

# 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 31-12-2014

**CD** Included  
INSIDE BACK COVER



Report PowerPoint  
**SLIDES**

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Editors: S.V. Lynch, G.A. Balderson

## STATISTICAL METHODS

Kaplan-Meier survival curves have been produced using IBM SPSS® for Windows™ Release 22.0.

## 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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# Preface

We are pleased to present the 26th Report of the Australia and New Zealand Liver Transplant Registry (ANZLTR). This report contains data to the 31st December 2014 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.

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](http://www.anzltr.org) from where the report can be downloaded. Slides are available on request from the Coordinating Centre.

Stephen Lynch  
Glenda Balderson





# Summary

## Page

5. Between January 1985 and 31st December 2014, 4864 orthotopic liver transplants (OLT) were performed in Australia and New Zealand on 4506 patients, 3711 adult patients [82%] and 795 children (< 16 years) [18%]. The median age of all recipients was 48.3 years. The ages ranged from 24 days to 73.1 years. There is a significant difference in gender distribution between children (M=48%) and adults (M=66%).
6. Two hundred and sixty-three new patients were transplanted in 2014 compared with 264 in 2013.
7. The trend to increasing age of adult recipients in recent years continued and the overall adult median age is now 51.2 years. The median age of new adult recipients in 2010-14 was 54.3 years.
- 8-9. In 2014, 6 fewer transplants were performed than in 2013 [278 vs 284]. Split grafts continue to make a significant contribution to the total number of paediatric transplants performed providing 18 of 42 [43%] grafts in 2014 and 237 of 900 [26%] overall. In children, other reduced size grafts have been used in 392 [44%] cases including 73 living donor grafts. One child has been treated with liver cell implantation. Of adult patients, 284 have received reduced size grafts - 241 split liver grafts (including 1 as auxiliary graft), 30 other reduced size grafts (1 as auxiliary graft) and 13 living donor grafts. Two 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 22.9% of recipients and chronic hepatitis B [CVH : HBV] in 6.0 %. 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 continued to increase with 16 new patients transplanted in 2014 bringing the total to 111. While the proportion of adult patients transplanted with a primary diagnosis of chronic viral Hepatitis B, C or B/C/D has fallen slightly in era 2010-14 compared with the previous eras, the number of patients with a primary diagnosis of hepatocellular carcinoma [HCC] is increasing each year and now account for 14% in 2010-14. The majority of these patients have a secondary diagnosis of CVH. When patients with either primary or secondary diagnosis of Hepatitis B,C or both are included, the overall incidence of CVH in new adult patients in 2014 was 47%.
16. Overall 1 year patient survival of all patients is 89.5% at 1 year, 82% at 5 years and 73.5% at 10 years. Children have a significantly better survival rate than adults with an actuarial survival of 72% at 25 years post-transplant.
17. Whilst older children had superior early survival than infants and babies, long term survival is similar. Older adult recipients 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 2010-14 cohort was 93% for all patients [93% for children, 94% for adults].
20. In both children and adults, there are worse early outcomes in patients receiving a deceased donor reduced size graft as their primary graft compared with split liver graft or whole liver grafts. Split liver grafts and whole livers have similar early outcomes in both children and adults.



# Summary

## Page

21. Smaller children and babies weighing < 8 kg at the time of transplant had inferior early survival compared to heavier children but similar long term results.
22. Adult patients transplanted for biliary atresia or hepatitis virus co-infections had the best longer term survival while those whose primary disease was malignancy or Hepatitis C have significantly lower survival rates.
23. In children, patient survival was similar for all disease groups though lower in patients whose primary disease was malignancy. There were no differences in survival between adults and children transplanted for fulminant hepatic failure [acute and sub-acute] with overall 5 year survival of 78%.
24. Recent cohorts of adult patients with a primary diagnosis of hepatitis B continue to show a significantly improved survival which is not seen in adult patients with hepatitis C as primary disease. Patients transplanted for malignancy continue to have a poor outcome but some improvement in longer term outcome is seen in patients transplanted since 2000.
- 25-26. Overall graft survival was 77% at 5 years with significantly better graft survival longer term in children. 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.
- 28-29. Vascular complications and rejection were the commonest indications for re-transplantation. Twelve percent of retransplants were due to poor early graft function. Re-transplantation for recurrent disease was most prevalent in adults [10% PSC, PBC, AIH and 8% HBV, HCV].
- 30-33. Sepsis is the most frequent cause of death in both adults and children. Full details of Miscellaneous and Other Graft Failure deaths are listed in Appendix V. Thirty percent of all deaths occurred within 6 months of transplant. Deaths from early graft failure were due to poor or no early graft function. By 1 year malignancy and graft failure from recurrent disease or chronic rejection cause most deaths. Deaths due to de novo malignancy and chronic rejection are increasing with longer survival time particularly in children surviving 15 years or longer.
34. There was a slight fall in the number of cadaveric donors in 2014 with 272 grafts transplanted from deceased donors. The number of livers split to produce two transplantable grafts was 18 in 2014. Fifteen liver grafts donated after cardiac death were transplanted. The number of people on the waiting list at 31 December 2014 was higher than the number on the waiting list at 31 December 2013.
35. Donor age has increased significantly in recent years. Long term graft survival trends lower in several older donor age groups.
36. Eighty-eight patients [73 children, 15 adults] have now received a living donor graft with 6 performed in 2014. In 82 patients the living donor graft was a primary graft, in 5 as a second and 1 as a third graft. The median age of the donors was 34.0 years with a range of 19.0 to 54.5 years. Two adult grafts were domino whole liver graft.



# Summary

## Page

37. Waiting list activity for 2014 shows the number of patients listed for transplantation continued to increase with 204 remaining on the waiting list at 31 December 2014. Patient delistings due to death, becoming too ill or tumour [HCC] progression accounted for 8% of all delistings while 278 [49%] were transplanted. Thirty patients were listed as urgent in 2014 [8 with initial listing as Category 1 and 22 Category 2]. Seven [88%] of Category 1 and 21 [95%] of Category 2 patients had a positive outcome.
- 38-39. Median waiting times tended to be higher in 2014 in some blood groups. Blood group B patients had the longest waiting times.
- 40-42. Cancer in liver transplant recipients was analysed from two perspectives. Firstly, those who had a liver cancer diagnosis at the time of transplantation (as primary, secondary or incidental) and secondly those who developed a cancer post transplantation (de novo skin and de novo non - skin cancer). Overall 950 (21%) patients were transplanted who had a liver malignancy – 384 (9%) as a primary diagnosis and 572 (13%) as a secondary diagnosis or incidental tumour, with Hepatocellular Carcinoma being the most common. Post transplant 127 (13%) of these patients developed a recurrent cancer whilst in 113 (12%) of these patients' death was related to their initial cancer.
42. There continues to be an increase in the number of patients being transplanted for primary malignancy.
- 43-46. Patient survival was significantly worse in the 857 (20%) patients with pre-transplant liver malignancy compared with patients with other forms of liver disease with the exception of those with a diagnosis of Hepatocellular Carcinoma and Hepatoblastoma whose survival rates are close to those with other liver diseases. Of these 106 (12%) died from their malignancy. Those with Cholangiocarcinoma had significantly poorer survival. The number of patients transplanted with liver cancer present at transplant has increased significantly in the last decade from 247 (1995-2005) to 643 (2005 -14).
- 46-51. Three hundred and fifty-two de novo non-skin types of cancer developed in 323 (7%) recipients. Twenty seven patients developed more than one de novo cancer. The three most common categories of de novo non-skin cancer were – cancers of the Alimentary Tract (125), Lymphoma (91) and Genitourinary (47). The incidence of de novo non-skin cancers appears to be related to the type of pre-transplant underlying disease. Most notable is the significant incidence of de novo non-skin malignancy in patients with underlying Primary Sclerosing Cholangitis, alcoholic cirrhosis and HCV ( $p<0.0001$ ).
- 51-52. Six hundred and fifty-four patients (15%) developed skin cancers with a peak 1 - 3years after transplantation for appearance of first cancer. Multiple skin cancers developed in 316 patients. Thirty-two patients developed Melanoma.

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



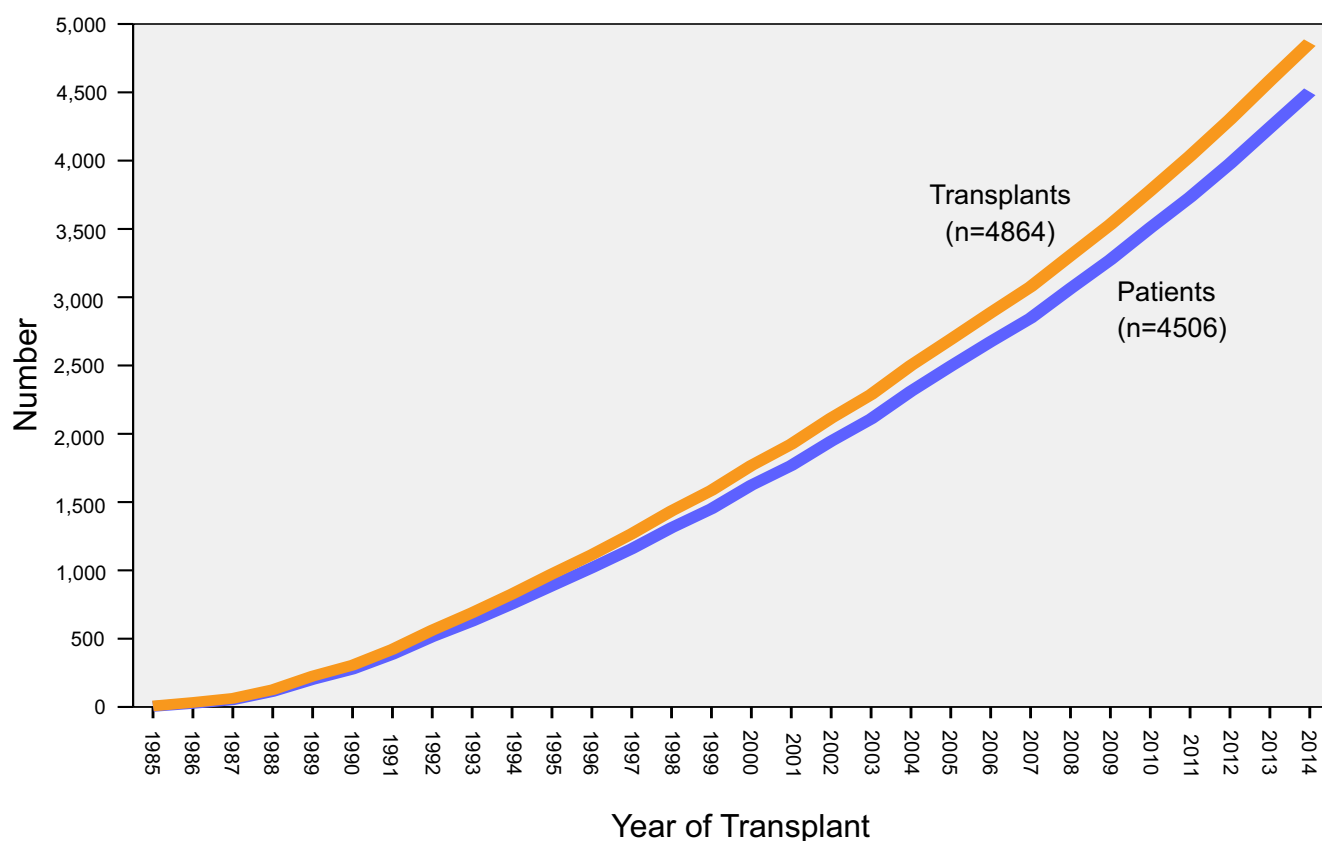


# Section 1

## Demographic Data



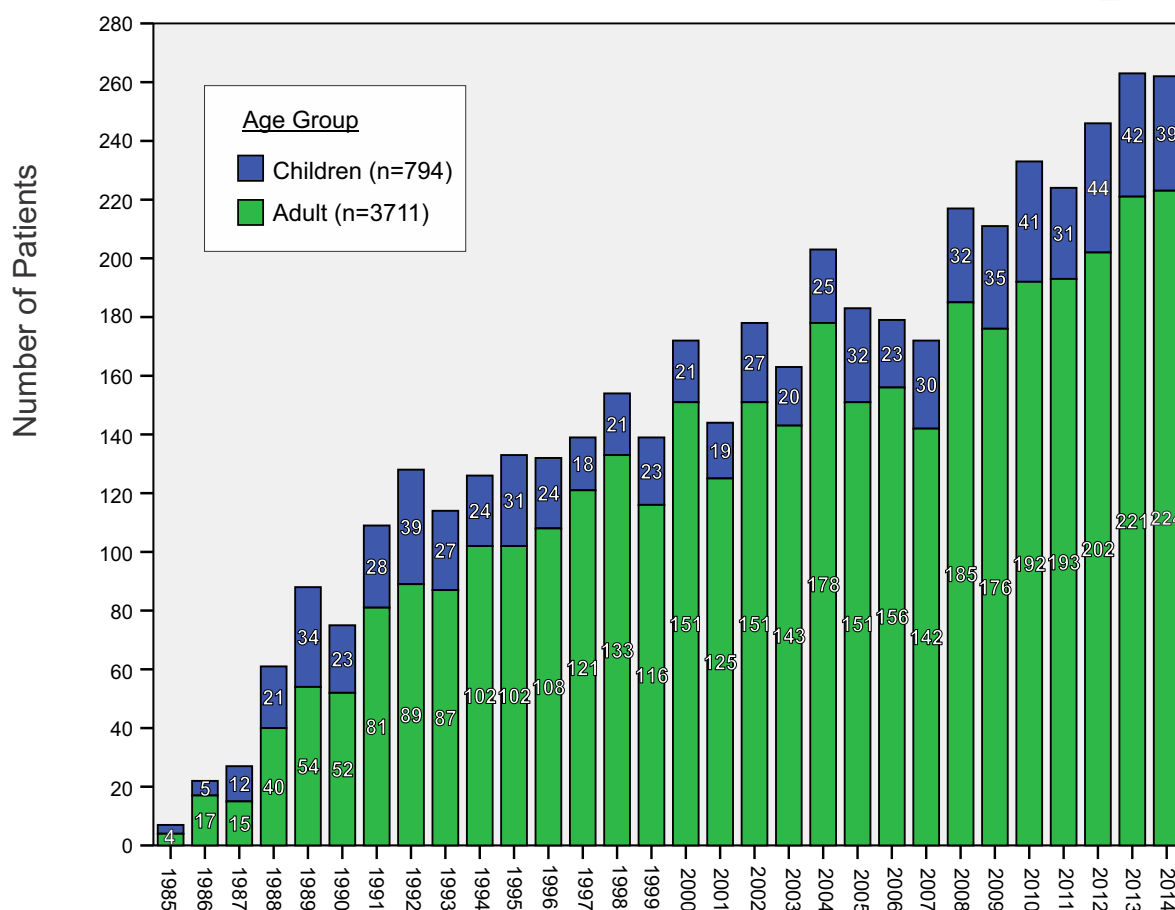




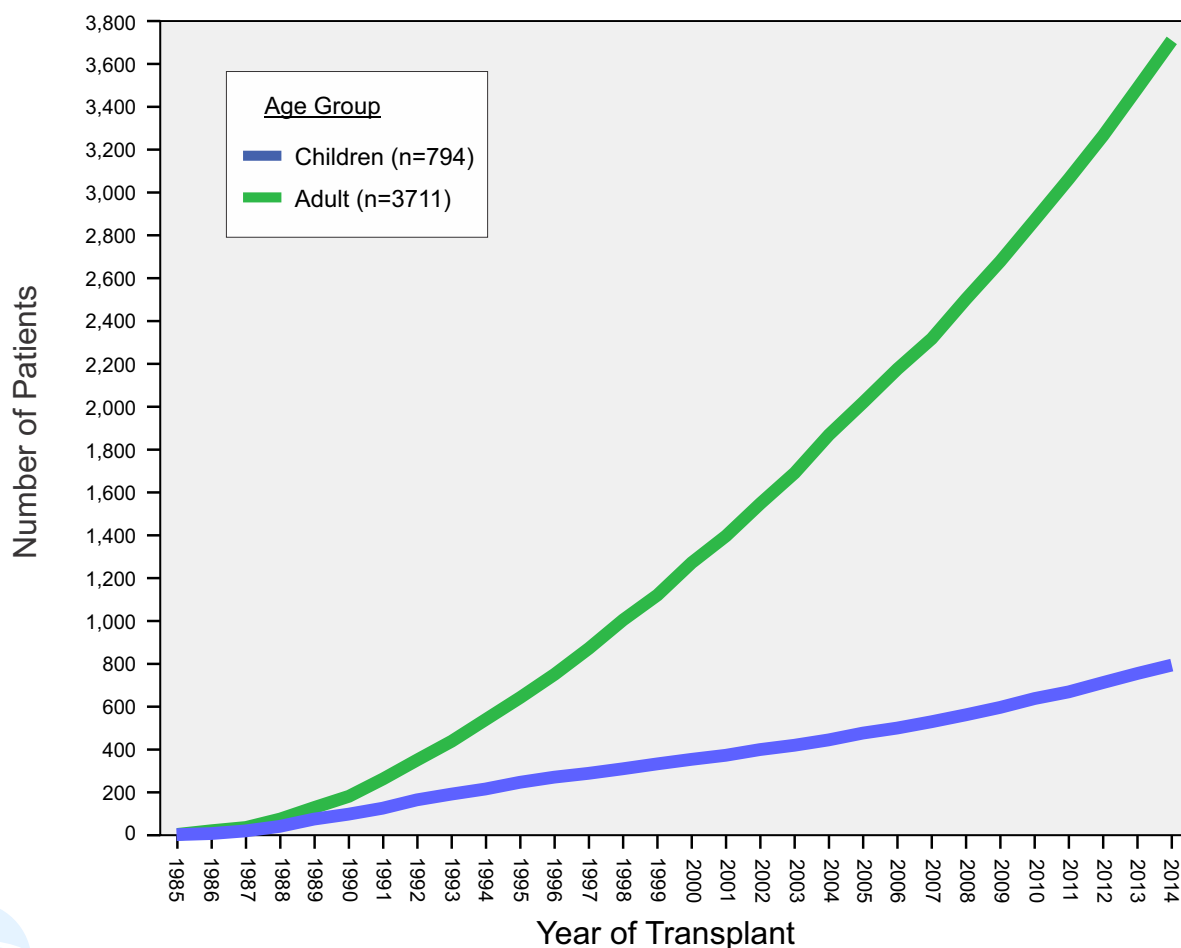
## Summary Statistics - Age and Gender

### ALL PATIENTS TRANSPLANTED

	Children [<16y]	Adults	Total
<i>Patients</i>	795	3711	4506
<b>Age</b>			
<i>Mean ± SD</i>	4.5 ± 4.5y	49.0 ± 11.6y	41.1 ± 20.0y
<i>Median</i>	2.4y	51.2y	48.3y
<i>Range</i>	24d - 15.9y	16.0 - 73.1y	24d - 73.1y
<b>Gender</b>			
<i>Female</i>	414 (52%)	1277 (34%)	1691 (37.5%)
<i>Male</i>	380 (48%)	2434 (66%)	2814 (62.5%)
<b>Surviving</b>	642 (81%)	2604 (70%)	3246 (72%)

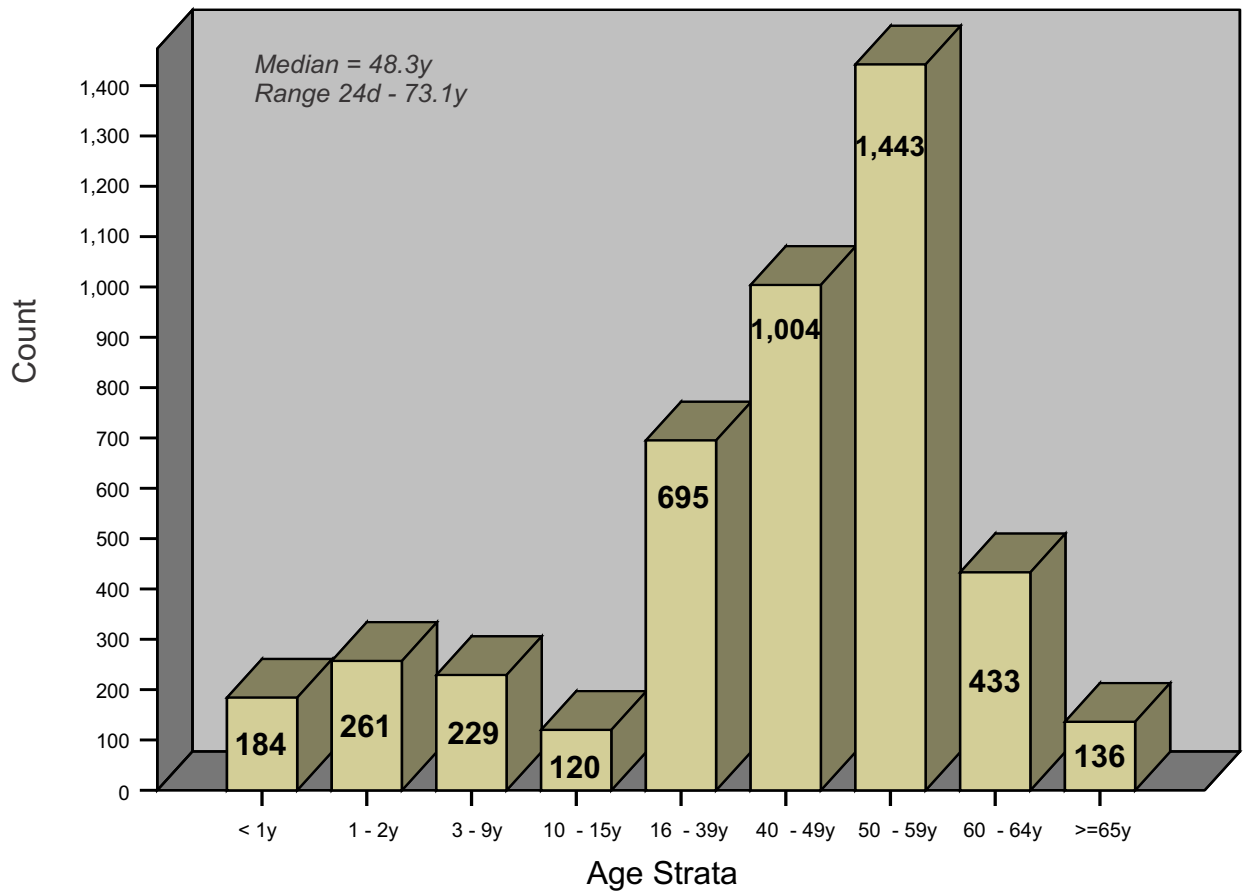


## Cumulative Number of New Patients Transplanted

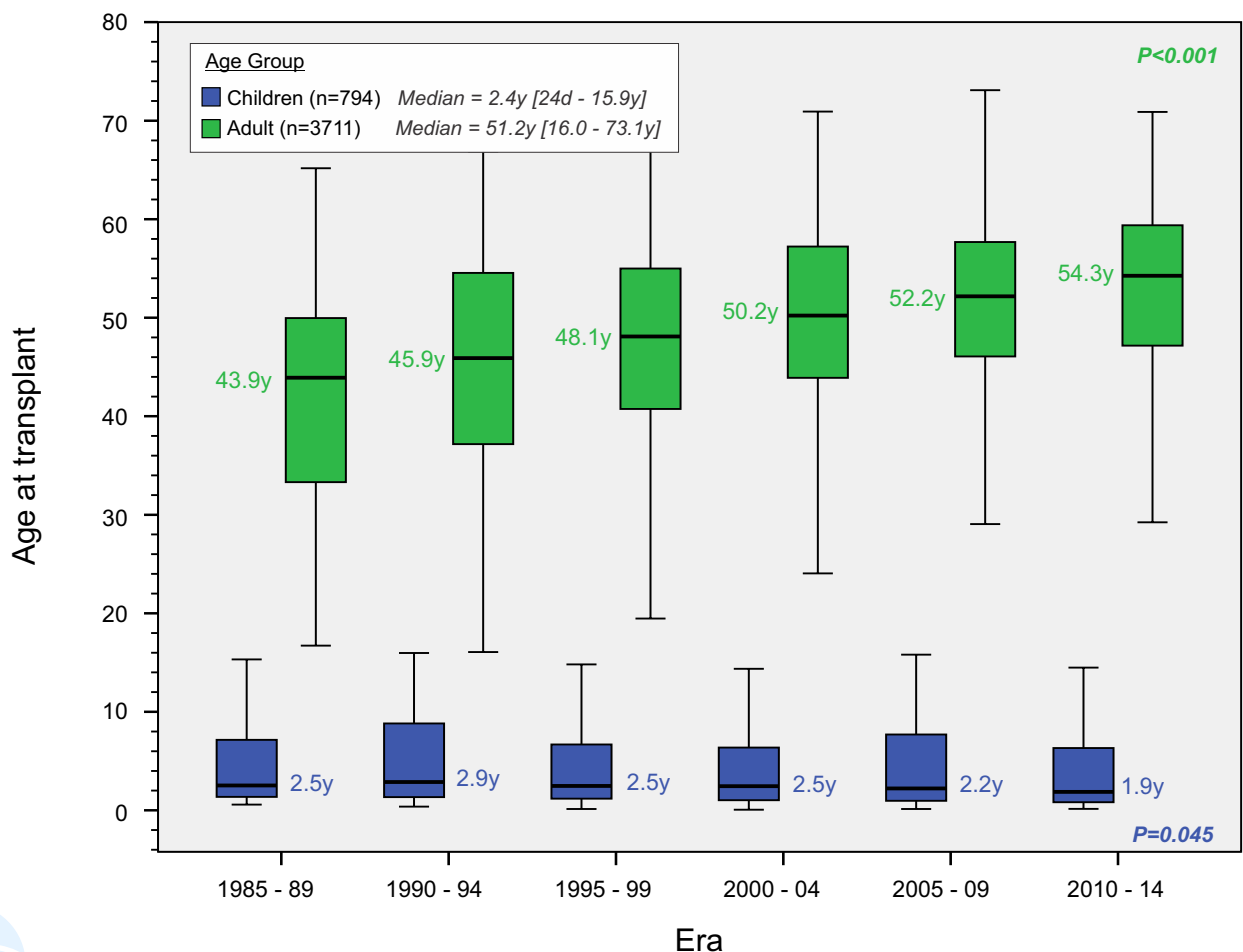


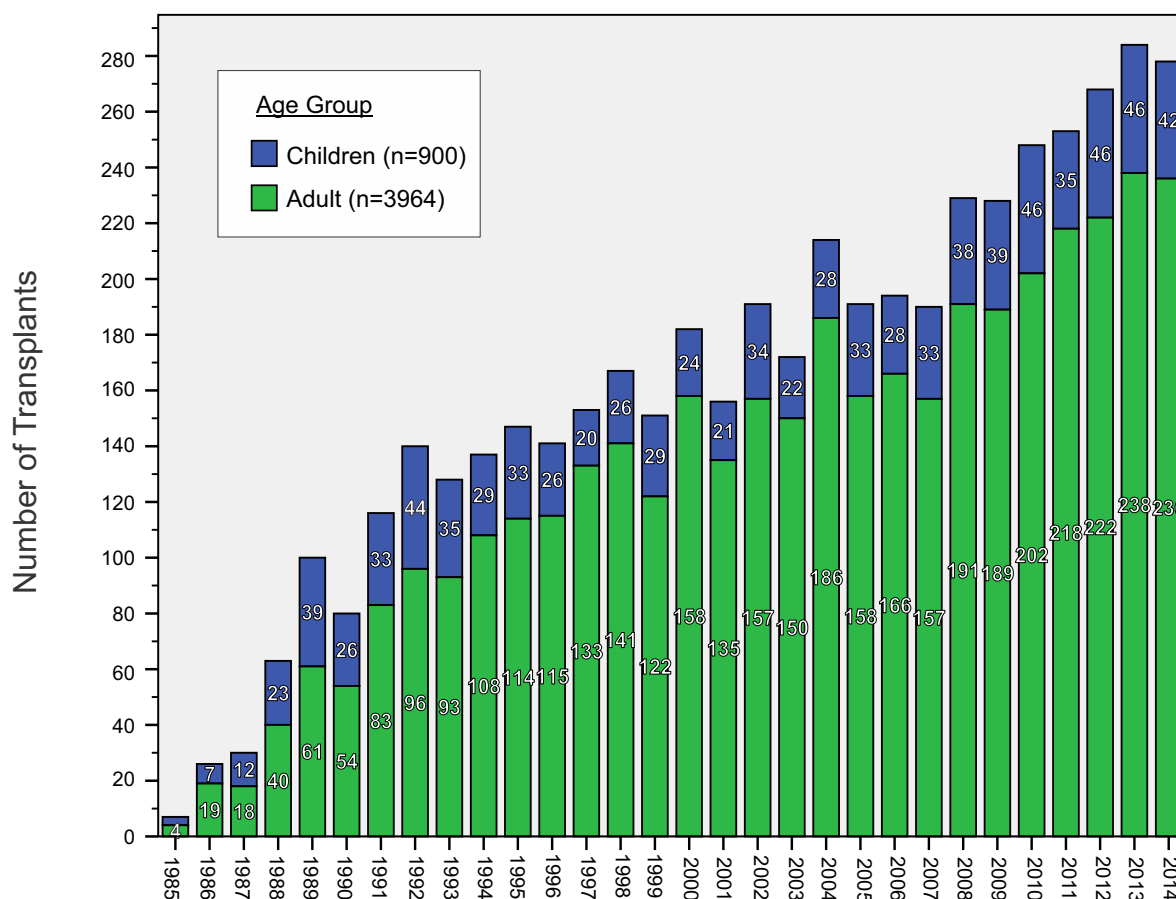
# Number of Recipients By Age at Primary Transplant

N=4506

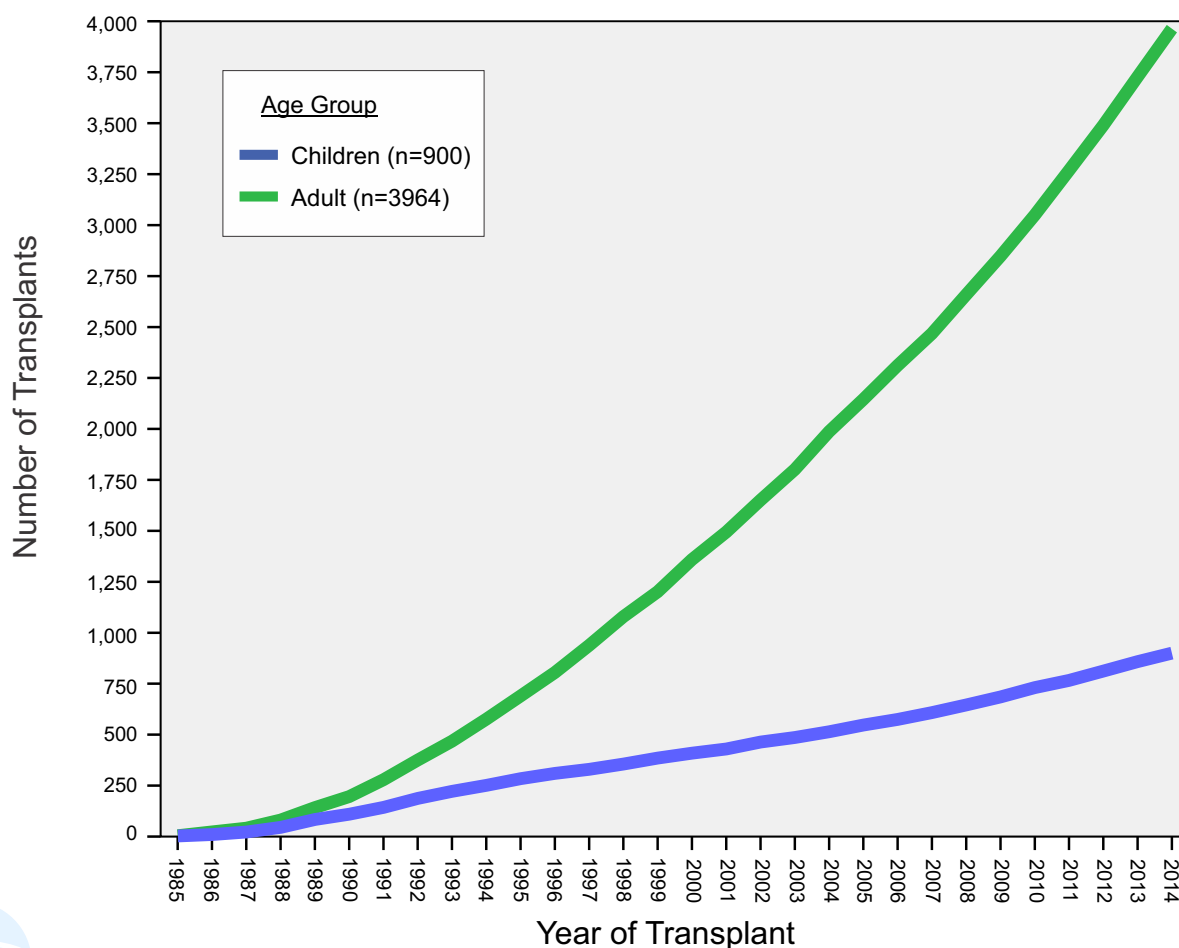


## Age at Primary Transplant by Era





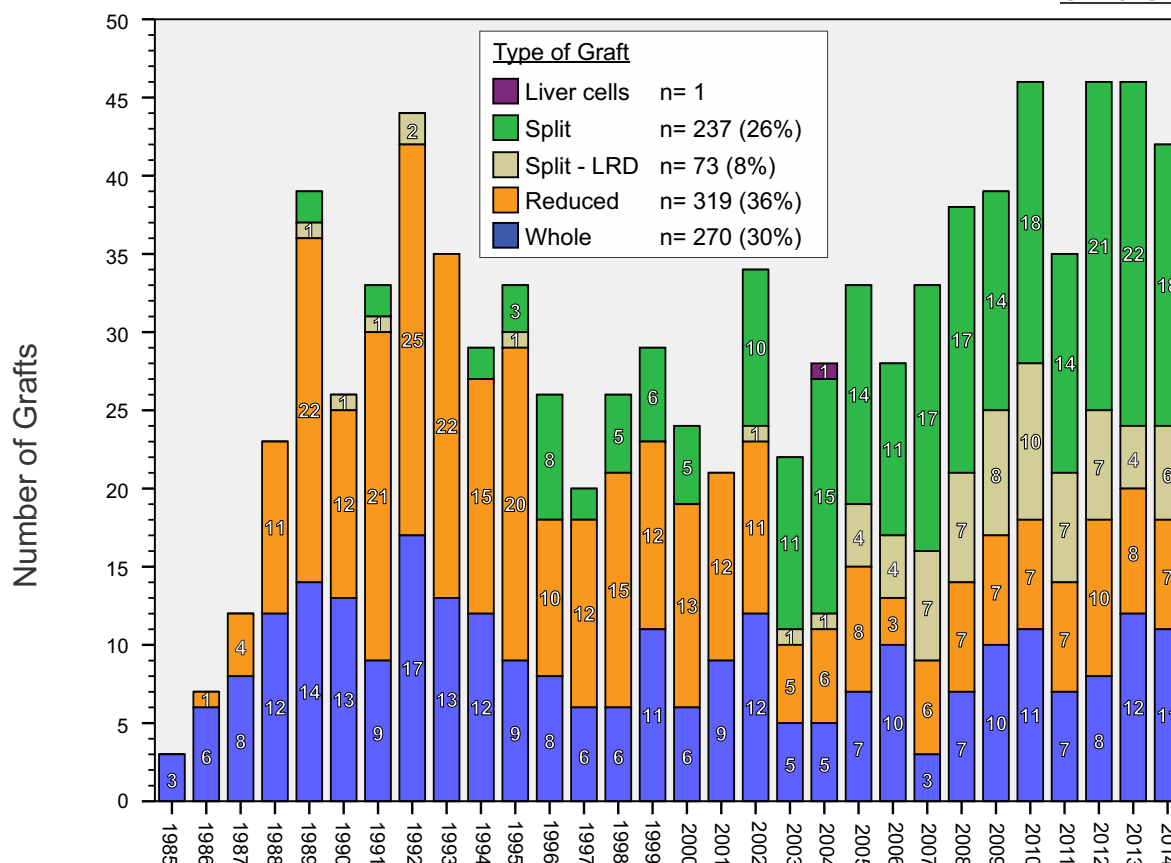
## Cumulative Number of Transplants



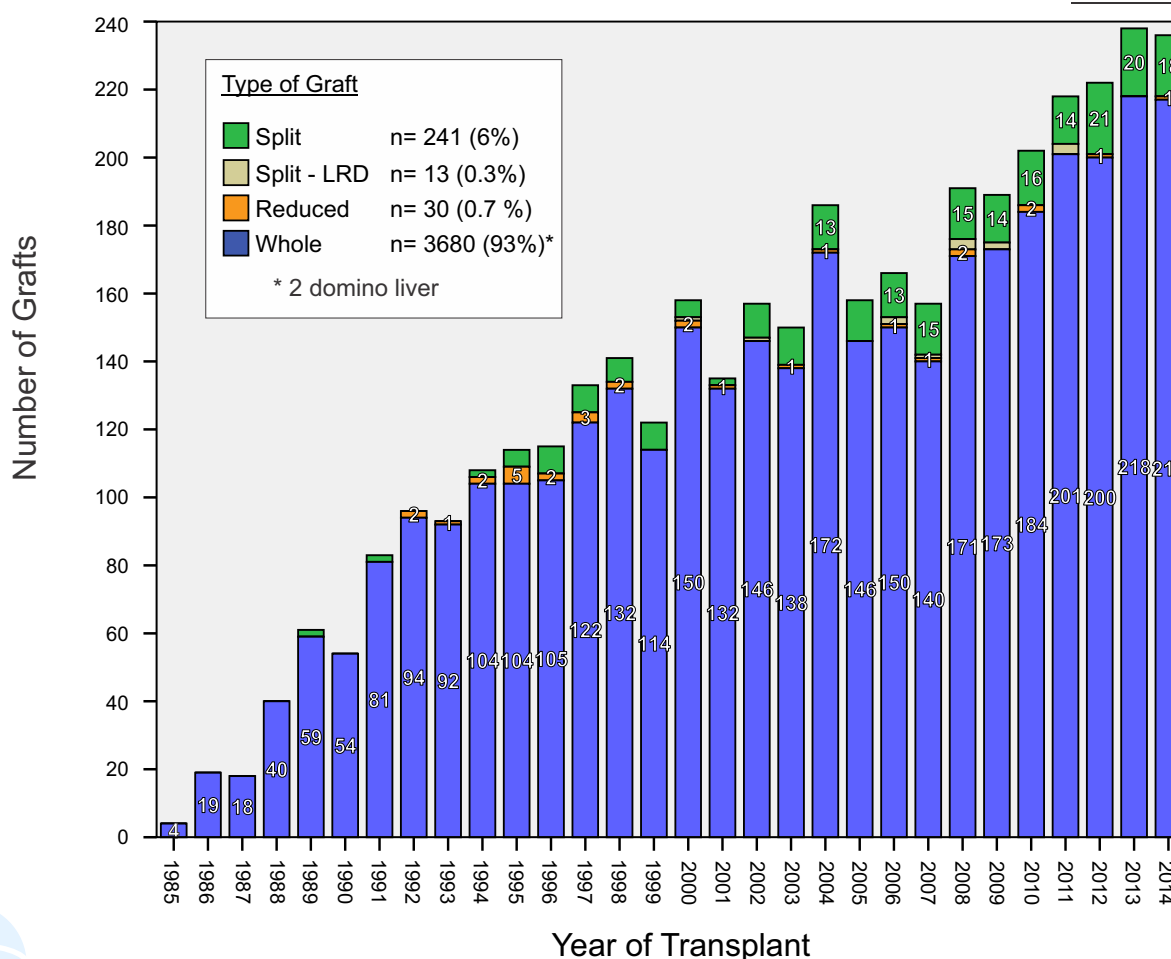
# Type of Graft by Year

## Split vs Reduced vs Whole

Children (n = 900)



Adults (n = 3964)

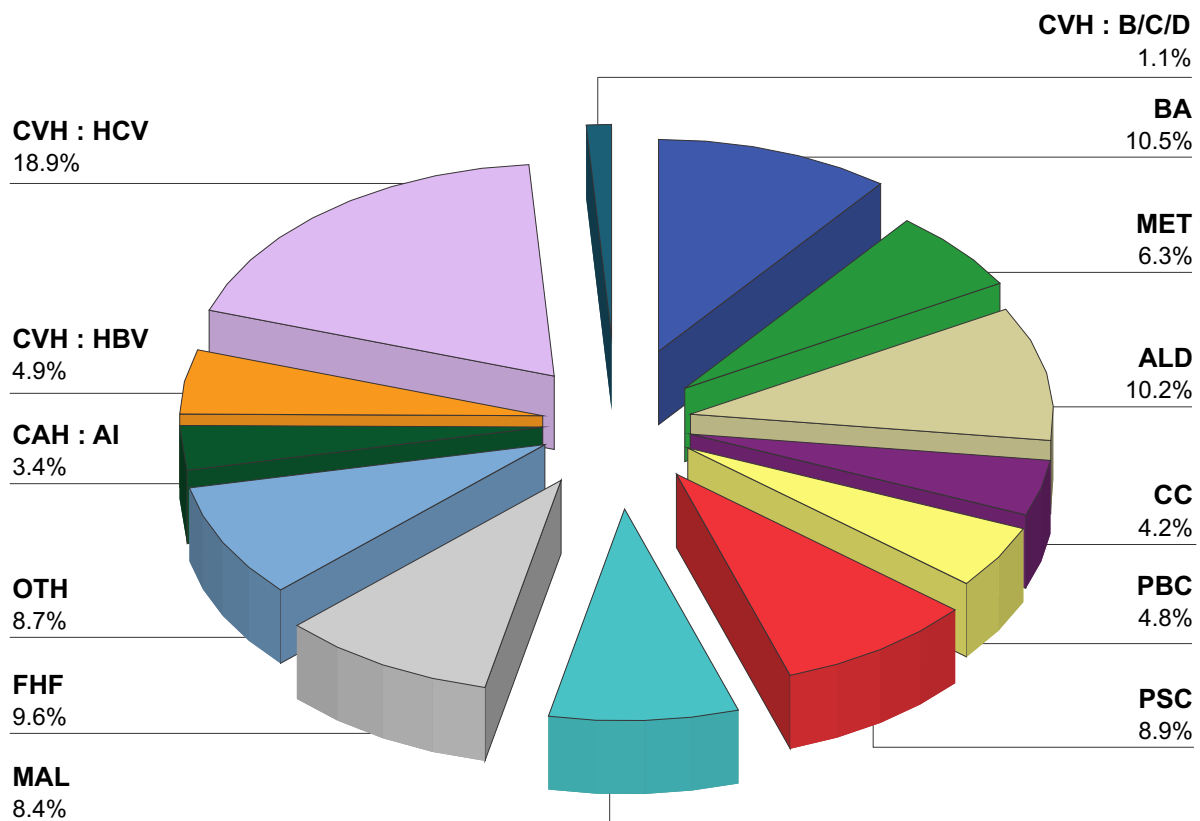




# Section 2

## Primary Diagnosis





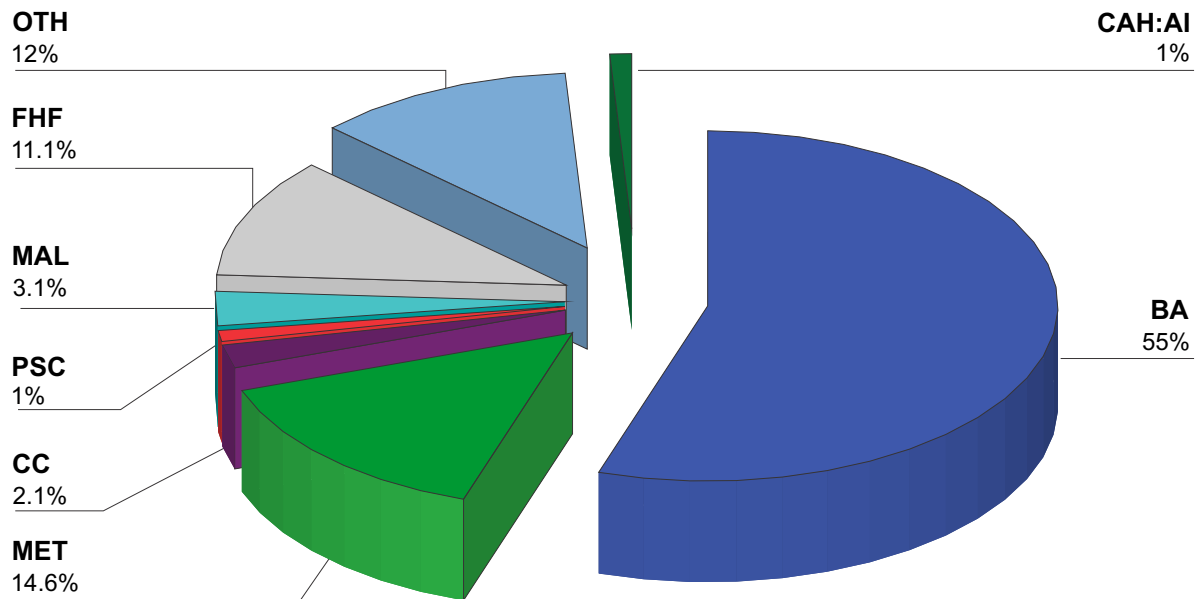
## Diagnosis Group

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

\* See Appendices for details

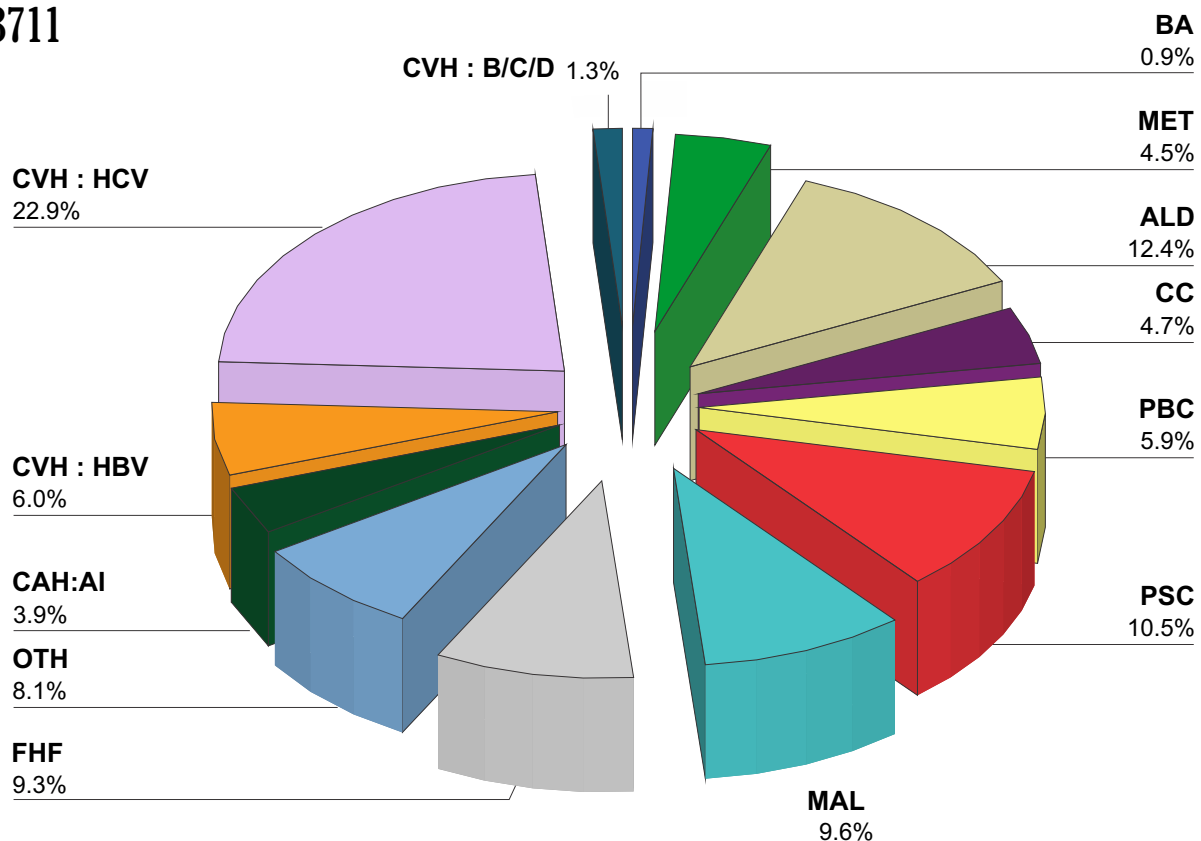
## Primary Diseases of Children

n = 794



## Primary Diseases of Adult Recipients

n = 3711

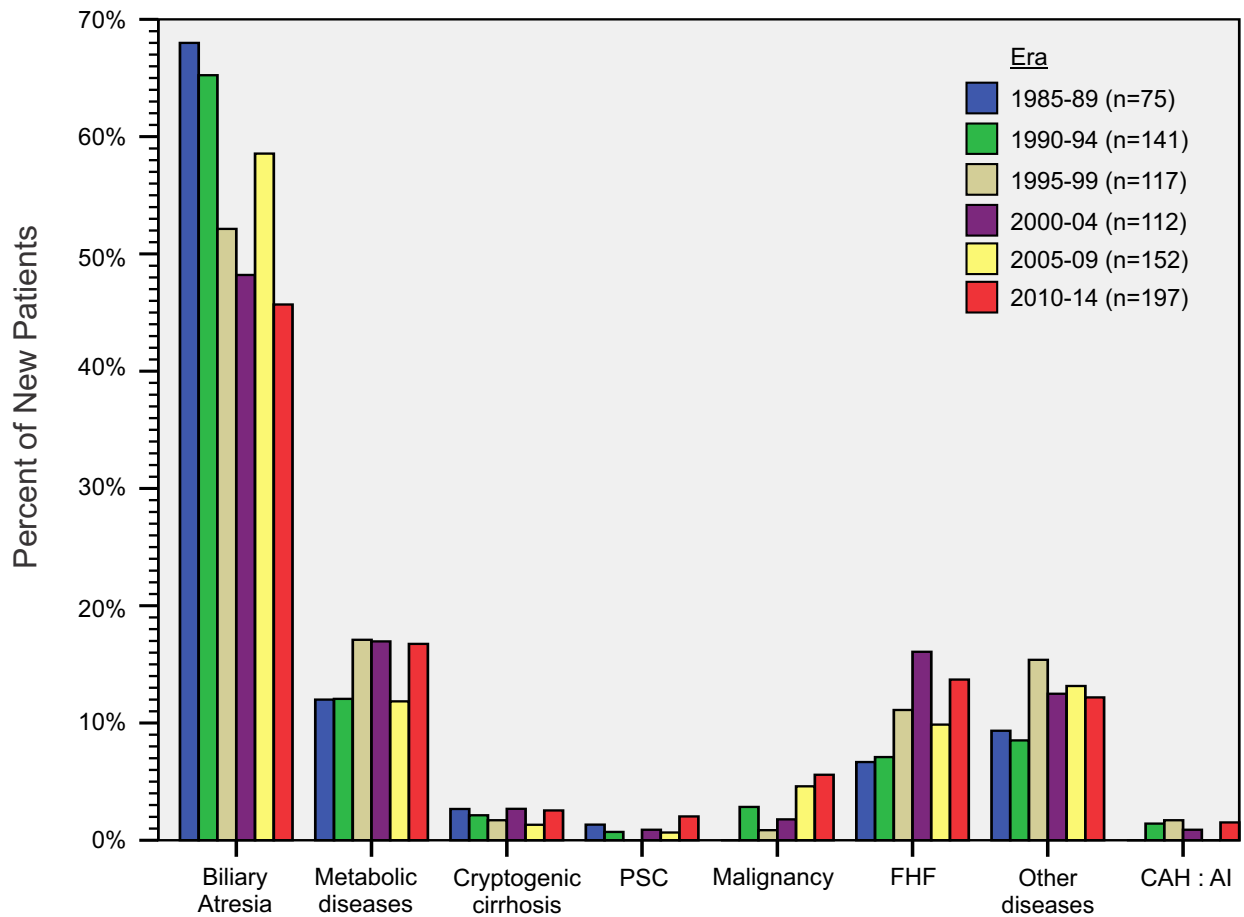


### Diagnosis Group

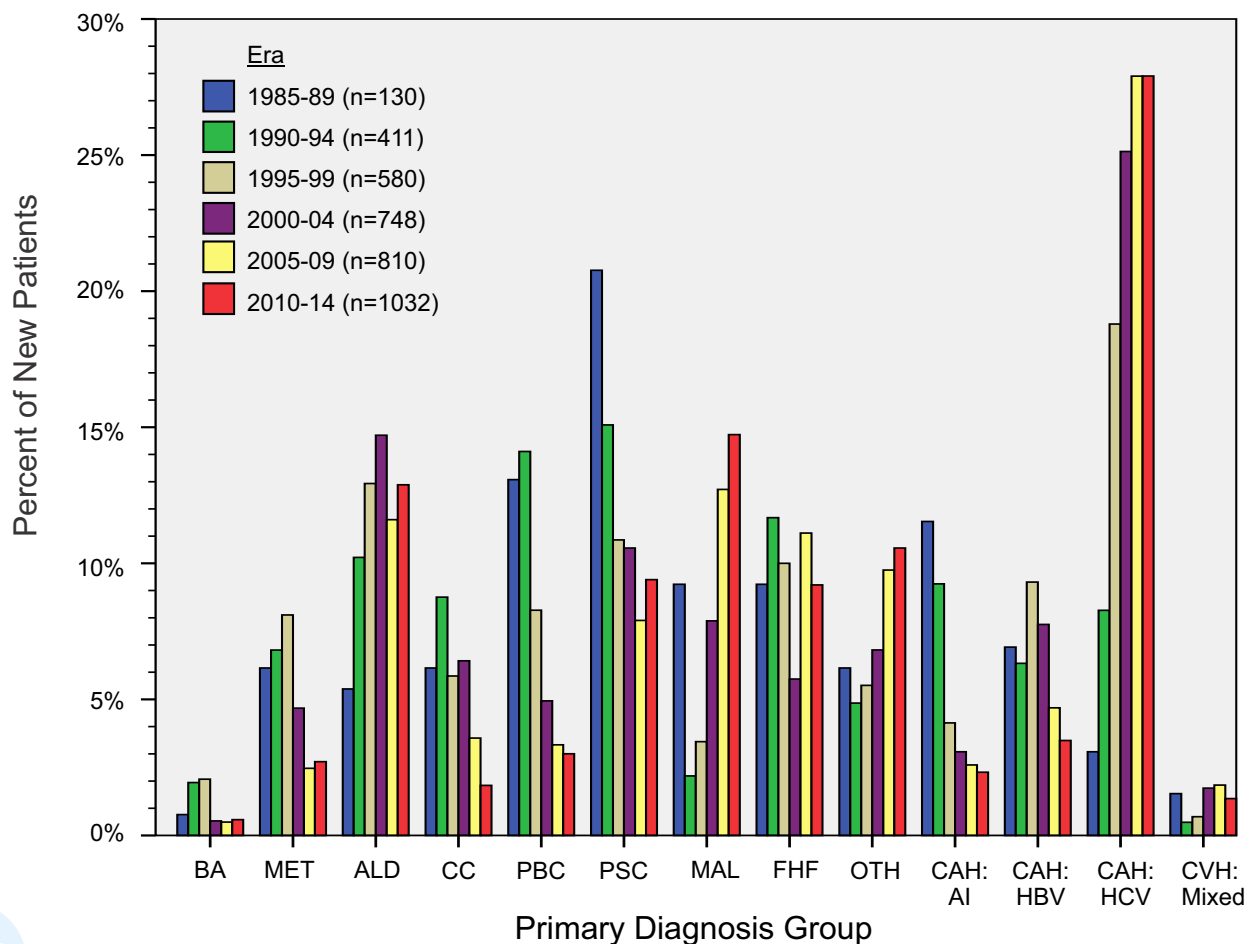
BA	- Biliary atresia	MAL	- Malignancy
MET	- Metabolic diseases	FHF	- Fulminant hepatic failure
ALD	- Alcoholic cirrhosis	OTH	- Other diseases
CC	- Cryptogenic cirrhosis	CAH : AI	- Chronic active hepatitis [autoimmune]
PBC	- Primary biliary cirrhosis	CVH : HBV	- Chronic viral hepatitis B
PSC	- Primary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

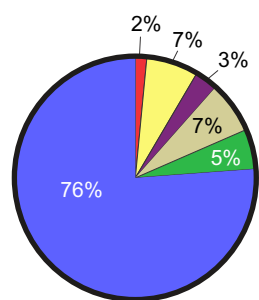


## Children (n=794)

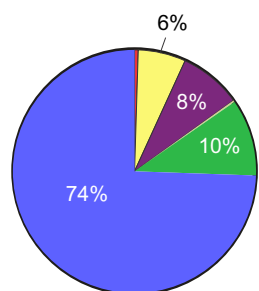


## Adults (n = 3711)

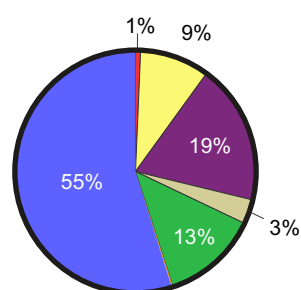




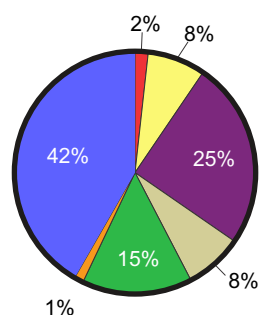
— 1985 - 89  
(n=130)



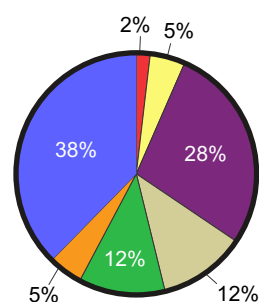
— 1990 - 94  
(n=411)



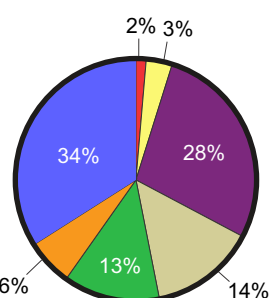
— 1995 - 99  
(n=580)



— 2000 - 04  
(n=748)



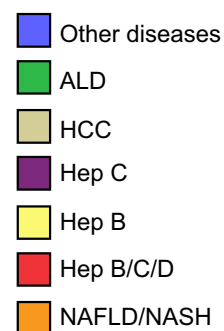
— 2005 - 09  
(n=810)

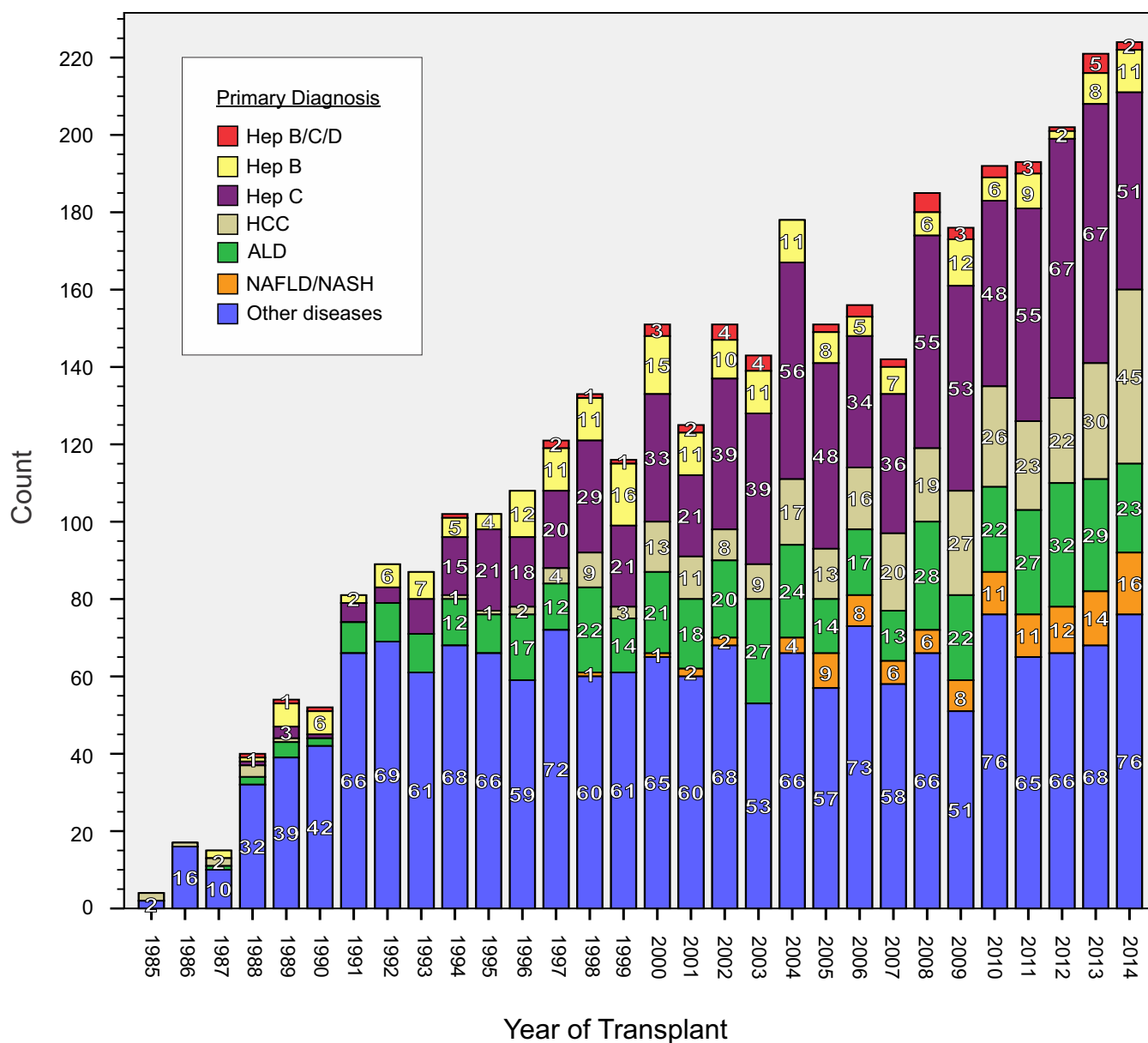


— 2010 - 14  
(n=1032)

**Era**

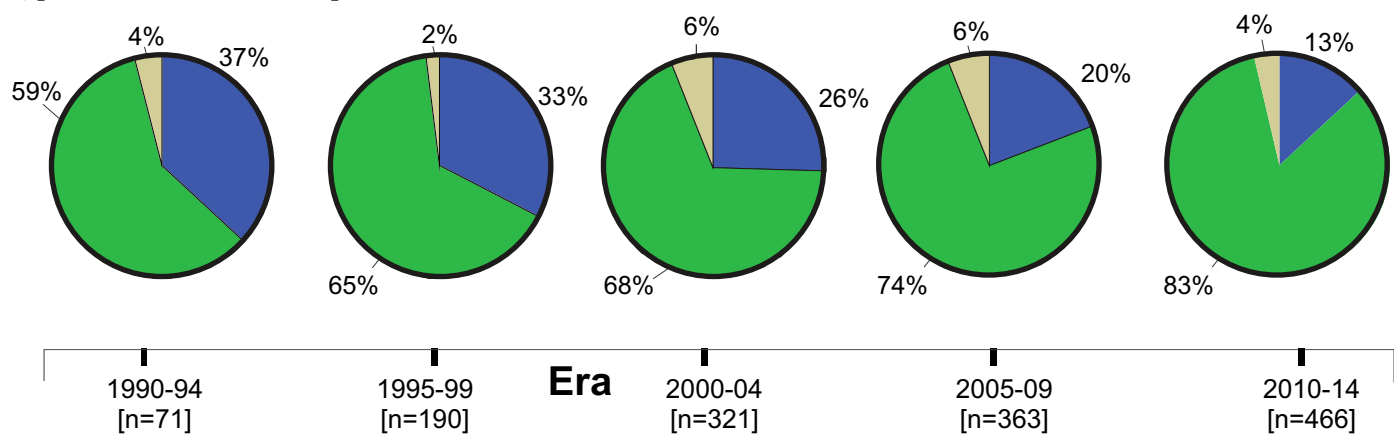
## Adult Diagnosis



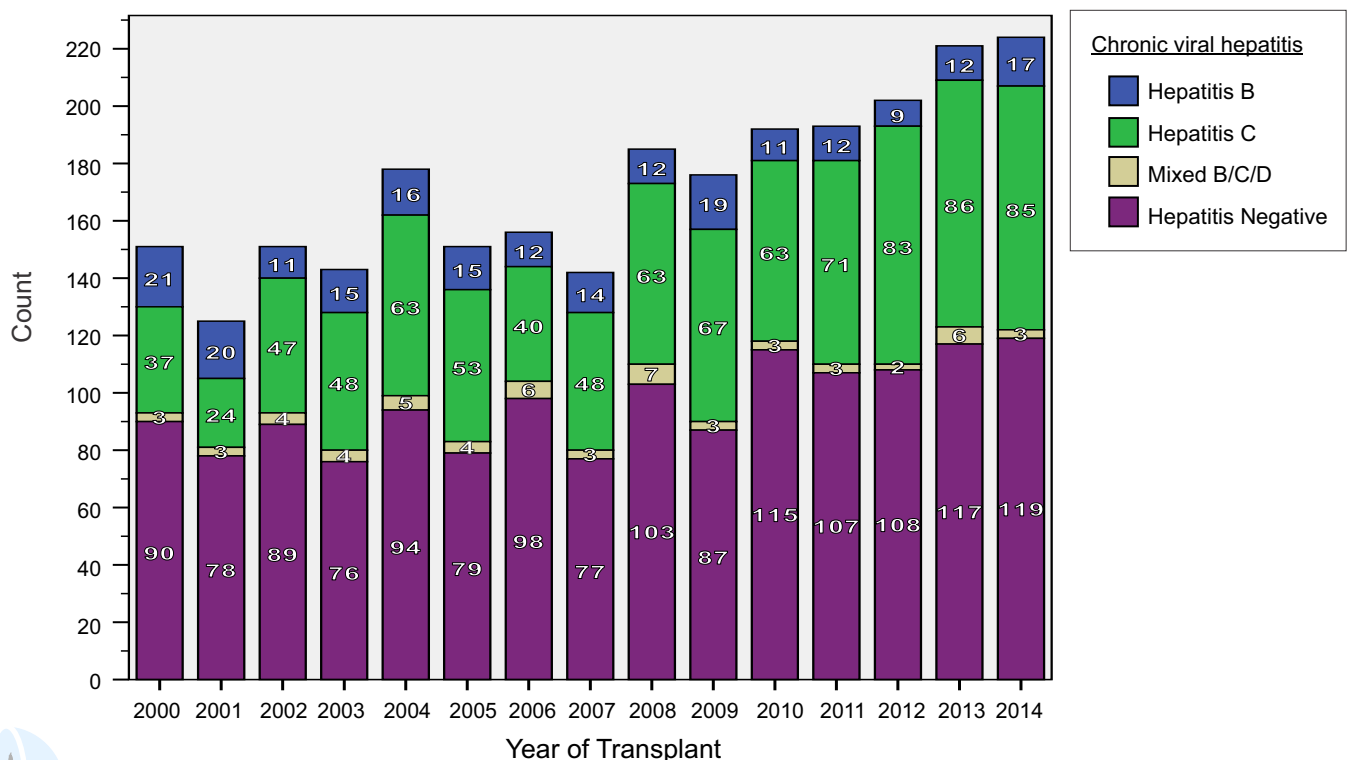


			Secondary / Tertiary diagnosis					
Primary Diagnosis		n =	Hepatitis C	Hepatitis B	Hepatitis B,C	HCC	NAFLD	ALD
	Hepatitis C	849		7		252	5	226
	Hepatitis B	220	3			83	1	6
	Hepatitis BD/BC/BCD	51				9		7
	HCC + cirrhosis	328	167	88	7		13	69
	ALD	461	22	3		59	9	
	NAFLD	111		2		24		5
	Other	1691	18	8		55	3	22
	TOTAL	3711						

## Type of Chronic Viral Hepatitis in Adult Patients



## Hepatitis diagnosis



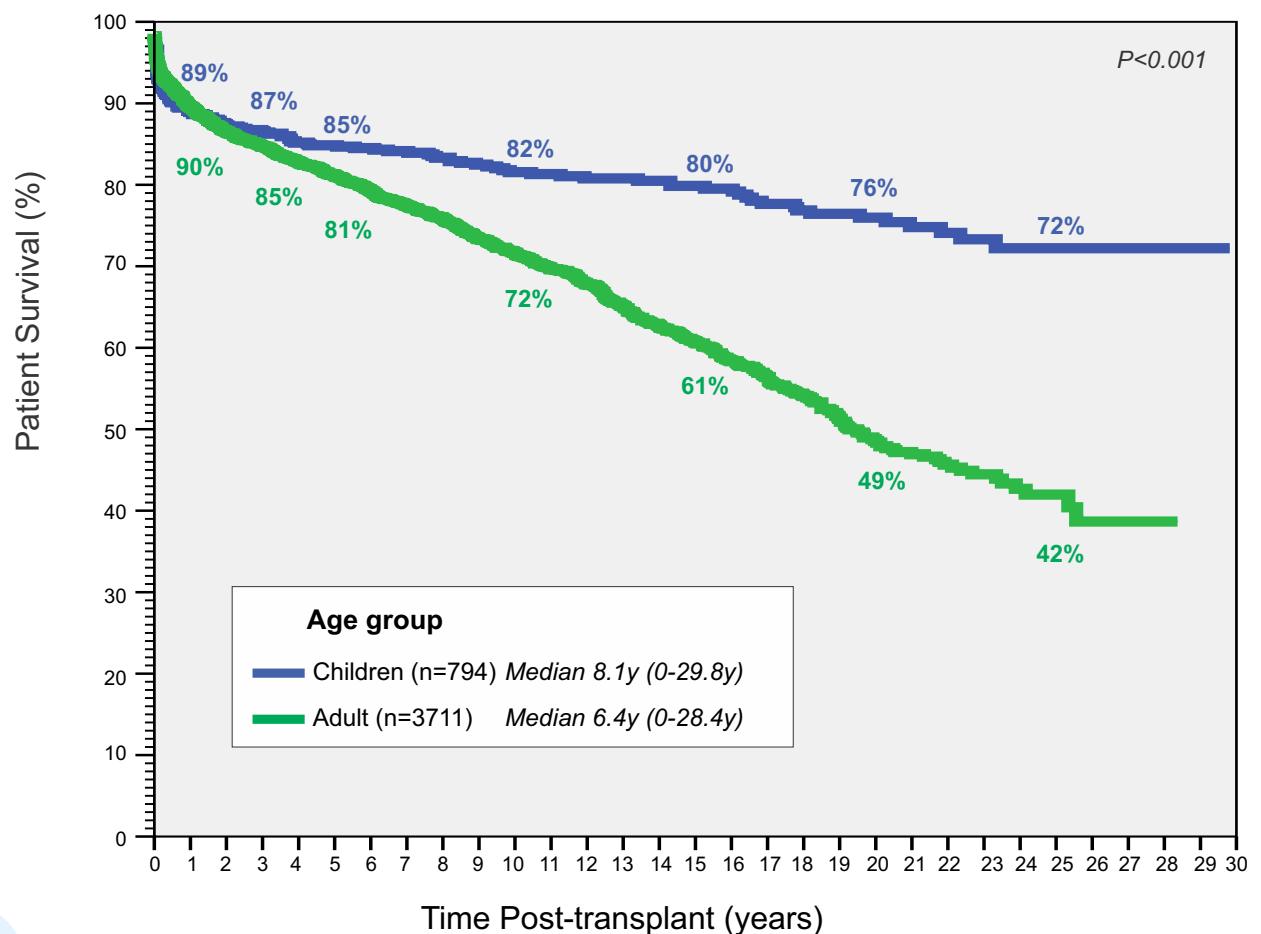
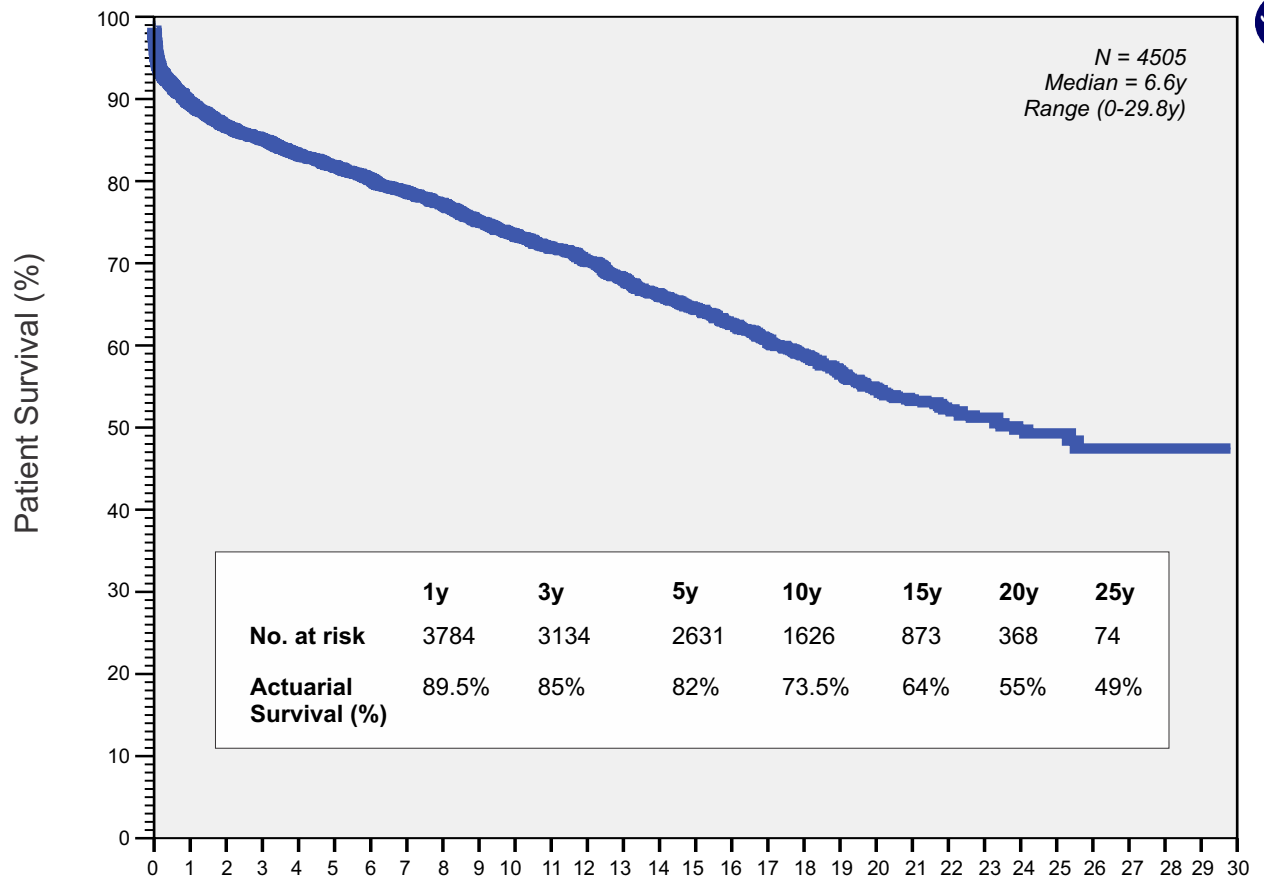


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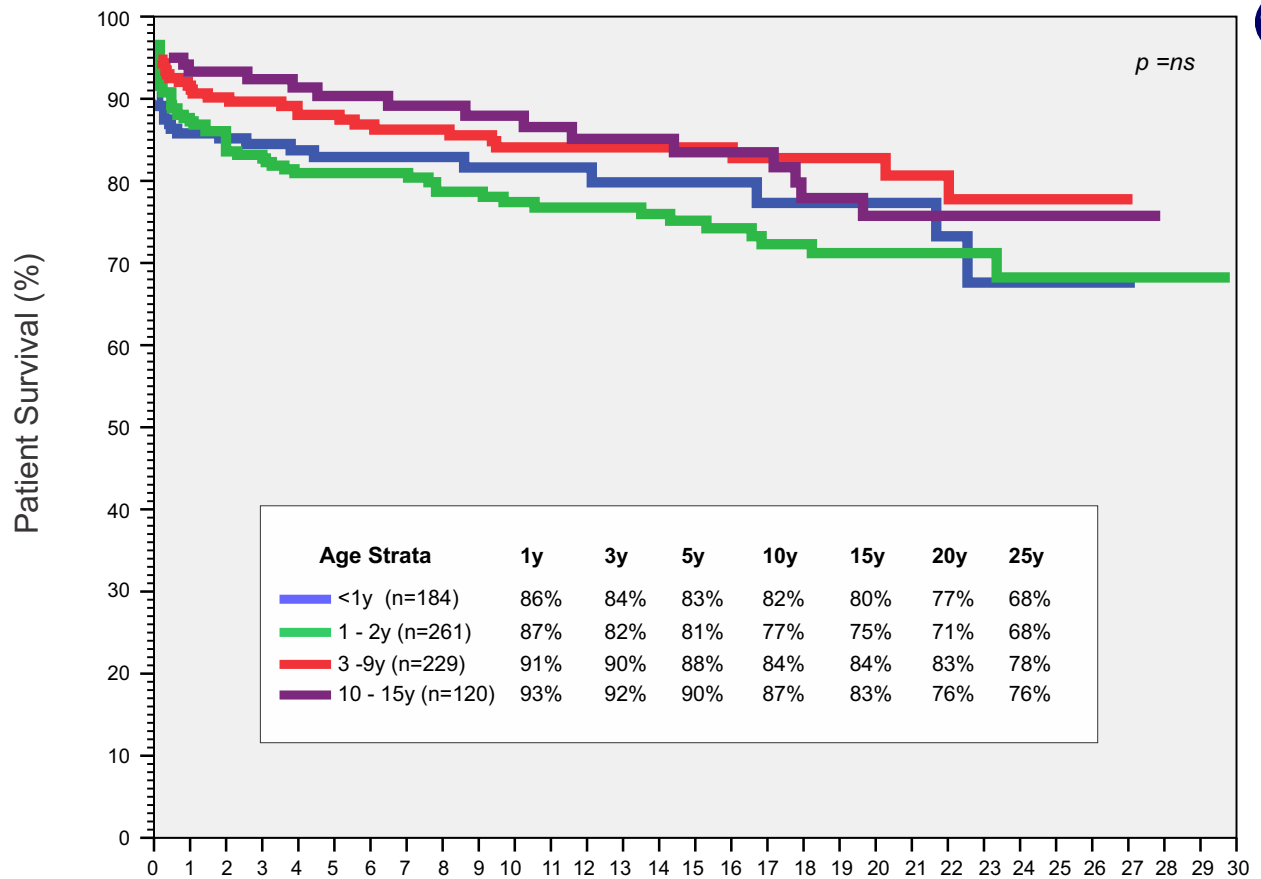
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## Patient Survival

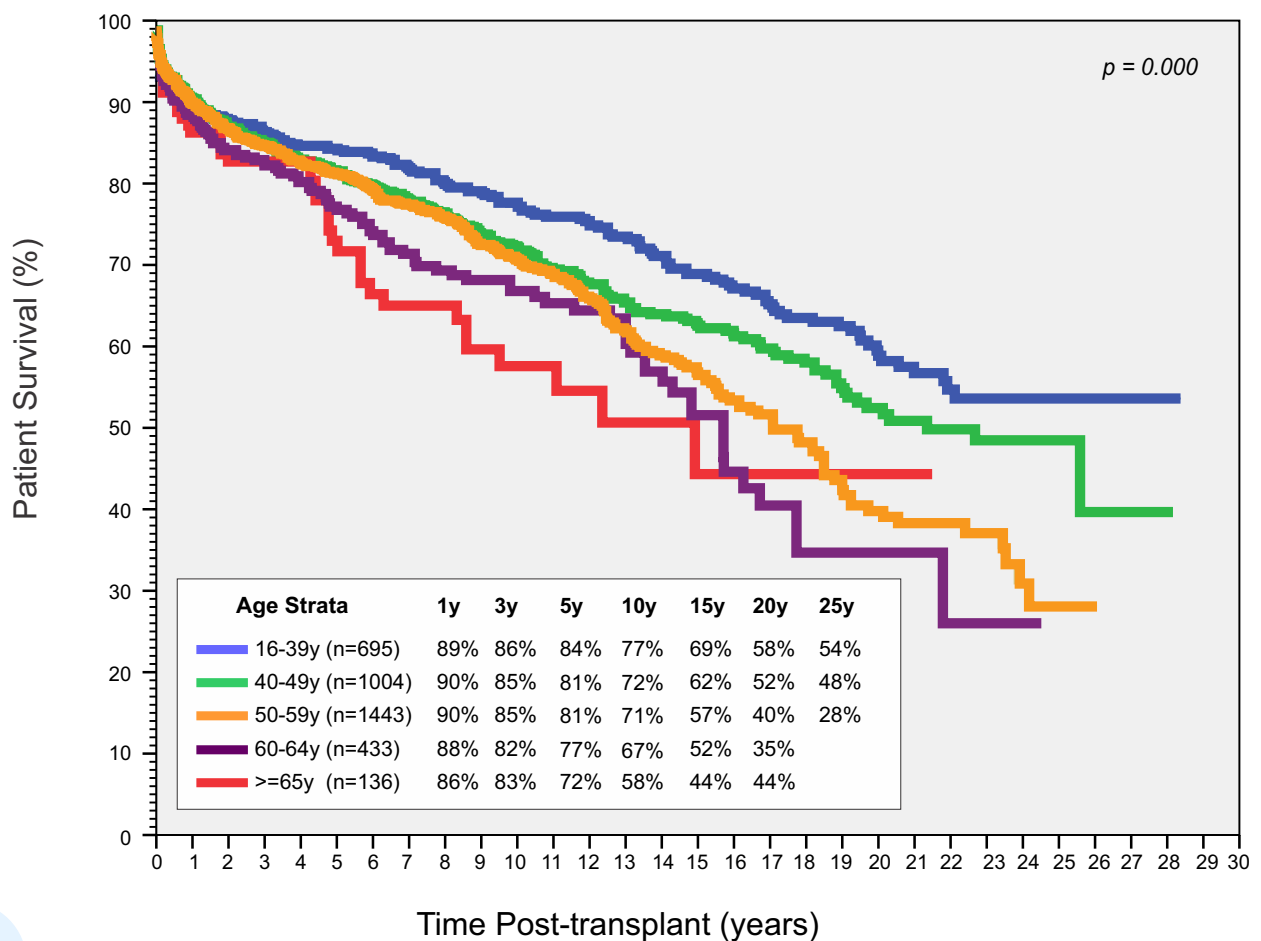


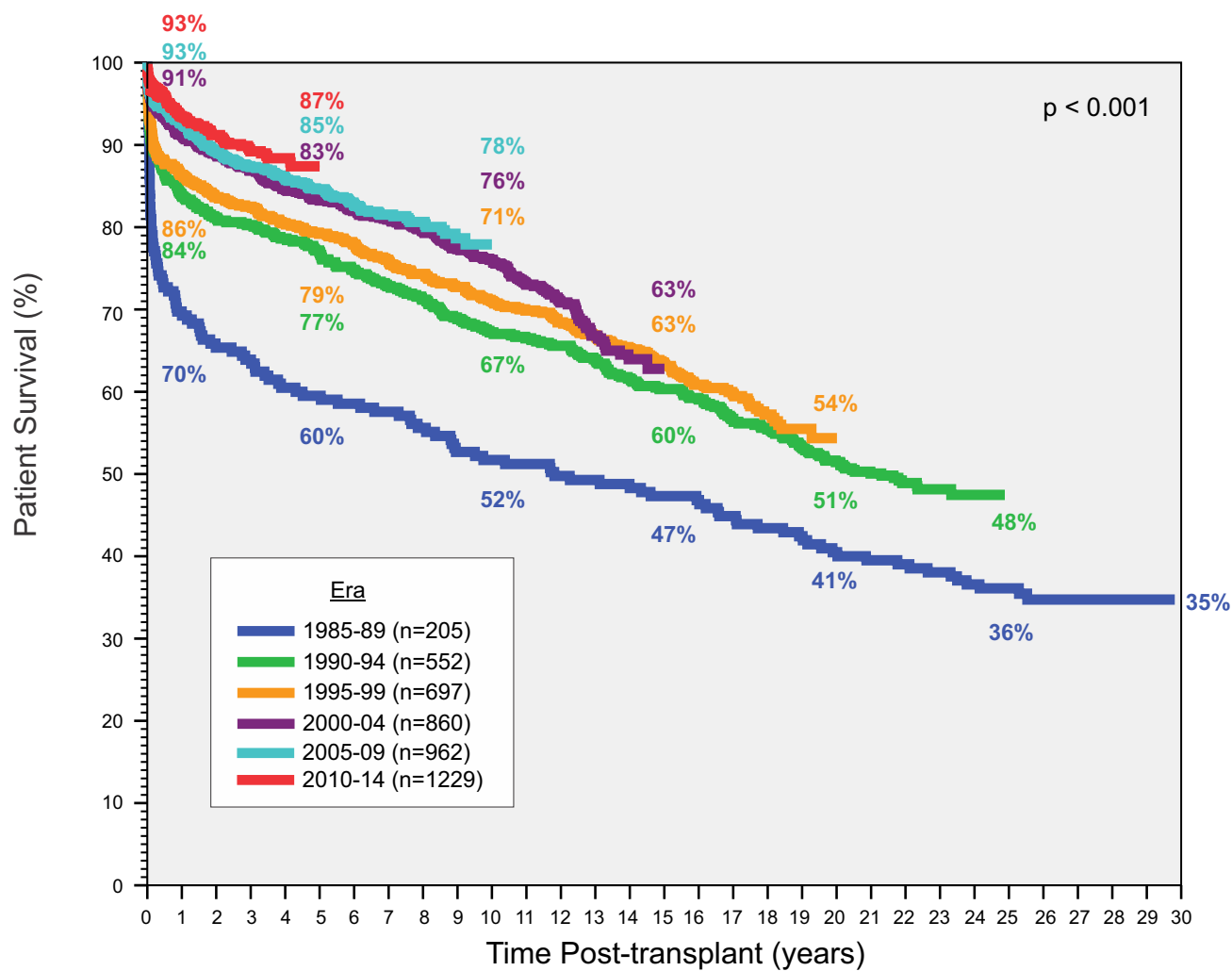


## Children n = 794

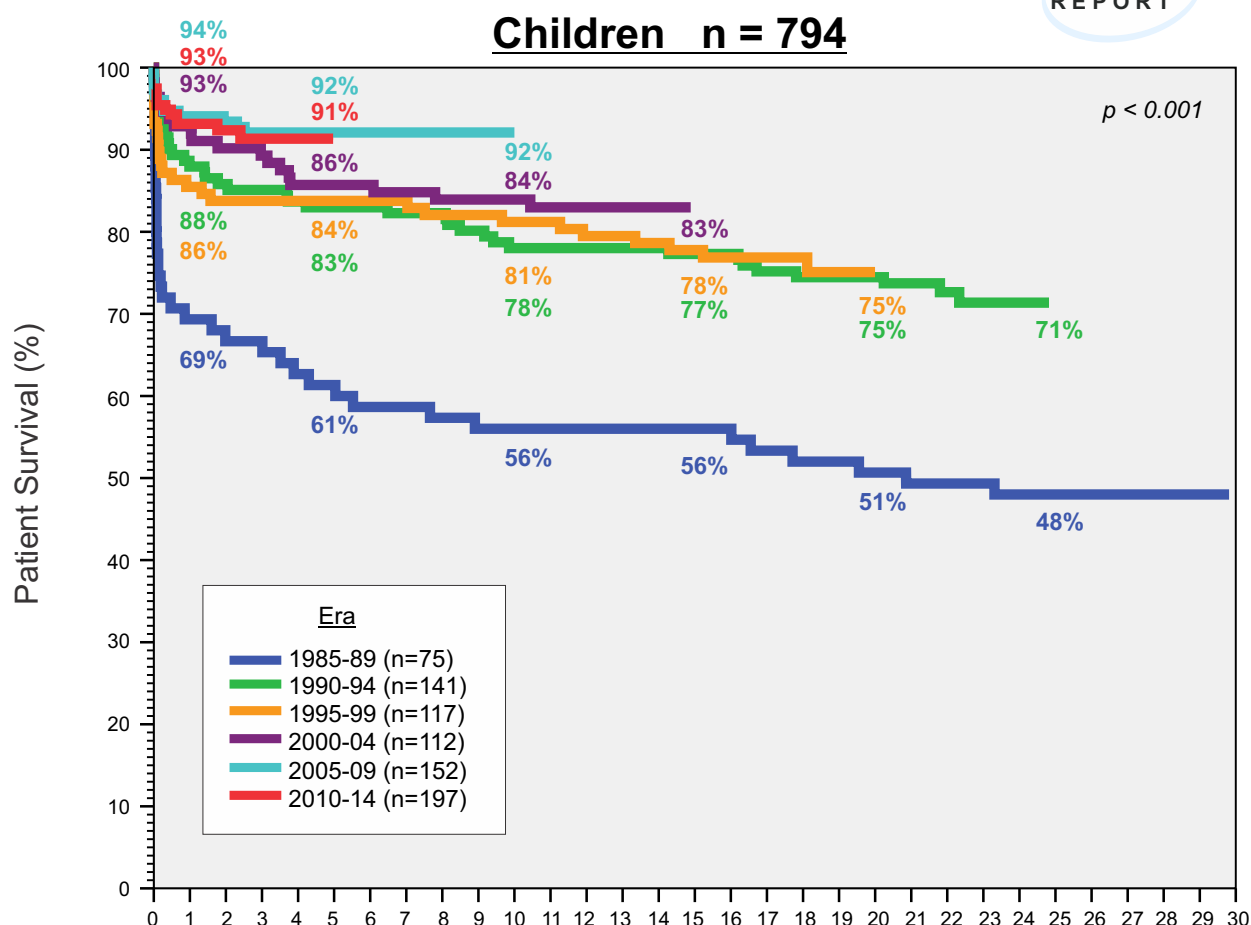


## Adults n = 3711



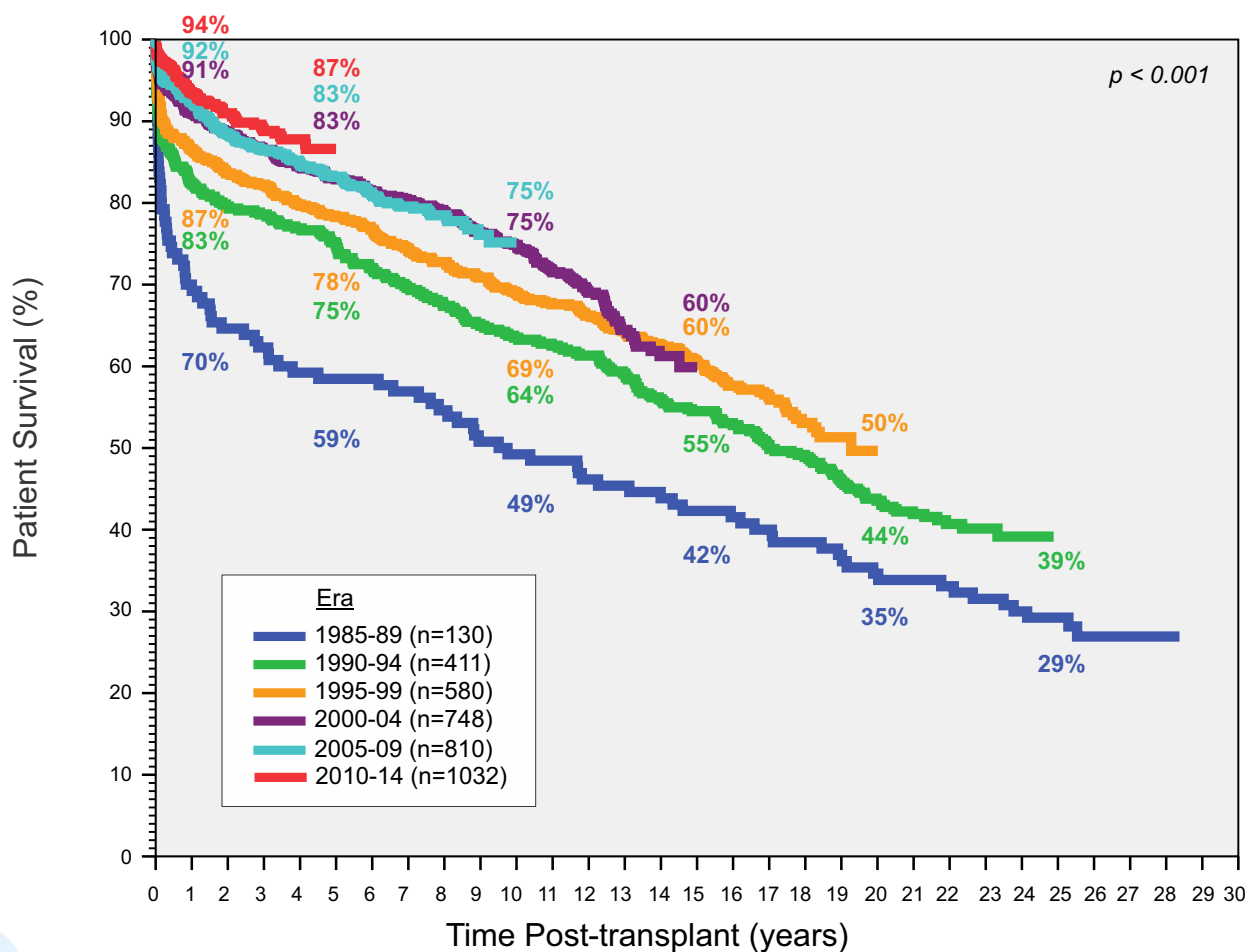






# Patient Survival - Adults

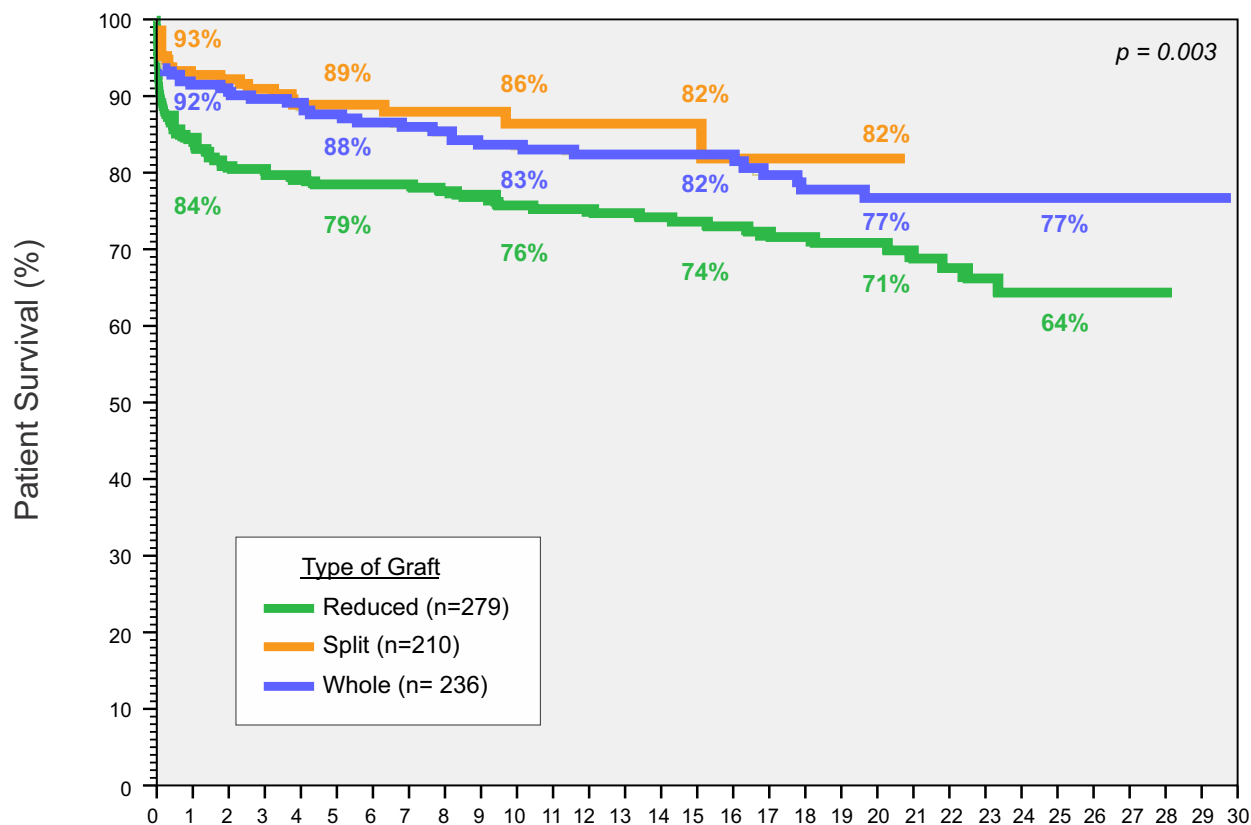
## Adults n = 3711



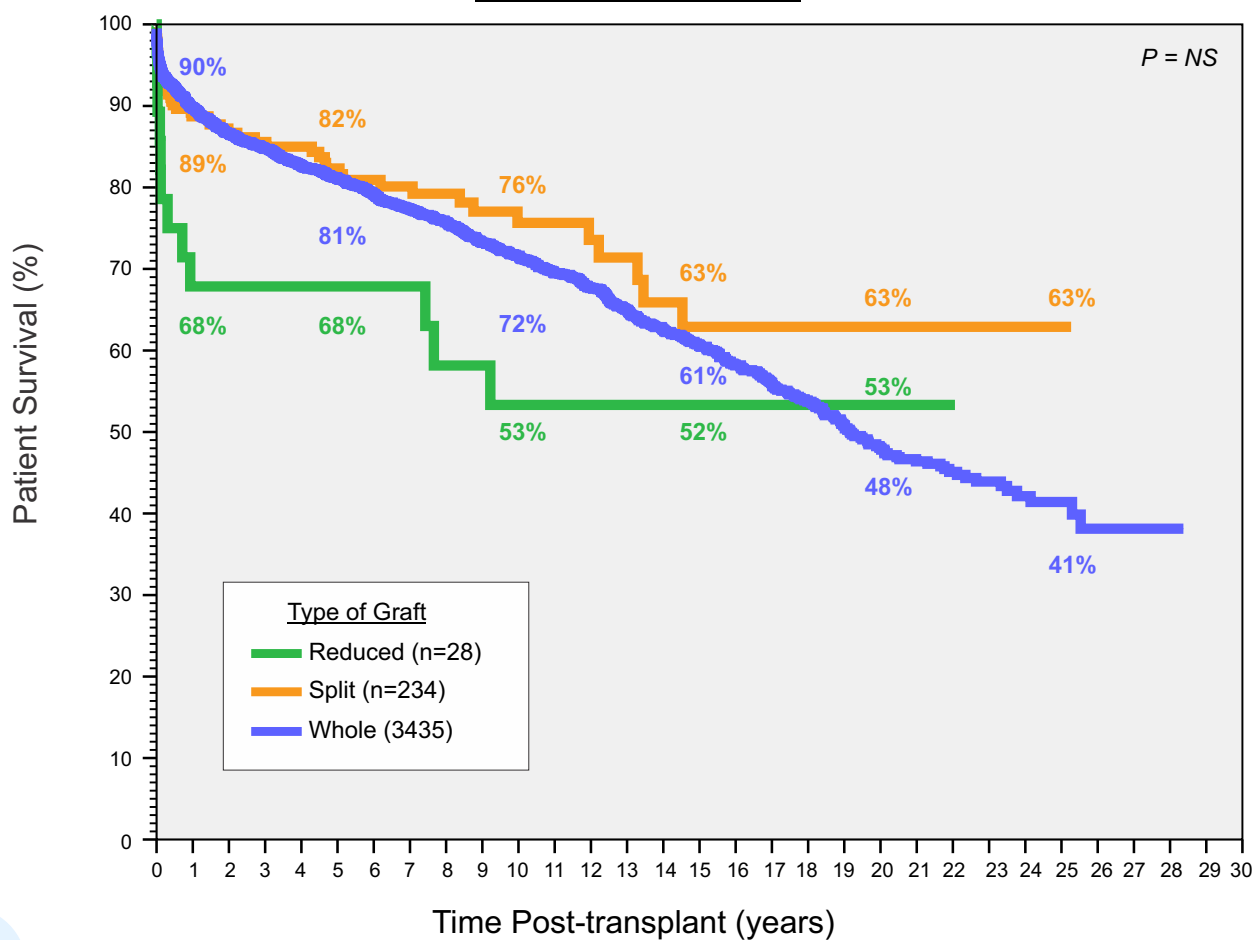
# Patient Survival by Type of Primary Graft [Deceased donors]

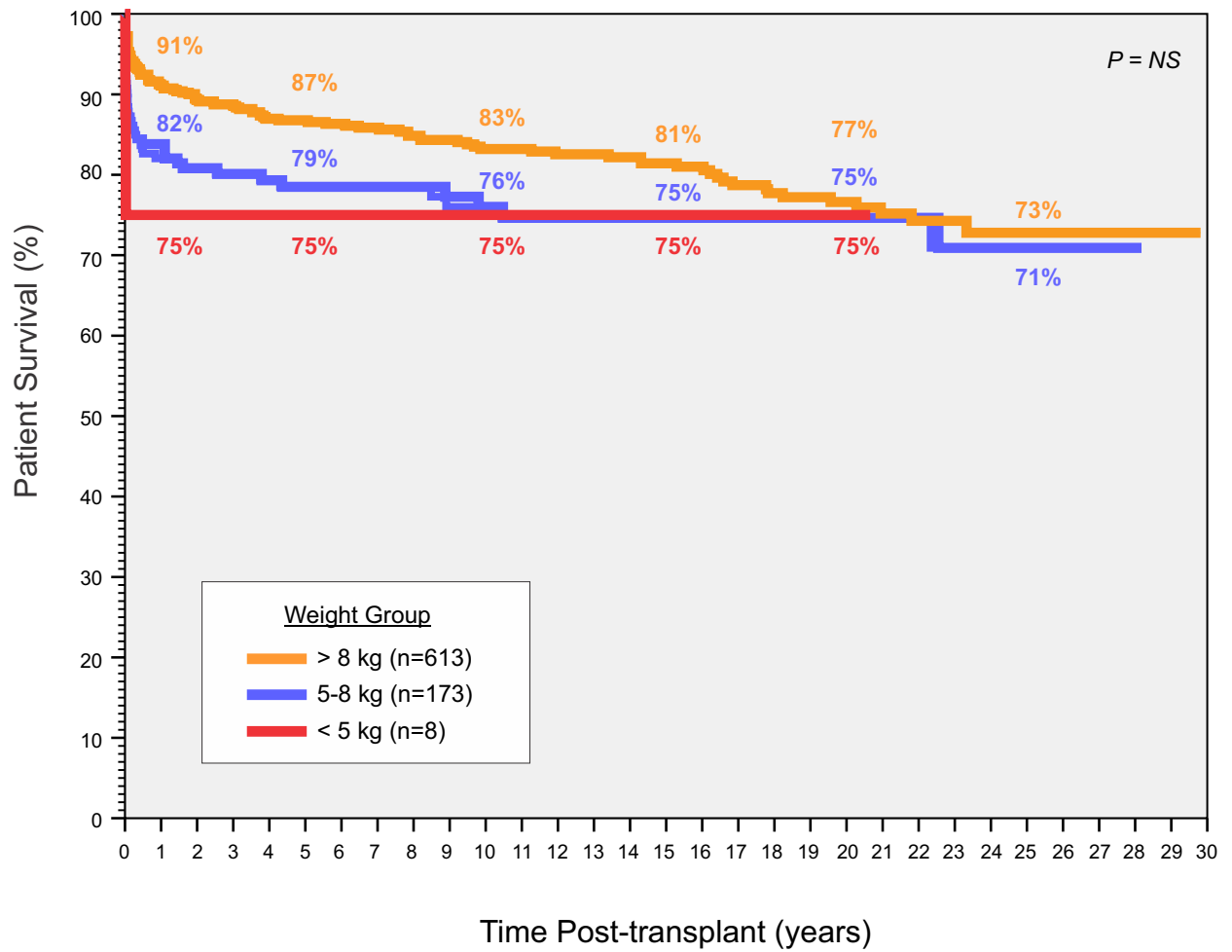


## Children n = 725

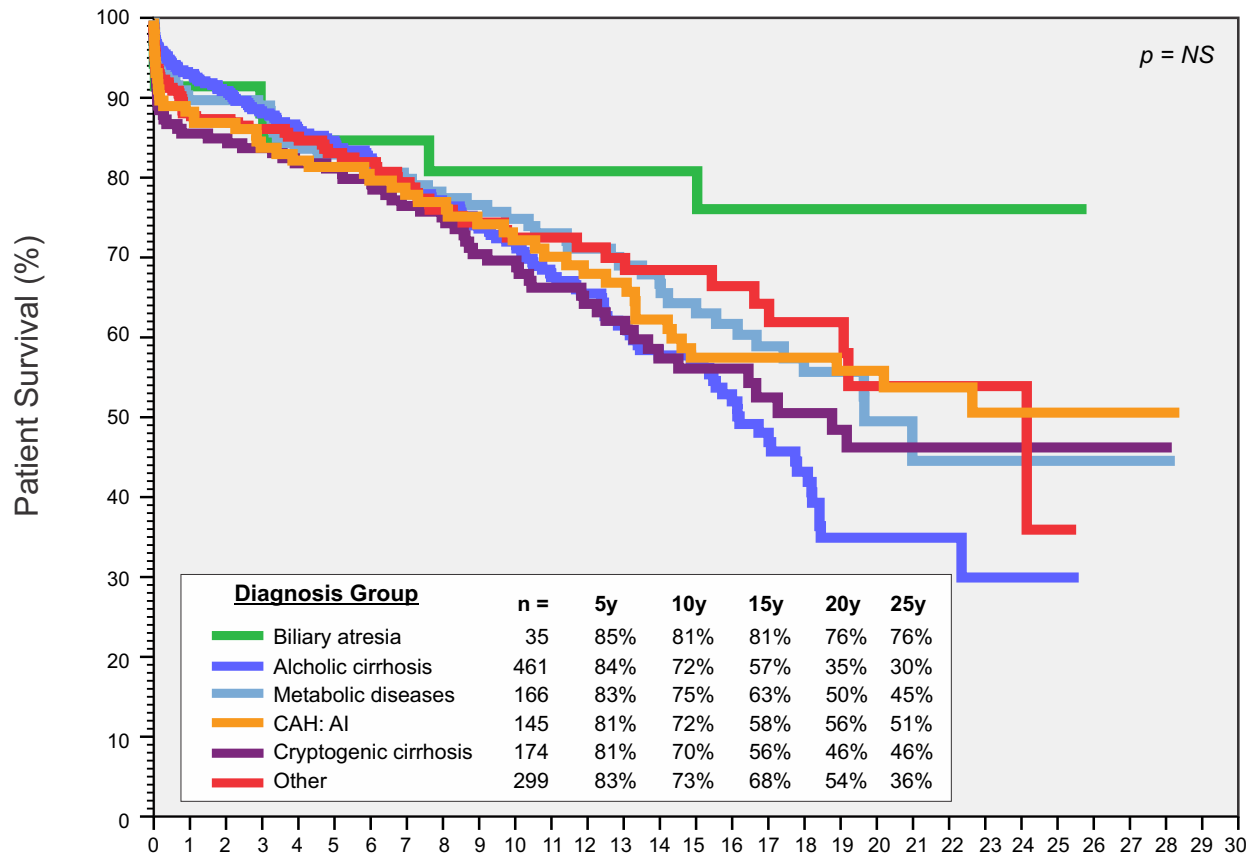


## Adults n = 3697

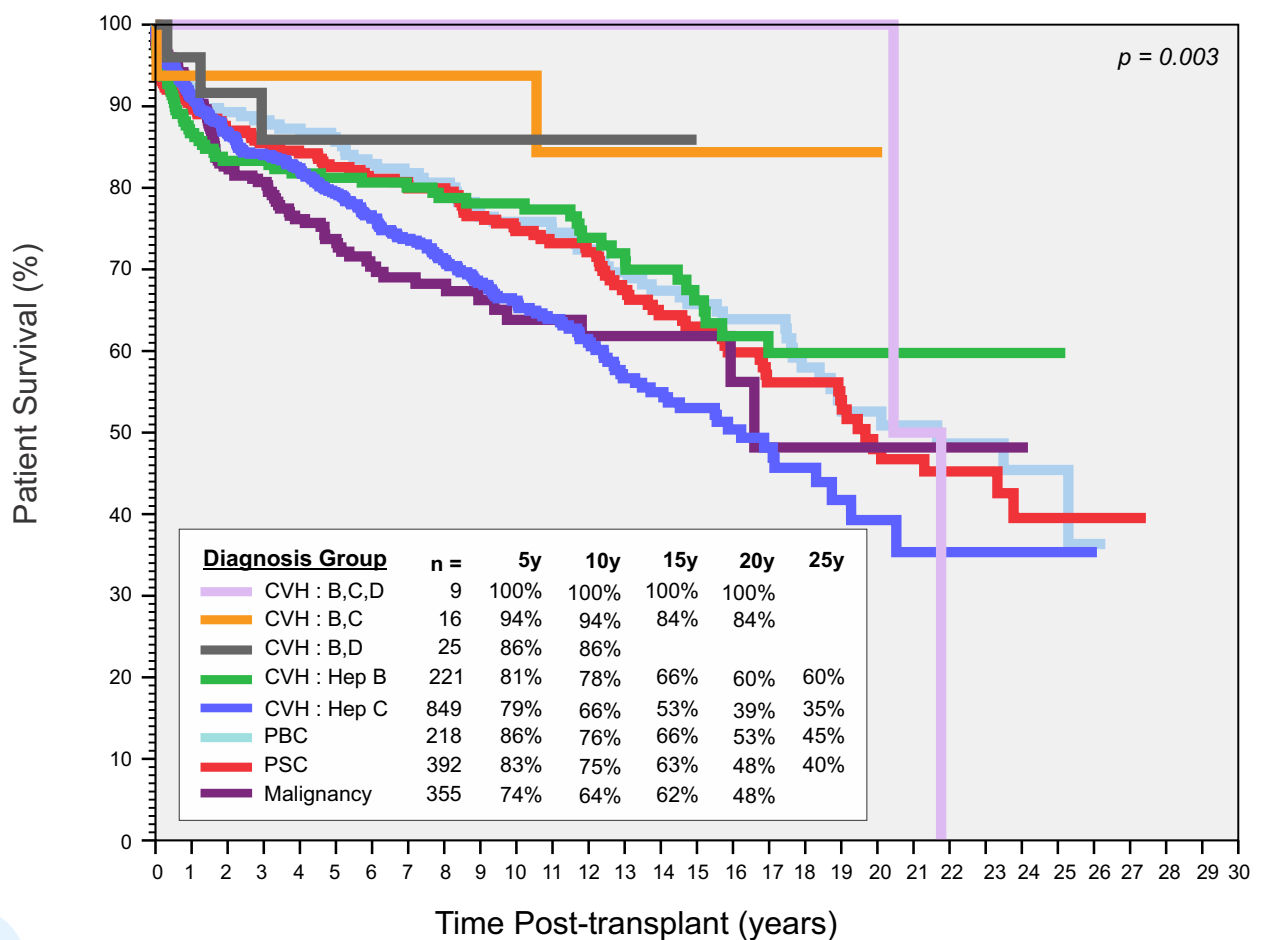




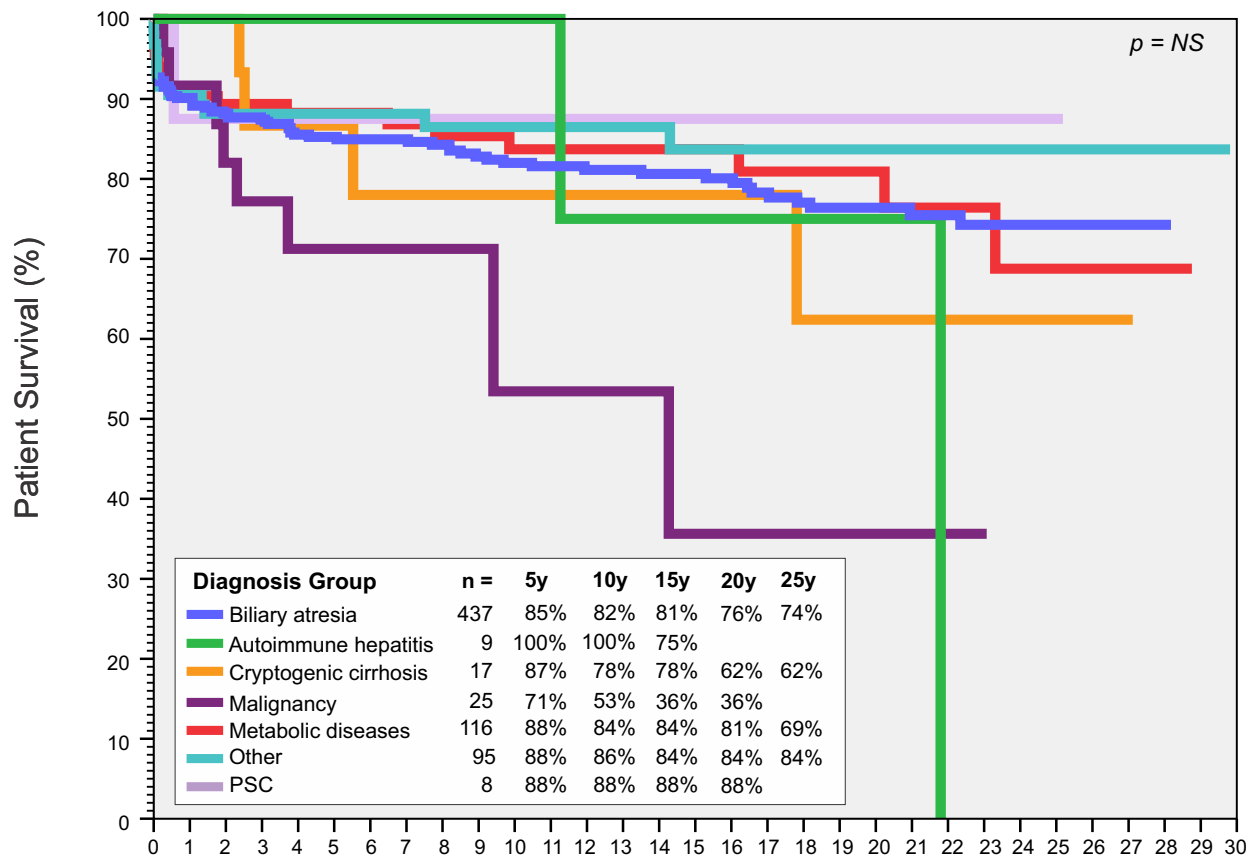
## (1) Adults [excluding FHF] n = 1280



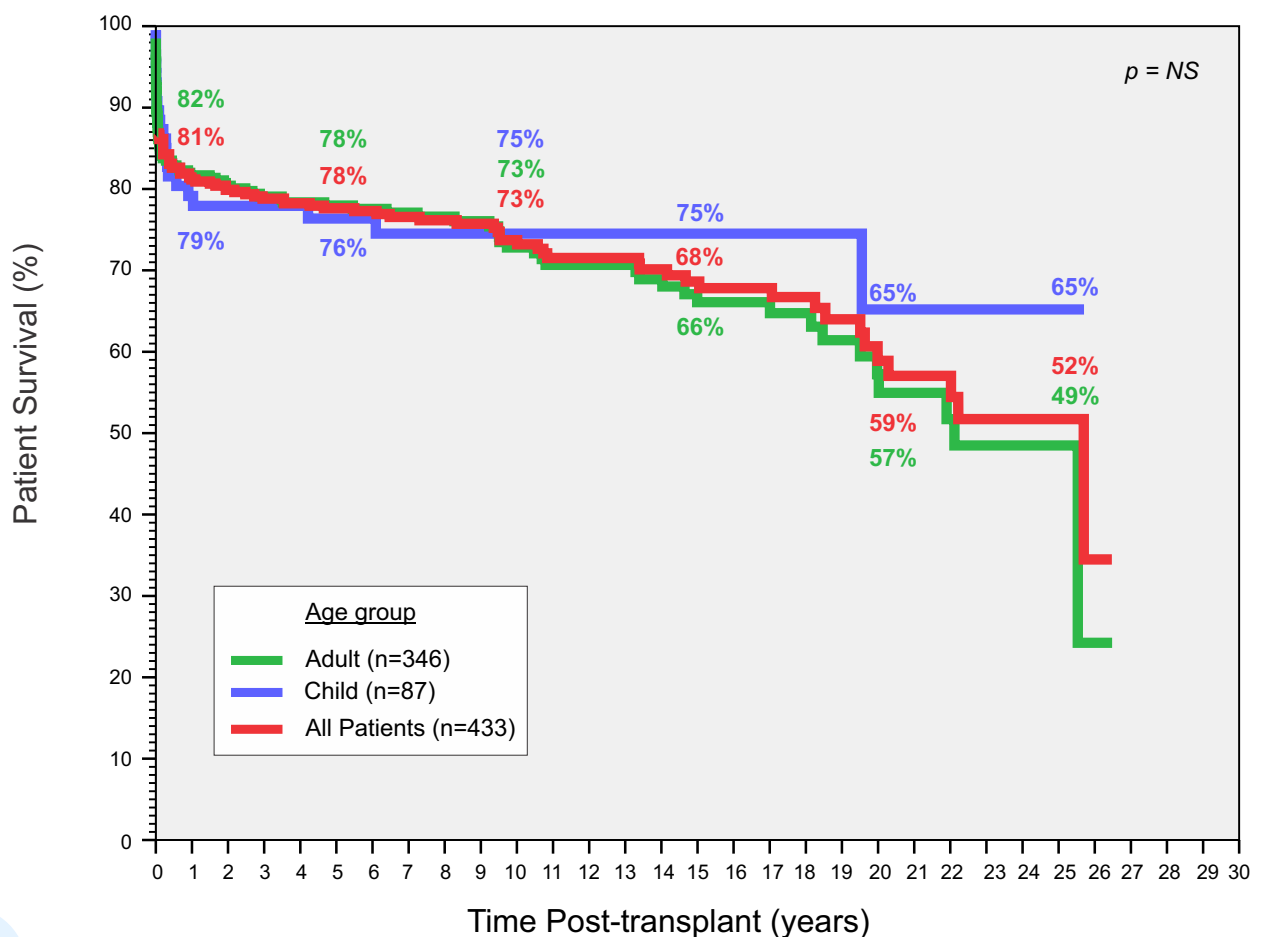
## (2) Adults [excluding FHF] n = 2085

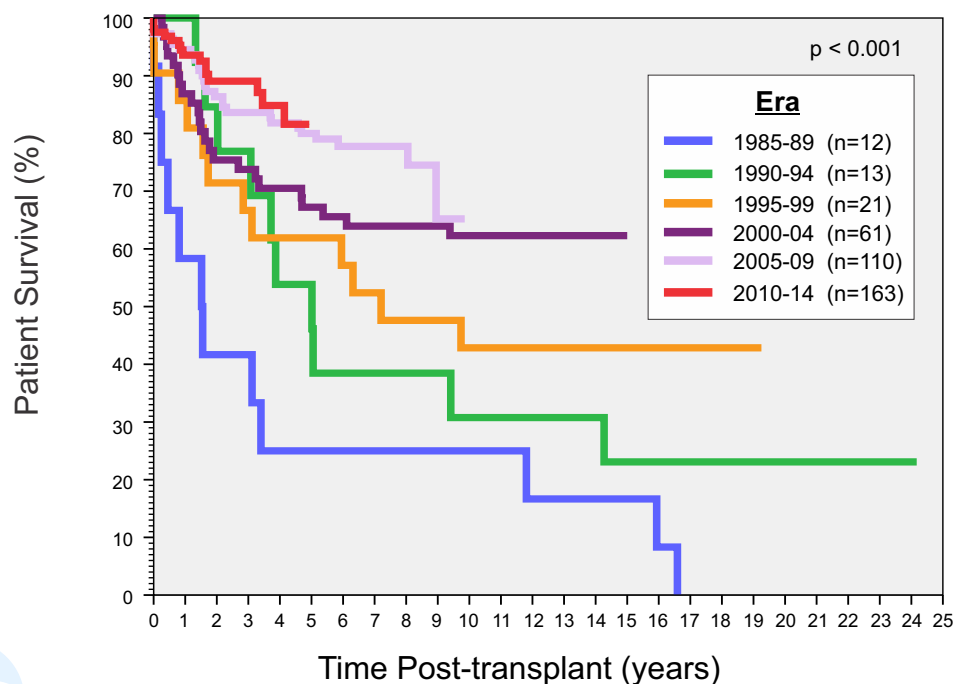
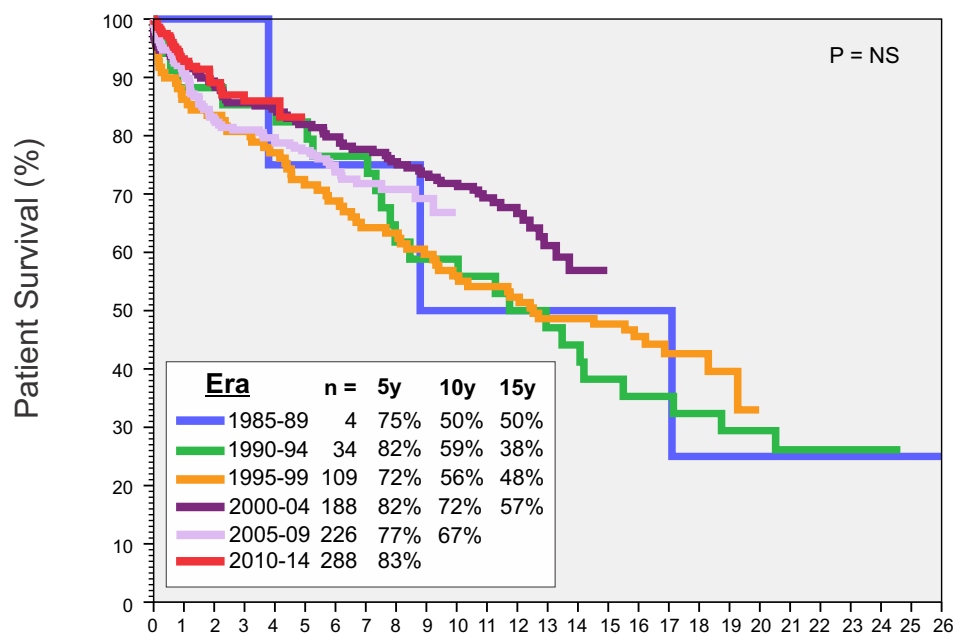
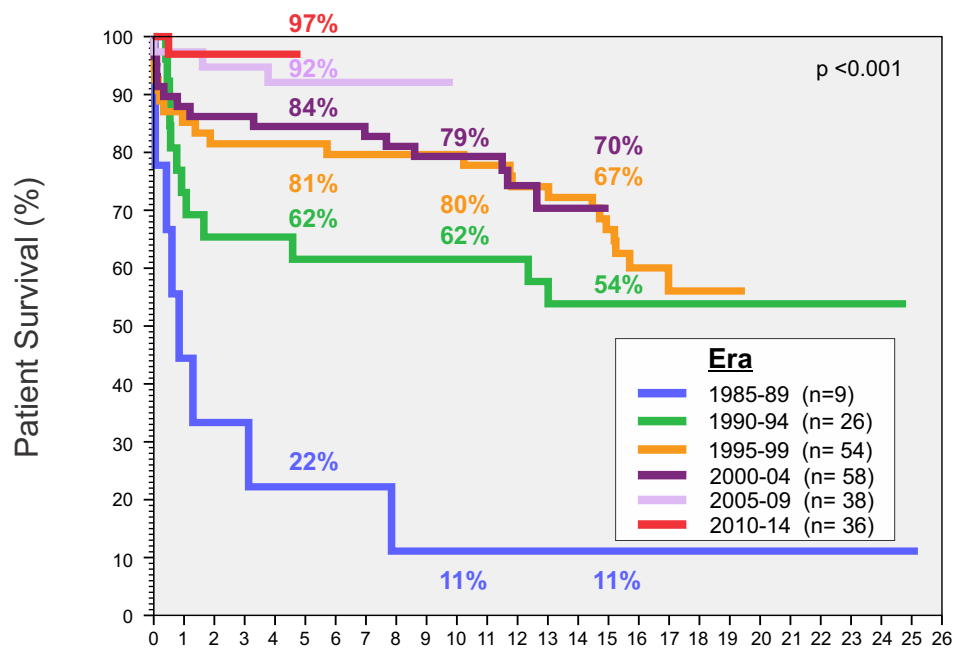


## (3) Paediatric recipients [excluding FHF] n = 707



## (4) Fulminant hepatic failure n = 433





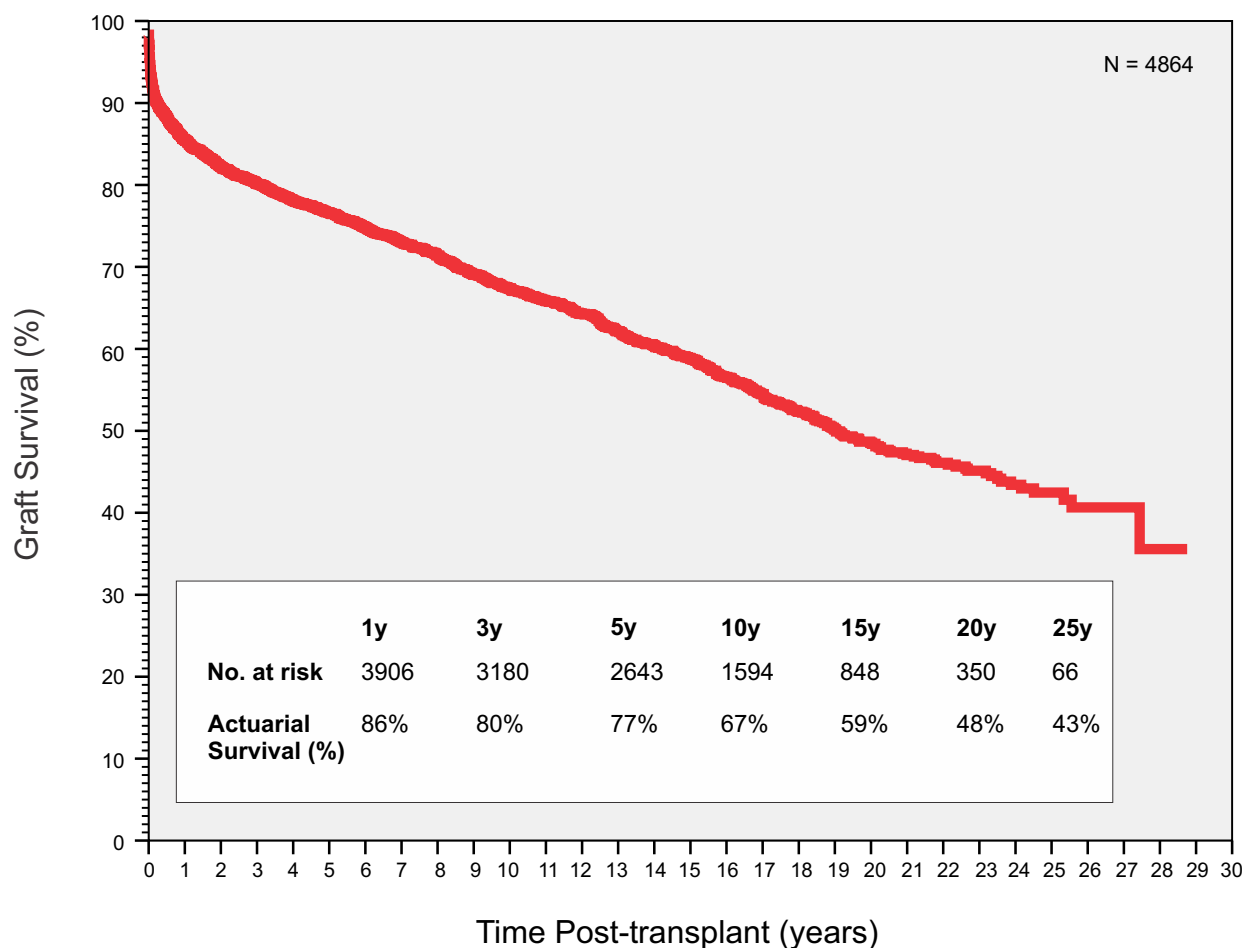


# Section 4

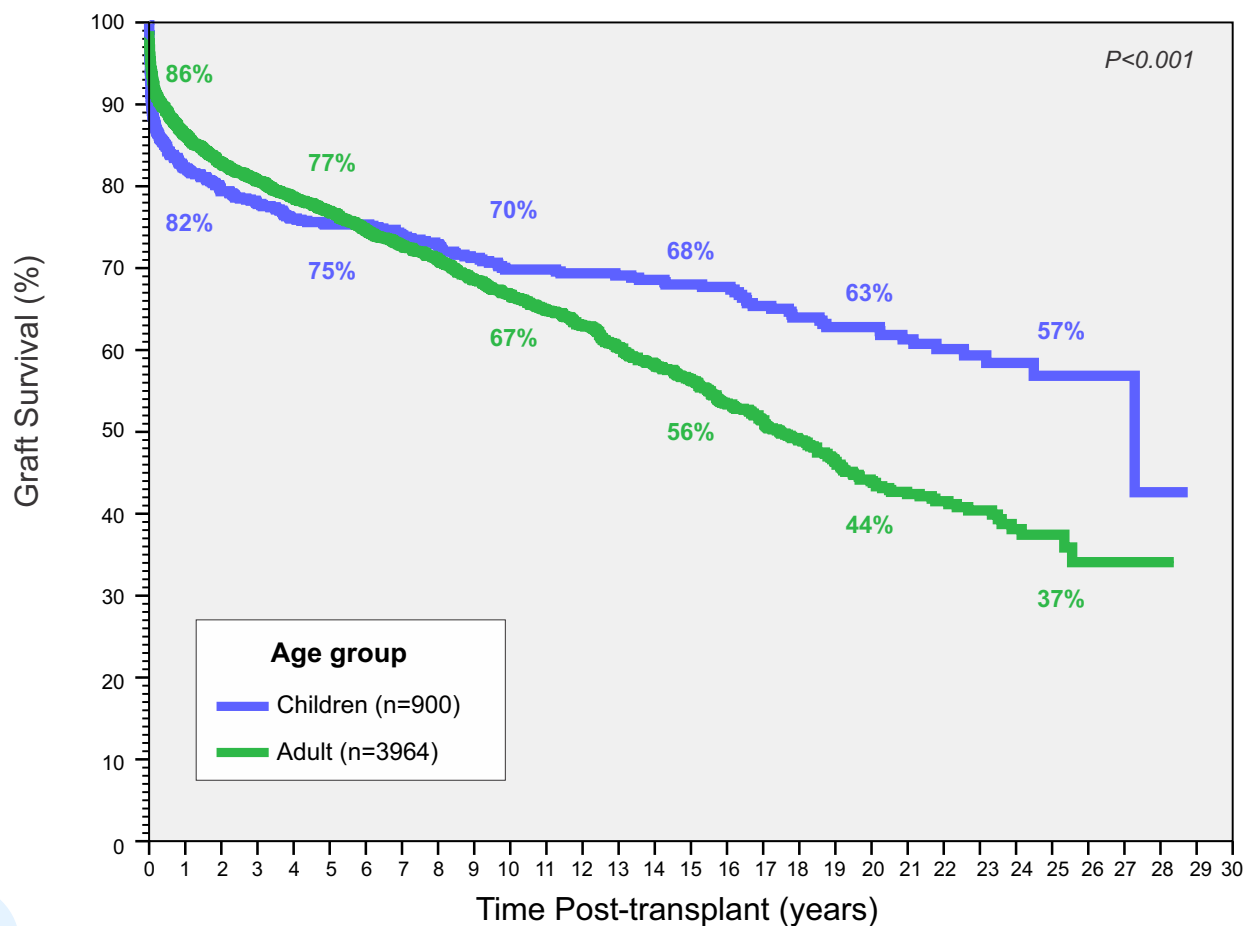
---

## Graft Outcome





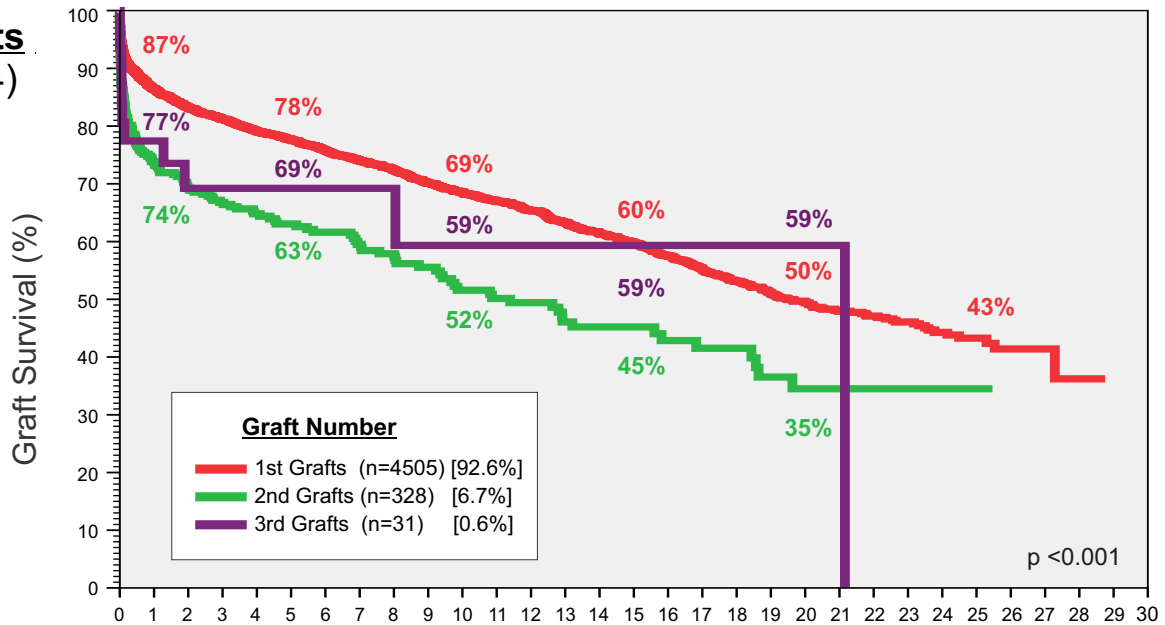
## Graft Survival by Age Group



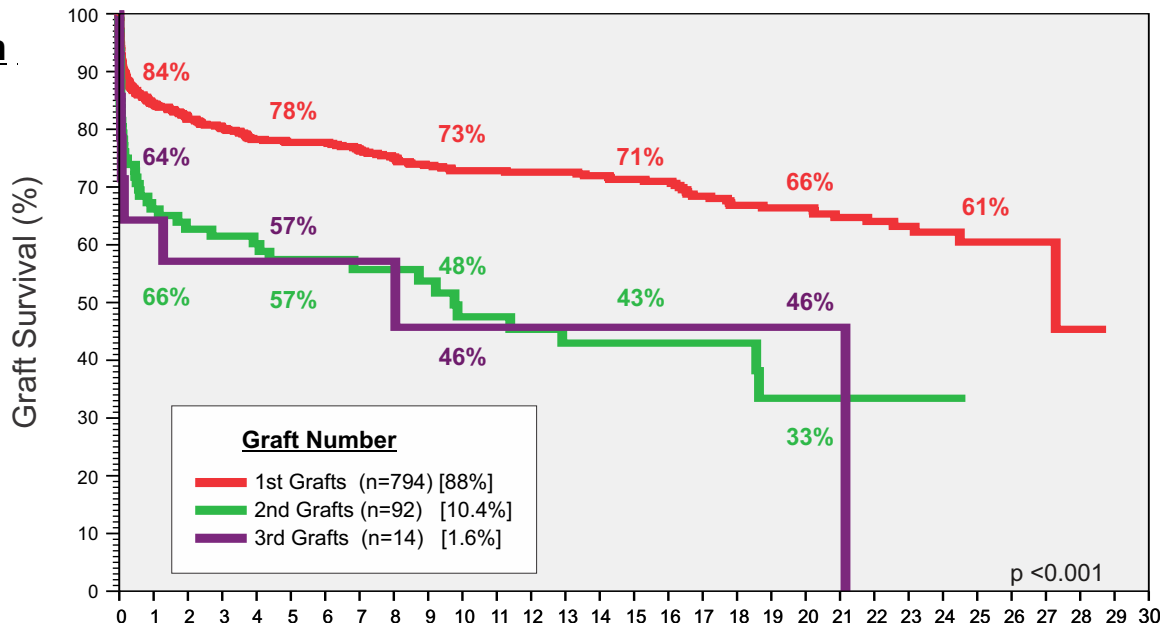




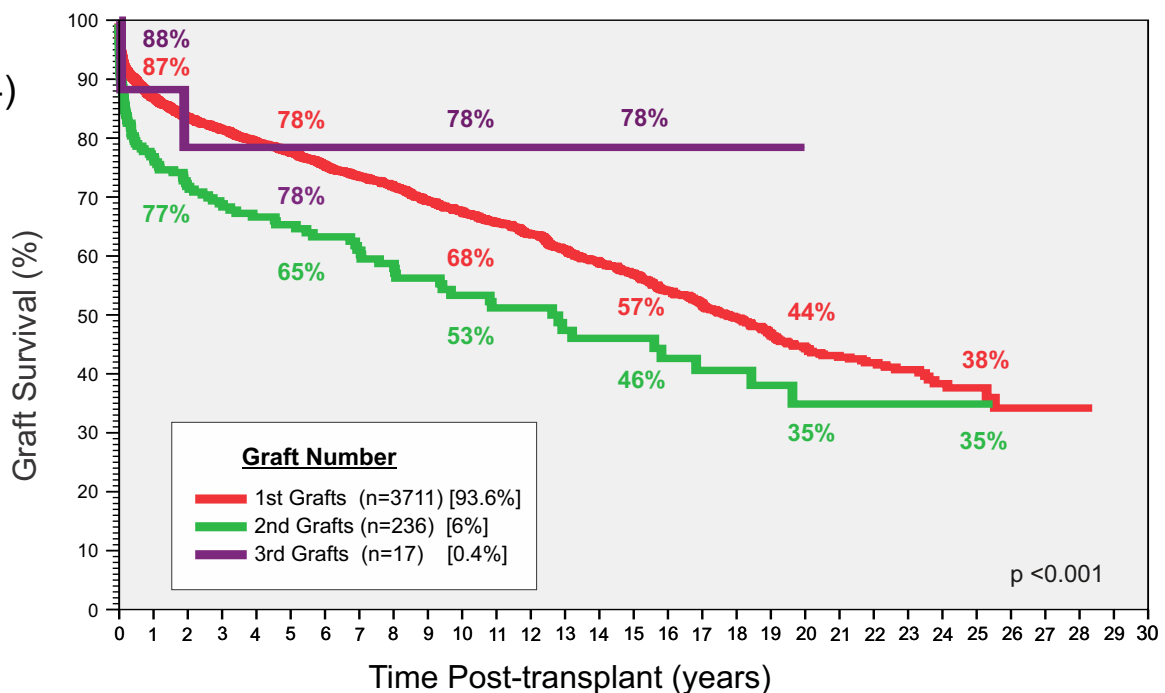
## All Grafts (n= 4864)



## Children (n= 900)

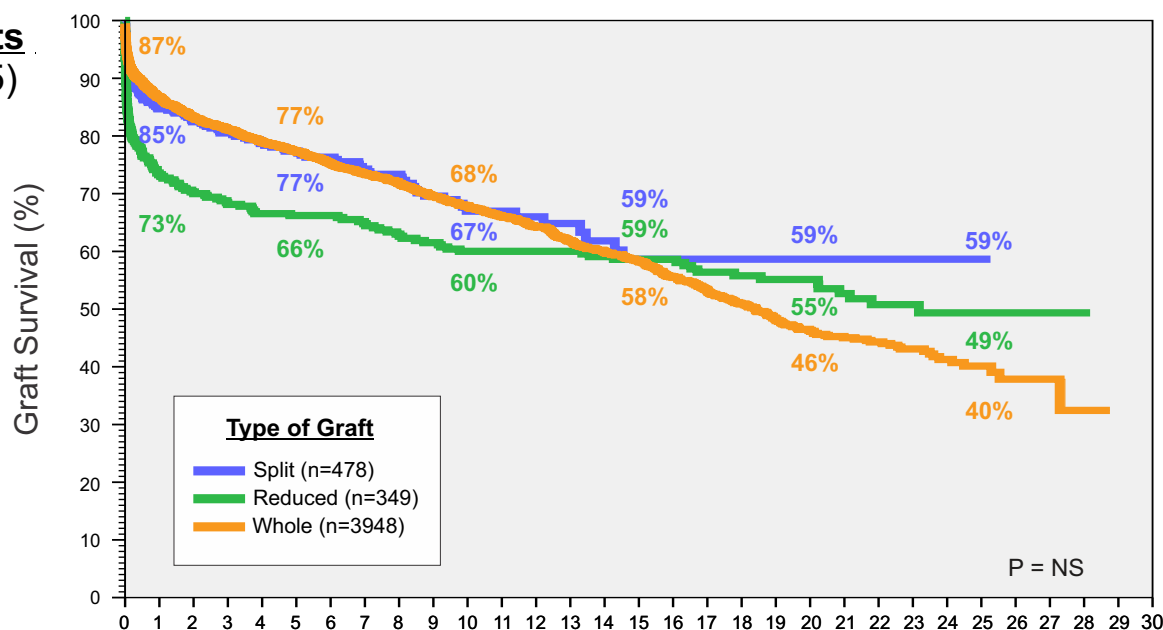


## Adult (n= 3964)

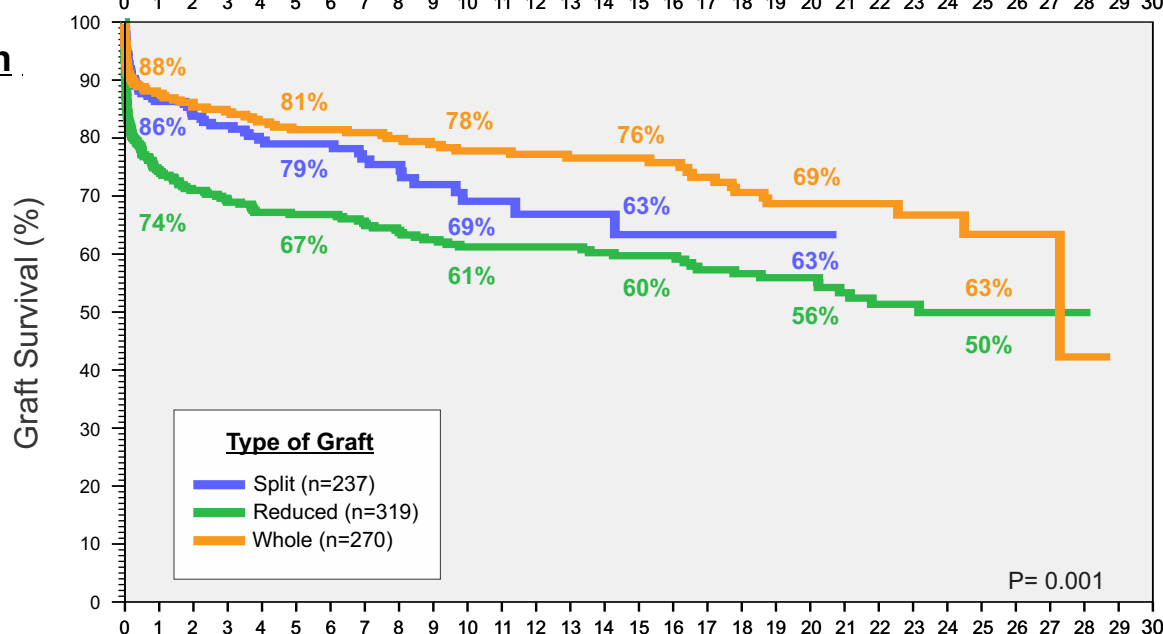




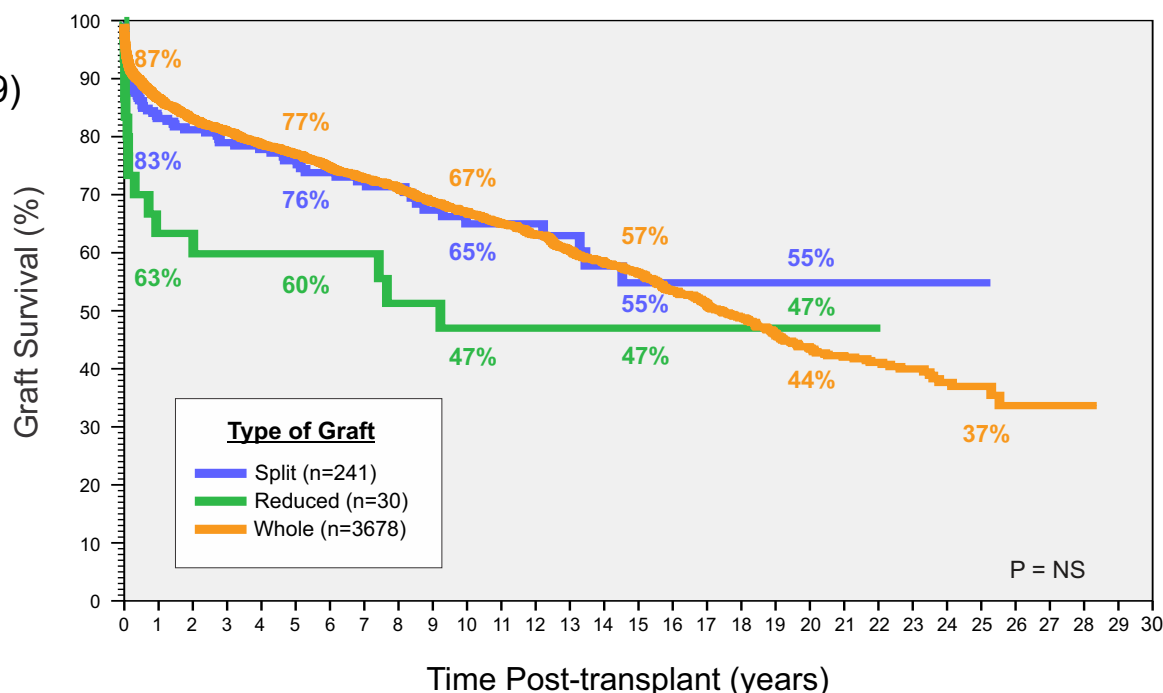
## All Grafts (n= 4775)



## Children (n= 826)

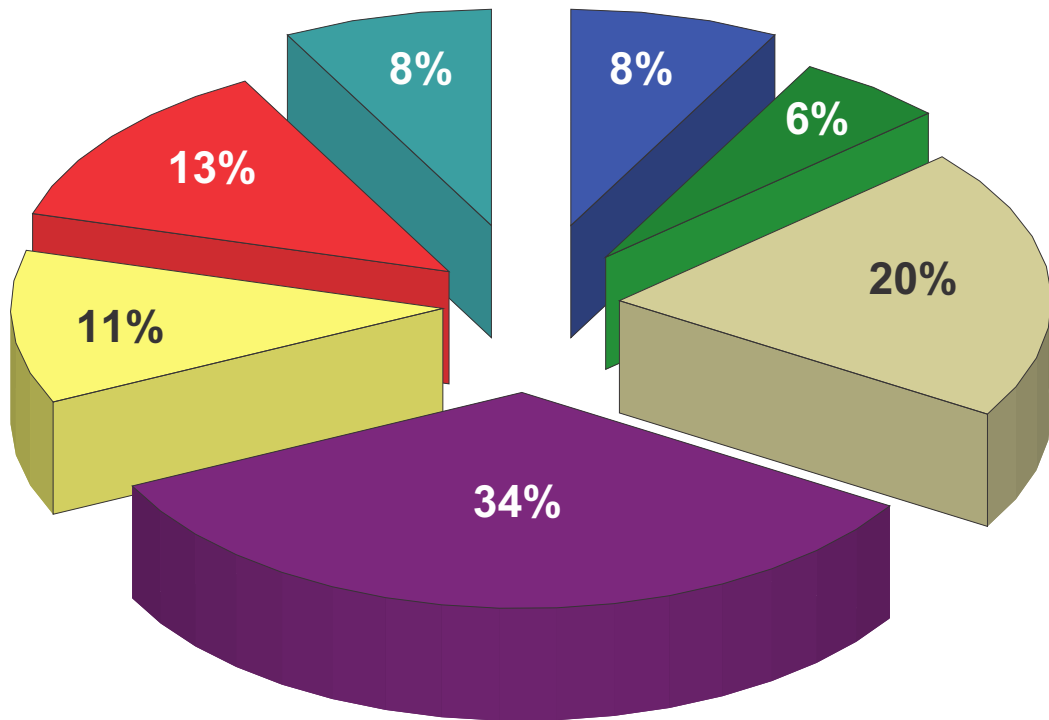


## Adult (n= 3949)



## Indication for Retransplantation

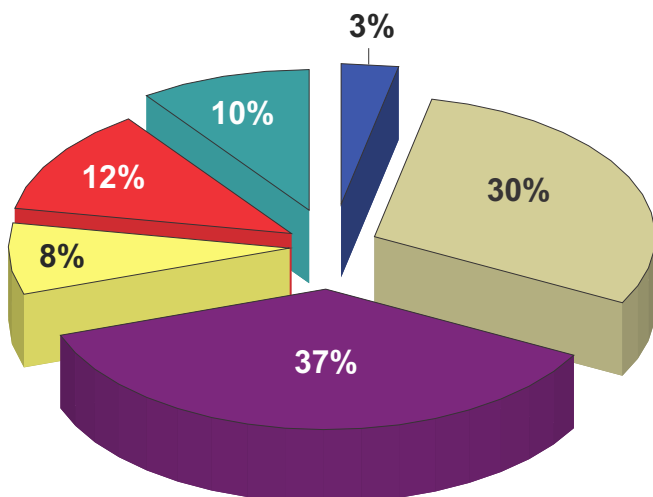
n = 358 (327 2nd grafts, 31 3rd grafts)



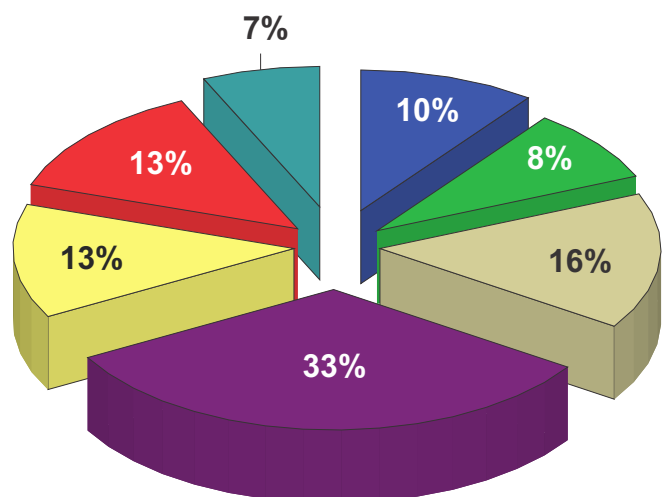
- |  |   |
|--|---|
| <span style="color: blue;">■</span> Recurrent PBC/PSC/CAH:AI | <span style="color: yellow;">■</span> PNF/poor graft function |
| <span style="color: green;">■</span> Recurrent HBV /HCV      | <span style="color: red;">■</span> Biliary                    |
| <span style="color: tan;">■</span> Rejection                 | <span style="color: teal;">■</span> Other                     |
| <span style="color: purple;">■</span> Vascular               |   |

## Age Group

### Children (n= 122)

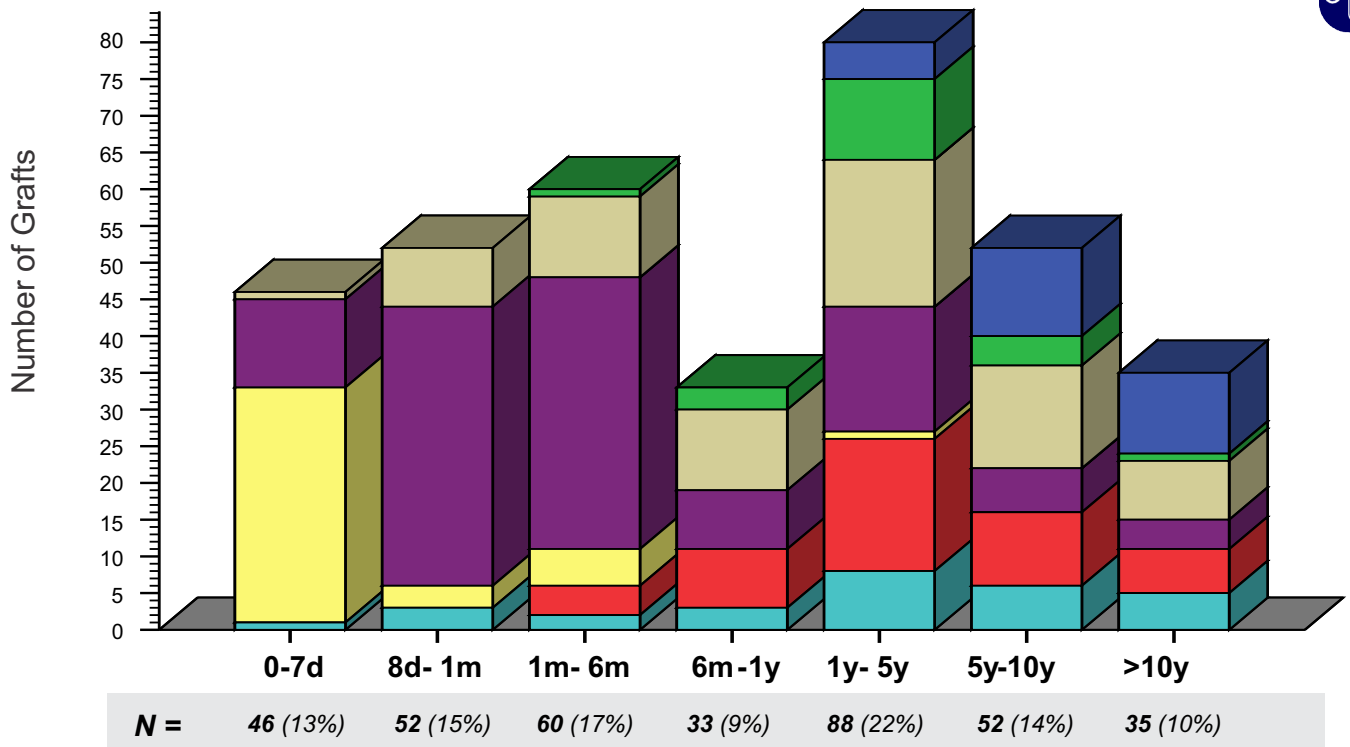


### Adults (n= 236)

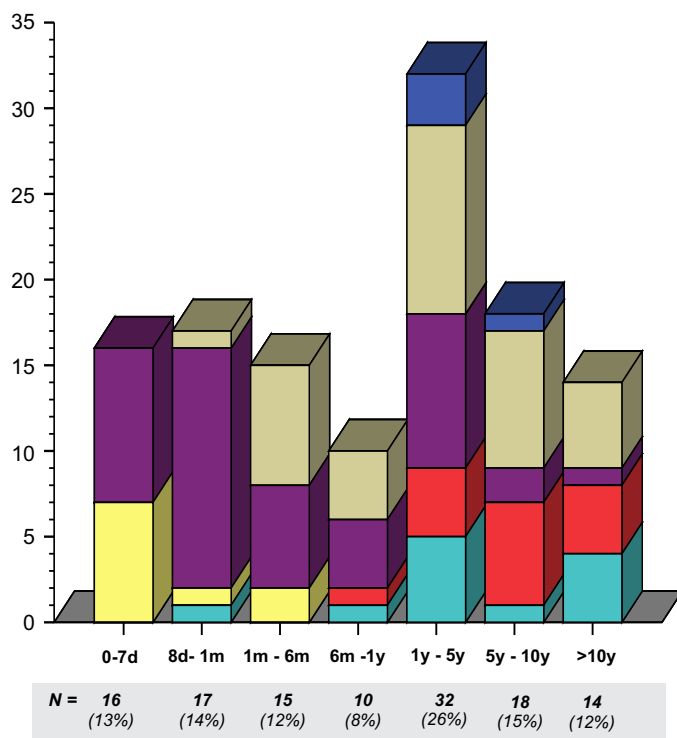


# Indication for Retransplantation

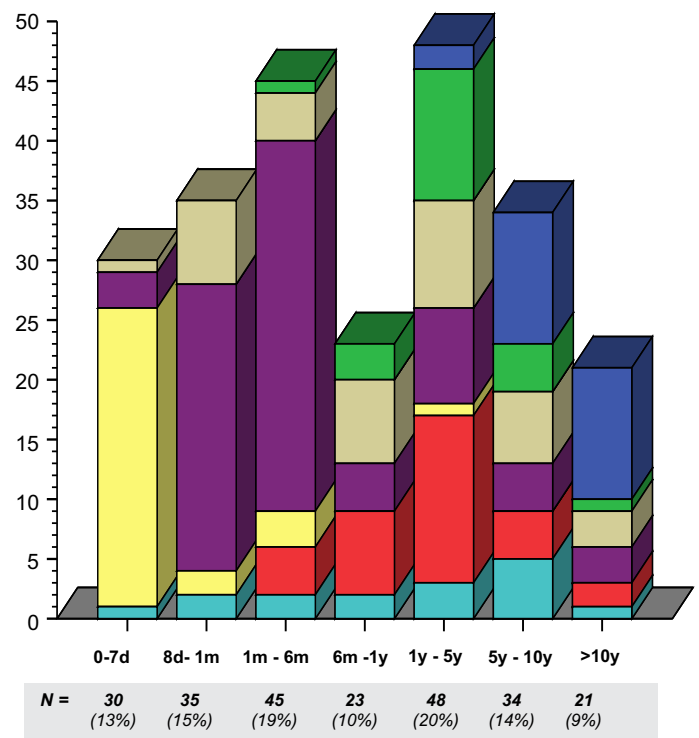
n = 358 (327 2nd grafts, 31 3rd grafts)



## Children (n=122)



## Adults (n=236)





# Section 5

## Cause of Patient Death

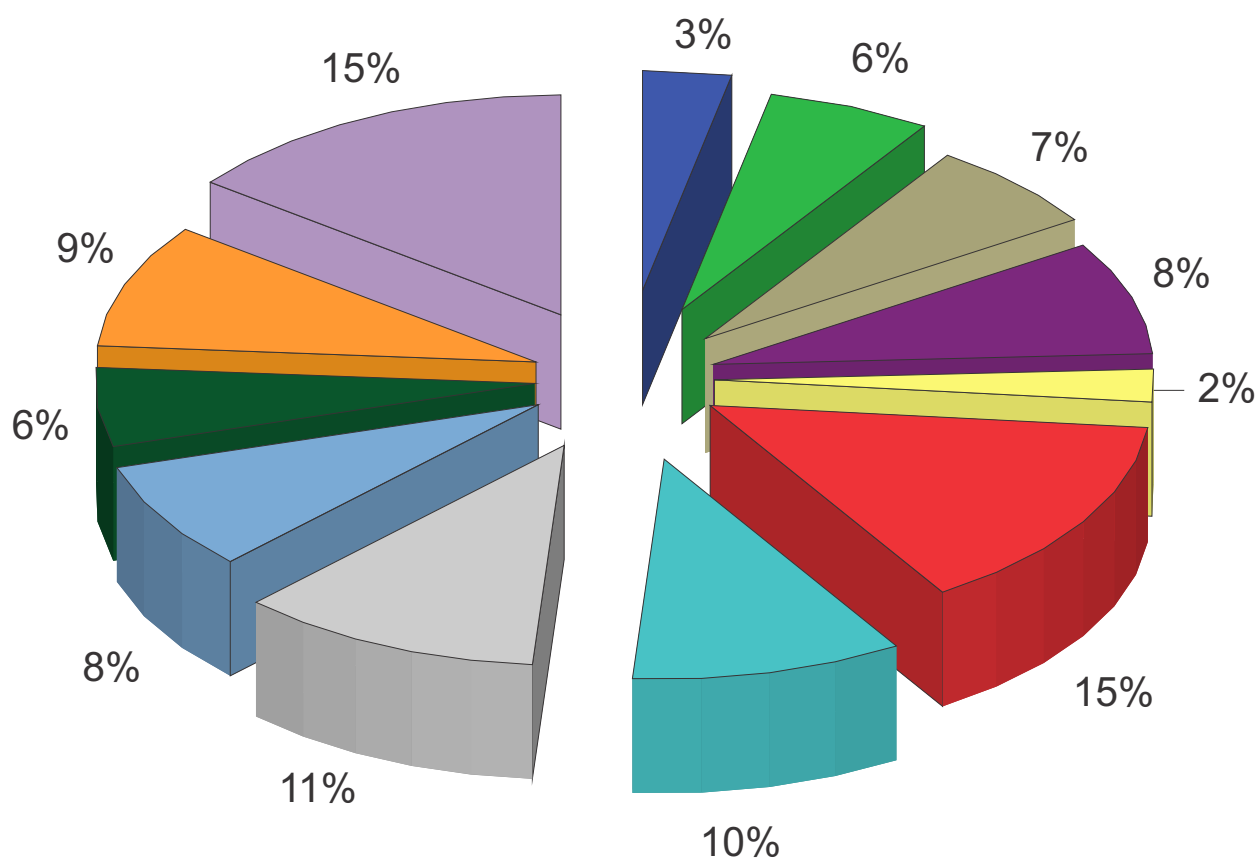




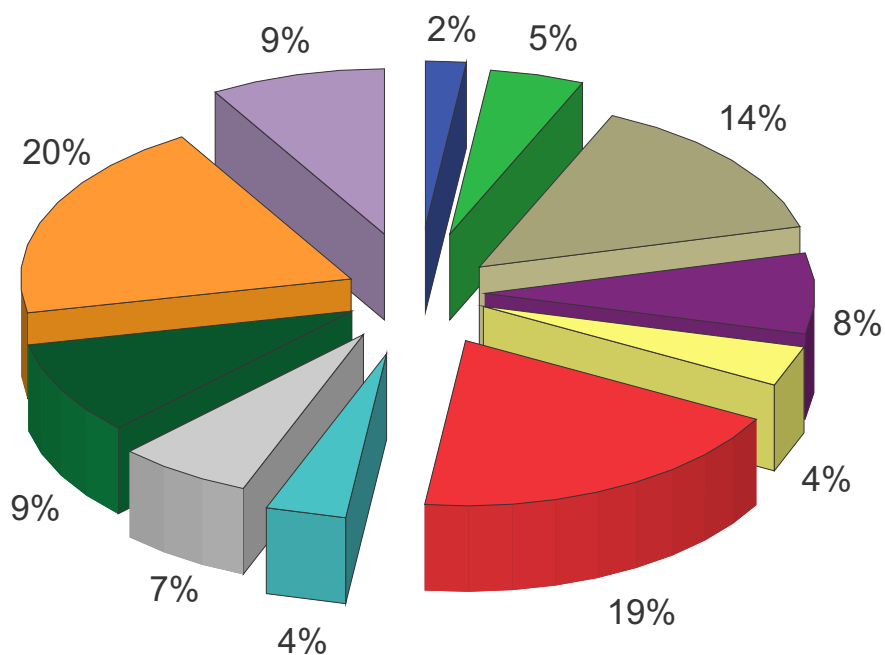
## All Patients n = 1259

- Operative
- Respiratory
- Cerebrovascular
- Cardiovascular
- Gastrointestinal
- Sepsis
- Malignancy - recurrent
- Malignancy - de novo
- Graft failure
  - Recurrent HBV / HCV
  - Rejection
  - Other\*
- Miscellaneous\*

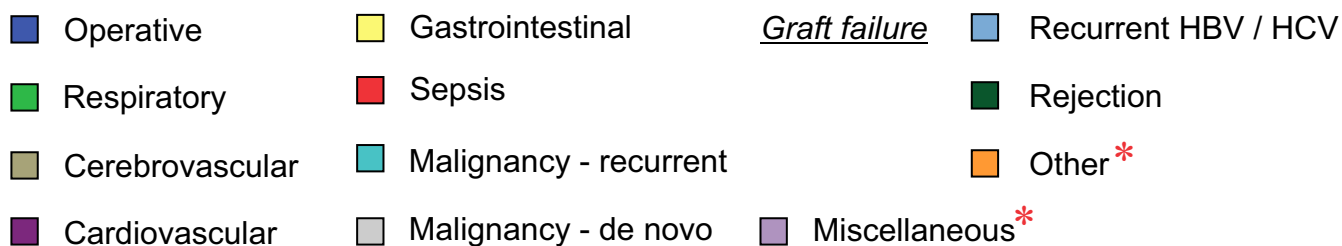
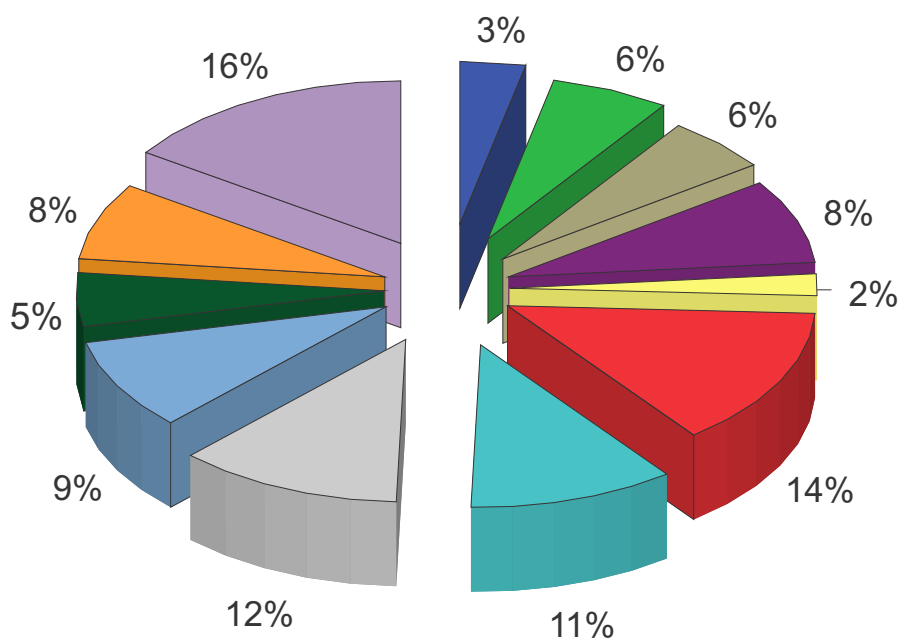
\* See Appendix V for details



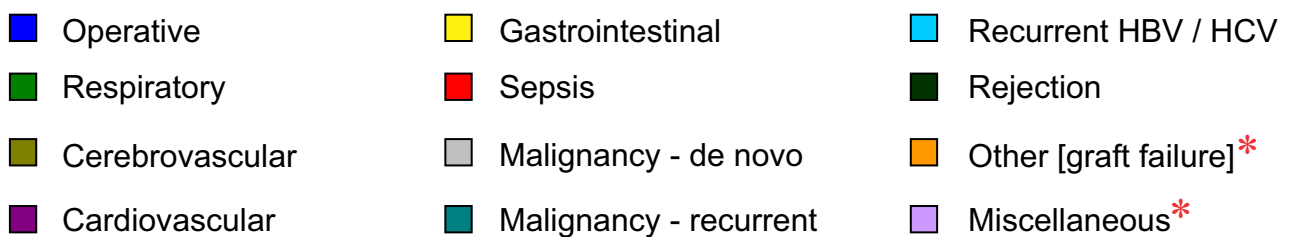
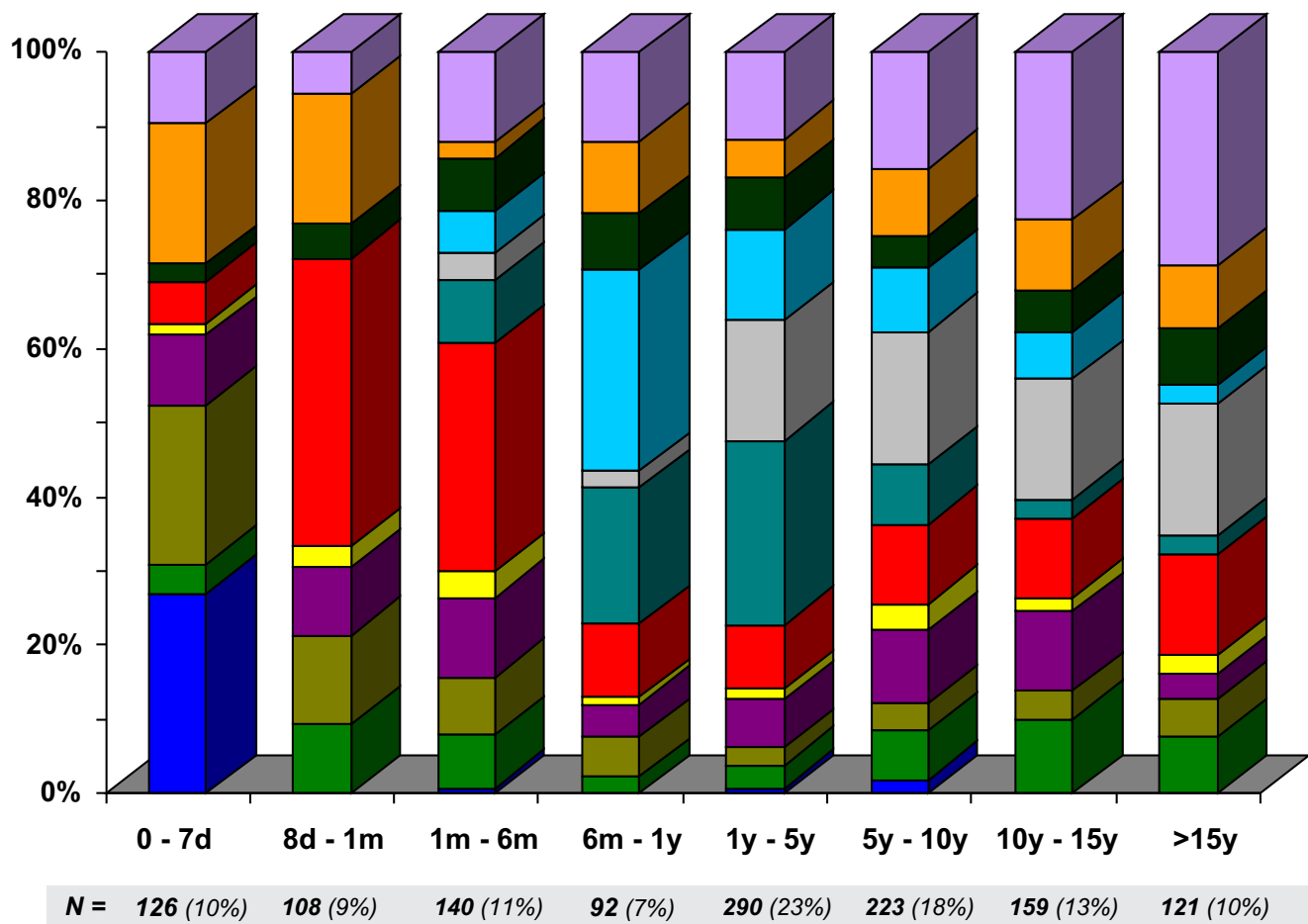
## Causes of Death in Children n = 152



## Causes of Death in Adult n = 1107



\* See Appendix V for details



\* See Appendix V for details

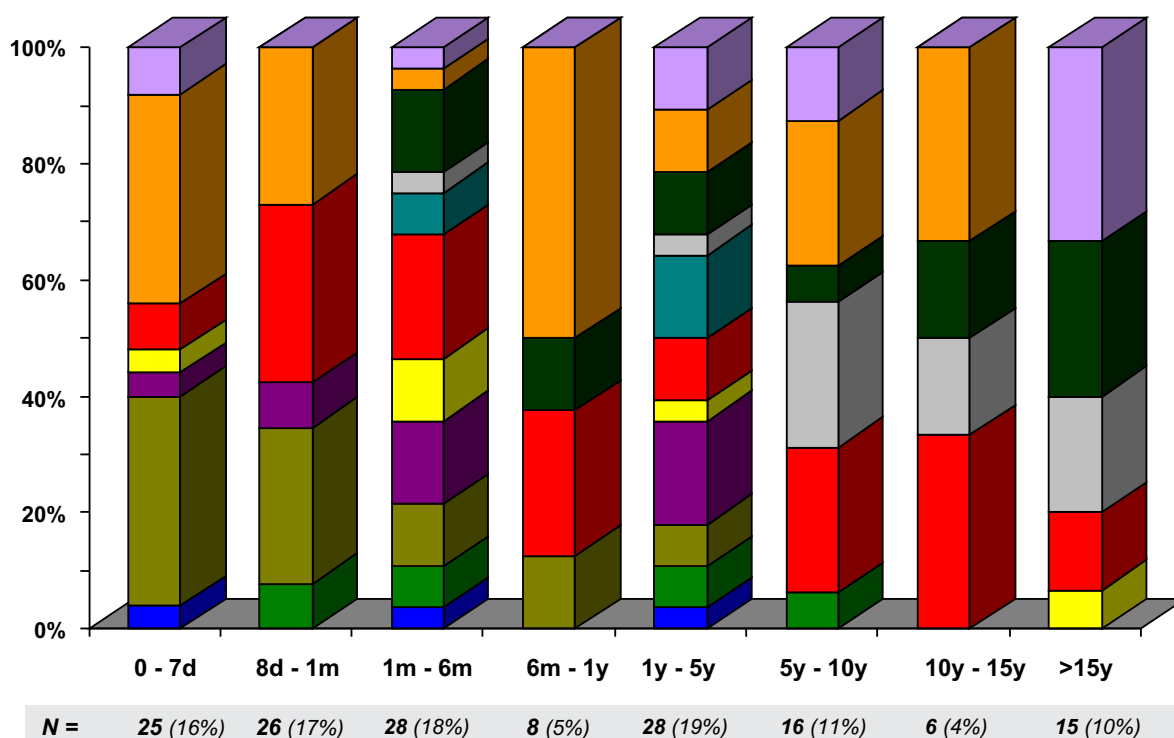


## Cause of Death by Time Post Transplant Children (n=152)

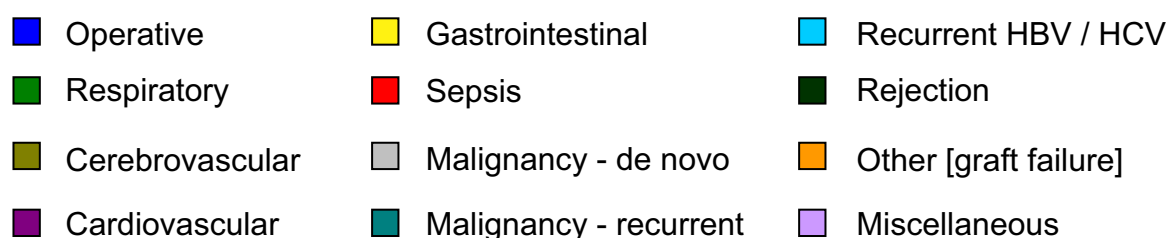
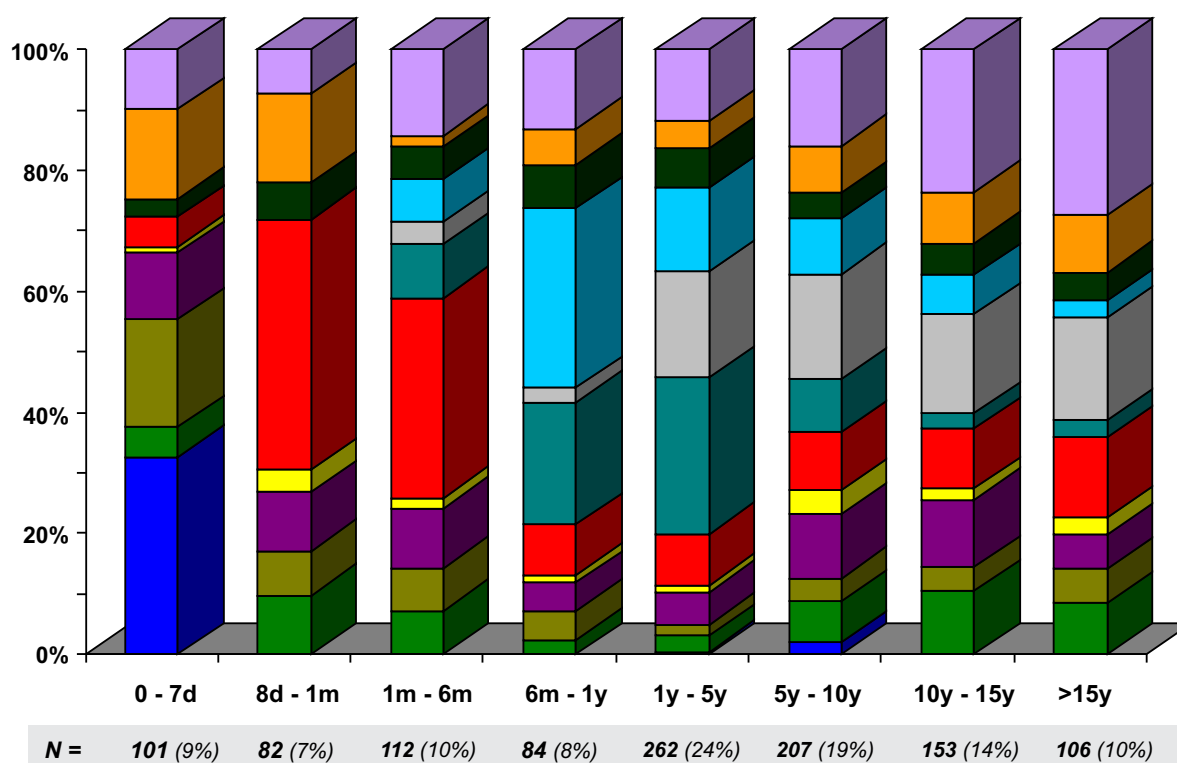
26<sup>TH</sup> ANZLT REGISTRY  
REPORT



CLICK HERE  
to go to Contents page



## Cause of Death by Time Post Transplant Adult (n=1107)





# Section 6

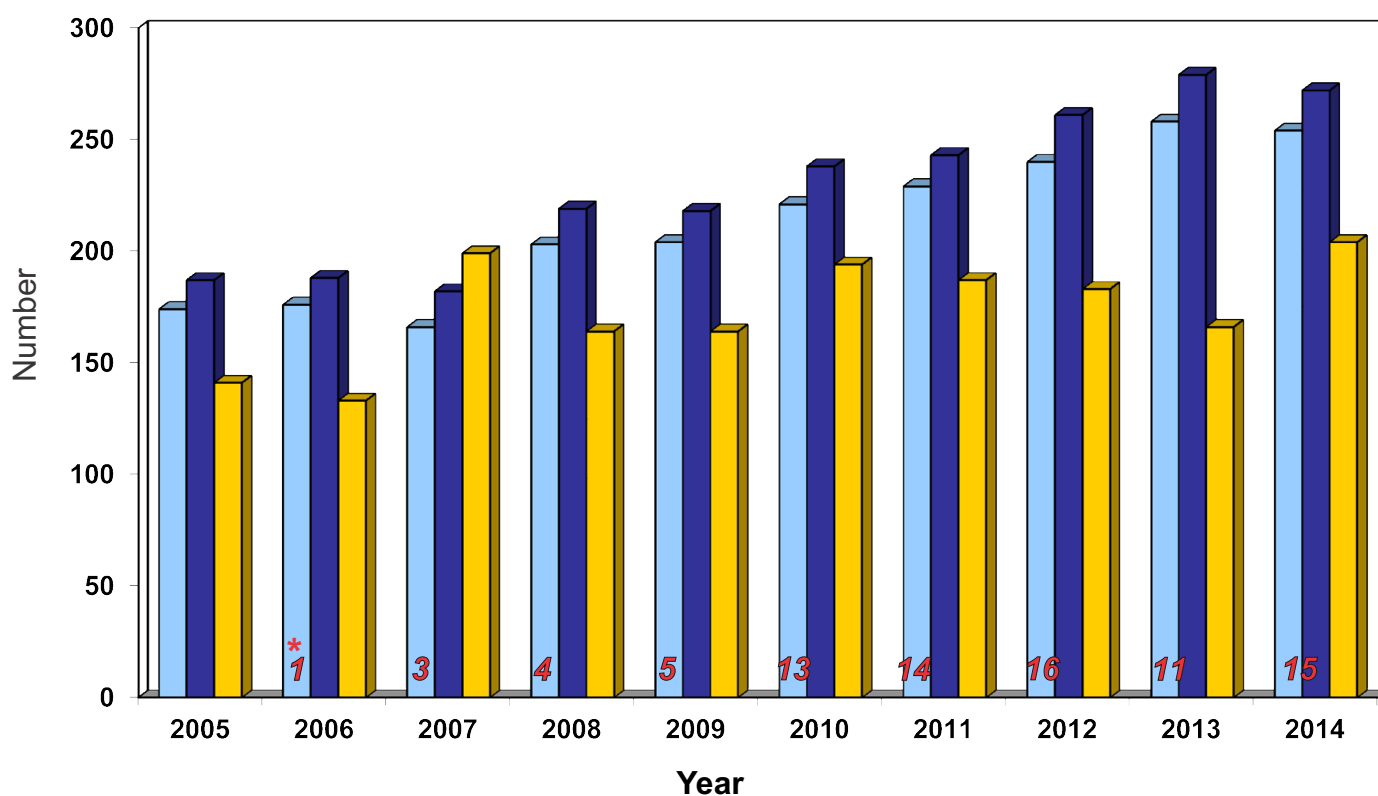
## Deceased Donor Information





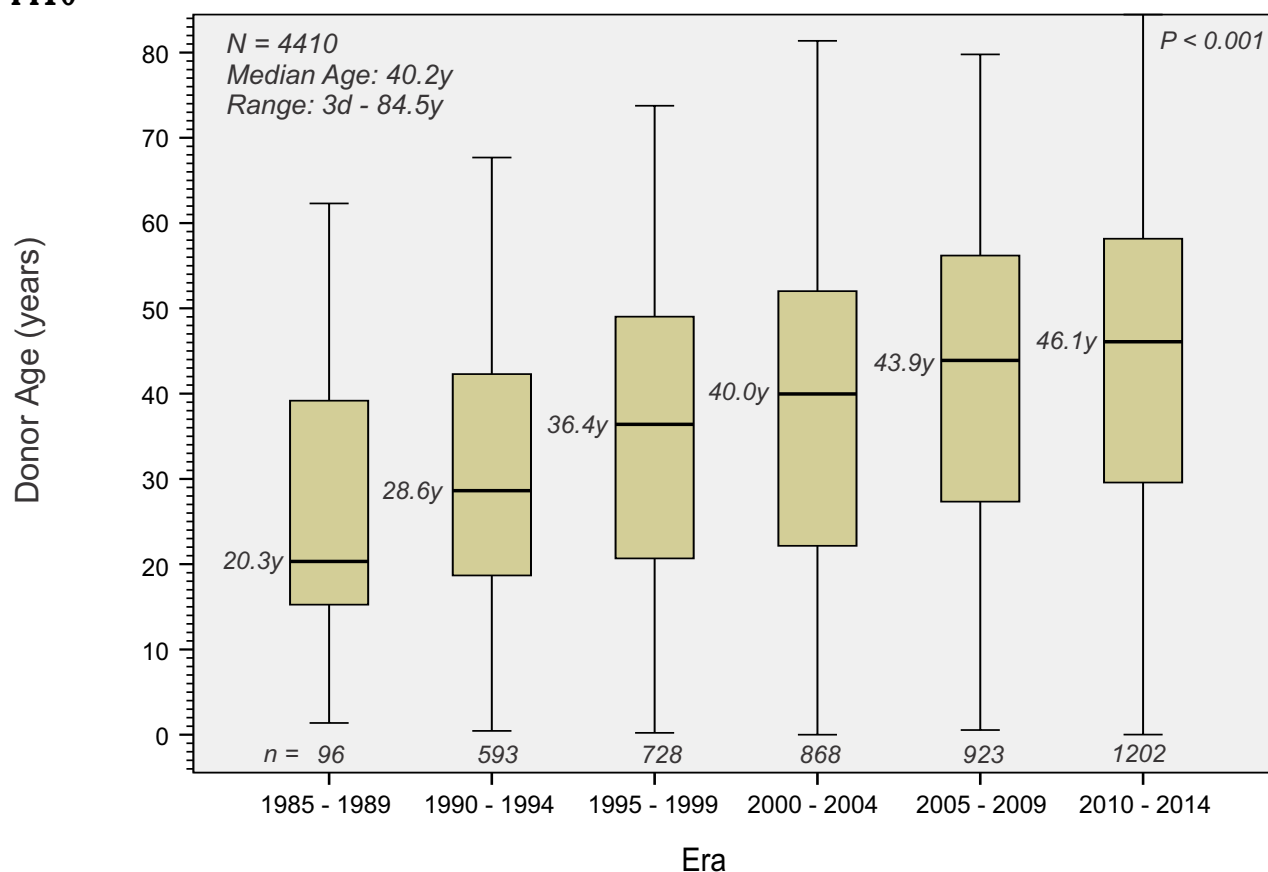
	QLD	NSW/ACT	VIC/TAS	SA/NT	WA	NZ	TOTAL
2005	24	36/8	38/2	17/3	25	21	174
2006	28	34/3	39/6	25	17	24	176
2007	25	36/1	36	19/2	15	32	166
2008	33	40/3	41/5	31/1	25	23	203
2009	35	46/4	36/5	28/2	15	33	204
2010	30	55/8	53/6	18/2	17	32	221
2011	44	52/7	49/3	22/2	20	30	229
2012	46	50/7	52/10	21/6	20	28	240
2013	40	66/5	54/7	23/5	33	25	258
2014	44	45/7	62/8	27/4	25	32	254

## Grafts from deceased donors



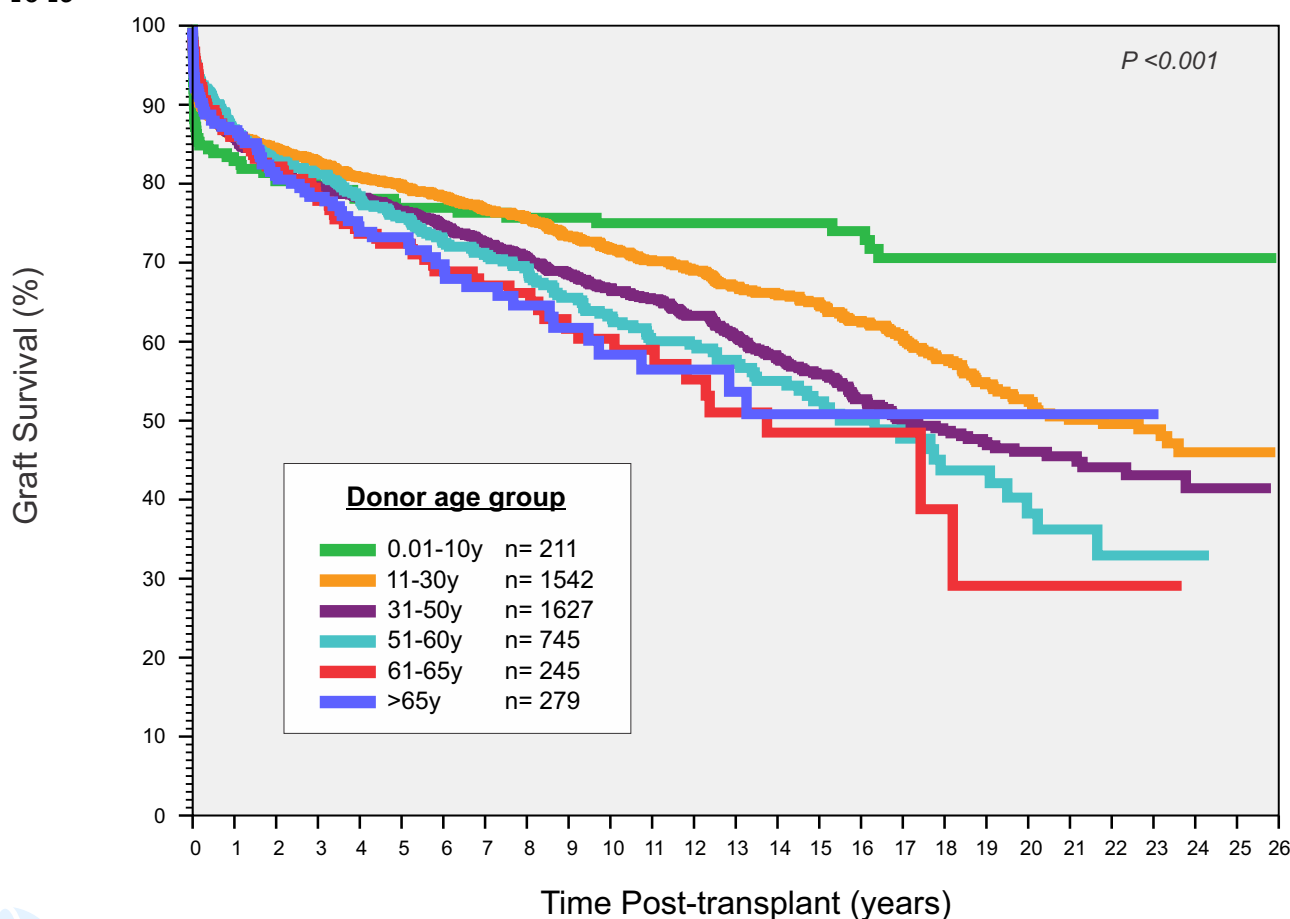
## Donor Age by Era

N = 4410



## Graft Survival by Donor Age

N = 4649





# Section 7

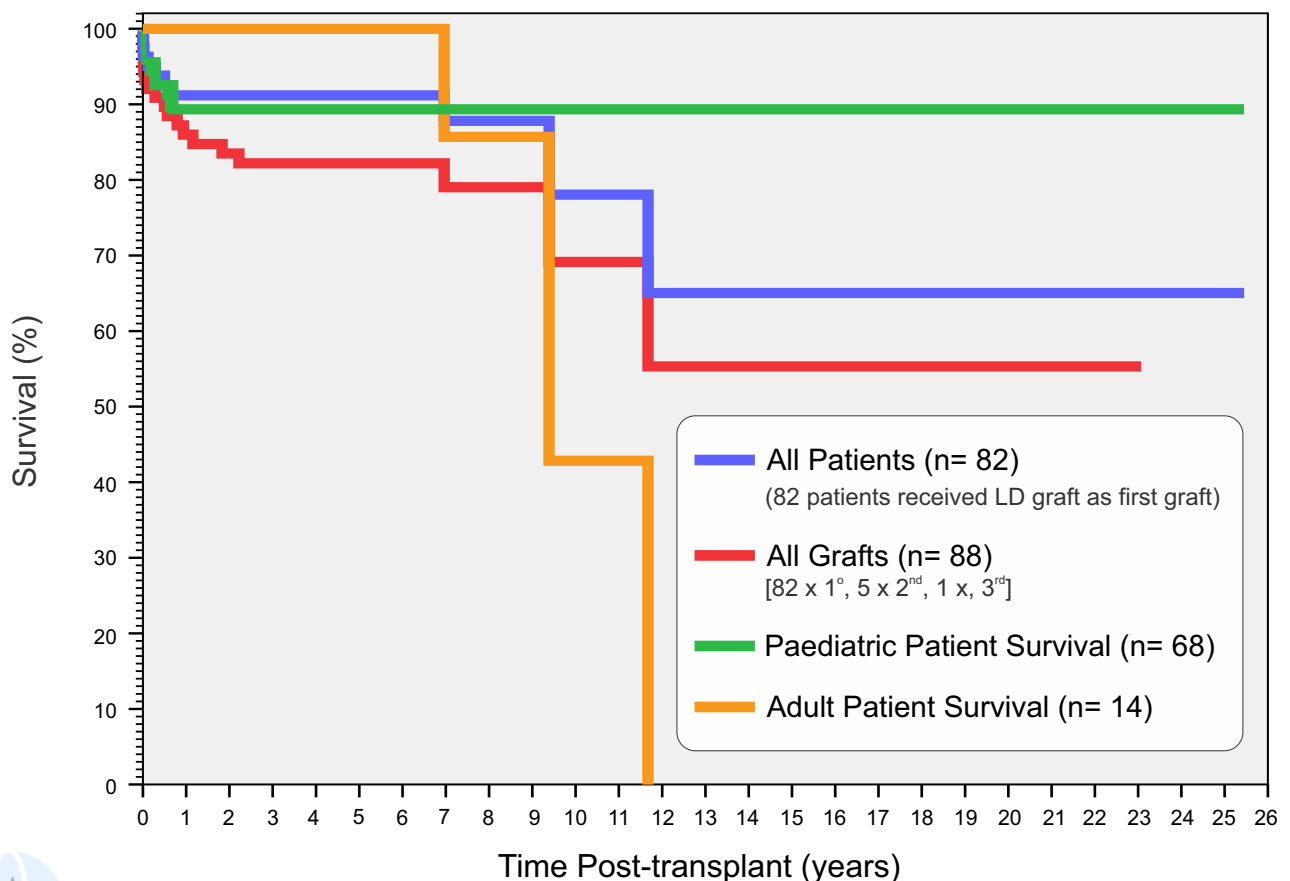
## Living Donor Transplantation





	Recipient Age Group		
	Child [n=73]	Adult [n=15]*	All [n=88]
<b>Donor gender</b>	-	-	-
Male	43	9	52
Female	30	6	36
<b>Donor age</b>	-	-	-
Median	35.3y	30.4y	34y
Range	19.9 - 54.5y	22.8 - 54.3y	19 - 54.5y
<b>Donor relationship</b>	-	-	-
Mother	18	-	18
Father	35	-	35
Son	-	4	4
Daughter	-	1	1
Grandmother	1	-	1
Grandfather	1	-	1
Sister	-	3	3
Brother	2	3	5
Aunt	6	-	6
Uncle	1	-	1
Family friend	5	1	6
Cousin	4	-	4
Spouse	-	1	1

\* 2 x whole liver domino transplant





# Section 8

## Waiting List



# Waiting List Activity

## [ Data 1/1/10 - 31/12/14 ]



Activity	2010	2011	2012	2013			2014		
Listed at 1 January	175	194	192	186	164	-			
New listings	335	336	351	360	-	401	TOTAL 2014	Adult	Paediatric
TOTAL	510	530	543	546	164	401	565	500	65
OUTCOME					OUTCOME				
Transplant	248 [49%]	253 [49%]	268 [50%]	284 [52%]	88	190	278 [49%]	235 [47%]	43 [66%]
Delisted	68 [13%]	85 [13%]	89 [13%]	98 [18%]	25	58	83	78	5
Died on list	12	17	29	26	8	10	18	15	3
Too sick	12 } 8%	17 } 8%	16 } 8%	11 } 10%	3	7	10 } [8%]	10 } 8%	- } 5%
Tumour progression	12	20	10	16	4	11	15	15	-
Improved	16	12	17	24	5	13	18	16	2
Other	12*	19*	17*	21*	5	17	22*	22	-
Still listed at 31 Dec	194 [38%]	192 [36%]	186 [34%]	164 [34%]	51	153	204 [36%]	187	17

[\* Patient declined, malignancy, drug use, infection, further investigations, medical]

## Outcome of Initial Urgent Listing

OUTCOME	CATEGORY 1						
	2010 (n=19)	2011 (n=15)	2012 (n=16)	2013 (n=19)	2014		
					N=8	Adult n=6	Paediatric n=2
TRANSPLANTED	13 } 74%	12 } 80%	11 } 81%	11 } 74%	6 } 88%	4	2
IMPROVED	1 }	- }	2 }	3 }	1 }	1	-
DIED / TOO SICK	5	3	3	5	1	1	-
OTHER TREATMENT	-	-	-	-	-	-	-

OUTCOME	CATEGORY 2						
	2010 (n=30)	2011 (n=28)	2012 (n=19)	2013 (n=29)	2014		
					N=22	Adult n=14	Paediatric n=8
TRANSPLANTED	23 } 93%	22 } 86%	14 } 89%	22 } 89%	18 } 95%	12	6
IMPROVED	5 }	2 }	3 }	4 }	3 }	2*	1
DIED / TOO SICK	1 / 1	3	1	2	-	-	-
OTHER TREATMENT	-	1 active 31/12/11	1 active 31/12/12	1 active 31/12/13	1 active 31/12/14	-	1 active 31/12/14

[\* 1 temporary listing chronic patient; later transplanted]



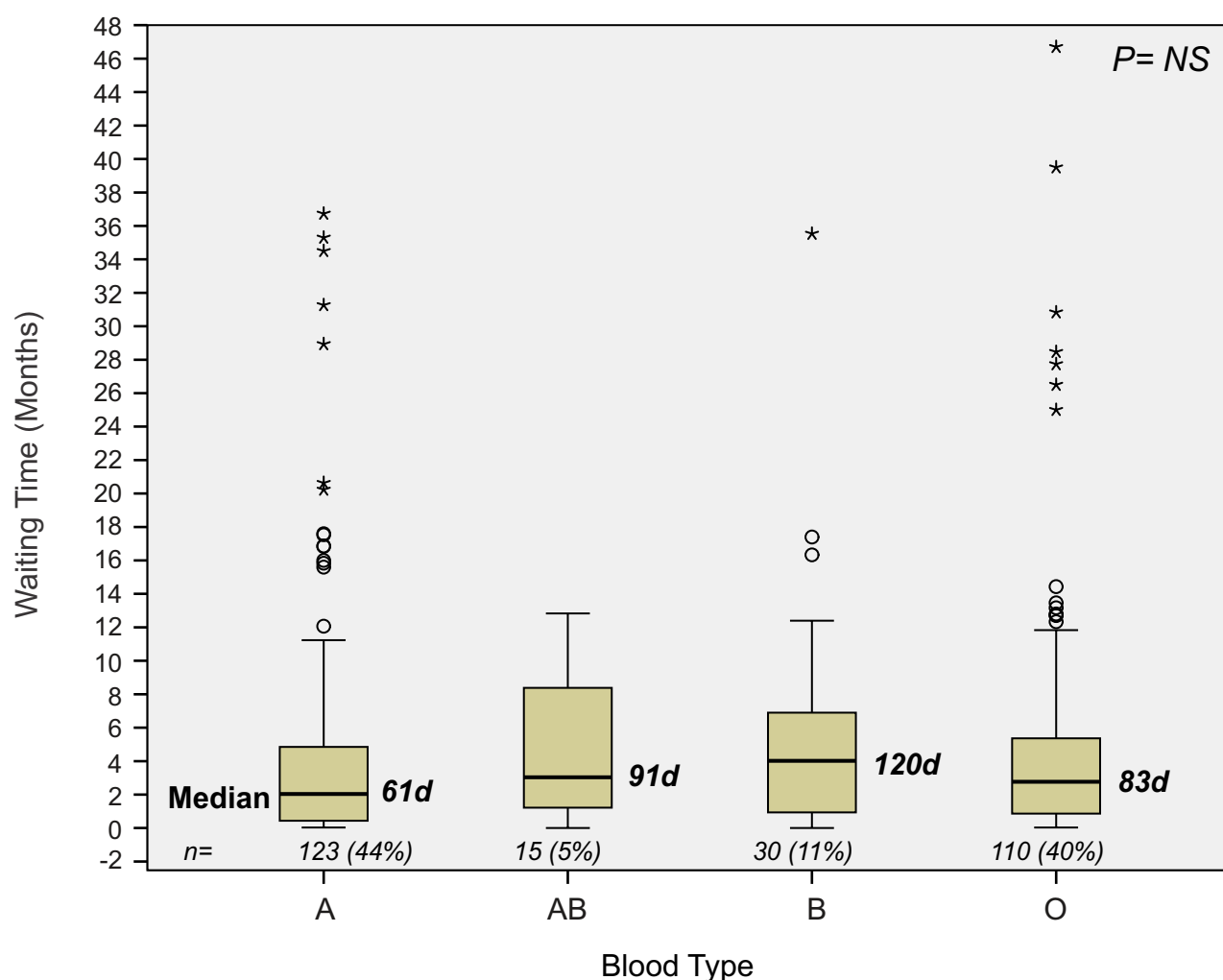


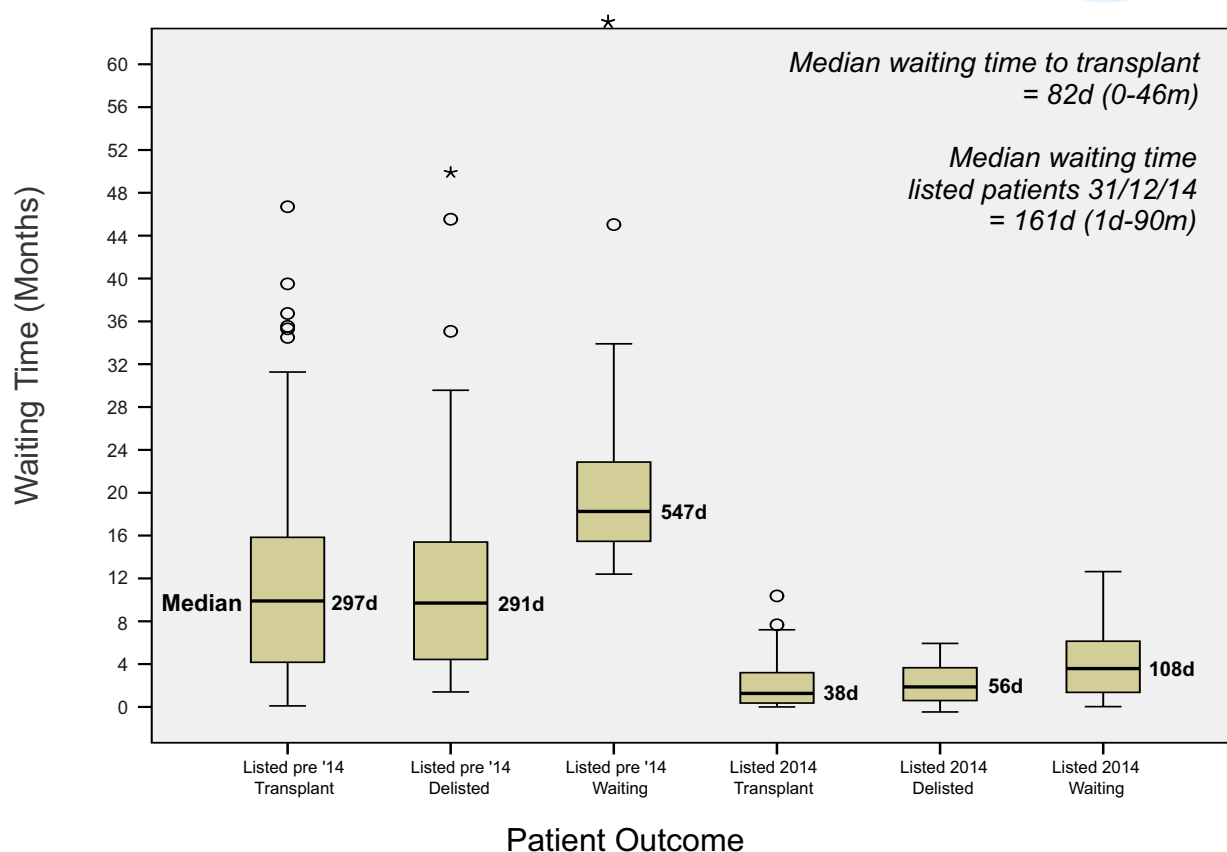
	Blood Group				
	A	O	B	AB	TOTAL
n=	215 (38%)*	254 (45%)	78 (14%)	20 (3%)	567
Not transplanted	92	144	48	5	289
Transplanted	123 (57%)**	110 (43%)	30 (38%)	15 (75%)	278 (49%)

\* % of total number listed

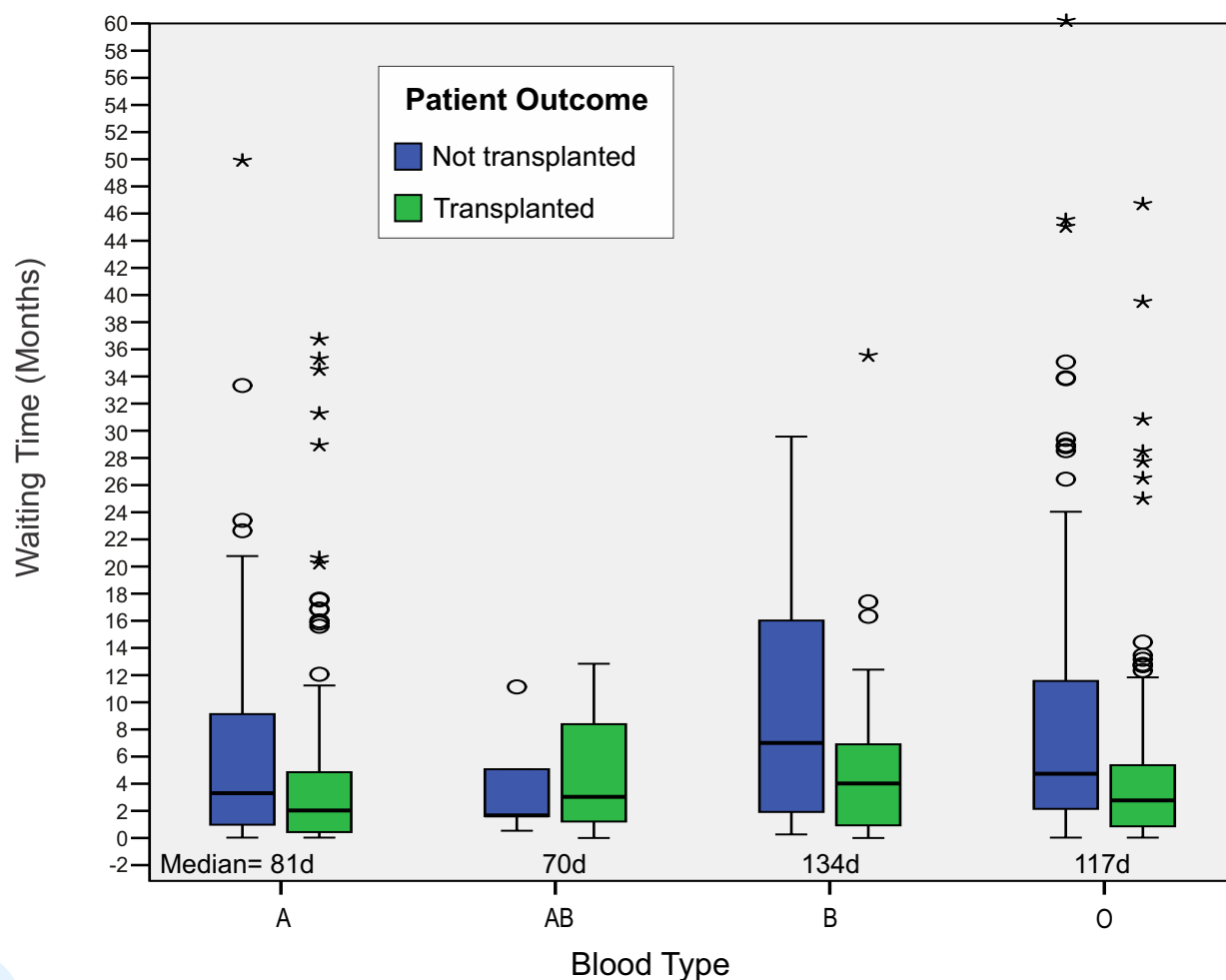
\*\* % of blood group

## Waiting Time to Transplant 2014





## Waiting Time by Outcome & Blood Group





# Section 9

## Liver Transplantation and Cancer



# Cancer in Liver Transplant Recipients

n = 4506



At Tx	Total number pts. transplanted = 4506	
Liver Cancer as indication for Transplant	384	(9%)
Liver Ca as a Secondary Diagnosis	572	(13%) 574 Ca
Total	950*	(21%)
Post Tx		
Recurrent Liver Ca	127	(3% of all pts, 13% pts with Ca atTx)
De Novo Ca	323	(7%) 352 Ca
Skin Ca	653	(14%)
Total	1103	(24%)
Multiple Cancer types (non skin and skin)	215	(5% of all pts)
Multiple non skin cancers	88	(2% of all pts)
Transferred from Donor	2	
Developed non skin Ca < 90days	9	

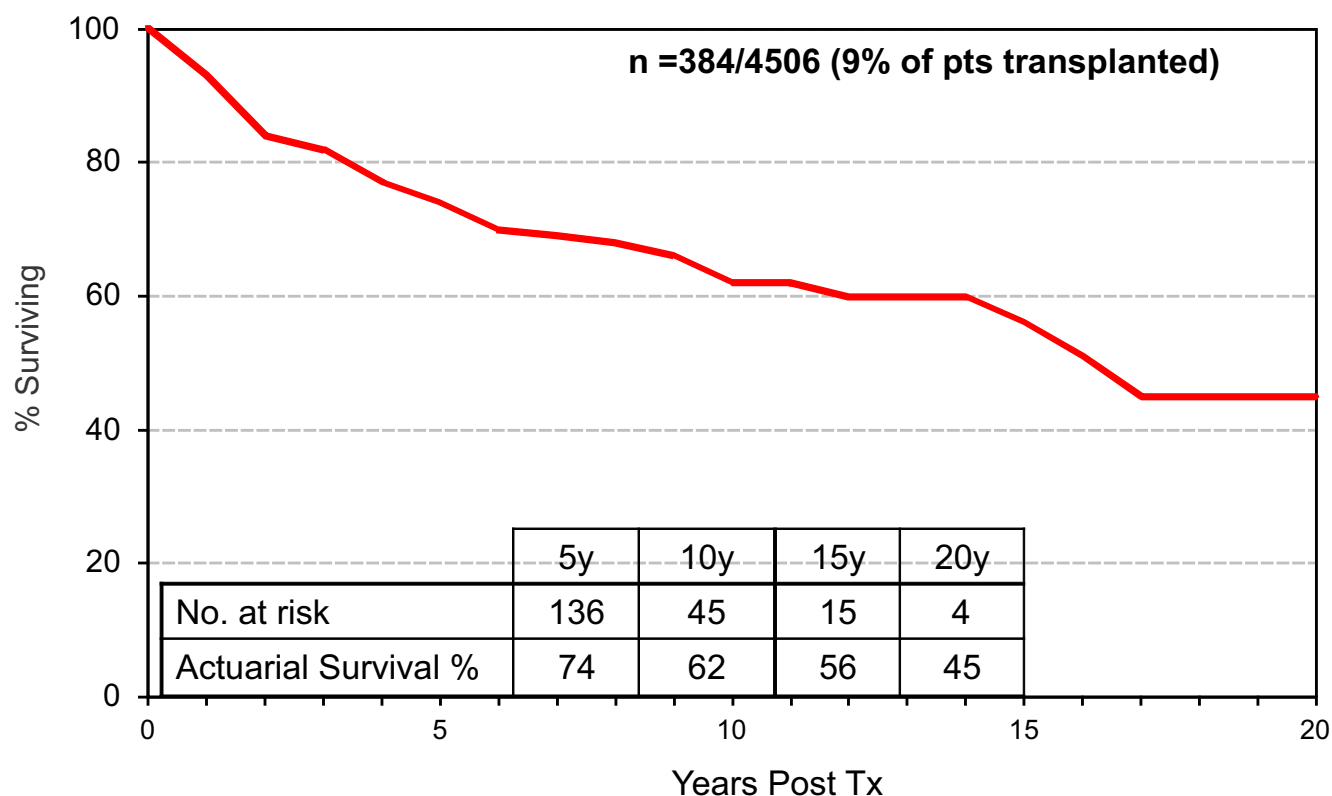
\* 2 pts had primary and a secondary liver cancer; 2 pts had multiple secondary liver cancers

## Liver Cancer as Primary Diagnosis

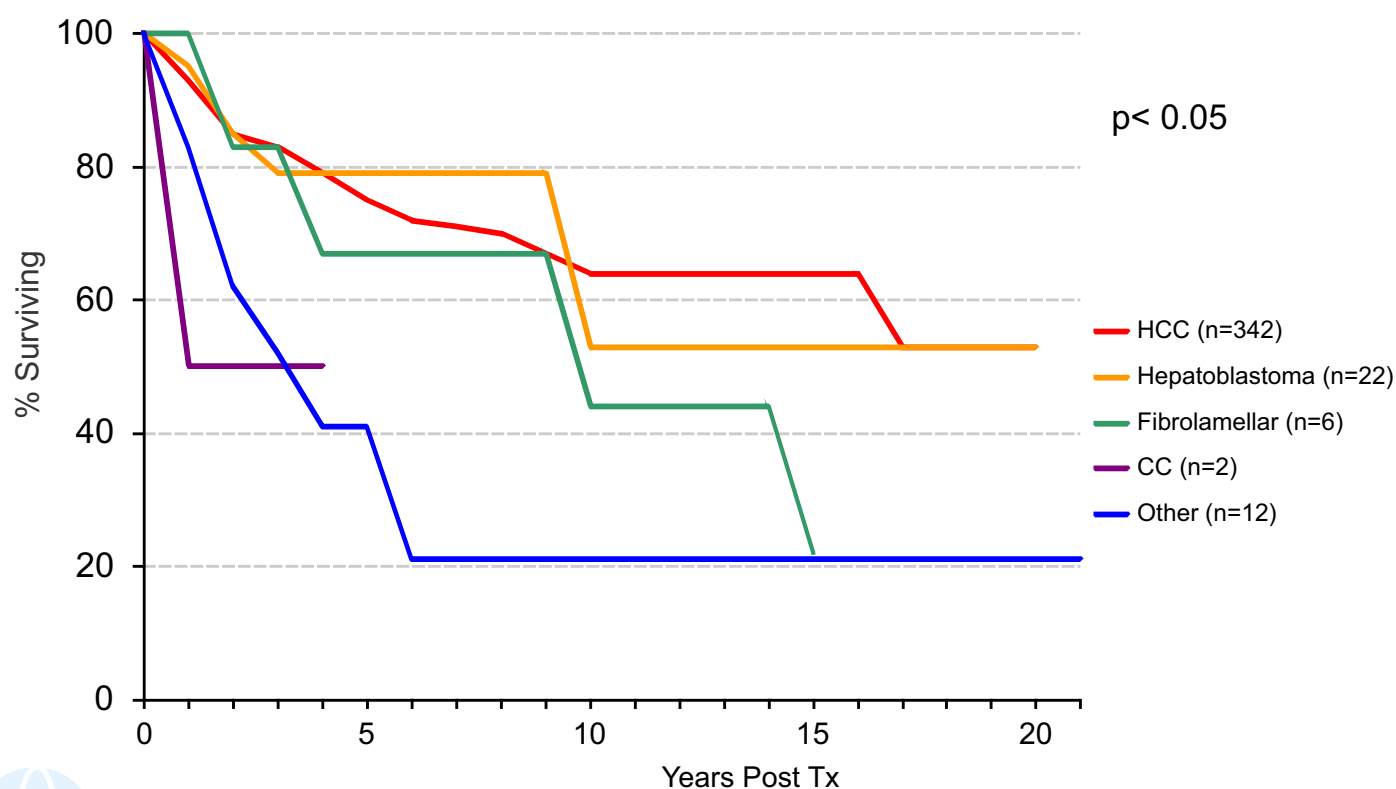
n = 384/4506

TYPE OF CA	No	DIED	DIED OF THIS CA
HEPATOCELLULAR CA	342	76	39 (11%)
HEPATOBLASTOMA	22	5	4 (18%)
FIBROLAMELLAR	6	5	2 (33%)
CARCINOID	4	4	4 (100%)
EPITHELOID HAEMANGIOENDOTHELIOMA	4	0	0
CHOLANGIOCARCINOMA	2	1	1 (50%)
ANGIOSARCOMA	1	1	1 (100%)
GASTRINOMA	1	1	1 (100%)
PANCREATIC ISLET CELL	1	1	1 (100%)
ERYTHROID LEUKAEMIA	1	1	1 (100%)
TOTALS	384 (9% of pts)	95 (25% of those with PCa)	54 (14% of those with PCa)

# Overall Survival Primary Liver Cancer n = 384/4506 (9% of pts transplanted)



## Overall Survival Primary Liver Cancer n= 384/4506 (9%)



# Primary Liver Cancer

## Actuarial Survival Summary

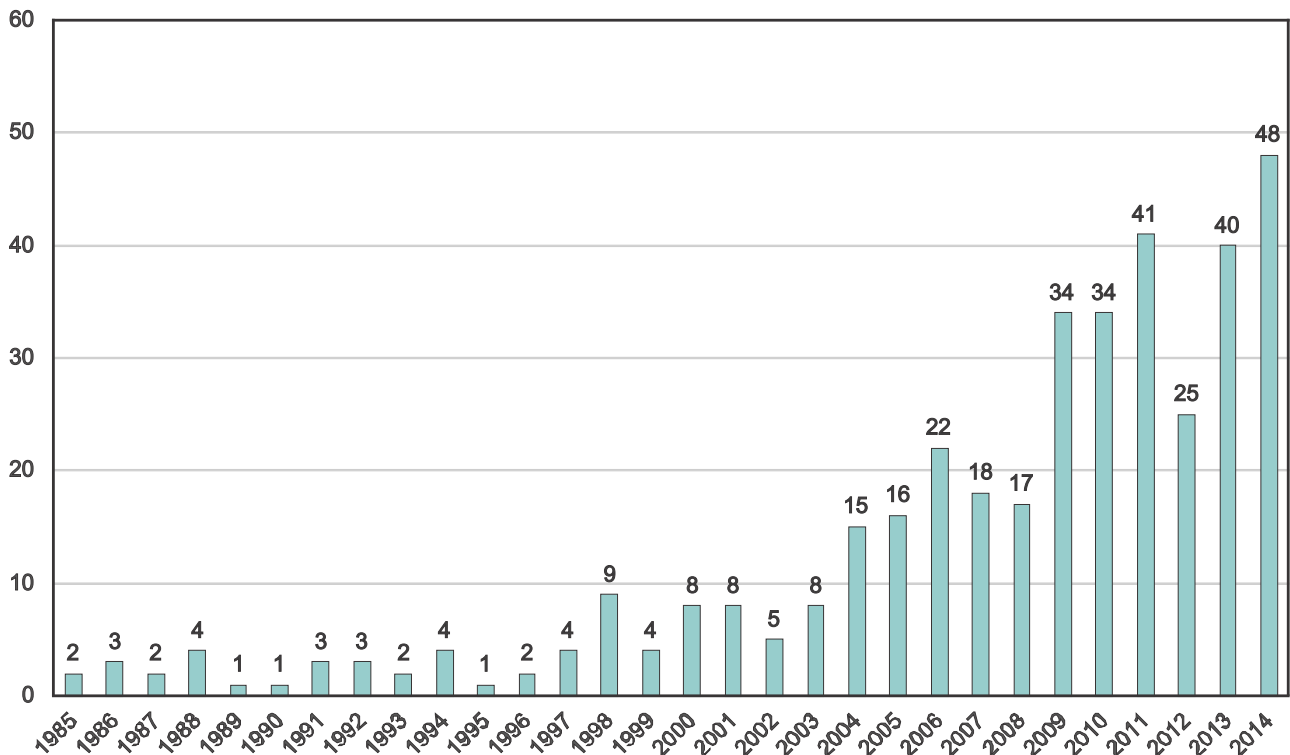
n = 384/4506



		1yr	5yr	10yr	15yr	20yr
<b>HCC (n=342)</b>	n	275	121	39	11	2
	%	92	75	64	64	53
<b>Hepatoblastoma (n=22)</b>	n	20	9	3	3	2
	%	95	79	53	53	53
<b>Other (n=12)</b>	n	10	5	2	2	2
	%	83	41	21	21	21
<b>Fibrolamellar (n=6)</b>	n	6	4	4	2	
	%	83	67	65	22	
<b>CC (n=2)</b>	n	2	1			
	%	50	50			

## Primary Liver Cancer Incidence

n= 384/4506





## Liver Cancer as a Secondary Diagnosis

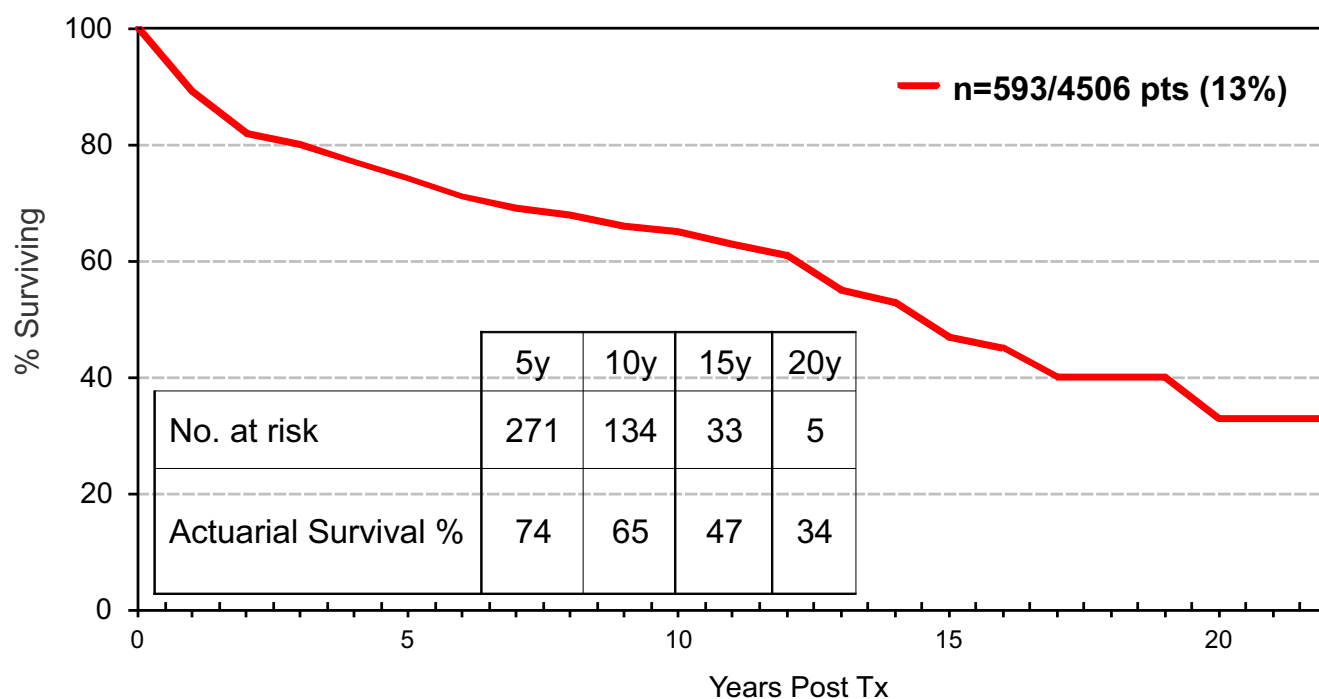
n = 572/4506

	No	Died	Died of This Cancer
HEPATOCELLULAR CA*	523	143	40 (8%)
CHOLANGIO CA	37	29	17 (46%)
OTHER	7	5	2 (29%)
FIBROLAMELLAR	4	0	0
HEPATOBLASTOMA*	3	1	0
<b>Total</b>	<b>574* in 572 pts (13%)</b>	<b>178 (31% of pts with SCa)</b>	<b>59 (10% of pts with SCa)</b>

\* 2 patients had 2 secondary cancers

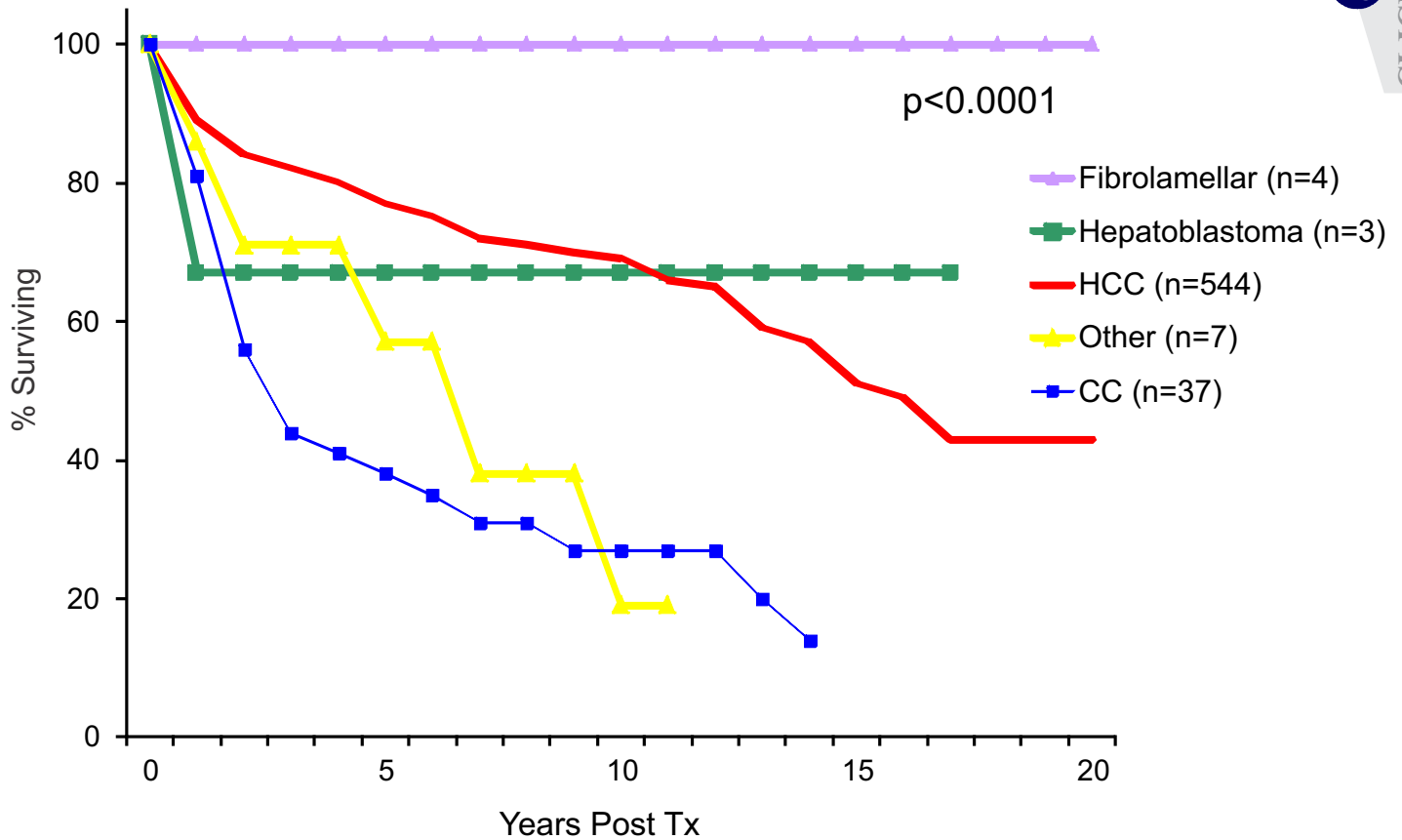
## Overall Survival

## Liver Cancer as a Secondary Diagnosis



## Liver Cancer as a Secondary Diagnosis

n =593/ 4506 (13%)



## Secondary Liver Cancer

### Actuarial Survival Summary

n =572/ 4506 (13%)

		1yr	5yr	10yr	15yr
HCC (n=523)	n	420	251	124	30
	%	89	77	69	51
CC (n=37)	n	31	13	8	2
	%	81	38	27	6
Other (n=7)	n	7	4	2	
	%	86	57	19	
Fibrolamellar (n=4)	n	4	4	4	4
	%	100	100	100	100
Hepatoblastoma (n=3)	n	3	3	2	2
	%	67	67	67	67



# Liver Cancer

## (Primary or Secondary Diagnosis)

n = 953/4506



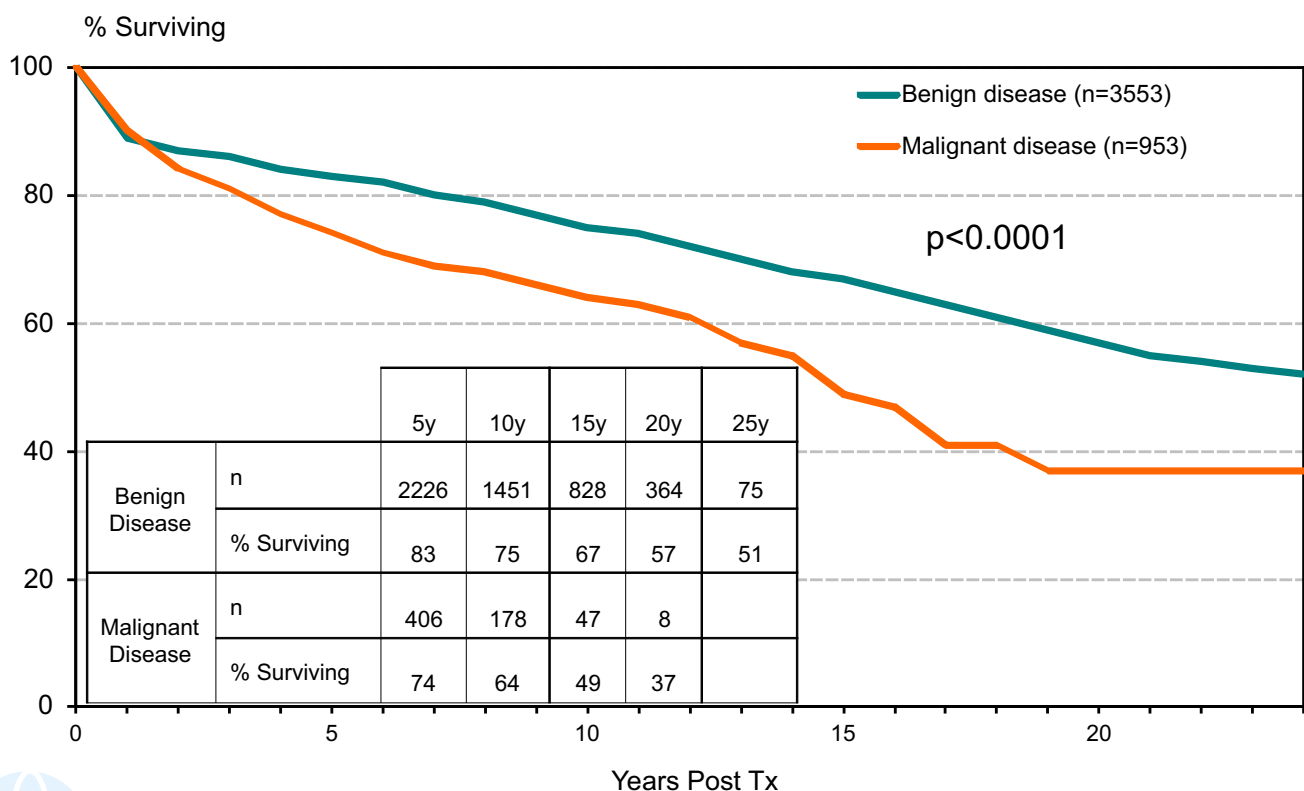
TYPE OF CA	No.	DIED	DIED OF THIS CA
HEPATOCELLULAR CA*	864	219	79 (9%)
CHOLANGIOCARCINOMA*	39	30	18 (46%)
HEPATOBLASTOMA*	25	6	4 (16%)
FIBROLAMELLAR	10	5	2 (20%)
CARCINOID	4	4	4 (100%)
ADENOCARCINOMA	5	4	1 (20%)
EPITHELOID HAEMANGIOENDOTHELIOMA	4	0	0
ANGIOSARCOMA	2	2	2 (100%)
GASTRINOMA	1	1	1 (100%)
PANCREATIC ISLET CELL	1	1	1 (100%)
ERYTHROID LEUKAEMIA	1	1	1 (100%)
<b>TOTALS</b>	<b>958* Ca in 953 pts (21% of pts)</b>	<b>273 (29% of those with Ca)</b>	<b>113 (12% of those with Ca at Tx)</b>

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

## Patient Actuarial Survival

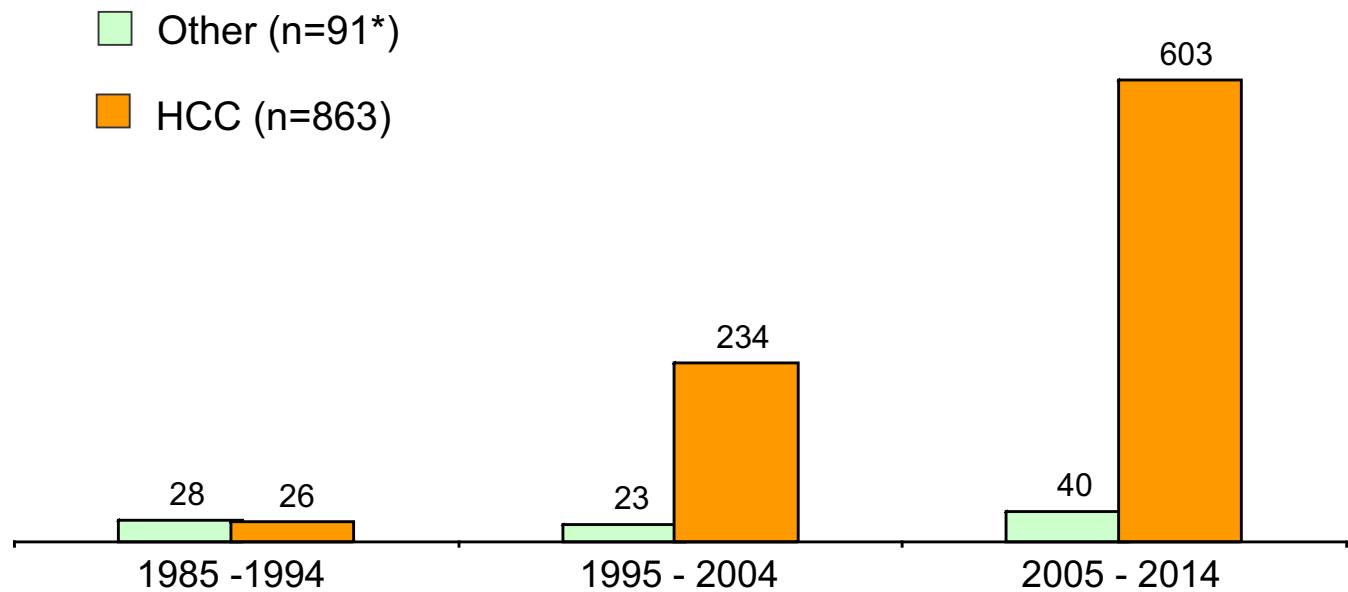
### Benign Disease vs Pre Transplant Liver Malignancy

n = 4506



## Liver Cancer at Transplantation

n = 954/4506 (21%)



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

## De Novo Non - Skin Cancer

n = 323/4506

	No	Male	Female	Age of pts (yrs)	Time to diagnosis (mths)	Died of This Cancer
Alimentary*	125	95	30	12.6 – 83 (m 59)	3 – 281 (m 54)	59 (45%)
Lymphoma*	91	54	37	1– 70 (m 48)	1 – 217 (m 5)	32 (37%)
Genitourinary*	47	31	16	21 – 75 (m 61)	2 – 348 (m 20)	4 (10%)
Breast	25	-	25	30 – 74 (m 55)	11 – 241 (m 79)	10 (36%)
Respiratory	33	27	6	29 – 75(m 60)	7 – 212 (m 39)	25 (76%)
Endocrine	9	4	5	35 – 70 (m 56)	35 – 213 (m 64)	3 (33%)
CNS	7	5	2	16 – 75 (m 57)	14– 211 (m 99)	6 (86%)
Kaposi's	5	4	1	32 – 65 (m 51)	2 – 48 (m 16)	0
Leukaemia	4	2	2	3 – 66 (m 43)	16 – 155 (m 37)	0
Miscellaneous	4	2	2	62 – 73 (m 68)	60– 234 (m 87)	1(25%)
<b>Total</b>	<b>*352 ca in 323 pts</b>	<b>225</b>	<b>127</b>	<b>1 – 83 (m 56)</b>	<b>1 – 348 (m 53)</b>	<b>140 (43% of pts with Ca)</b>

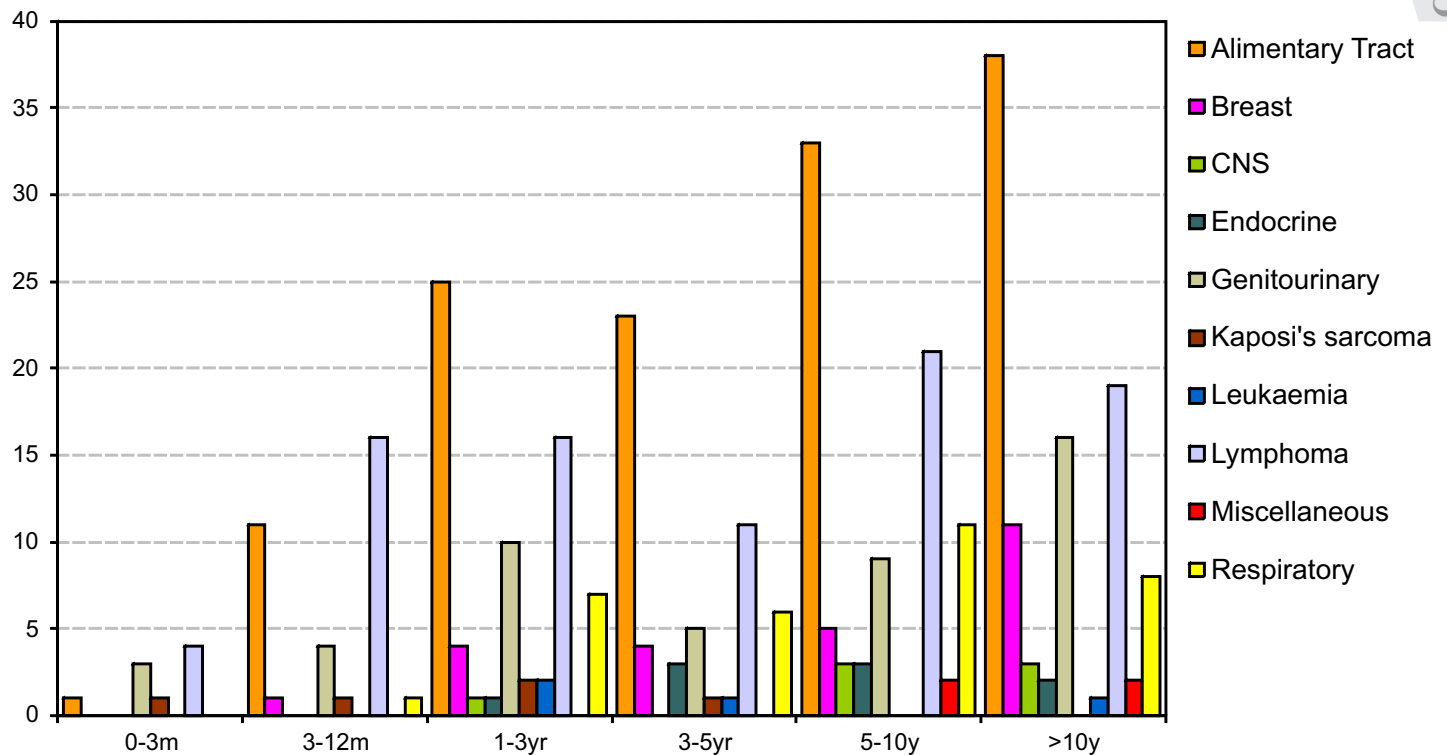
\* 27 patients had more than 1 de novo cancer

m = median

## Time to De Novo Non - Skin Cancer

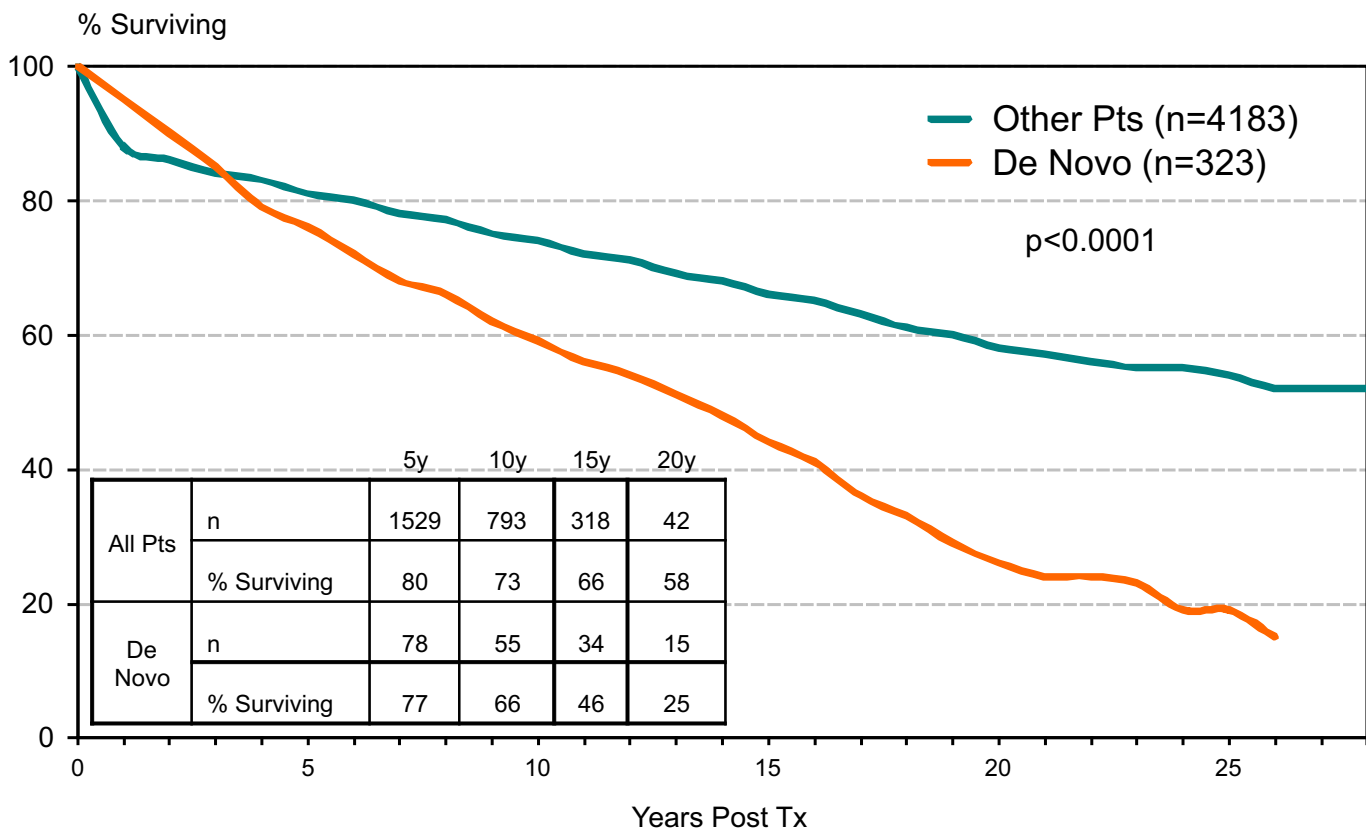
n = 4506

352 cancers in 323 pts (7% of all pts)

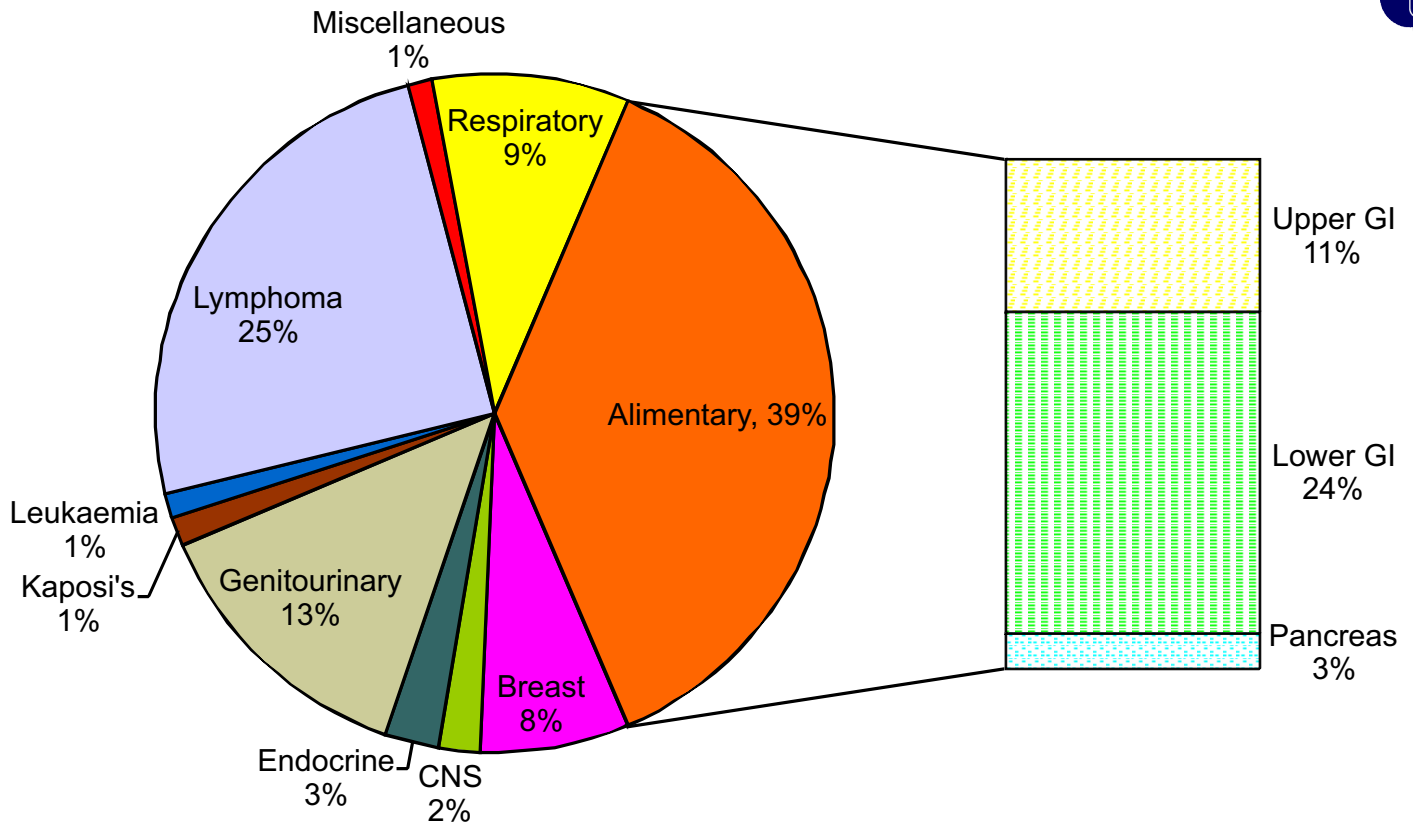


## De Novo Non - Skin Cancer vs All Patients

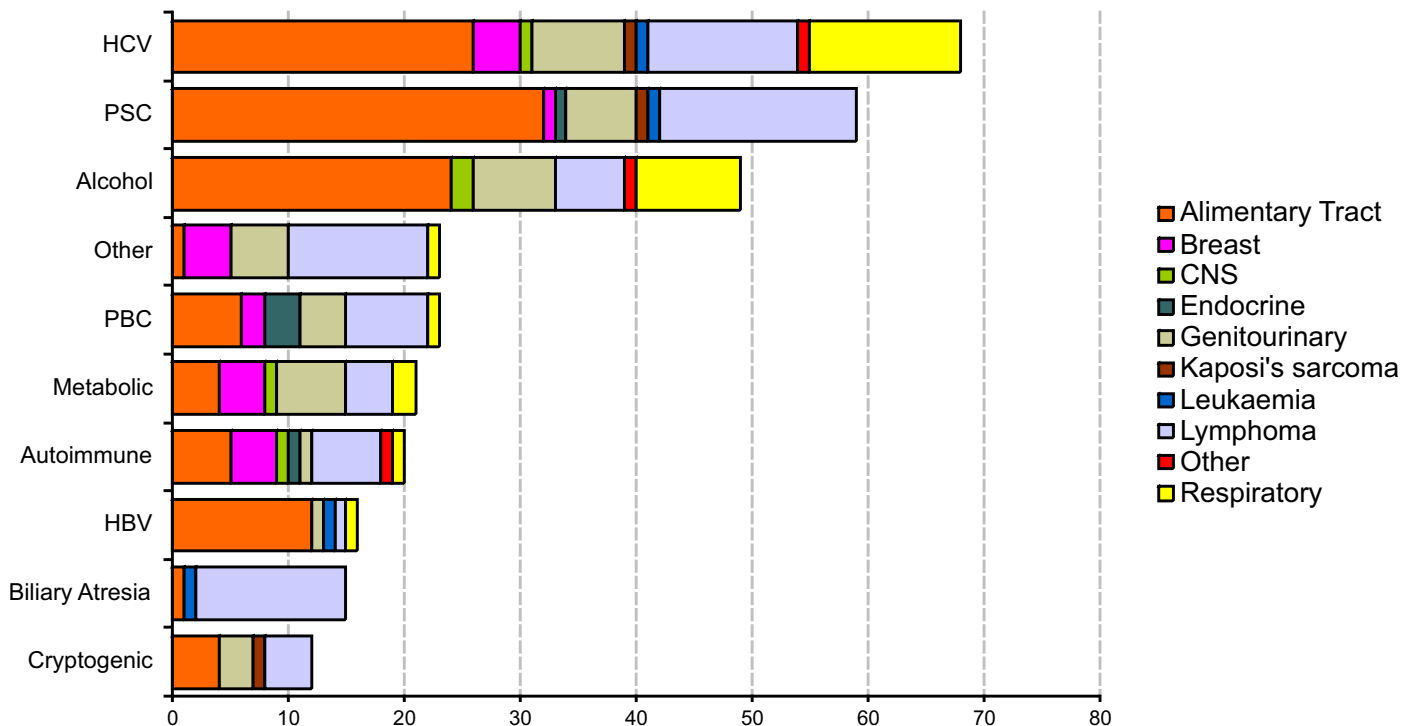
n = 4506



## De Novo Non - Skin Cancer n = 323/4506 (7%)

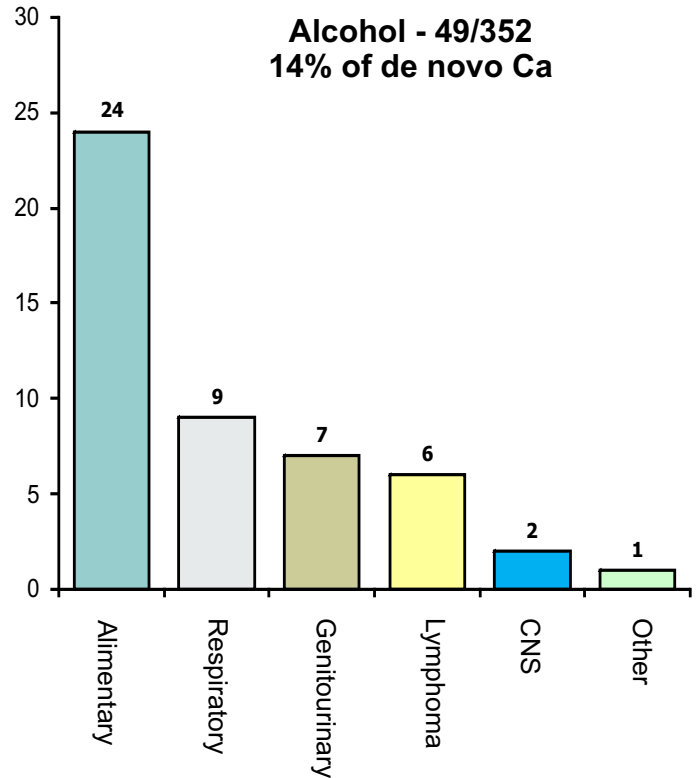
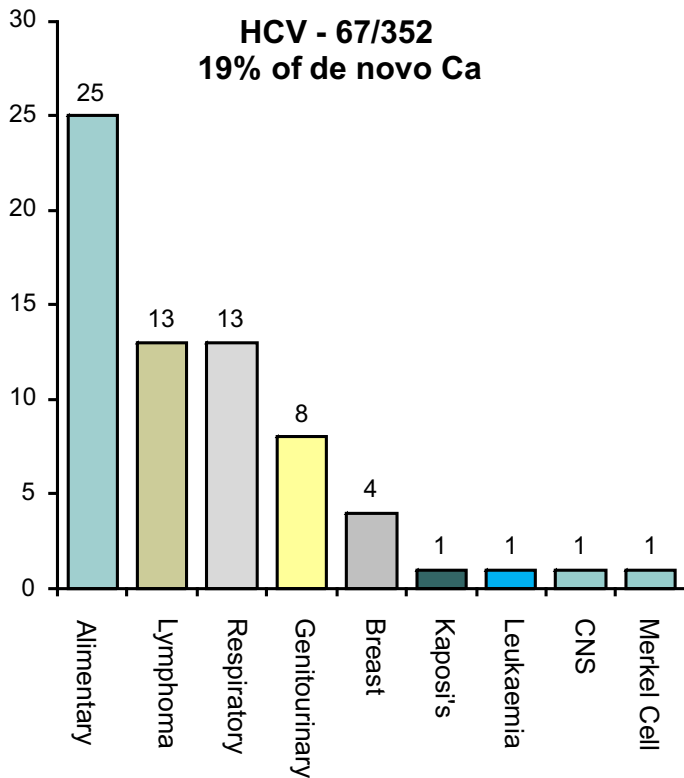


## Pre Transplant Liver Disease and De Novo Non - Skin Cancer n = 323/4506 pts (7%)



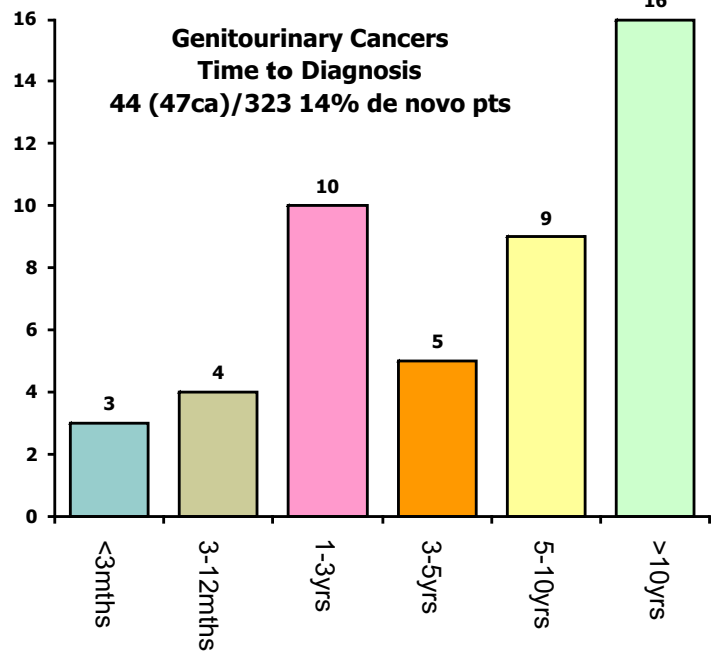
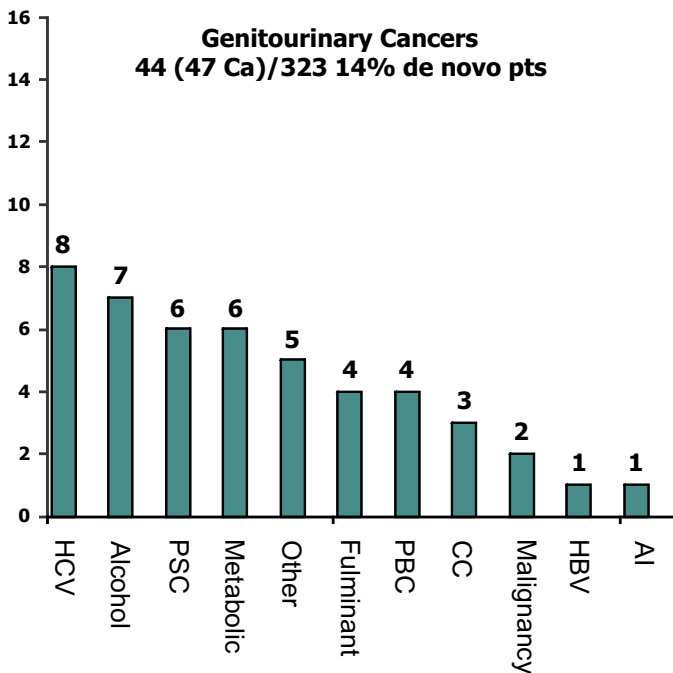
## Pre Transplant Primary Disease and De Novo Non - Skin Cancer

n = 323 (352 Ca)/4506 pts (7%)

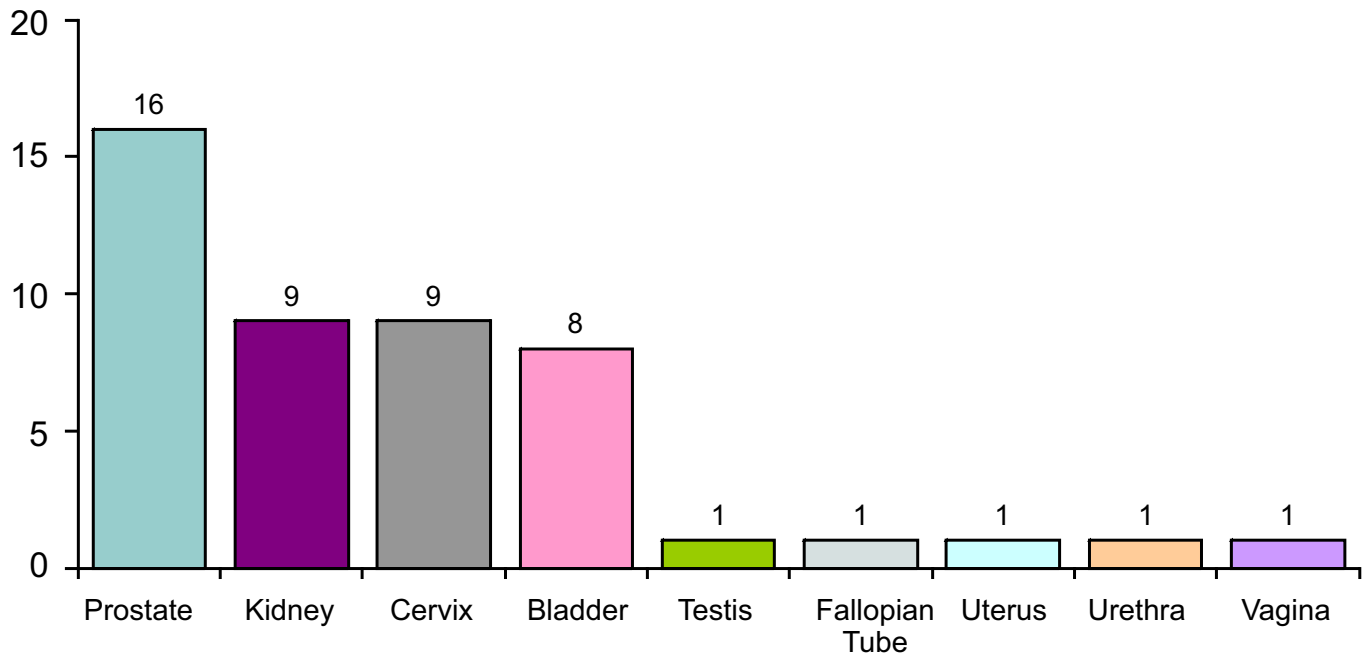


## Pre Transplant Primary Liver Disease and De Novo Non - Skin Cancer

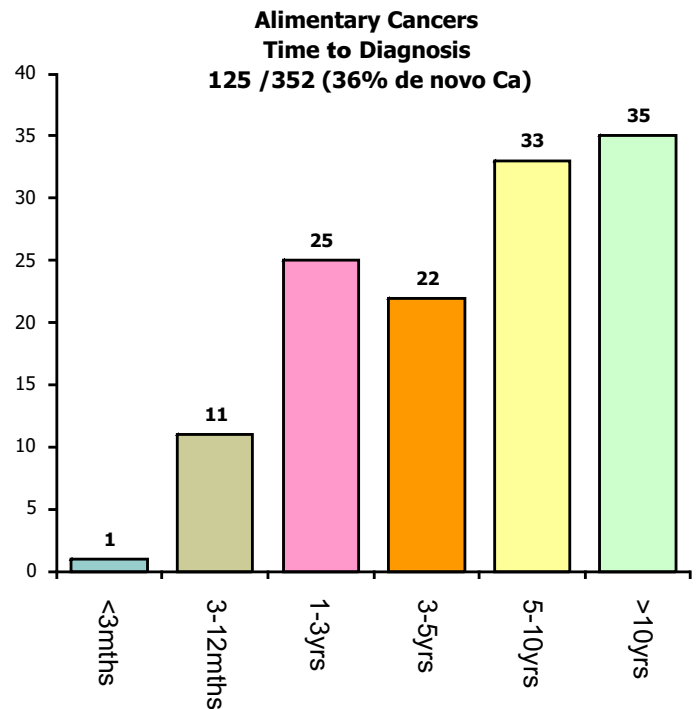
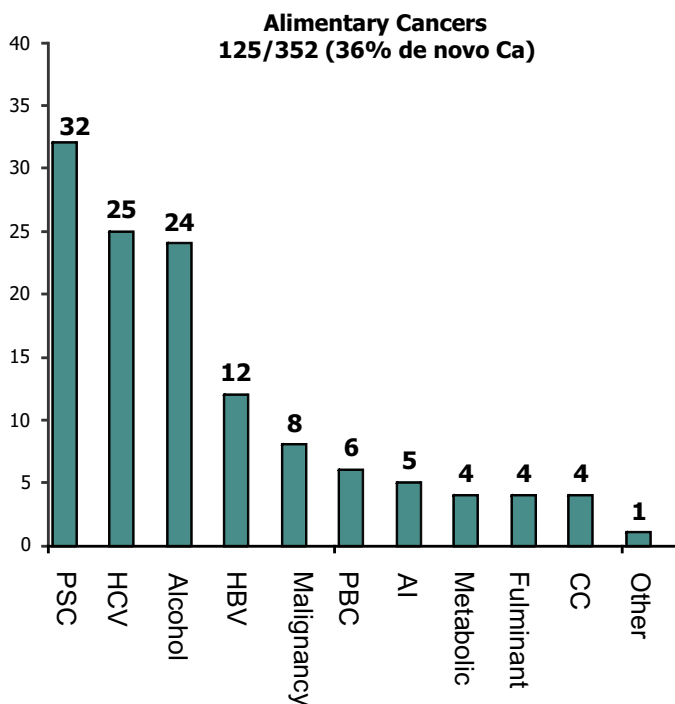
n = 323 (352 Ca)/4506 pts (7%)



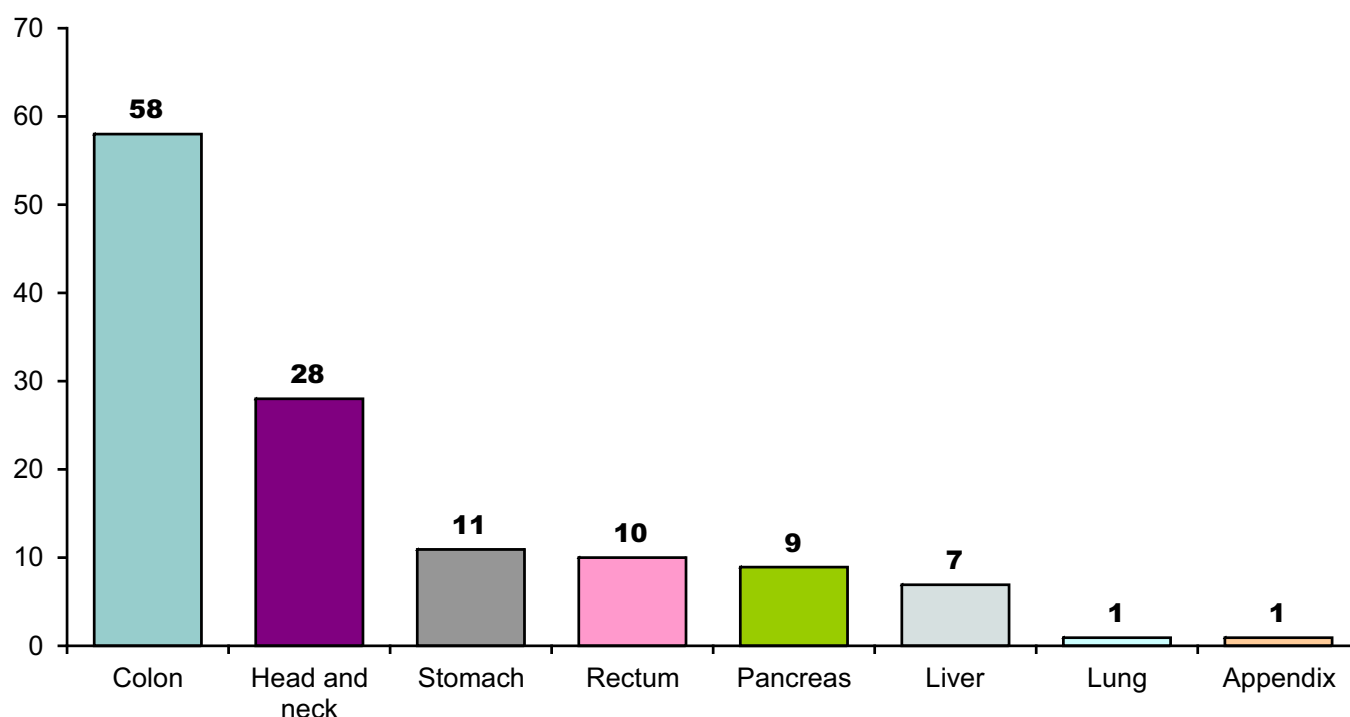
## De Novo Non - Skin Cancer Genitourinary Tract Incidence n = 47/352 cancers (13%)



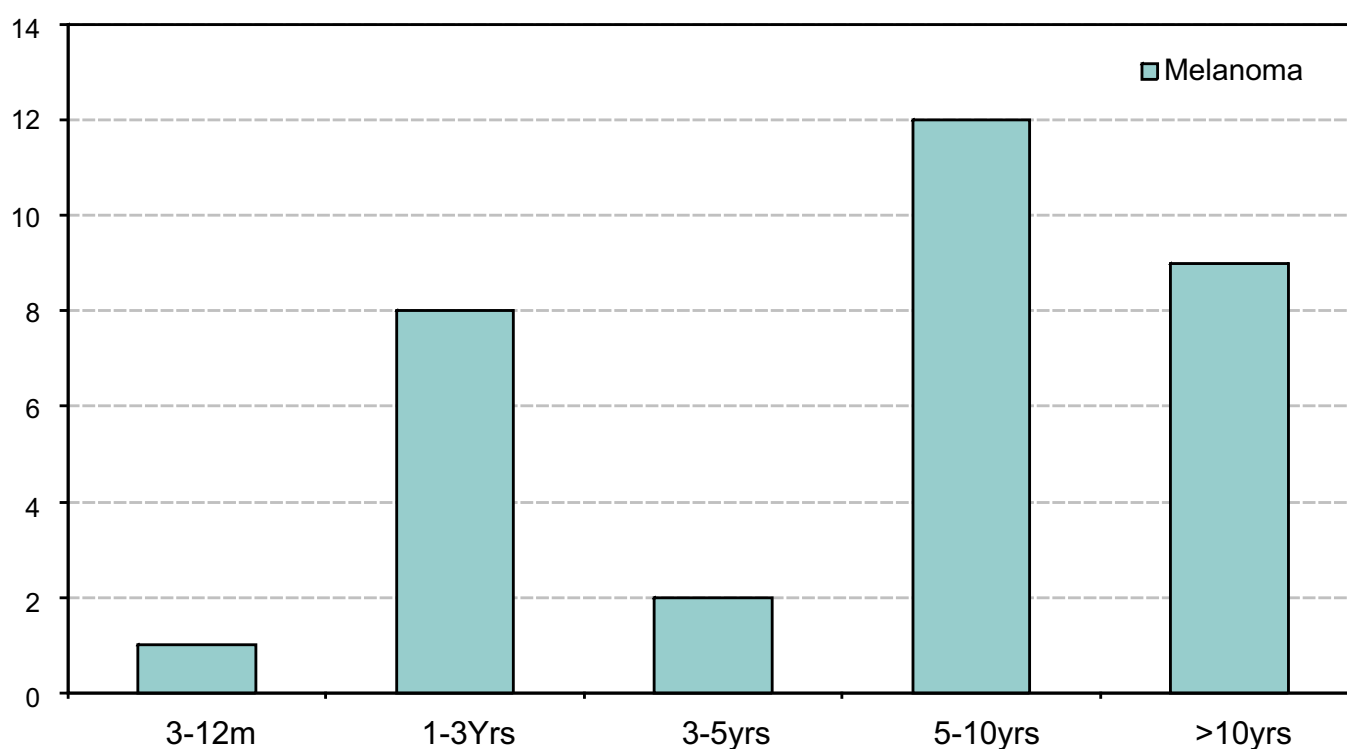
## Pre Transplant Primary Disease and De Novo Non - Skin Cancer n = 323 (352 Ca)/4506 pts (7%)



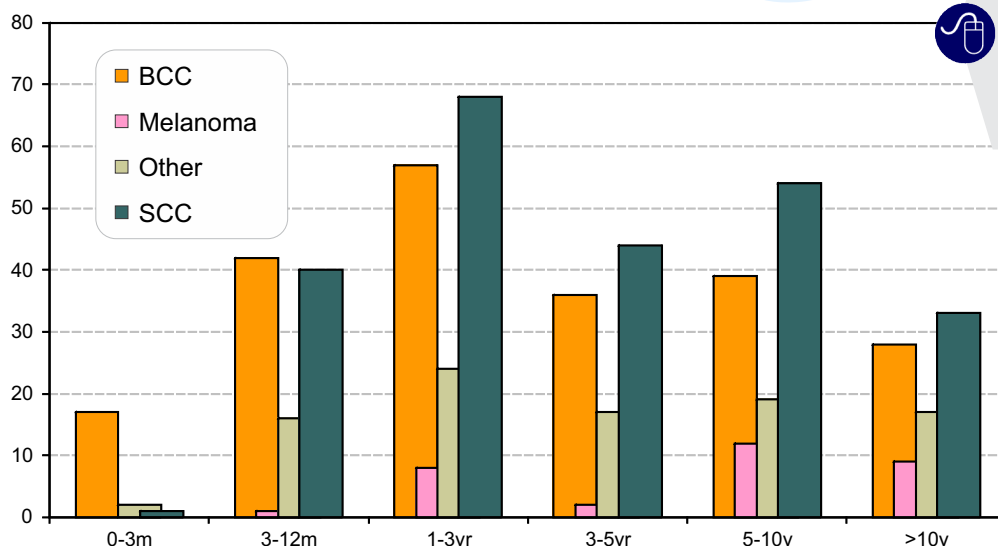
## De Novo Non - Skin Cancer Alimentary Tract Incidence n = 125/352 cancers (36%)



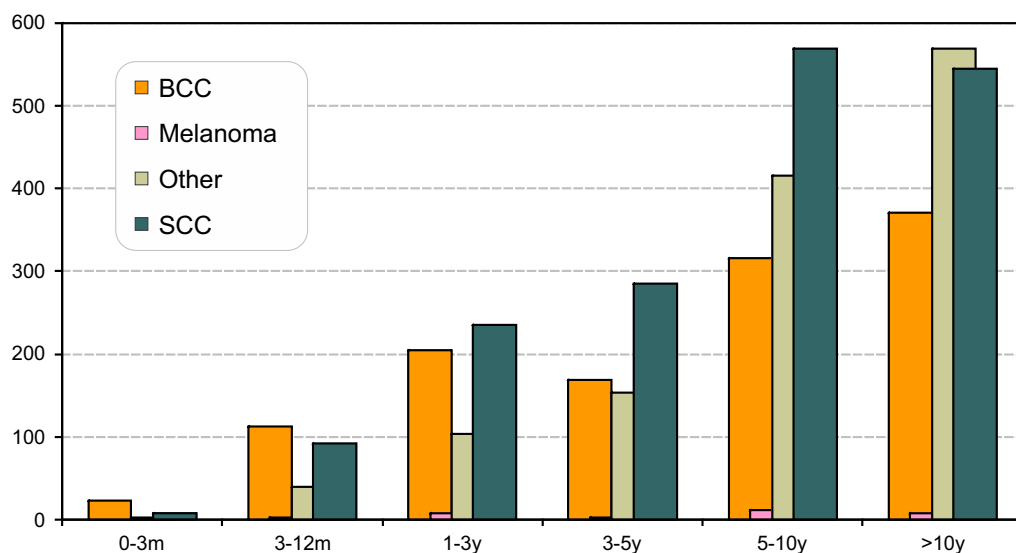
## Time to Melanoma Skin Cancer Development Post Tx. n = 4506 32 (0.7% of all pts)



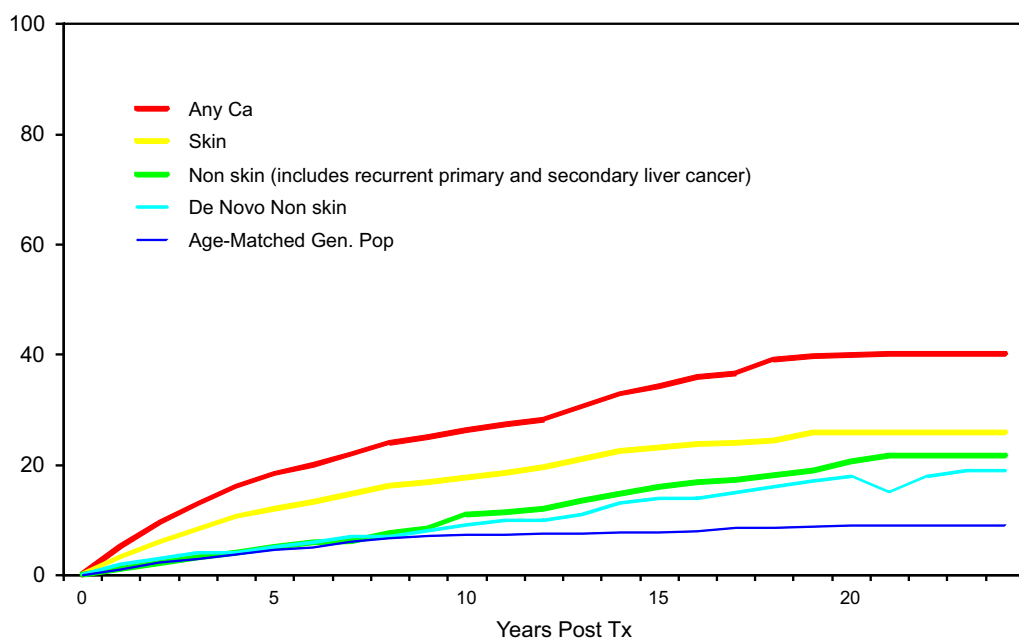
## Time to 1st Skin Cancer Development 654/4506 (15% of all pts)



## Time to Multiple Skin Cancer Development 316/4506 (5% of all pts)



## Cumulative Risk of Diagnosis of Cancer Following Liver Tx. 1985-2014 Patients at Risk (4506)







# Appendix I

## Liver Transplant Units of Australia and New Zealand

Australian National Liver Transplant Unit  
Royal Prince Alfred Hospital  
Missenden Road  
CAMPERDOWN NSW 2050  
Email: [pamela.dilworth@sswahs.nsw.gov.au](mailto:pamela.dilworth@sswahs.nsw.gov.au)  
<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.nzliver.org/>

*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	
$\alpha$ -1 Antitrypsin deficiency	38	49	87
Crigler-Najjar	10	1	11
Familial amyloid polyneuropathy	0	35	35
Glycogen storage disease	4	6	10
Haemochromatosis	3	29	32
Homozygous Hypercholesterolemia	6	2	8
Idiopathic copper toxicosis	1	0	1
Indian childhood cirrhosis	1	0	1
Other*	13	6	19
Primary hyperoxaluria	9	6	15
Tyrosinemia	4	0	4
Urea cycle disorders**	20	4	24
Wilsoms disease	8	28	36
<b>Total</b>	<b>117</b>	<b>166</b>	<b>283</b>

\* Maple syrup urine disease 4  
Amyloidosis 2  
Bile acid Transport disorder 2  
Protein C deficiency 2  
Propionic acidemia 2  
Methylmalonic acidemia  
Familial immunodeficiency  
Mitochondrial disease  
Porphyria

\*\* OTC deficiency 13  
Citrullinemia 4  
Argininosuccinic aciduria 4  
Carbamyl phosphate synthetase deficiency 3



# Appendix III

## ANZLTR PRIMARY Diagnosis - Other by Age Group

Primary Diagnosis	Age group		Total
	Child	Adult	
Alagille syndrome	29	7	36
Alagille non-syndromic	2	0	2
Benign liver tumour - Adenomatosis	0	2	2
Benign liver tumour - Hemangioma	0	3	3
Caroli's disease / congenital hepatic fibrosis	2	20	22
Choledocal cyst	2	2	4
Cholestatic disease-Other	4	10	14
Chronic Budd Chiari	1	30	31
Congenital biliary fibrosis	0	2	2
Ductopenia	1	3	4
Granulomatous hepatitis / sarcoidosis	0	4	4
Histiocytosis X	4	1	5
Liver Trauma	0	1	1
Neonatal hepatitis	4	0	4
Nodular regenerative hyperplasia	0	7	7
Non alcoholic fatty liver (NAFLD or NASH)	0	111	111
Polycystic Liver disease	0	22	22
Polycystic liver and kidney disease	1	12	13
Progressive familial intrahepatic cholestasis(PFIC)	20	5	25
Secondary biliary cirrhosis	3	13	16
Secondary biliary cirrhosis - Hepatolithiasis	0	4	4
Secondary biliary cirrhosis - Cystic fibrosis	12	18	30
Other - specify <sup>#</sup>	9	22	31
Total	94	299	393

# Vanishing bile duct syndrome  
Haemangioteliectasia  
Veno-occlusive disease  
Chronic Active Hepatitis A  
Non-cirrhotic portal hypertension  
Kassabach-Merritt syndrome  
Arterial-venous malformation  
Hereditary haemorrhagic telangiectasia / OWRD  
Oriental cholangio hepatitis

COACH syndrome  
Biliary sclerosis  
Cornelia De Lange Syndrome  
Hepatic Lymphangiomatosis



# Appendix IV

## ANZLTR PRIMARY Diagnosis Fulminant Hepatic Failure by Age Group

Primary Diagnosis	Age group		Total
	Children	Adult	
Acute - Budd Chiari	0	2	2
Acute - Wilson's	8	16	24
Acute - $\alpha$ -1 -AAT	2	0	2
Acute Autoimmune hepatitis	0	6	6
Acute Unknown / unspecified	44	94	138
Acute - Paracetamol	4	15	19
Acute - Other drugs	3	25	28
Acute Herbs / mushrooms	1	8	9
Acute - Hepatitis A	1	3	4
Acute - Hepatitis B	0	60	60
Acute - Non A-G	13	20	33
Acute - Hepatitis E	0	1	1
Acute - Post liver resection/trauma	1	3	4
Subacute - Budd Chiari	1	2	3
Subacute - Wilson's	2	4	6
Subacute Autoimmune hepatitis	1	17	18
Subacute - Drug / Herbs	1	15	16
Subacute - Unknown / unspecified	5	30	35
Subacute - Hepatitis A	0	2	2
Subacute - Hepatitis B	0	19	19
Subacute - Non A-G	0	4	4
<b>Total</b>	<b>87</b>	<b>346</b>	<b>433</b>



# Appendix V

## ANZLTR Causes of Patient death

<u>Graft failure - other</u>	Age group		Total
	Children	Adult	
Vascular thrombosis	8	16	24
<i>Hepatic artery</i>	4	9	13
<i>Portal vein</i>	2	7	9
<i>Hepatic vein</i>	2	-	2
Non thrombotic infarction	3	-	3
Primary non function	4	17	21
Massive haemorrhagic necrosis	4	0	4
Recurrent disease ( <i>ALD, PSC, CAH:AI</i> )	-	19	19
De novo Hep C	-	2	2
Biliary Complications	3	12	15
Other ( <i>PNC, immune hepatitis, outflow obstruction</i> )	7	19	26
<b>TOTAL</b>	<b>29</b>	<b>85</b>	<b>114</b>

<u>Miscellaneous</u>	Children	Adult	
Multiorgan failure	8	71	79
Renal Failure	1	33	34
Graft vs Host disease	-	7	7
Social ( <i>accident, suicide, non-compliance, Rx withdrawn</i> )	1	16	17
Sudden death ( <i>cause unknown</i> )	2	29	31
Other ( <i>Hyperkalaemia, motor neurone disease, diabetes complications, drug reaction, progression FAP, essential thrombocythemia</i> )	1	19	20
<b>TOTAL</b>	<b>13</b>	<b>175</b>	<b>188</b>