

AUSTRALIA & NEW ZEALAND



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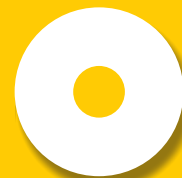
LIVER TRANSPLANT REGISTRY



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

DATA TO 31-12-2017

CD Included
INSIDE BACK COVER



Report PowerPoint
SLIDES

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FUNDING

ANZLTR is funded by the Australian Organ and Tissue Authority.
Additional funding is received from Astellas Pharma Australia Pty Ltd.

CITATION

The suggested citation for this report is as follows:

ANZLT Registry Report 2017
Australia and New Zealand Liver Transplant Registry
Brisbane, QLD, AUSTRALIA
Editors: S.V. Lynch, G.A. Balderson

STATISTICAL METHODS

Kaplan-Meier survival curves have been produced using IBM SPSS® for Windows™ Release 23.0.

ACKNOWLEDGMENT

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

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All queries to: Dr Deborah Verran

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Preface

We are pleased to present the 29th Report of the Australia and New Zealand Liver Transplant Registry (ANZLTR). This report contains data to the 31st December 2017 and analyses the cumulative data since the establishment of the first liver transplantation unit in Australia or New Zealand in 1985.

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

Donor data have been supplied by the Australia and New Zealand Organ Donor Registry and we thank them for their collaboration.

The Editors would also like to thank the staff of all the liver transplant units who contribute their data by direct entry into the ANZLTR database. A full list of the units and their contact information can be found in Appendix I. In particular we are grateful to the efforts of Pamela Dilworth, Program Manager and Marie Mulhearn for their continuing contribution to the maintenance of the Cancer Registry which is based at the Royal Prince Alfred Hospital, Sydney and who, together with Dr Deborah Verran, prepare the Cancer Report.

We are grateful to the Australian Government, through the Australian Organ and Tissue Authority, for their ongoing financial support. We would also like to thank Astellas Pharma Australia Pty Ltd for additional financial support.

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 **www3.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 2017, 5890 orthotopic liver transplants (OLT) were performed in Australia and New Zealand on 5450* patients, 4515 adult patients [83%] and 935 children (<16 years) [17%]. (*Three patients had their primary transplant overseas, one adult and two children). The median age of all recipients was 49.2 years. The ages ranged from 24 days to 73.0 years. There is a significant difference in gender distribution between children (M=48%) and adults (M=66%).
6. Three hundred and thirteen new patients were transplanted in 2017 compared with 336 in 2016.
7. The trend to increasing age of adult recipients in recent years continued and the overall adult median age is now 52.2 years. The median age of new adult recipients in 2015 -17 was 56.9 years.
- 8-9. In 2017, there was a decrease in the number of transplants with 36 less performed [337 vs 373]. Split grafts continue to make a significant contribution to the total number of paediatric transplants performed providing 28 of 48 [58%] of deceased donor grafts in 2017 and 325 of 978 [30.5%] overall. In children, other reduced size grafts have been used in 425 [40%] cases including 85 living donor grafts. One child has been treated with liver cell implantation. Of adult patients, 338 have received reduced size grafts - 321 split liver grafts (including one as auxiliary graft), 32 other reduced size grafts (one as auxiliary graft) and 16 living donor grafts. Four domino transplants of a whole liver have 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 18.2% of recipients and chronic hepatitis B [CVH : HBV] in 4.6%. Full details of specific diagnoses categories by age group are listed in the Appendices for – Metabolic disorders (Appendix II), Other diseases (Appendix III) and Fulminant Hepatic Failure (Appendix IV).
- 12-15. The number of patients transplanted with non-alcoholic fatty liver disease [NAFLD/NASH] as the primary diagnosis was 24 [9%] of new patients transplanted in 2017 bringing the total to 180. The proportion of adult patients transplanted with a primary diagnosis of chronic viral Hepatitis B, C or B/C/D fell in 2017 compared with the previous eras but the number of patients with a primary diagnosis of hepatocellular carcinoma [HCC] increased and accounted for 23% in 2017. The majority of these patients have a secondary diagnosis of CVH: HCV or HBV. 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 2017 was 37%.
16. Overall one year patient survival of all patients is 90% at one year, 86% at 5 years and 75% at 10 years. Children have a significantly better survival rate than adults with an actuarial survival of 73% at 30 years post-transplant.
17. Whilst older children had superior early survival than infants and babies, long term survival is similar. Older adult recipients had poorer longer term outcomes.
- 18-19. Patient survival in later cohorts show continued improvement in outcome for the first 10 years compared with earlier cohorts. This is seen in both children and adults. One year patient survival in 2015-17 cohort was 95% for all patients [98% for children, 95% for adults].
20. In both children and adults, there are worse early outcomes in patients receiving a deceased donor reduced size graft as their primary graft compared with split liver graft or whole liver grafts. Split liver grafts and whole livers have similar early outcomes in both children and adults.



Summary

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21. Smaller children and babies weighing < 8 kg at the time of transplant had inferior early survival compared to heavier children but similar long term results.
22. Adult patients transplanted for biliary atresia or hepatitis virus co-infections had the best longer term survival while those whose primary disease was primary biliary cirrhosis or primary sclerosing cholangitis or Hepatitis C have significantly lower long term survival rates.
23. In children, patient survival was similar for all disease groups though lower in patients whose primary disease was malignancy. There were no differences in survival between adults and children transplanted for fulminant hepatic failure [acute and sub-acute] with overall five year survival of 77%.
24. Recent cohorts of adult patients with a primary diagnosis of hepatitis B continue to show a significantly improved survival. Adult patients with hepatitis C as primary disease show some improvement in survival in more recent cohorts. Patients transplanted for malignancy continue to have a poor outcome but some improvement in longer term outcome is seen in patients transplanted since 2000.
- 25-26. Overall graft survival was 86% at one year and 78% at five years with significantly better graft survival longer term in children. Graft survival was significantly worse in second grafts in both children and adults. Third grafts in adults have better outcomes than in children.
27. Overall split liver grafts have similar graft survival to whole liver grafts. Reduced grafts have lower graft survival in the early post-transplant years in both children and adults.
28. Graft survival has increased significantly over time for all deceased donor grafts.
- 29-30. Vascular complications and rejection were the commonest indications for retransplantation. Fifteen percent of retransplants were due to poor early graft function. Re-transplantation for recurrent disease was most prevalent in adults [10% PSC, PBC, AIH and 9% HBV, HCV].
- 31-34. Sepsis is the most frequent cause of death in both adults and children. Full details of miscellaneous and other graft failure deaths are listed in Appendix V. Twenty-eight percent of all deaths occurred within six months of transplant. Deaths from early graft failure were due to poor or no early graft function. By one year malignancy and graft failure from recurrent disease or chronic rejection cause most deaths. Deaths due to de novo malignancy and chronic rejection are increasing with longer survival times.
35. There was an decrease in the number of cadaveric donors in 2017 to 304 and fewer liver transplant grafts with 332 grafts transplanted from deceased donors. The number of livers split to produce two transplantable grafts was 28 in 2017. Eleven liver grafts donated after cardiac death were transplanted. The number of people on the waiting list at 31 December 2017 was lower than the number on the waiting list at 31 December 2016.
36. Donor age has increased significantly in recent years. Long term graft survival trends lower in several older donor age groups.
37. One hundred and five patients [85 children, 20 adults] have now received a living donor graft with five performed in 2017. In 98 patients the living donor graft was a primary graft, in six as a second and one as a third graft. The median age of the donors was 33.8 years with a range of 18.3 to 54.5 years. Four adult grafts were domino whole liver graft.





Summary

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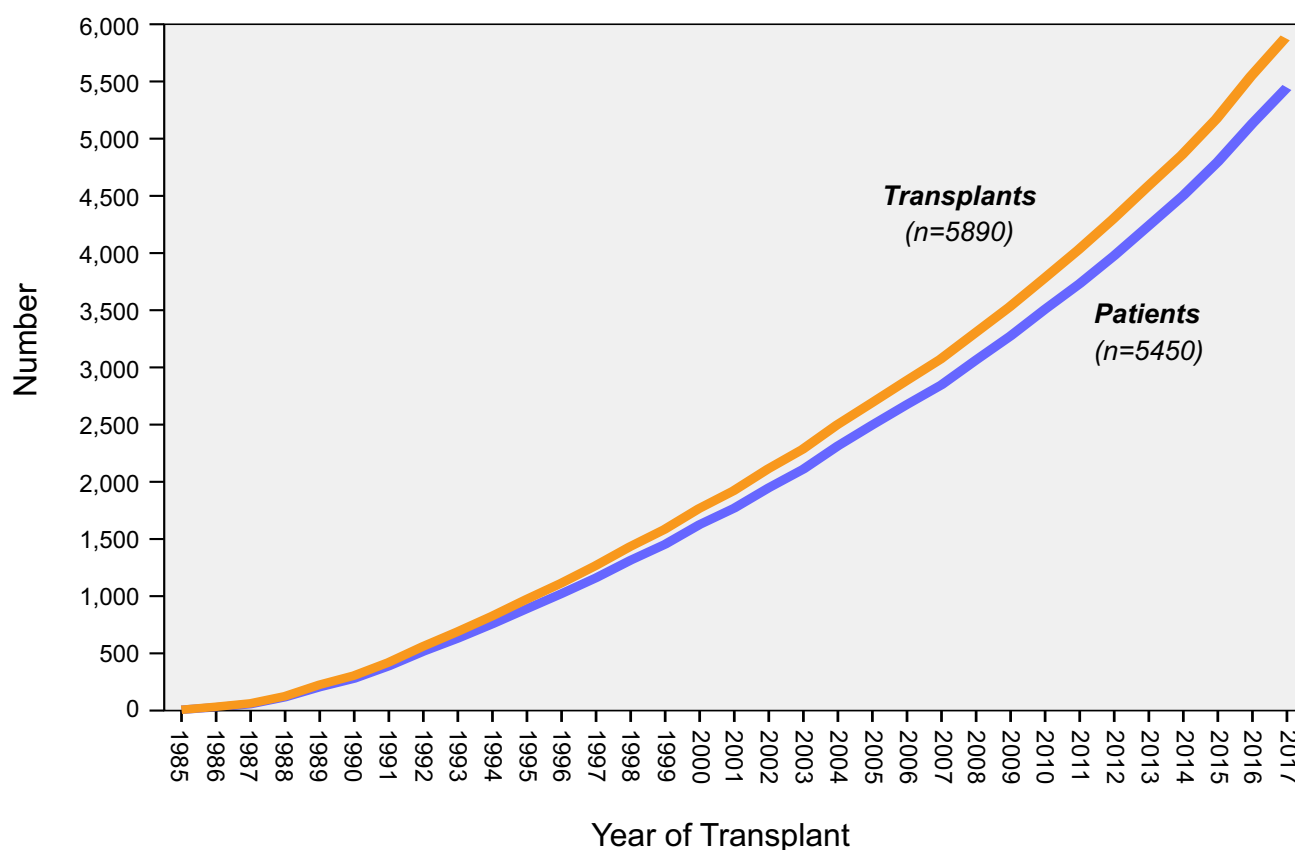
38. Waiting list activity for 2017 showed fewer patients listed for transplantation and an increase with 167 remaining on the waiting list at 31 December 2017. Patient delistings due to death, becoming too ill or tumour [HCC] progression accounted for 5% of all delistings. Three hundred and thirty-seven patients were transplanted [58%]. Thirty-six patients were listed as urgent in 2017 [17 with initial listing as Category 1 and 19 Category 2]. Fifteen [88%] of Category 1 and 19 [100%] of Category 2 patients had a positive outcome.
- 39-40. Median waiting times varied across the blood groups. Blood group A & O patients had similar waiting times to transplant but O patients was longest overall.
41. Cancer in liver transplant recipients are analysed from two perspectives. Firstly, those who had a liver cancer diagnosis at the time of transplantation (as primary, secondary or incidental) and secondly those who developed a cancer post transplantation (de novo skin and de novo non - skin cancer). Overall 1256 patients (23%) had a liver cancer at the time of transplantation with HCC being the most common (90%). Five hundred and eight patients (9%) were transplanted for primary liver cancer, 751 patients (14%) had liver cancer as a secondary or incidental diagnosis, of which 167 (23%) were undiagnosed prior to transplantation. Three of 1256 patients had both primary and secondary liver cancers and 3 had multiple secondary or incidental liver cancers.
- Post transplant 165 (12%) of pretransplant cancers recurred and 150 (11% of those with cancer at transplantation) died as a result of recurrence.
- 42-43. Actuarial patient survival was 52% at 20 years in patients with primary liver cancer. Patients with a diagnosis of HCC or hepatoblastoma had the best survival rate [58% and 61%]. Those with cholangiocarcinoma had significantly poorer survival.
- 44-47. In patients with liver cancer as a secondary diagnosis, 20 year patient survival was 40%. Eighty-three [12% of patients] died from recurrence of their cancer.
- Overall patients with a diagnosis of pretransplant malignancy had worse survival than patients with benign diseases.
- Incidence of liver cancer at time of transplantation continues to increase, climbing from 304 to 951 over the last decade.
- 47-53. Four hundred and seventy-one de novo non-skin types of cancer developed in 439 (8%) of patients. Thirty-two patients developed more than one de novo non-skin cancer.
- Adult recipient cancer is being more commonly diagnosed from 10 years post transplantation.
- The three most common categories of de novo non-skin cancer were cancers of the alimentary tract 165 (38%), lymphoma 114 (4%) and genitourinary 67 (15%).
- Incidence of de novo non-skin malignancy is greatest in those with underlying hepatitis C, primary sclerosing cholangitis and alcoholic cirrhosis ($p < 0.0001$).
- 54-55. Eight hundred and forty-four (16%) developed a first skin cancer, with a peak of 1-3 years after transplantation, with 400 going on to develop multiple types of skin cancer. Forty-eight patients developed 49 melanomas.



Section 1

Demographic Data

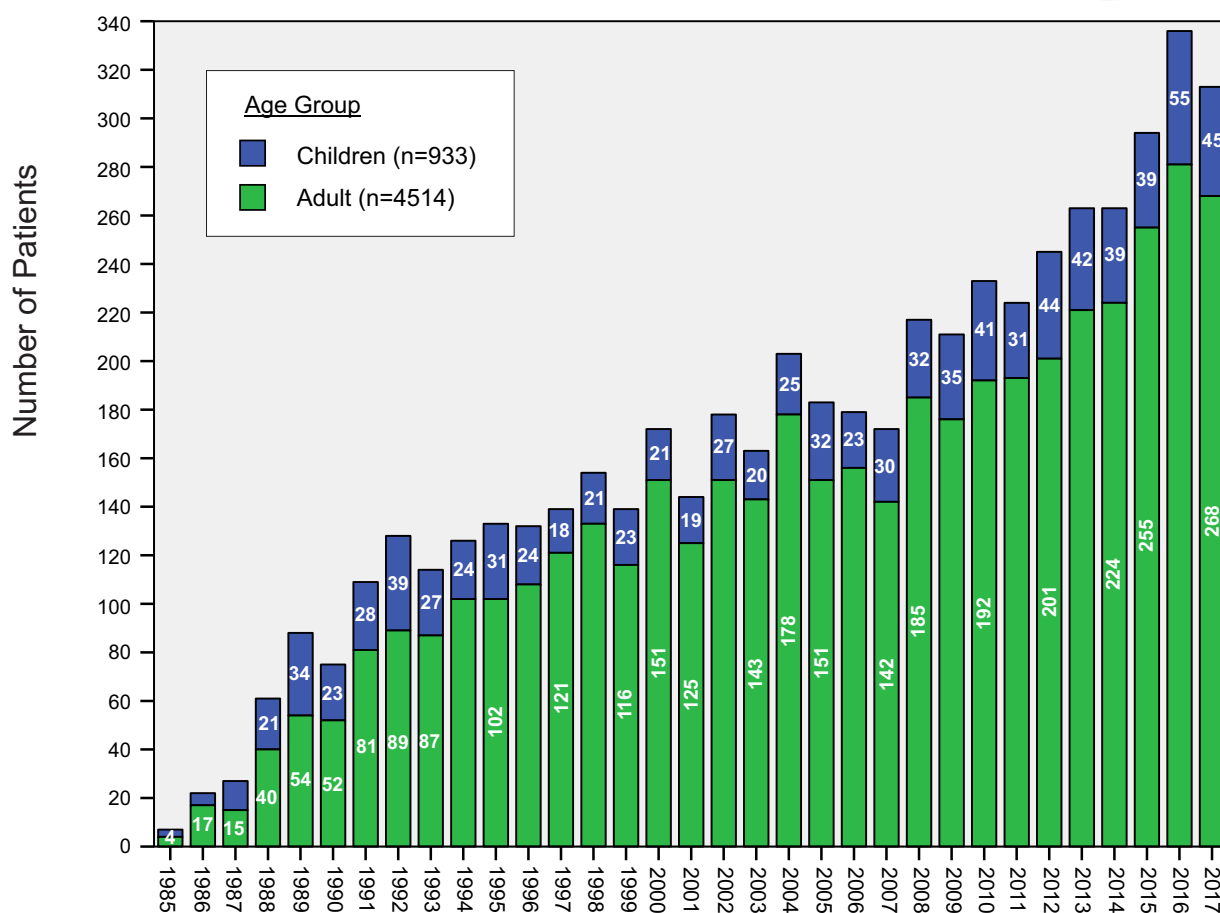




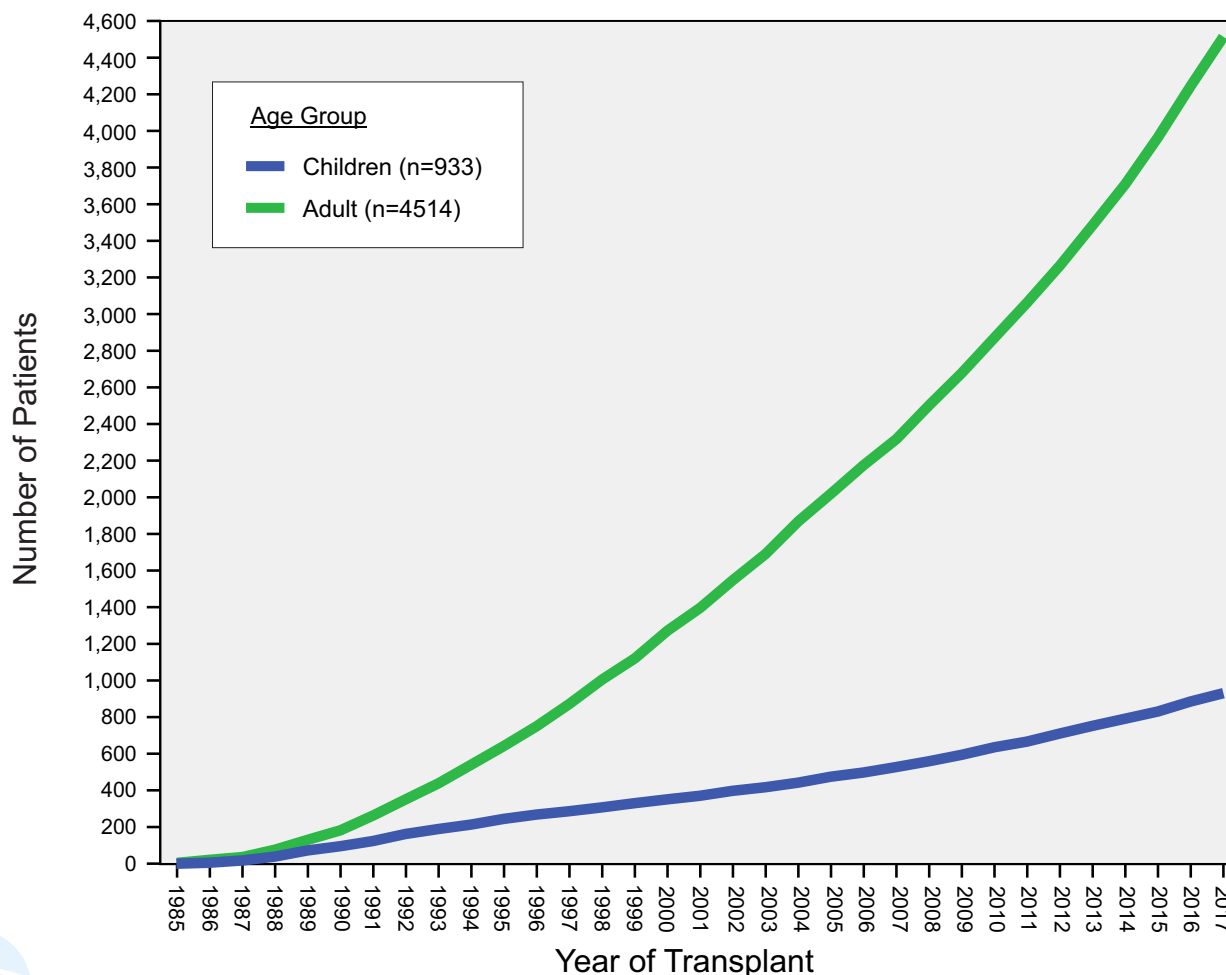
Summary Statistics by Age and Gender

ALL PATIENTS TRANSPLANTED

	Children [<16y]	Adults	Total
Patients	935	4515	5450
Age			
<i>Mean ± SD</i>	4.5 ± 4.5y	49.8 ± 11.7y	42.0 ± 20.2y
<i>Median</i>	2.4y	52.2y	49.2y
<i>Range</i>	24d -15.9y	16.0 - 73.1y	24d - 73.0y
Gender			
<i>Female</i>	482 (52%)	1524 (34%)	2006 (37%)
<i>Male</i>	453 (48%)	2991 (66%)	3444 (63%)
Surviving	767 (82%)	3161 (70%)	3928 (72%)

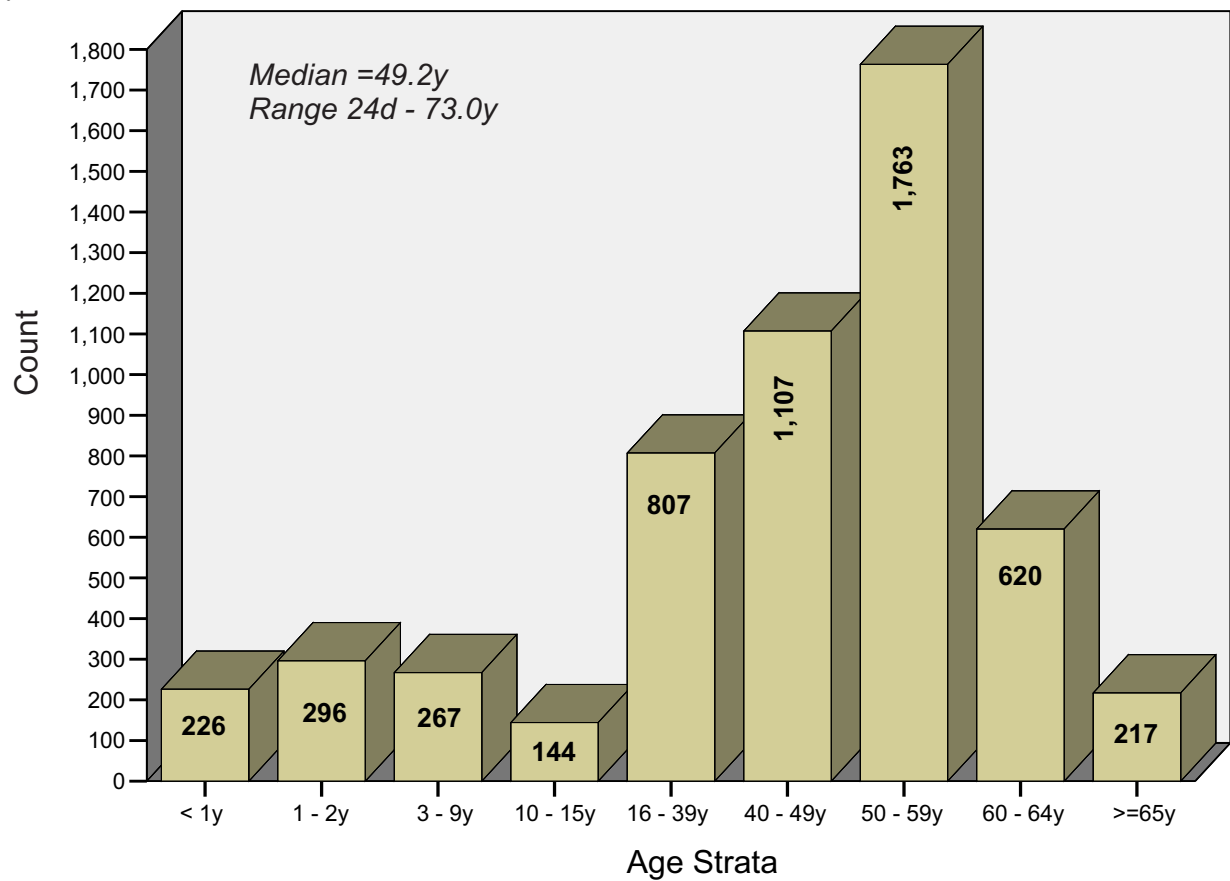


Cumulative Number of New Patients Transplanted

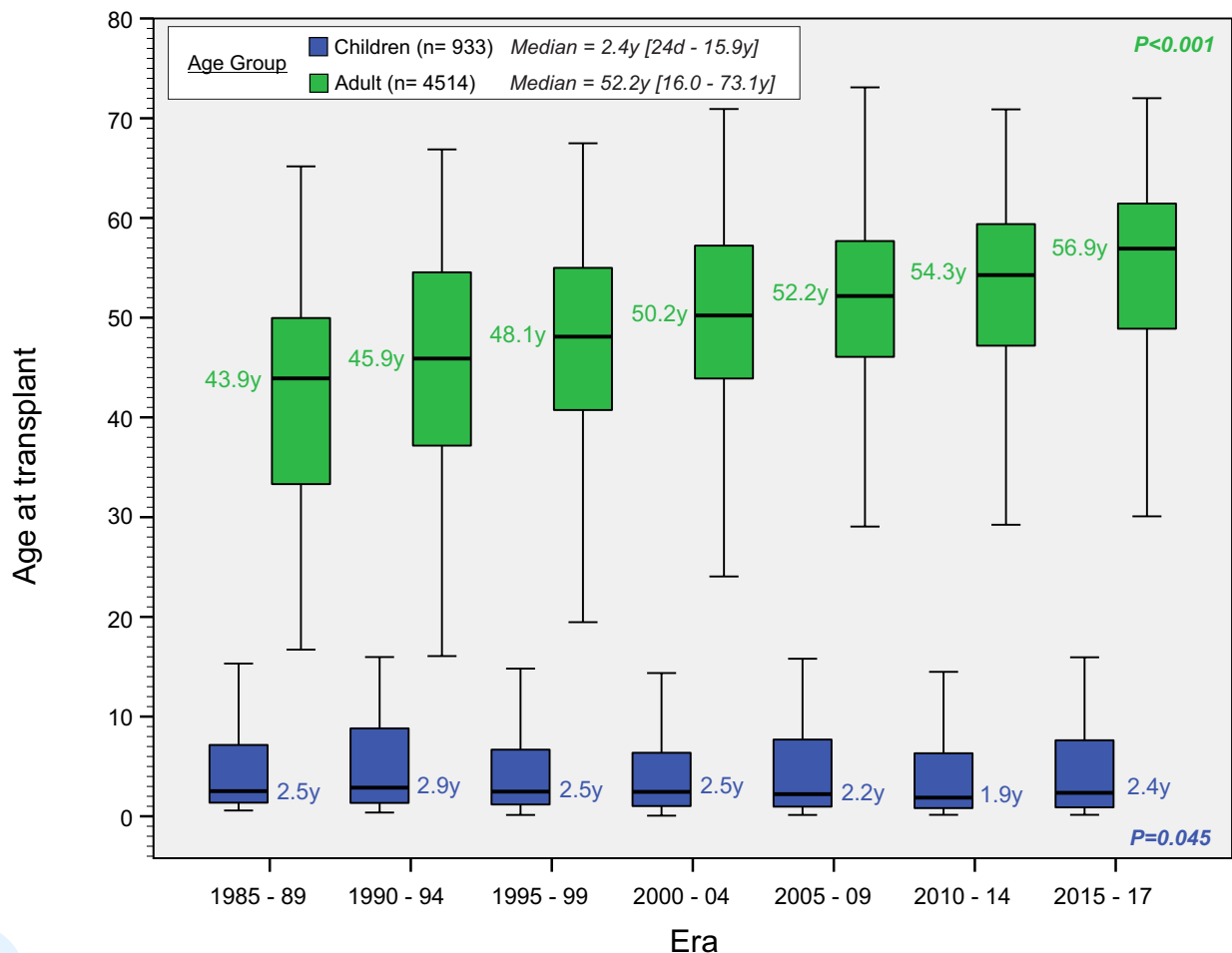


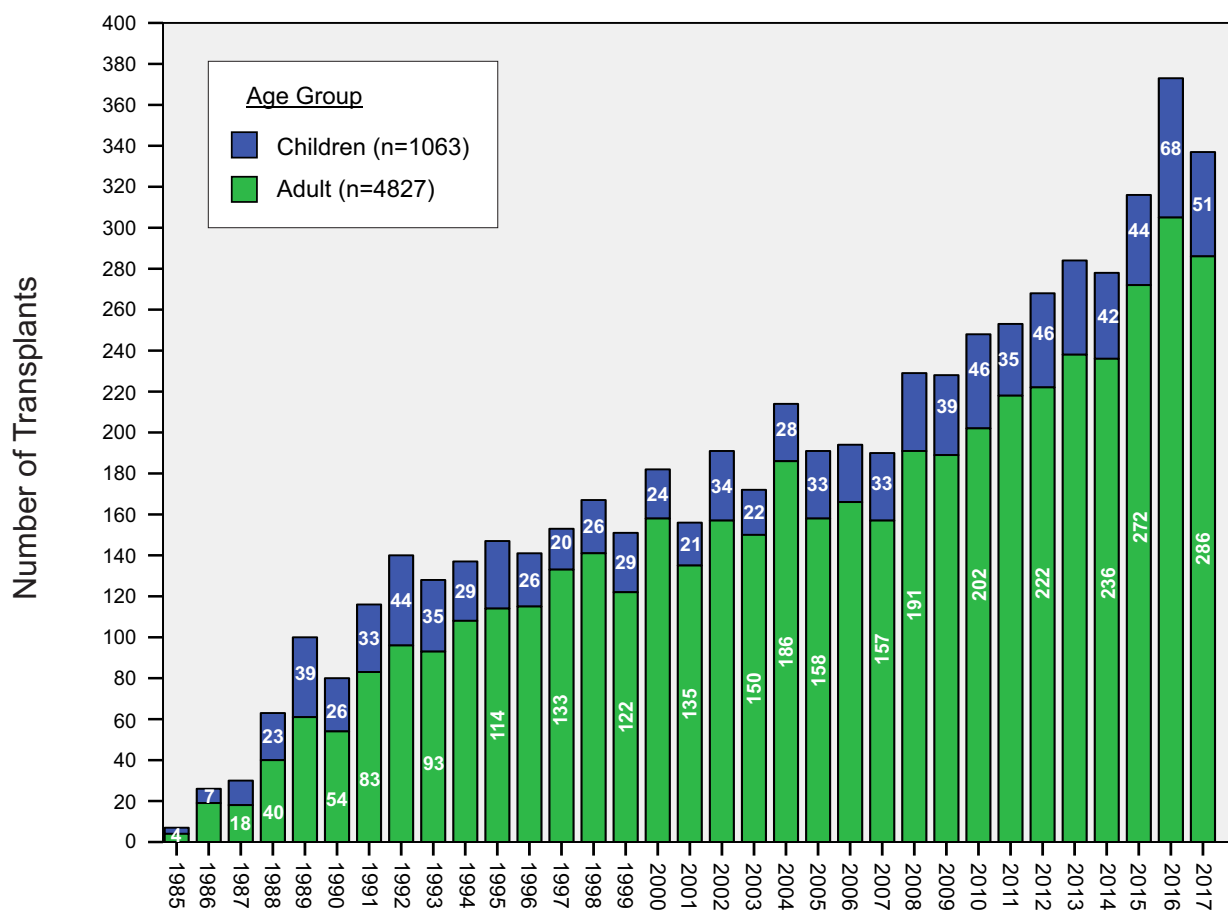
Number of Recipients by Age at Primary Transplant

N=5447

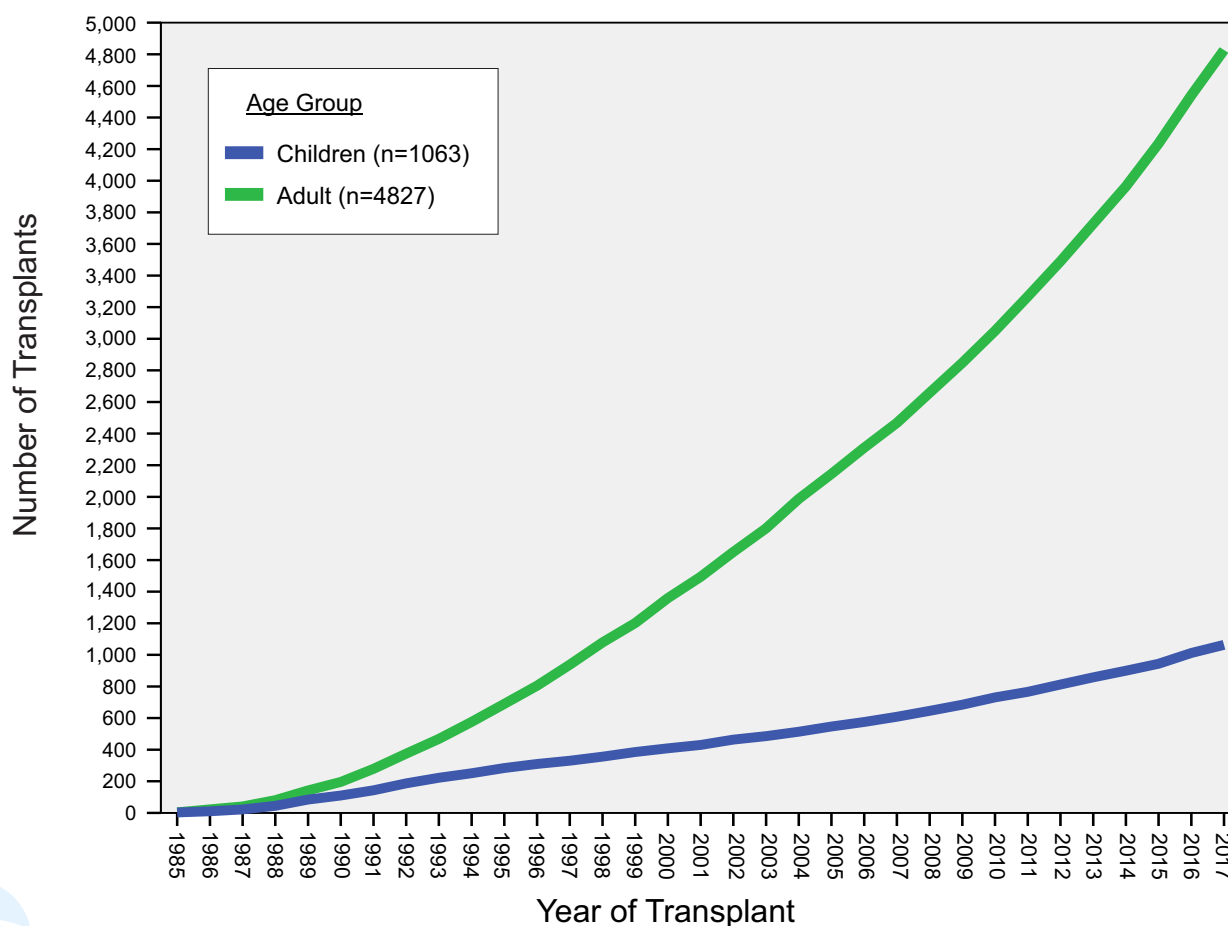


Age at Primary Transplant by Era





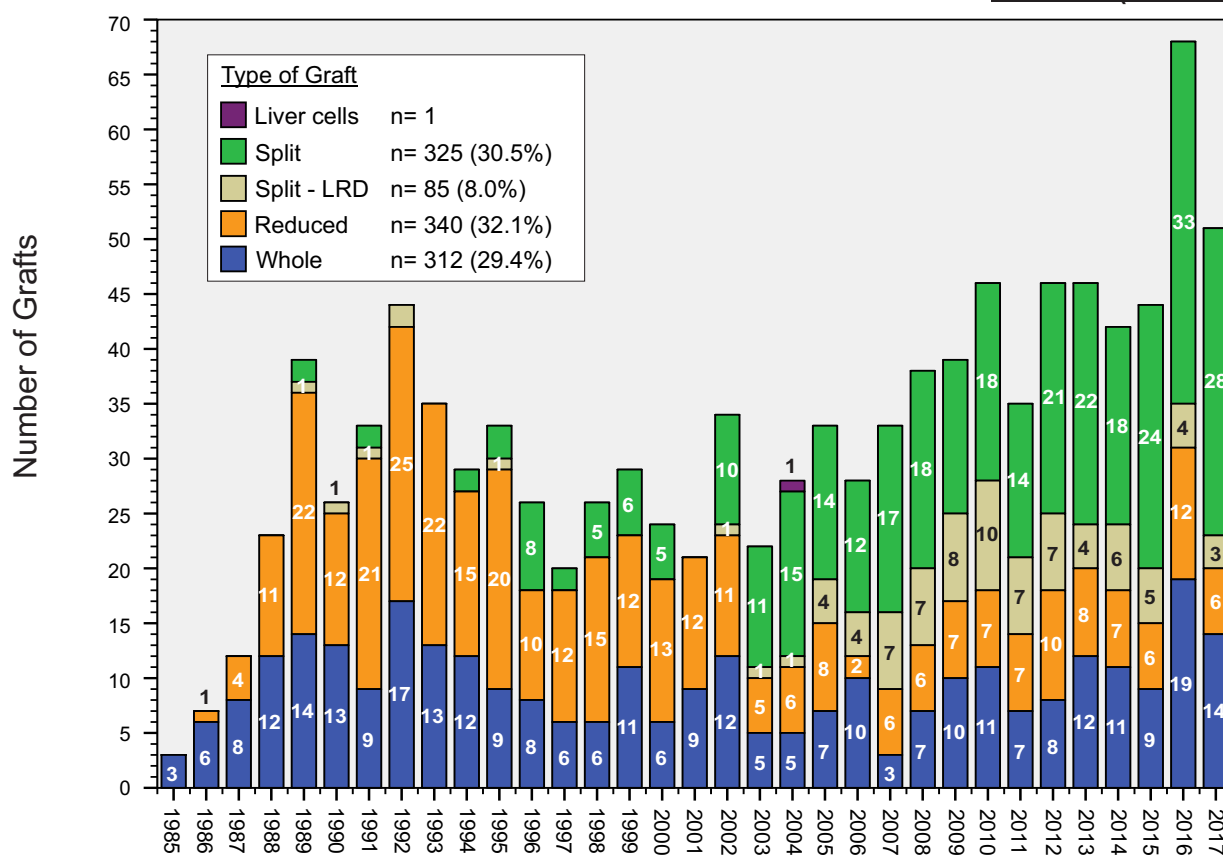
Cumulative Number of Transplants



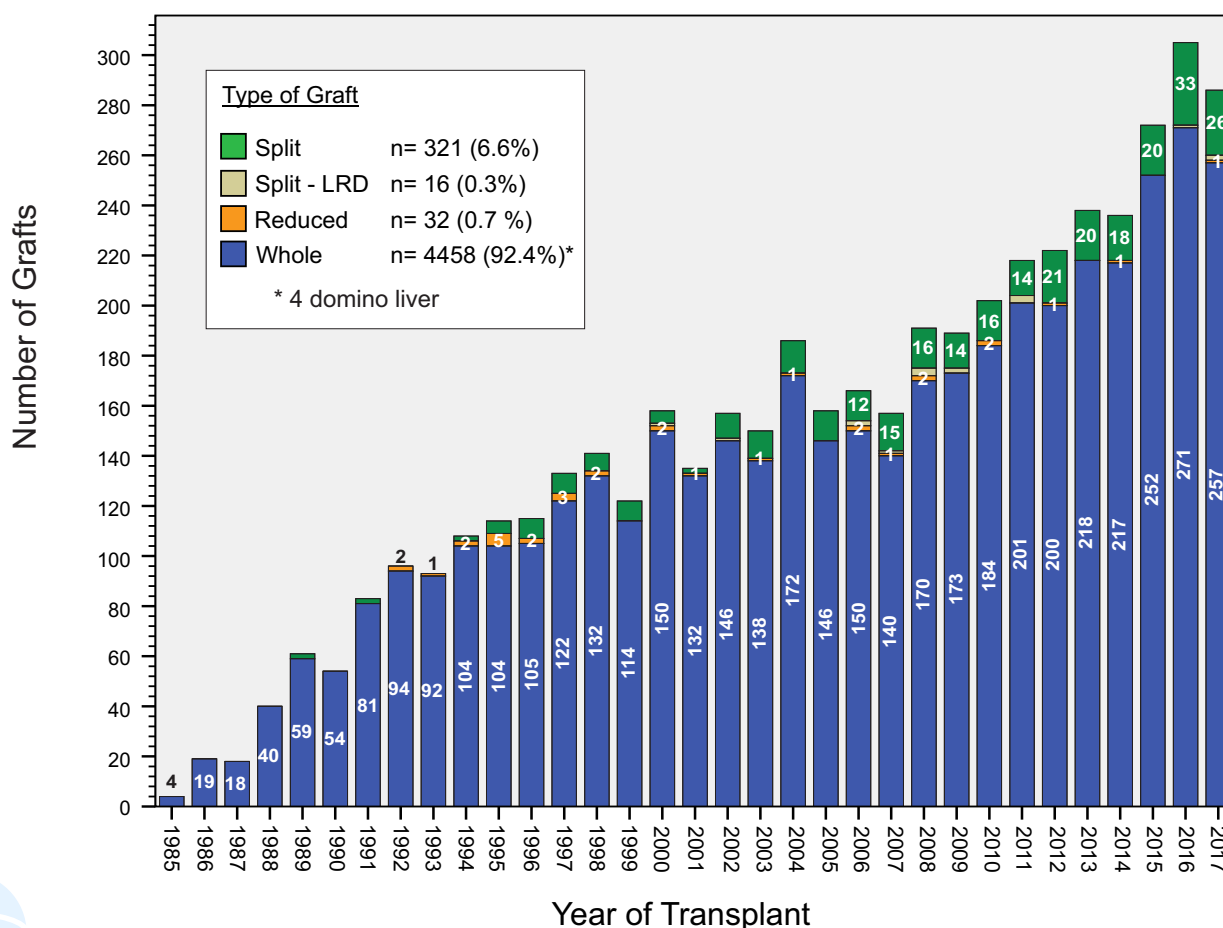
Type of Graft by Year

Split vs Reduced vs Whole

Children (N = 1063)



Adults (N = 4827)





Section 2

Primary Diagnosis





CVH : B/C/D
1%

CVH : HCV
18.2%

CVH : HBV
4.6%

CAH : AI
3.2%

OTH
6.5%

NAFLD
3.3%

FHF
9.2%

Malignancy
10.3%

BA
10%

MET
6.1%

ALD
10.6%

CC
3.9%

PBC
4.5%

PSC
8.7%

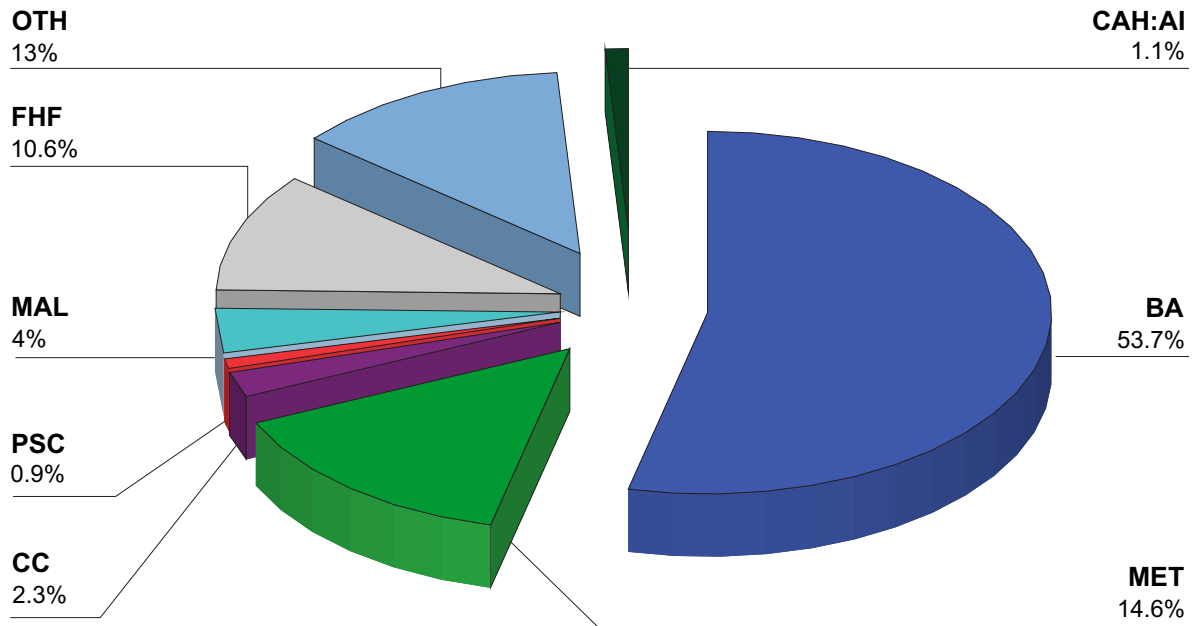
Diagnosis Group

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*
NAFLD	- Non-alcoholic fatty liver disease
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

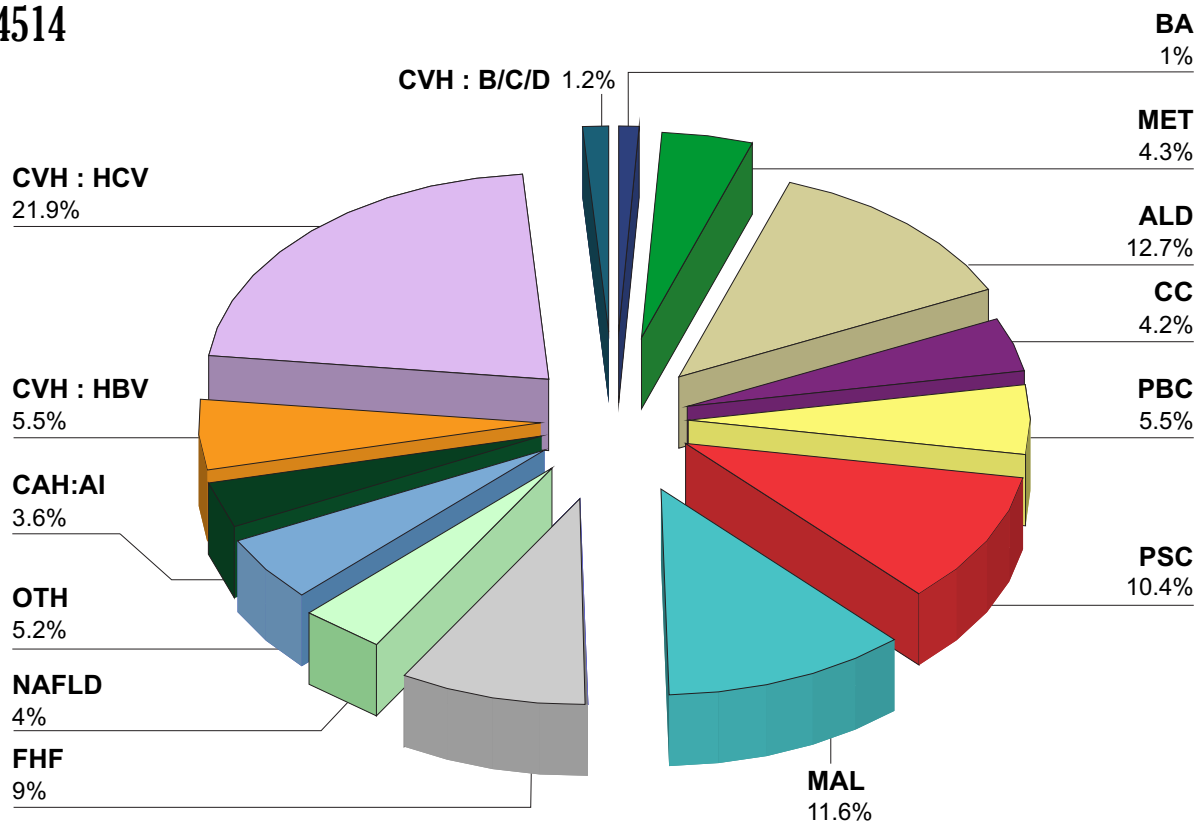
Primary Diseases of Children

N = 933



Primary Diseases of Adult Recipients

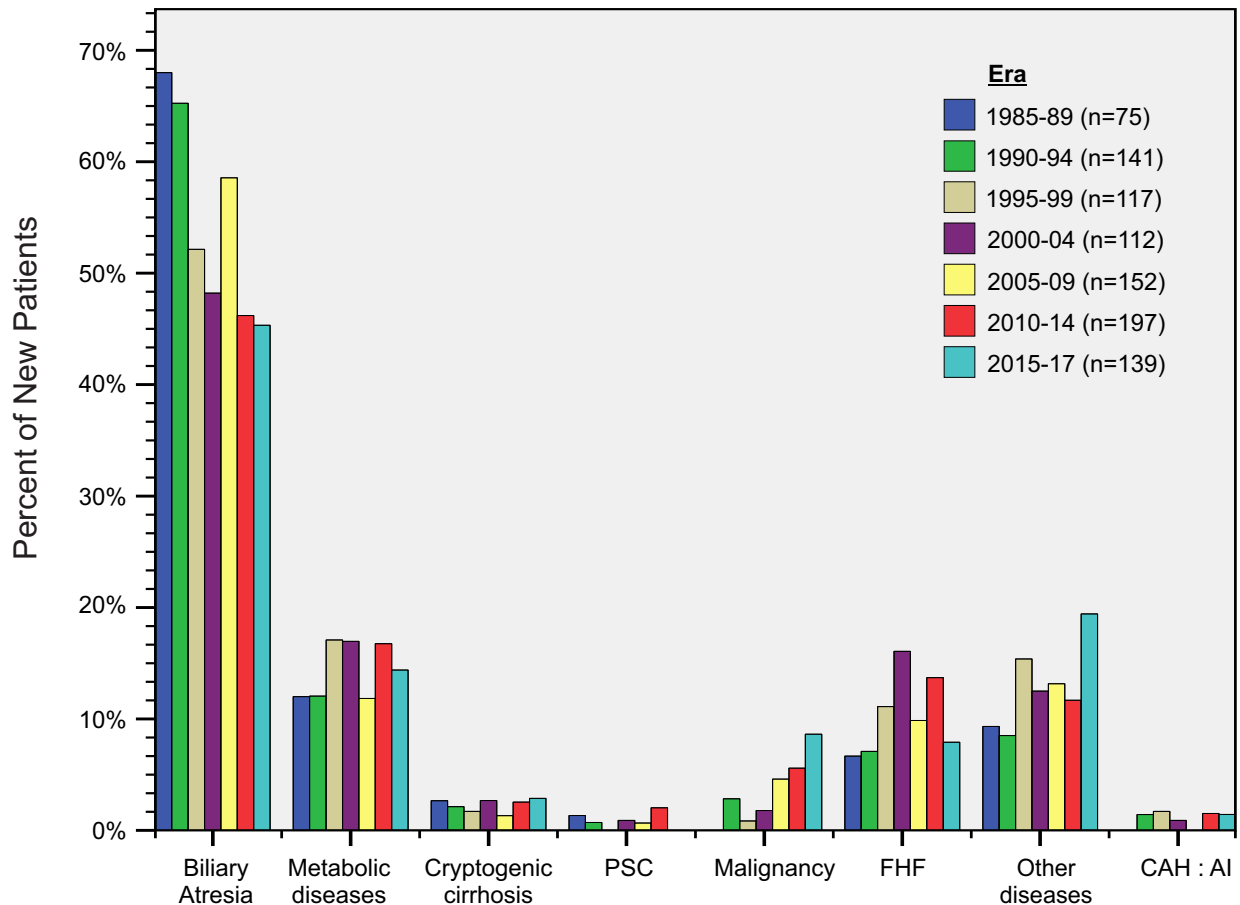
N = 4514



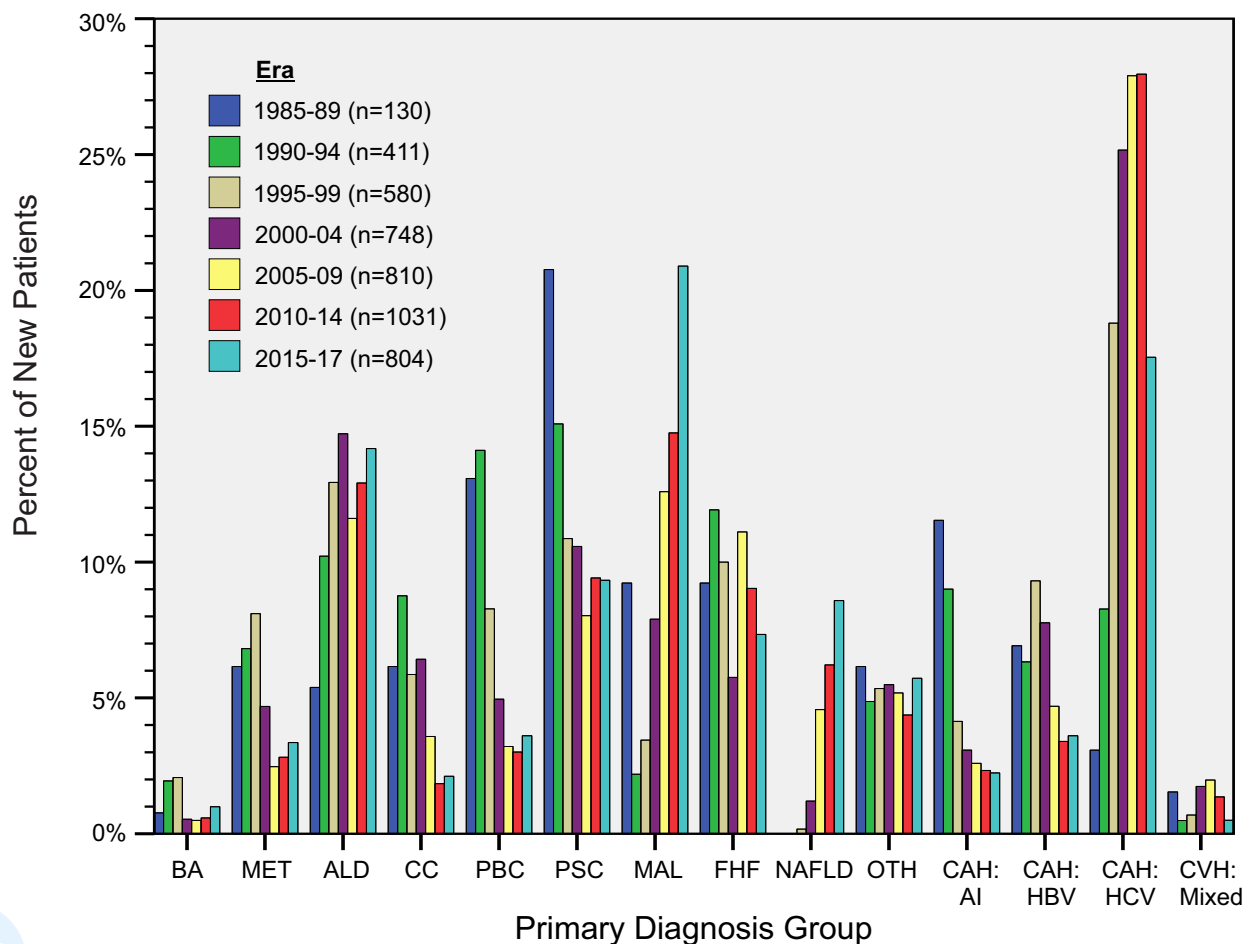
Diagnosis Group

BA	- Biliary atresia	FHF	- Fulminant hepatic failure
MET	- Metabolic diseases	NAFLD	- Non-alcoholic fatty liver disease
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
MAL	- Malignancy	CVH : B/C/D	- Chronic viral hepatitis B / C / D

Children (N=933)



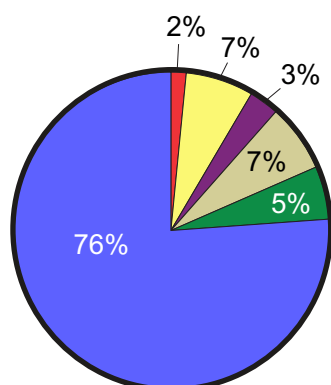
Adults (N = 4514)





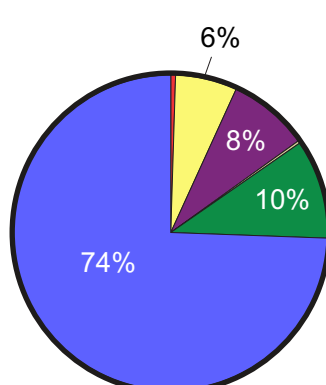
1985 - 89

(n=130)



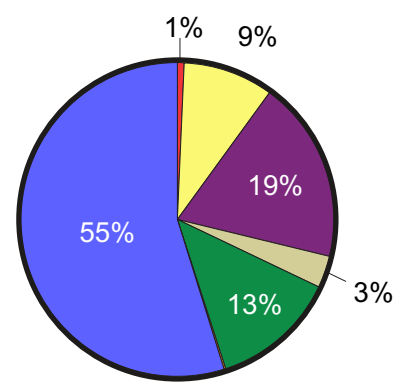
1990 - 94

(n=411)



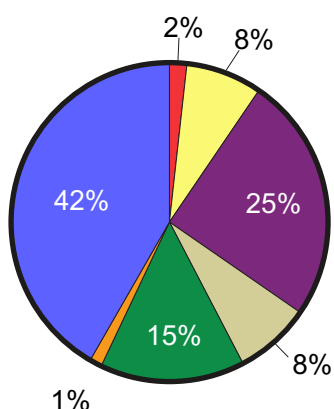
1995 - 99

(n=580)



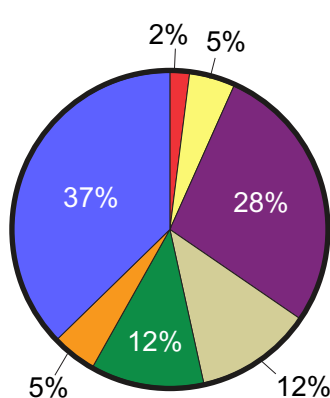
2000 - 04

(n=748)



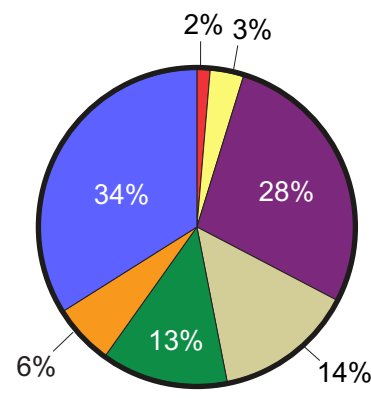
2005 - 09

(n=810)



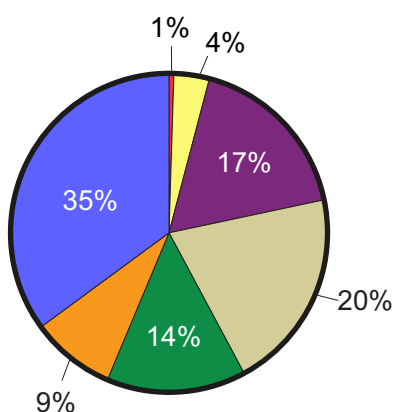
2010 - 14

(n=1031)

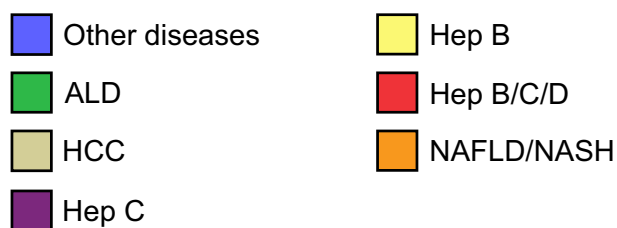


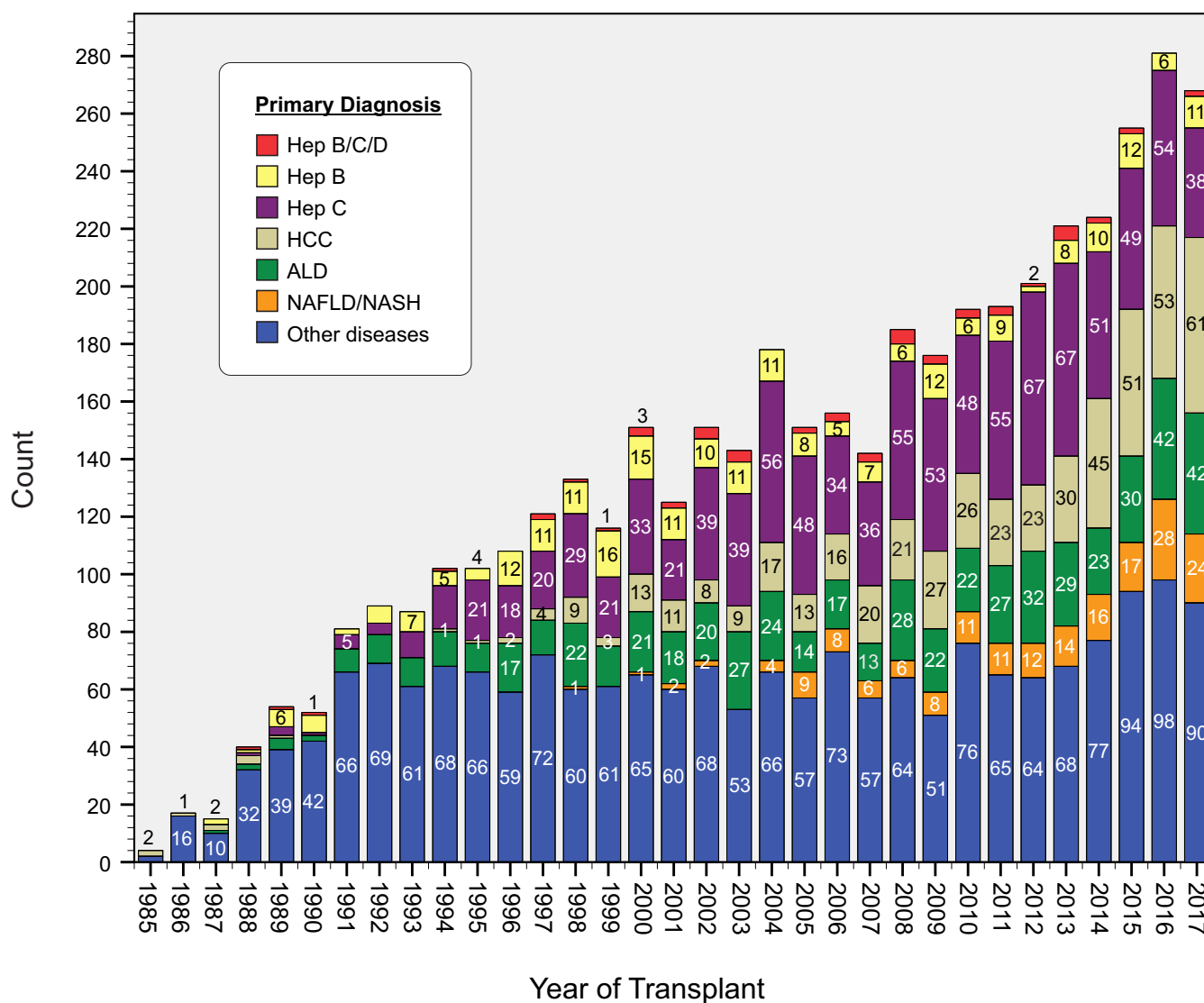
2015 - 2017

(n=804)



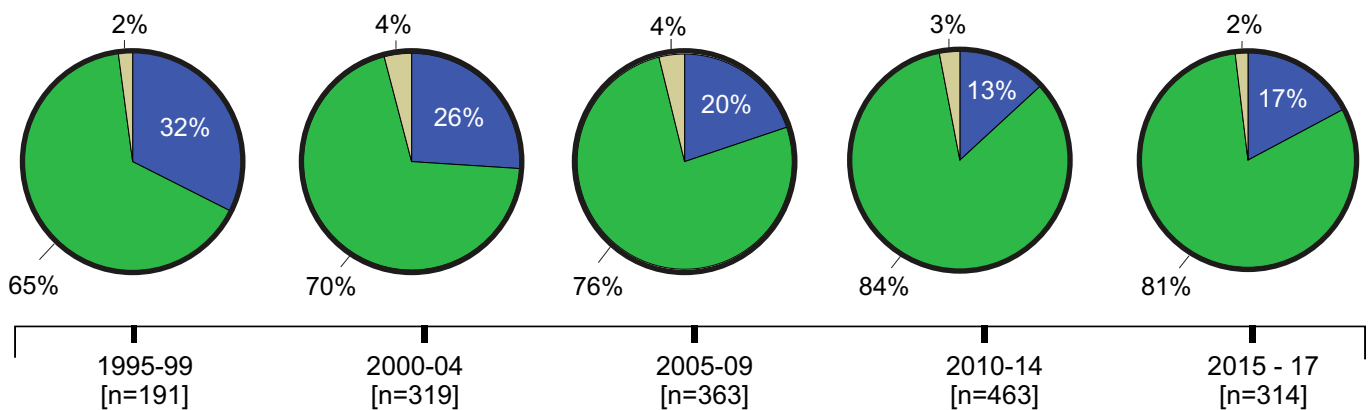
Adult Diagnosis



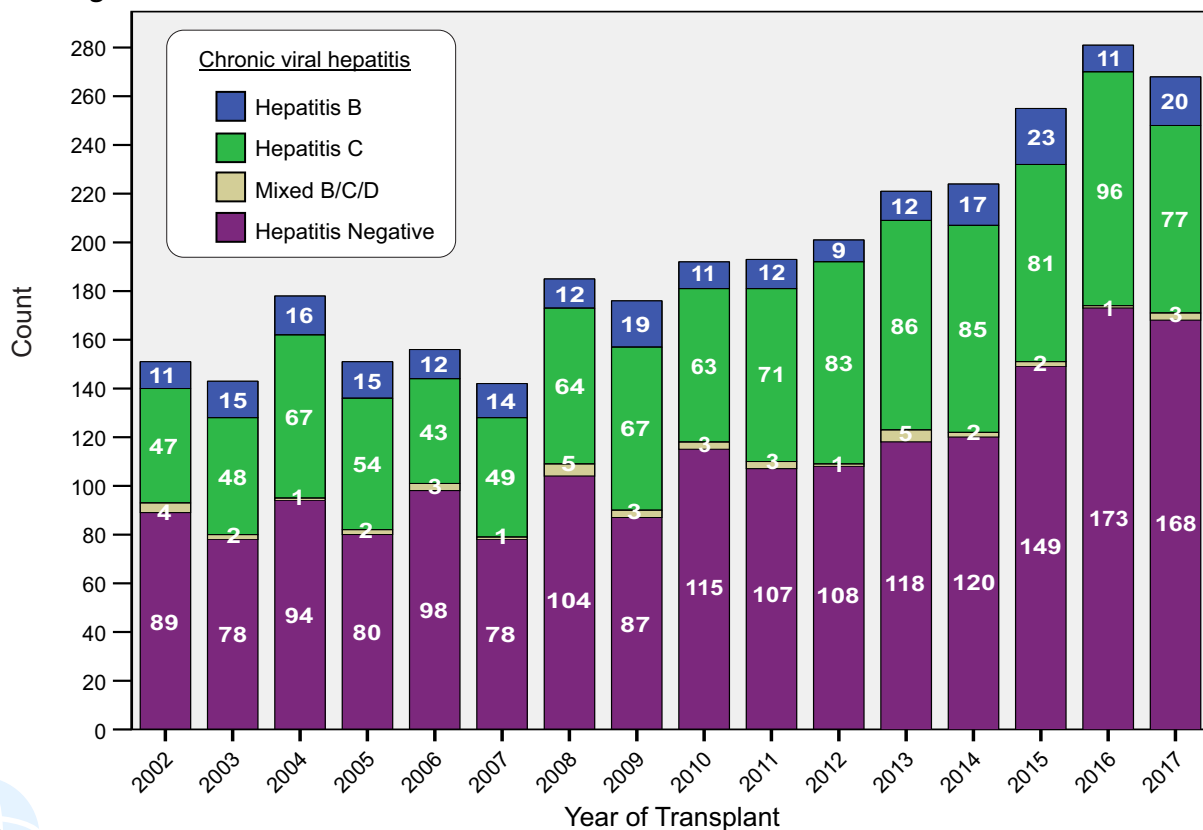


			Secondary / Tertiary diagnosis					
Primary Diagnosis		n =	Hepatitis C	Hepatitis B	Hepatitis B,C	HCC	NAFLD	ALD
	Hepatitis C	990		7		319	13	273
	Hepatitis B	249	2			105	3	8
	Hepatitis BD/BC/BCD	55				10		8
	HCC + cirrhosis	496	269	119	11		22	122
	ALD	575	32	3		69	18	
	NAFLD	180	1	2		44		16
	Other	1969	18	8		65	7	28
TOTAL		4514						

Type of Chronic Viral Hepatitis in Adult Patients by Era



Hepatitis Diagnosis

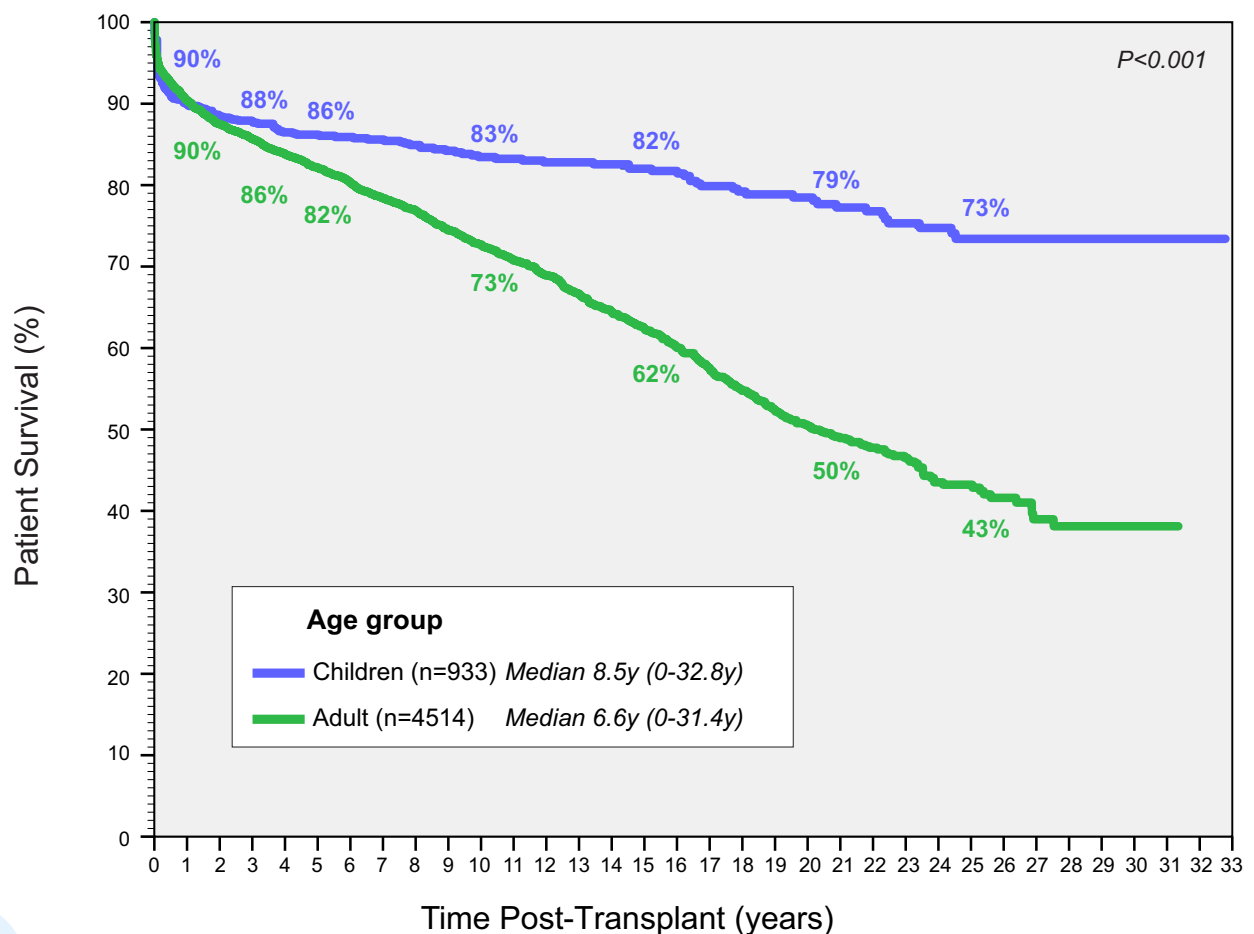
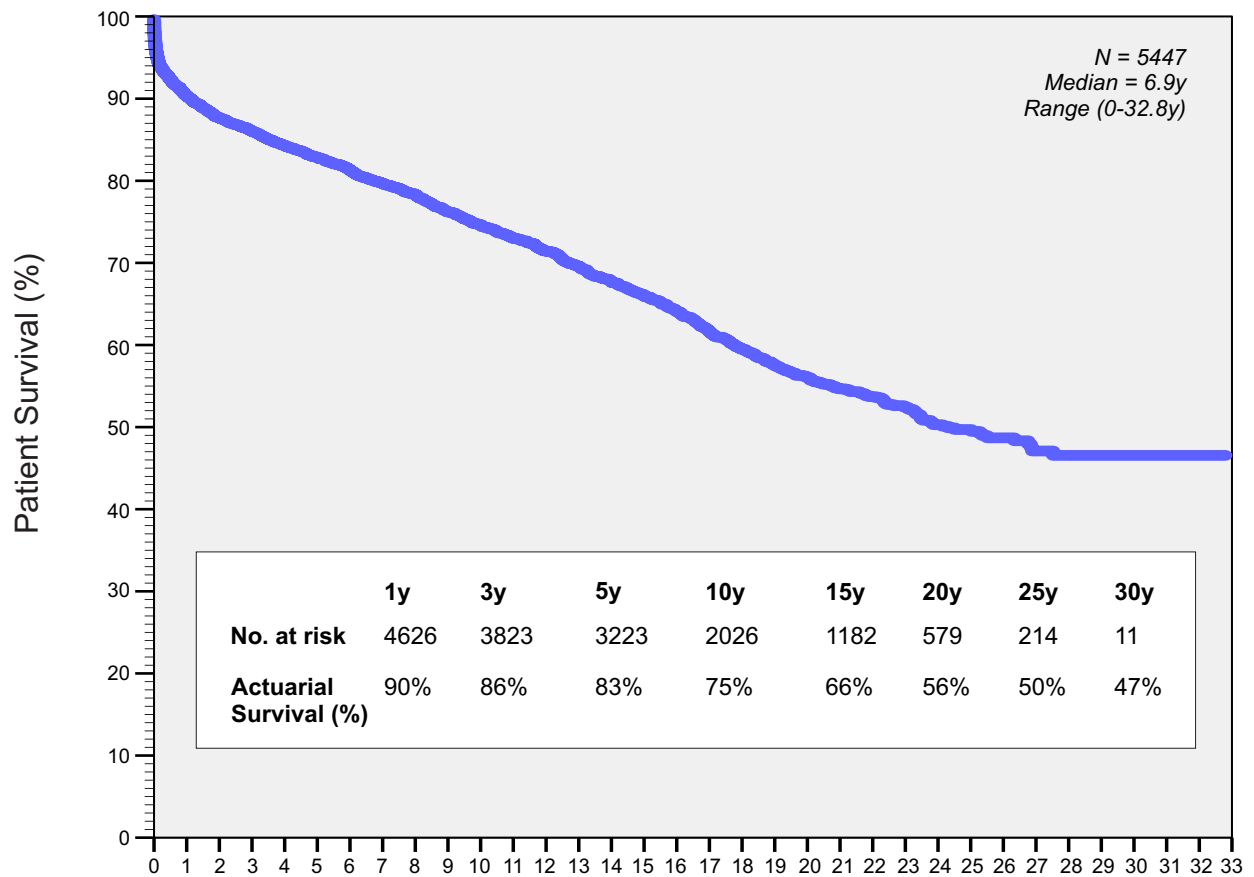




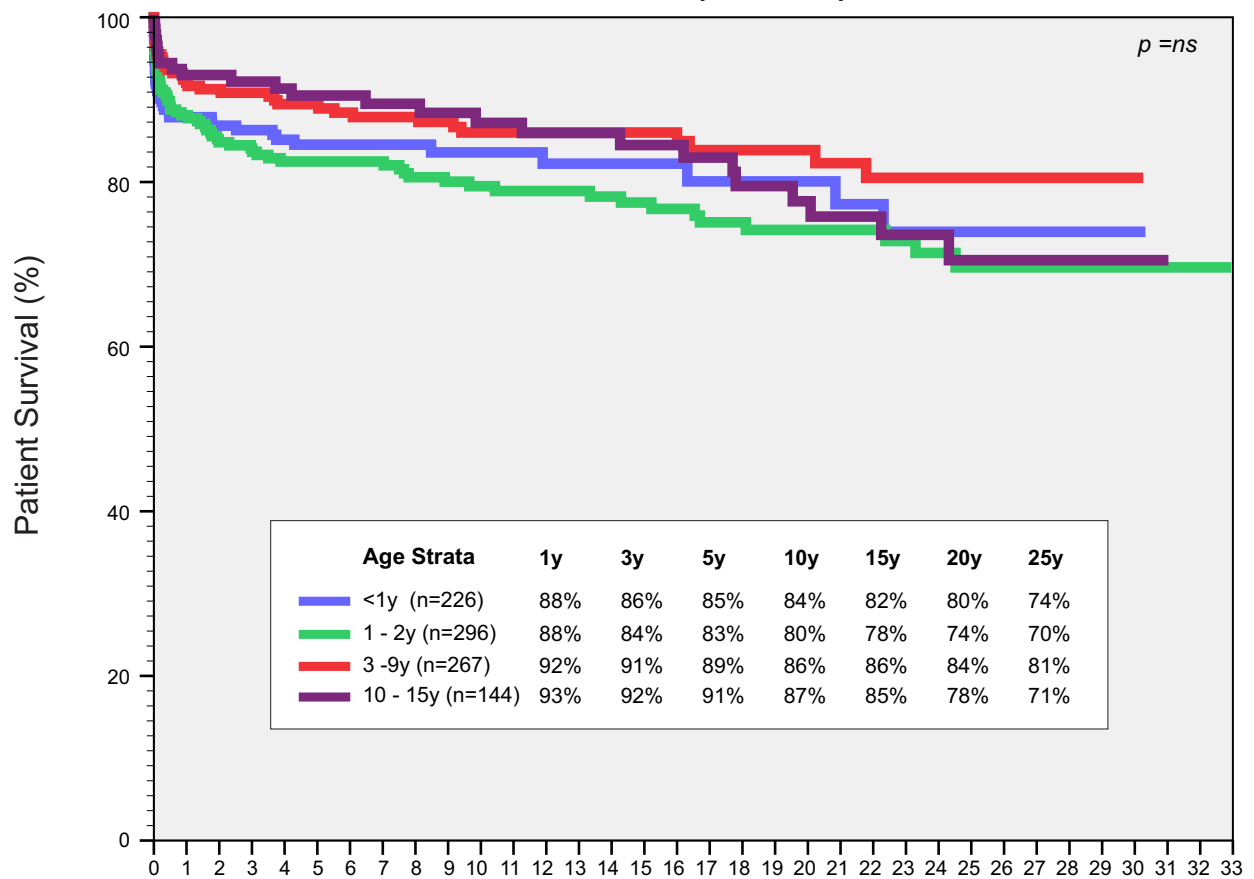
Section 3

Patient Survival

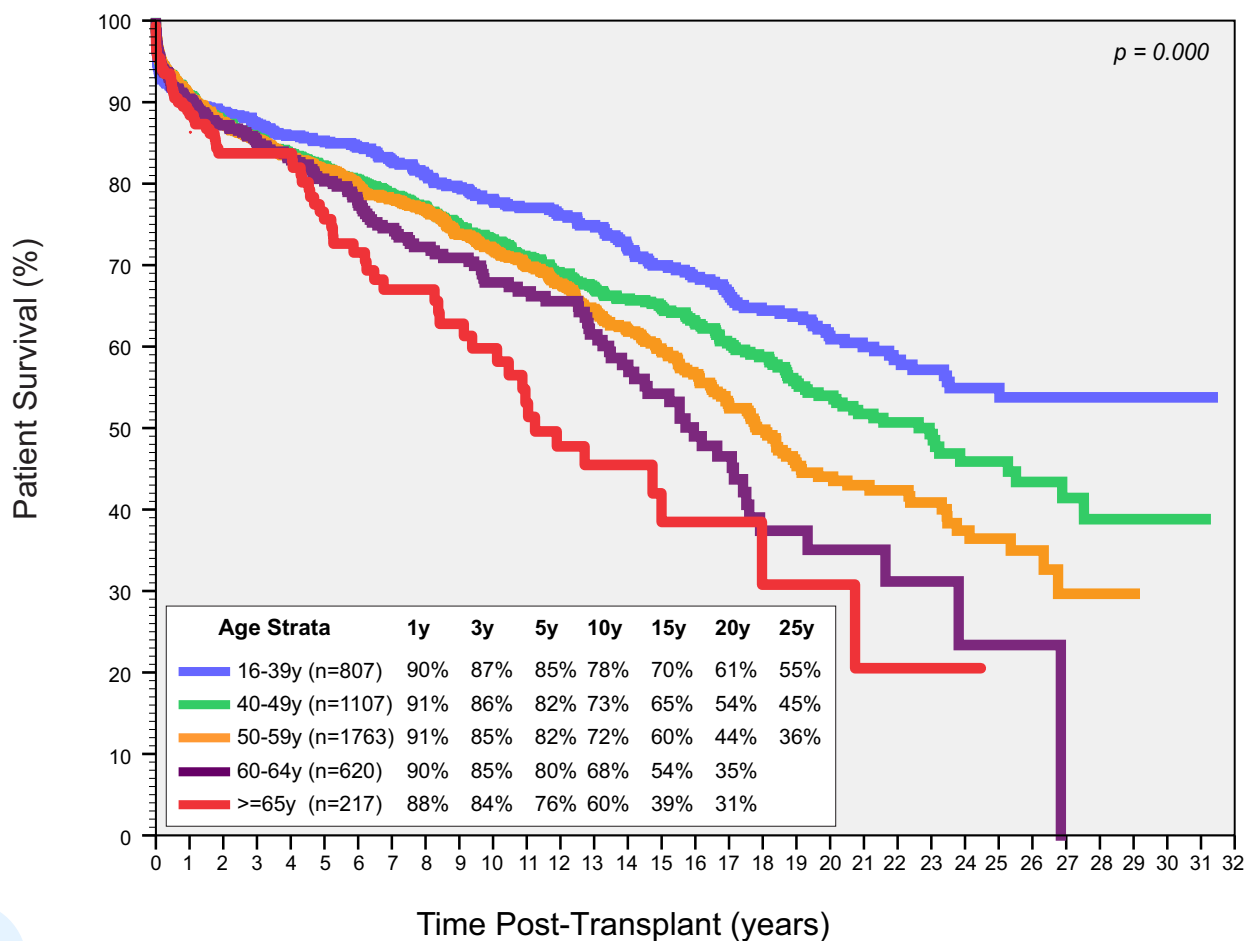


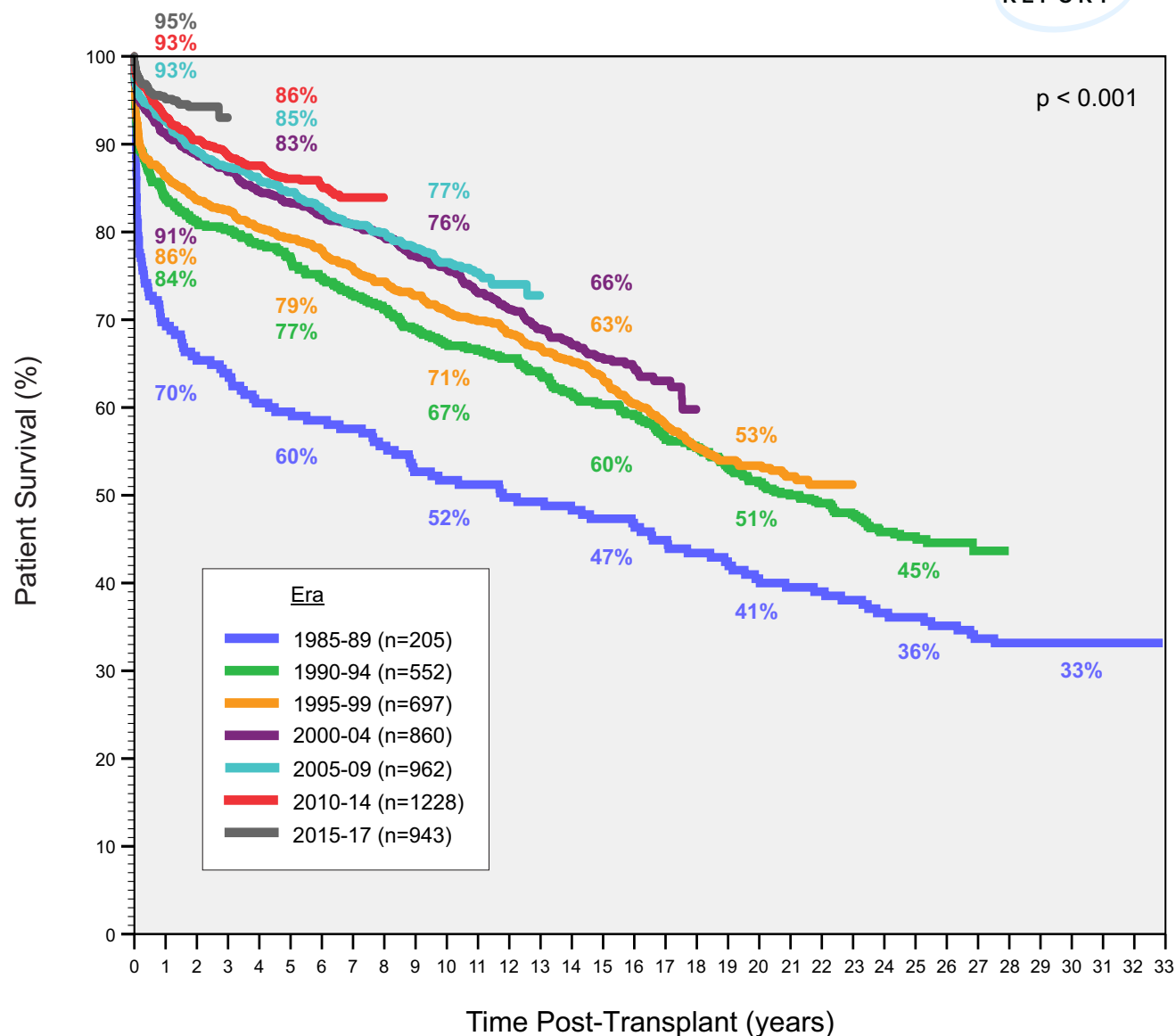


Children (N = 933)

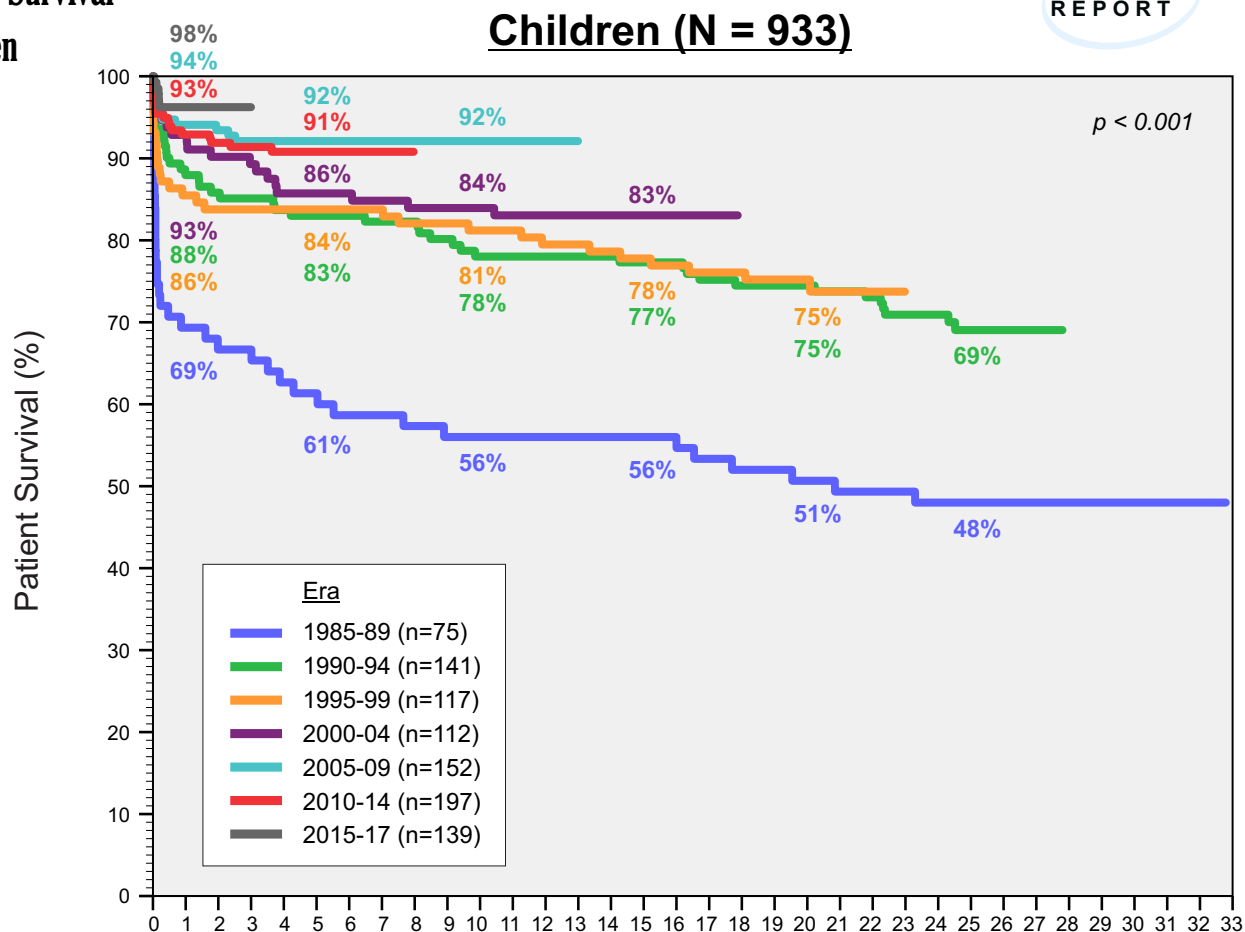


Adults (N = 4514)

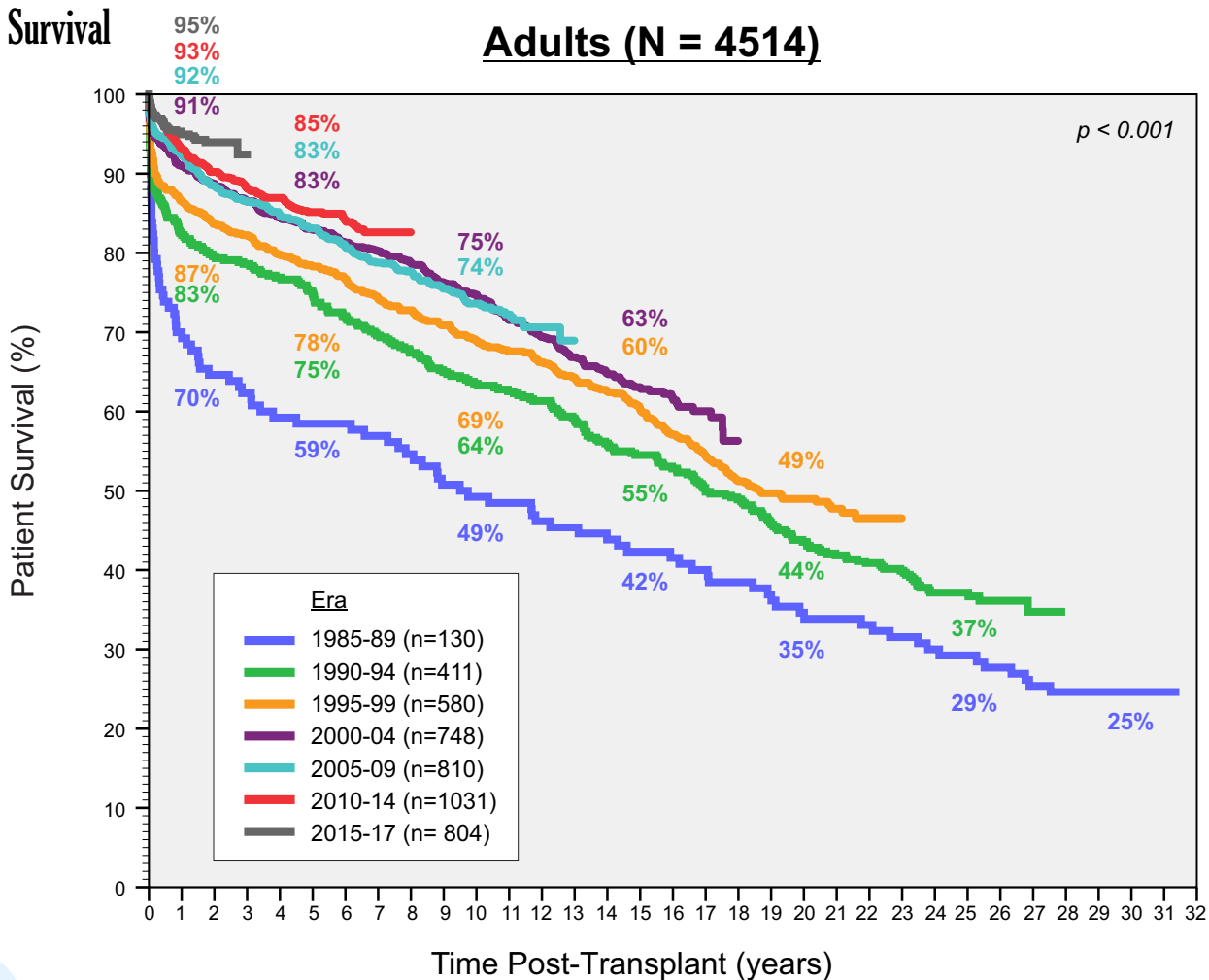




Patient Survival Children



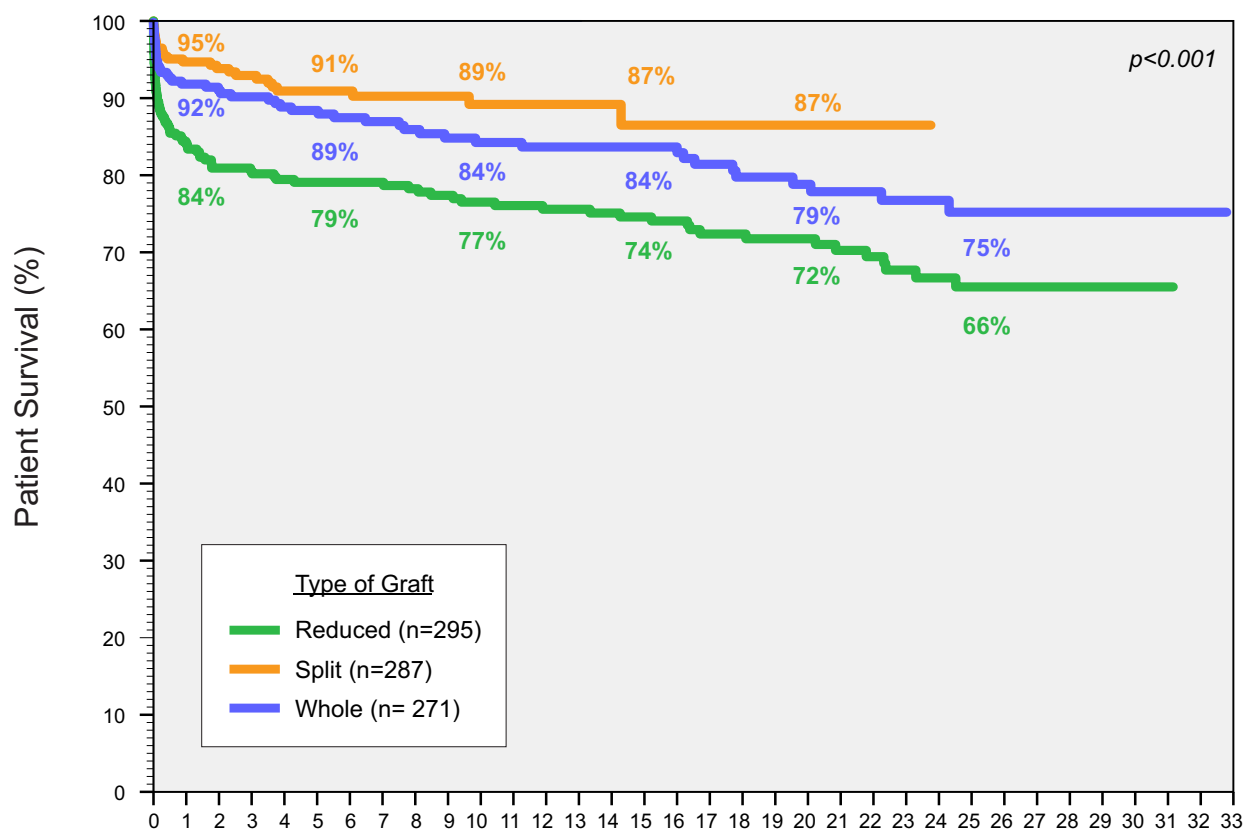
Patient Survival Adults



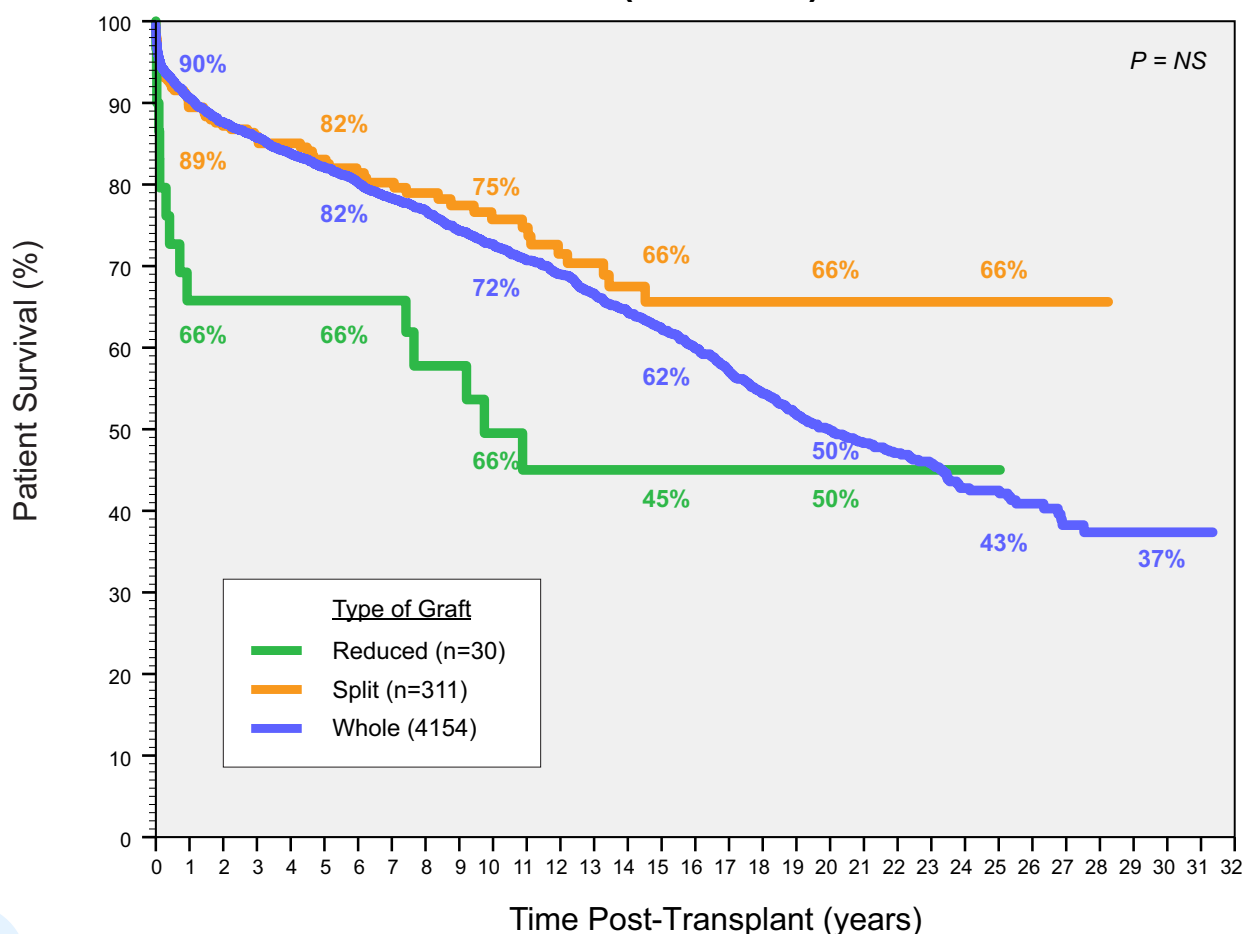
Patient Survival by Type of Primary Graft [deceased donors]

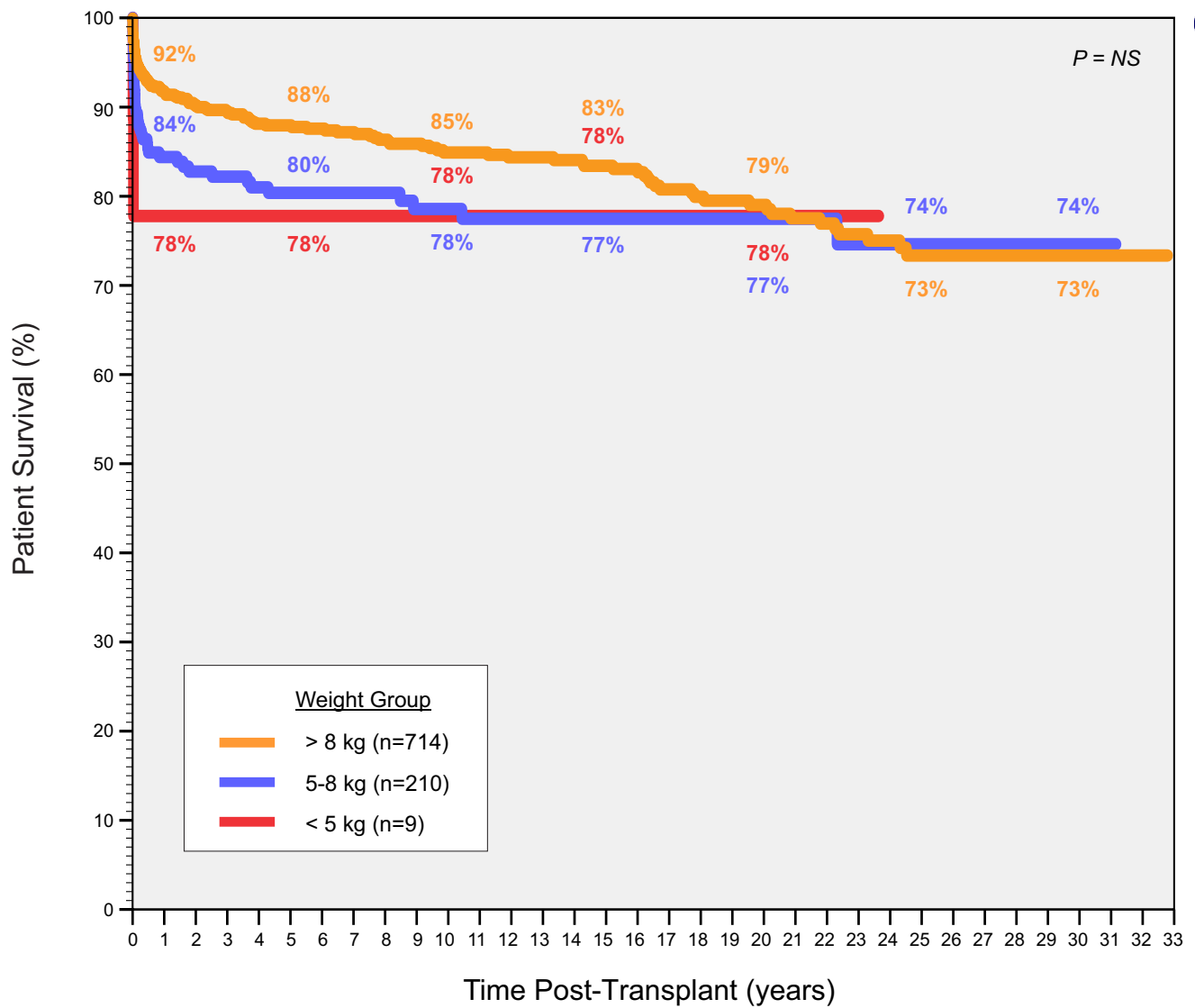


Children (N = 853)

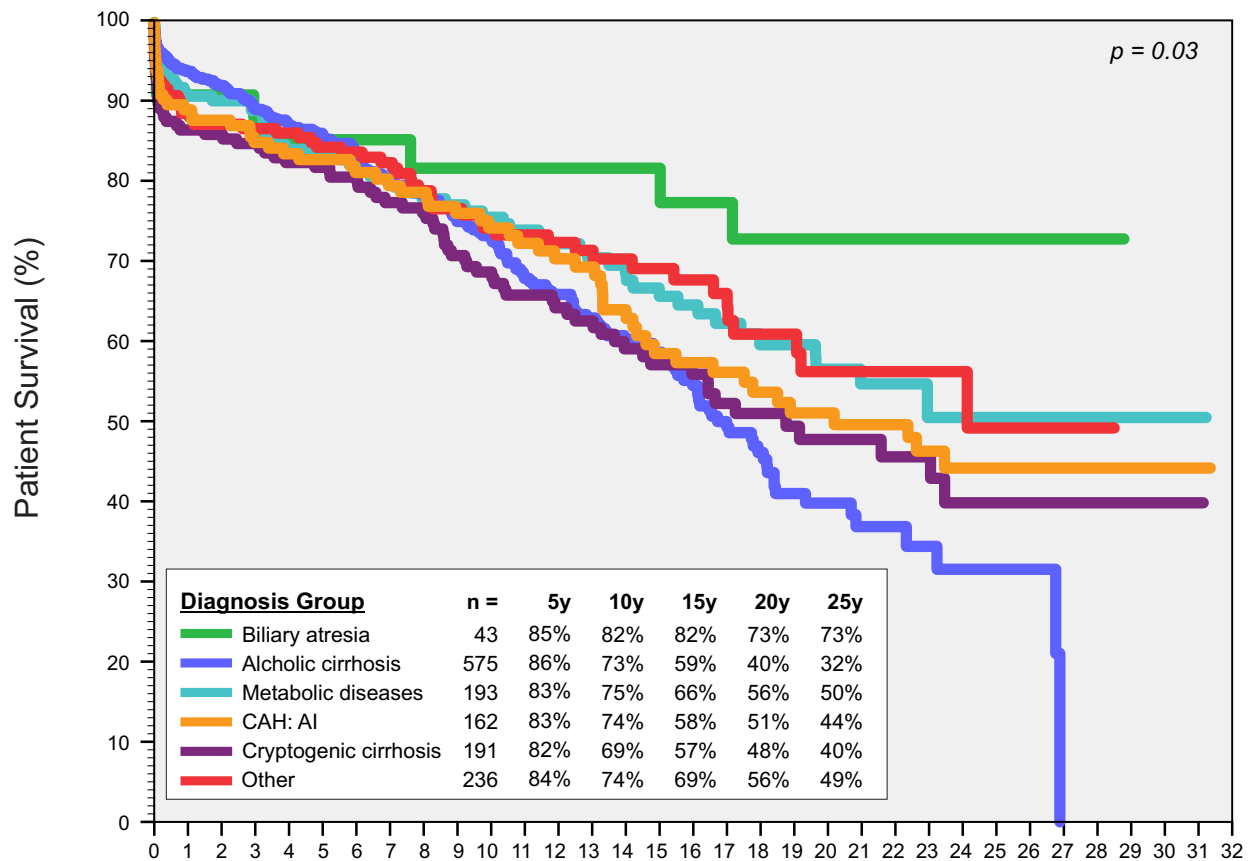


Adults (N = 4495)

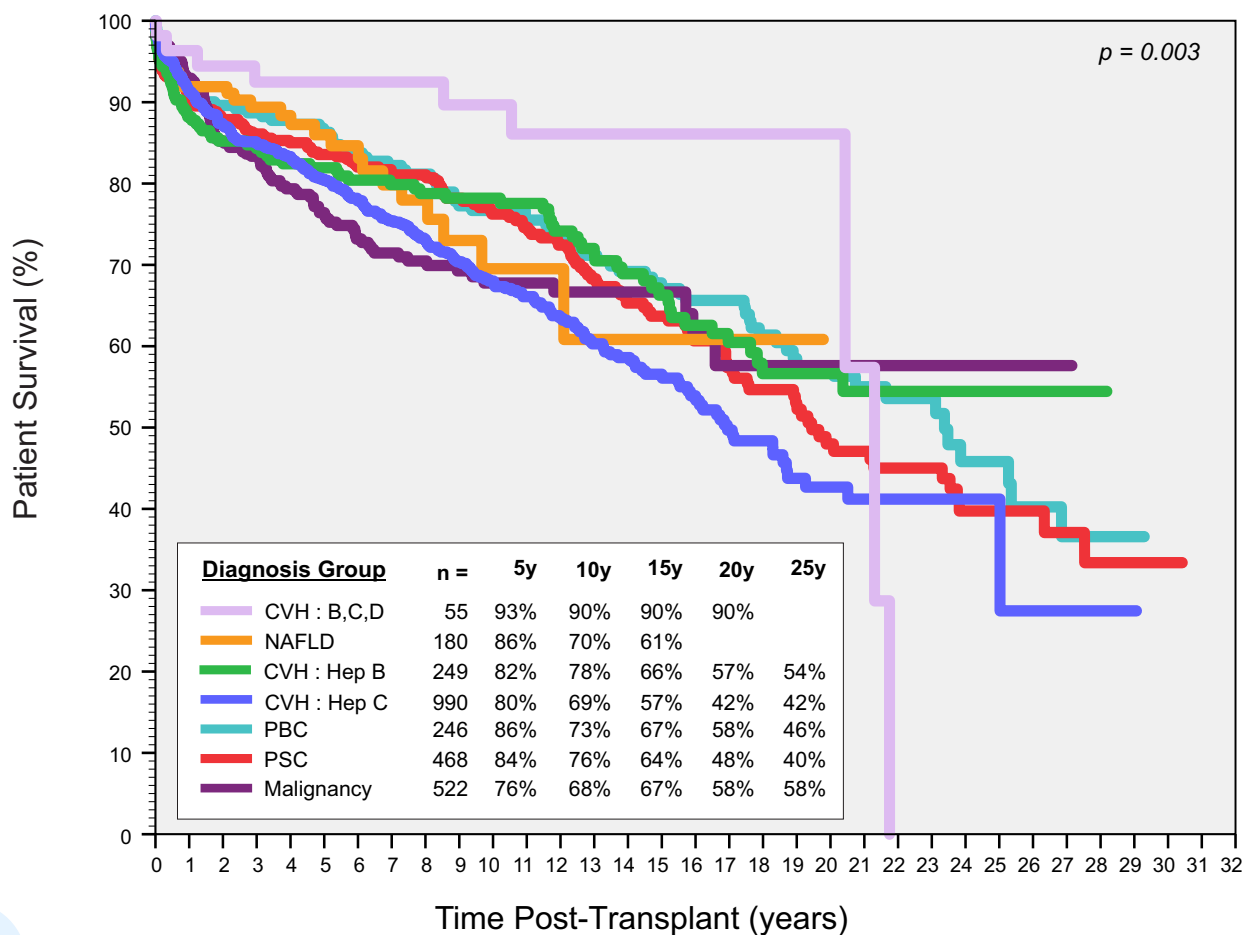




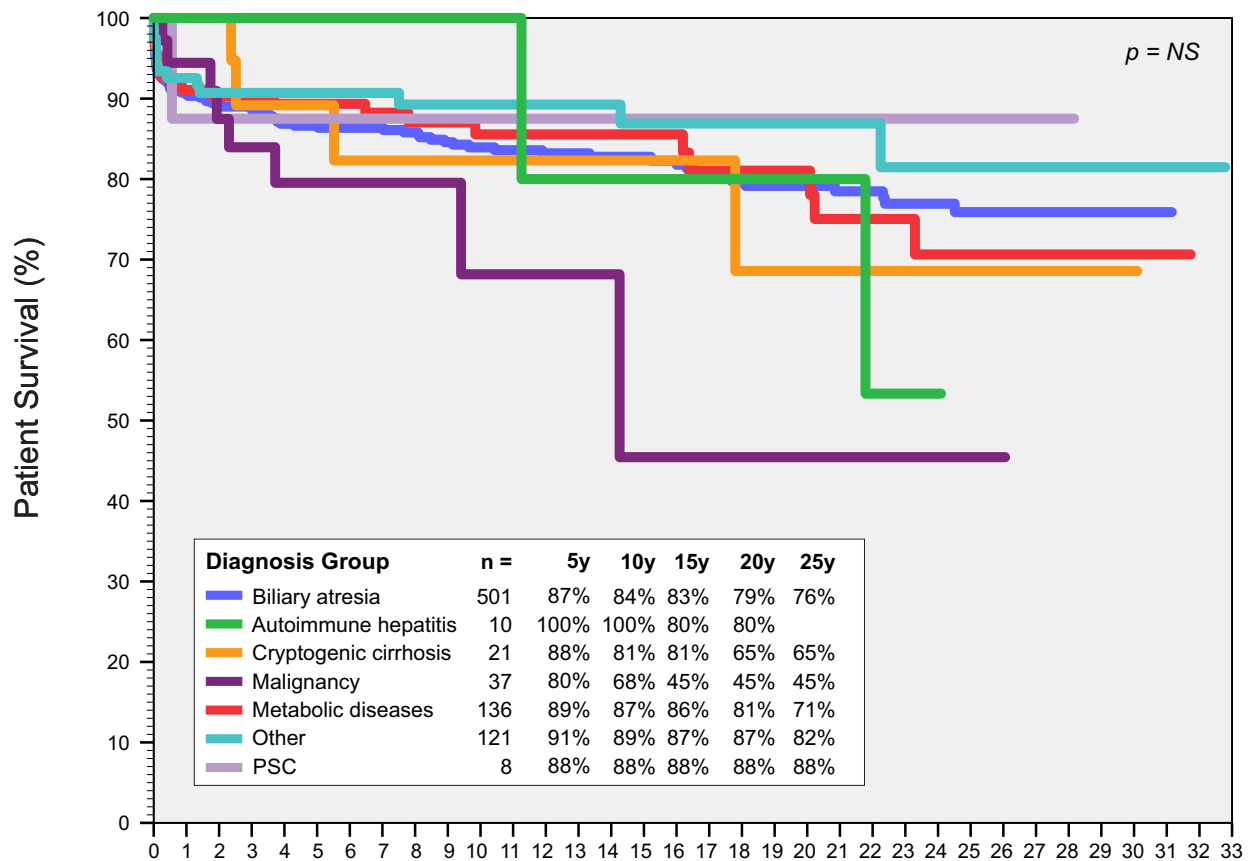
(1) Adults [excluding FHF] (N = 1400)



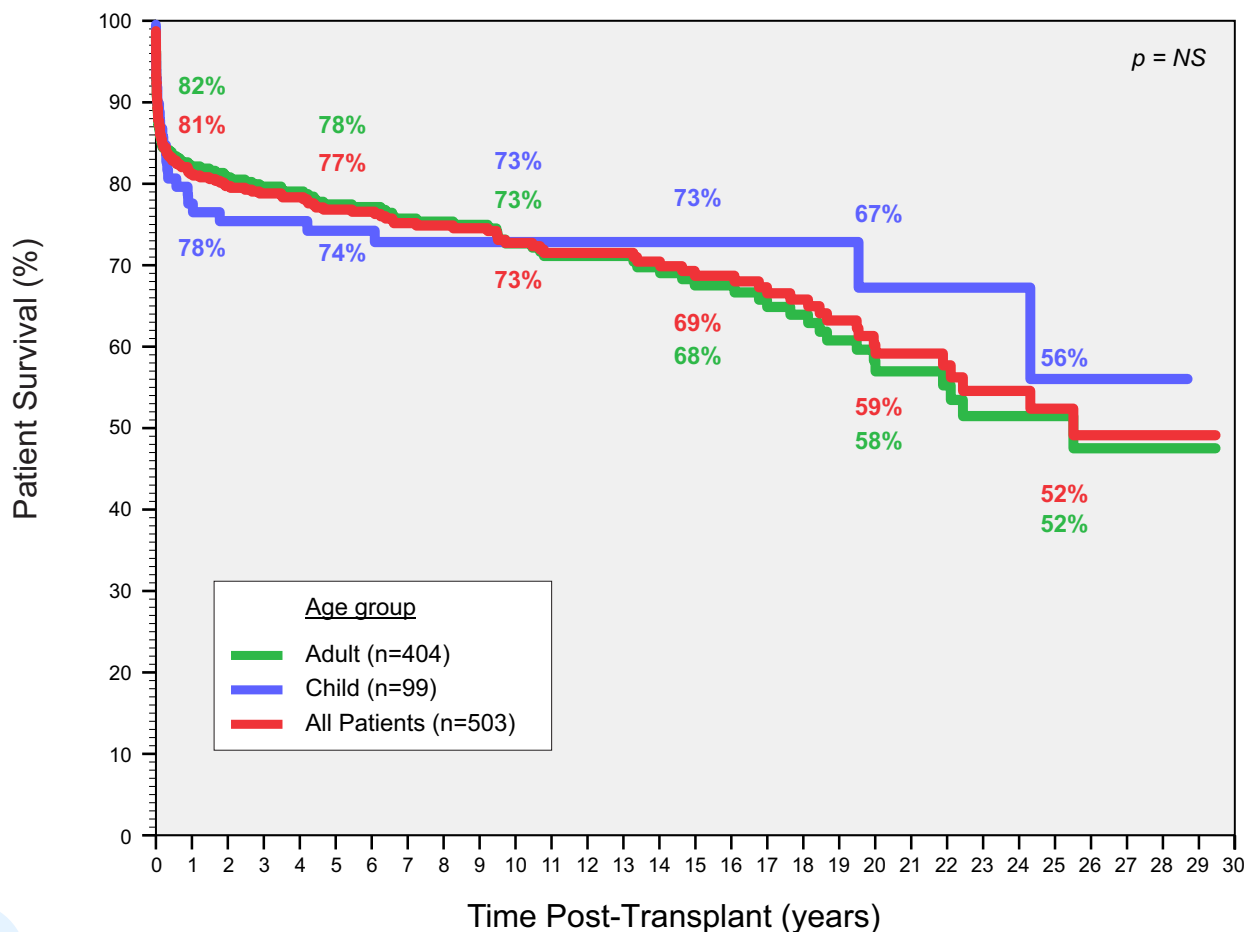
(2) Adults [excluding FHF] (N = 2710)

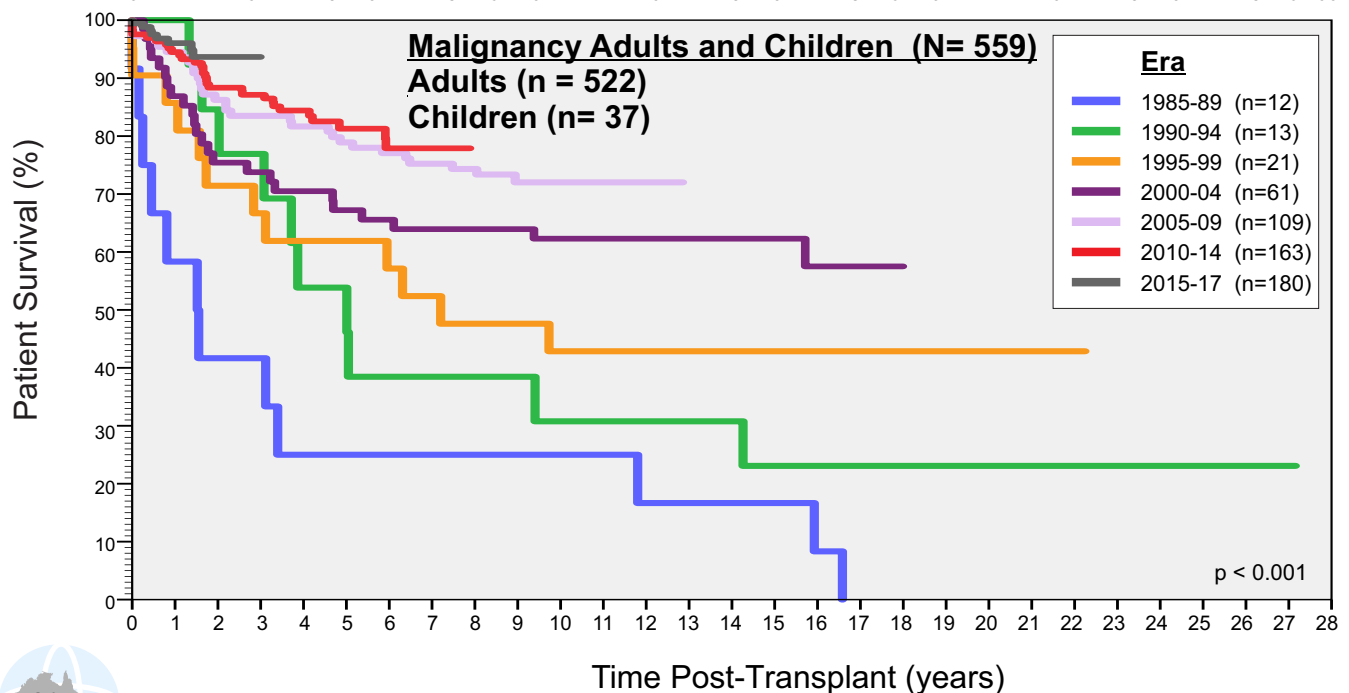
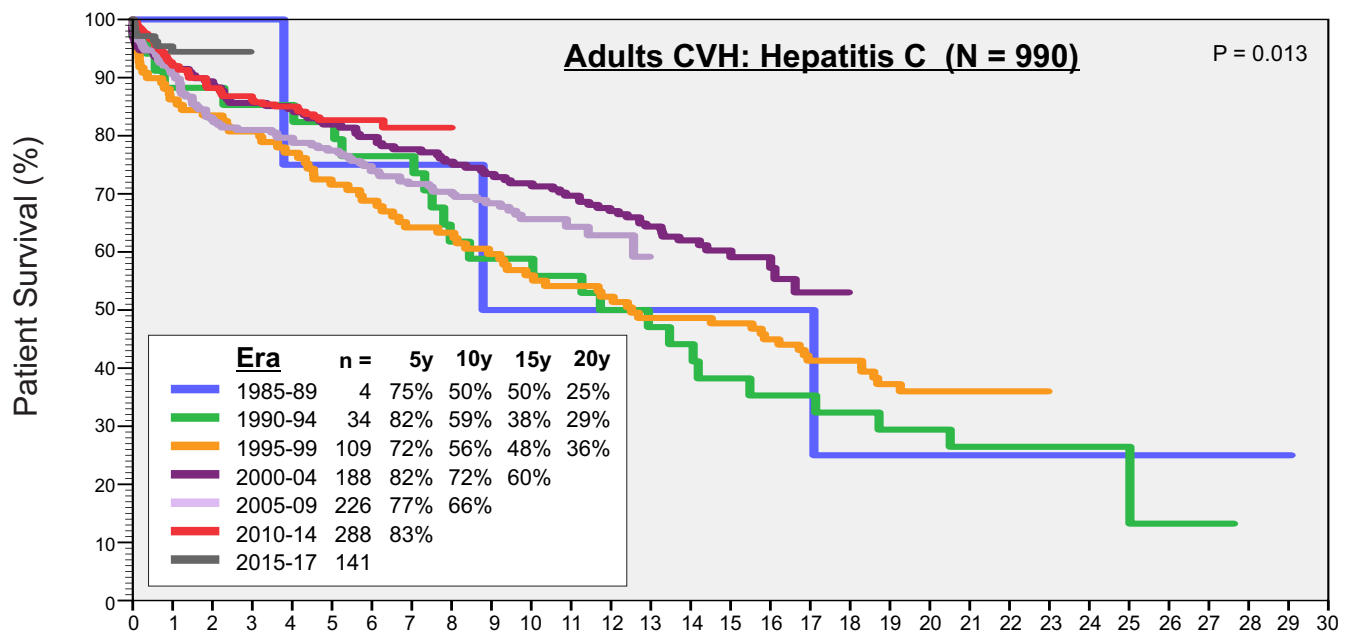
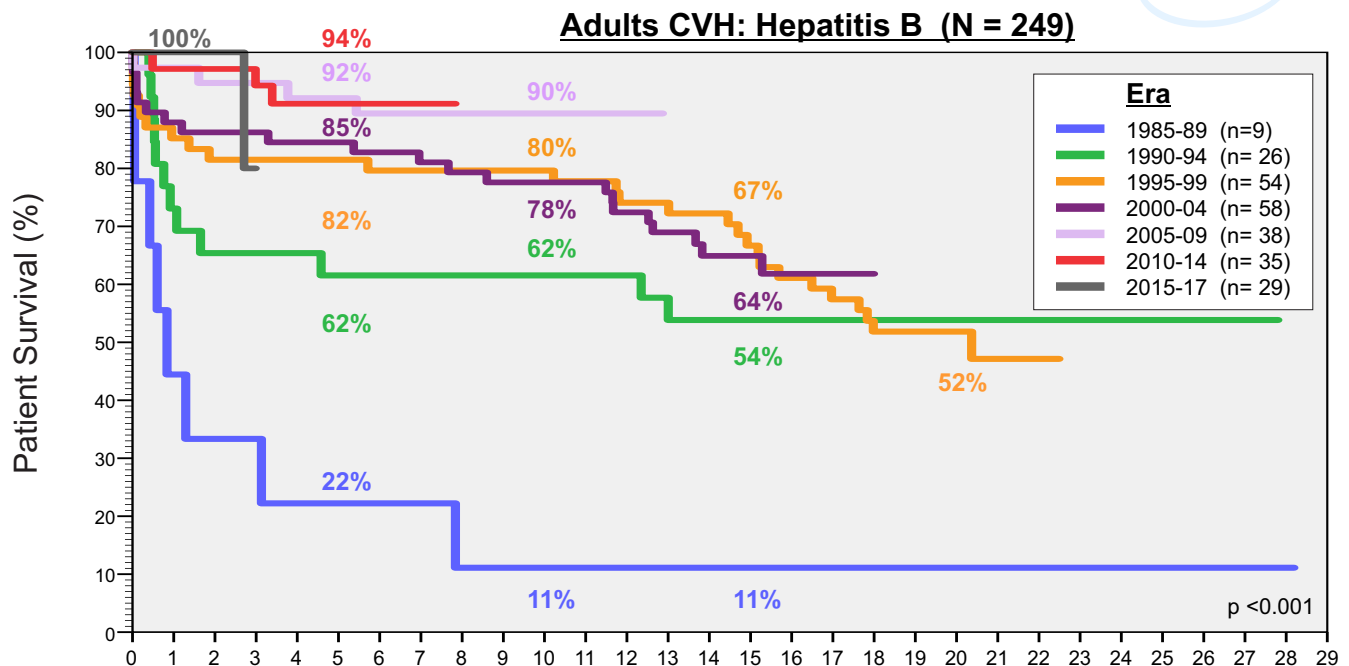


(3) Paediatric recipients [excluding FHF] (N = 834)



(4) Fulminant hepatic failure (N = 503)



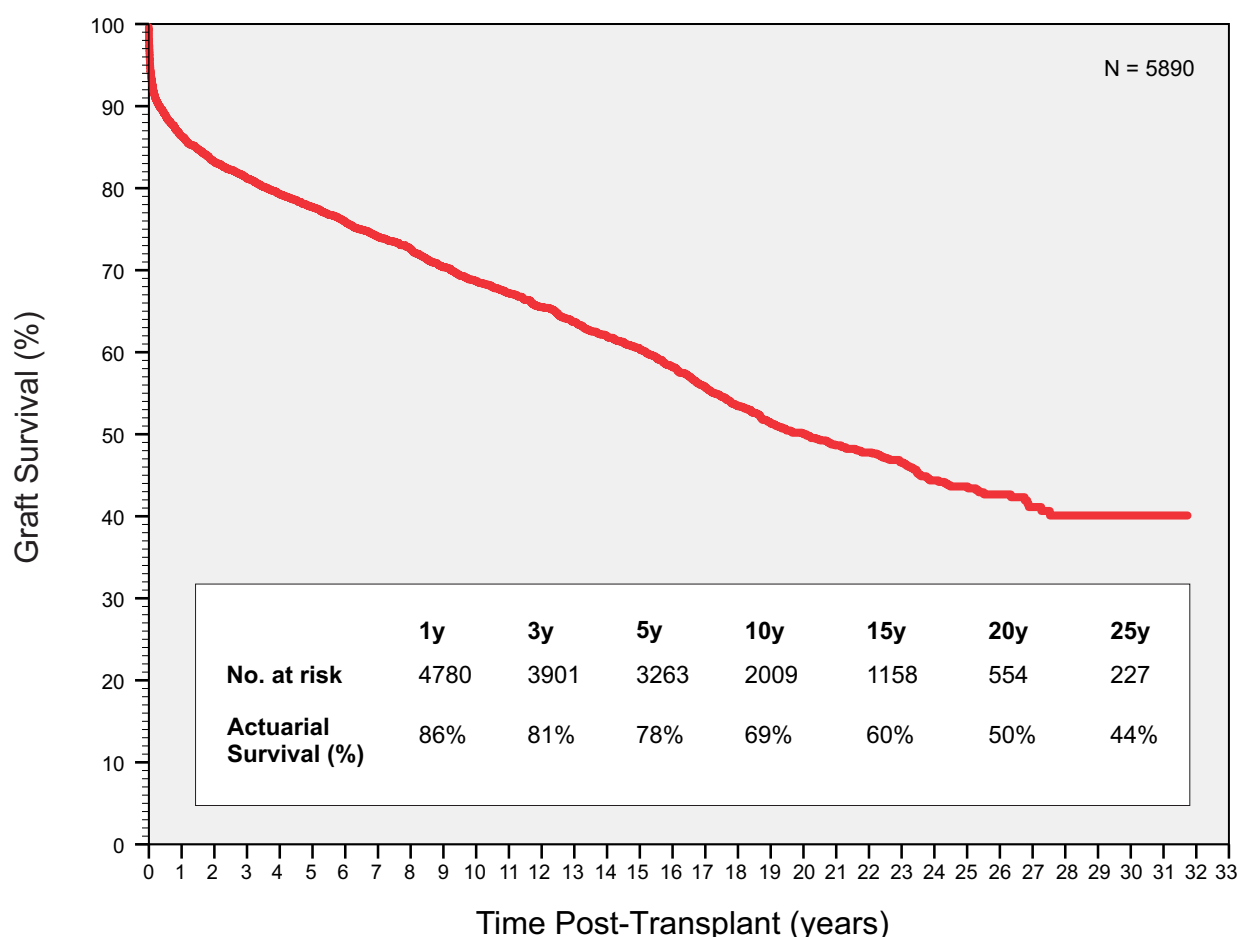




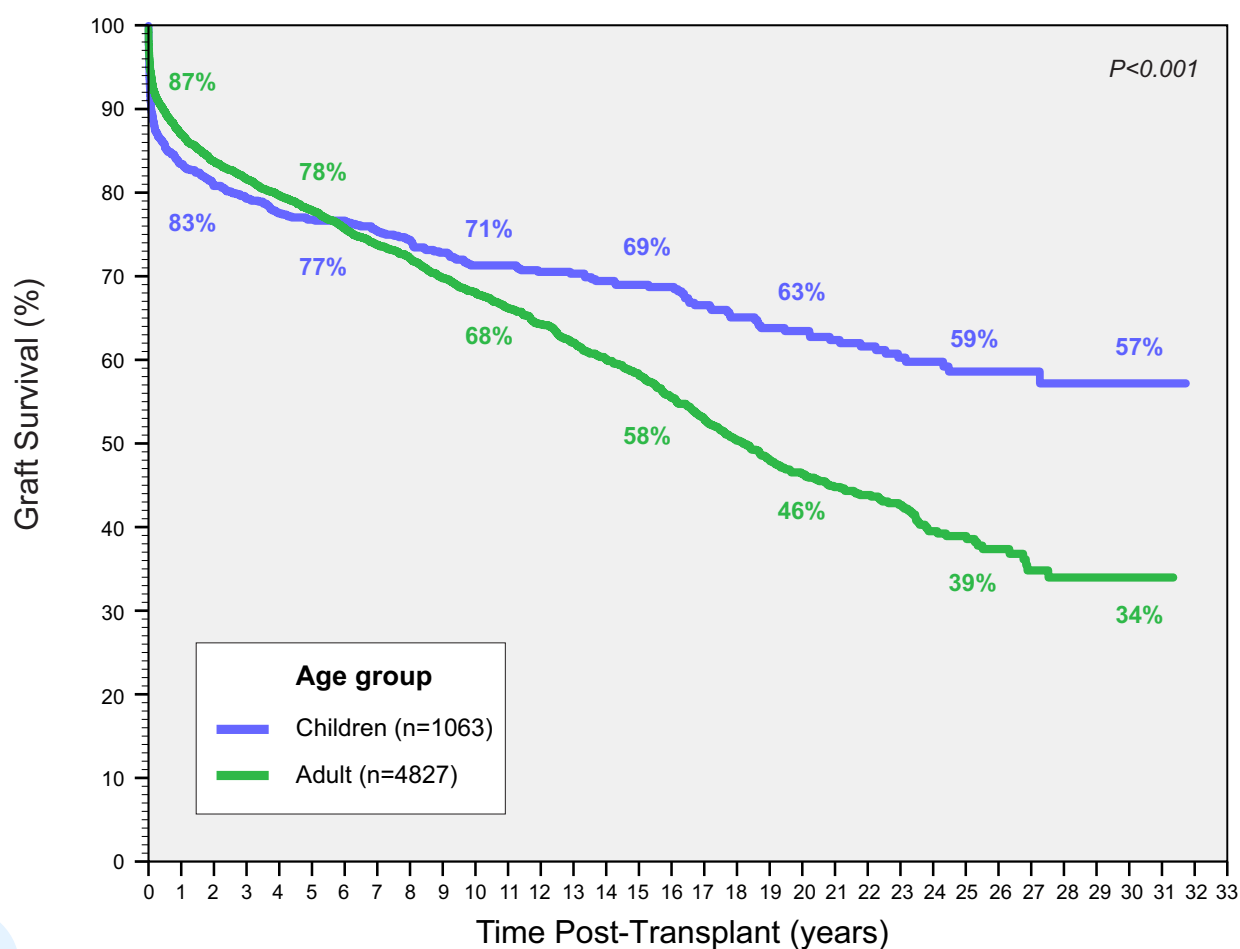
Section 4

Graft Outcome

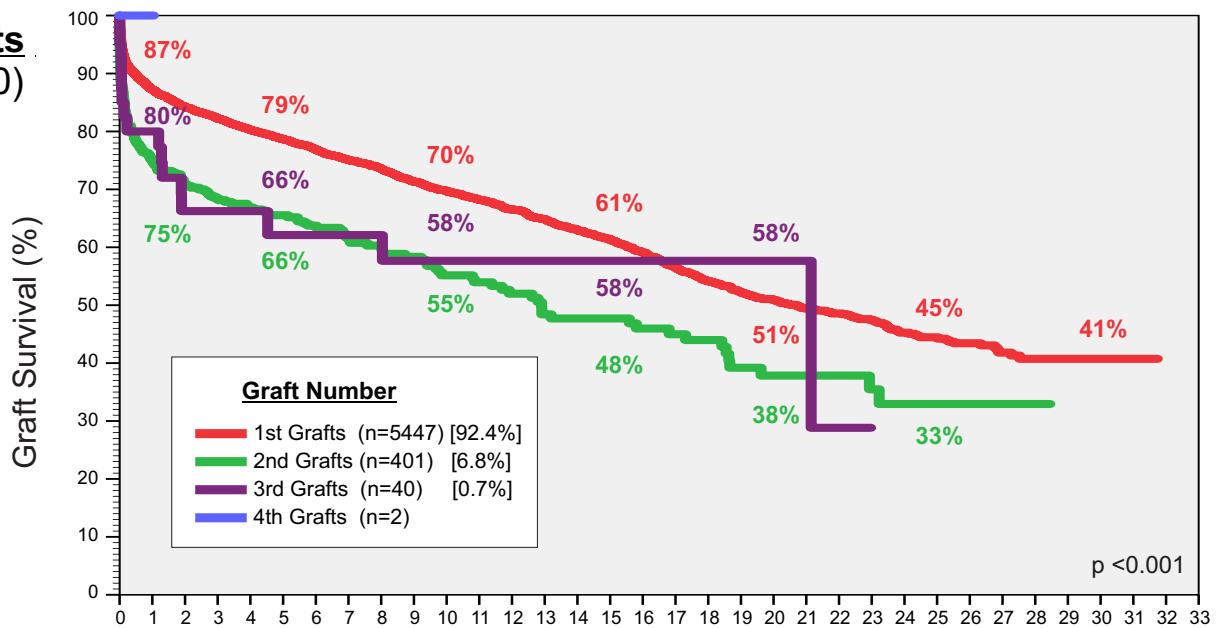




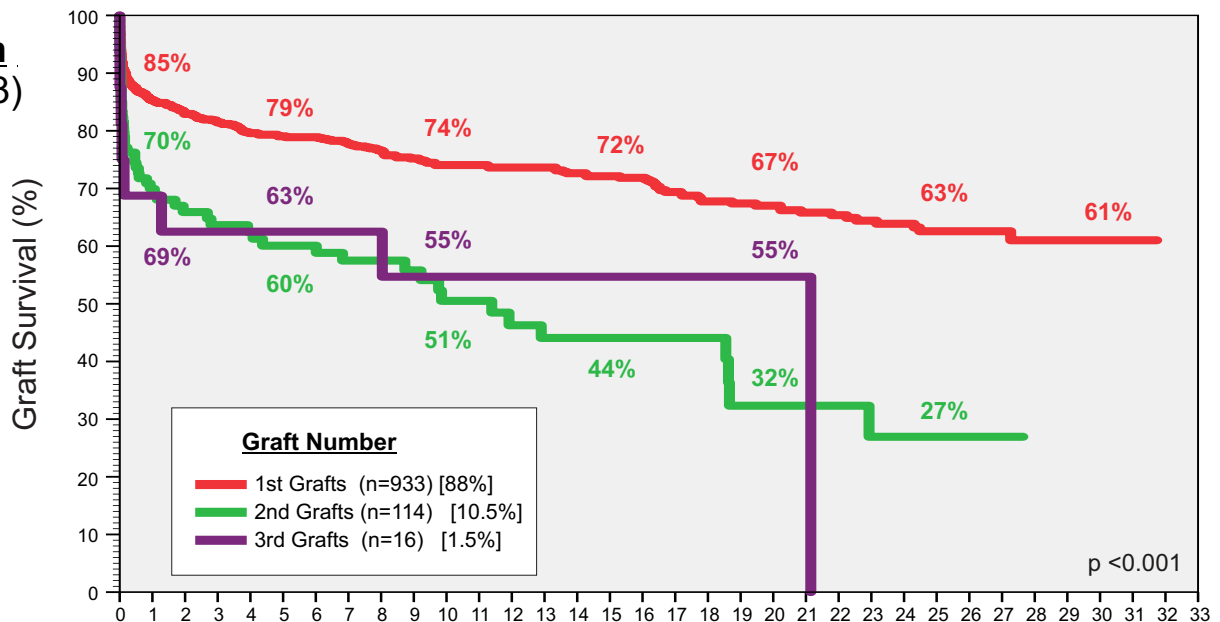
Graft Survival by Age Group



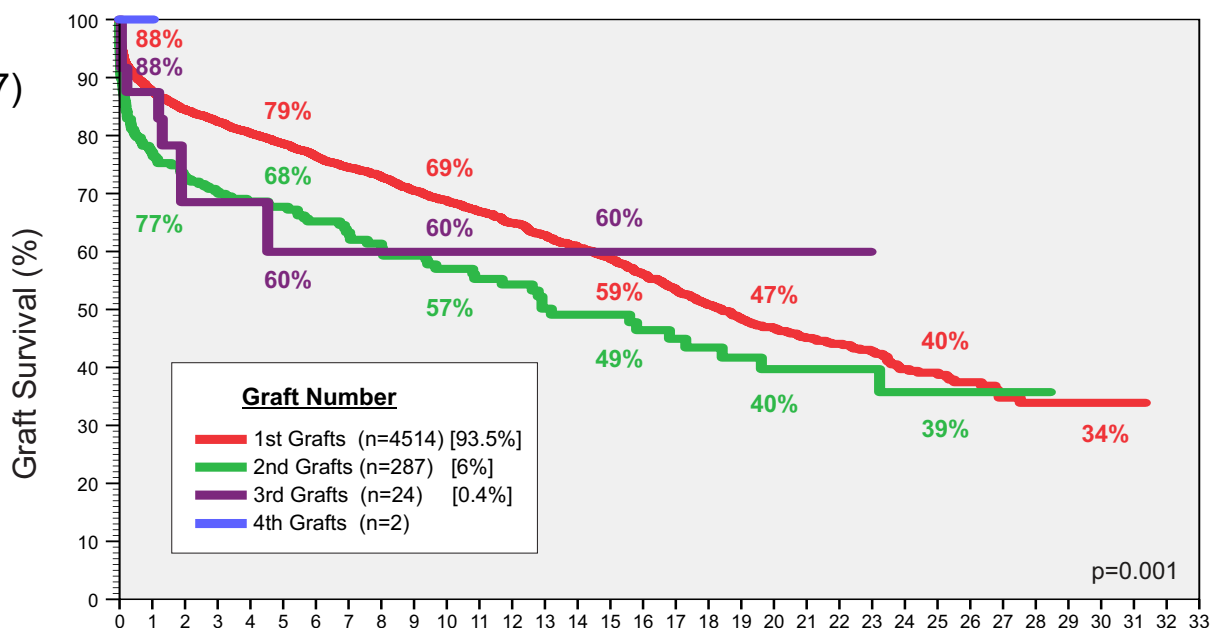
All Grafts (N= 5890)



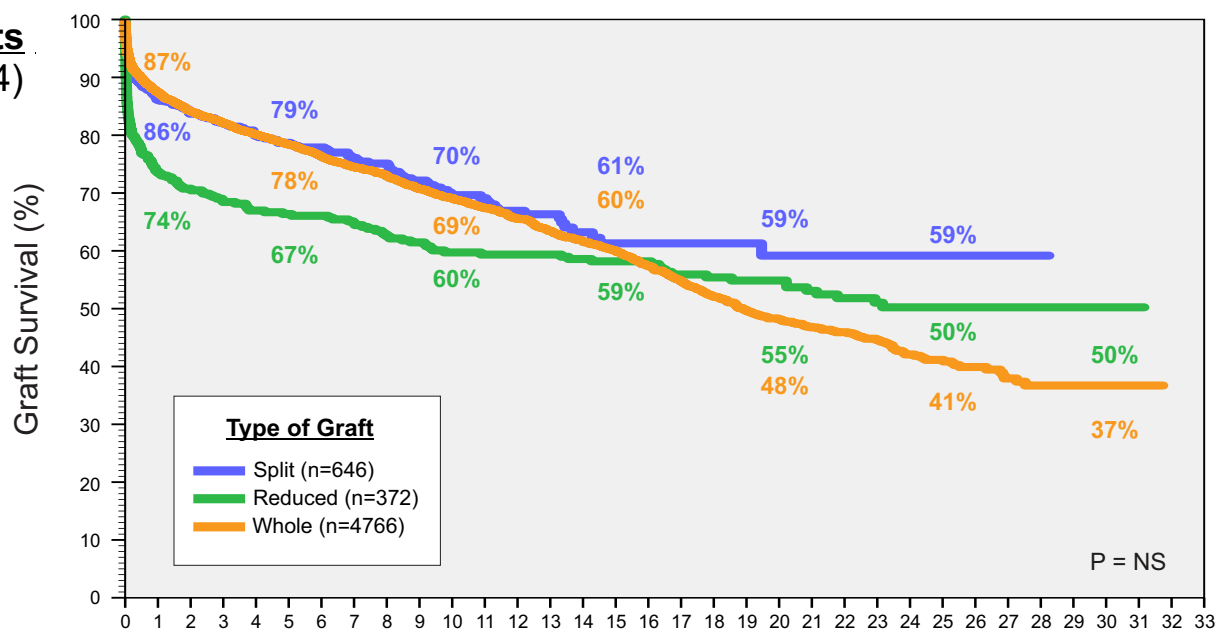
Children (N= 1063)



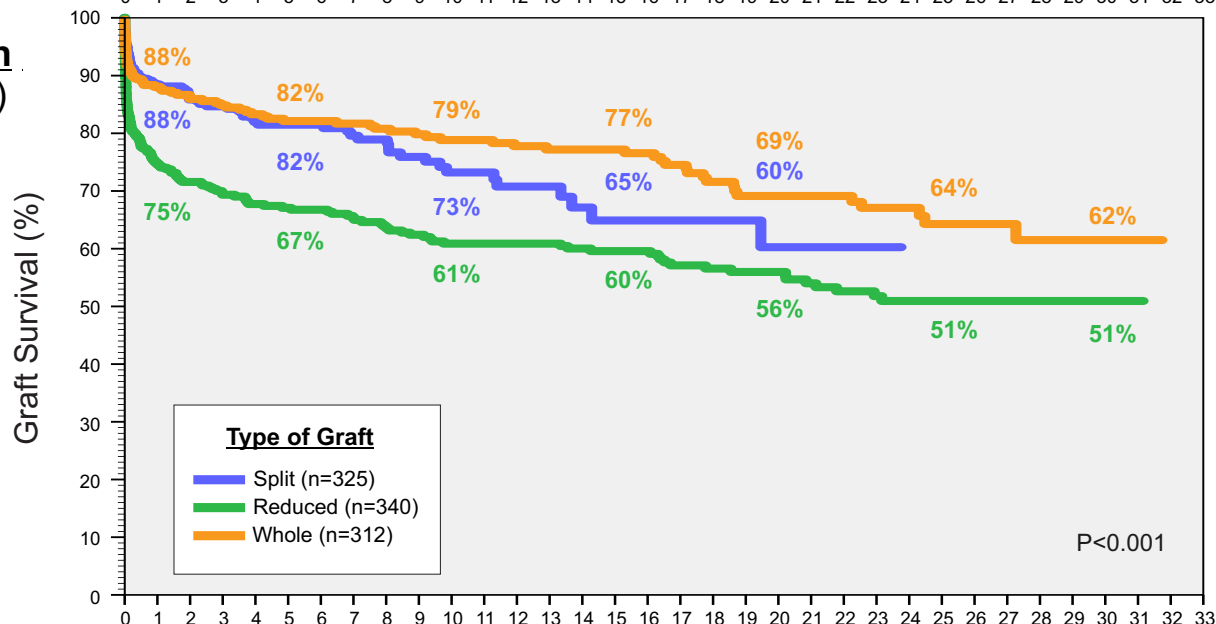
Adult (N= 4827)



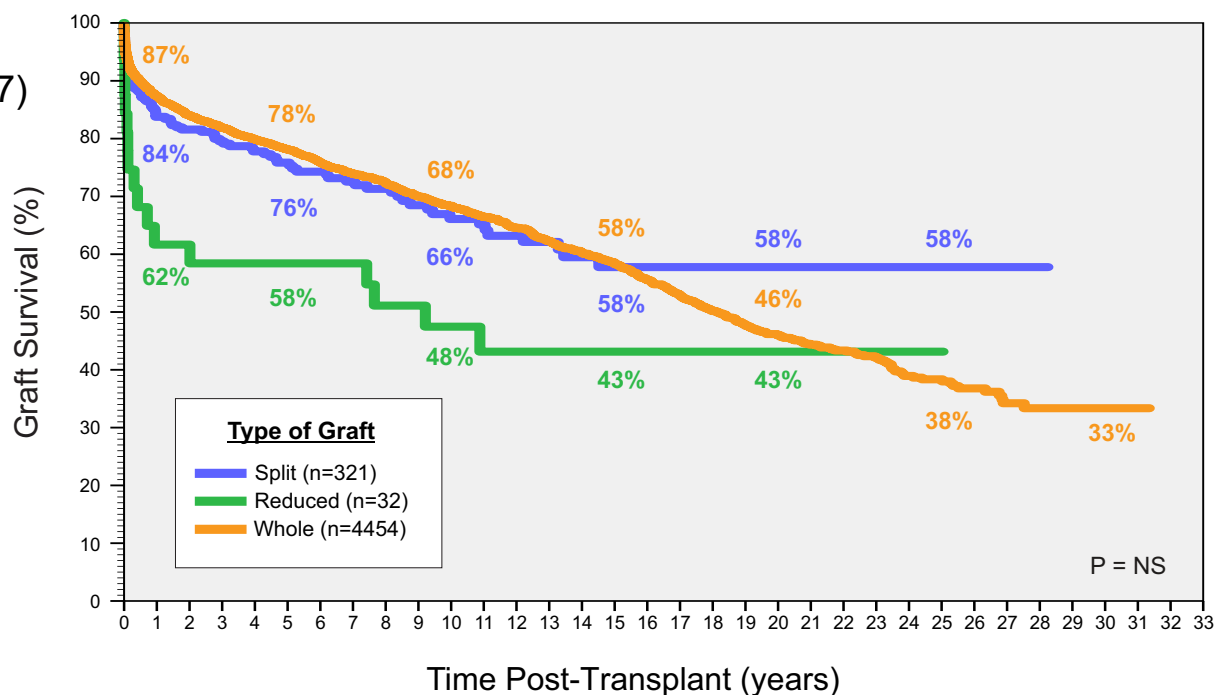
All Grafts (N= 5784)

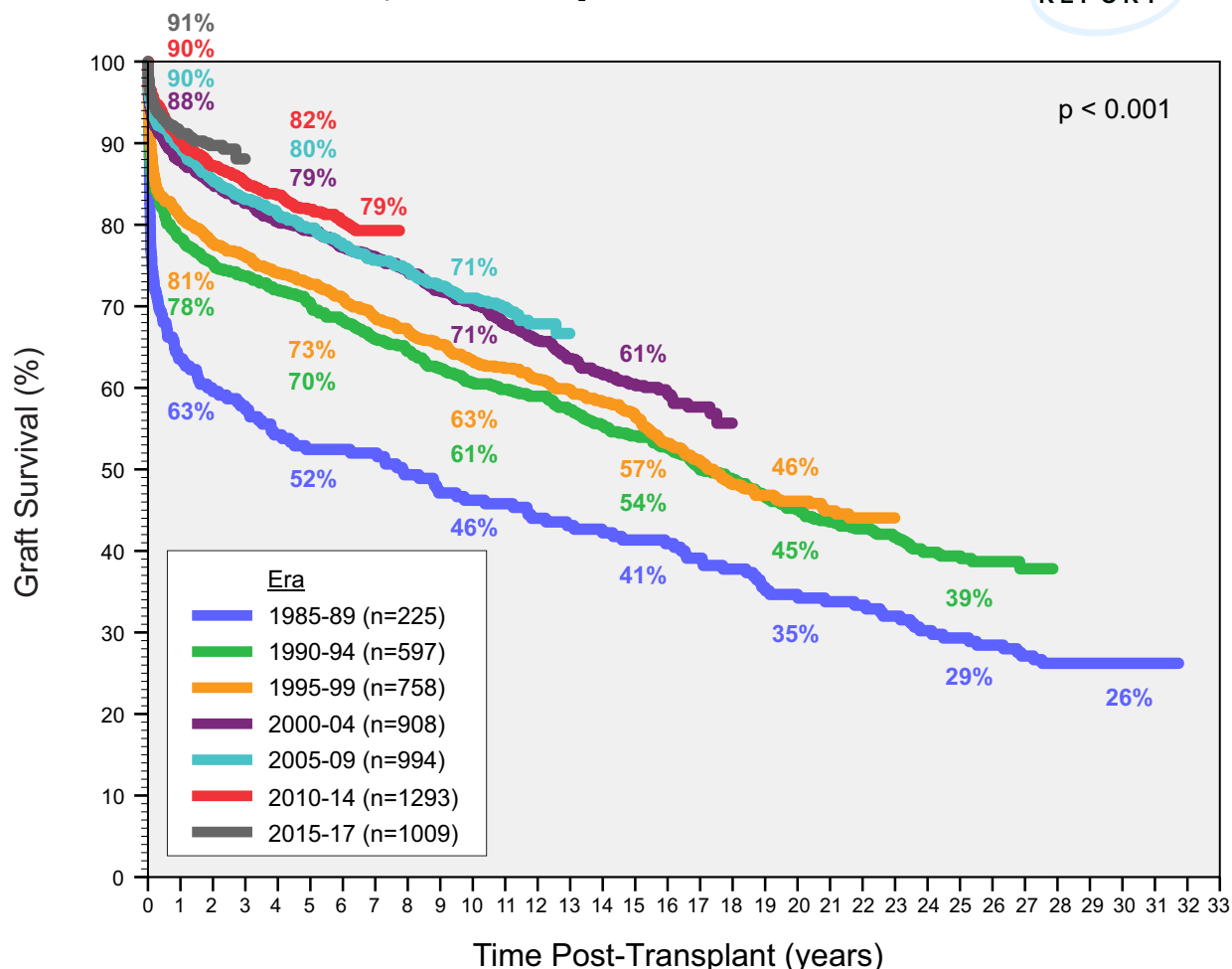


Children (N= 977)

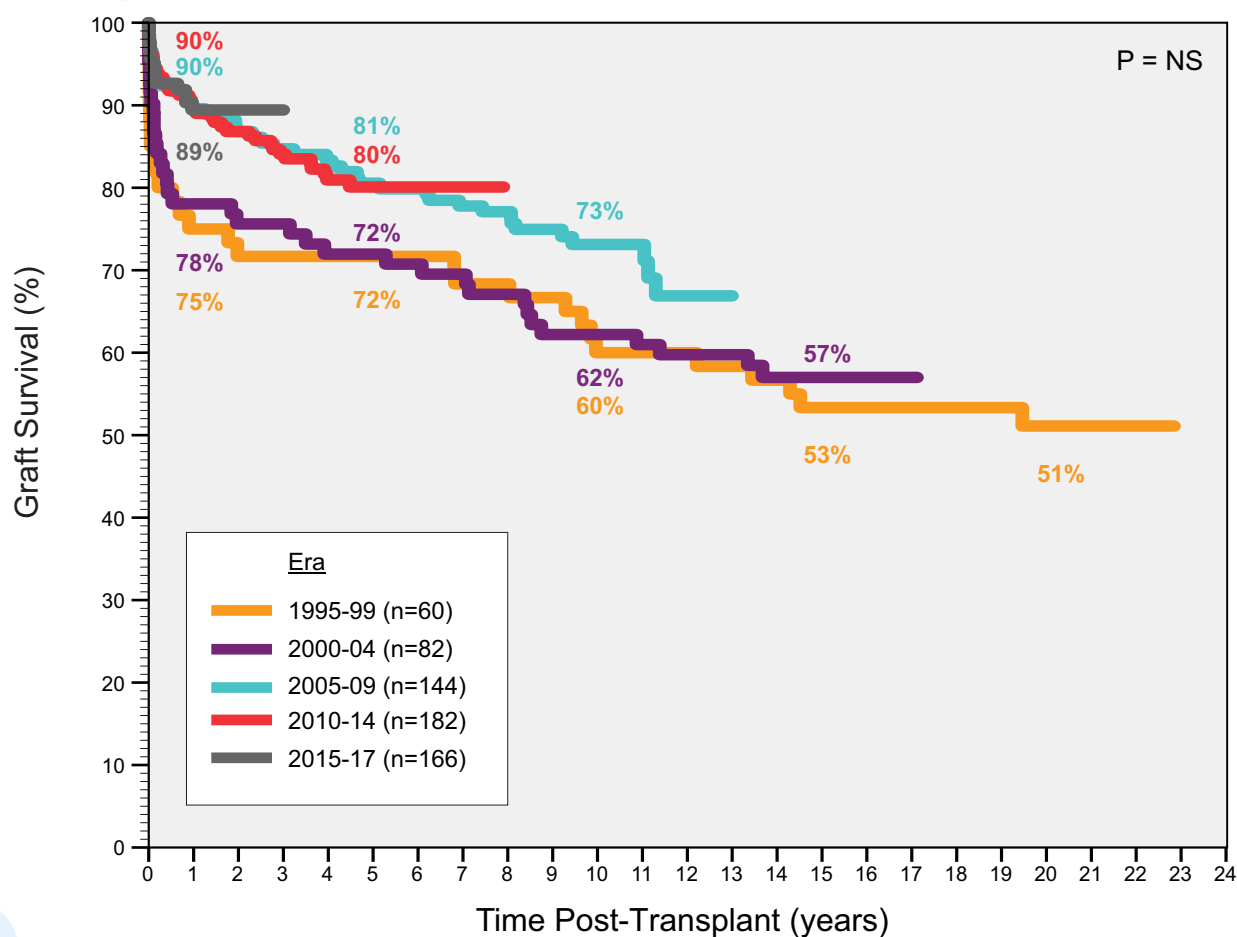


Adult (N= 4807)



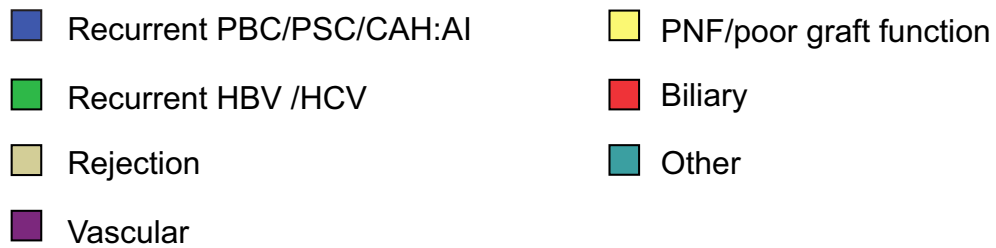
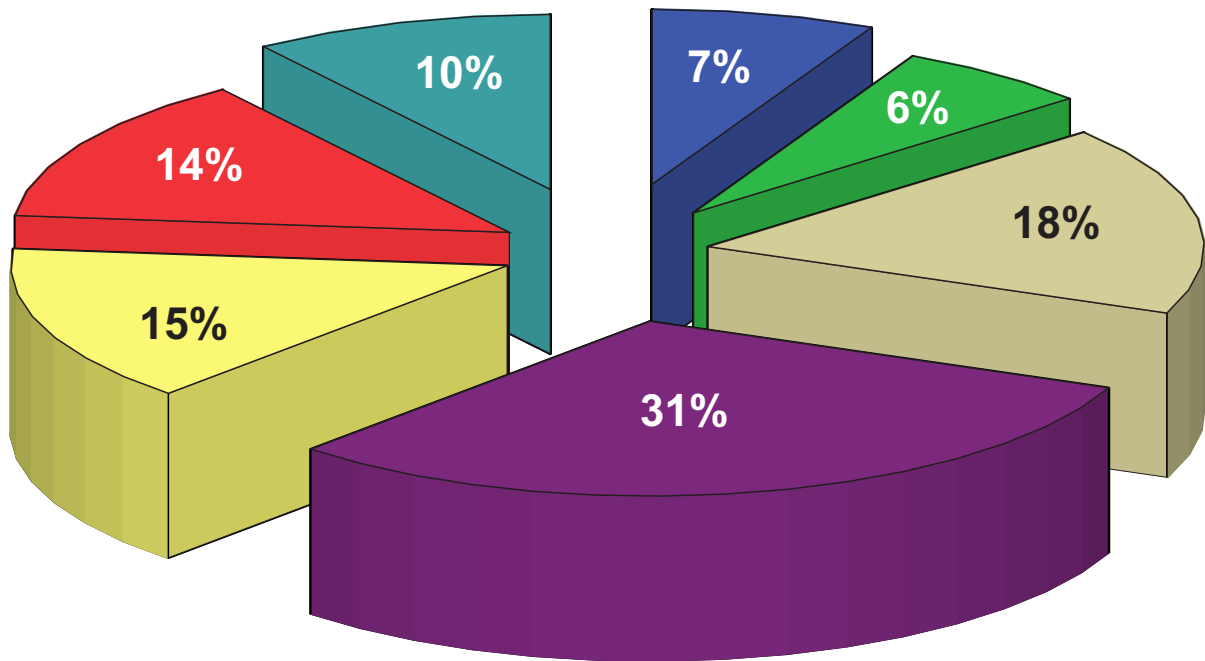


Deceased Donor Split Liver Grafts by Era



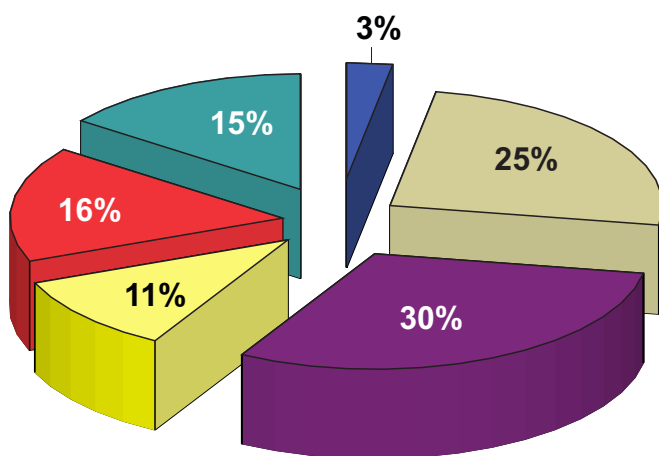
Indication for Retransplantation

N = 440 (398 2nd grafts, 40 3rd grafts & 2 4th graft)

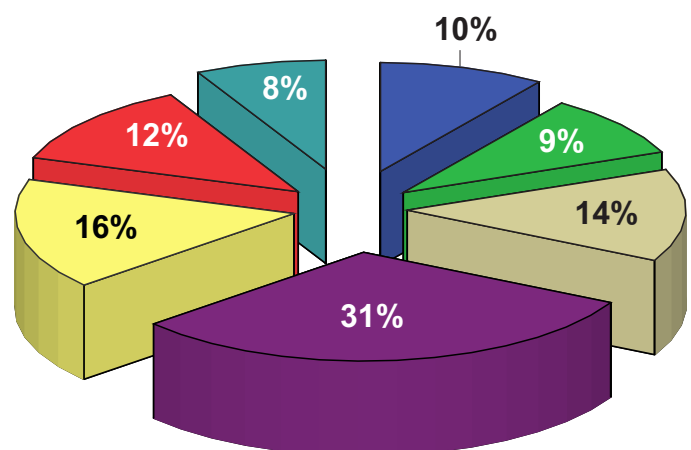


Age Group

Children (n= 149)

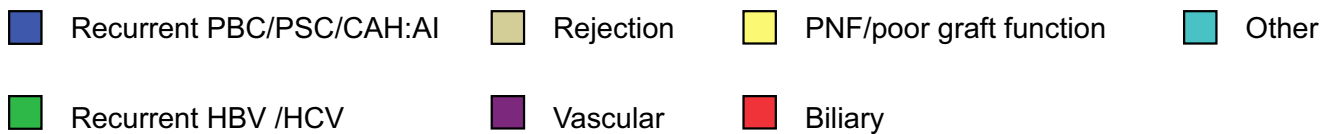
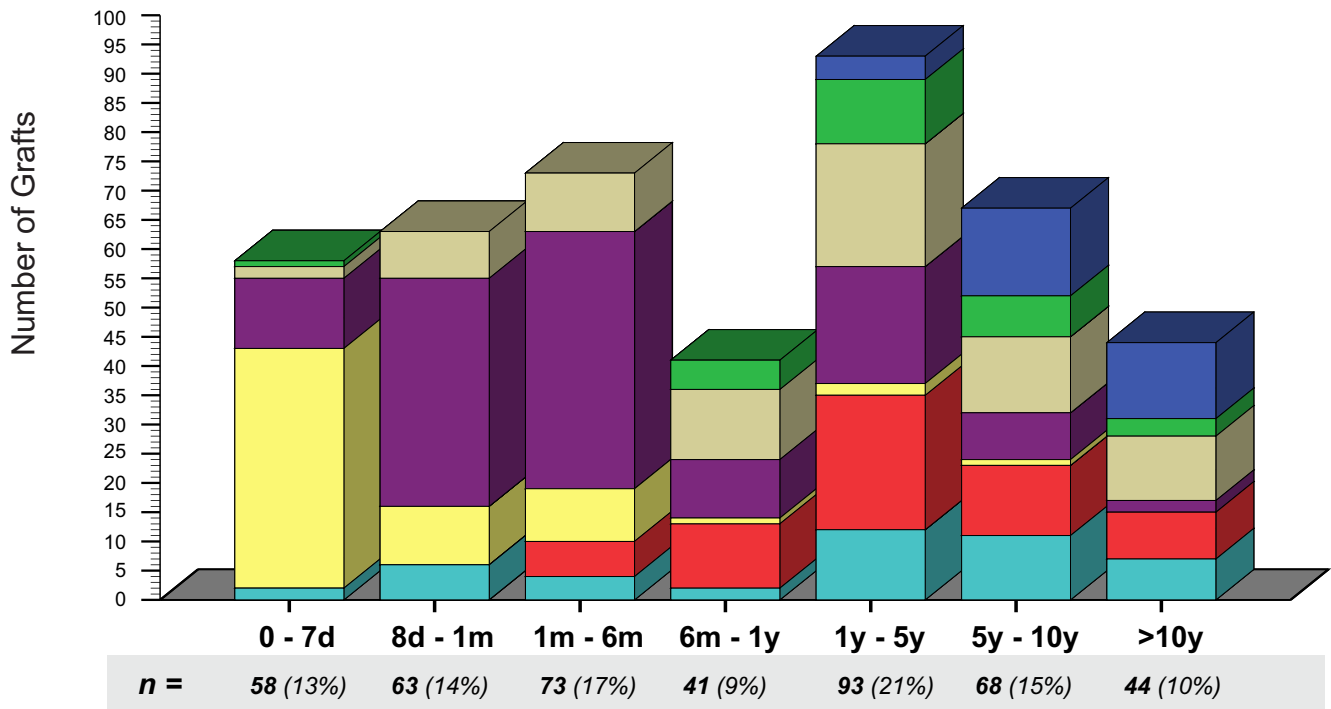


Adults (n= 291)

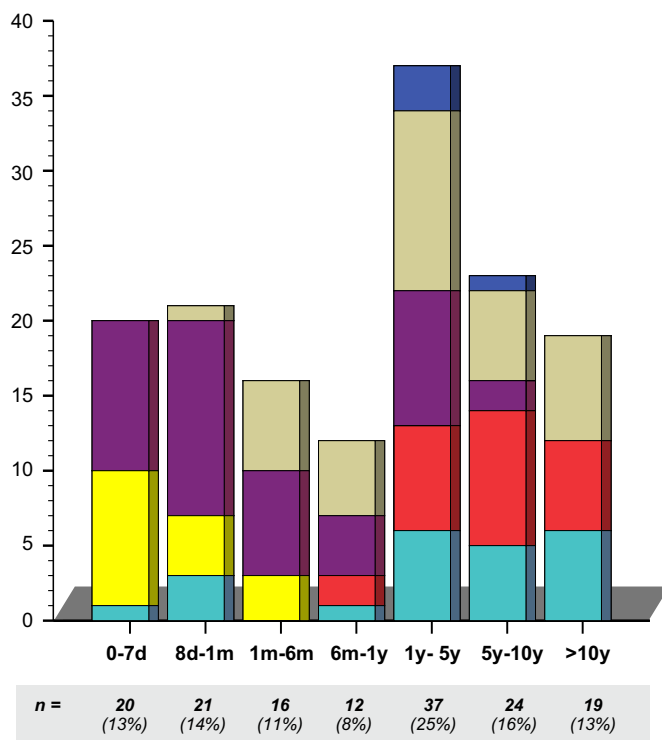


Indication for Retransplantation

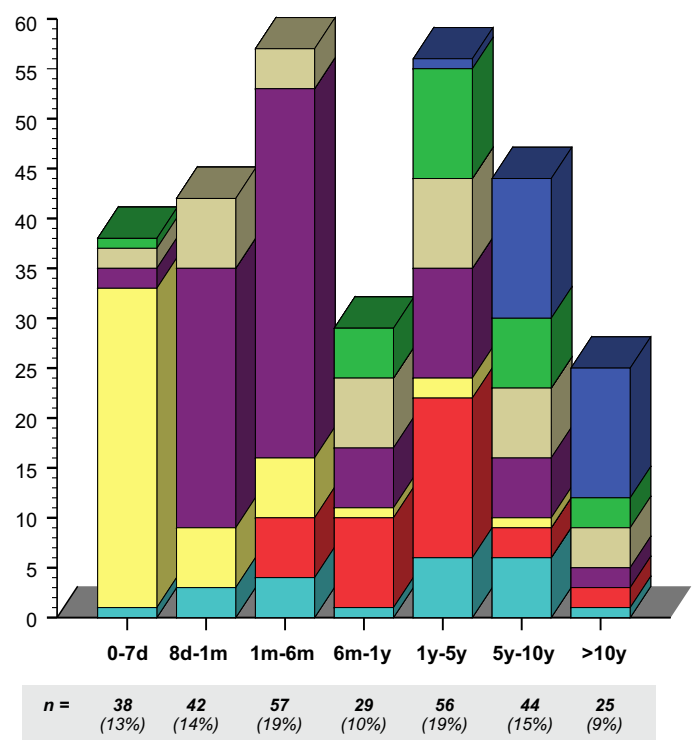
N = 440 (398 2nd grafts, 40 3rd grafts & 2 4th graft)



Children (n=149)



Adults (n=291)





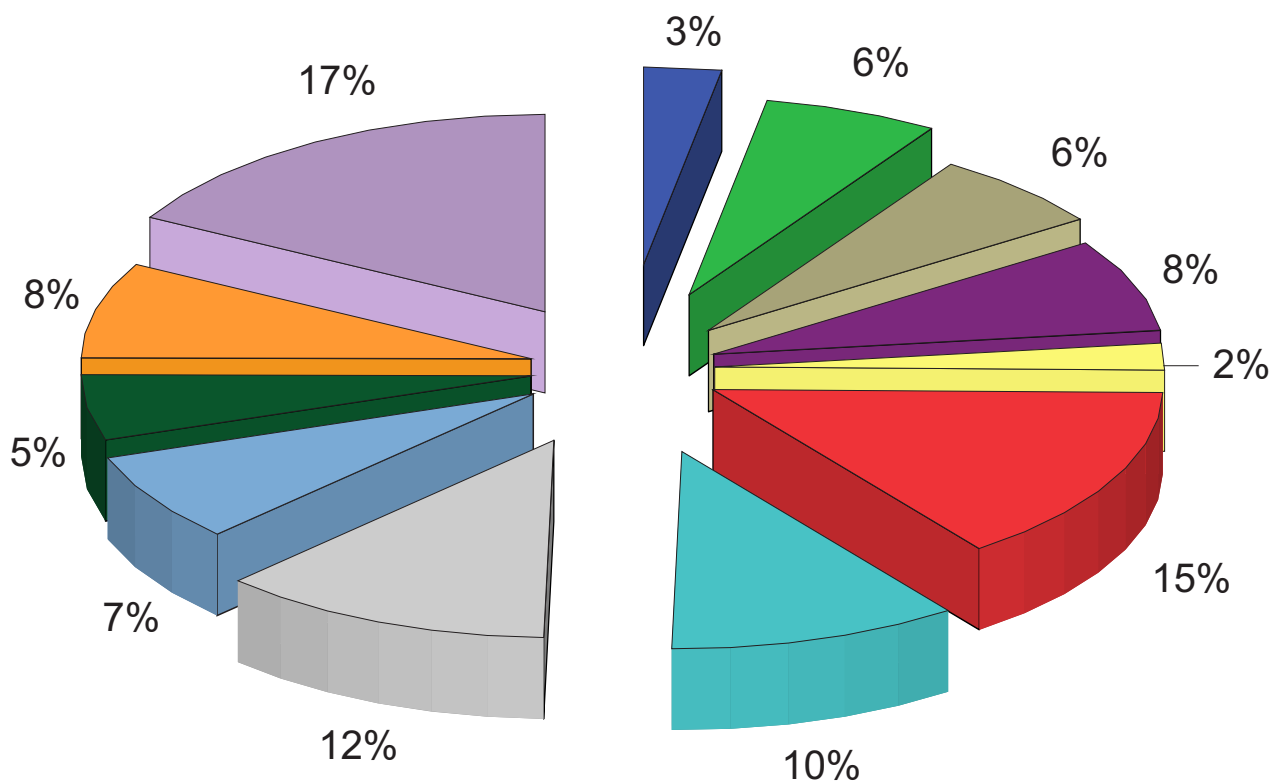
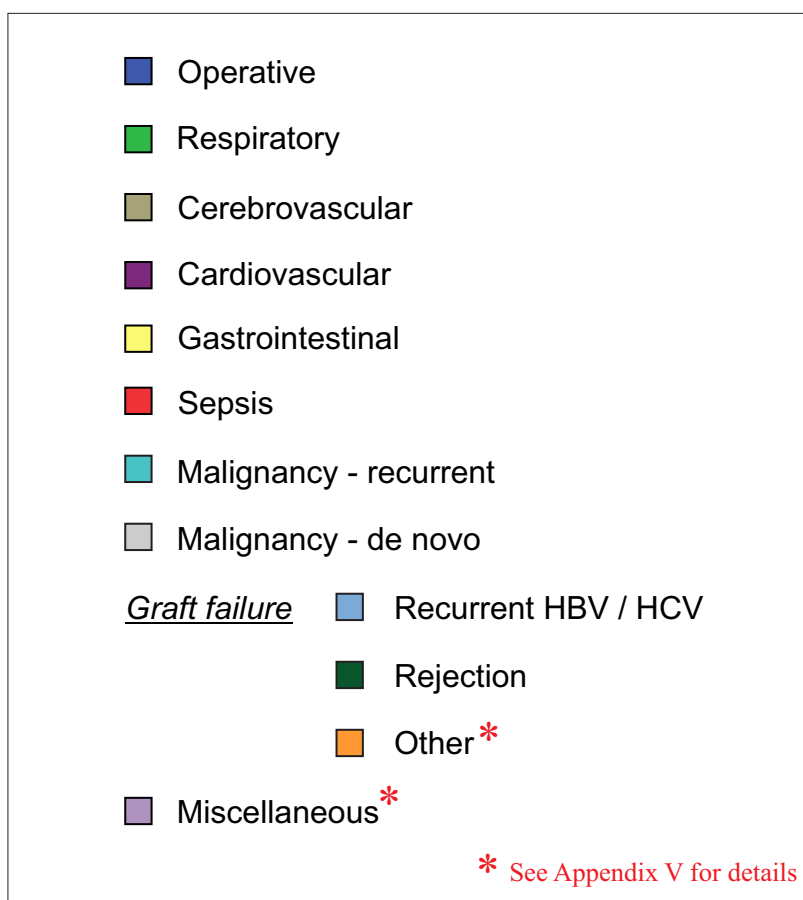
Section 5

Cause of Patient Death

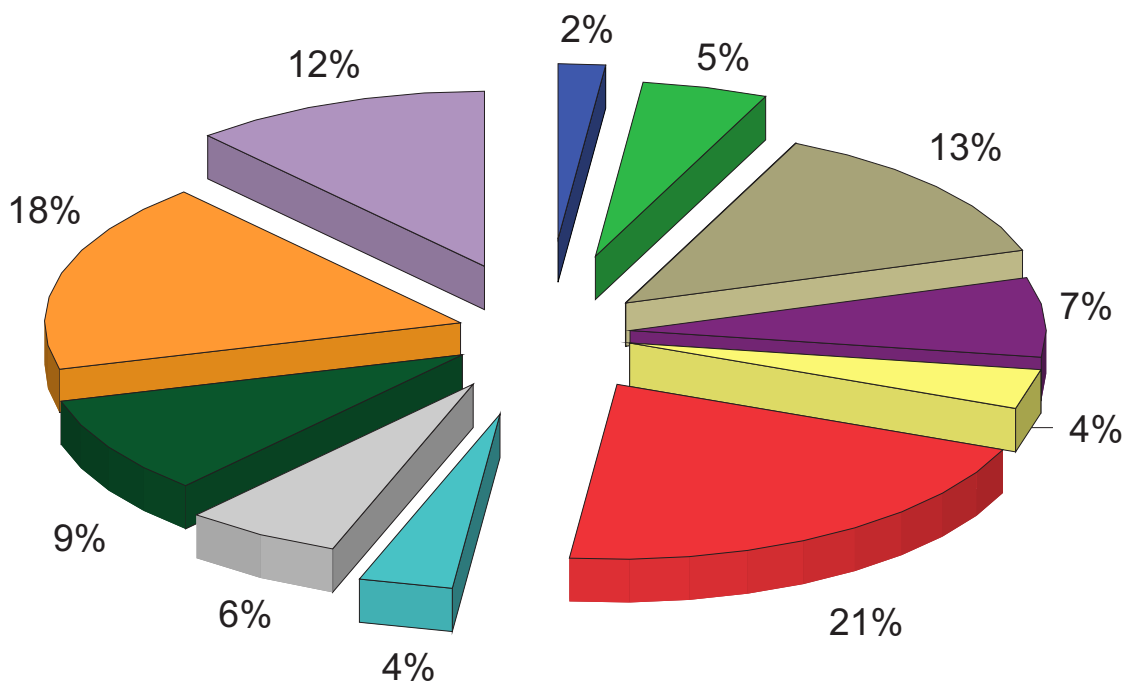




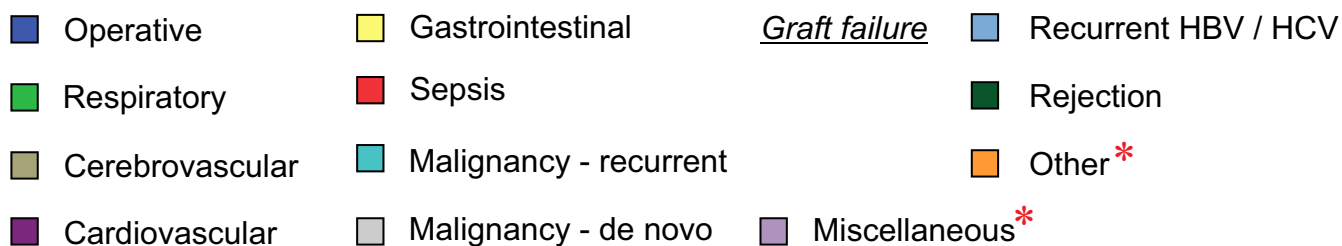
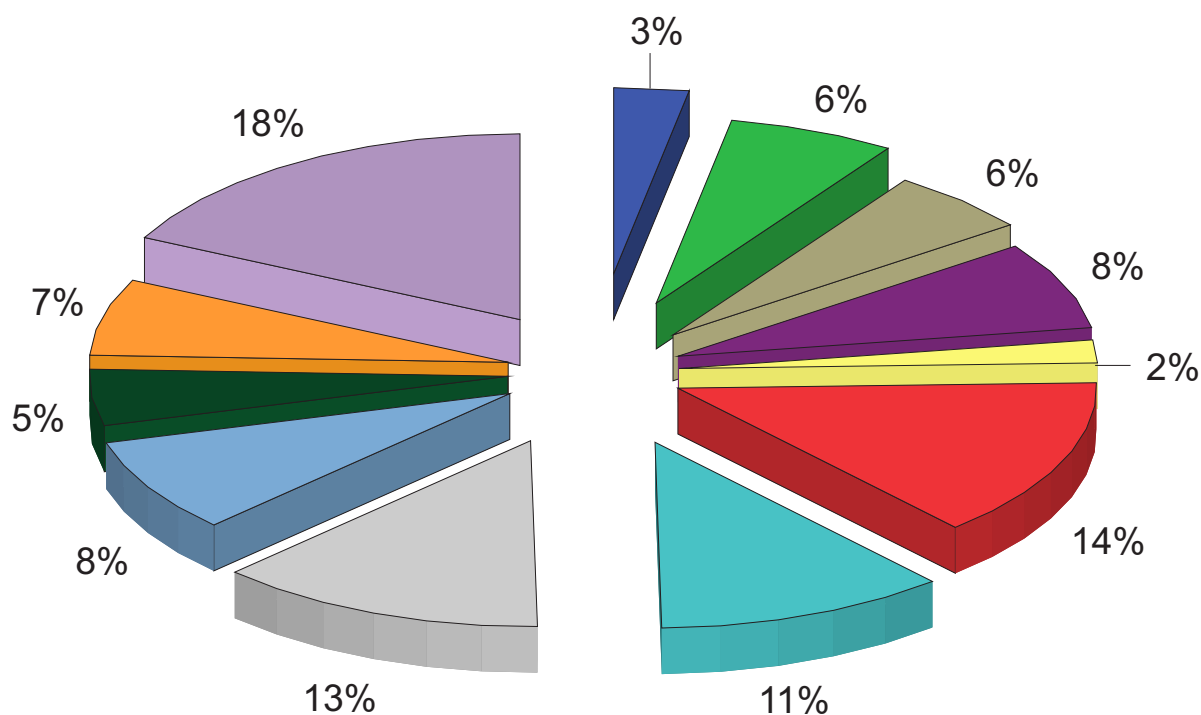
All Patients (N = 1519)



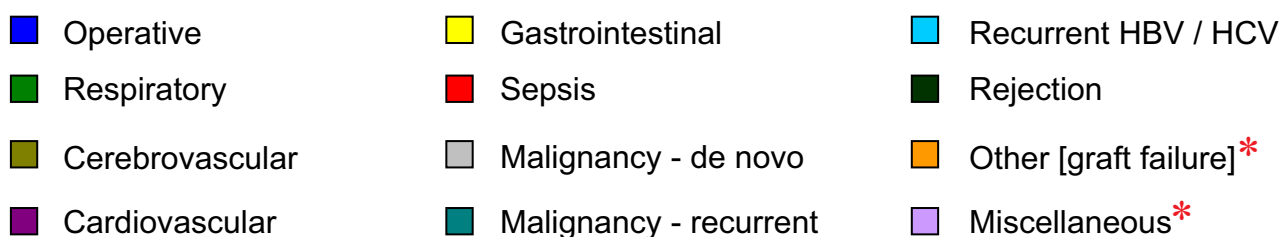
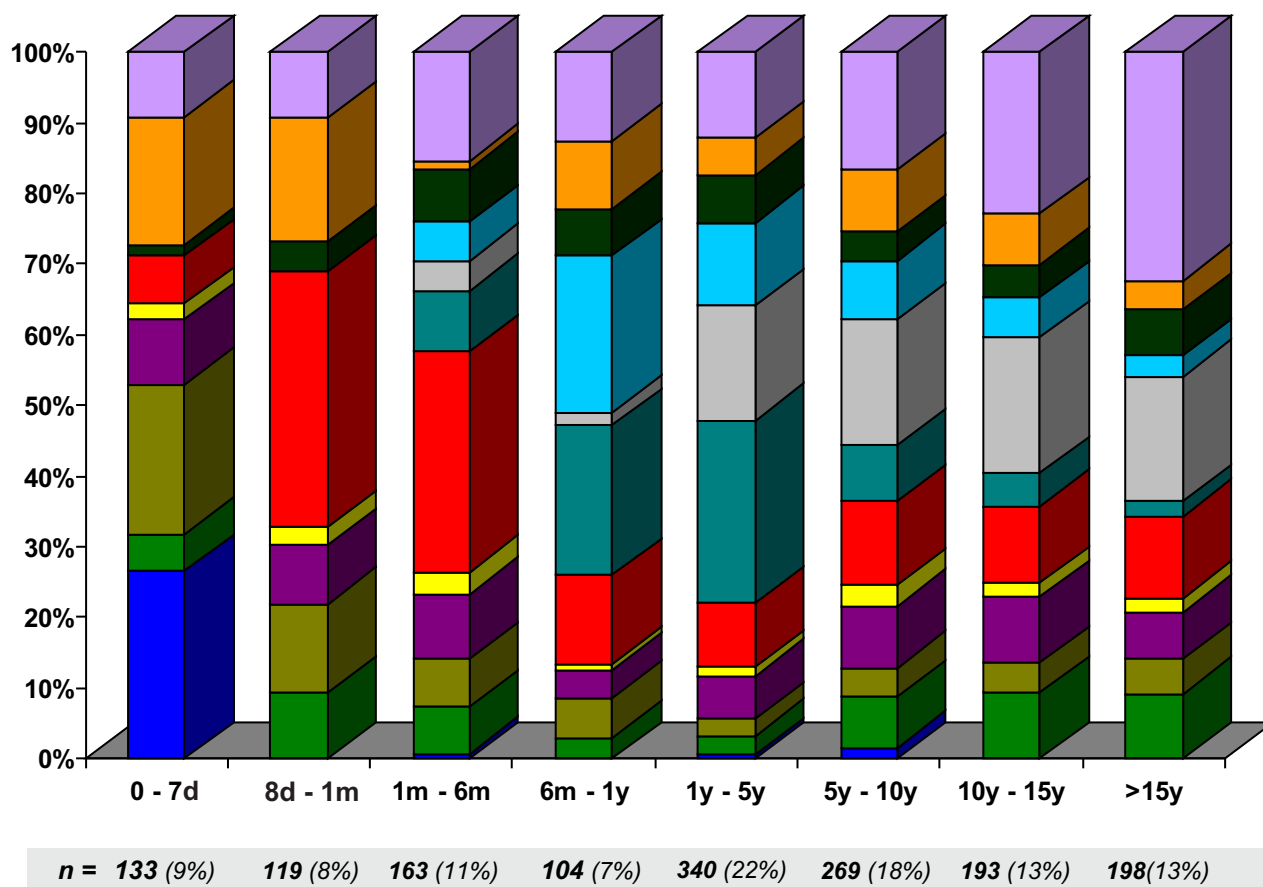
Causes of Death in Children N = 165



Causes of Death in Adult N = 1354



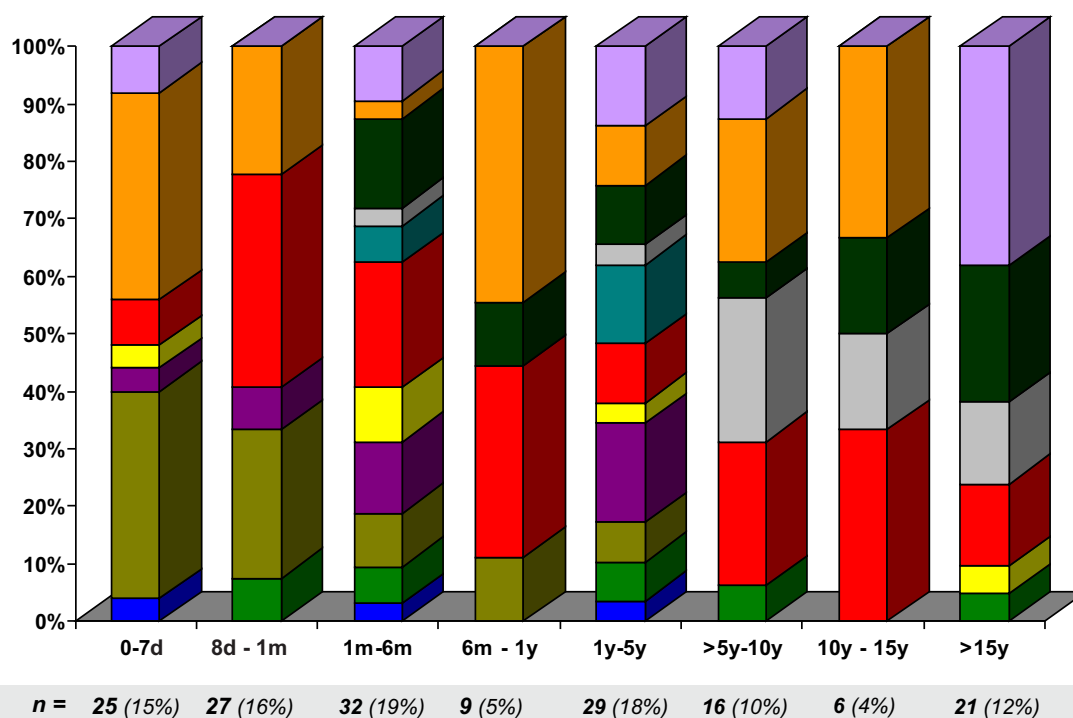
* See Appendix V for details



* See Appendix V for details

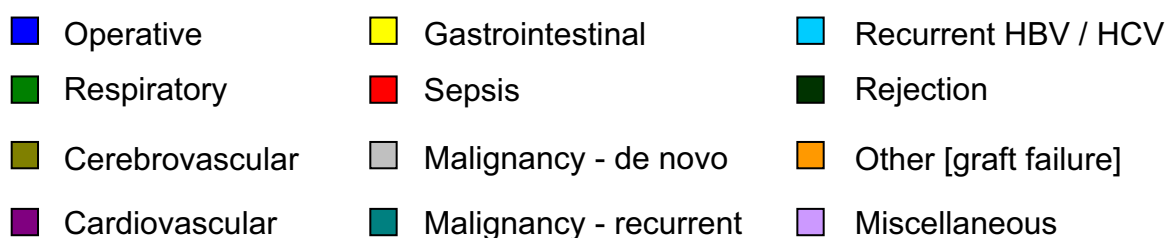
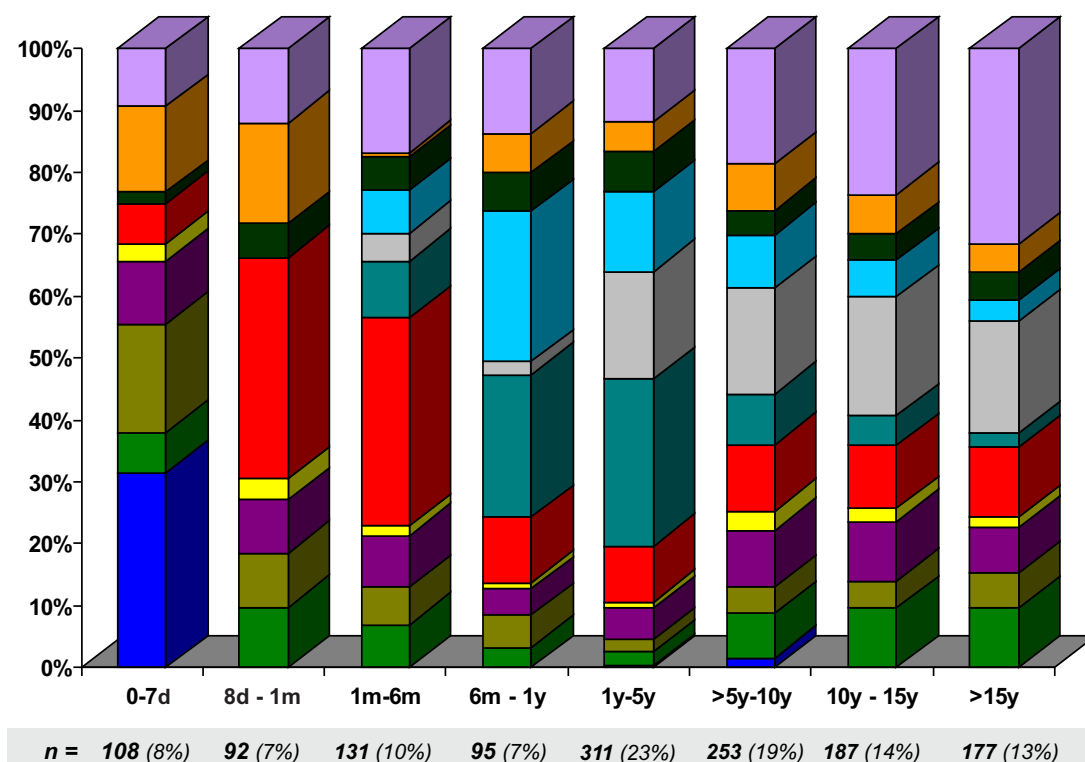


Children (N=165)



Cause of Death by Time Post Transplant

Adult (N=1354)





Section 6

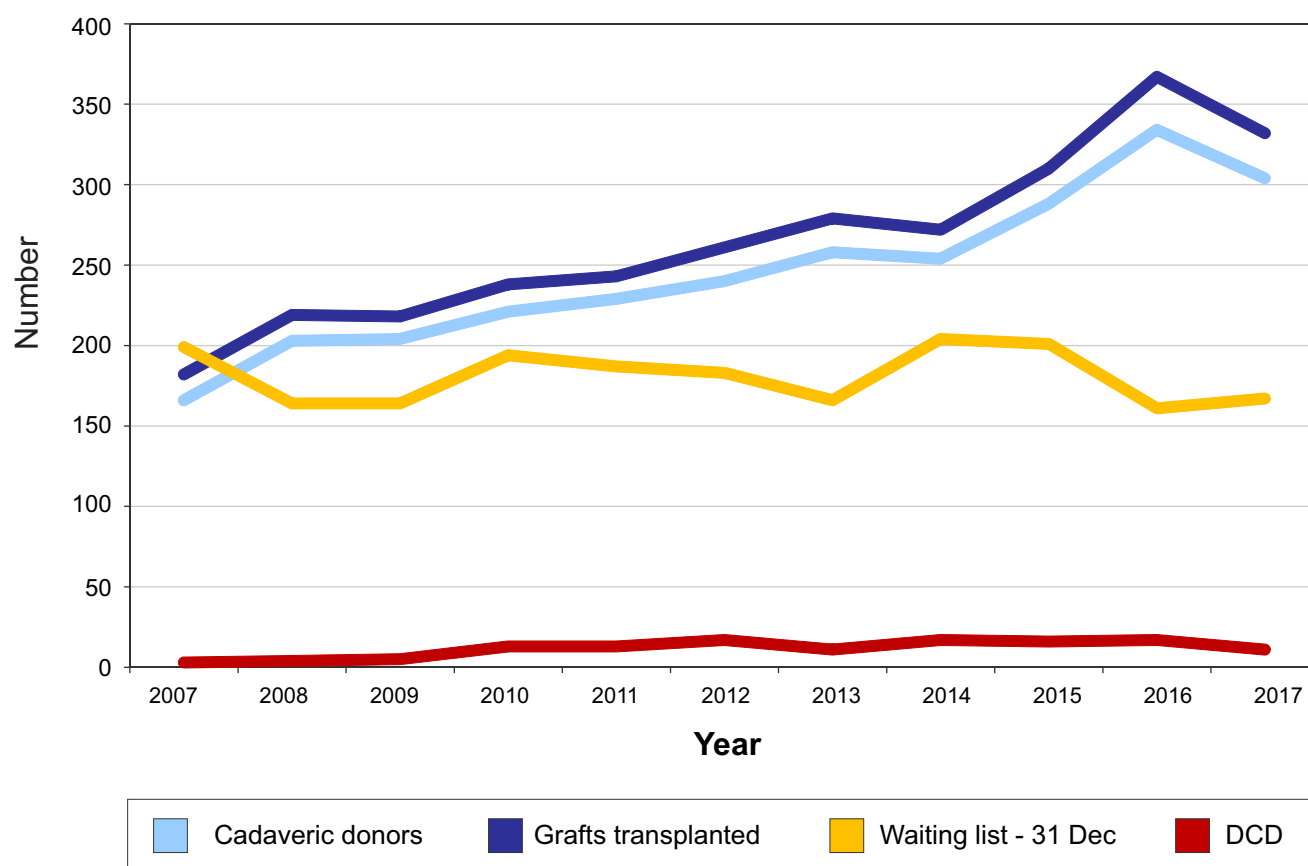
Deceased Donor Information





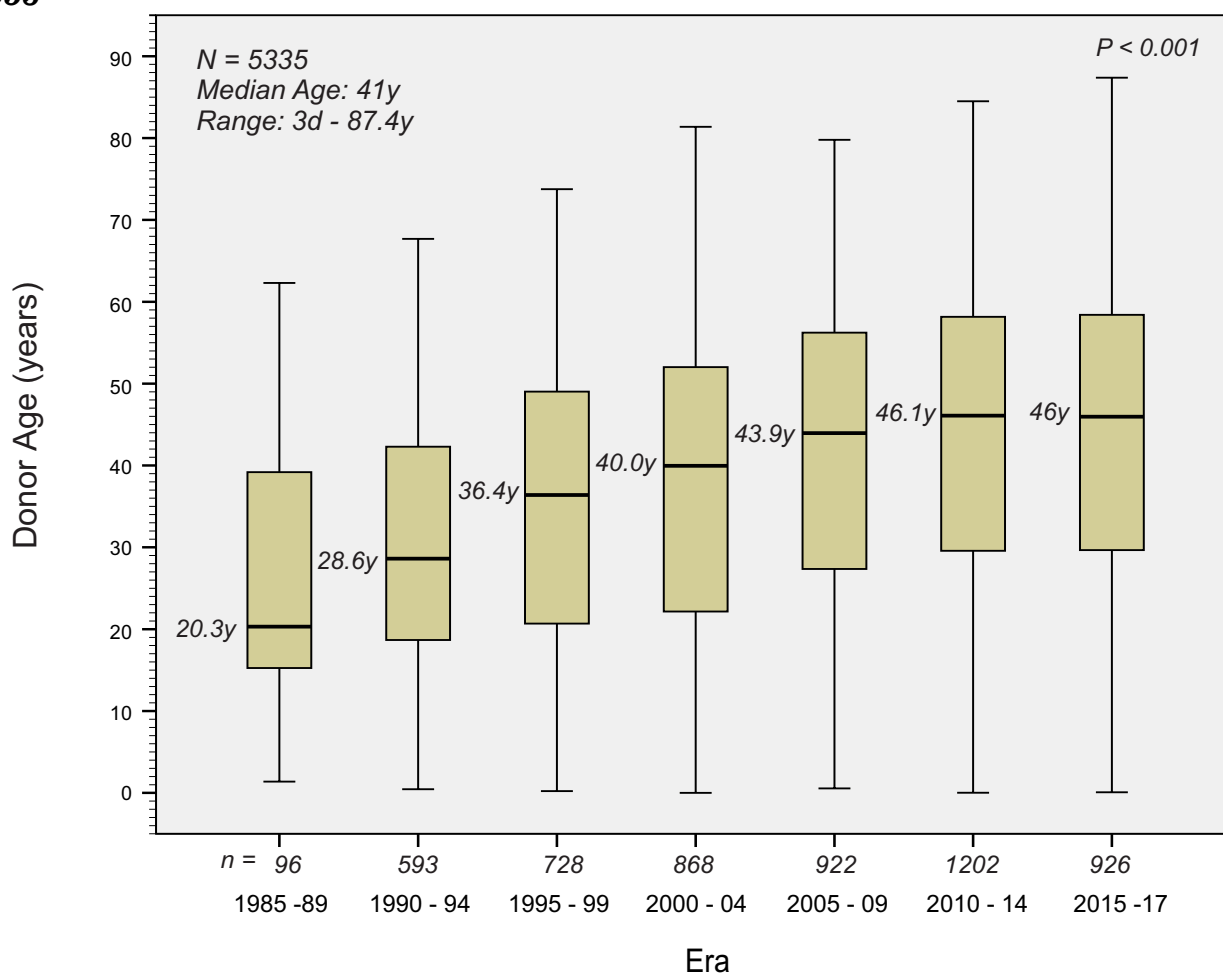
	QLD	NSW/ACT	VIC/TAS	SA/NT	WA	NZ	TOTAL
2008	33	40/3	41/5	31/1	25	23	203
2009	35	46/4	36/5	28/2	15	33	204
2010	30	55/8	53/6	18/2	17	32	221
2011	44	52/7	49/3	22/2	20	30	229
2012	46	50/7	52/10	21/6	20	28	240
2013	40	66/5	54/7	23/5	33	25	258
2014	44	45/7	62/8	27/4	25	32	254
2015	48	72/8	52/7	26/4	30	41	288
2016	69	74/12	61/4	28/4	33	51	334
2017	56	69/4	58/12	20/3	34	48	304

Grafts from deceased donors



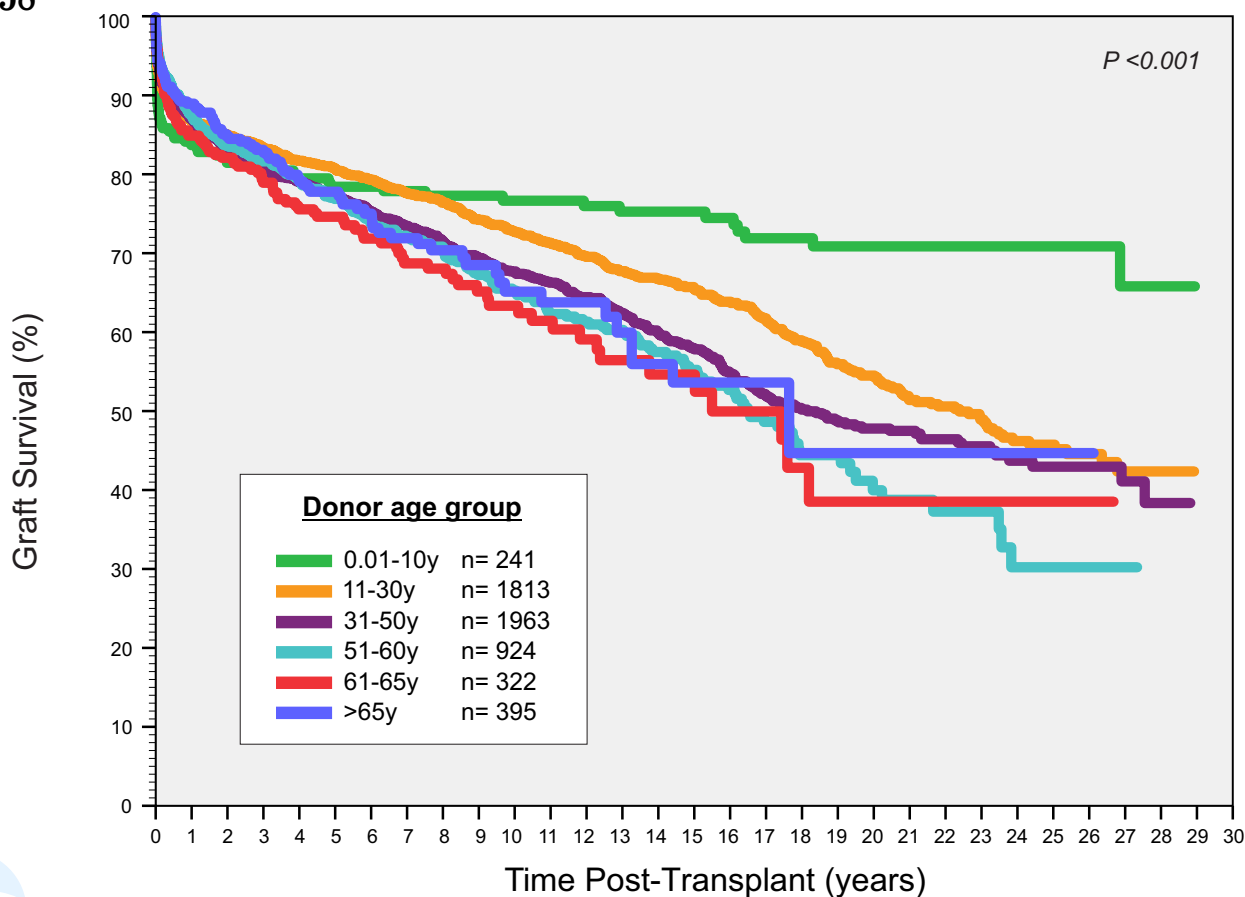
Donor Age by Era

N = 5335



Graft Survival by Donor Age

N = 5658





Section 7

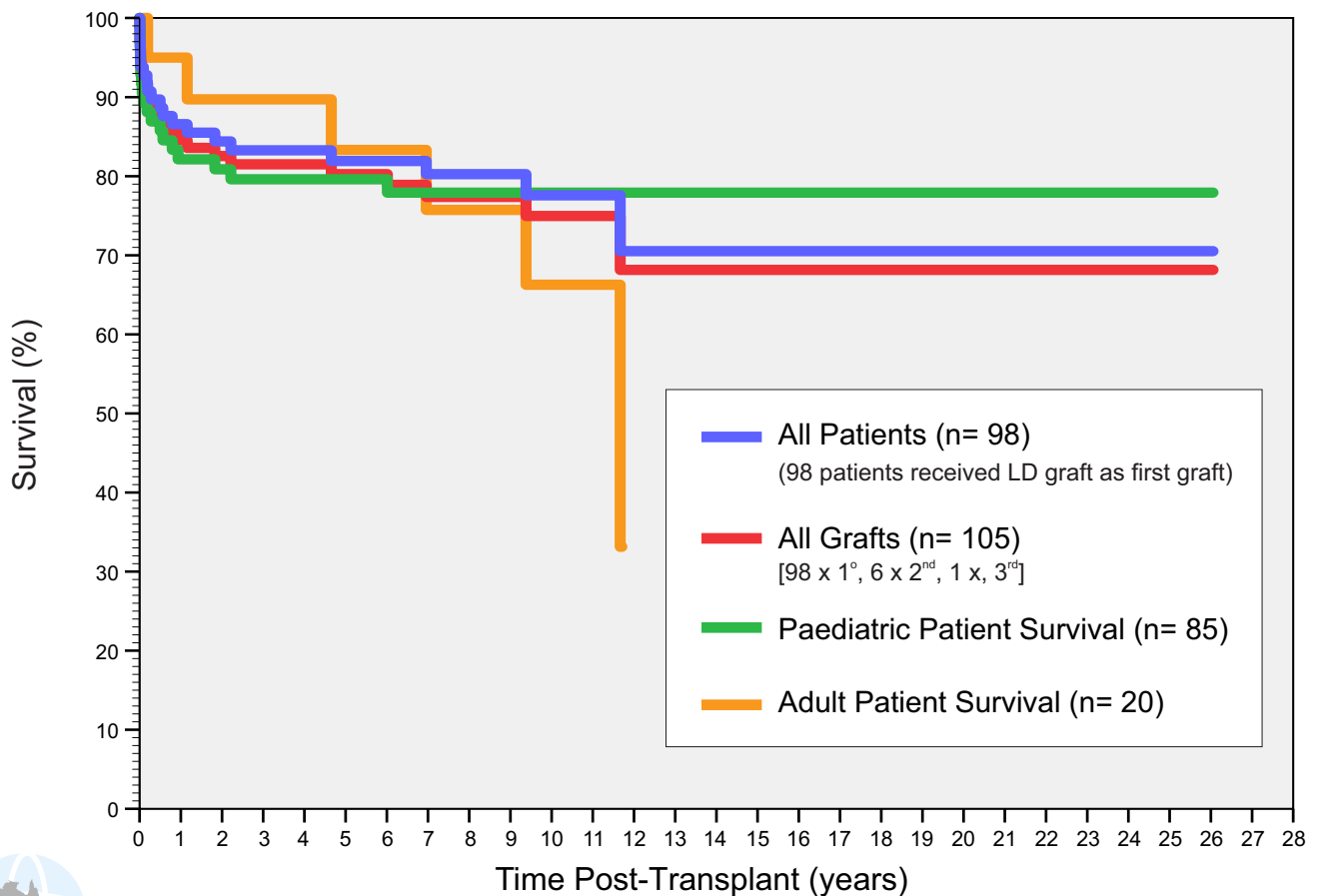
Living Donor Transplantation





	Recipient Age Group		
	Child [n=85]	Adult [n=20]*	All [n=105]
Donor gender	-	-	-
Male	45	13	58
Female	40	7	47
Donor age	-	-	-
Median	34.5y	31.7y	33.8y
Range	19.0 - 54.5y	18.3 - 54.4y	18.3 - 54.5y
Donor relationship	-	-	-
Mother	23	-	23
Father	35	1	36
Son	-	5	5
Daughter	-	2	2
Grandmother	2	-	2
Grandfather	1	-	1
Sister	-	3	3
Brother	2	3	5
Aunt	8	-	8
Uncle	2	-	2
Family friend	8	1	9
Cousin	4	-	4
Spouse	-	1	1

* 4 x whole liver domino transplant





Section 8

Waiting List



Waiting List Activity

[Data 1/1/13 - 31/12/17]



Activity	2013	2014	2015	2016	2017				
Listed at 1 January	186	164	206	211	161	-	TOTAL 2017	Adult	Paediatric
Activated	360	407	404	406	-	416			
TOTAL	546	571	610	617	161	416	577	344	72
OUTCOME					OUTCOME				
Transplant	284 [52%]	278 [49%]	316 [52%]	373 [60%]	101	236	337 [58%]	286 [83%]	51 [71%]
Delisted	98 [18%]	87 [16%]	83 [14%]	83 [13%]	28	45	73 [13%]	69	4
Died on list	26	18	21	12	4	9	13	12	1
Too sick	11	10	5	7	2	1	3	3	0
Tumour progression	16	15	20	17	6	9	15	15	0
Improved	24	18	17	25	10	9	19	17	2
Other	21*	26*	20*	22*	6	17	23*	22	1
Active at 31 Dec	164 [34%]	206 [36%]	211 [34%]	161 [26%]	32	135	167 [29%]	154	13

[* Patient declined, malignancy, drug use, infection, temporary delist for further investigations, medical]

Outcome of Initial Urgent Listing

OUTCOME	CATEGORY 1						
	2013 (n=19)	2014 (n=8)	2015 (n=25)	2016 (n=20)	2017		
					N=17	Adult n=14	Paediatric n=3
TRANSPLANTED	11 } 74%	6 } 88%	21 } 88%	17 } 95%	13 } 88%	10	3
IMPROVED	3 }	1 }	1 }	2 }	2 }	2	-
DIED / TOO SICK	5	1	3	1	2	2	-
OTHER TREATMENT	-	-	-	-	-	-	-

OUTCOME	CATEGORY 2						
	2013 (n=29)	2014 (n=22)	2015 (n=22)	2016 (n=25)	2017		
					N=19	Adult n=9	Paediatric n=10
TRANSPLANTED	22 } 89%	18 } 95%	20 } 95%	21 } 100%	18 } 100%	8	10
IMPROVED	4 }	3 }	1 }	3 }	1 }	1	
DIED / TOO SICK	2	-	-	-	-	-	-
OTHER TREATMENT	1 active 31/12/13	1 active 31/12/14	1 active 31/12/15	1 active 31/12/16			

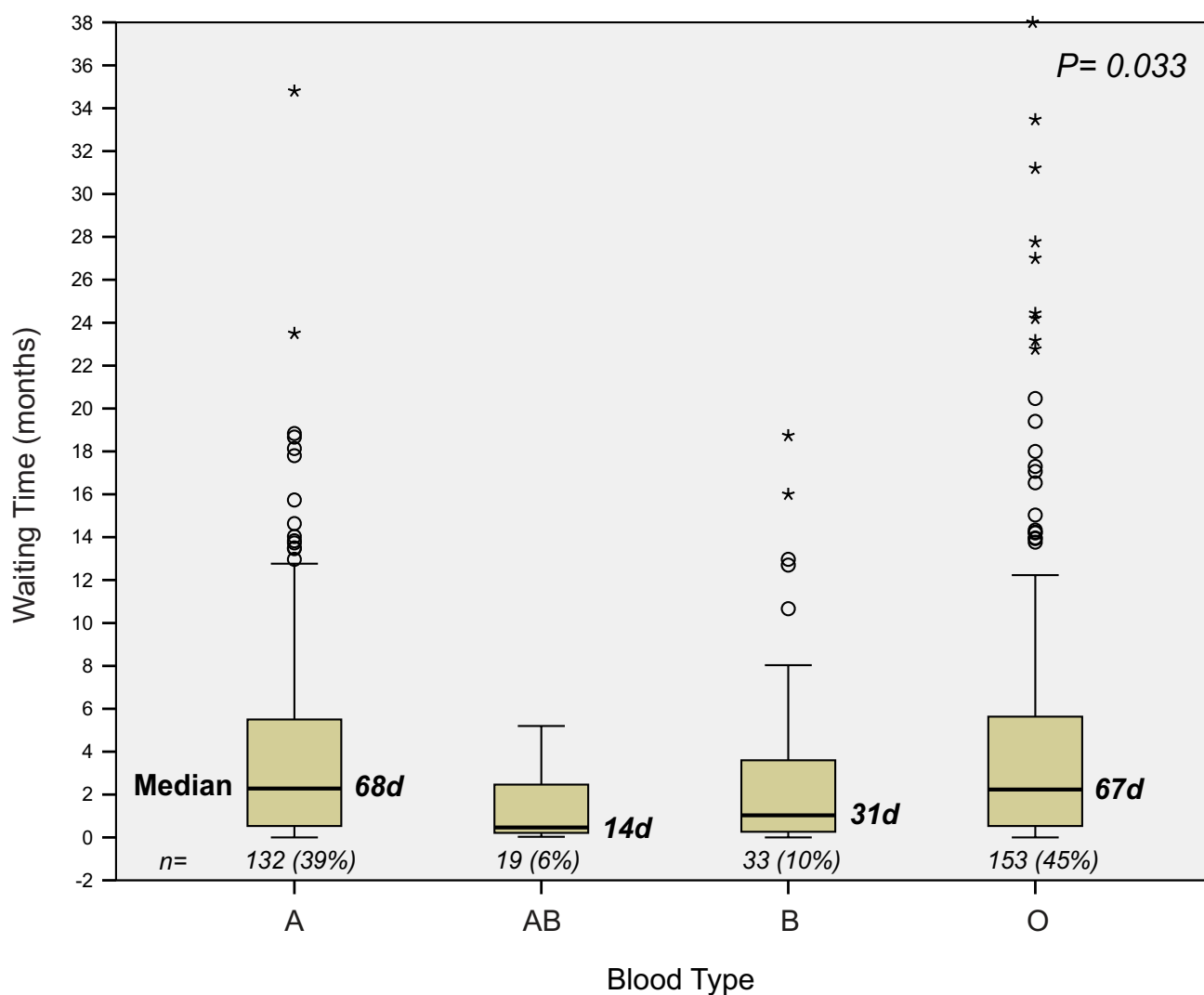


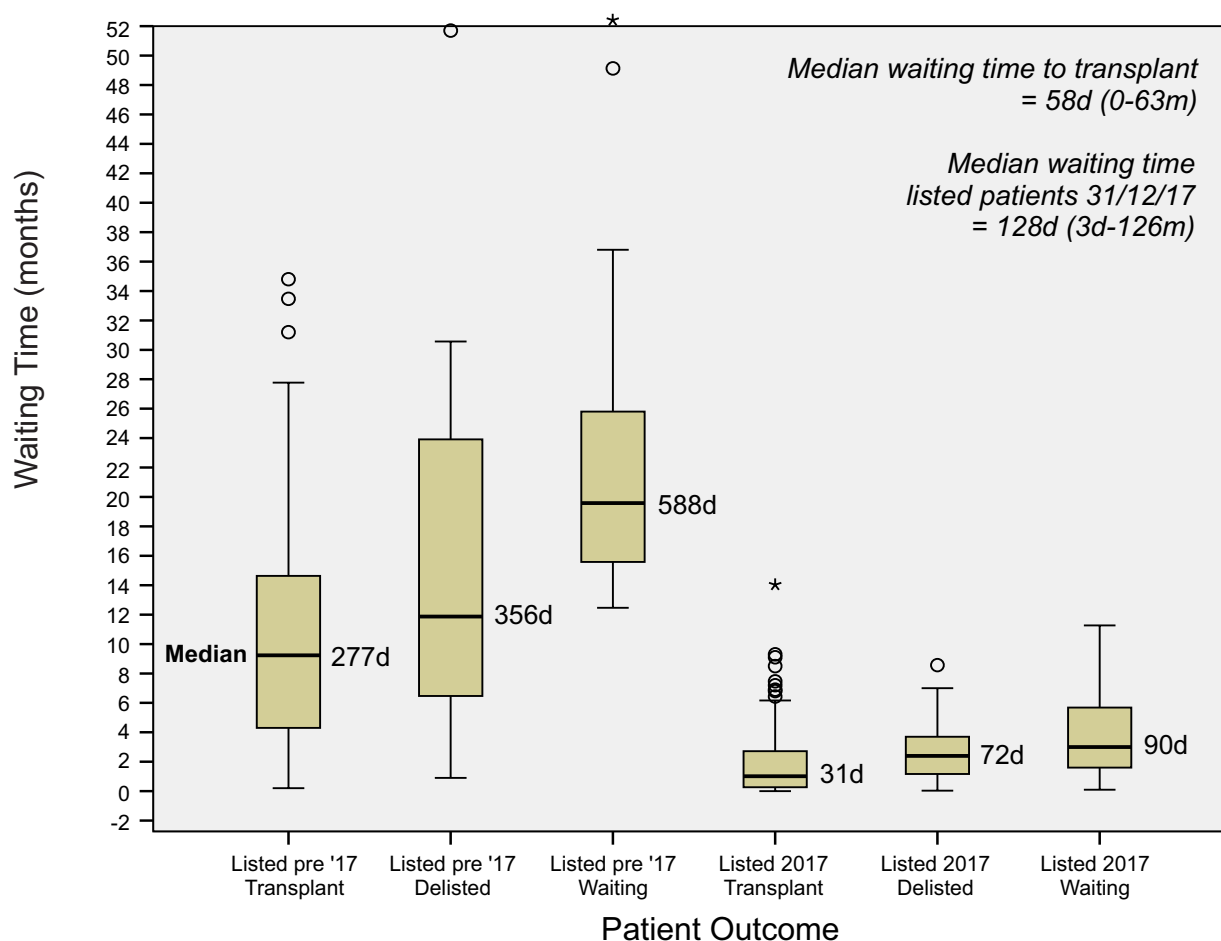
	Blood Group				
	A	O	B	AB	TOTAL
n=	224 (39%)*	257 (44%)	70 (12%)	27 (5%)	578
Not transplanted	92	104	37	8	241
Transplanted	132 (59%)**	153 (60%)	33 (47%)	19 (70%)	337 (58%)

* % of total number listed

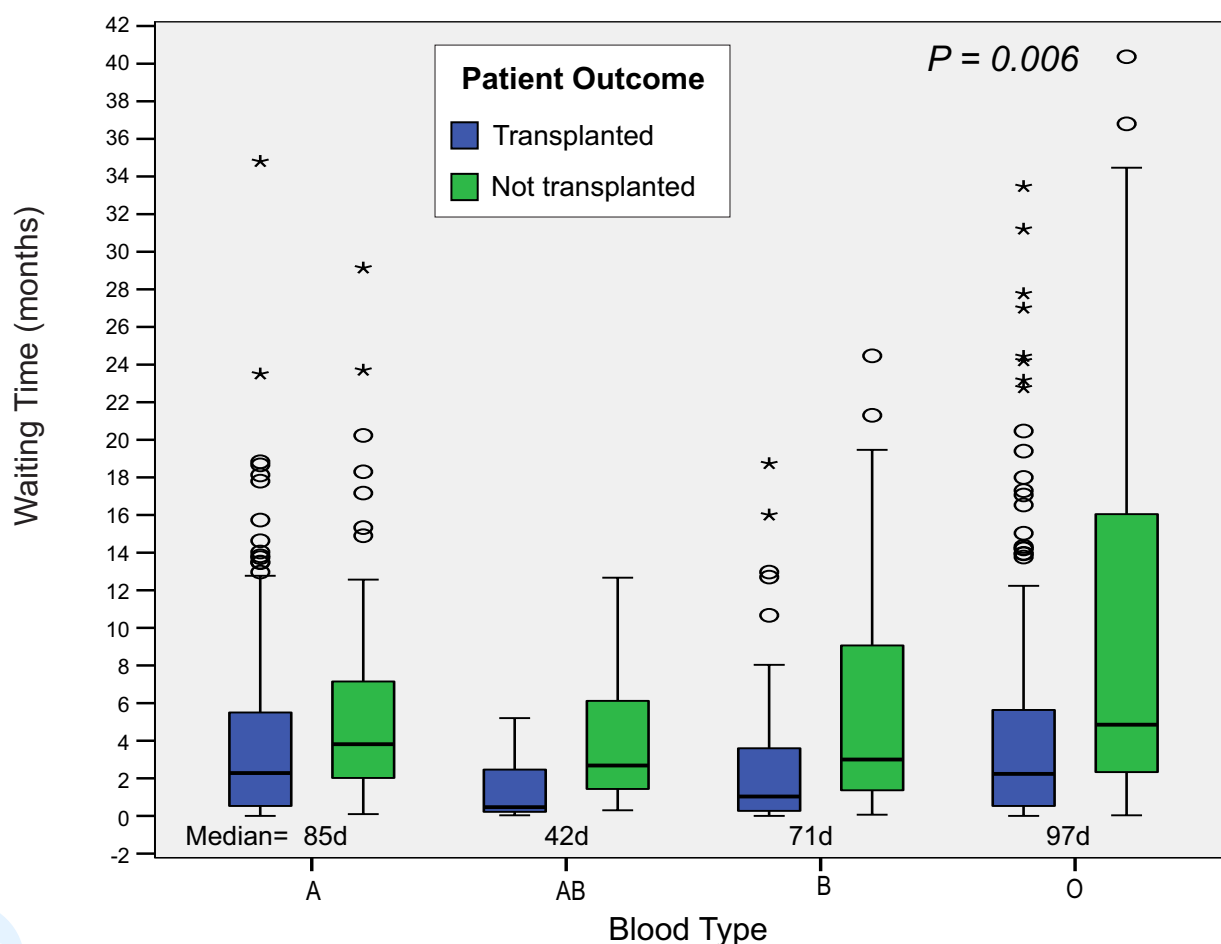
** % of blood group

Waiting Time to Transplant 2017





Waiting Time by Outcome & Blood Group





Section 9

Liver Transplantation and Cancer



Cancer in Liver Transplant Recipients

N = 5448



At Tx	Total number pts. transplanted = 5448	
Liver Cancer as indication for Transplant	508 (9%)	511 Ca
Liver Ca as a Secondary Diagnosis	751 (14%)	754 Ca
Total	1256*	(23%)
Post Tx		
Recurrent Liver Ca	165 (12% pts with Ca at Tx)	
De Novo Ca	439 (7%)	471 Ca
Skin Ca	844 (15%)	
Total	1448 (27%)	
Multiple Cancer types (non skin and skin)	343 (6% of all pts)	
Multiple non skin cancers	124 (2% of all pts)	
Developed non skin Ca < 90days	10	

* 3 pts had primary and a secondary liver cancer; 3 pts had multiple secondary liver cancers

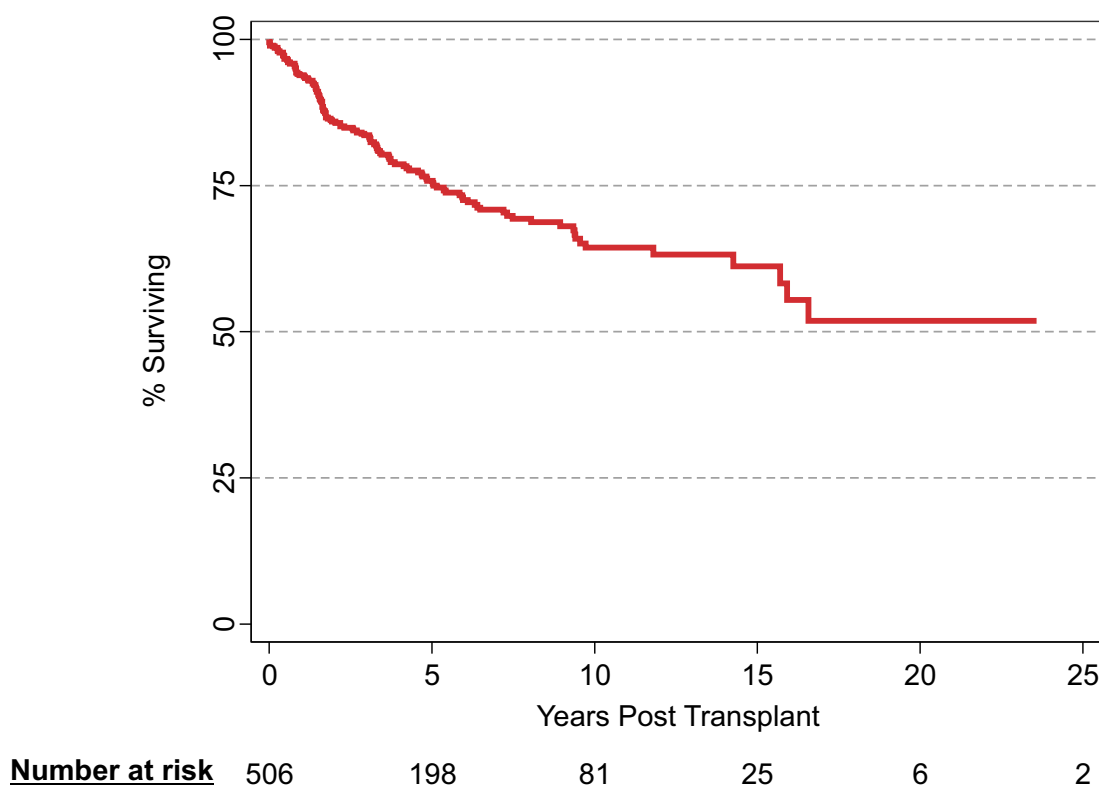
Liver Cancer as Primary Diagnosis

N = 508/5448 (9%)

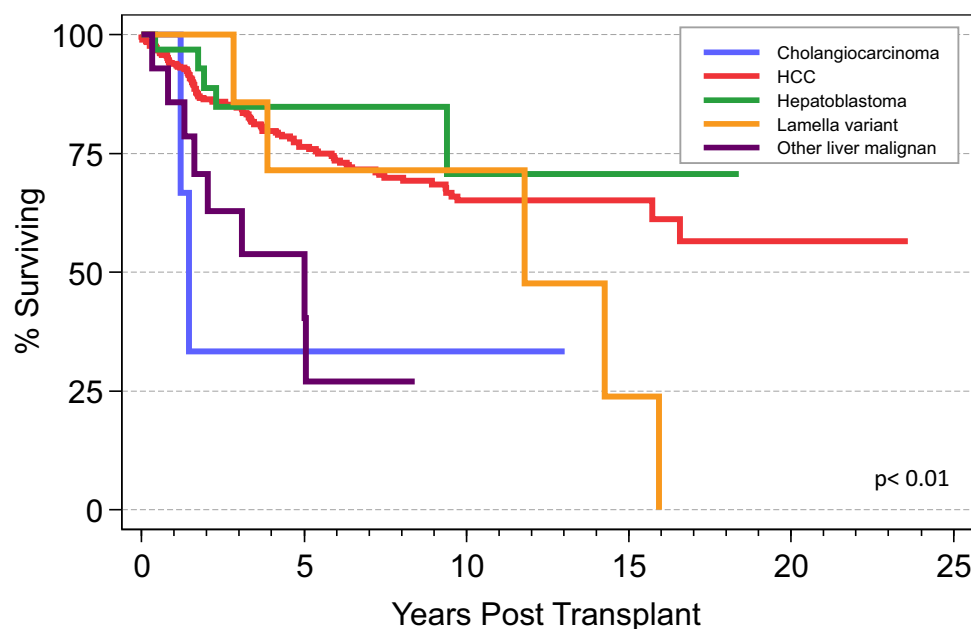
TYPE OF CA	No	DIED	DIED OF THIS CA
HEPATOCELLULAR CA	453	106	52 (12%)
HEPATOBLASTOMA	32	5	4 (14%)
FIBROLAMELLAR	7	5	2 (29%)
EPITHELOID HAEMANGIOENDOTHELIOMA	5	0	0
CHOLANGIOCARCINOMA	5	2	1 (25%)
CARCINOID	4	4	4 (100%)
HEPATOCELLULAR MALIGNANT NEOPLASM	1	0	0
ANGIOSARCOMA	1	1	1 (100%)
GASTRINOMA	1	1	1 (100%)
PANCREATIC ISLET CELL	1	1	1 (100%)
ERYTHROID LEUKAEMIA	1	1	1 (100%)
TOTALS	511* (9% of pts)	126 (25% of those with PCa)	67 (13% of those with PCa)

* 3 pts had two primary liver cancers

Overall Survival
Primary Liver Cancer
N = 508/5448 (9% of pts transplanted)



Overall Survival
Primary Liver Cancer
N=508*/5448 (9%)

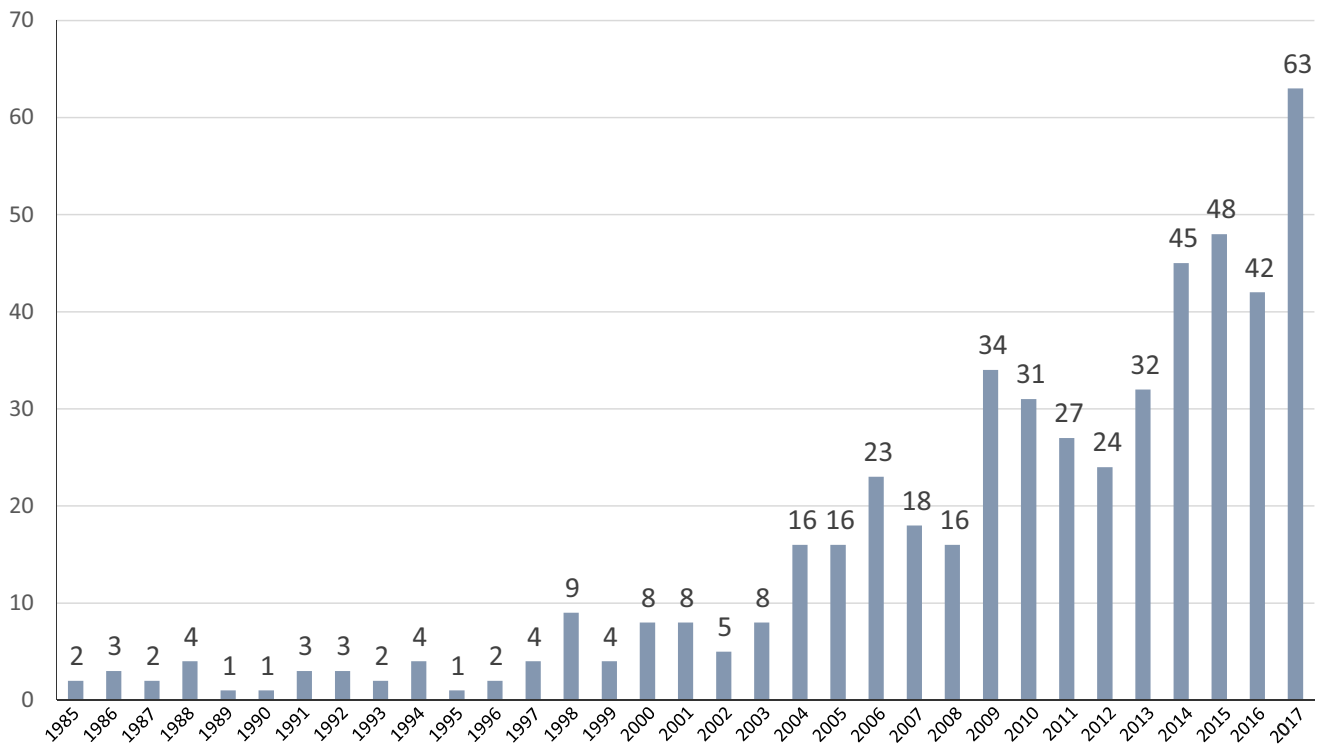


	Number at risk					
	5	1	1	0	0	0
Cholangiocarcinoma	5	1	1	0	0	0
HCC	448	173	72	21	4	0
Hepatoblastoma	32	15	4	2	1	1
Lamella variant	7	5	3	1	0	0
Other liver malignan	14	4	1	1	1	1

* 3 pts had two primary liver cancers

Primary Liver Cancer Incidence

N = 508/5448 (9%)



* 3 pts had two primary liver cancers

Liver Cancer as a Secondary Diagnosis

N=751/5448 (14% pts)

	No	Died	Died of This Cancer
HEPATOCELLULAR CA*	694	195	59 (9%)
CHOLANGIO CA	46	34	22 (48%)
OTHER	7	5	2 (29%)
FIBROLAMELLAR	4	0	0
HEPATOBLASTOMA*	3	2	0
Total	754* Ca in 751 pts	236 (31% of pts with SCa)	83 (12% of pts with SCa)

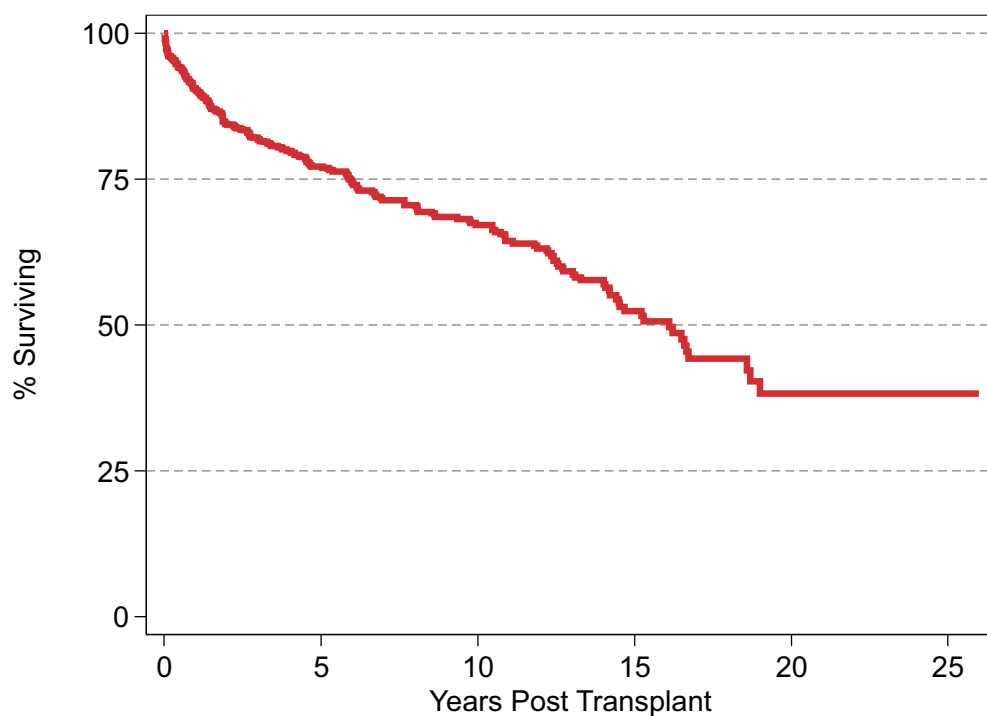
* 3 patients had 2 secondary cancers



Overall Survival

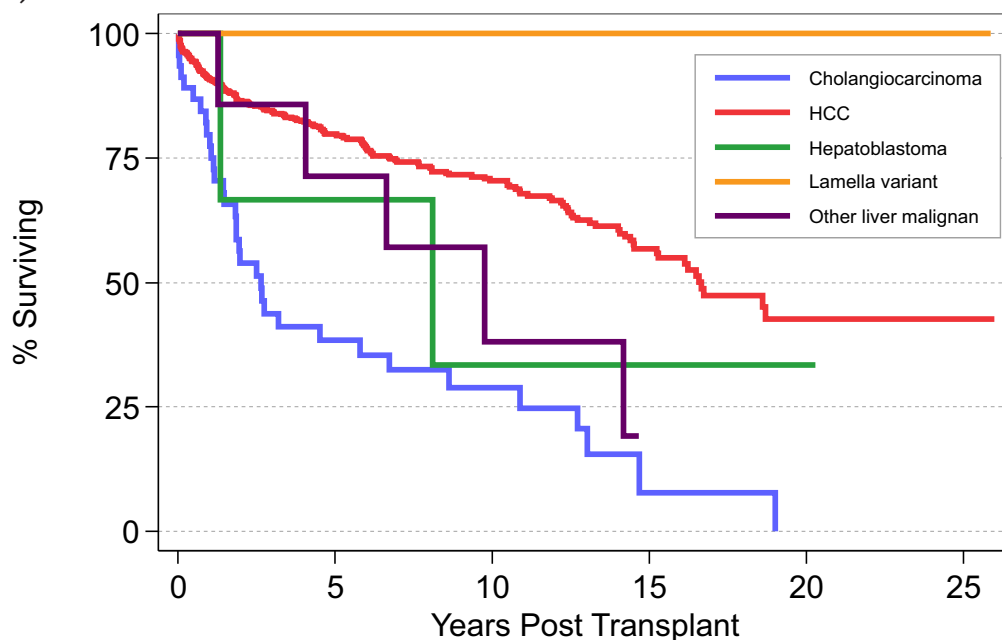
Liver Cancer as a Secondary Diagnosis

N = 751/5448 (14% pts)



Liver Cancer as a Secondary Diagnosis

N = 751/5448 (14% pts)



	Number at risk					
Cholangiocarcinoma	46	14	7	1	0	0
HCC	689	342	172	62	11	2
Hepatoblastoma	3	2	1	1	1	0
Lamella variant	4	4	1	1	1	1
Other liver malignan	7	5	2	0	0	0

Liver Cancer - (Primary or Secondary Diagnosis)

N= 1306/5448 (23%)



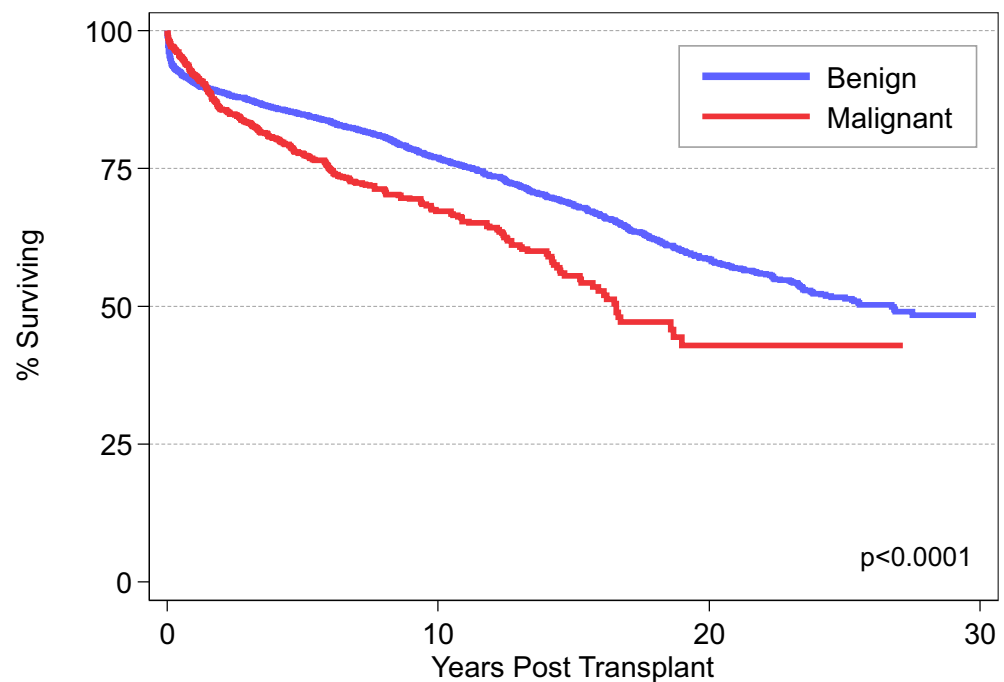
TYPE OF CA	No.	DIED	DIED OF THIS CA
HEPATOCELLULAR CA*	1198	301	111 (9%)
CHOLANGIOCARCINOMA*	49	35	23 (47%)
HEPATOBLASTOMA*	35	7	4 (11%)
FIBROLAMELLAR	10	5	2 (20%)
EPITHELOID HAEMANGIOENDOTHELIOMA	7	1	1 (14%)
ADENOCARCINOMA	4	3	0
CARCINOID	4	4	4 (100%)
ANGIOSARCOMA	2	2	2 (100%)
GASTRINOMA	1	1	1 (100%)
PANCREATIC ISLET CELL	1	1	1 (100%)
ERYTHROID LEUKAEMIA	1	1	1 (100%)
HEPATOCELLULAR MALIGNANT NEOPLASM (NOS)	1	0	0
TOTALS	1313* Ca in 1306 pts	361 (27% of those with Ca)	150 (11% of those with Ca at Tx)

* 4 patients had 2 secondary cancers; 3 patients had a primary and secondary cancer

Patient Actuarial Survival

Benign Disease vs Pre Transplant Liver Malignancy

N = 5448



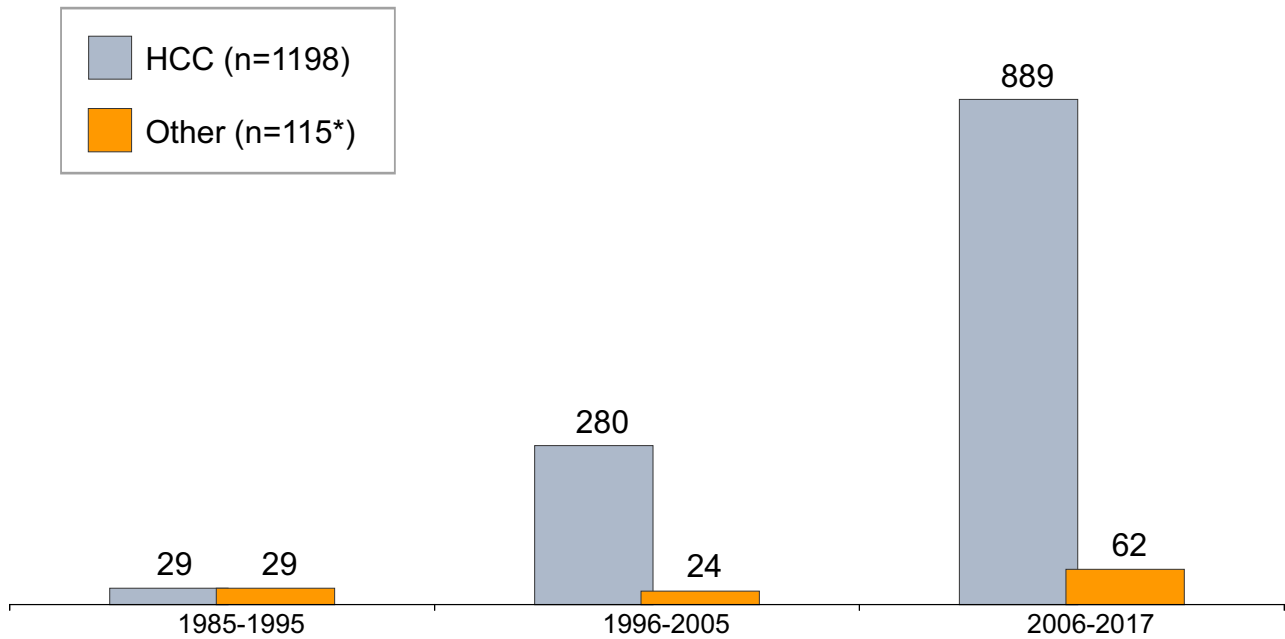
Number at risk

Benign	4094	1758	561	12
Malignant	1297	265	20	0



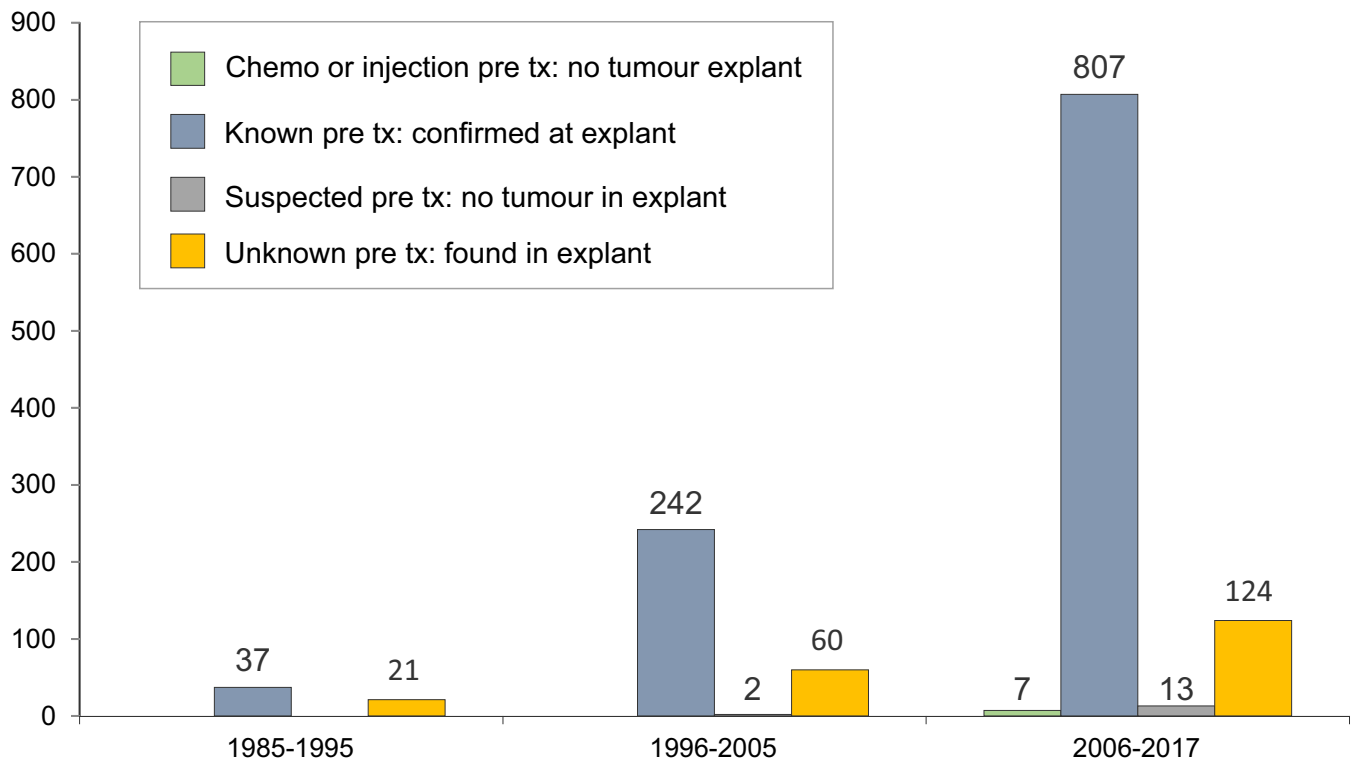
Liver Cancer at Transplantation

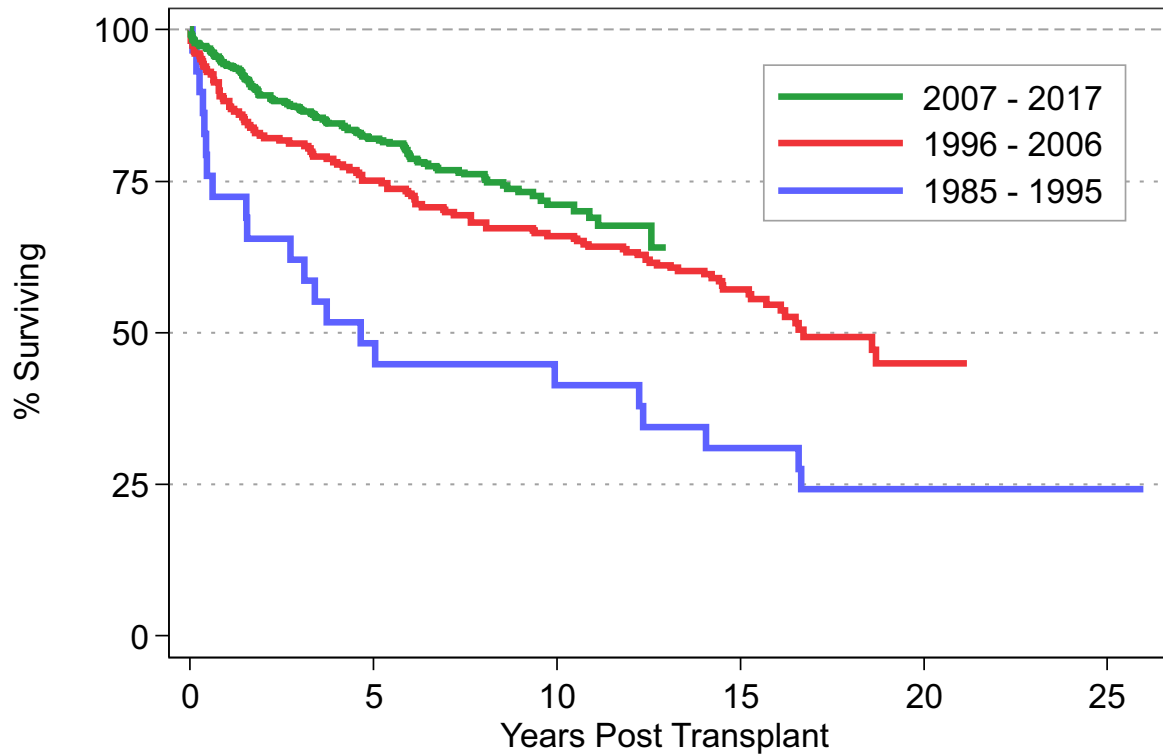
N = 1306/5448 (23%)



* 4 patients had 2 secondary cancers; 3 patients had a primary and secondary cancers

HCC at Transplantation



**Number at risk**

1985-1995	29	14	12	9	7	3
1996-2006	229	172	151	76	9	0
2007-2017	934	350	84	0	0	0

De Novo Non Skin Cancer

N = 439/5448 (8%)

	No	Male	Female	Age of pts (yrs)	Time to diagnosis (mths)	Died of This Cancer
Alimentary*	168	121	47	5 – 83 (m 59)	3 – 316 (m 79)	73 (43%)
Lymphoma*	114	64	50	1 – 79 (m 50)	1 – 283 (m 66)	43 (38%)
Genitourinary*	70	44	26	21 – 82 (m 61)	1 – 350 (m 81)	7 (10%)
Respiratory*	52	40	12	29 – 80 (m 60)	7 – 278 (m 102)	37 (71%)
Breast*	30	1	29	30 – 74 (m 55)	11 – 282 (m 98)	11 (37%)
Endocrine	11	5	6	36 – 70 (m 55)	35 – 346 (m 82)	3 (27%)
CNS*	8	5	3	16 – 75 (m 65)	14 – 212 (m 93)	6 (75%)
Miscellaneous*	6	3	3	57 – 73 (m 67)	61 – 191 (m 96)	4 (67%)
Leukaemia*	6	3	2	3 – 66 (m 49)	16 – 157 (m 37)	2 (33%)
Kaposi's	6	4	2	32 – 76 (m 56)	2 – 254 (m 17)	0
Total	*471 ca in 439 pts	291	180	1 – 83 (m 59)	1 – 350 (m 64)	186 (39% of pts with Ca)

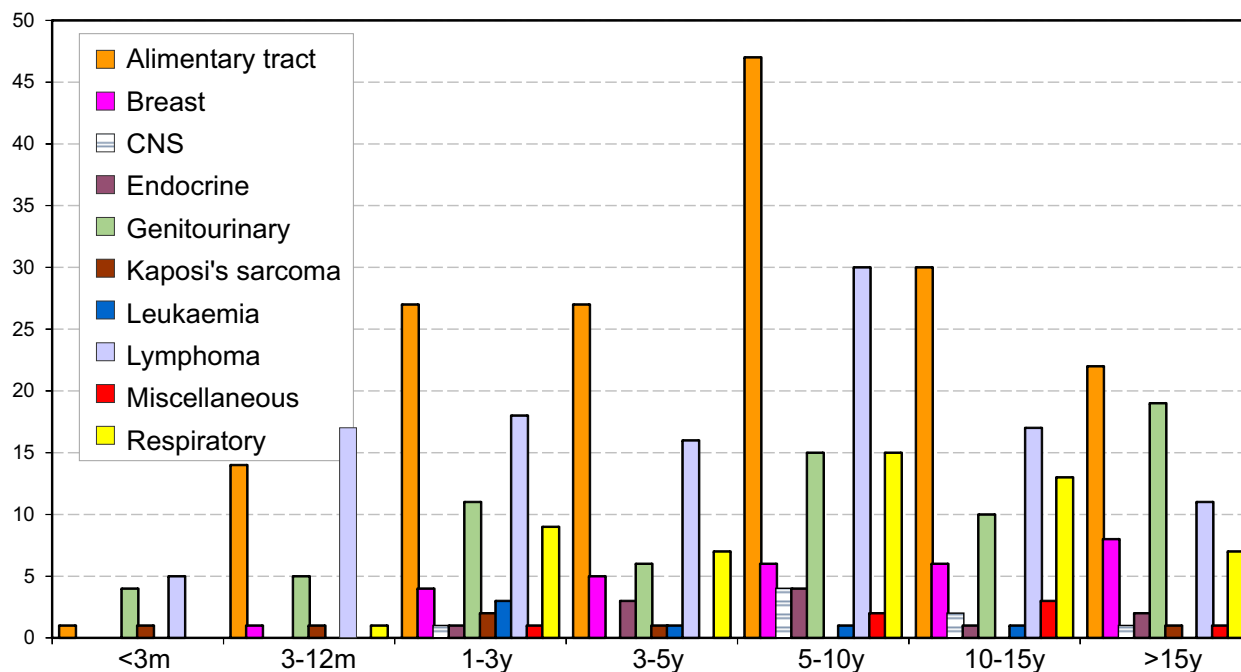
* 29 patients had 2 de novo cancer, 3 patients had 3 de novo cancers
m=median

Time to Diagnosis of De Novo Non Skin Cancer (3m - >15y)

N = 5448



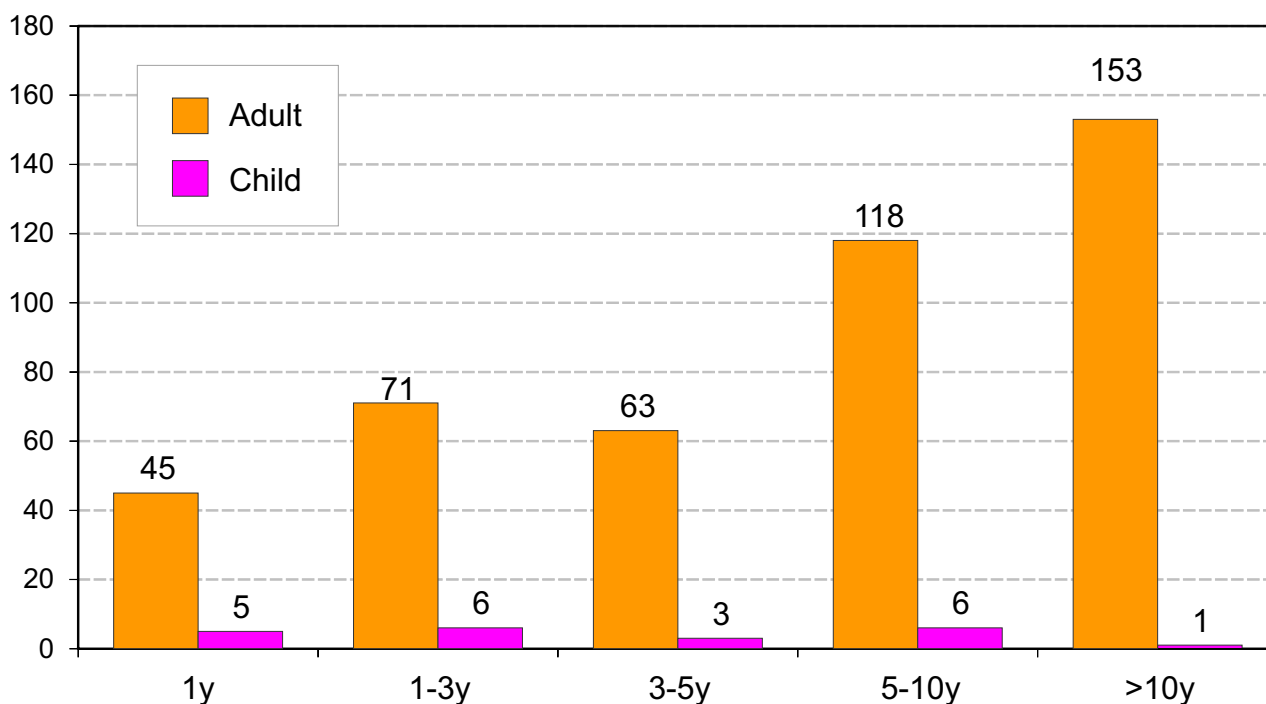
471 cancers in 439 pts (8% of all pts)



Time to Diagnosis of Any Non Skin Cancer (3m - >10y)

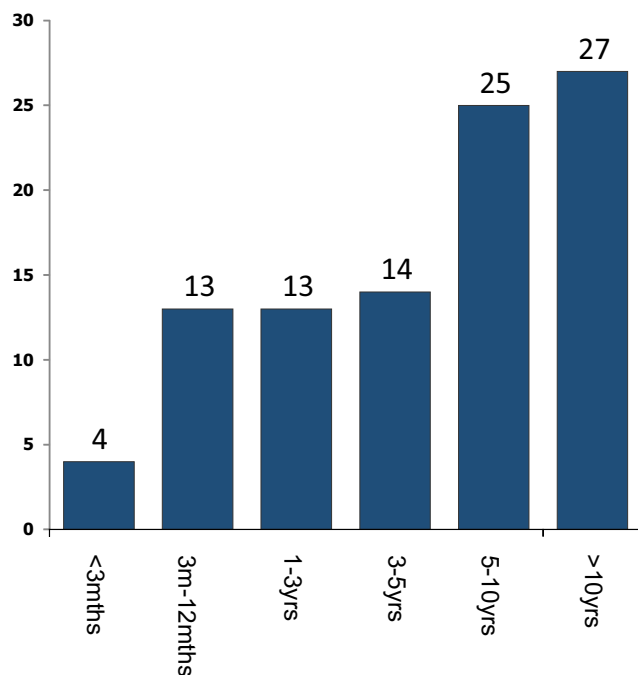
N = 5448

471 cancers in 439 pts (8% of all pts)

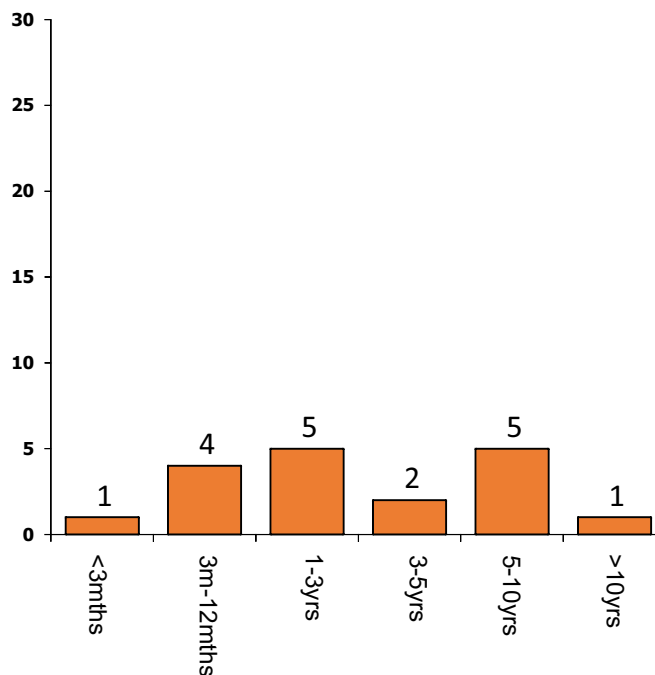




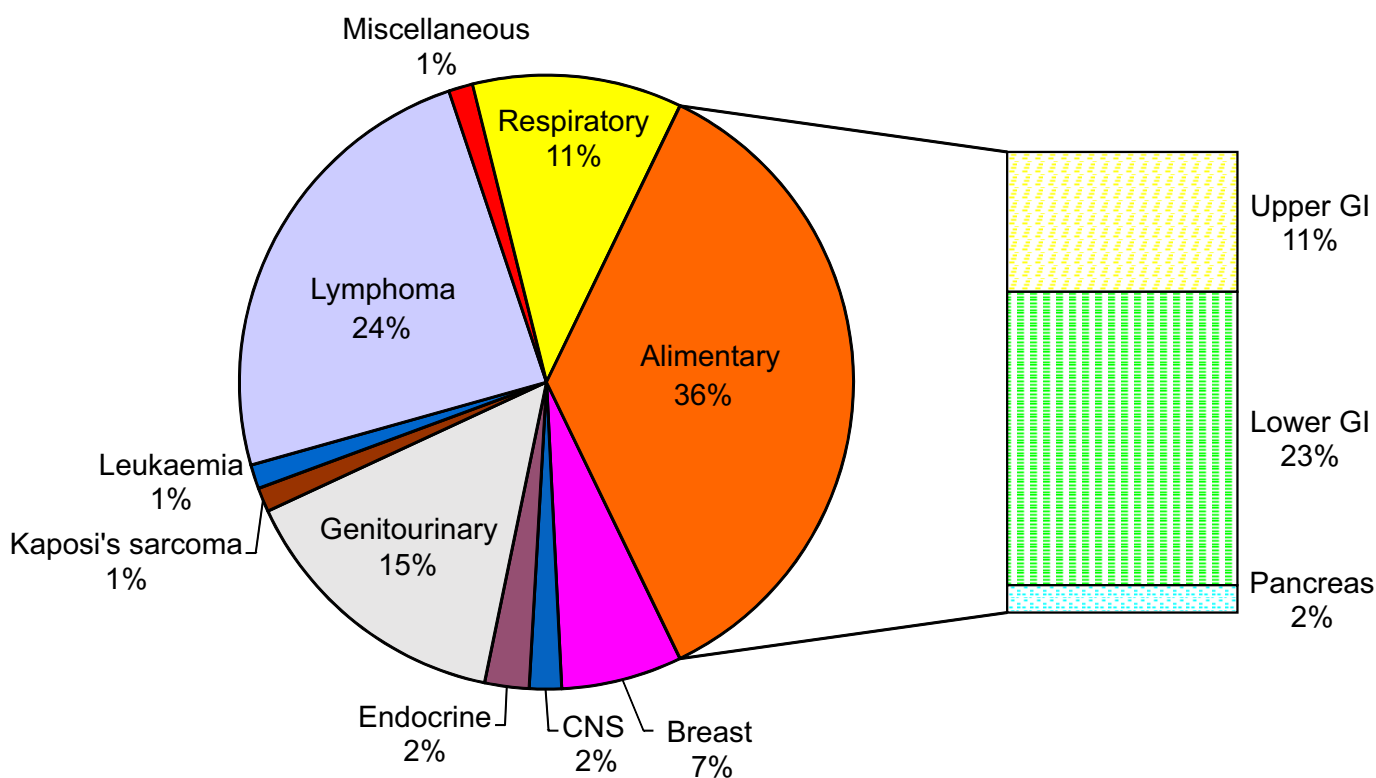
Lymphoma - Adults
n = 96 (21% adults with de novo Ca)



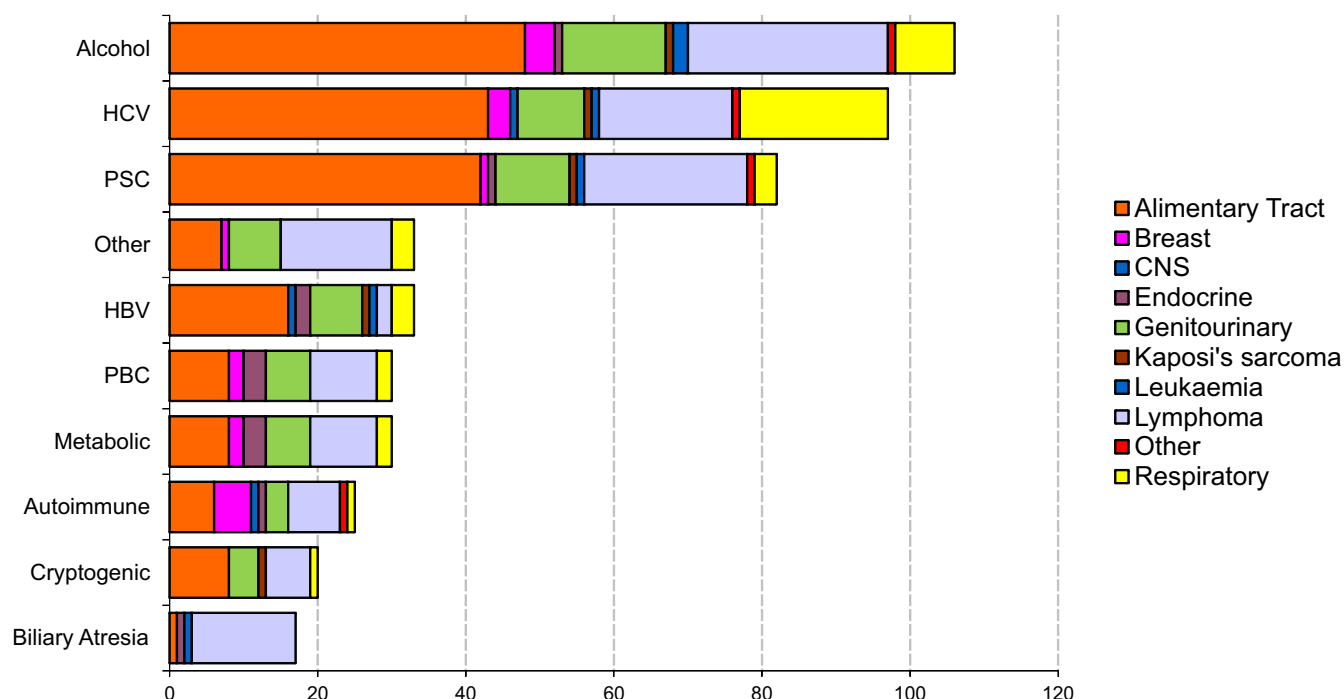
Lymphoma - Children
n = 18 (86% children with de novo Ca)



De Novo Non Skin Cancer
N = 439/5448 (8%)

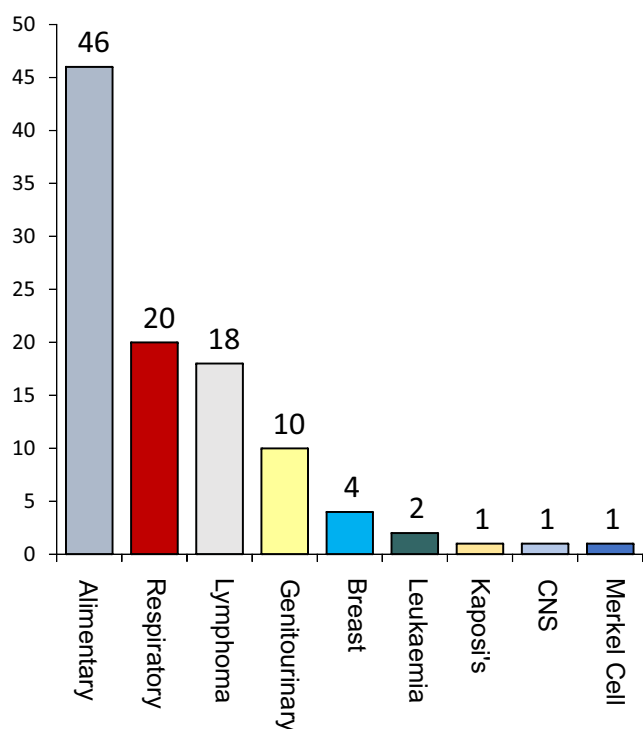


Pre Transplant Disease and De Novo Non Skin Cancer N = 439/5448 pts (8%)

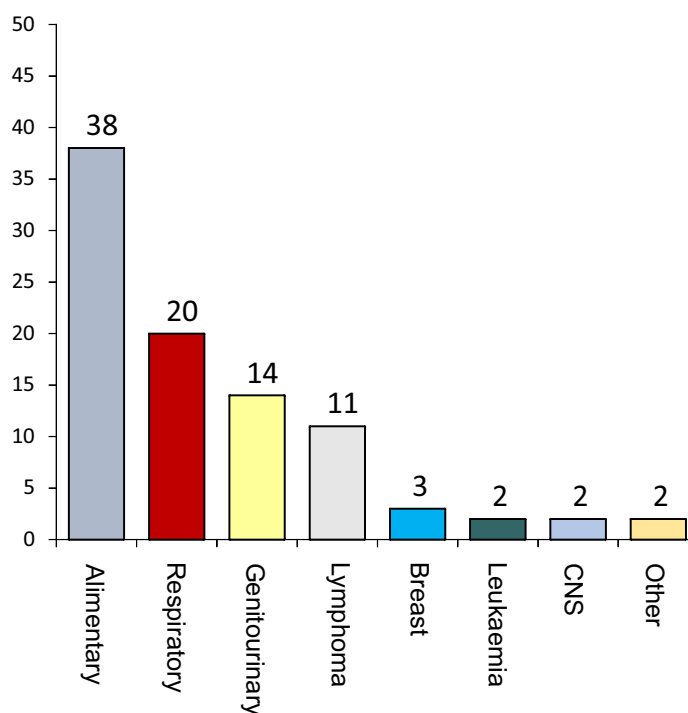


Pre Transplant Disease and De Novo Non Skin Cancer N = 439 (470 Ca)/5448 pts (8%)

HCV - 103/439
24% of de novo Ca



Alcohol - 92/439
21% of de novo CA

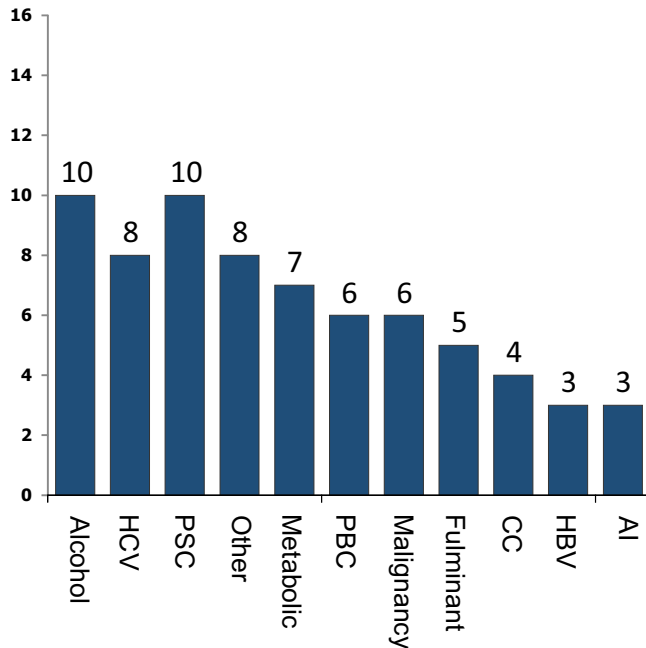


Pre Transplant Primary Liver Disease and De Novo Non Skin Cancer

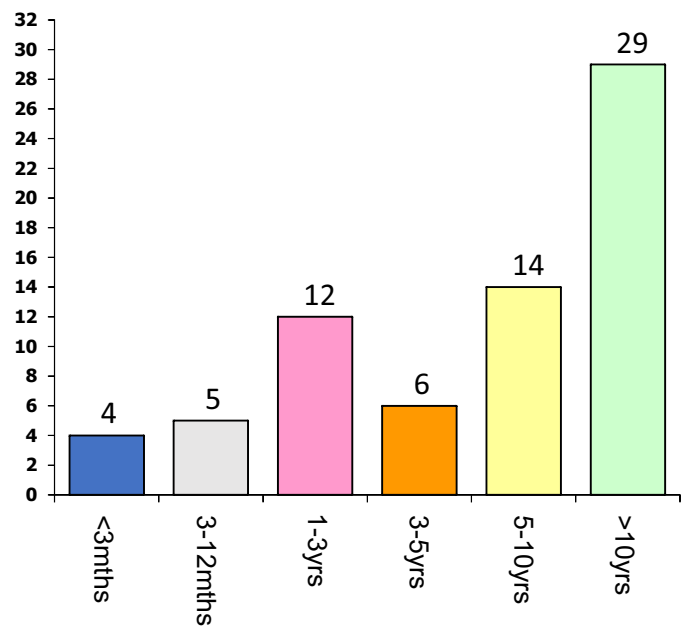
N = 439 (470 Ca)/5448 pts (8%)



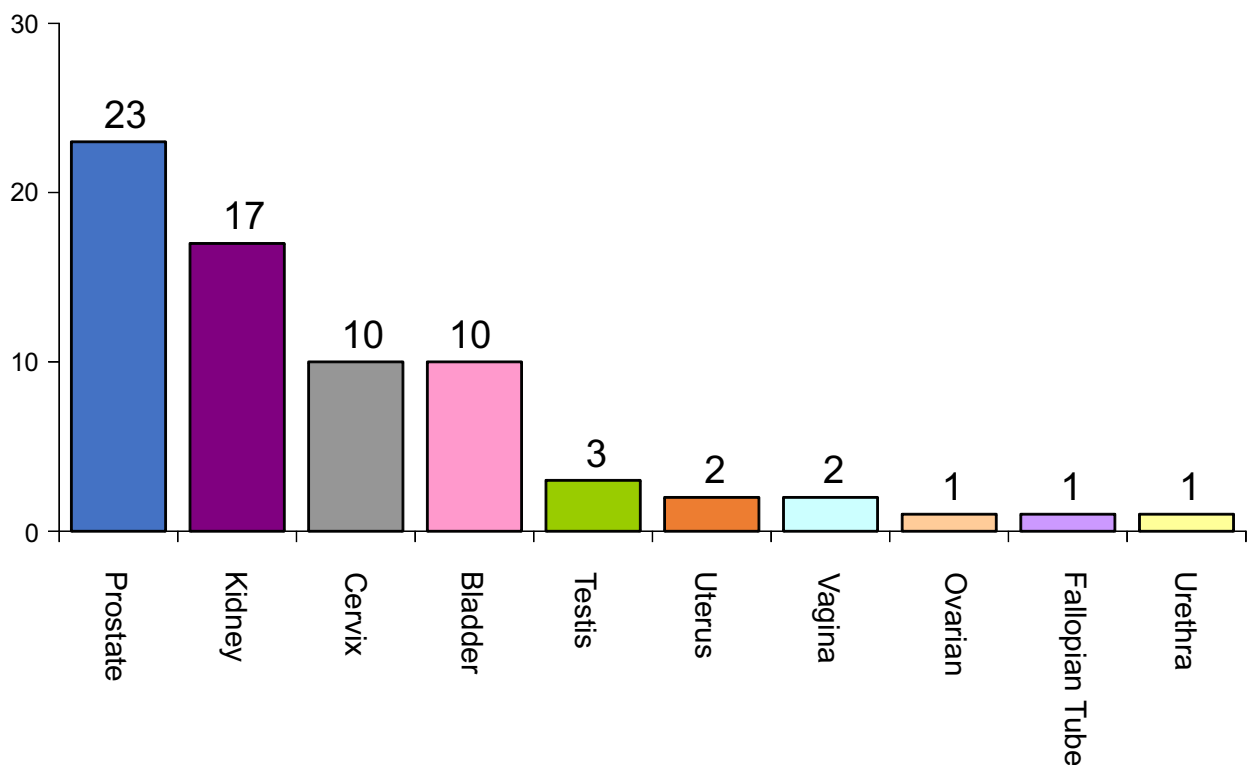
Genitourinary Cancers 67 (70 Ca)/439 (15% de novo pts)



Genitourinary Cancers Time to Diagnosis 67 (70 Ca)/439 (15% de novo pts)



De Novo Non Skin Cancer - Genitourinary Tract Incidence N = 70/470 cancers (15%)

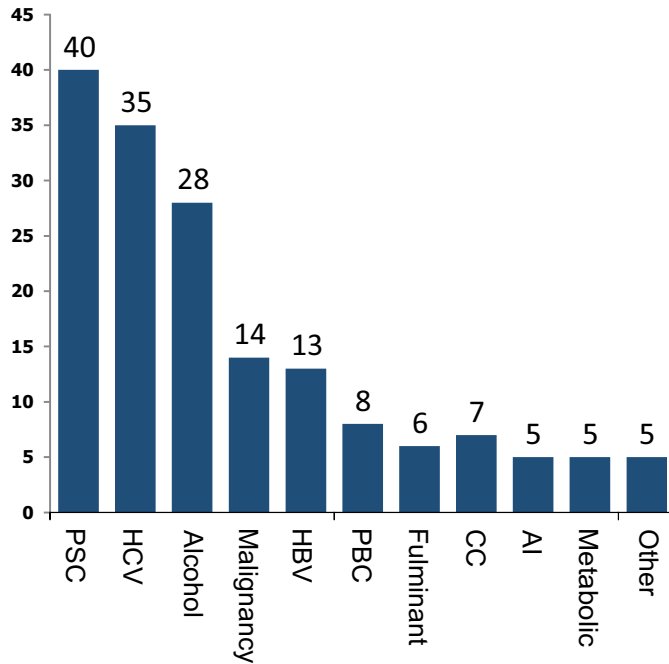


Pre Transplant Primary Disease and Alimentary Cancer

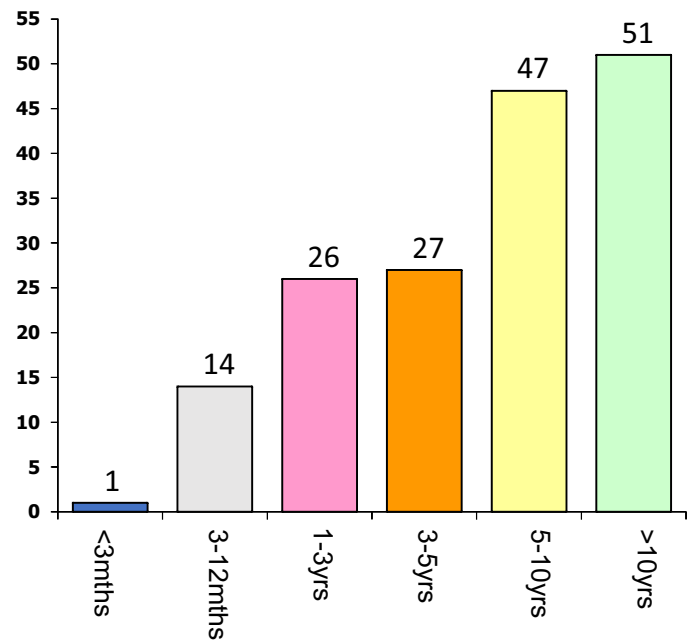
N = 439 (470 Ca)/5448 pts (8%)



Alimentary Cancers
165 (166 ca)/439 (38% de novo pts)

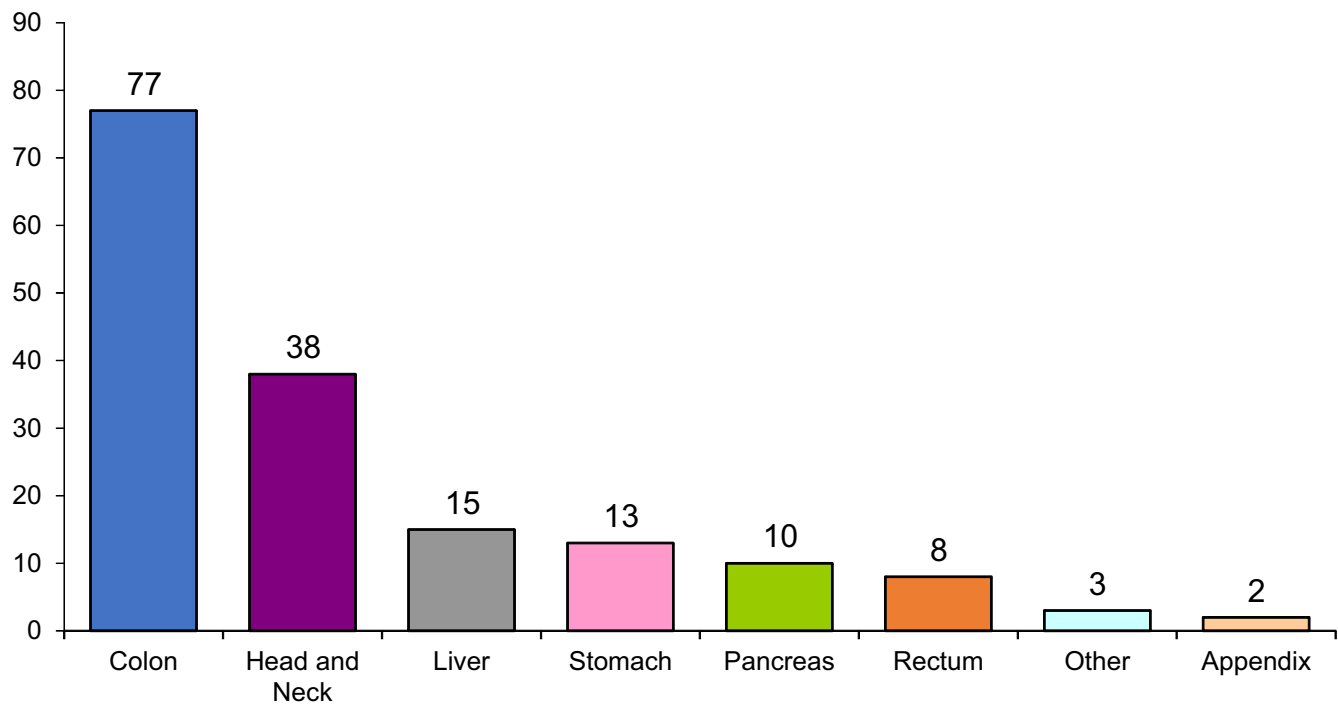


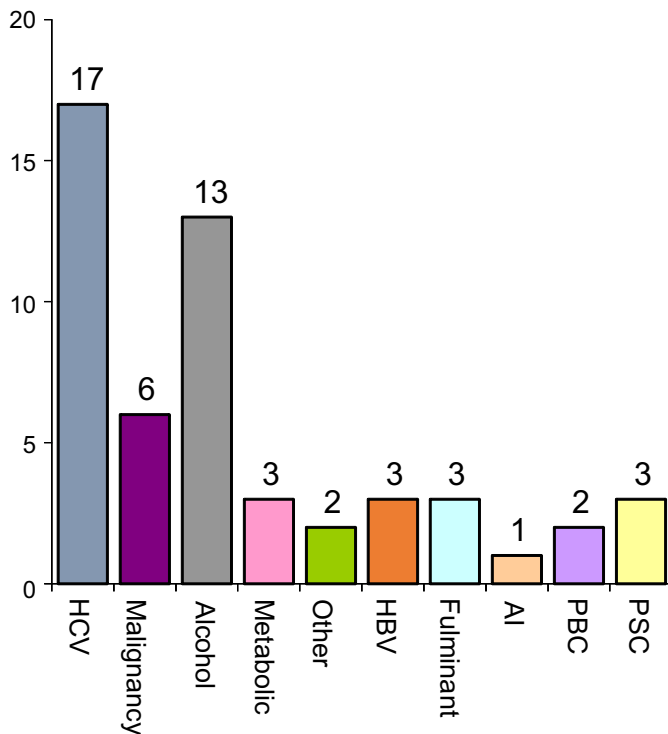
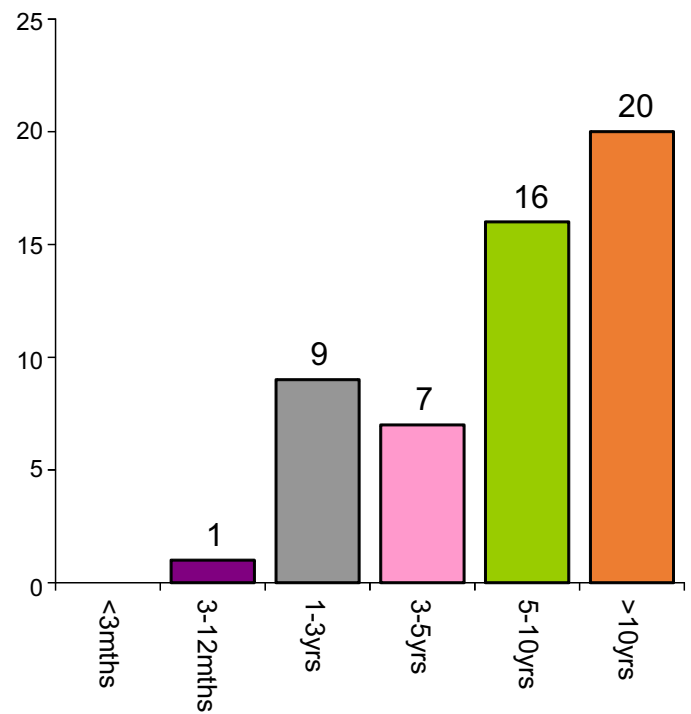
Alimentary Cancers
Time to Diagnosis
165 (166 ca)/439 (38% de novo pts)



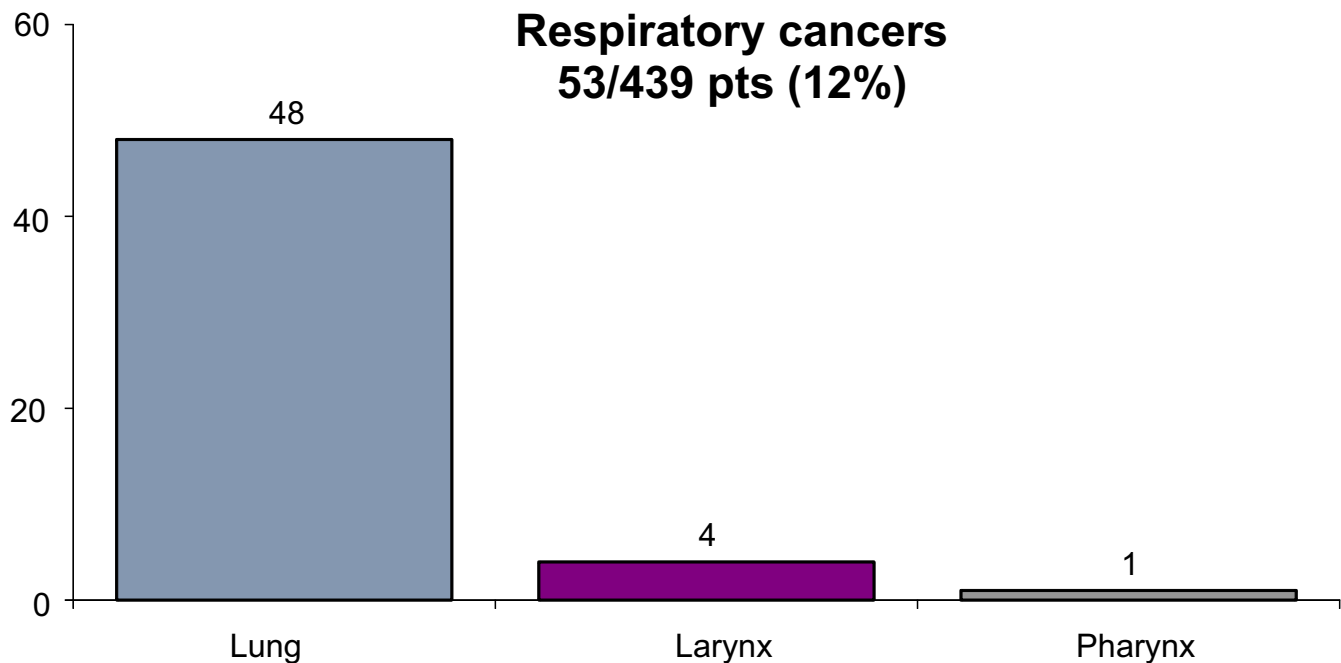
De Novo Non Skin Cancer - Alimentary Tract Incidence

N = 165 (166 ca) /439 pts (38%)



**Respiratory cancers**
53/439 pts (12%)**Respiratory cancers**
53/439 pts (12%)

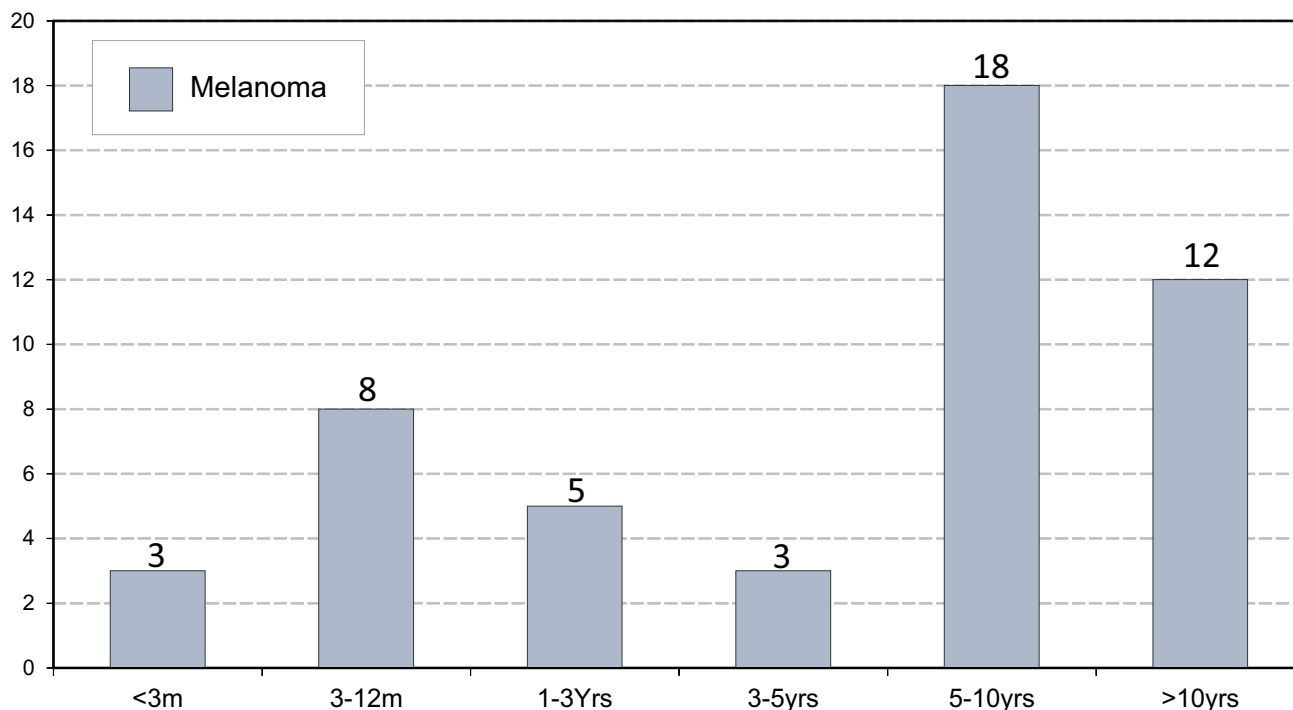
De Novo Non Skin Cancer - Respiratory Cancer Incidence

Respiratory cancers
53/439 pts (12%)

Time to Melanoma Skin Cancer Development Post Tx.

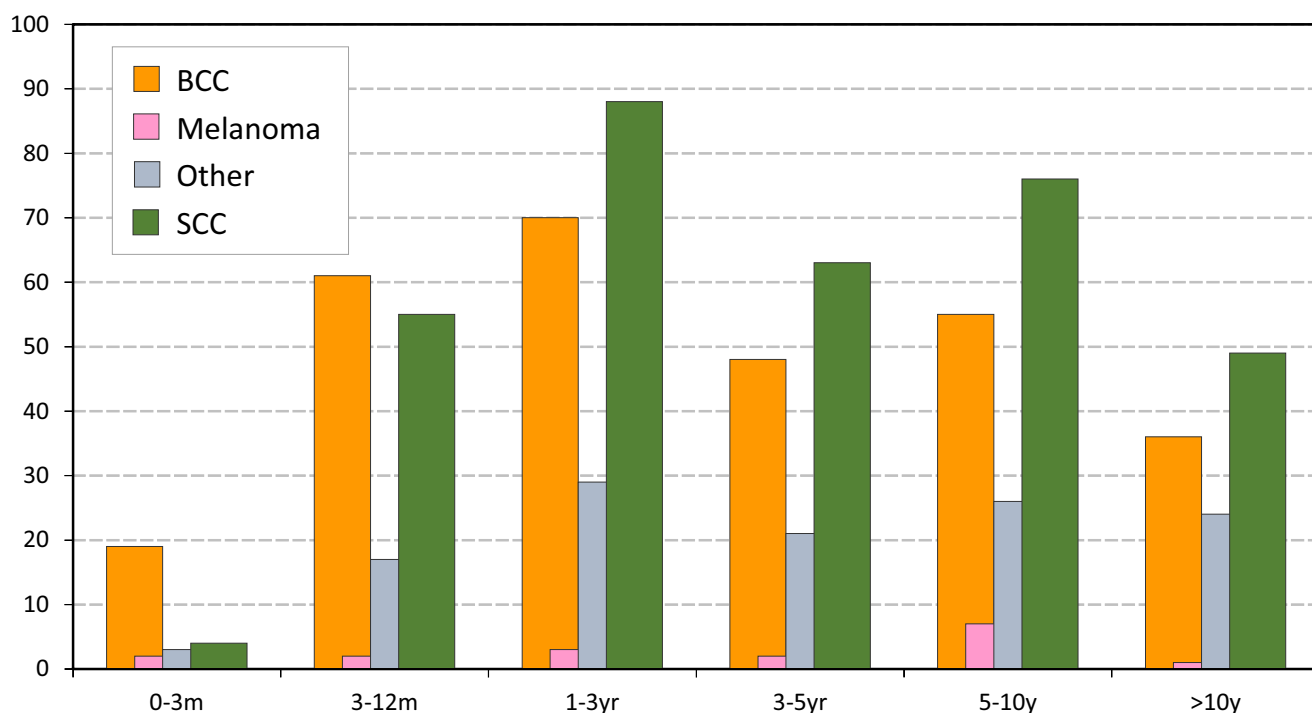
N = 5448

48 (49 ca) (0.9% of all pts)

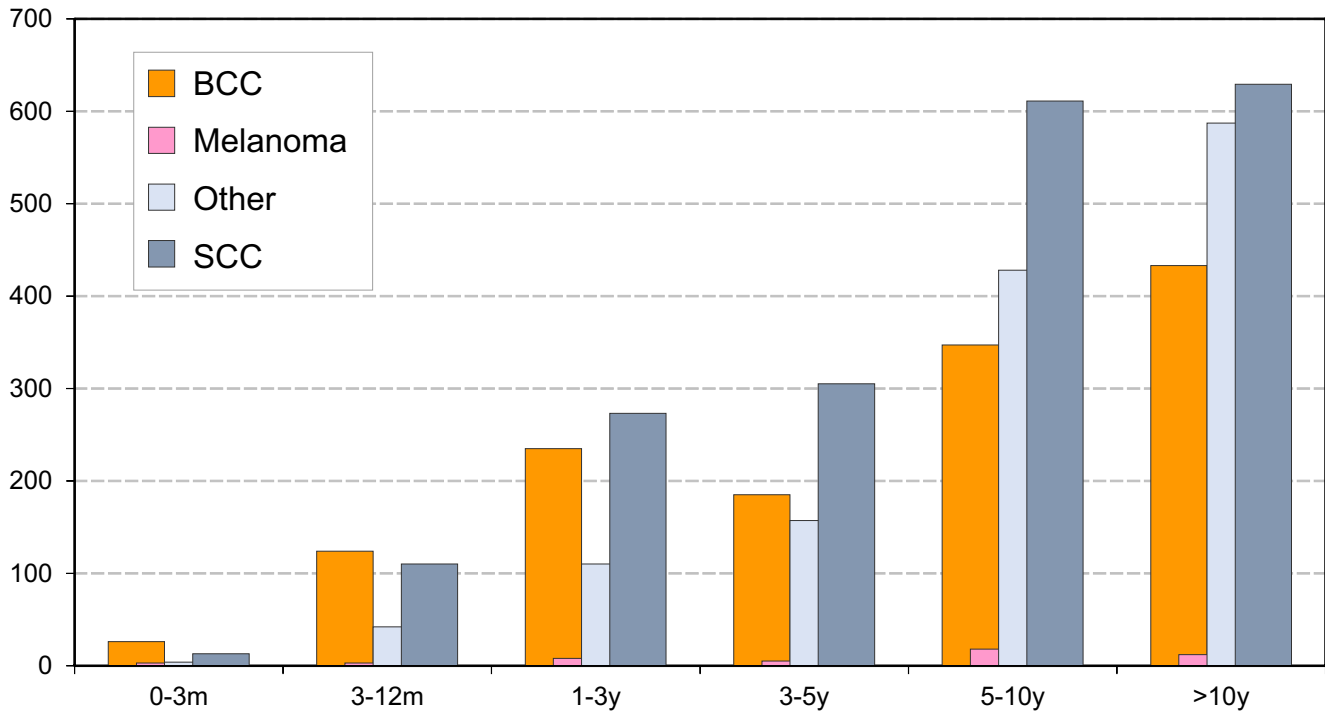


Time to 1st Skin Cancer Development

844/5448 (16% of all pts)

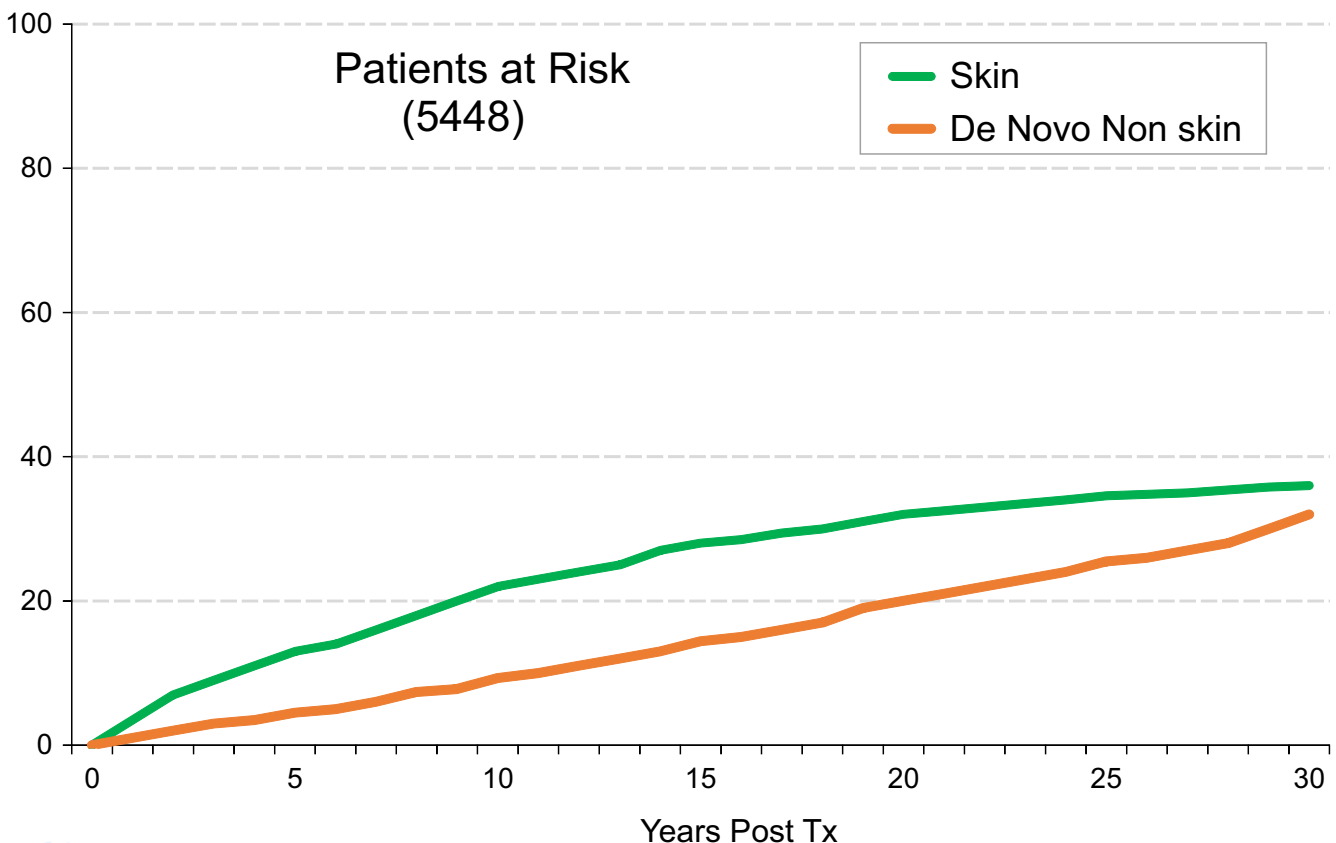


Time to Any Skin Cancer Development 844/5448 (15% of all pts)



844 (15%) pts developed skin cancer post Tx. 400 (47%) pts have multiple skin cancer types.

Cumulative Risk of Diagnosis of Skin or Non Skin Cancer Following Liver Tx. 1985-2017





Appendix I

Liver Transplant Units of Australia and New Zealand

Australian National Liver Transplant Unit
Royal Prince Alfred Hospital
Missenden Road
CAMPERDOWN NSW 2050
<http://www.anltu.com.au/>

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/page/209>

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 Lady Cilento Children's Hospital
Stanley Street
SOUTH BRISBANE QLD 4101

South Australian Liver Transplant Unit
Flinders Medical Centre
Flinders Drive
BEDFORD PARK SA 5042
<http://www.flinders.sa.gov.au/surgical/pages/livertrans/6984/>

WA Liver Transplantation Service
Sir Charles Gairdner Hospital
Verdun Street
NEDLANDS WA 6009

New Zealand Liver Transplant Unit
Auckland City Hospital
Park Road
Auckland
New Zealand
<http://www.livers.org.nz/>

and

Starship Children's Hospital
Park Road
AUCKLAND
New Zealand



Appendix II

ANZLTR PRIMARY Diagnosis Metabolic disorders by Age Group

Primary Diagnosis	Age group		Total
	Child	Adult	
α -1 Antitrypsin deficiency	39	56	95
Crigler-Najjar	12	1	13
Familial amyloid polyneuropathy	0	40	40
Glycogen storage disease	4	9	13
Haemochromatosis	3	32	35
Homozygous hypercholesterolemia	7	2	9
Maple syrup urine disease	6	1	7
Indian childhood cirrhosis	1	0	1
Other*	15	7	22
Primary hyperoxaluria	10	9	19
Tyrosinemia	6	0	6
Urea cycle disorders**	24	4	28
Wilsoms disease	8	32	40
Total	135	193	328

* Amyloidosis 1
 Bile acid transport disorder 3
 Protein C deficiency 3
 Propionic acidemia 6
 Methylmalonic acidemia 2
 Familial immunodeficiency 1
 Mitochondrial disease 3
 Porphyria 1
 aB Lipoprotein Amyloid 1
 Niemann-Pick 1

** OTC deficiency 15
 ASL deficiency 5
 CPS deficiency 3
 ASS deficiency 5



Appendix III

ANZLTR PRIMARY Diagnosis - Other by Age Group

Primary Diagnosis	Age group		Total
	Child	Adult	
Alagille syndrome	36	10	46
Alagille non-syndromic	2	0	2
Benign liver tumour - adenomatosis	0	1	1
Benign liver tumour - hemangioma	0	4	4
Caroli's disease / congenital hepatic fibrosis	4	18	22
Choledocal cyst	3	2	5
Cholestatic disease-Other	4	10	14
Chronic Budd Chiari	1	33	34
Congenital biliary fibrosis	0	2	2
Ductopenia	1	3	4
Granulomatous hepatitis / sarcoidosis	0	5	5
Histiocytosis X	5	1	6
Hereditary haemorrhagic telangiectasia / OWRD	0	7	7
Neonatal hepatitis	4	0	4
Nodular regenerative hyperplasia	0	7	7
Polycystic liver disease	0	24	24
Polycystic liver and kidney disease	2	22	24
Progressive familial intrahepatic cholestasis (PFIC)	23	6	29
Secondary biliary cirrhosis	3	19	22
Secondary biliary cirrhosis - hepatolithiasis	0	4	4
Secondary biliary cirrhosis - cystic fibrosis	15	22	37
Other - specify [#]	11	22	33
Total	121	236	357

Haemangiotelangiectasia
Veno-occlusive disease
Non-cirrhotic portal hypertension
Arterial-venous malformation
Oriental cholangio hepatitis
Liver trauma
Cholestatic cirrhosis parvovirus
Osler-weber-rendu disease

Biliary sclerosis
Drug induced cholestasis
Graft vs host disease
Ischaemic sclerosing cholangitis
Choledochal cyst
Langerhans cell histiocytosis



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	8	19	27
Acute - α -1 -AAT	2	0	2
Acute autoimmune hepatitis	1	9	10
Acute unknown / unspecified	47	95	142
Acute - paracetamol	4	22	26
Acute - other drugs	3	30	33
Acute herbs / mushrooms	0	8	8
Acute - hepatitis A	1	3	4
Acute - hepatitis B	0	73	73
Acute - hepatitis non A-G	15	21	36
Acute - hepatitis E	0	1	1
Acute - other virus	1	1	2
Acute - post liver resection/trauma	1	3	4
Subacute - Budd Chiari	1	2	3
Subacute - Wilson's	2	7	9
Subacute autoimmune hepatitis	2	21	23
Subacute - drug / herbs	1	16	17
Subacute - unknown / unspecified	5	31	36
Subacute - hepatitis A	0	2	2
Subacute - hepatitis B	0	21	21
Subacute - hepatitis non A-G	0	6	6
Total	99	404	503



Appendix V

ANZLTR Causes of Patient death

<u>Graft failure - other</u>	Age group		Total
	Children	Adult	
Vascular thrombosis	8	18	26
<i>Hepatic artery</i>	4	9	13
<i>Portal vein</i>	2	9	11
<i>Hepatic vein</i>	2	-	2
Non thrombotic infarction	3	-	3
Primary non function	3	18	21
Massive haemorrhagic necrosis	4	0	4
Recurrent disease (<i>ALD, PSC, CAH:AI</i>)	-	25	25
De novo hepatitis C	-	2	2
Biliary complications	3	13	16
Other (<i>PNC, immune hepatitis, outflow obstruction</i>)	8	12	20
TOTAL	29	88	117

<u>Miscellaneous</u>	Children	Adult	
Multiorgan failure	11	88	99
Renal failure	1	44	45
Graft vs Host disease	-	6	6
Social (<i>accident, suicide, non-compliance, Rx withdrawn</i>)	1	21	22
Sudden death (<i>cause unknown</i>)	3	44	47
Other (<i>hyperkalaemia, motor neurone disease, diabetes complications, drug reaction, progression FAP, essential thrombocythemia</i>)	3	37	40
TOTAL	19	240	259