

AUSTRALIA & NEW ZEALAND

LIVER TRANSPLANT REGISTRY



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

DATA TO 31-12-2009

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STATISTICAL METHODS

Kaplan-Meier survival curves have been produced using SPSS® for Windows™ Release 18.0, SPSS Inc.

ACKNOWLEDGMENT

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

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Preface

We are pleased to present the 21st Report of the Australia and New Zealand Liver Transplant Registry (ANZLTR). This report contains data to the 31st December 2009 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 who are 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, for her continuing contribution to the maintenance of the Cancer Registry which is based at the Royal Prince Alfred Hospital, Sydney and who, together with Dr Deborah Verran, prepares 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 2009, 3533 orthotopic liver transplants (OLT) were performed in Australia and New Zealand on 3277 patients, 2692 adult patients (> 15 years) [82%] and 585 children [18%]. The median age of all recipients was 46.8 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=63%)
6. Fewer new patients were transplanted in 2009 compared with 2008 with 211 new patients.
7. The trend to increasing age of adult recipients in recent years continued and the overall adult median age is now 49.65 years. The median age of new adult recipients in 2005-08 was 52.2 years.
- 8-9. In 2009, one less transplant was performed then in 2008 [228 vs 229]. Split grafts continue to make a significant contribution to the total number of paediatric transplants performed providing 14 of 39 [36%] grafts in 2009 and 142 of 668 [21%] overall. In children, other reduced size grafts have been used in 319 [48%] cases including 39 living donor grafts. One child has been treated with liver cell implantation. Of adult patients, 190 have received reduced size grafts - 154 split liver grafts (including 1 as auxiliary graft), 26 other reduced size grafts (1 as auxiliary graft) and 10 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 21% 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). The number of patients transplanted for non alcoholic fatty liver disease [NAFLD/NASH] continued to increase with 8 new patients transplanted in 2009 bringing the total to 47 (Appendix III).
- 12-14. While the total number of adult patients transplanted with a primary diagnosis of chronic viral Hepatitis B, C or B/C/D remained static in 2005-09 compared with the previous era [35% primary diagnosis CVH], the number with a primary diagnosis of CVH : Hepatitis C increased [25% Hepatitis C, 8% Hepatitis B and 2% Hepatitis B,C,D in 2000-04 ; 28% Hep C, 5% Hep B, 2% Hep B/C/D in 2005-09]. 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 2009 was 50%.
15. Overall 1 year patient survival of all patients is 88% at 1 year, 80% at 5 years and 71.5% at 10 years. Children had a significantly better survival rate than adults.
16. Whilst older children had superior early survival than infants and babies, older adult recipients (60-65 and >65 years) had poorer longer term outcomes.
- 17-18. Patient survival in 2000-04 cohort shows continued improvement in outcome for the first 5 years compared with earlier cohorts. This is seen in both children and adults. Current 1year patient survival in 2005-09 cohort is 93% for all patients [94% for children, 93% for adults].
19. The type of primary graft, (whole , reduced or split liver), had no significant effect on patient survival in either children or adults.
20. Children weighing < 8 kg at the time of transplant had inferior early survival compared to heavier patients.

Summary

21. Adult patients transplanted for biliary atresia or hepatitis virus co-infections had the best long 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.
22. 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 5 year survival of 71%.
23. Recent cohorts of adult patients with a primary diagnosis of hepatitis B show a significantly improved survival which is not seen in adult patients with hepatitis C as primary disease. Patients transplanted for malignancy continue to have a poor outcome.
24. Graft survival was significantly worse in second and third grafts.
25. Overall split liver grafts have only a slightly lower graft survival then whole liver grafts. Reduced grafts have lower survival in the early post-transplant years in both children and adults.
26. Vascular complications and rejection were the commonest indications for retransplantation. Eleven percent of retransplants were due to poor early graft function. Recurrent disease was the indication for retransplantation in 12% of cases [6% PSC, PBC and 6% HBV, HCV].
- 27-28. Overall, sepsis is the most frequent cause of death. Full details of Miscellaneous and Other Graft Failure deaths are listed in Appendix V. Thirty-eight 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.
29. While there was an increase in the number of cadaveric donors in 2009, fewer grafts were transplanted from deceased donors. The number of livers split to produce two transplantable grafts reduced for 16 in 2008 to 14 in 2009. Five liver grafts donated after cardiac death were transplanted. The number of people on the waiting list at 31 December 2009 remained similar to the number on the waiting list at 31 December 2008.
30. Donor age has increased significantly in recent years. Long term graft survival trends lower in several donor age groups but not for those aged over 60 years.
31. Fifty patients [39 children, 11 adults] have now received a living donor graft with 10 performed in 2009. Forty-six were transplanted as a primary graft, 3 as second and 1 as a third graft. The median age of the donors was 35.4 years with a range of 22.8 to 54.5 years. One adult graft was a domino graft.
32. The numbers of patients waiting for transplant decreased slightly with 164 patients awaiting a transplant at 31 December 2009 compared with 2008. Patient delistings due to death, becoming too ill or tumour (HCC) progression were 12%. Thirty-eight patients were listed as urgent in 2009 [17 Category 1 and 21 Category 2]. In 2009 65% of patients listed urgently as Category 1 had a positive outcome compared with 90% listed as Category 2.
- 33-34. Median waiting times tended to be lower in 2009 in some blood groups. Blood group O patients tend to have the longest waiting times.

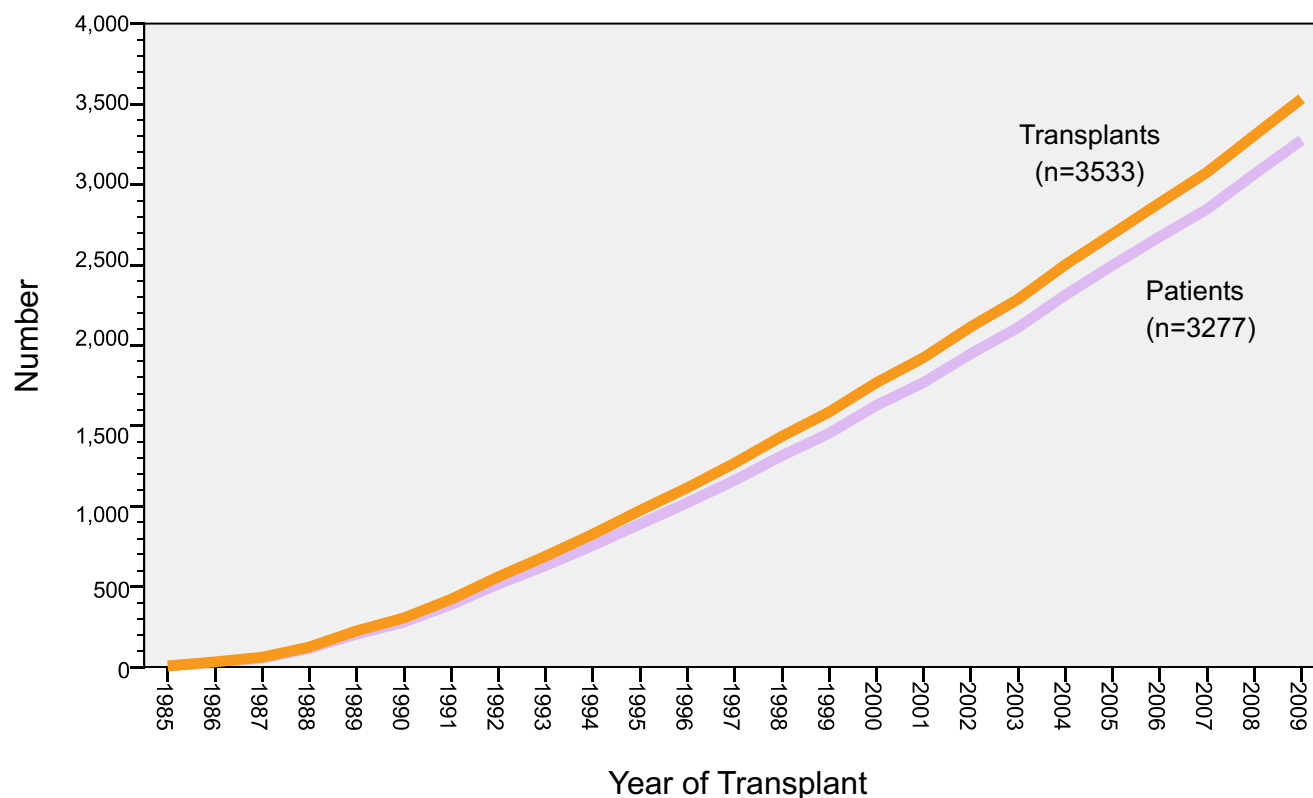
Summary

35. Cancer in liver transplant recipients was analysed from two perspectives:
1. Those who had a liver cancer at the time of transplantation (primary, secondary or incidental) Of 3277 patients who have undergone liver transplantation, 557 (17%) had a liver cancer at transplantation. Three hundred and sixty six (11%) patients had liver cancer as an incidental (Secondary) diagnosis.
 2. Those who developed a cancer post transplantation (de novo skin and de novo non skin cancer) 603 (19%) patients developed either non skin or skin cancer (de novo) post transplant. One hundred and fortyfive (4%) of all patients developed multiple cancer types, 2 patients developed cancers transferred from their donor and 10 patients developed a non skin cancer < 90 days post transplant.
- A flow diagram of cancer in liver transplantation is shown in Appendix VI
- One hundred and ninety three (6%) patients were transplanted for liver malignancy (Primary), 180 (93%) were adults and 13 (7%) children. 34 adults (19%) and 3 (23%) children died from their malignancy.
- 36-37. Longer term survival of patients with primary liver cancers is significantly poorer for patients with cholangiocarcinoma. There has been a marked increase in the number of patients being transplanted for primary malignancy in the patient cohort 2004-09.
- 38-40 Three hundred and sixty six (11%) patients had liver cancer as an incidental (Secondary) diagnosis with hepatocellular carcinoma the most common. Of these 43 (12%) died from their malignancy. Those with cholangiocarcinoma had significantly poorer survival.
- 40-41 Patient survival was significantly worse in the 557(17%) patients with pre transplant liver malignancy compared with patients with benign liver disease. The number of patients with liver malignancy at transplant has continued to increase over the last decade.
- 42 Two hundred and nine (6%) patients developed two hundred and twenty-three non skin cancers. Eighty nine (40%) died from this cancer. Twelve patients (6%) had more than one de novo non skin cancer. Cancers of the alimentary tract 74 (33%) and lymphoma 62 (28%) predominate. Ten (2%) patients developed non skin malignancy within 90 days of transplantation. Thirty-one (6%) patients with liver malignancy at transplantation developed de novo cancer.
- 43 Patients with de novo non skin cancers have significantly worse long term survival. There were 44 lower GI cancers which account for 59% of the alimentary tract cancers.
- 44-45 The incidence of de novo non skin cancers varies according to pre transplant liver disease, with the incidence of Primary Sclerosing Cholangitis and de novo malignancy being statistically significant ($p < 0.0001$).
- 46 Four hundred and fourteen (13%) patients developed skin cancer, 186 (45%) having multiple skin cancer types and 21 (5%) developed melanoma.
- 47 The cumulative risk of diagnosis of any cancer at twenty years post transplant is 40%.

Section 1

Demographic Data

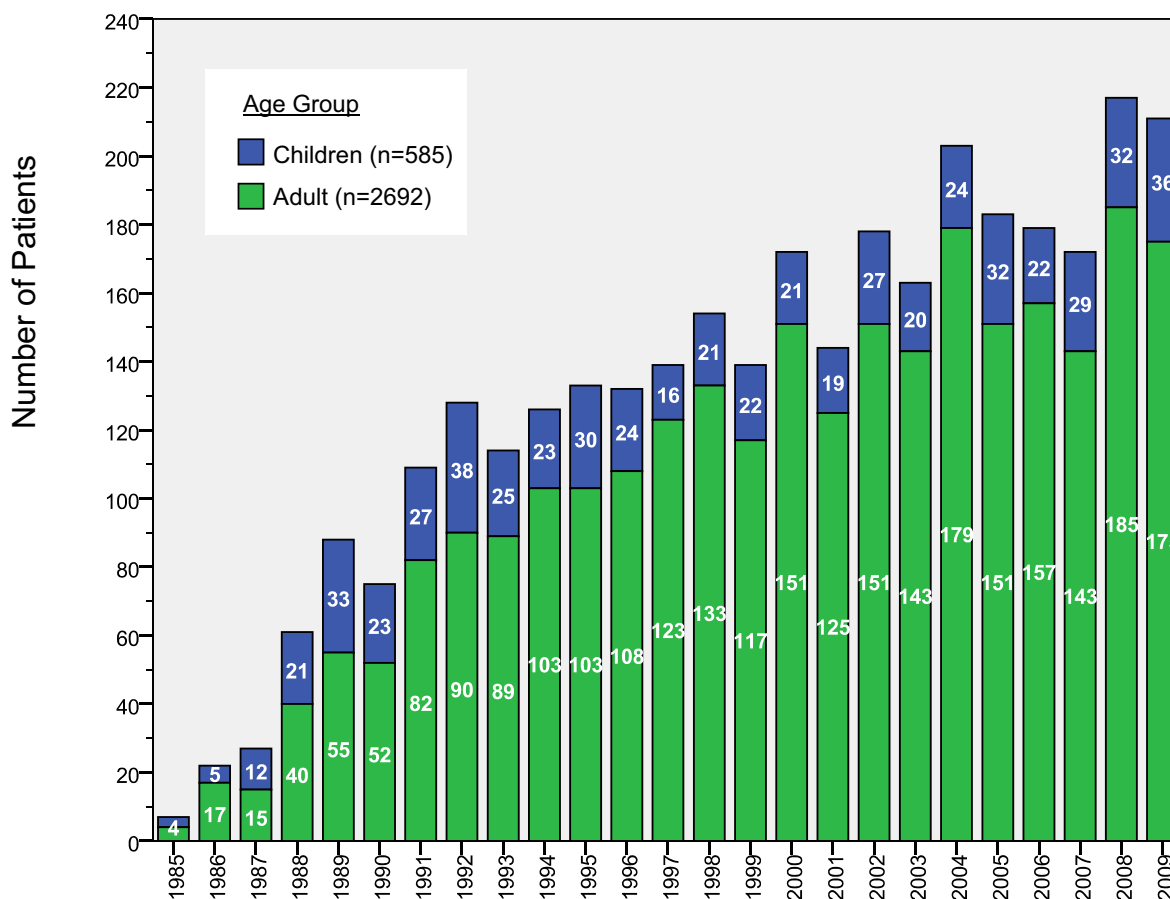




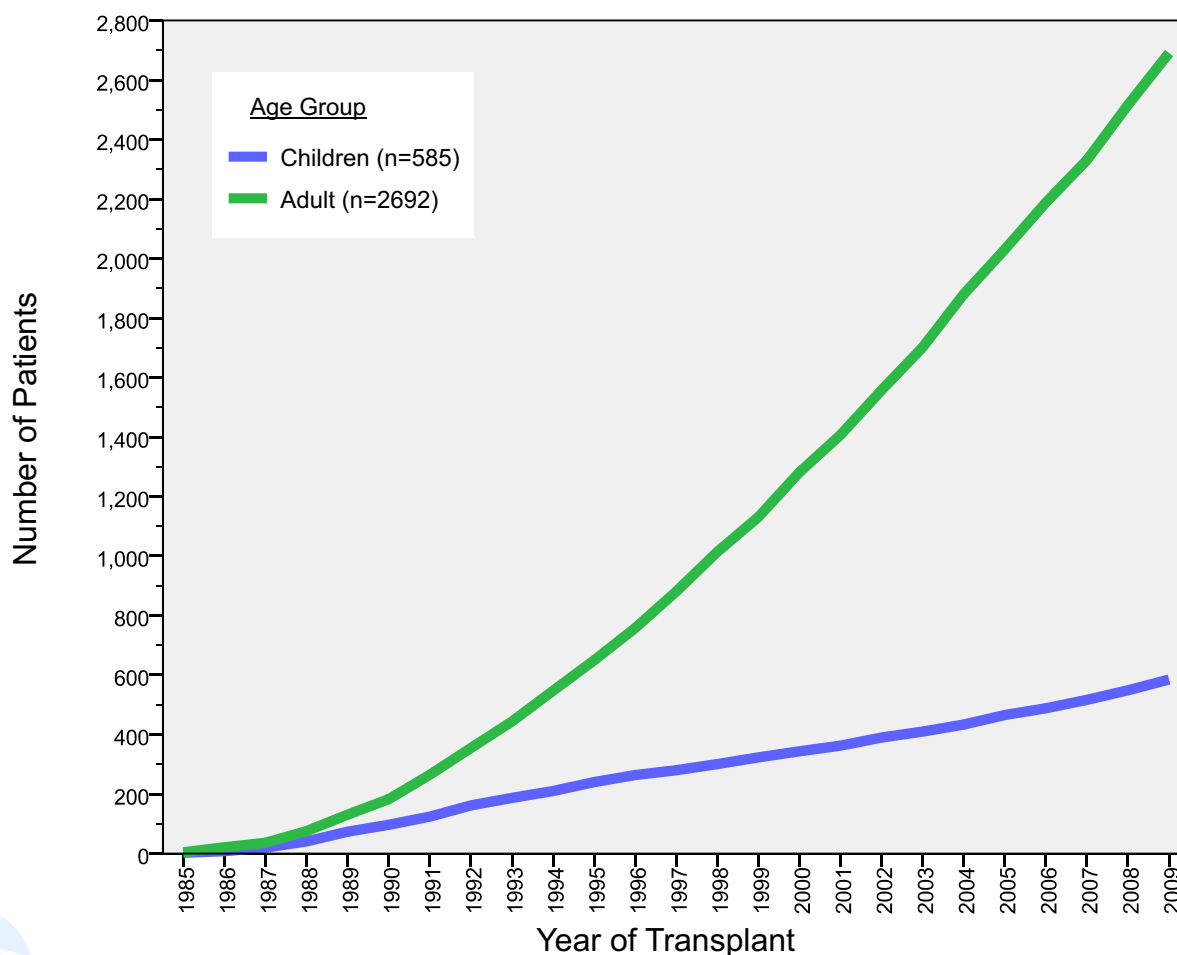
Summary Statistics - Age and Gender

ALL PATIENTS TRANSPLANTED

	Children [<15y]	Adults	Total
Patients	585	2692	3277
Age			
<i>Mean ± SD</i>	4.3 ± 4.2y	47.8 ± 11.7y	40.0 ± 19.8y
<i>Median</i>	2.4y	49.65y	46.8y
<i>Range</i>	24d -14.9y	15.0 - 73.1y	24d - 73.1y
Gender			
<i>Female</i>	310 (53%)	988 (37%)	1298 (40%)
<i>Male</i>	275 (47%)	1704 (63%)	1979 (60%)
Surviving	464 (79.5%)	1950 (72%)	2414 (74%)

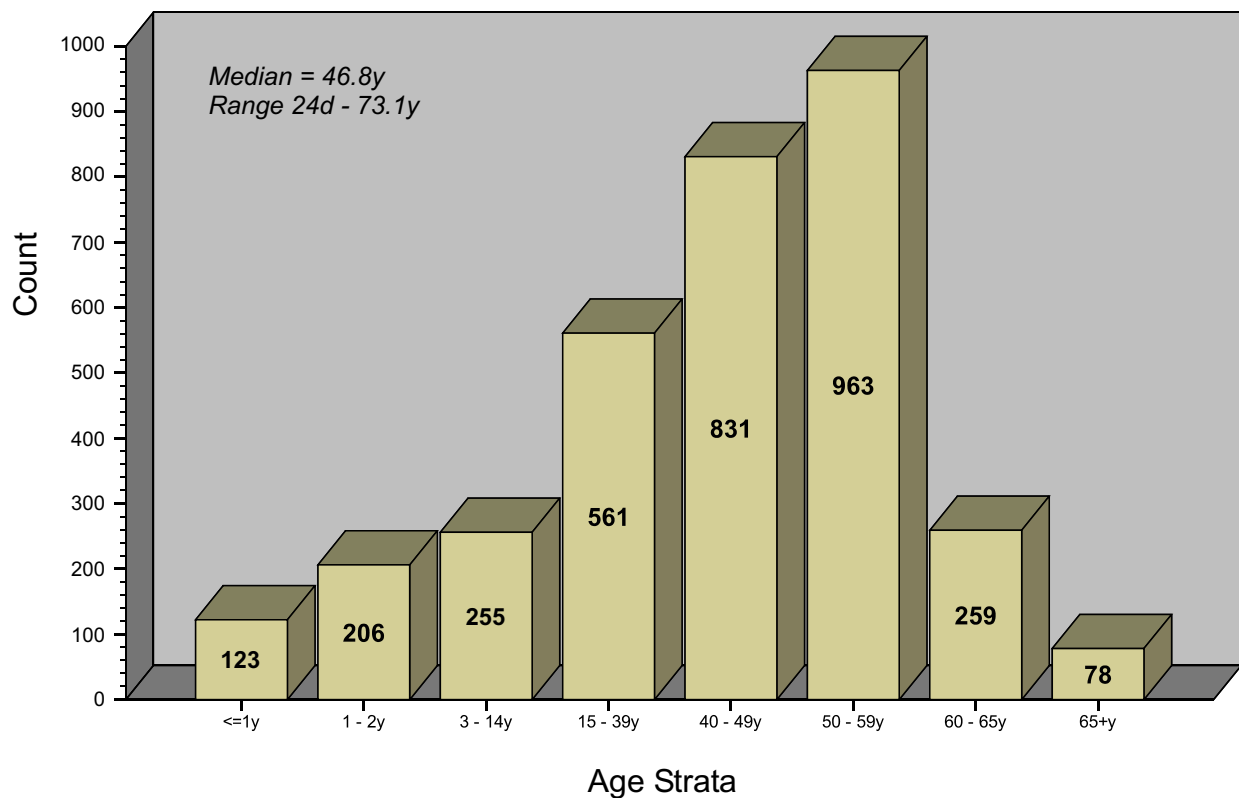


Cumulative Number of New Patients Transplanted

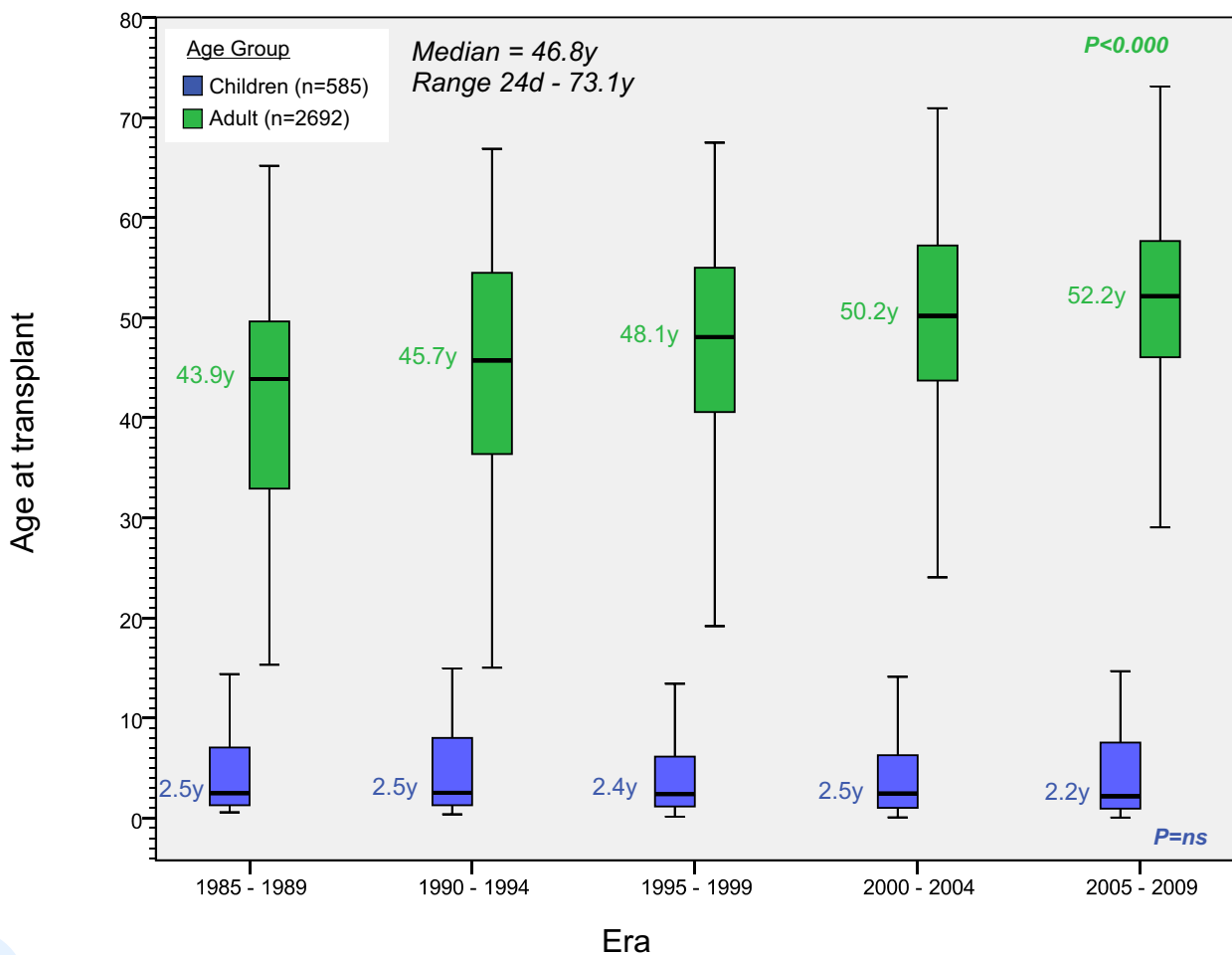


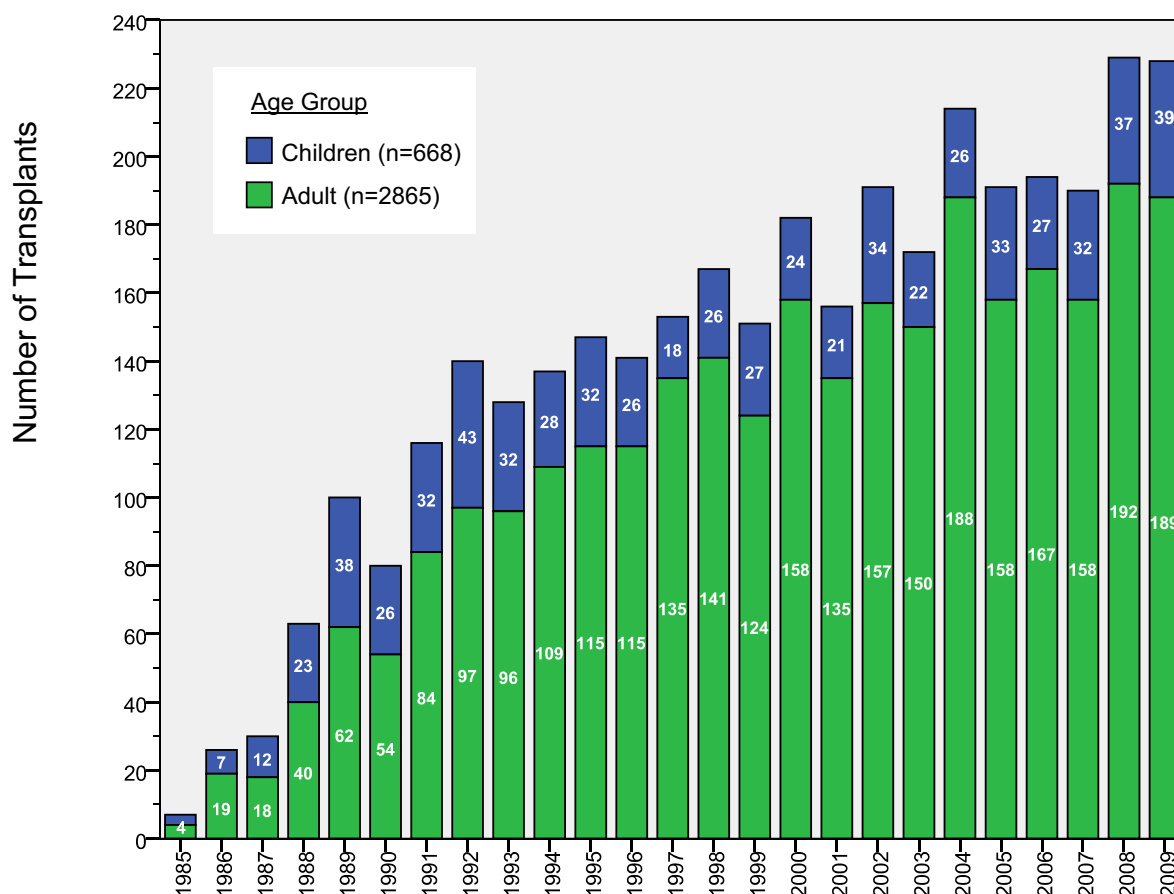
Number of Recipients By Age at Primary Transplant

N=3277

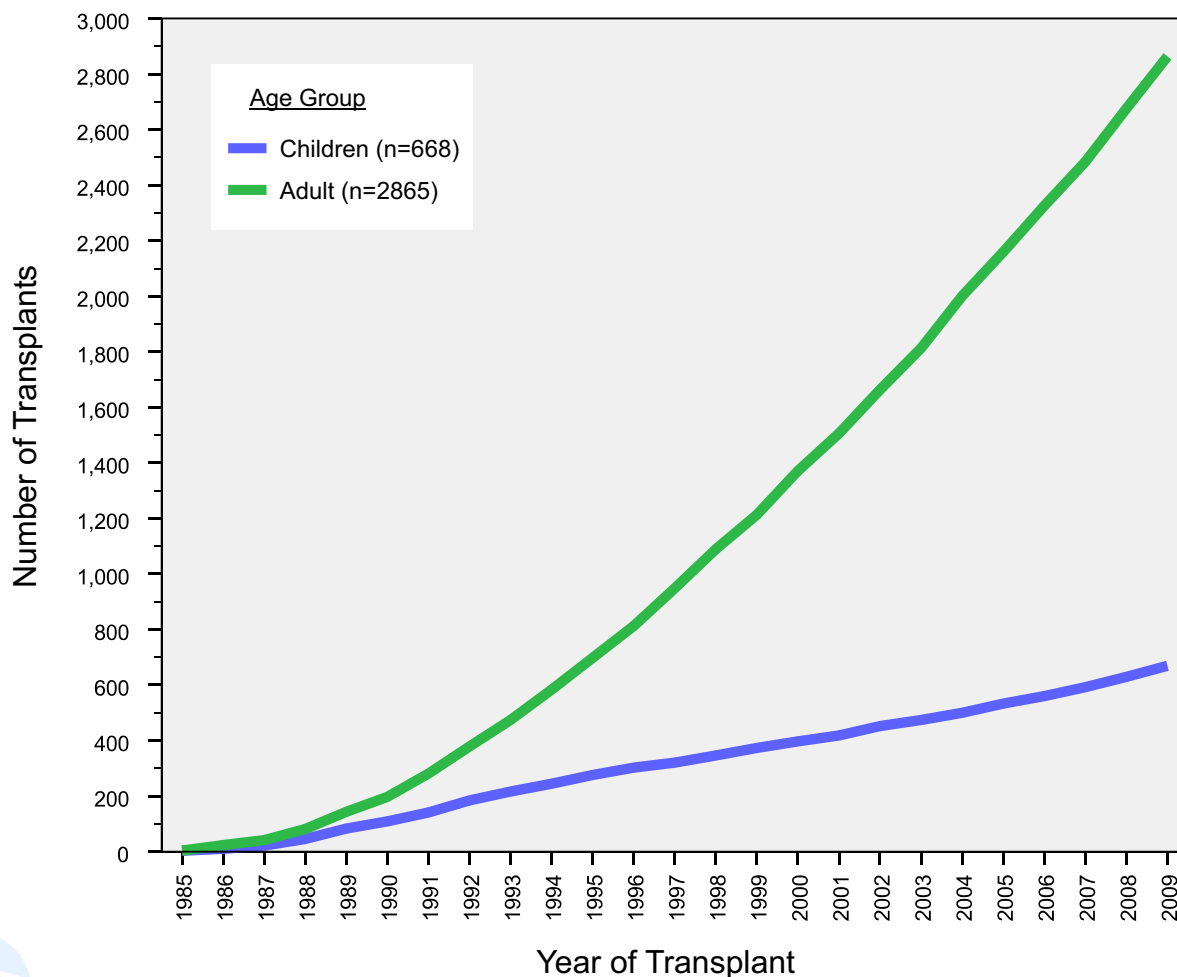


Age at Primary Transplant by Era



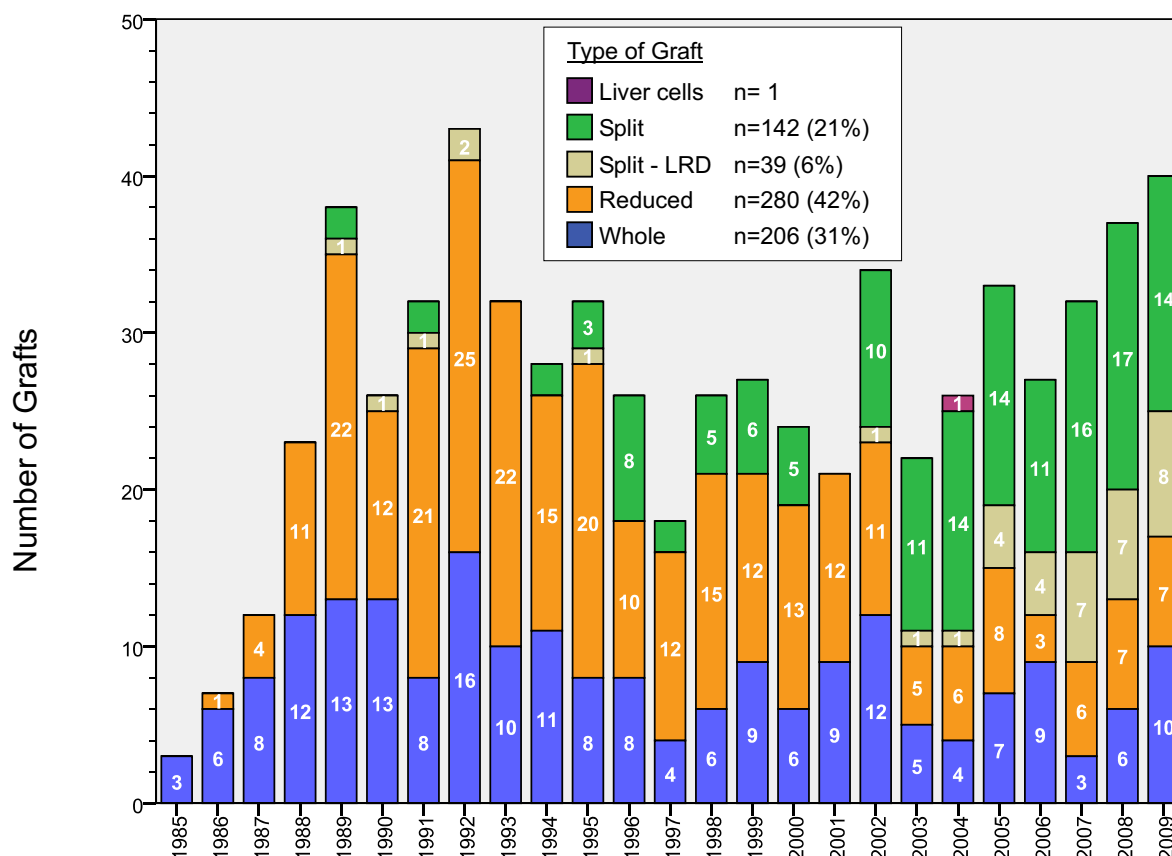


Cumulative Number of Transplants

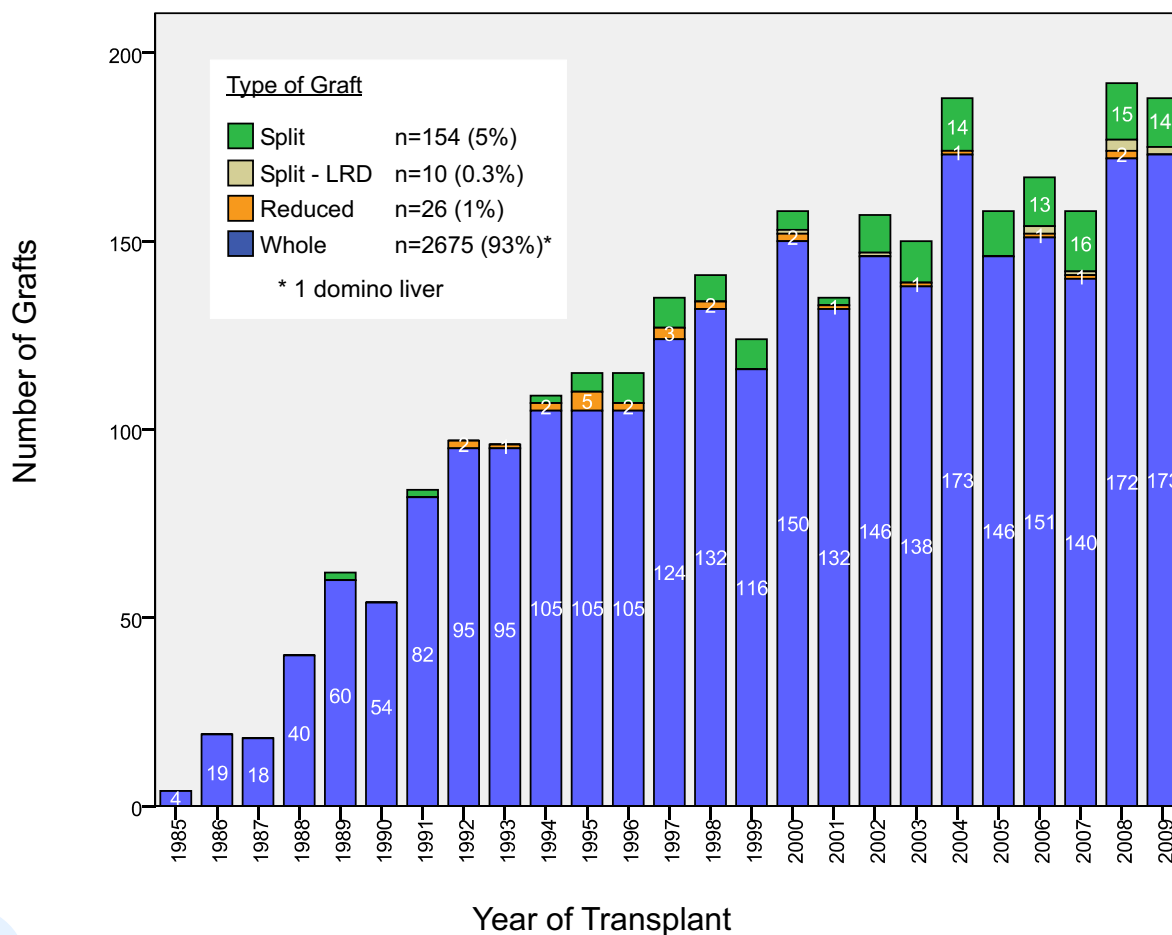


Type of Graft by Year Split vs Reduced vs Whole

Children (n = 668)



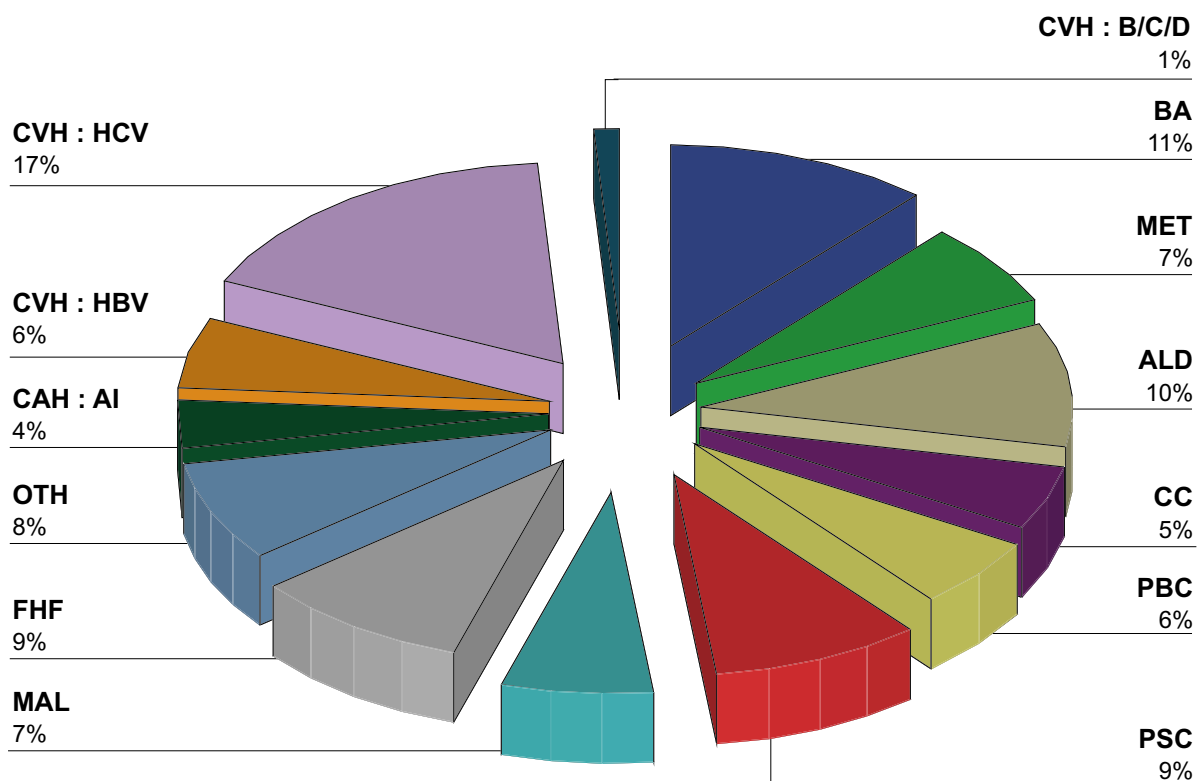
Adults (n = 2865)



Section 2

Primary Diagnosis





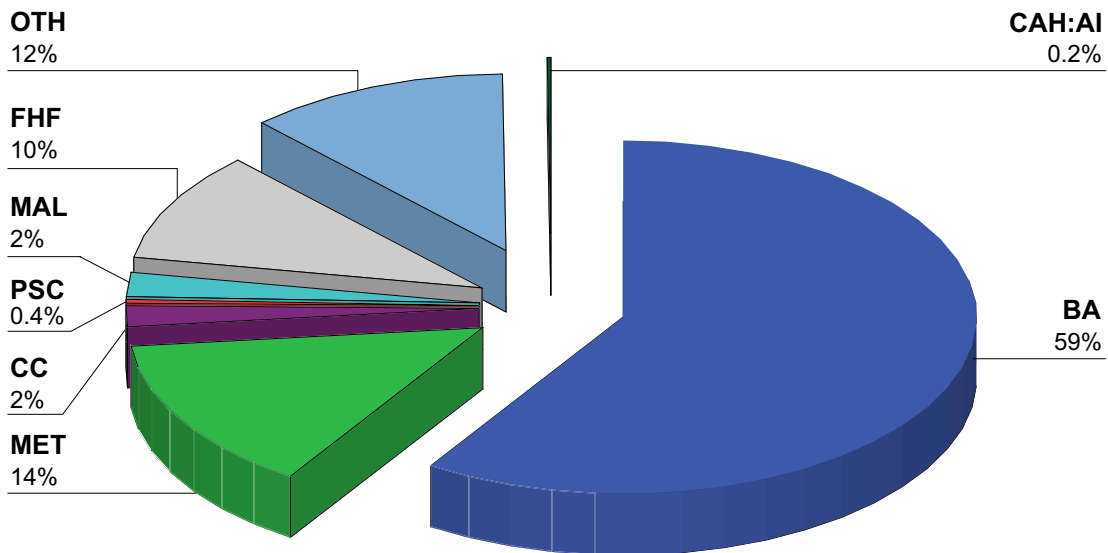
Diagnosis Group

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

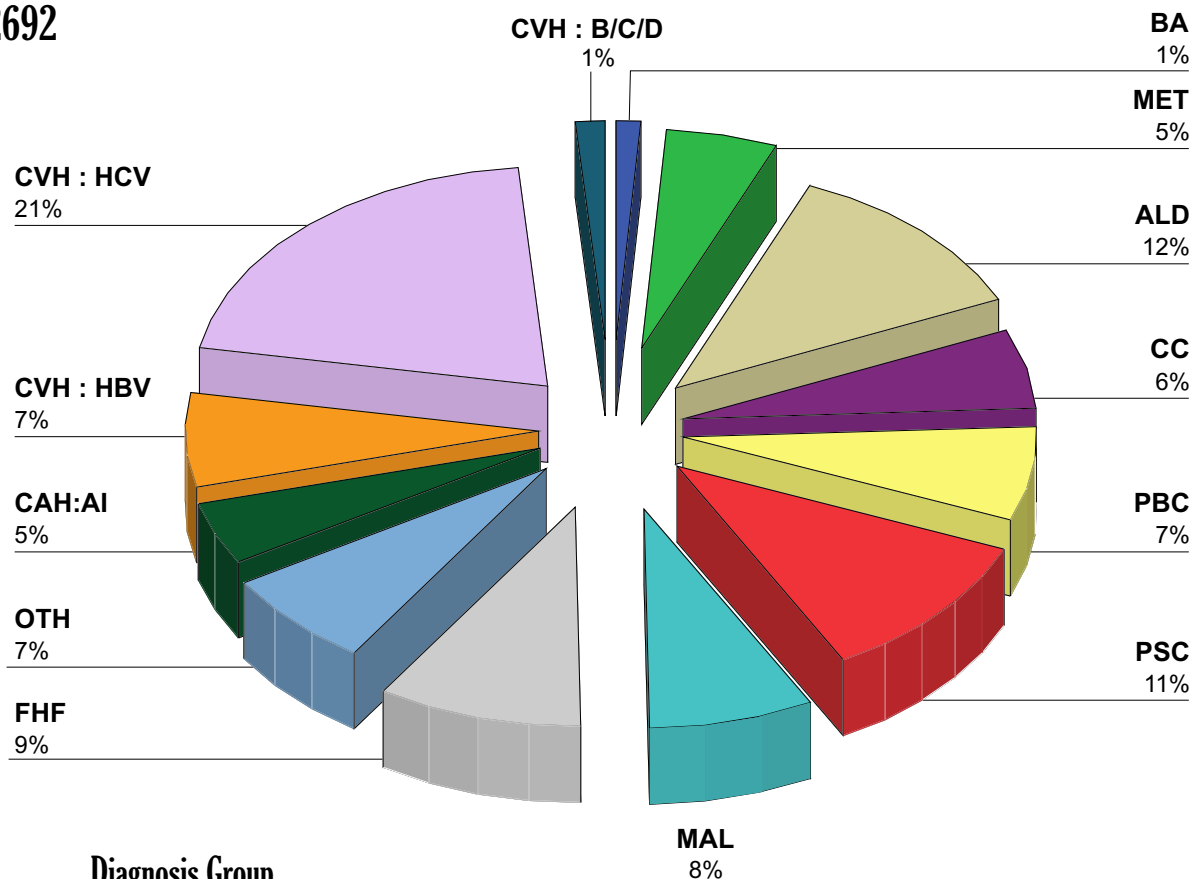
Primary Diseases of Children

n = 585



Primary Diseases of Adult Recipients

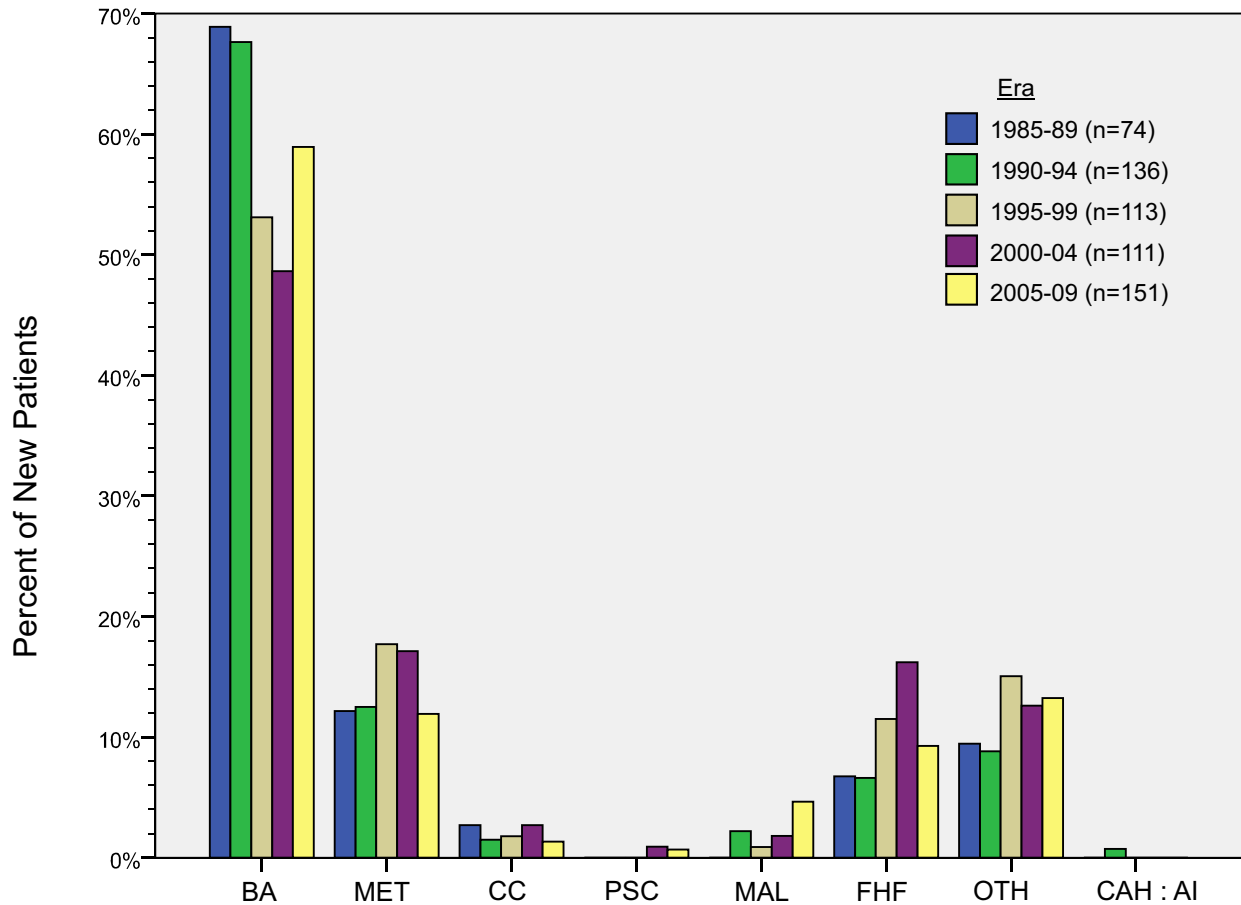
n = 2692



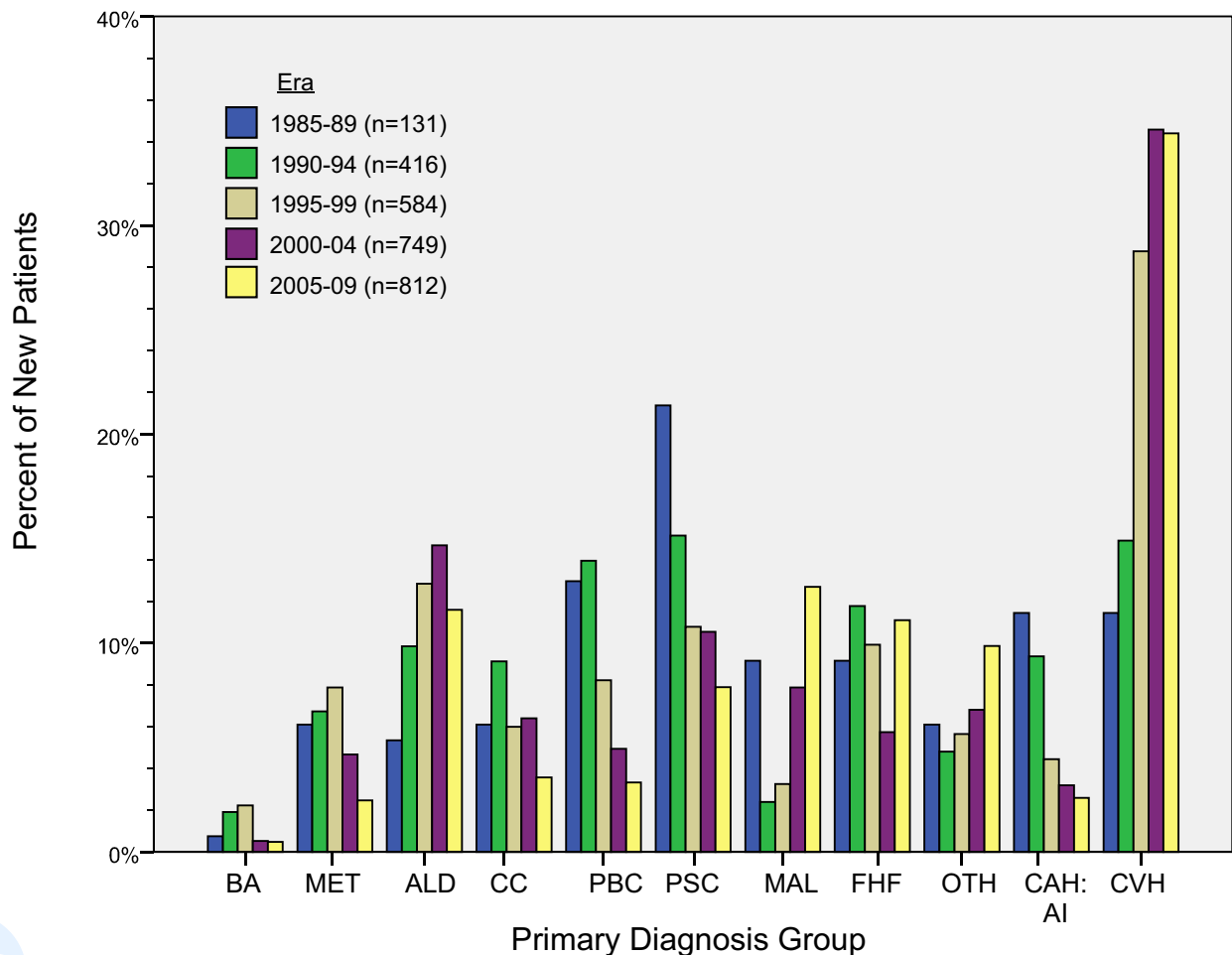
Diagnosis Group

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

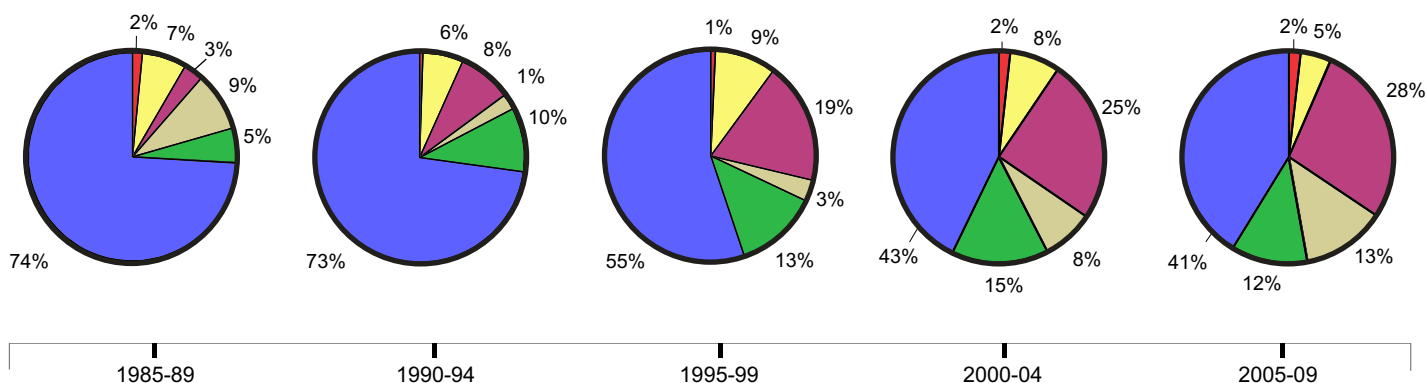
Children (n=585)



Adults (n = 2692)

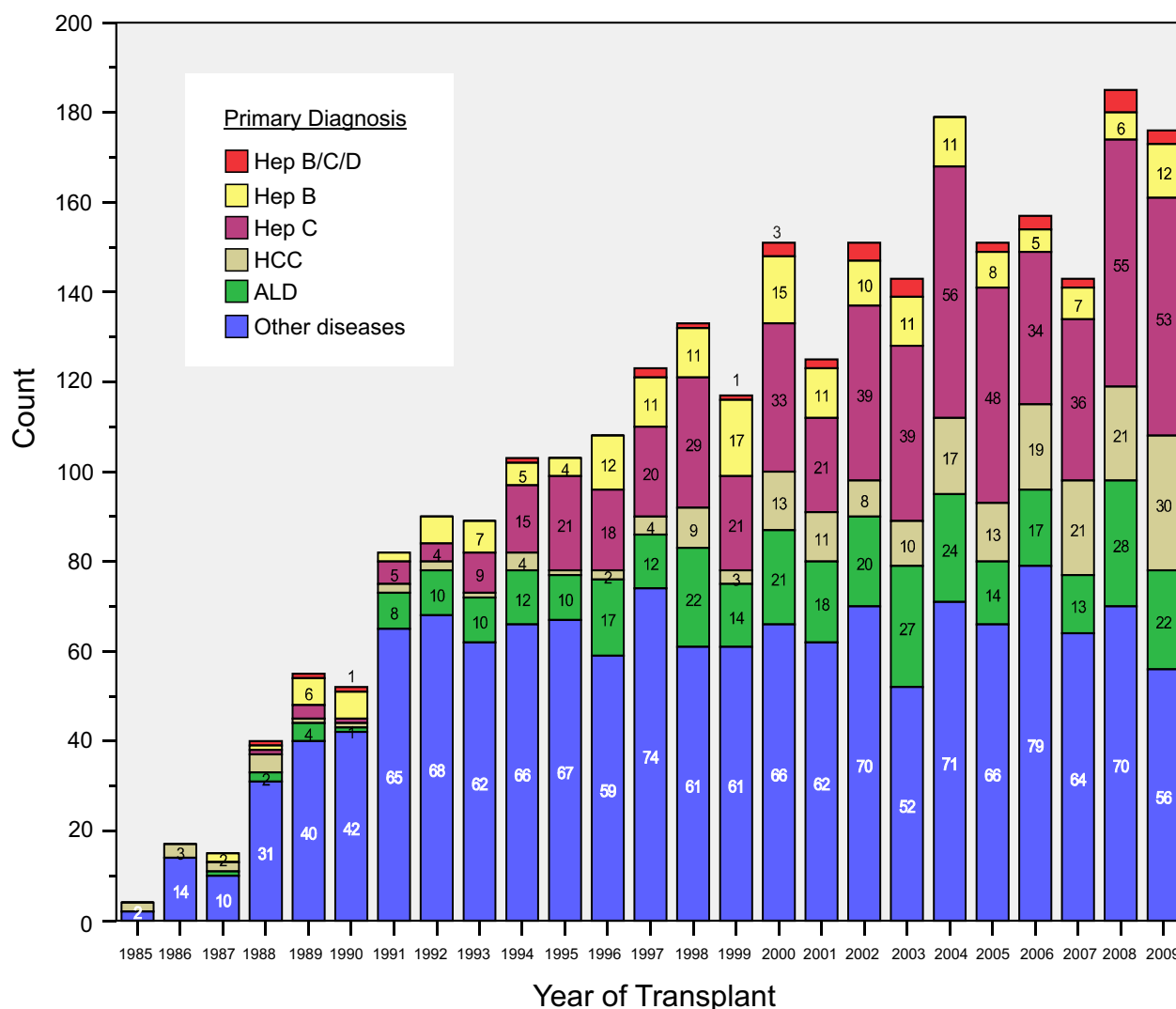


Adult Diagnosis



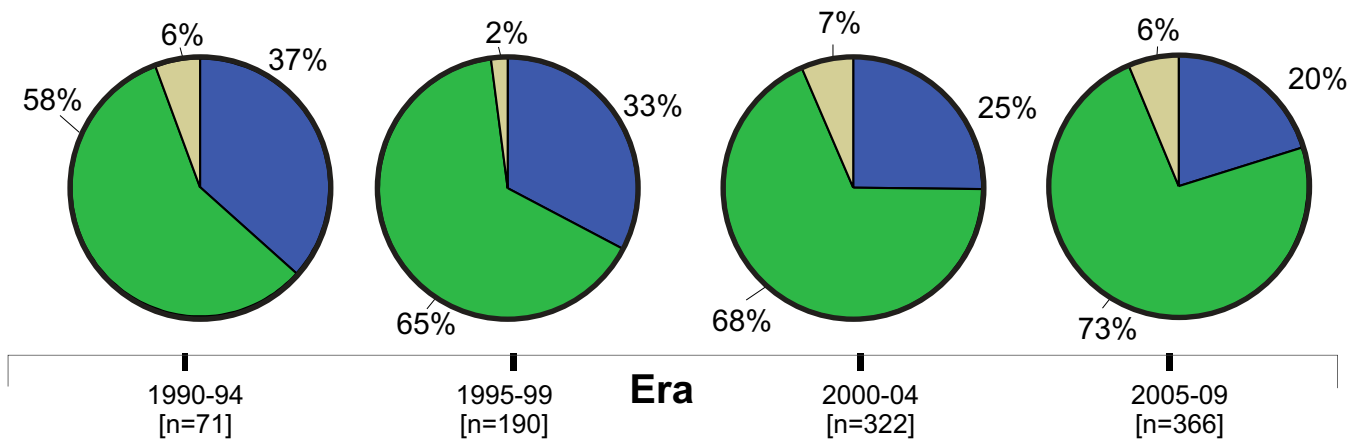
Era

Adult Primary Diagnosis by Year

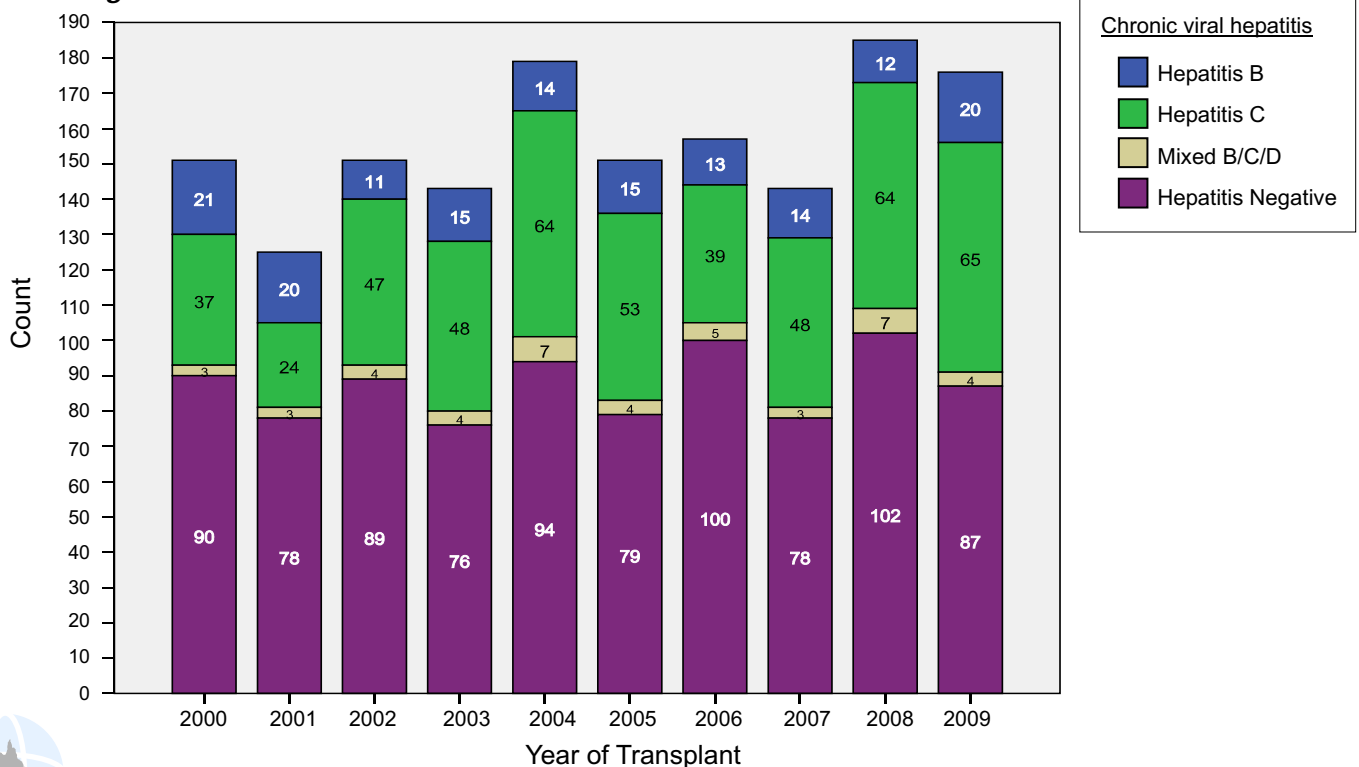


		n =	Secondary / Tertiary diagnosis				
			Hepatitis C	Hepatitis B	Hepatitis B,C	HCC	ALD
Primary Diagnosis	Hepatitis C	561		7		122	135
	Hepatitis B	186	4			60	4
	Hepatitis BD/BC/BCD	36				3	6
	HCC + cirrhosis	189	81	63	5		23
	ALD	327	12	3		35	
	Other	1393	13	8		43	19
	TOTAL	2692					

Type of Chronic Viral Hepatitis in Adult Patients



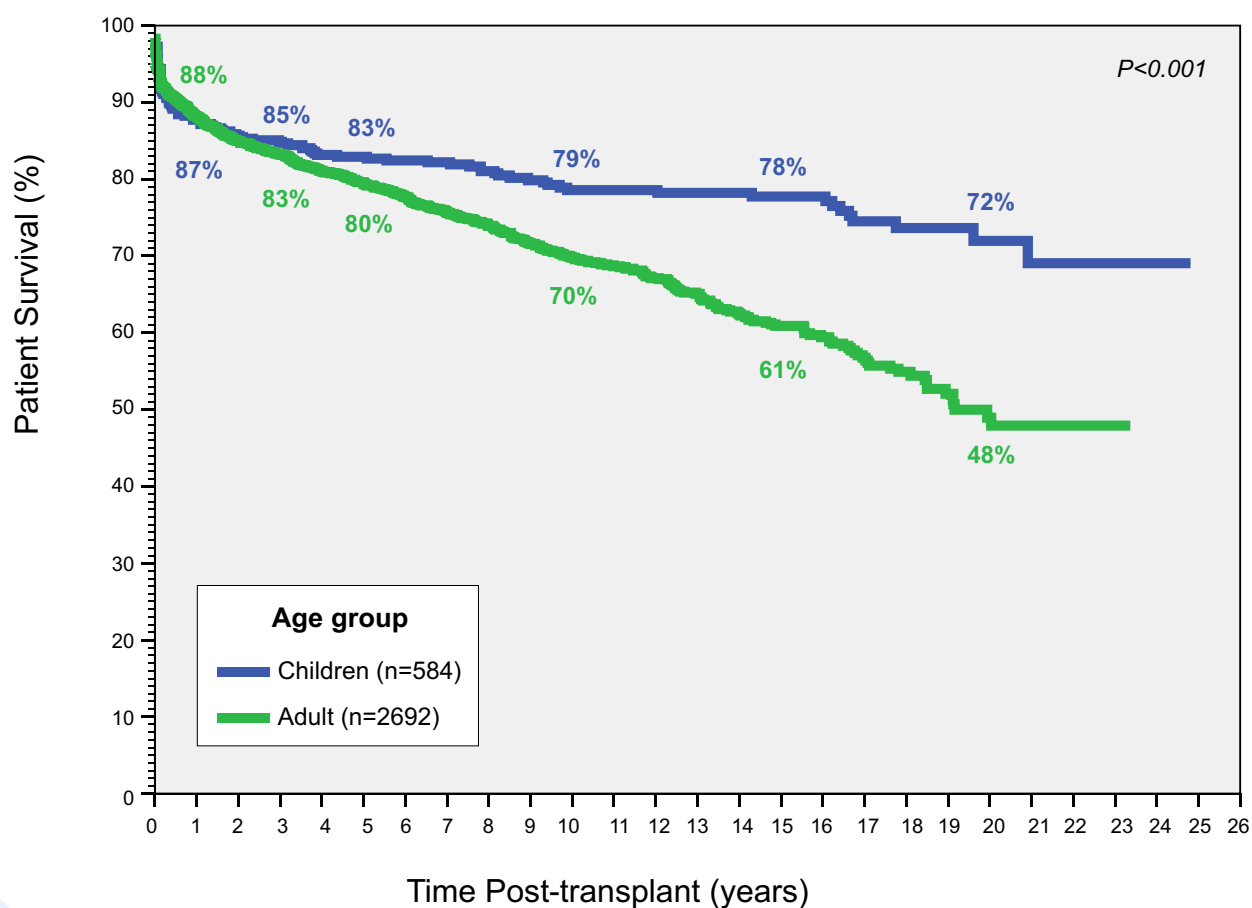
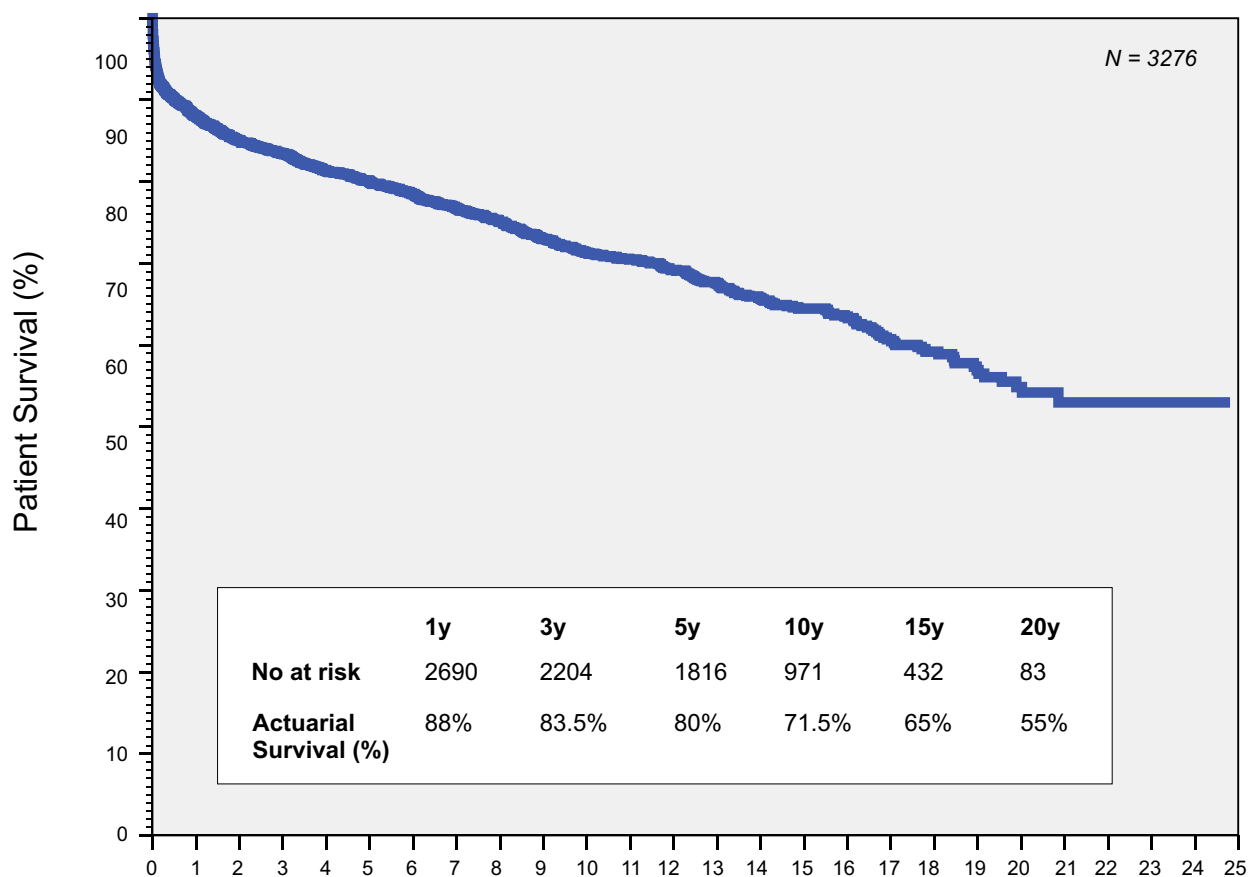
Hepatitis diagnosis

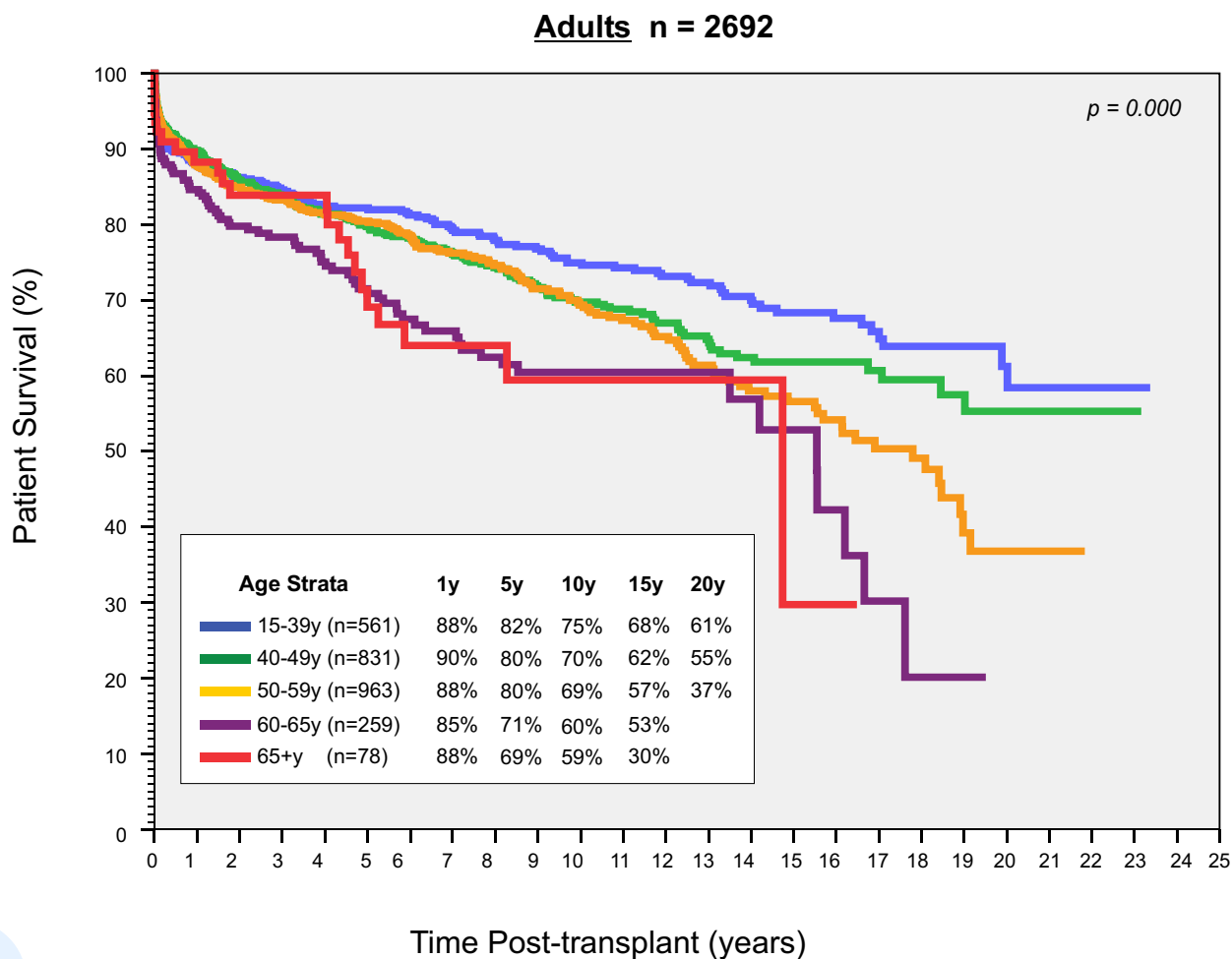
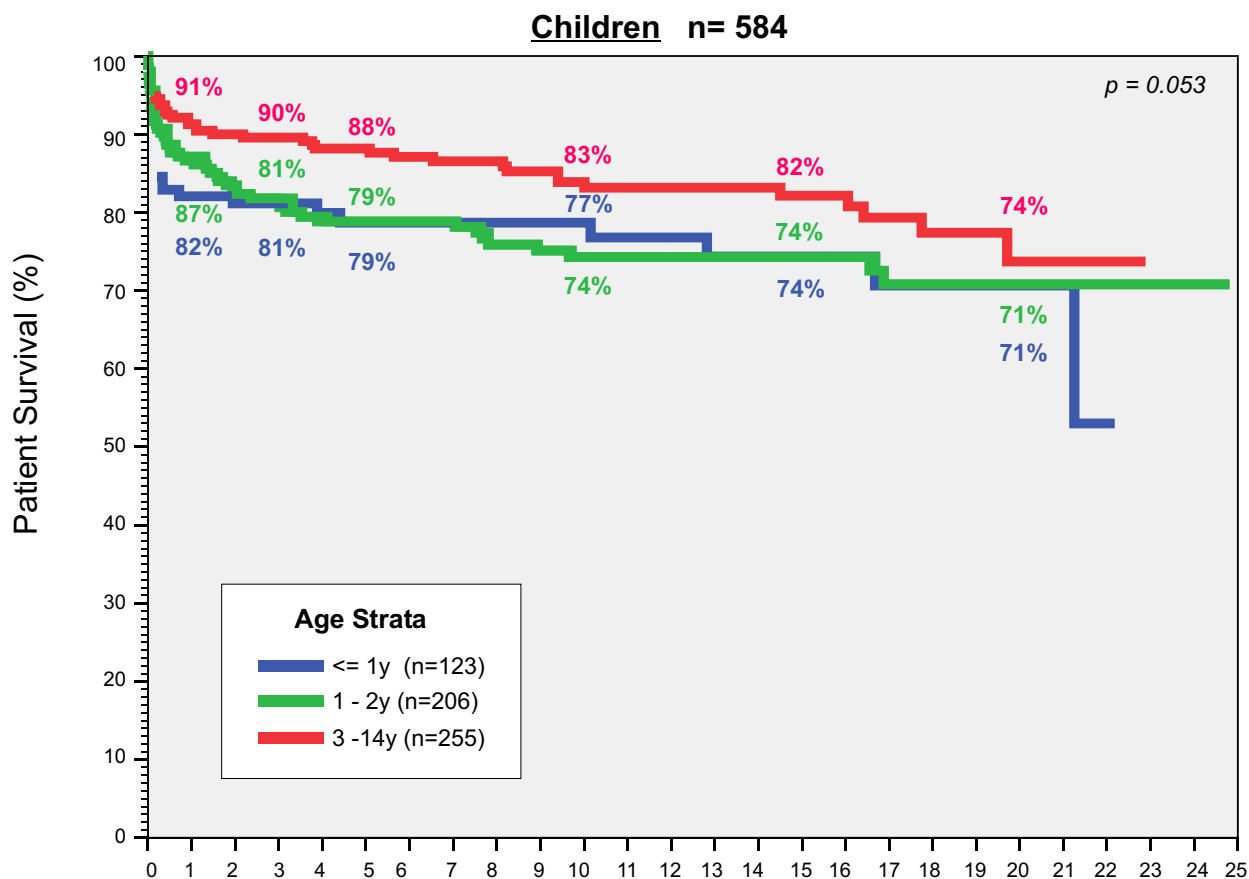


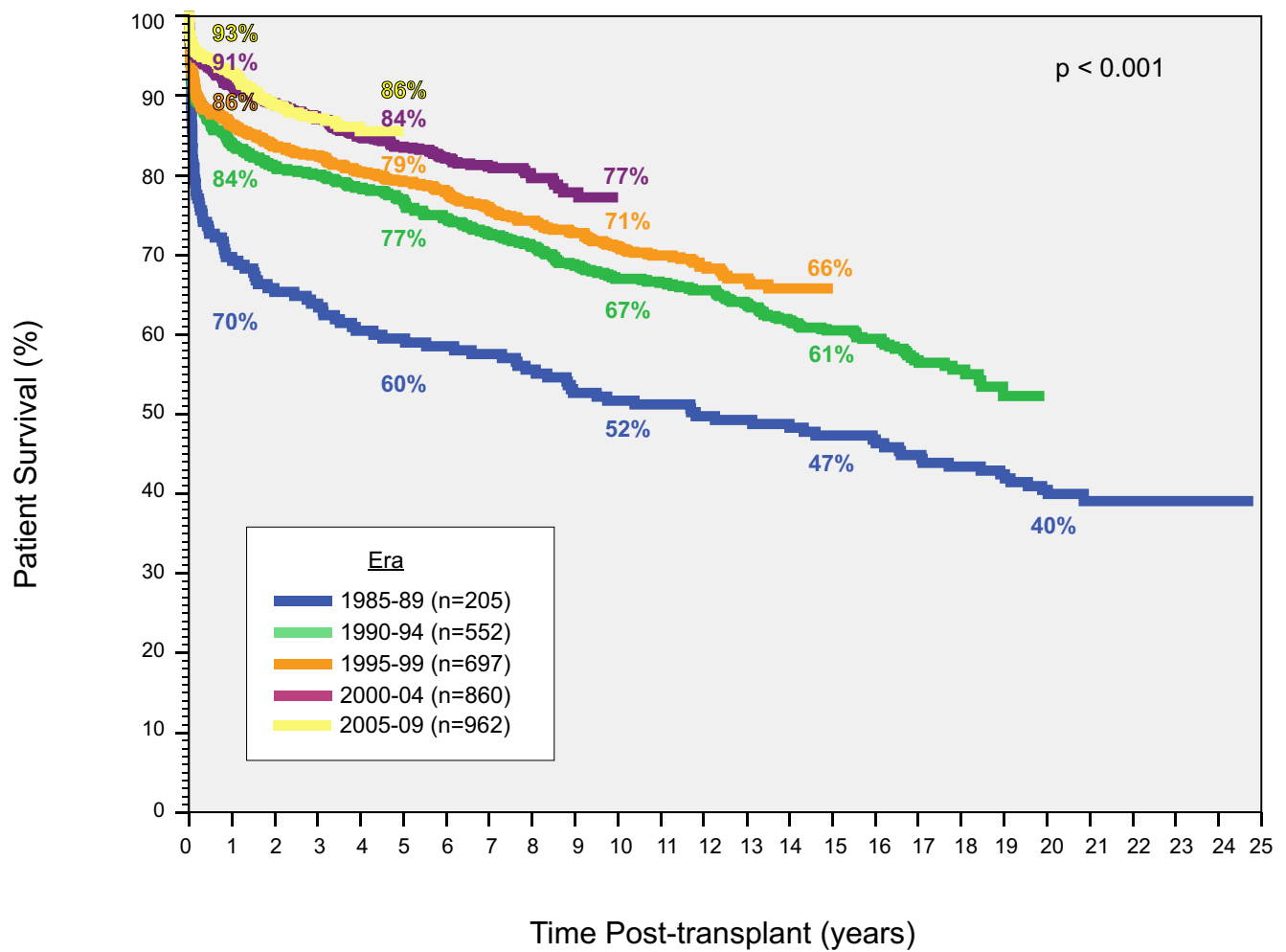
Section 3

Patient Survival

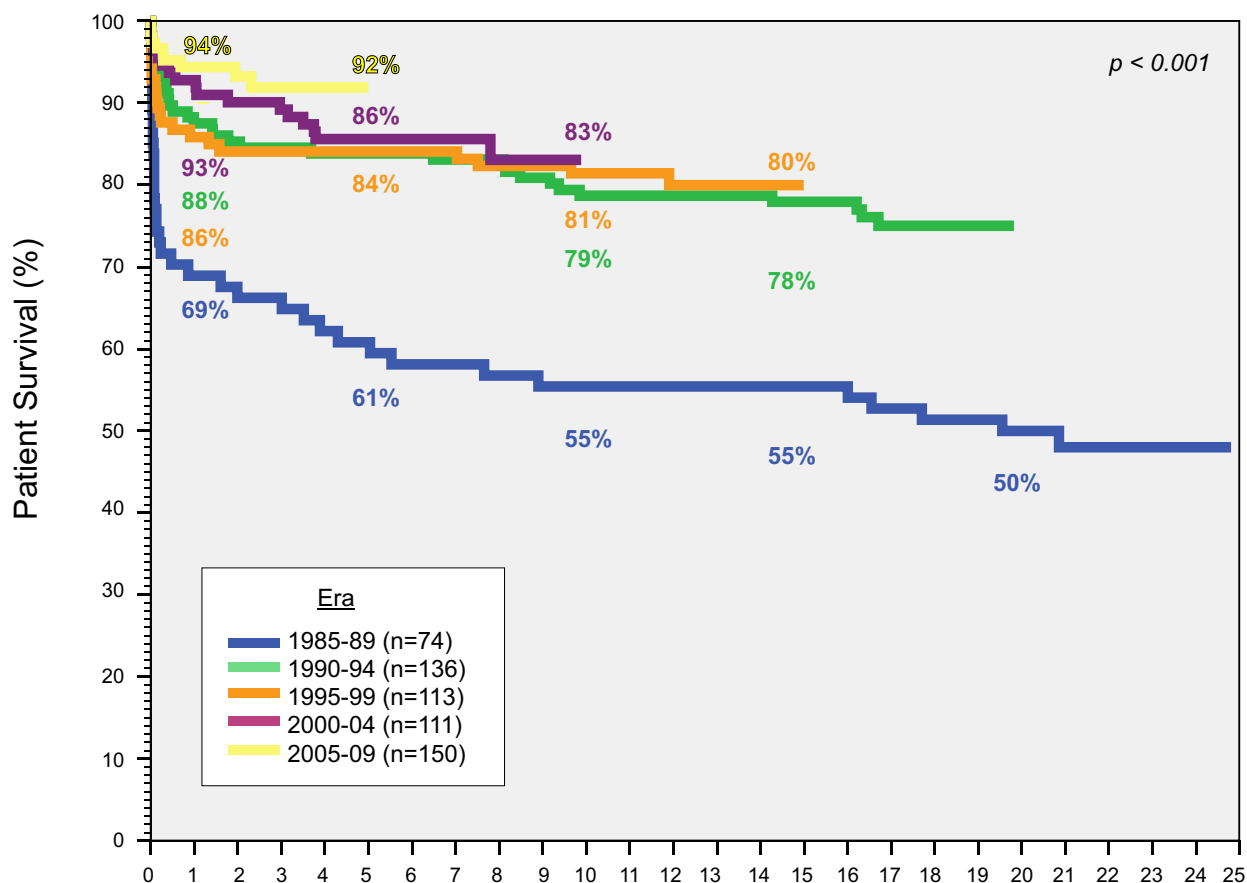






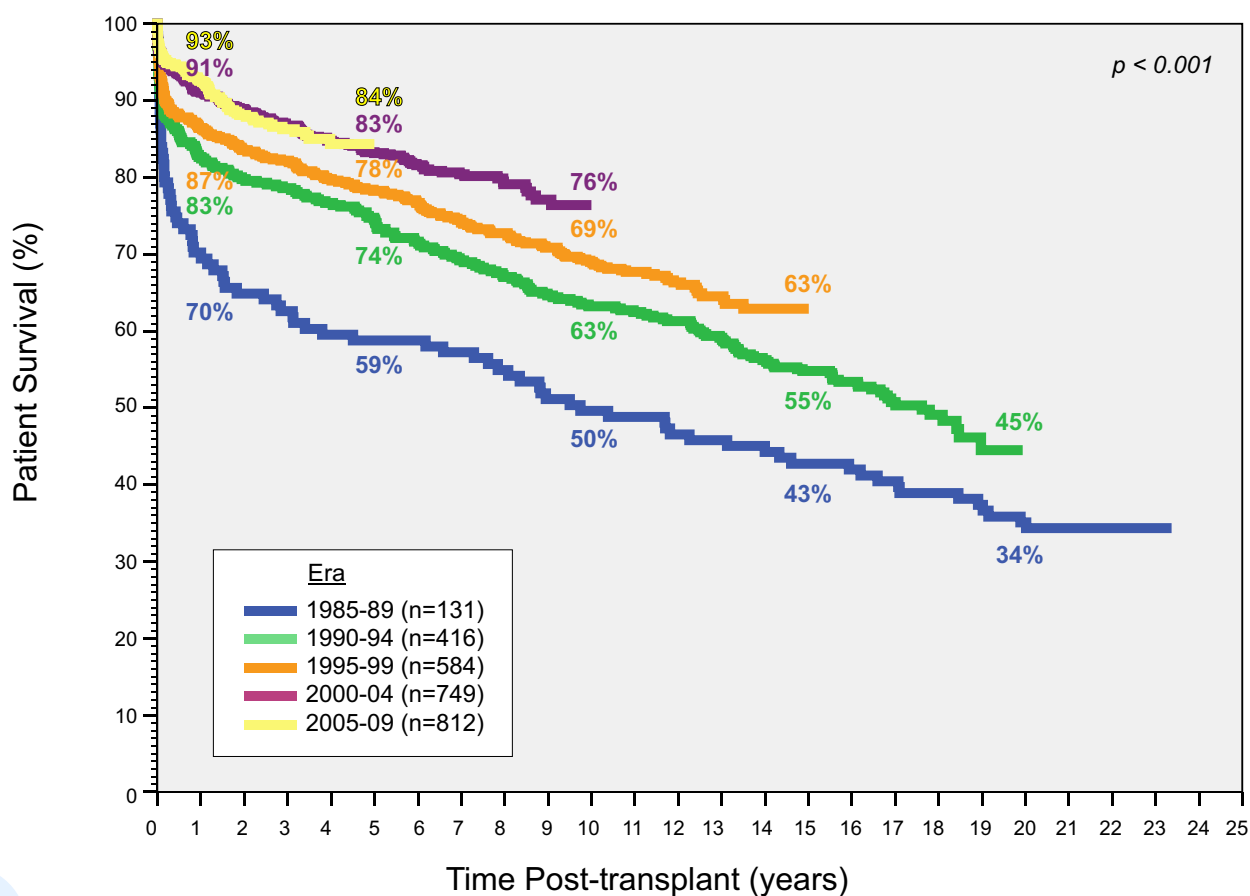


Children n=584



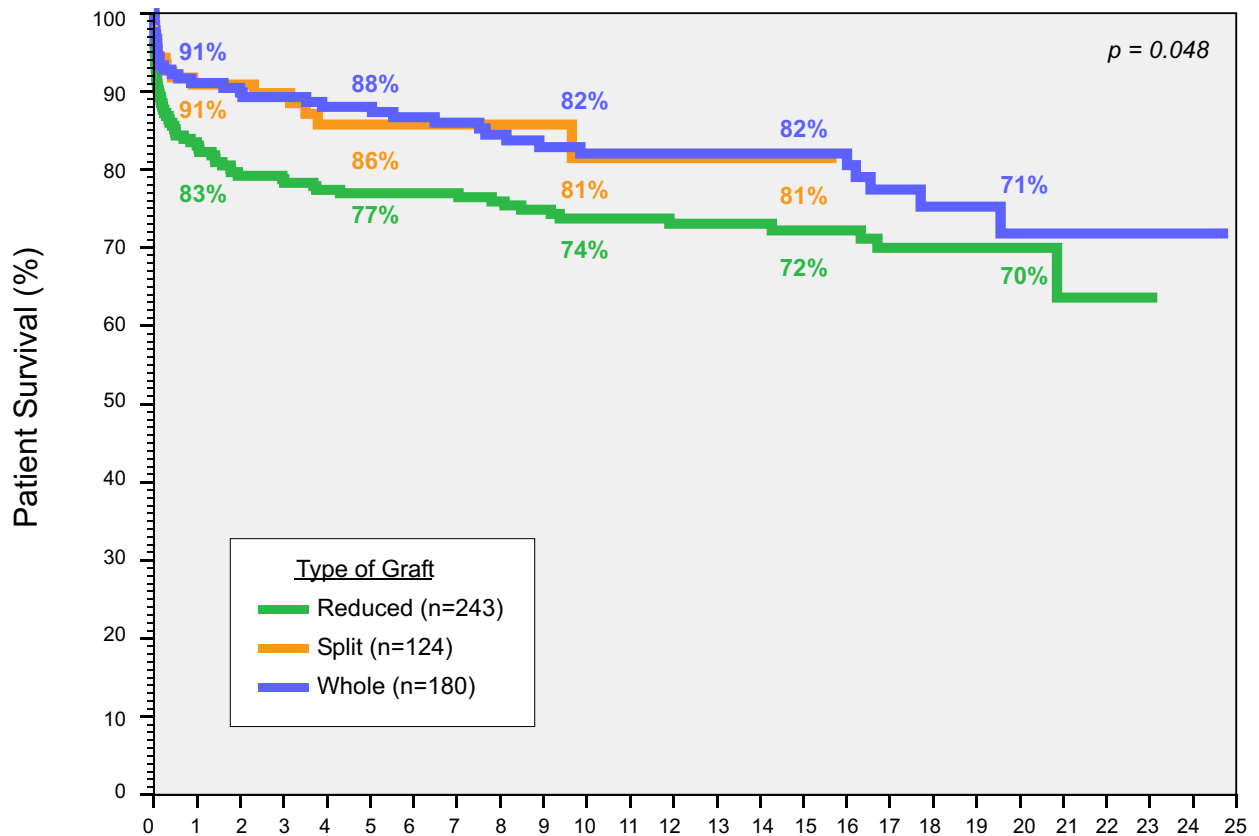
Patient Survival - Adults

Adults n = 2692

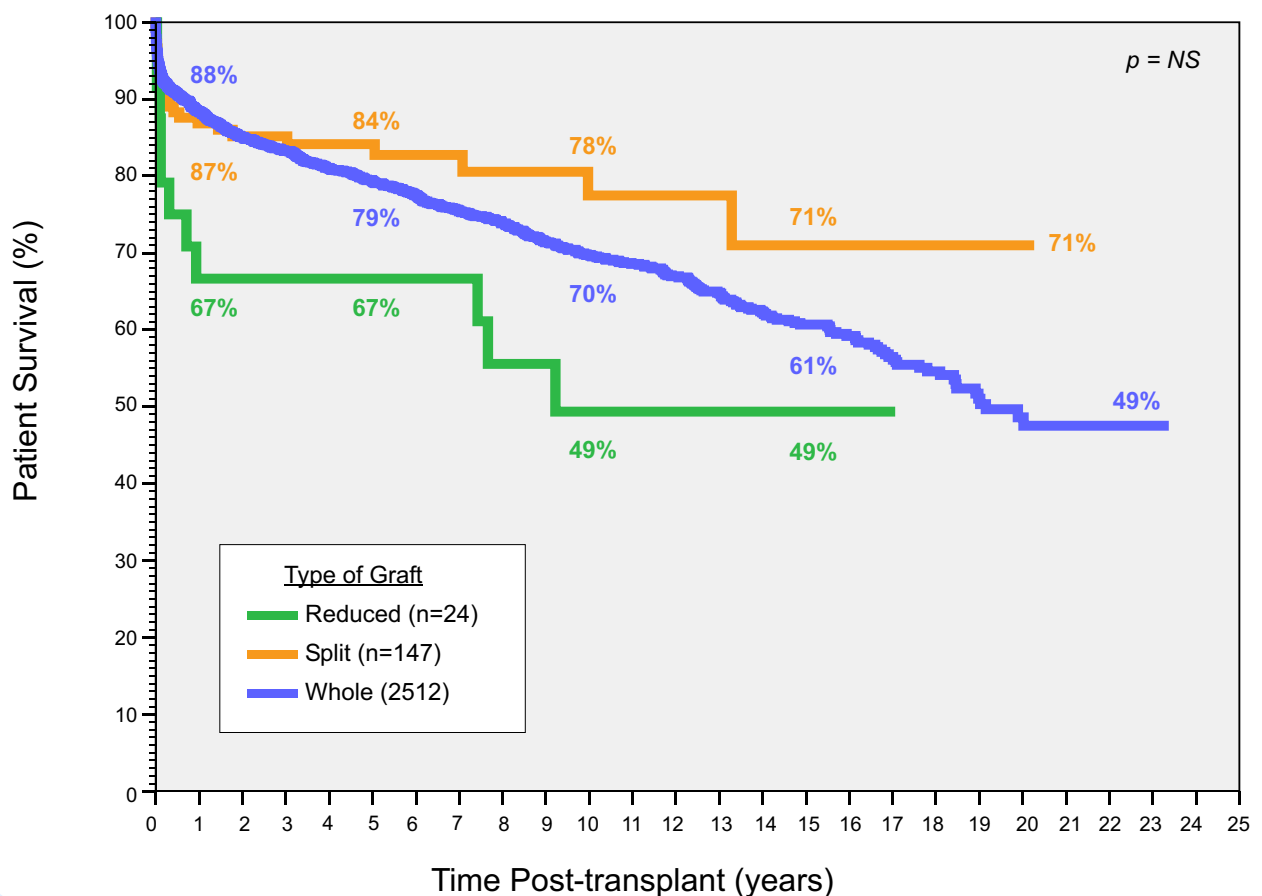


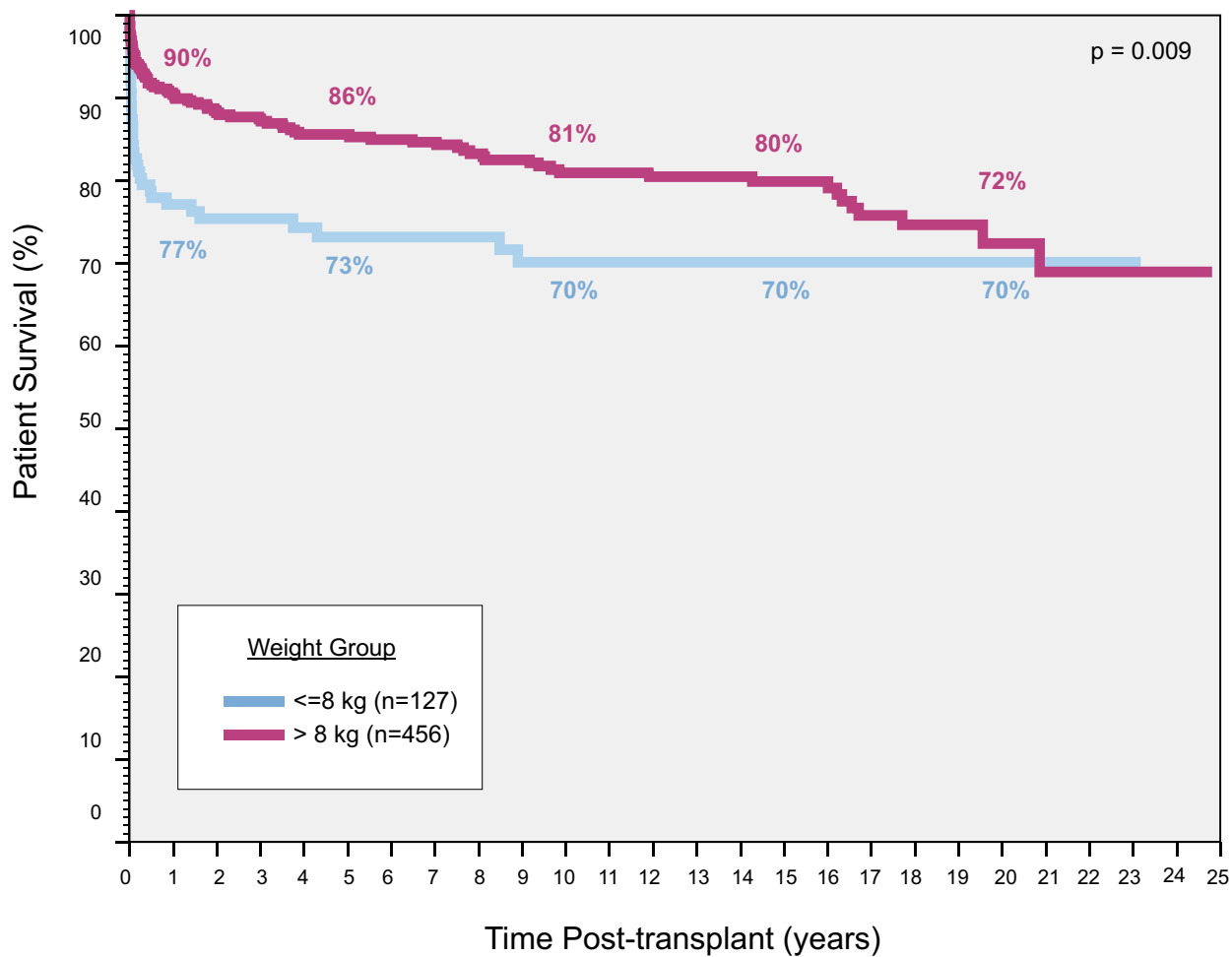
Patient Survival by Type of Primary Graft [Deceased donors]

Children - n = 547

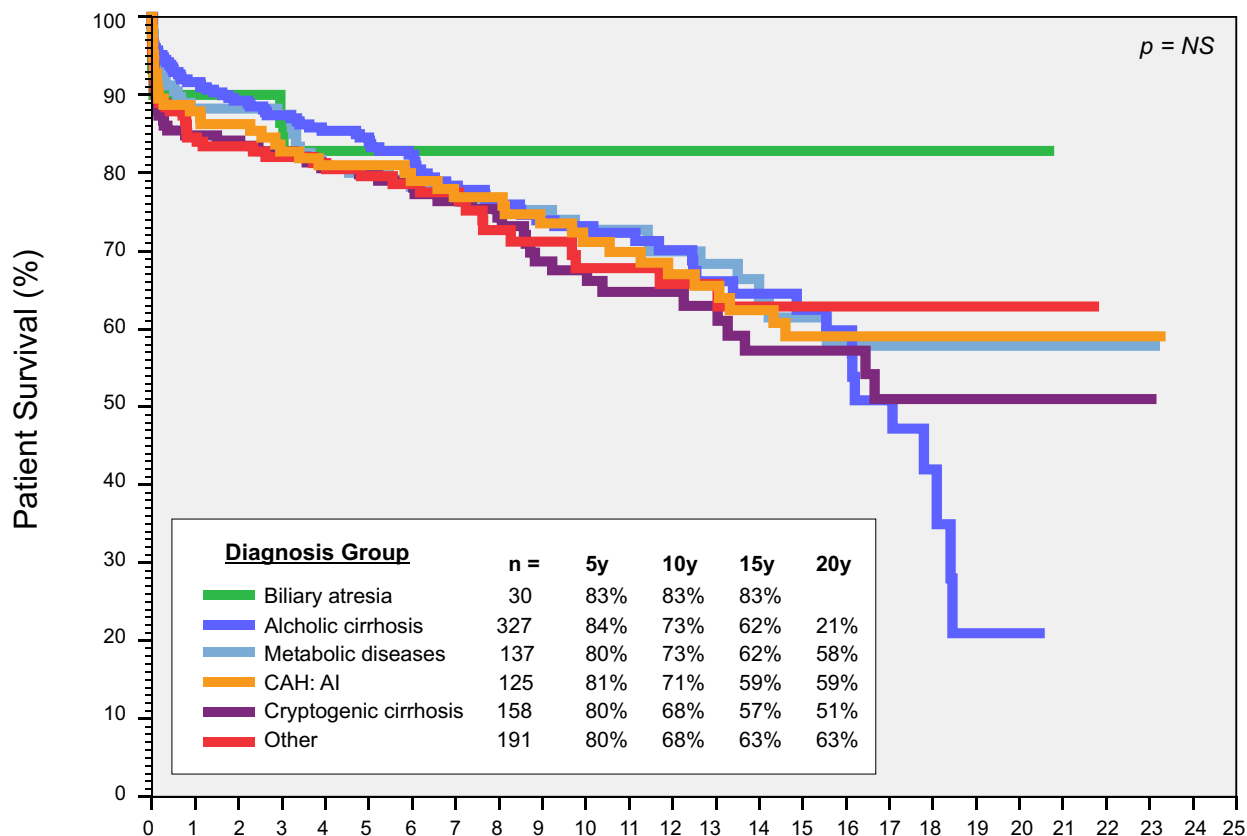


Adults - n = 2683

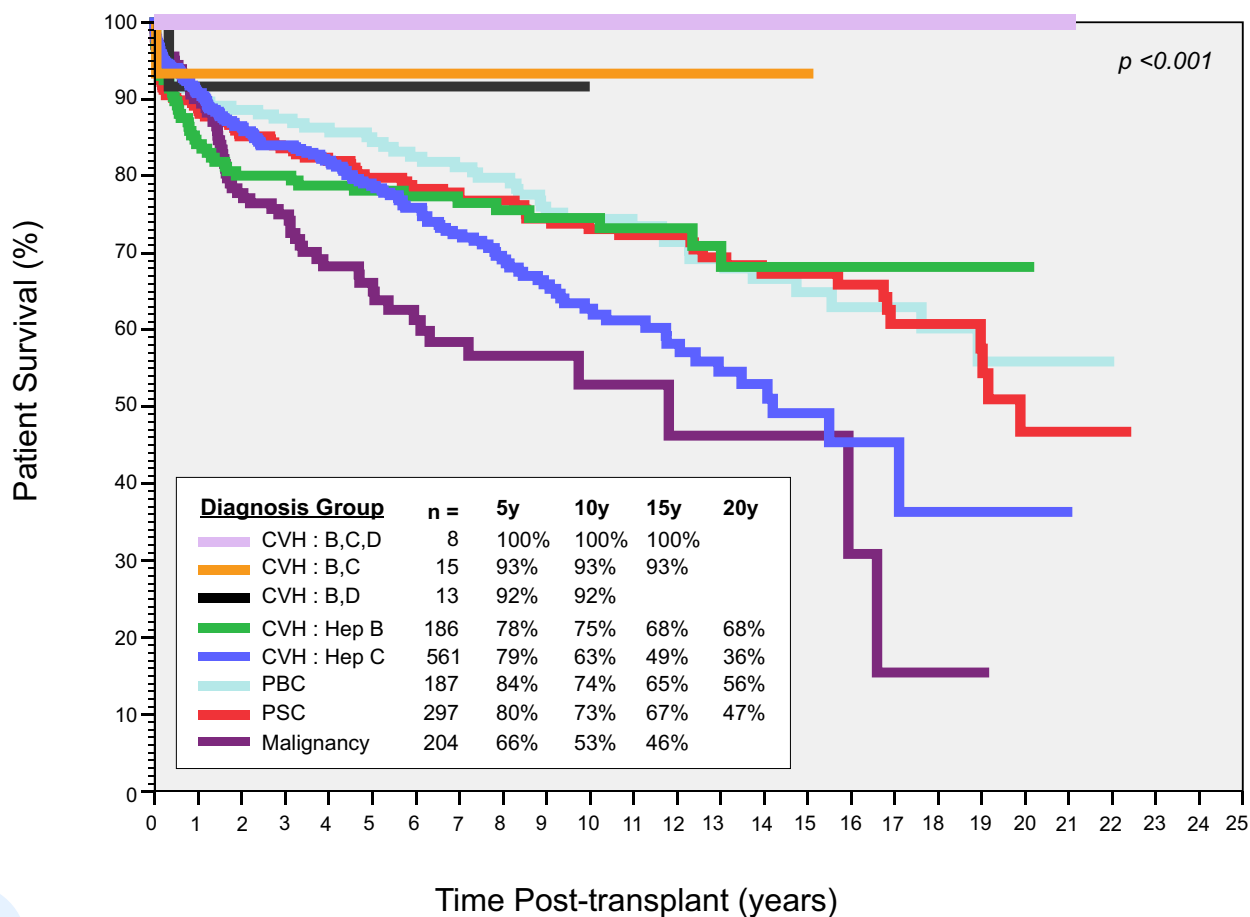




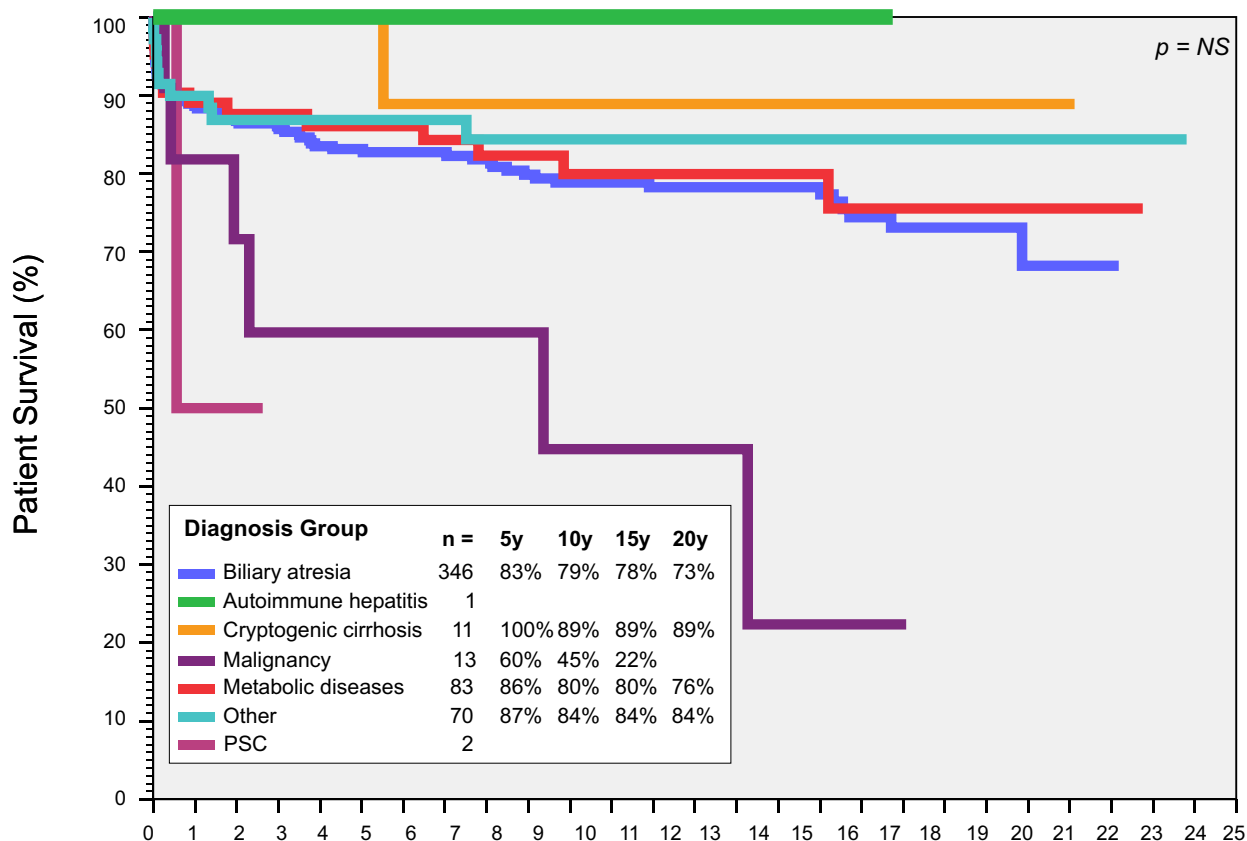
(1) Adults [excluding FHF] - n=968



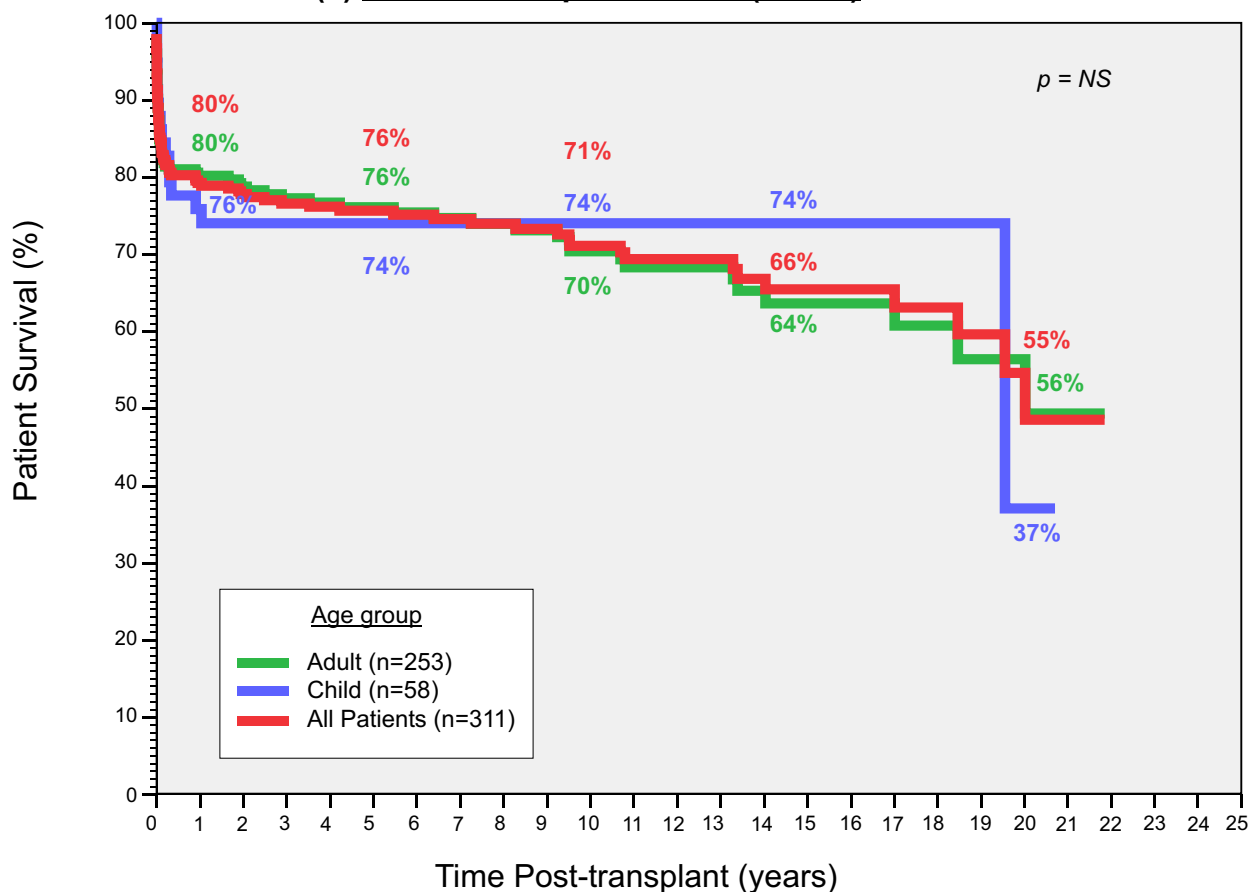
(2) Adults [excluding FHF] - n=1471

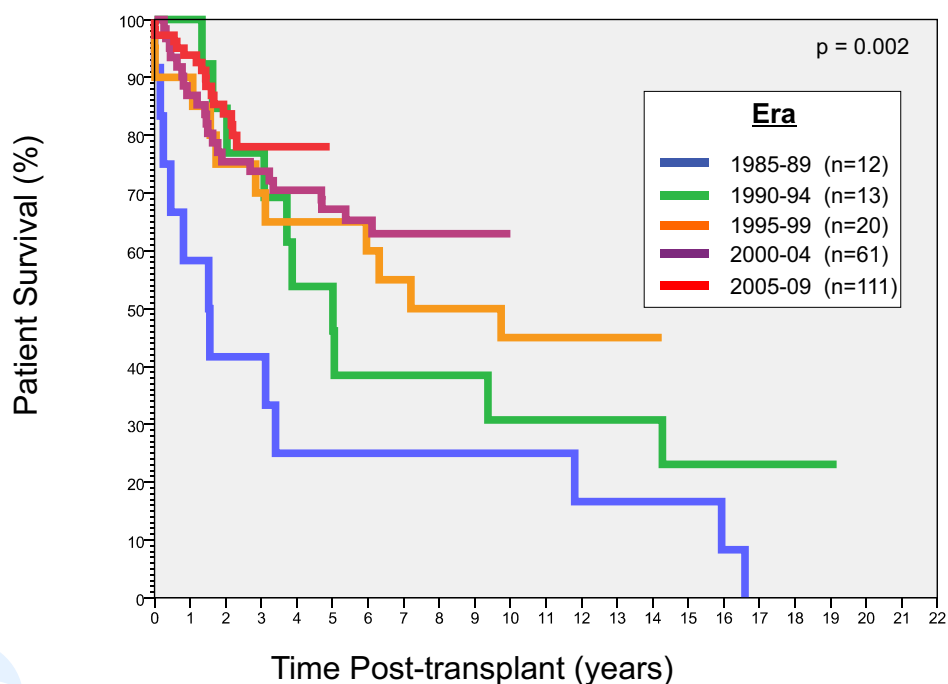
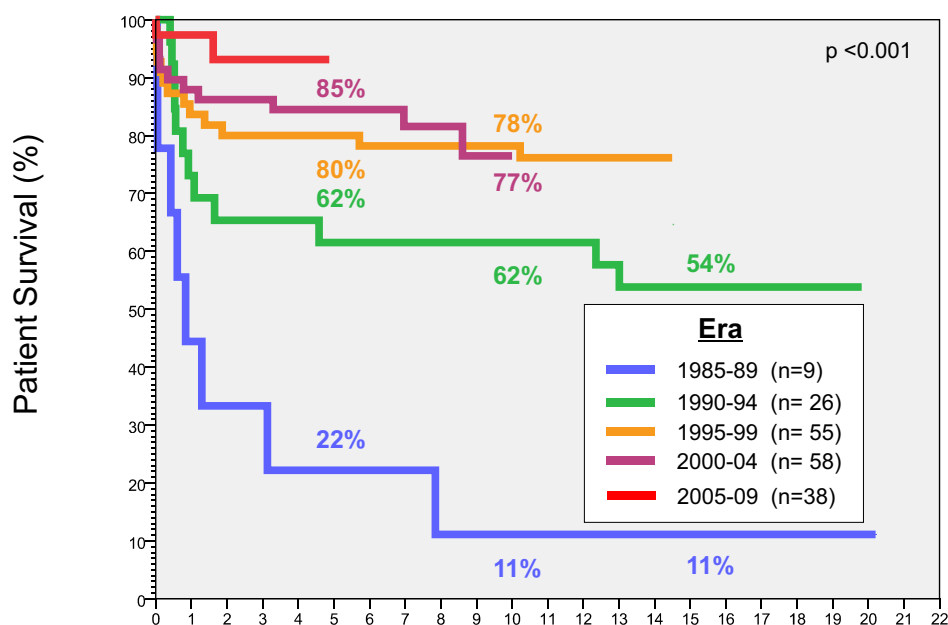
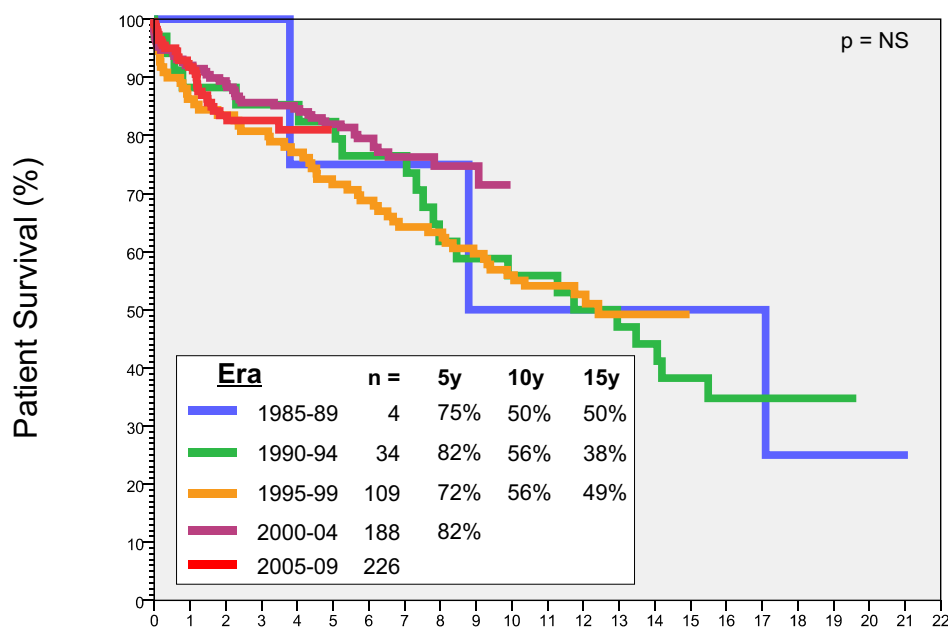


(3) Paediatric recipients [excluding FHF] - n=526



(4) Fulminant hepatic failure (n=311)

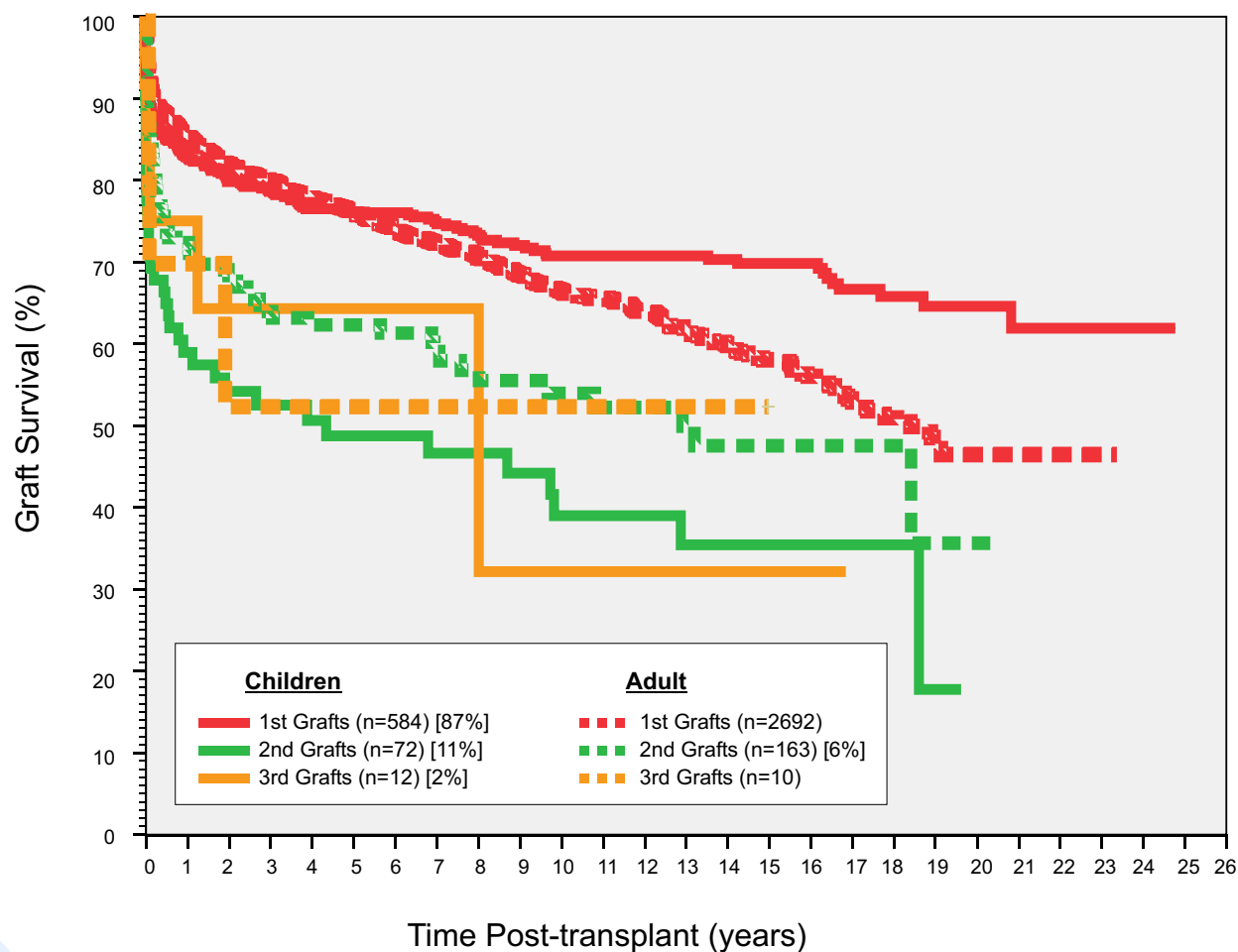
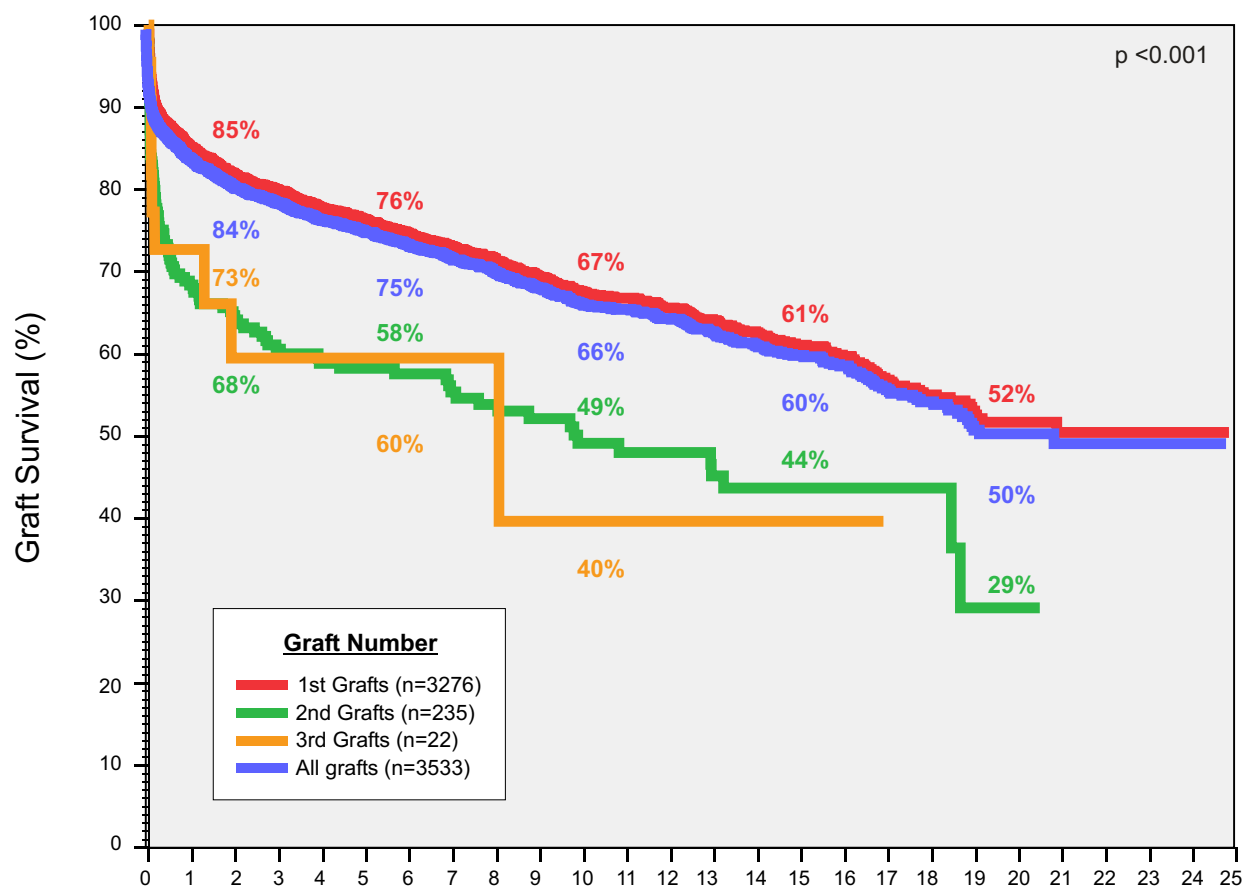




Section 4

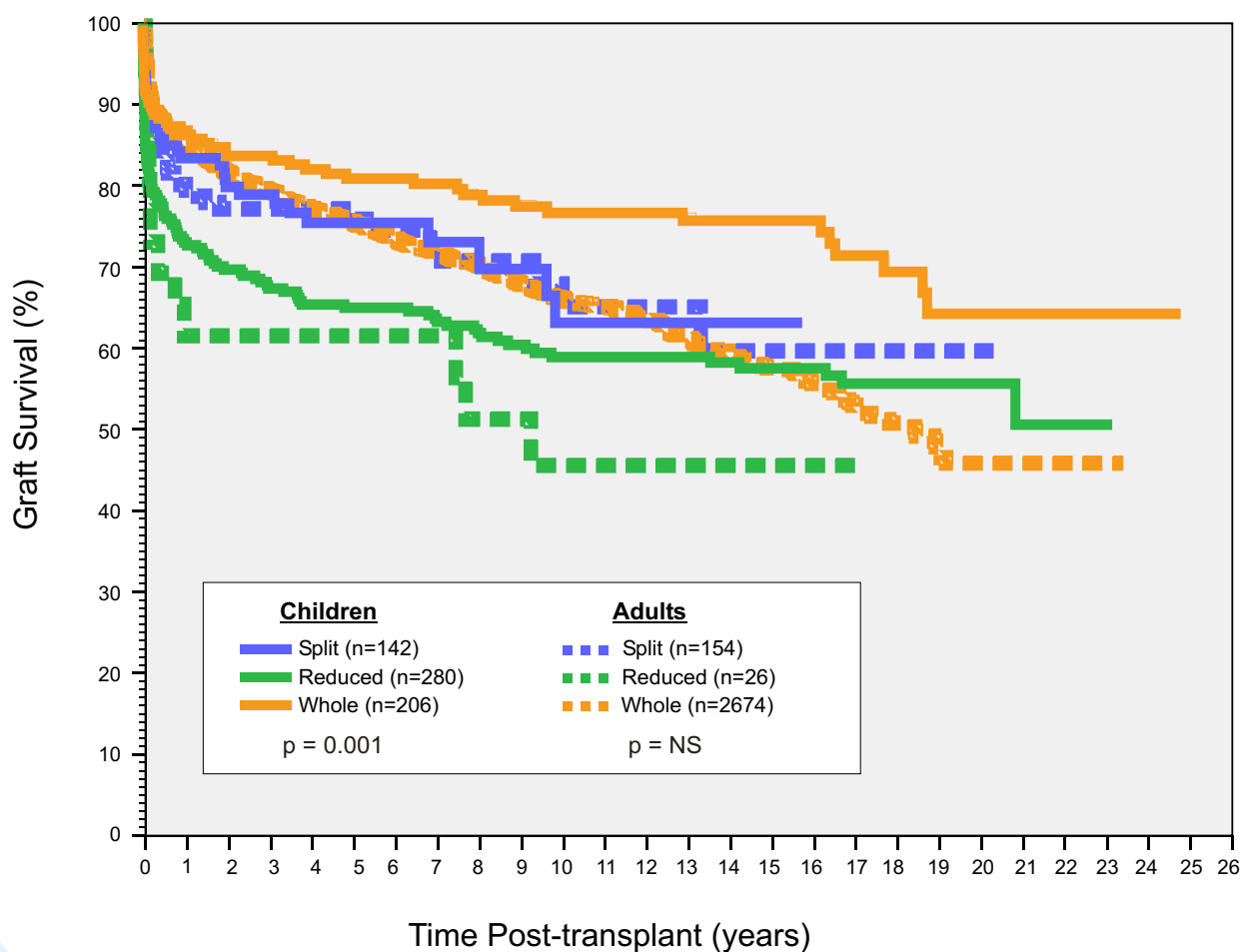
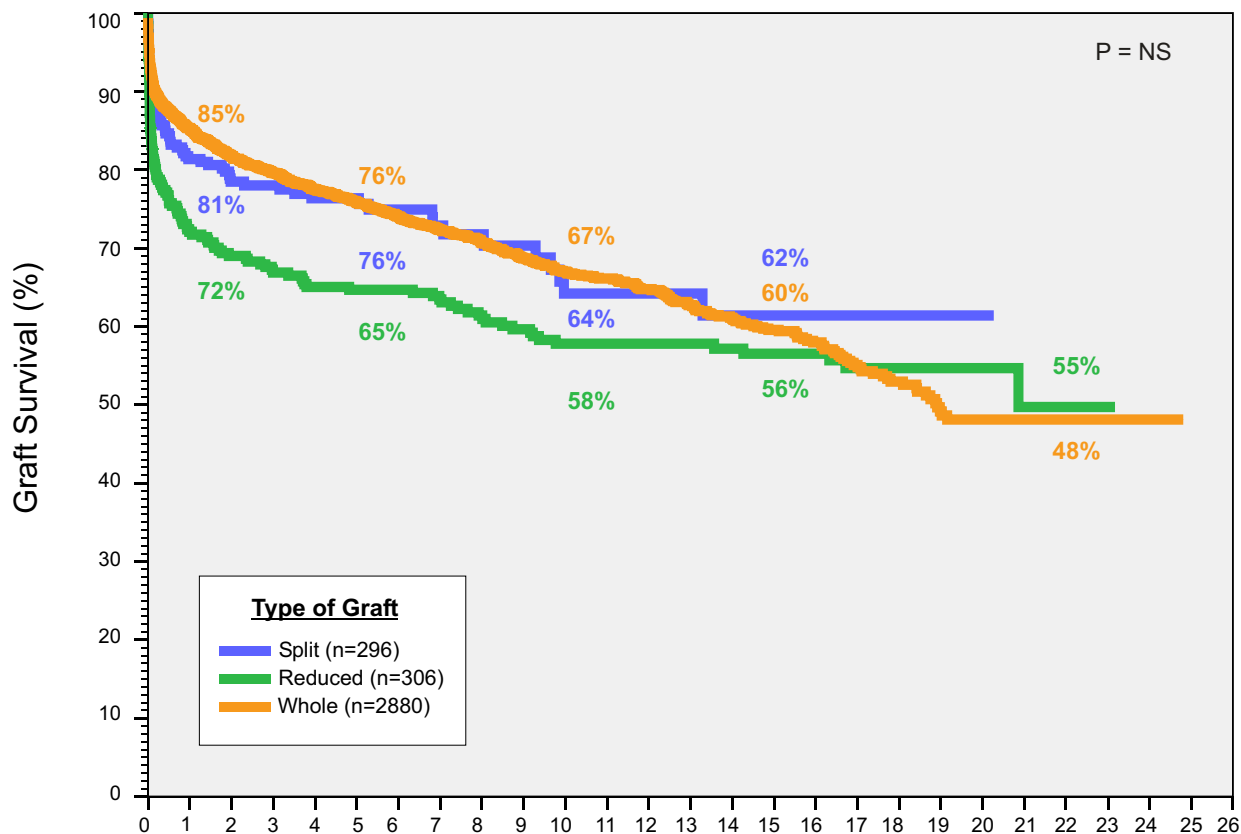
Graft Outcome





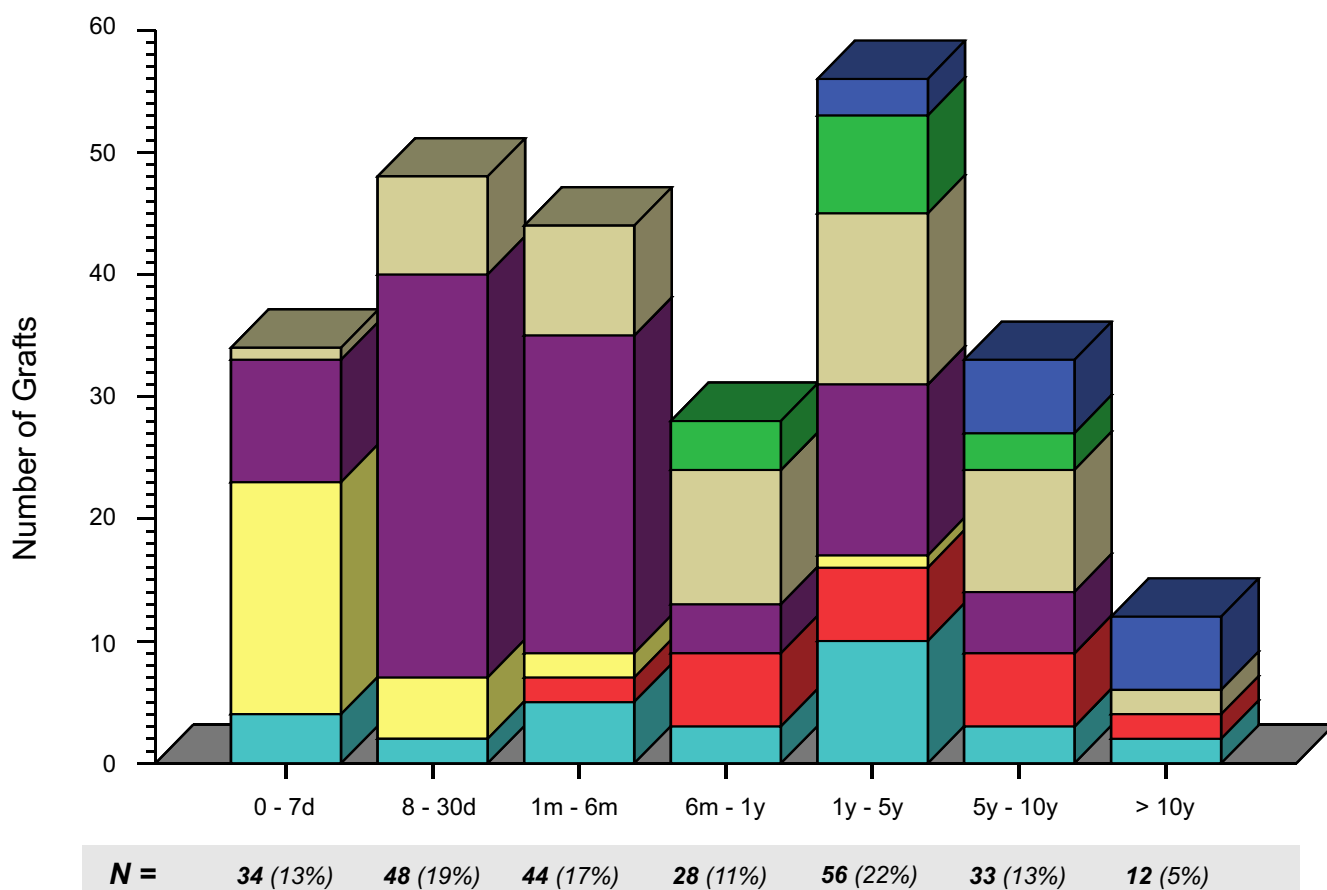
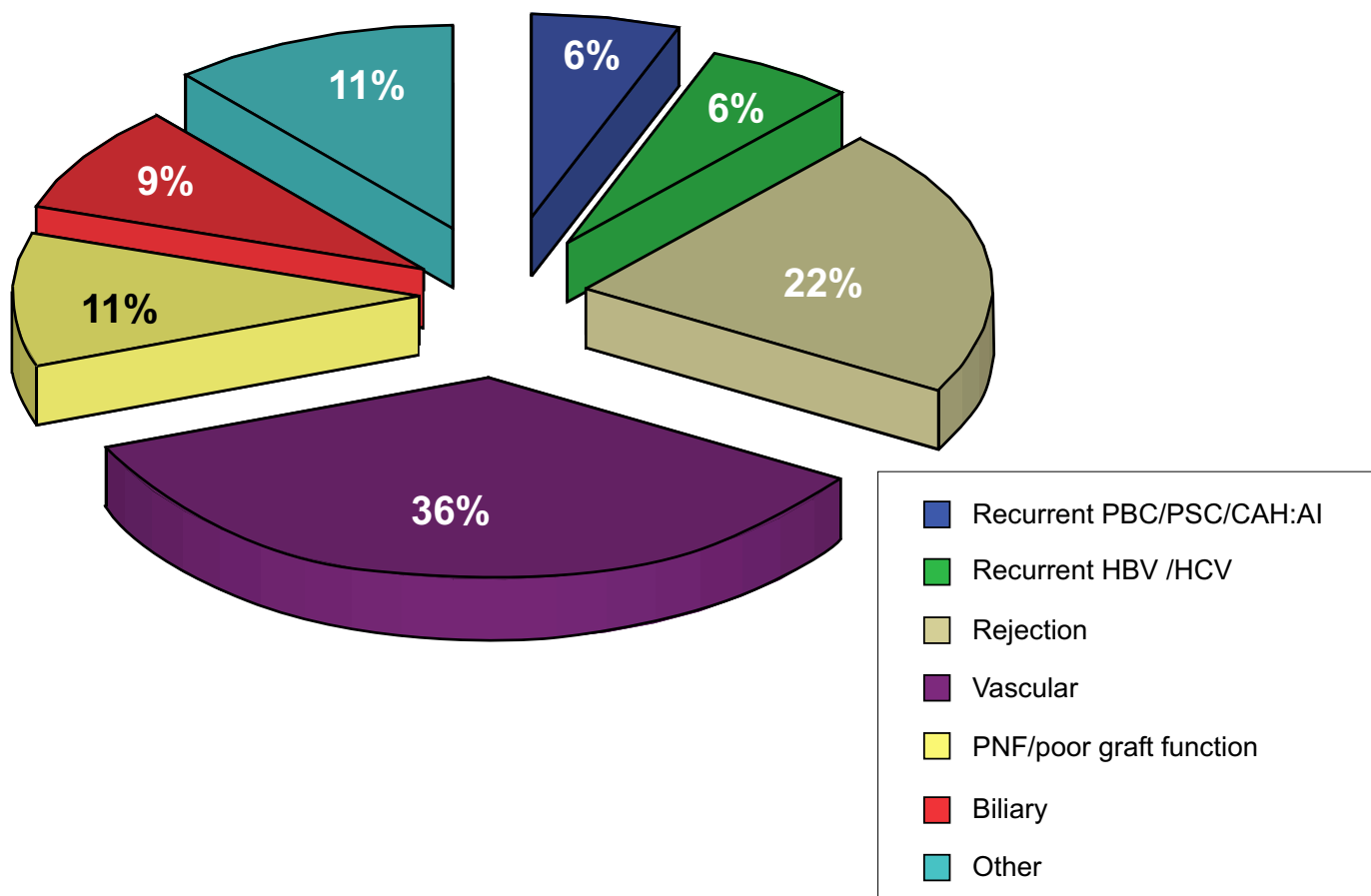
Graft Survival by Type of Graft [Deceased Donors]

All grafts (n = 3482)



Indication for Retransplantation

n = 257 (235 2nd grafts, 22 3rd grafts)

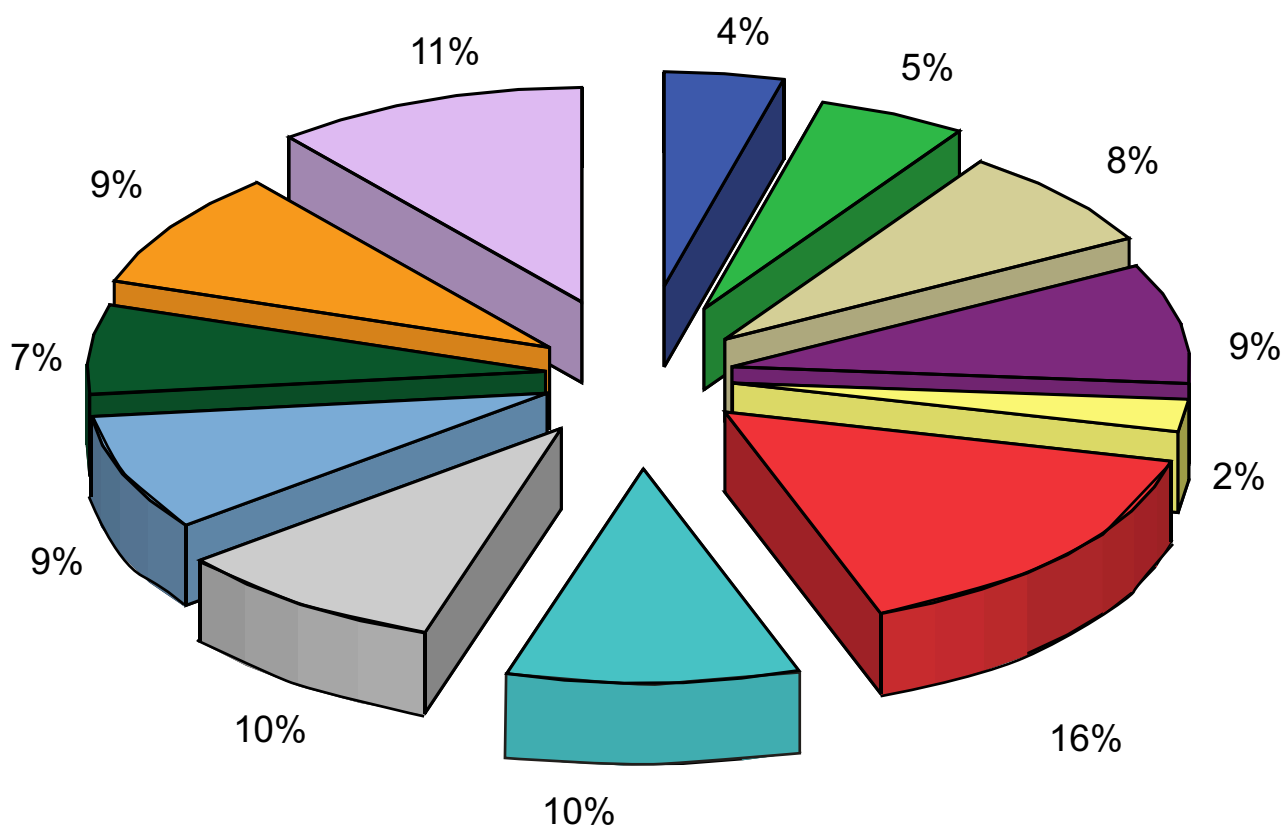
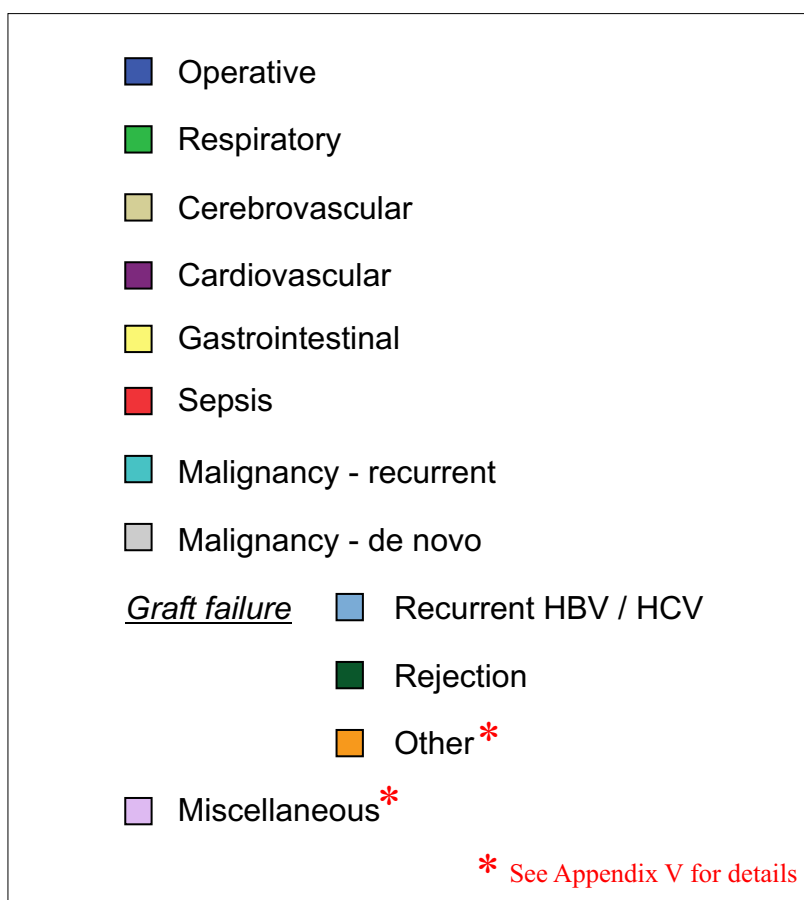


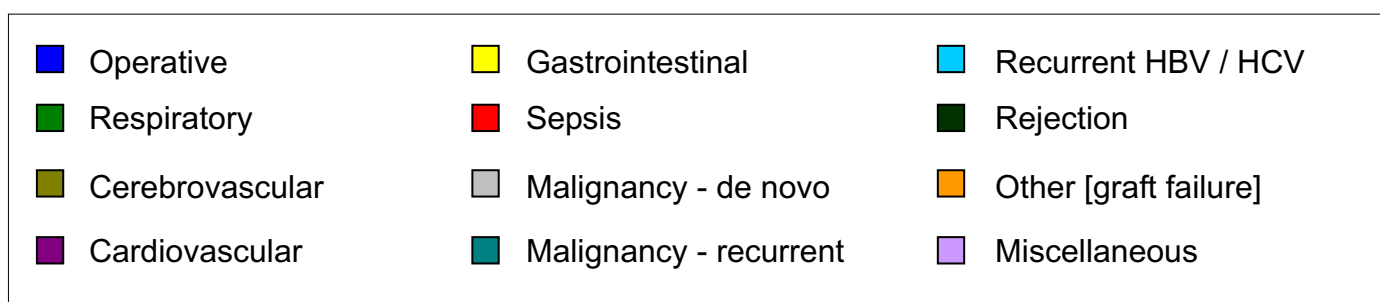
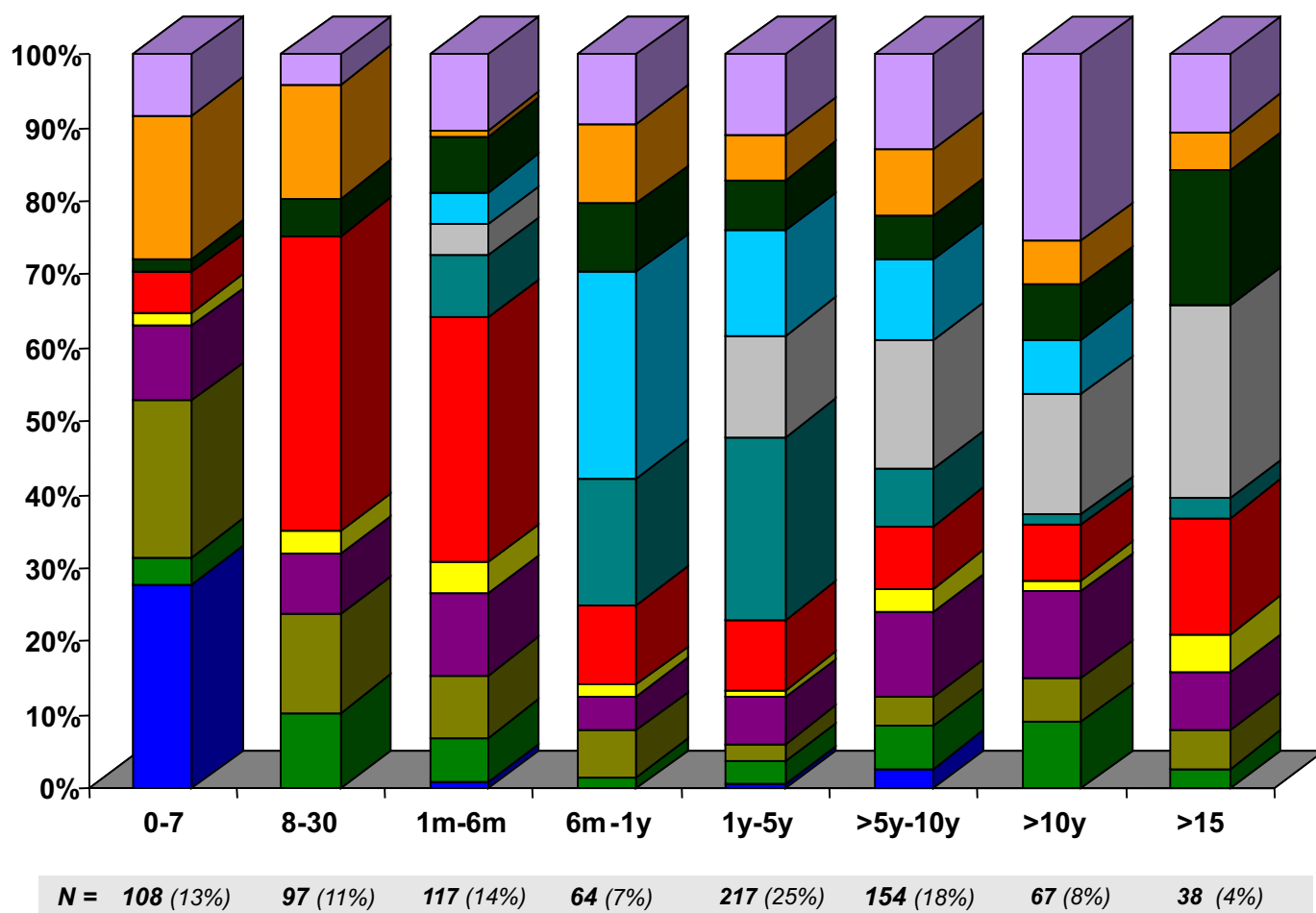
Section 5

Cause of Patient Death



All Patients n = 862





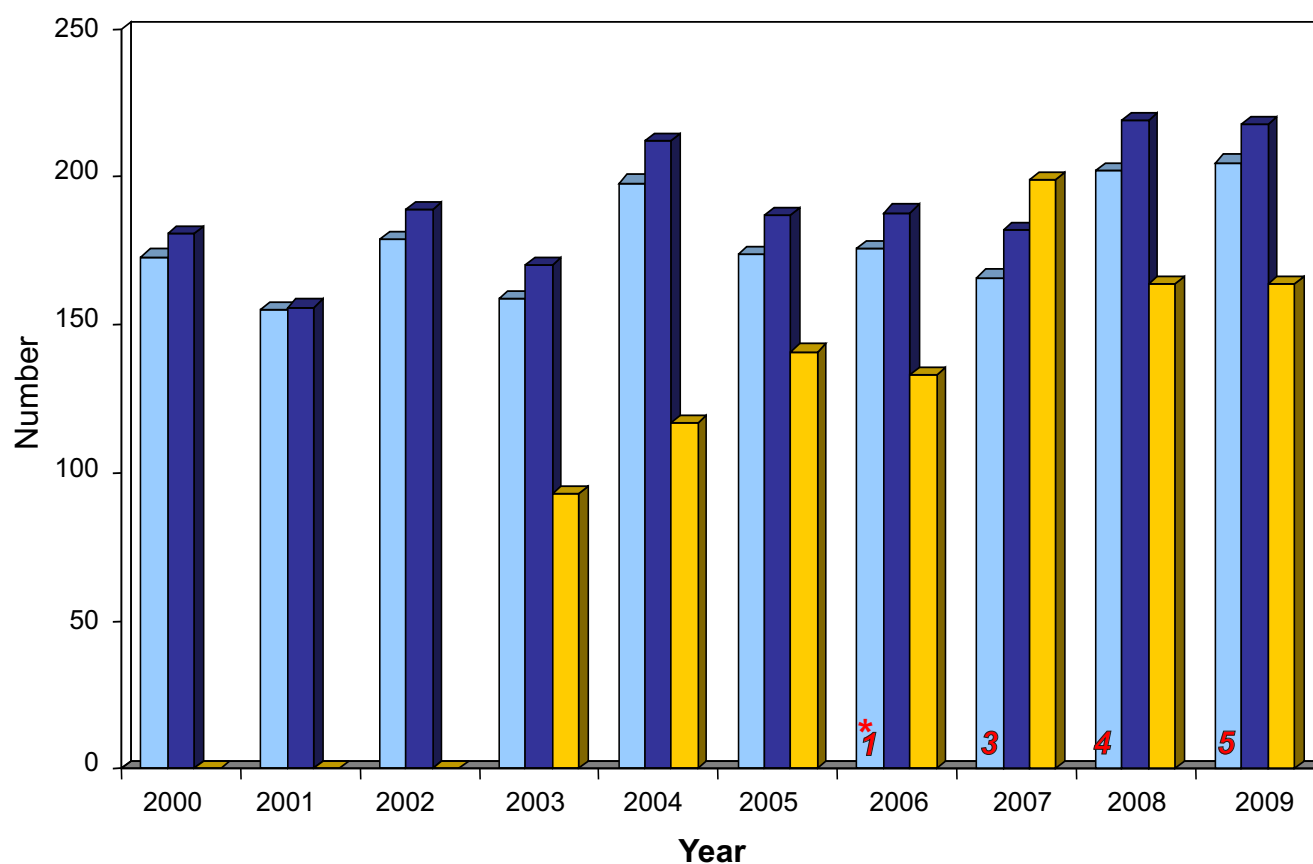
Section 6

Deceased Donor Information

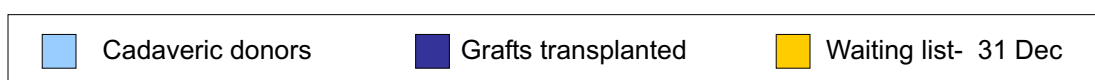


	QLD	NSW/ACT	VIC/TAS	SA/NT	WA	NZ	TOTAL
2000	26	51	26	24	12	34	173
2001	37	40	26	14	9	29	155
2002	34	42	38	24	11	30	179
2003	34	32/3	29/2	13	15	31	159
2004	30	49/4	35/1	26/1	17	35	198
2005	24	36/8	38/2	17/3	25	21	174
2006	28	34/3	39/6	25	17	24	176
2007	25	36/1	36	19/2	15	32	166
2008	33	40/3	41/5	31/1	25	23	203
2009	35	46/4	36/5	28/2	15	33	204

Grafts from deceased donors

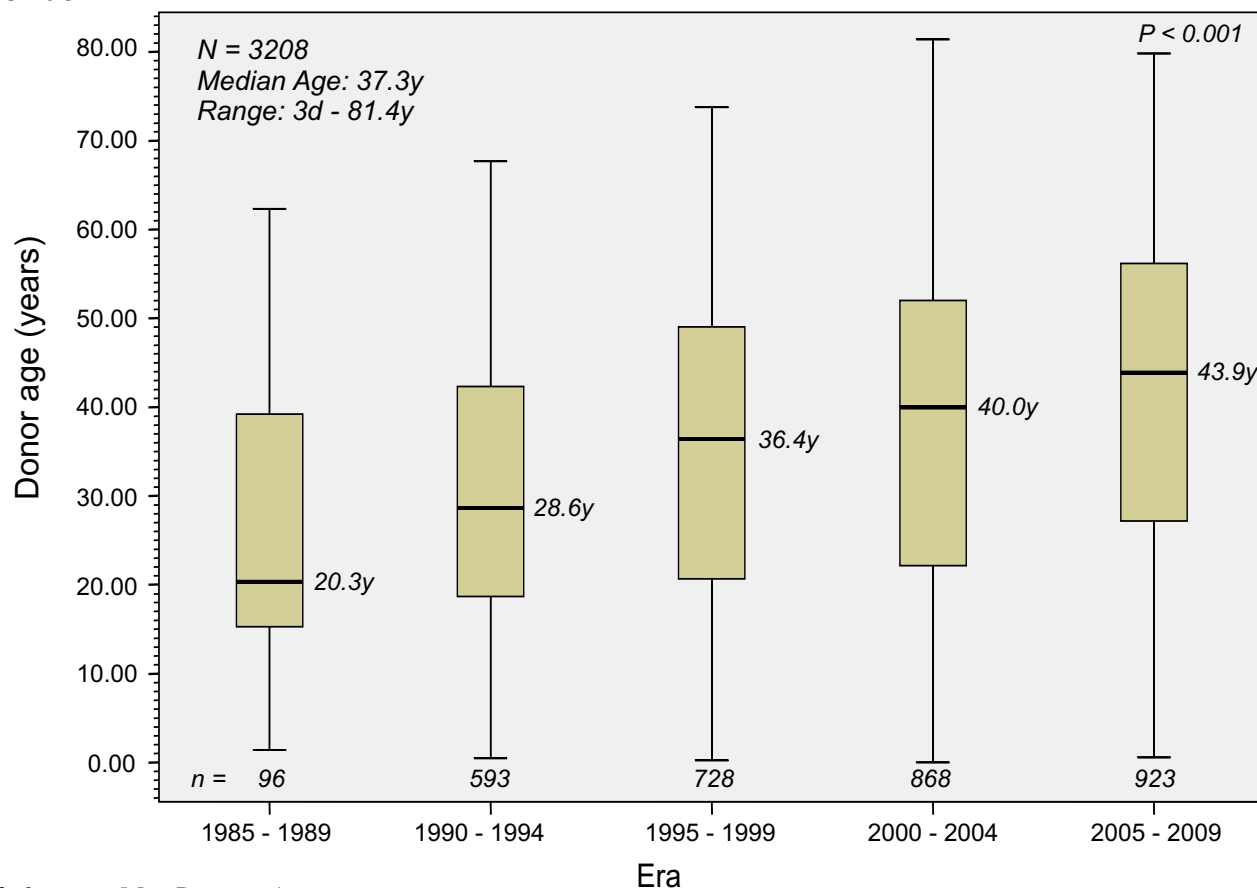


DCD donors*



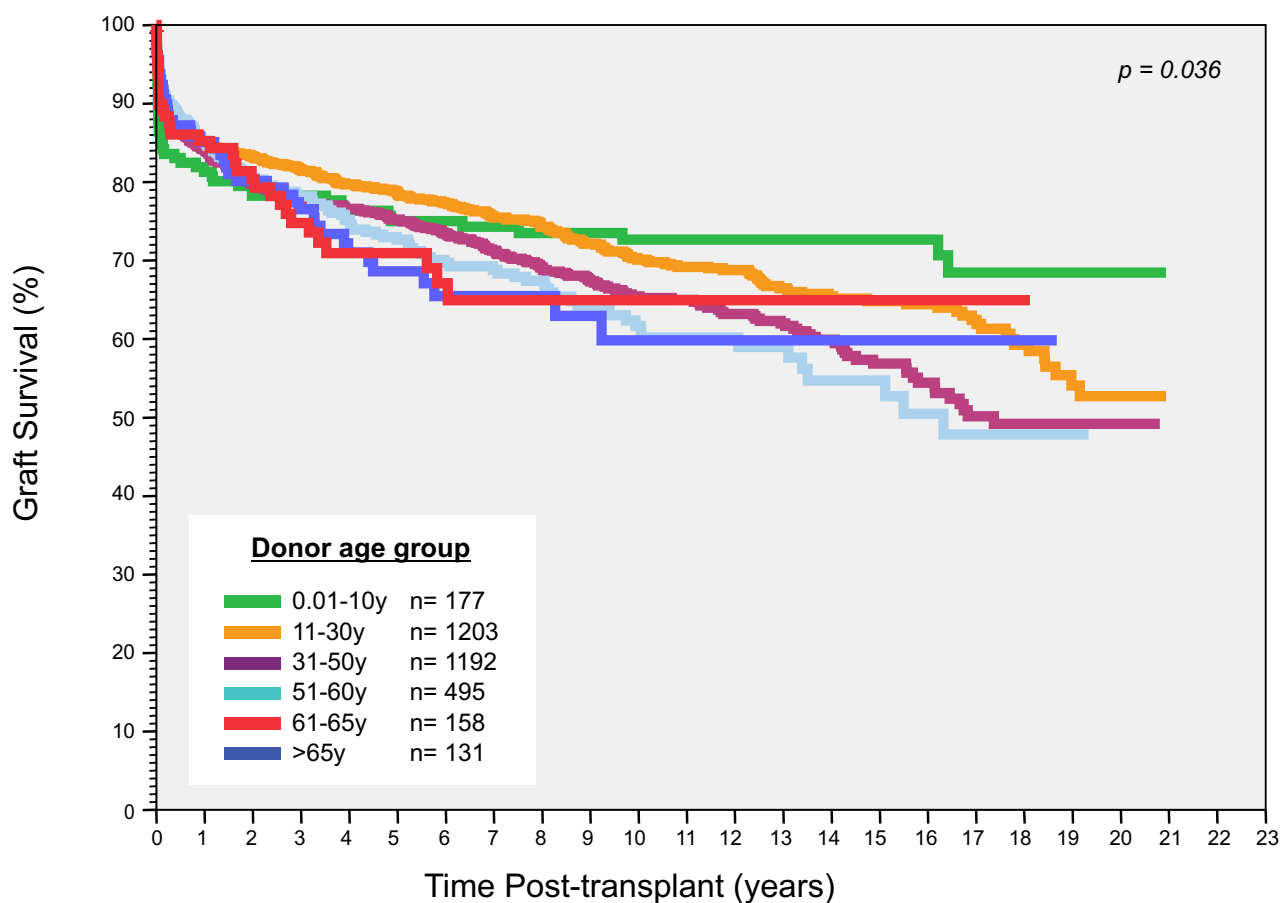
Donor Age by Era

N = 3208



Graft Survival by Donor Age

N = 3356



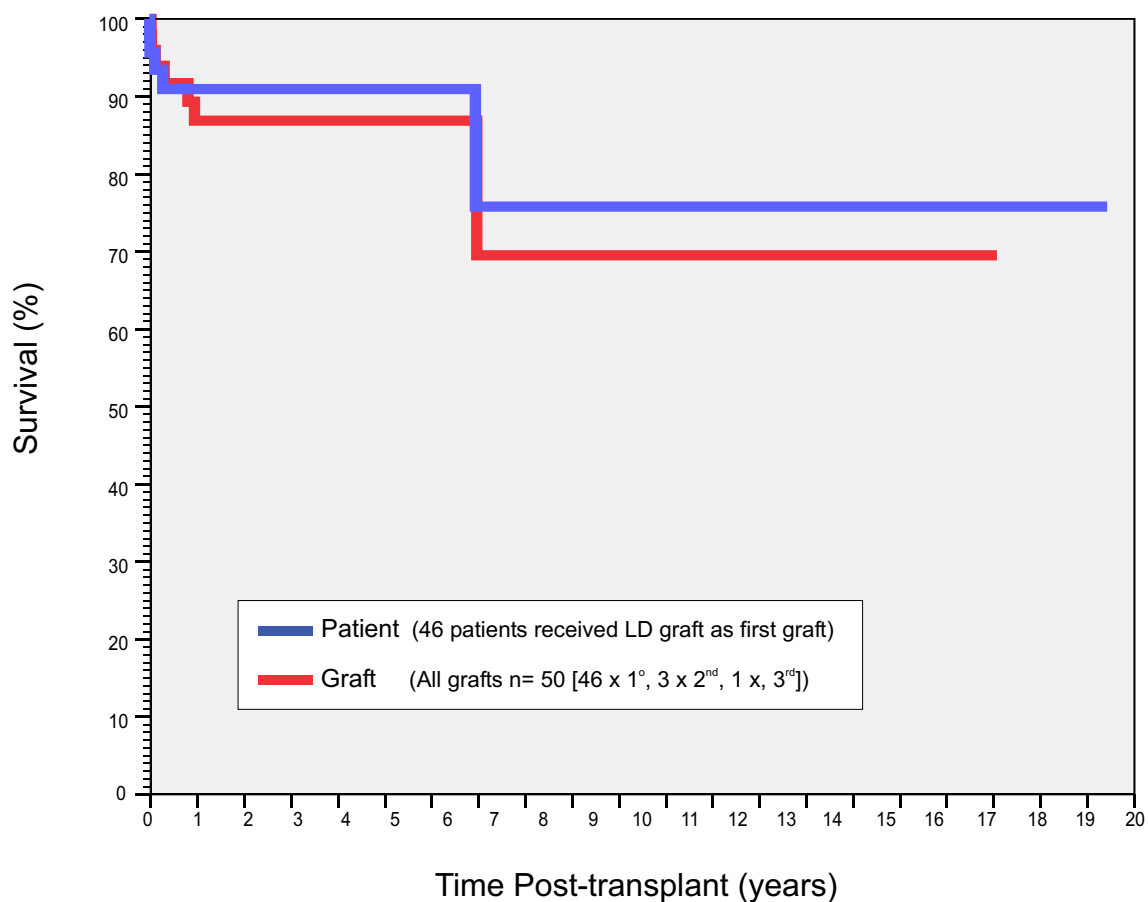
Section 7

Living Donor Transplantation



	Recipient Age Group		
	Child [n=39]	Adult [n=11] [*]	All [n=50]
Donor gender	-	-	-
Male	25	6	31
Female	14	5	19
Donor age	-	-	-
Median	36.2y	33.3y	35.4y
Range	23.0 - 54.5y	22.8 - 44.2y	22.8 - 54.5y
Donor relationship	-	-	-
Mother	9	-	9
Father	21	-	21
Son	-	3	3
Daughter	-	1	1
Grandmother	1	-	1
Grandfather	1	-	1
Sister	-	3	2
Brother	-	2	2
Aunt	3	-	3
Family friend	3	1	4
Cousin	1	-	1

^{*} 1 x whole liver domino transplant



Section 8

Waiting List



Waiting List Activity

[Data 1/1/04 - 31/12/09]

Activity	2004	2005	2006	2007	2008	2009		
Listed at 1 January	93	117	145	133	199	169	-	TOTAL 2009
New listings	279	292	259	338	290	-	324	
TOTAL	372	409	404	471	489	169	324	493
OUTCOME OUTCOME OUTCOME								
Transplant	214 [58%]	191 [47%]	194 [48%]	190 [40%]	229 [47%]	86	142	228 [46%]
Delisted	41 [10%]	72 [18%]	77 [19%]	86 [18%]	96 [20%]	44	57	101 [20%]
Died on list	14	26	18	35	48	10	22	32
Too sick	8	9	13	13	14	6	11	17
Tumour progression	2	9	8	11	7	3	5	8
Improved	8	15	16	17	15	11	7	18
Other	9	13	22	10*	11	14	12	26*
Still listed at 31 Dec	117 [32%]	146 [35%]	133 [33%]	199 [43%]	169 [34%]	39	125	164 (33%)

[*Social/psychiatric 5; Moved overseas 1;Temp delist 1; Stable - 1; Alcohol 1; Malignancy 1; Cardiac - 1.]

Outcome of Urgent Listing

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

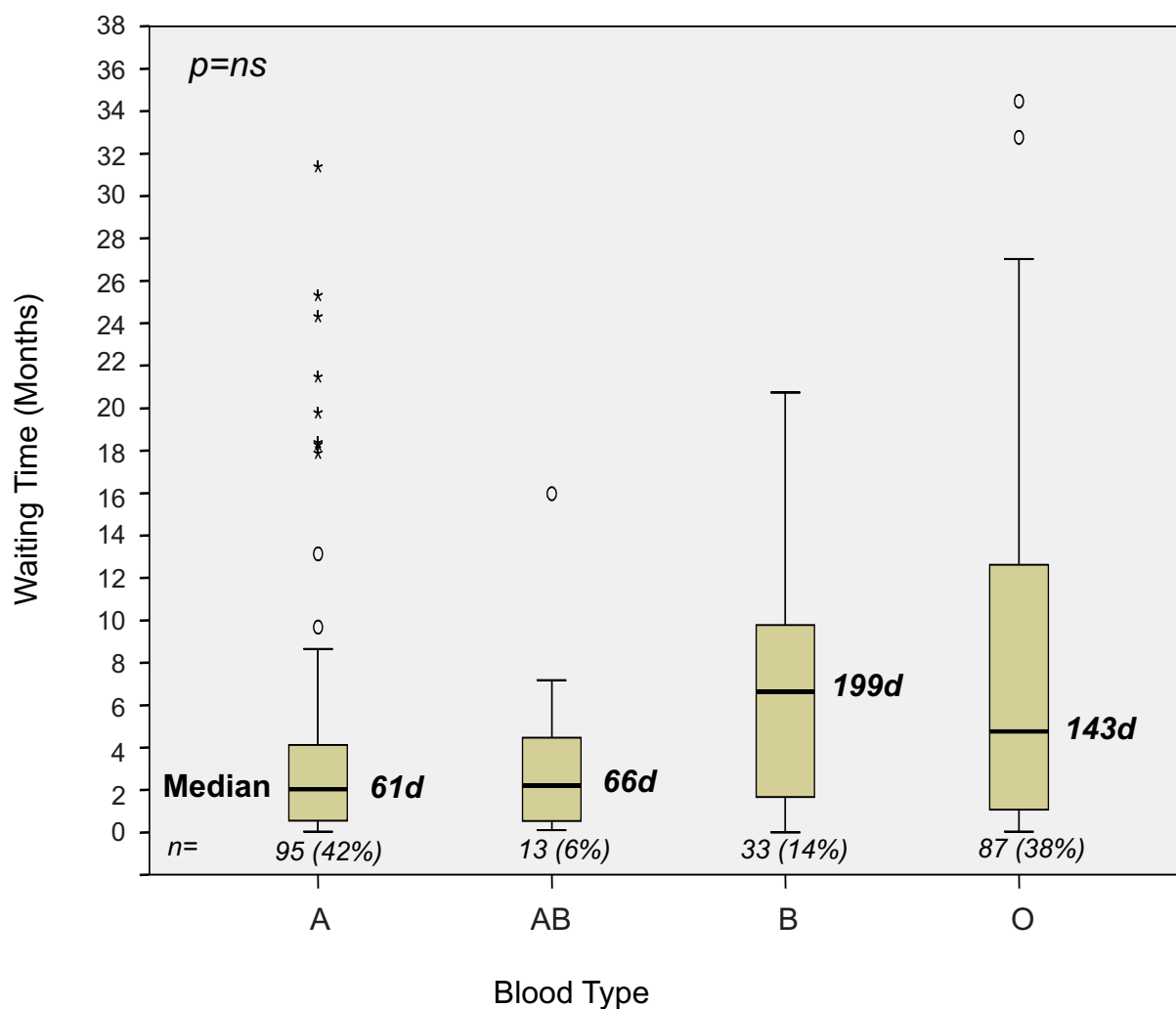
OUTCOME	CATEGORY 2				
	2005 (n=31)	2006 (n=26)	2007 (n=32)	2008 (n=24)	2009 (n=21)
TRANSPLANTED	20 } 68%	21 } 88%	24 } 88%	20 } 83%	18 } 90%
IMPROVED	1 }	2 }	4 }	1 }	1 }
DIED / TOO SICK	10	2	2	3	2
OTHER TREATMENT	-	1	-	-	-

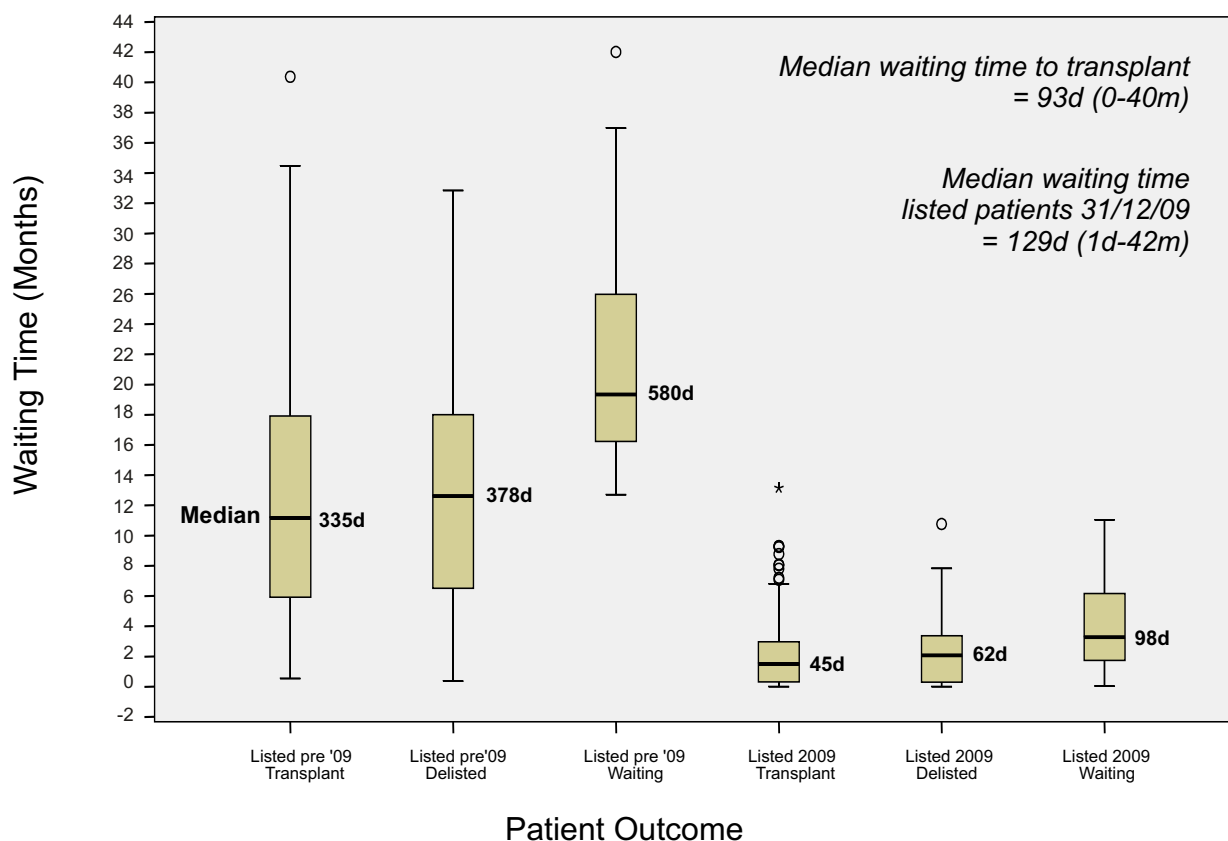
	Blood Group				
	A	O	B	AB	TOTAL
n=	186 (38%)*	210 (46%)	80 (16%)	17 (3%)	493
Not transplanted	91	123	47	4	265
Transplanted	95 (51%)**	87 (41%)	33 (41%)	13 (76%)	228

* % of total number listed

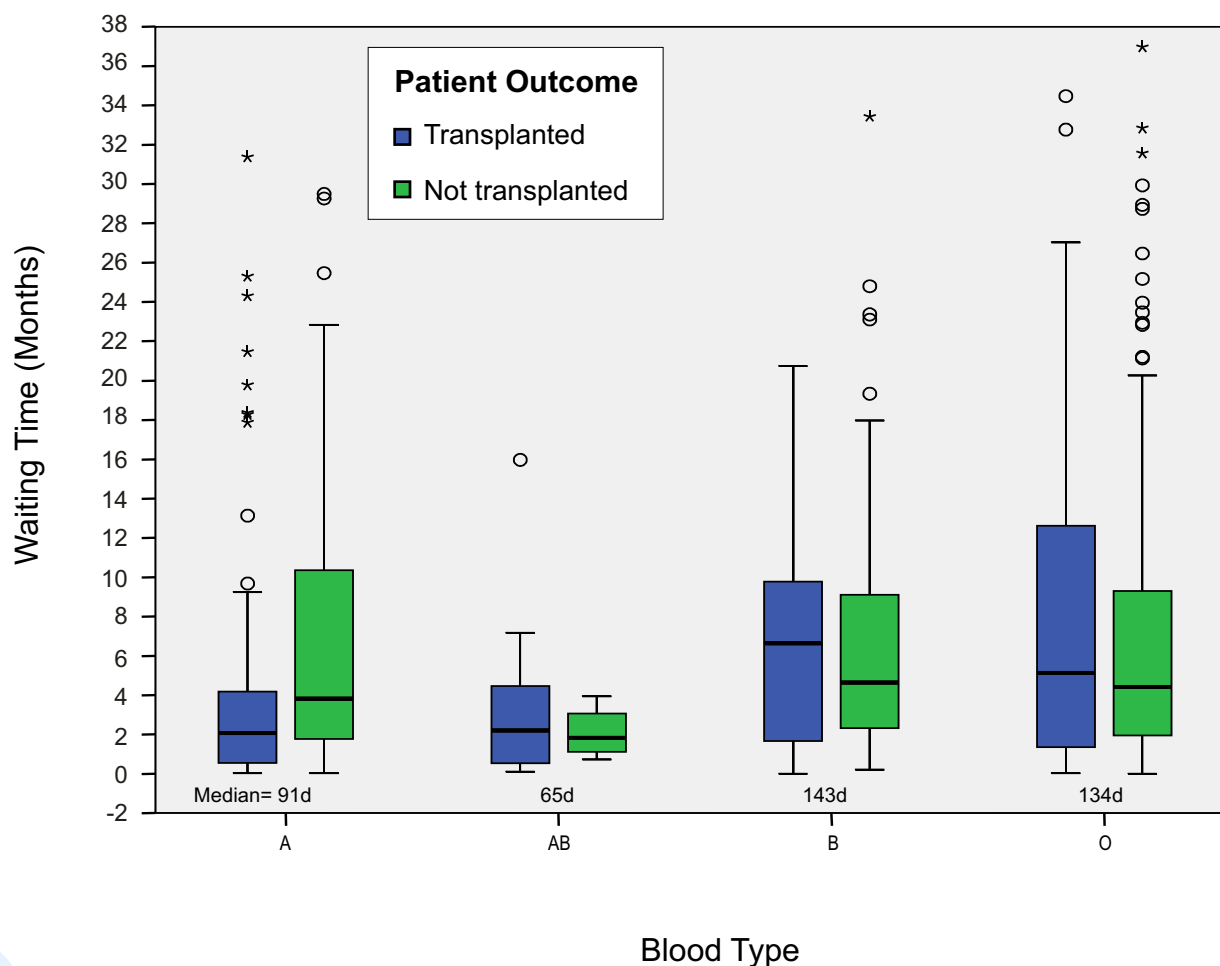
** % of blood group

Waiting Time to Transplant 2009





Waiting Time by Outcome & Blood Group



Section 9

Liver Transplantation and Cancer



Cancer in Liver Transplant Recipients

N = 3277

At Tx	
Tx for Liver Ca	193 (6%)
Liver Ca as a Secondary Diagnosis	366 (11%) 368 Ca
Total	557* (17%)
Post Tx	
Recurrent Liver Ca	92 (3% of all pts, 17% pts with Ca at Tx)
De Novo Ca	209 (6%) 223 Ca
Skin Ca	414 (13%)
Total	715 (22%)
Multiple Ca types	145 (4% of all pts)
Pre-Tx cancer developed de novo non skin cancer	31 (6% of pts with Ca at Tx)
Transferred from Donor	2
Developed non skin Ca < 90days	10

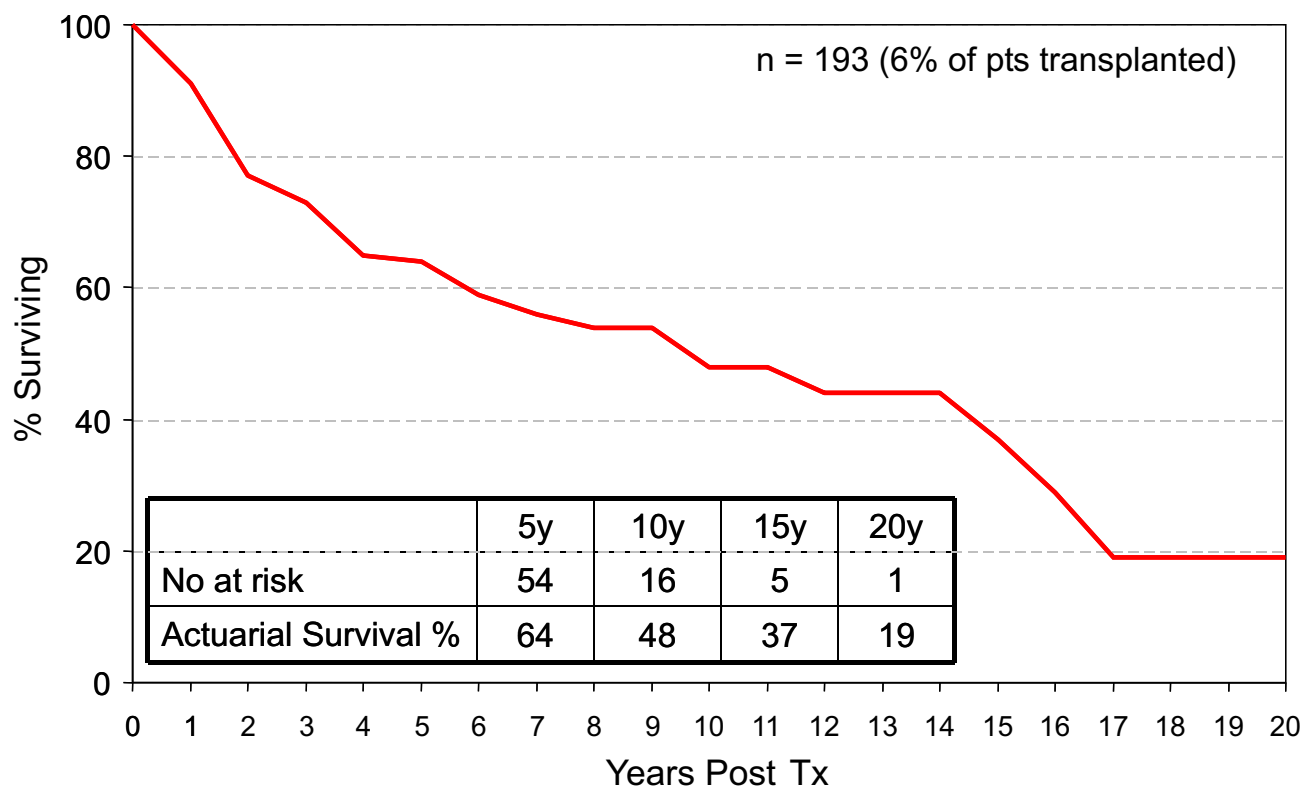
* 2 pts had primary and a secondary liver cancer; 2 pts had multiple secondary liver cancers

Liver Cancer as Primary Diagnosis

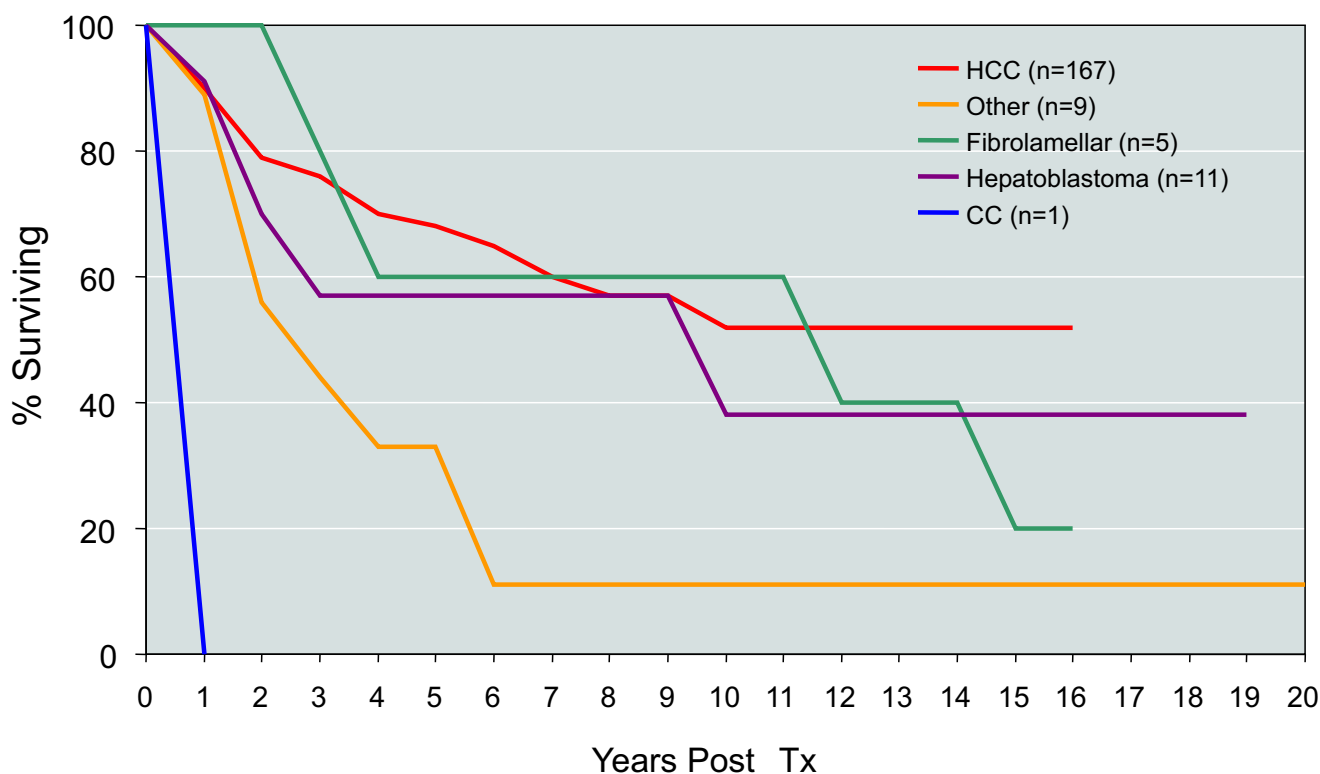
N= 3277

TYPE OF CA	No	DIED	DIED OF THIS CA
HEPATOCELLULAR CA	167	47	24 (14%)
HEPATOBLASTOMA	11	4	3 (25%)
FIBROLAMELLAR	5	5	2 (40%)
CARCINOID	4	4	4
EPITHELOID HAEMANGIOENDOTHELIOMA	2	0	0
CHOLANGIOCARCINOMA	1	1	1
ANGIOSARCOMA	1	1	1
GASTRINOMA	1	1	1
PANCREATIC ISLET CELL	1	1	1
TOTALS	193 (6% of pts)	64 (33% of those with PCa)	37 (19% of those with PCa)

Overall Survival
Primary Liver Cancer
N = 193 (6% of patients transplanted)



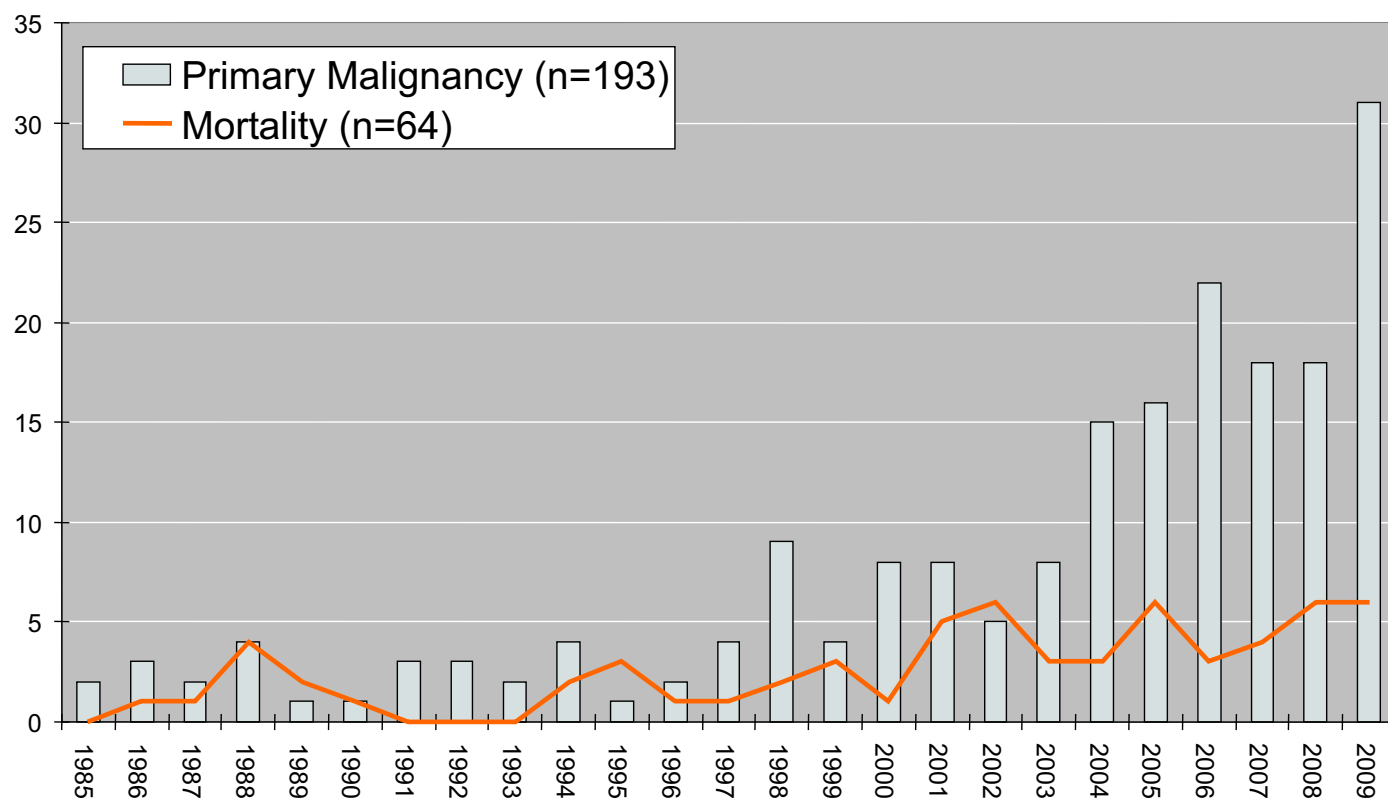
Overall Survival
Primary Liver Cancer
N = 193/3277 (6%)



Primary Liver Cancer Actuarial Survival Summary n = 3277

		1yr	5yr	10yr	15yr
HCC (n=167)	n	124	45	10	2
	%	90	68	52	52
Hepatoblastoma (n=11)	n	9	3	2	1
	%	91	57	38	38
Other (n=9)	n	8	3	1	1
	%	89	33	11	11
Fibrolamellar (n=5)	n	3	3	3	1
	%	60	60	60	20
CC (n=1)	n	1	0		
	%	100			

Primary Liver Cancer Incidence and Mortality

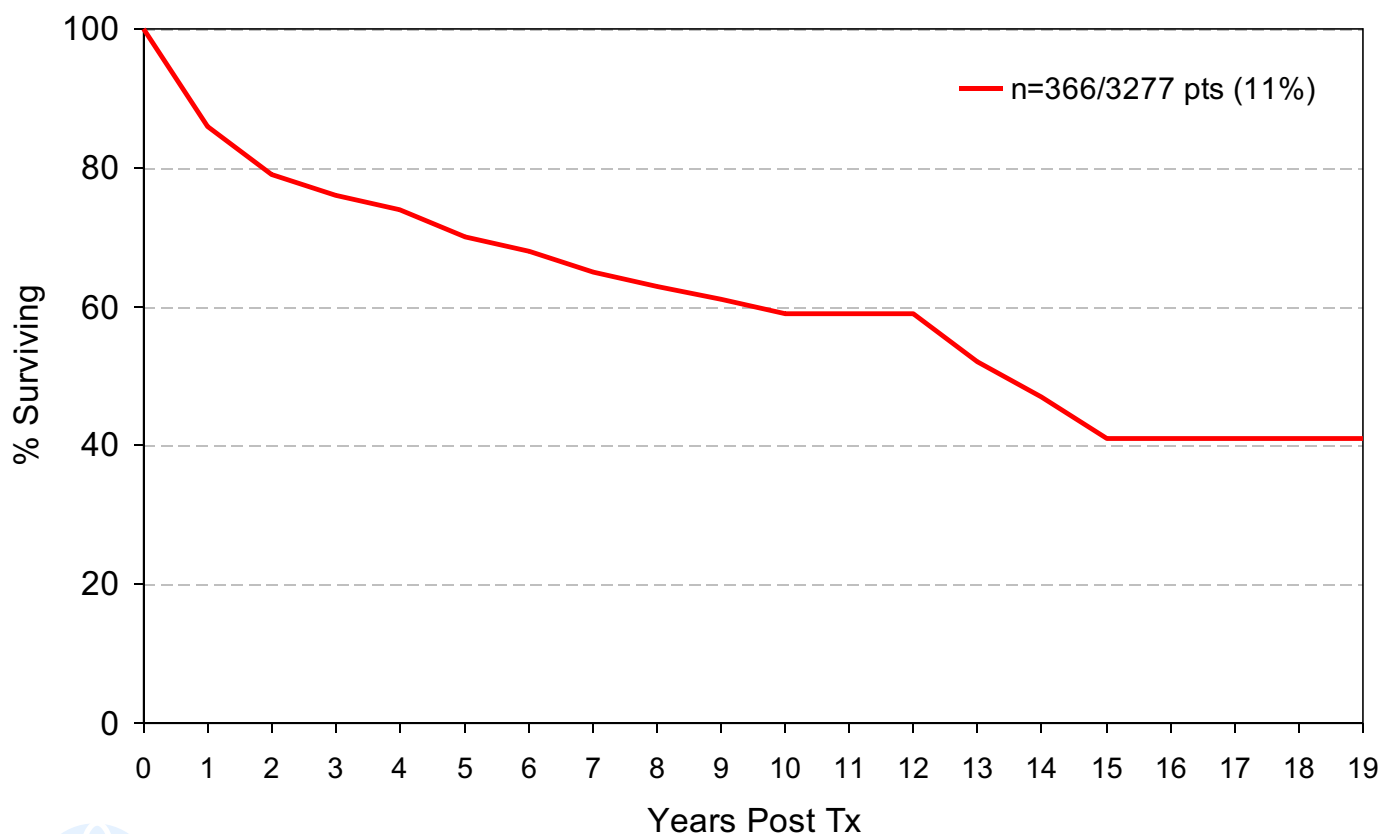


Liver Cancer as a Secondary Diagnosis N=3277

	No	Died	Died of This Cancer
HEPATOCELLULAR CA*	328	85	27 (8%)
CHOLANGIO CA	29	20	13 (45%)
ADENOCARCINOMA	4	4	1
FIBROLAMELLAR	3	1	1
HEPATOBLASTOMA*	2	1	0
ANGIOSARCOMA	1	1	1
EPITHELOID HAEMANGIOCA	1	0	0
Total	368* in 366 pts (11%)	112 (32% of pts with SCa)	43 (12% of pts with SCa)

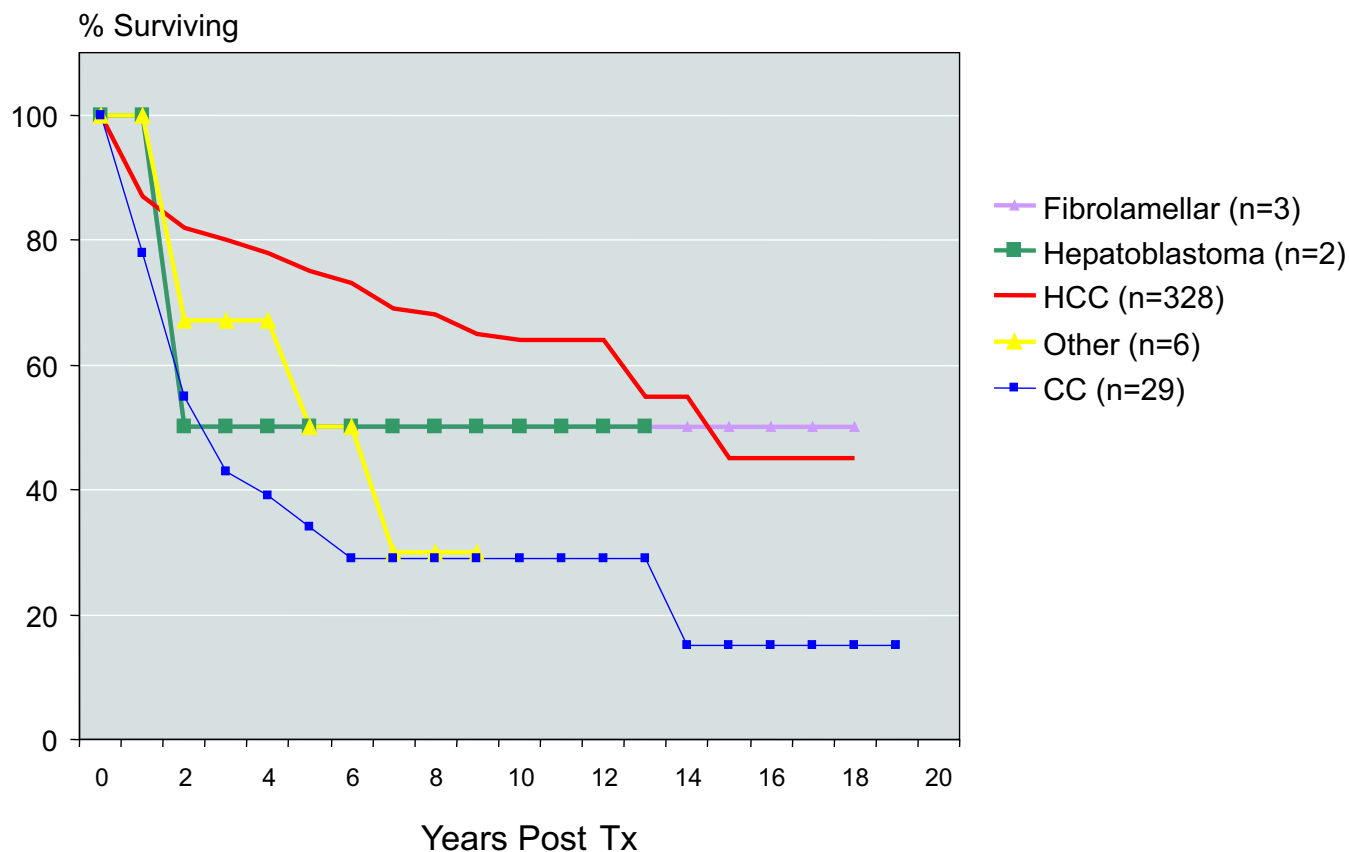
* 2 patients had 2 secondary cancers

Overall Survival Liver Cancer as a Secondary Diagnosis



Liver Cancer as a Secondary Diagnosis

N = 3277



Secondary Liver Cancer

Actuarial Survival Summary

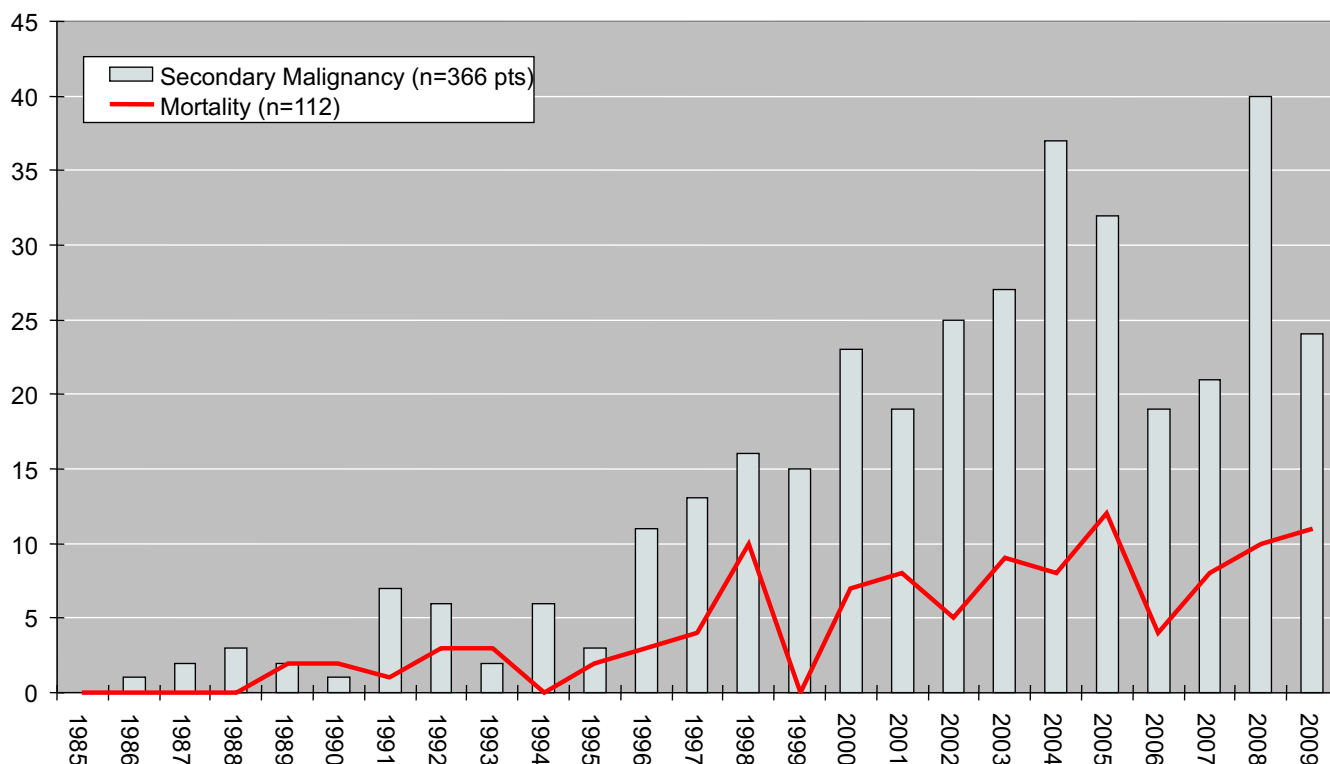
N=3277

		1yr	5yr	10yr	15yr
CC (n=29)	n	21	8	3	1
	%	78	34	29	15
HCC (n=328)	n	252	136	37	4
	%	87	75	64	
Hepatoblastoma (n=2)	n	2	1	1	
	%	50	50	50	50
Fibrolamellar (n=3)	n	2	1	1	1
	%	100	50	50	50
Other (n=6)	n	6	3		
	%	100	50		

Liver Cancer as a Secondary Diagnosis

Incidence and Mortality

n=366/3277 pts (11%)



Liver Cancer

(Primary or Secondary Diagnosis)

N = 3277

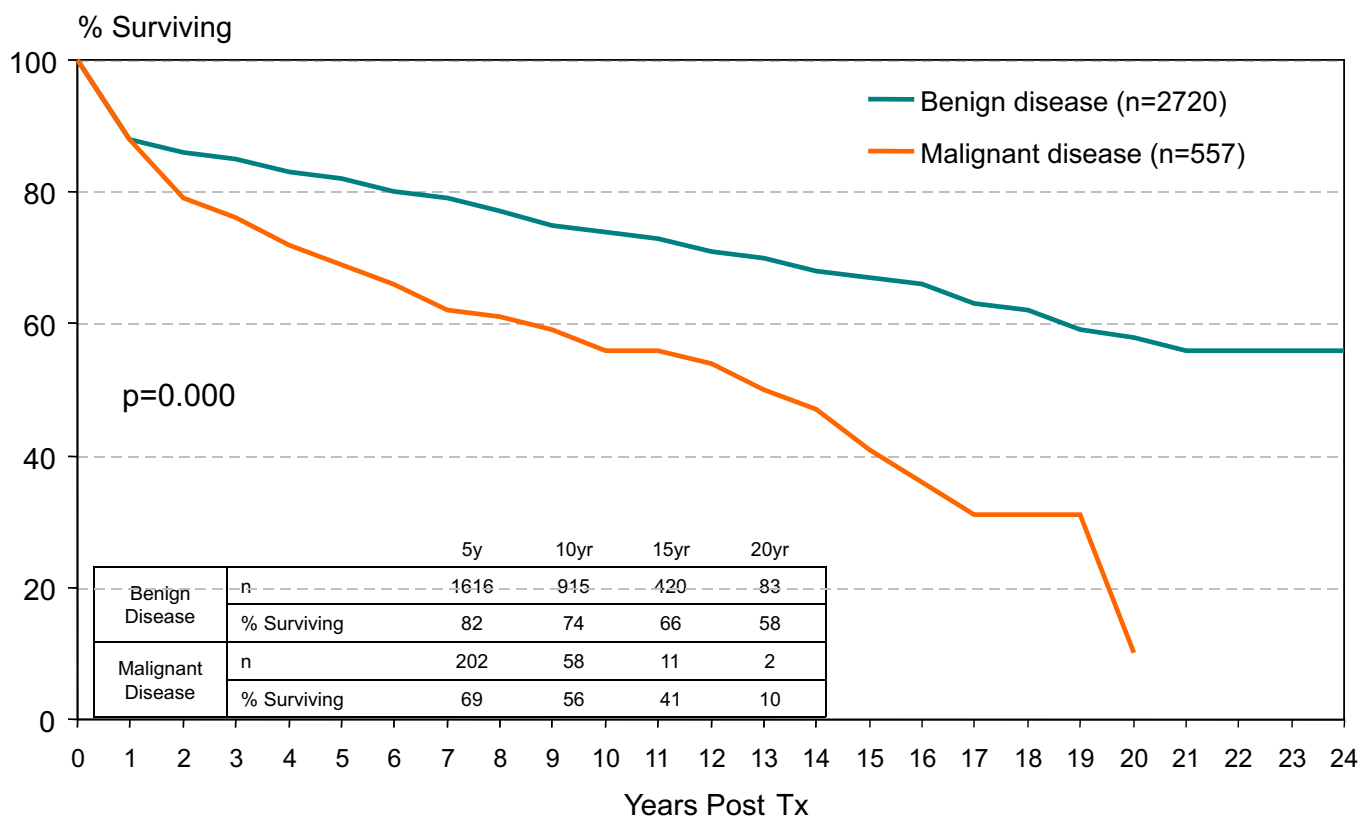
TYPE OF CA	NO	DIED	DIED OF THIS CA
HEPATOCELLULAR CA*	495	132	51 (10%)
CHOLANGIOCARCINOMA*	30	21	14 (48%)
HEPATOBLASTOMA*	13	5	3 (23%)
FIBROLAMELLAR	8	6	3 (38%)
CARCINOID	4	4	4
ADENOCARCINOMA	4	4	1 (25%)
EPITHELOID HAEMANGIOENDOTHELIOMA	3	0	0
ANGIOSARCOMA	2	2	2
GASTRINOMA	1	1	1
PANCREATIC ISLET CELL	1	1	1
TOTALS	561* Ca in 557 pts (17% of pts)	176 (31% of those with Ca)	80 (14% of those with Ca at Tx)

* 2 patients had 2 secondary cancers; 2 patients had a primary and secondary liver malignancy

Patient Actuarial Survival

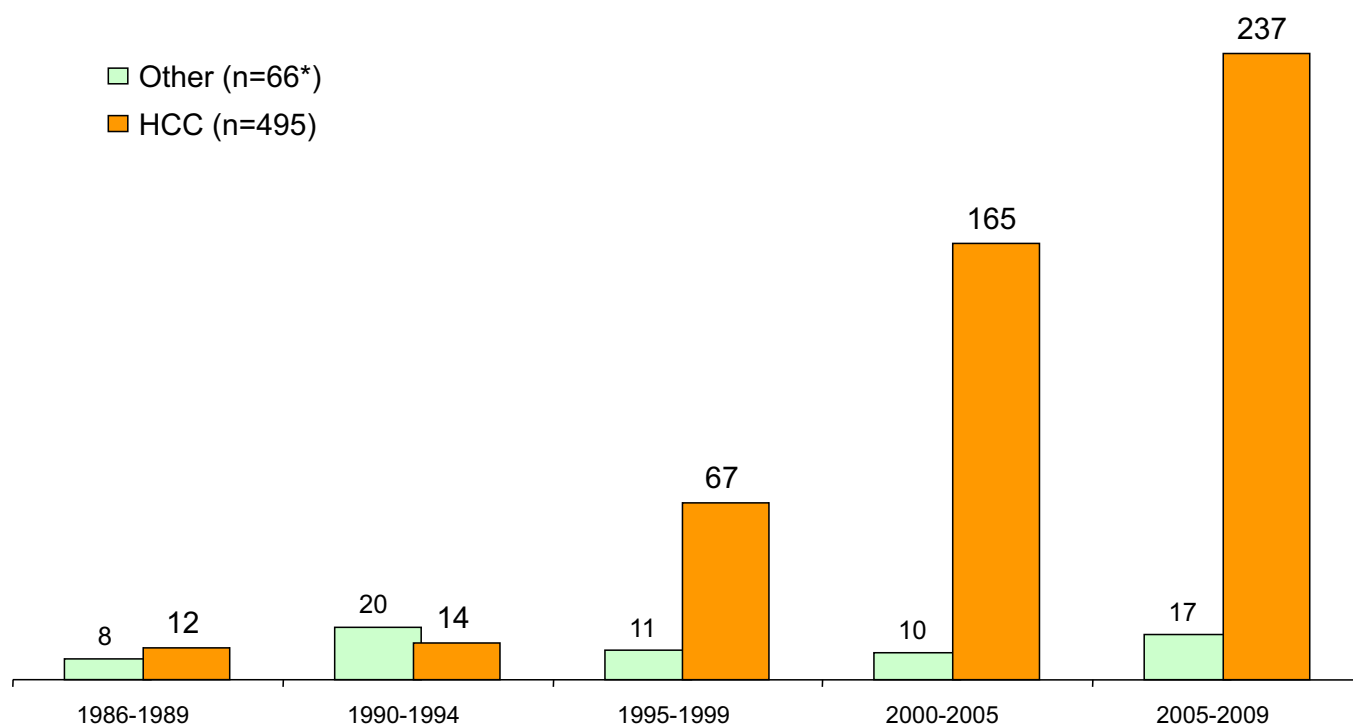
Benign Disease vs Pre Transplant Liver Malignancy

N=3277



Liver Cancer at Transplantation

N = 557/3277 (17%)



* 2 patients had 2 secondary cancers; 2 patients had a primary and secondary liver malignancy

De Novo Non Skin Cancer

N = 3277

m = median

n = 3277

	No	Male	Female	Age of pts (yrs)	Time to diagnosis (mths)	Died of This Cancer
Alimentary*	74	56	18	12.6 – 78 (m 58)	1 – 219 (m 57)	36 (47%)
Lymphoma*	62	40	22	1.5 – 70 (m 46)	1 – 183 (m 45)	25 (40%)
Genitourinary*	28	16	12	32– 75 (m 60)	2 – 225 (m 43)	4 (14%)
Breast	19	-	19	30 – 74.2 (m 50)	11 – 241 (m 89)	4 (21%)
Respiratory	18	14	4	4 – 72 (m 56)	13 – 212 (m 63)	13 (72%)
Kaposi's	5	4	1	32 – 65 (m 49)	2 – 48 (m 16)	0
Endocrine	5	2	3	36 – 70 (m 63)	47 – 144 (m 55)	2 (40%)
CNS	6	4	2	16.5 – 75 (m 65)	14 – 211 (m 121)	5 (83%)
Leukaemia	3	1	2	2.9 – 49.5 (m 37)	16 – 44 (m 30)	0
Miscellaneous	3	1	2	62 – 67 (m 64)	6 – 213 (m 60)	0
Total	*223 ca in 211 pts	138	85	1.5 – 78 (m 55)	1 – 241 (m 57)	89 (40% of pts with Ca)

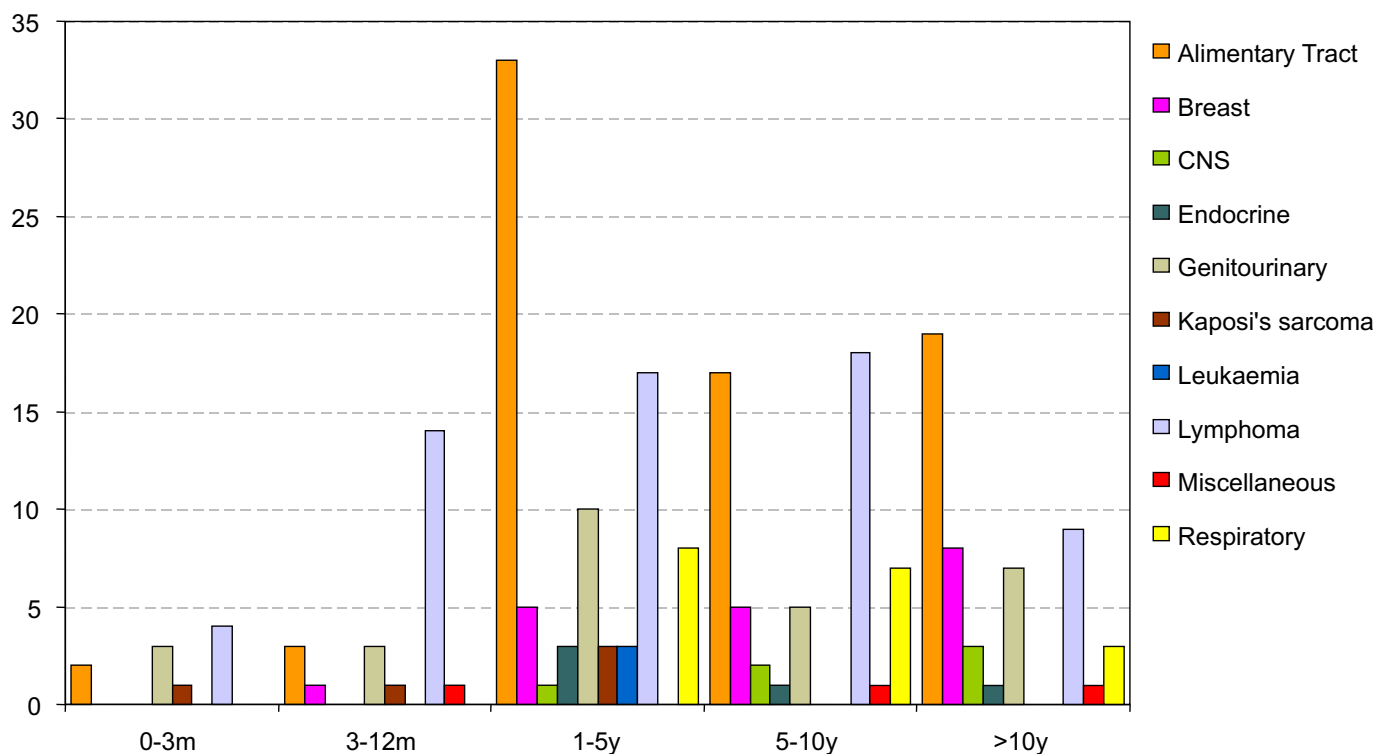
Thirty one pts with liver cancer at Tx developed non skin de novo cancer

* 12 patients had more than 1 de novo malignancies

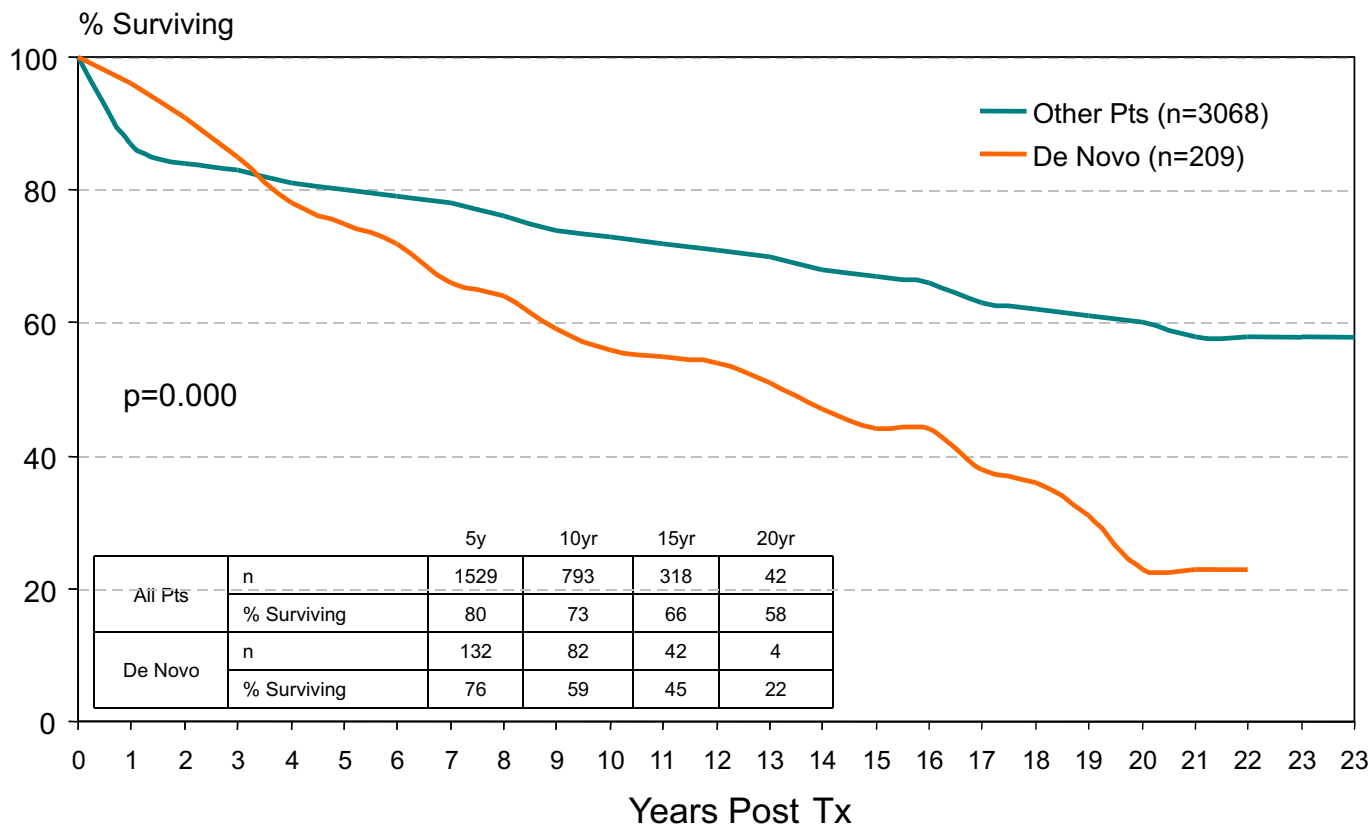
Time to De Novo Non Skin Cancer

N = 3277

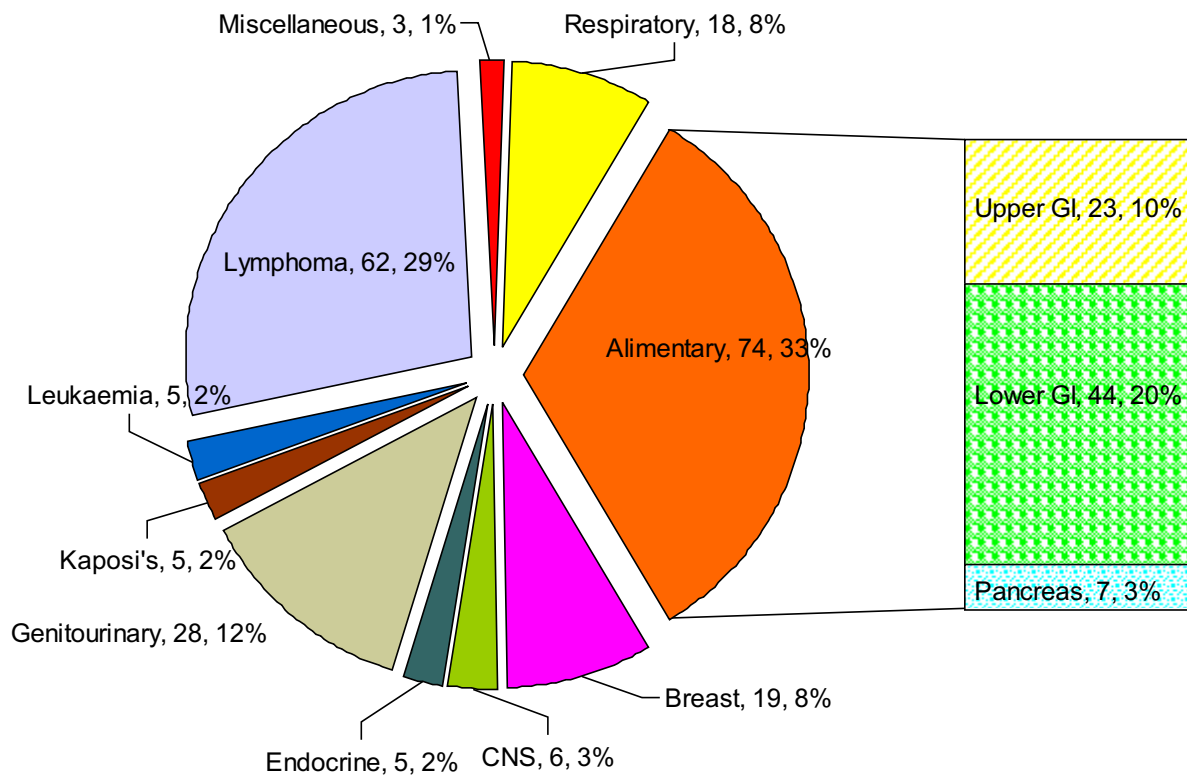
223 cancers in 209 pts (6% of all pts)



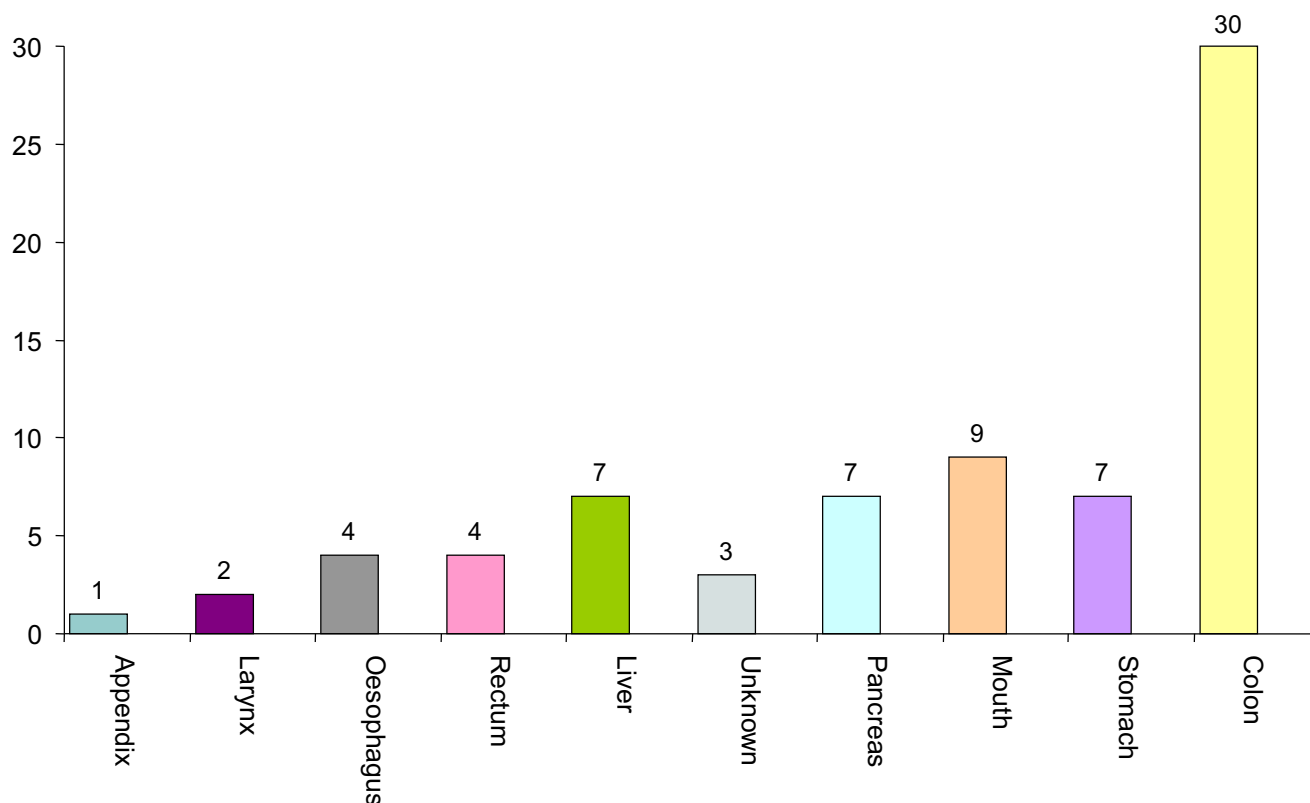
De Novo Non Skin Cancer vs All Patients N = 3277



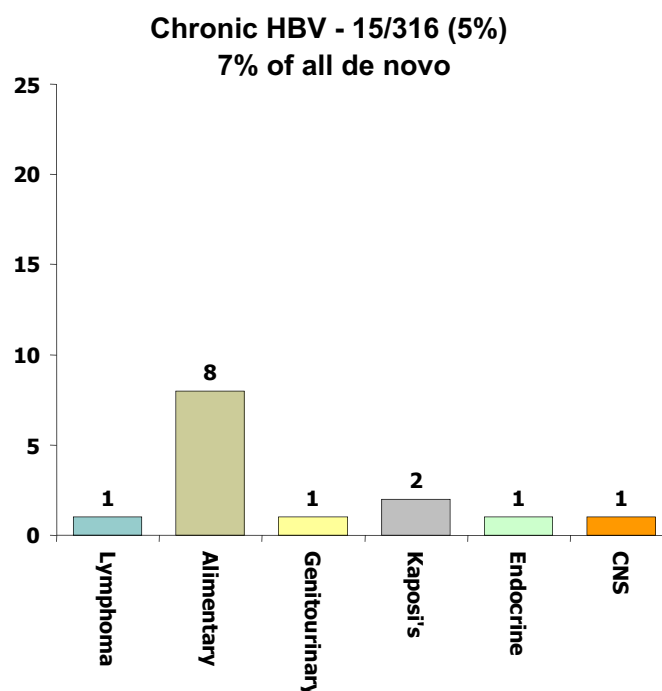
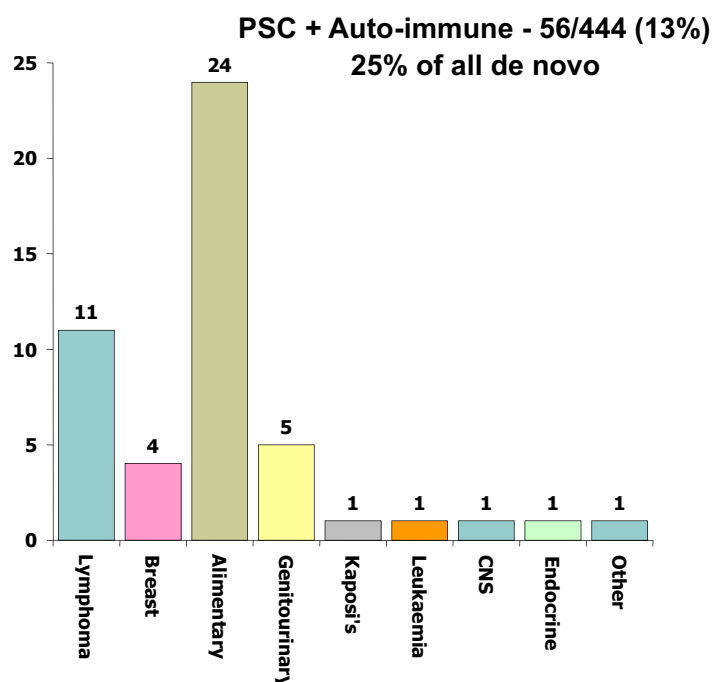
De Novo Non Skin Cancer n = 209/3277 (6%)



De Novo Non Skin Cancer Alimentary Tract Incidence n = 74/223 cancers (33%)

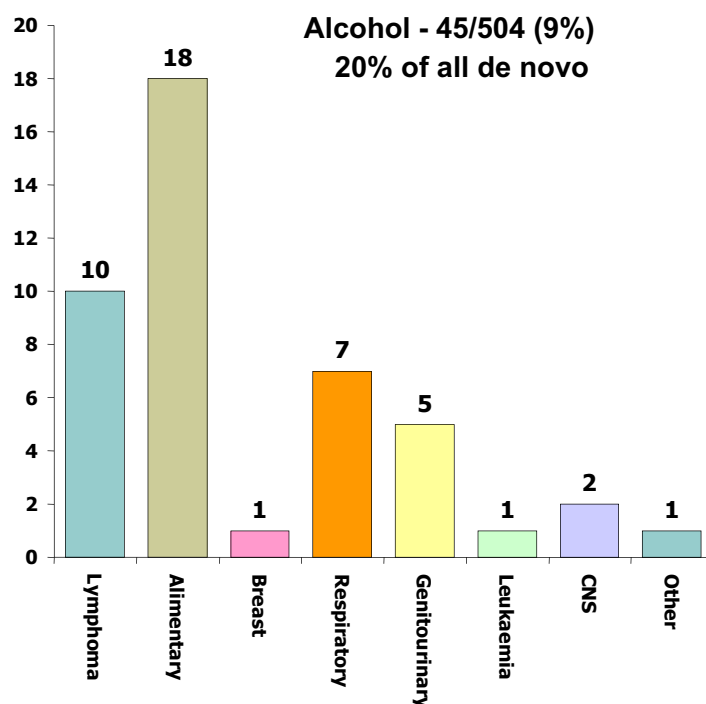
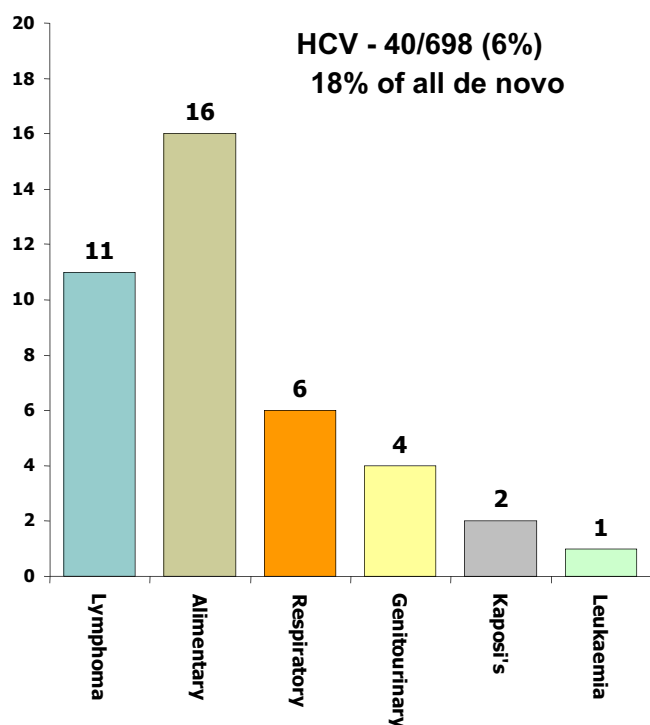


Pre Transplant Liver Disease and De Novo Non Skin Cancer n = 209/3277 pts (6%)



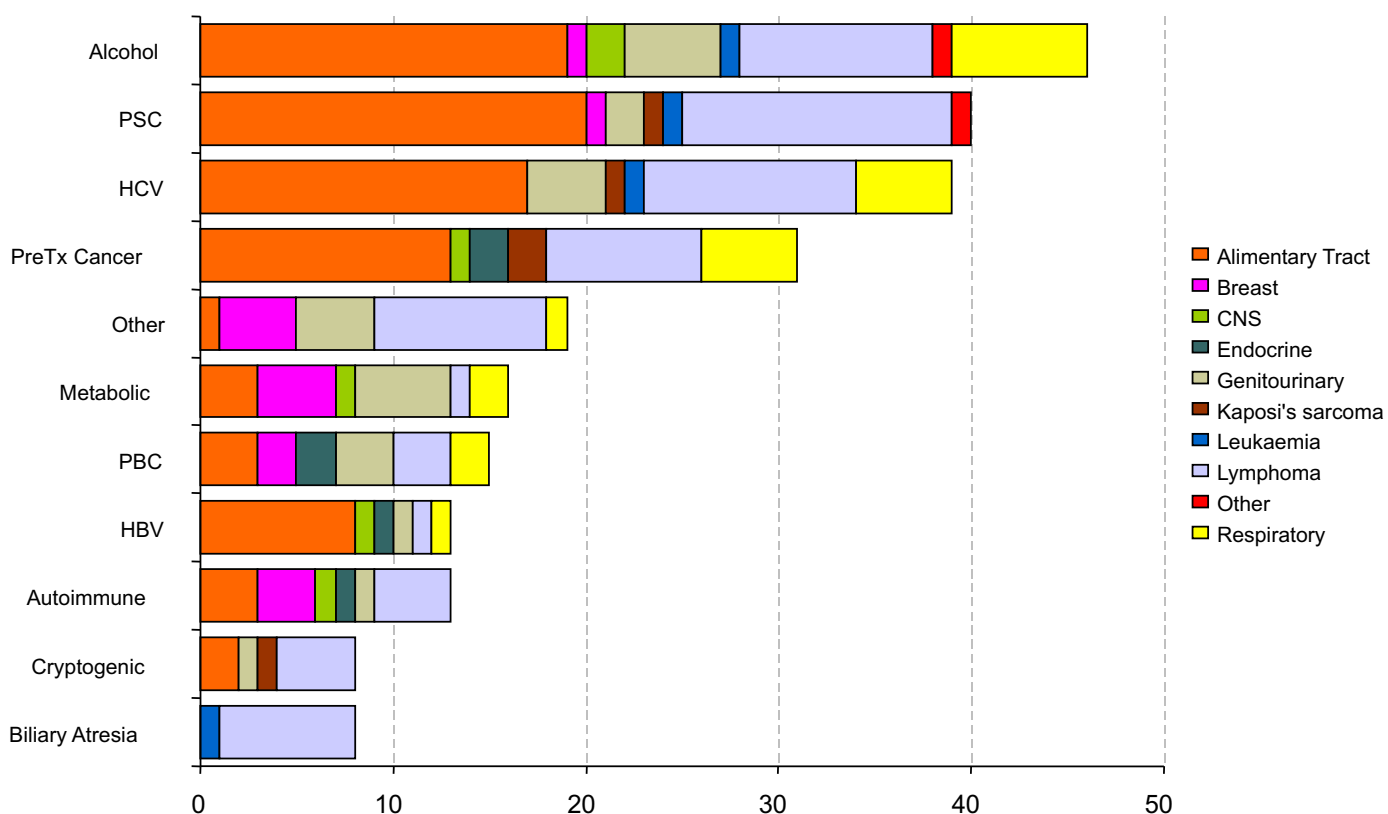
Pre Transplant Liver Disease and De Novo Non Skin Cancer

n = 209/3277 pts (6%)



Pre Transplant Liver Disease and De Novo Non Skin Cancer

n = 209/3277 pts (6%)



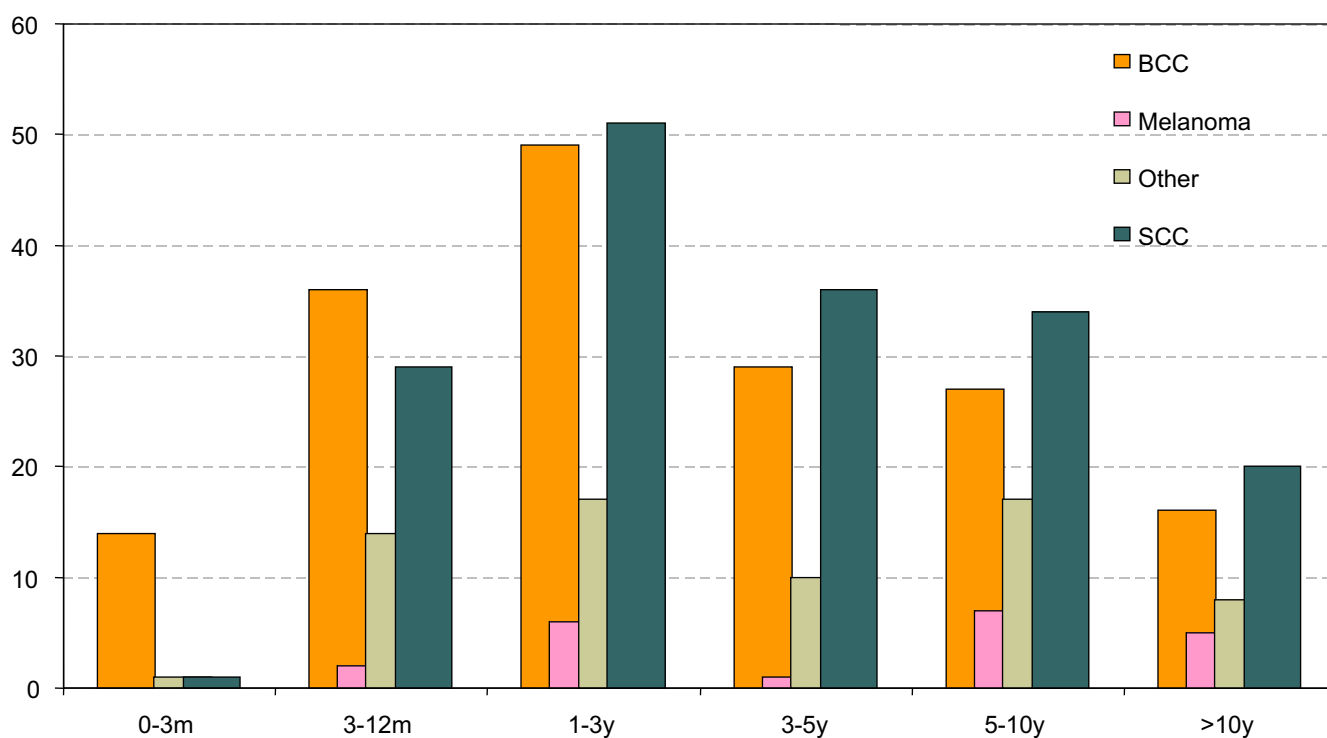
Type of Skin Cancer	Pts	Cancers
BCC	255	784
SCC	265	1130
Melanoma	21	21
Other	168	957
Total	414 (13% of all pts)**	2490

**** 186 pts had multiple skin cancer types**

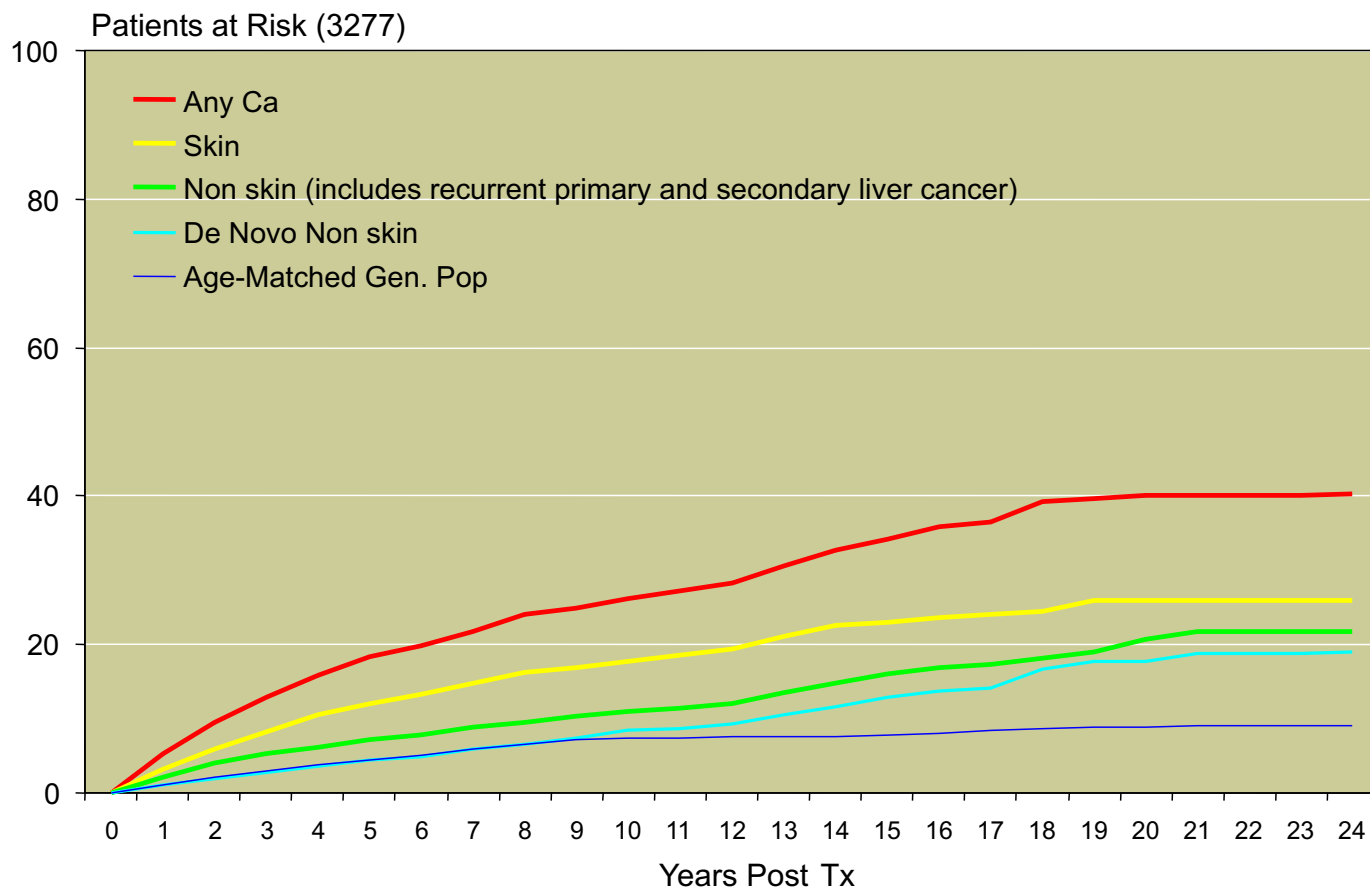
Time to 1st Skin Cancer Development

n = 3277

414 (13% of all pts)



Cumulative Risk of Diagnosis of Cancer Following Liver Transplant 1985-2009



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: anltu@cs.nsw.gov.au

<http://www.cs.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	
-1 Antitrypsin deficiency	31	43	74
Crigler-Najjar	5	1	6
Familial amyloid polyneuropathy	0	28	28
Glycogen storage disease	0	2	2
Haemochromatosis	2	25	27
Homozygous Hypercholesterolemia	4	1	5
Indian childhood cirrhosis	1	0	1
Other *	8	2	10
Primary hyperoxaluria	7	6	13
Tyrosinemia	4	0	4
Urea cycle disorders **	14	3	17
Wilsos disease	7	26	33
Total	83	137	220

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

** OTC deficiency 10; citrullinemia 4; argininosuccinic aciduria 3

Appendix III

ANZLTR PRIMARY Diagnosis - Other by Age Group

Primary Diagnosis	Age group		Total
	Child	Adult	
Alagille syndrome	25	2	27
Alagille non-syndromic	2	0	2
Benign liver tumour -Adenomatosis	0	2	2
Benign liver tumour-Hemangioma	0	2	2
Caroli's disease	1	13	14
Choledocal cyst	1	2	3
Cholestatic disease-Other	1	7	8
Chronic Budd Chiari	1	29	30
Congenital biliary fibrosis	2	3	5
Ductopenia	1	3	4
Granulomatous hepatitis / sarcoidosis	0	4	4
Histiocytosis X	4	0	4
Liver Trauma	0	1	1
Neonatal hepatitis	3	0	3
Nodular regenerative hyperplasia	0	6	6
Non alcoholic fatty liver (NAFLD or NASH)	0	47	47
Polycystic Liver disease	0	14	14
Polycystic liver and kidney disease	0	7	7
Progressive familial intrahepatic cholestasis(PFIC)	16	4	20
Secondary biliary cirrhosis	2	10	12
Secondary biliary cirrhosis - Hepatolithiasis	0	4	4
Secondary biliary cirrhosis - Cystic fibrosis	8	14	22
Other -specify #	3	17	20
Total	70	191	261

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

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	5	14	19
Acute - -1 -AAT	2	0	2
Acute Autoimmune hepatitis	0	7	7
Acute Unknown / unspecified	38	74	112
Acute -Paracetamol	0	12	12
Acute -Other drugs	2	16	18
Acute Herbs / mushrooms	0	5	5
Acute - Hepatitis A	0	2	2
Acute - Hepatitis B	0	47	47
Acute - NonA-NonB	4	12	16
Acute - Hepatitis E	0	1	1
Acute - Post liver resection	1	1	2
Subacute - Budd Chiari	0	1	1
Subacute - Wilson's	2	2	4
Subacute Autoimmune hepatitis	1	8	9
Subacute - Drug / Herbs	0	6	6
Subacute - Unknown / unspecified	3	31	34
Subacute - Hepatitis A	0	2	2
Subacute - Hepatitis B	0	10	10
Total	58	253	311

Appendix V

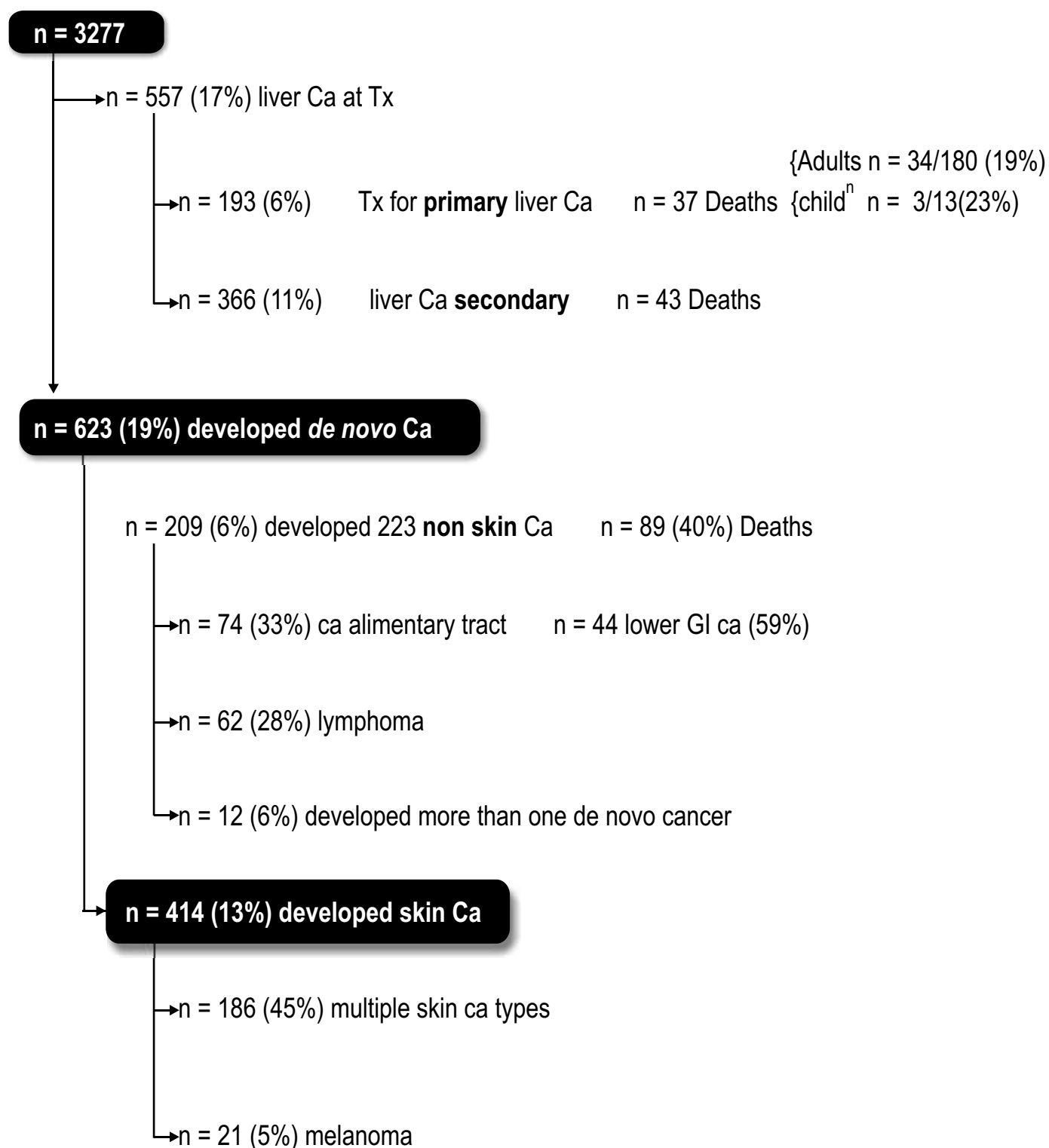
ANZLTR Causes of Patient death

<u>Graft failure - other</u>		
Vascular thrombosis		18
Hepatic artery	10	
Portal vein	7	
Hepatic vein	1	
Non thrombotic infarction		3
Primary non function		20
Massive haemorrhagic necrosis		4
Recurrent disease (ALD, PSC, CAH:AI)		10
De novo Hep C		3
Biliary Complications		11
Other (PNC, immune hepatitis, outflow obstruction)		9
<u>Miscellaneous</u>		
Multiorgan failure		29
Renal Failure		21
Graft vs Host disease		6
Social (accident, suicide, non-compliance, Rx withdrawn)		11
Sudden death (cause unknown)		19
Other (Hyperkalaemia, motor neurone disease diabetes complications, drug reaction, progression FAP)		10

Appendix VI

SUMMARY

Cancer in Liver Transplant Recipients



Cumulative risk of diagnosis of any cancer twenty years post transplant is 40%