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AUSTRALIA & NEW ZEALAND

LIVER TRANSPLANT REGISTRY

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

DATA TO 31-12-2007

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ANZLT Registry Report 2008
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Editors : S.V. Lynch, G.A. Balderson

STATISTICAL METHODS

Kaplan-Meier survival curves have been produced using SPSS® for Windows™ Release 16.0, 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 19th Report of the Australia and New Zealand Liver Transplant Registry (ANZLTR). This report contains data to the 31st December 2007 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 now contribute their data by direct entry into the ANZLTR database. A full list of the Units and their contact information can be found in 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 Commonwealth Department of Health and Aging [DHA] for their financial contribution. Recent additional support from the DHA is allowing expansion of the information collected in the data base and we look forwarding 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

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Summary

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5. Between January 1985 and 31st December 2007, 3076 orthotopic liver transplants (OLT) were performed in Australia and New Zealand on 2850 patients, 2332 adult patients (> 15 years) [82%] and 518 children [18%]. The median age of all recipients was 46.2 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. There was a decrease in the total number of new patients transplanted in 2007 compared with the previous 3 years, particularly for adult recipients. but there was an increase in the number of new paediatric patients compared with 2006.

7. The trend to increasing age of adult recipients in recent years continued and the overall adult median age is now 49.1 years. The median age of new adult recipients in 2005-07 was 51.4 years.

8-9. Four fewer transplants were performed in 2007 then in 2006. Split grafts now make a significant contribution to the total number of paediatric transplants performed providing 16 of 32 [50%] grafts in 2007 and 111 of 592 [19%] overall. In children, other reduced size grafts have been used in 290 [49%] cases including 24 living donor grafts. One child has been treated with liver cell implantation. Of adult patients, 152 have received reduced size grafts - 125 split liver grafts (including 1 as auxiliary graft), 24 other reduced size grafts (1 as auxiliary graft) and 5 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 19% 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 2007 (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 2005-07 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 -07, 34% primary diagnosis CVH [27% Hep C,5% 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 2007 was 45%.

15. Current 1 year patient survival of all patients is 87% at 1 year, 79% at 5 years and 71% at 10 years. Children had a significantly better survival rate then adults.

16. Whilst older children had superior 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.

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 coinfections 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. There were no differences in survival between adults and children transplanted for fulminant hepatic failure [acute and sub-acute] with 5 year survival of 74%.

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.

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Summary

24. Graft survival was significantly worse in second and third grafts.

25. Both split and other reduced grafts had lower graft survival in the early post-transplant years in both children and adults but had an improving longer term outcome particularly for split grafts.

26. Vascular complications and rejection were the commonest indications for retransplantation. Ten percent of retransplants were due to poor early graft function. Recurrent disease was the indication for retransplantation in 11% of cases [5% 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. Forty-one 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 a fall in the in number of cadaveric donors in 2007 resulting in fewer transplants from deceased donors then in 2006. The number of transplantable grafts was increased by splitting sixteen deceased donor grafts and using livers donated after cardiac death [3 in 2007]. However for the first time , the number of people on the waiting list at 31 December 2007 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 age groups but not for those over 65 years.

31. Thirty patients [24 children, 6 adults] have now received a living donor graft with 8 performed in 2007. Twenty eight were transplanted as a primary graft , 1 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 increased markedly with 195 patients awaiting a transplant at the end of 2007 compared with 133 at 31st December 2006. Delistings due to death, becoming too ill or tumour (HCC) progression were increased to 12.5%. Fifty patients were listed as urgent in 2007 [18 Category 1 and 32 Category 2]. In 2007 the majority of urgently listed patients 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.

35-38 Five hundred and eighty six patients (21%) have had a pre- or post-transplant cancer. One hundred and forty four (5%) of patients were transplanted for liver malignancy and 33 [23% of these patients] have died from this cancer.

39-42 Two hundred and ninety one patients had liver cancer as a secondary diagnosis with hepatocellular carcinoma the most common. However those with cholangiocarcinoma had significantly poorer survival.

42-43 De novo non skin cancers (170) have developed in 161 (6%) patients and 61 [38%] have died from this cancer. Cancers of the alimentary tract (54, 34%) and lymphoma (54, 34%) predominate.
Patients with either de novo non skin cancers or liver cancers have significantly worse long term survival.

44 Lower GI cancers (35) account for 65% of alimentary tract cancers.

45-46 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 ($p<0.0001$).

46-47 Three hundred and forty eight (12%) patients have developed 2223 skin cancers with 147 patients having multiple skin cancer types.

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

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Section 1

Demographic Data

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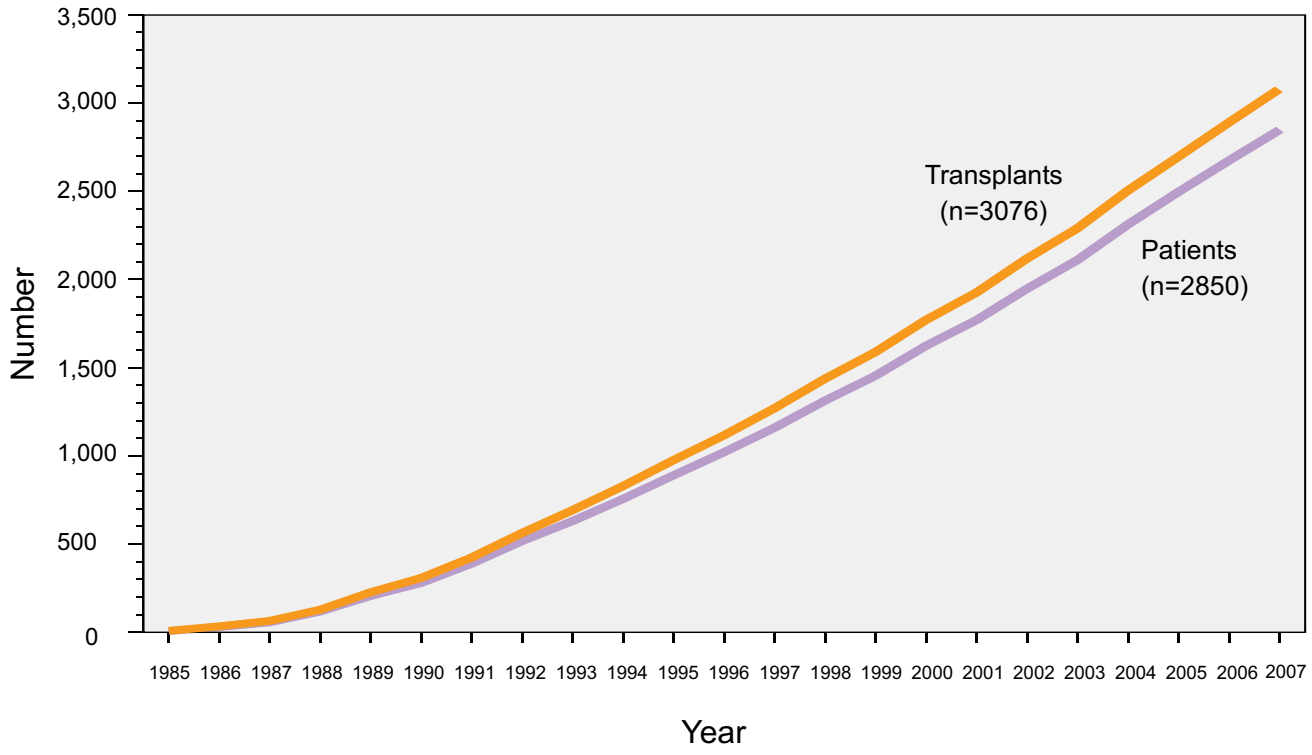
Cumulative Number of Patients & Transplants



Summary Statistics - Age and Gender

ALL PATIENTS TRANSPLANTED

	Children	Adults	Total
Patients	518	2332	2850
Age			
Mean ± SD	4.3 ± 4.2y	47.3 ± 11.8y	39.5 ± 19.8y
Median	2.4y	49.1y	46.2y
Range	24d -14.9y	15.0 - 73.1y	24d - 73.1y
Gender			
Female	275 (53%)	871 (37%)	1146 (40%)
Male	243 (47%)	1461 (63%)	1704 (60%)
Surviving	411 (79%)	1708 (73%)	2119 (74%)

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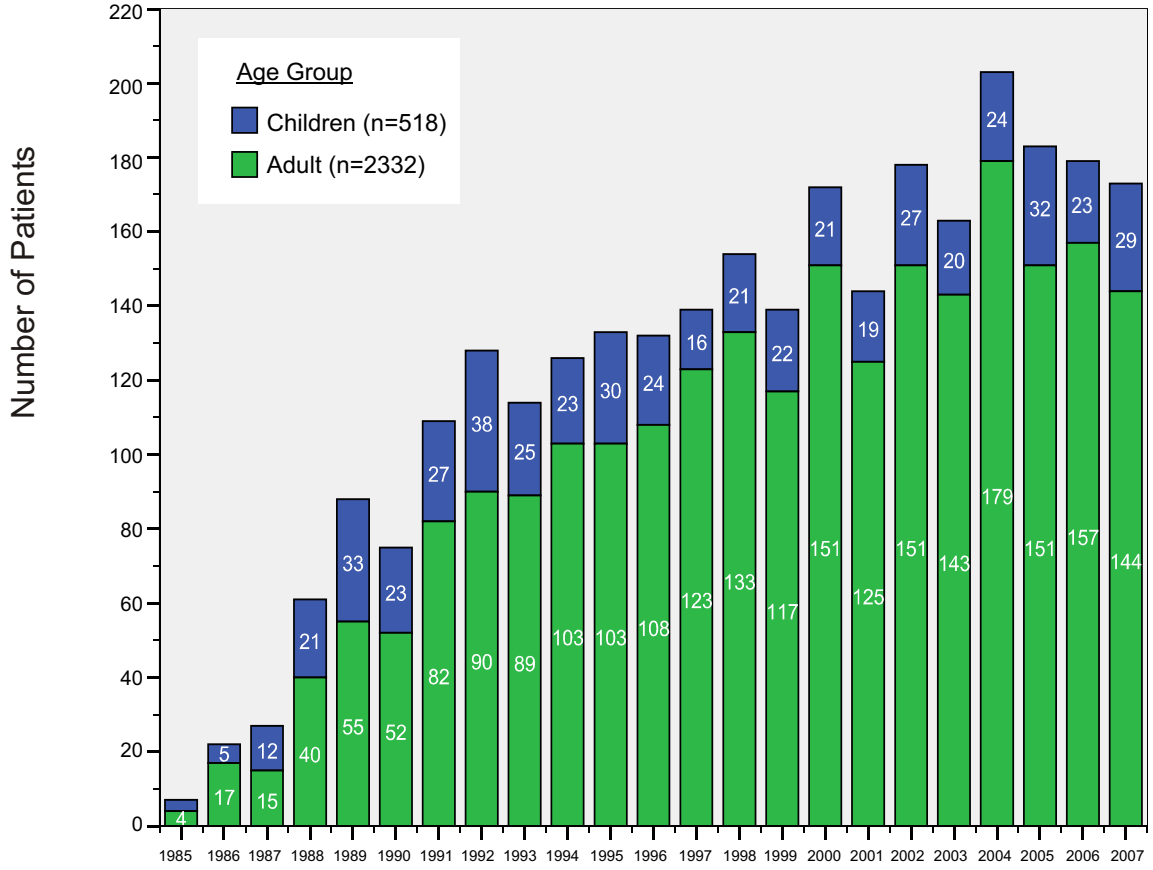
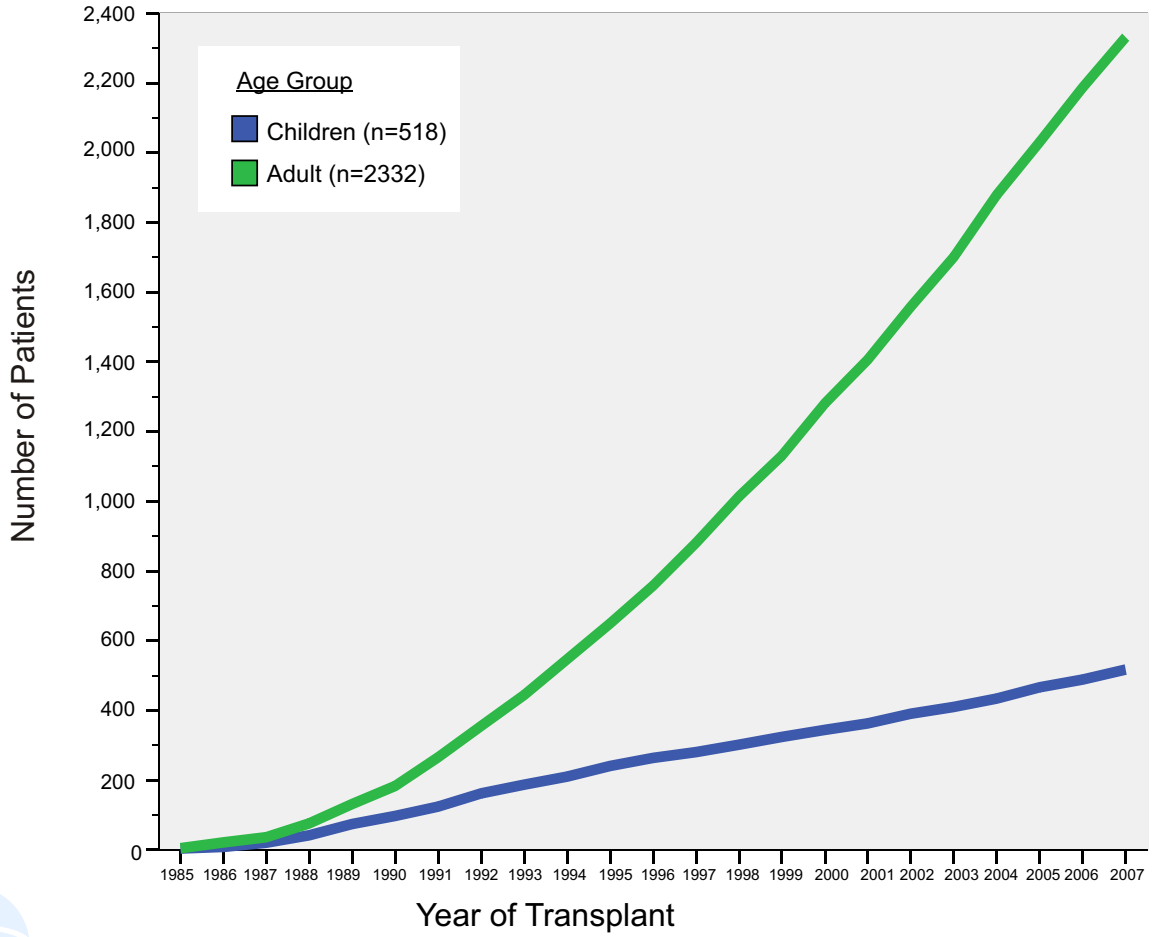
Number of New Patients Transplanted by Year



Cumulative Number of New Patients Transplanted



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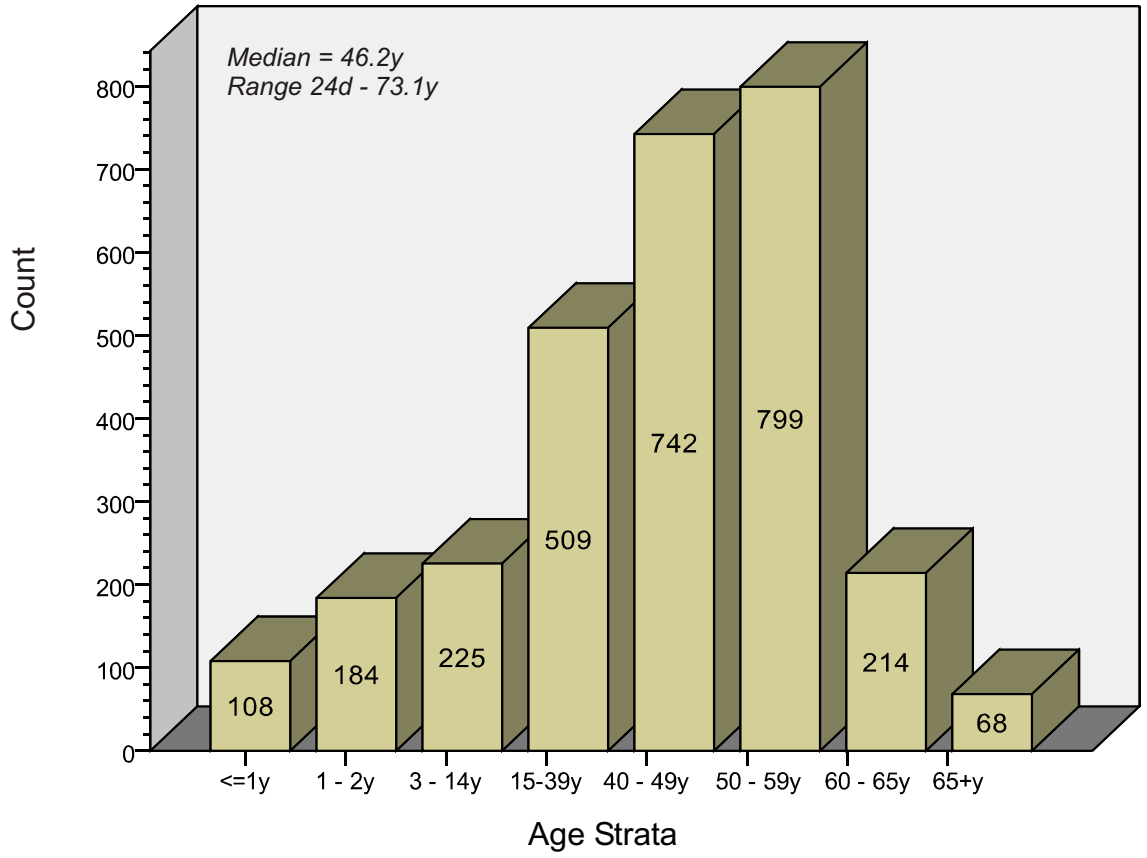
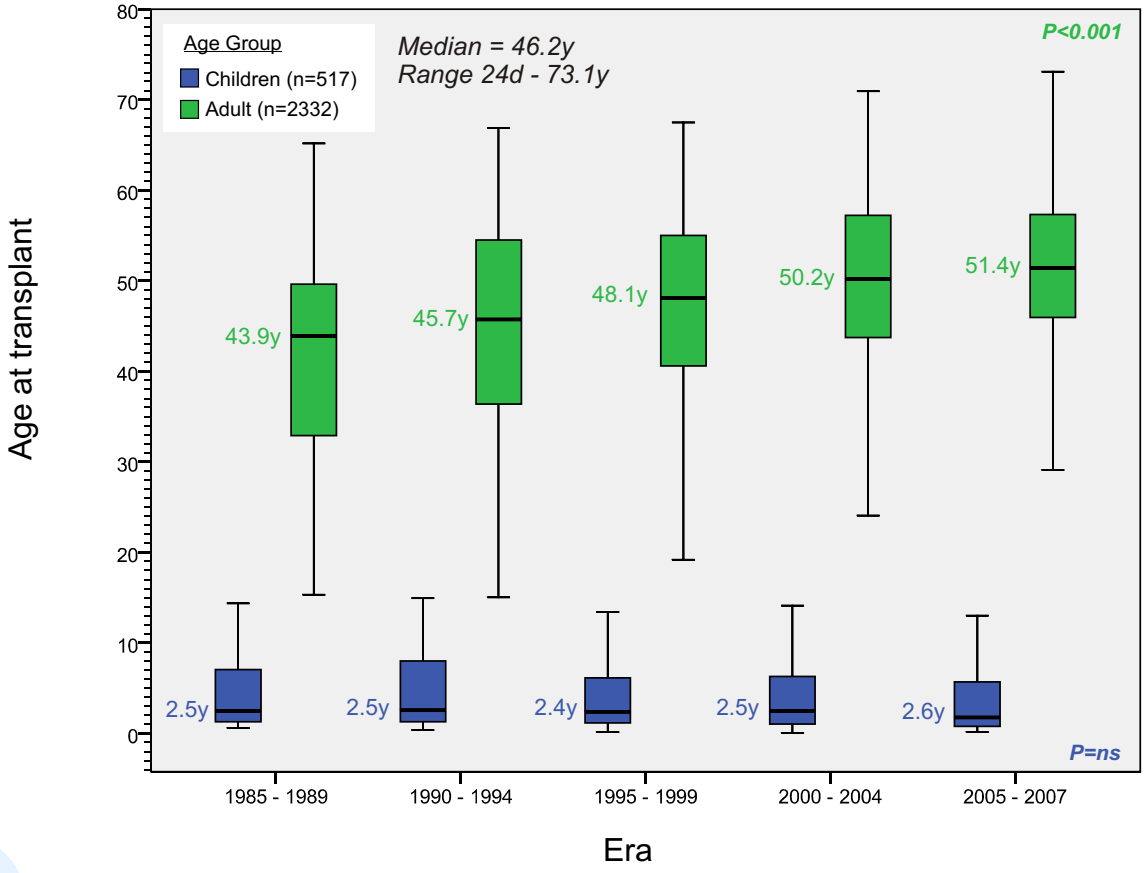
Number of Recipients By Age at Primary Transplant N=2849



Age at Primary Transplant by Era



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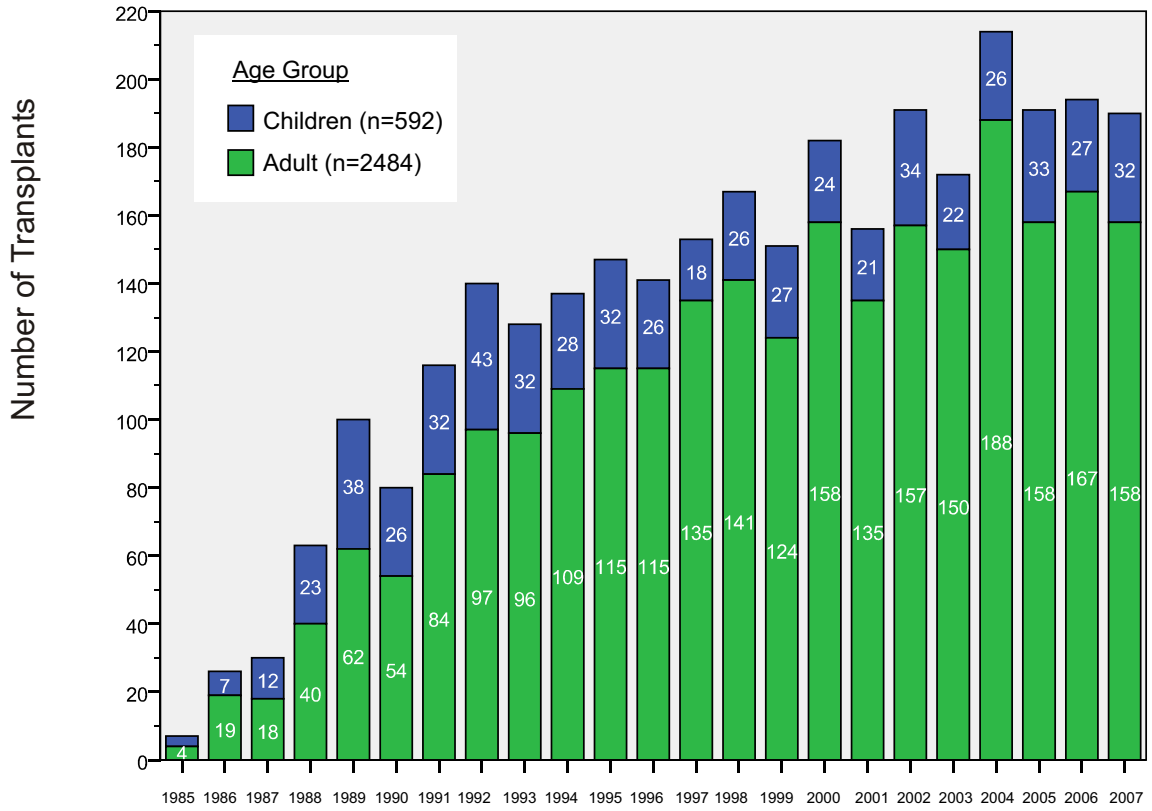
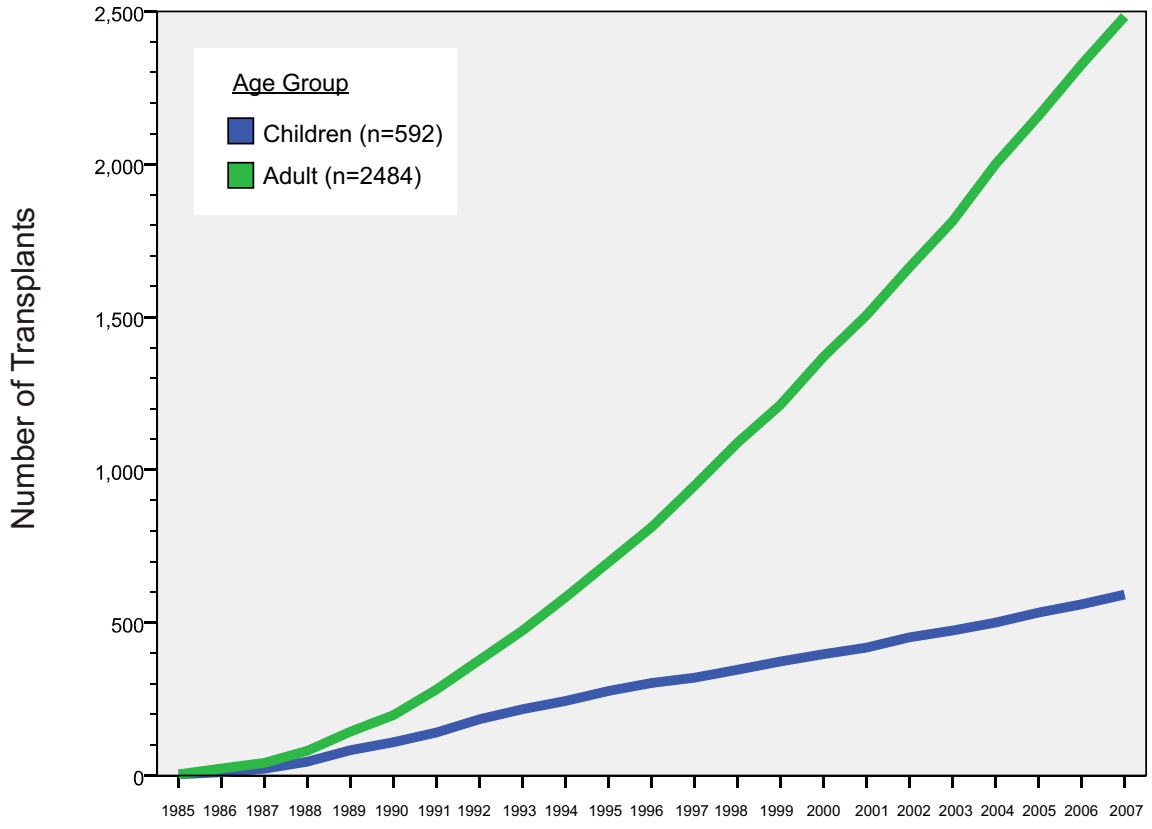
Number of Transplants by Year



Cumulative Number of Transplants



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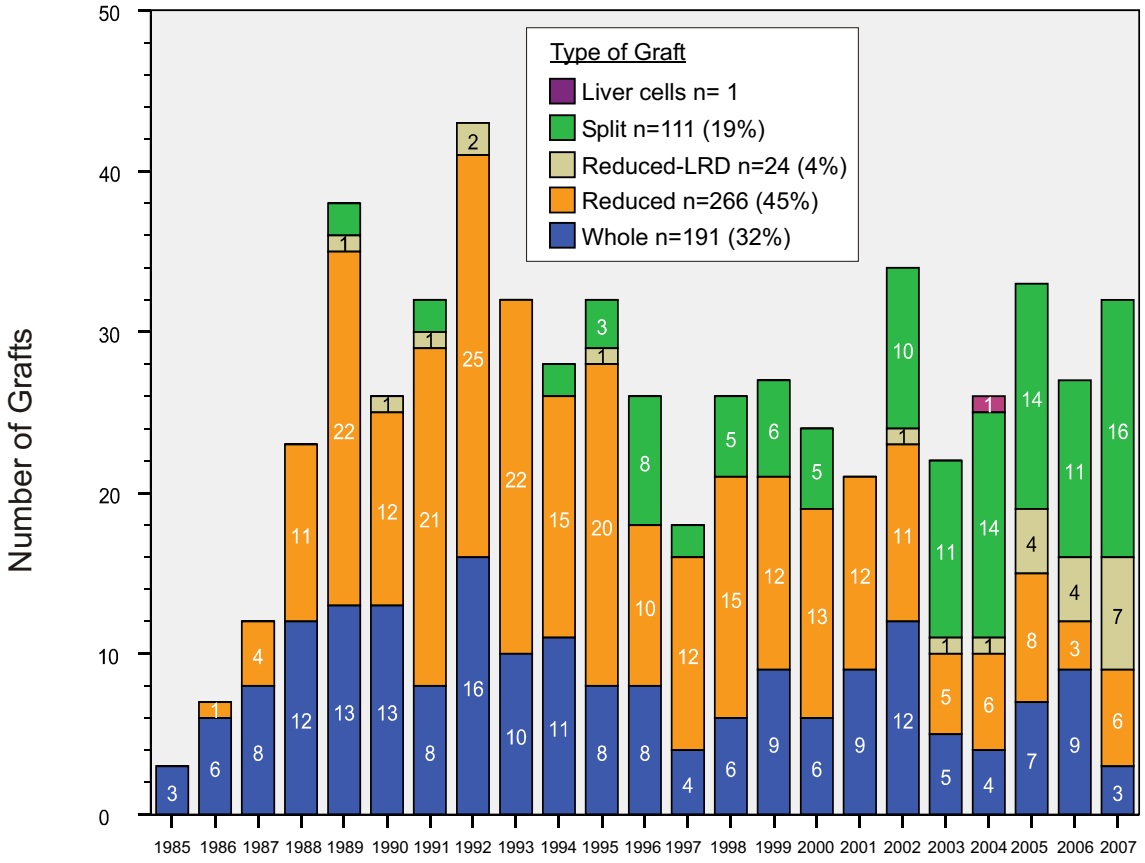
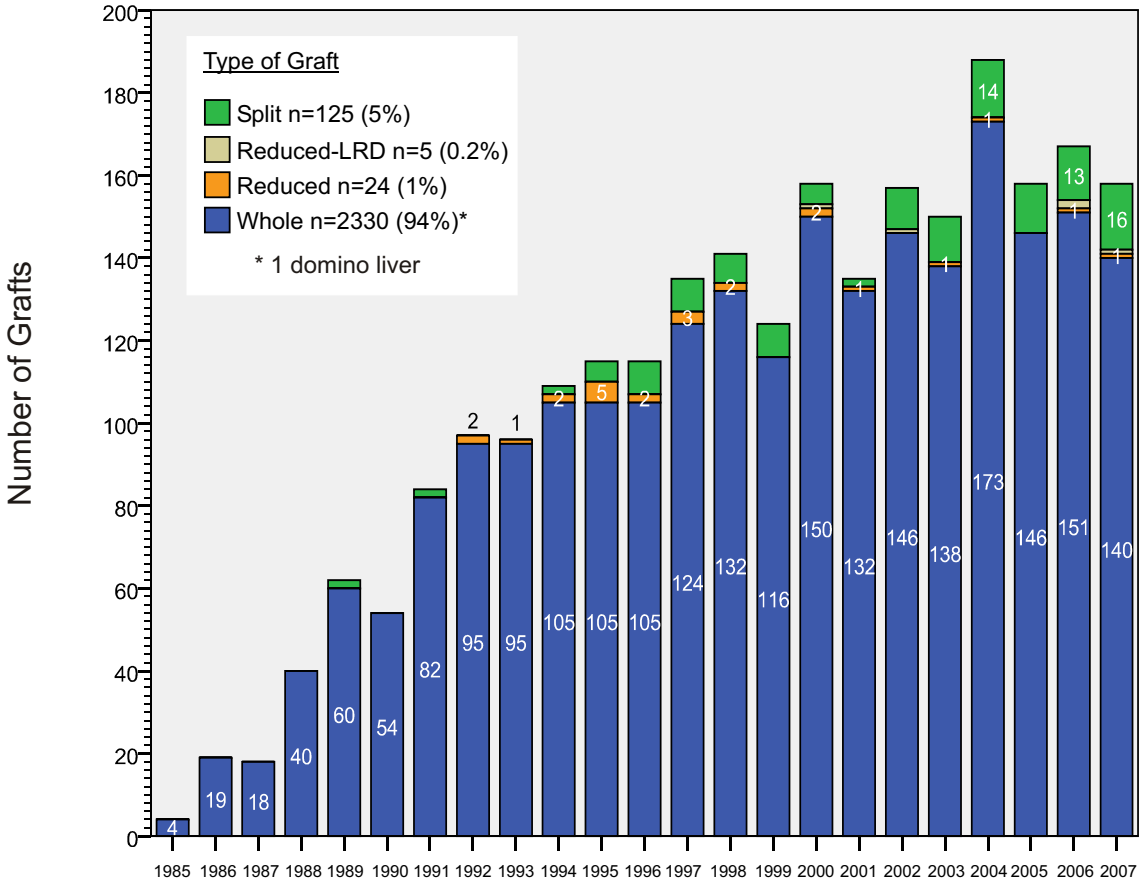
Type of Graft by Year
Split vs Reduced vs Whole

Children (n = 592)



Adults (n = 2484)



Year of Transplant

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Section 2

Primary Diagnosis

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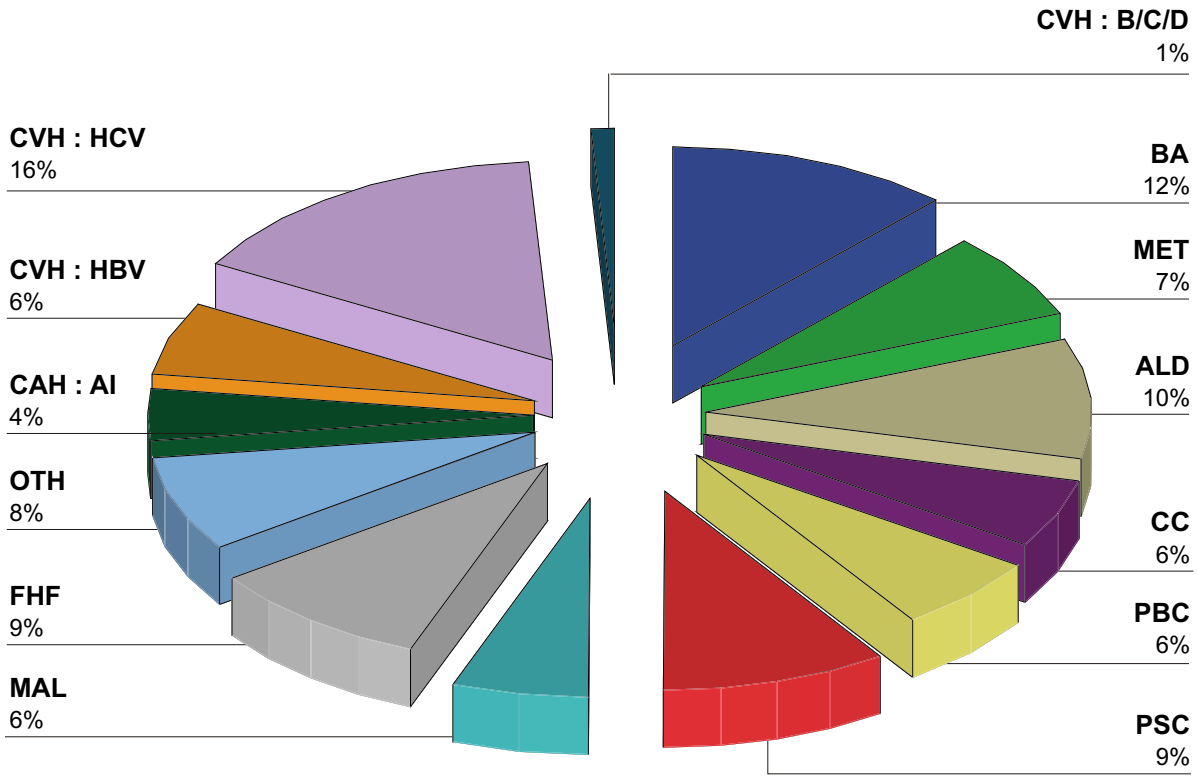

Diagnosis Group

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

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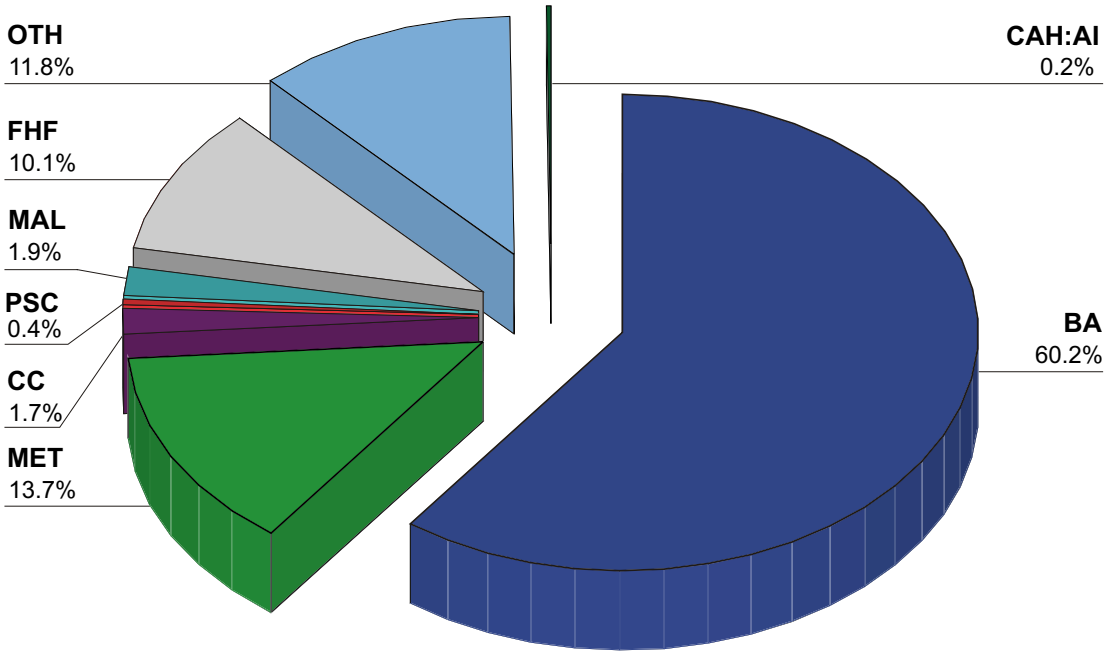
# Primary Diseases of Children
n = 518



# Primary Diseases of Adult Recipients
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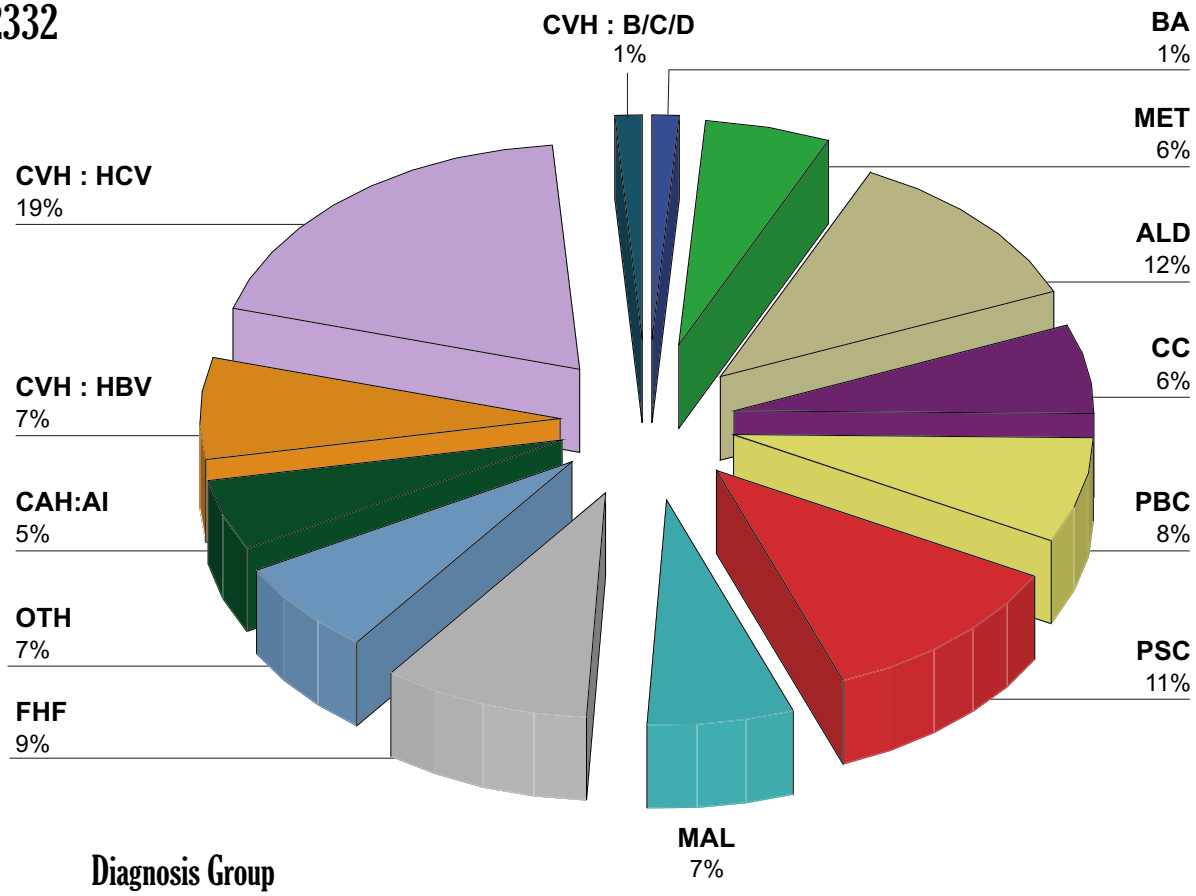

Diagnosis Group

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

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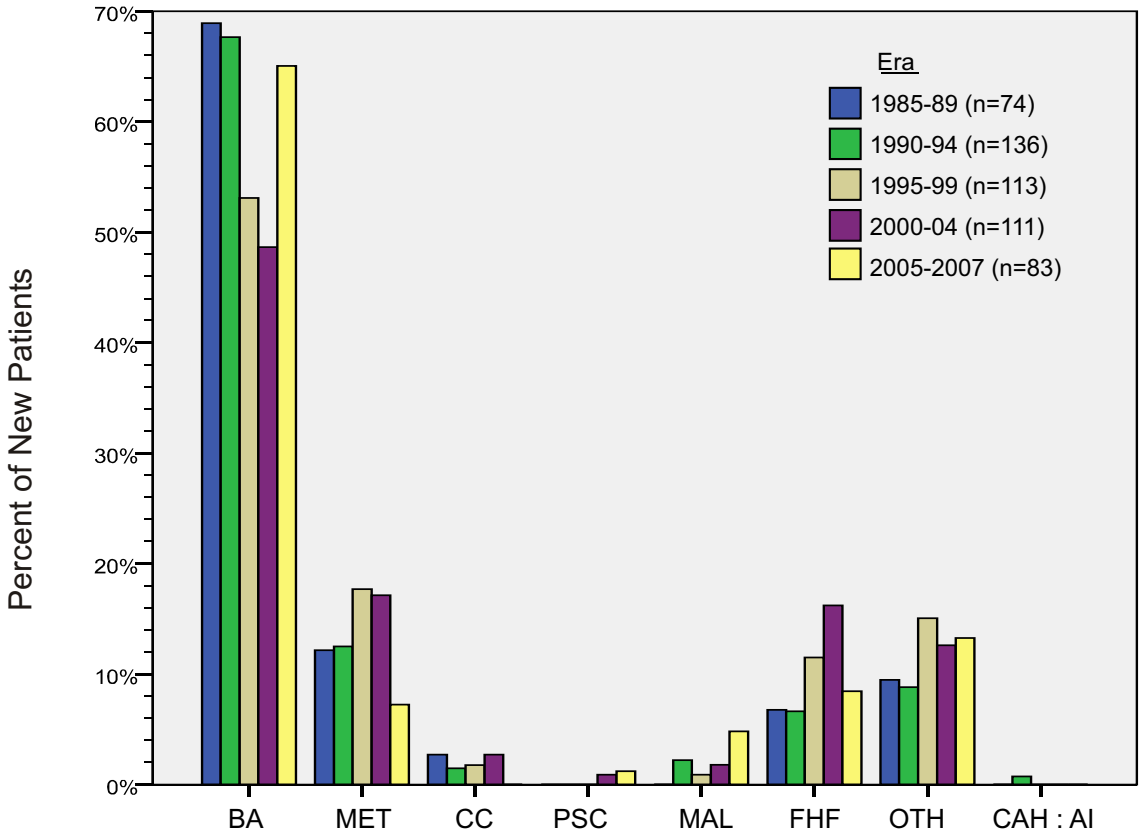
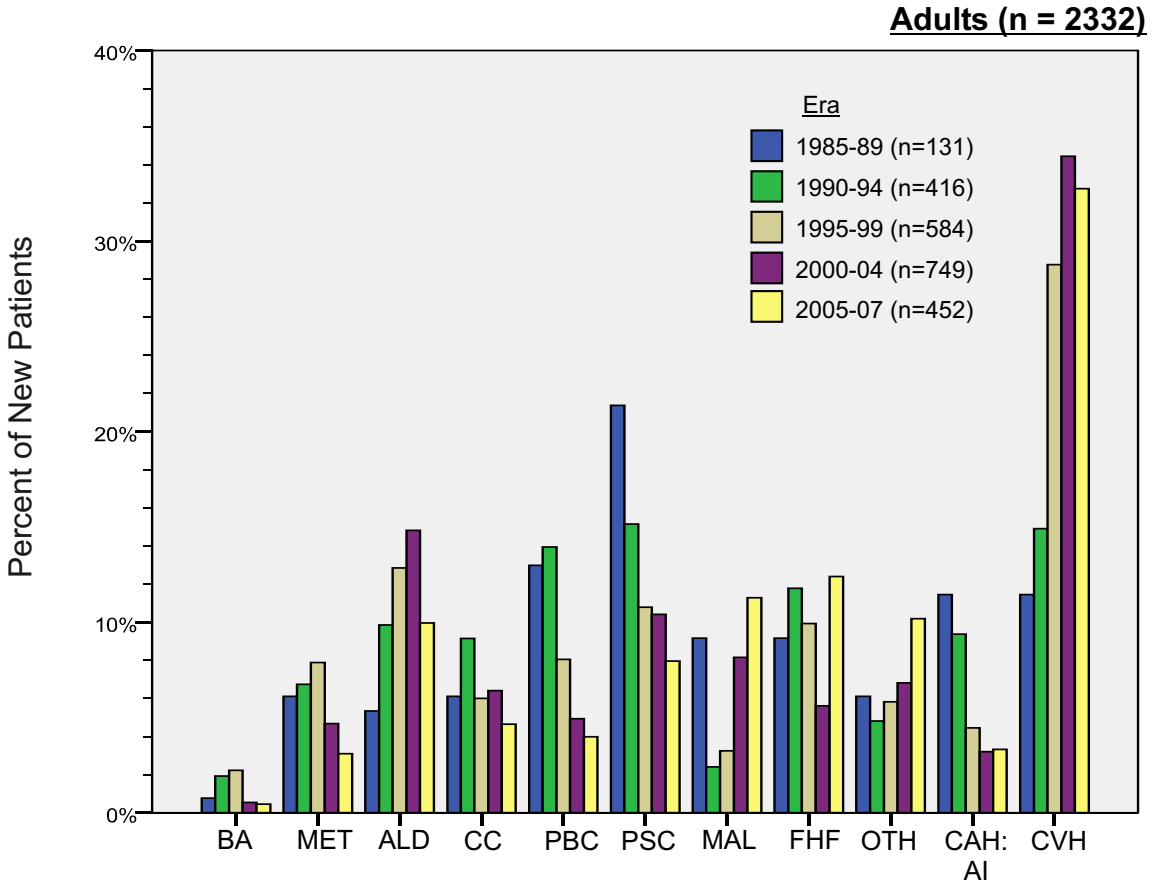
Children (n=517)



Adults (n = 2332)



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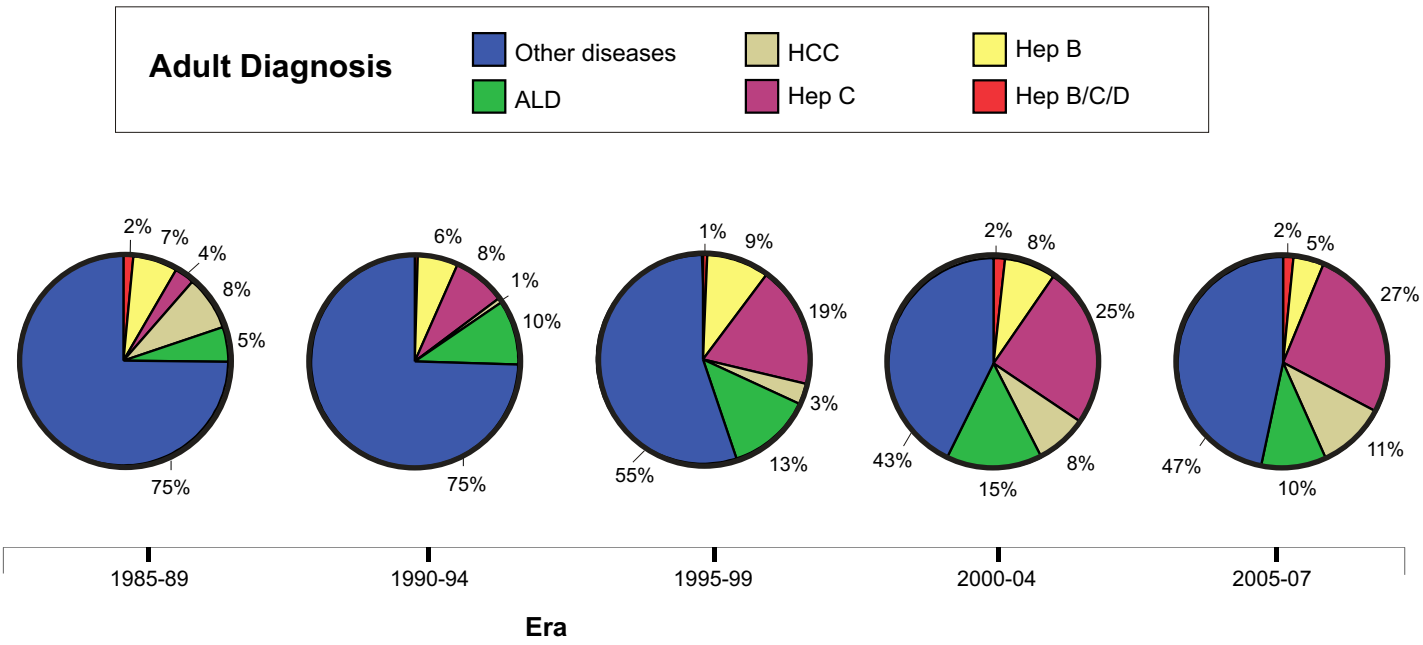
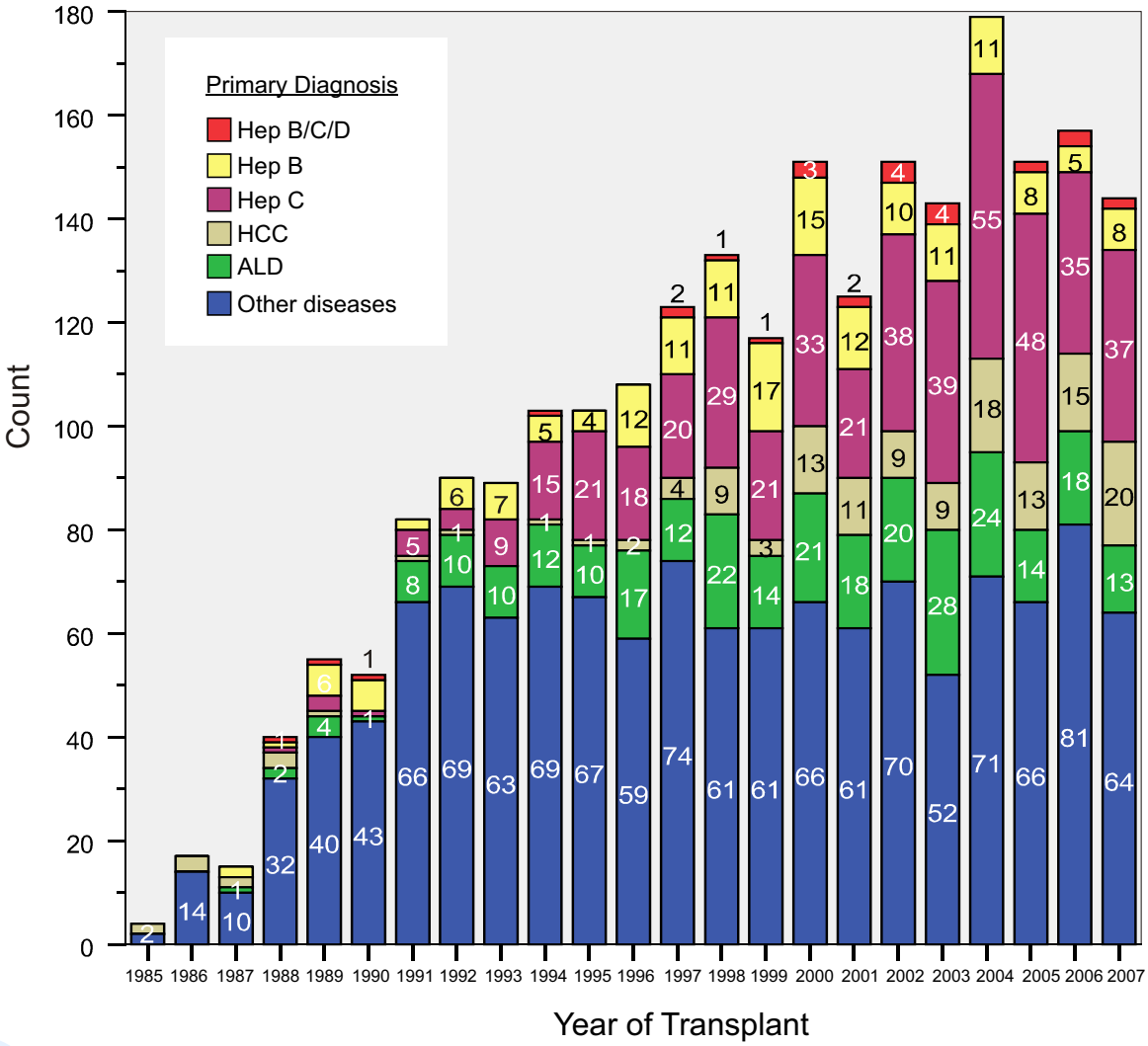
Adult Primary Diagnosis by Era



Adult Primary Diagnosis by Year



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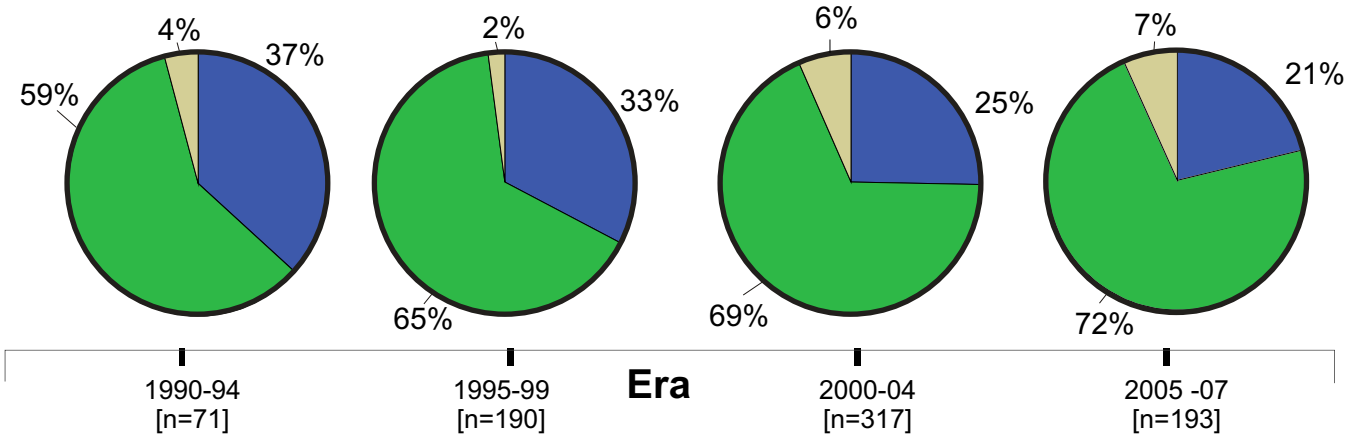
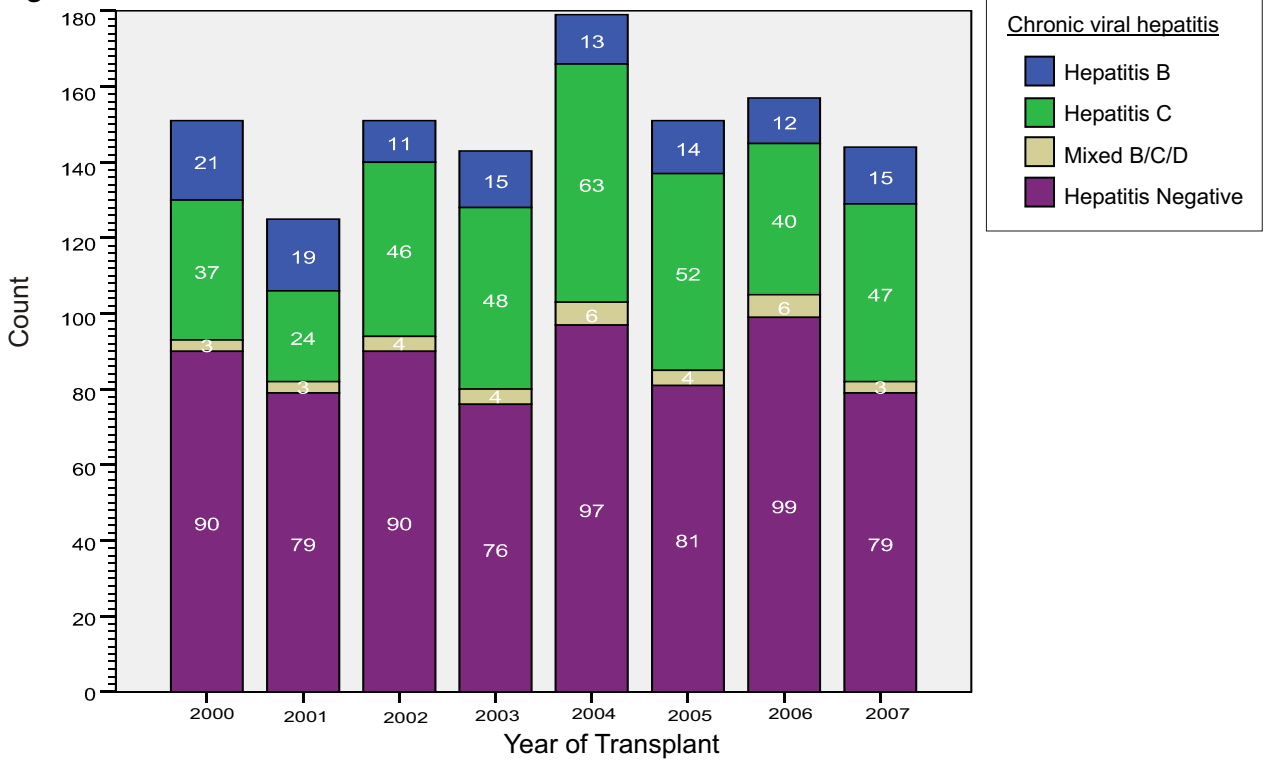
Chronic Viral Hepatitis as Primary or Secondary Diagnosis in Adult Patients

Primary Diagnosis		Secondary / Tertiary diagnosis					
		n =	Hepatitis C	Hepatitis B	Hepatitis B,C	HCC	ALD
	Hepatitis C	453		6		89	107
	Hepatitis B	170	4			47	4
	Hepatitis BD/BC/BCD	28				3	6
	HCC + cirrhosis	141	61	52	4		14
	ALD	279	10	2		25	
	Other	1261	11	4		39	20
	TOTAL	2332					

Type of Chronic Viral Hepatitis in Adult Patients



Hepatitis diagnosis



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Section 3

Patient Survival

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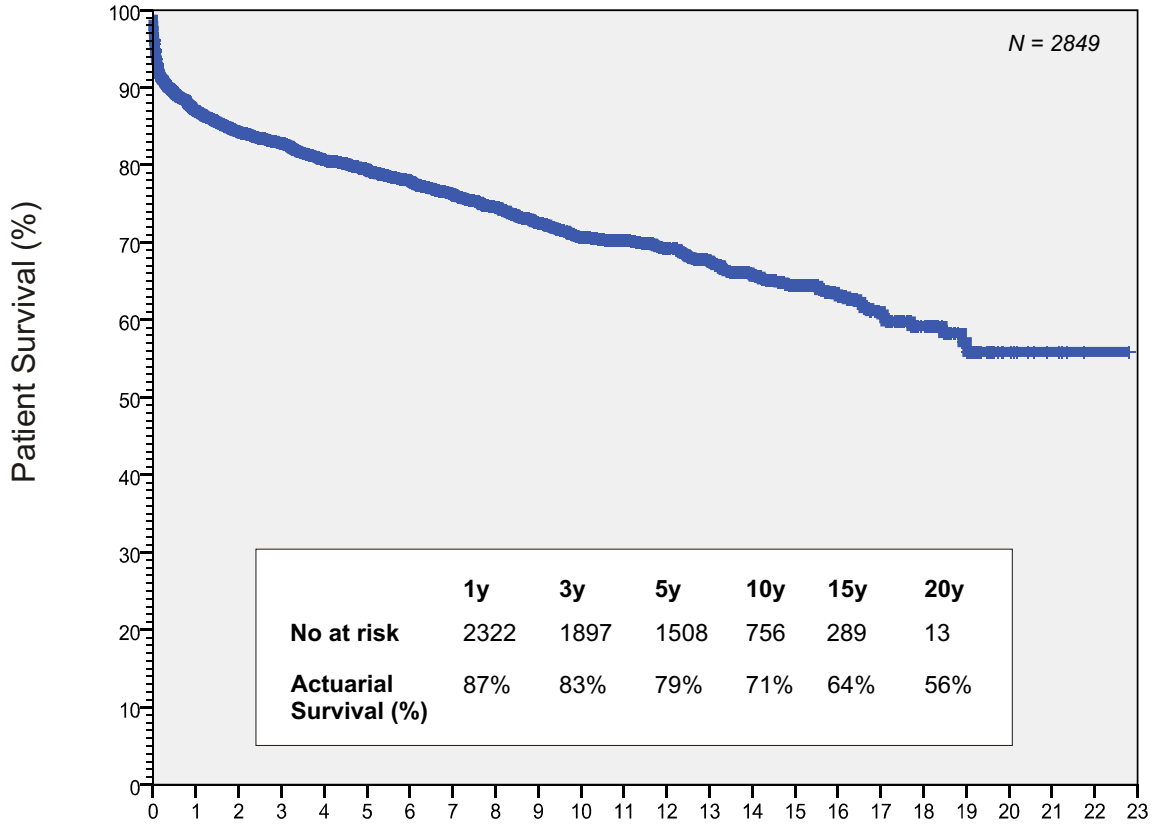
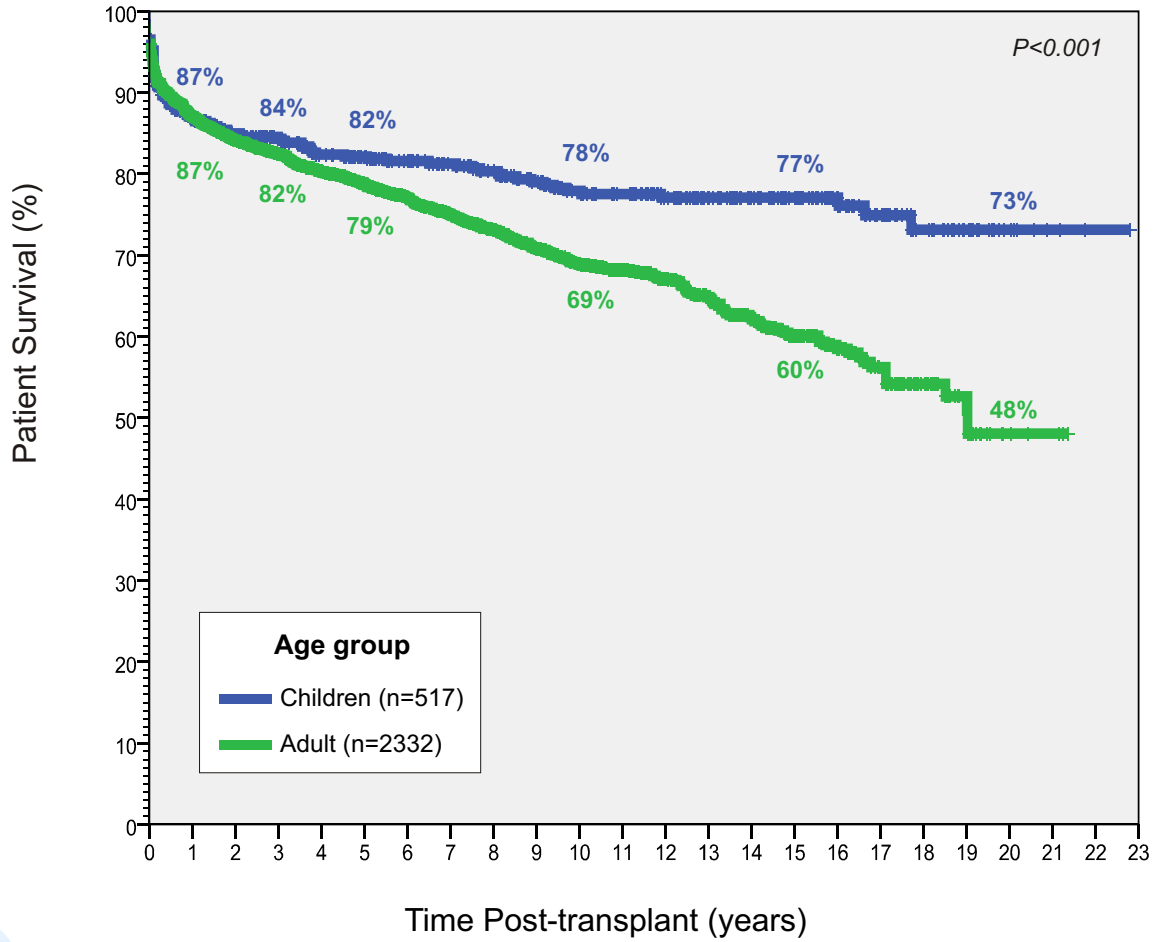


	1y	3y	5y	10y	15y	20y
No at risk	2322	1897	1508	756	289	13
Actuarial Survival (%)	87%	83%	79%	71%	64%	56%



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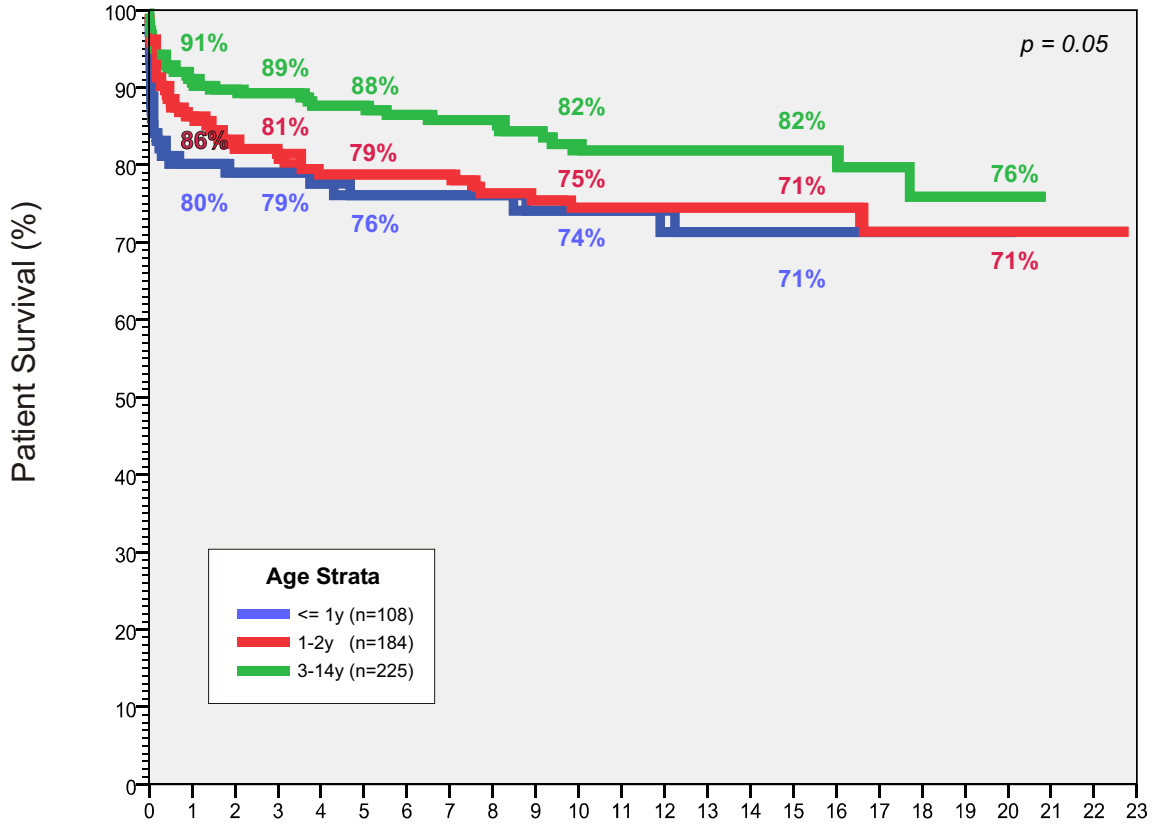
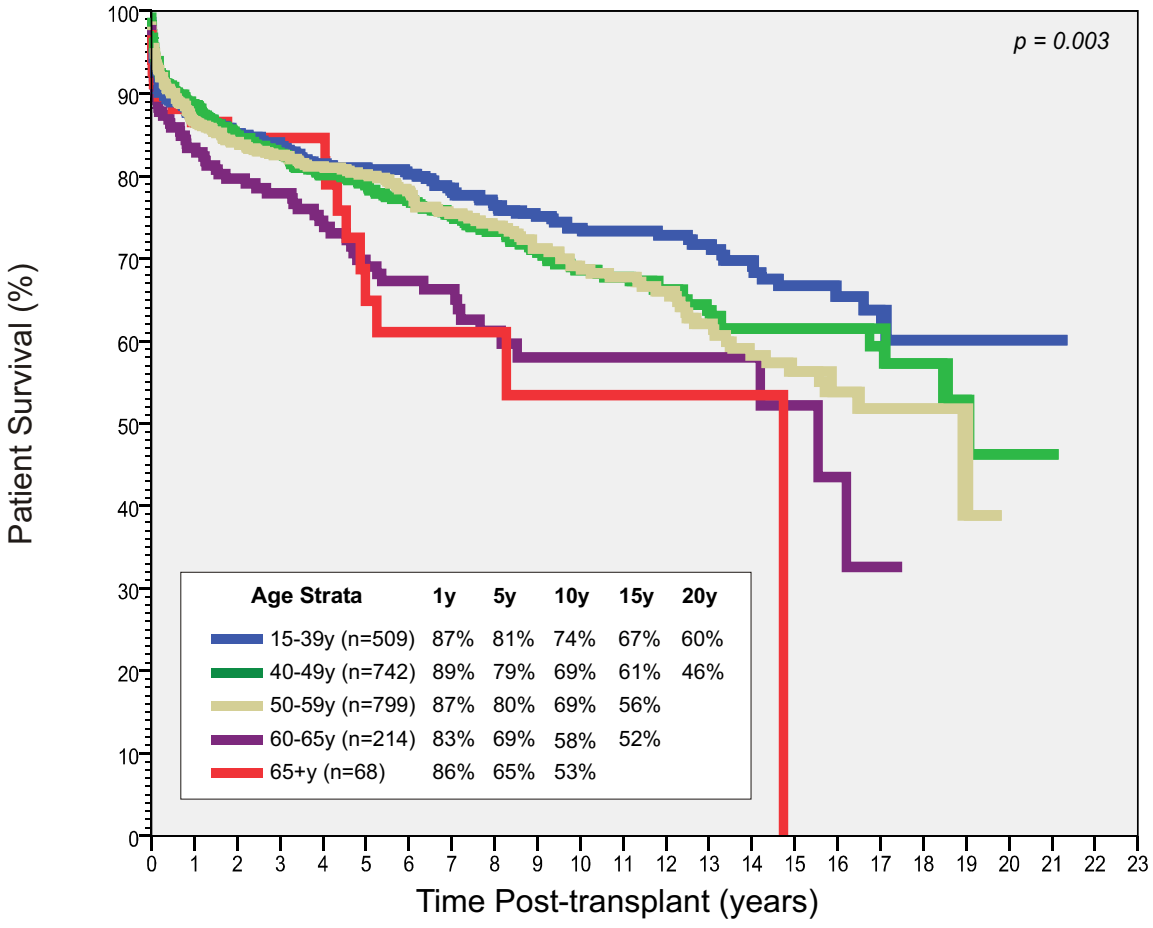
Children n= 517



Adults n = 2332



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All Patient Survival by Year of Transplant

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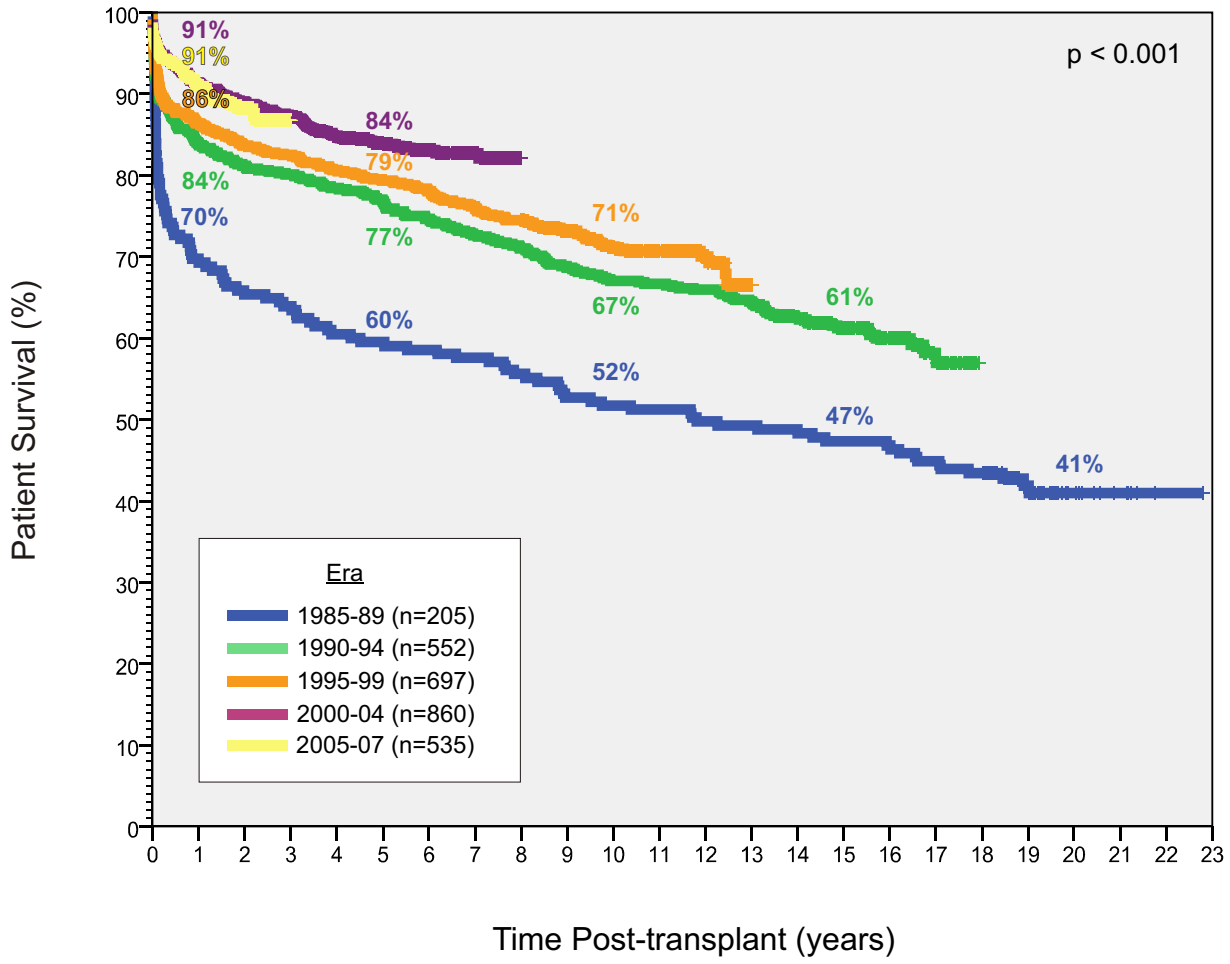

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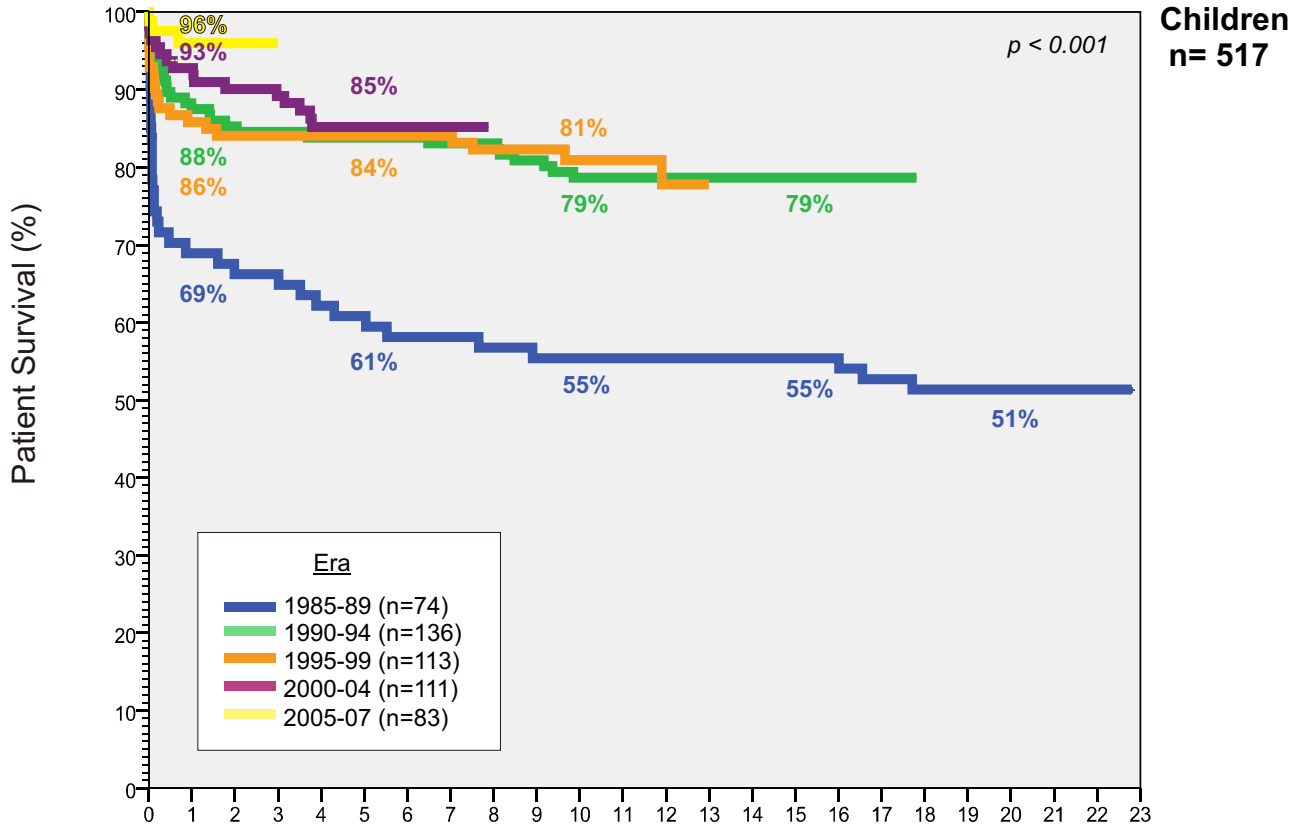
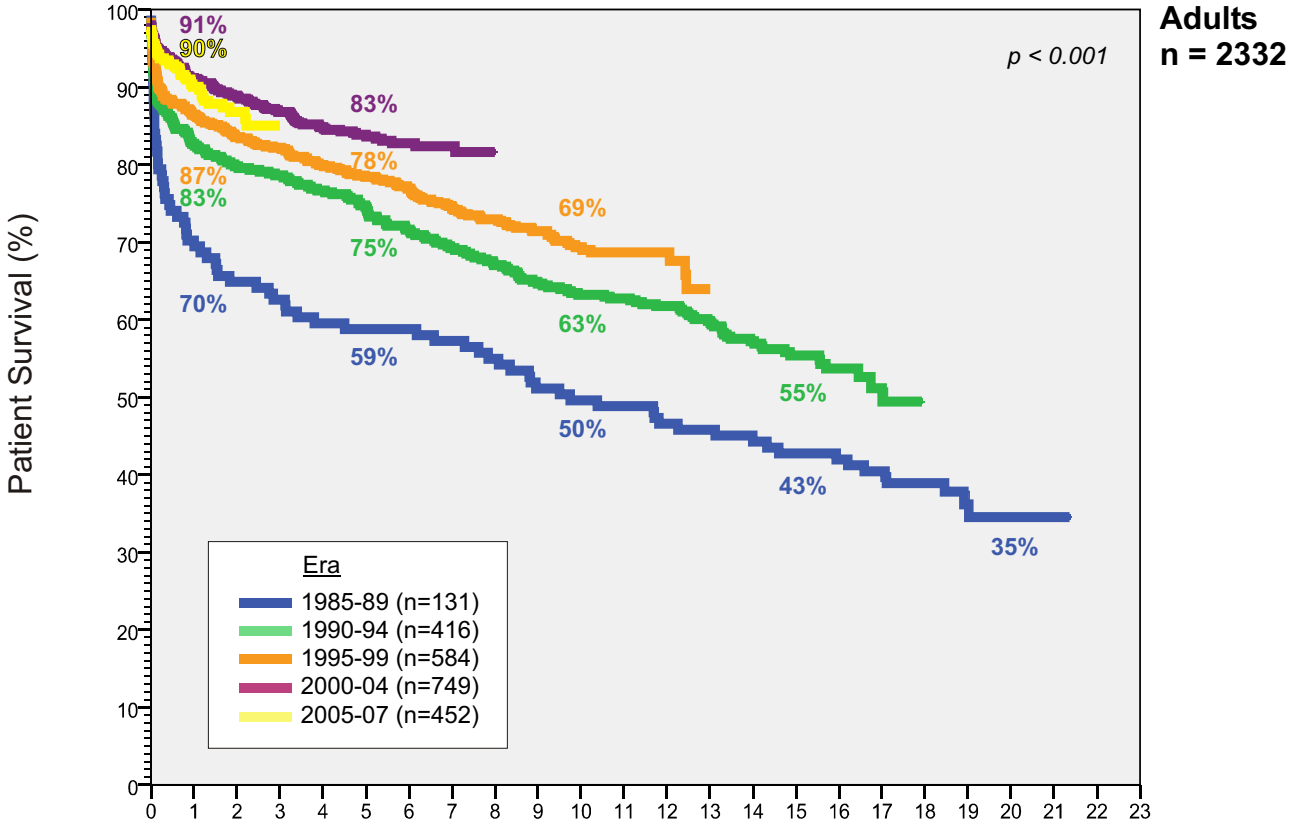
Patient Survival - Children



Patient Survival - Adults



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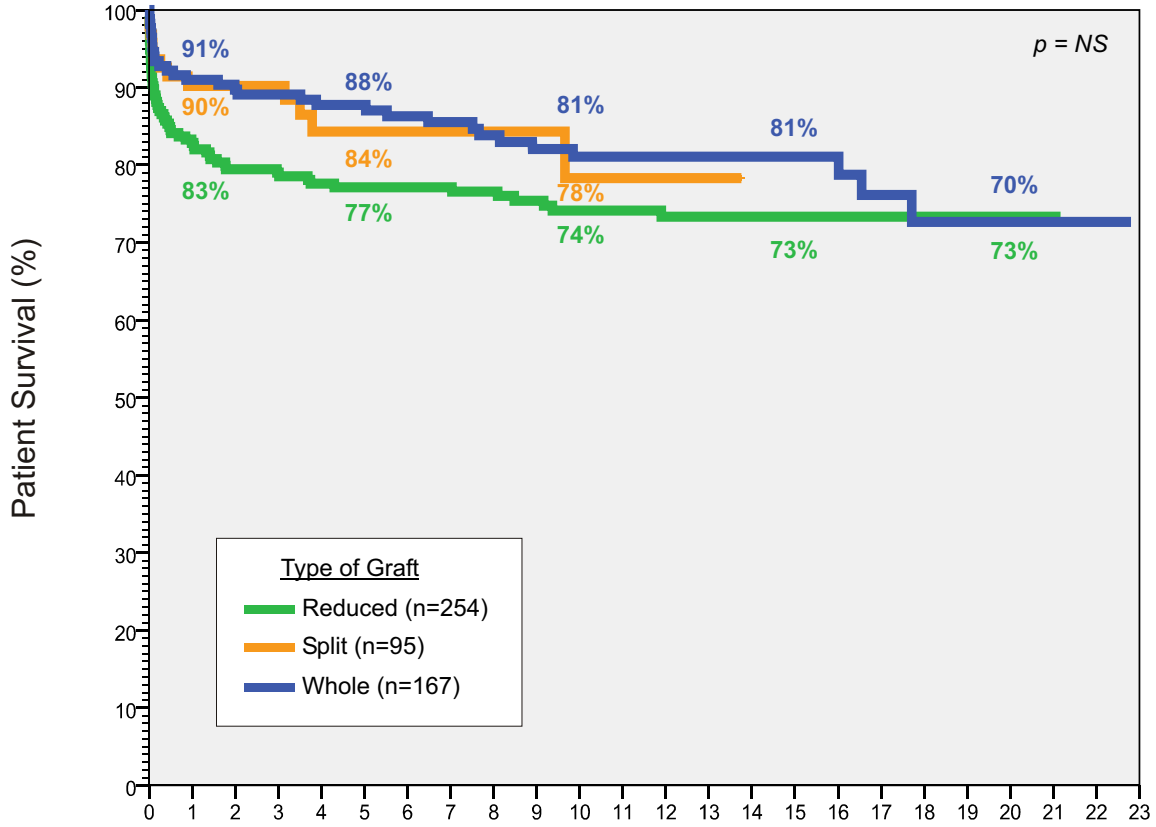
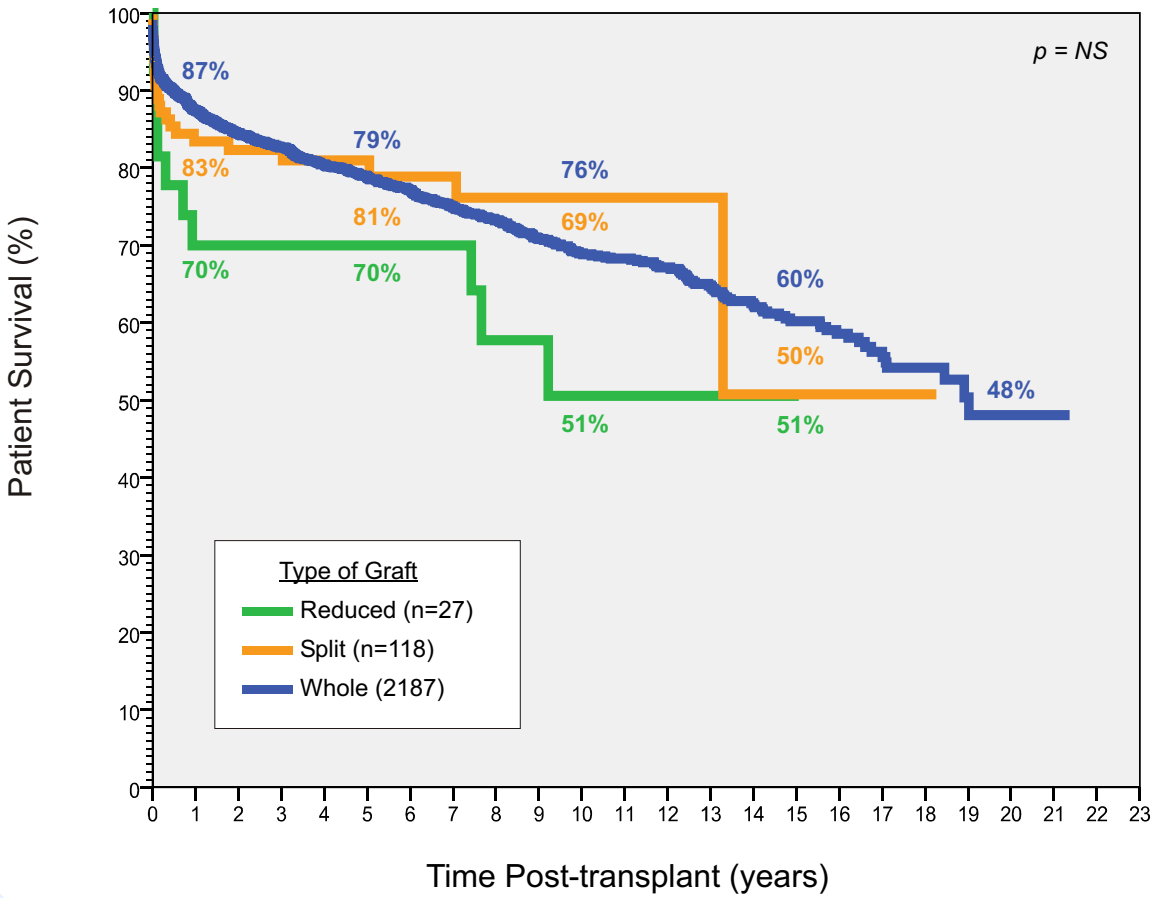
Children - n = 516



Adults - n = 2332



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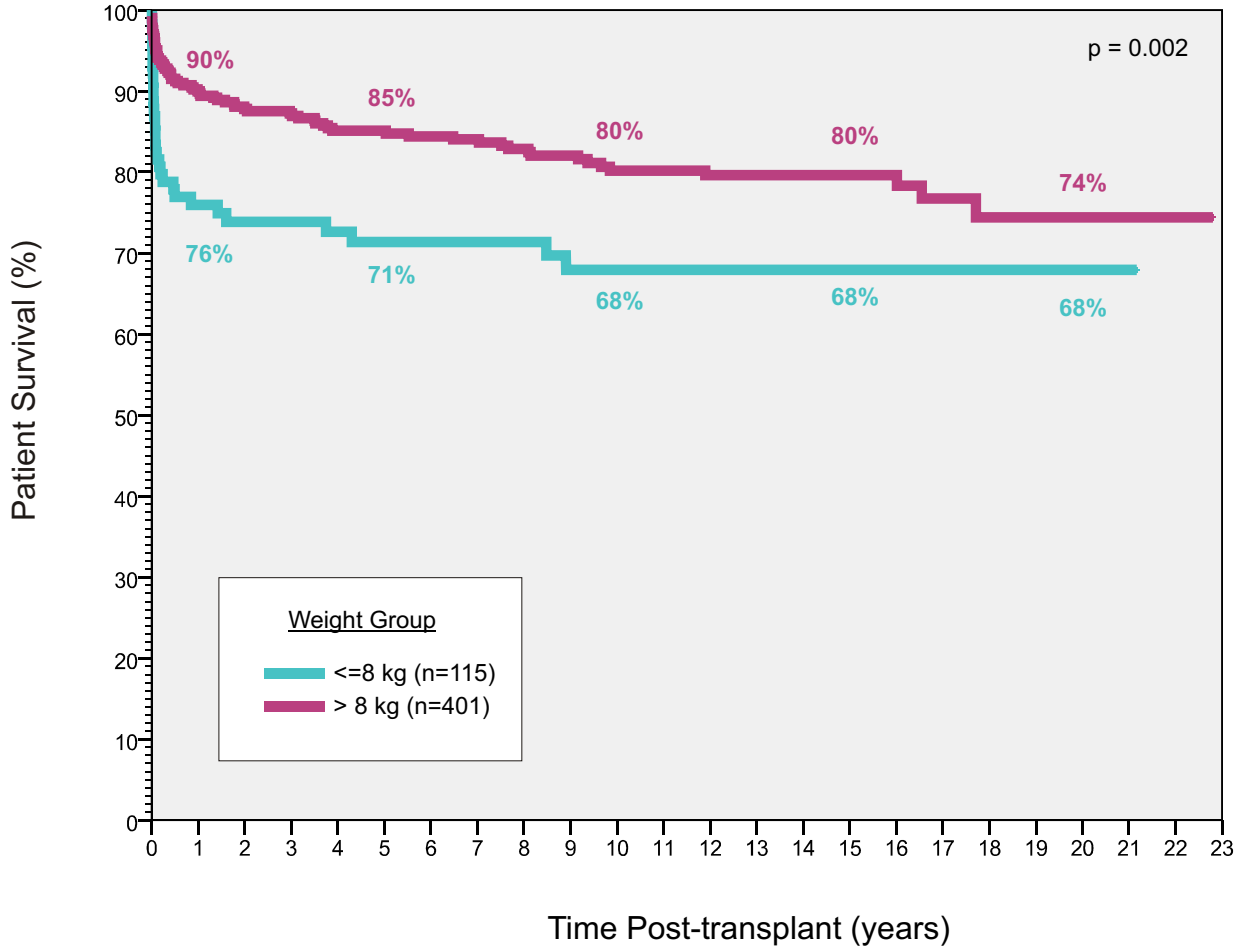

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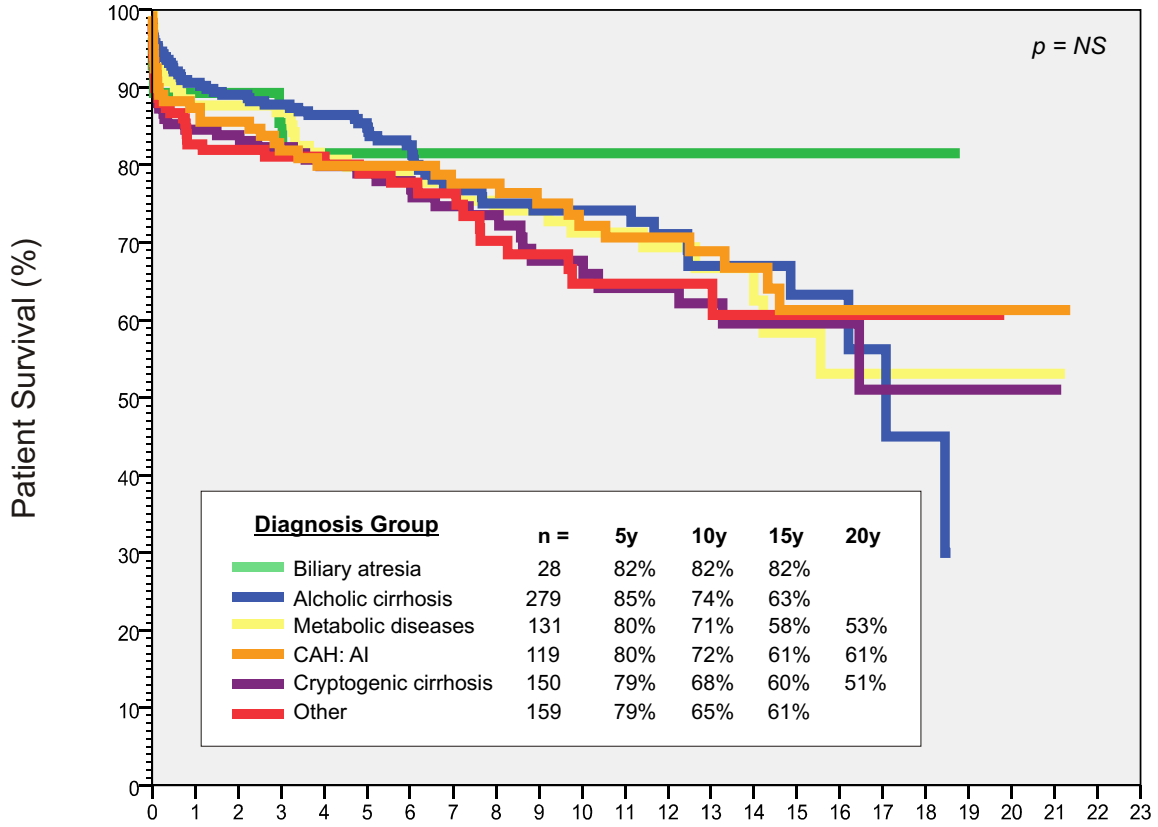
(1) Adults [excluding FHF] - n=866



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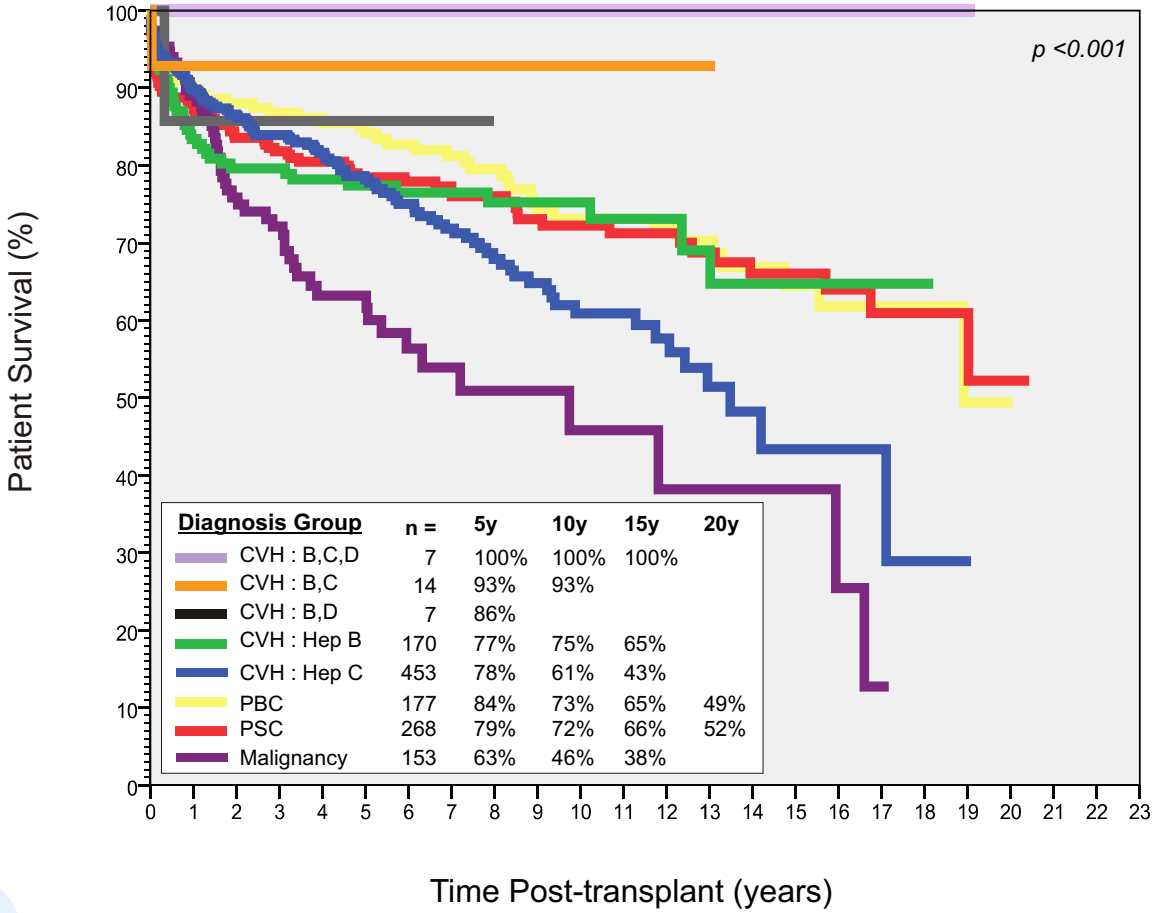

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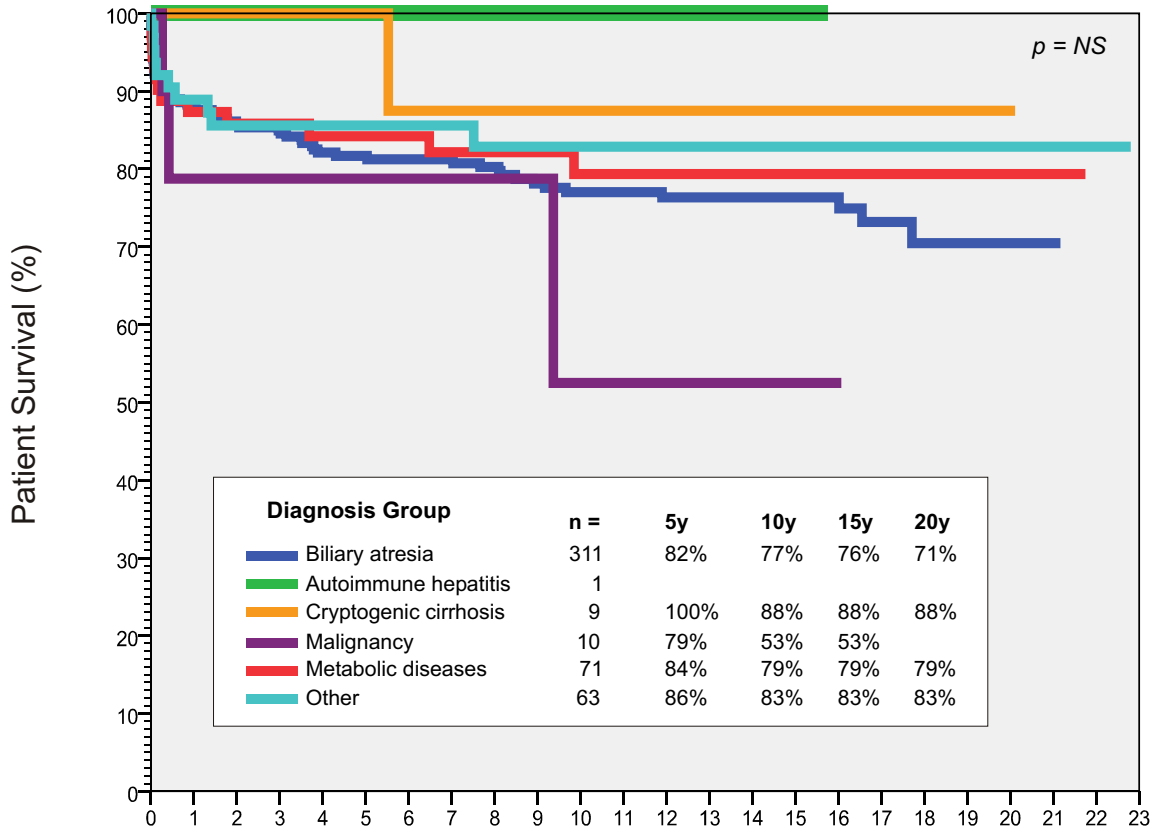
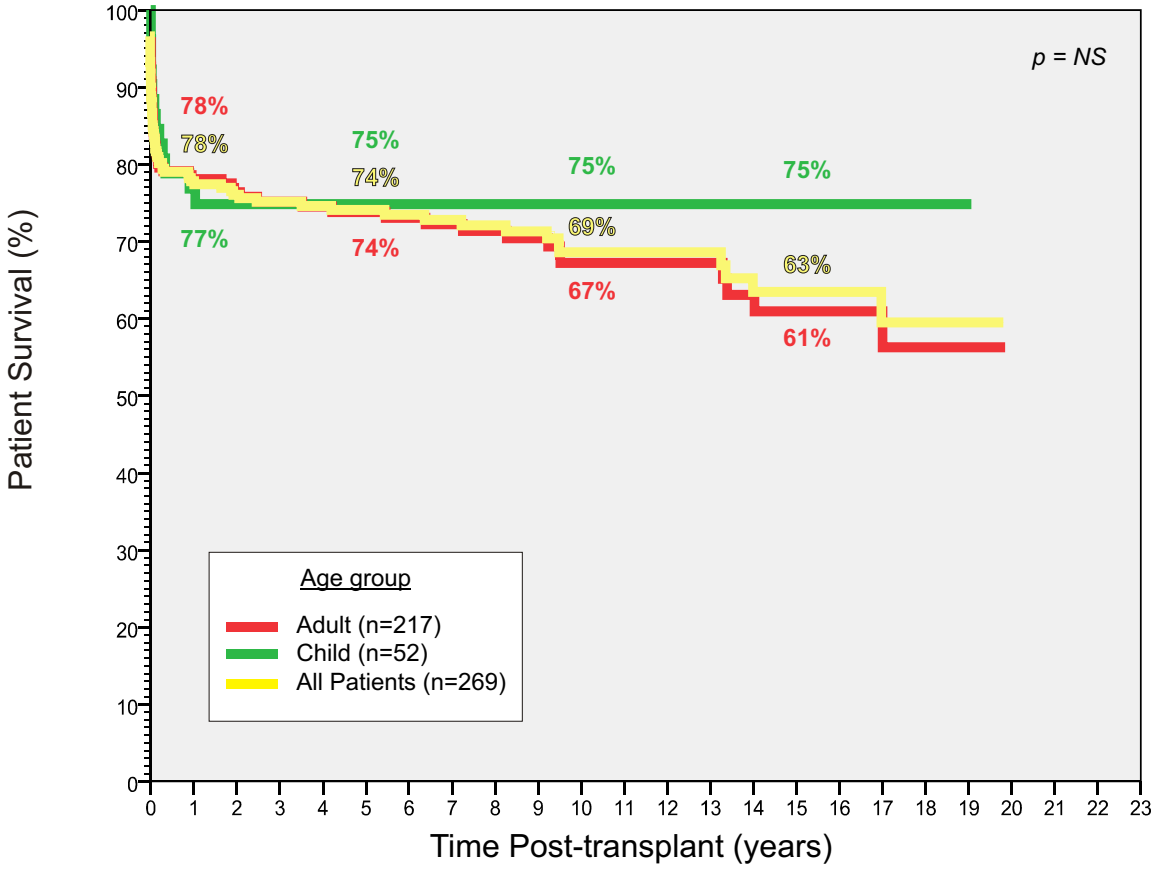
(3) Paediatric recipients [excluding FHF] - n=438



(4) Fulminant hepatic failure (n=269)



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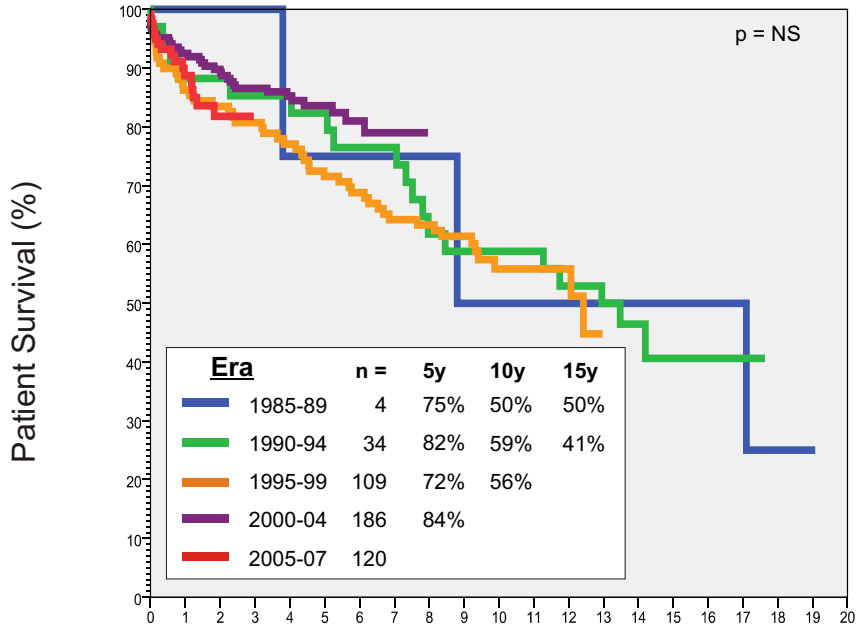
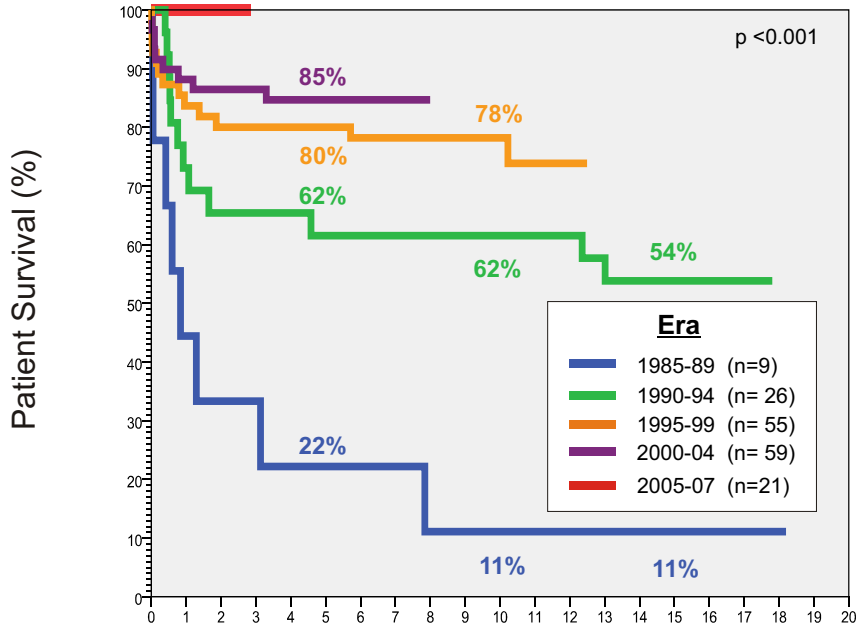
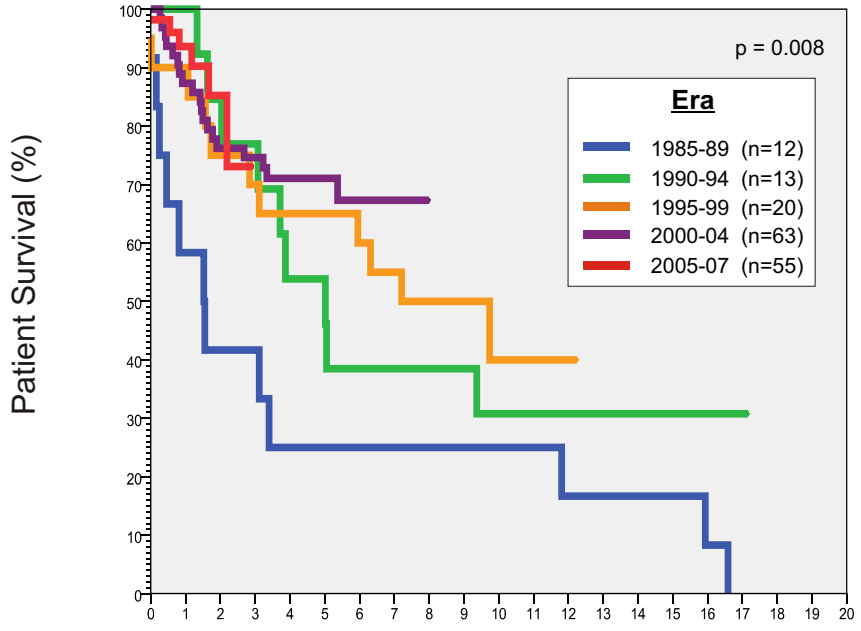


Adults CVH: Hepatitis C
n = 453



Adults CVH: Hepatitis B
n = 170



Malignancy
Adults and Children
n = 163

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Section 4

Graft Outcome

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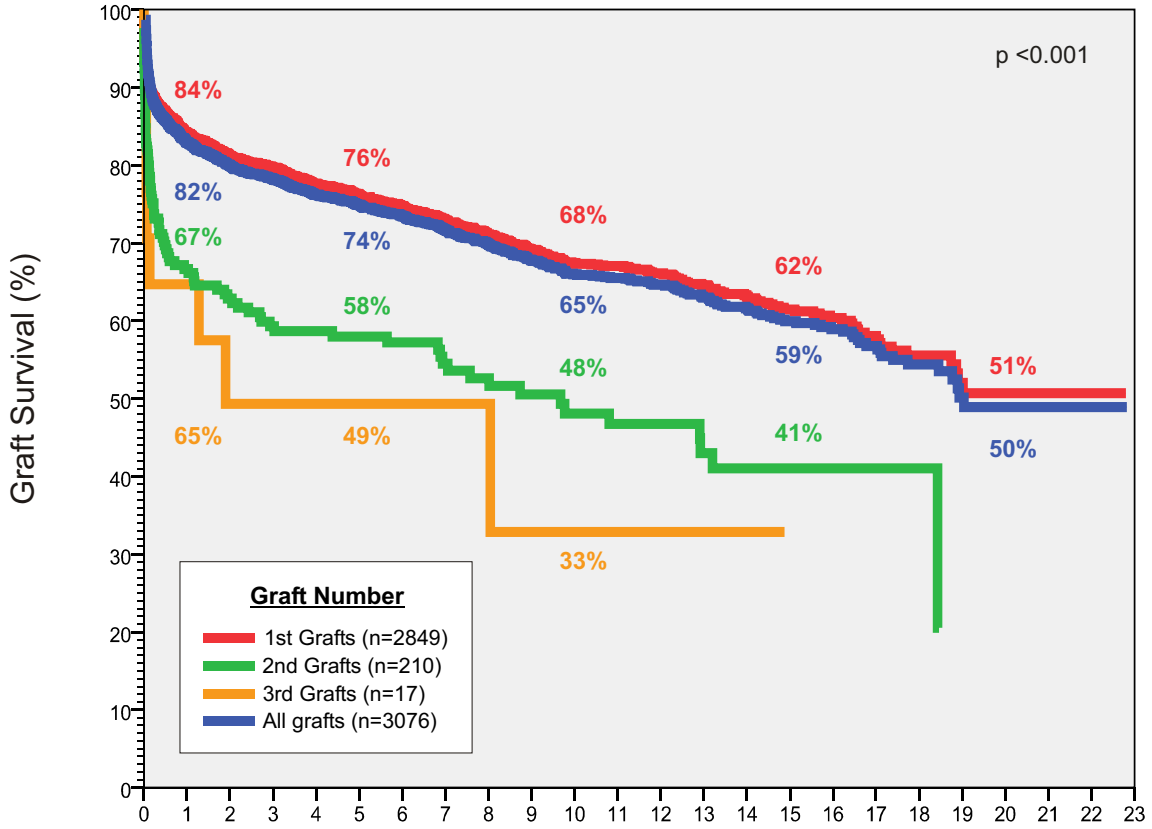

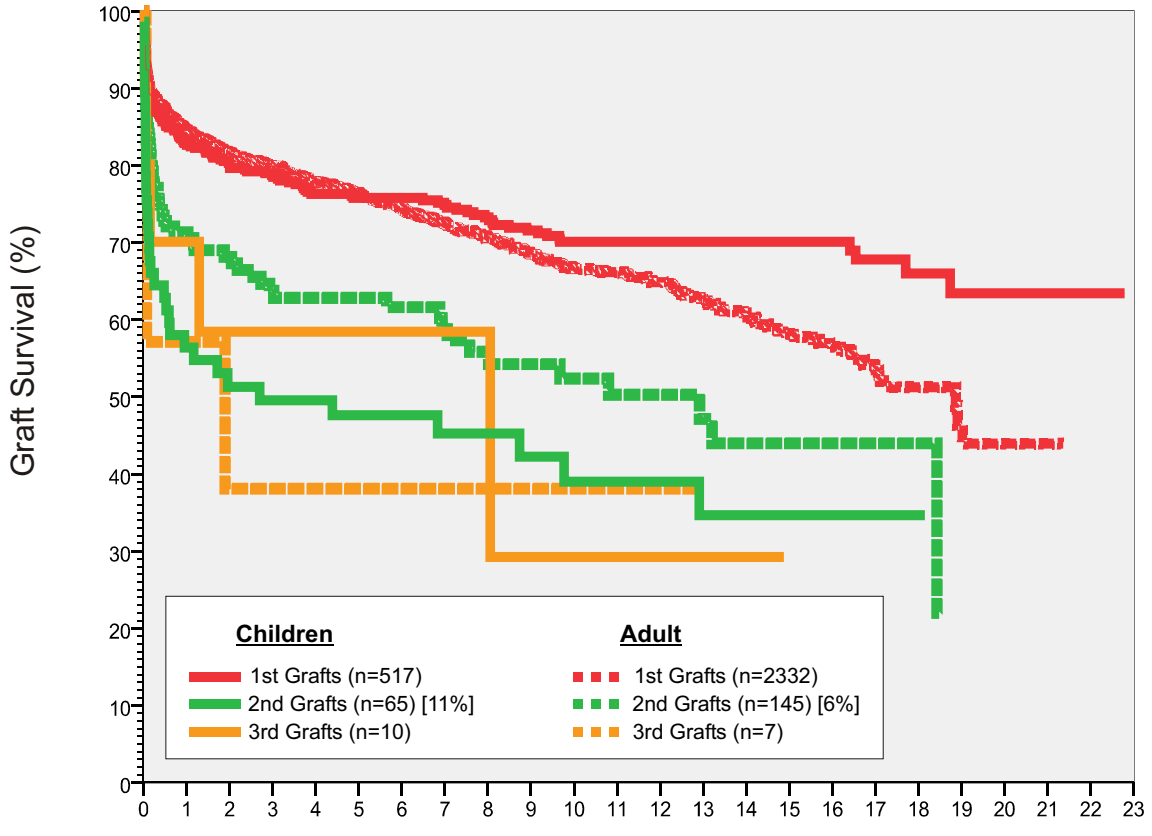

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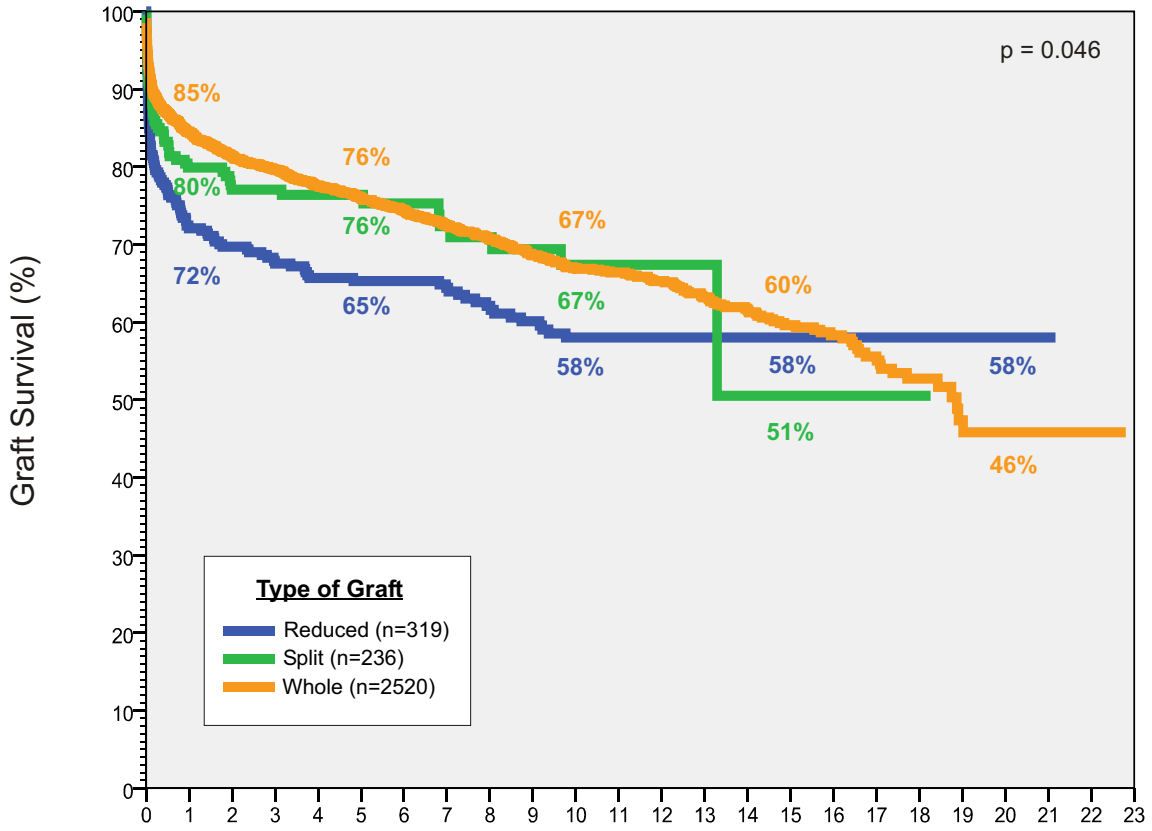
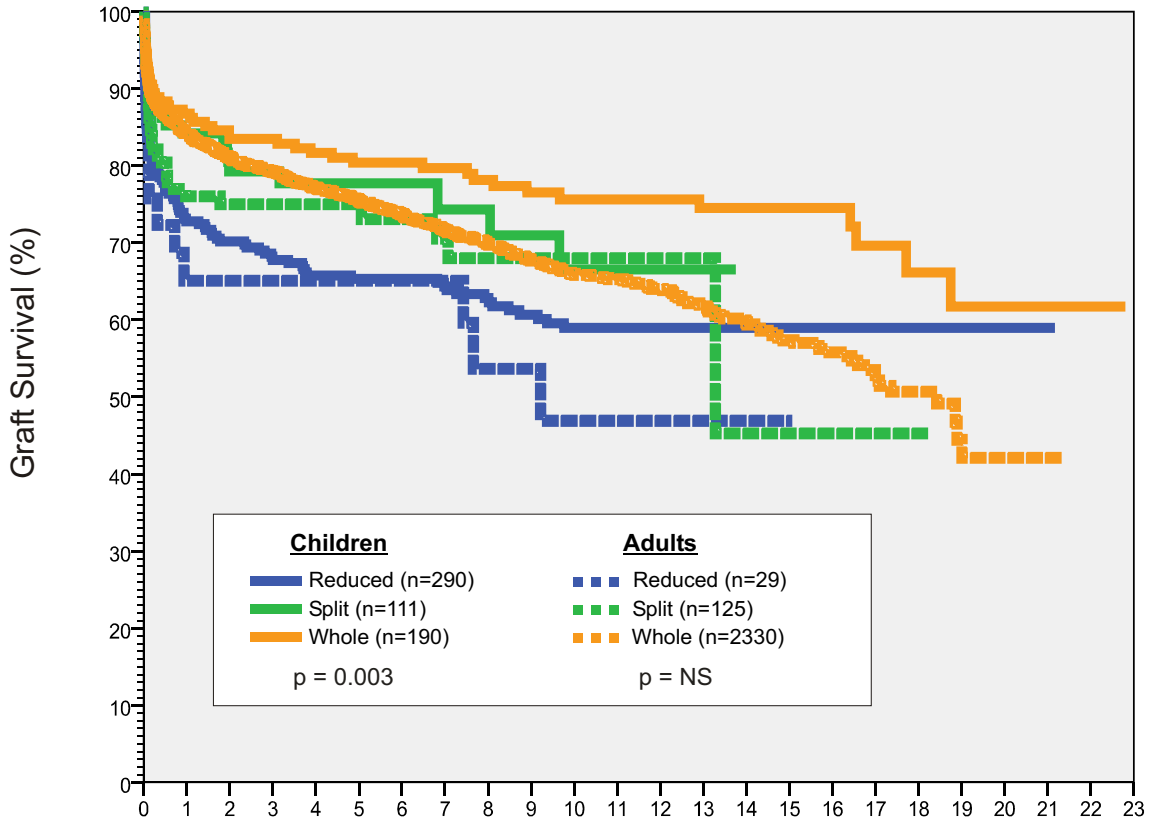
All grafts (n = 3075)





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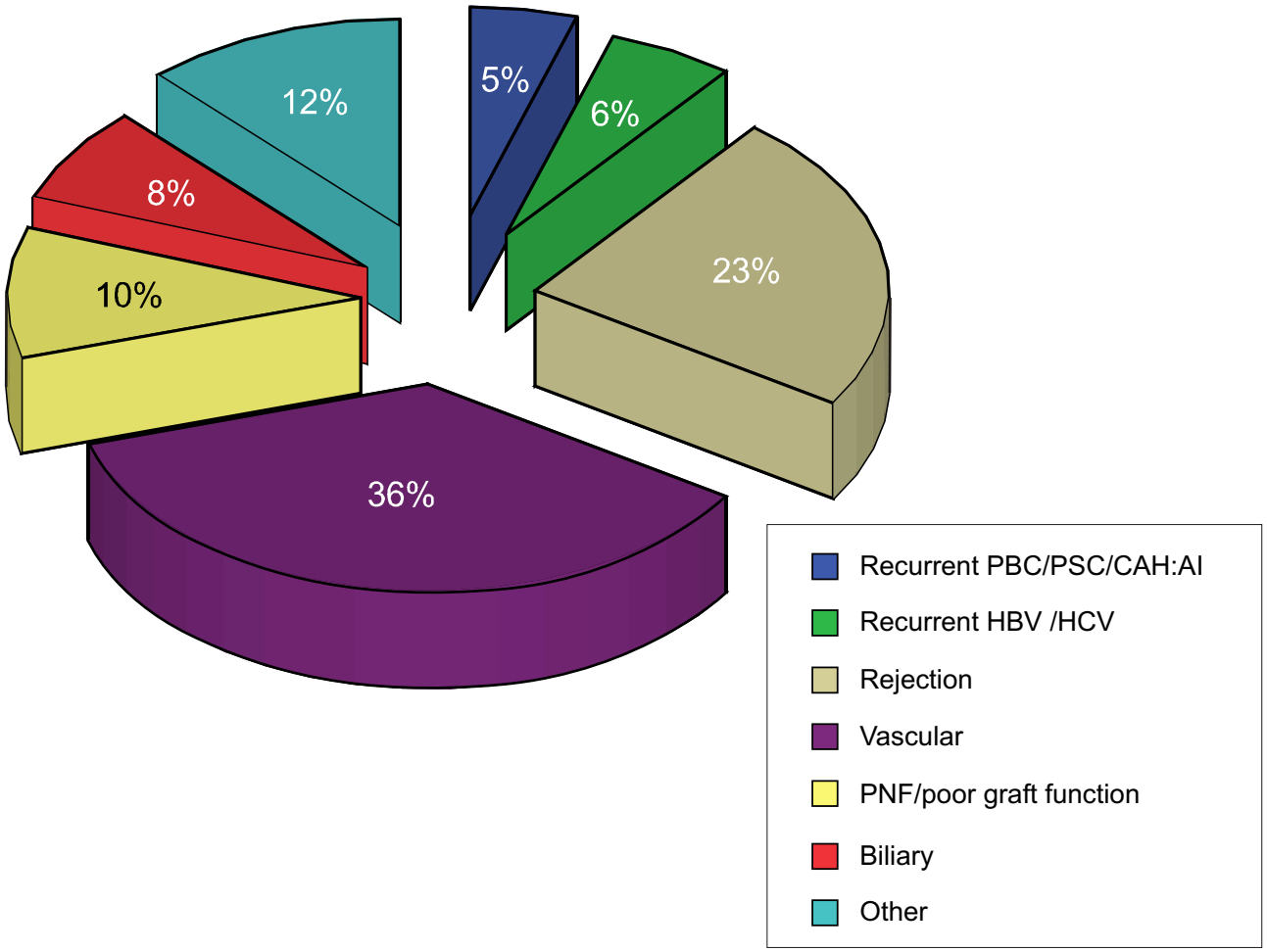
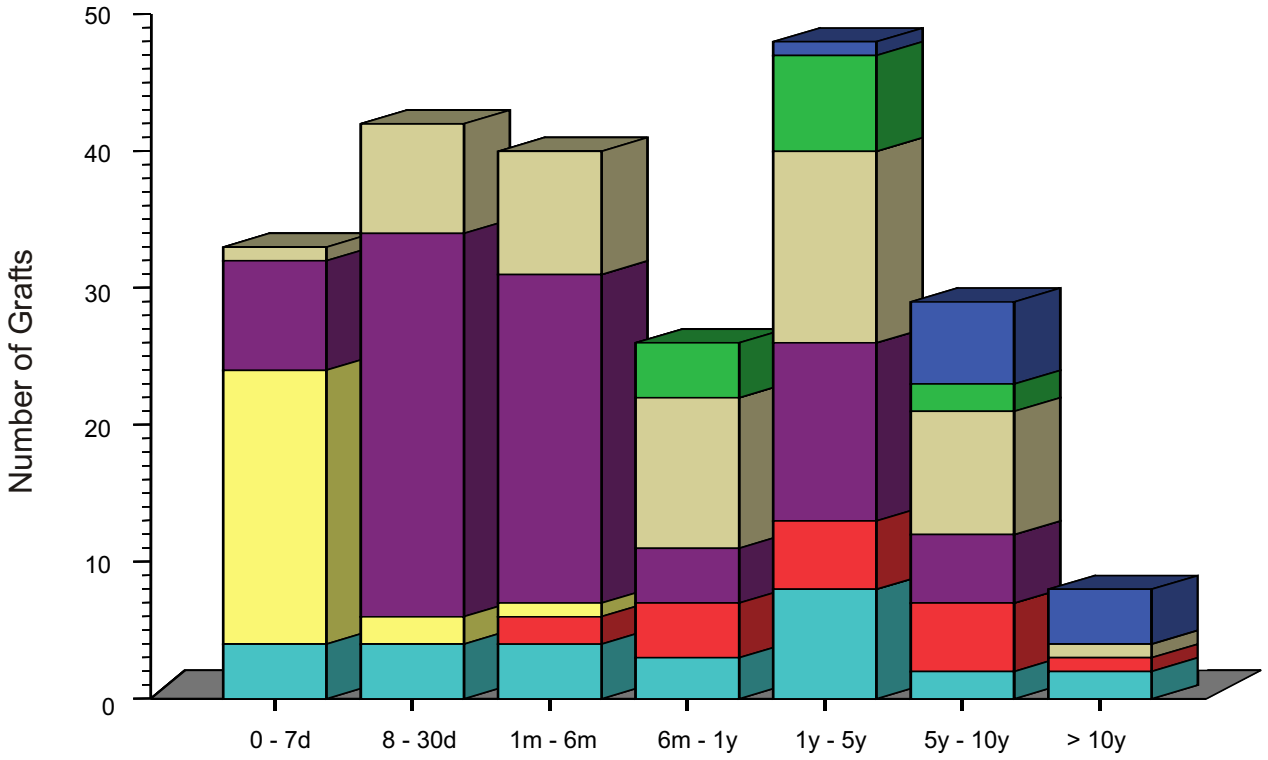
Indication for Retransplantation

n = 226 *(209 2nd grafts, 17 3rd grafts)*





N =	***33*** *(15%)*	***42*** *(19%)*	***40*** *(18%)*	***26*** *(11%)*	***48*** *(21%)*	***29*** *(13%)*	***8*** *(3%)*

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Section 5

Cause of Patient Death

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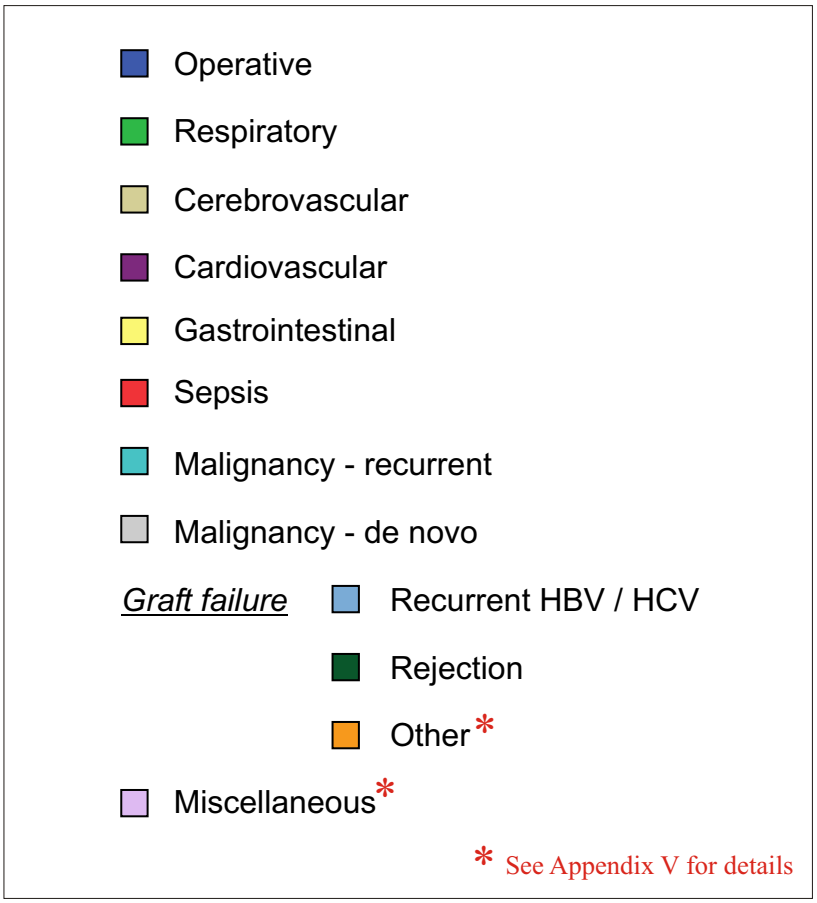
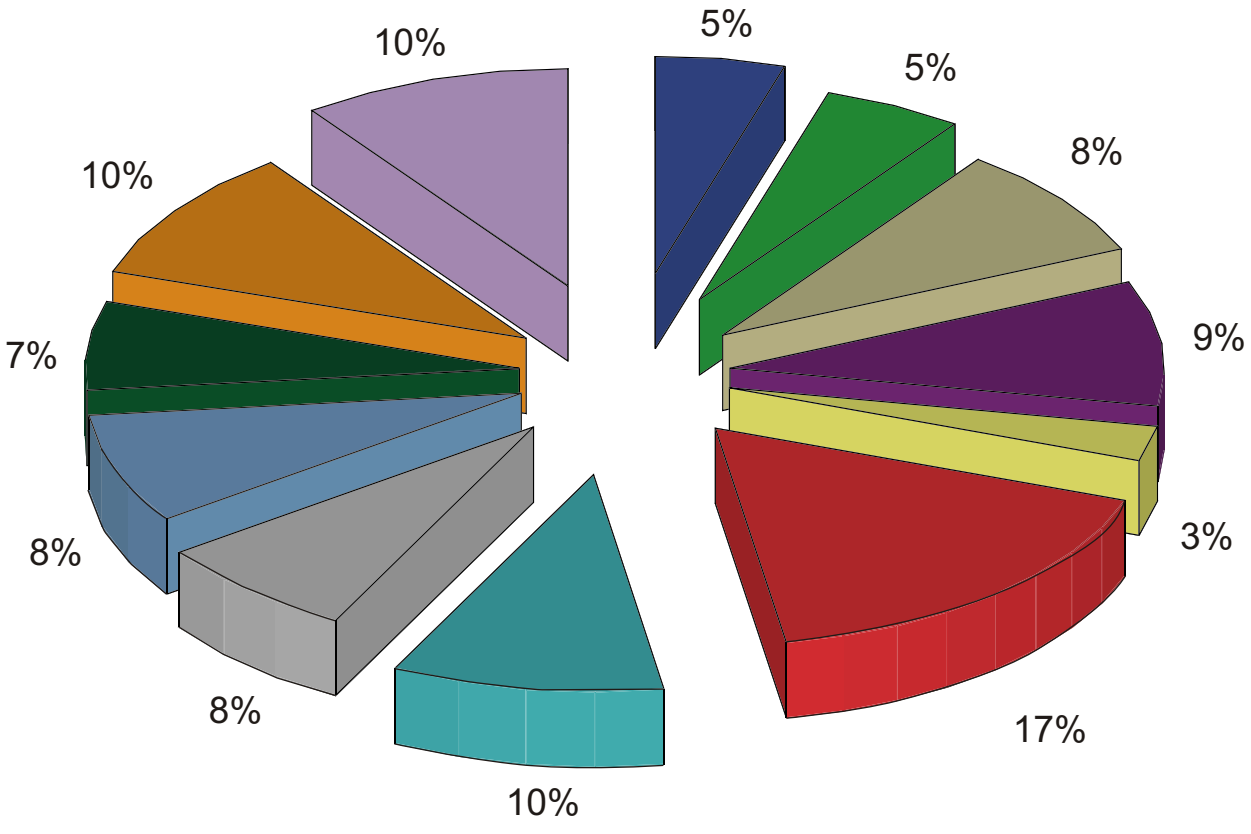
All Patients n = 730





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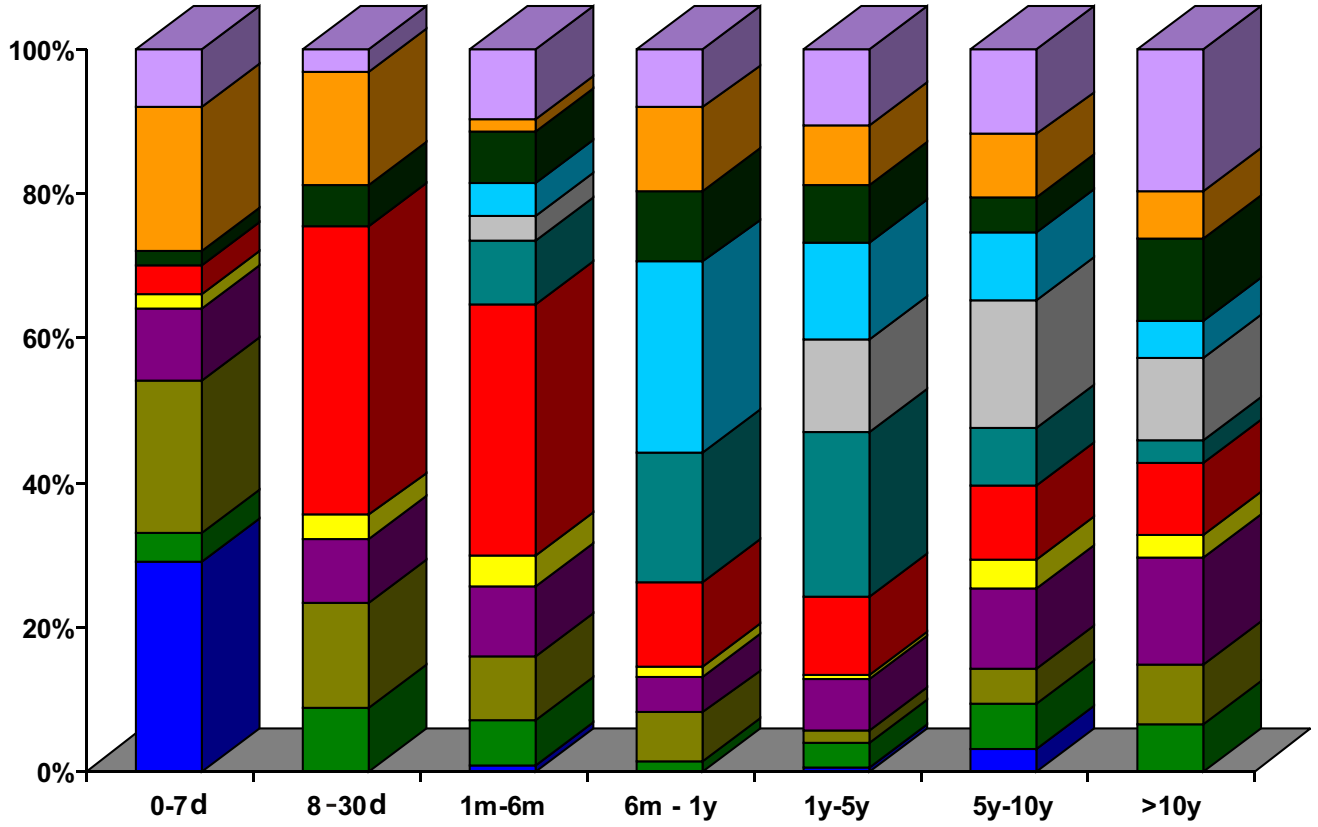
Cause of Death by Time Post Transplant



	0-7 d	8 -30 d	1m-6m	6m - 1y	1y-5y	5y-10y	>10y
N =	100 (14%)	90 (12%)	113 (15%)	61 (8%)	179 (24%)	126 (17%)	61 (8%)

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

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Section 6

Deceased Donor Information

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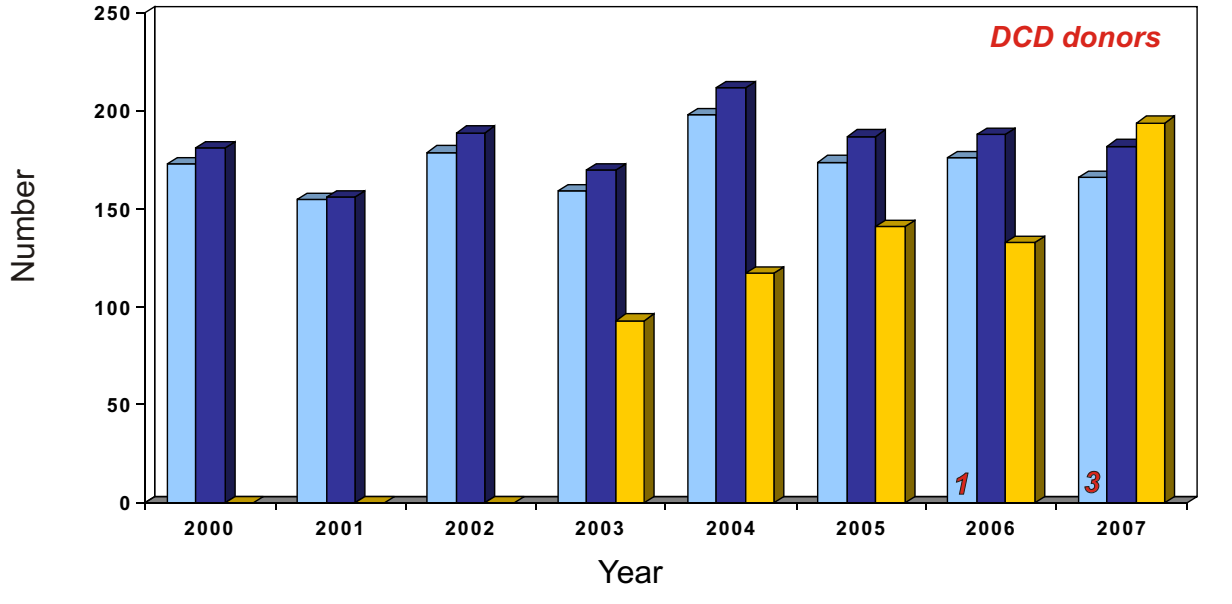
Deceased Donation by Year

	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

Grafts from deceased donors



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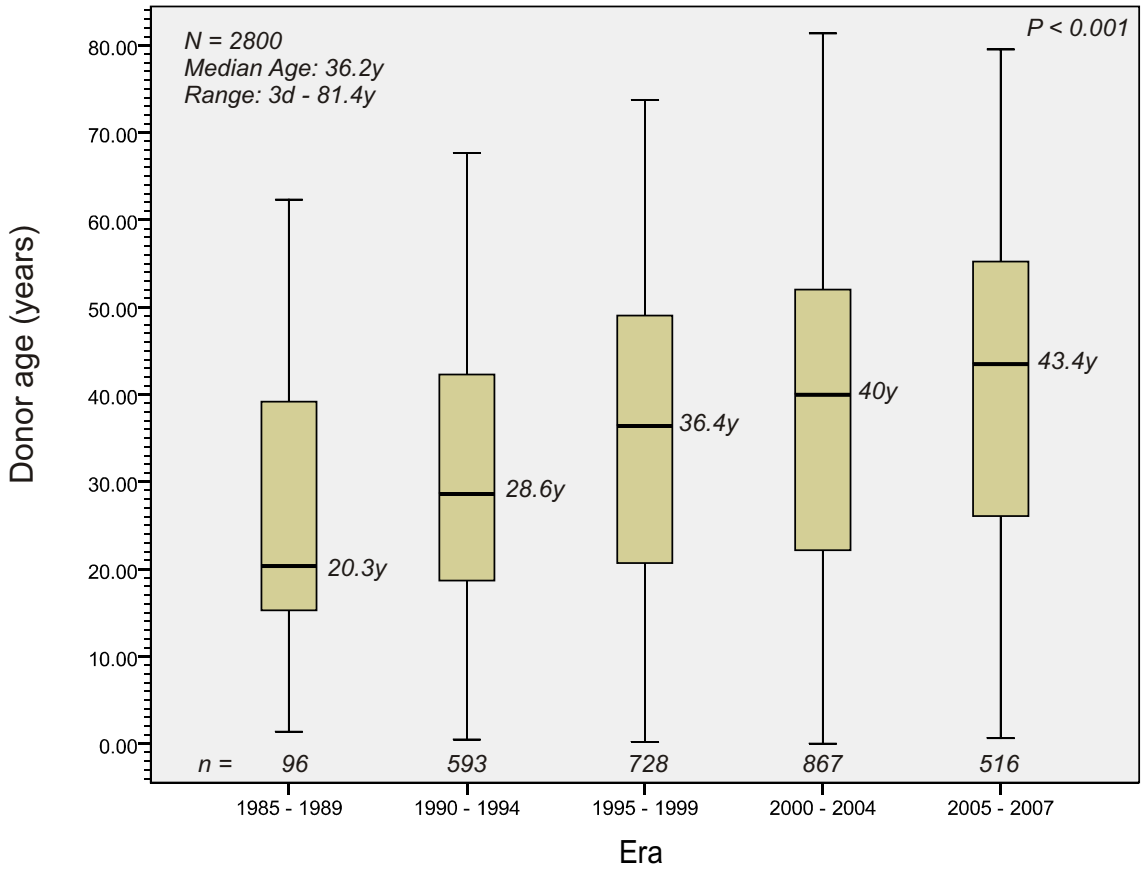
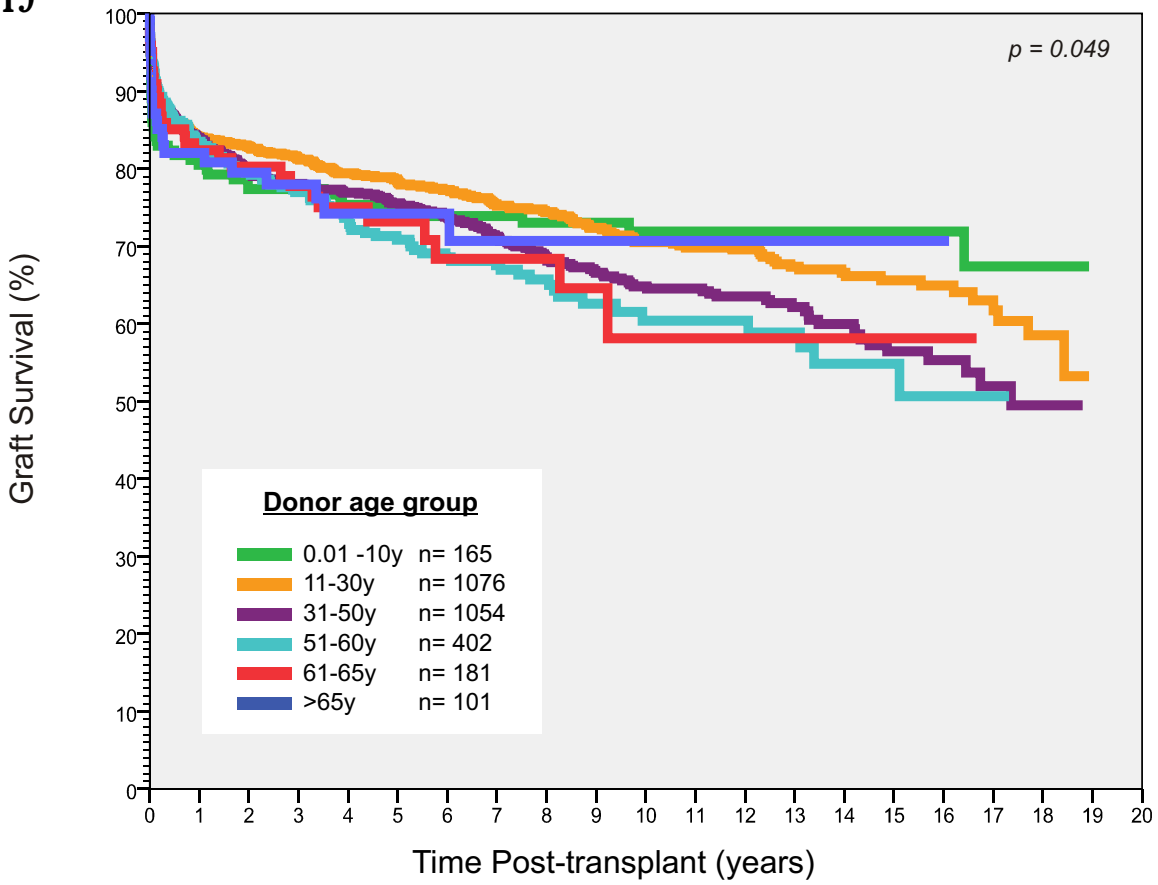
Donor Age by Era
N = 2800



Graft Survival by Donor Age
N = 2919



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Section 7

Living Donor Transplantation

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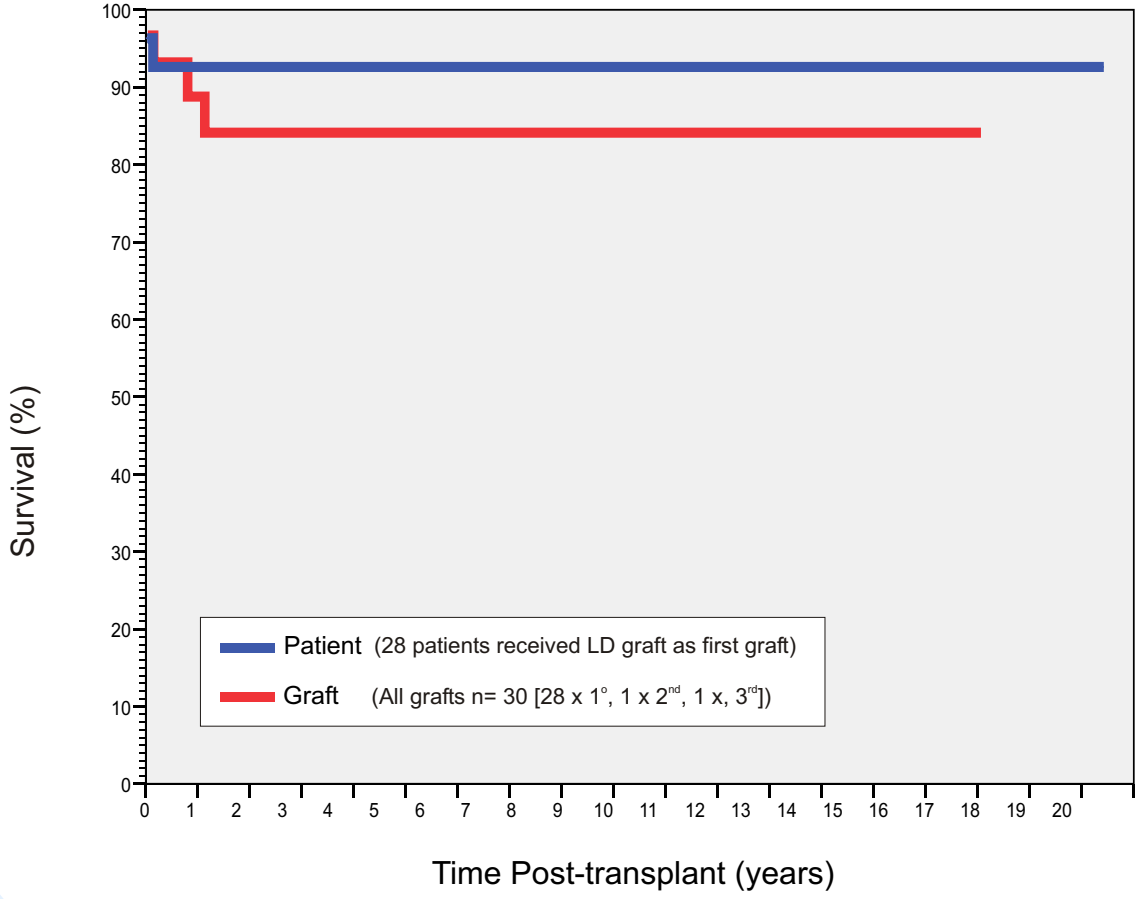
	Recipient Age Group		
	Child [n=24]	Adult [n=6]*	All [n=30]
Donor gender	-	-	-
Male	13	4	17
Female	11	2	13
Donor age	-	-	-
Median	35.9y	30.3y	35.3y
Range	29.7 - 54.5y	22.8 - 35.7y	22.8 - 54.5y
Donor relationship	-	-	-
Mother	5	-	5
Father	12	-	12
Son	-	1	1
Grandmother	1	-	1
Grandfather	1	-	1
Sister	-	2	2
Brother	-	2	2
Aunt	3	-	3
Family friend	2	-	2

* *1 x whole liver domino transplant*



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Section 8

Waiting List

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Waiting List Activity
[Data 1/1/04 - 31/12/07]

Activity	2004	2005	2006	2007		
Listed at 1 January	93	117	145	133	-	TOTAL 2007
New listings	279	292	259	-	338	
TOTAL	**372**	**409**	**404**	**133**	**338**	**471**
OUTCOME						
Transplant	**214 [58%]**	**191 [47%]**	**194 [48%]**	**67**	**123**	**190 [40%]**
Delisted	**41 [10%]**	**72 [18%]**	**77 [19%]**	**33**	**53**	**86 [18%]**
Died on list	14 } 6%	26 } 11%	18 } 10%	15	20	35 } [12.5%]
Too sick	8	9	13	4	9	13
Tumour progression	2	9	8	3	8	11
Improved	8	15	16	7	10	17
Other	9	13	22	4	6	10*
Still listed at 31 Dec	117 [32%]	146 [35%]	133 [33%]	33	162	195 [41%]

[*Other: Temporary delist - 4; Moved interstate - 2; Cardiac - 1; Respiratory - 1; Alcohol - 2; Patient wish - 1]

Outcome of Urgent Listing

OUTCOME	CATEGORY 1			CATEGORY 2		
	2005 (n=14)	2006 (n=16)	2007 (n=18)	2005 (n=31)	2006 (n=26)	2007 (n=32)
TRANSPLANTED	4 } 64%	12 } 88%	10 } 67%	20 } 68%	21 } 88%	24 } 88%
IMPROVED	5	2	2	1	2	4
DIED	5	2	6	10	2	2
OTHER TREATMENT	-	-	-	-	1	-

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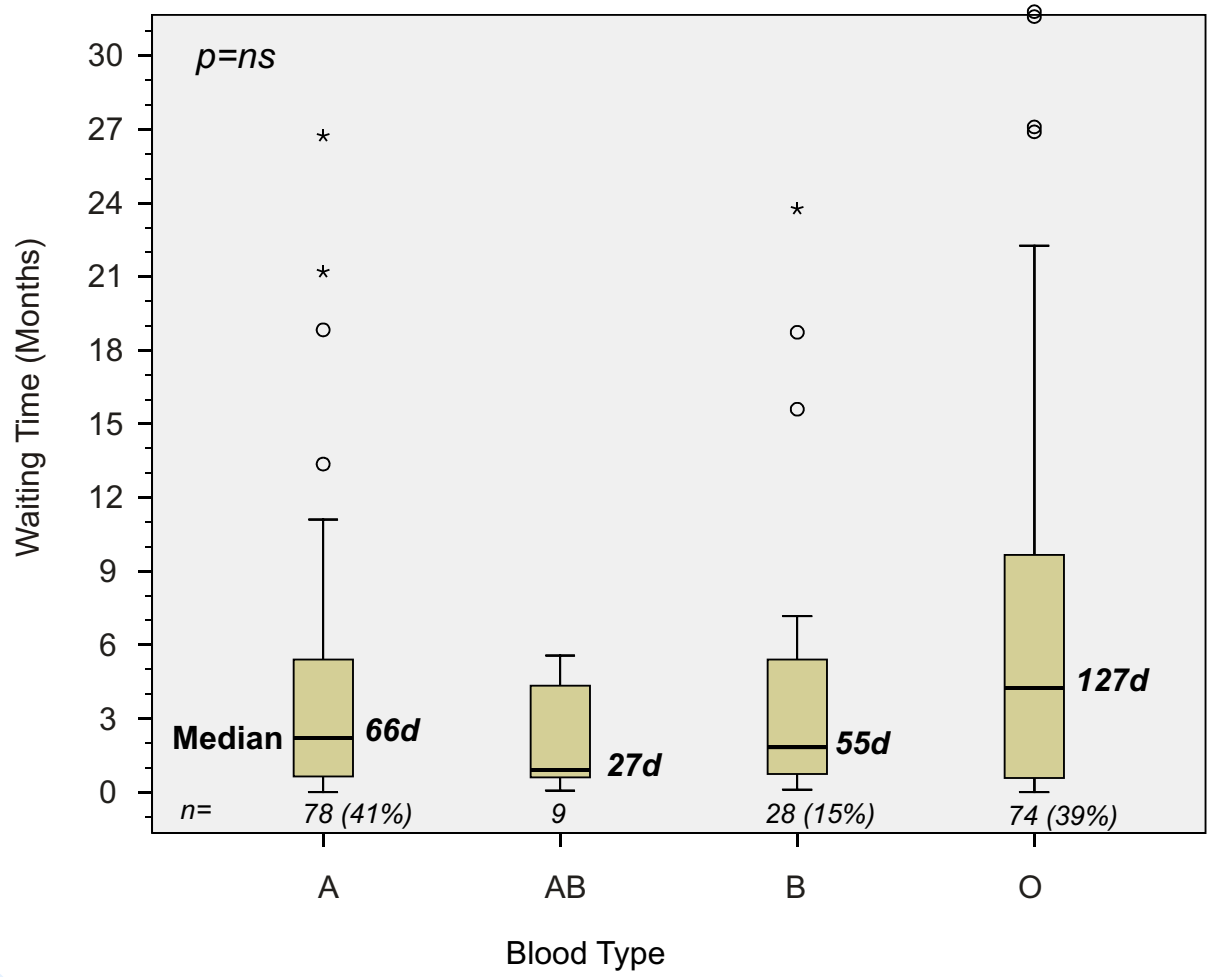
Outcome by Blood Group

	Blood Group				
	A	O	B	AB	TOTAL
n=	167 (35.5%)*	218 (46%)	71 (15%)	15 (3%)	471
Not transplanted	89	144	42	6	281
Transplanted	78 (47%)**	74 (34%)	29 (41%)	9 (60%)	190

* *% of total number listed*

** *% of blood group*

Waiting Time to Transplant 2007



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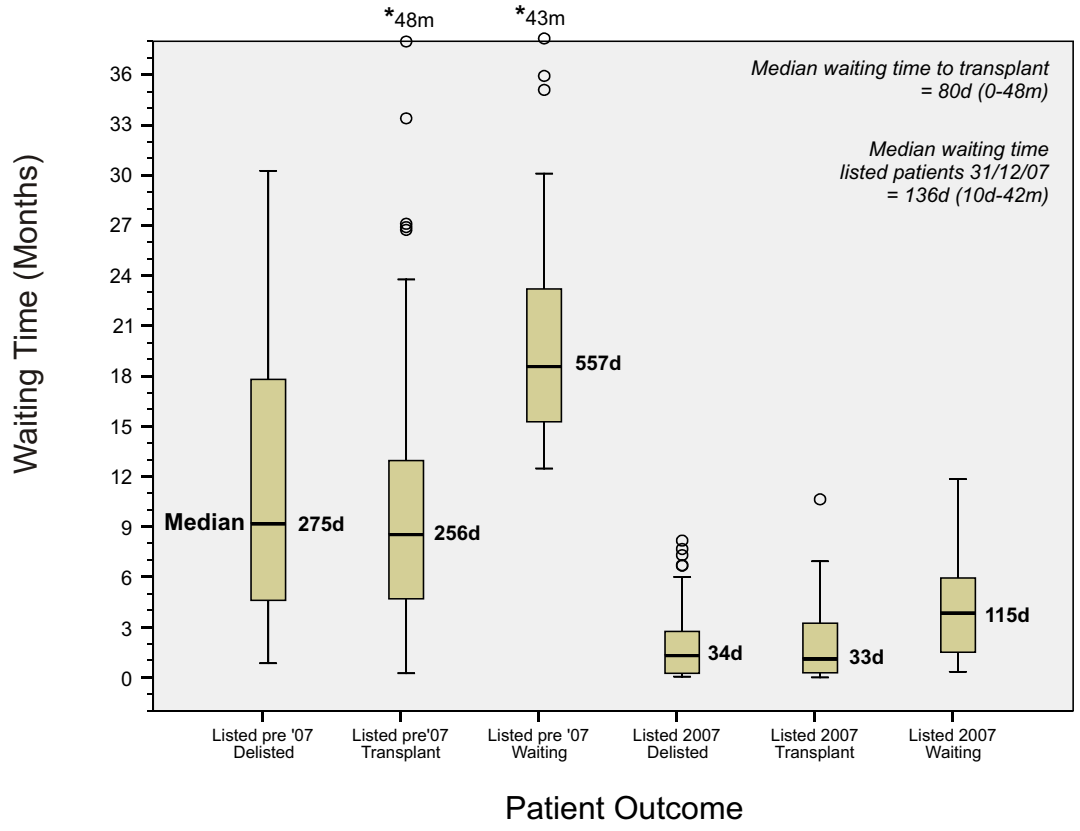
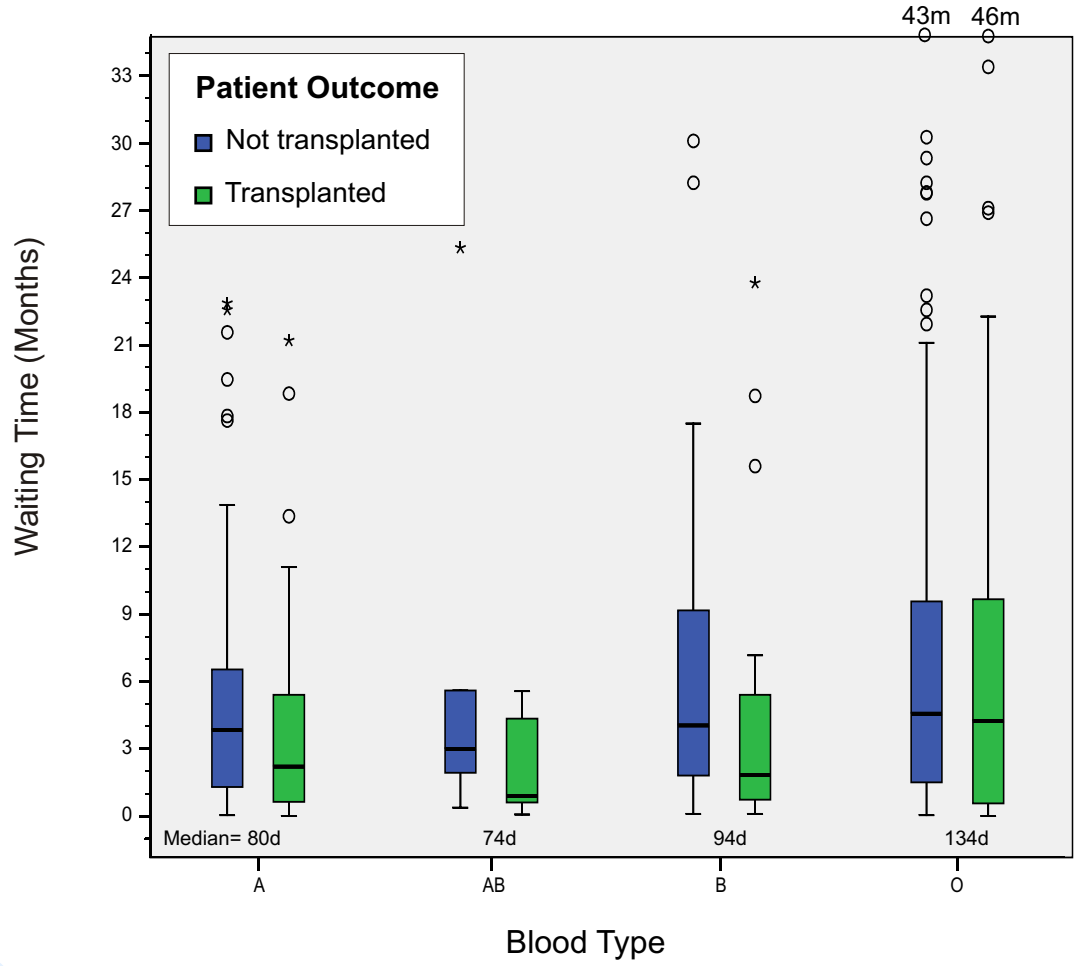
Waiting Time by Outcome



Waiting Time by Outcome & Blood Group



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Section 9

Liver Transplantation and Cancer

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# Cancer in Liver Transplant Recipients
N = 2850

At Tx		
Tx for Liver Ca	144	(5%)
Liver Ca as a Secondary Diagnosis	291	(10%) 292 Ca
Total	435	(15%)
Post Tx		
Recurrent Liver Ca	77	(3% of all pts, 18% of pts with Ca at Tx)
De Novo Ca	161	(6%) 170 Ca
Skin Ca	348	(12%)
Total	586	(21%)
Multiple Ca	68	
Pre-Tx cancer developed de novo cancer	15	(3% of pts with Ca at Tx)
Transferred from Donor	2	
Developed non skin Ca < 90days	8	

# Liver Cancer as Primary Diagnosis
N= 2850

TYPE OF CA	No	DIED	DIED OF THIS CA
HEPATOCELLULAR CA	122	38	22 (18%)
HEPATOBLASTOMA	8	2	1 (12%)
FIBROLAMELLAR	5	5	2 (40%)
HEPATOBLASTOMA	8	2	1 (12%)
CARCINOID	4	4	4 (100%)
CHOLANGIOCARCINOMA	1	1	1 (100%)
ANGIOSARCOMA	1	1	1 (100%)
EPITHELOID HAEMANGIOENDOTHELIOMA	1	0	0
GASTRINOMA	1	1	1 (100%)
PANCREATIC ISLET CELL	1	1	1 (100%)
TOTALS	**144 (5% of pts)**	**53 (37% of those with PCa)**	**33 (23% of those with PCa)**

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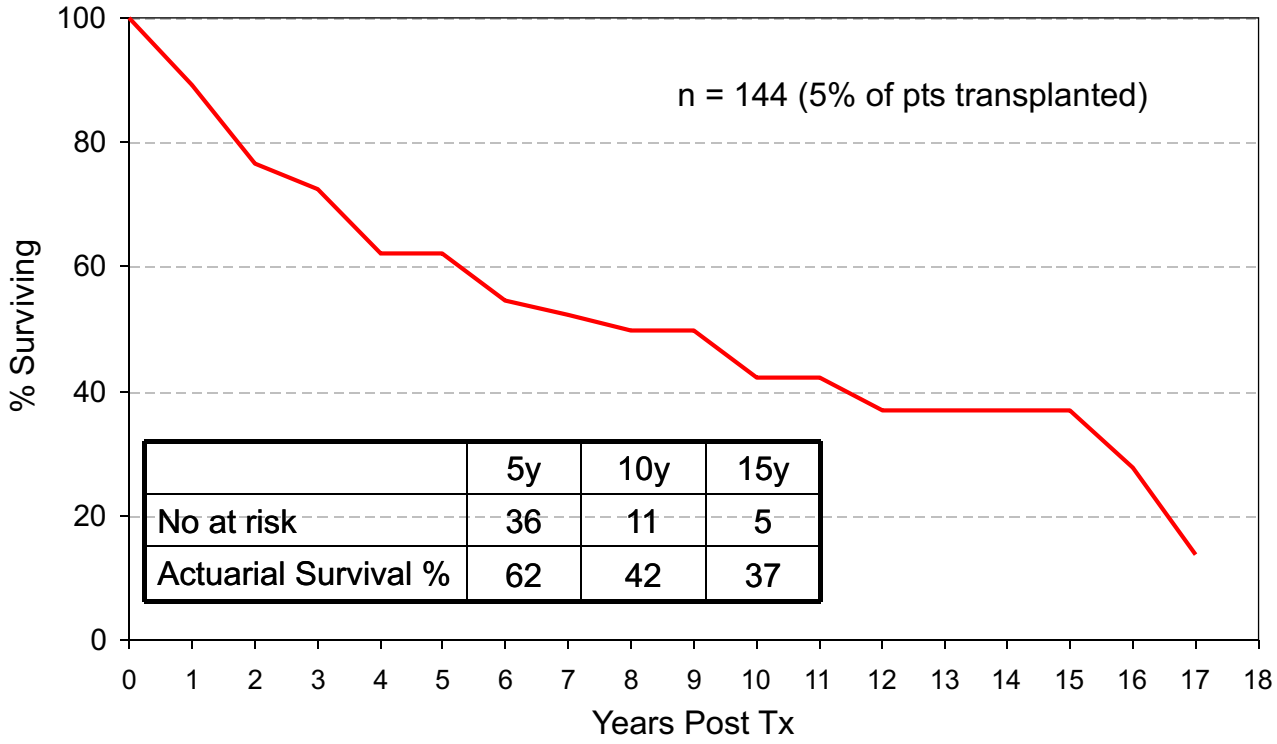
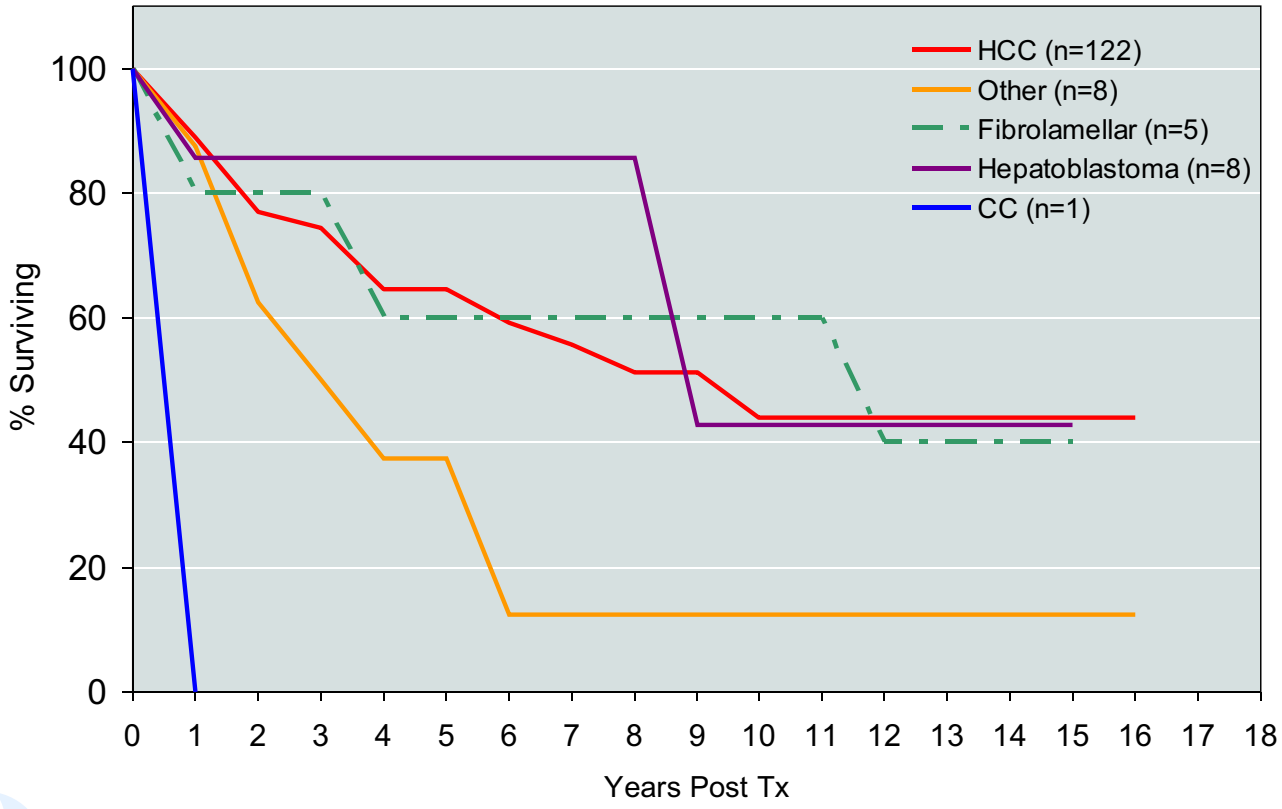
Overall Survival
Primary Liver Cancer
N = 144 (5% of patients transplanted)



	5y	10y	15y
No at risk	36	11	5
Actuarial Survival %	62	42	37

Overall Survival
Primary Liver Cancer
N = 144 / 2850 (5%)



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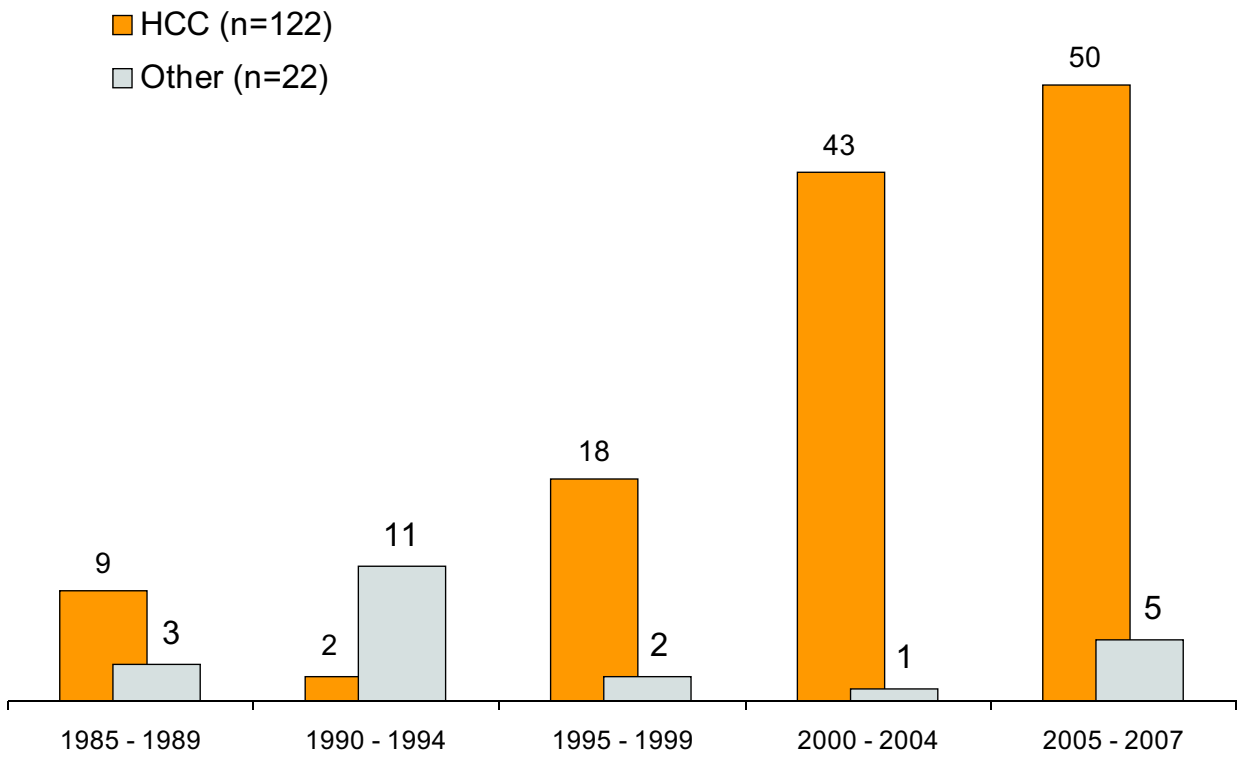
Primary Liver Cancer
Actuarial Survival Summary
N = 2850

		1yr	5yr	10yr	15yr
HCC (n=122)	n	95	27	6	2
	%	89	65	44	44
Other (n=8)	n	8	4	2	2
	%	88	38	13	13
Hepatoblastoma (n=8)	n	6	4	2	2
	%	86	86	43	43
Lamella Variant (n=5)	n	5	4	4	2
	%	80	60	60	40
CC (n=1)	n	1			
	%	1			

Liver Cancer as Primary Diagnosis
n = 144



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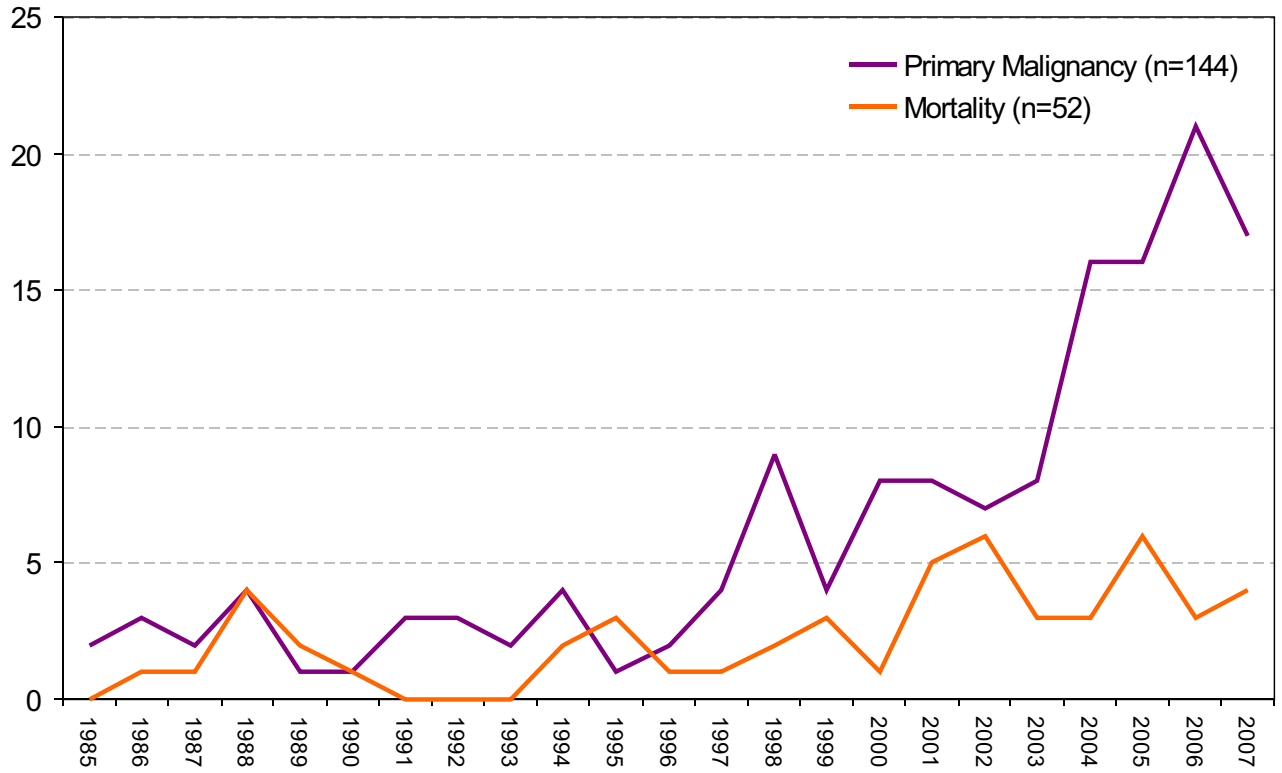
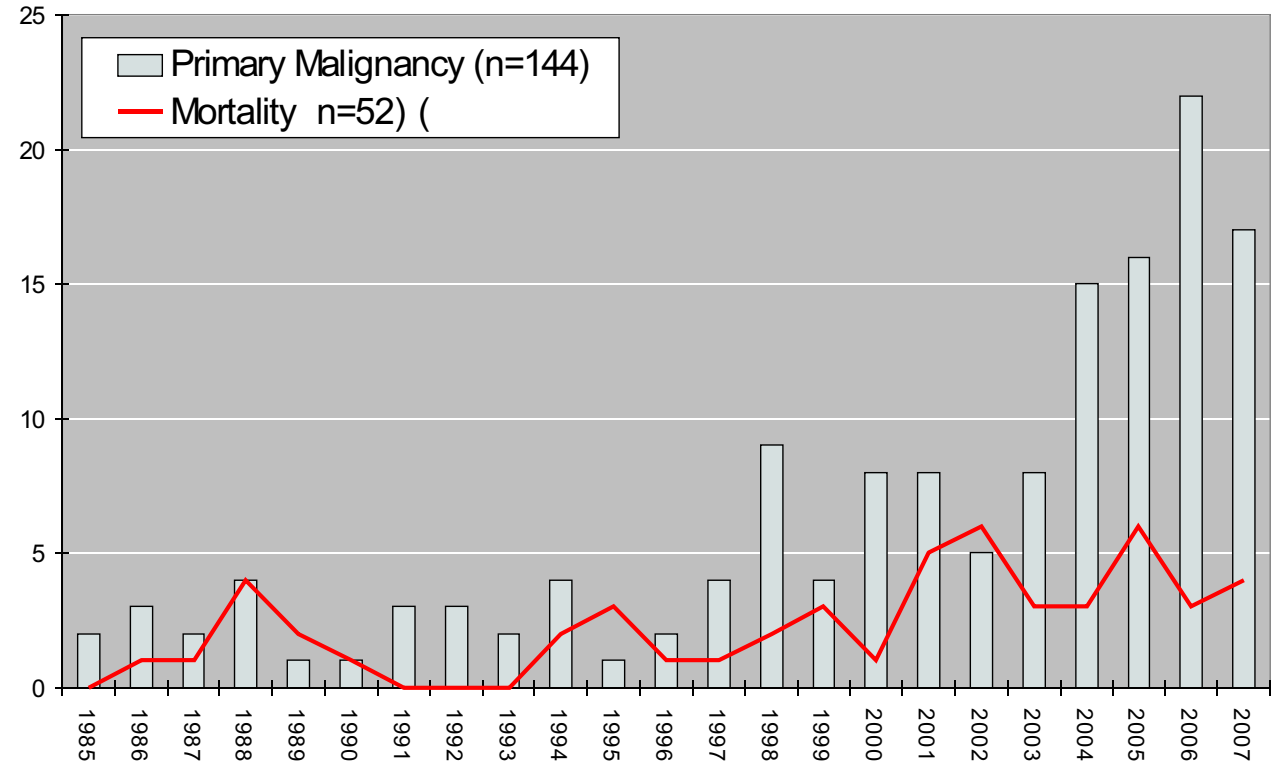
Primary Liver Cancer Incidence and Mortality n=144/2850 (5%)



Primary Liver Cancer Incidence and Mortality



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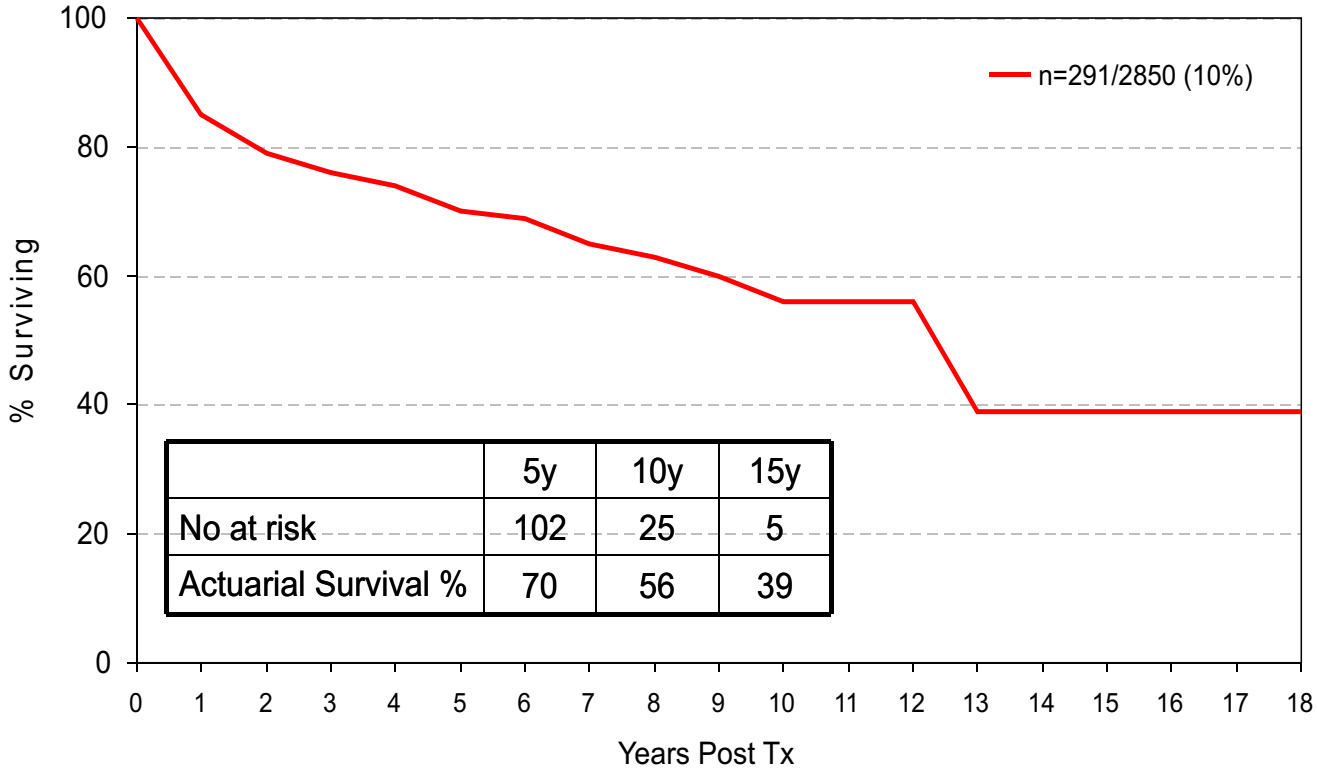
Liver Cancer as a Secondary Diagnosis
N = 2850

	No	Died	Died of This Cancer
HEPATOCELLULAR CA*	258	65	21 (8%)
CHOLANGIO CA	25	16	13 (52%)
ADENOCARCINOMA	3	3	0
HEPATOBLASTOMA*	2	1	0
FIBROLAMELLAR	2	1	1
ANGIOSARCOMA	1	1	1
EPITHELOID HAEMANGIOCA	1	0	0
Total	**292* in 291 pts (10%)**	**88 (31% of pts with SCa)**	**36 (12.5% of pts with SCa)**

*** 1 patient had 2 secondary cancers**

Overall Survival
Liver Cancer as a Secondary Diagnosis



	5y	10y	15y
No at risk	102	25	5
Actuarial Survival %	70	56	39

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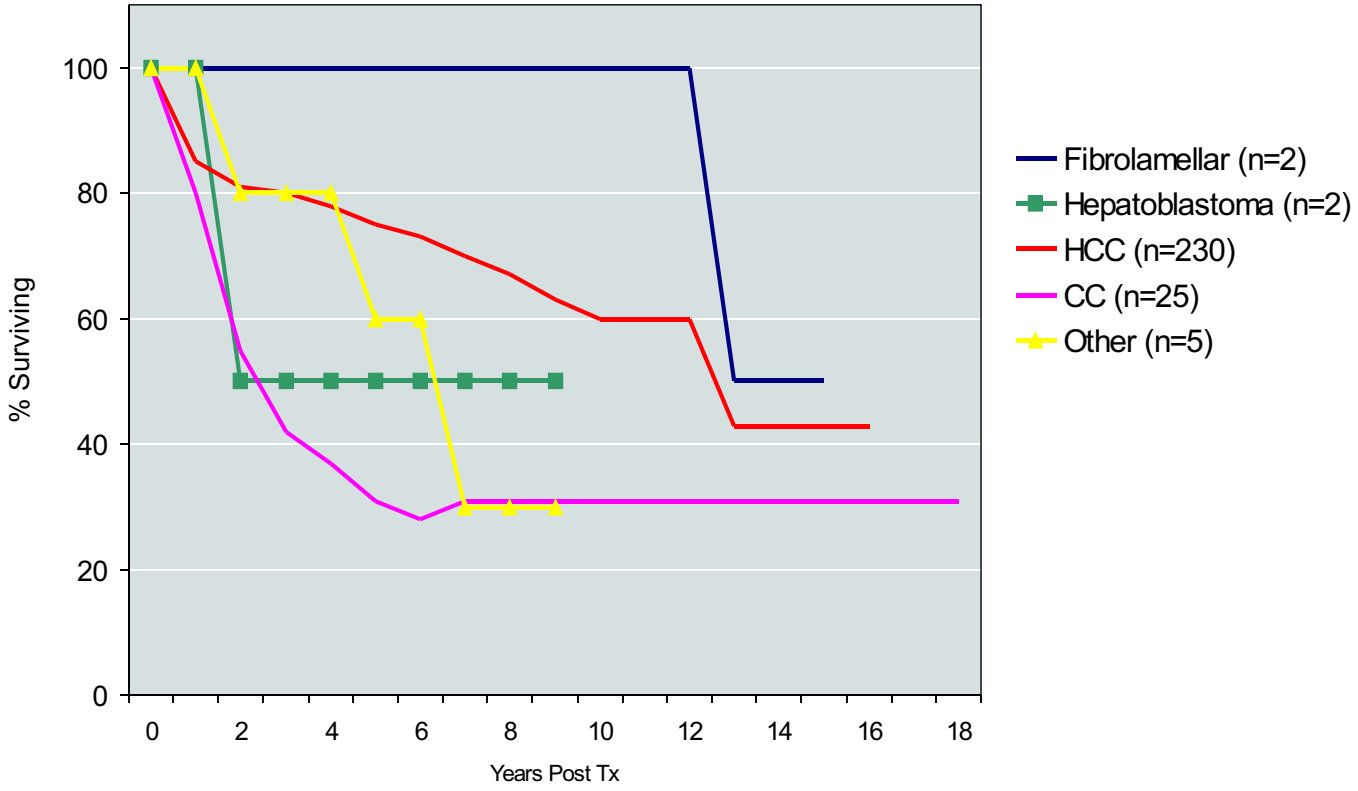
Liver Cancer as a Secondary Diagnosis
N = 2850



Secondary Liver Cancer
Actuarial Survival Summary
N = 2850

		1yr	5yr	10yr	15yr
CC (n=25)	n	20	6	4	2
	%	80	31	31	31
HCC (n=258)	n	201	92	19	3
	%	85	75	60	43
Hepatoblastoma (n=2)	n	2	2	2	1
	%	50	50	50	50
Lamella Variant (n=2)	n	2	2	2	1
	%	50	50	50	50
Other (n=5)	n	5	5		
	%	80	60		

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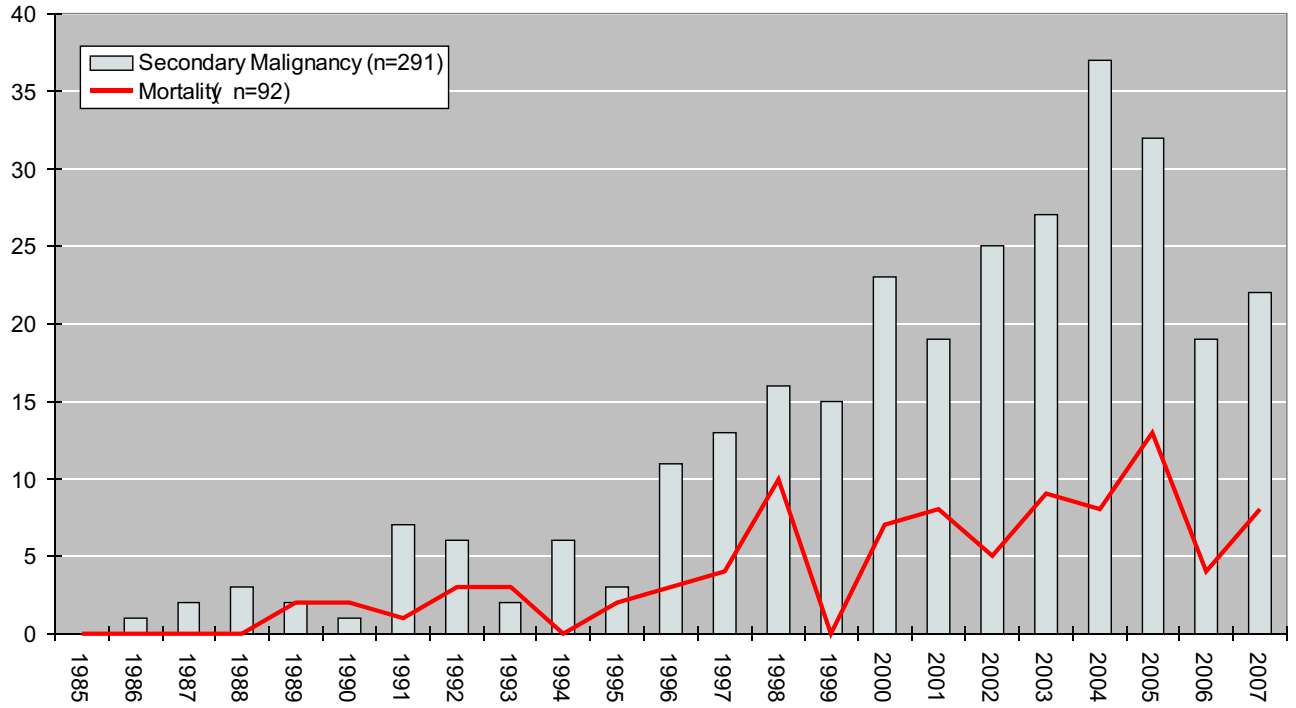
Liver Cancer as a Secondary Diagnosis Incidence and Mortality n=291/2850 (10%)



Liver Cancer (Primary or Secondary Diagnosis) N = 2850

TYPE OF CA	NO	DIED	DIED OF THIS CA
HEPATOCELLULAR CA*	380	103	43 (11%)
CHOLANGIOCARCINOMA	26	17	14 (54%)
HEPATOBLASTOMA*	10	3	1 (10%)
FIBROLAMELLAR	7	6	3 (43%)
CARCINOID	4	4	4 (100%)
ADENOCARCINOMA	3	3	0
EPITHELOID HAEMANGIOENDOTHELIOMA	2	0	0
GASTRINOMA	1	1	1 (100%)
PANCREATIC ISLET CELL	1	1	1 (100%)
ANGIOSARCOMA	1	1	1 (100%)
TOTALS	**435 (15% of pts)**	**140 (32%of those with Ca)**	**69 (16% of those with Ca at Tx)**

*** 1 patient had 2 secondary cancers**

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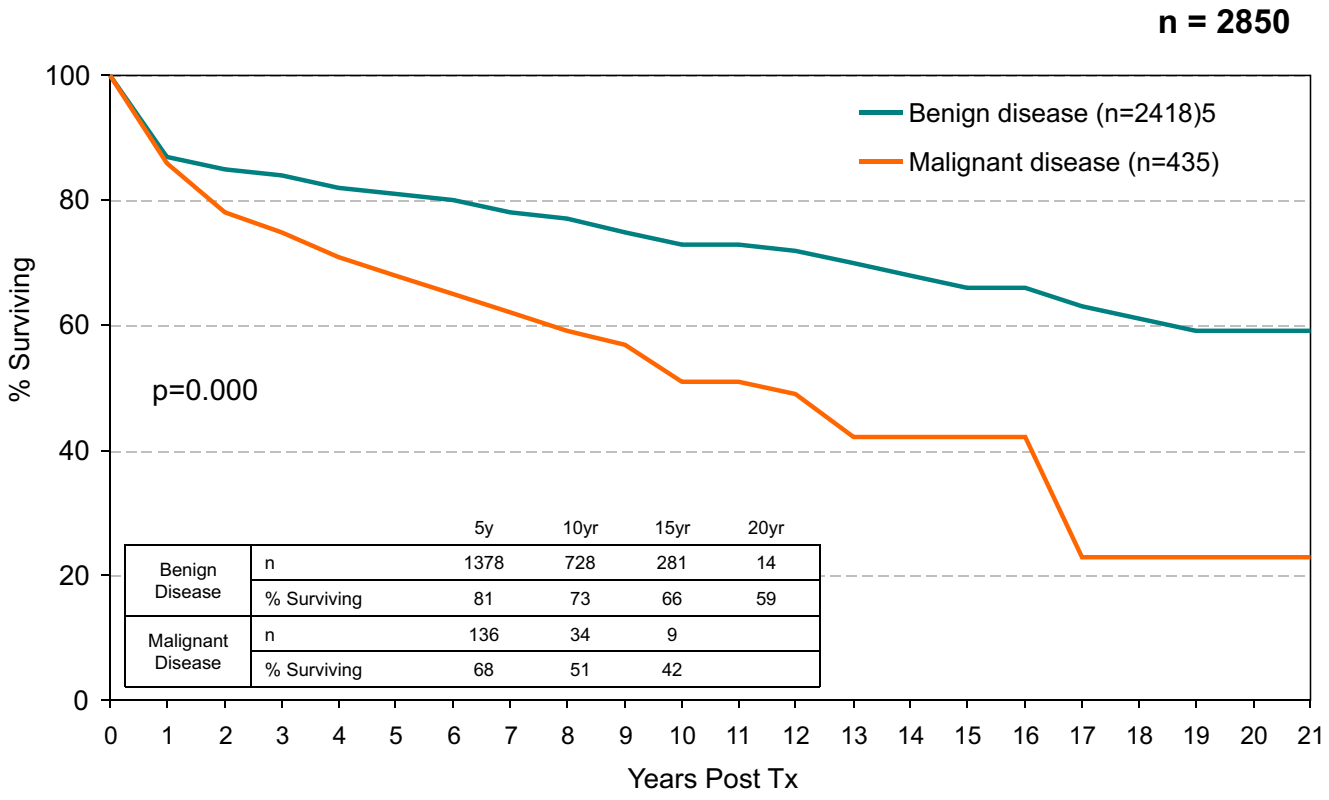
Patient Actuarial Survival
Benign Disease vs Pre Transplant Liver Malignancy
N = 2850



		5y	10yr	15yr	20yr
Benign Disease	n	1378	728	281	14
	% Surviving	81	73	66	59
Malignant Disease	n	136	34	9	
	% Surviving	68	51	42	

De Novo Non Skin Cancer
N = 2850

	No	Male	Female	Age of pts (yrs)	Time to diagnosis (mths)	Died of This Cancer
Alimentary*	54	38	16	12.6 – 78 (m 58)	3 – 207 (m 58)	24 (44%)
Lymphoma*	54	34	20	1.5 – 69 (m 45)	1 – 182 (m 51)	21 (39%)
Genitourinary*	21	11	10	38.5 – 70.5 (m 60)	2 – 164 (m 29)	2 (10%)
Breast	12	-	12	30 – 62.8 (m 50)	11 – 204 (m 80)	2 (17%)
Respiratory	10	7	3	29 – 61.1(m 51)	13 – 170(m 57)	7 (70%)
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	4	2	2	16.5 – 75 (m 50)	66 – 174 (m 120)	3 (75%)
Leukaemia	3	1	2	2.9 – 49.5 (m 37)	16 – 44 (m 30)	0
Miscellaneous	2	1	1	63 – 67 (m 65)	6 – 145 (m 75)	0
Total	***170 ca in 161 pts**	**100**	**70**	**1.5 – 78 (m 52)**	**1 – 207 (m 55)**	**61 (38% of pts with Ca)**

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

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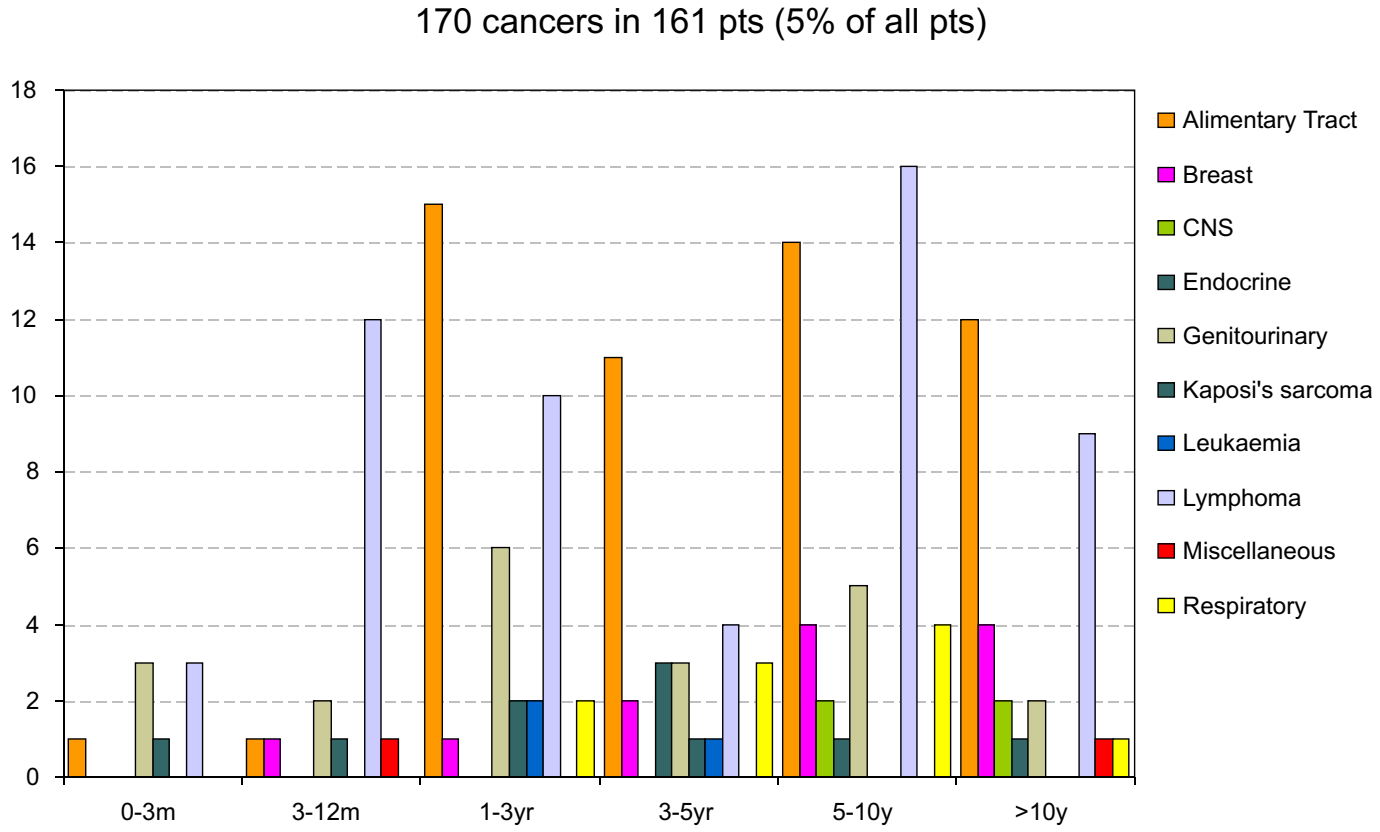
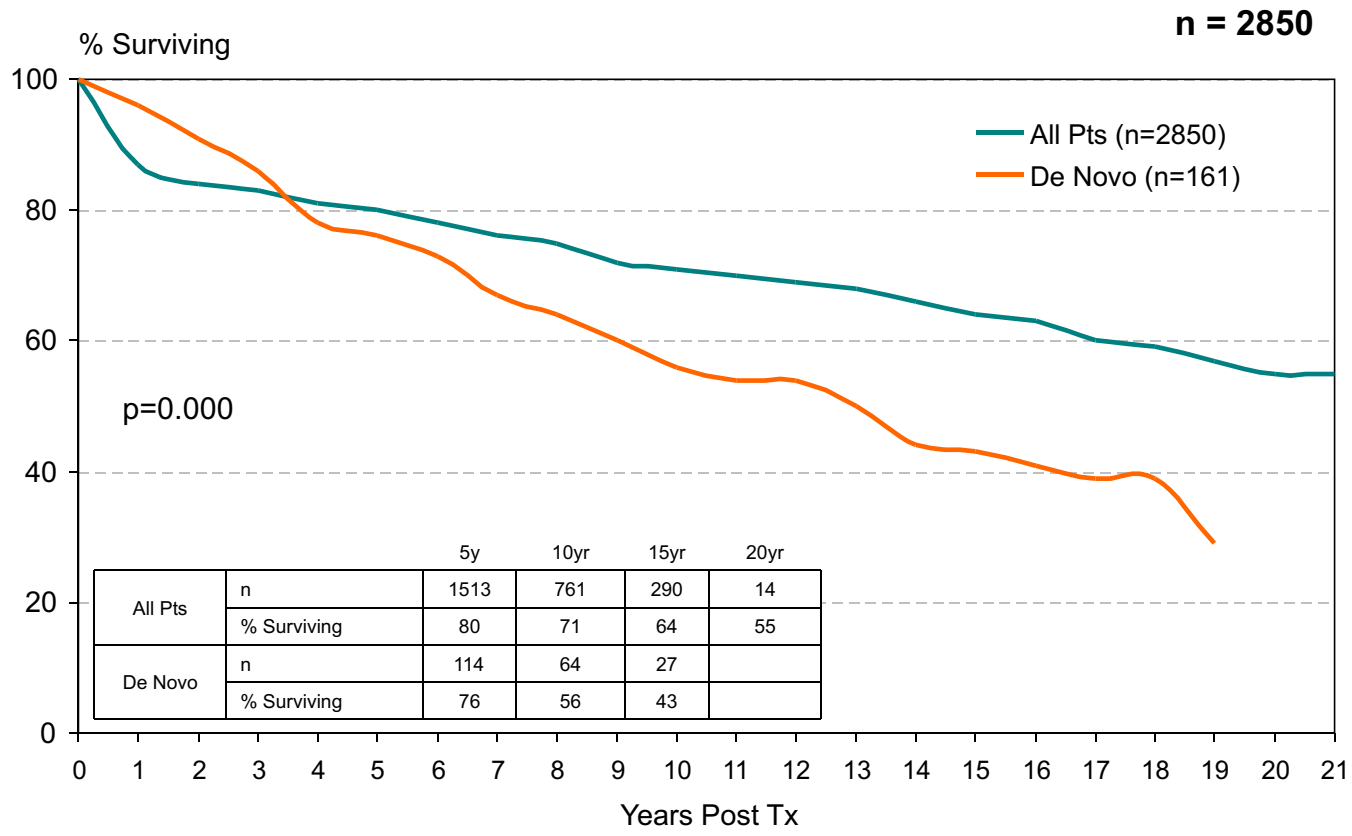
Time to 1st De Novo Non Skin Cancer
N = 2850



De Novo Non Skin Cancer vs All Patients
N = 2850



		5y	10yr	15yr	20yr
All Pts	n	1513	761	290	14
	% Surviving	80	71	64	55
De Novo	n	114	64	27	
	% Surviving	76	56	43	

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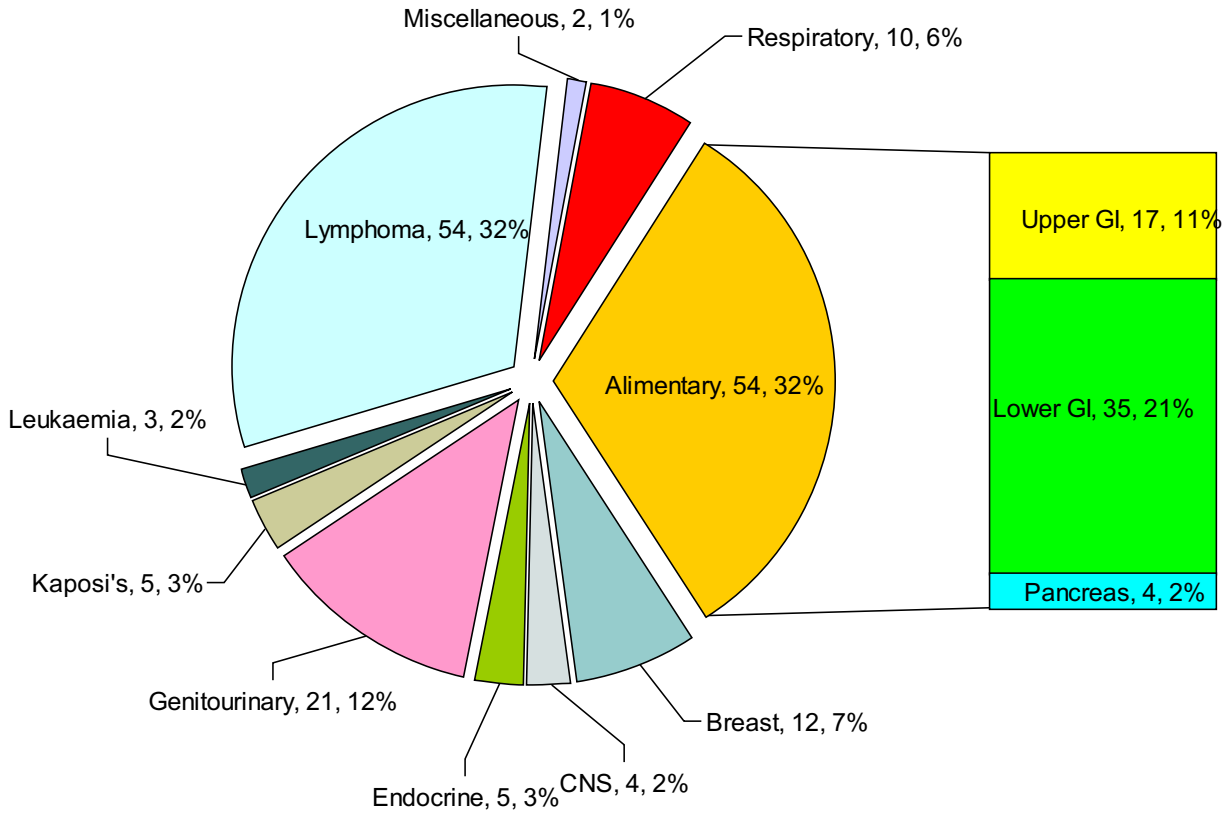
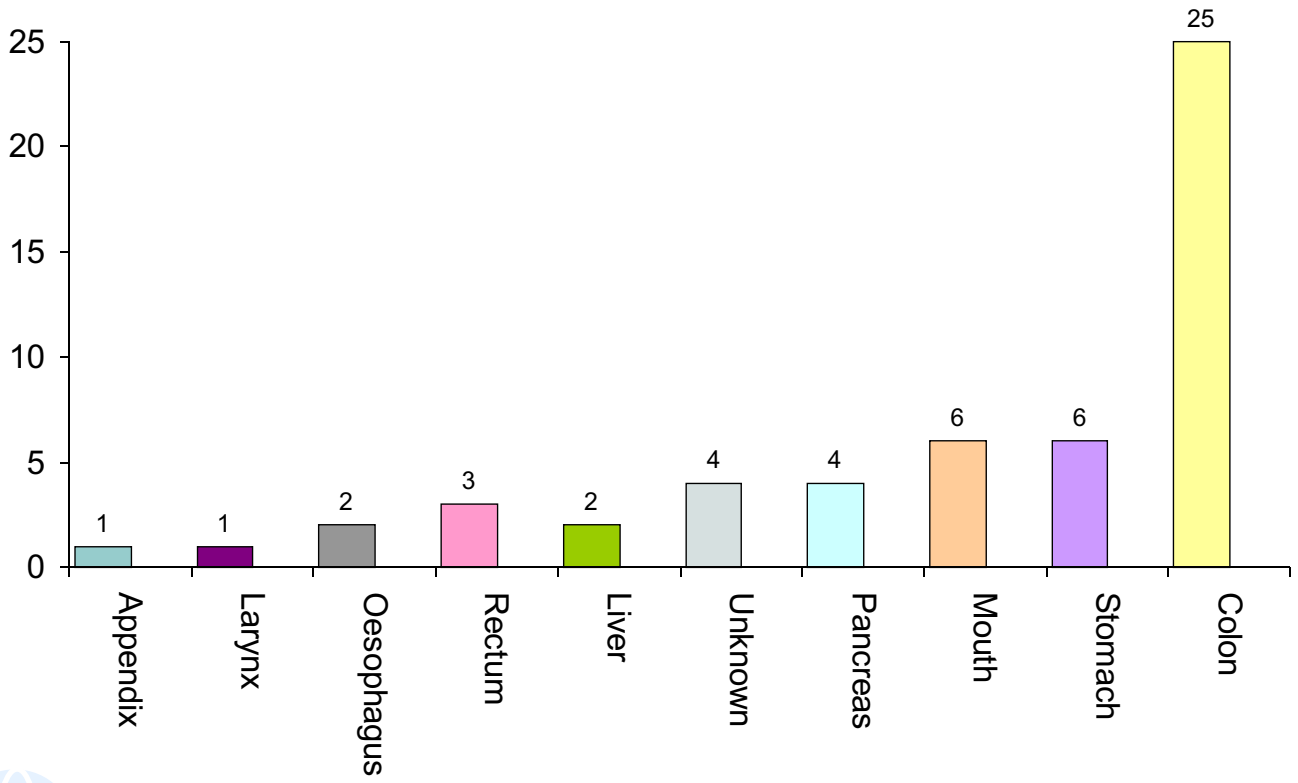
De Novo Non Skin Cancer
n = 161/2850 (6%)



De Novo Non Skin Cancer
Alimentary Tract Incidence
n = 54/170 cancers (32%)



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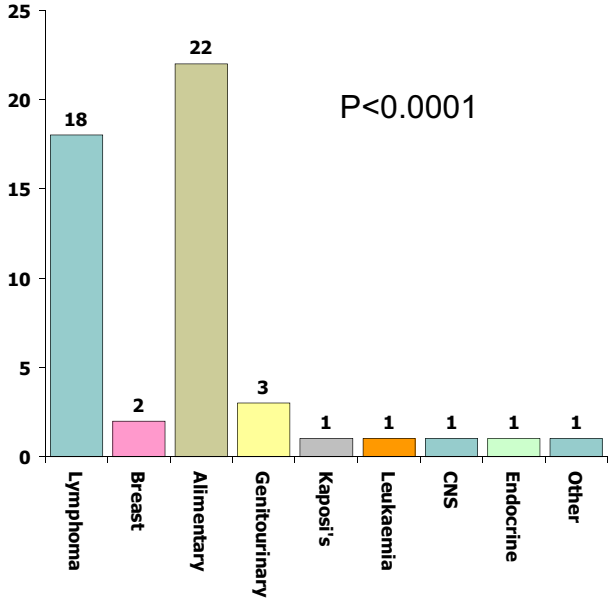
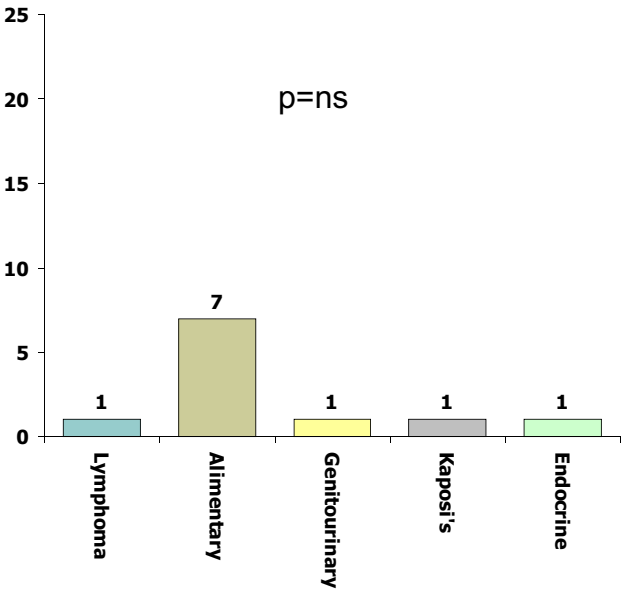
Pre Transplant Liver Disease and De Novo Non Skin Cancer n = 161/2850 (6%)

PSC + Auto-immune - 50/417 (12%)
31% of all de novo

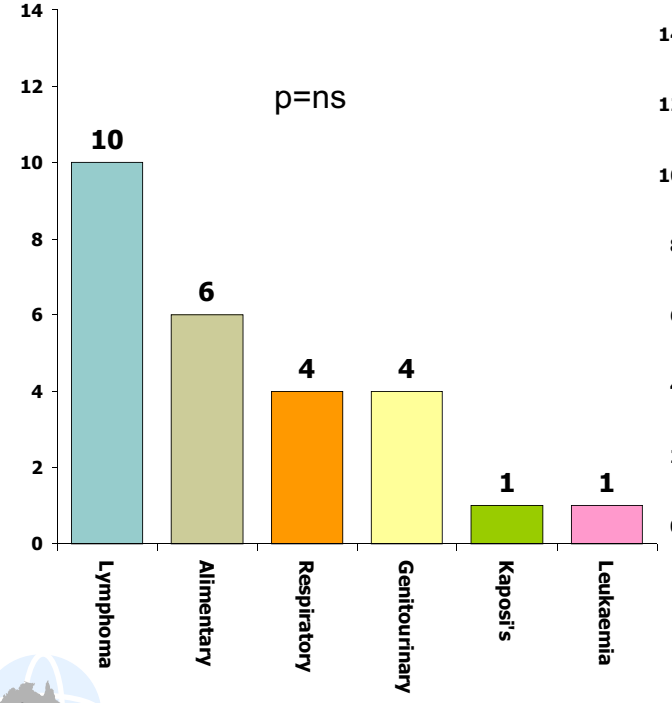


HBV - 11/315 (3%)
7% of all de novo

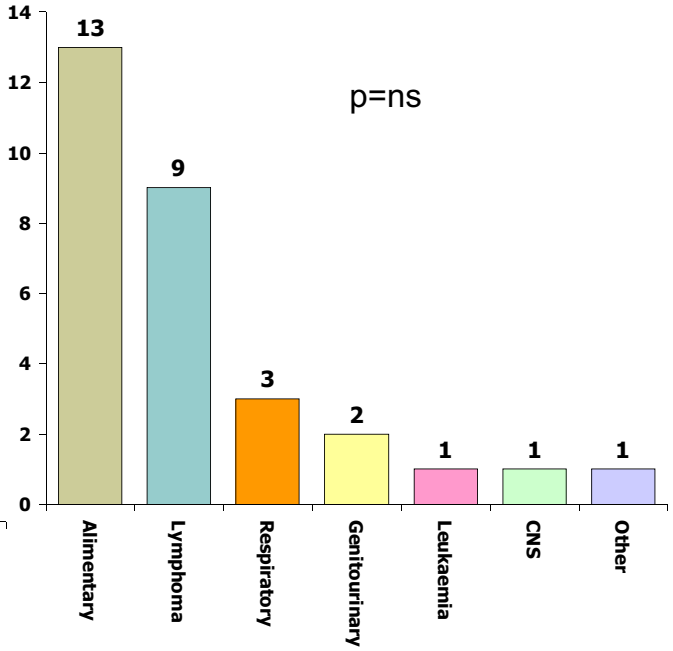


Pre Transplant Liver Disease and De Novo Non Skin Cancer n = 161/2850 (6%)

HCV - 26/565 (5%)
16% of all de novo



Alcohol - 30/410 (7%)
19% of all de novo



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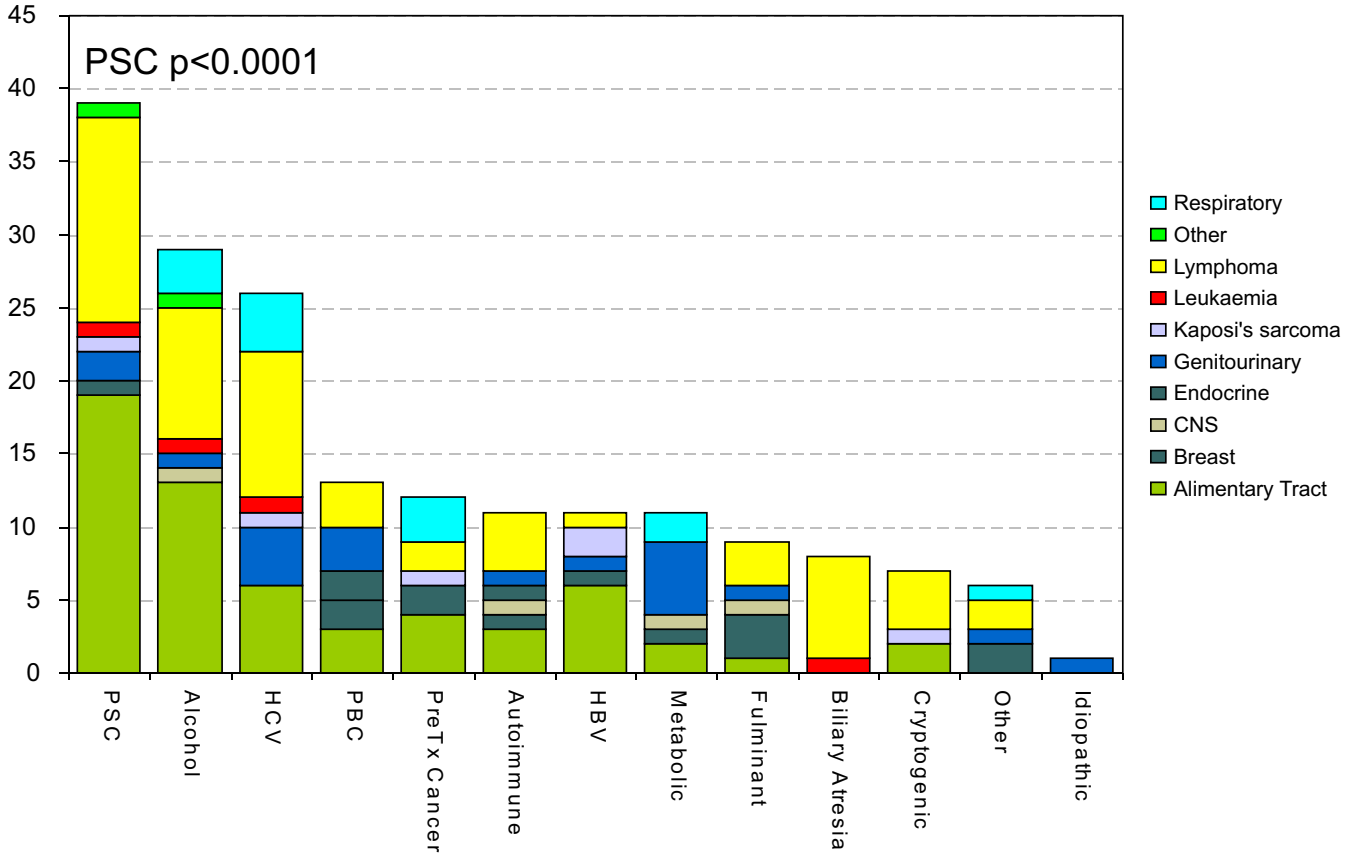
Pre Transplant Liver Disease and De Novo Non Skin Cancer
n = 161/2850 (6%)



Skin Ca Post Liver Transplant
n = 2850

Type of Skin Cancer	Pts	Cancers
BCC	**208**	**616**
SCC	**219**	**879**
Melanoma	**15**	**15**
Total	**348 (12% of all pts)****	**2223**

**** 147 pts had multiple skin cancer types**

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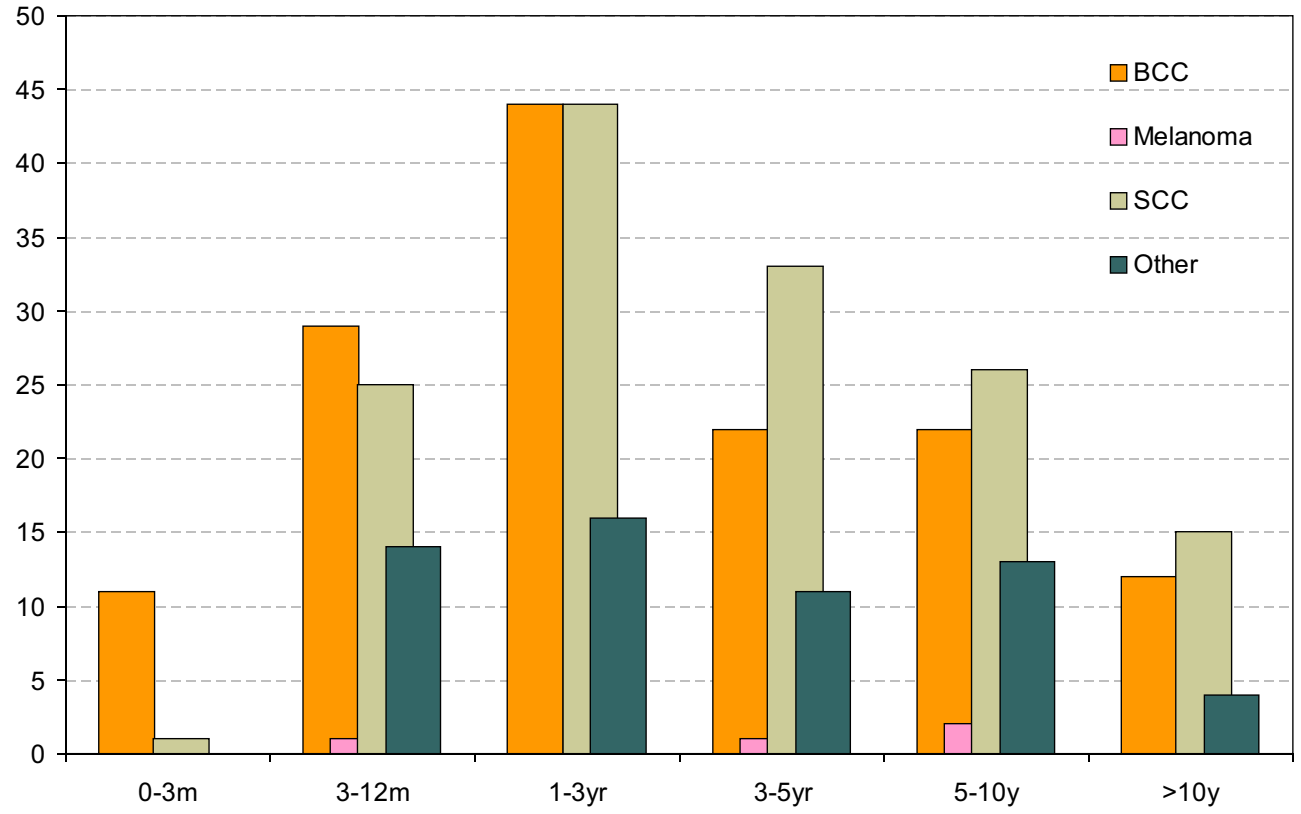
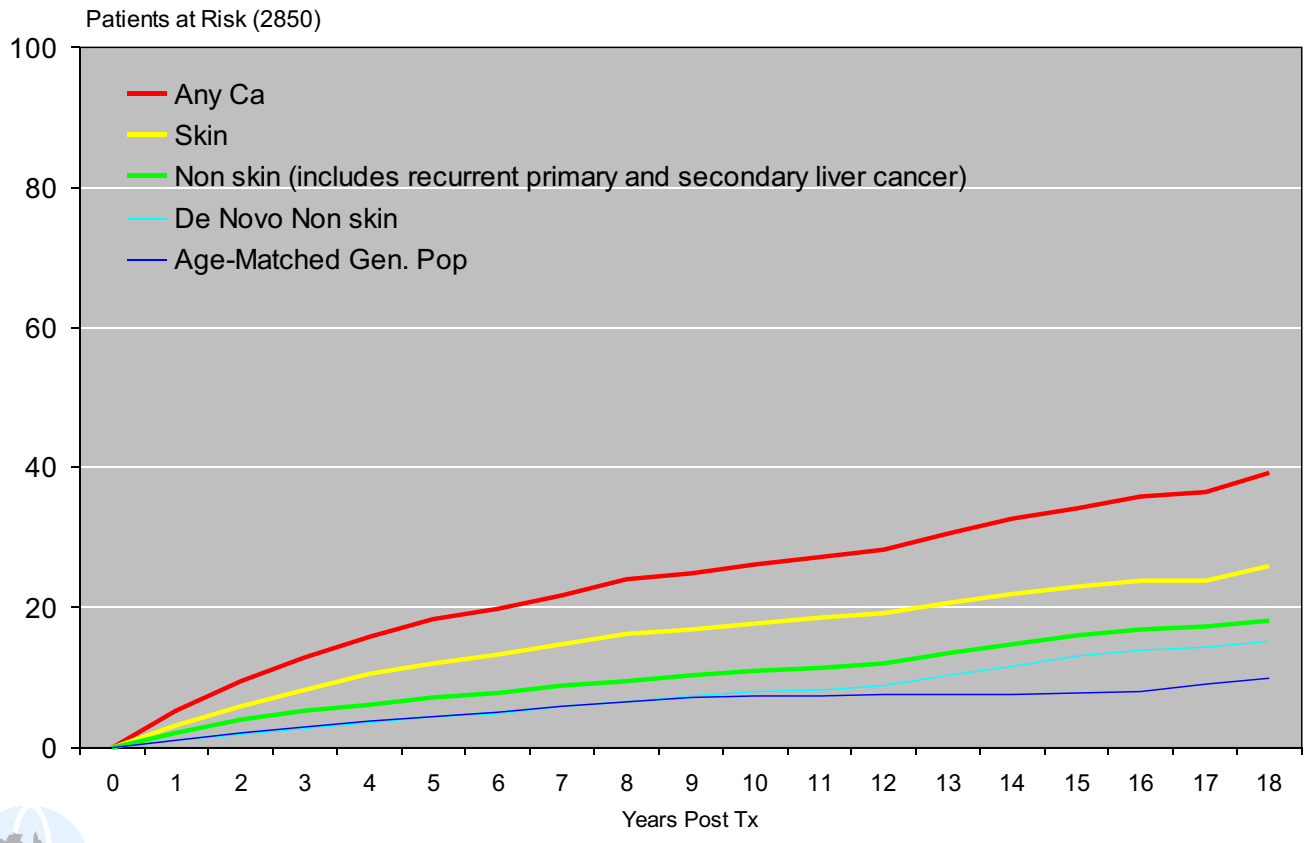
# Time to 1st Skin Cancer Development
n = 2850
348 (12% of all pts)



Cumulative Risk of Diagnosis of Cancer Following Liver Transplant 1985-2007



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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/

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Appendix II

ANZLTR PRIMARY Diagnosis
Metabolic disorders by Age Group

Primary Diagnosis	Age group		Total
	Child	Adult	
-1 Antitrypsin deficiency	30	42	72
Crigler-Najjar	4	1	5
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 *	7	0	7
Primary hyperoxaluria	5	6	11
Tyrosinemia	4	0	4
Urea cycle disorders **	8	3	11
Wilsons disease	7	26	33
Total	71	131	202

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

** OTC deficiency 6; citrullinemia 3; argininosuccinic aciduria 2

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Appendix III

ANZLTR PRIMARY Diagnosis - Other by Age Group

Primary Diagnosis	Age group		Total
	Child	Adult	
Alagille syndrome	22	1	23
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	3	4
Chronic Budd Chiari	1	28	29
Congenital biliary fibrosis	1	1	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	5	5
Non alcoholic fatty liver (NAFLD or NASH)	0	33	33
Polycystic Liver disease	0	11	11
Polycystic liver and kidney disease	0	7	7
Progressive familial intrahepatic cholestasis(PFIC)	13	4	17
Secondary biliary cirrhosis	1	9	10
Secondary biliary cirrhosis - Hepatolithiasis	0	4	4
Secondary biliary cirrhosis - Cystic fibrosis	7	11	18
Other -specify #	3	15	18
Total	62	158	220

\# *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.

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Appendix IV

ANZLTR PRIMARY Diagnosis
Fulminant Hepatic Failure by Age Group

Primary Diagnosis	Age group		Total
	Children	Adult	
Acute - Budd Chiari	0	2	2
Acute - Wilson's	4	11	15
Acute - -1 -AAT	2	0	2
Acute Autoimmune hepatitis	0	6	6
Acute Unknown / unspecified	34	62	96
Acute -Paracetamol	0	11	11
Acute -Other drugs	2	14	16
Acute Herbs / mushrooms	0	4	4
Acute - Hepatitis A	0	2	2
Acute - Hepatitis B	0	39	39
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	0	6	6
Subacute - Drug	0	5	5
Subacute - Unknown / unspecified	3	27	30
Subacute - Hepatitis A	0	2	2
Subacute - Hepatitis B	0	9	9
Total	52	217	269

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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	19
Massive haemorrhagic necrosis	4
Recurrent disease *(ALD, PSC, CAH:AI)*	6
De novo Hep C	2
Biliary Complications	11
Other *(PNC, immune hepatitis, outflow obstruction)*	9

Miscellaneous	
Multiorgan failure	20
Renal Failure	15
Graft vs Host disease	5
Social (accident, suicide,non-compliance, Rx withdrawn)	11
Sudden death (cause unknown)	15
Other (Hyperkalaemia,motor neurone disease diabetes complications, drug reaction, progression FAP)	7

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