AUSTRALIA & NEW ZEALAND

LIVER TRANSPLANT REGISTRY

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

DATA TO 31-12-2008

COORDINATING CENTRE

ANZLT Registry
Princess Alexandra Hospital
Ipswich Rd
WOOLLOONGABBA, QLD, 4102

www.anzltr.org

Professor Stephen Lynch — Editor
Ms Glenda Balderson — Editor/Liaison Officer
Ms Debra Cormack — Graphics

Phone (61-7) 3240 2385 — G.Balderson
Fax (61-7) 3240 2999 — G.Balderson

Email Glenda_Balderson@health.qld.gov.au

MANAGEMENT COMMITTEE

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STATISTICAL METHODS

Kaplan-Meier survival curves have been produced using SPSS® for Windows™ Release 17.0, 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.

Director: Professor G.W McCaughan
All queries to: Dr Deborah Verran — Email deborah@email.cs.nsw.gov.au

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Preface

We are pleased to present the 20th Report of the Australia and New Zealand Liver Transplant Registry (ANZLTR). This report contains data to the 31st December 2008 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 now has financial support and we are grateful to the Australian Government, formerly through the Department of Health and Aging [DHA], and more recently the Australian Organ and Tissue Donation and Transplantation Authority, for their financial contribution. Recent additional support from the DHA is allowing expansion of the information collected in the data base and we look forward to incorporating the new data in future reports.

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 2008, 3305 orthotopic liver transplants (OLT) were performed in Australia and New Zealand on 3066 patients, 2516 adult patients (> 15 years) [82%] and 550 children [18%]. The median age of all recipients was 46.6 years. The ages ranged from 24 days to 73.1 years. There is a significant difference in gender distribution between children (M=46%) and adults (M=63%)

6. There was a marked increase in the total number of new patients transplanted in 2008 compared with 2007 with 217 new patients being the highest number yet reached.

7. The trend to increasing age of adult recipients in recent years continued and the overall adult median age is now 49.4 years. The median age of new adult recipients in 2005-08 was 51.8 years.

8-9. 2008 was also a record year for transplants with 229 performed. Split grafts continue to make a significant contribution to the total number of paediatric transplants performed providing 18 of 37 [50%] grafts in 2008 and 129 of 629 [21%] overall. In children, other reduced size grafts have been used in 303 [49%] cases including 31 living donor grafts. One child has been treated with liver cell implantation. Of adult patients, 176 have received reduced size grafts - 141 split liver grafts (including 1 as auxiliary graft), 26 other reduced size grafts (1 as auxiliary graft) and 9 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 20% 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 6 new patients transplanted in 2008 (Appendix III).

12-14. The number of adult patients transplanted with a primary diagnosis of chronic viral Hepatitis B, C or B/C/D remained static in 2005-08 compared with the previous era - 2000-04, 35% primary diagnosis CVH [25% Hepatitis C, 8% Hepatitis B and 2% Hepatitis B,C,D]; in 2005 -08, 34% primary diagnosis CVH [27% Hep C,4% Hep B, 2% Hep B/C/D]. 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 2008 was 44%.

15. Current 1 year patient survival of all patients is 88% at 1 year, 80% at 8 years and 71% at 10 years. Children had a significantly better survival rate then adults.

16. Whilst older children had superior early survival then 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 survivals in 2005-08 cohort is 93% for all patients [95% for children, 92% for adults].

19. The type of primary graft, (whole , reduced or split liver), had no effect on patient survival in either children or adults.

20. Children weighing < 8 kg at the time of transplant had inferior early survival compared to heavier patients.

21. Adult patients transplanted for biliary atresia 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 70%.

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.

Summary

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-nine 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.

29. There was an increase in the in number of cadaveric donors in 2008 resulting in a record number of transplants from deceased donors. The number of transplantable grafts was increased by splitting 14 deceased donor grafts and using livers donated after cardiac death [4 in 2008]. As a result the number of people on the waiting list at 31 December 2008 fell as compared with 2007 when the number on the waiting list at 31 December 2007 had exceeded the total number of transplants performed in 2007.

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 65 years.

31. Forty patients [31 children, 9 adults] have now received a living donor graft with 10 performed in 2008. Thirty-seven were transplanted as a primary graft , 2 as second and 1 as a third graft. The median age of the donors was 35.3 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 with 164 patients awaiting a transplant at the end of 2008 compared with 199 at 31st December 2007. Delistings due to death, becoming too ill or tumour (HCC) progression were increased to 14%. Thirty-seven patients were listed as urgent in 2008 [13 Category 1 and 24 Category 2]. In 2008 only 46% of patients listed urgently as Category 1 had a positive outcome compared with 83% listed as Category 2 who received a timely transplant

33-34 Waiting times continue to increase with some patients waiting years to receive a graft. Blood group O patients tend to have the longest waiting times.

35 A flow diagram of cancer in liver transplant recipients can be seen in Appendix VI. Of the 3066 patients who have undergone liver transplantation, 488 (16%) had a liver cancer at transplantation 161 (5%) patients were transplanted for liver malignancy (Primary), 150 (93%) were adults and 11 (7%) children. Of these 161 patients 33 (22%) adults and 2 (18%) children died from their malignancy. Hepatocellular carcinoma [HCC] was the predominant primary cancer in adults, hepatoblastoma in children.Three hundred and twenty eight (11%) patients had 329 liver cancers as an incidental (Secondary) diagnosis. Five hundred and forty nine (18%) patients developed either non skin [179] or skin cancer [370] *(de novo)* post transplant - 91 (3%) of patients developed multiple types; 10 (2%) patients developed non skin malignancy within 90 days of transplant; 19 patients with pre transplant cancer developed a *de novo* cancer post transplant; in 2 patients the cancer was of donor origin.

36-38 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 2005-08.

39-42 HCC was the predominant diagnosis for liver cancers as a secondary diagnosis. Longer term survival overall was poor particularly for patients with cholangiocarcinoma. The incidence of liver cancer as a secondary diagnosis has increased in the last decade. Patients with any pre-transplant liver malignancy have significantly worse survival then patients transplanted with benign diseases.

42-43 *De novo* non skin cancers (188) have developed in 179 (6%) patients and 69 [39%] have died from this cancer. Cancers of the alimentary tract (59, 33%) and lymphoma (58, 32%) predominate. Patients with *de novo* non skin cancers have significantly worse long term survival.

44 Lower GI cancers (35) account for 59% of alimentary tract cancers.

45-46 The incidence of *de novo* non skin cancers varies according to pre transplant liver disease, with the incidence in patients with primary sclerosing cholangitis [PSC] and autoimmune hepatitis being statistically significant ($p<0.0001$).

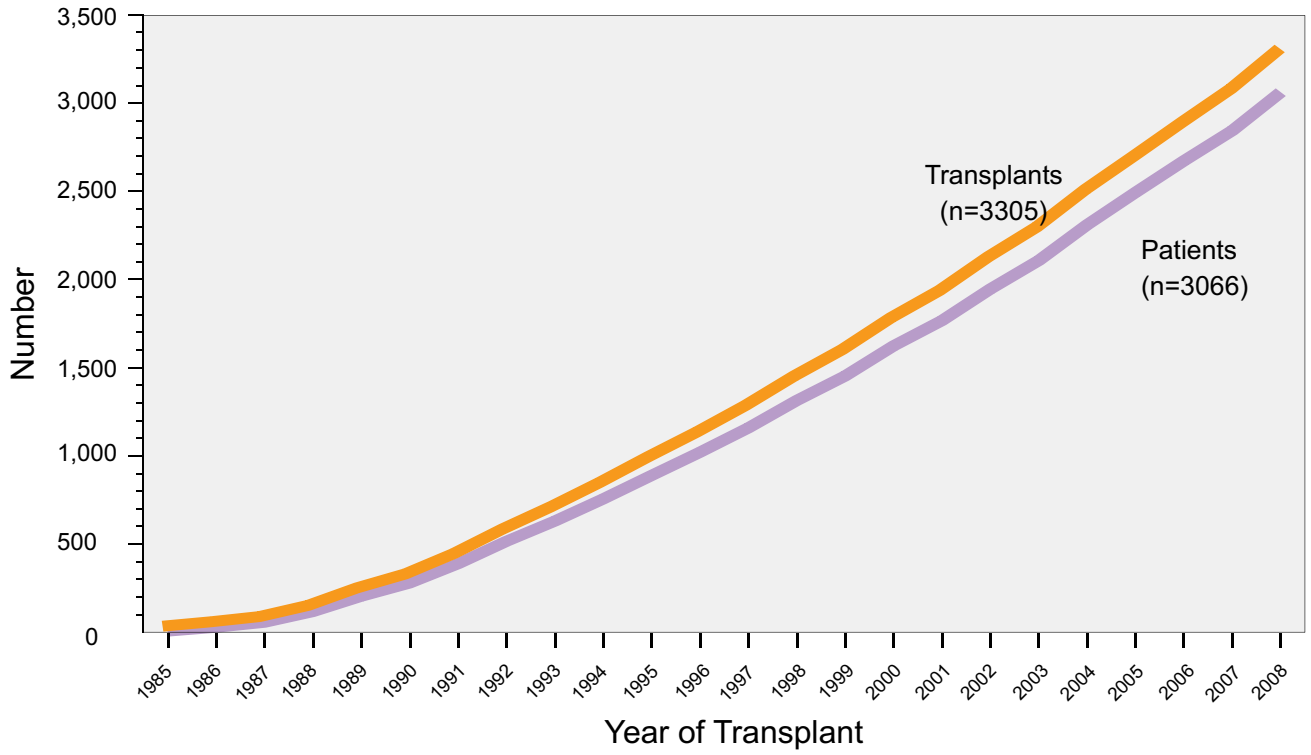
46-47 Three hundred and seventy (12%) patients have developed 2490 skin cancers with 163 patients having multiple skin cancer types and 16 (4%) developing melanoma.

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

Section 1

Demographic Data

Cumulative Number of Patients & Transplants

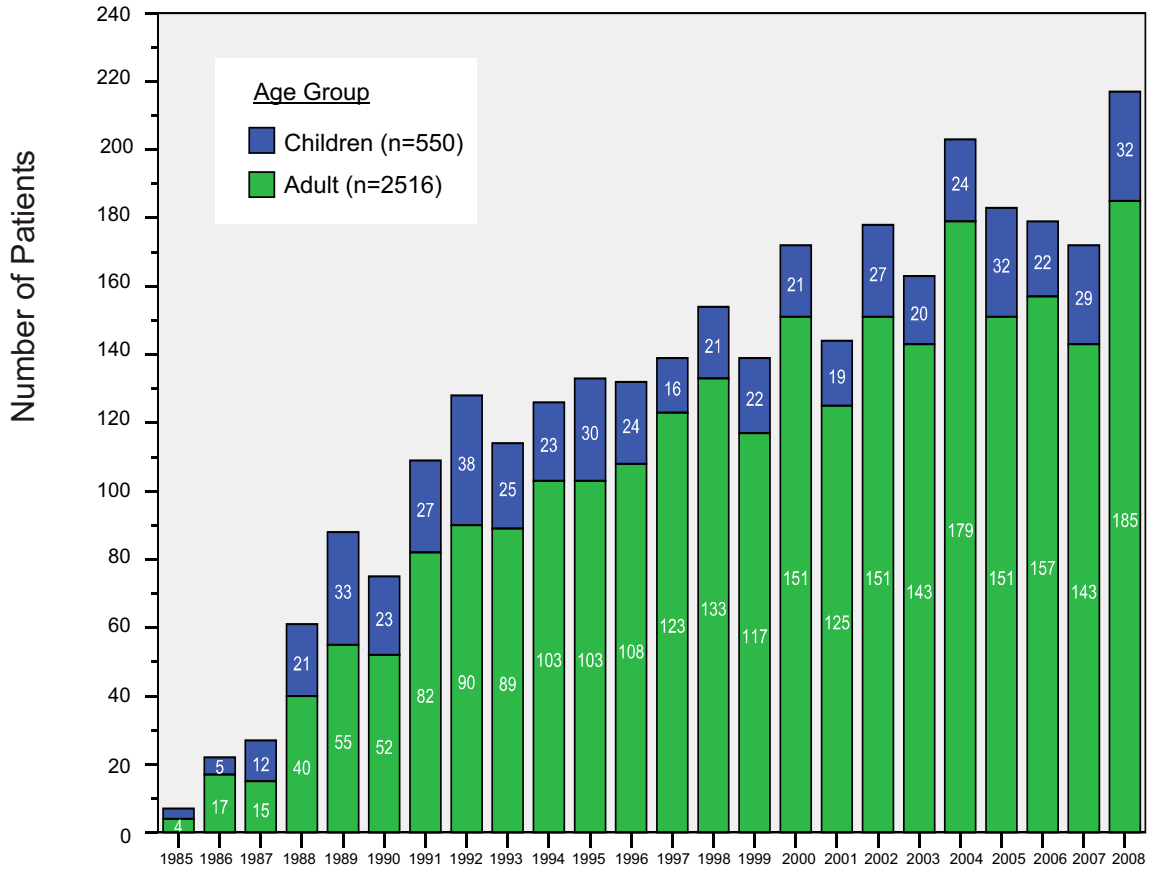


Summary Statistics - Age and Gender

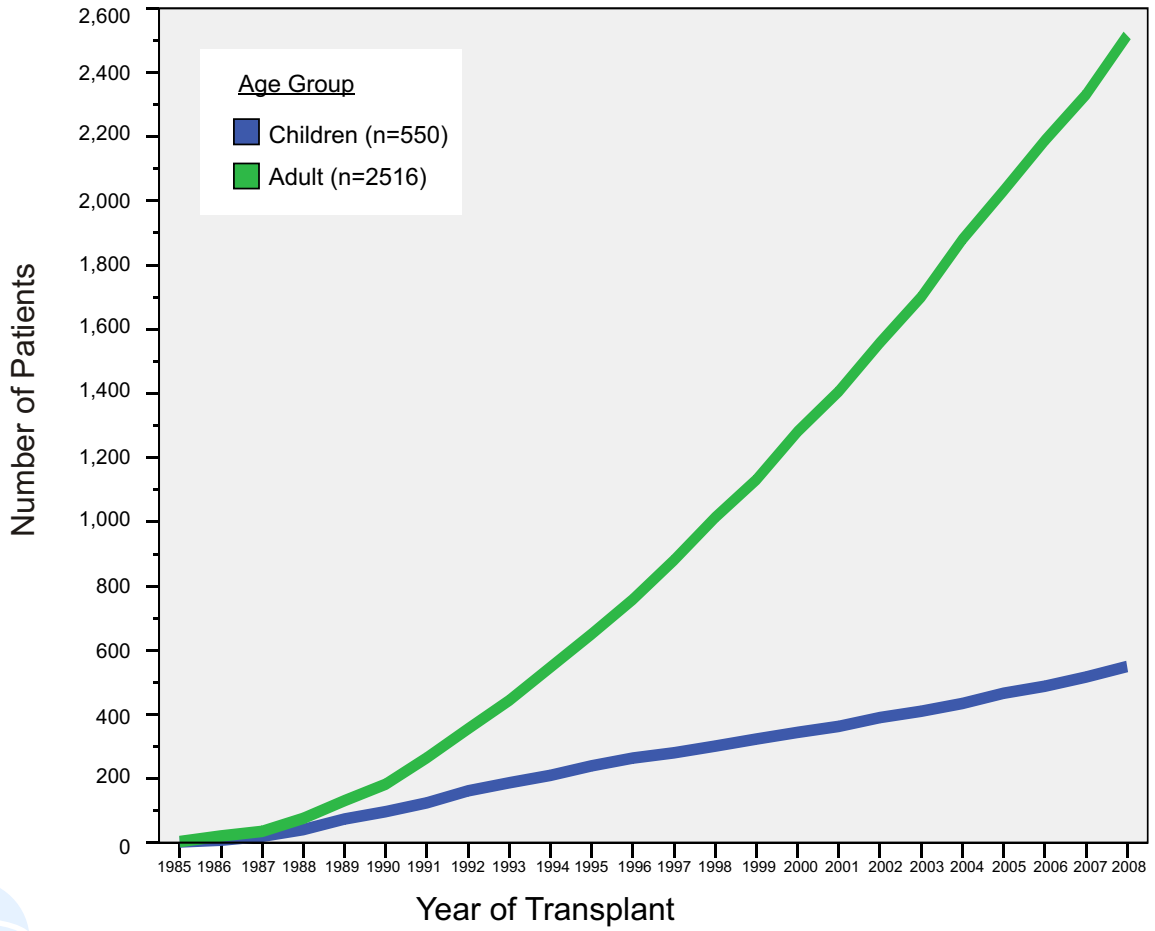
ALL PATIENTS TRANSPLANTED

	Children [<15y]	**Adults**	**Total**
Patients	550	2516	3066
Age			
Mean ± SD	4.3 ± 4.2y	47.5 ± 11.8y	39.8 ± 19.8y
Median	2.3y	49.4y	46.6y
Range	24d -14.9y	15.0 - 73.1y	24d - 73.1y
Gender			
Female	294 (54%)	932 (37%)	1226 (40%)
Male	256 (46%)	1584 (63%)	1840 (60%)
Surviving	435 (79%)	1837 (73%)	2271 (74%)

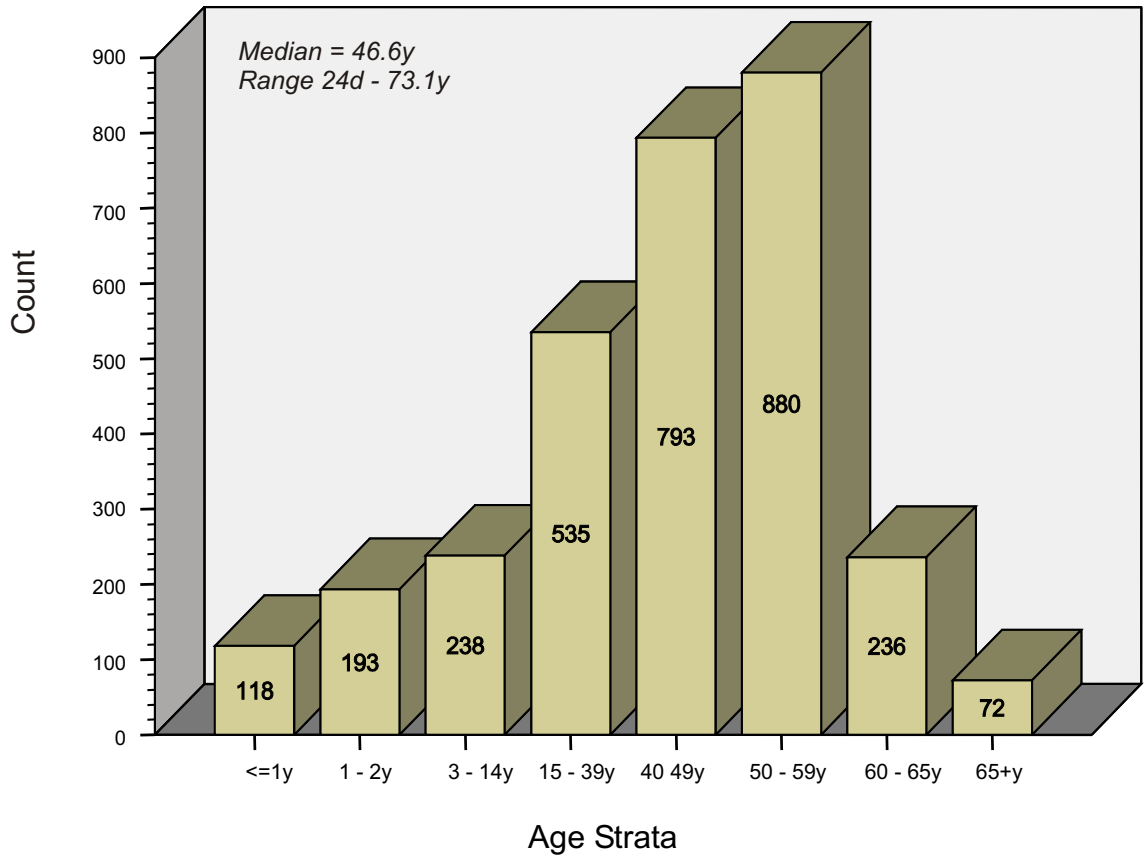
Number of New Patients Transplanted by Year



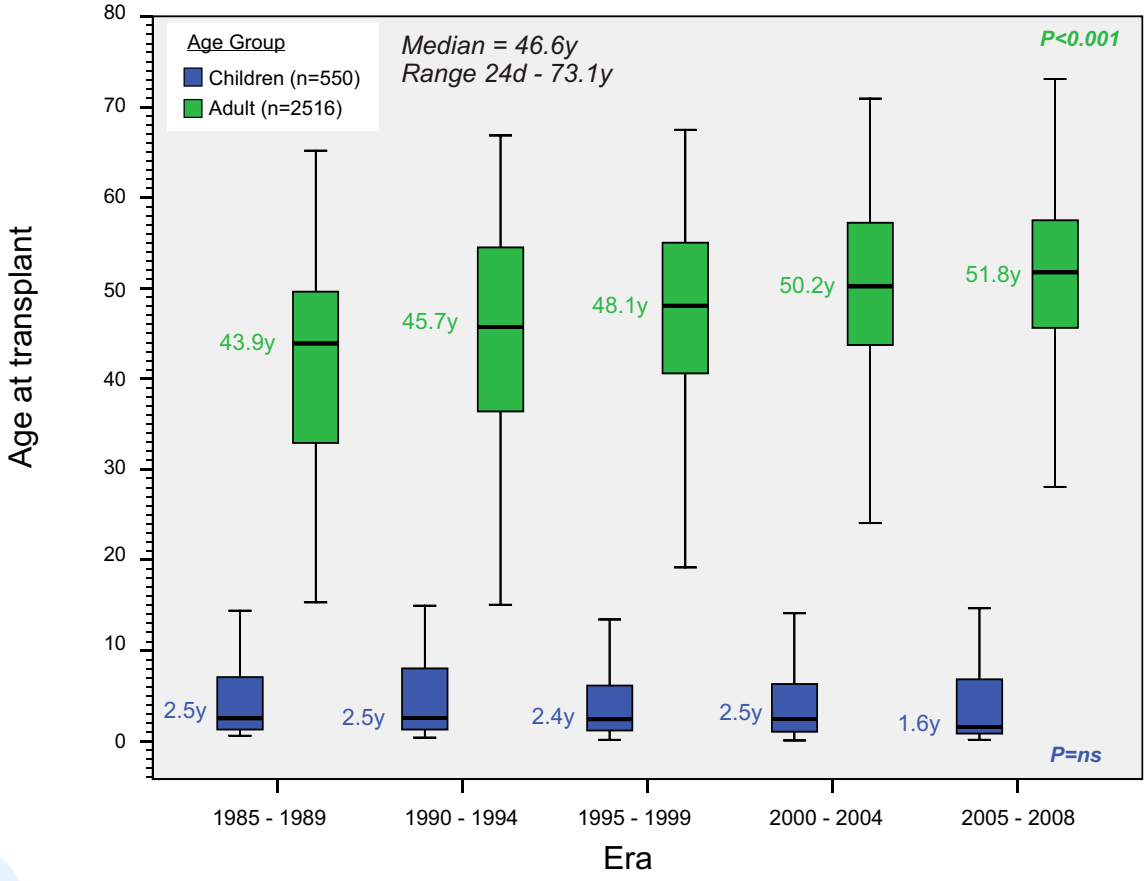
Cumulative Number of New Patients Transplanted



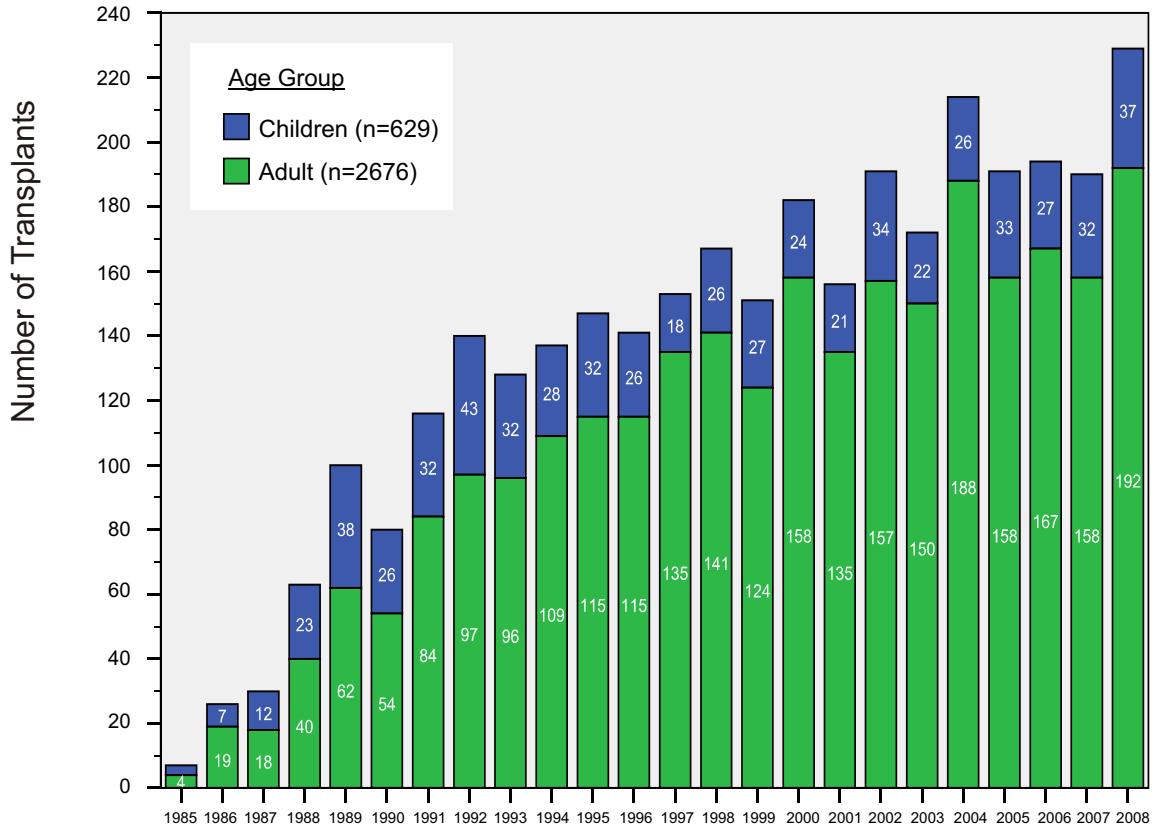
Number of Recipients By Age at Primary Transplant N=3066



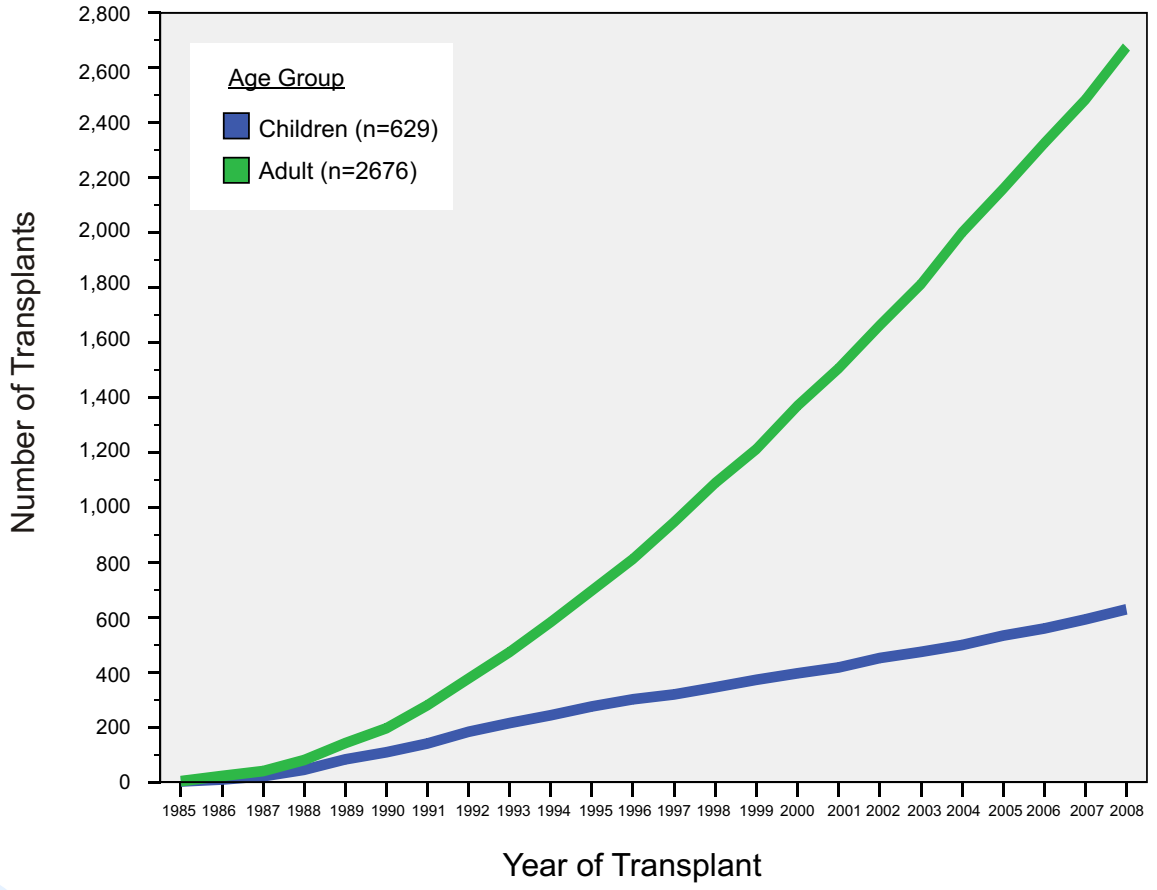
Age at Primary Transplant by Era



Number of Transplants by Year

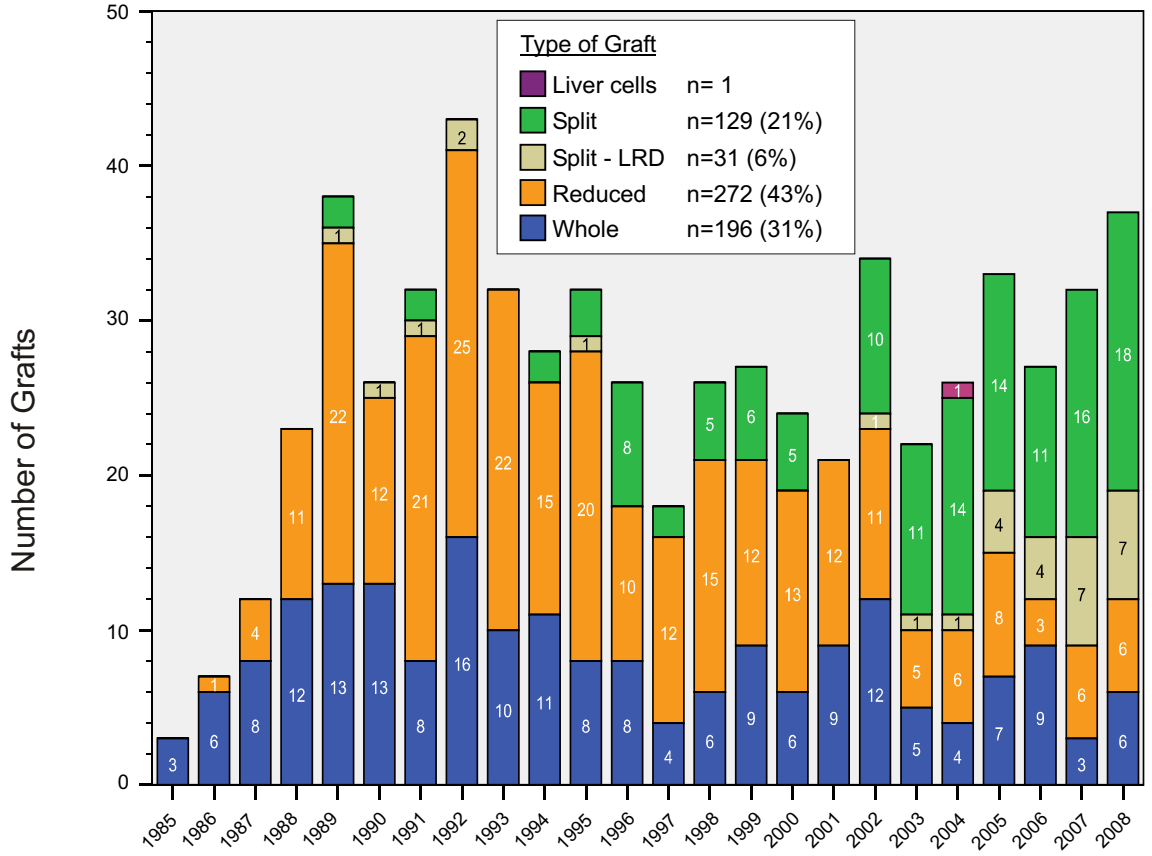


Cumulative Number of Transplants

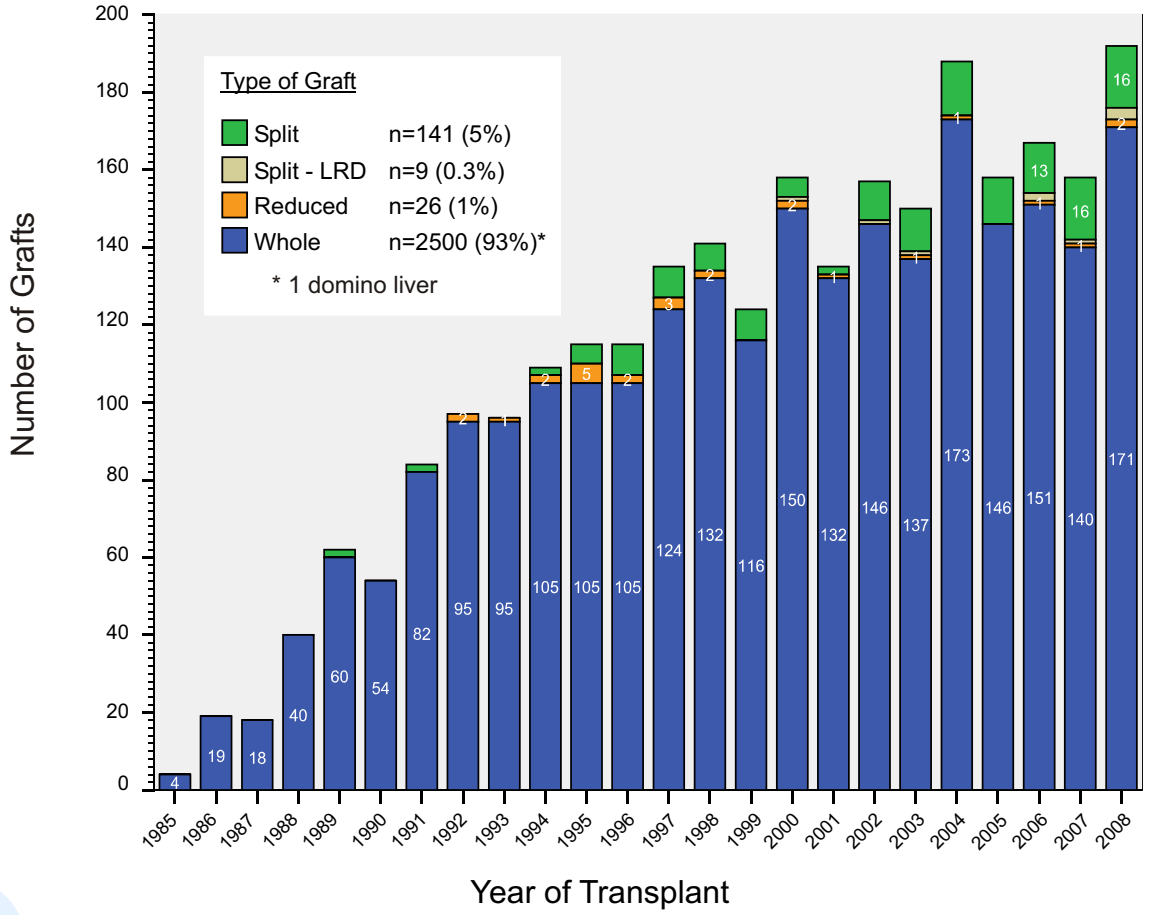


Type of Graft by Year
Split vs Reduced vs Whole

Children (n = 629)

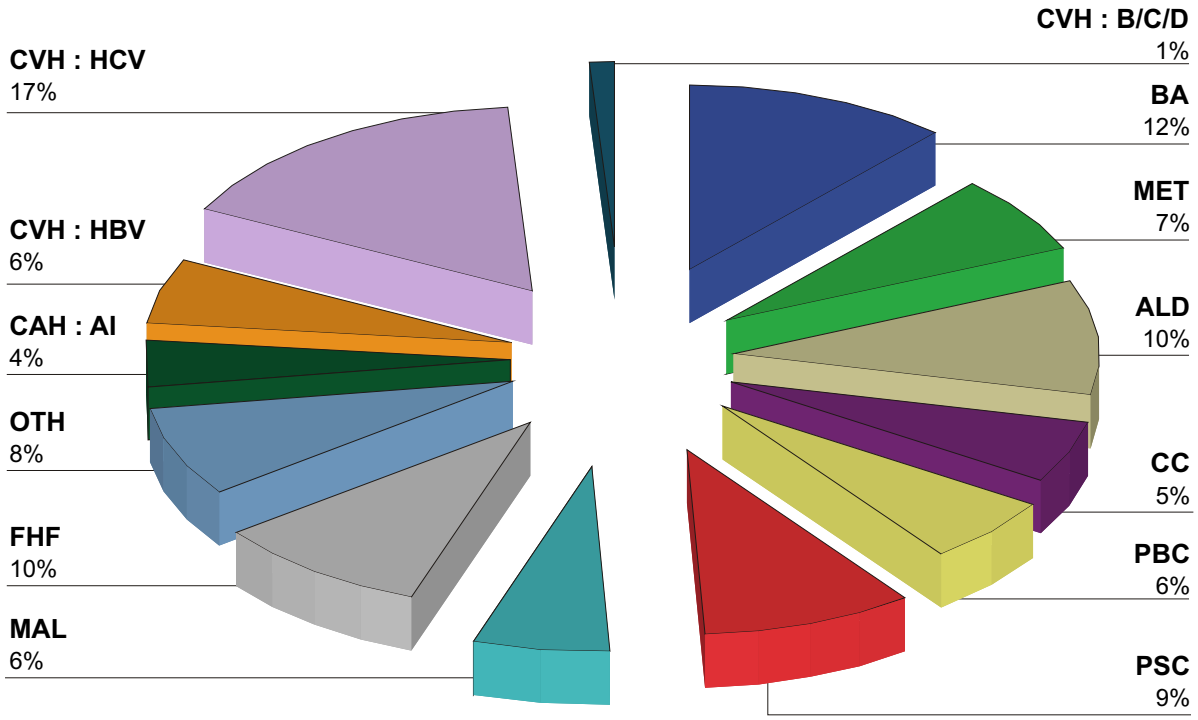


Adults (n = 2676)



Section 2

Primary Diagnosis

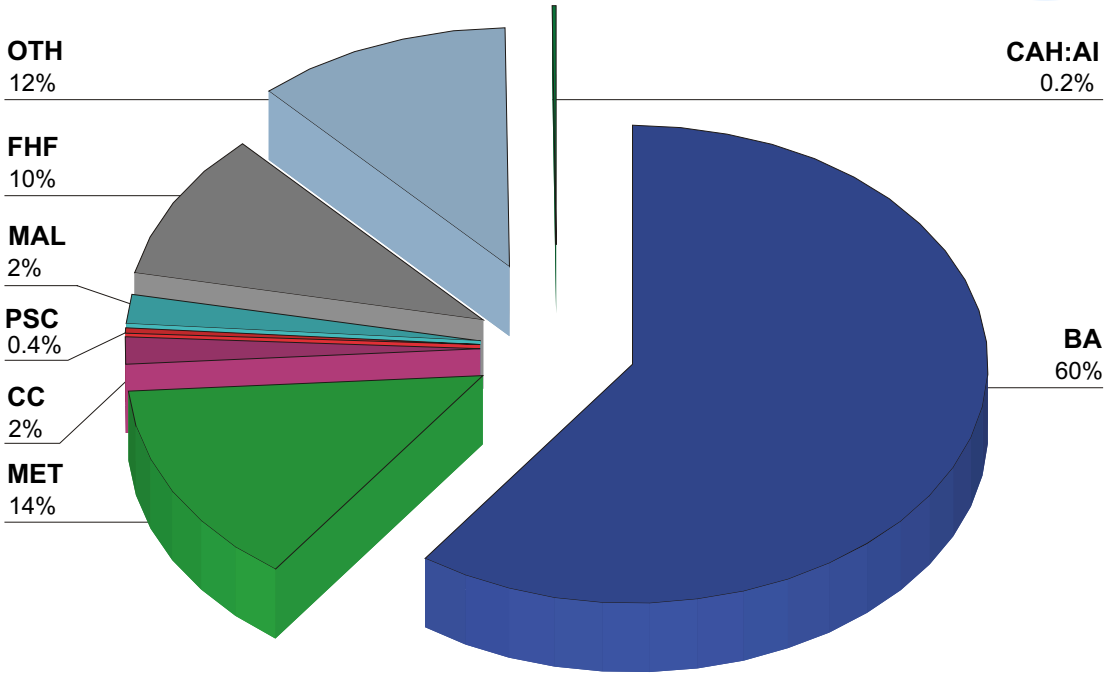


Diagnosis Group

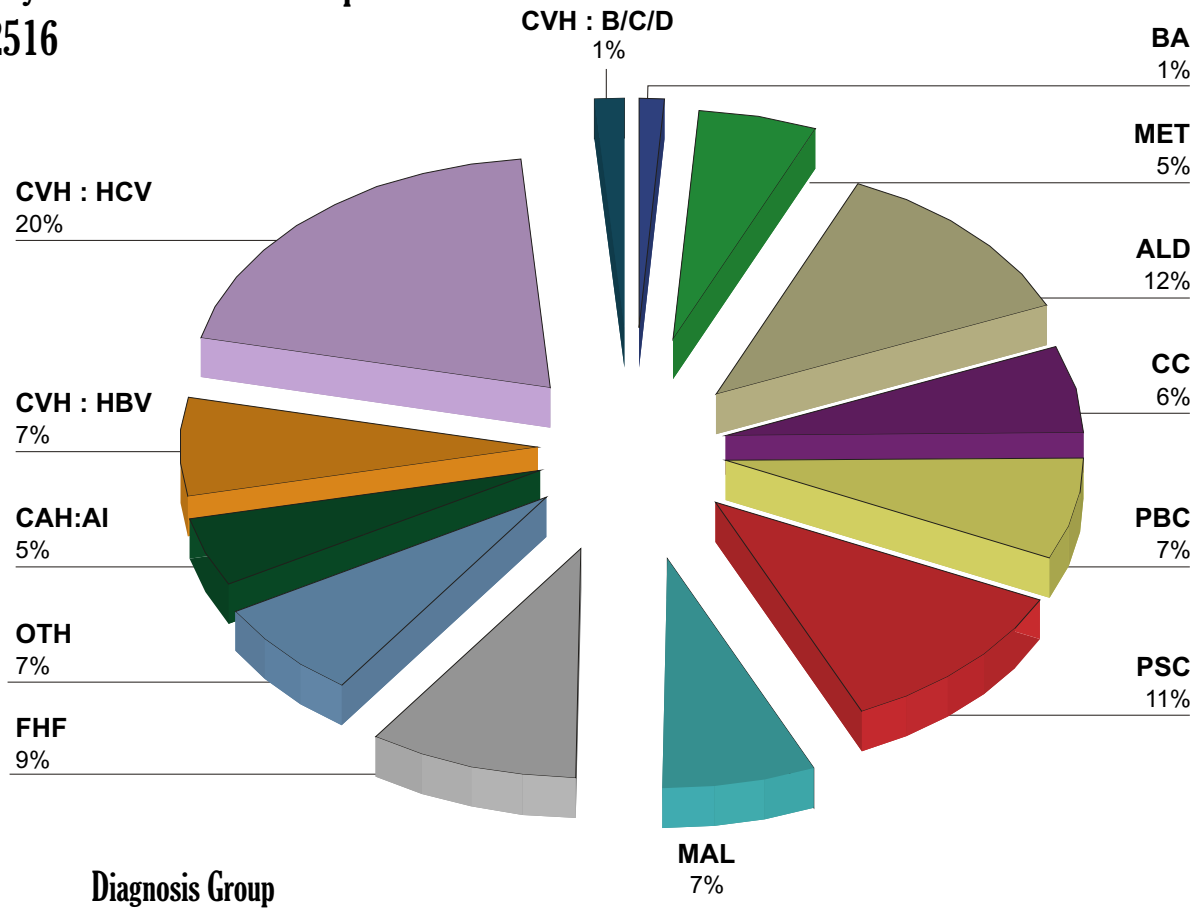
BA	- Biliary atresia
MET	- Metabolic diseases*
ALD	- Alcoholic cirrhosis
CC	- Cryptogenic cirrhosis
PBC	- Primary biliary cirrhosis
PSC	- Primary sclerosing cholangitis
MAL	- Malignancy
FHF	- Fulminant hepatic failure*
OTH	- Other diseases*
CAH : AI	- Chronic active hepatitis [autoimmune]
CVH : HBV	- 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 = 549



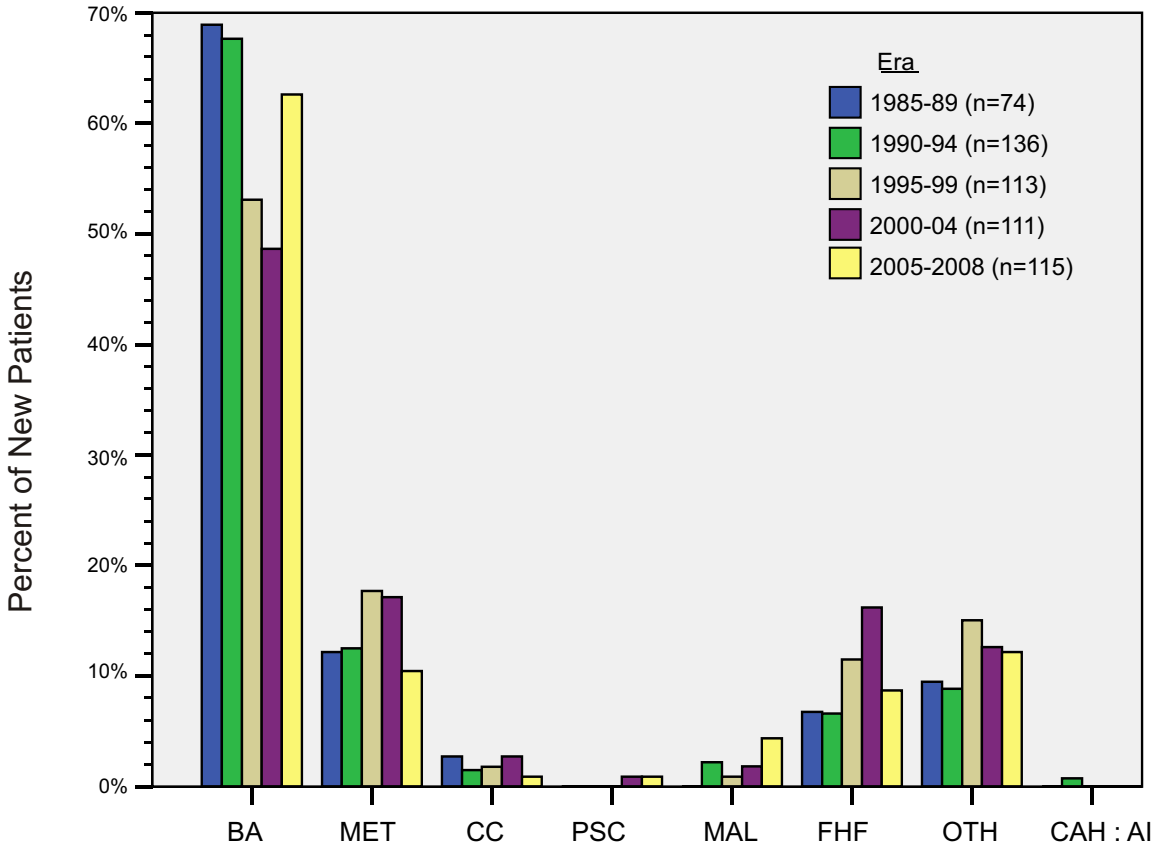
Primary Diseases of Adult Recipients
n = 2516



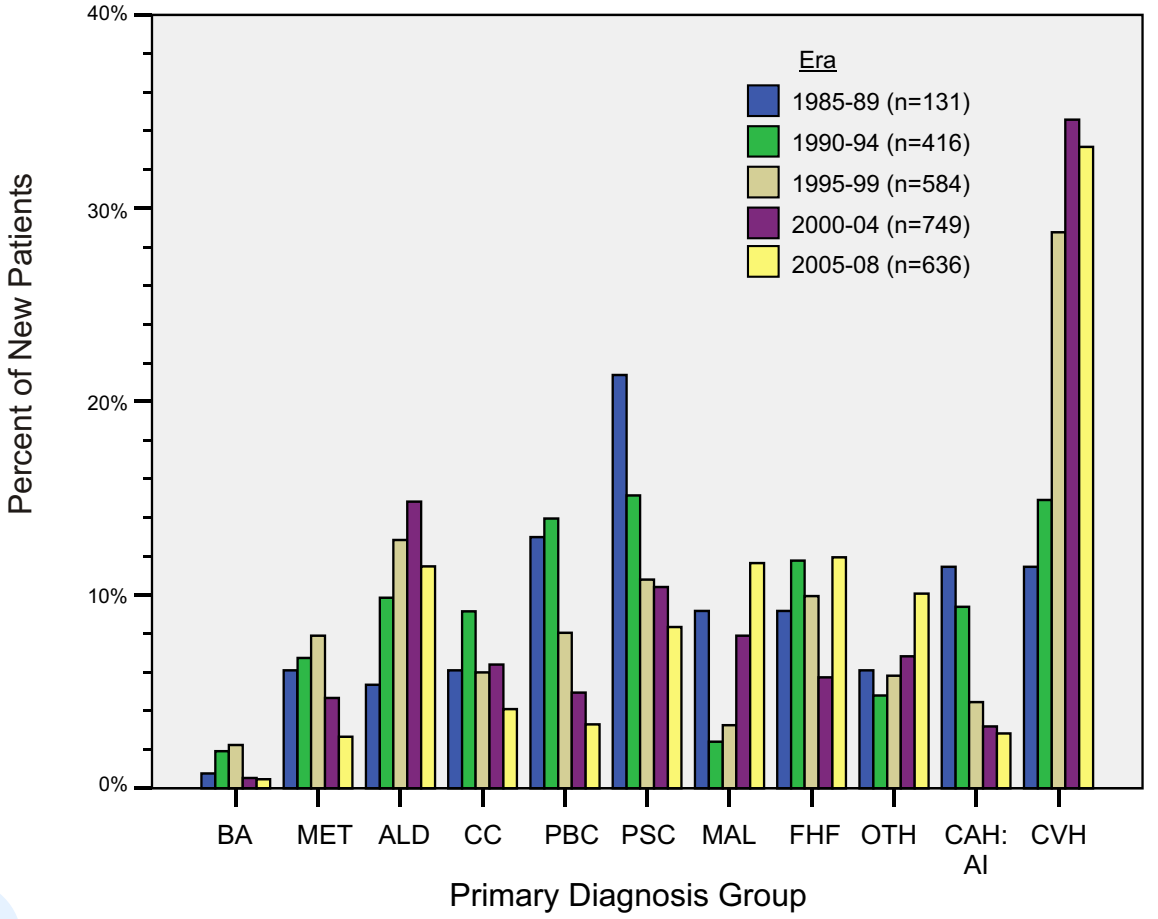
Diagnosis Group

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

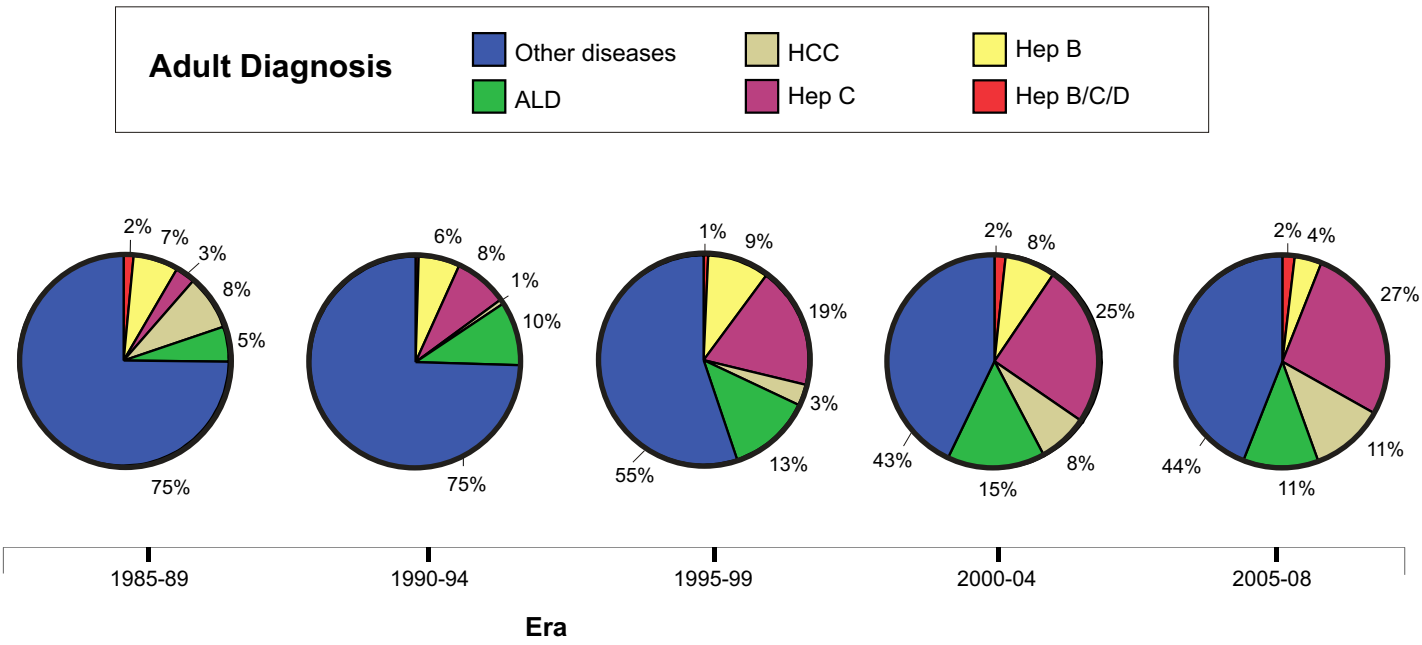
Children (n=549)



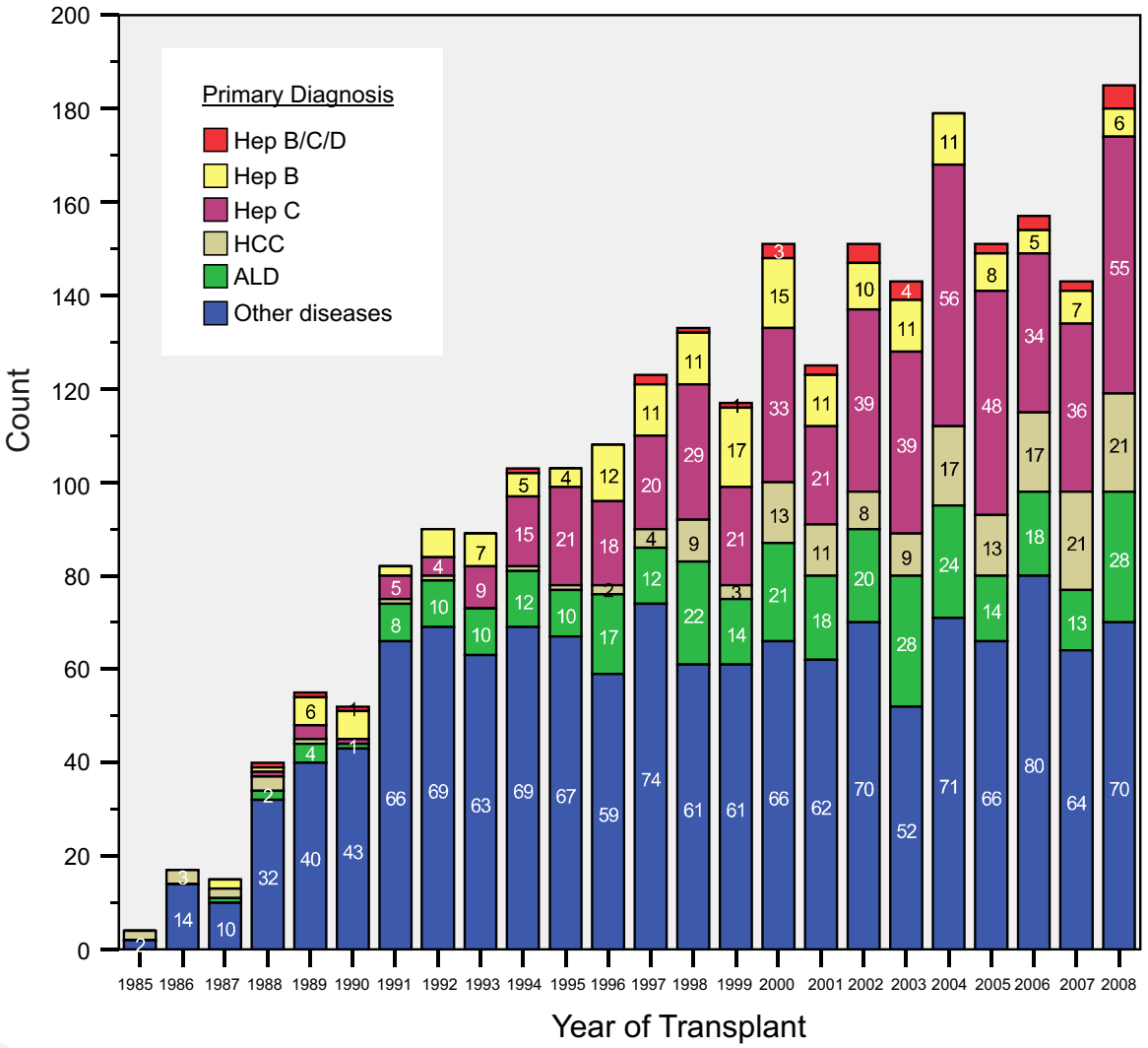
Adults (n = 2516)



Adult Primary Diagnosis by Era



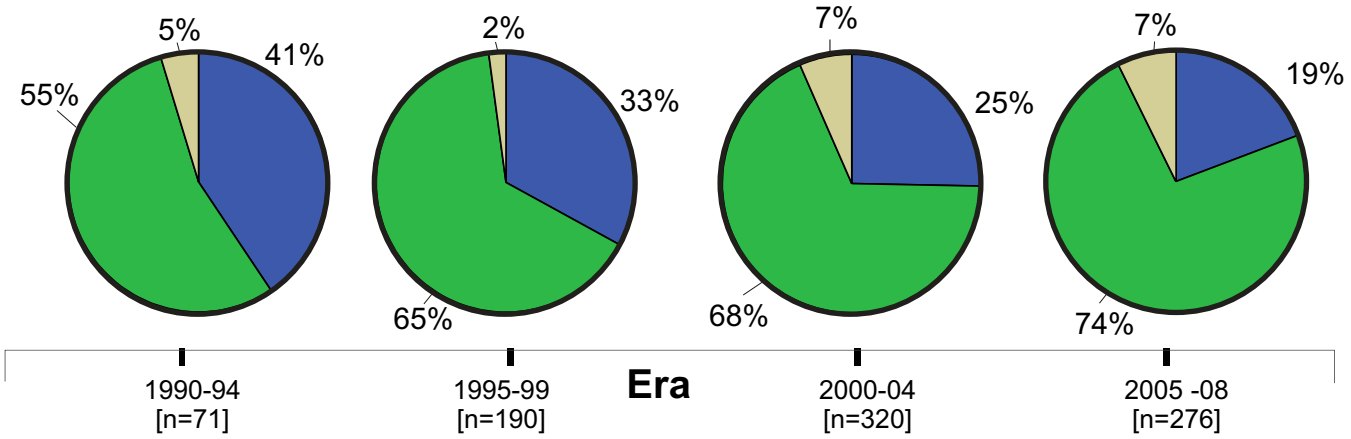
Adult Primary Diagnosis by Year



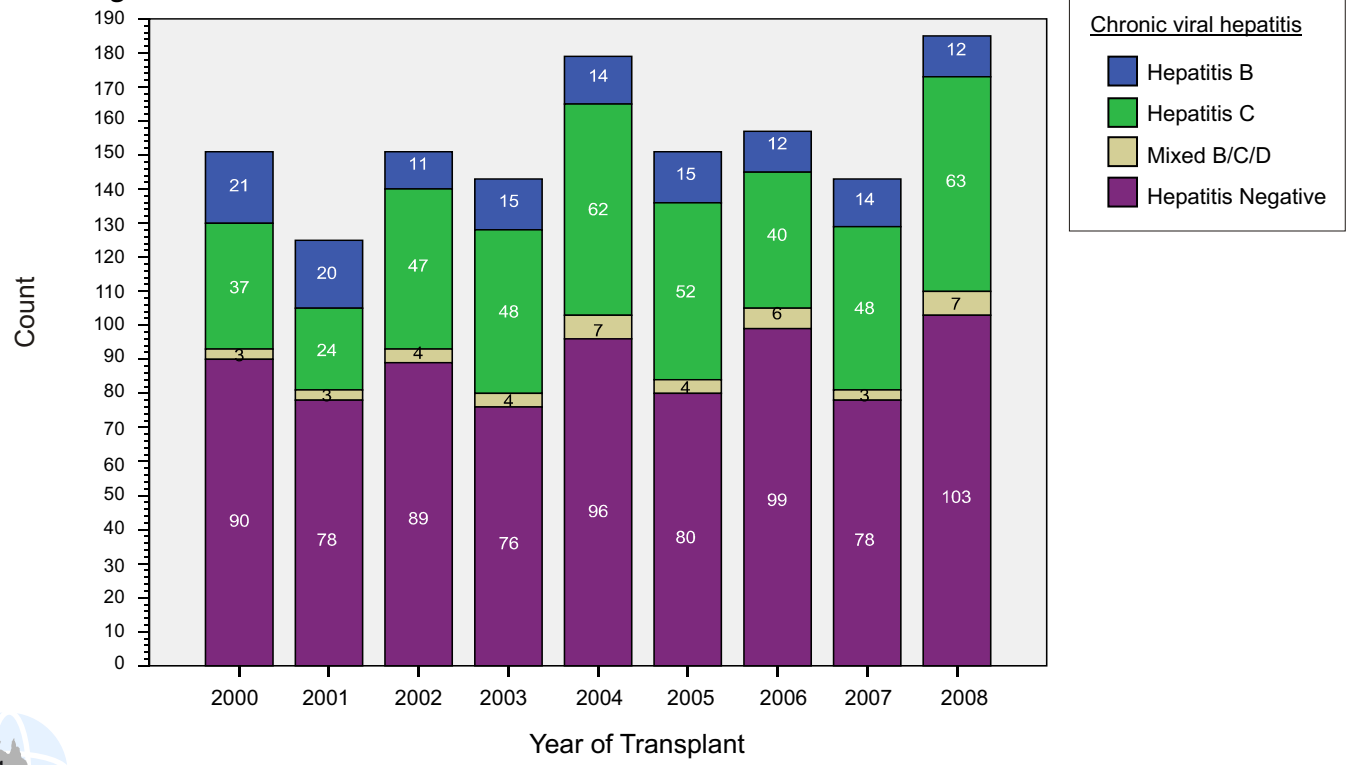
Chronic Viral Hepatitis as Primary or Secondary Diagnosis in Adult Patients

Primary Diagnosis		Secondary / Tertiary diagnosis					
		n =	Hepatitis C	Hepatitis B	Hepatitis B,C	HCC	ALD
	Hepatitis C	508		7		107	122
	Hepatitis B	174	4			50	4
	Hepatitis BD/BC/BCD	33				3	6
	HCC + cirrhosis	163	70	58	5		17
	ALD	307	10	2		31	
	Other	1331	11	6		42	19
	TOTAL	2516					

Type of Chronic Viral Hepatitis in Adult Patients

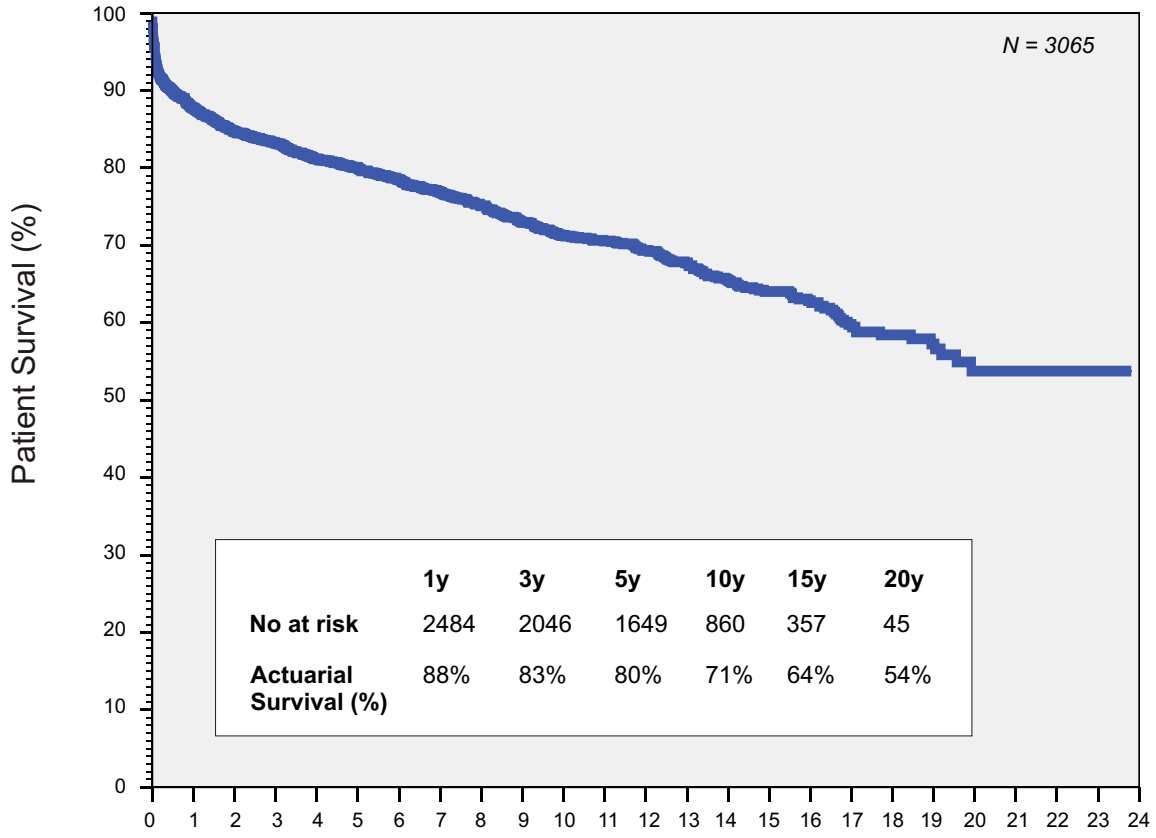


Hepatitis diagnosis

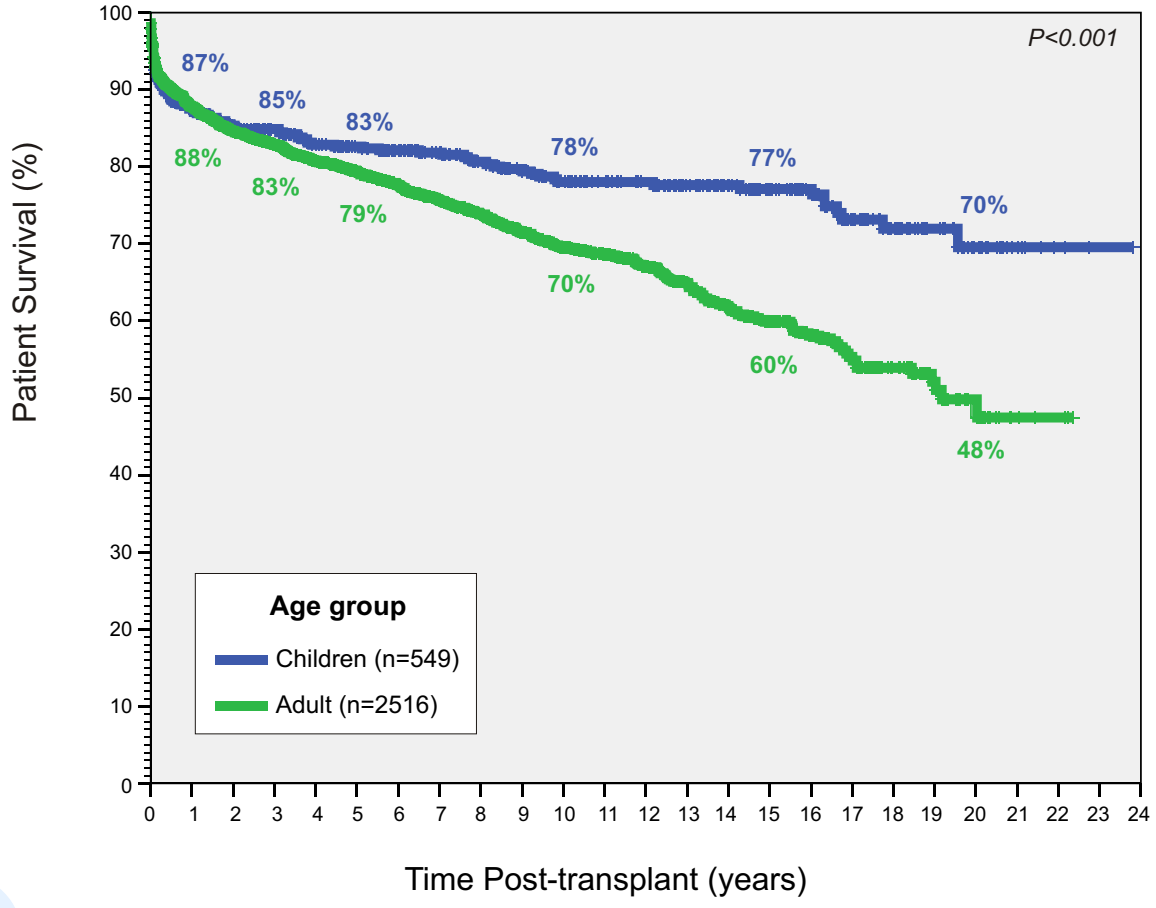


Section 3

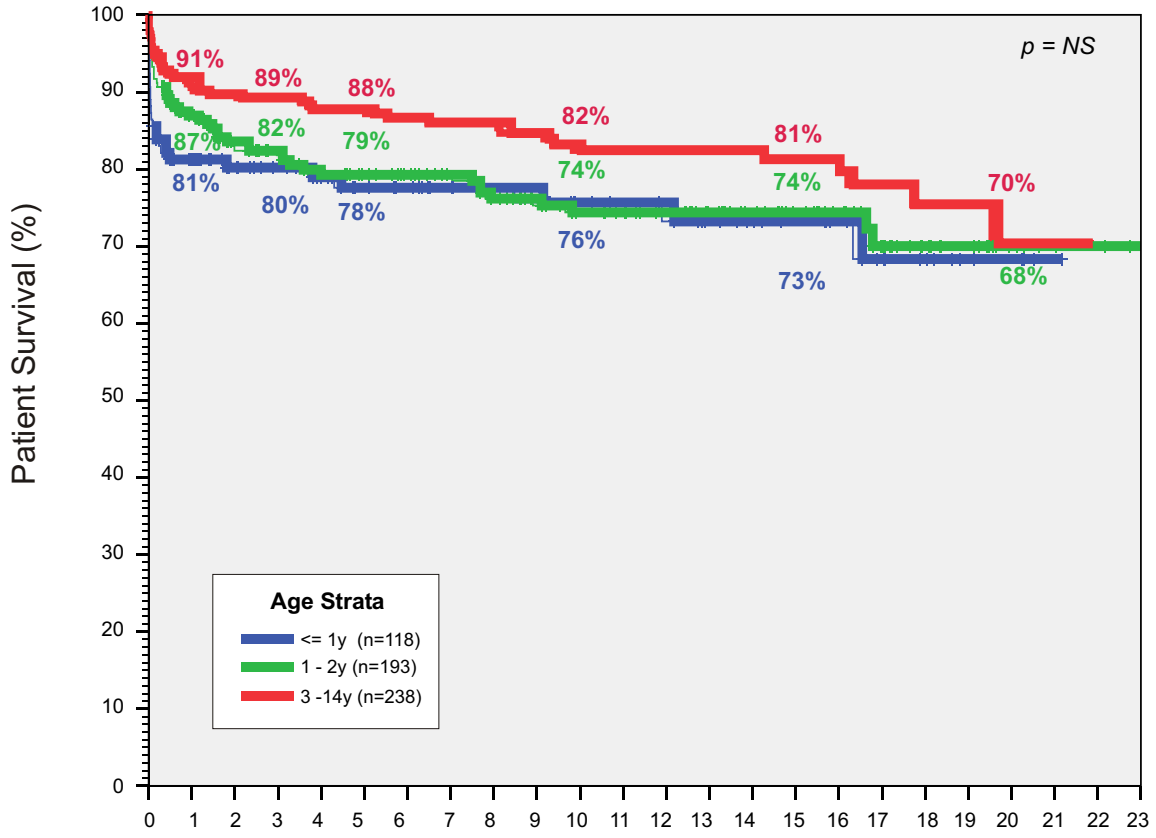
Patient Survival



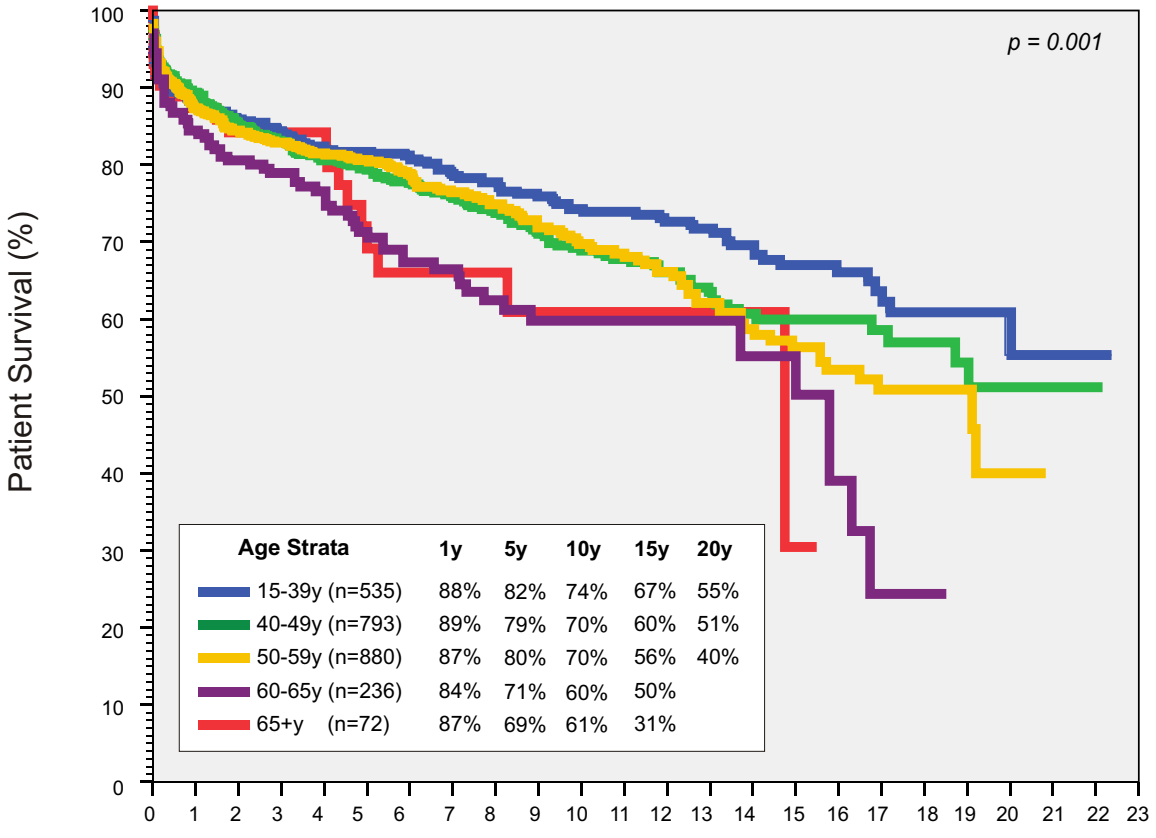
	1y	3y	5y	10y	15y	20y
No at risk	2484	2046	1649	860	357	45
Actuarial Survival (%)	88%	83%	80%	71%	64%	54%



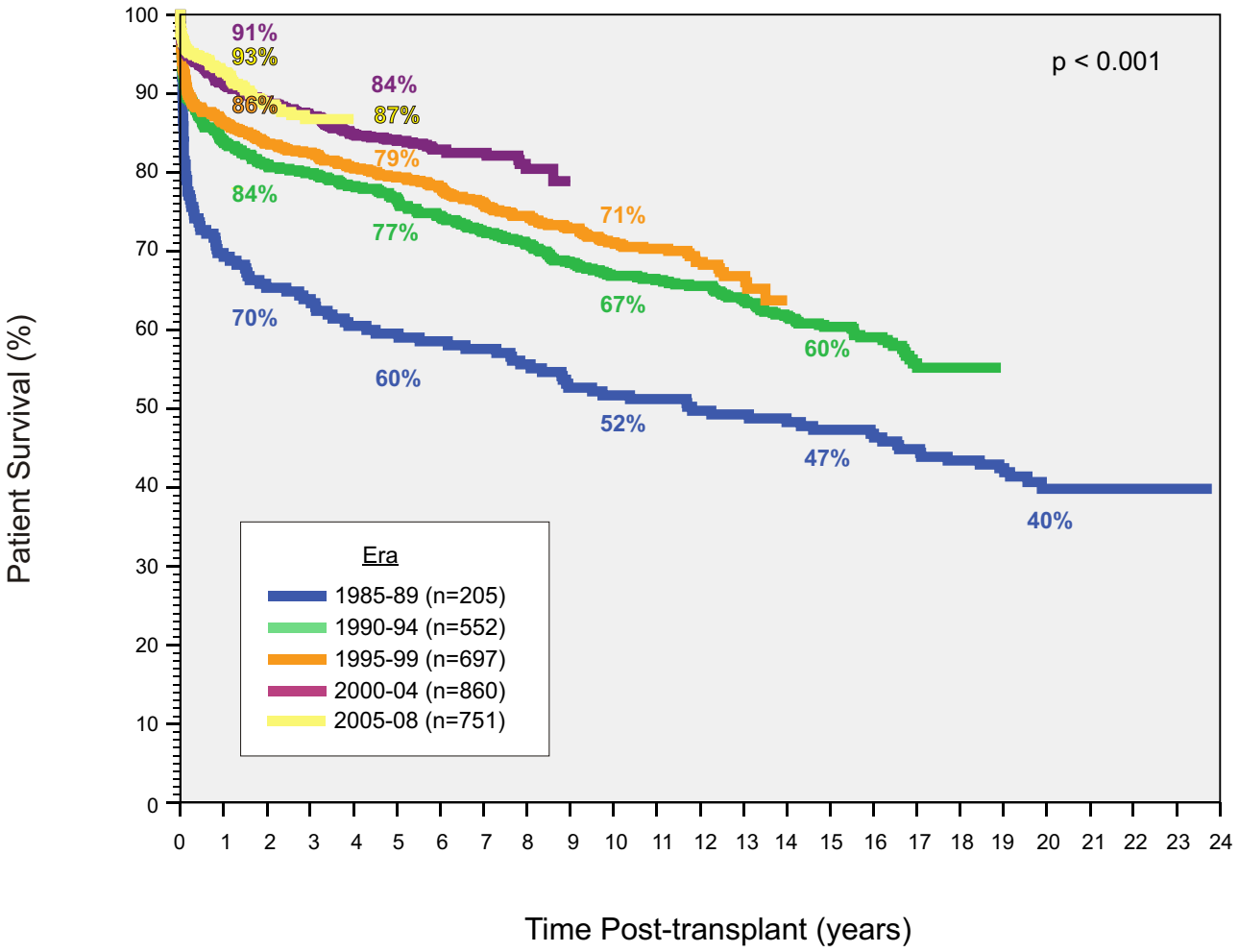
Children n= 549



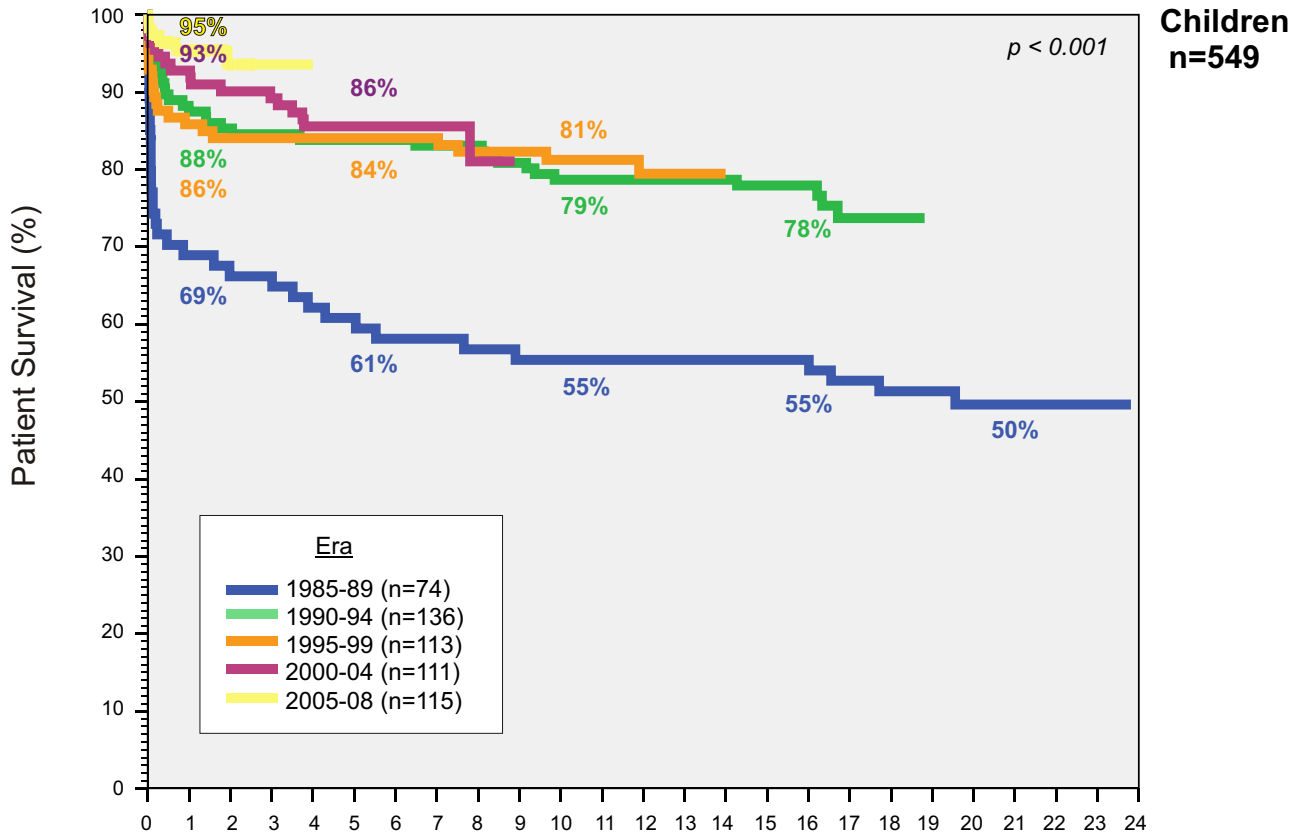
Adults n = 2516



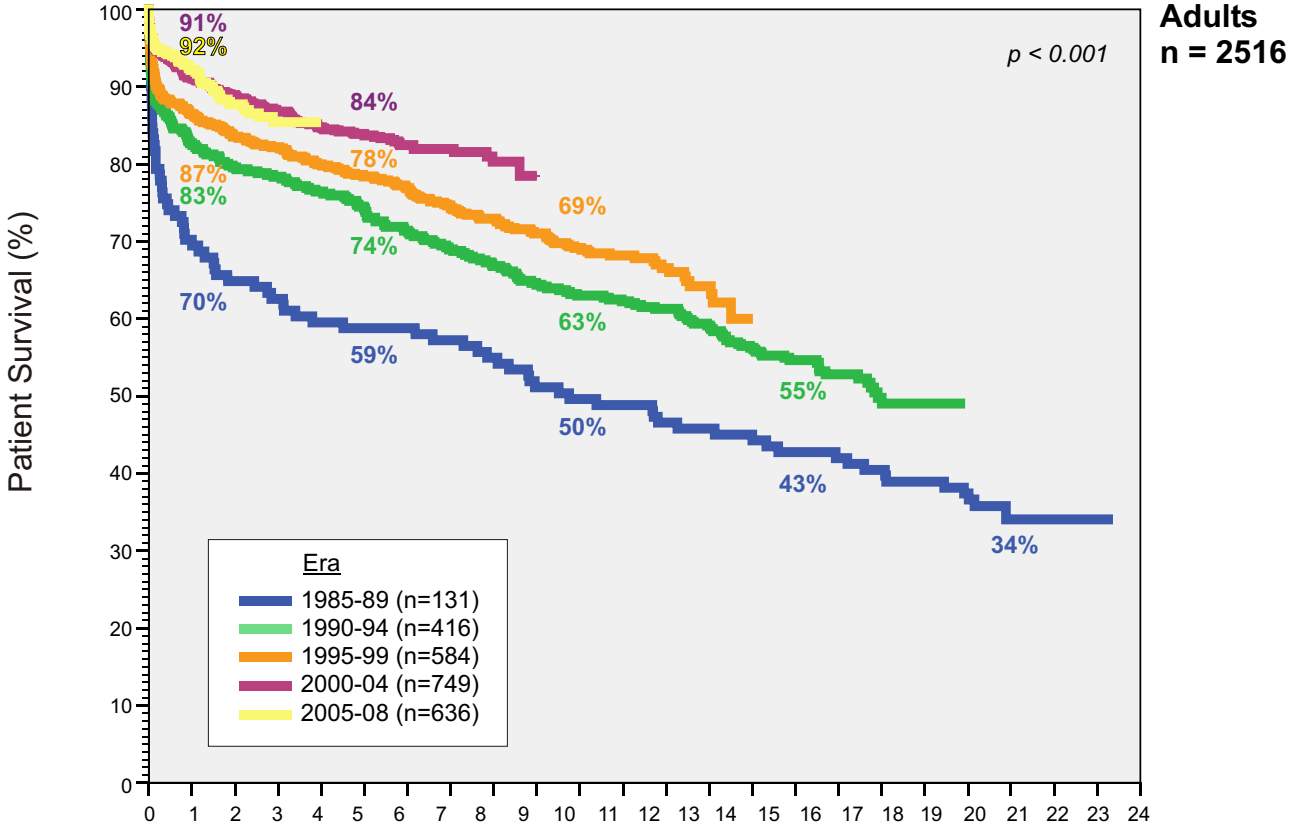
All Patient Survival by Year of Transplant



Patient Survival - Children

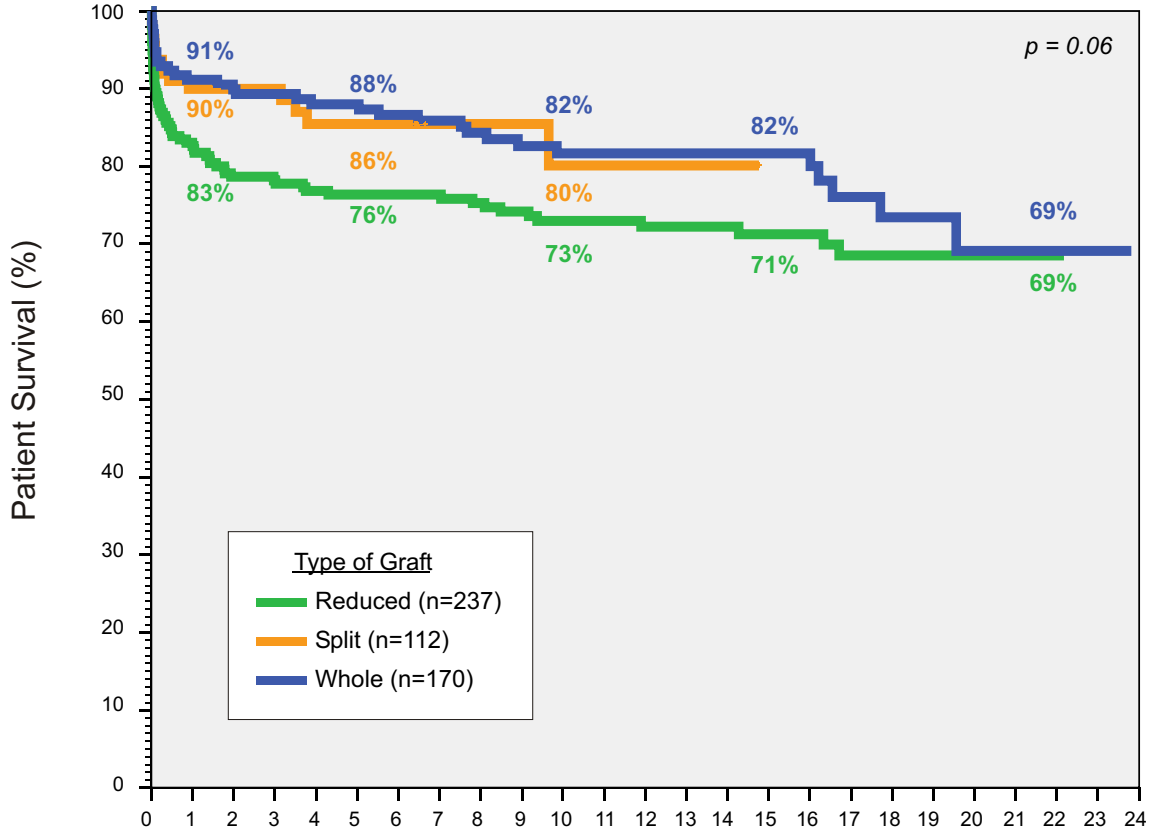


Patient Survival - Adults

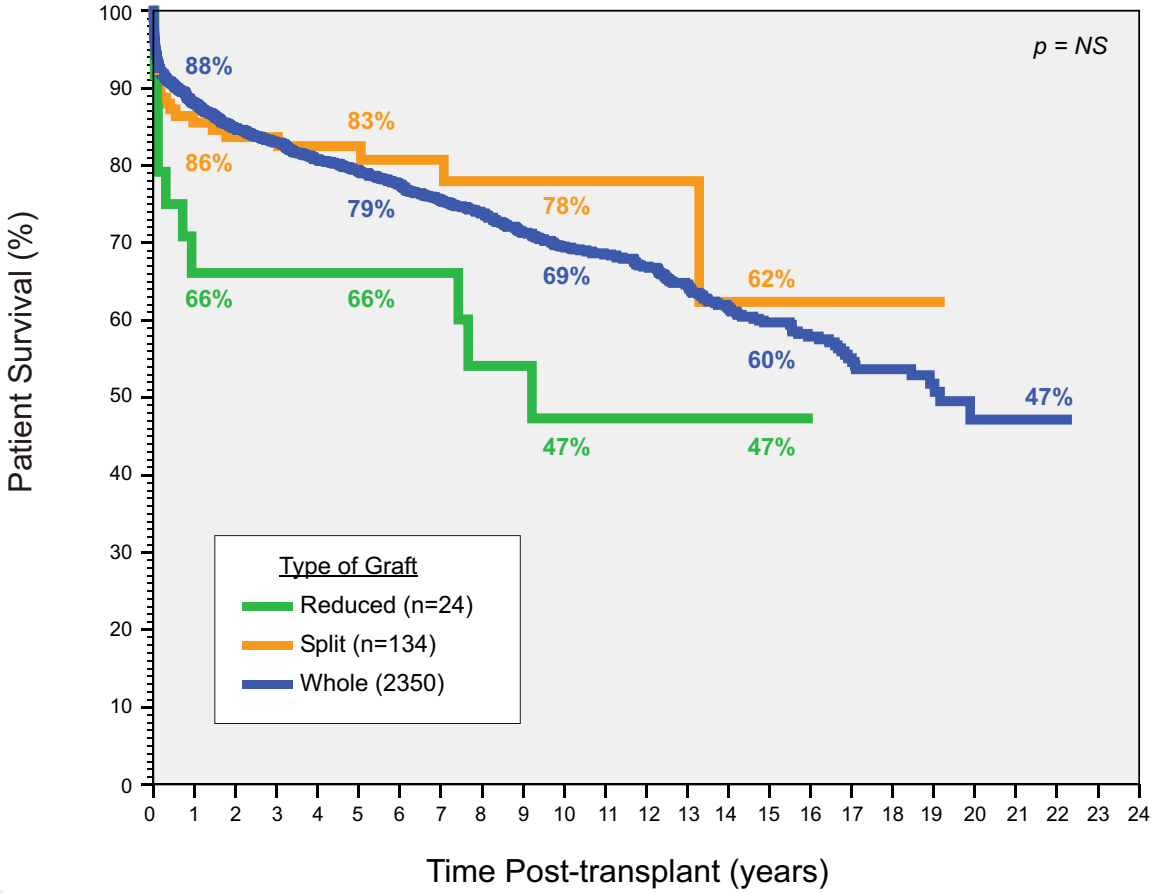


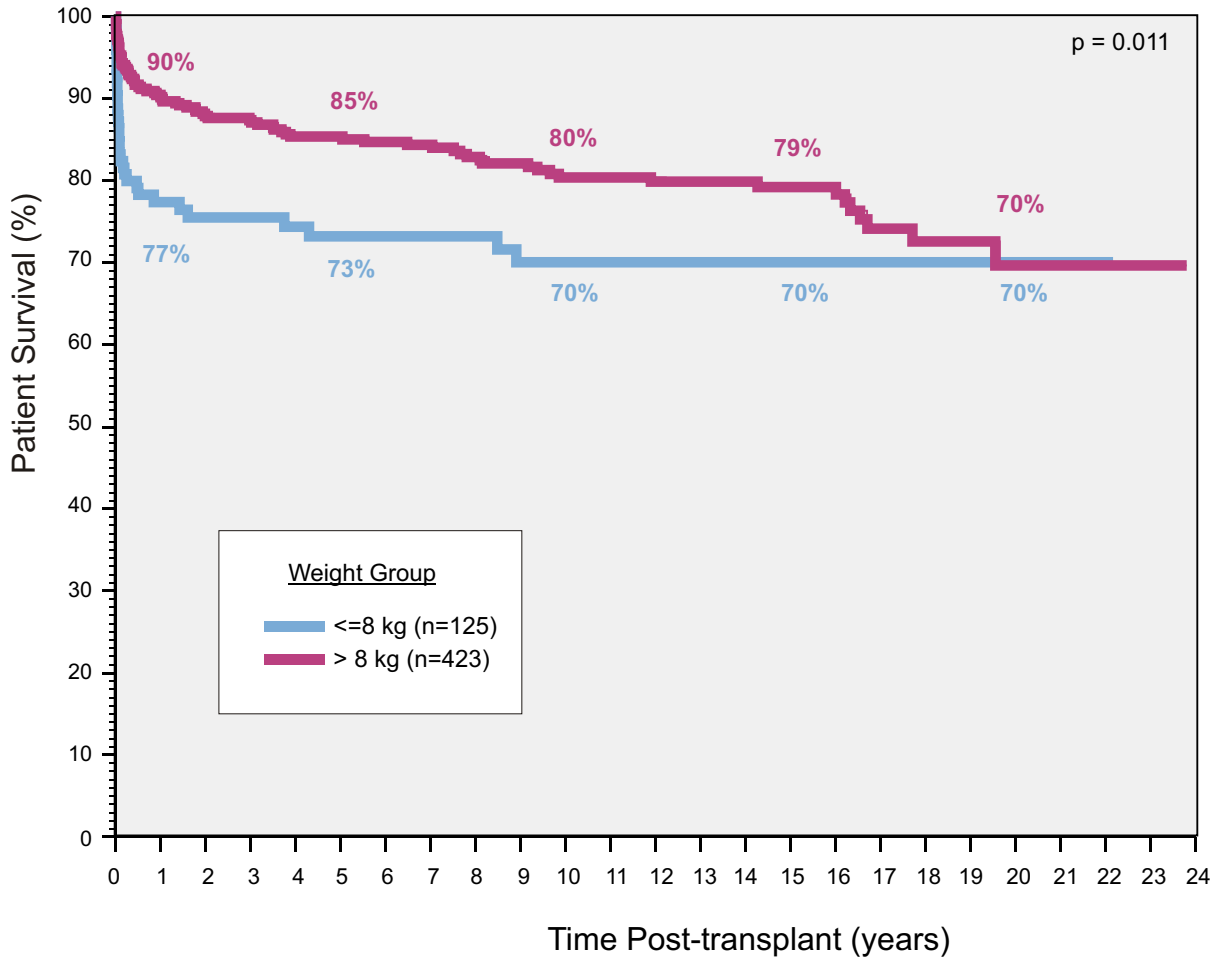
Patient Survival by Type of Primary Graft [Deceased donors]

Children - n = 519

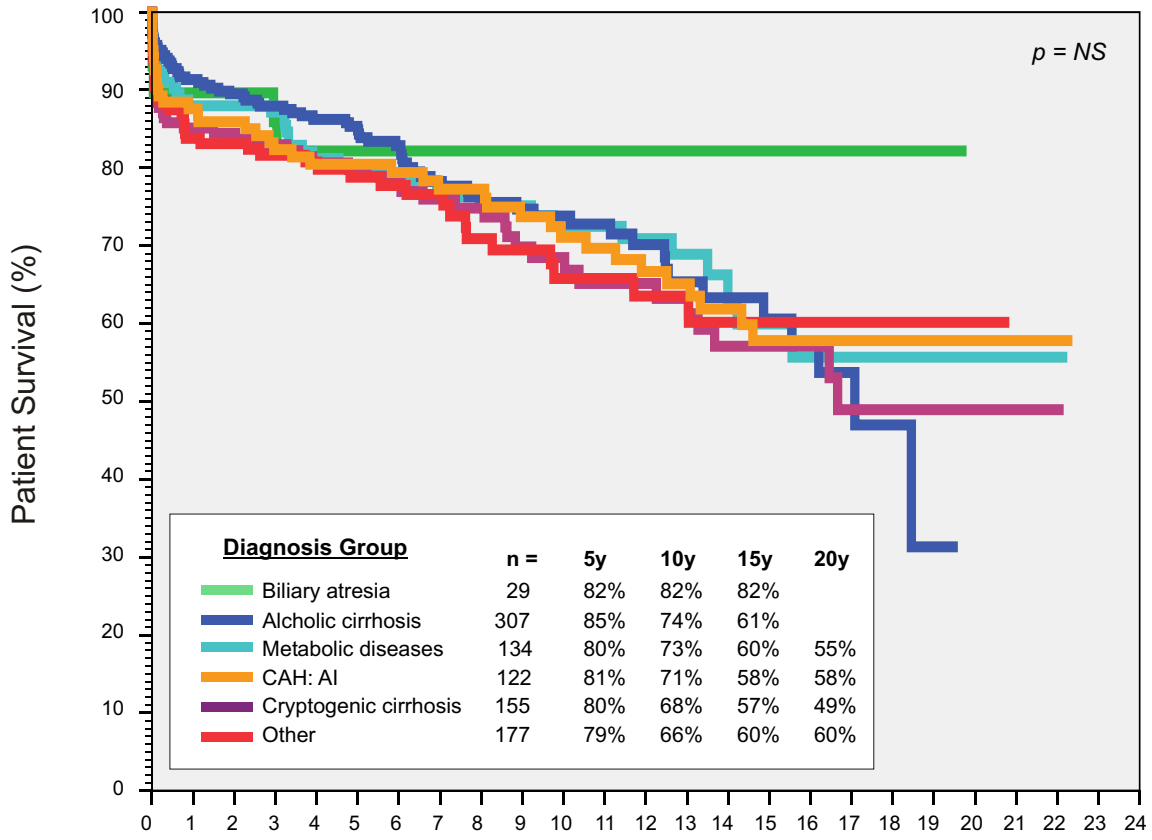


Adults - n = 2508

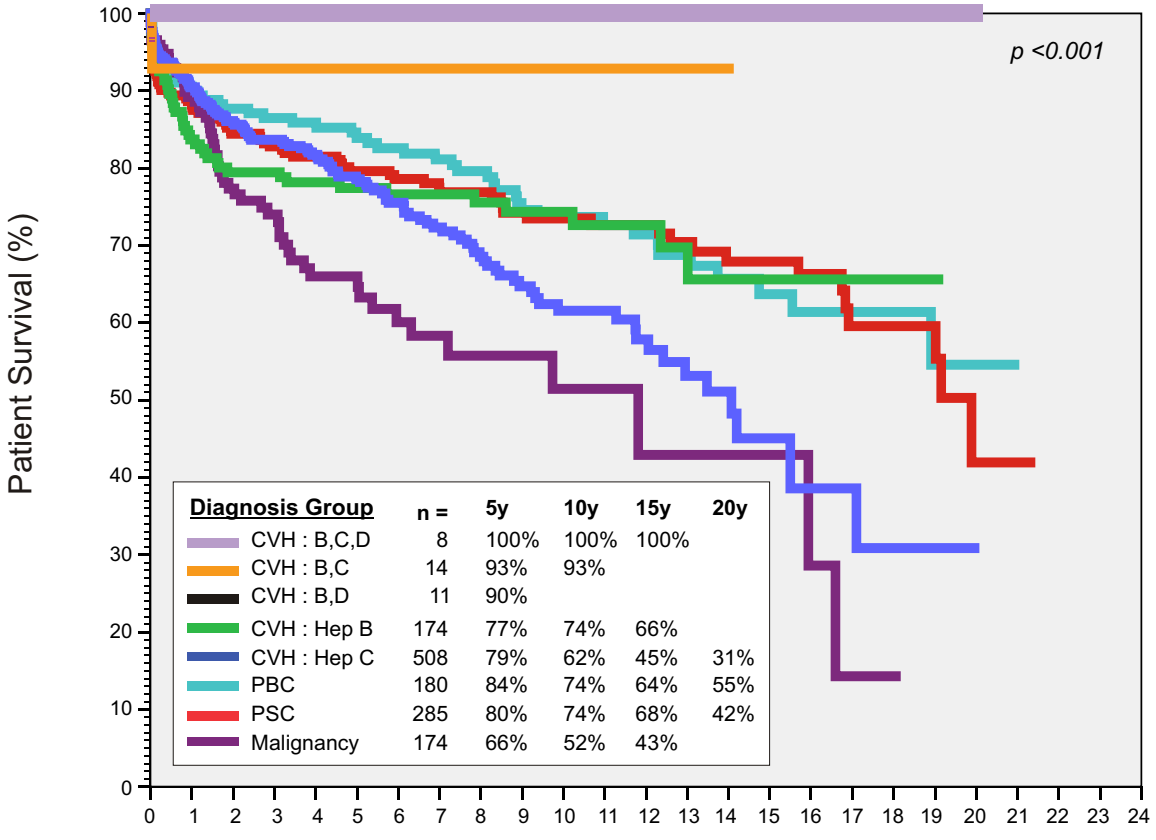




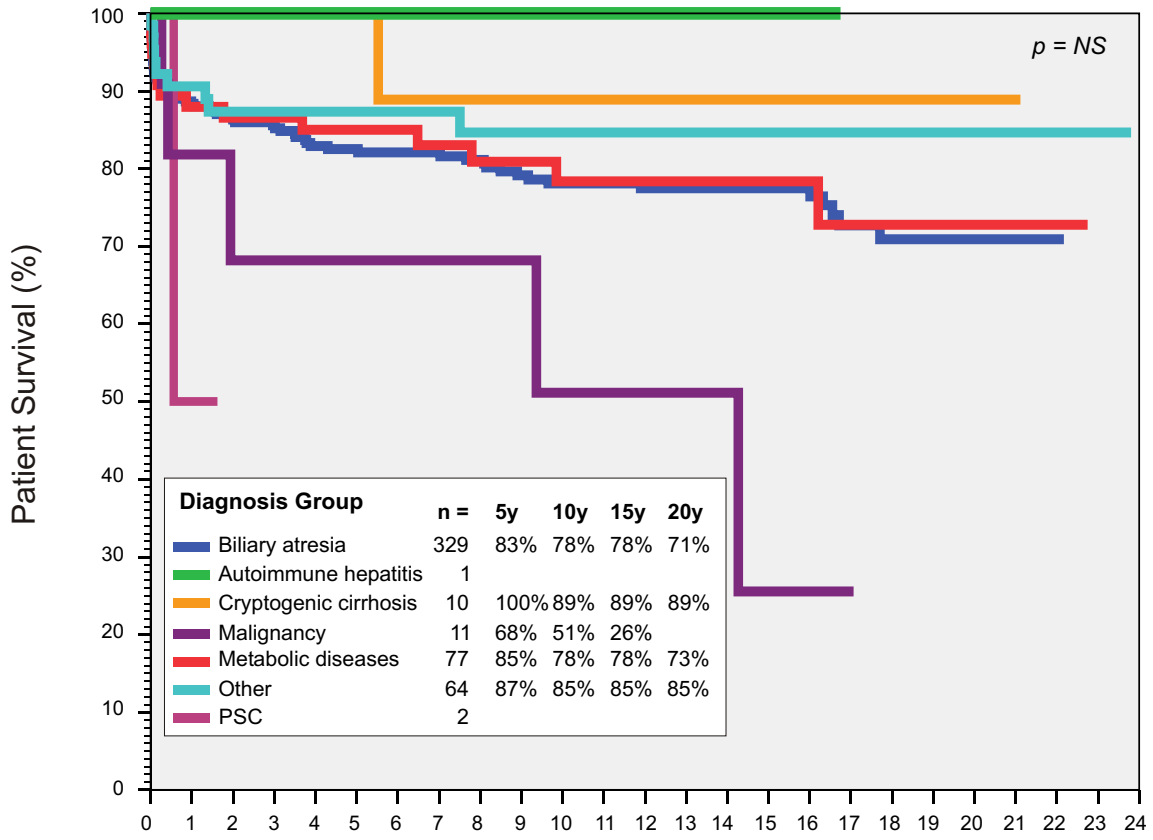
(1) Adults [excluding FHF] - n=924



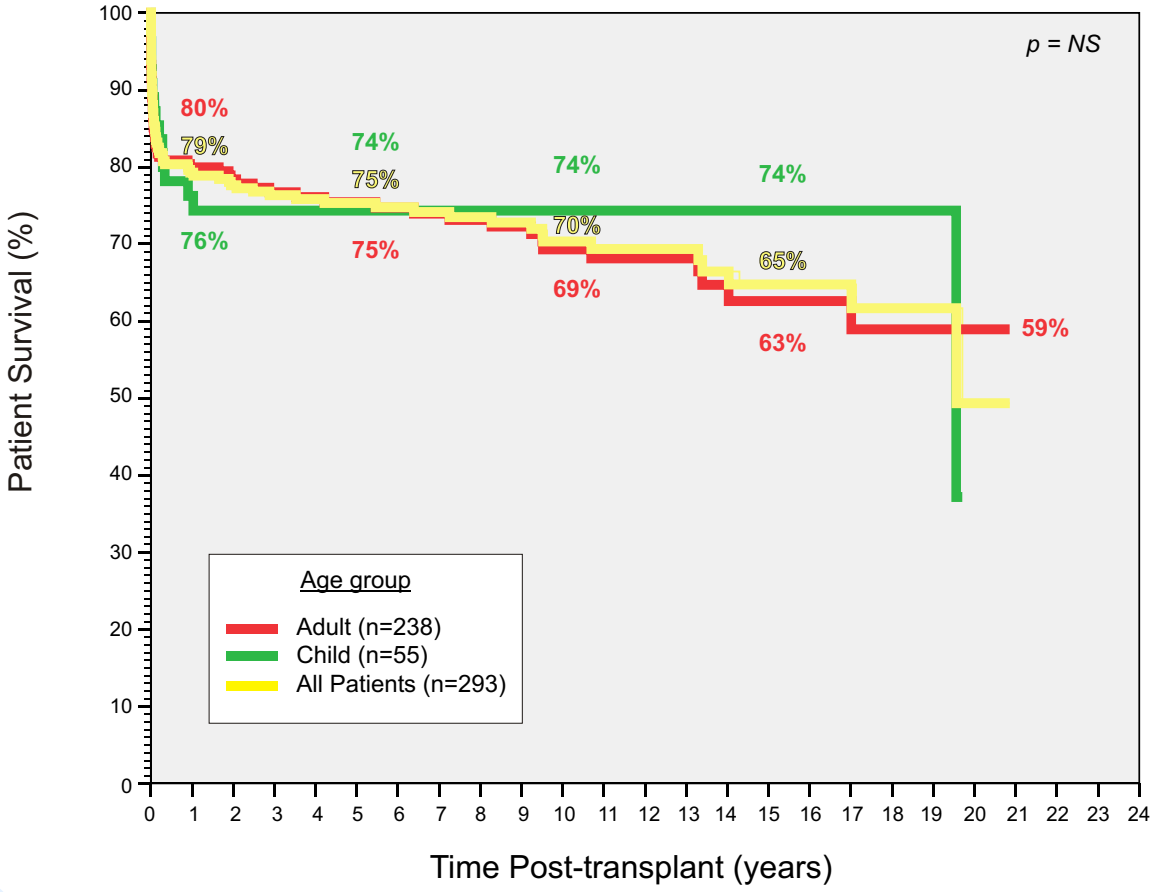
(2) Adults [excluding FHF] - n=1354

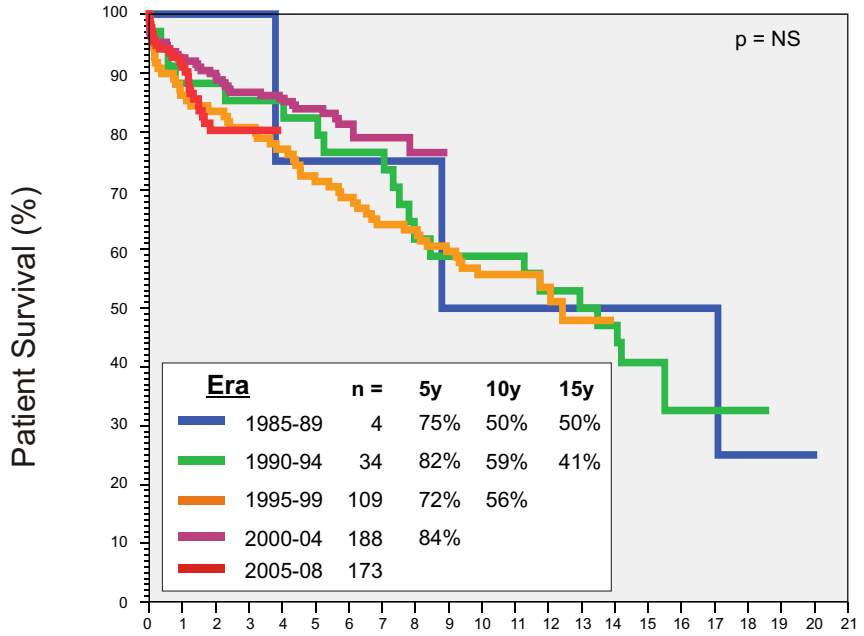


(3) Paediatric recipients [excluding FHF] - n=494

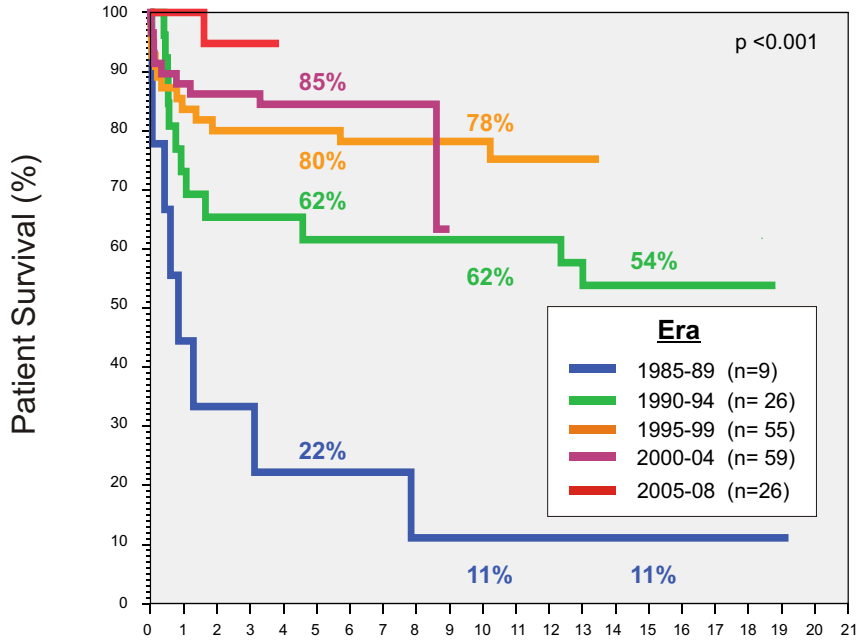


(4) Fulminant hepatic failure (n=293)

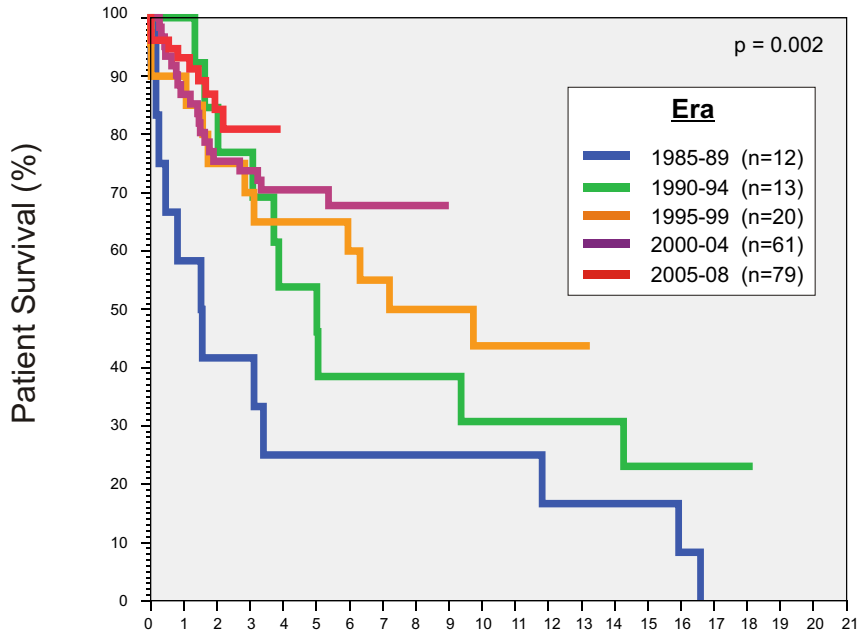




Adults CVH: Hepatitis C
n = 508



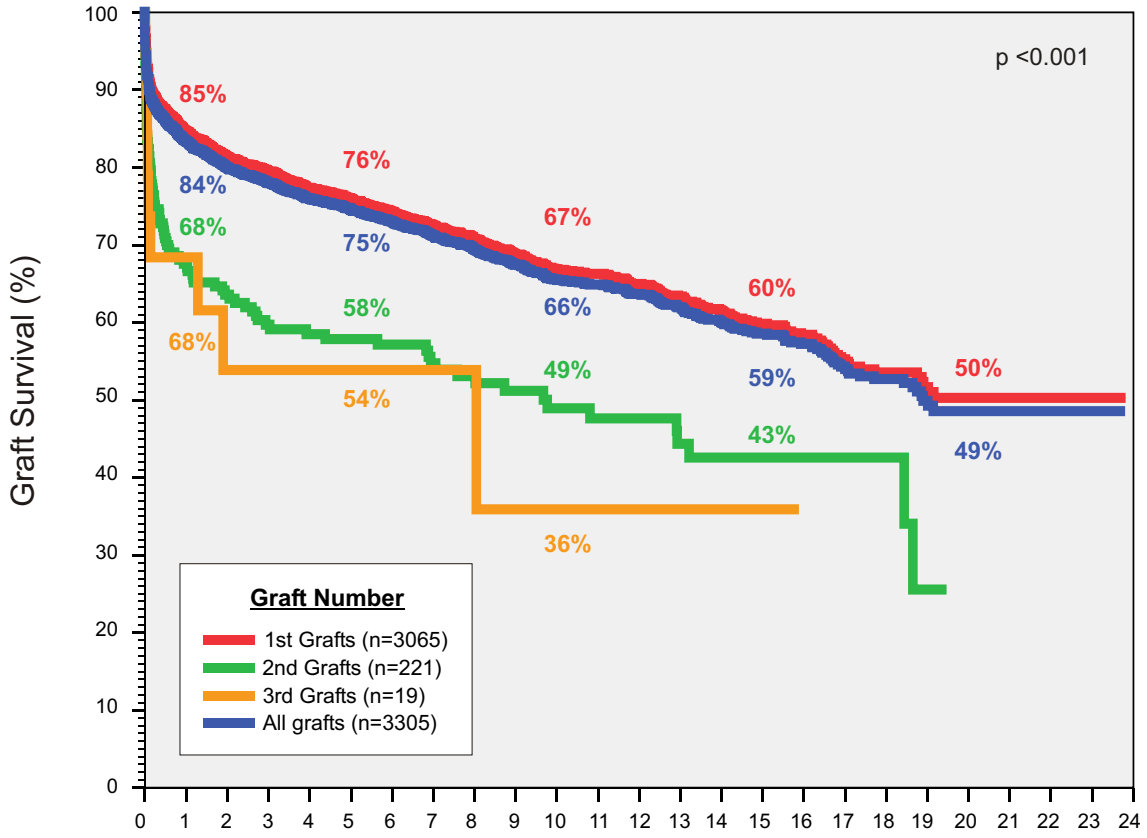
Adults CVH: Hepatitis B
n = 174

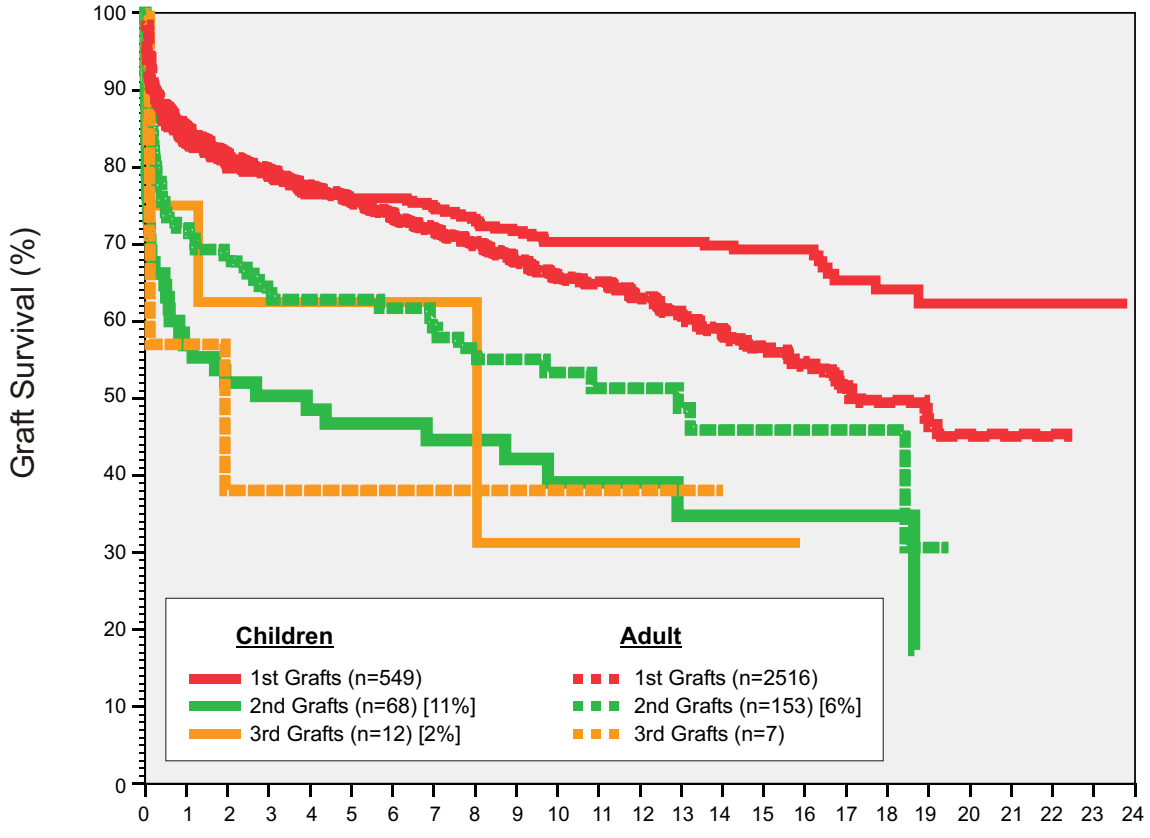


Malignancy
Adults and Children
n = 185

Section 4

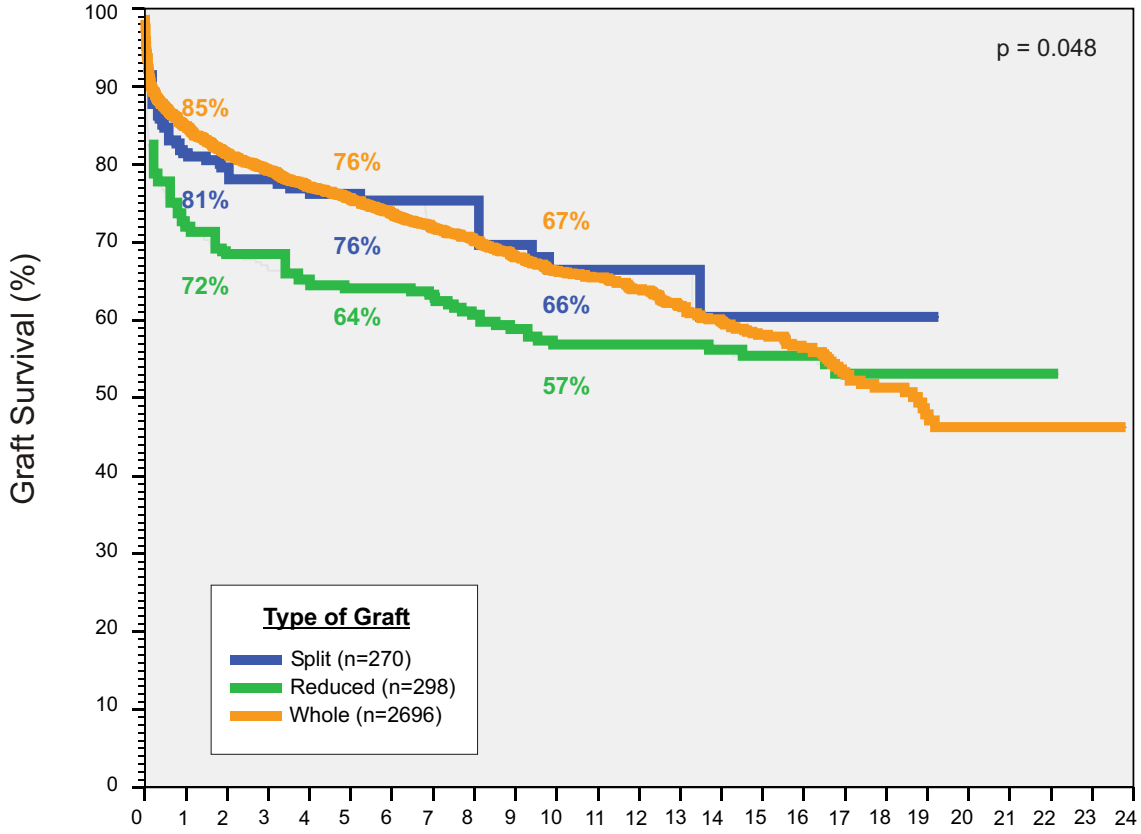
Graft Outcome

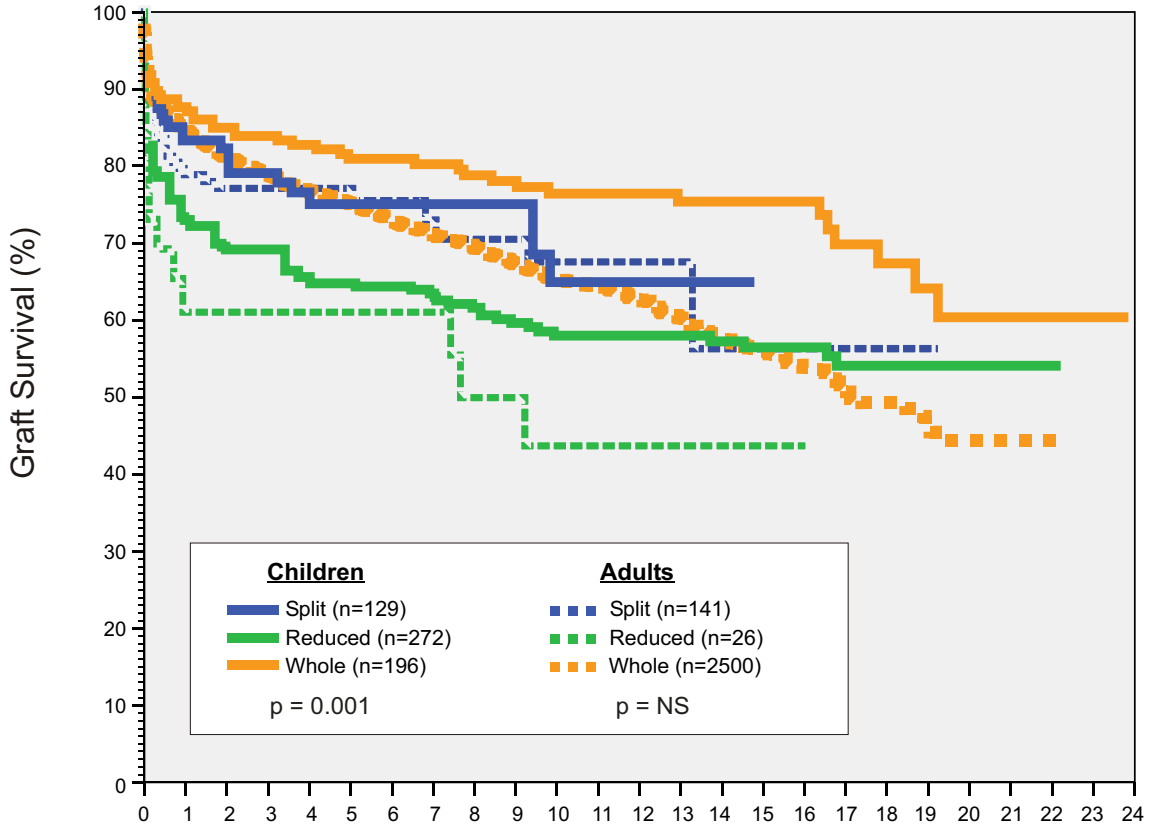




Graft Survival by Type of Graft [Deceased Donors]

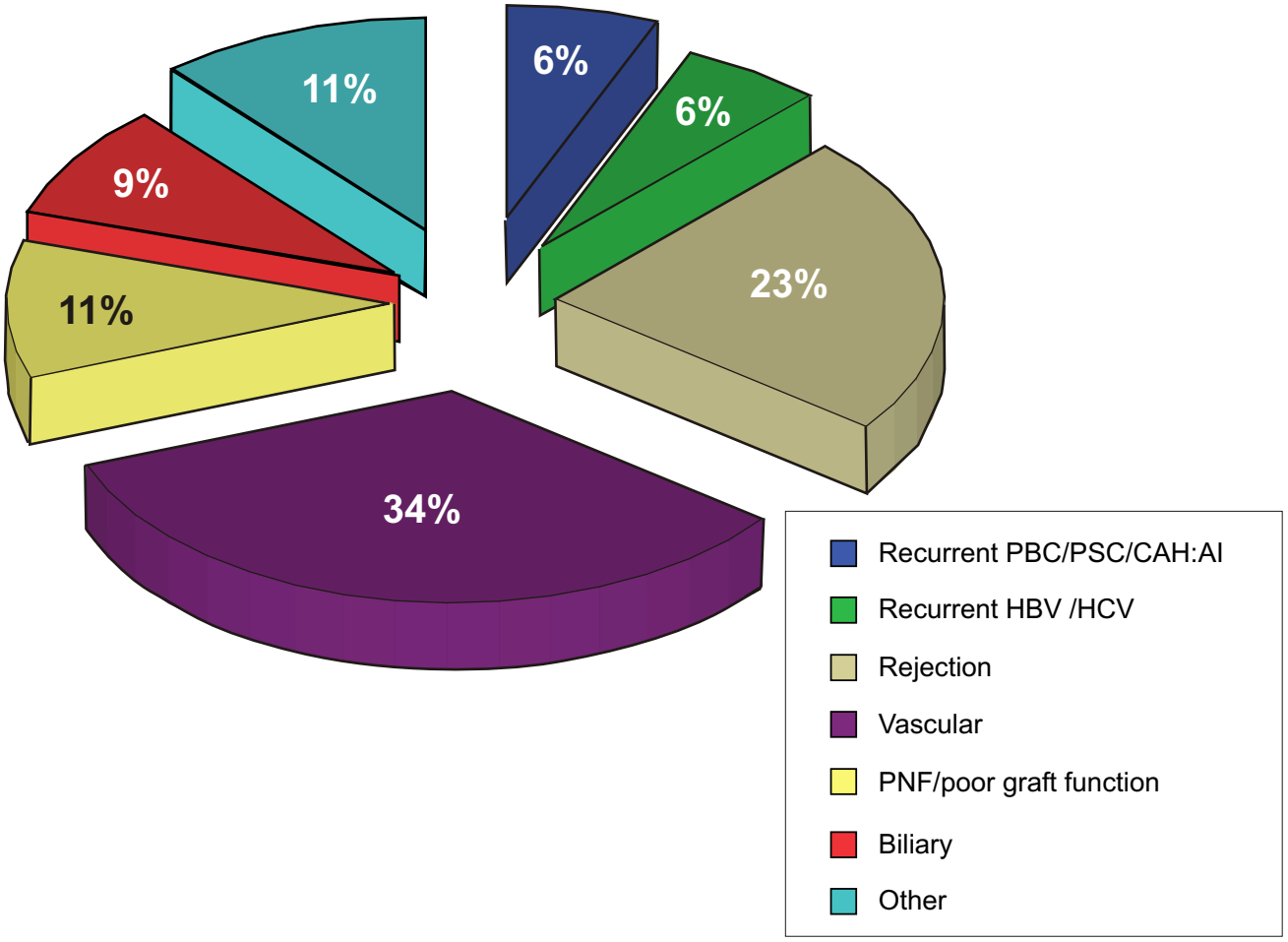
All grafts (n = 3264)

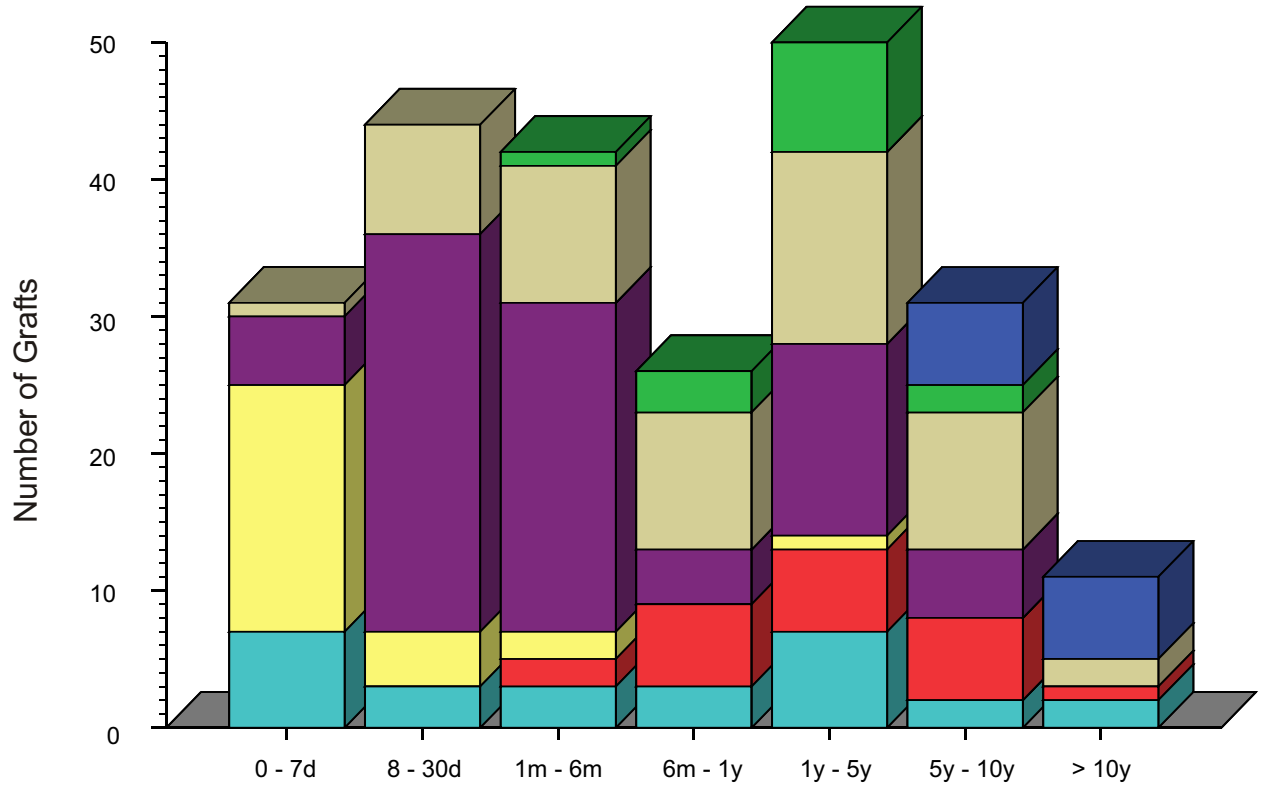




Indication for Retransplantation

n = 240 *(221 2nd grafts, 19 3rd grafts)*



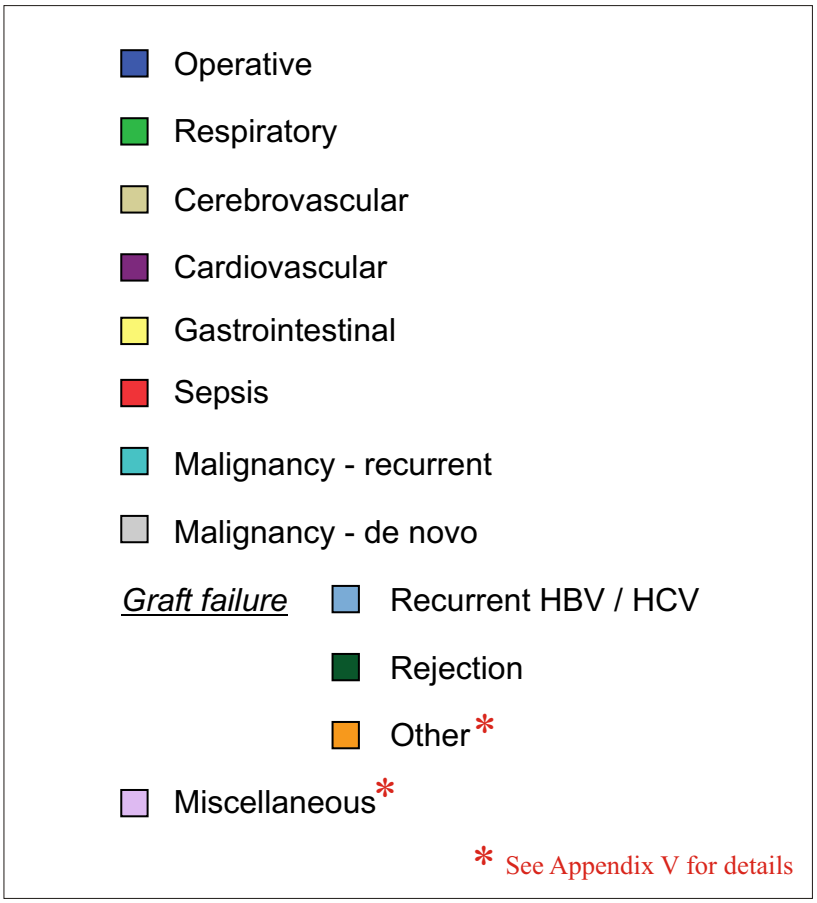


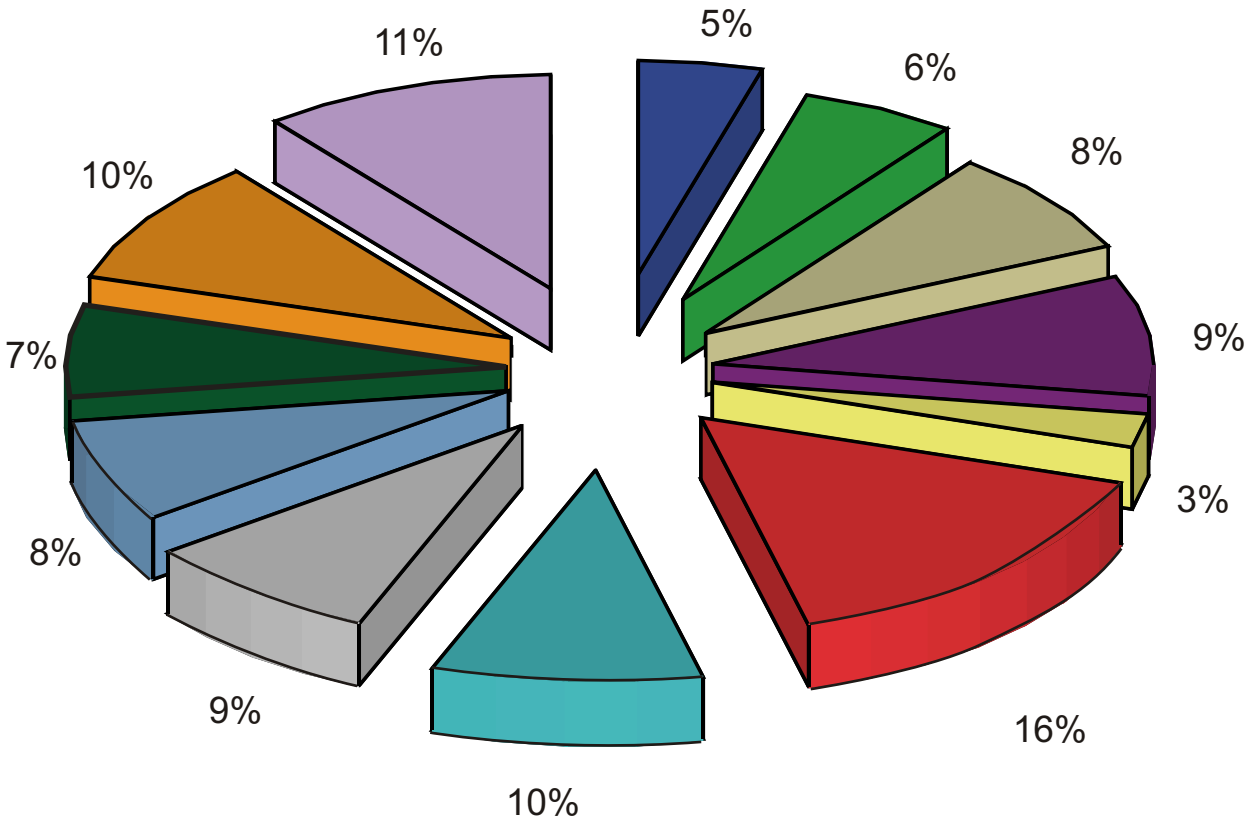
N =	***31*** *(13%)*	***44*** *(18%)*	***42*** *(18%)*	***26*** *(11%)*	***53*** *(22%)*	***31*** *(13%)*	***12*** *(5%)*

Section 5

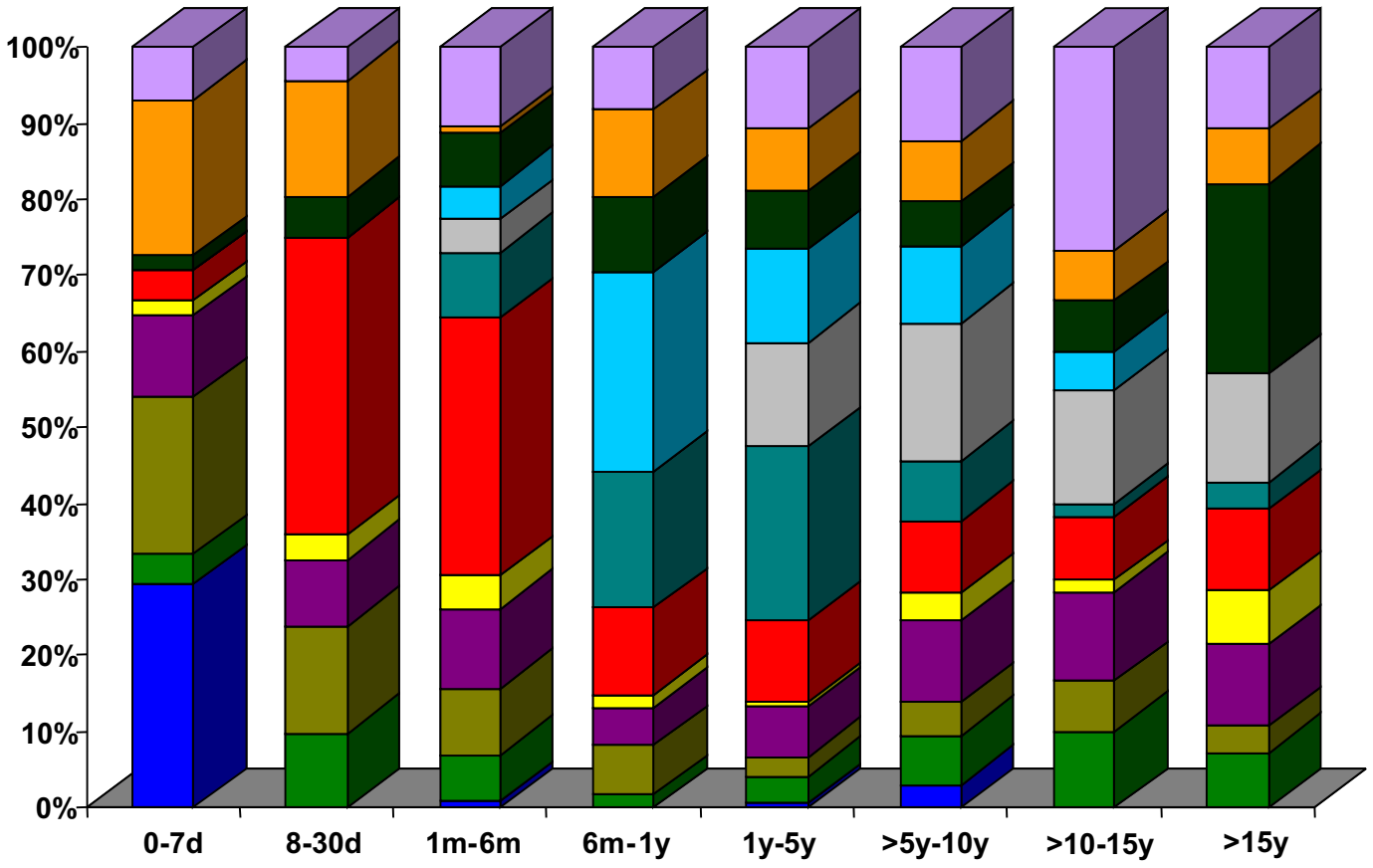
Cause of Patient Death

All Patients n = 730





Cause of Death by Time Post Transplant



	0-7d	8-30d	1m-6m	6m-1y	1y-5y	>5y-10y	>10-15y	>15y
N =	103 (13%)	92 (12%)	115 (14%)	61 (8%)	196 (25%)	139 (17%)	60 (8%)	28 (3%)

- Operative
- Respiratory
- Cerebrovascular
- Cardiovascular
- Gastrointestinal
- Sepsis
- Malignancy - de novo
- Malignancy - recurrent
- Recurrent HBV / HCV
- Rejection
- Other [graft failure]
- Miscellaneous

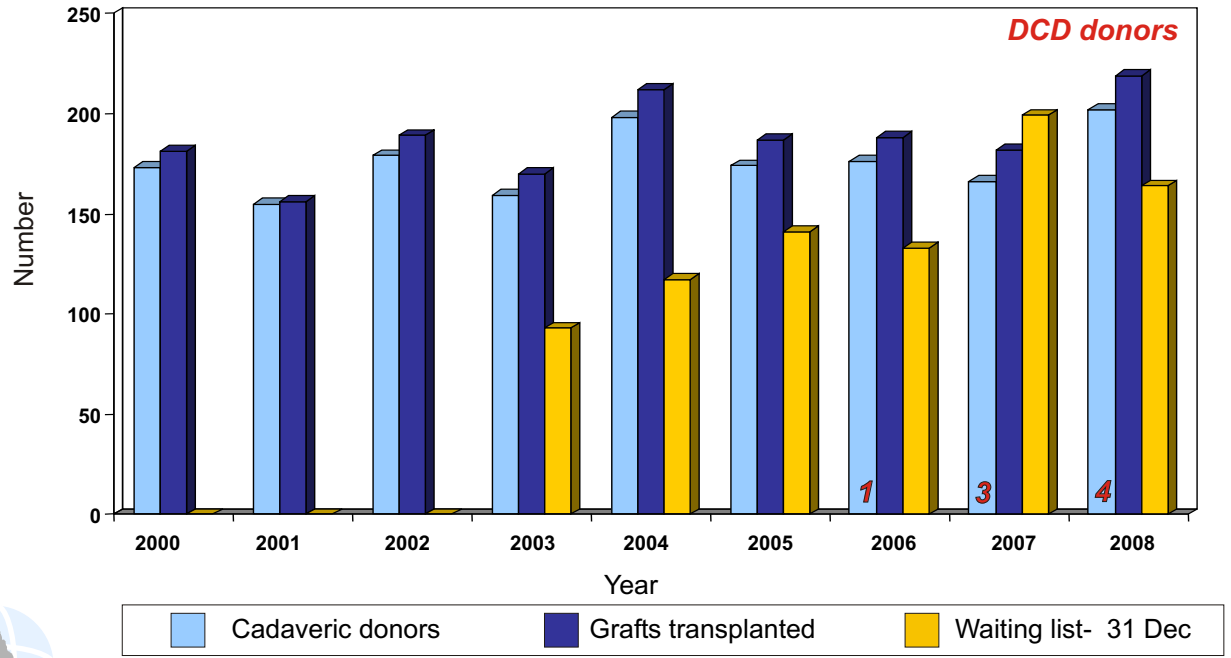
Section 6

Deceased Donor Information

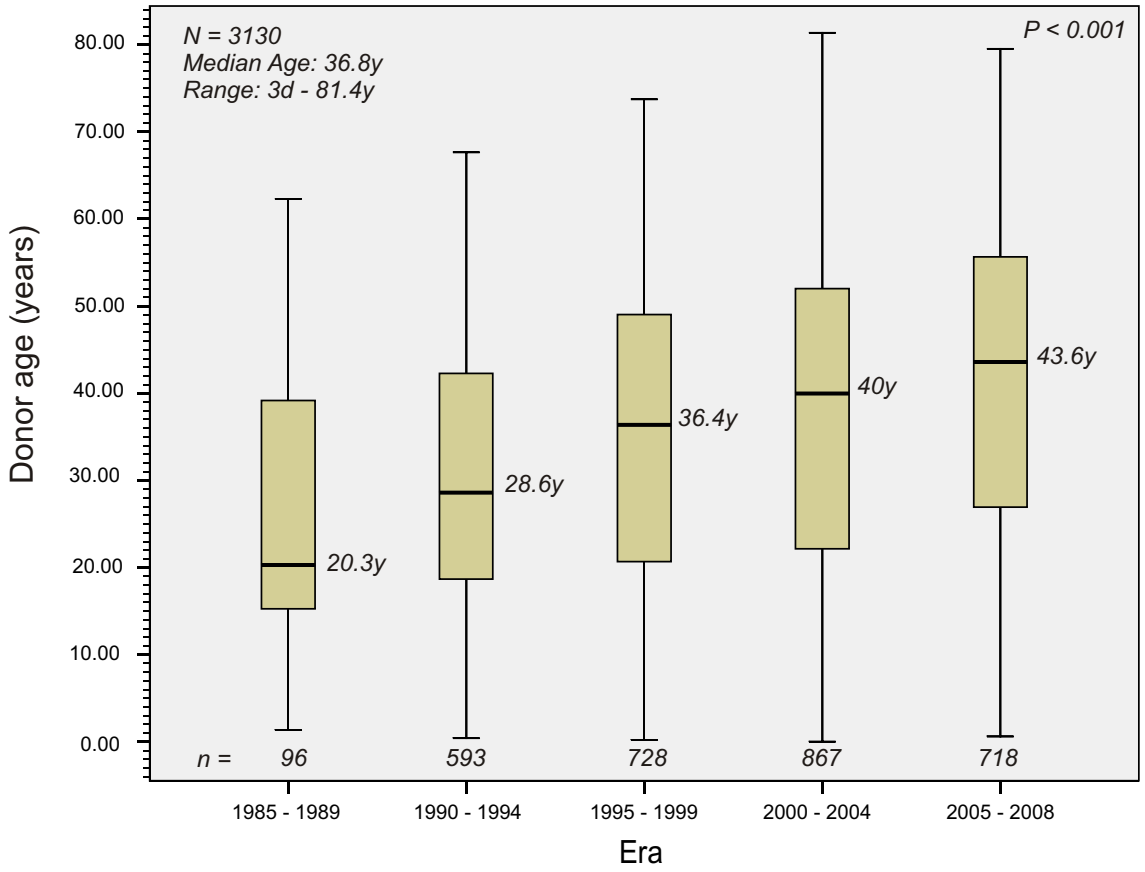
Deceased Donation by Year

	QLD	NSW/ACT	VIC/TAS	SA/NT	WA	NZ	TOTAL
1990	22	27	16	5		7	77
1991	29	35	20	6	8	11	109
1992	43	32	18	9	8	24	134
1993	28	40	25	12	6	16	127
1994	29	39	23	12	10	21	134
1995	29	44	24	17	8	21	143
1996	26	37	19	17	10	24	133
1997	31	49	19	19	8	22	148
1998	29	44	27	22	13	27	162
1999	15	31	31	29	11	27	144
2000	26	51	26	24	12	34	173
2001	37	40	26	14	9	29	155
2002	34	42	38	24	11	30	179
2003	34	32/3	29/2	13	15	31	159
2004	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	202

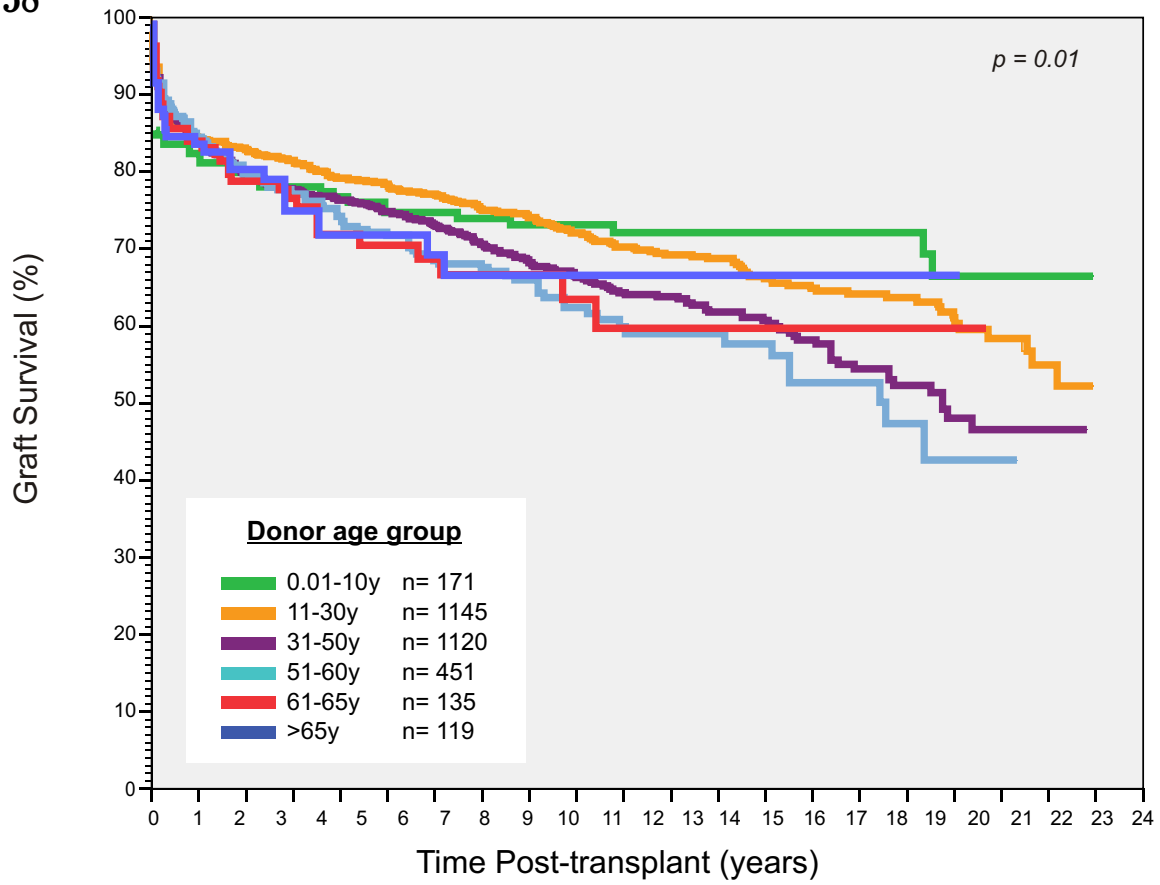
Grafts from deceased donors



Donor Age by Era
N = 3130



Graft Survival by Donor Age
N = 3138

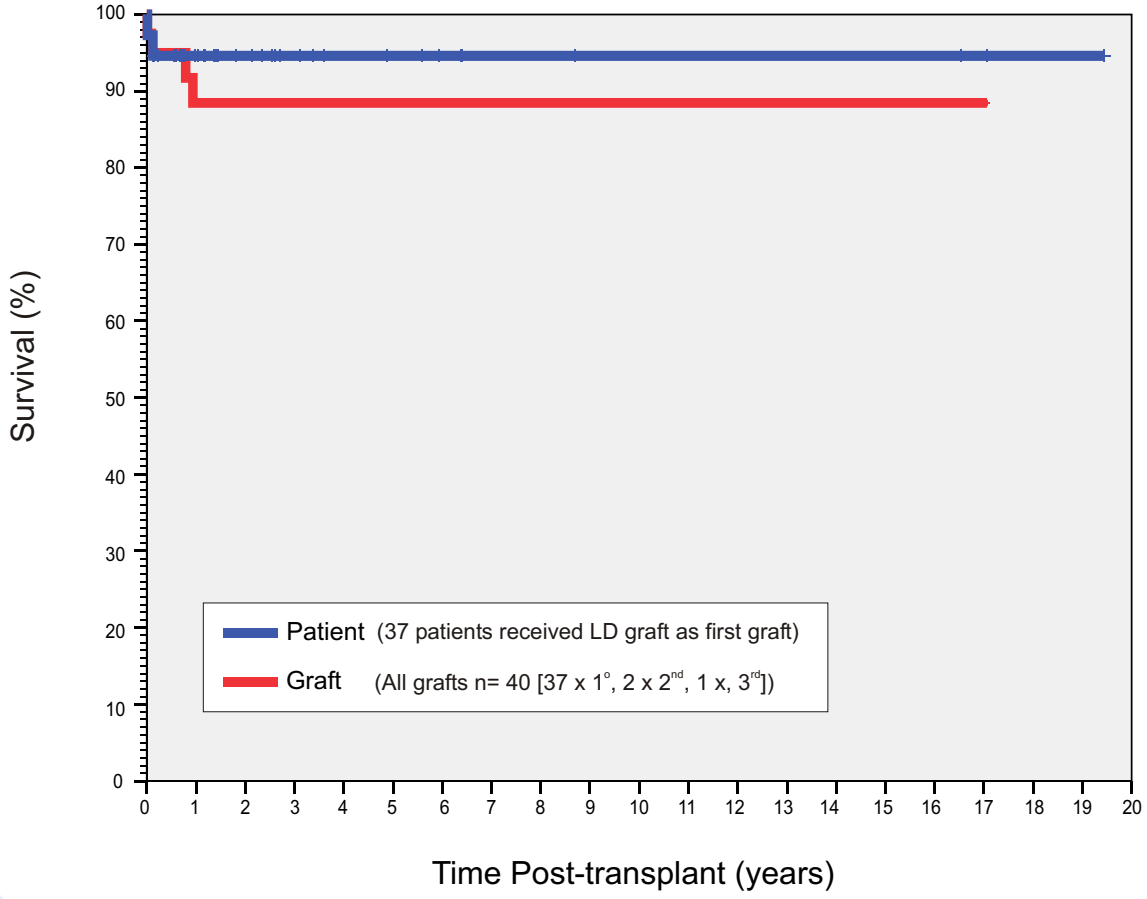


Section 7

Living Donor Transplantation

	Recipient Age Group		
	Child [n=31]	Adult [n=9]*	All [n=40]
Donor gender	-	-	-
Male	17	6	23
Female	14	3	17
Donor age	-	-	-
Median	35.9y	30.3y	35.3y
Range	29.7 - 54.5y	22.8 - 35.7y	22.8 - 54.5y
Donor relationship	-	-	-
Mother	7	-	7
Father	16	-	16
Son	-	3	3
Grandmother	1	-	1
Grandfather	1	-	1
Sister	-	2	2
Brother	-	2	2
Aunt	3	-	3
Family friend	3	1	4

* *1 x whole liver domino transplant*



Section 8

Waiting List

Waiting List Activity [Data 1/1/04 - 31/12/08]

Activity	2004	2005	2006	2007	2008		
Listed at 1 January	*93*	*117*	*145*	*133*	*199*	*-*	TOTAL 2008
New listings	*279*	*292*	*259*	*338*	*-*	*290*	
TOTAL	***372***	***409***	***404***	***471***	***199***	***290***	**489**
			OUTCOME	OUTCOME			
Transplant	***214 [58%]***	***191 [47%]***	***194 [48%]***	***190 [40%]***	***110***	***119***	**229 [47%]**
Delisted	***41 [10%]***	***72 [18%]***	***77 [19%]***	***86 [18%]***	***40***	***56***	**96 [20%]**
Died on list	*14*	*26*	*18*	*35*	*19*	*29*	**48**
Too sick	*8* } *6%*	*9* } *11%*	*13* } *10%*	*13* } *12%*	*7*	*7*	**14** } **69 [14%]**
Tumour progression	*2*	*9*	*8*	*11*	*3*	*4*	**7**
Improved	*8*	*15*	*16*	*17*	*7*	*8*	**15**
Other	*9*	*13*	*22*	*10**	*4*	*7*	**11***
Still listed at 31 Dec	*117 [32%]*	*146 [35%]*	*133 [33%]*	*199 [43%]*	*49*	*115*	**164 (34%)**

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

Outcome of Urgent Listing

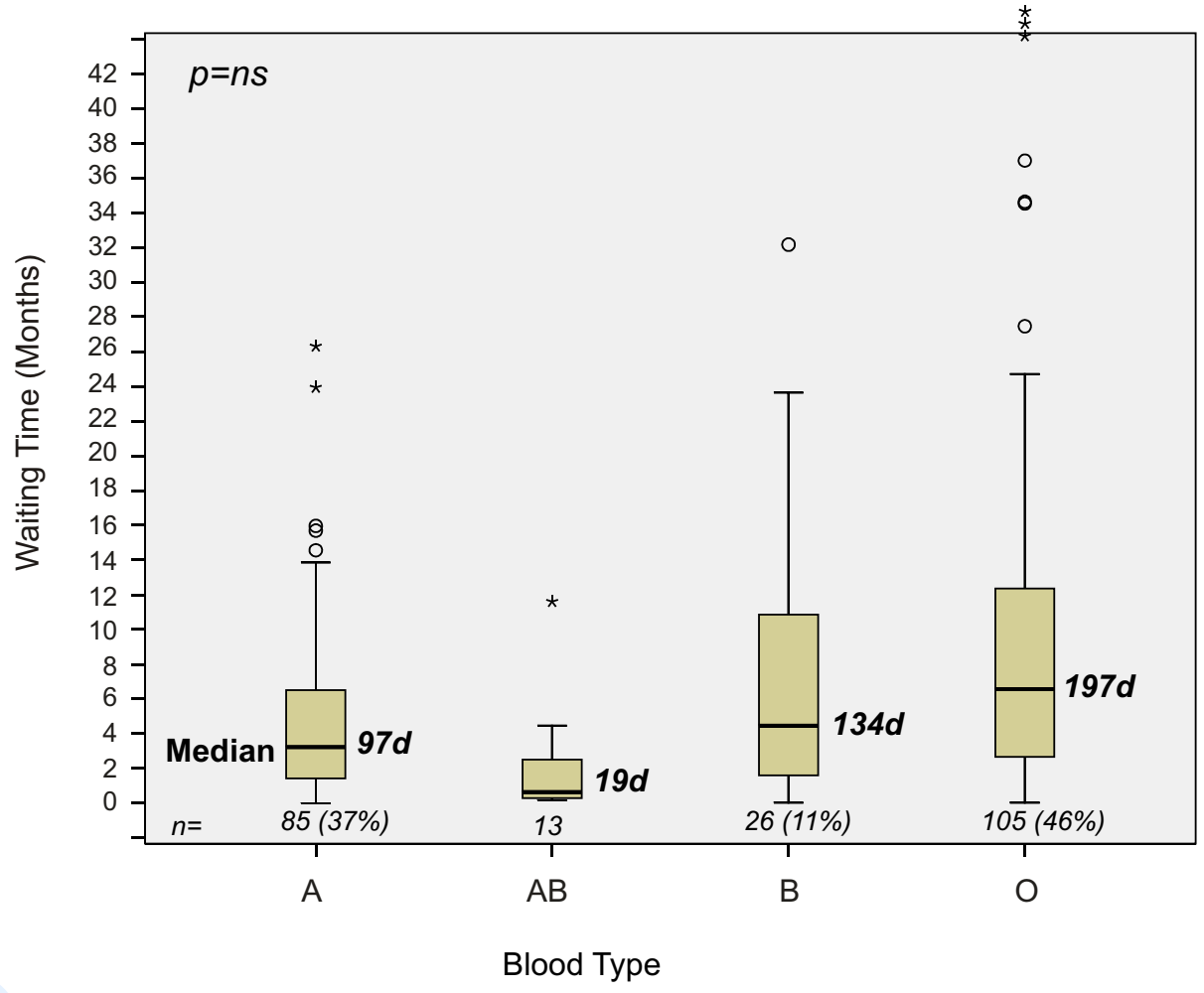
OUTCOME	CATEGORY 1				CATEGORY 2			
	2005 (n=14)	**2006** (n=16)	**2007** (n=18)	**2008** (n=13)	**2005** (n=31)	**2006** (n=26)	**2007** (n=32)	**2008** (n=24)
TRANSPLANTED	4 } *64%*	12 } *88%*	10 } *67%*	3 } *46%*	20 } *68%*	21 } *88%*	24 } *88%*	20 } *83%*
IMPROVED	5	2	2	3	1	2	4	1
DIED / TOO SICK	5	2	6	7	10	2	2	3
OTHER TREATMENT	-	-	-	-	-	1	-	-

	Blood Group				
	A	O	B	AB	TOTAL
n=	167 (34%)*	226 (46%)	77 (16%)	20 (4%)	489
Not transplanted	82	121	51	7	260
Transplanted	85 (51%)**	105 (46%)	26 (34%)	13 (65%)	229

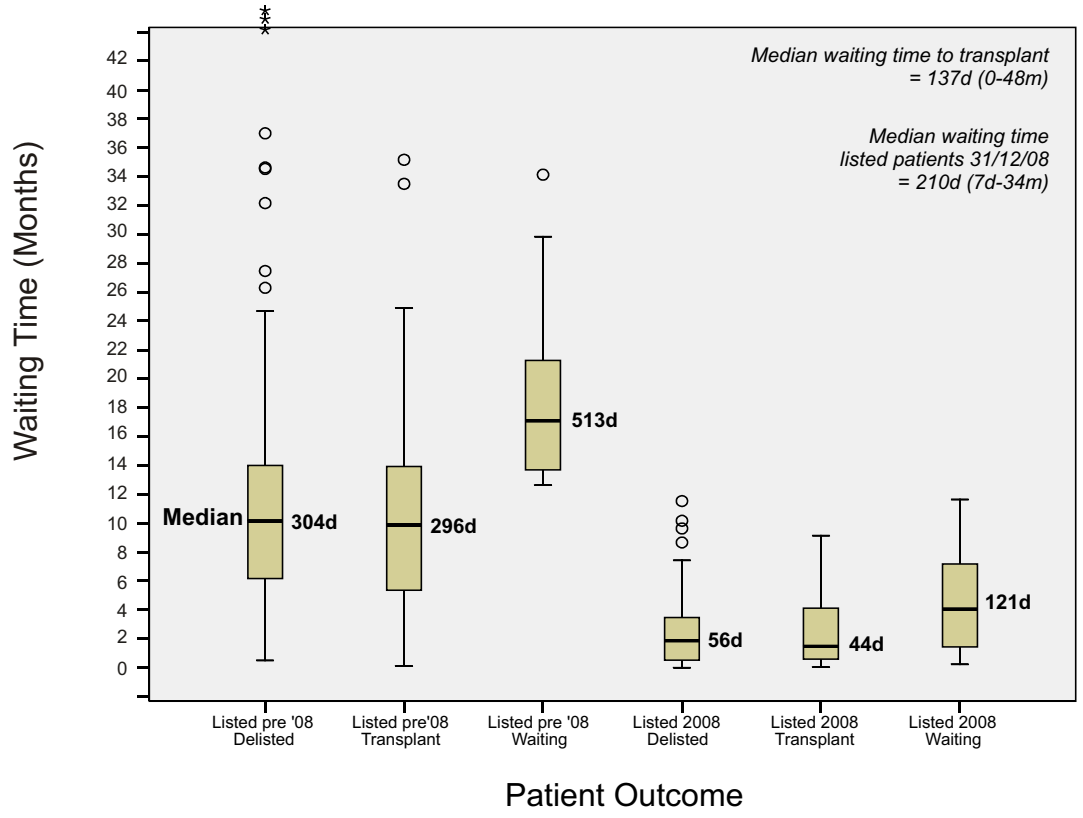
* *% of total number listed*

** *% of blood group*

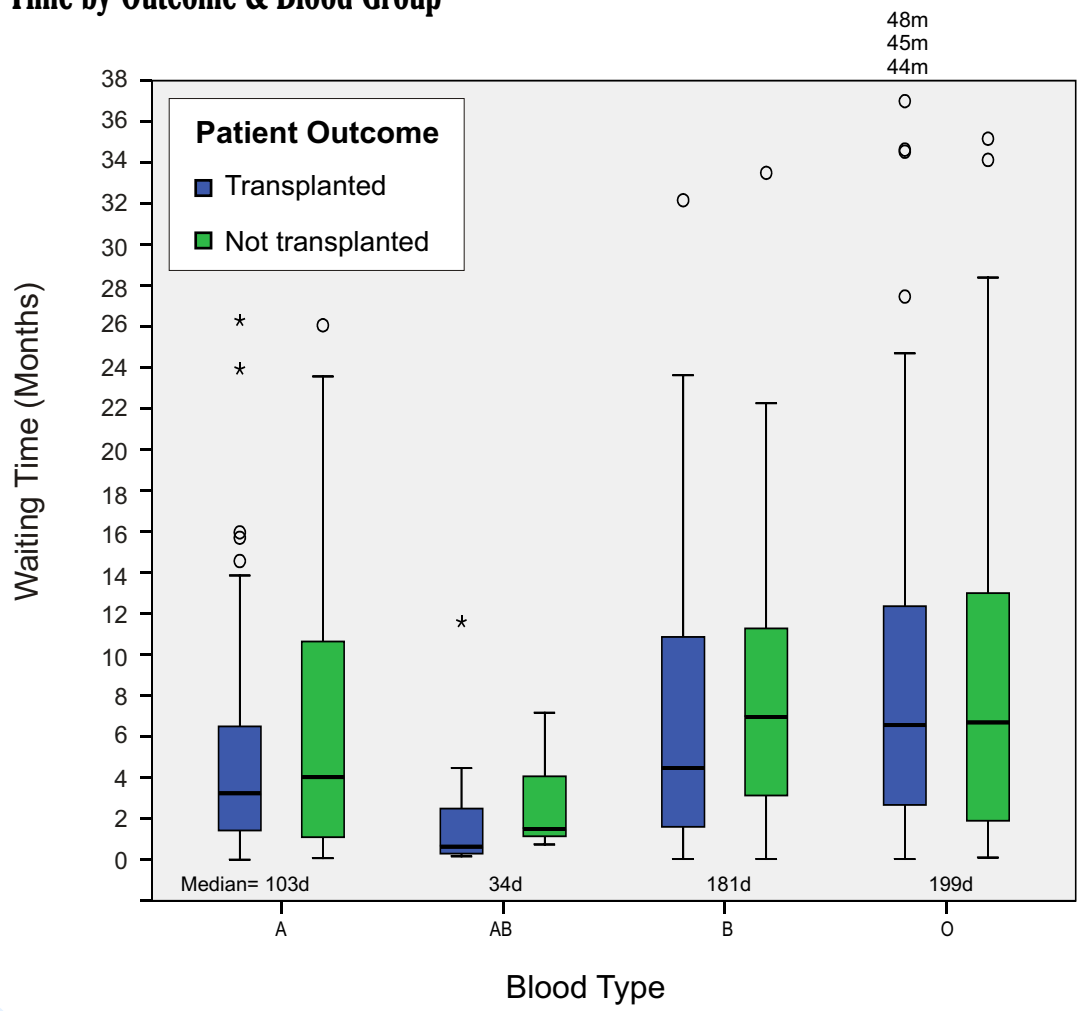
Waiting Time to Transplant 2008



Waiting Time by Outcome



Waiting Time by Outcome & Blood Group



Section 9

Liver Transplantation and Cancer

Cancer in Liver Transplant Recipients
N = 3066

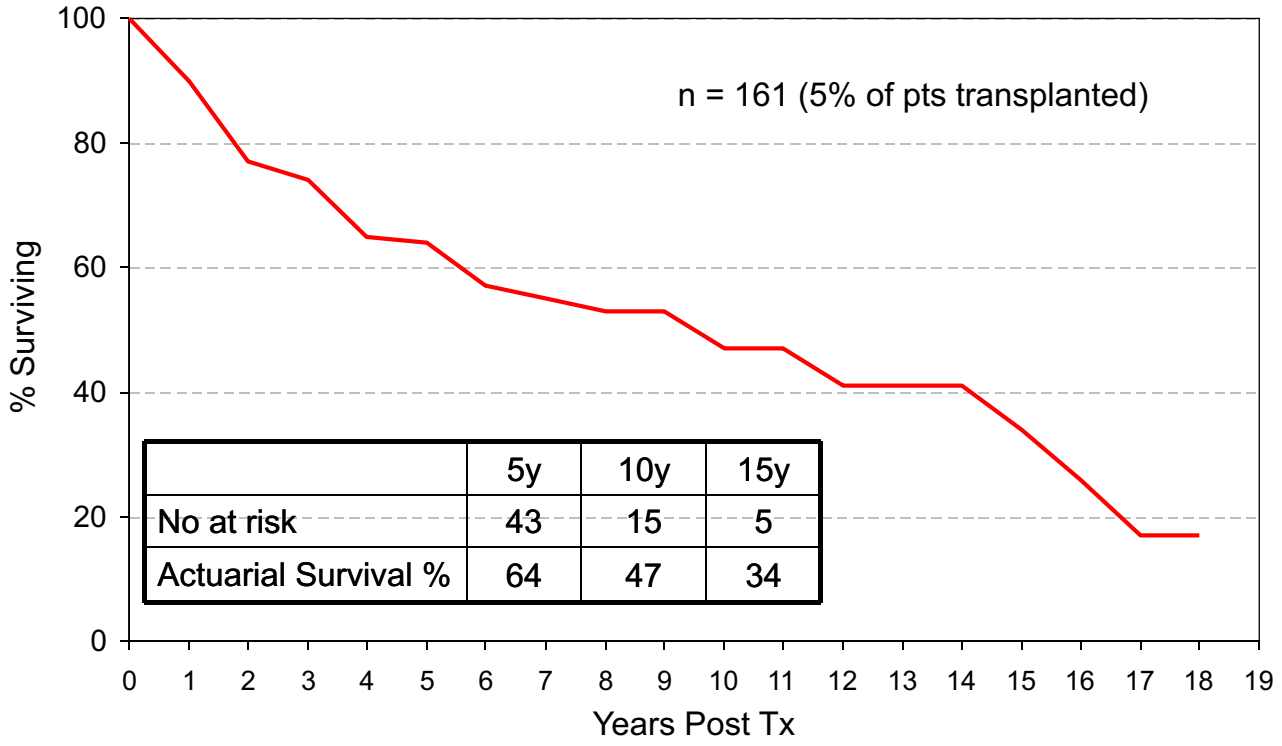
At Tx		
Tx for Liver Ca	161	(5%)
Liver Ca as a Secondary Diagnosis	328	(11%) 329 Ca
Total	488*	(16%) 490 Ca
Post Tx		
Recurrent Liver Ca	80	(3% of all pts, 16% of pts with Ca at Tx)
De Novo Ca	179	(6%) 188 Ca
Skin Ca	370	(12%)
Total	629	(21%)
Multiple Ca types	91	(3% of all pts)
Pre-Tx cancer developed de novo cancer	19	(4% of pts with Ca at Tx)
Transferred from Donor	2	
Developed non skin Ca < 90days	10	

* 1 patient had a primary and a secondary liver cancer

Liver Cancer as Primary Diagnosis
N= 3066

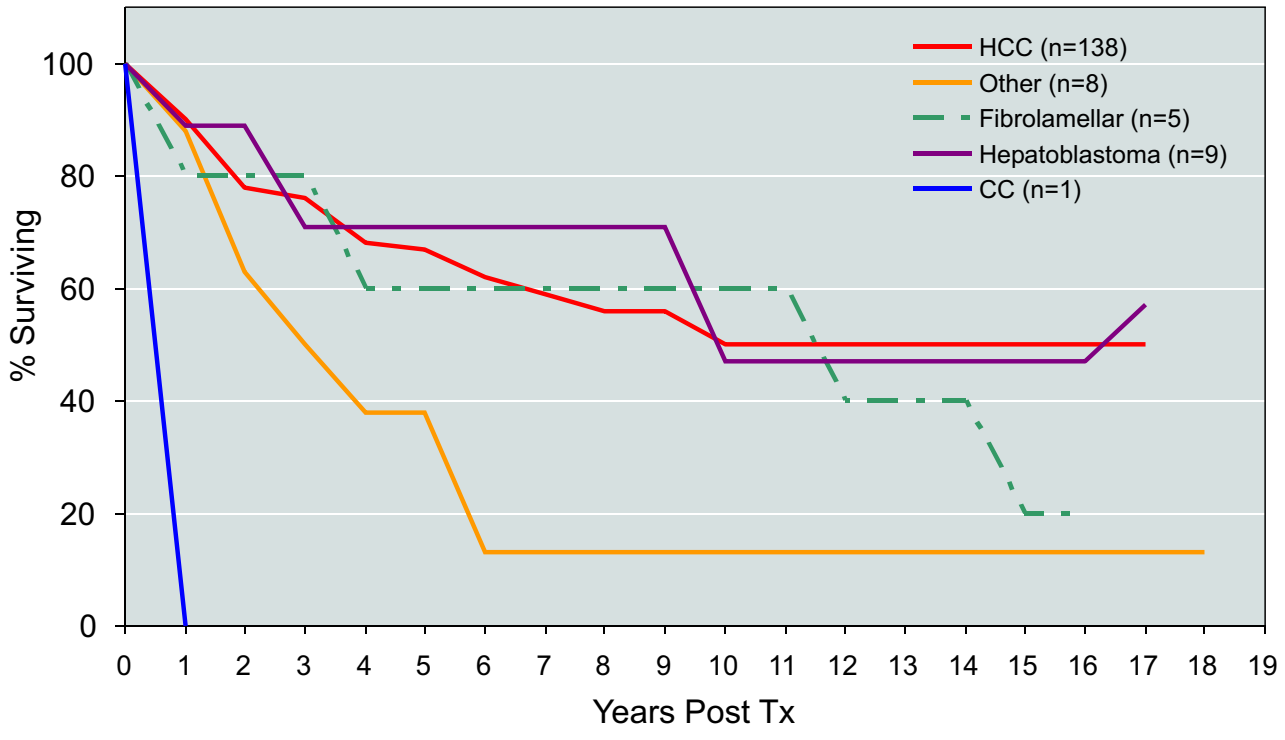
TYPE OF CA	No	DIED	DIED OF THIS CA
HEPATOCELLULAR CA	138	41	23 (18%)
HEPATOBLASTOMA	9	3	2 (12%)
FIBROLAMELLAR	5	5	2 (40%)
CARCINOID	4	4	4 (100%)
CHOLANGIOCARCINOMA	1	1	1 (100%)
ANGIOSARCOMA	1	1	1 (100%)
GASTRINOMA	1	1	1 (100%)
PANCREATIC ISLET CELL	1	1	1 (100%)
EPITHELOID HAEMANGIOENDOTHELIOMA	1	0	0
TOTALS	**161 (5% of pts)**	**57 (35% of those with PCa)**	**35 (22% of those with PCa)**

Overall Survival
Primary Liver Cancer
N = 161 (5% of patients transplanted)



	5y	10y	15y
No at risk	43	15	5
Actuarial Survival %	64	47	34

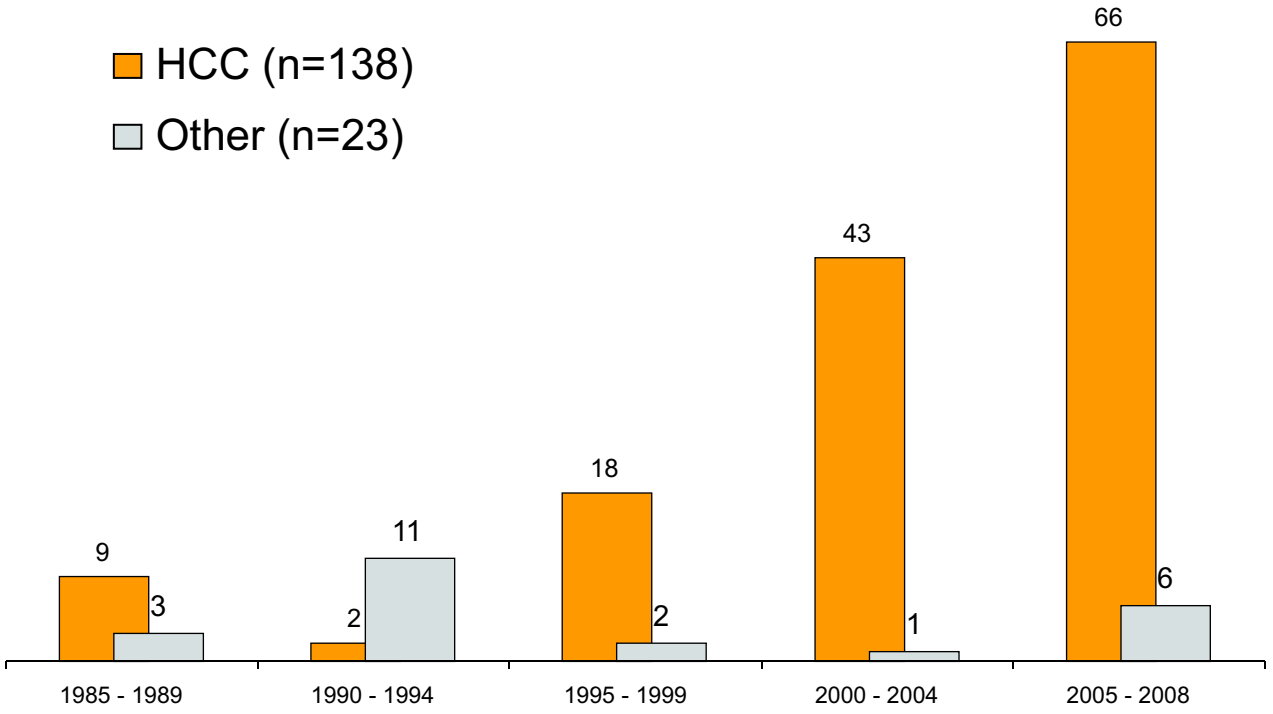
Overall Survival
Primary Liver Cancer
N = 161/3066 (5%)



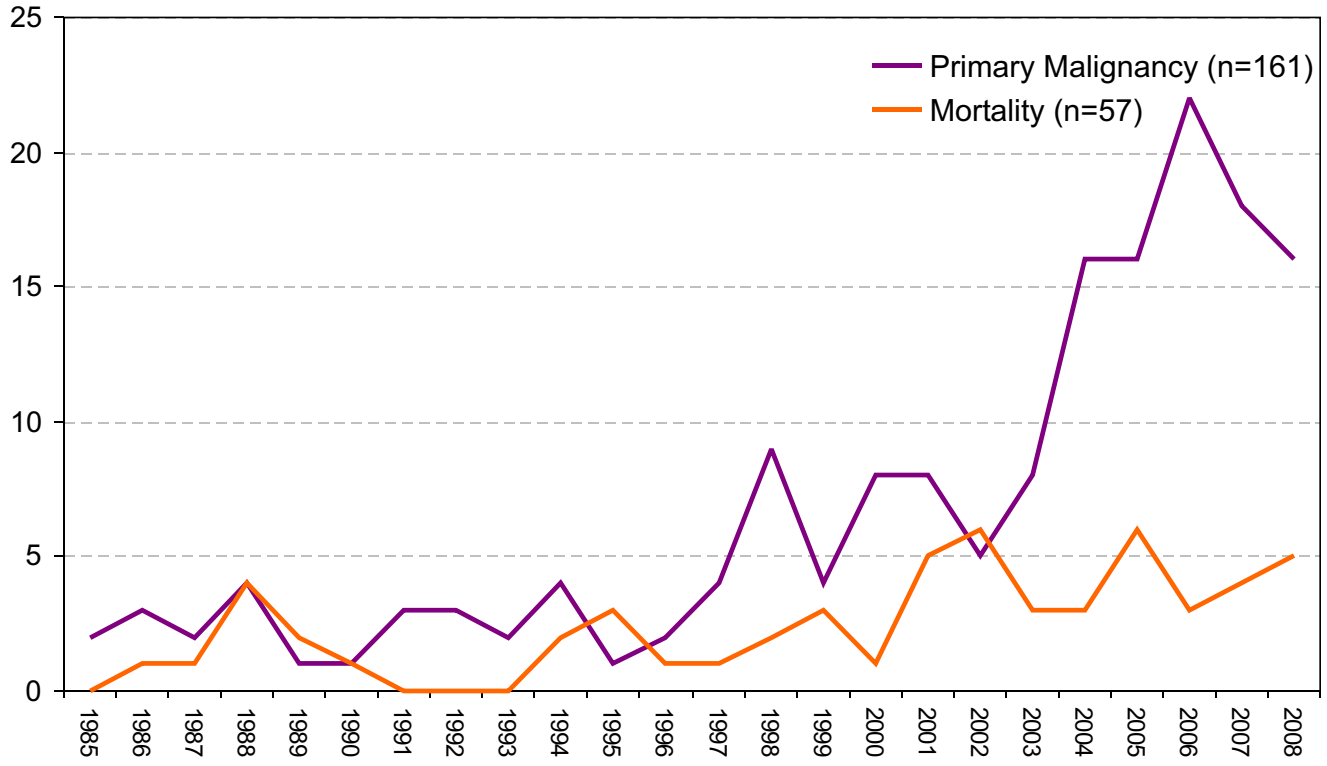
Primary Liver Cancer
Actuarial Survival Summary
N = 3066

		1yr	5yr	10yr	15yr
HCC (n=138)	n	112	34	10	2
	%	90	67	50	50
Hepatoblastoma (n=9	n	89	4	2	2
	%	88	71	47	47
Other (n=8)	n	8	4	2	2
	%	86	38	13	13
Fibrolamellar (n=5)	n	5	4	4	2
	%	80	60	60	20
CC (n=1)	n	1			
	%	1			

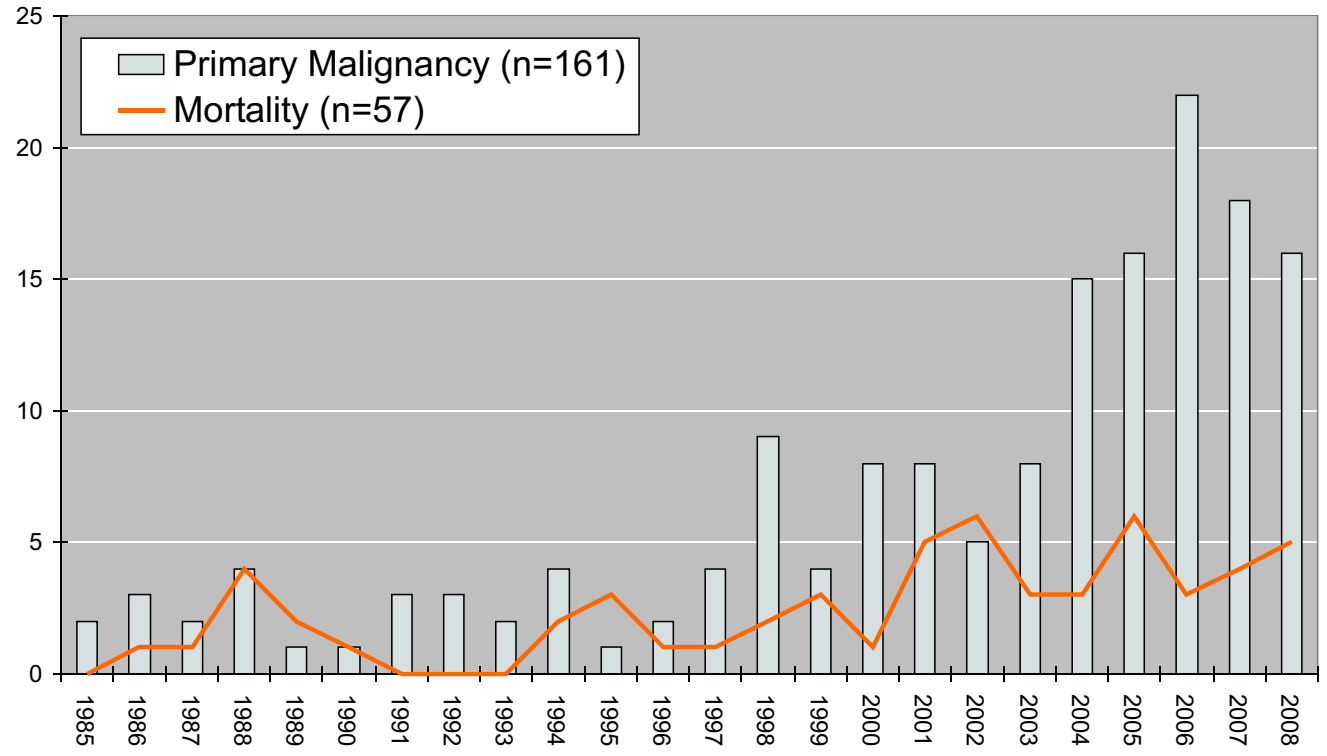
Liver Cancer as Primary Diagnosis
n = 161/3066 (5%)



Primary Liver Cancer Incidence and Mortality n=161/3066 (5%)



Primary Liver Cancer Incidence and Mortality

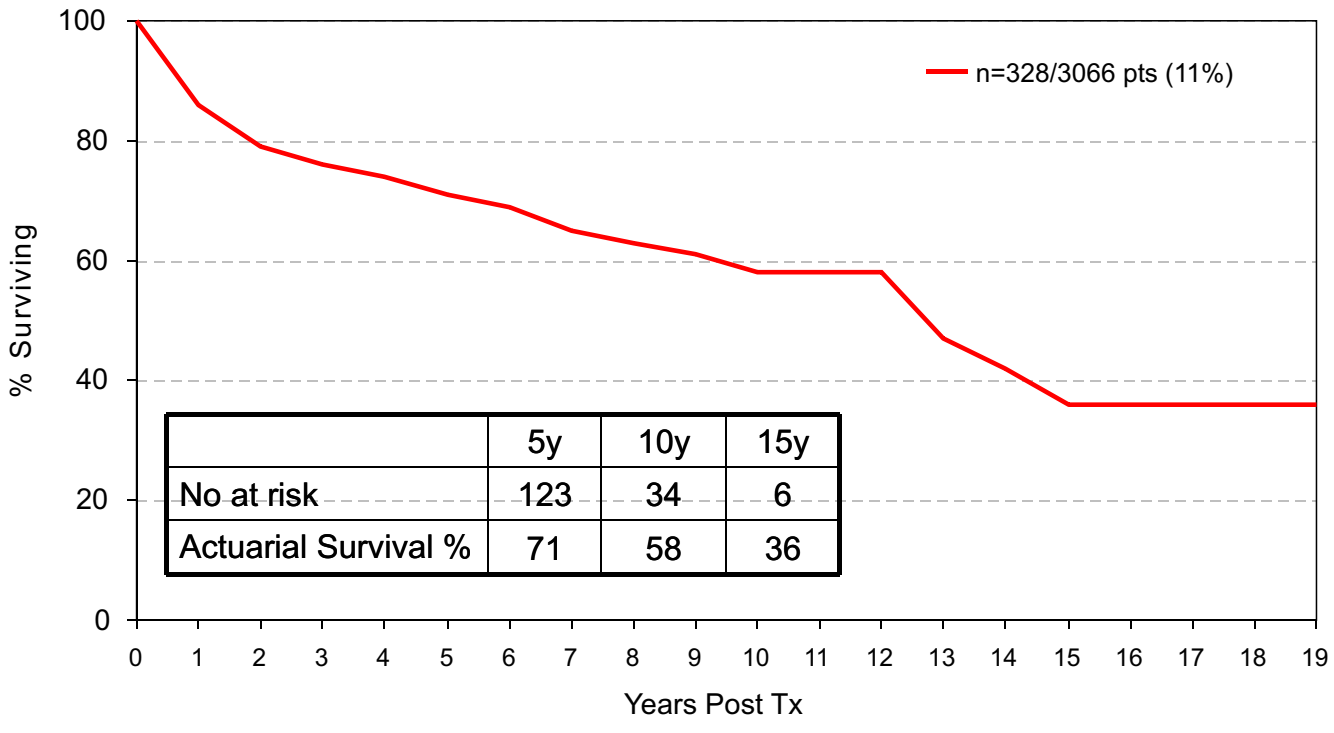


Liver Cancer as a Secondary Diagnosis
N = 3066

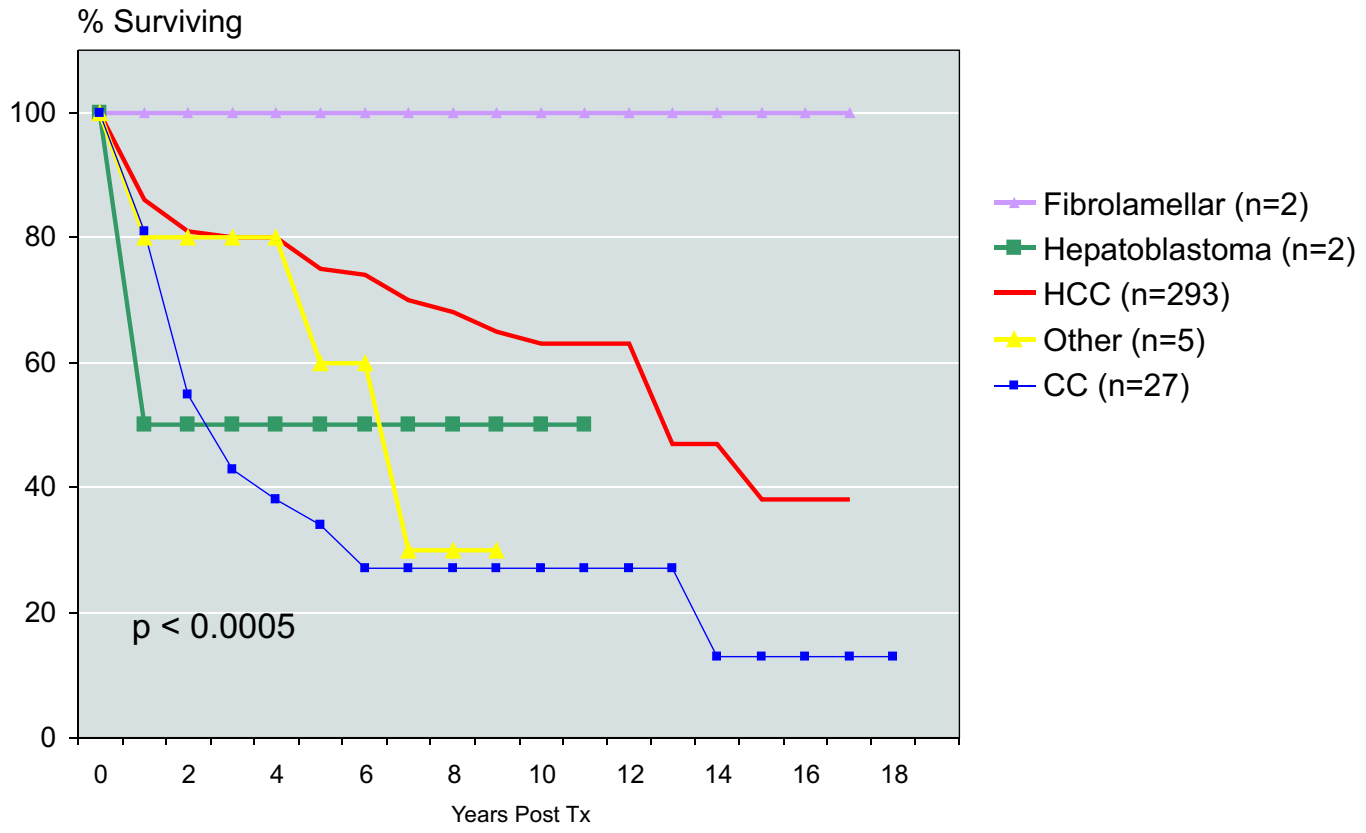
	No	Died	Died of This Cancer
HEPATOCELLULAR CA*	293	77	22 (7.5%)
CHOLANGIO CA	27	19	13 (48%)
ADENOCARCINOMA	3	3	0
FIBROLAMELLAR	2	0	0
HEPATOBLASTOMA*	2	1	0
ANGIOSARCOMA	1	1	1
EPITHELOID HAEMANGIOCA	1	0	0
Total	**329* in 328 pts (11%)**	**101 (31% of pts with SCa)**	**36 (11.5% of pts with SCa)**

*** 1 patient had 2 secondary cancers**

Overall Survival
Liver Cancer as a Secondary Diagnosis



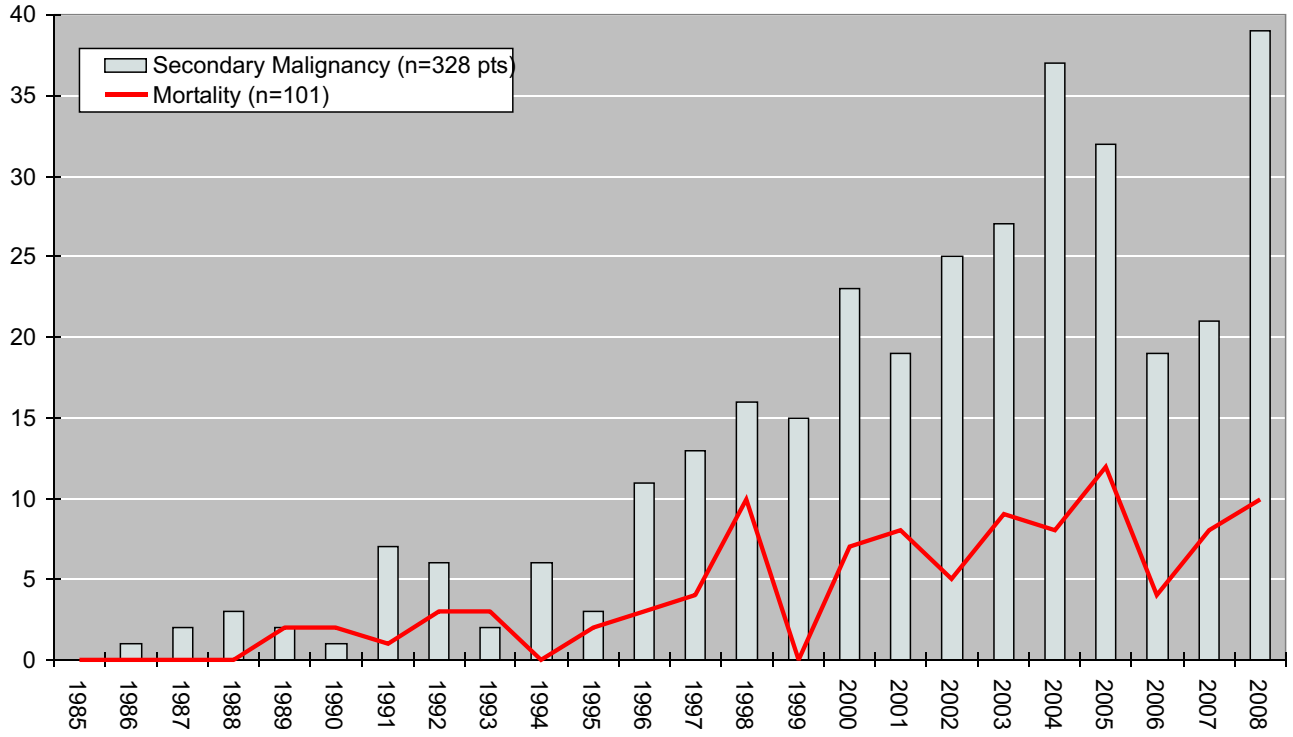
Liver Cancer as a Secondary Diagnosis
N = 3066



Secondary Liver Cancer
Actuarial Survival Summary
N = 3066

		1yr	5yr	10yr	15yr
CC (n=27)	n	21	6	4	2
	%	81	34	27	13
HCC (n=293)	n	219	113	29	4
	%	86	75	63	38
Hepatoblastoma (n=2)	n	2	2	2	1
	%	50	50	50	50
Fibrolamellar (n=2)	N	2	2	2	2
	%	100	100	100	100
Other (n=5)	n	5	3		
	%	80	60		

Liver Cancer as a Secondary Diagnosis Incidence and Mortality n=328/3066 pts (11%)

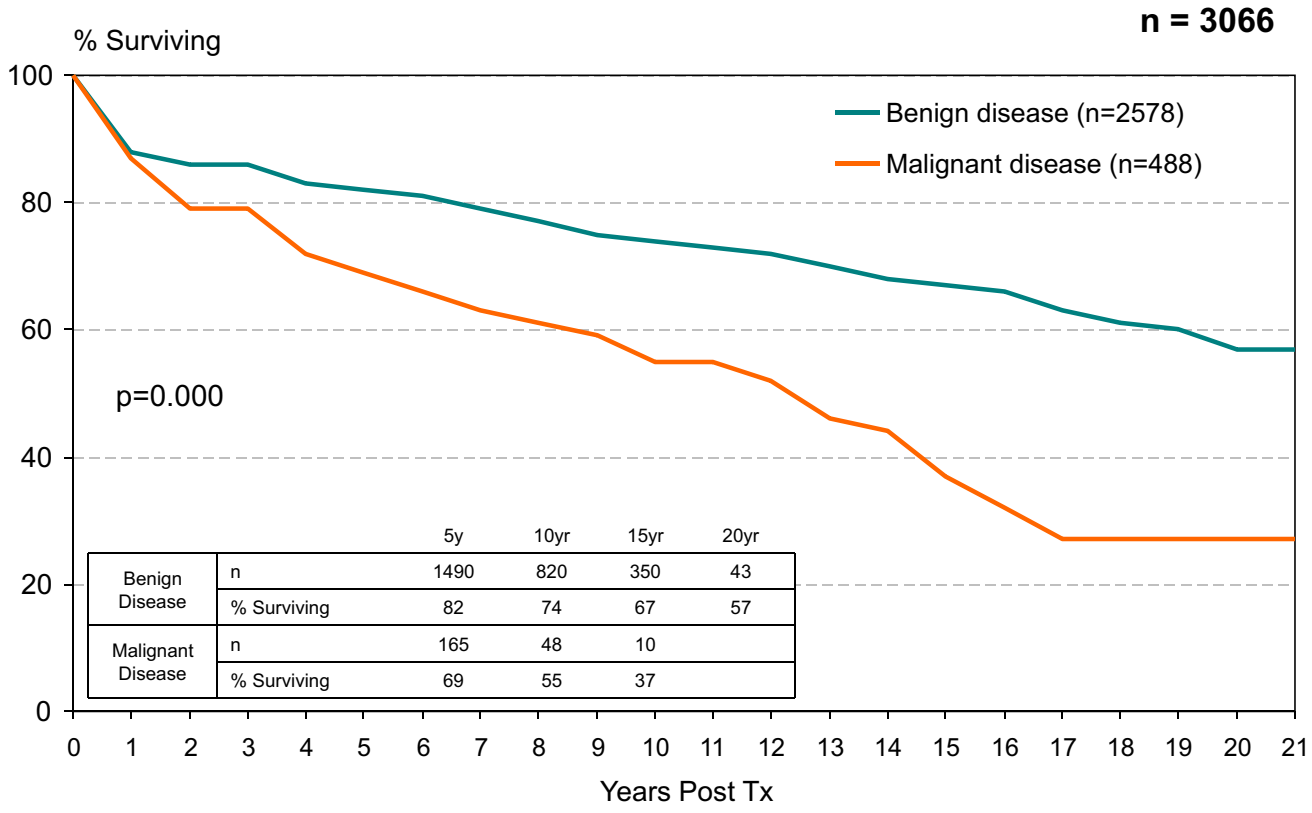


Liver Cancer (Primary or Secondary Diagnosis) N = 3066

TYPE OF CA	NO	DIED	DIED OF THIS CA
HEPATOCELLULAR CA*#	431	118	45 (10%)
CHOLANGIOCARCINOMA#	28	20	14 (50%)
HEPATOBLASTOMA*	11	4	2 (18%)
FIBROLAMELLAR	7	5	2 (29%)
CARCINOID	4	4	4 (100%)
ADENOCARCINOMA	3	3	0
EPITHELOID HAEMANGIOENDOTHELIOMA	2	0	0
ANGIOSARCOMA	2	2	2 (100%)
GASTRINOMA	1	1	1 (100%)
PANCREATIC ISLET CELL	1	1	1 (100%)
TOTALS	**490 Ca in 488 pts (16% of pts)**	**158 (32%of those with Ca)**	**71 (15% of those with Ca at Tx)**

*** 1 patient had 2 secondary cancers; # 1 patient had a primary and secondary liver malignancy**

Patient Actuarial Survival
Benign Disease vs Pre Transplant Liver Malignancy
N = 3066



		5y	10yr	15yr	20yr
Benign Disease	n	1490	820	350	43
	% Surviving	82	74	67	57
Malignant Disease	n	165	48	10	
	% Surviving	69	55	37	

De Novo Non Skin Cancer
N = 3066

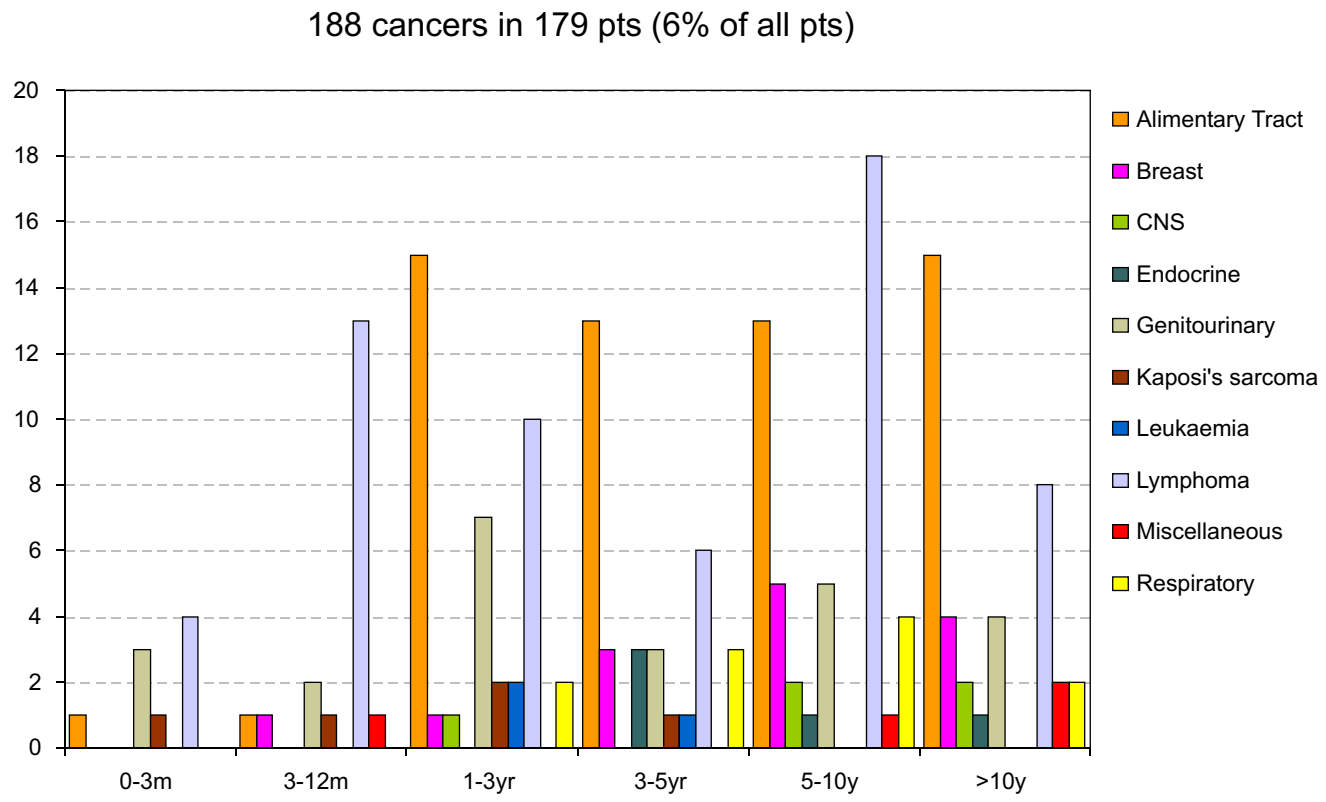
m = median

n = 3066

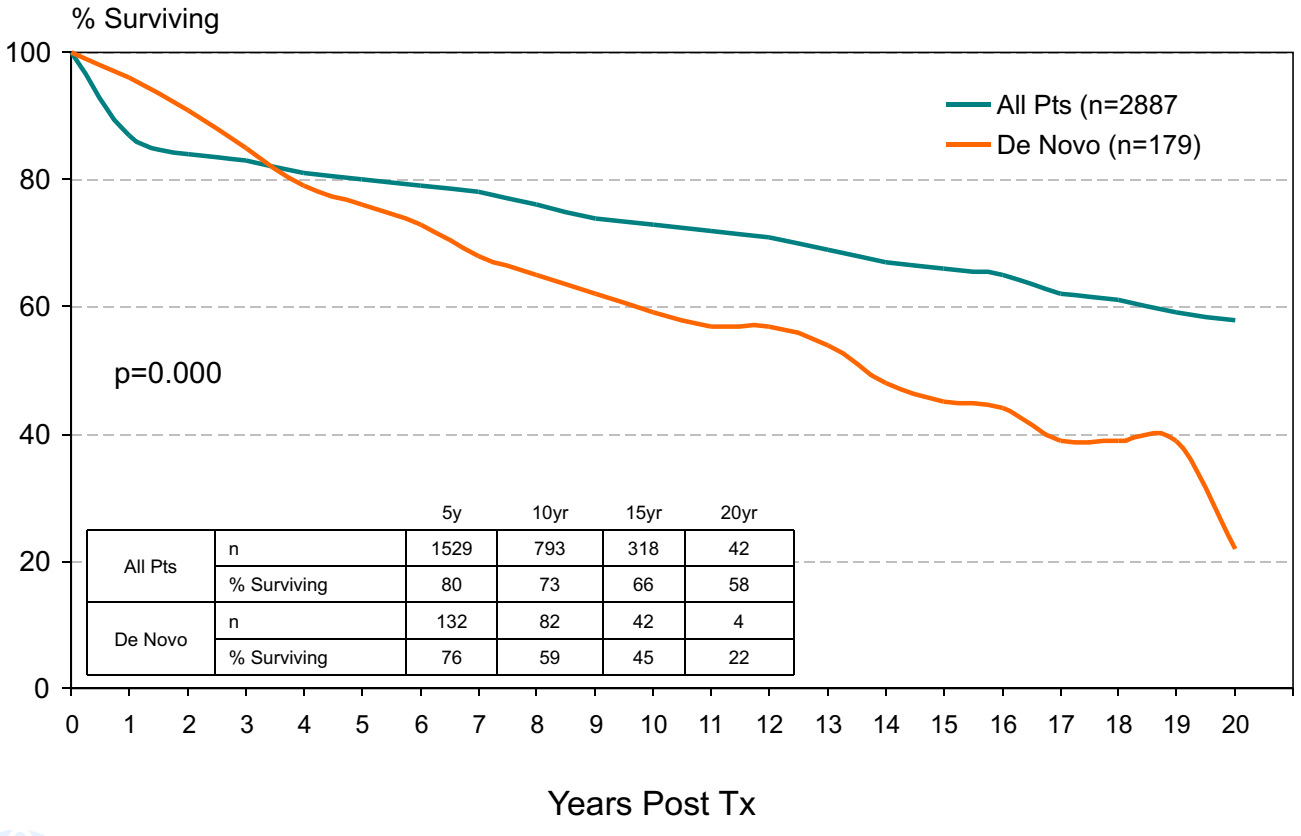
	No	Male	Female	Age of pts (yrs)	Time to diagnosis (mths)	Died of This Cancer
Alimentary*	59	42	17	12.6 – 78 (m 58)	1 – 217 (m 58)	26 (44%)
Lymphoma*	59	38	21	1.5 – 70 (m 46)	1 – 182 (m 46)	24 (41%)
Genitourinary*	24	14	10	38.5 – 70.5 (m 60)	2 – 165 (m 29)	2 (8%)
Breast	14	-	14	30 – 63 (m 45)	11 – 204 (m 80)	3 (21%)
Respiratory	11	8	3	29 – 68 (m 52)	13 – 121(m 63)	8 (73%)
Kaposi's	5	4	1	32.1 – 64 (m 49)	2 – 48 (m 16)	0
Endocrine	5	2	3	36 – 70 (m 63)	47 – 144 (m 55)	2 (40%)
CNS	5	3	2	16.5 – 75 (m 65)	13 – 174 (m 93)	4 (80%)
Leukaemia	3	1	2	2.9 – 49.5 (m 37)	16 – 44 (m 30)	0
Miscellaneous	4	2	2	62 – 67 (m 64)	6 – 213 (m 102)	0
Total	***188 ca in 179 pts**	**114**	**75**	**1.5 – 78 (m 53)**	**1 – 217 (m 55)**	**69 (39% of pts with Ca)**

Fifteen patients also had a livercancer at Tx; * 7 patients had more than 1de novo malignancies

Time to 1st De Novo Non Skin Cancer
N = 3066

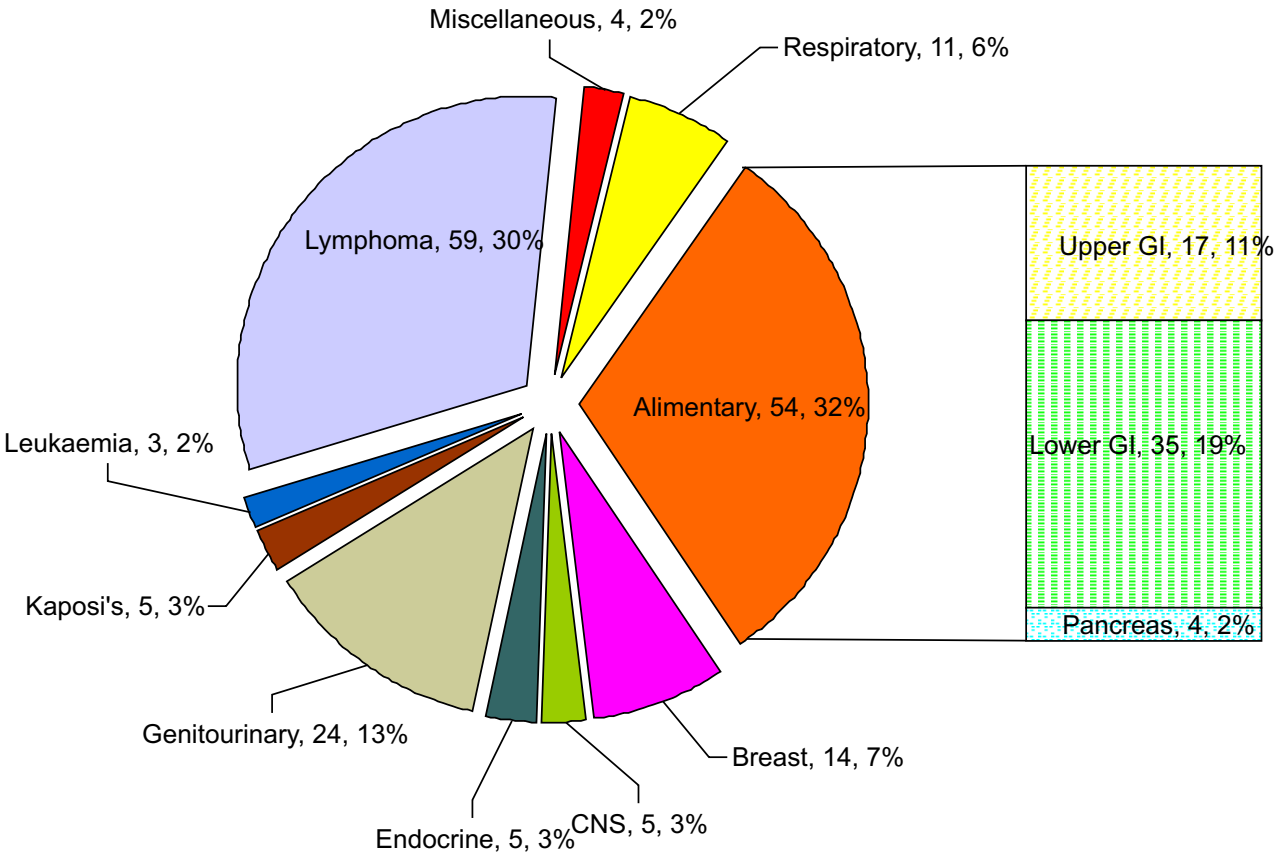


De Novo Non Skin Cancer vs All Patients
N = 3066

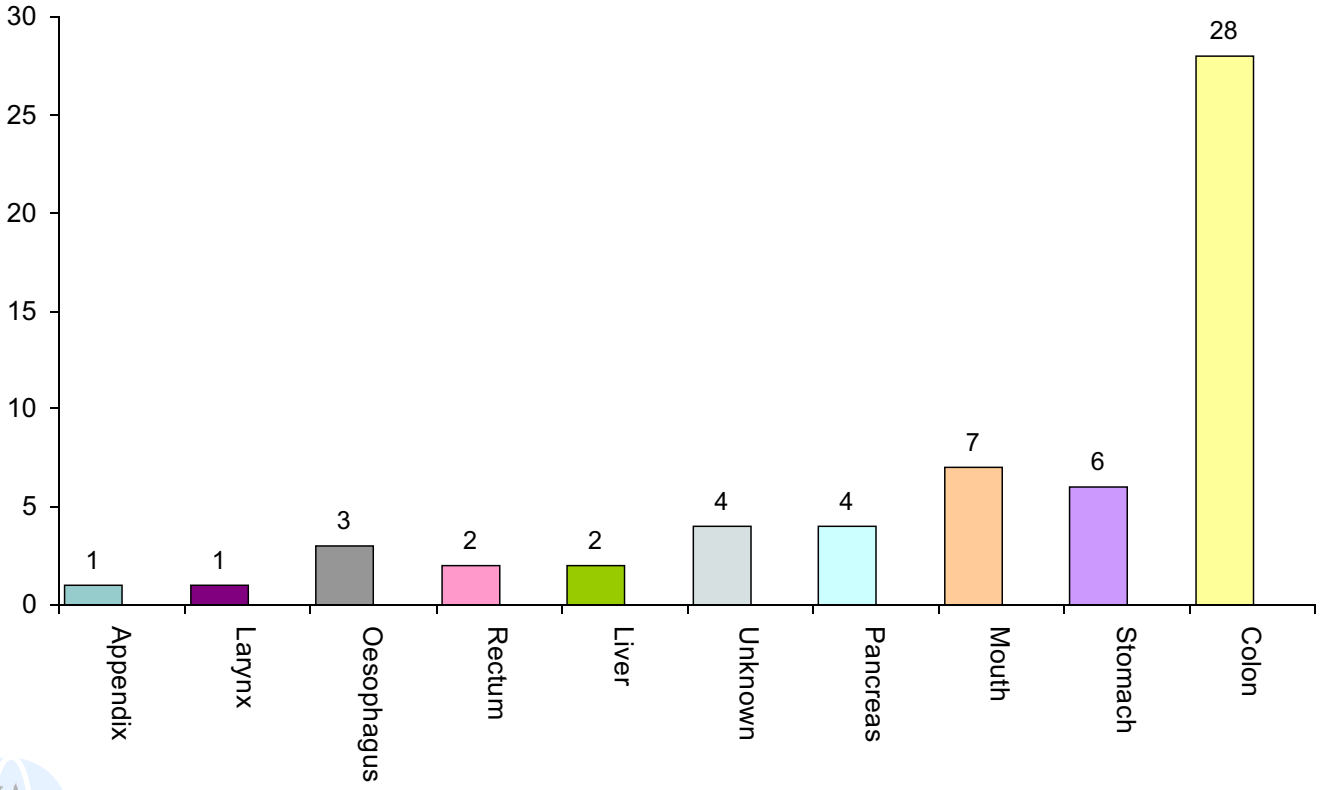


		5y	10yr	15yr	20yr
All Pts	n	1529	793	318	42
	% Surviving	80	73	66	58
De Novo	n	132	82	42	4
	% Surviving	76	59	45	22

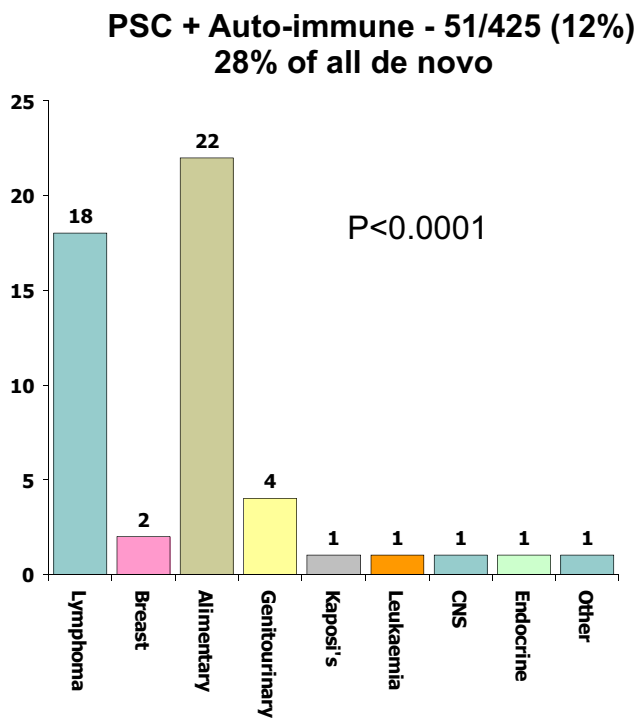
De Novo Non Skin Cancer
n = 179/3066 (6%)

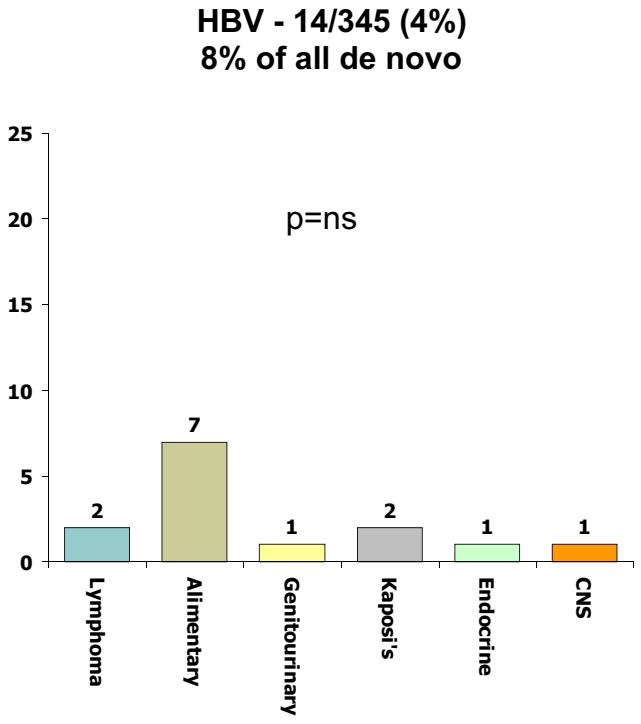


De Novo Non Skin Cancer
Alimentary Tract Incidence
n = 58/188 cancers (31%)

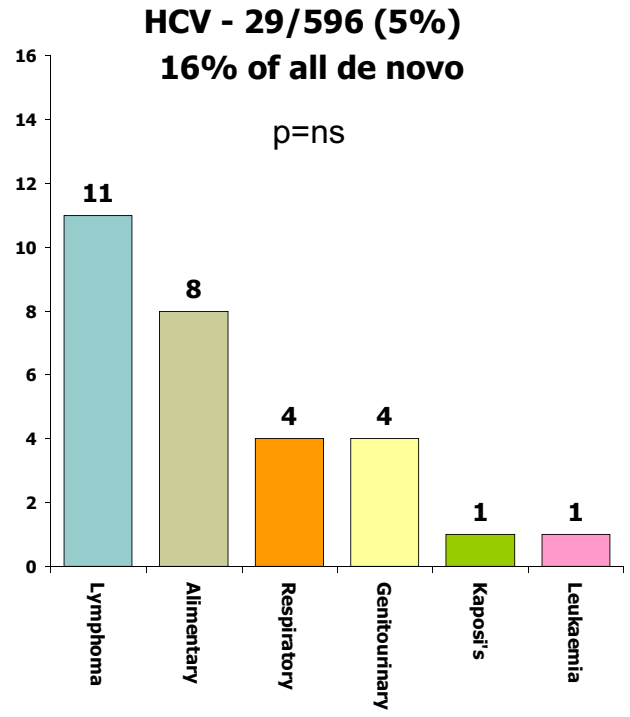


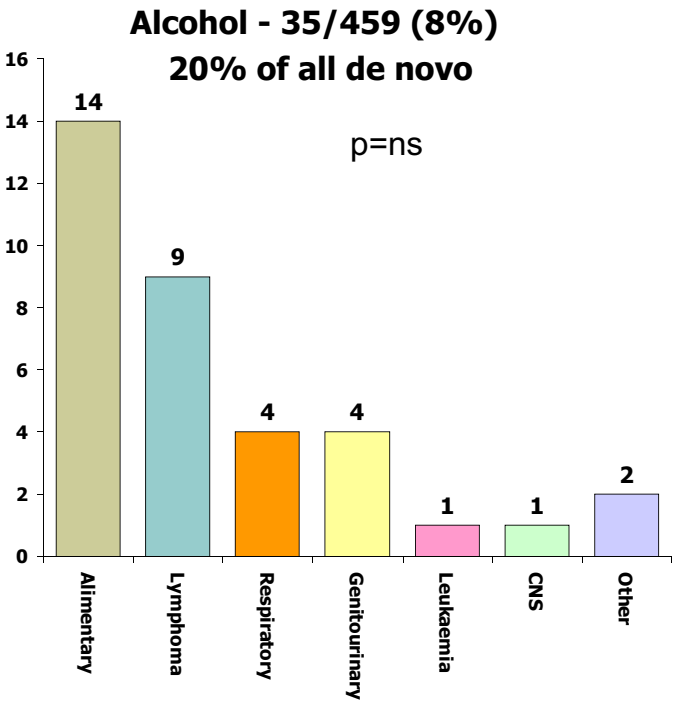
Pre Transplant Liver Disease and De Novo Non Skin Cancer n =179/3066 (6%)



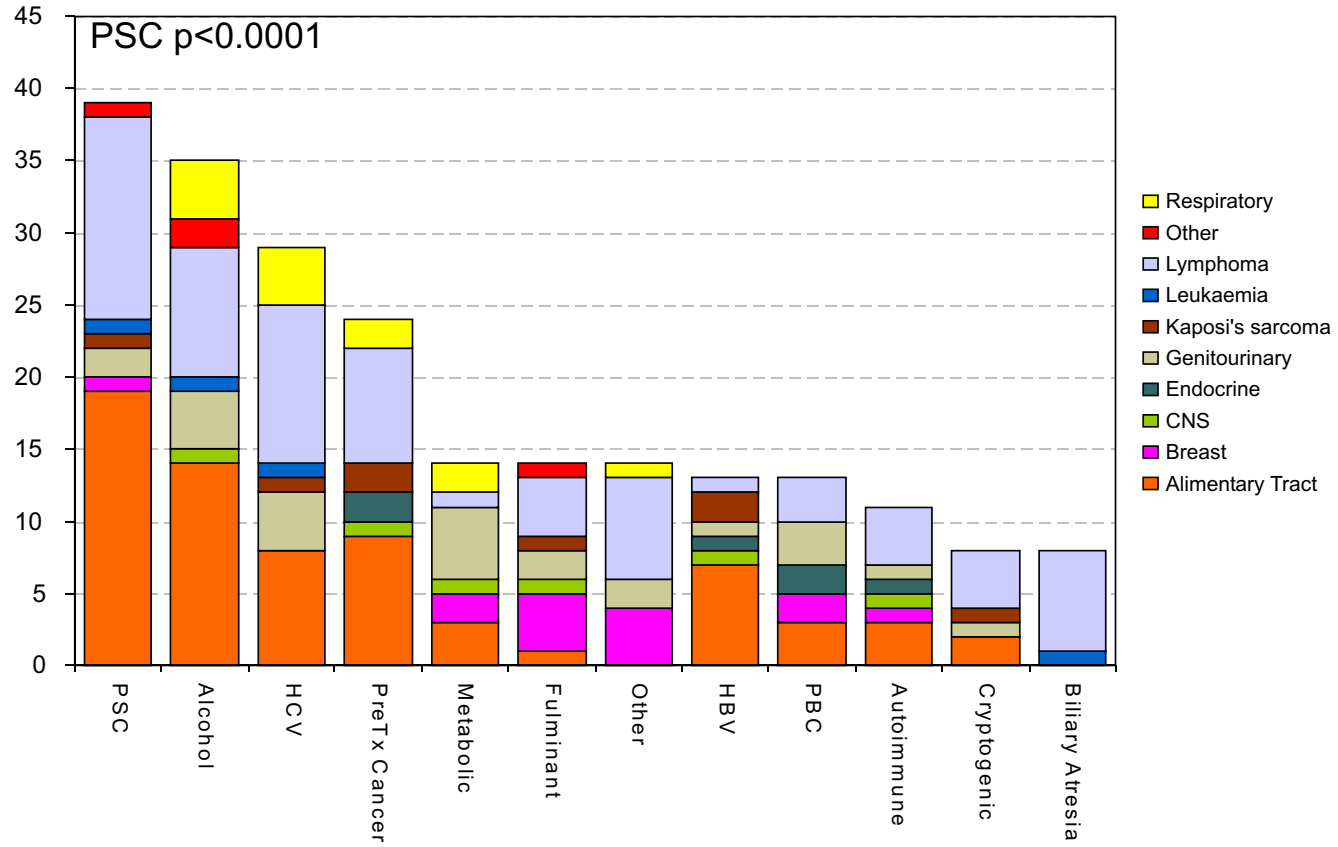


Pre Transplant Liver Disease and De Novo Non Skin Cancer n =179/3066 (6%)





Pre Transplant Liver Disease and De Novo Non Skin Cancer n = 179/3066 (6%)

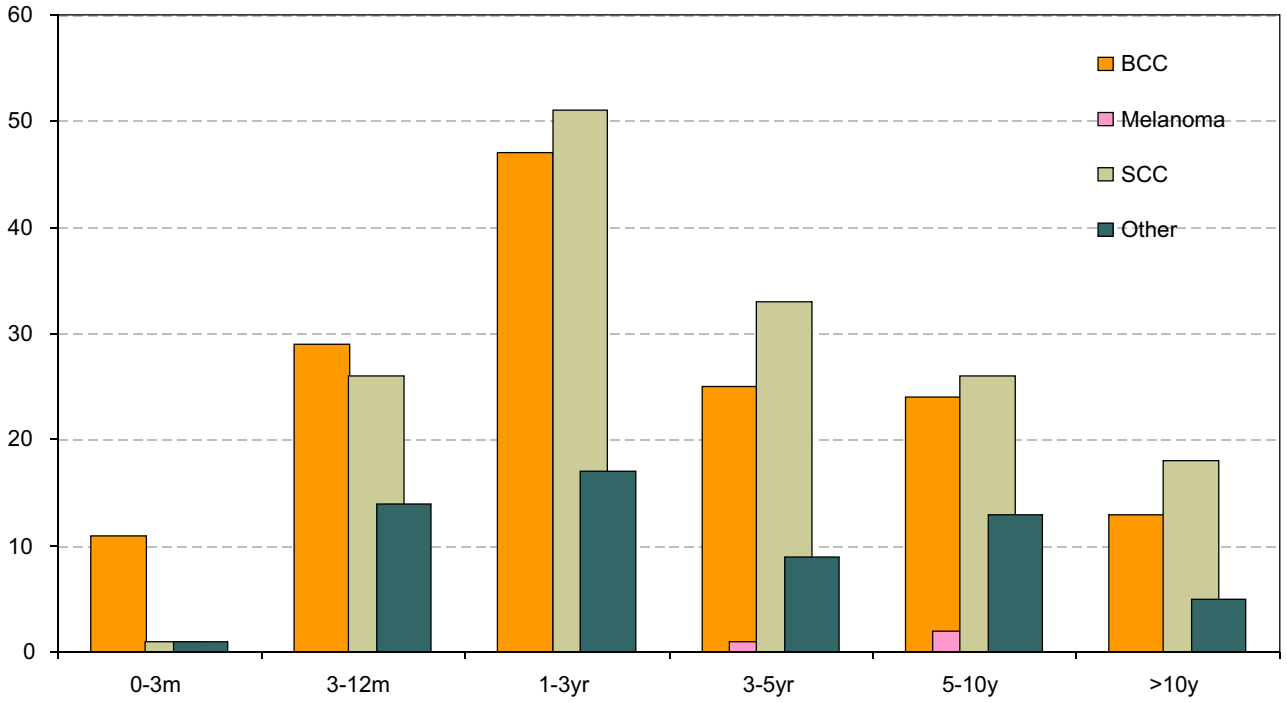


Skin Ca Post Liver Transplant n = 3066

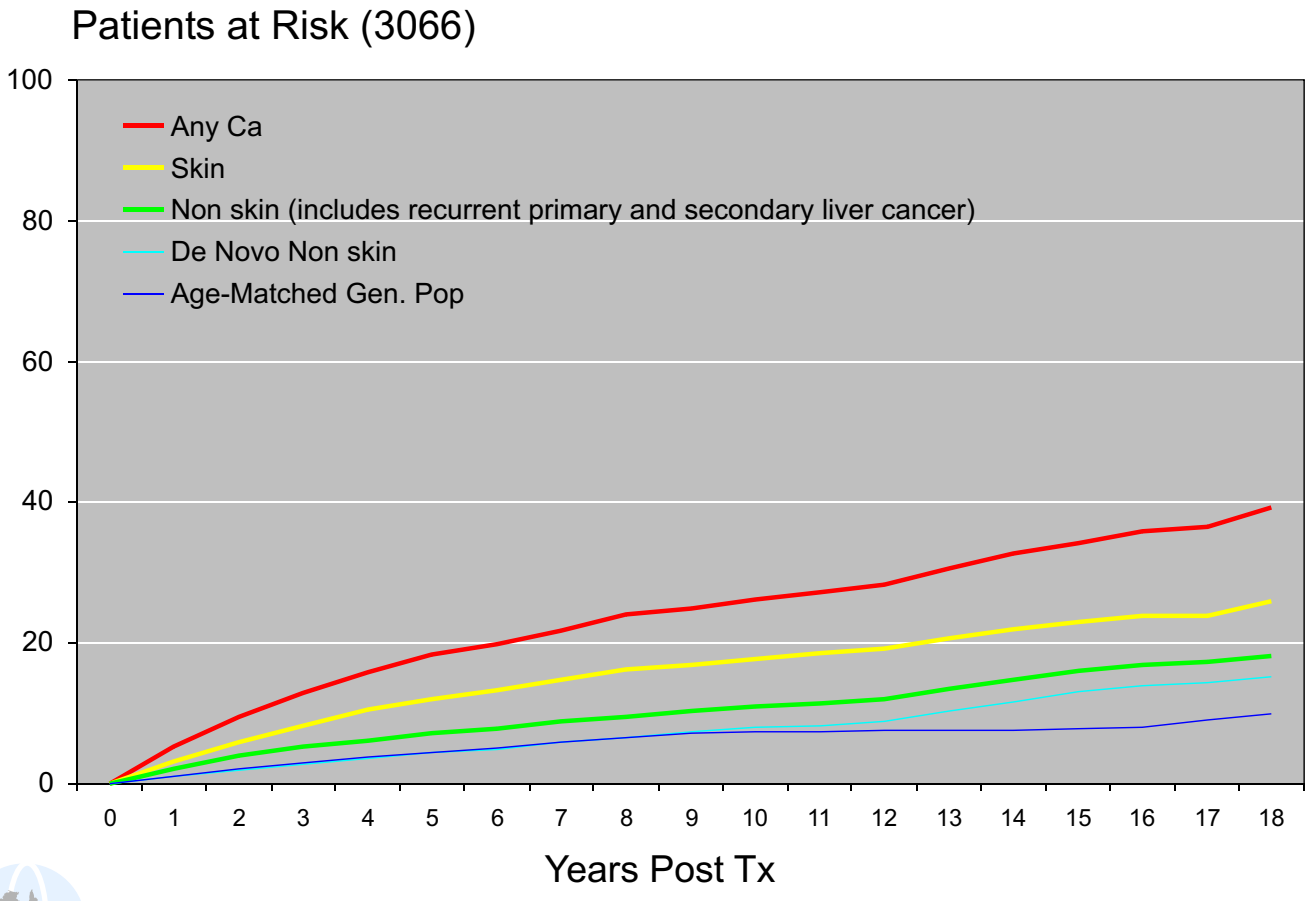
Type of Skin Cancer	Pts	Cancers
BCC	**226**	**685**
SCC	**232**	**961**
Melanoma	**16**	**16**
Other	**151**	**828**
Total	**370 (12% of all pts)****	**2490**

**** 163 pts had multiple skin cancer types**

Time to 1st Skin Cancer Development
n = 3066
370 (12% of all pts)



Cumulative Risk of Diagnosis of Cancer Following Liver Transplant 1985-2008



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/

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	1	1
Haemochromatosis	2	23	25
Homozygous Hypercholesterolemia	3	1	4
Indian childhood cirrhosis	1	0	1
Other *	6	2	8
Primary hyperoxaluria	6	6	12
Tyrosinemia	4	0	4
Urea cycle disorders **	12	3	15
Wilsons disease	7	26	33
Total	77	134	211

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

** OTC deficiency 10; citrullinemia 3; argininosuccinic aciduria 2

Appendix III

ANZLTR PRIMARY Diagnosis - Other by Age Group

Primary Diagnosis	Age group		Total
	Child	Adult	
Alagille syndrome	24	2	26
Alagille non-syndromic	2	0	2
Benign liver tumour -Adenomatosis	0	2	2
Benign liver tumour-Hemangioma	0	2	2
Caroli's disease	1	12	13
Choledocal cyst	1	2	3
Cholestatic disease-Other	1	5	6
Chronic Budd Chiari	1	29	30
Congenital biliary fibrosis	1	3	4
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	39	39
Polycystic Liver disease	0	14	14
Polycystic liver and kidney disease	0	7	7
Progressive familial intrahepatic cholestasis(PFIC)	14	4	18
Secondary biliary cirrhosis	1	11	12
Secondary biliary cirrhosis - Hepatolithiasis	0	4	4
Secondary biliary cirrhosis - Cystic fibrosis	7	11	18
Other -specify #	3	15	18
Total	64	176	240

\# *Vanishing bile duct syndrome*
Haemangiotelangiectasia
Veno-occlusive disease
Chronic Active Hepatitis A
Non-cirrhotic portal hypertension
Kassabach-Merritt syndrome
Arterial-venous malformation
Hereditary haemorrhagic telengectasia / 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	6	6
Acute Unknown / unspecified	35	67	102
Acute -Paracetamol	0	11	11
Acute -Other drugs	2	14	16
Acute Herbs / mushrooms	0	5	5
Acute - Hepatitis A	0	2	2
Acute - Hepatitis B	0	44	44
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	9	9
Total	55	238	293

Appendix V

ANZLTR Causes of Patient death

Graft failure - other		
Vascular thrombosis		19
	Hepatic artery 11 Portal vein 7 Hepatic vein 1	
Non thrombotic infarction		3
Primary non function		20
Massive haemorrhagic necrosis		4
Recurrent disease *(ALD, PSC, CAH:AI)*		7
De novo Hep C		2
Biliary Complications		11
Other *(PNC, immune hepatitis, outflow obstruction)*		9

Miscellaneous		
Multiorgan failure		26
Renal Failure		18
Graft vs Host disease		6
Social (accident, suicide,non-compliance, Rx withdrawn)		9
Sudden death (cause unknown)		18
Other (Hyperkalaemia,motor neurone disease diabetes complications, drug reaction, progression FAP)		10

Appendix VI

SUMMARY
Cancer in Liver Transplant Recipients