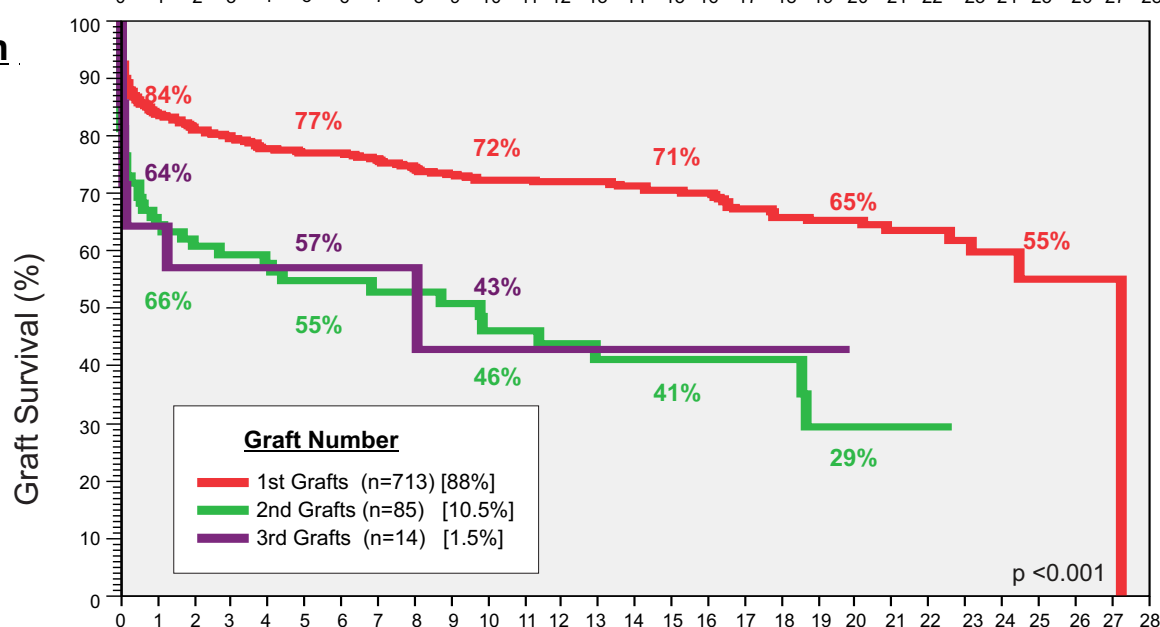
Graft Survival by Age Group



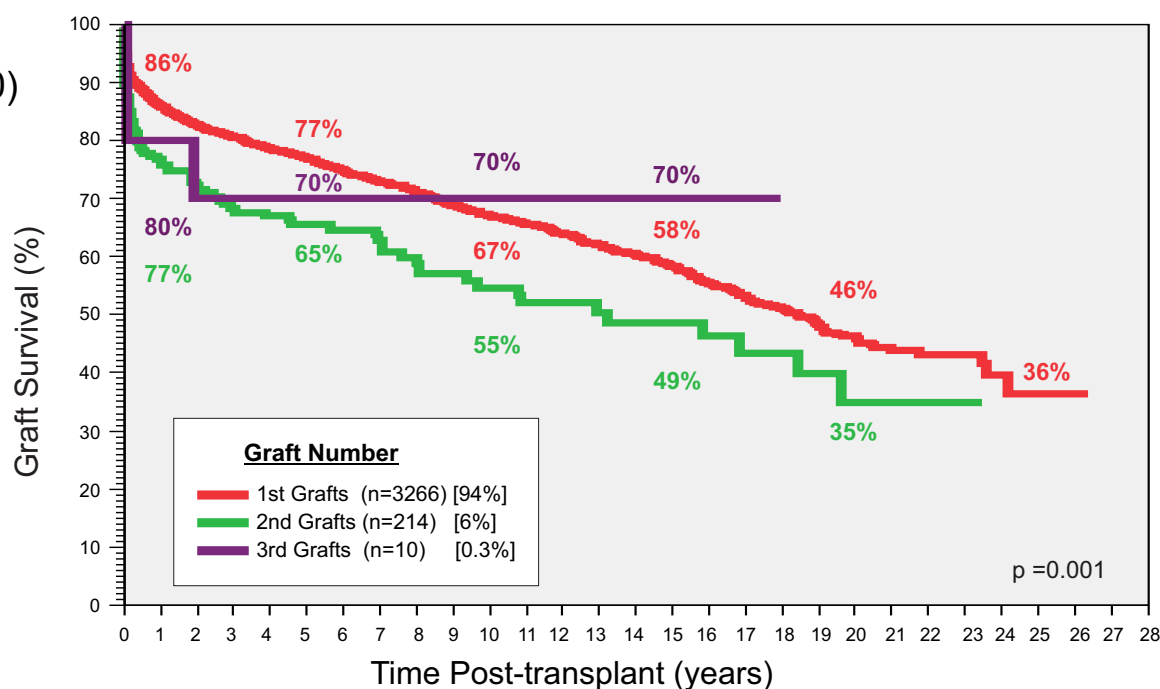
All Grafts (n= 4302)



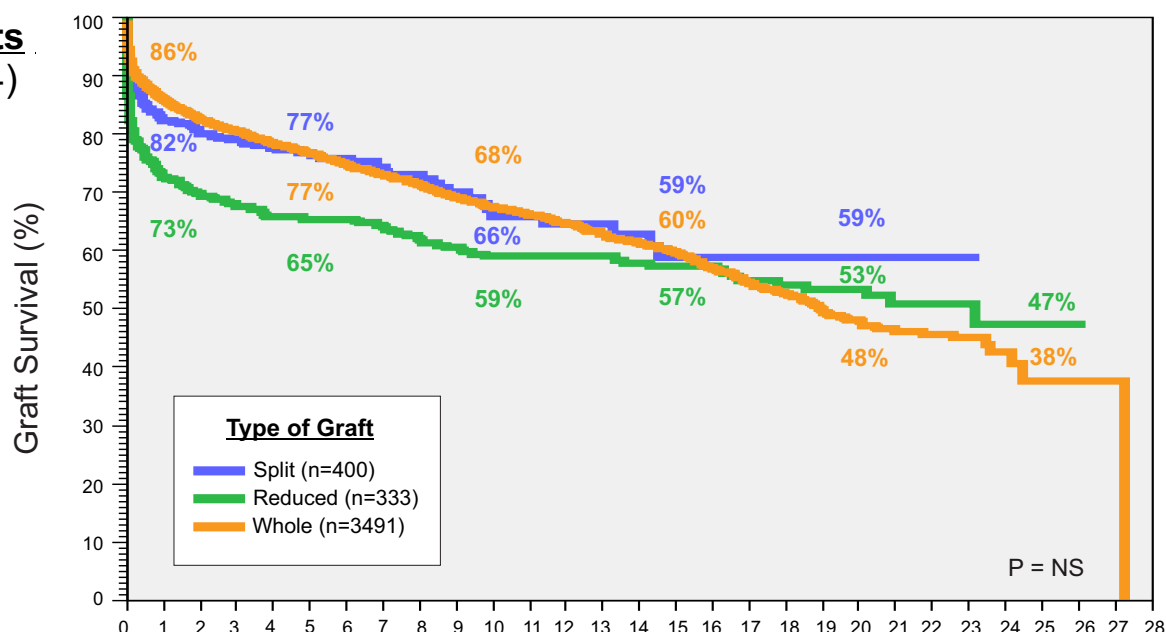
Children (n= 812)



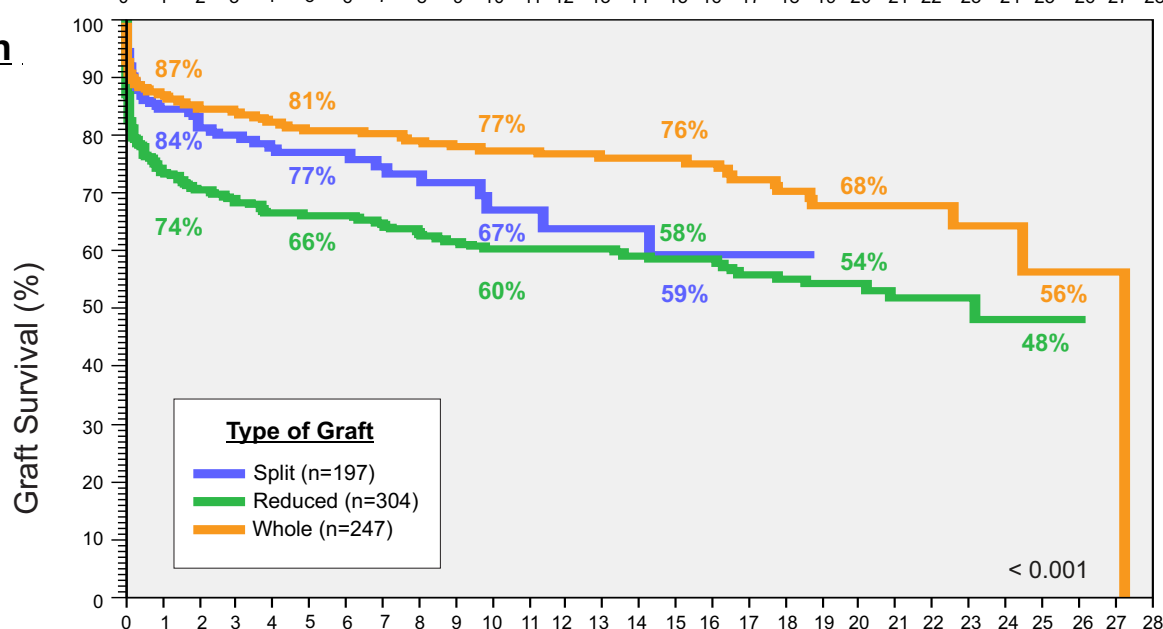
Adult (n= 3490)



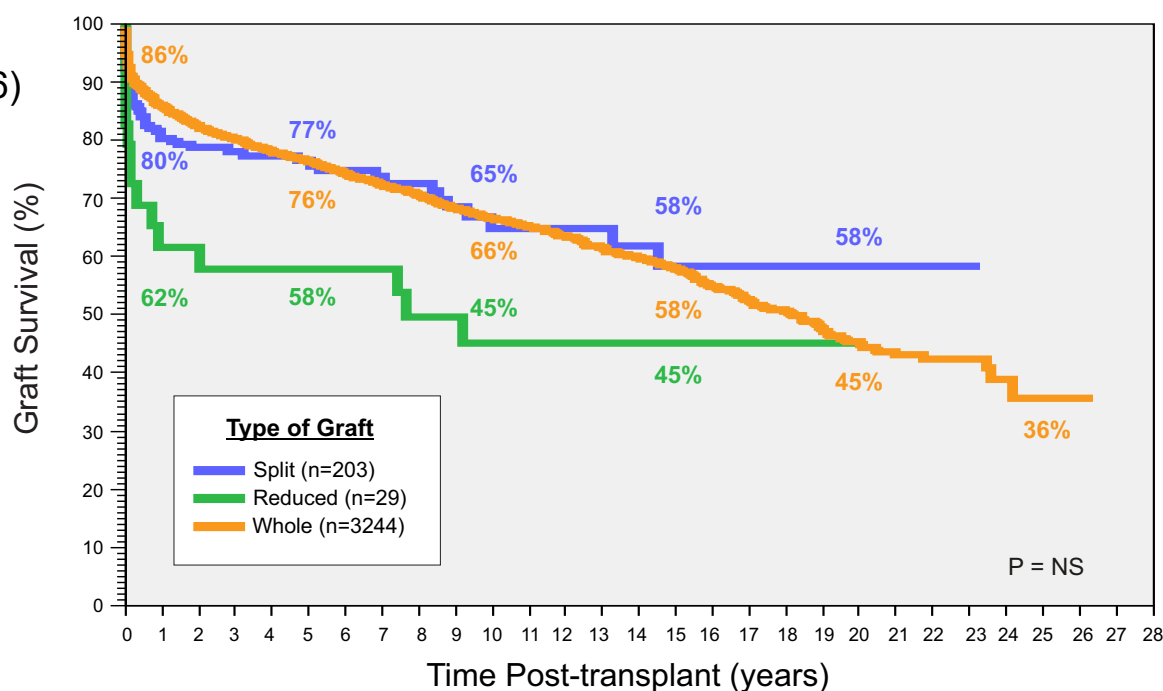
All Grafts (n= 4224)



Children (n= 748)

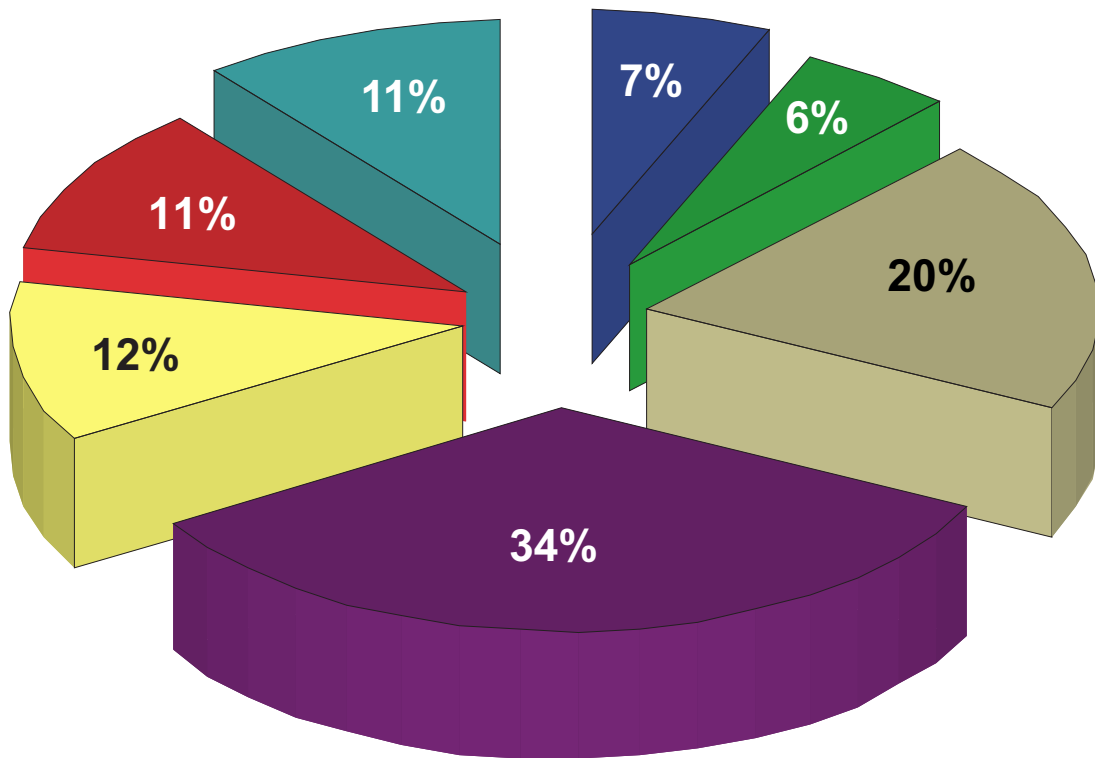


Adult (n= 3476)



Indication for Retransplantation

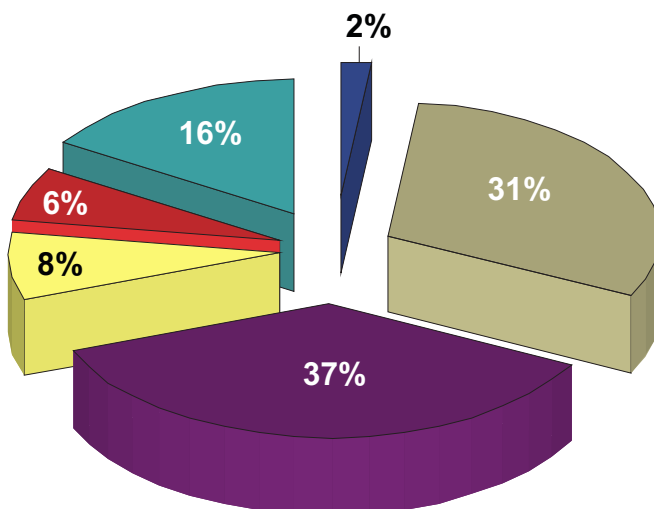
n = 322 (298 2nd grafts, 24 3rd grafts)



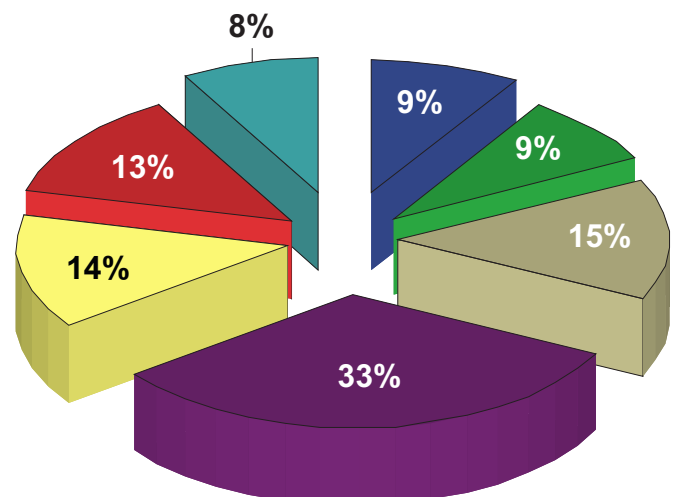
- | | |
|--|---|
| ■ Recurrent PBC/PSC/CAH:AI | ■ PNF/poor graft function |
| ■ Recurrent HBV /HCV | ■ Biliary |
| ■ Rejection | ■ Other |
| ■ Vascular | |

Age Group

Children (n= 111)

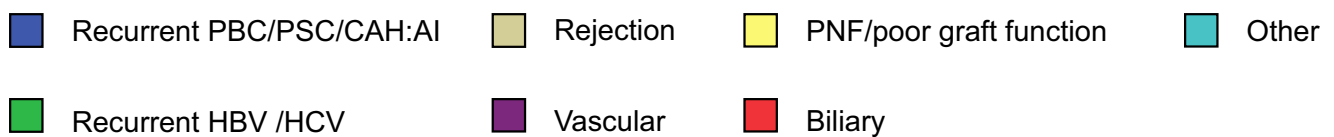
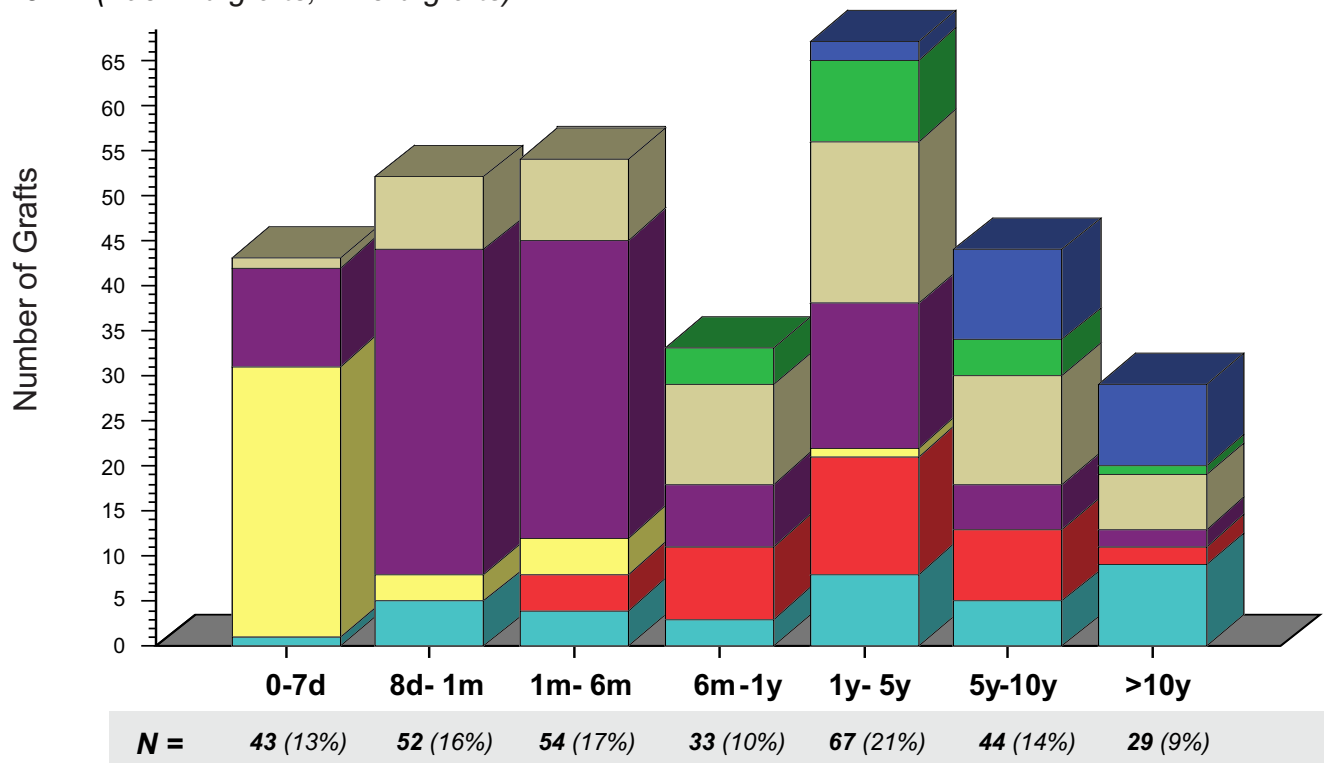


Adults (n= 211)

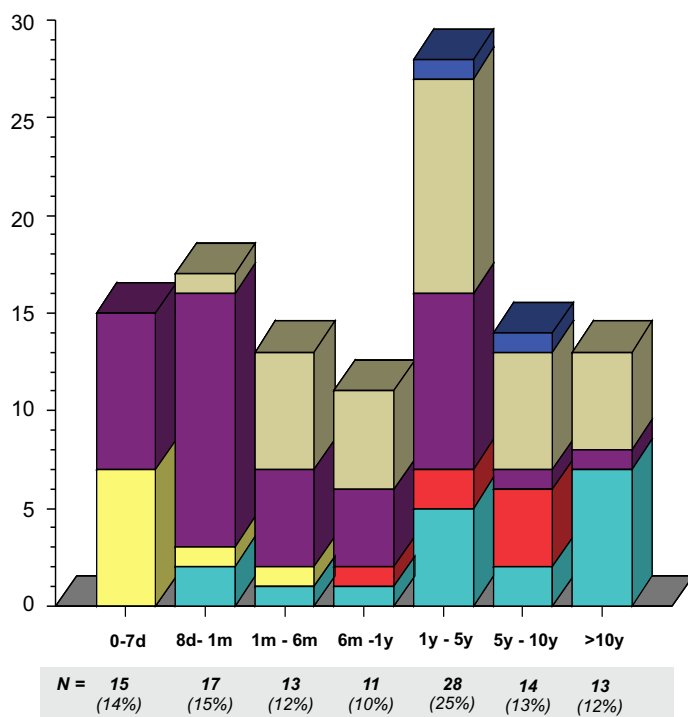


Indication for Retransplantation

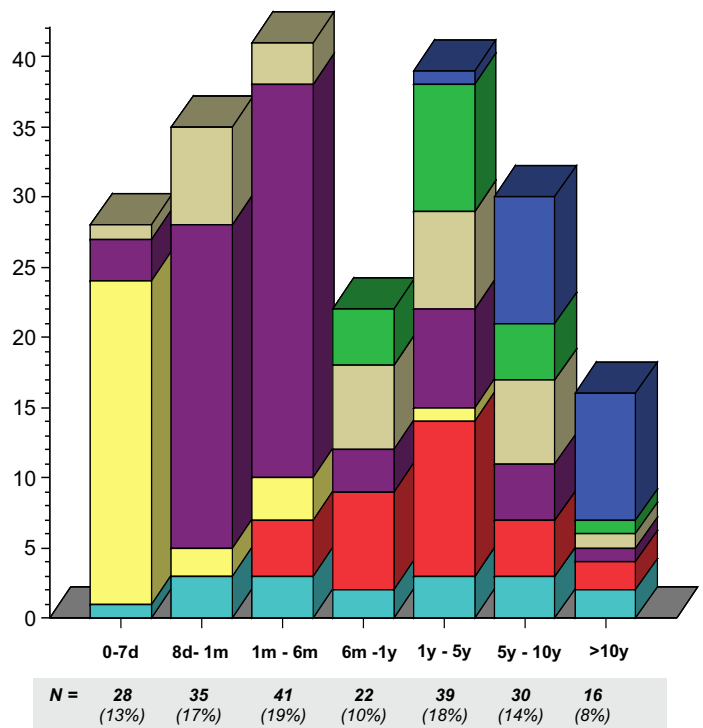
n = 322 (298 2nd grafts, 24 3rd grafts)



Children (n=111)



Adults (n=211)

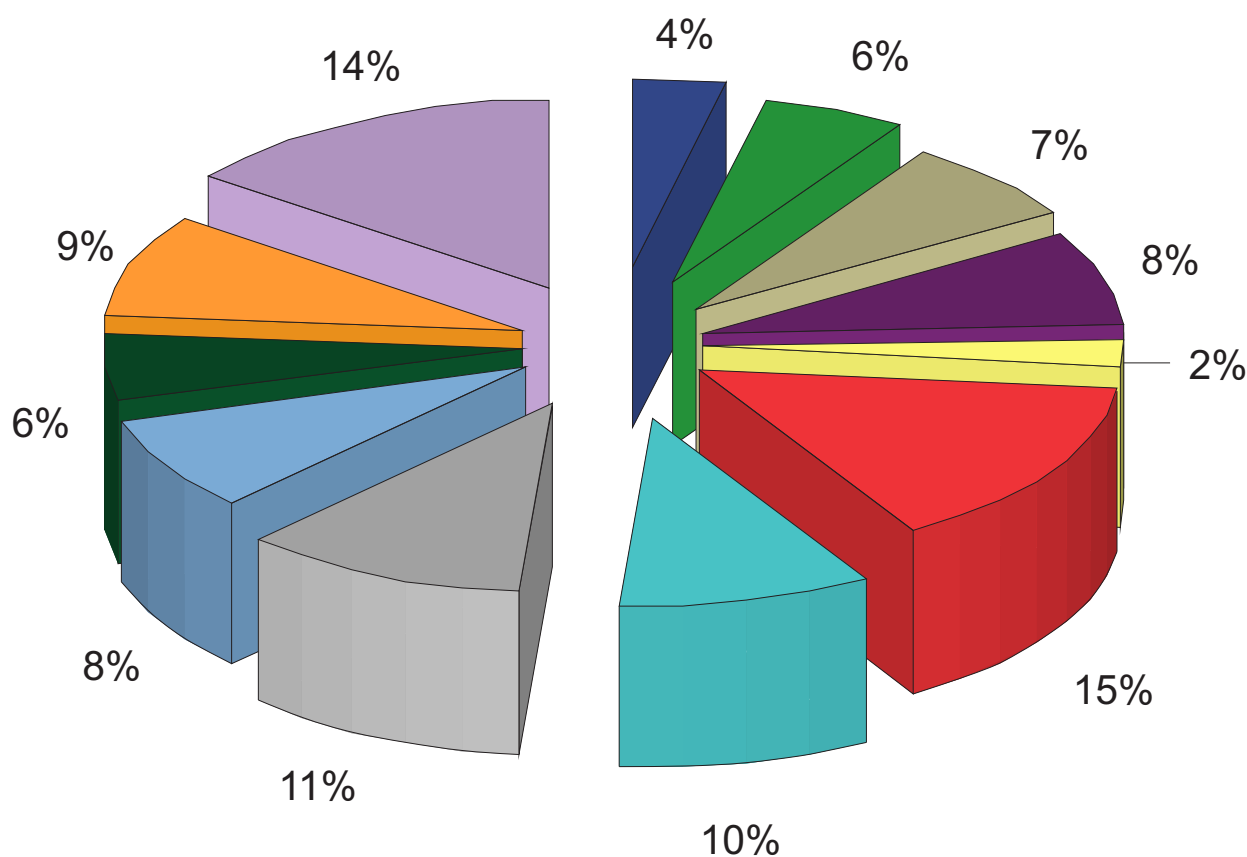
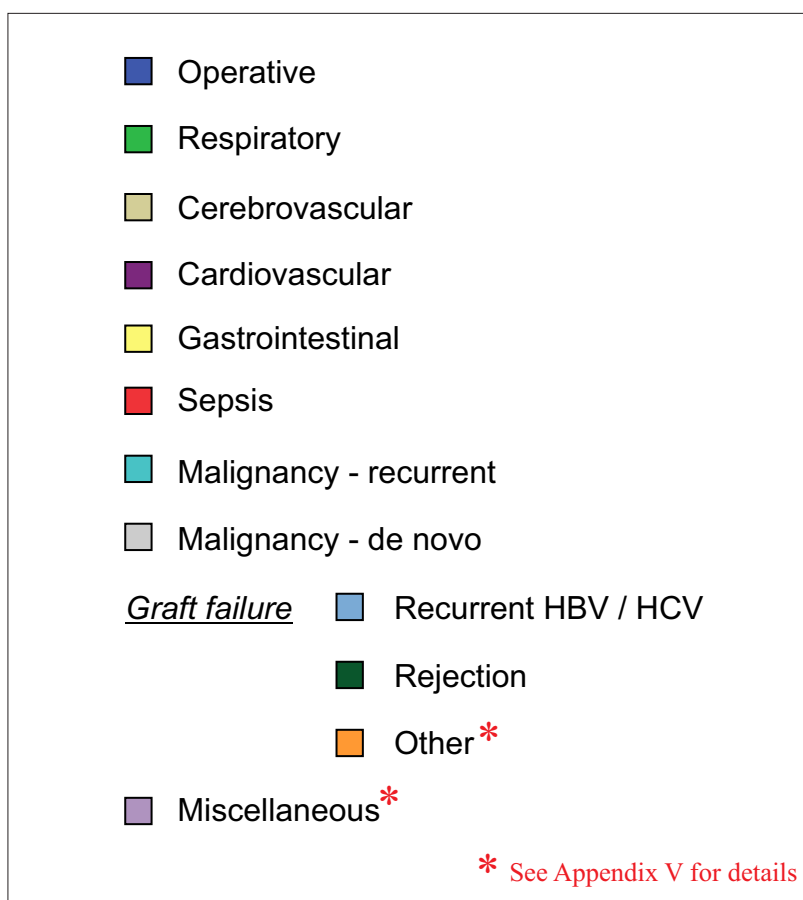


Section 5

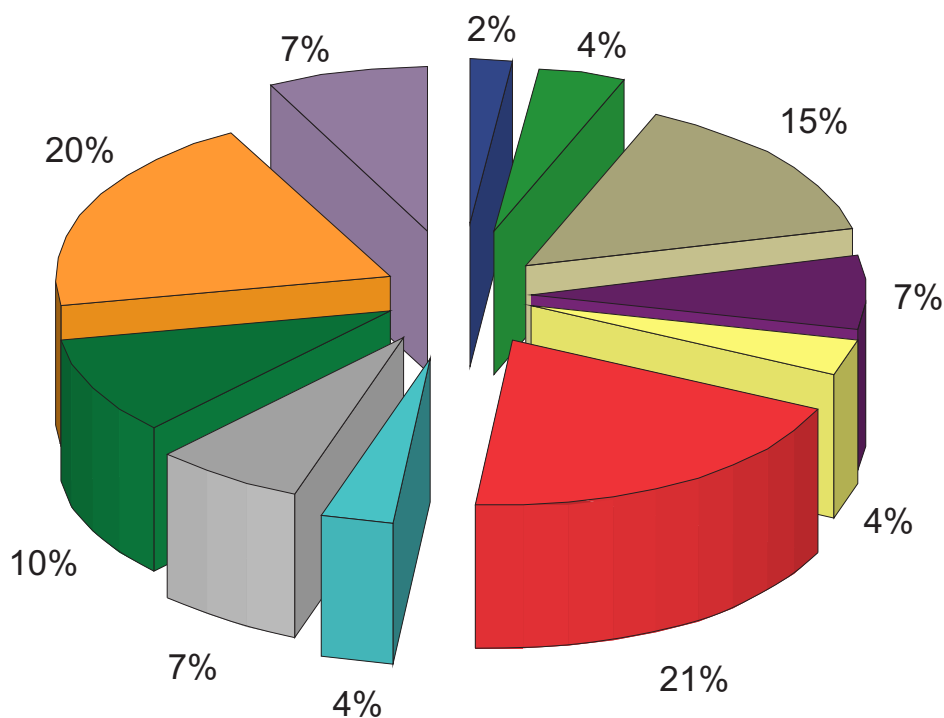
Cause of Patient Death



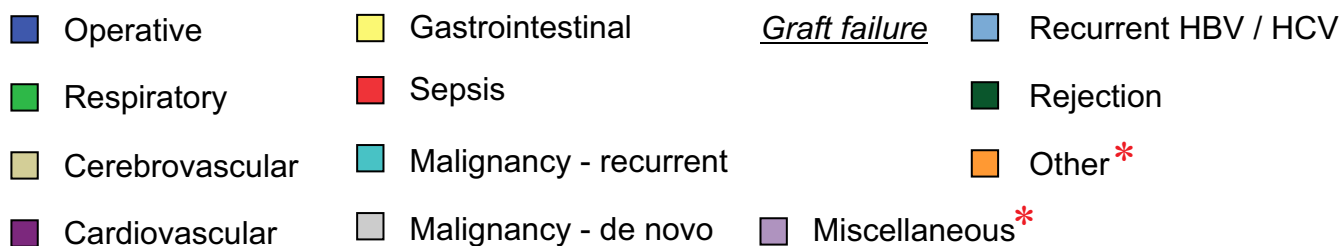
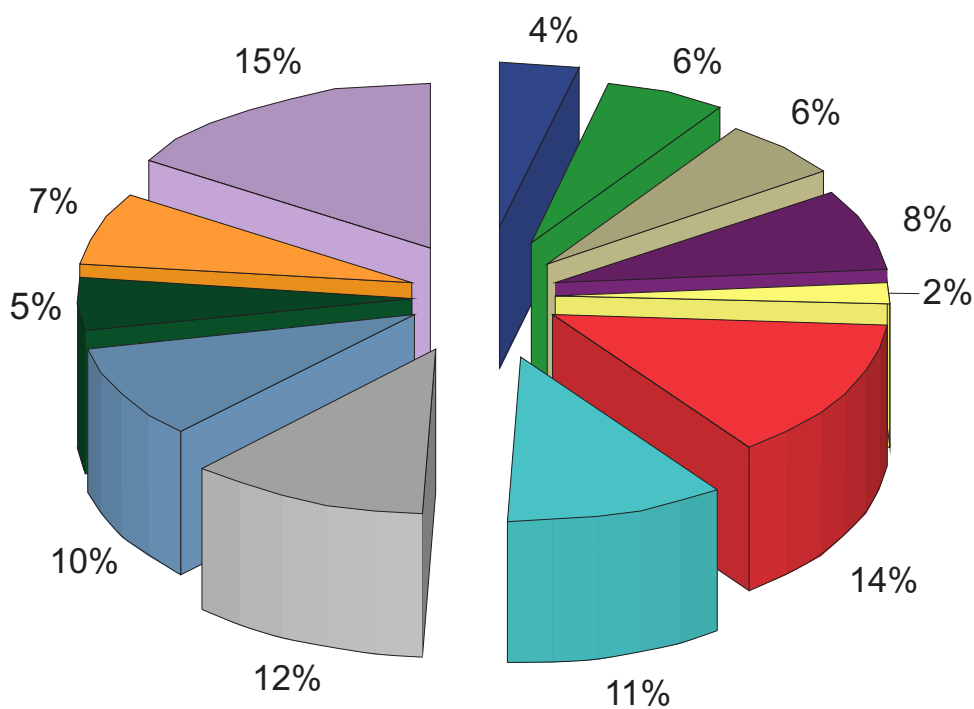
All Patients n = 1093



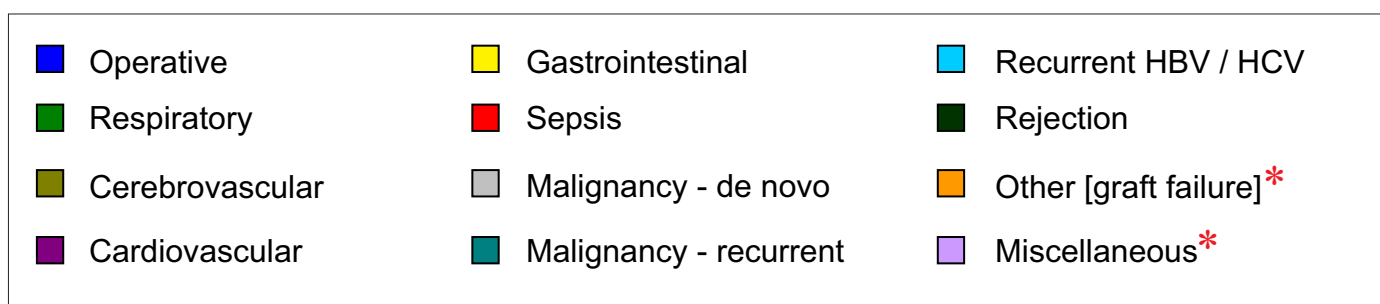
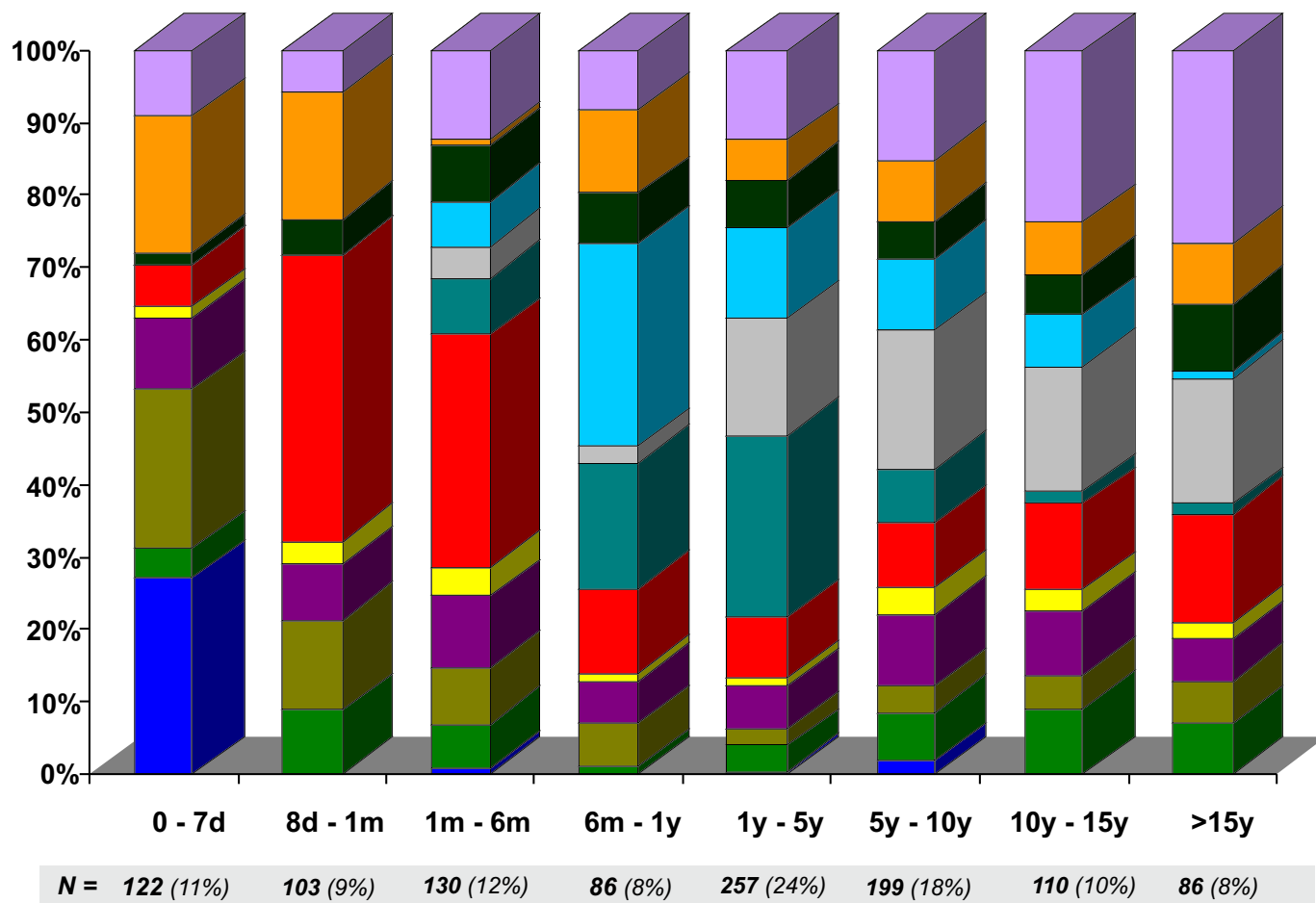
Causes of Death in Children n = 141



Causes of Death in Adult n = 952

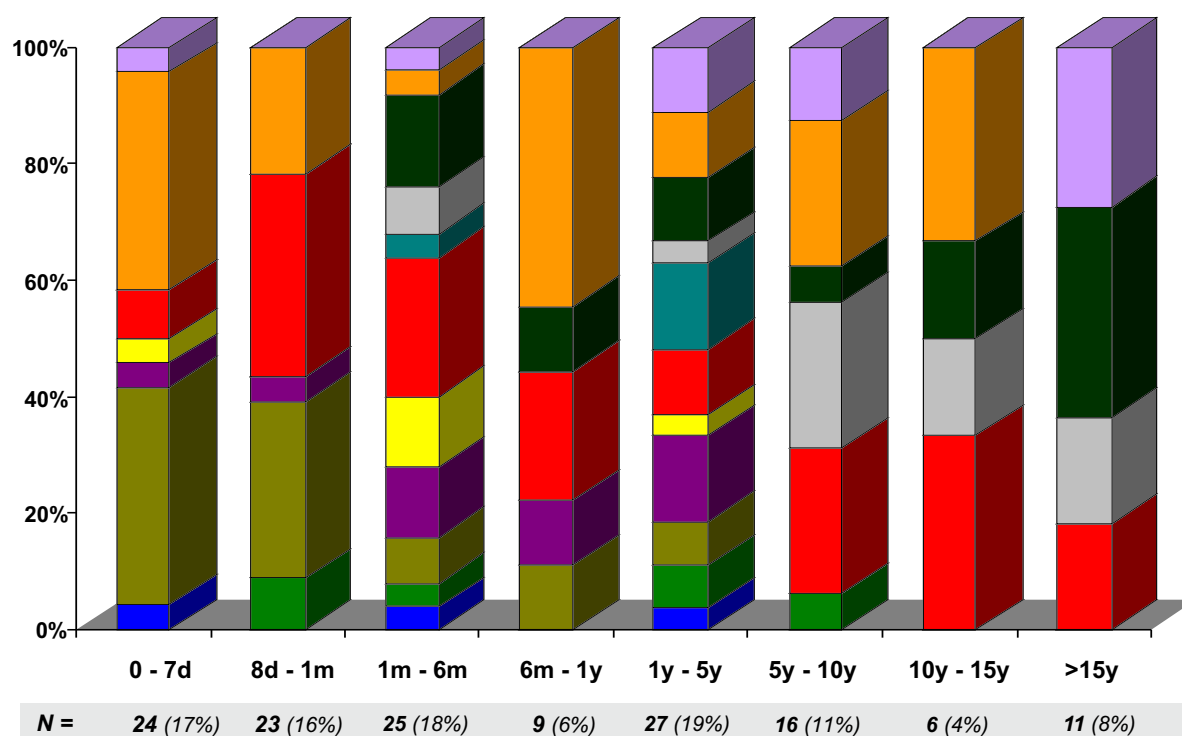


* See Appendix V for details

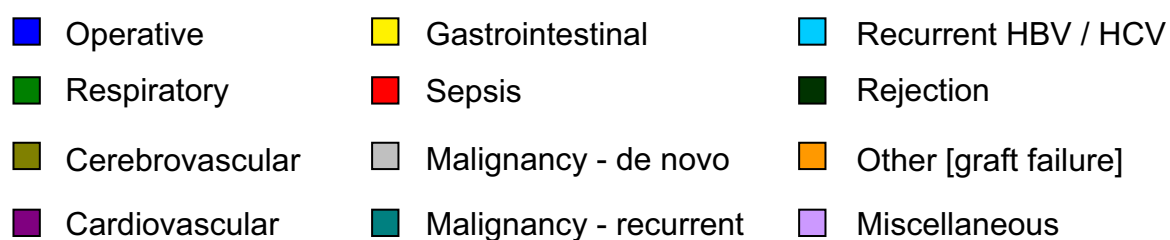
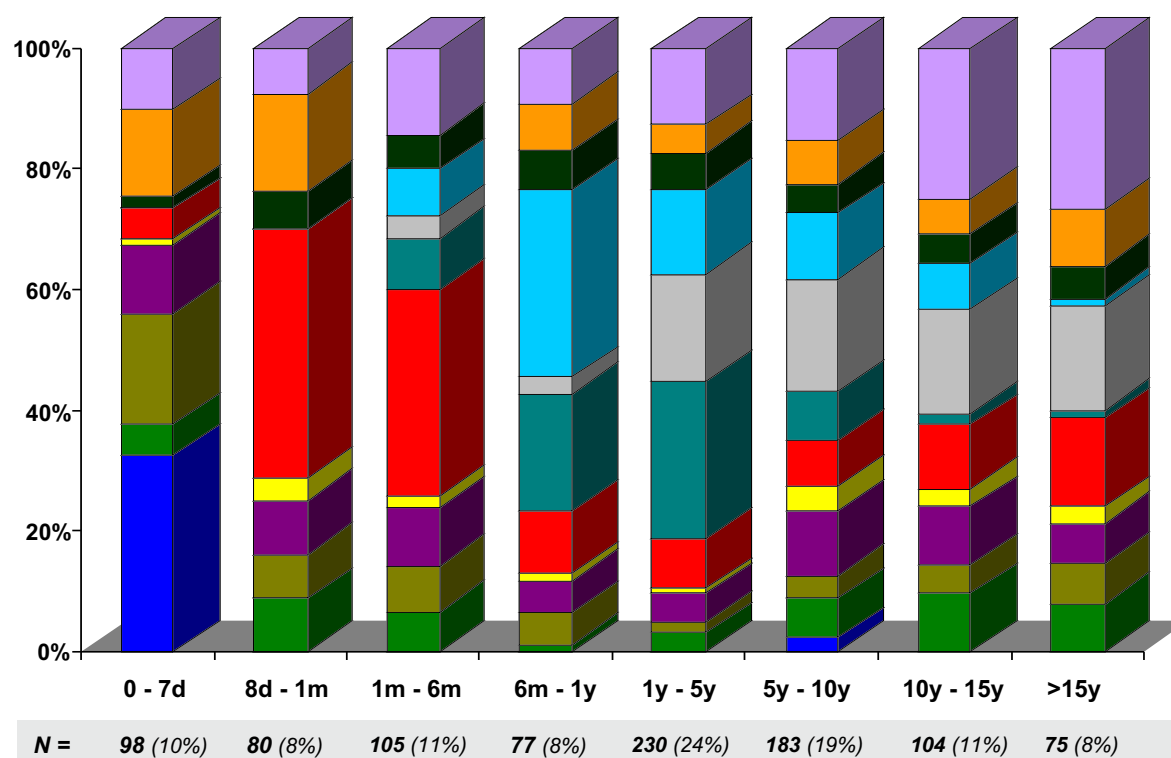


* See Appendix V for details

Cause of Death by Time Post Transplant Children (n=141)



Cause of Death by Time Post Transplant Adult (n=952)



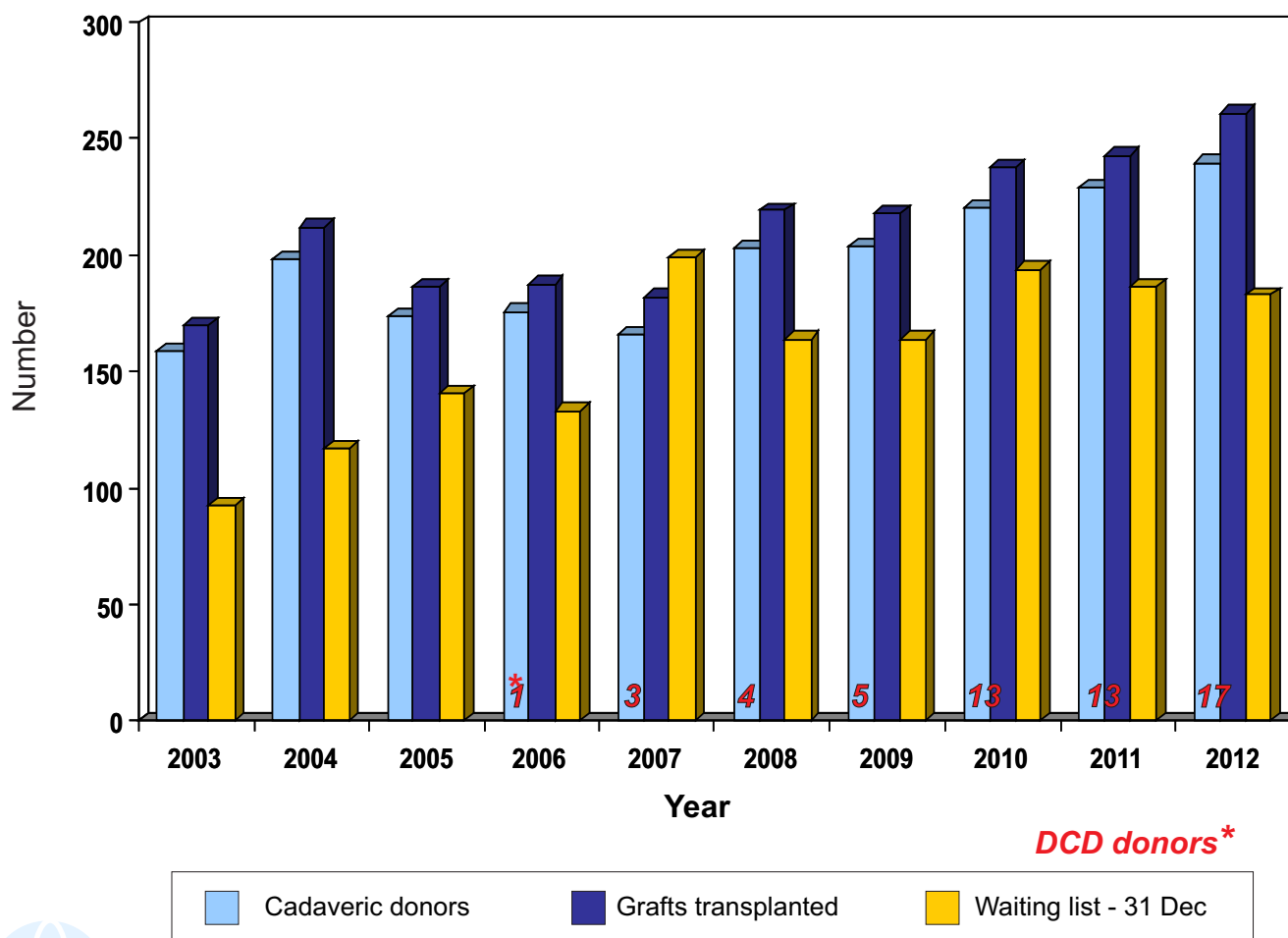
Section 6

Deceased Donor Information



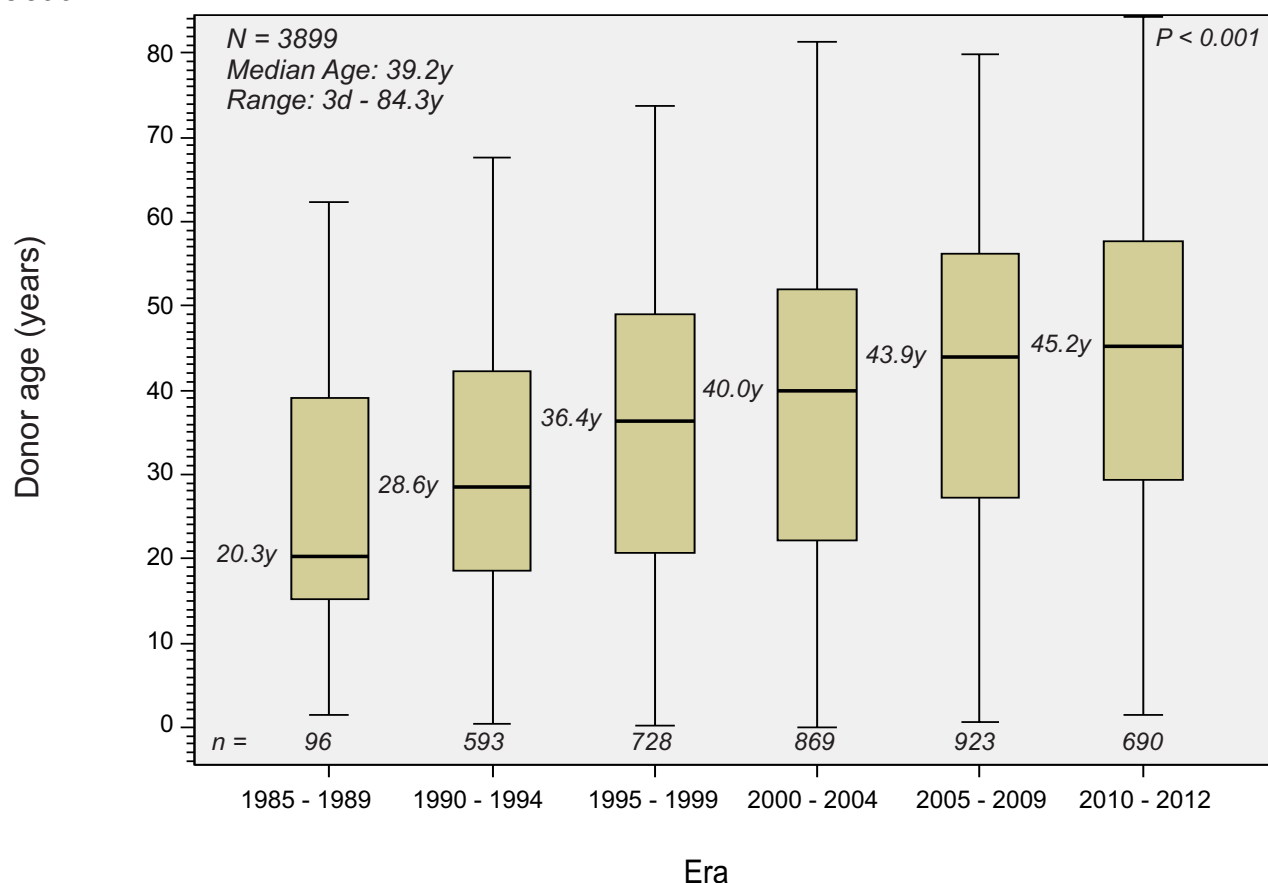
	QLD	NSW/ACT	VIC/TAS	SA/NT	WA	NZ	TOTAL
2003	34	32/3	29/2	13	15	31	159
2004	30	49/4	35/1	26/1	17	35	198
2005	24	36/8	38/2	17/3	25	21	174
2006	28	34/3	39/6	25	17	24	176
2007	25	36/1	36	19/2	15	32	166
2008	33	40/3	41/5	31/1	25	23	203
2009	35	46/4	36/5	28/2	15	33	204
2010	30	55/8	53/6	18/2	17	32	221
2011	44	52/7	49/3	22/2	20	30	229
2012	46	50/7	52/10	21/6	20	28	240

Grafts from deceased donors



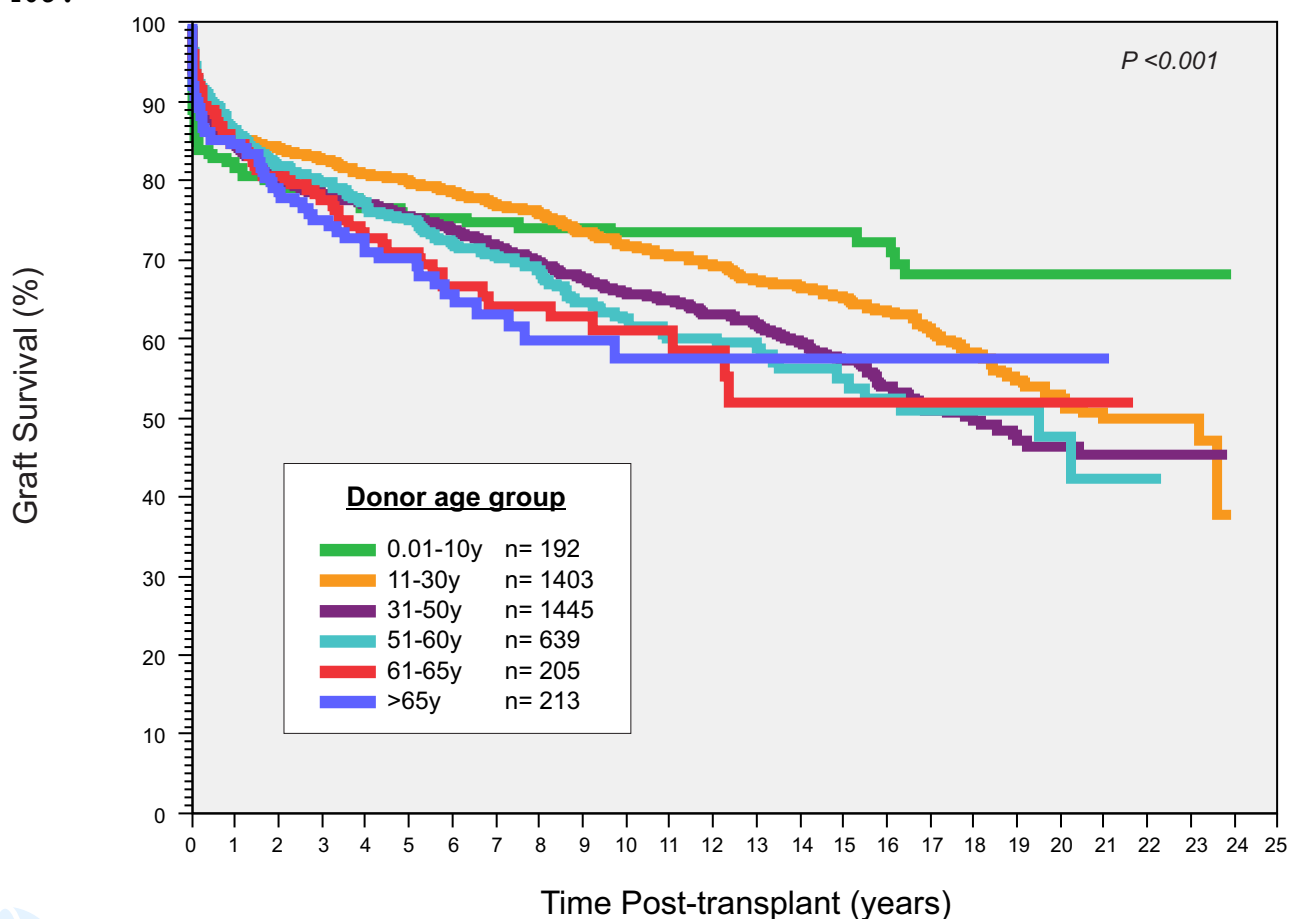
Donor Age by Era

N = 3899



Graft Survival by Donor Age

N = 4097



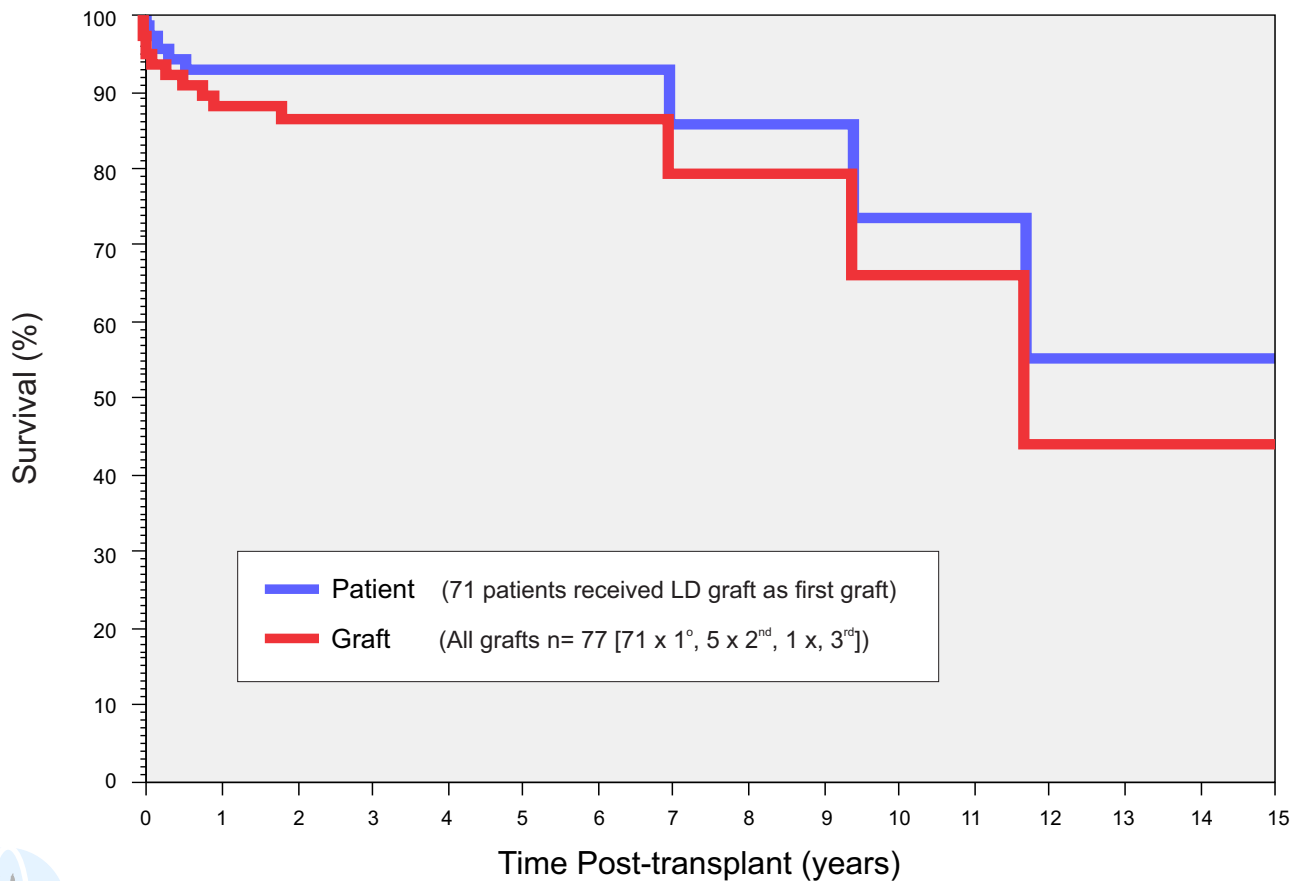
Section 7

Living Donor Transplantation



	Recipient Age Group		
	Child [n=63]	Adult [n=14] [*]	All [n=77]
Donor gender	-	-	-
Male	38	9	47
Female	25	5	30
Donor age	-	-	-
Median	34.7y	30.3y	33.8y
Range	20.1 - 54.5y	22.8 - 44.2y	20.1 - 54.5y
Donor relationship	-	-	-
Mother	15	-	15
Father	31	-	31
Son	-	4	4
Daughter	-	1	1
Grandmother	1	-	1
Grandfather	1	-	1
Sister	-	3	3
Brother	2	3	5
Aunt	6	-	6
Family friend	5	1	6
Cousin	2	-	2
Spouse	-	1	1

^{*} 1 x whole liver domino transplant



Section 8

Waiting List



Waiting List Activity

[Data 1/1/08 - 31/12/12]

Activity	2008	2009	2010	2011	2012				
Listed at 1 January	199	169	175	194	192	-	TOTAL 2012	Adult	Paediatric
New listings	290	335	335	336	-	347			
TOTAL	489	504	510	530	192	347	539	464	75
OUTCOME					OUTCOME				
Transplant	229 [47%]	228 [46%]	248 [49%]	253 [49%]	106	162	268 [50%]	121 [26%]	47 [63%]
Delisted	96 [20%]	101 [20%]	68 [13%]	85 [13%]	41	48	89 [16%]	83 [18%]	6 [8%]
Died on list	48	32	12	17	11	18	29	28	1
Too sick	14 } 14%	17 } 14%	12 } 8%	17 } 8%	8	8	16 } [10%]	14 } 11%	2 } 4%
Tumour progression	7	8	12	20	5	5	10	10	-
Improved	15	18	16	12	9	8	17	15	2
Other	11	26	12*	19*	8	9	17*	16	1
Still listed at 31 Dec	169 [34%]	175 [34%]	194 [38%]	192 [36%]	45	137	182 [34%]	160	22

[* Patient decline, Malignancy, Drug Use, Infection, Further investigations, Medical]

Outcome of Initial Urgent Listing

OUTCOME	CATEGORY 1						
	2008	2009	2010	2011	2012		
	(n=13)	(n=17)	(n=19)	(n=15)	N=16	Adult n=13	Paediatric n=3
TRANSPLANTED	3 } 46%	9 } 65%	13 } 74%	12 } 80%	11 } 81%	9	2
IMPROVED	3 }	2 }	1 }	- }	2 }	1	1
DIED / TOO SICK	7	6	5	3	3	3	-
OTHER TREATMENT	-	-	-	-	-	-	-

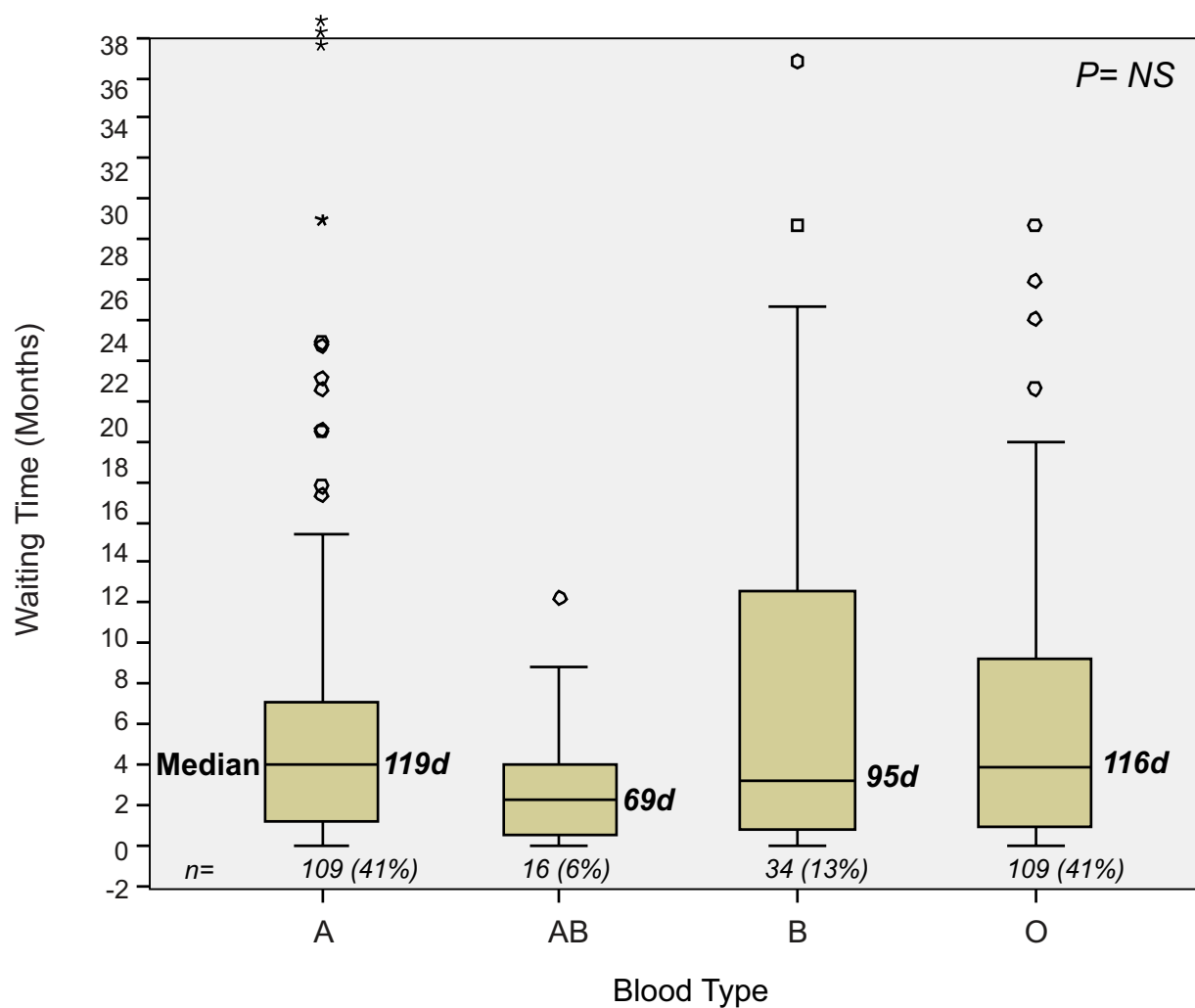
OUTCOME	CATEGORY 2						
	2008	2009	2010	2011	2012		
	(n=24)	(n=21)	(n=30)	(n=28)	N=19	Adult n=10	Paediatric n=9
TRANSPLANTED	20 } 83%	18 } 90%	23 } 93%	22 } 86%	14 } 89%	8	6
IMPROVED	1 }	1 }	5 }	2 }	3 }	1	2
DIED / TOO SICK	3	2	1 / 1	3	1	1	-
OTHER TREATMENT	-	-	-	1 active 31/12/11	1 active 31/12/12	-	1 active 31/12/12

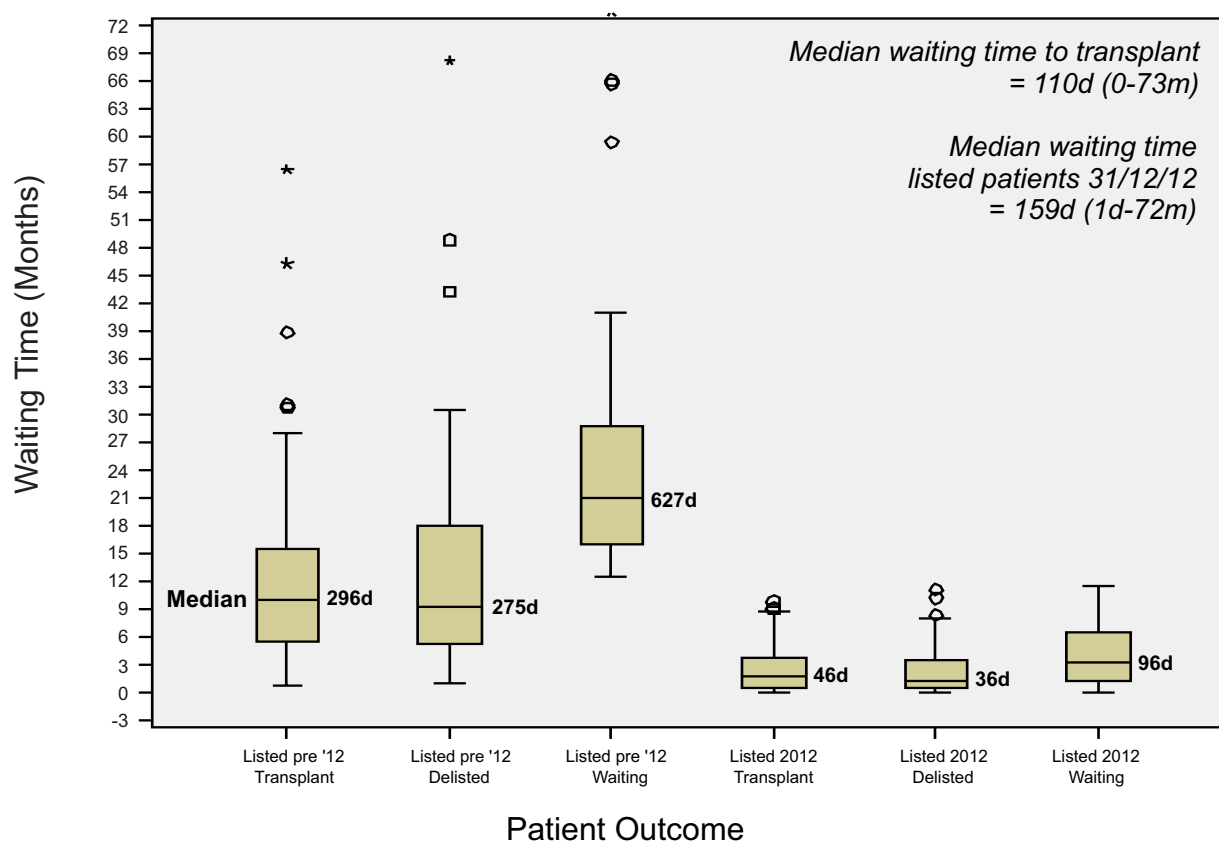
	Blood Group				
	A	O	B	AB	TOTAL
n=	210 (39%)*	234 (43%)	67 (12%)	27 (5%)	539
Not transplanted	101	125	33	11	271
Transplanted	109 (52%)**	109 (47%)	34 (51%)	16 (59%)	268

* % of total number listed

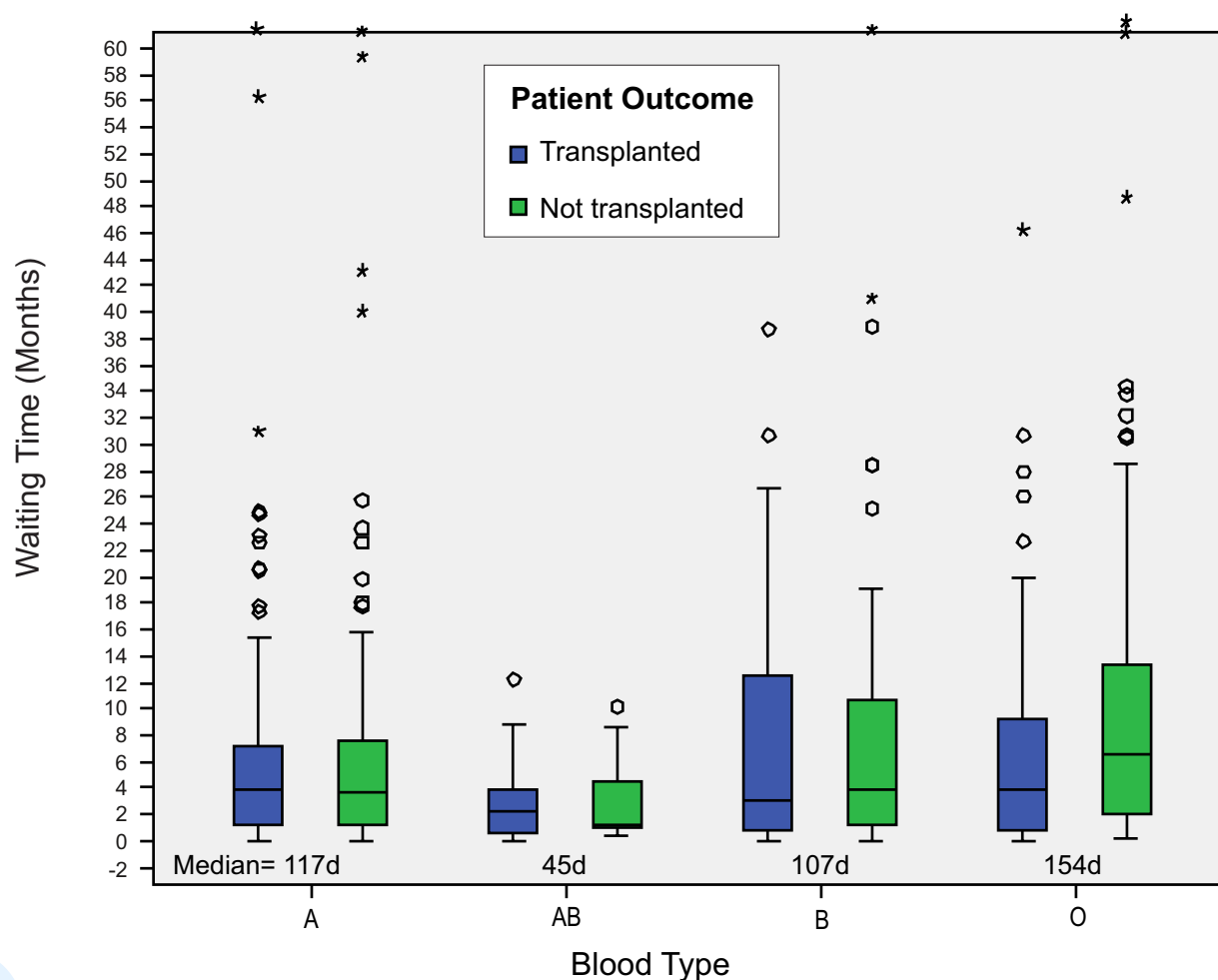
** % of blood group

Waiting Time to Transplant 2012





Waiting Time by Outcome & Blood Group



Section 9

Liver Transplantation and Cancer



Cancer in Liver Transplant Recipients

n = 3980

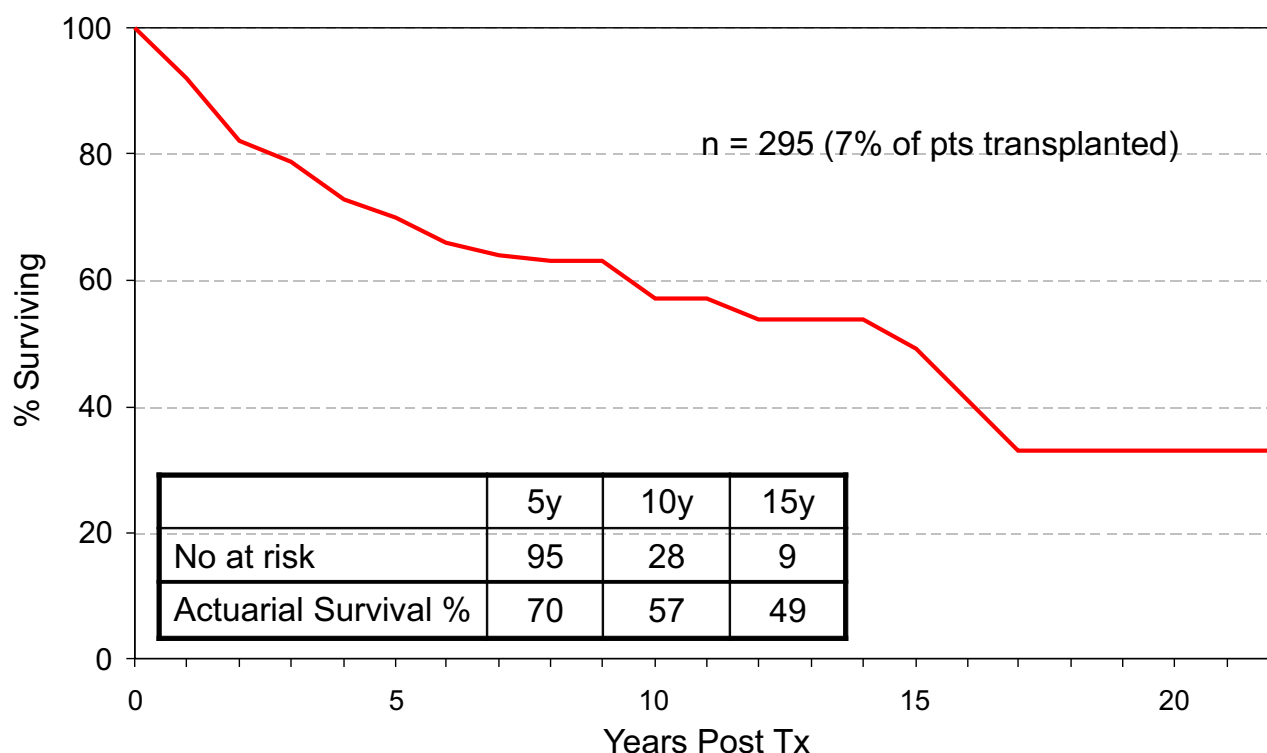
At Tx	n = 3980	
Liver Cancer as Primary Diagnosis	295	(7%)
Liver Ca as a Secondary Diagnosis	471	(12%) 473 Ca
Total	766	(18%)
Post Tx		
Recurrent Liver Ca	113	(3% of all pts, 16% of pts with Ca at Tx)
De Novo Ca	295	(7%) 309 Ca
Skin Ca	984	(25%) 3809 Ca
Total	1392	(35%)
Multiple Ca	555	
Pre-Tx cancer developed de novo cancer	25	(3% of pts with Ca at Tx)
Transferred from Donor	2	
Developed non skin Ca < 90days	9	

Liver Cancer as Primary Diagnosis

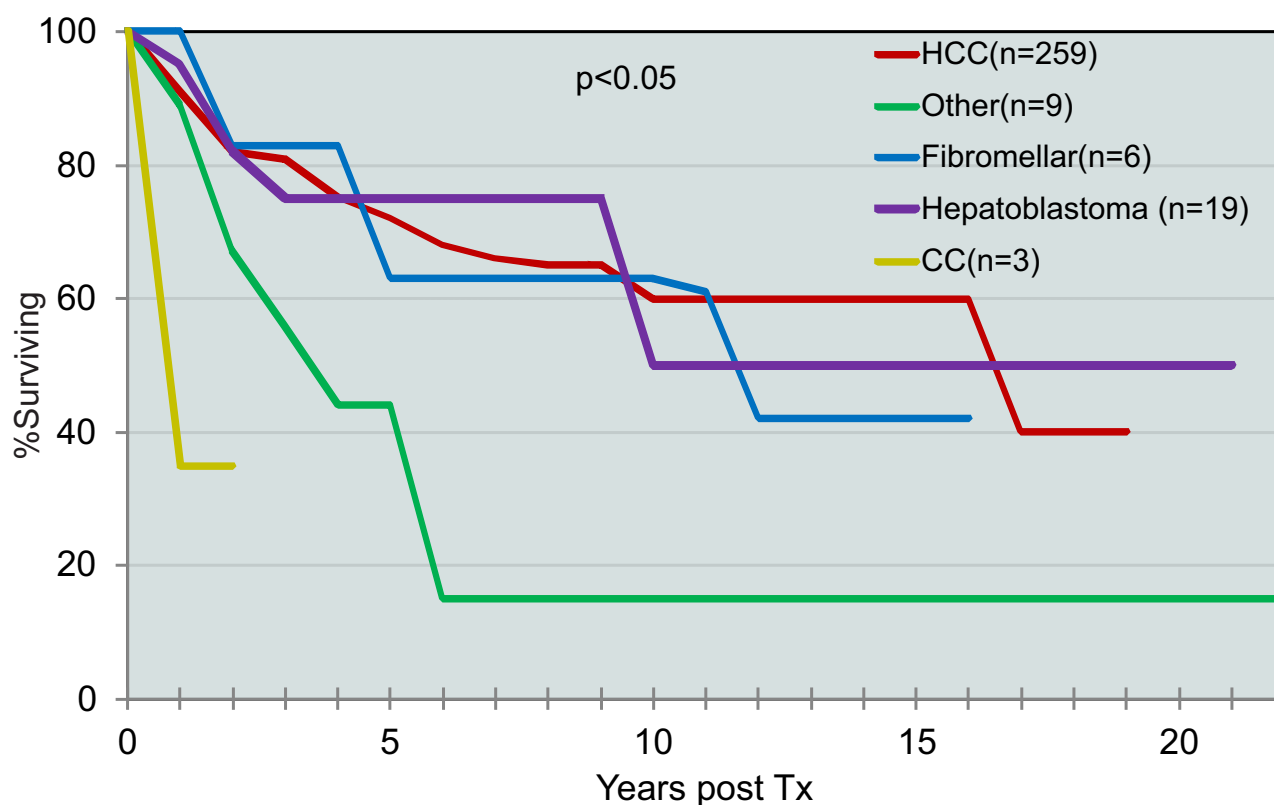
n= 3980

TYPE OF CA	No	DIED	DIED OF THIS CA
HEPATOCELLULAR CA	259	64	34 (36%)
HEPATOBLASTOMA	19	5	4 (67%)
FIBROLAMELLAR	6	5	2 (40%)
CARCINOID	4	4	4 (100%)
CHOLANGIOCARCINOMA	2	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	295 (7% of pts)	82 (28% of those with PCa)	48 (16% of those with PCa)

Overall Survival
Primary Liver Cancer
n = 295 (7% of patients transplanted)



Overall Survival
Primary Liver Cancer
n = 295/3980 (7%)



Primary Liver Cancer

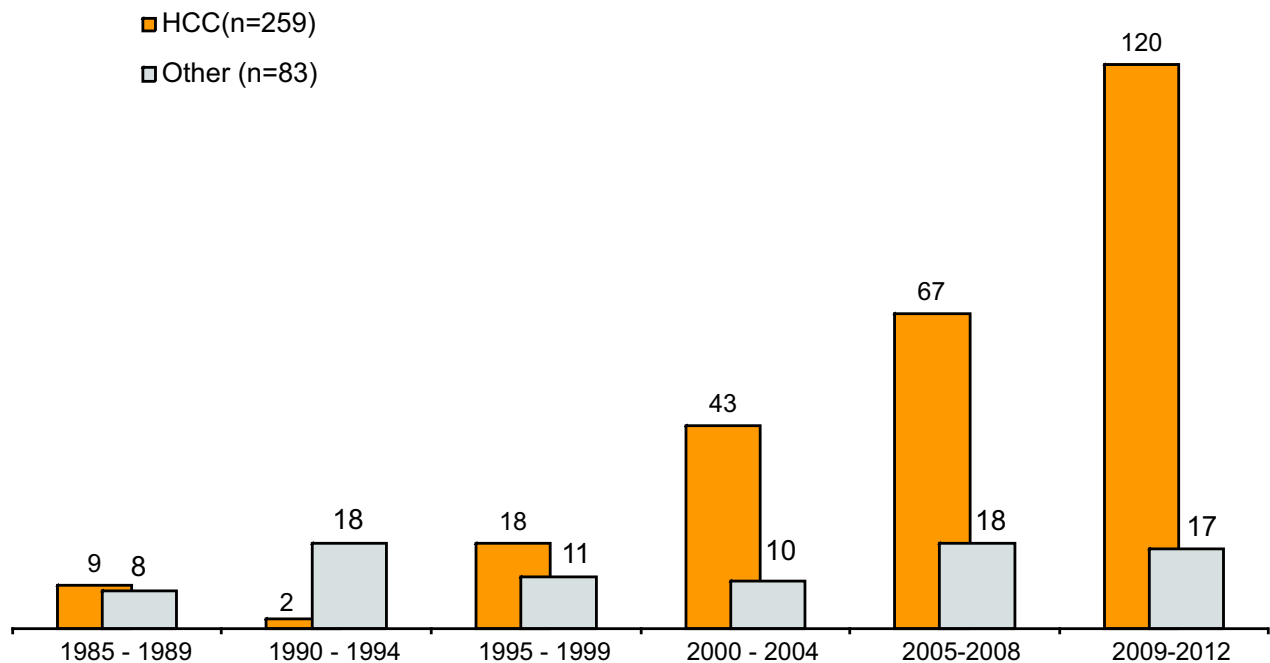
Actuarial Survival Summary

n = 3980

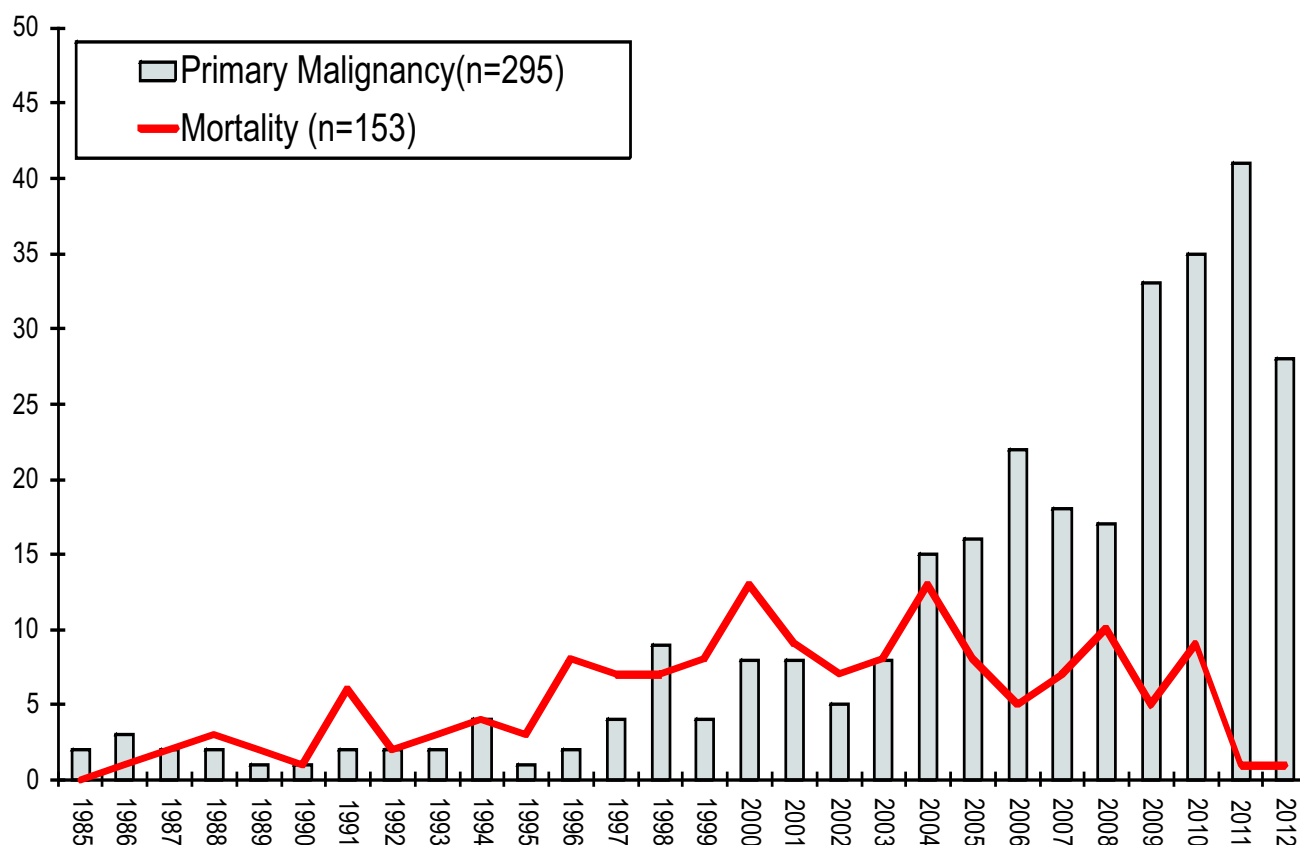
		1yr	5yr	10yr	15yr
HCC (n=259)	n	217	84	22	6
	%	91	72	60	60
Other (n=9)	n	9	4	2	2
	%	89	44	15	15
Hepatoblastoma(n=19)	n	18	6	3	2
	%	95	75	50	50
Fibrolamellar (n=6)	n	6	4	4	2
	%	83	63	63	21
CC (n=3)	n	23			
	%	50			

Liver Cancer as Primary Diagnosis

n = 295



Primary Liver Cancer Incidence and Mortality



Liver Cancer as a Secondary Diagnosis

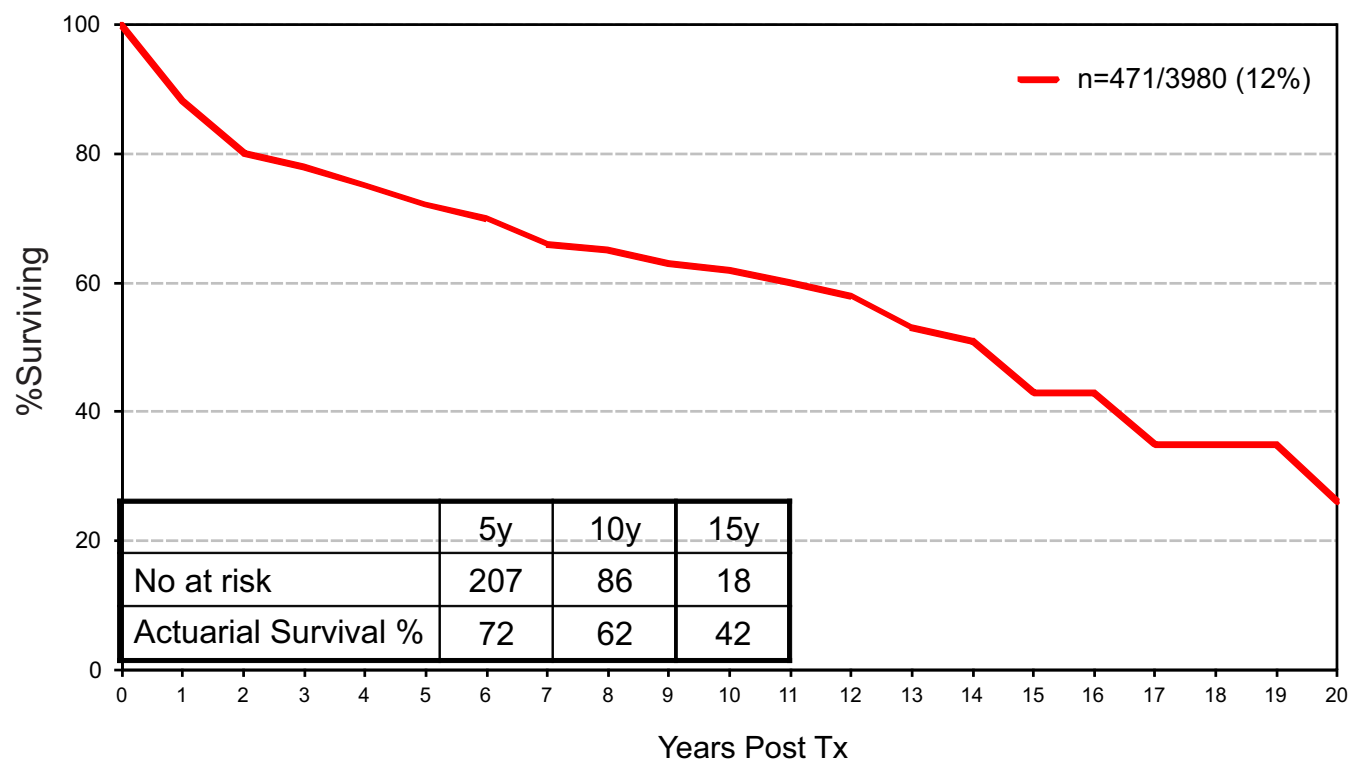
n = 3980

	No	Died	Died of This Cancer
HEPATOCELLULAR CA*	426	122	33 (27%)
CHOLANGIO CA	34	25	13(52%)
HEPATOBLASTOMA*	3	1	0
LAMELLA VARIANT	4	2	0
OTHER	6	4	2 (50%)
Total	473* in 471pts (12%)	152 (32% of pts with SCa)	48 (10% of pts with SCa)

* 1 patient had 2 secondary cancers

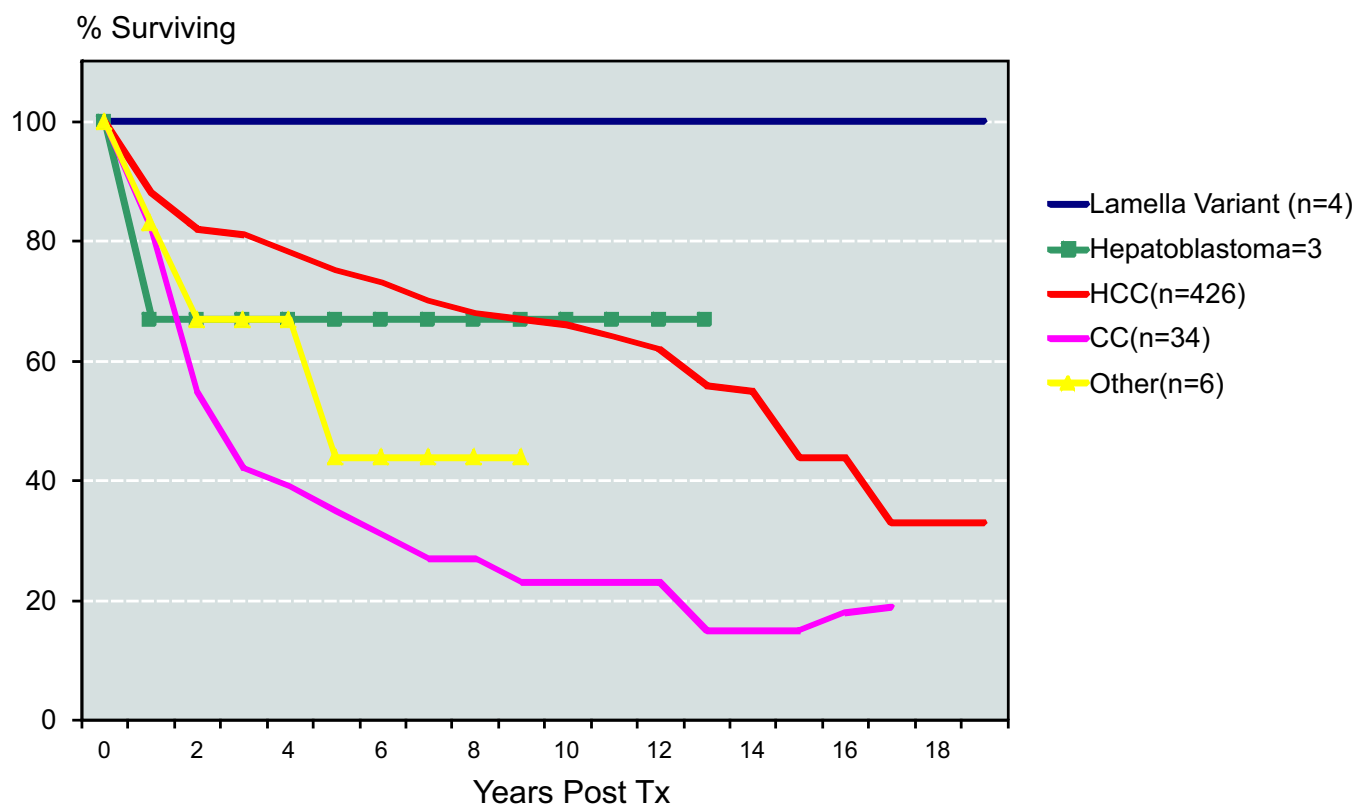
Overall Survival

Liver Cancer as a Secondary Diagnosis



Liver Cancer as a Secondary Diagnosis

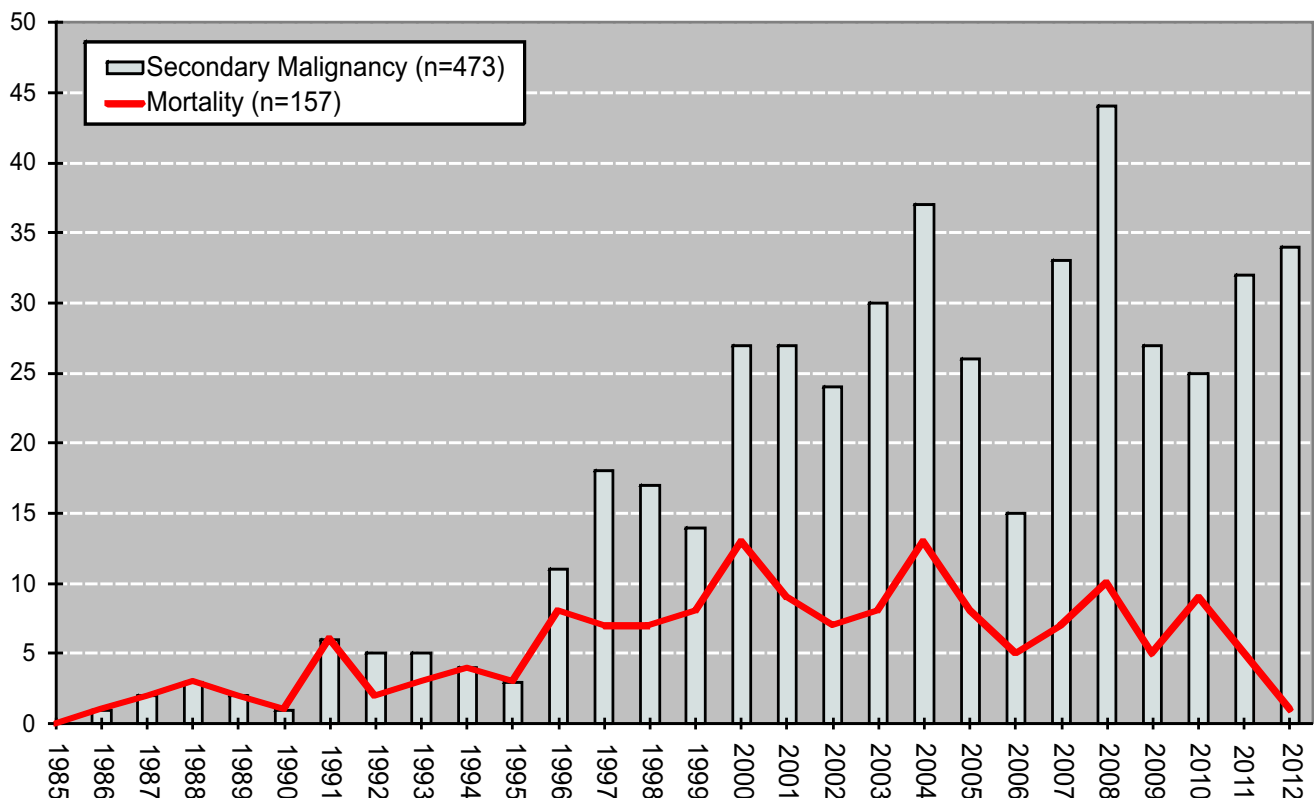
n = 3980



Secondary Liver Cancer Actuarial Survival Summary n =473/ 3980 (12%)

		1yr	5yr	10yr	15yr
HCC (n=385)	n	305	178	65	7
	%	79	46	17	2
CC (n=33)	n	27	10	5	2
	%	82	30	15	6
Hepatoblastoma (n=3)	n	3	2	2	1
	%	100	67	67	33
Fibrolamellar (n=4)	n	4	4	2	2
	%	100	100	50	50
Other (n=7)	n	7	4	1	0
	%	100	57	14	0

Liver Cancer as a Secondary Diagnosis Incidence and Mortality n=473/3890 (12%)



Liver Cancer

(Primary or Secondary Diagnosis)

n = 3980

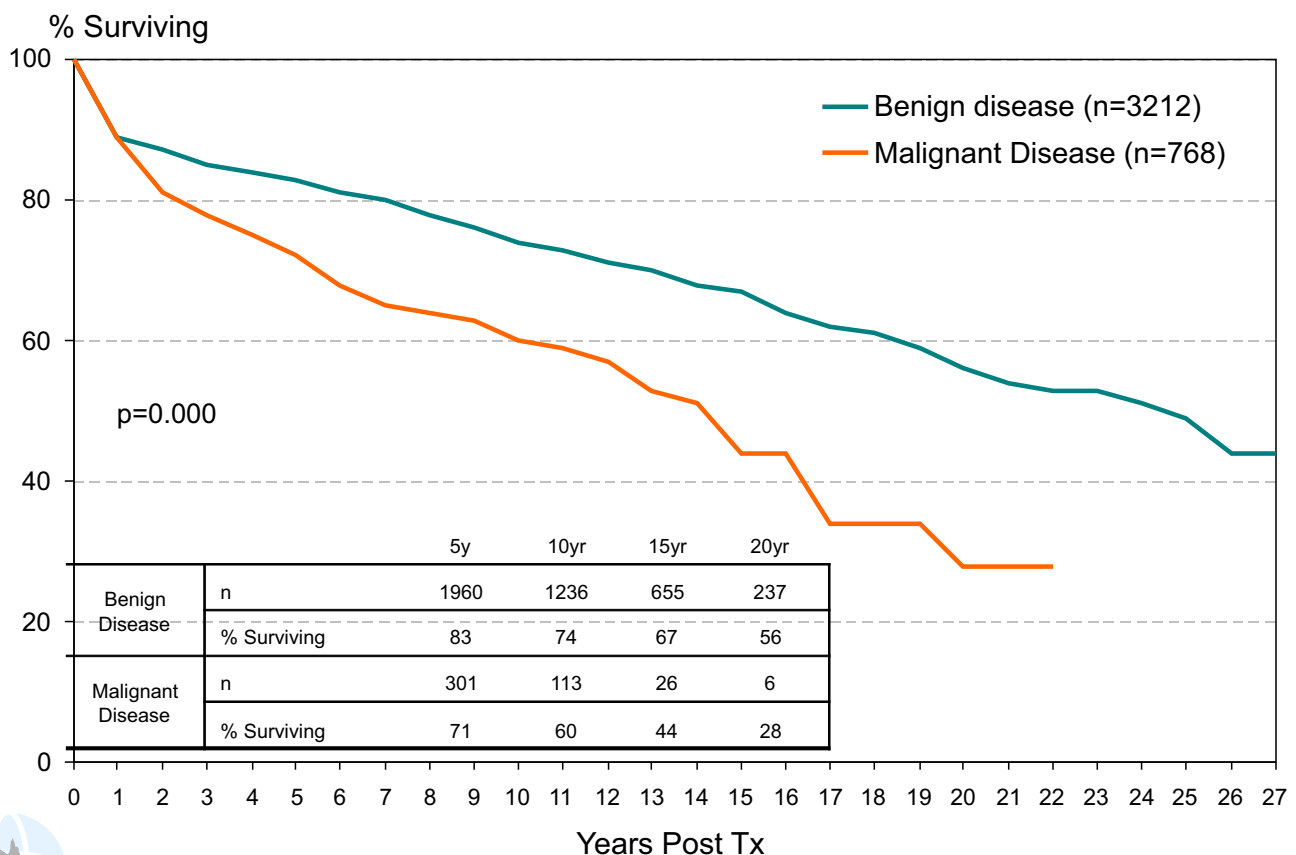
TYPE OF CA	NO	DIED	DIED OF THIS CA
HEPATOCELLULAR CA*	685	188	67 (41%)
CHOLANGIOCARCINOMA	36	27	15 (53%)
HEPATOBLASTOMA*	22	6	4 (66%)
FIBROLAMELLAR	10	5	2 (40%)
CARCINOID	4	4	4 (100%)
ADENOCARCINOMA	4	3	1 ((20%)
EPITHELOID HAEMANGIOENDOTHELIOMA	3	0	0
GASTRINOMA	1	1	1 (100%)
PANCREATIC ISLET CELL	1	1	1 (100%)
ANGIOSARCOMA	2	2	2 (100%)
TOTALS	768 (19% of pts)	237 (31% of those with Ca)	97 (13% of those with Ca at Tx)

* 1 patient had 2 secondary cancers

Patient Actuarial Survival

Benign Disease vs Pre Transplant Liver Malignancy

n = 3980



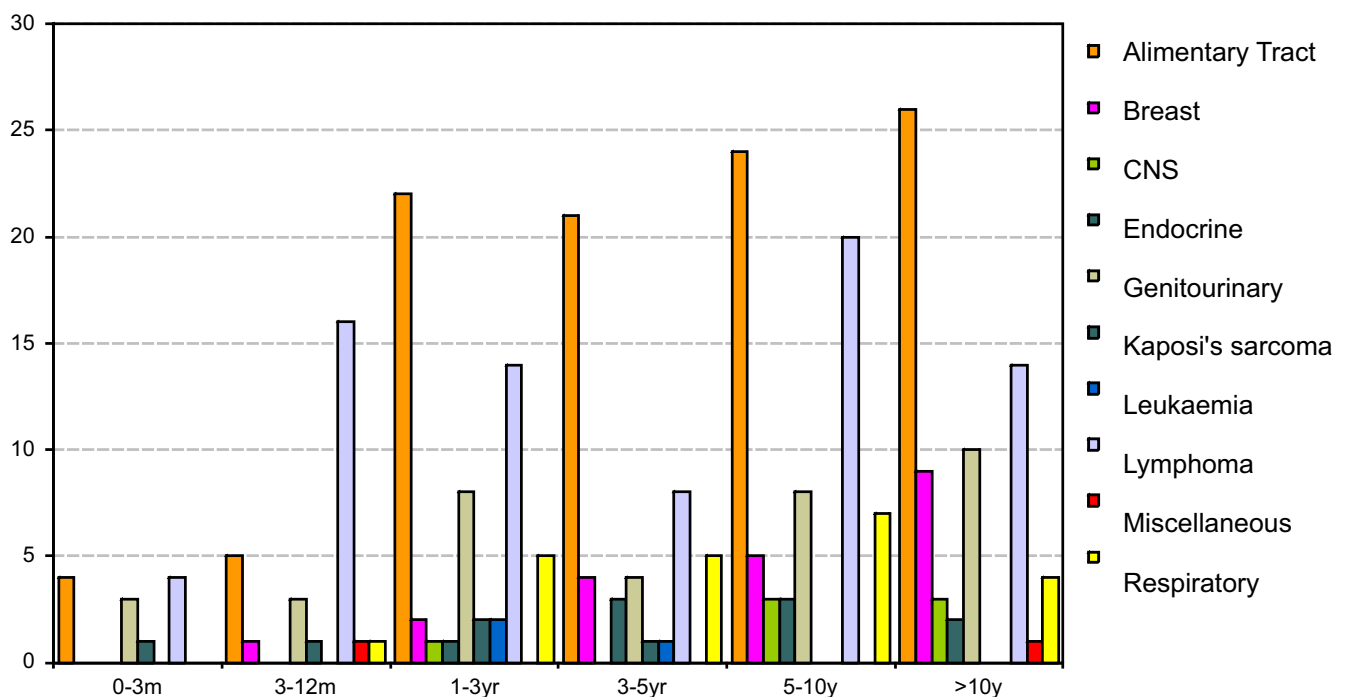
	No	Male	Female	Age of pts (yrs)	Time to diagnosis (mths)	Died of This Cancer
Alimentary*	114	83	31	13 – 78 (m 57)	3 – 232 (m 107)	52 (46%)
Lymphoma*	79	49	30	1– 70 (m 49)	1 – 214 (m 64)	28 (35%)
Genitourinary*	39	26	13	21 – 75 (m 60)	2 – 231 (m 87)	4(10%)
Breast	23	-	23	30 – 74 (m 53)	11 –241(m 112)	9 (39%)
Respiratory	26	21	5	29 – 75(m 58)	7 – 212(m70)	19(73%)
Kaposi's	5	4	1	32 – 65 (m 51)	2 – 48 (m 21)	0
Endocrine	9	4	5	36 – 70 (m 55)	35 – 213 (m89)	3 (33%)
CNS	7	5	2	16 – 75 (m 57)	14 –211(m118)	6(86%)
Leukaemia	3	1	2	3.– 50 (m 30)	16 – 44 (m 30)	0
Miscellaneous	4	2	2	62 – 73 (m 65)	6 – 234 (m 75)	1 (25%)
Total	*309ca in 295pts	195	114	1 – 78 (m 53)	1 – 242 (m 72)	122 (41% of pts with Ca)

Fifteen patients also had a liver cancer at Tx; * 11 patients had more than 1 de novo malignancy

Time to 1st De Novo Non Skin Cancer

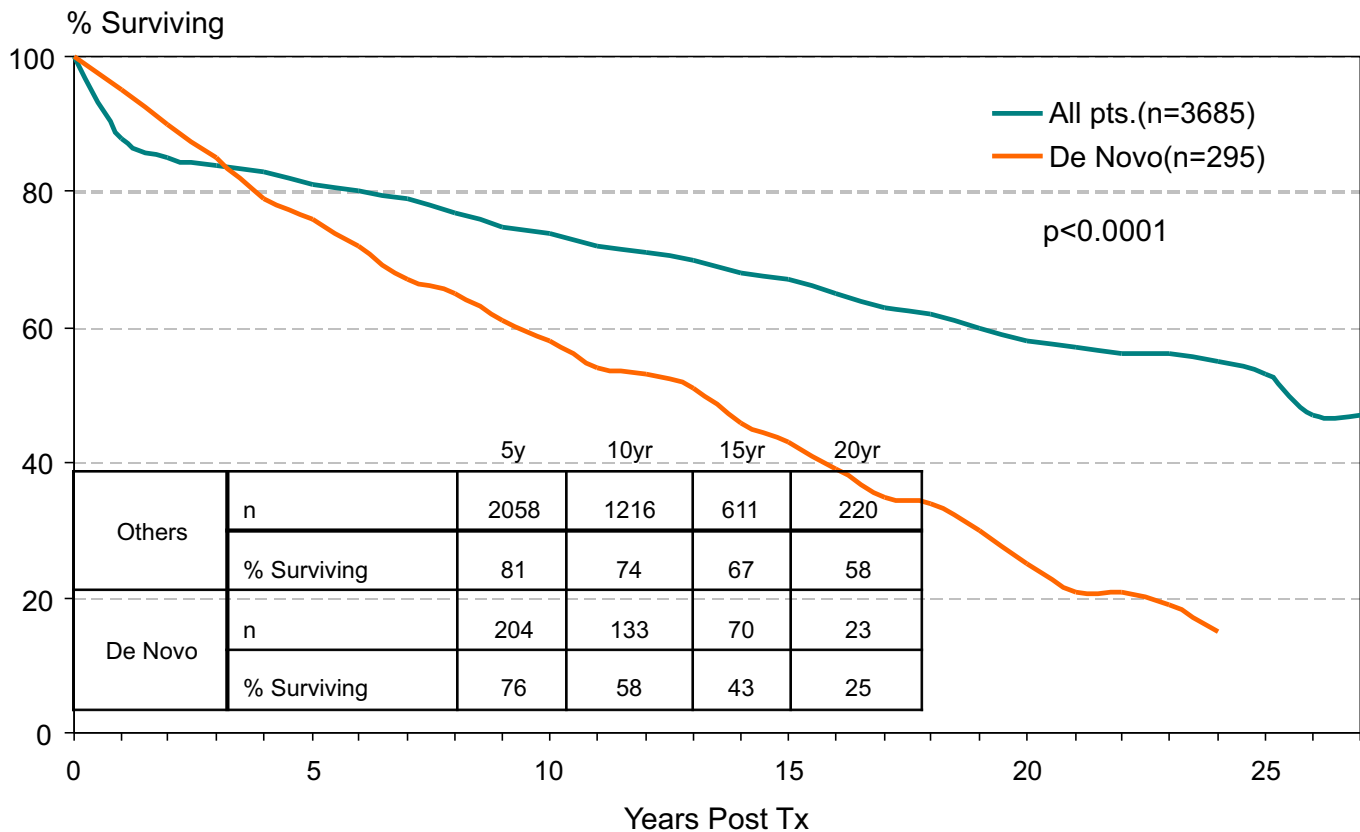
n = 3980

309 cancers in 295 pts (7% of all pts)



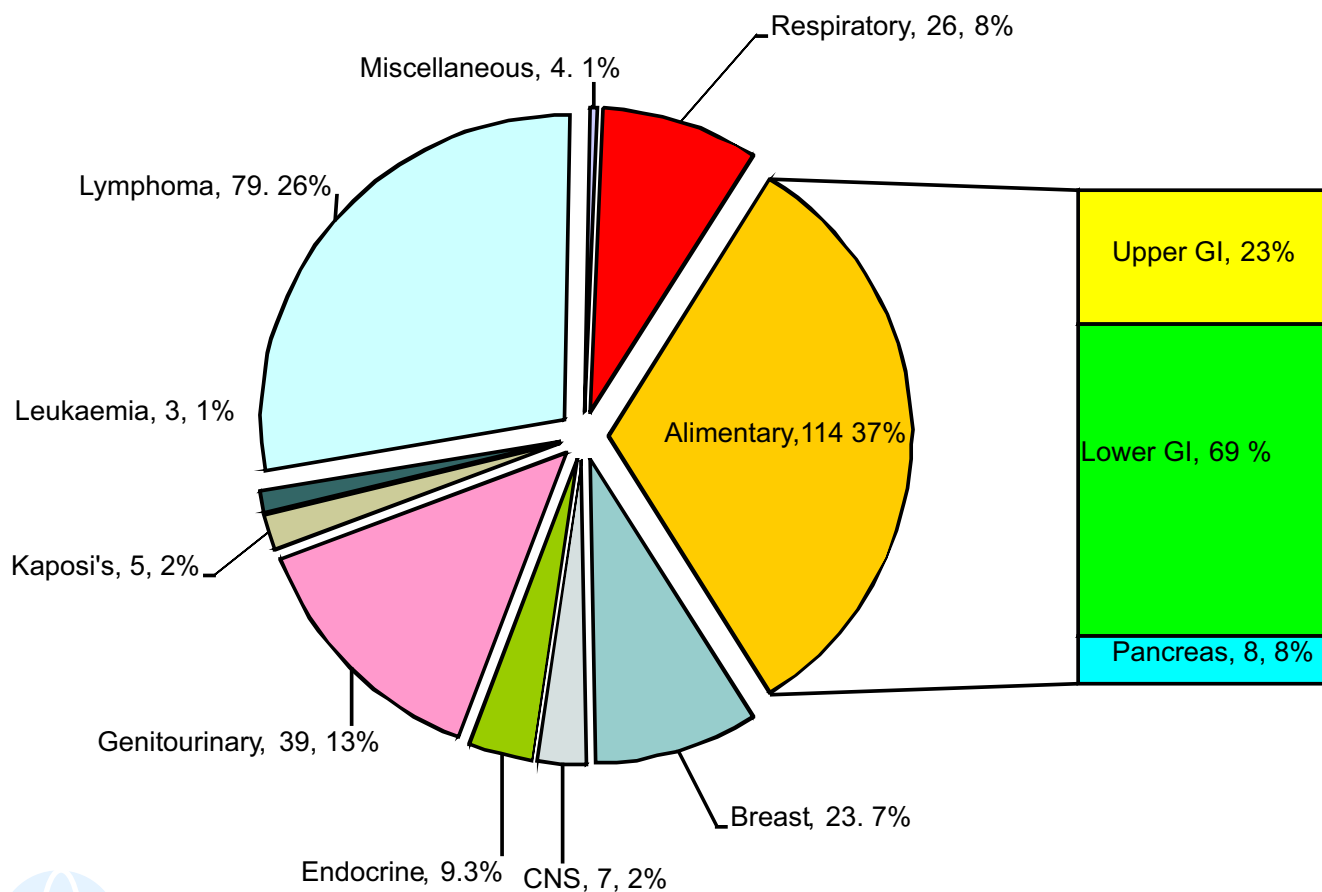
De Novo Non Skin Cancer vs All Patients

n = 3980

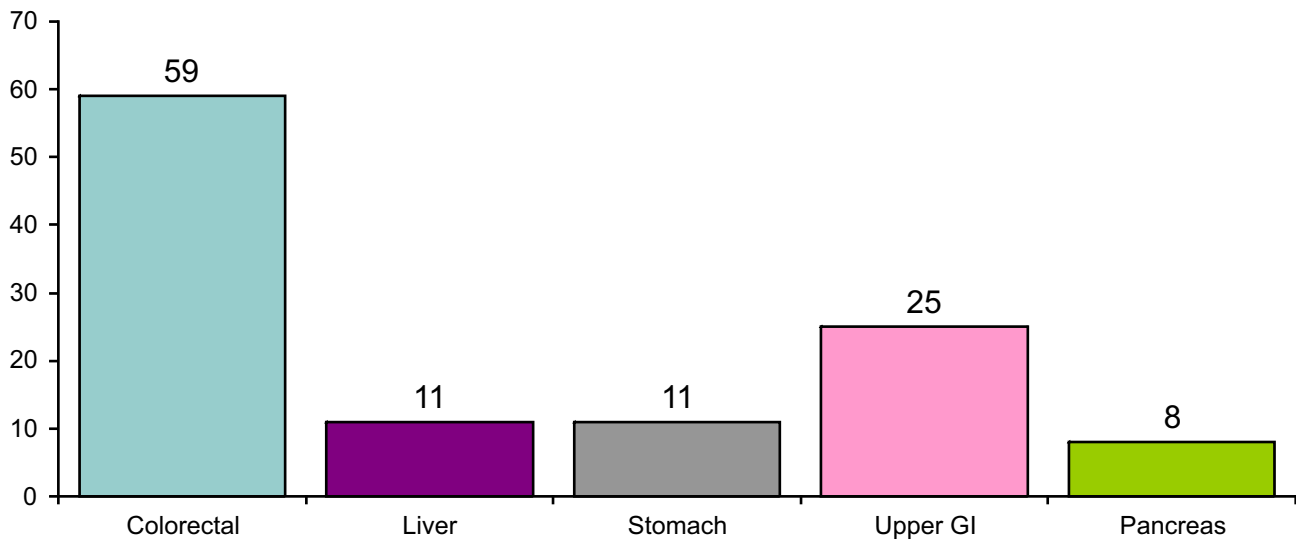


De Novo Non Skin Cancer

n = 309/3980(8%)



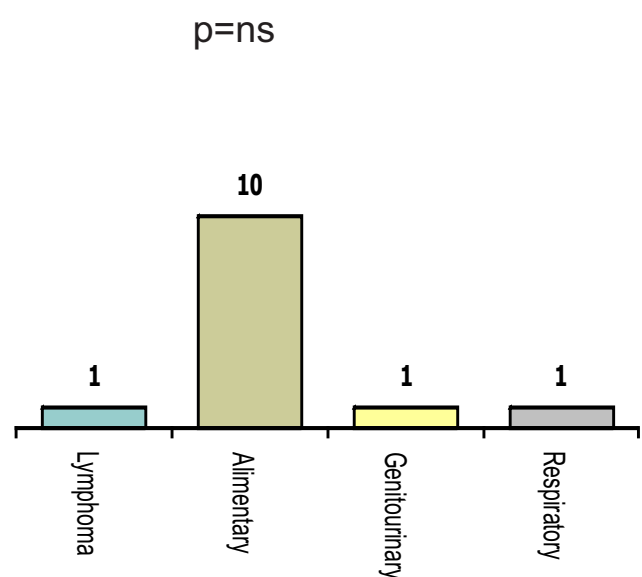
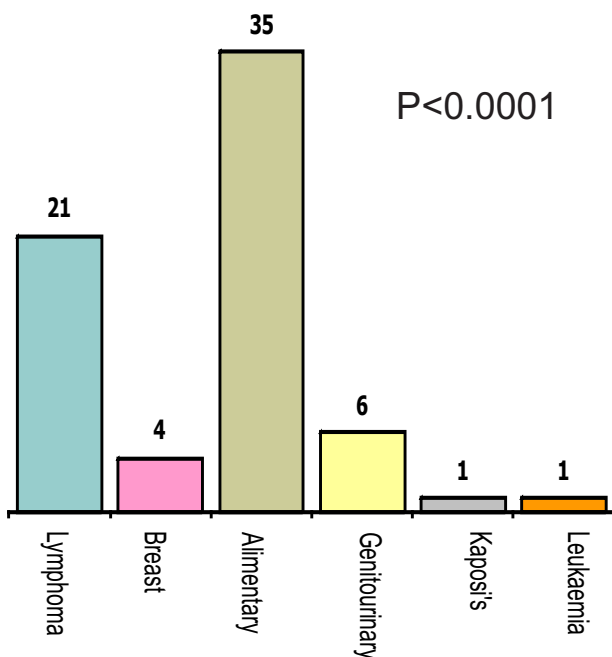
De Novo Non Skin Cancer Alimentary Tract Incidence n = 114/309 cancers (37%)



Pre Transplant Liver Disease and De Novo Non Skin Cancer n = 309/3980 (7%)

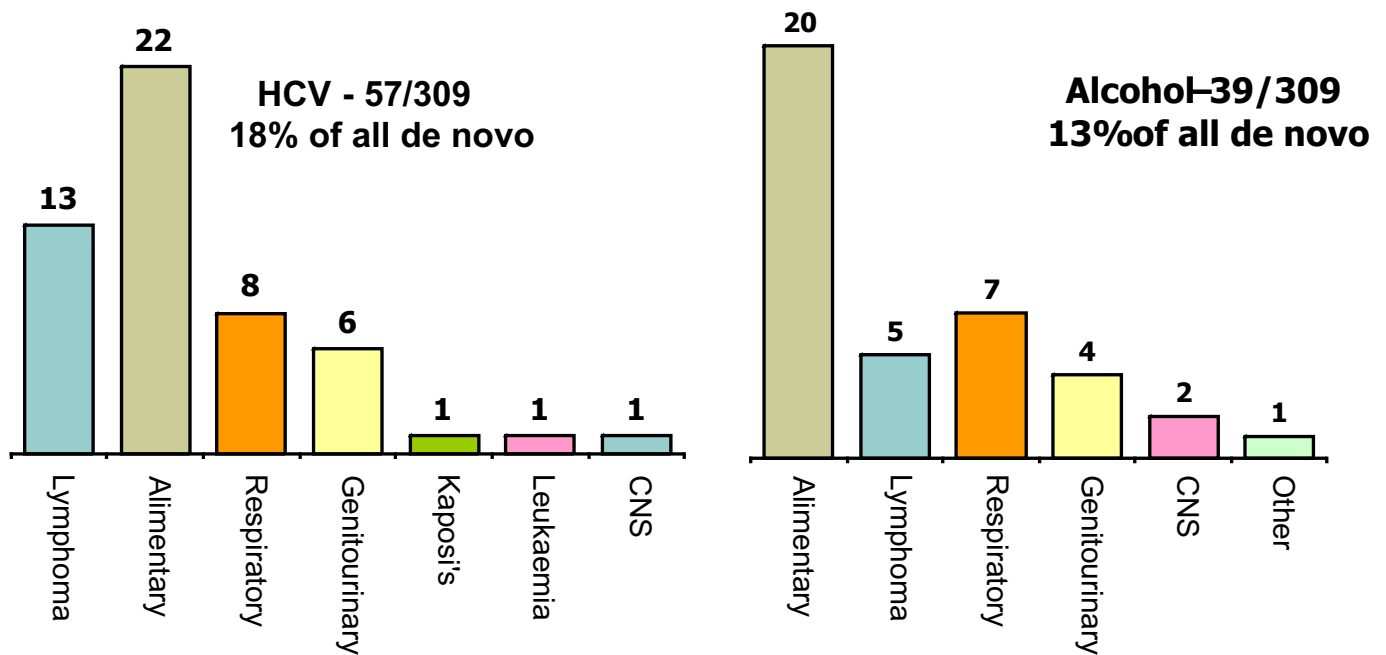
PSC + Auto-immune - 73/309
24% of all de novo

HBV - 13/309 4%
of all de novo



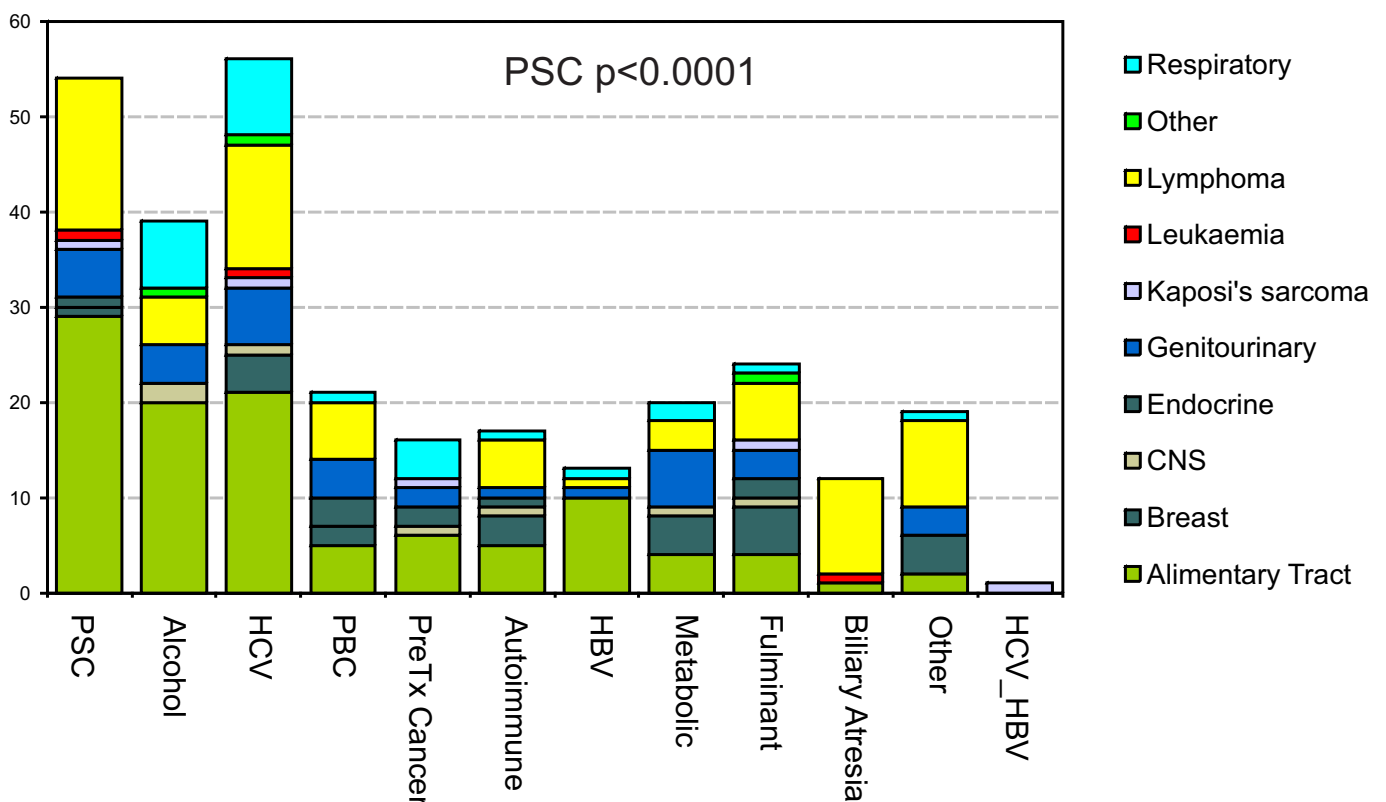
Pre Transplant Liver Disease and De Novo Non Skin Cancer

n = 309/3980 (7%)



Primary Liver Disease and De Novo Non Skin Cancer

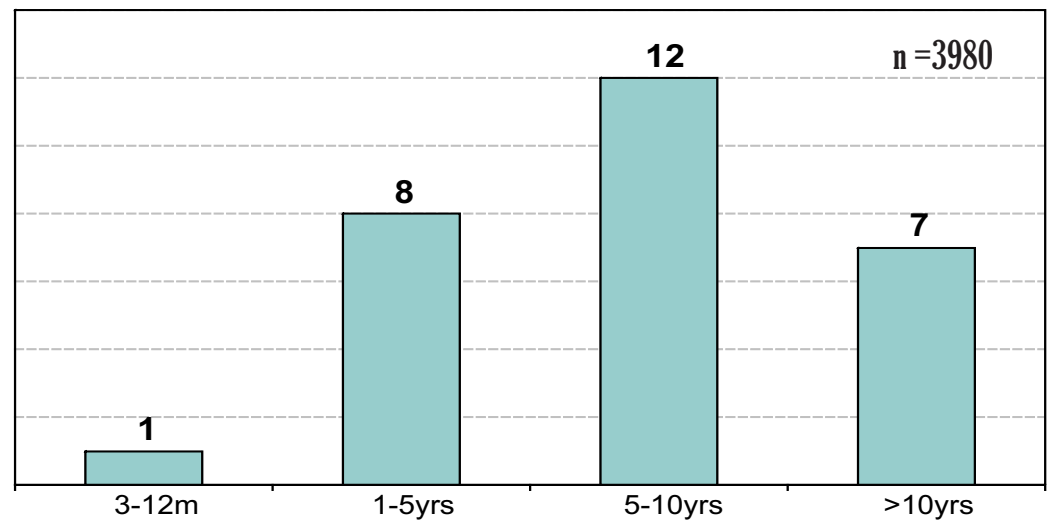
n = 309/3980 (7%)



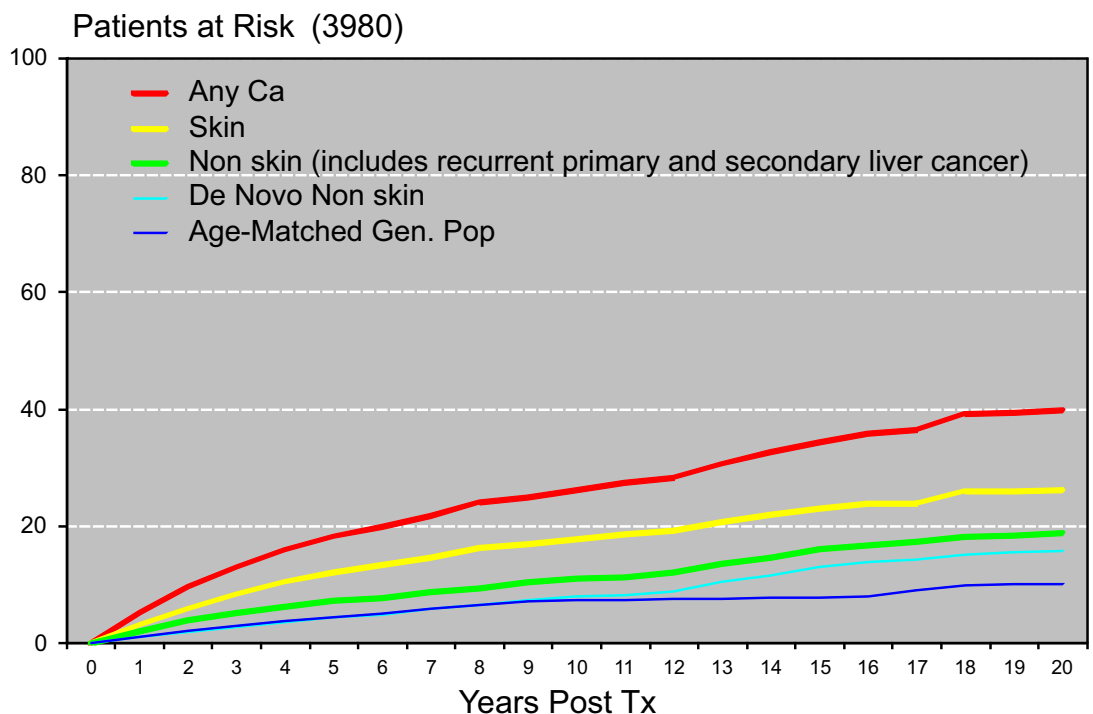
Type of Skin Cancer	Pts	Cancers
BCC	333	1071
SCC	364	1532
Melanoma	29	29
Total	948 (26% of all pts)**	3809

****555 pts had multiple skin cancer types**

Time to Melanoma Skin Cancer Development n = 29(0.7% of all pts)



Cumulative Risk of Diagnosis of Cancer Following Liver Tx. 1985-2012



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

Studley Road

HEIDELBERG VIC 3084

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

and

The Royal Children's Hospital

Flemington Road

PARKVILLE VIC 3052

Queensland Liver Transplant Service

Princess Alexandra Hospital

Ipswich Road

WOOLLOONGABBA QLD 4102

and

The Royal Children's Hospital

Bowen Bridge Road

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

Sir Charles Gardiner Hospital

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	
α -1 Antitrypsin deficiency	36	48	84
Crigler-Najjar	9	1	10
Familial amyloid polyneuropathy	0	31	31
Glycogen storage disease	2	3	5
Haemochromatosis	3	28	31
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**	18	4	22
Wilsonts disease	8	28	36
Total	103	156	259

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

** *OTC deficiency 13*
Citrullinemia 4
Argininosuccinic aciduria 4
Carbamyl phosphate synthetase deficiency

Appendix III

ANZLTR PRIMARY Diagnosis - Other by Age Group

Primary Diagnosis	Age group		Total
	Child	Adult	
Alagille syndrome	24	6	30
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	19	22
Choledocal cyst	2	2	4
Cholestatic disease-Other	1	7	8
Chronic Budd Chiari	1	30	31
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	7	7
Non alcoholic fatty liver (NAFLD or NASH)	0	81	81
Polycystic Liver disease	0	19	19
Polycystic liver and kidney disease	0	9	9
Progressive familial intrahepatic cholestasis(PFIC)	20	5	25
Secondary biliary cirrhosis	2	12	14
Secondary biliary cirrhosis - Hepatolithiasis	0	4	4
Secondary biliary cirrhosis - Cystic fibrosis	11	17	28
Other - specify [#]	8	22	30
Total	83	254	337

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
Cornelia De Lange Syndrome
Hepatic Lymphangiomatosis

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 - α -1 -AAT	2	0	2
Acute Autoimmune hepatitis	0	6	6
Acute Unknown / unspecified	43	89	132
Acute - Paracetamol	3	15	18
Acute - Other drugs	3	21	24
Acute Herbs / mushrooms	0	6	6
Acute - Hepatitis A	0	3	3
Acute - Hepatitis B	0	56	56
Acute - Non A-E	6	15	21
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	14	15
Subacute - Drug / Herbs	1	10	11
Subacute - Unknown / unspecified	5	31	36
Subacute - Hepatitis A	0	2	2
Subacute - Hepatitis B	0	16	16
Subacute - NonA - NonB	0	1	1
Total	75	311	386

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	3	-	3
Primary non function	4	17	21
Massive haemorrhagic necrosis	4	0	4
Recurrent disease (<i>ALD, PSC, CAH:AI</i>)	-	17	17
De novo Hep C	-	2	2
Biliary Complications	3	11	14
Other (<i>PNC, immune hepatitis, outflow obstruction</i>)	7	8	15
TOTAL	28	69	97

<u>Miscellaneous</u>	Children	Adult	
Multiorgan failure	5	48	53
Renal Failure	1	29	30
Graft vs Host disease	-	7	7
Social (<i>accident, suicide, non-compliance, Rx withdrawn</i>)	1	14	15
Sudden death (<i>cause unknown</i>)	1	23	24
Other (<i>Hyperkalaemia, motor neurone disease, diabetes complications, drug reaction, progression FAP, essential thrombocythemia</i>)	2	20	22
TOTAL	10	141	151