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AUSTRALIA & NEW ZEALAND

LIVER TRANSPLANT REGISTRY

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

CD Included
INSIDE BACK COVER

Report PowerPoint
SLIDES

DATA TO 31-12-2015

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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.

Director: Professor G.W McCaughan
All queries to: Dr Deborah Verran — Email verran@ausdoctors.net

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Preface

We are pleased to present the 27th Report of the Australia and New Zealand Liver Transplant Registry (ANZLTR). This report contains data to the 31st December 2015 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 from where the report can be downloaded. Slides are available on request from the Coordinating Centre.

Stephen Lynch
Glenda Balderson

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Summary

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5. Between January 1985 and 31st December 2015, 5180 orthotopic liver transplants (OLT) were performed in Australia and New Zealand on 4800 patients, 3966 adult patients [83%] and 834 children (< 16 years) [17%]. The median age of all recipients was 48.6 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 ninety-five new patients were transplanted in 2015 compared with 263 in 2014.

7. The trend to increasing age of adult recipients in recent years continued and the overall adult median age is now 51.5 years. The median age of new adult recipients in 2015 was 56.5 years.

8-9. In 2015, there was an increase in the number of transplants with 38 more performed [316 vs 278]. Split grafts continue to make a significant contribution to the total number of paediatric transplants performed providing 24 of 39 [62%] of deceased donor grafts in 2015 and 261 of 944 [27%] overall. In children, other reduced size grafts have been used in 403 [41%] cases including 78 living donor grafts. One child has been treated with liver cell implantation. Of adult patients, 304 have received reduced size grafts - 261 split liver grafts (including 1 as auxiliary graft), 30 other reduced size grafts (1 as auxiliary graft) and 13 living donor grafts. Three 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 22.6% of recipients and chronic hepatitis B [CVH : HBV] in 5.9 %. 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 18 [7%] of new patients transplanted in 2015 bringing the total to 129. The proportion of adult patients transplanted with a primary diagnosis of chronic viral Hepatitis B, C or B/C/D fell in 2015 compared with the previous eras but the number of patients with a primary diagnosis of hepatocellular carcinoma [HCC] increased and accounted for 20% in 2015. 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 2015 was 42%.

16. Overall 1 year patient survival of all patients is 90% at 1 year, 82% at 5 years and 74% at 10 years. Children have a significantly better survival rate than adults with an actuarial survival of 73% 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 2015 cohort was 96% for all patients [100% 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.

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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 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 77%.

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 86% at 1 year and 77% at 5 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, both for all deceased donor grafts and split liver grafts by era of transplantation.

29-30. Vascular complications and rejection were the commonest indications for retransplantation. Thirteen 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 nine 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.

35. There was an increase in the number of cadaveric donors in 2015 to 288 with 310 grafts transplanted from deceased donors. The number of livers split to produce two transplantable grafts was 22 in 2015. Sixteen liver grafts donated after cardiac death were transplanted. The number of people on the waiting list at 31 December 2015 was higher than the number on the waiting list at 31 December 2014.

36. Donor age has increased significantly in recent years. Long term graft survival trends lower in several older donor age groups.

37. Ninety-four patients [78 children, 16 adults] have now received a living donor graft with 6 performed in 2015. In 88 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. Three adult grafts were domino whole liver graft.

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Summary

Page

38. Waiting list activity for 2015 shows the number of patients listed for transplantation continued to increase with 207 remaining on the waiting list at 31 December 2015. Patient delistings due to death, becoming too ill or tumour [HCC] progression accounted for 7.5% of all delistings . Only 1 child was delisted in these categories for tumour progression. Three hundred and sixteen patients were transplanted [52%]. Forty seven patients were listed as urgent in 2014 [25 with initial listing as Category 1 and 22 Category 2]. Twenty two [88%] of Category 1 and 21 [95%] of Category 2 patients had a positive outcome.

39-40. Median waiting times tended to be higher in 2015 in some blood groups. Blood group B patients had the longest waiting times to transplant but blood group O longest waiting time 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 1059* patients (21%) had a liver cancer at the time of transplantation with HCC being the most common (95%). 397 patients (8%) were transplanted for liver cancer, 659 patients (13%) had liver cancer as a secondary or incidental diagnosis, of which 154 (23%) were undiagnosed prior to transplantation. Three patients had both primary and secondary liver cancers and 3 had multiple secondary or incidental liver cancers.

Post transplant 131 (13%) of pretransplant cancers recurred and 122 (11.5% of those with cancer at transplantation) died as a result of recurrence.

42-43. Actuarial patient survival was 49% 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 Cholangiocarinoma had significantly poorer survival.

44-46. In patients with liver cancer as a secondary diagnosis, 20 year patient survival was 33%. Sixty-six [10% of patients] died from recurrence of their cancer.
Overall patients with a diagnosis of pretransplant malignancy had worse survival than patients with benign diseases.

47. Incidence of liver cancer at time of transplantation continues to increase, climbing from 257 to 643 over the last decade.

47-53. Three hundred and eighty two de novo non-skin types of cancer developed in 351 (7%) of patients. Thirty patients developed more than one de novo non-skin cancer.

The three most common categories of de novo non-skin cancer were cancers of the alimentary tract (137), lymphoma (95) and genitourinary (57).

Patients who develop a de novo non-skin cancer post transplant have significantly worse survival than other patients.

Incidence of de novo non-skin malignancy is greatest in those with underlying hepatitis C, primary sclerosing cholangitis and alcoholic cirrhosis ($p<0.0001$).

53-54. Six hundred and seventy three (14%) developed a first skin cancer, with a peak of 1-3 years after transplantation, with 324 going on to develop multiple types of skin cancer. Thirty seven patients developed melanoma.

The cumulative risk of diagnosis of any cancer post transplant is approximately 40% at 20 years.

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Section 1

Demographic Data

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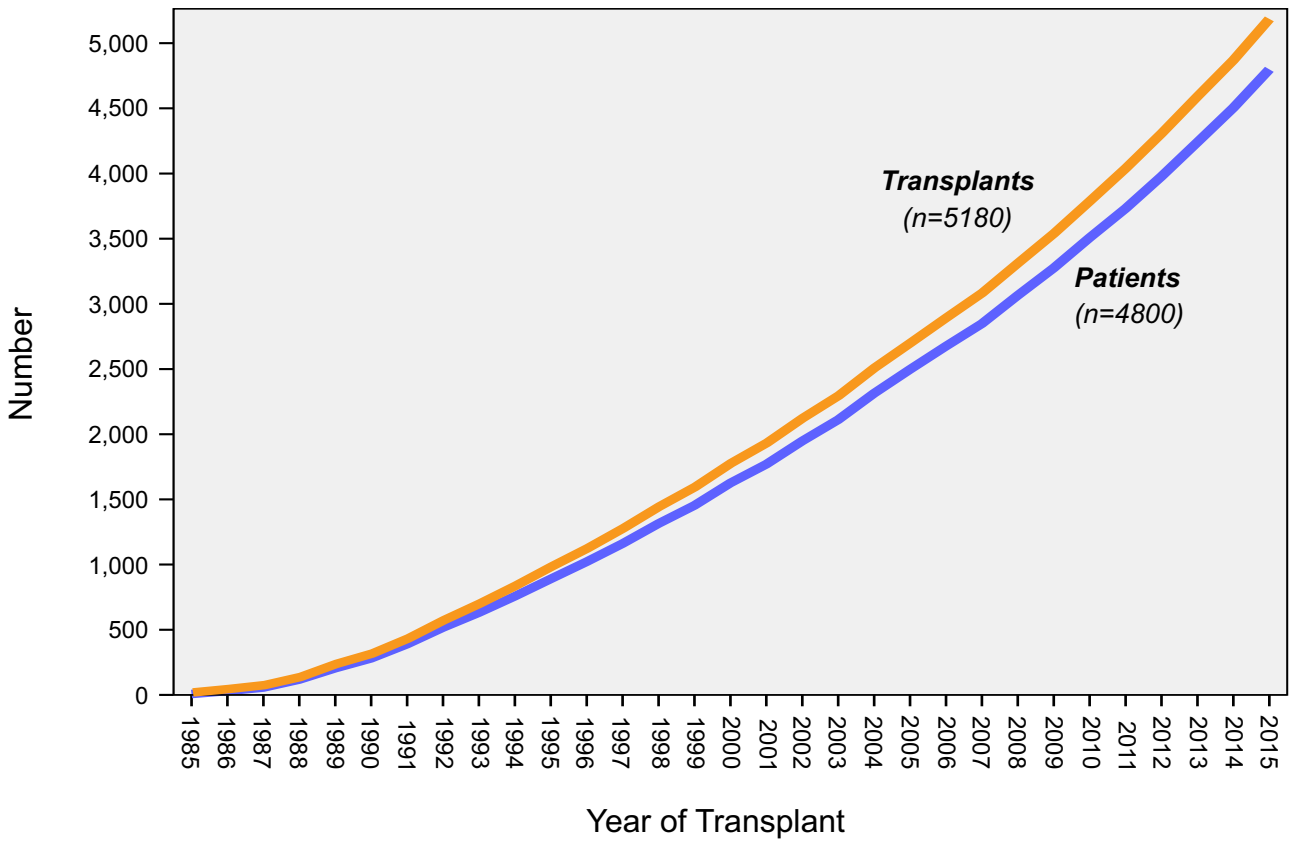
Cumulative Number of Patients & Transplants



Summary Statistics - Age and Gender

ALL PATIENTS TRANSPLANTED

	Children [<16y]	Adults	Total
Patients	834	3966	4800
Age			
Mean ± SD	4.5 ± 4.5y	49.3 ± 11.7y	41.5 ± 20.1y
Median	2.4y	51.5y	48.6y
Range	24d -15.9y	16.0 - 73.1y	24d - 73.1y
Gender			
Female	433 (52%)	1352 (34%)	1785 (37%)
Male	401 (48%)	2614 (66%)	3015 (63%)
Surviving	676 (81%)	2777 (70%)	3453 (72%)

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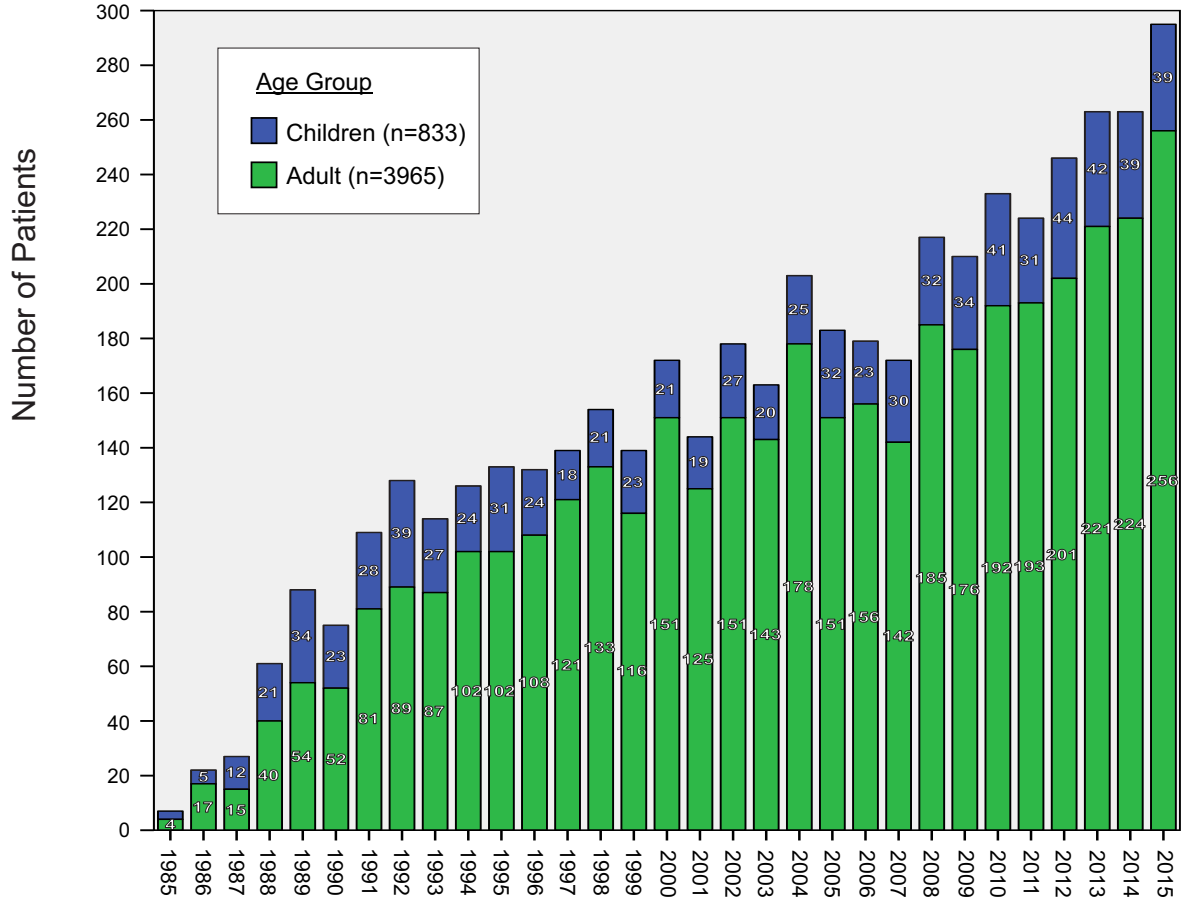
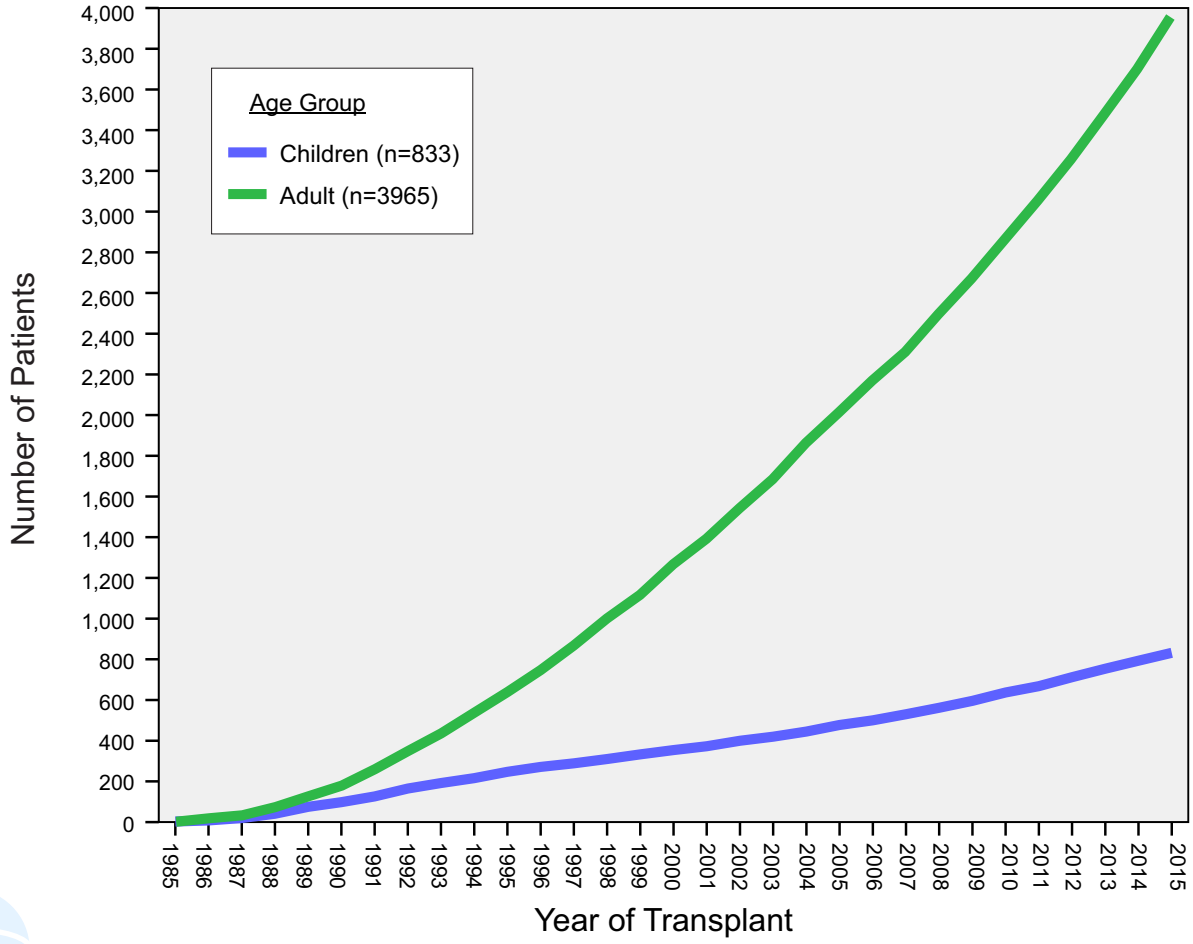
Number of New Patients Transplanted by Year



Cumulative Number of New Patients Transplanted



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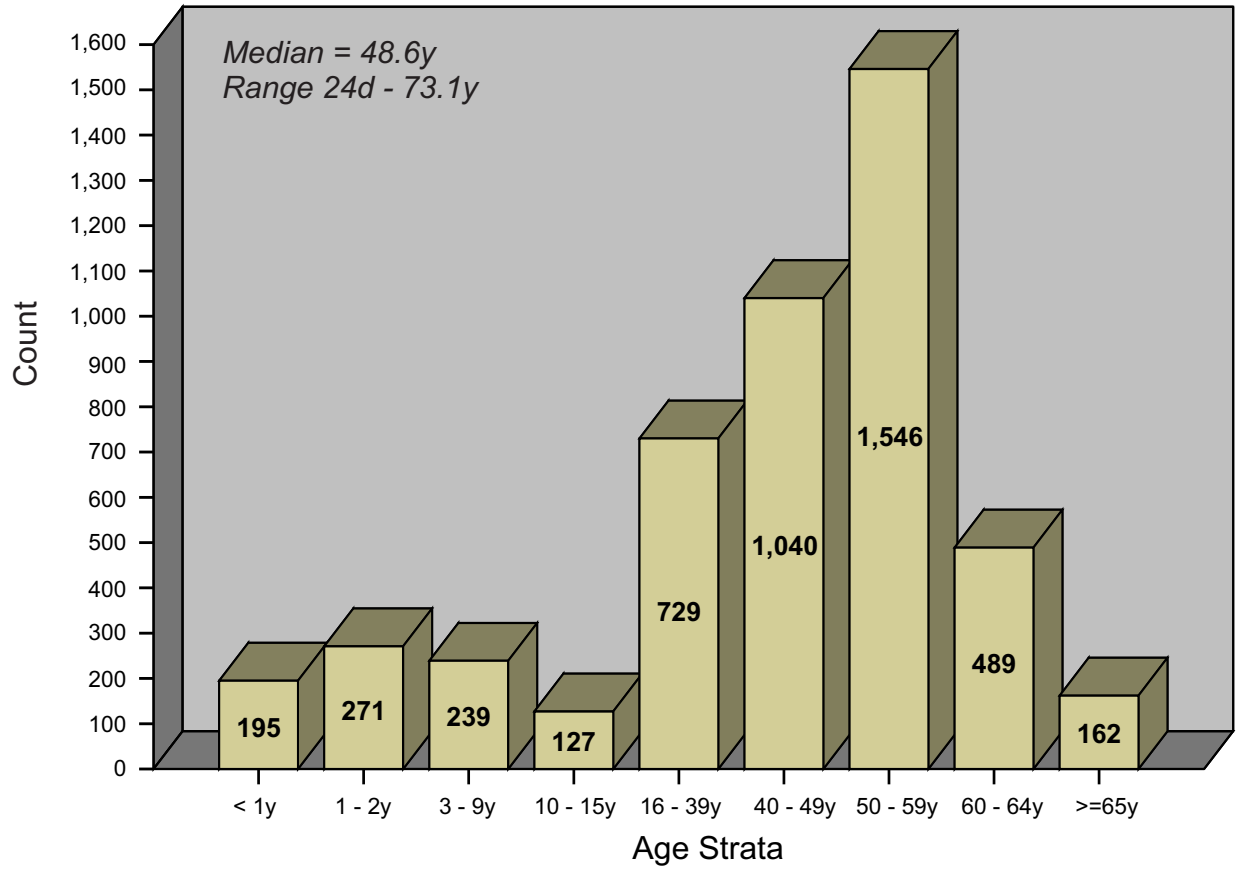
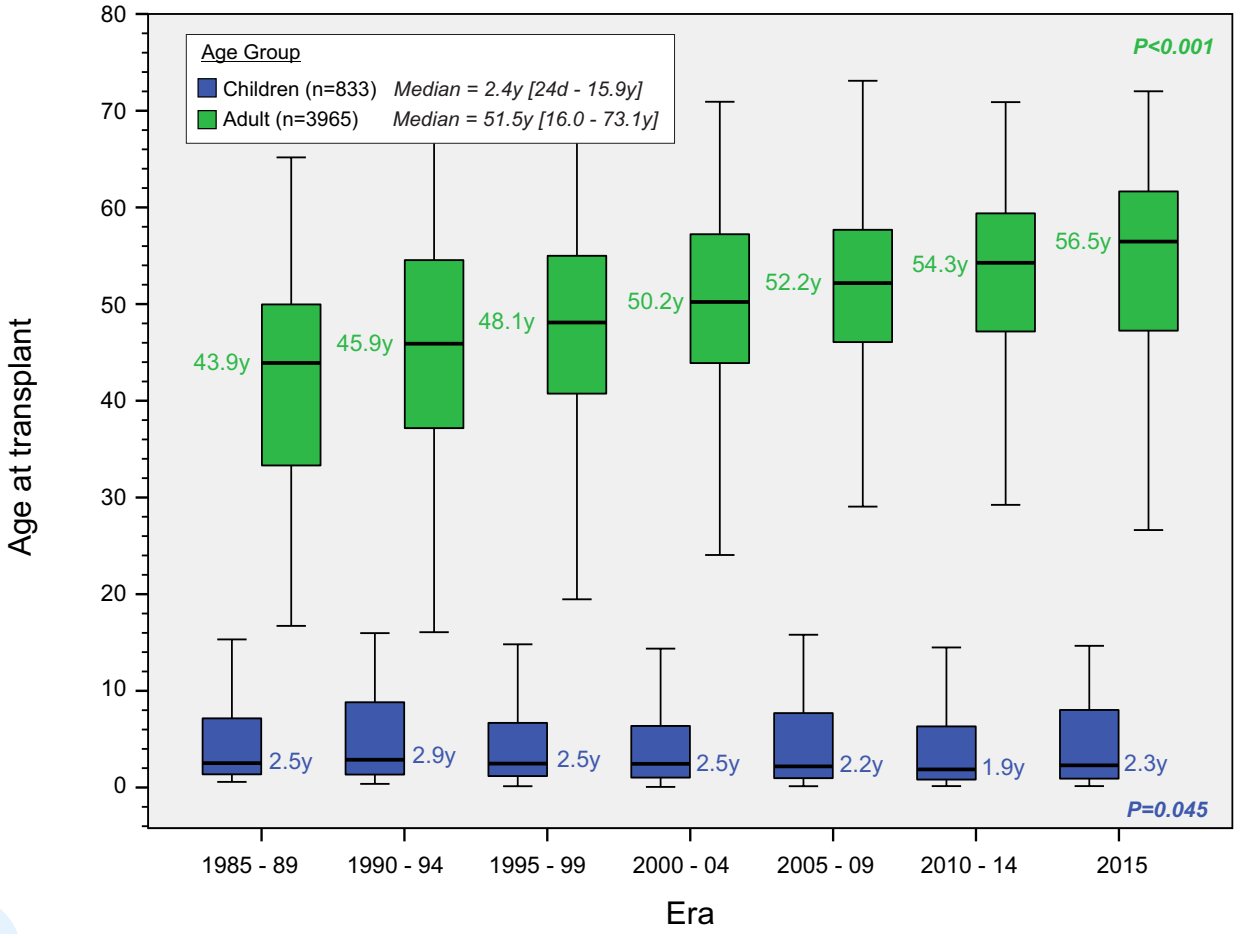
Number of Recipients By Age at Primary Transplant N=4798



Age at Primary Transplant by Era



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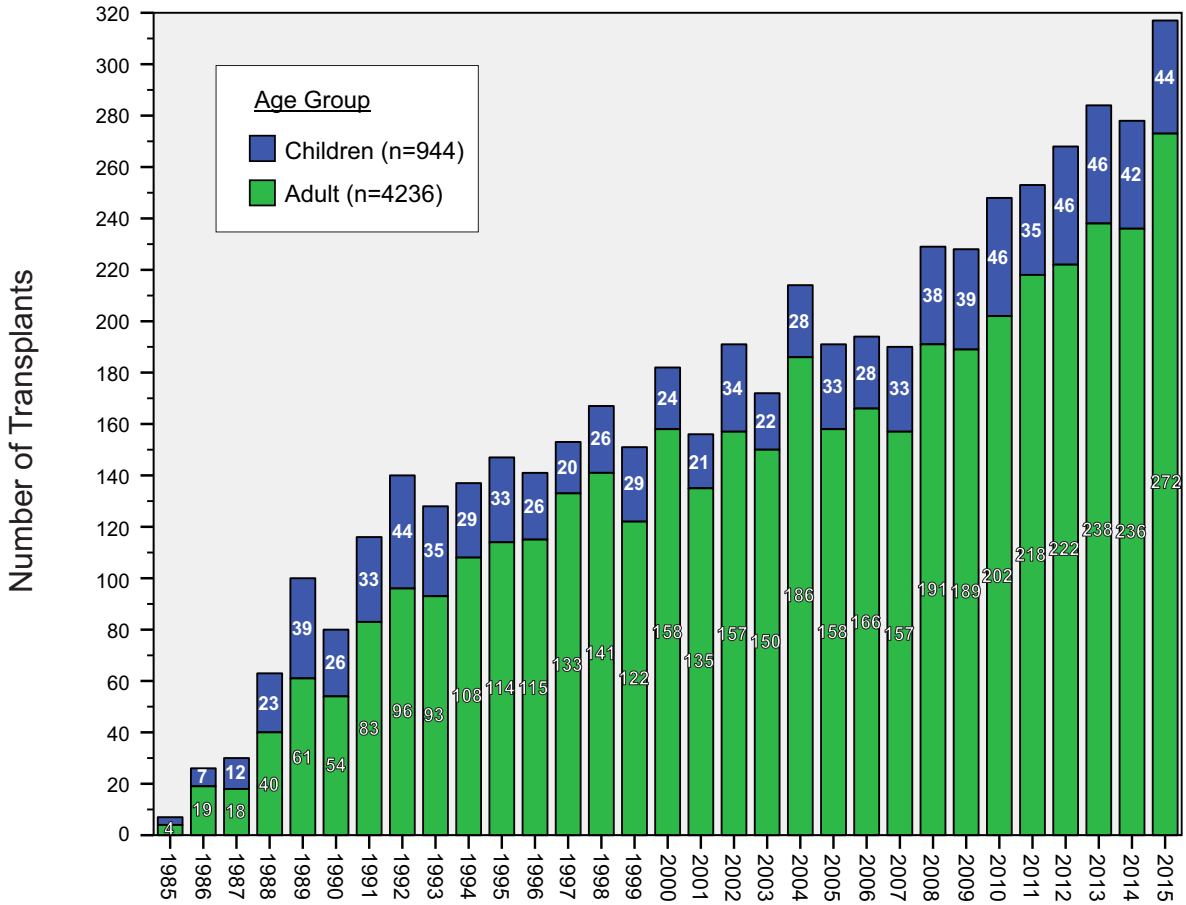
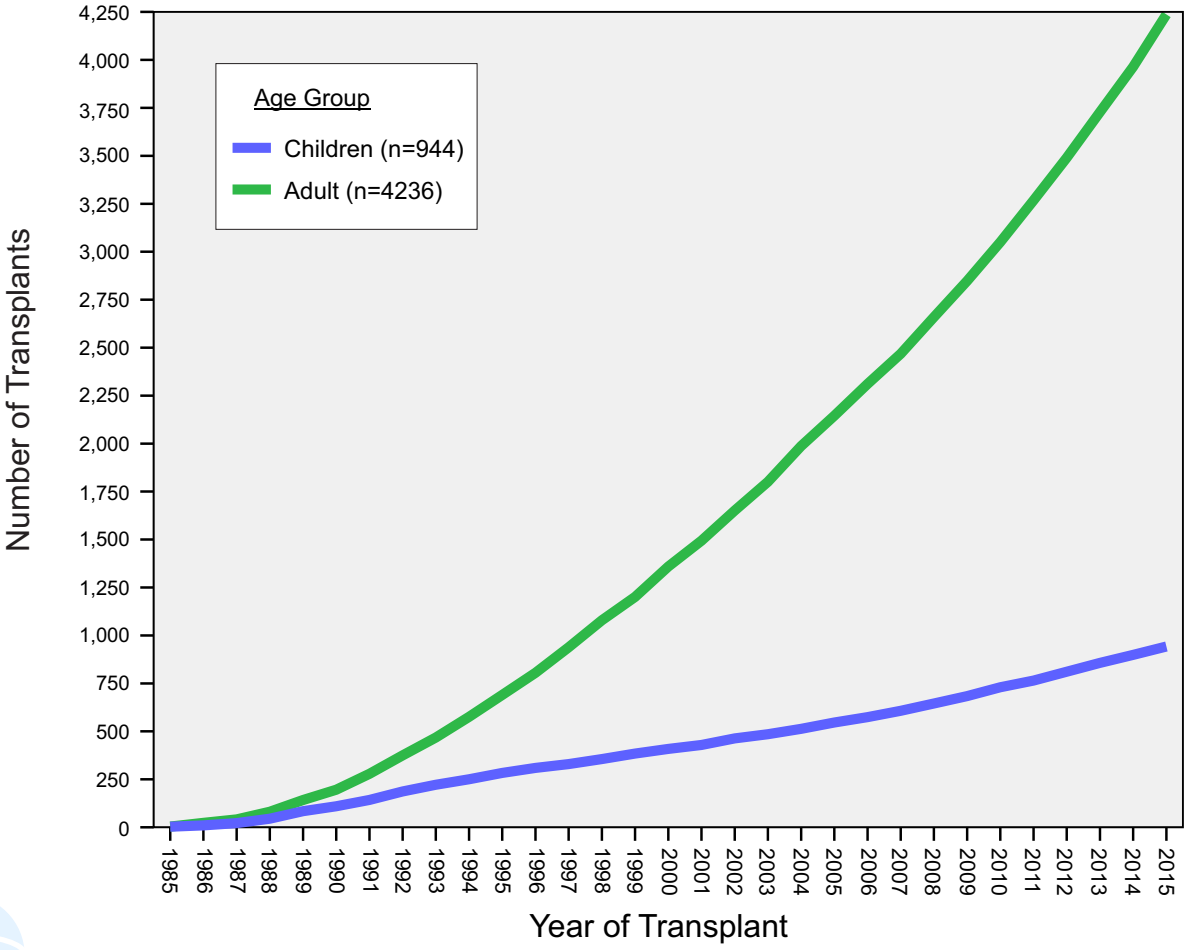
Number of Transplants by Year



Cumulative Number of Transplants



Type of Graft by Year
Split vs Reduced vs Whole

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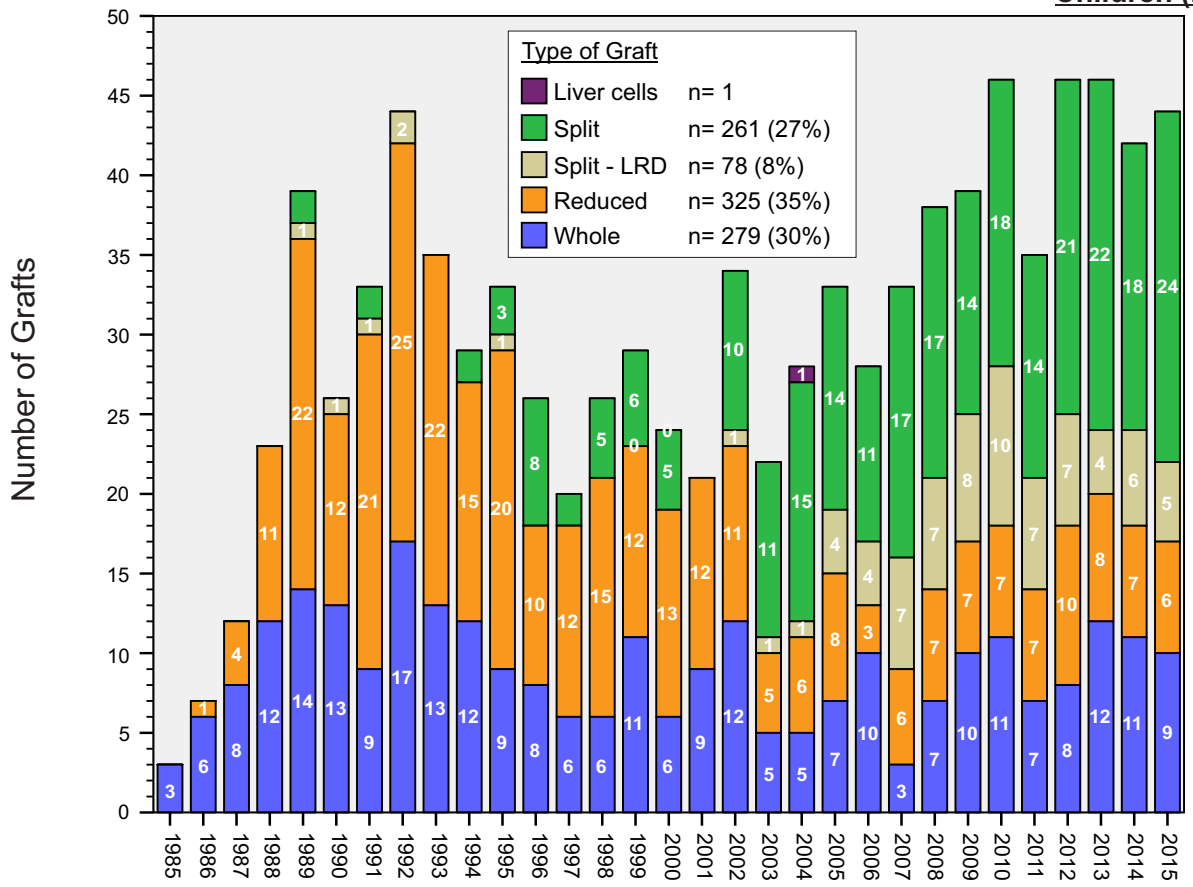
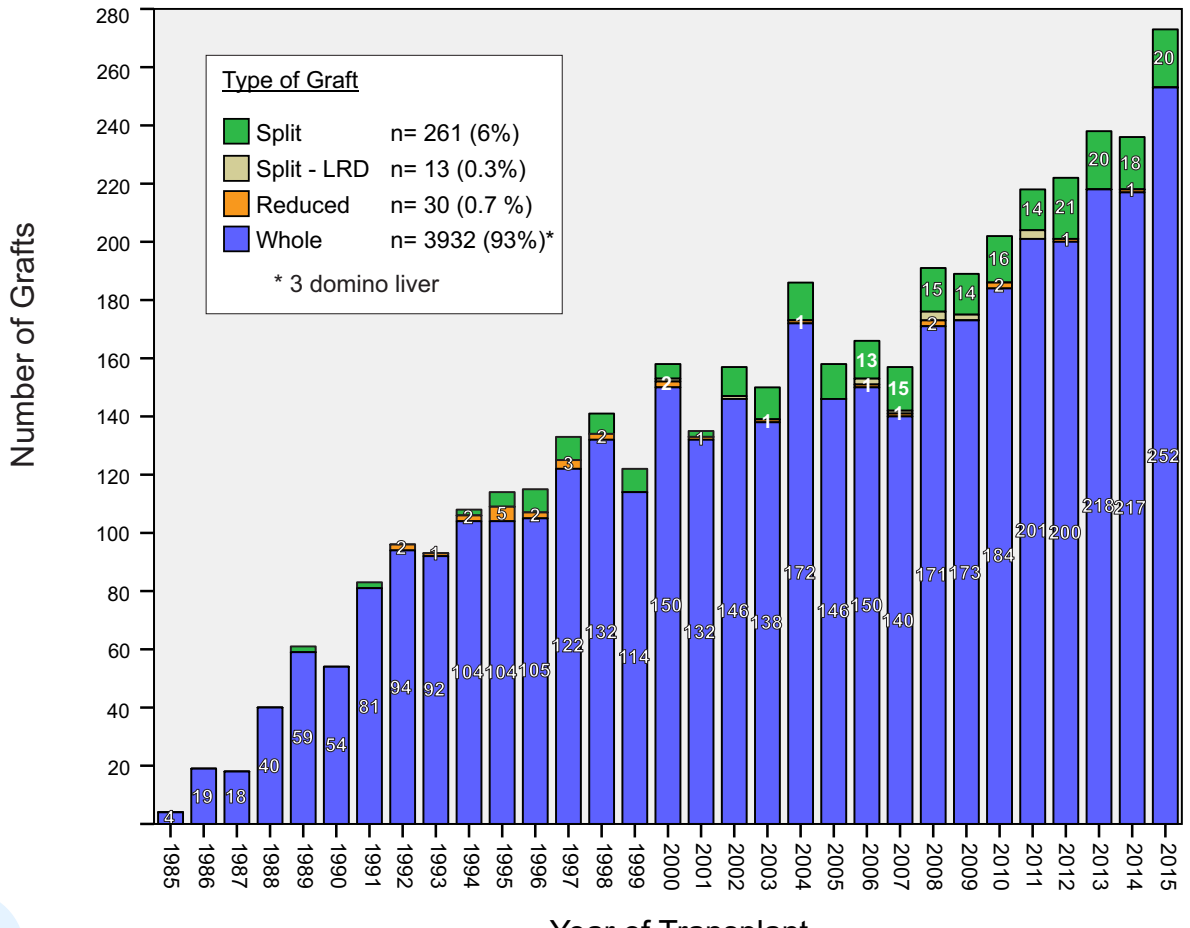
Children (n = 944)



Adults (n = 4236)



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Section 2

Primary Diagnosis

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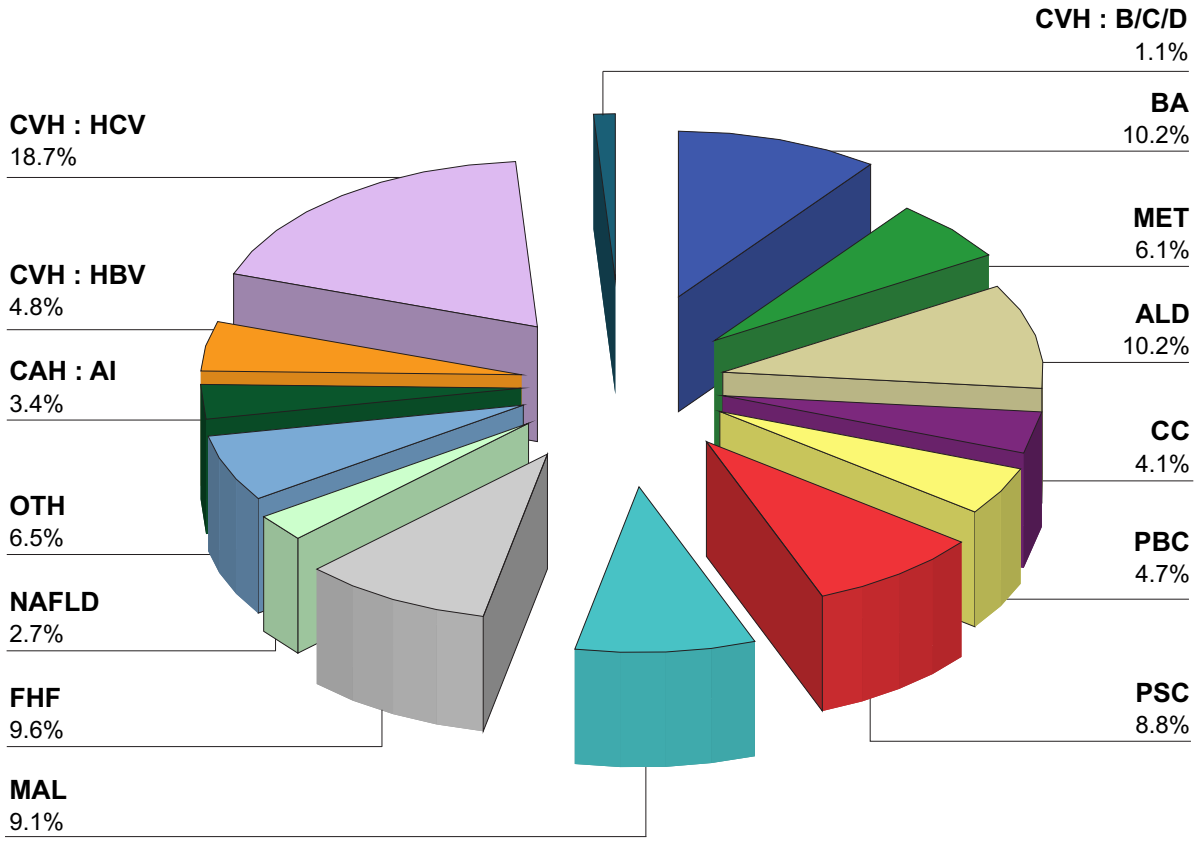
Primary Diseases of All Recipients



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

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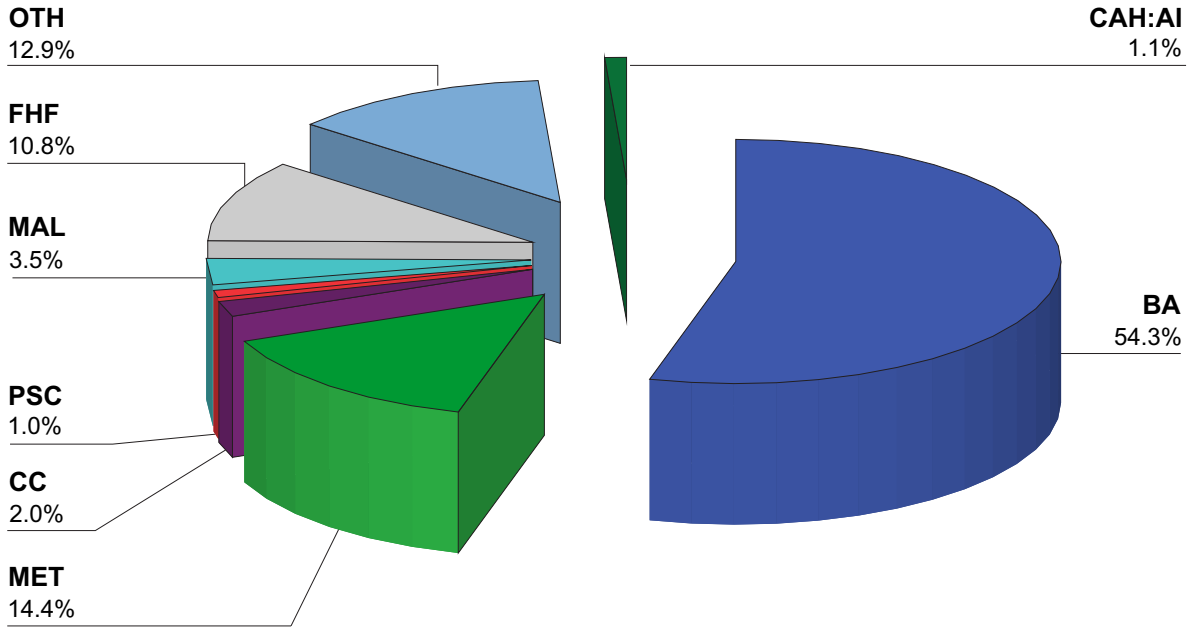
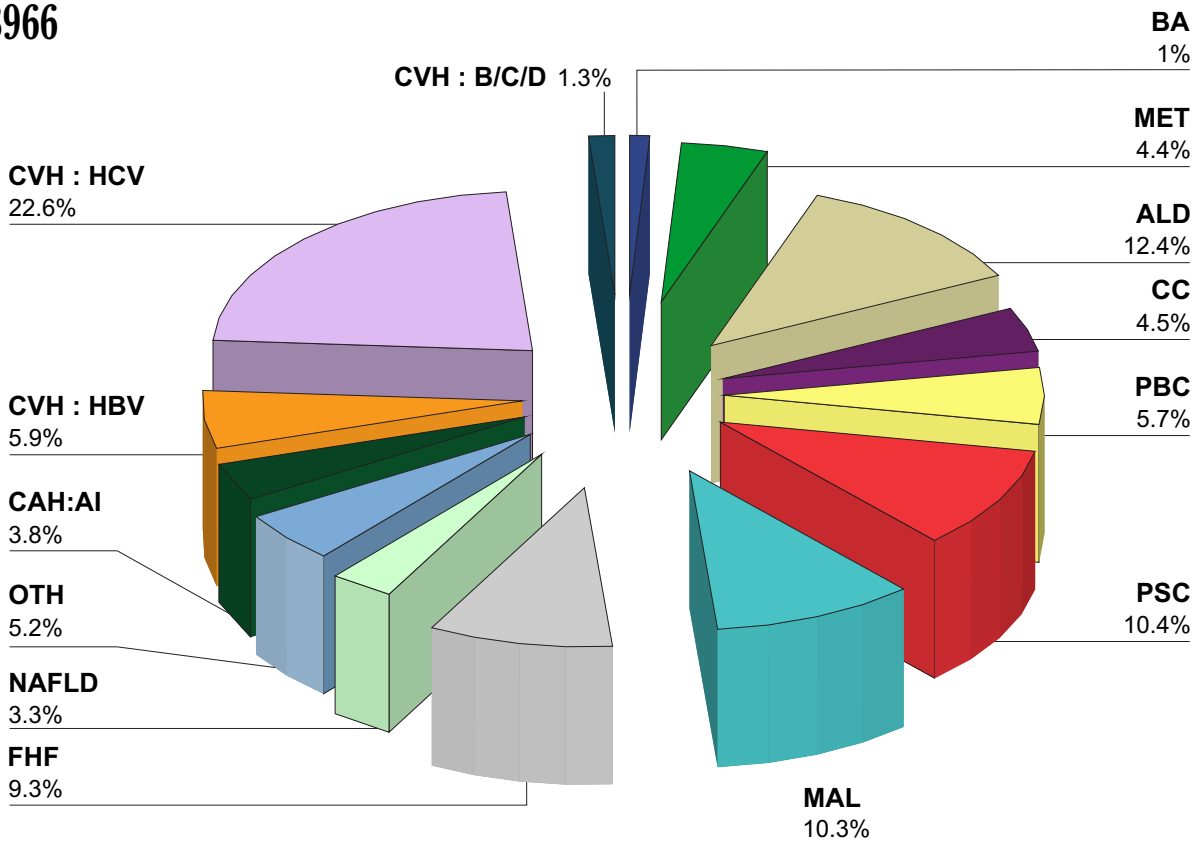
Primary Diseases of Children
n =832



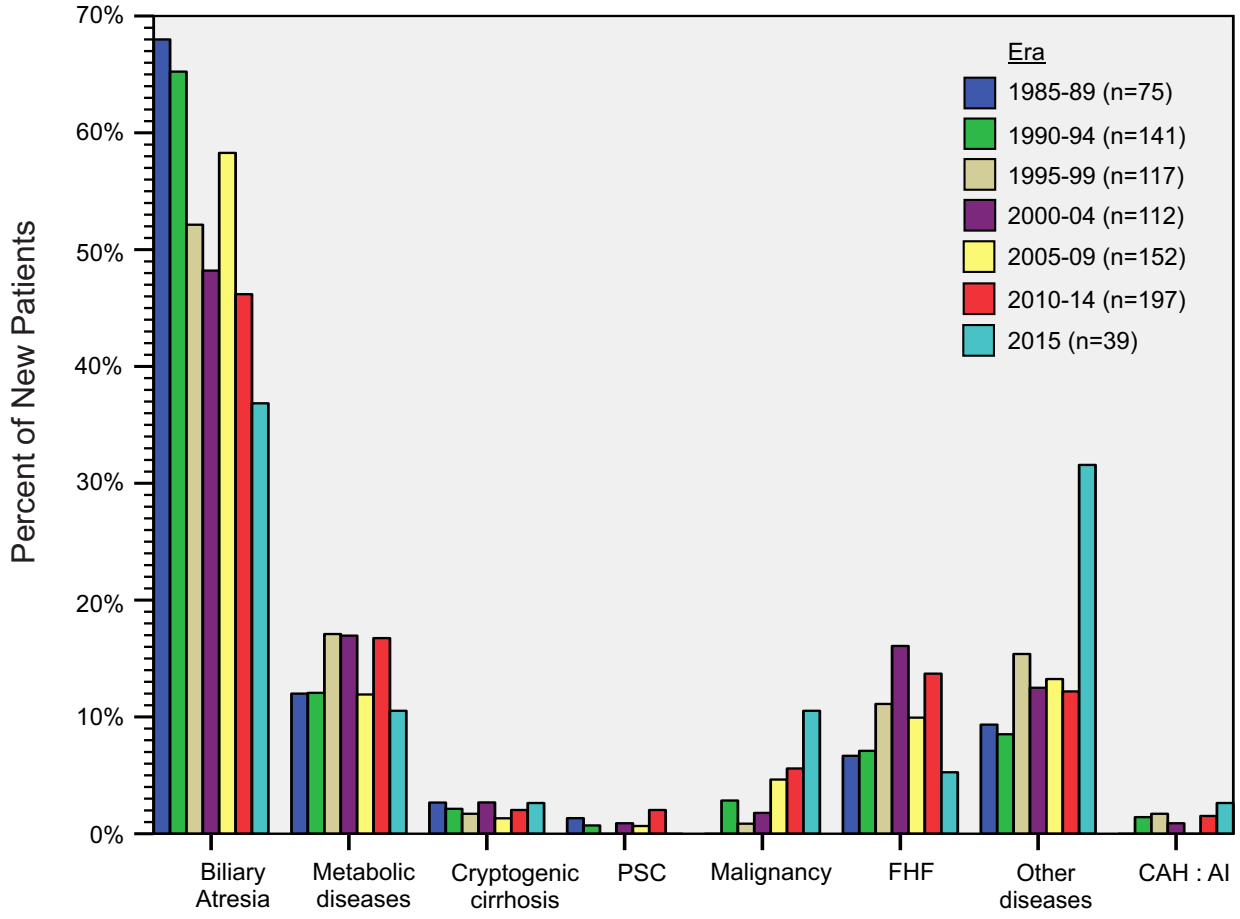
Primary Diseases of Adult Recipients
n = 3966



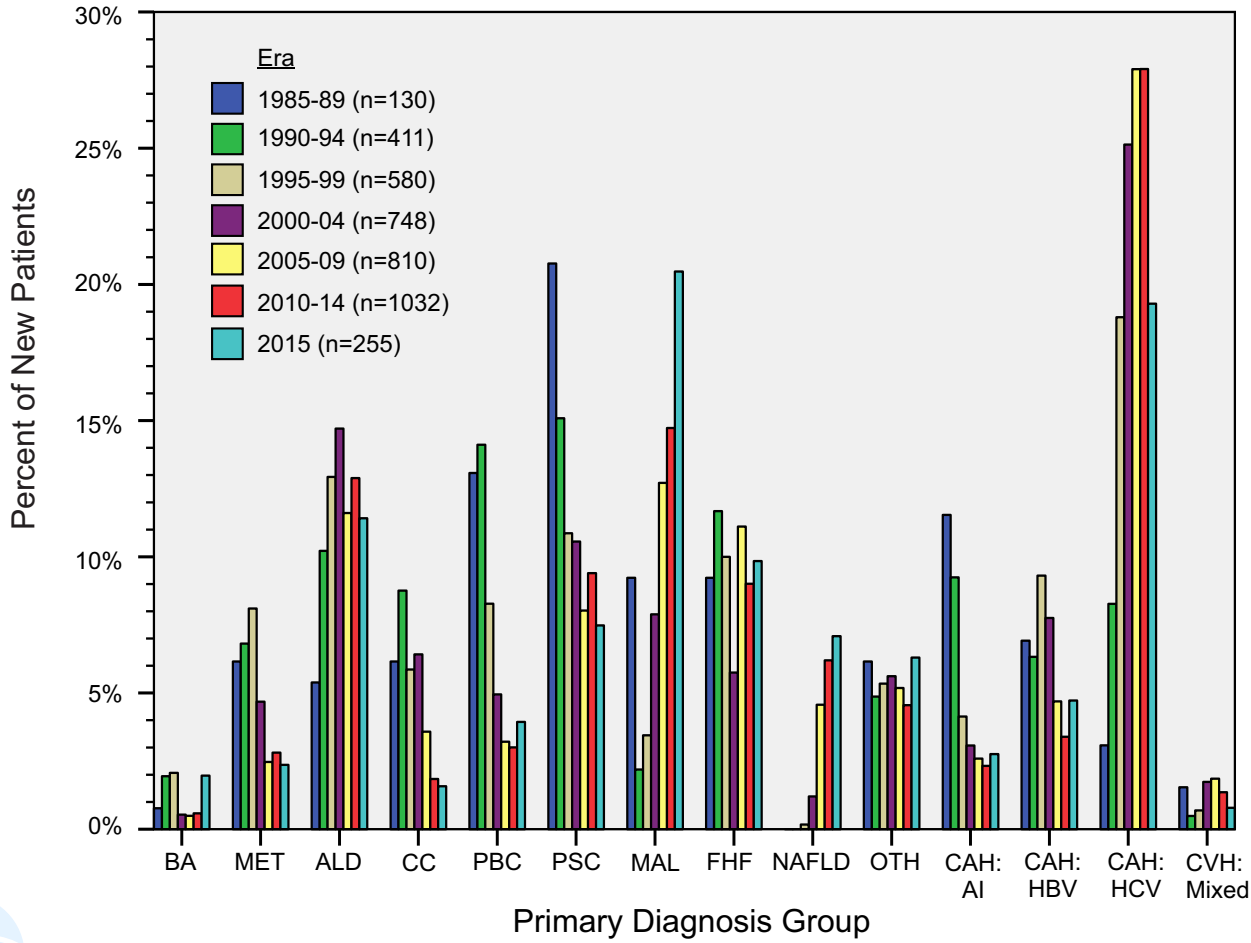
Diagnosis Group

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=832)



Adults (n = 3966)



Adult Primary Diagnosis by Era

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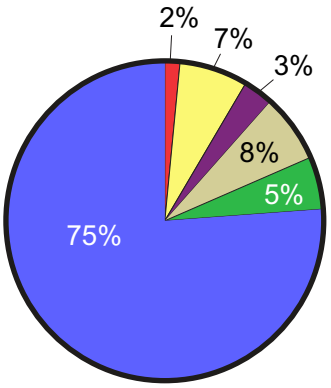
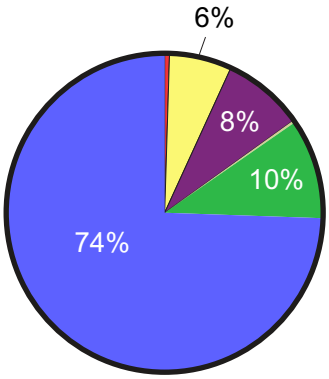
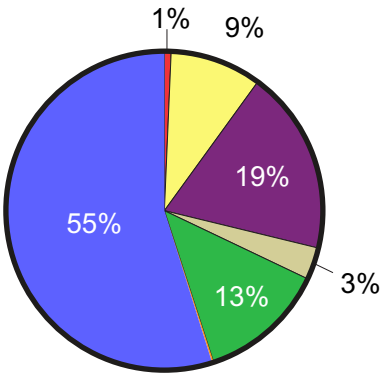
1985 - 89
(n=130)



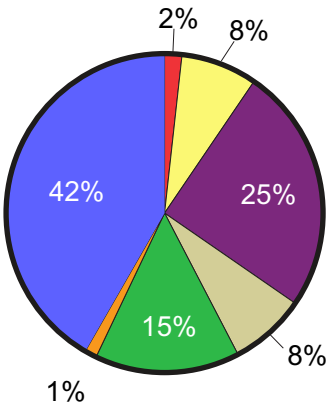
1990 - 94
(n-411)



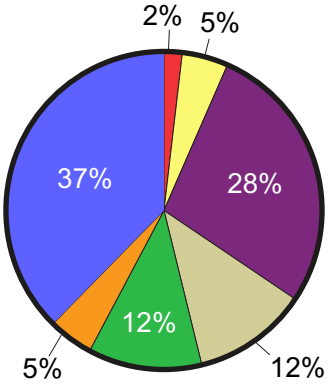
1995 - 99
(n=580)



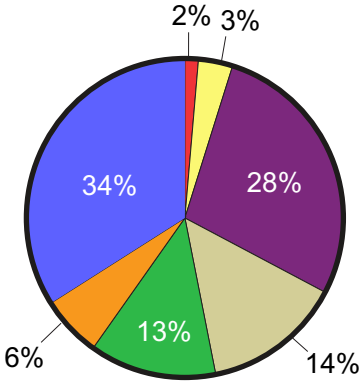
2000 - 04
(n=748)



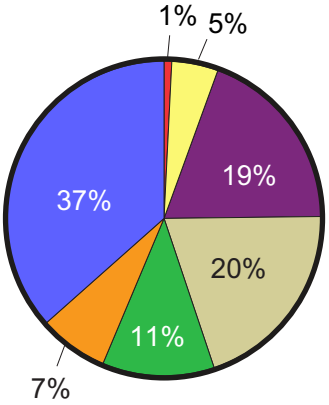
2005 - 09
(n=810)

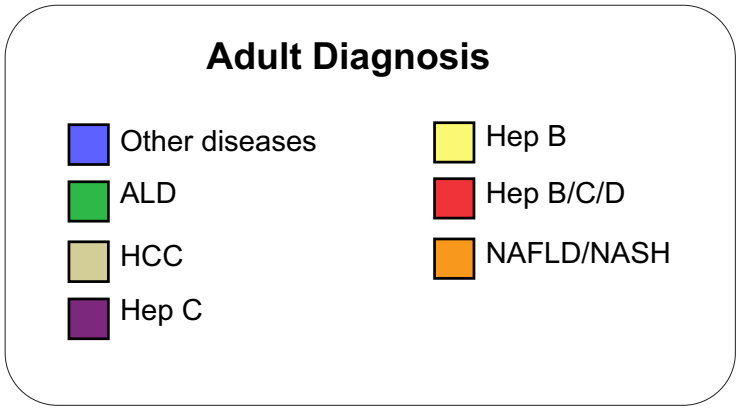


2010 - 14
(n=1032)



2015
(n=255)





Adult Primary Diagnosis by Year

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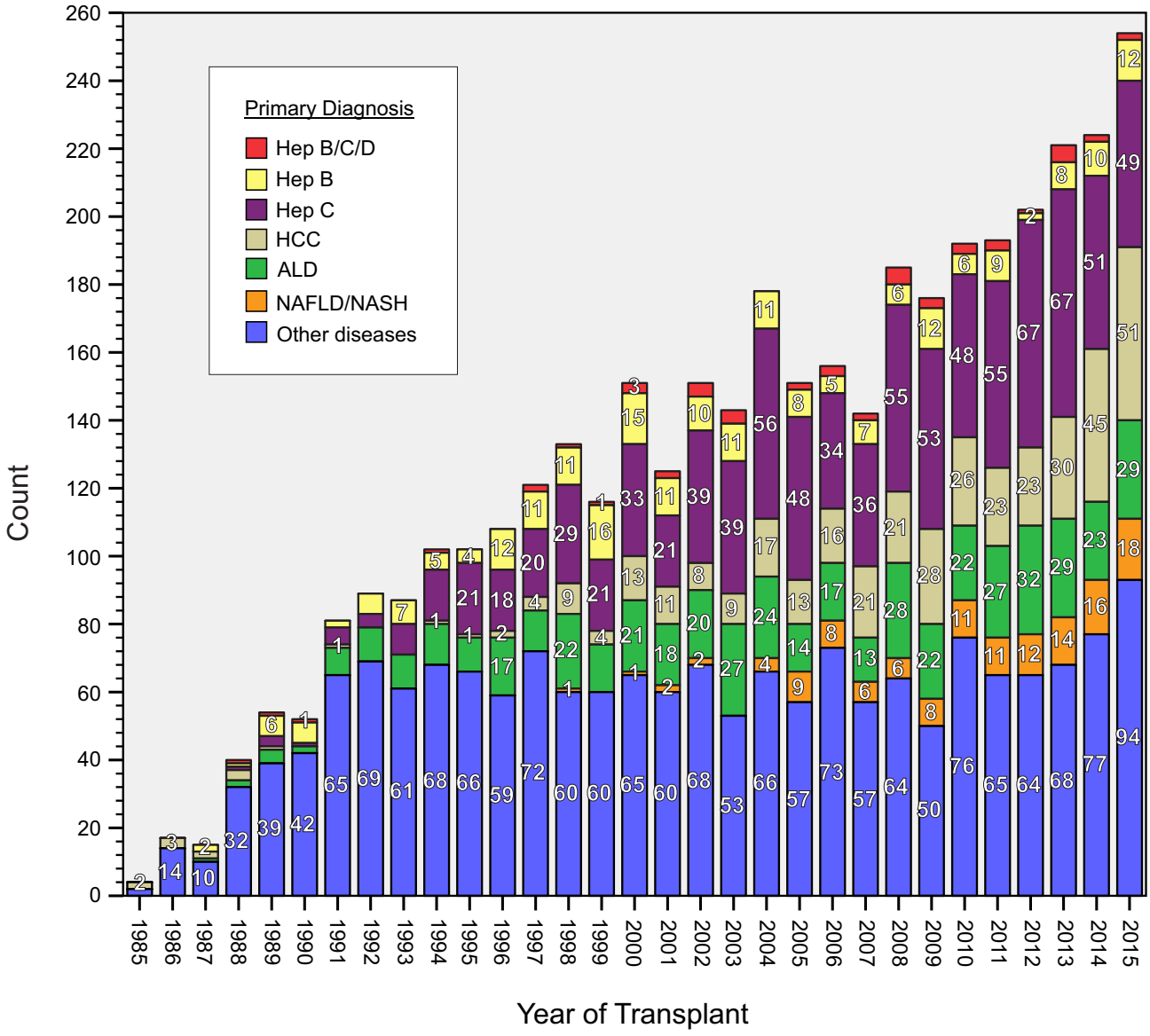

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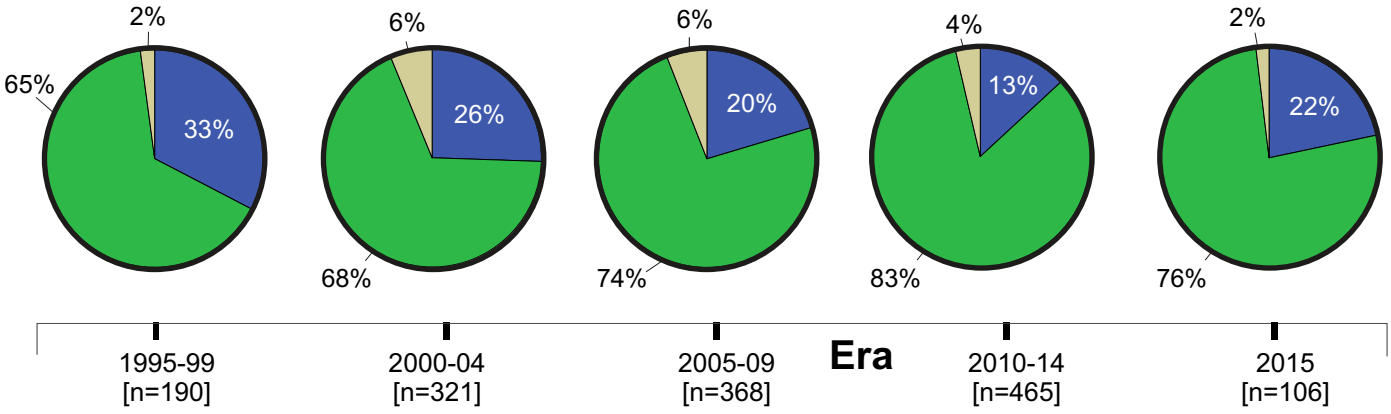
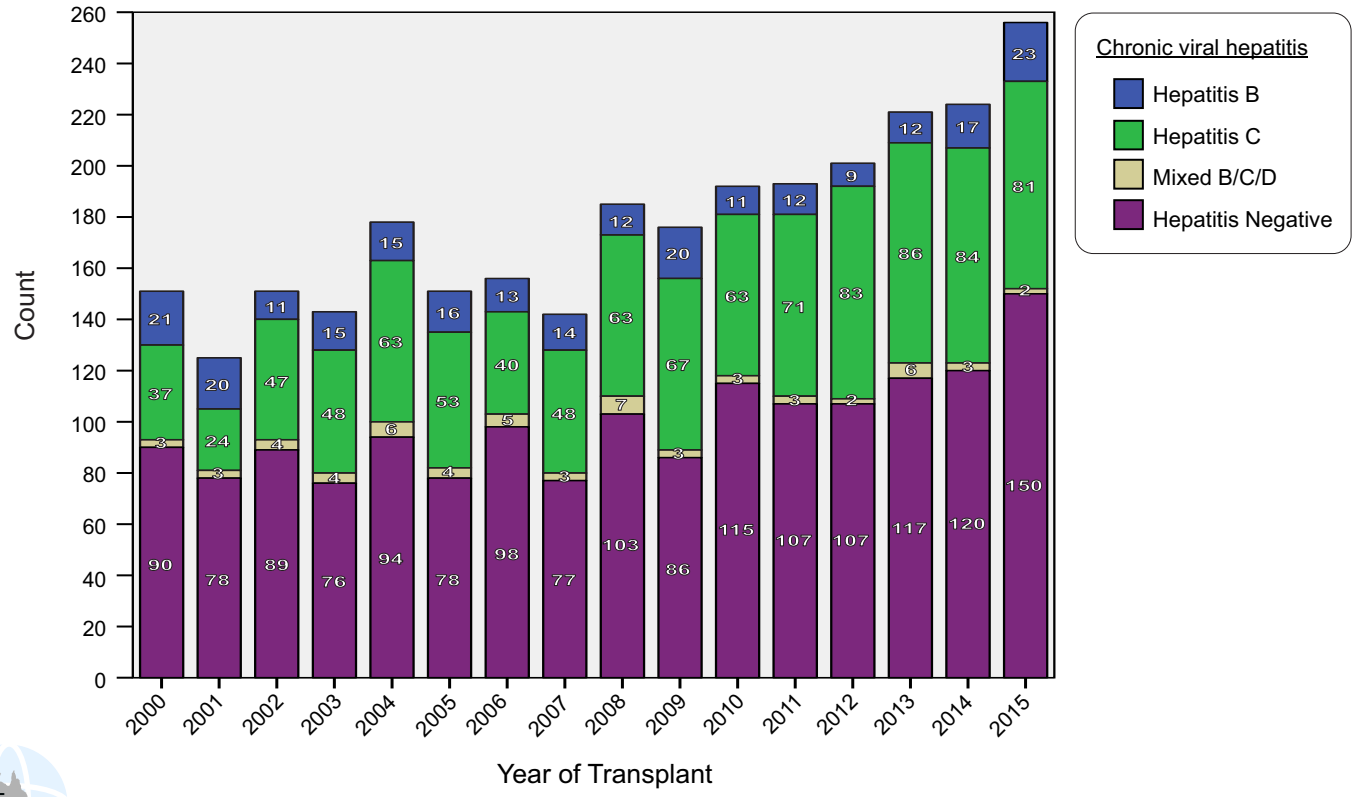
Chronic Viral Hepatitis as Primary or Secondary Diagnosis in Adult Patients

Primary Diagnosis	n =	Secondary / Tertiary diagnosis: Hepatitis C	Hepatitis B	Hepatitis B,C	HCC	NAFLD	ALD
Hepatitis C	898		7		271	9	238
Hepatitis B	232	3			93	2	6
Hepatitis BD/BC/BCD	52				10		7
HCC + cirrhosis	388	198	100	7		16	84
ALD	490	25	3		63	11	
NAFLD	129		2		30		9
Other	1777	16	9		61	4	23
TOTAL	3966						

Type of Chronic Viral Hepatitis in Adult Patients



Hepatitis diagnosis



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Patient Survival

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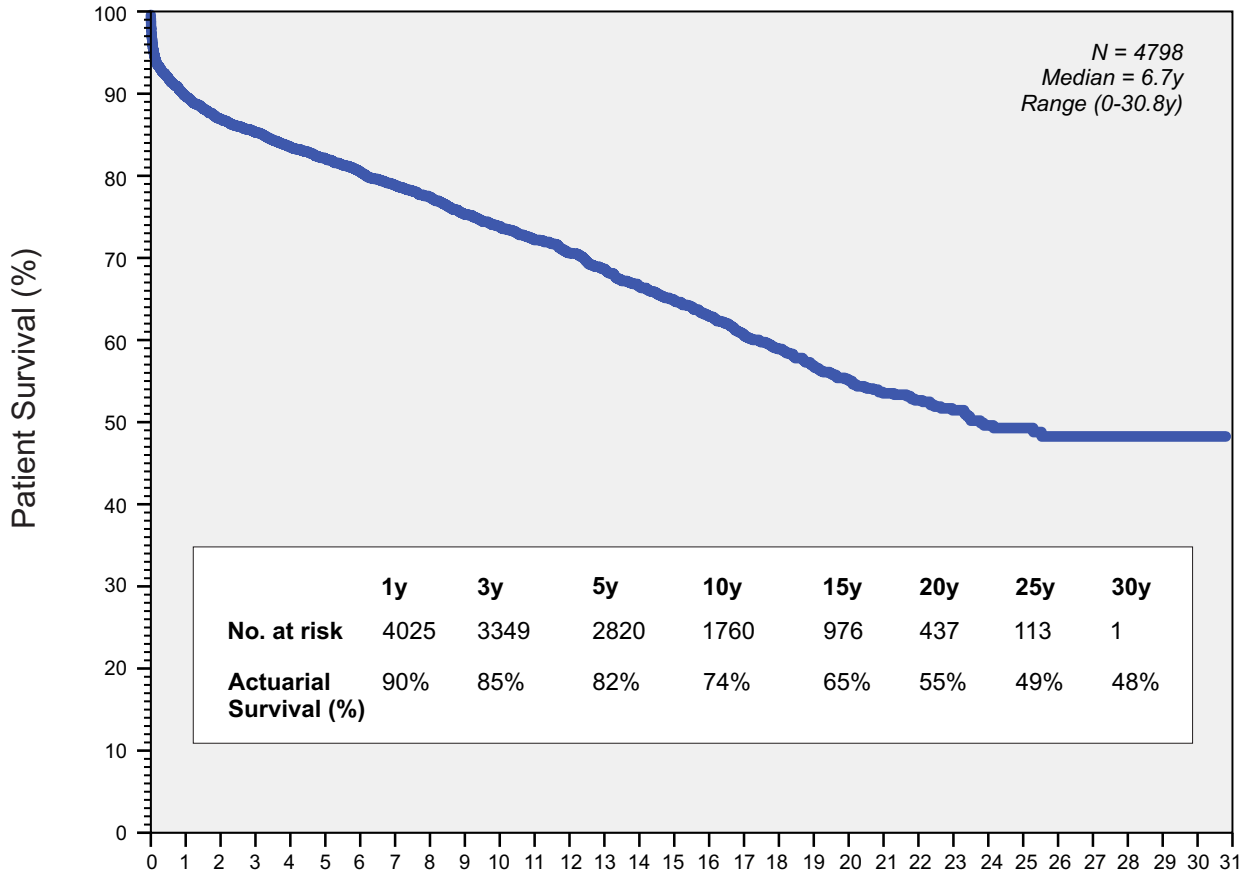
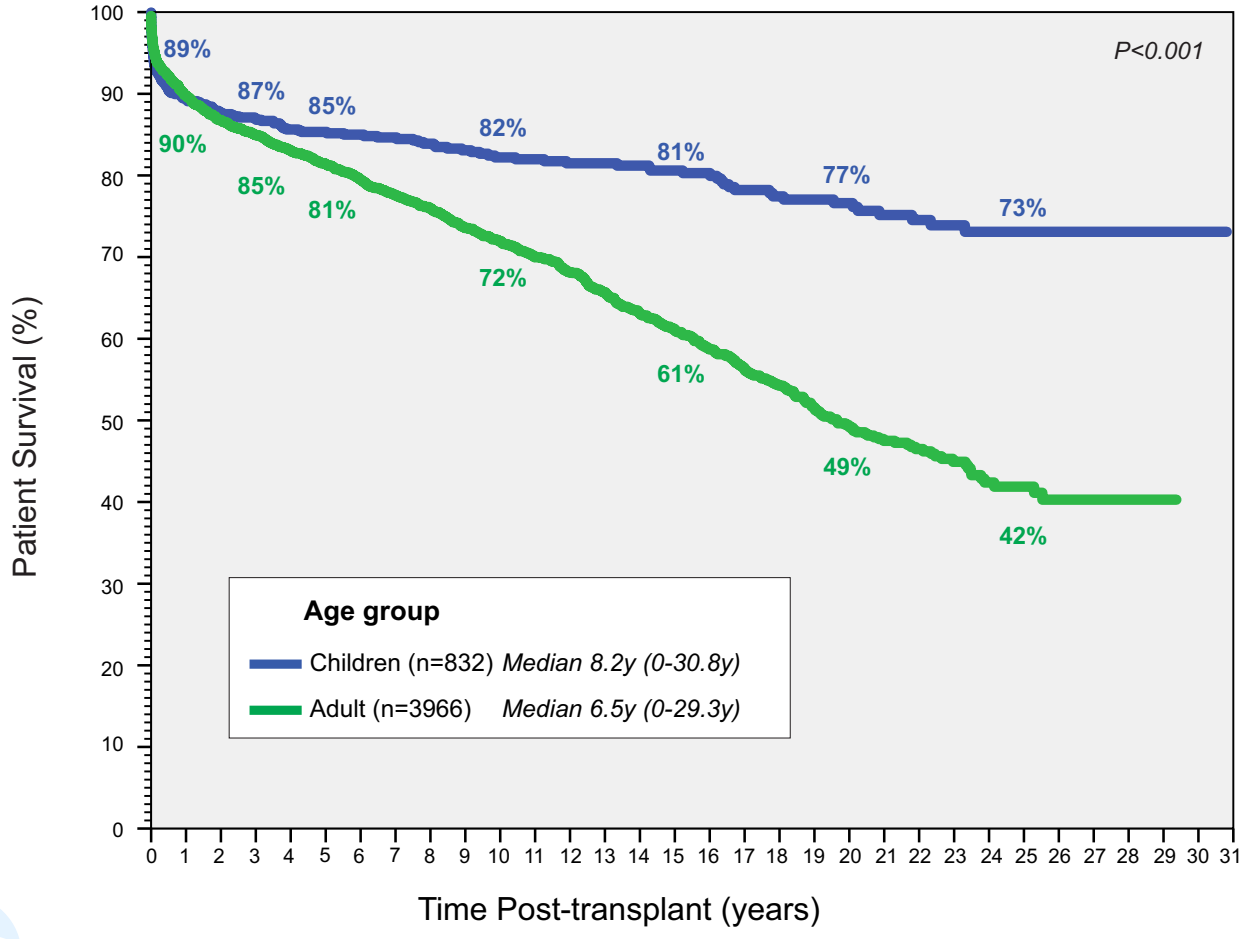
Patient Survival Post Transplant



	1y	3y	5y	10y	15y	20y	25y	30y
No. at risk	4025	3349	2820	1760	976	437	113	1
Actuarial Survival (%)	90%	85%	82%	74%	65%	55%	49%	48%



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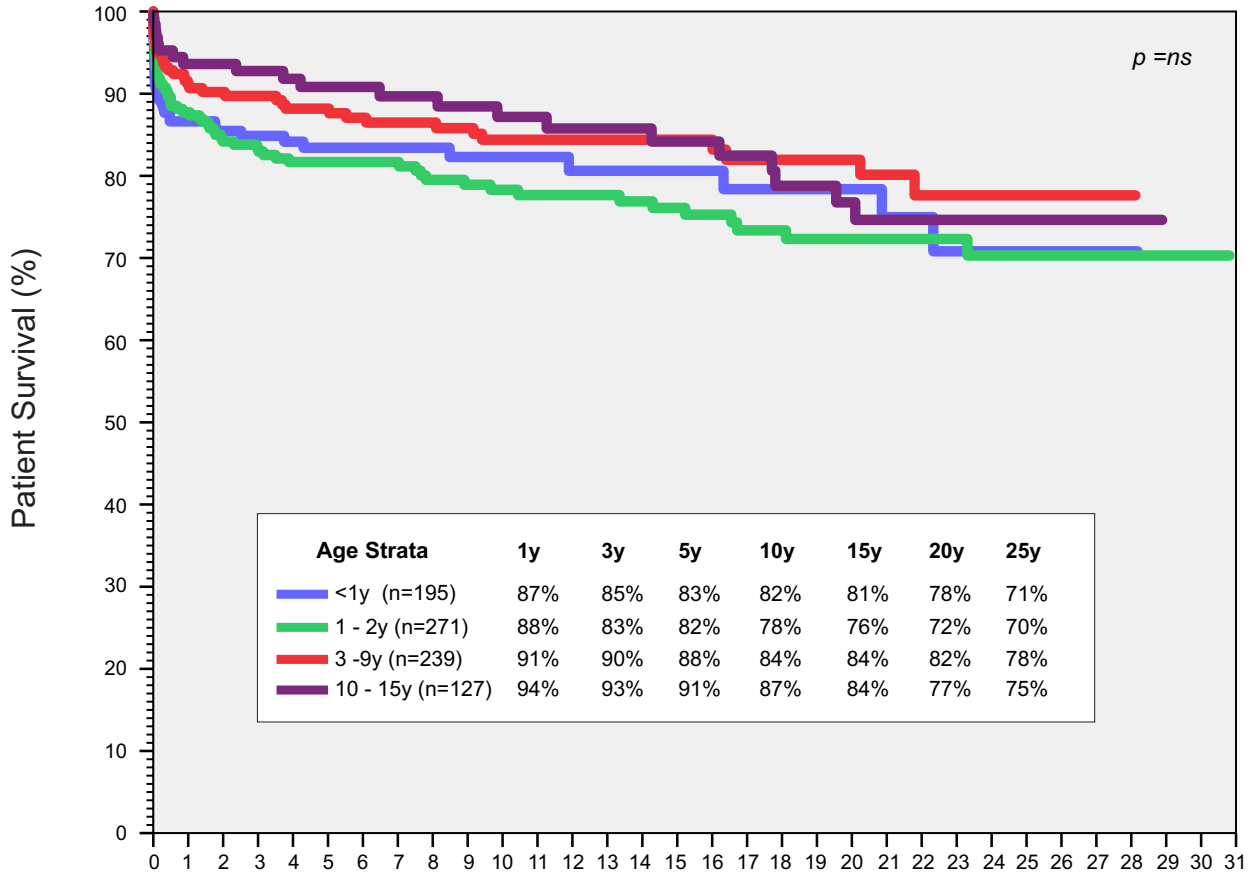
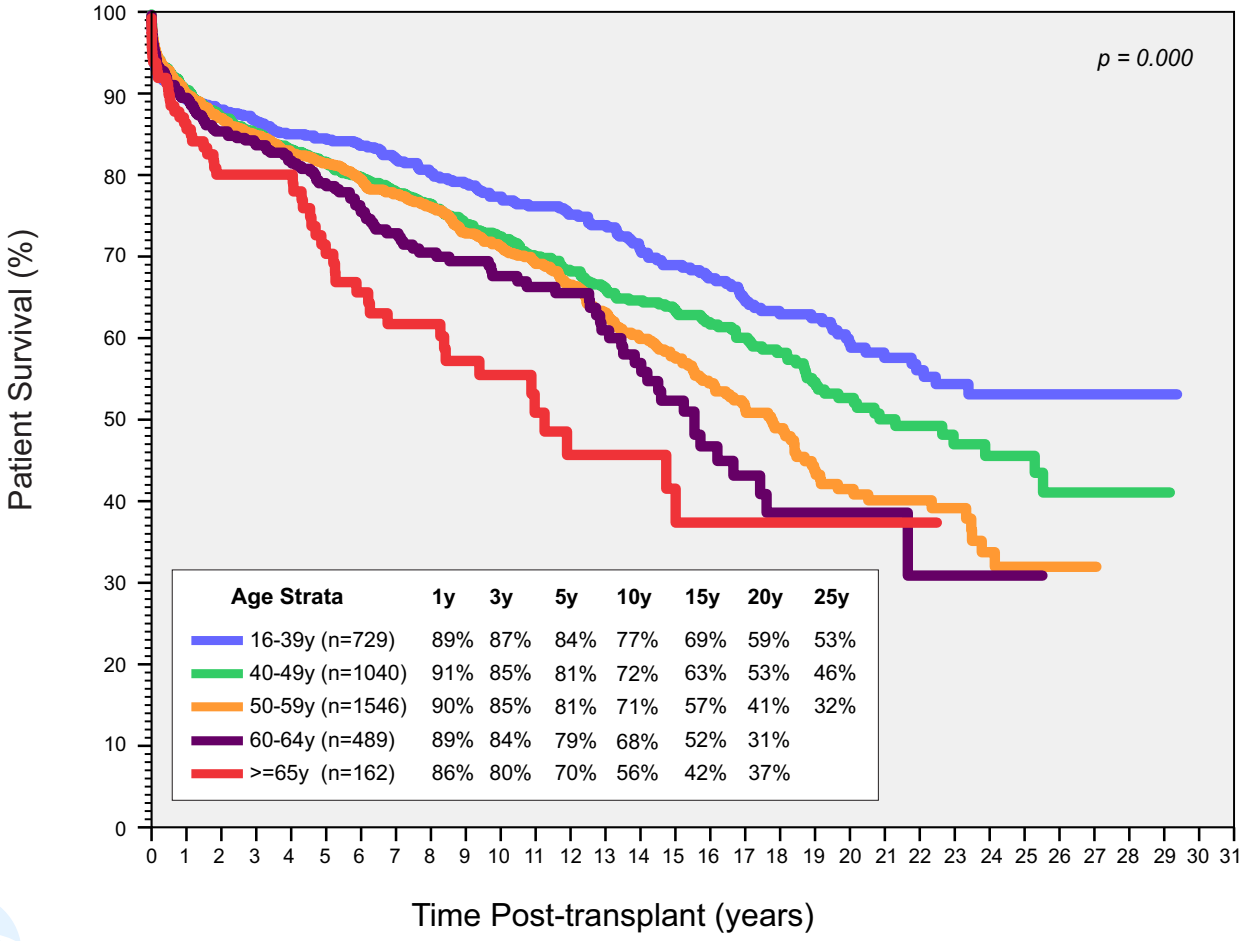
Children n= 832



Adults n = 3966



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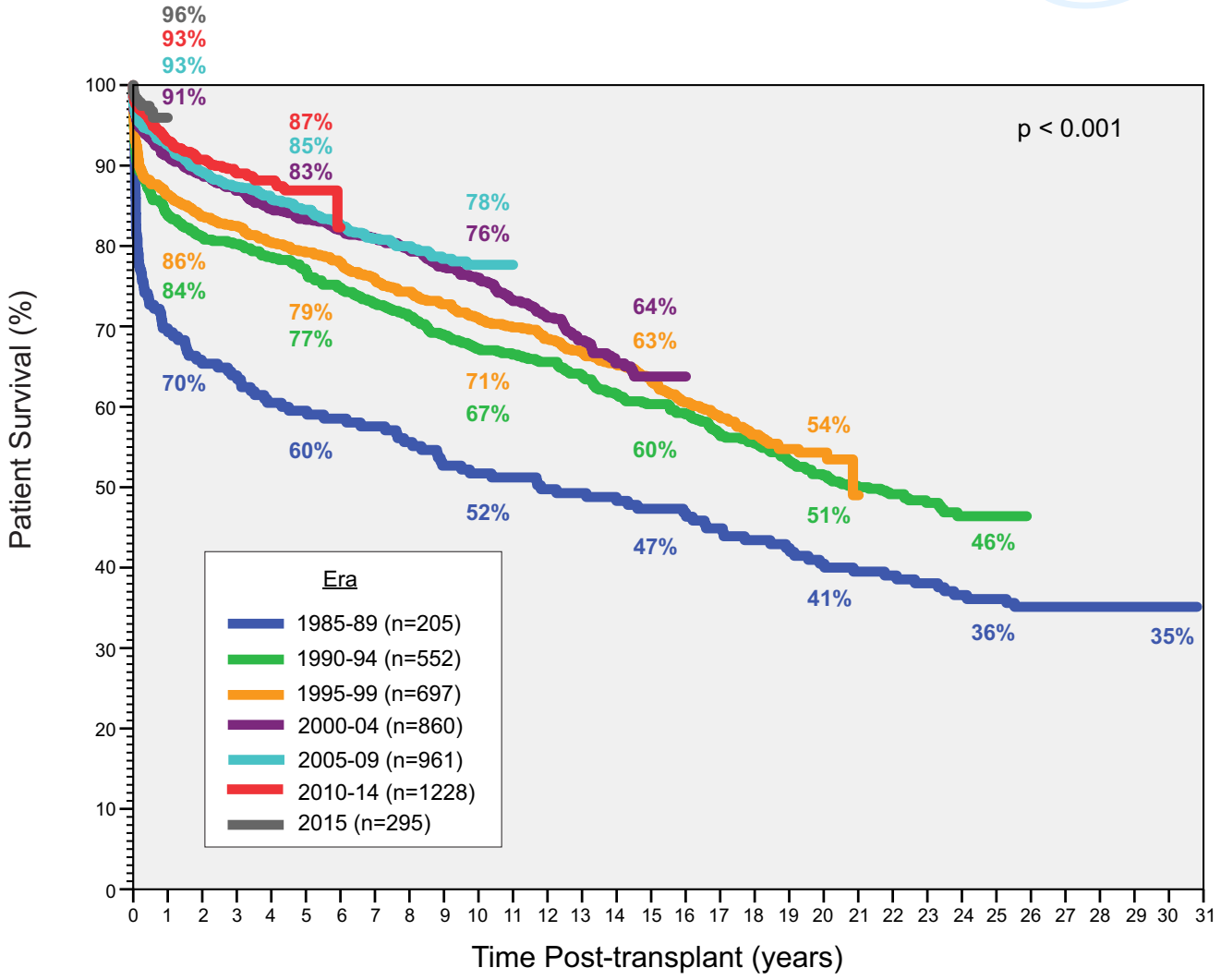
All Patient Survival by Year of Transplant



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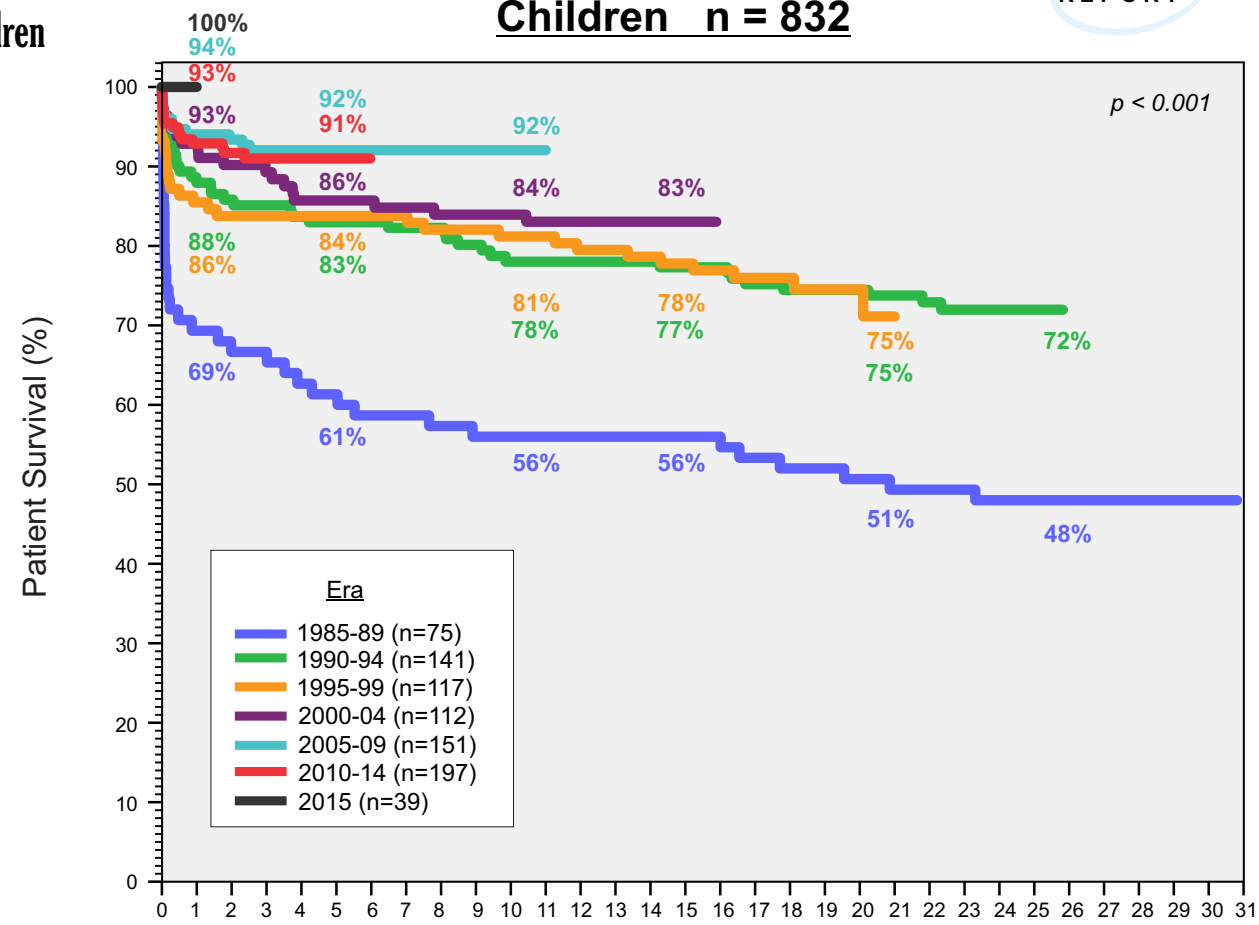
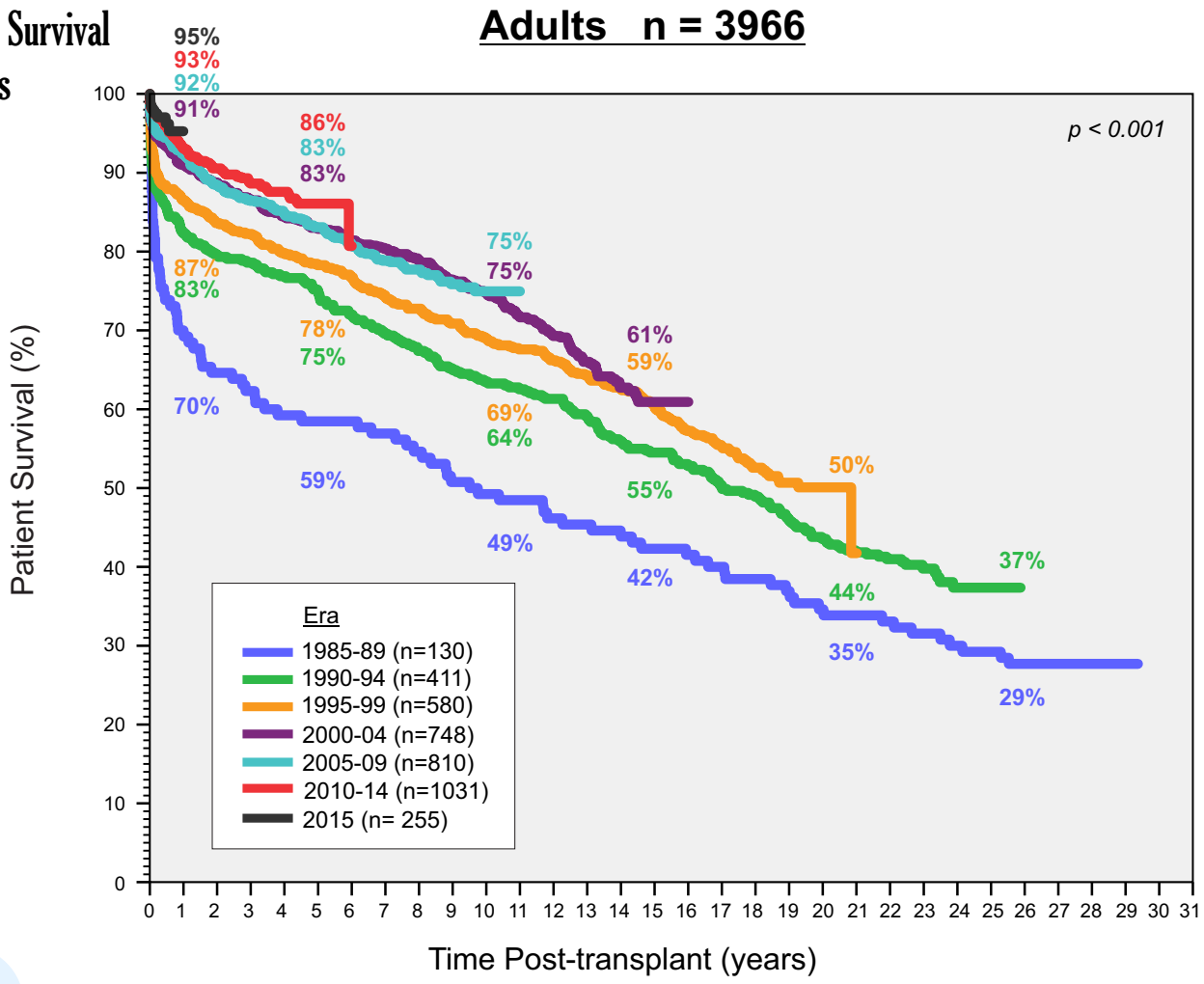
Patient Survival - Children



Patient Survival - Adults



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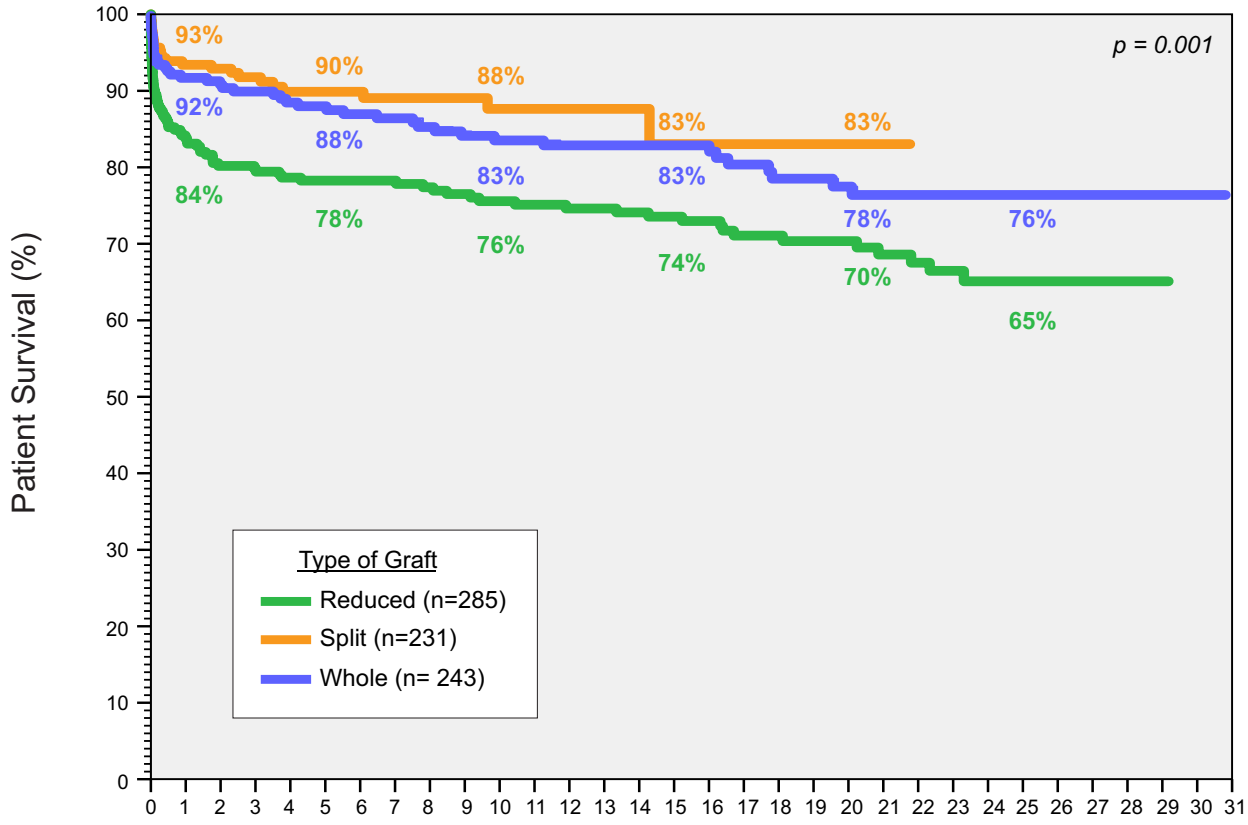
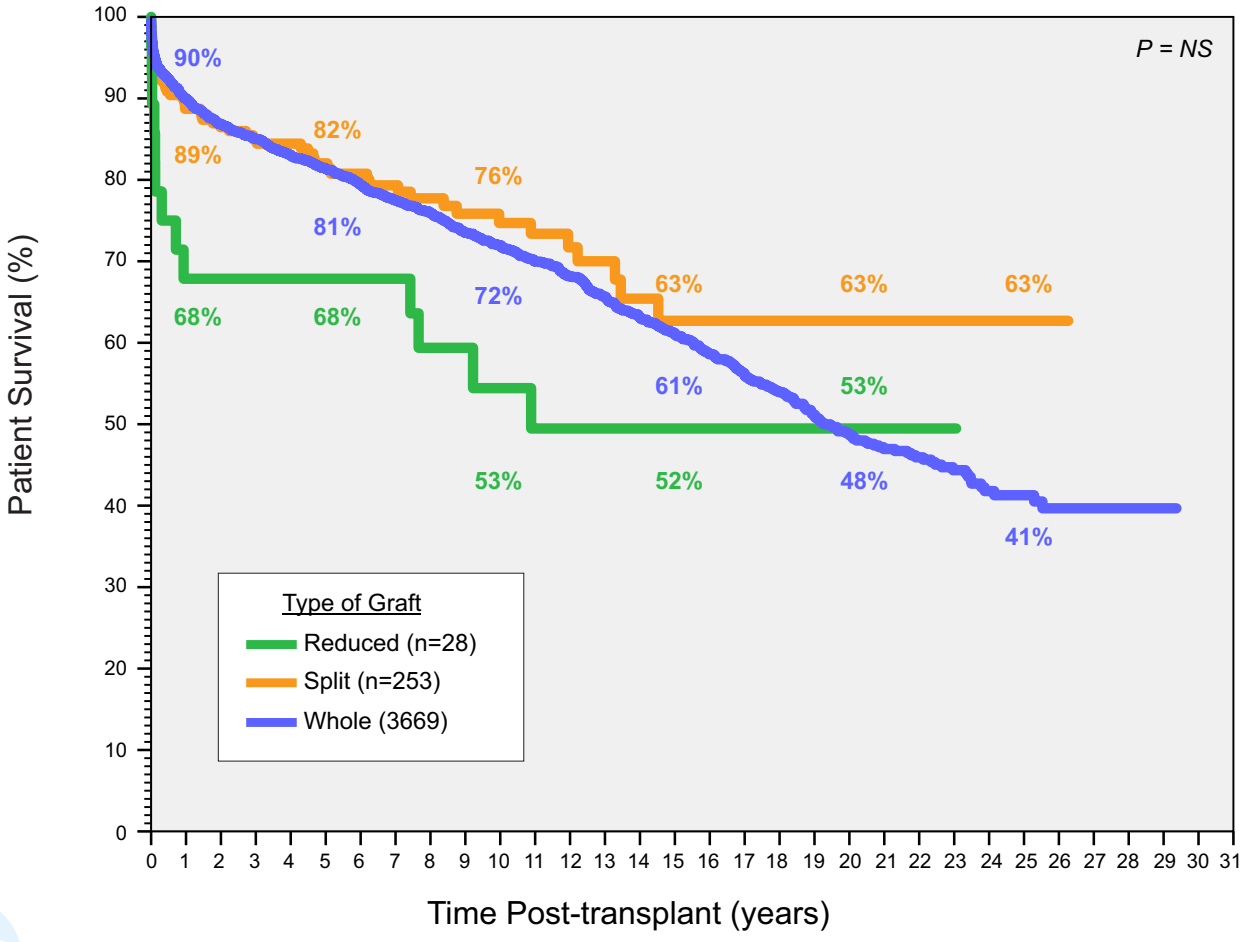
Patient Survival by Type of Primary Graft [Deceased donors]

Children n = 759



Adults n = 3950



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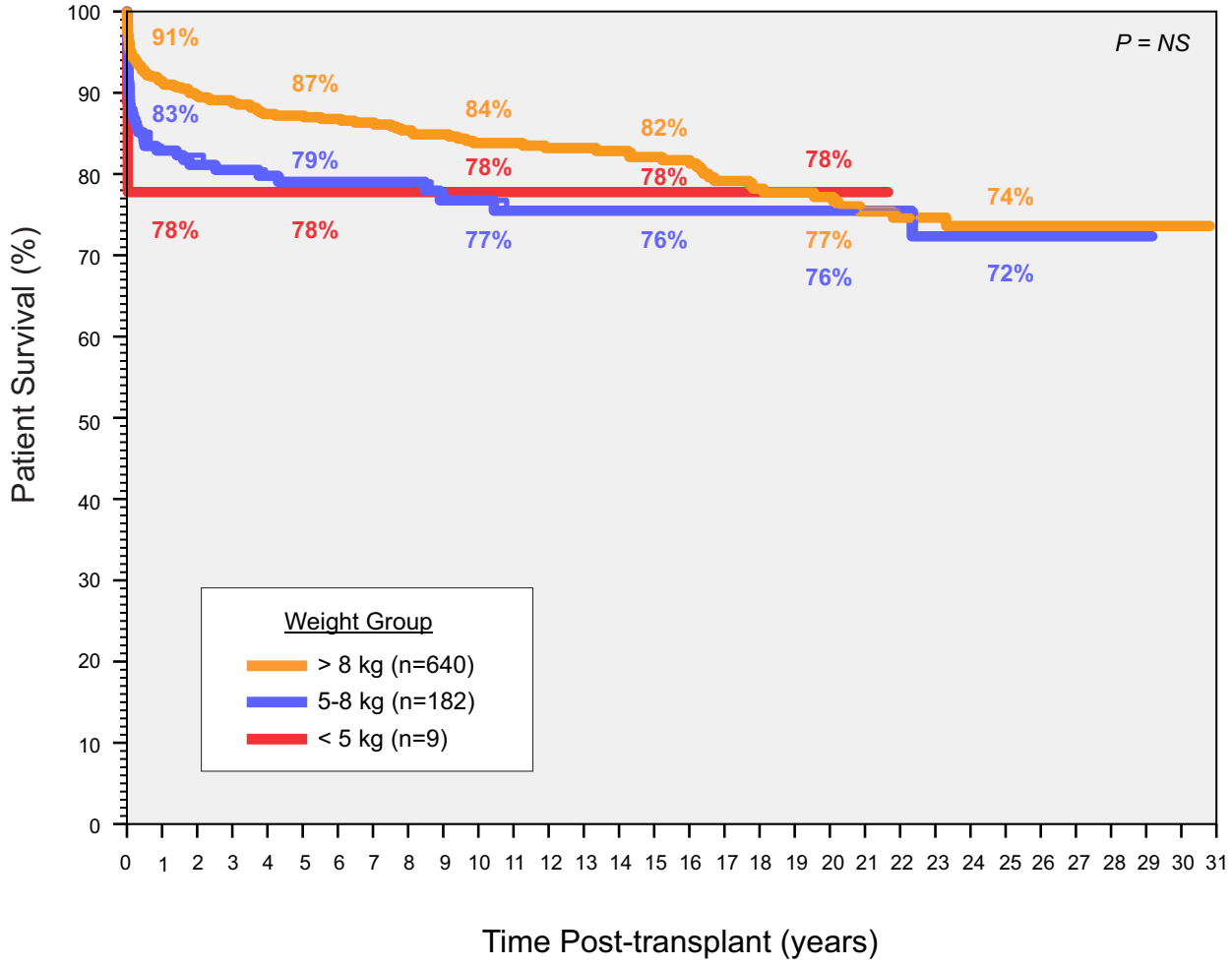
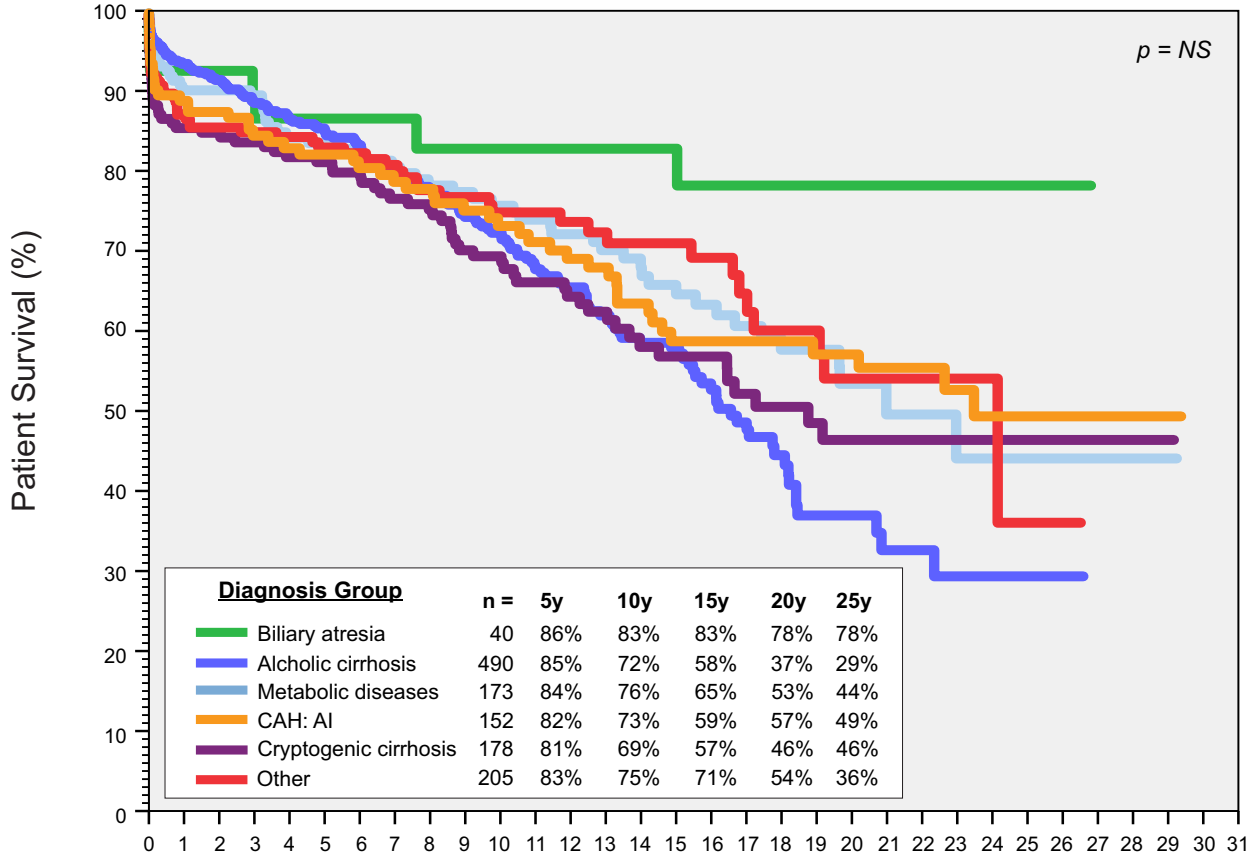
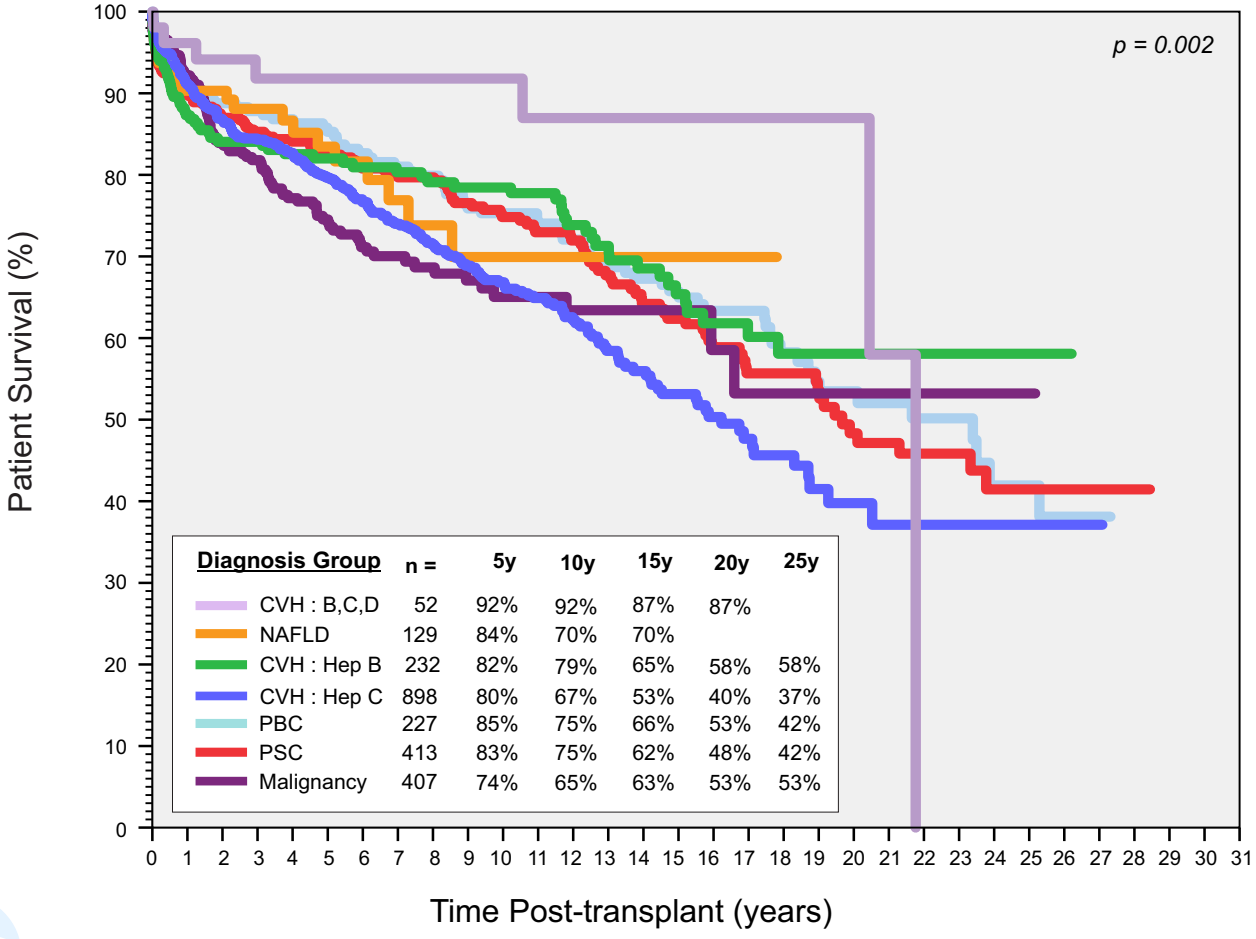
Patient Survival by Weight - Children



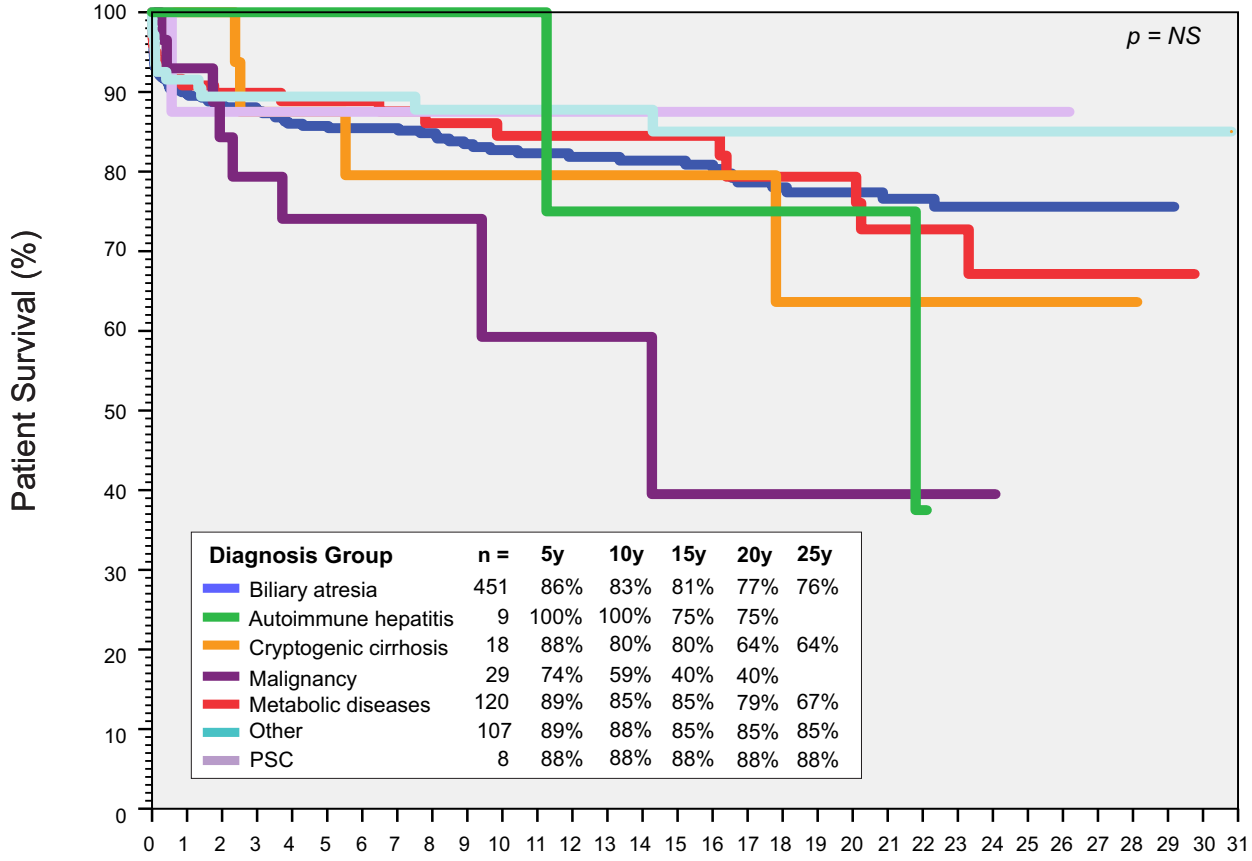
(1) Adults [excluding FHF] n = 1238



(2) Adults [excluding FHF] n = 2358

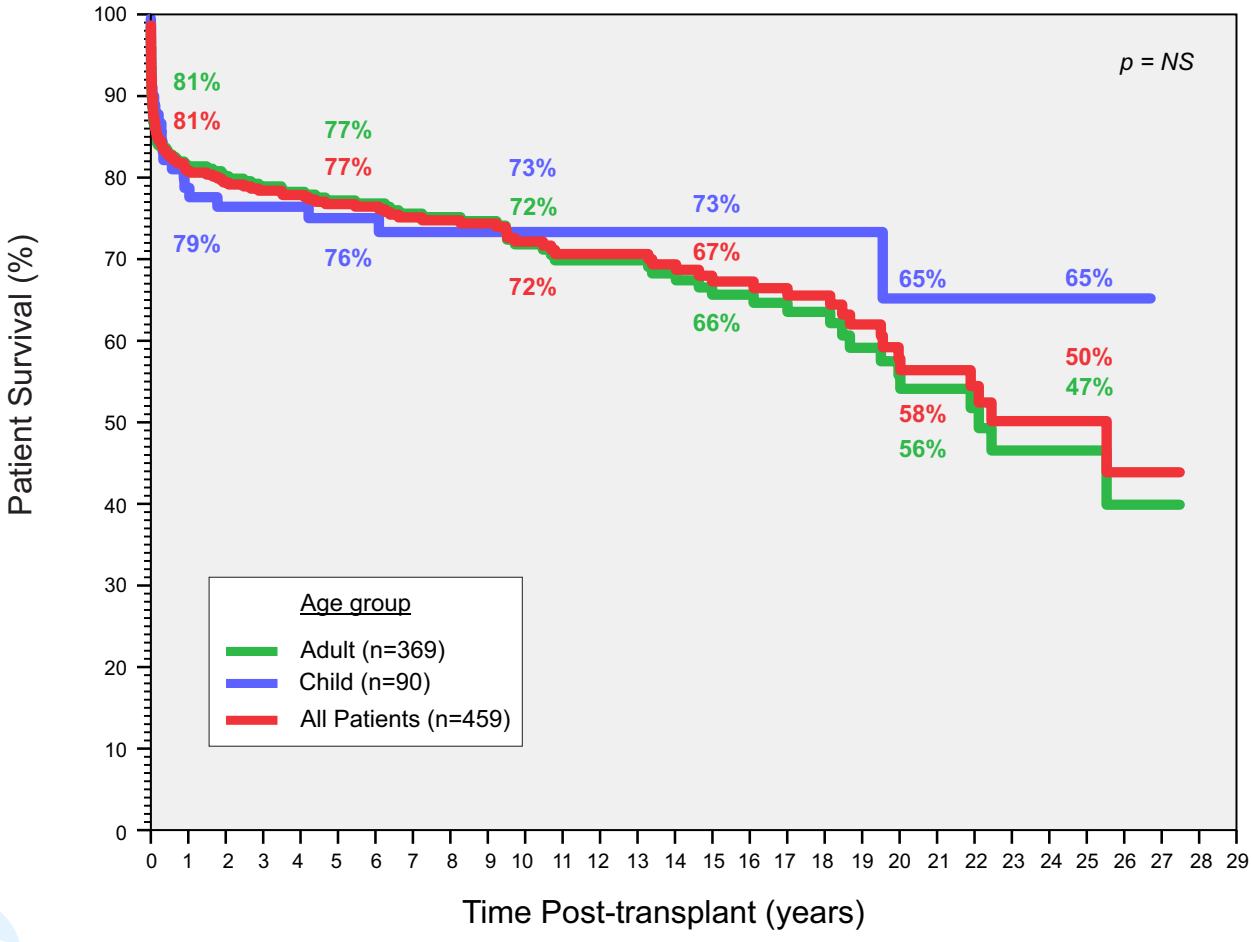


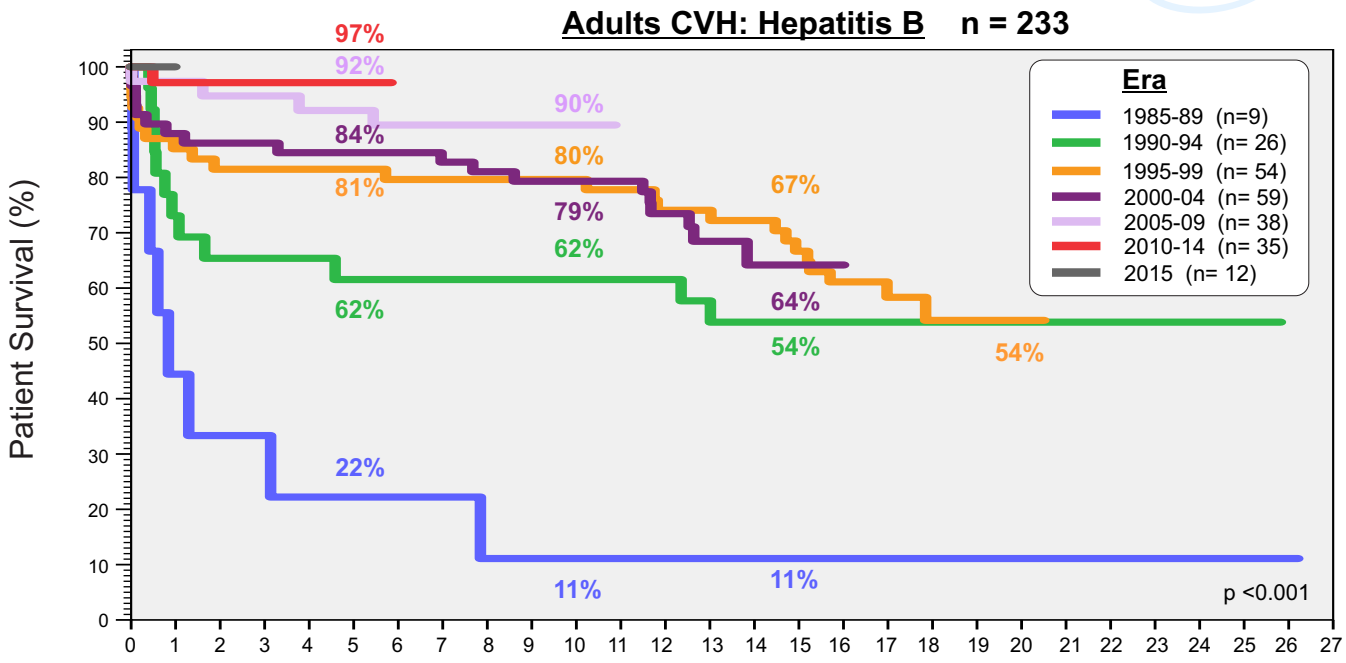
(3) Paediatric recipients [excluding FHF] n = 742

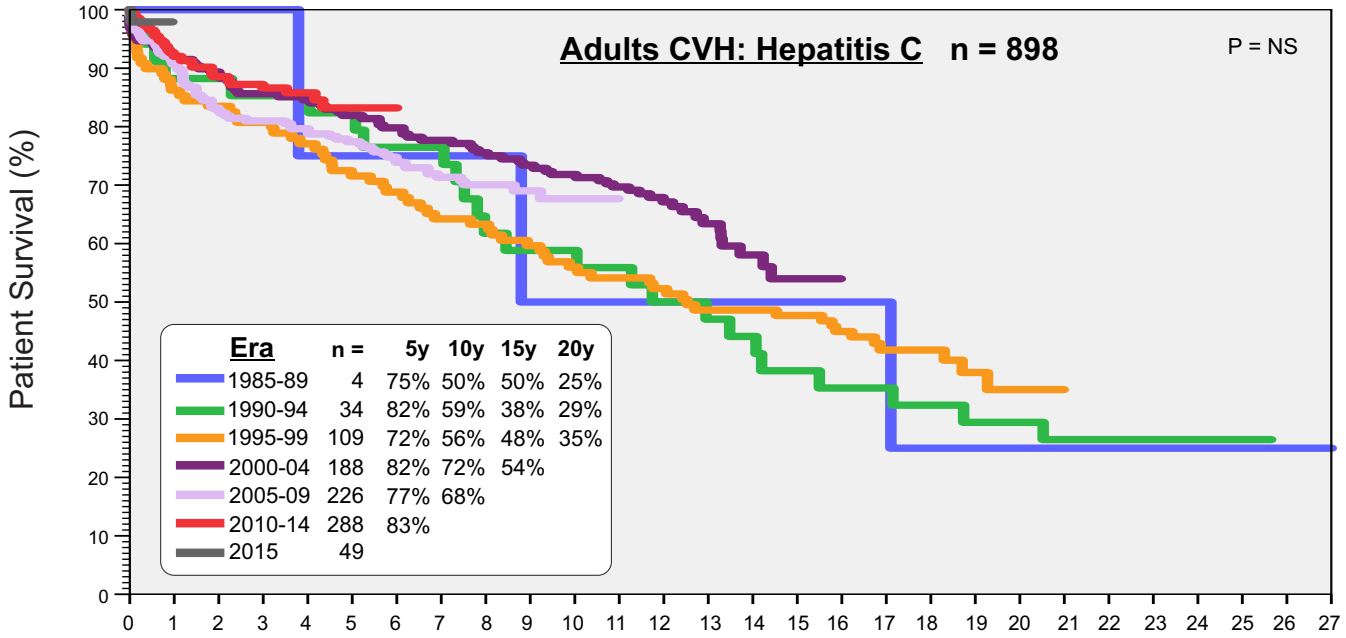


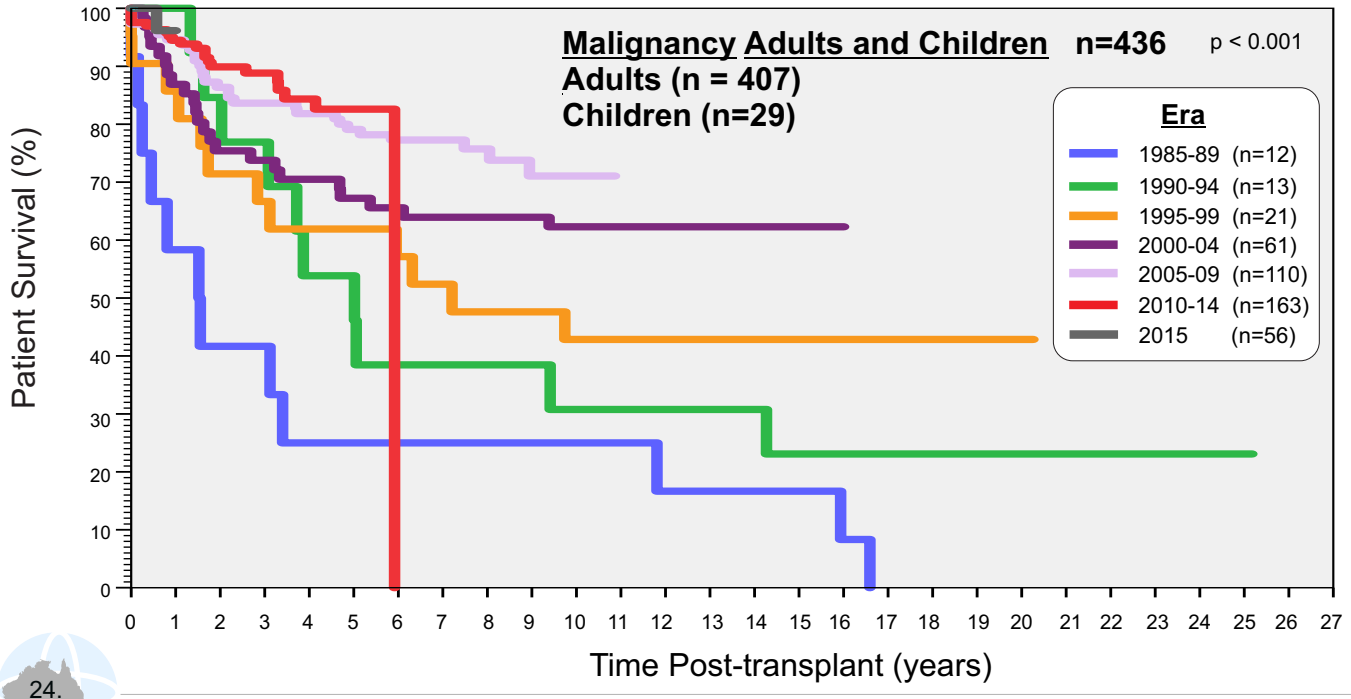
Diagnosis Group	n =	5y	10y	15y	20y	25y
Biliary atresia	451	86%	83%	81%	77%	76%
Autoimmune hepatitis	9	100%	100%	75%	75%	
Cryptogenic cirrhosis	18	88%	80%	80%	64%	64%
Malignancy	29	74%	59%	40%	40%	
Metabolic diseases	120	89%	85%	85%	79%	67%
Other	107	89%	88%	85%	85%	85%
PSC	8	88%	88%	88%	88%	88%

(4) Fulminant hepatic failure n = 459









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Section 4

Graft Outcome

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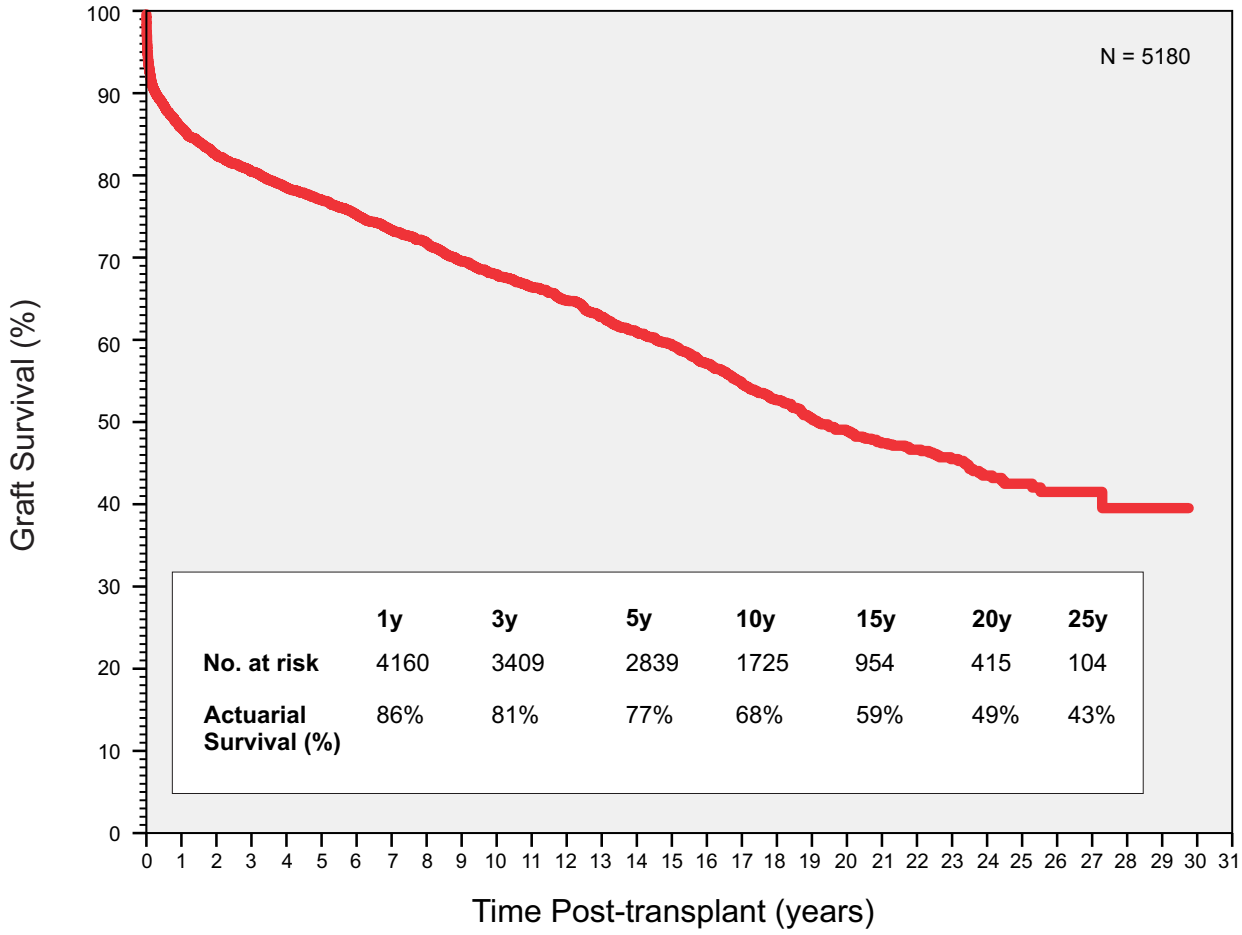
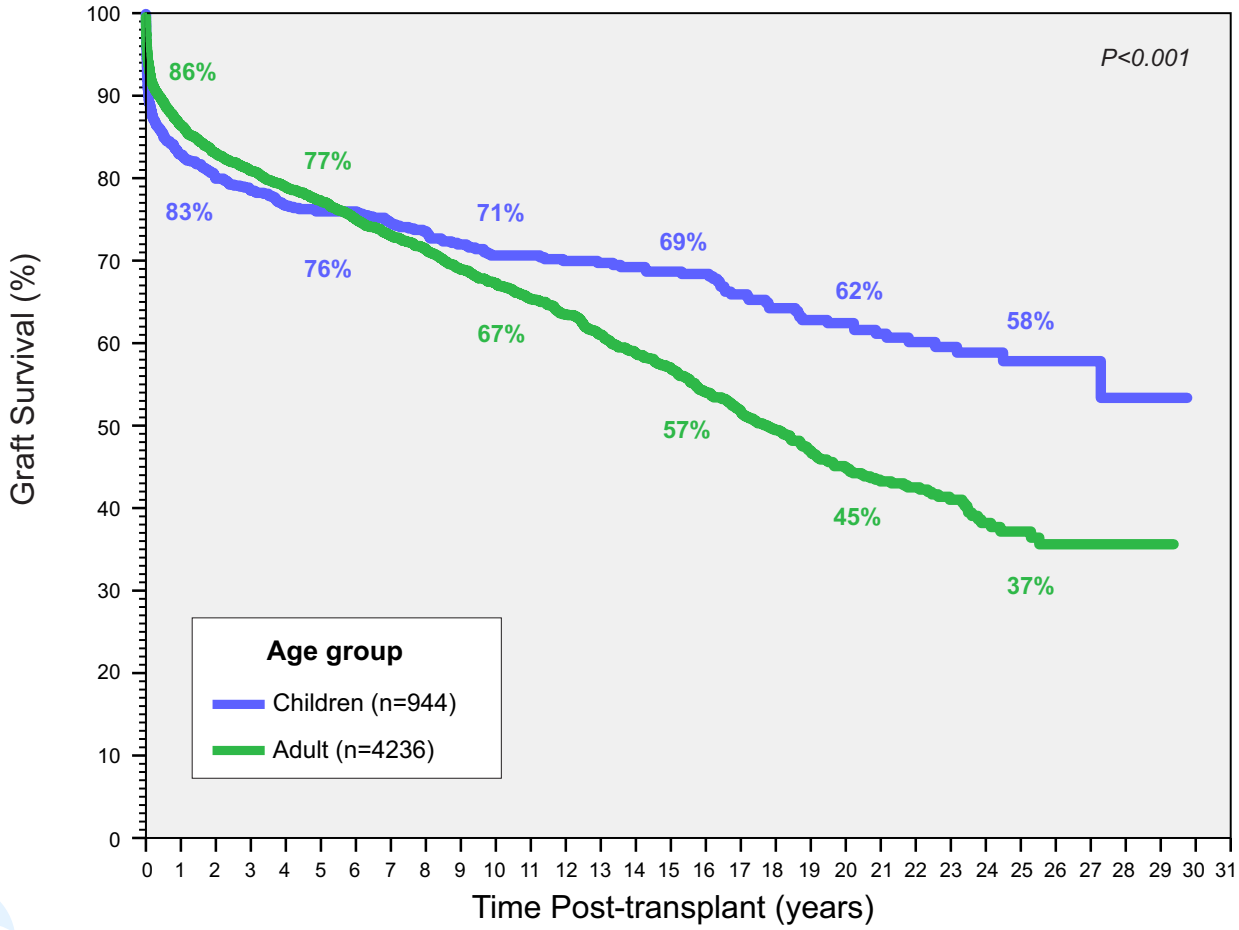
Graft Survival - All Grafts

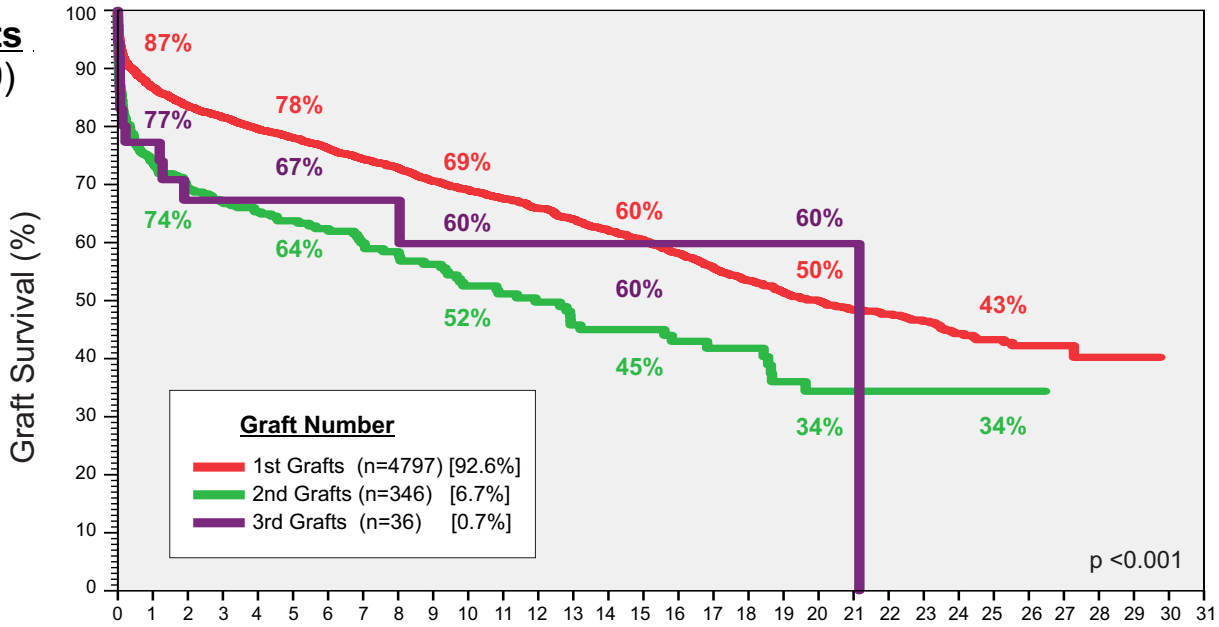


	1y	3y	5y	10y	15y	20y	25y
No. at risk	4160	3409	2839	1725	954	415	104
Actuarial Survival (%)	86%	81%	77%	68%	59%	49%	43%

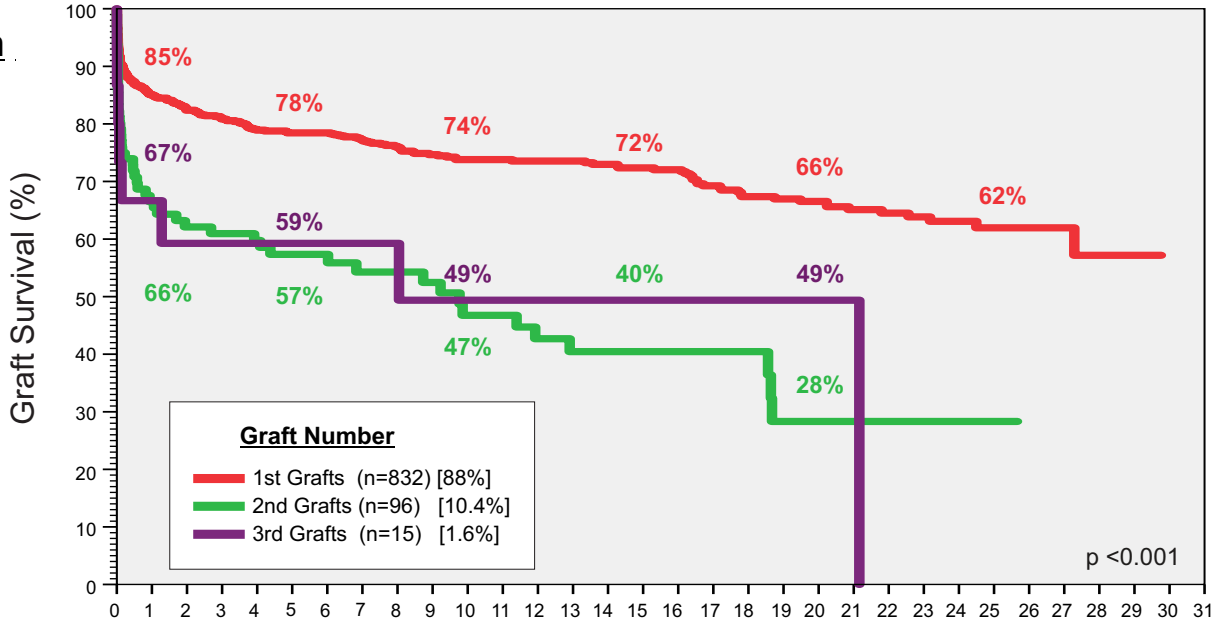
Graft Survival by Age Group



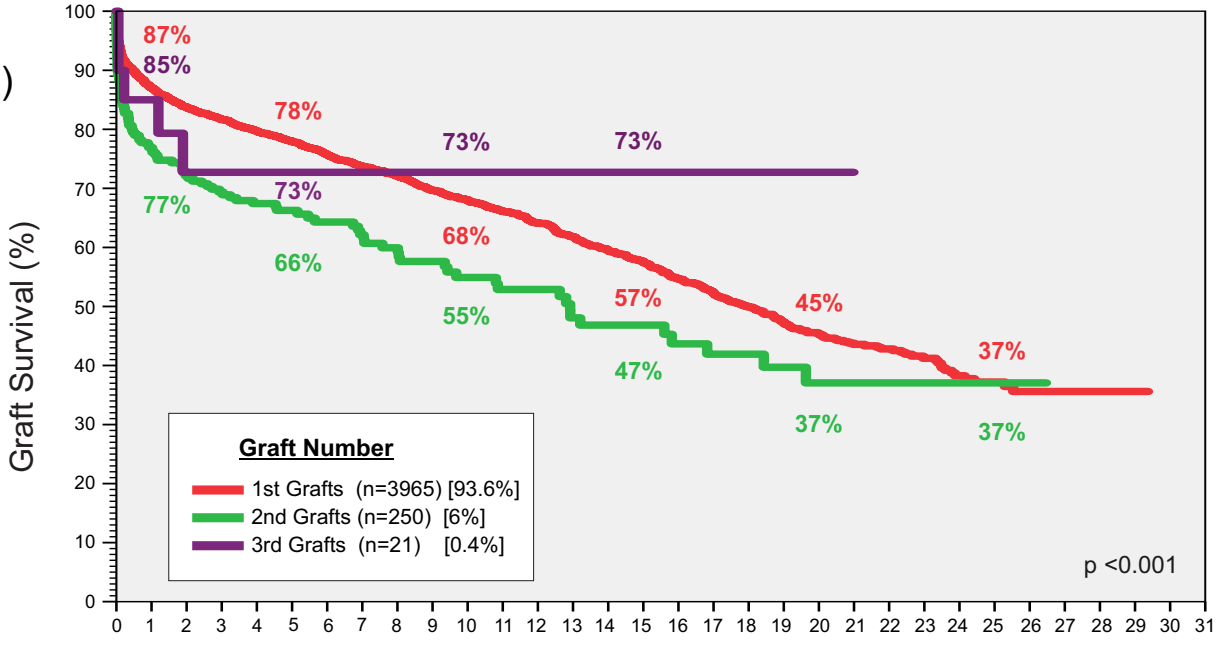
All Grafts
(n= 5179)



Children
(n= 943)



Adult
(n= 4236)



Graft Survival by Type of Graft [Deceased Donors]

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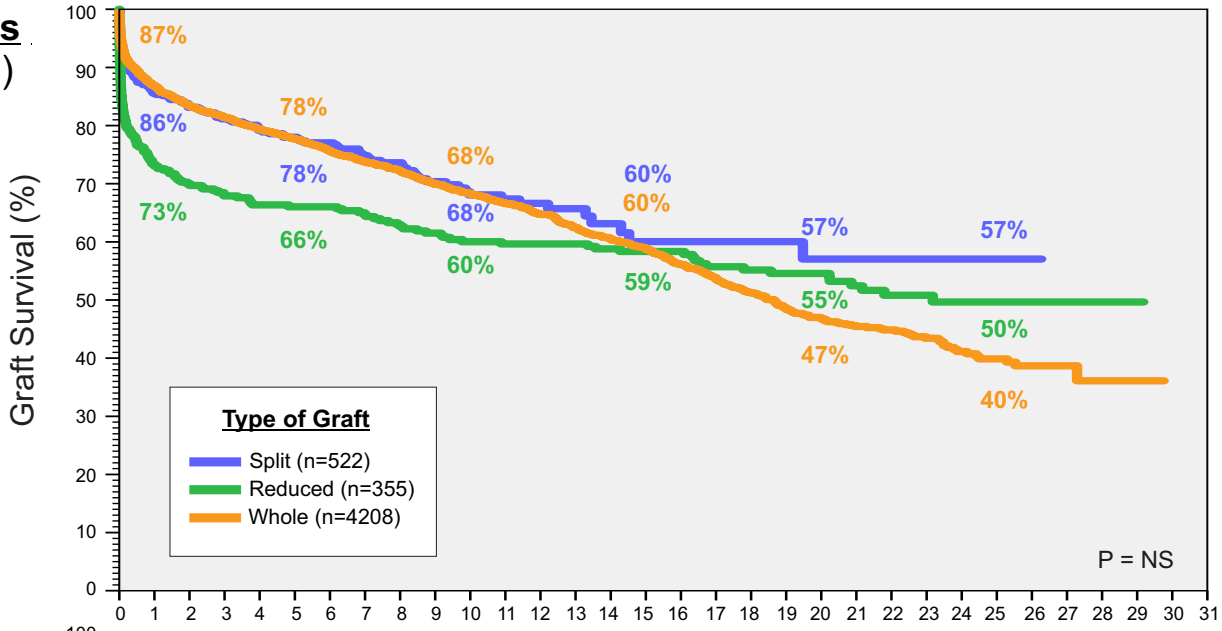
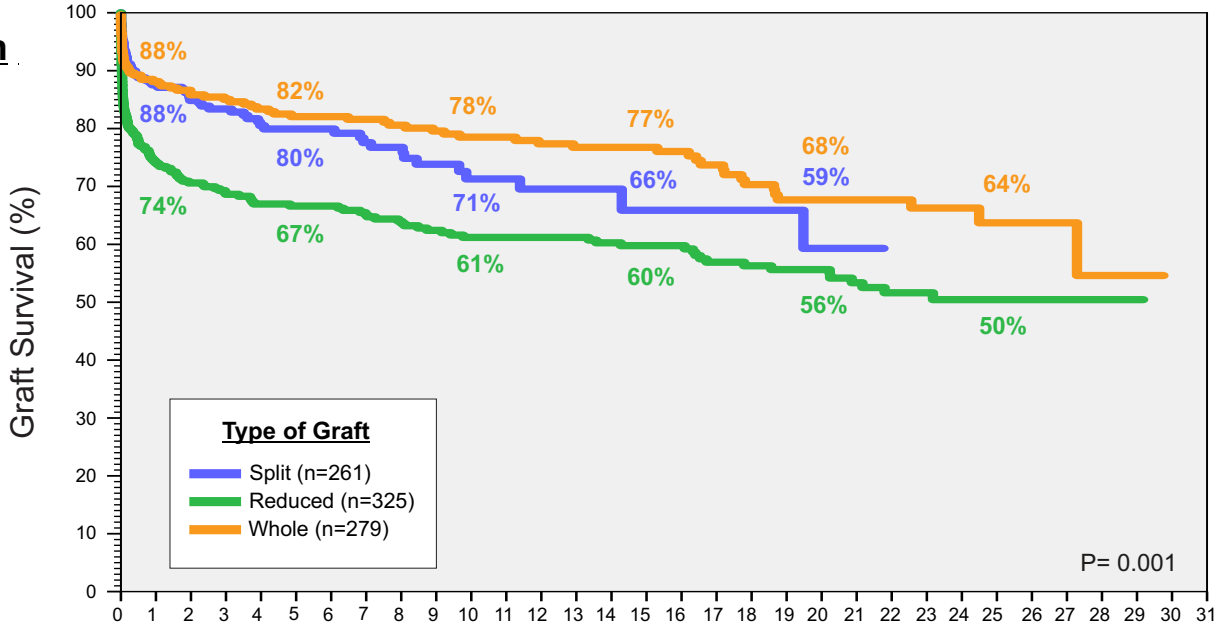
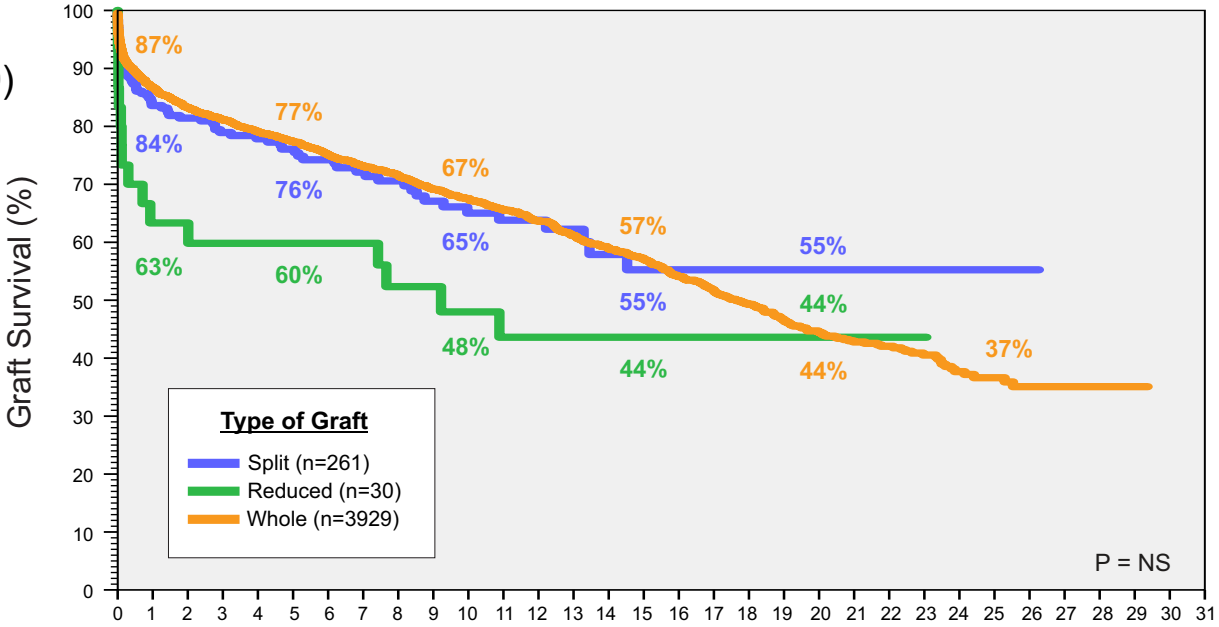
All Grafts
(n= 5085)



Children
(n= 865)



Adult
(n= 4220)



Time Post-transplant (years)

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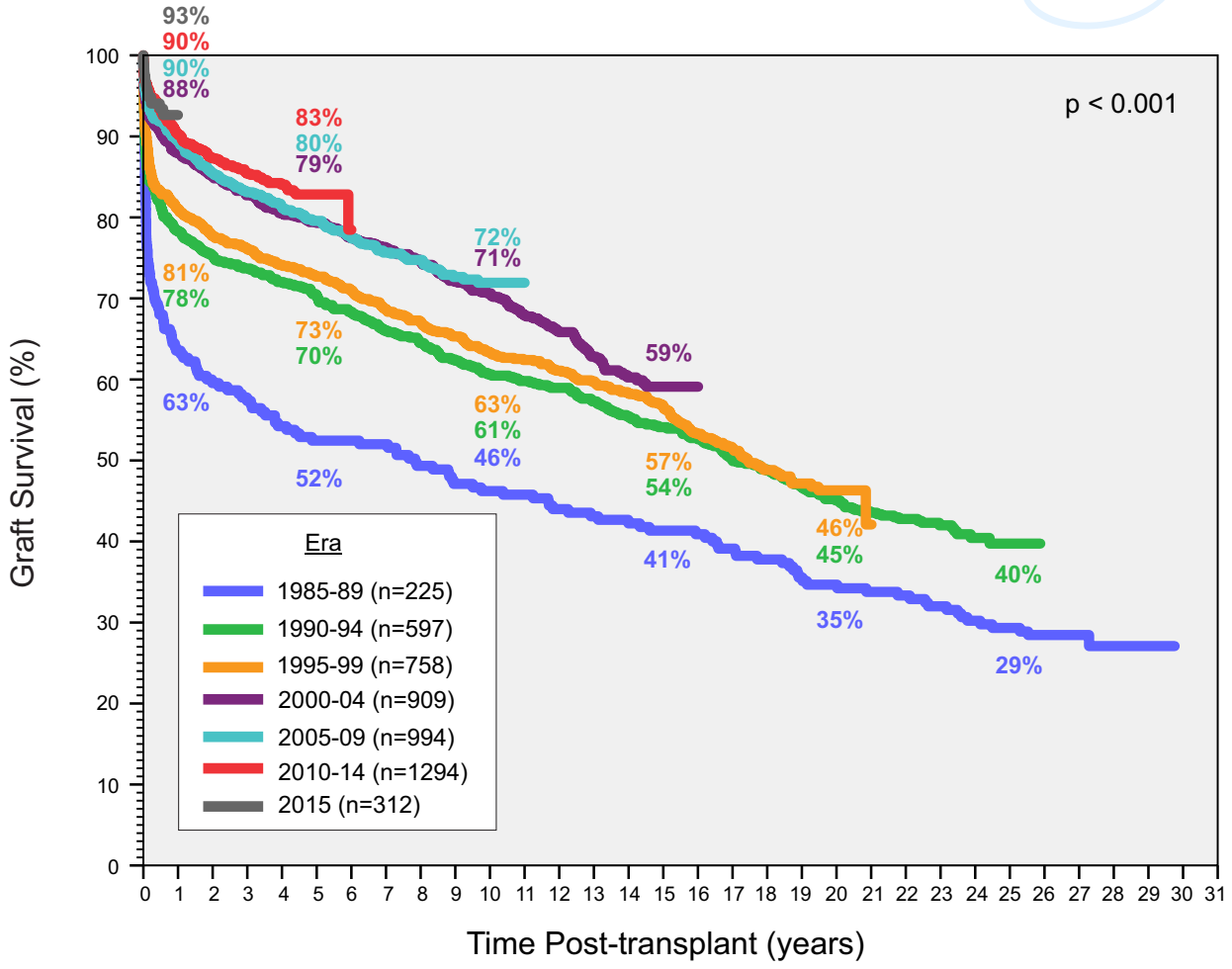
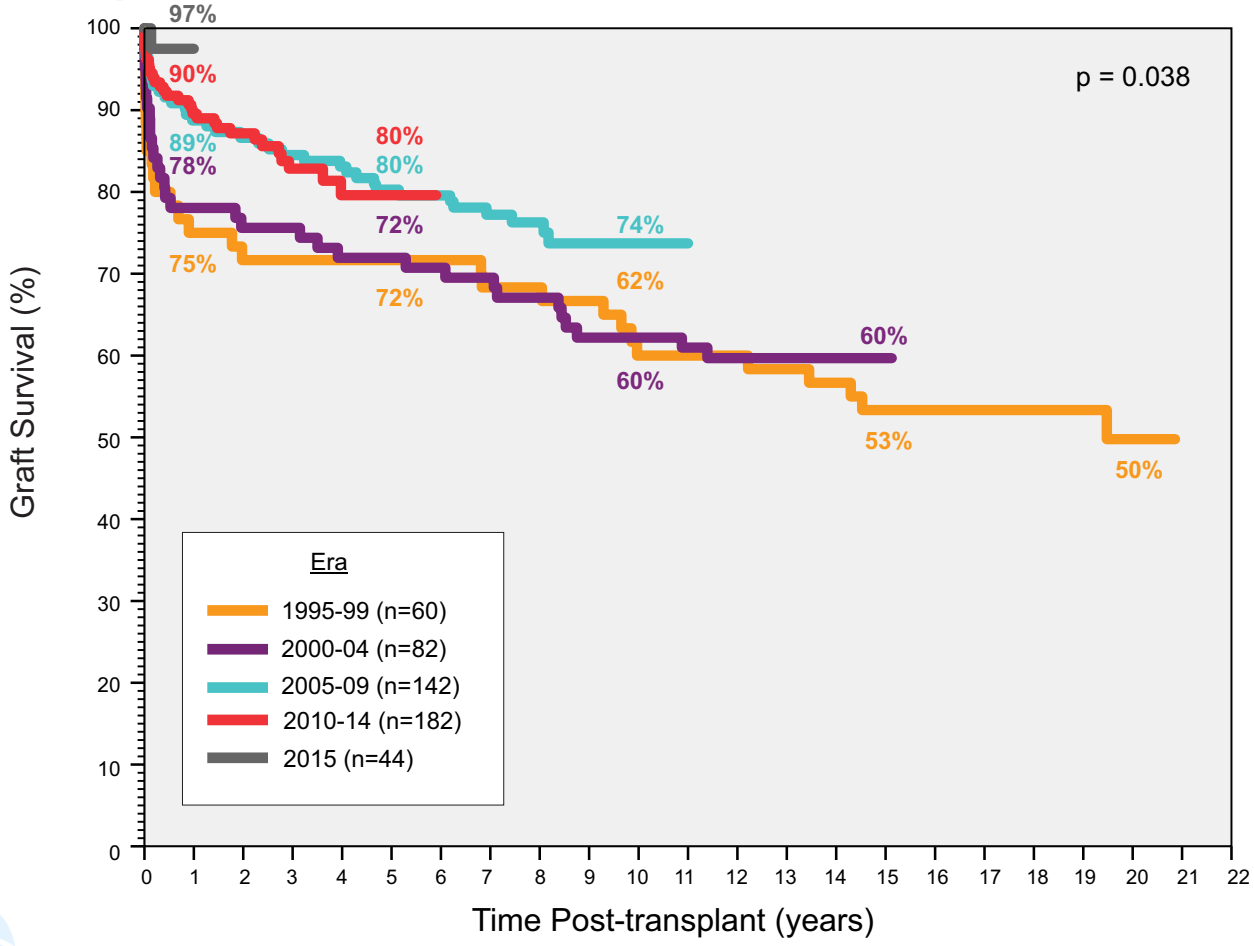
All Deceased Donor Grafts Survival by Year of Transplant



Deceased Donor Split Liver Grafts by Era



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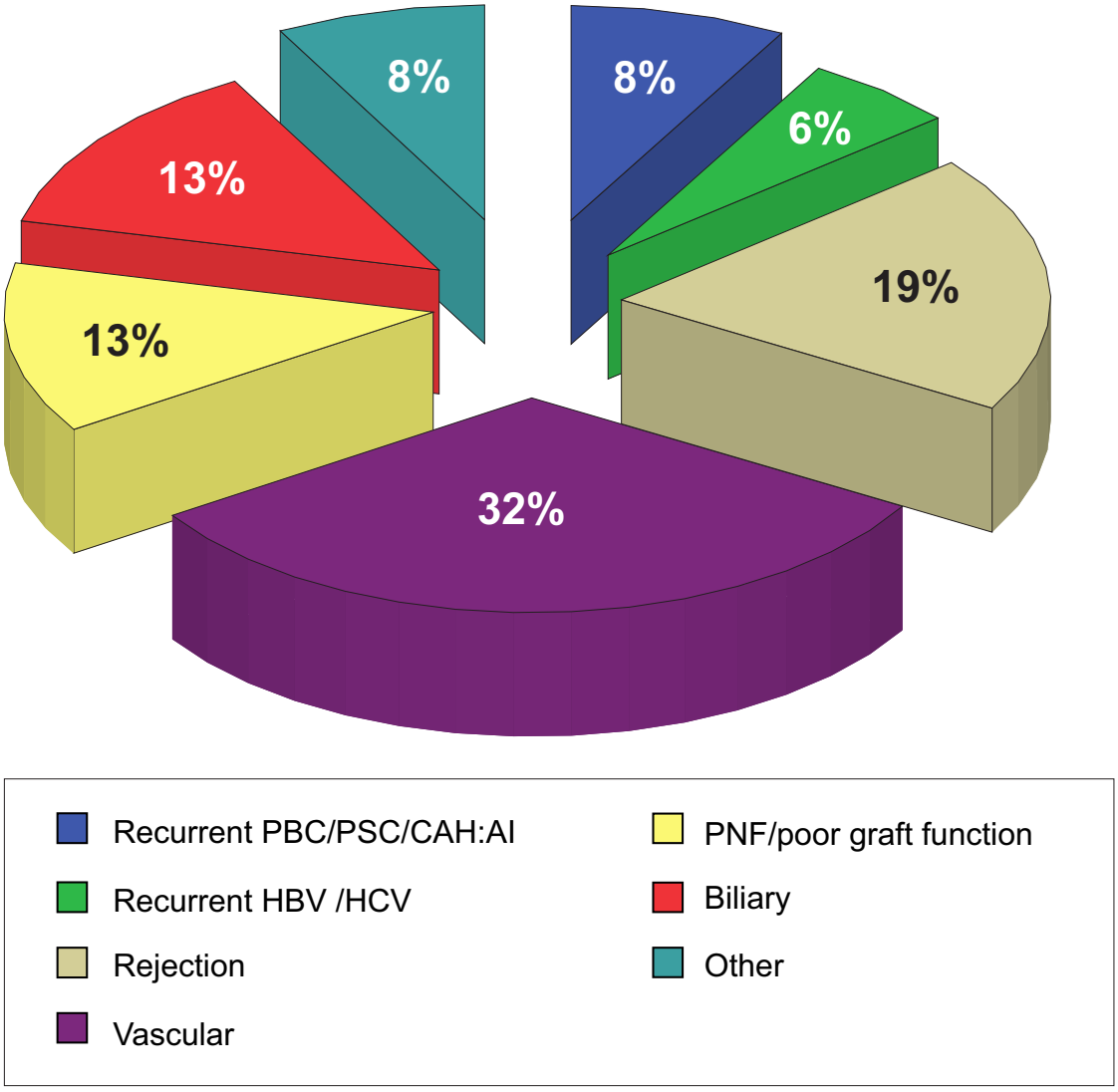
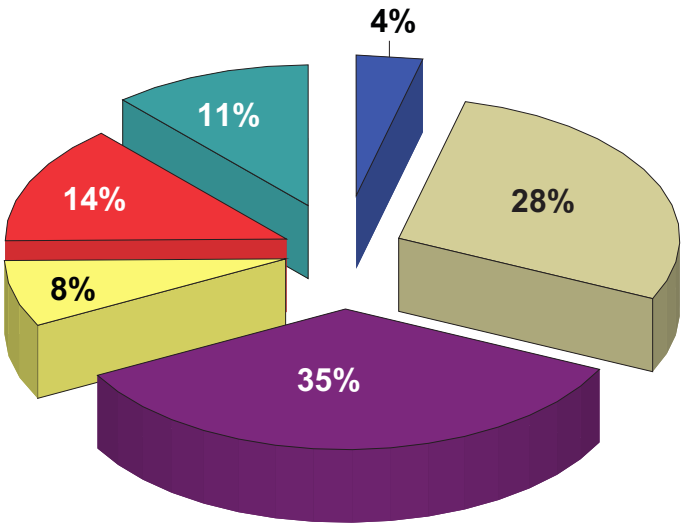
Indication for Retransplantation

n = 380 *(344 2nd grafts, 36 3rd grafts)*

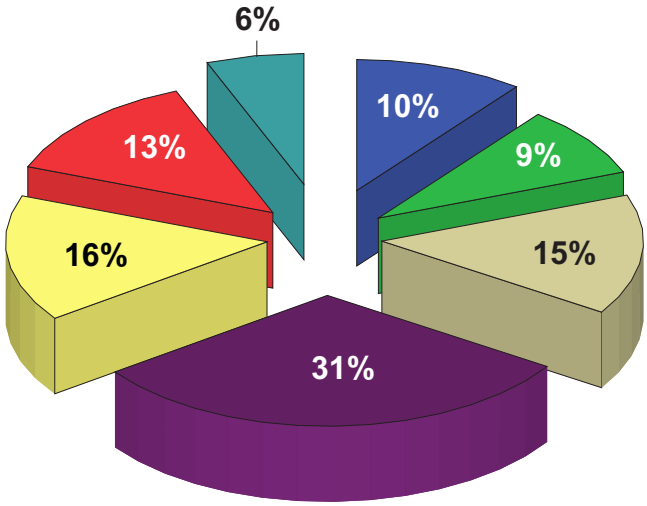


Age Group

Children
(n= 131)



Adults
(n= 249)



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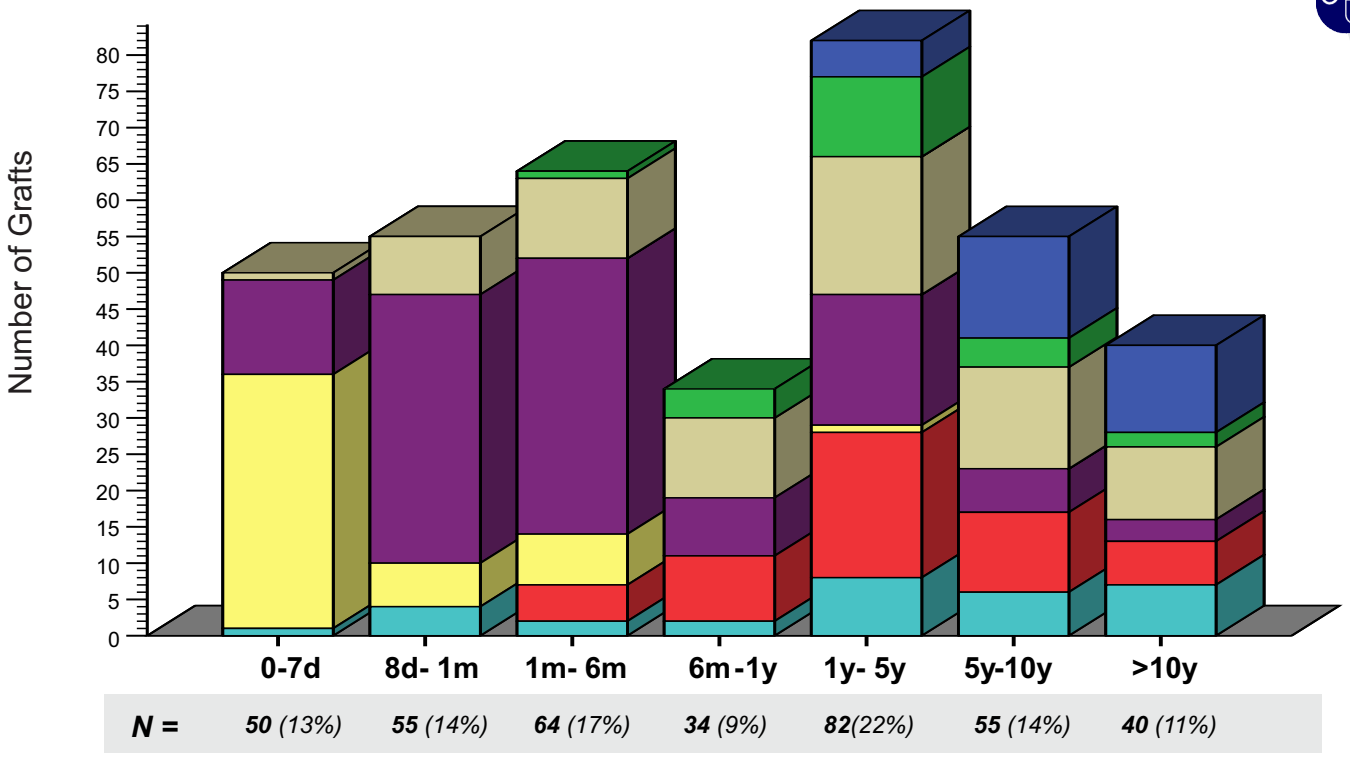
Indication for Retransplantation

n = 380 *(344 2nd grafts, 36 3rd grafts)*

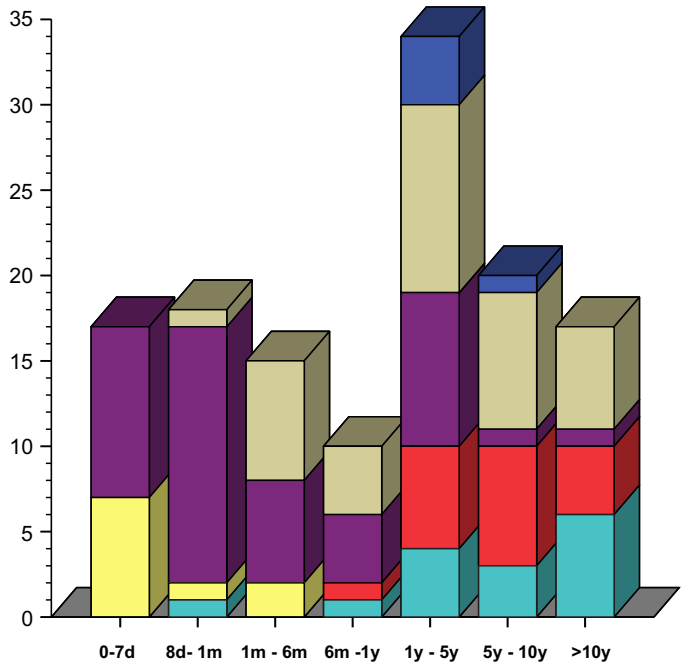


N =	0-7d	8d- 1m	1m- 6m	6m -1y	1y- 5y	5y-10y	>10y
	50 (13%)	55 (14%)	64 (17%)	34 (9%)	82(22%)	55 (14%)	40 (11%)

Recurrent PBC/PSC/CAH:AI | Rejection | PNF/poor graft function | Other

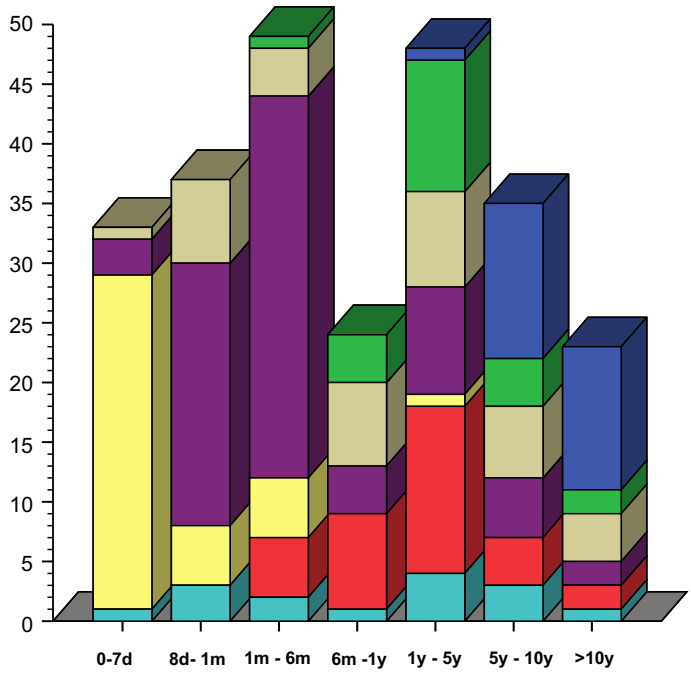
Recurrent HBV /HCV | Vascular | Biliary

Children (n=131)



N =	0-7d	8d- 1m	1m - 6m	6m -1y	1y - 5y	5y - 10y	>10y
	17 (13%)	18 (14%)	15 (11%)	10 (8%)	34 (26%)	20 (15%)	17 (13%)

Adults (n=249)



N =	0-7d	8d- 1m	1m - 6m	6m -1y	1y - 5y	5y - 10y	>10y
	33 (13%)	37 (15%)	49 (20%)	24 (10%)	48 (19%)	35 (14%)	23 (9%)

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Section 5

Cause of Patient Death

All Patients n = 1347

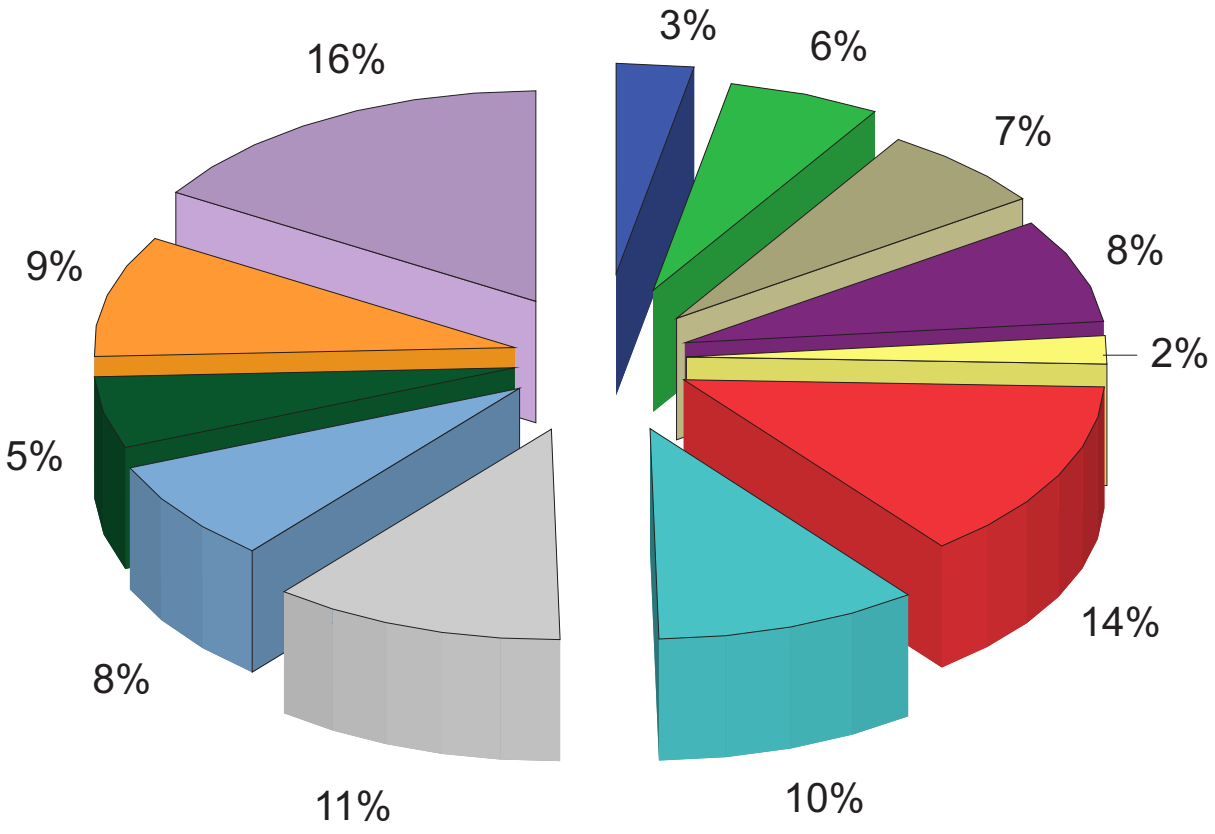
- Operative
- Respiratory
- Cerebrovascular
- Cardiovascular
- Gastrointestinal
- Sepsis
- Malignancy - recurrent
- Malignancy - de novo

Graft failure

- Recurrent HBV / HCV
- Rejection
- Other*

- Miscellaneous*

* See Appendix V for details



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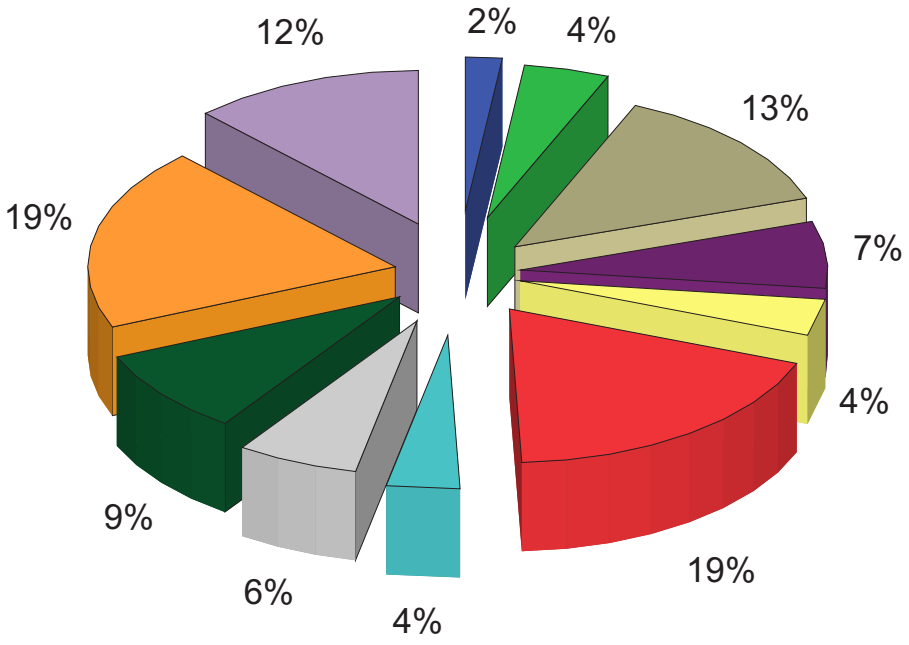
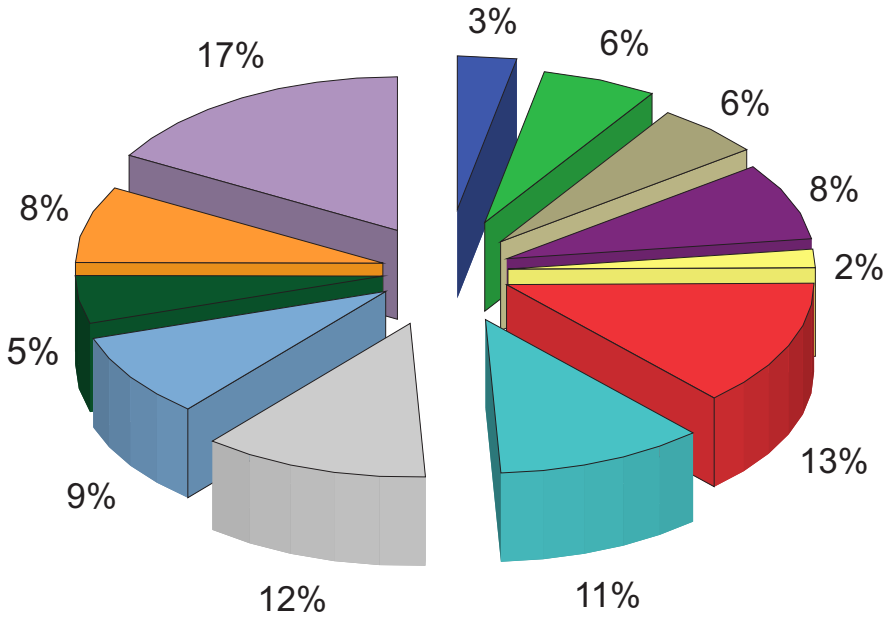
Causes of Death in Children
n =156



Causes of Death in Adult
n = 1191



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

* See Appendix V for details

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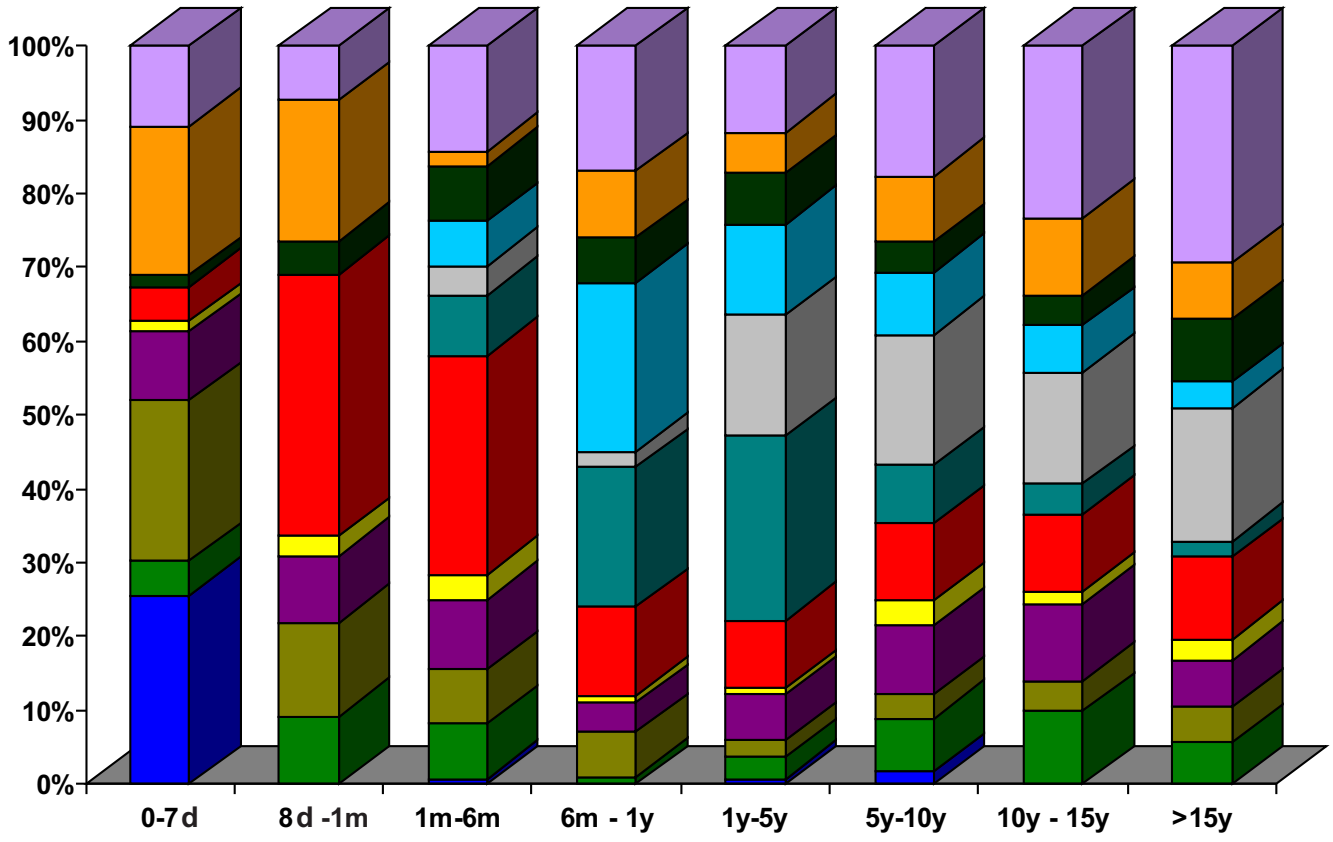
Cause of Death by Time Post Transplant



N =	129 (10%)	110 (8%)	148 (11%)	100 (7%)	307 (23%)	238 (18%)	172 (13%)	143 (11%)

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

* See Appendix V for details

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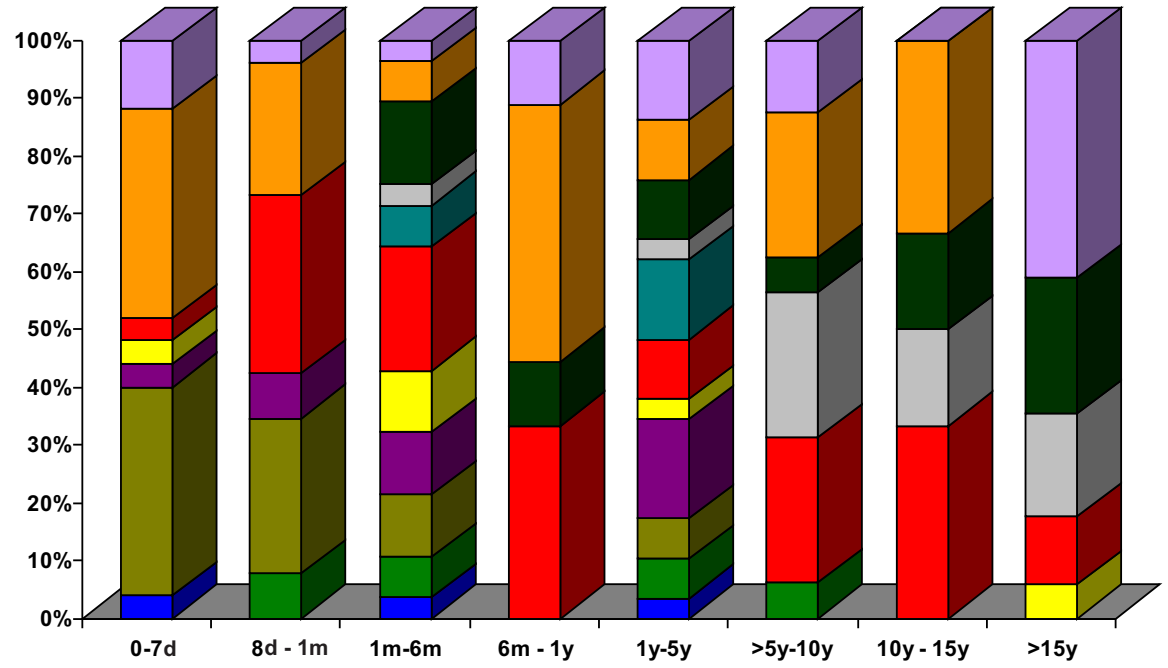
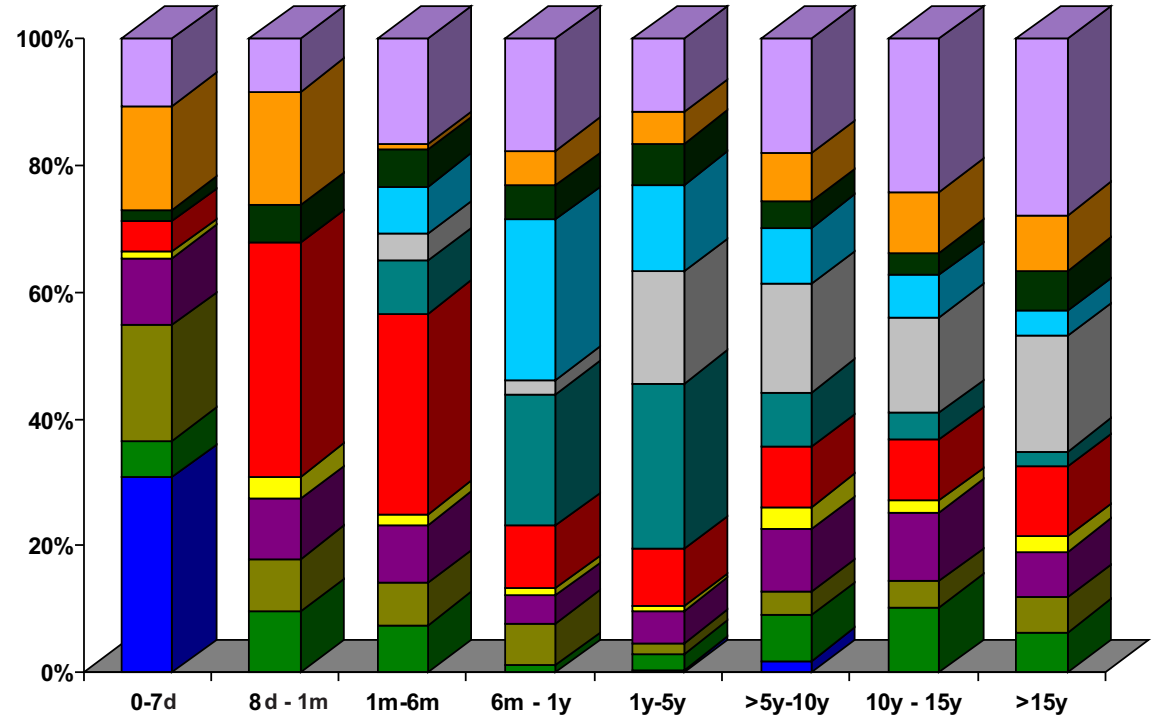
Cause of Death by Time Post Transplant Children (n=156)



	0-7d	8d - 1m	1m-6m	6m - 1y	1y-5y	>5y-10y	10y - 15y	>15y
N =	25 (16%)	26 (17%)	28 (18%)	9 (6%)	29 (19%)	16 (10%)	6 (4%)	17 (11%)

Cause of Death by Time Post Transplant Adult (n=1191)



	0-7d	8d - 1m	1m-6m	6m - 1y	1y-5y	>5y-10y	10y - 15y	>15y
N =	104 (9%)	84 (7%)	120 (10%)	91 (8%)	278 (23%)	222 (19%)	166 (14%)	126 (11%)

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

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Section 6

Deceased Donor Information

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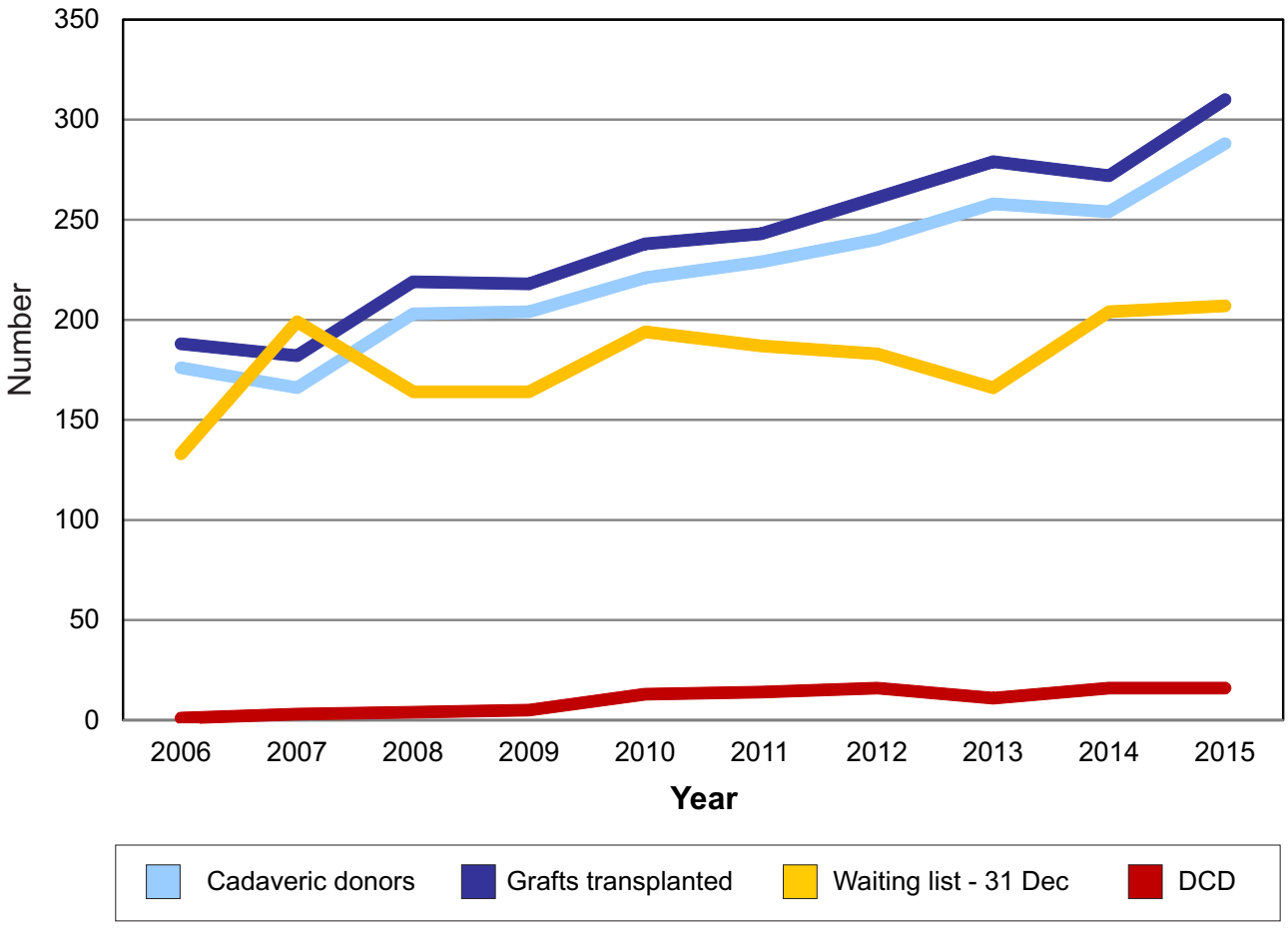
Deceased Donation by Year

	QLD	NSW/ACT	VIC/TAS	SA/NT	WA	NZ	TOTAL
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
2015	48	72/8	52/7	26/4	30	41	288

Grafts from deceased donors



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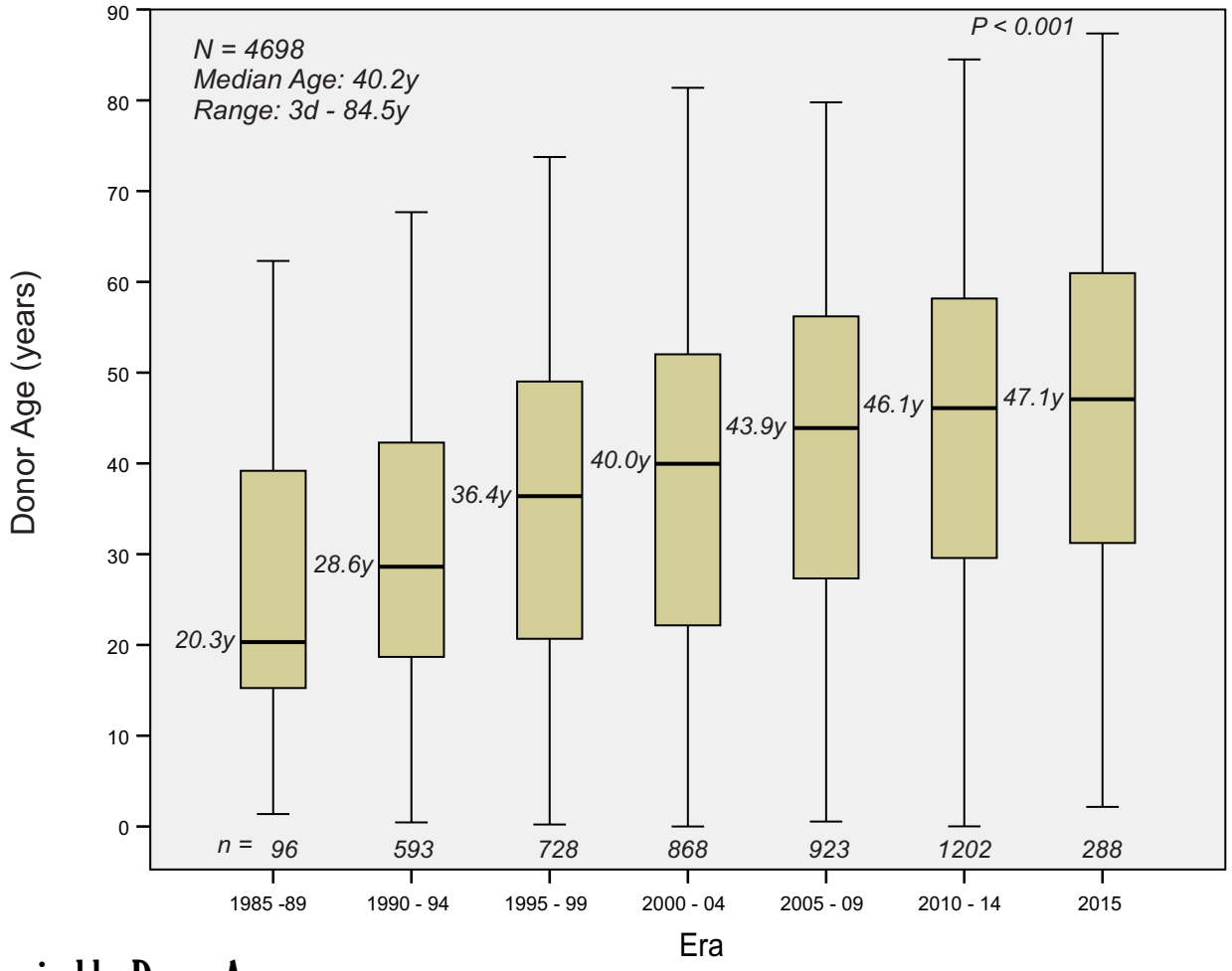
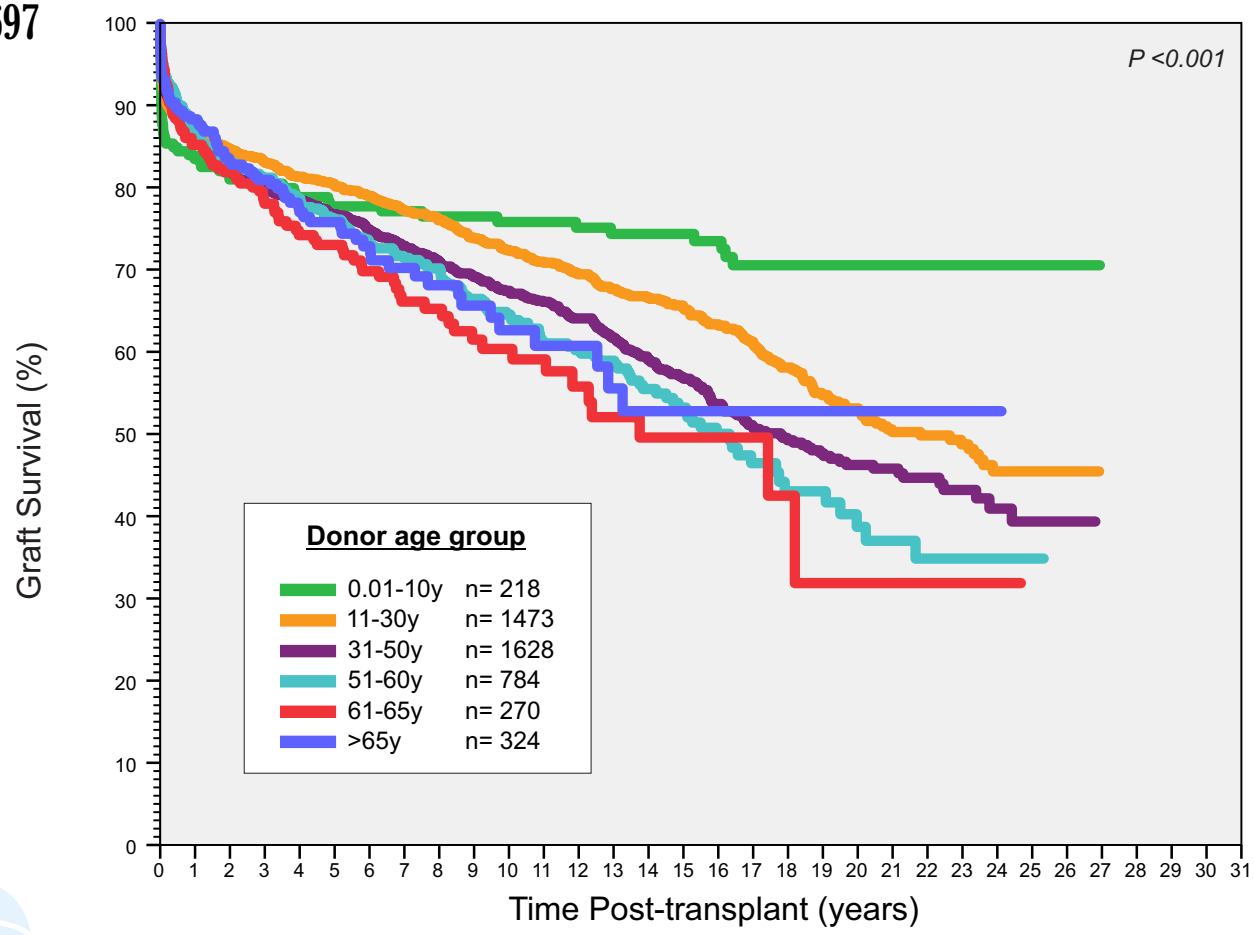
Donor Age by Era
N = 4698



Graft Survival by Donor Age
N = 4697



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Section 7

Living Donor Transplantation

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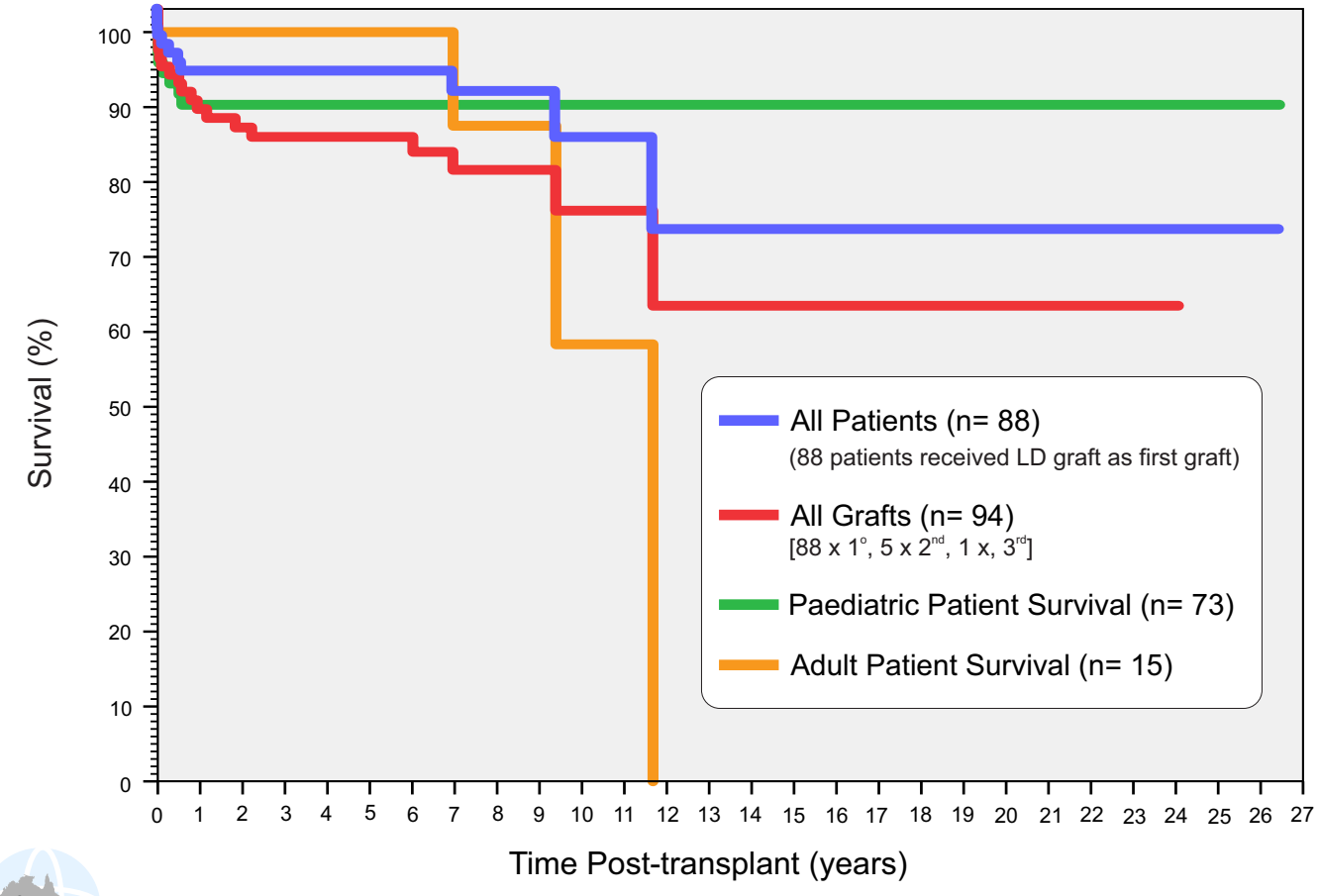
Living Donor Transplantation
N = 94

	Recipient Age Group		
	Child [n=78]	Adult [n=16]*	All [n=94]
Donor gender	-	-	-
Male	43	10	53
Female	35	6	41
Donor age	-	-	-
Median	35.4y	31.5y	33.8y
Range	19.0 - 54.5y	22.8 - 54.4y	19 - 54.5y
Donor relationship	-	-	-
Mother	20	-	20
Father	35	-	35
Son	-	4	4
Daughter	-	1	1
Grandmother	1	-	1
Grandfather	1	-	1
Sister	-	3	3
Brother	2	3	5
Aunt	8	-	8
Uncle	1	-	1
Family friend	6	1	7
Cousin	4	-	4
Spouse	-	1	1

* *3 x whole liver domino transplant*



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Section 8

Waiting List

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Waiting List Activity
[Data 1/1/11 - 31/12/15]

Activity	2011	2012	2013	2014	2015				
Listed at 1 January	194	192	186	164	204	-	TOTAL 2015	Adult	Paediatric
Activated	336	351	360	407	-	402			
TOTAL	**530**	**543**	**546**	**571**	**204**	**402**	**606**	**535**	**71**
	OUTCOME				OUTCOME				
Transplant	**253 [49%]**	**268 [50%]**	**284 [52%]**	**278 [49%]**	**113**	**203**	**316 [52%]**	**270 [51%]**	**46 [65%]**
Delisted	**85 [13%]**	**89 [13%]**	**98 [18%]**	**89 [16%]**	**42**	**41**	**83 [14%]**	**79**	**4**
Died on list	17	29	26	18	5	16	21	21	0
Too sick	17 } 8%	16 } 8%	11 } 10%	10 } 8%	2	3	5 [7.5%]	5 } 9%	0 } 1.5%
Tumour progression	20	10	16	15	13	7	20	19	1
Improved	12	17	24	18	12	5	17	16	1
Other	19*	17*	21*	28*	10	10	20*	18	2
Active at 31 Dec	192 [36%]	186 [34%]	164 [34%]	204 [36%]	55	152	207 [34%]	186	21

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

Outcome of Initial Urgent Listing

OUTCOME	CATEGORY 1						
	2011 (n=15)	2012 (n=16)	2013 (n=19)	2014 (n=8)	2015 N=25	2015 Adult n=23	2015 Paediatric n=2
TRANSPLANTED	12 } 80%	11 } 81%	11 } 74%	6 } 88%	21 } 88%	19	2
IMPROVED	- }	2 }	3 }	1 }	1 }	1	-
DIED / TOO SICK	3	3	5	1	3	3	-
OTHER TREATMENT	-	-	-	-	-	-	-

OUTCOME	CATEGORY 2						
	2011 (n=28)	2012 (n=19)	2013 (n=29)	2014 (n=22)	2015 N=22	2015 Adult n=9	2015 Paediatric n=13
TRANSPLANTED	22 }	14 } 86%	22 } 89%	18 } 95%	20 } 95%	8	12
IMPROVED	2 }	3 }	4 }	3 }	1 }		1
DIED / TOO SICK	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 31/12/15	1 active 31/12/15	

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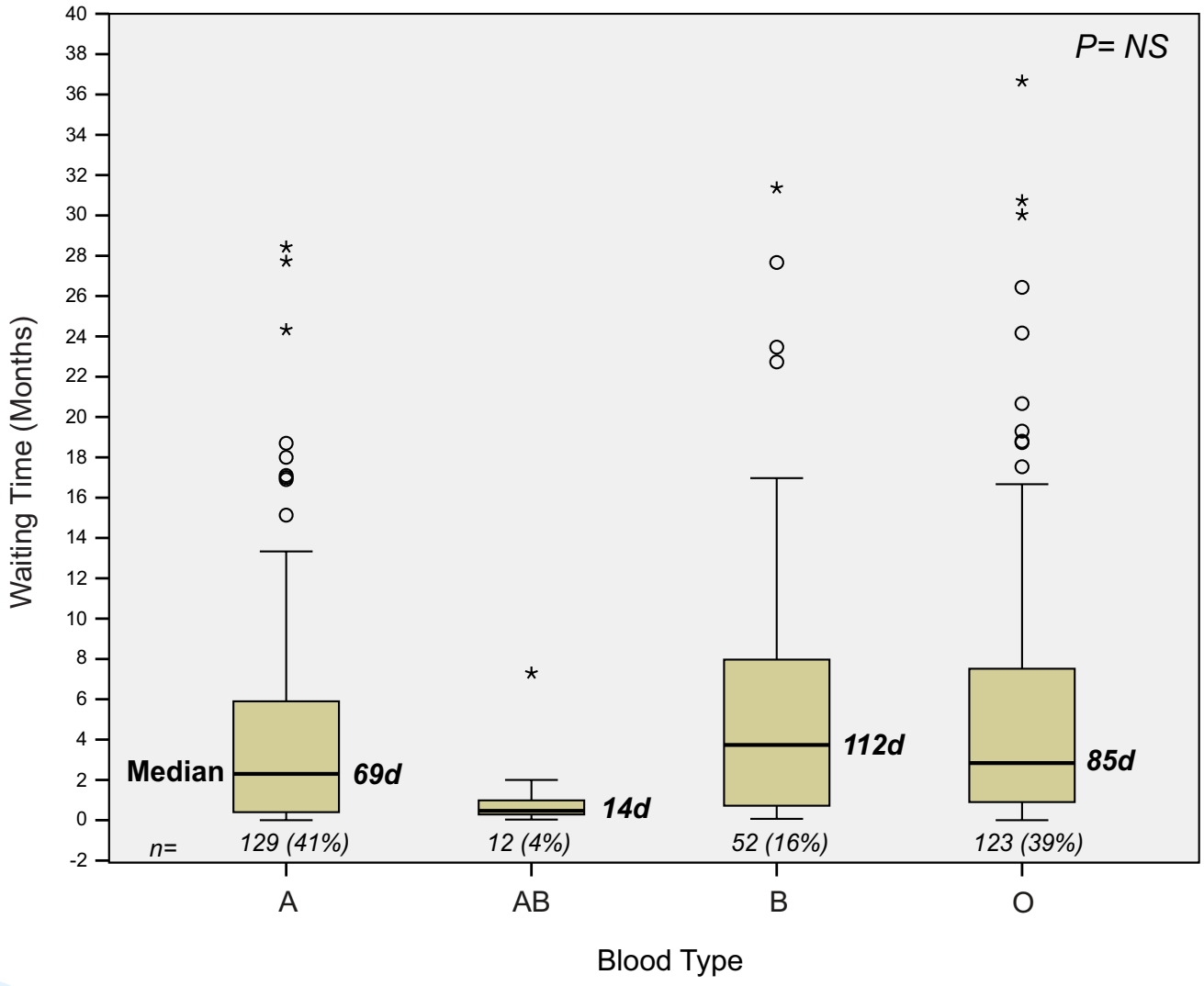
Outcome by Blood Group

	Blood Group				
	A	O	B	AB	TOTAL
n=	223 (37%)*	274 (45%)	94 (15%)	16 (3%)	607
Not transplanted	94	151	42	4	291
Transplanted	129 (58%)**	123 (45%)	52 (55%)	12 (75%)	316 (52%)

* *% of total number listed*

** *% of blood group*

Waiting Time to Transplant 2015



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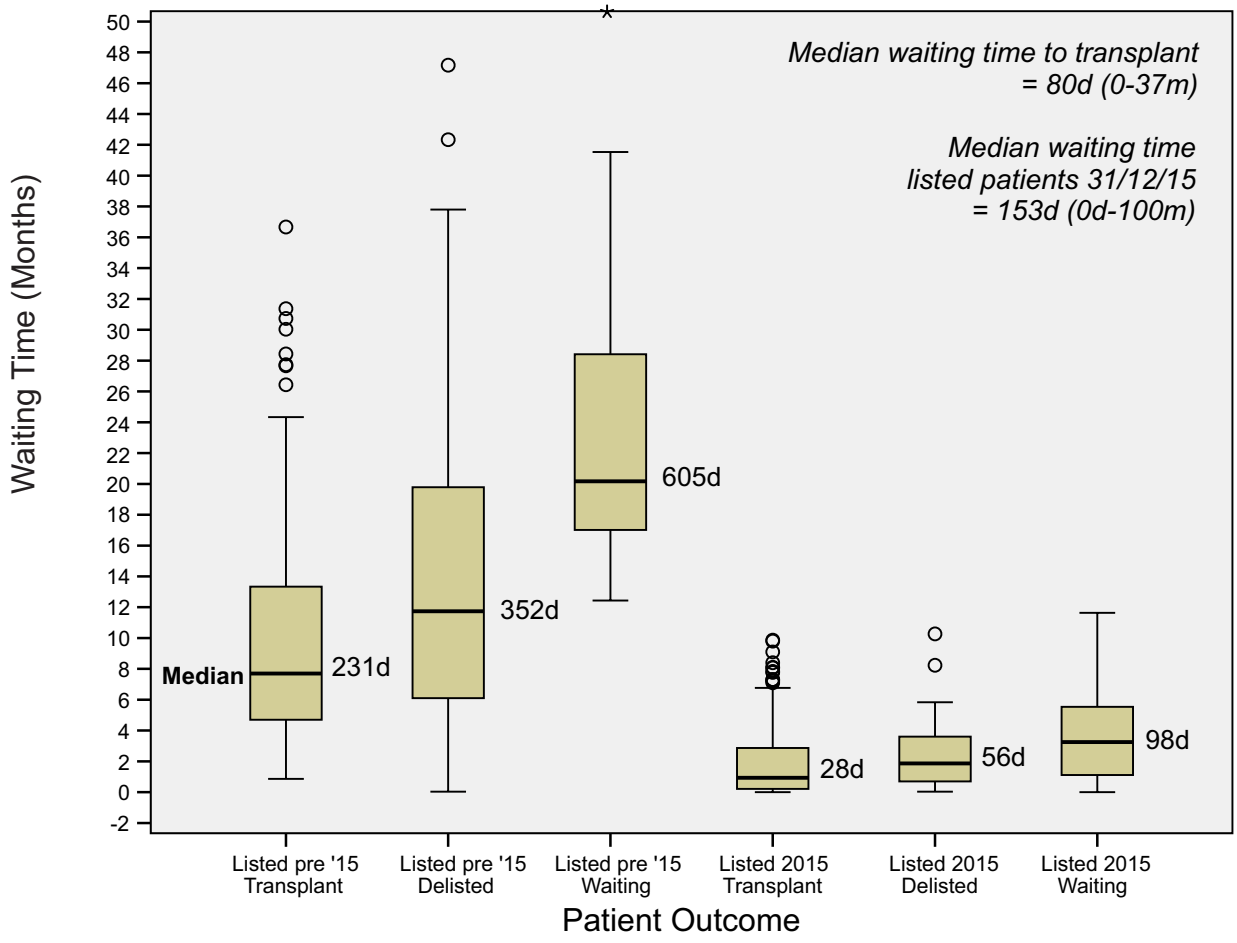
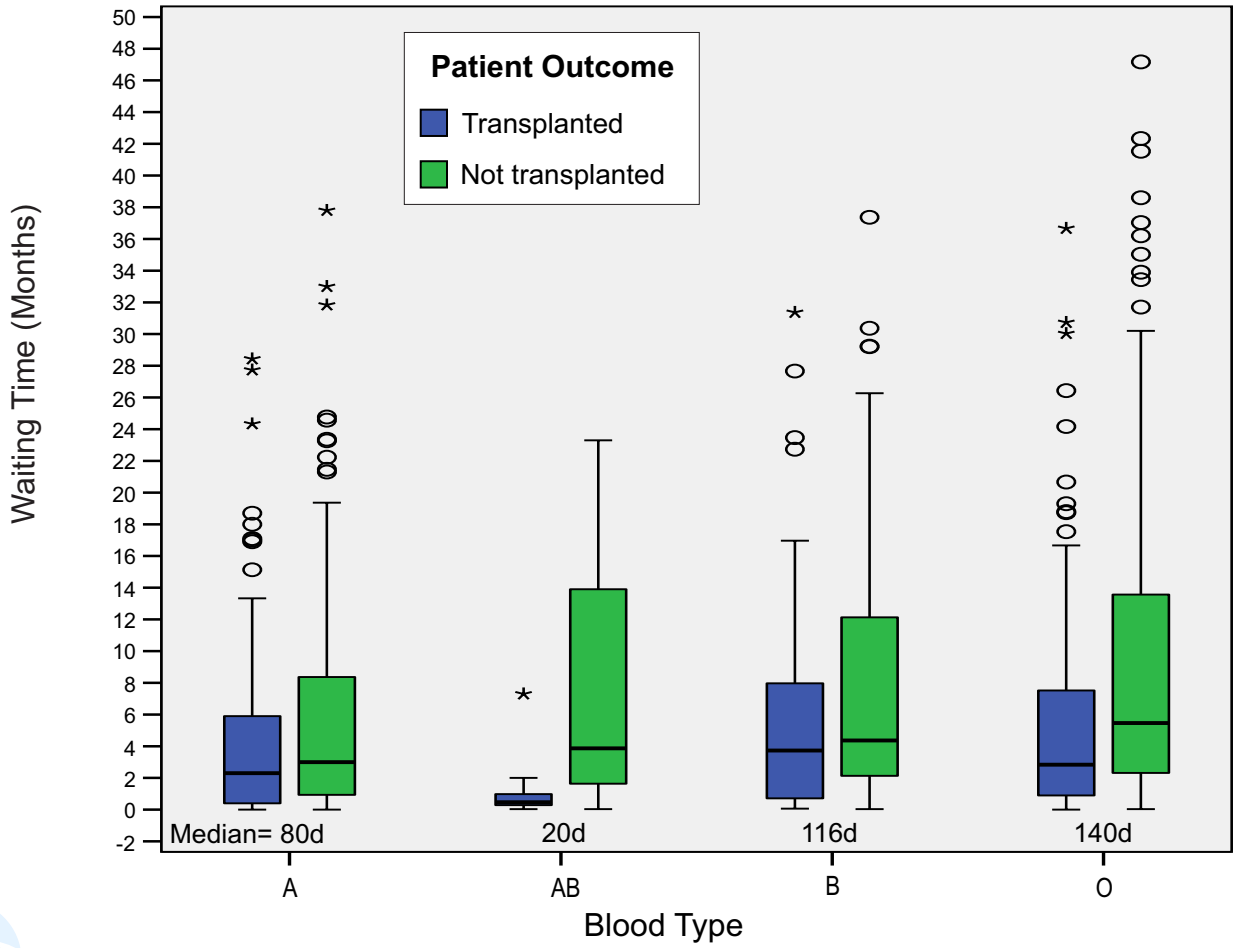
Waiting Time by Outcome



Waiting Time by Outcome & Blood Group



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Section 9

Liver Transplantation and Cancer

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Cancer in Liver Transplant Recipients
n = 4800

At Tx	Total number pts. transplanted = 4800
Liver Cancer as indication for Transplant	397 (8%) 400 Ca
Liver Ca as a Secondary Diagnosis	659 (14%) 665 Ca
Total	1059* (22%)
Post Tx	
Recurrent Liver Ca	131 (3% of all pts, 12% pts with Ca at Tx)
De Novo Ca	351 (7%) 382 Ca
Skin Ca	677 (14%)
Total	1159 (24%)
Multiple Cancer types (non skin and skin)	324 (7% of all pts)
Multiple non skin cancers	87 (2% of all pts)
Transferred from Donor	2
Developed non skin Ca < 90days	8

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

Liver Cancer as Primary Diagnosis
n = 397/4800 (8%)

TYPE OF CA	No	DIED	DIED OF THIS CA
HEPATOCELLULAR CA	351	78	41 (12%)
HEPATOBLASTOMA	25	5	4 (16%)
FIBROLAMELLAR	7	5	2 (29%)
CARCINOID	4	4	4 (100%)
EPITHELOID HAEMANGIOENDOTHELIOMA	4	0	0
HEPATOCELLULAR MALIGNANT NEOPLASM	1	0	0
CHOLANGIOCARCINOMA	4	2	1 (25%)
ANGIOSARCOMA	1	1	1 (100%)
GASTRINOMA	1	1	1 (100%)
PANCREATIC ISLET CELL	1	1	1 (100%)
ERYTHROID LEUKAEMIA	1	1	1 (100%)
TOTALS	**400* (8% of pts)**	**98 (25% of those with PCa)**	**56 (14% of those with PCa)**

* 3 pts had two primary liver cancers

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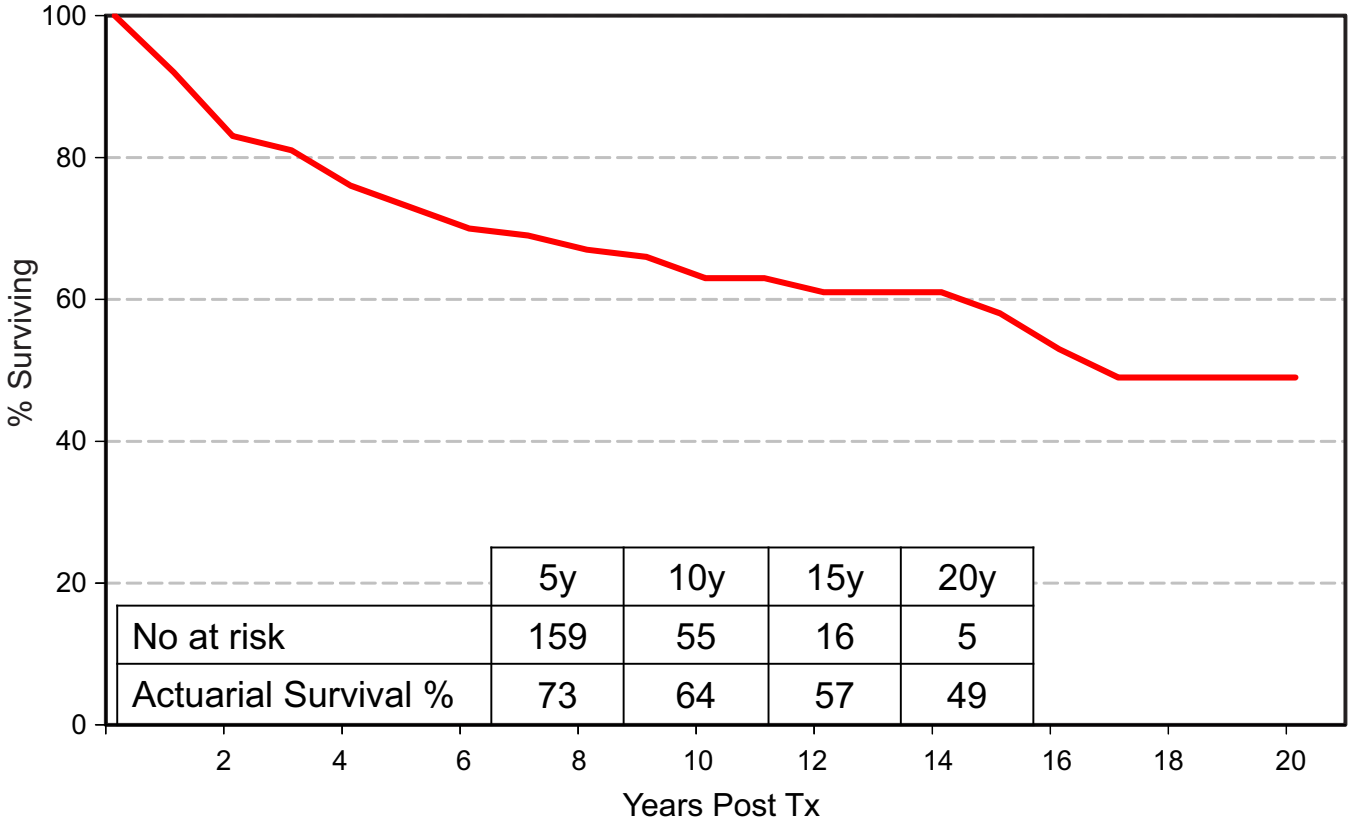
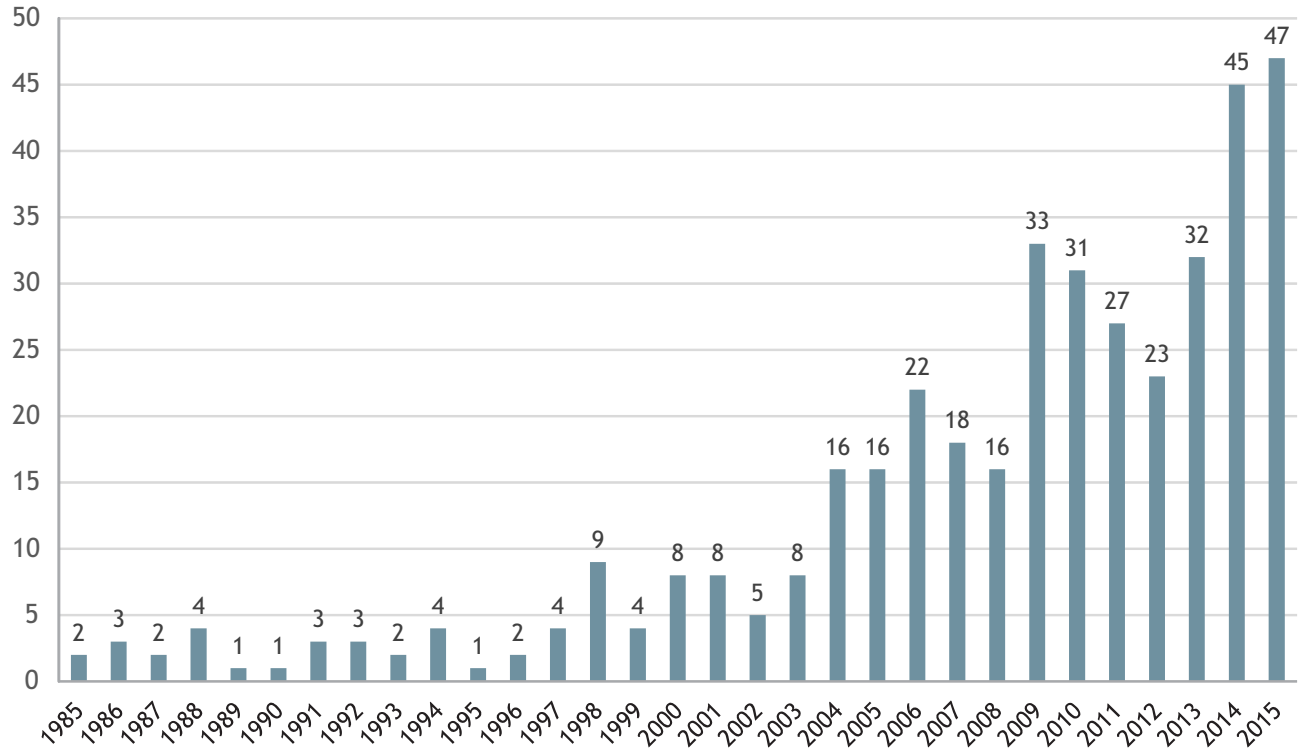
Overall Survival
Primary Liver Cancer
n =397/4800 (8% of pts transplanted)



	5y	10y	15y	20y
No at risk	159	55	16	5
Actuarial Survival %	73	64	57	49

Primary Liver Cancer Incidence
n=397/4800



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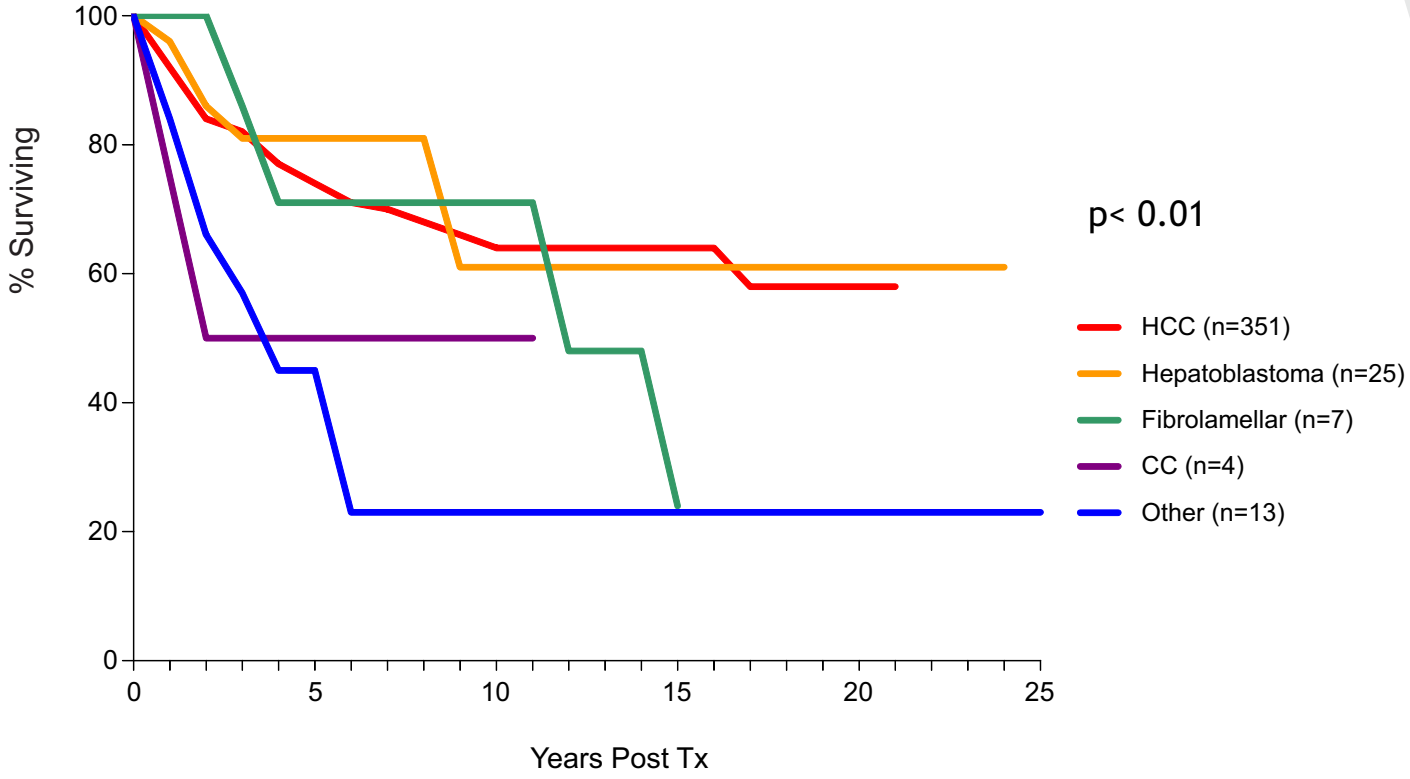
Overall Survival
Primary Liver Cancer
n=397/4800 (8%)



Primary Liver Cancer
Actuarial Survival Summary
n = 397/4800

		1yr	5yr	10yr	15yr	20yr	25yr
HCC (n=351)	n	282	136	48	12	3	
	%	92	74	64	64	58	
Hepatoblastoma (n=25)	n	22	13	3	3	2	
	%	96	81	61	61	61	
Other (n=13)	n	11	5	2	2	2	1
	%	84	45	23	23	23	23
Fibrolamellar (n=7)	n	7	6	4	2		
	%	86	71	71	24		
CC (n=4)	n	4	3	2			
	%	100	50	50			

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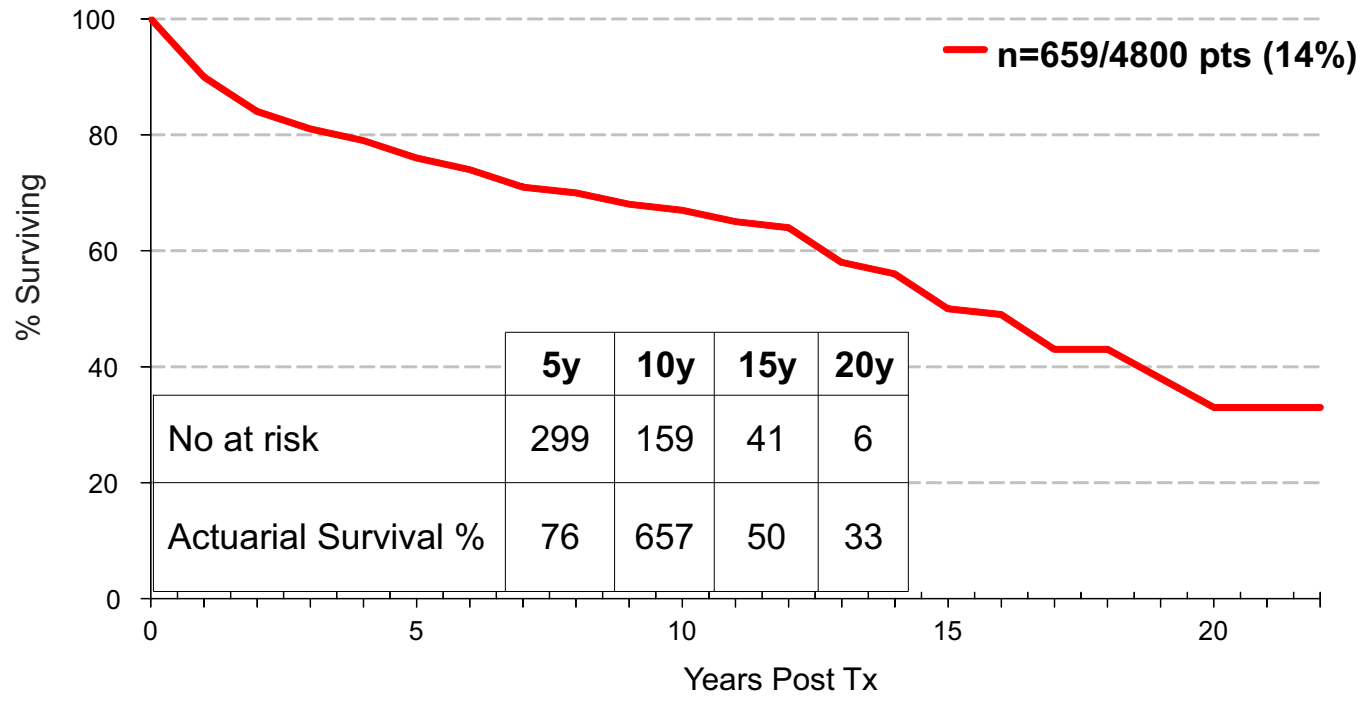
Liver Cancer as a Secondary Diagnosis
n = 659/4800 (14% pts)

	No	Died	Died of This Cancer
HEPATOCELLULAR CA*	612	159	45 (7%)
CHOLANGIO CA	39	31	19 (48%)
OTHER	8	5	2 (25%)
FIBROLAMELLAR	4	0	0
HEPATOBLASTOMA*	2	1	0
Total	**665* in 659 pts (14%)**	**196 (30% of pts with SCa)**	**66 (10% of pts with SCa)**

*** 3 patients had 2 secondary cancers**

Overall Survival
Liver Cancer as a Secondary Diagnosis



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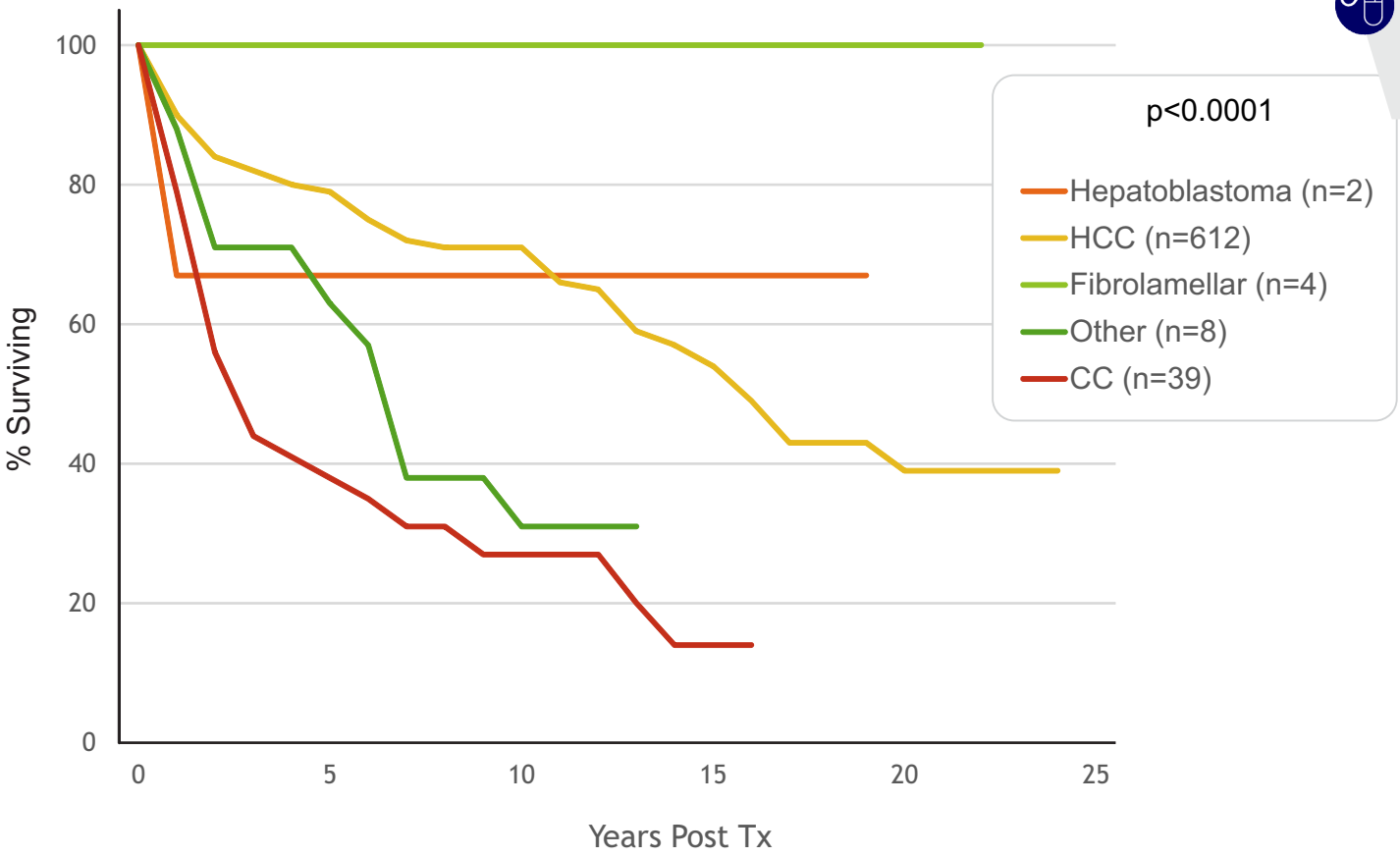
Liver Cancer as a Secondary Diagnosis
n =659/ 4800 (14%)



Secondary Liver Cancer
Actuarial Survival Summary
n =659/ 4800 (13%)

		1yr	5yr	10yr	15yr	20yr
HCC (n=612)	n	502	275	148	38	5
	%	90	79	71	54	39
CC (n=39)	n	30	14	8	2	
	%	79	38	27	6	
Other (n=8)	n	8	6	3		
	%	88	63	31		
Fibrolamellar (n=4)	n	4	4	4	4	
	%	100	100	100	100	
Hepatoblastoma (n=2)	n	3	3	2	2	
	%	67	67	67	67	

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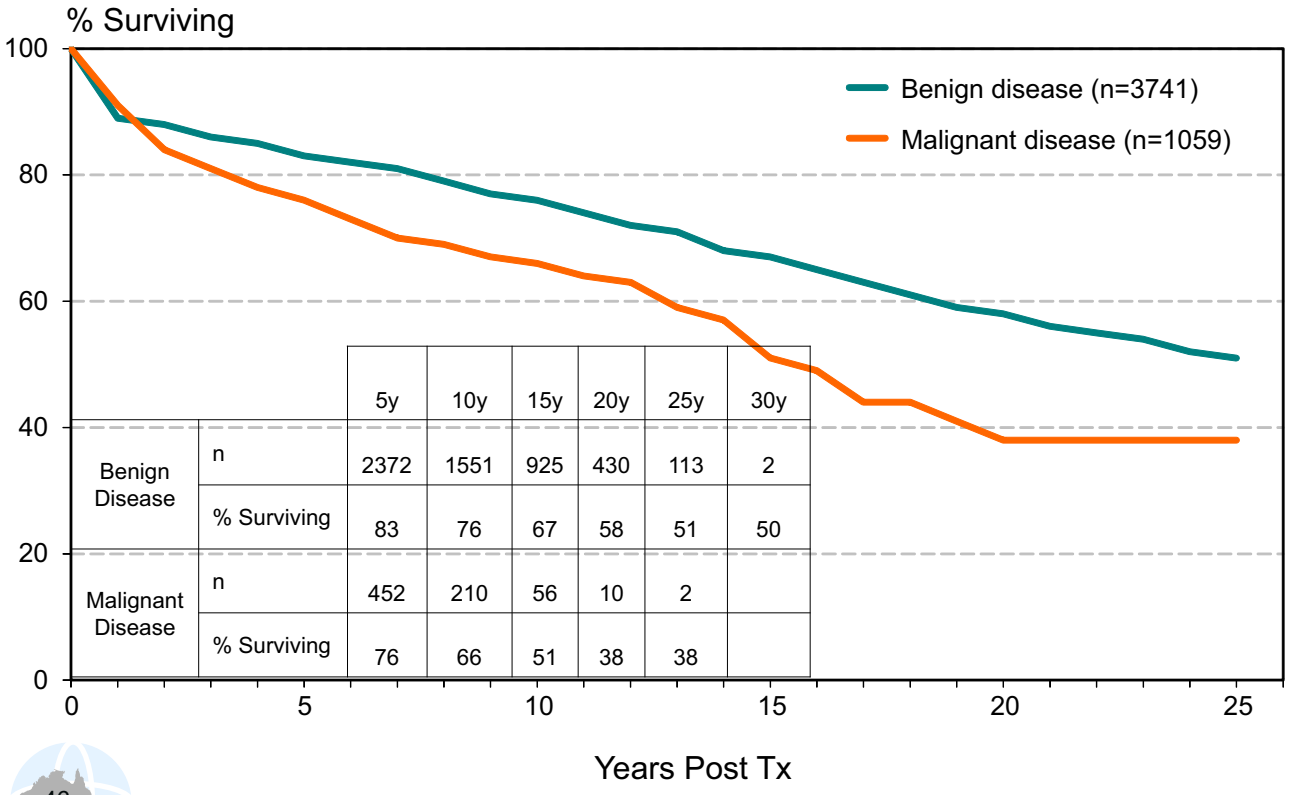
Liver Cancer (Primary or Secondary Diagnosis) n = 1059/4800 (22%)

n = 1059/4800 (22%)

TYPE OF CA	No.	DIED	DIED OF THIS CA
HEPATOCELLULAR CA*	965	236	86 (9%)
CHOLANGIOCARCINOMA*	41	32	20 (49%)
HEPATOBLASTOMA*	28	6	4 (14%)
FIBROLAMELLAR	10	5	2 (20%)
CARCINOID	4	4	4 (100%)
ADENOCARCINOMA	5	4	1 (20%)
EPITHELOID HAEMANGIOENDOTHELIOMA	6	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%)
HEPATOCELLULAR MALIGNANT NEOPLASM (NOS*)	1	0	0
TOTALS	**1059* Ca in 1065 pts (22% of pts)**	**292 (28%of those with Ca)**	**122 (12% of those with Ca at Tx)**

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

Patient Actuarial Survival Benign Disease vs Pre Transplant Liver Malignancy n = 4800



		5y	10y	15y	20y	25y	30y
Benign Disease	n	2372	1551	925	430	113	2
	% Surviving	83	76	67	58	51	50
Malignant Disease	n	452	210	56	10	2	
	% Surviving	76	66	51	38	38	

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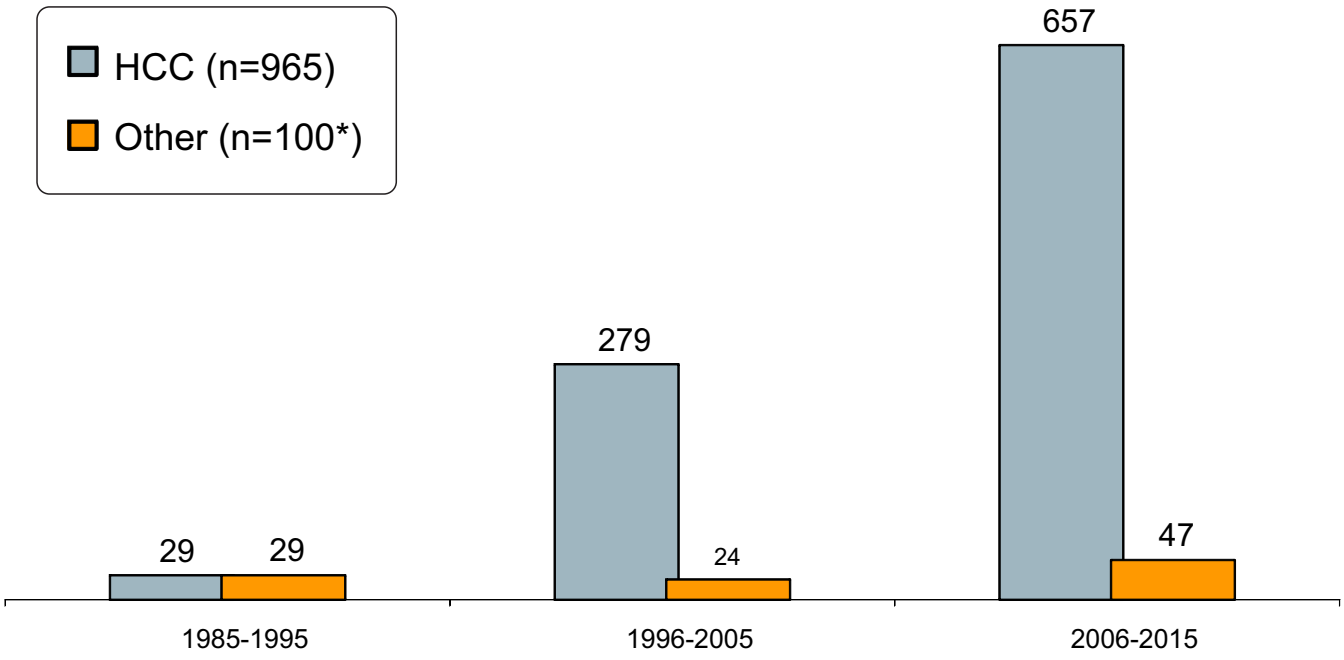
Liver Cancer at Transplantation
n = 1059/4800 (22%)



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

De Novo Non - Skin Cancer
n = 351/4800 (7%)

	No	Male	Female	Age of pts (yrs)	Time to diagnosis (mths)	Died of This Cancer
Alimentary*	137	101	36	13 – 83 (m 59)	3 – 277 (m 77)	61 (45%)
Lymphoma*	95	54	41	1– 70 (m 49)	1 – 283 (m 60)	35 (37%)
Genitourinary*	57	36	21	21 – 82 (m 61)	2 – 350 (m 73)	5 (9%)
Breast	27	-	27	30 – 74 (m 55)	11 – 282 (m 98)	10 (37%)
Respiratory	35	28	7	29 – 75(m 60)	7 – 213 (m 90)	26 (74%)
Endocrine	10	5	5	36 – 70 (m 56)	35 – 214 (m 82)	3 (30%)
CNS	7	5	2	16 – 75 (m 66)	14– 212 (m 93)	6 (86%)
Kaposi's	5	4	1	32 – 65 (m 48)	2 – 49 (m 17)	0
Leukaemia	4	2	2	3 – 66 (m 43)	16 – 157 (m 37)	0
Miscellaneous	5	2	3	62 – 73 (m 68)	61 – 235 (m 121)	1 (20%)
Total	***382 ca in 351 pts**	**237**	**145**	**1 – 83 (m 58)**	**1 – 350 (m 72)**	**147 (42% of pts with Ca)**

*** 29 patients had more than 1 de novo cancer**

m=median

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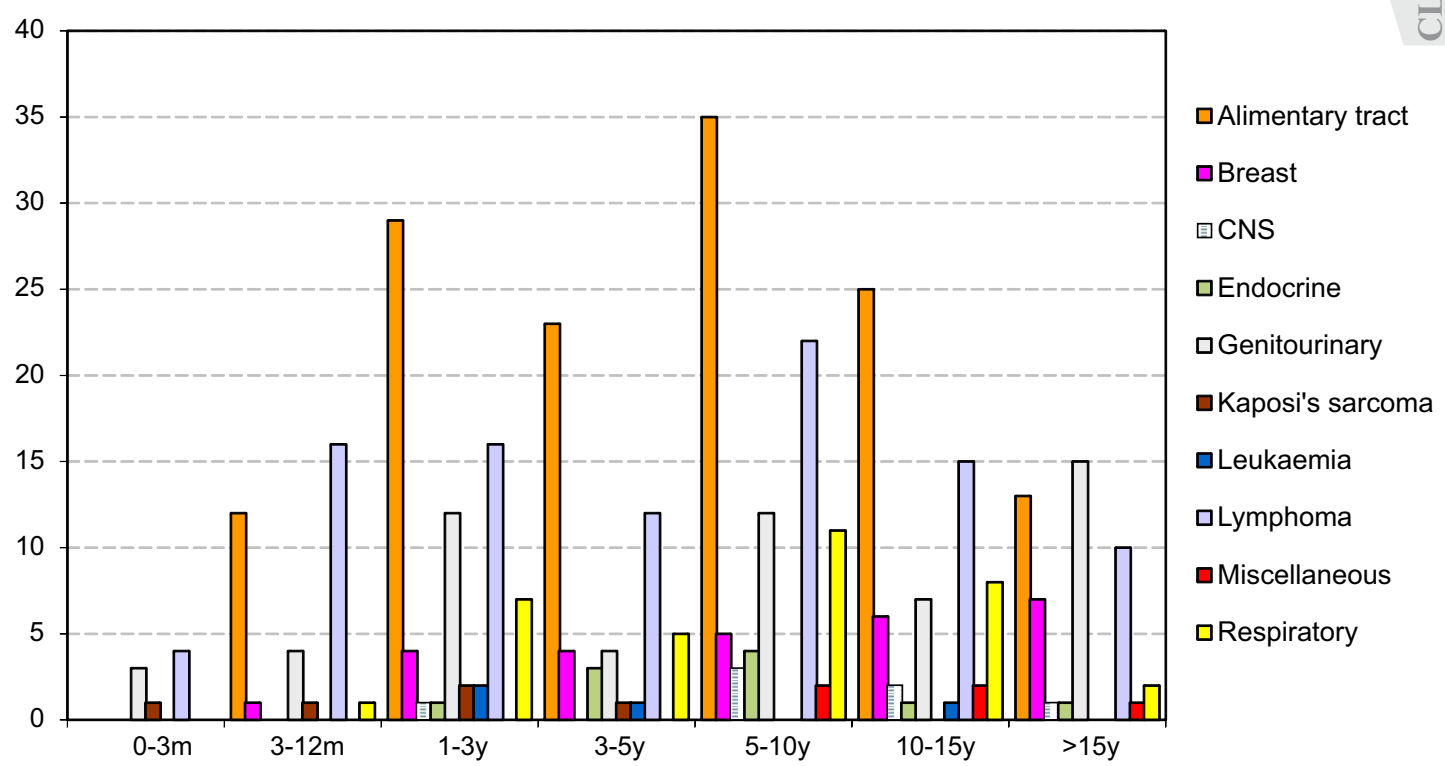
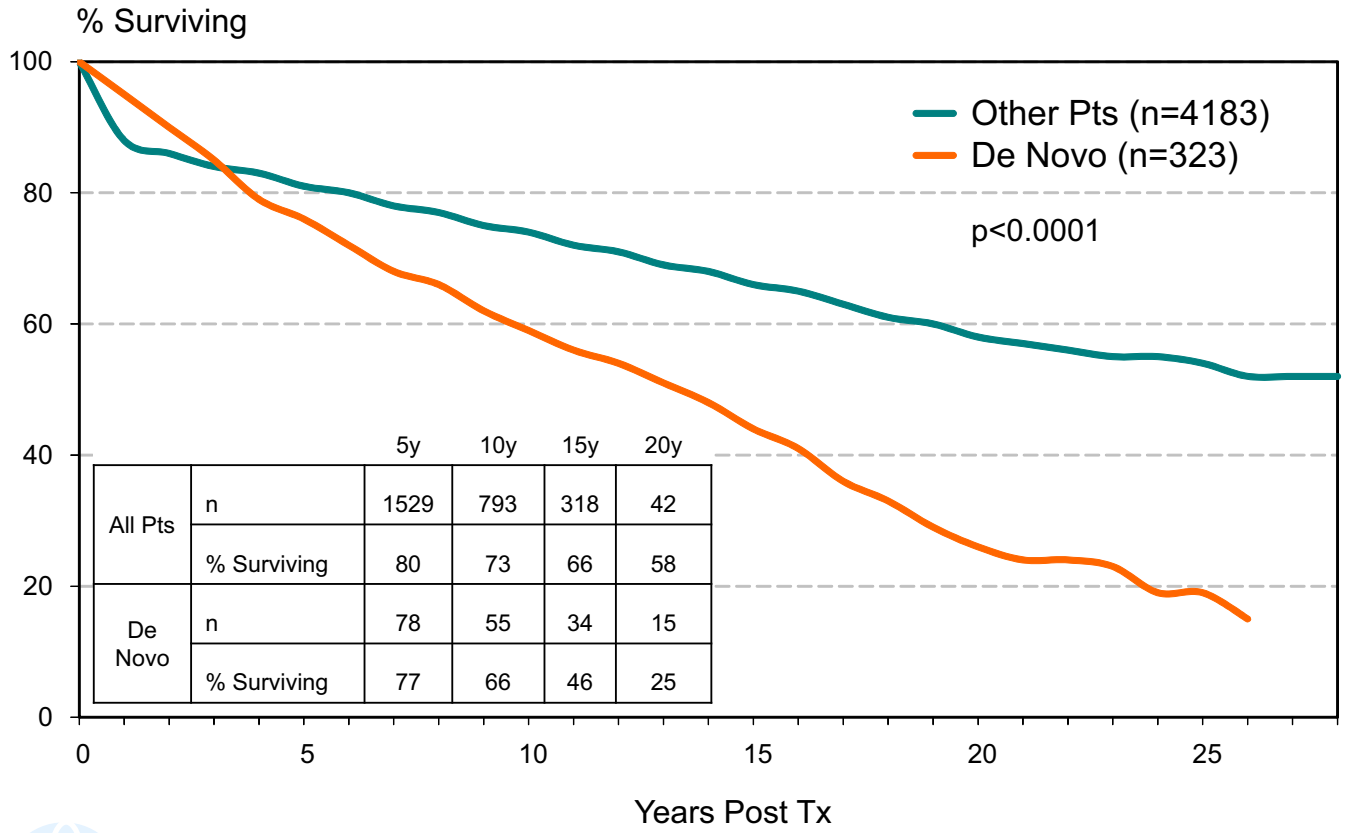
Time to De Novo Non - Skin Cancer
n = 4800
382 cancers in 351 pts (7% of all pts)



De Novo Non - Skin Cancer vs All Patients
n =4800



		5y	10y	15y	20y
All Pts	n	1529	793	318	42
	% Surviving	80	73	66	58
De Novo	n	78	55	34	15
	% Surviving	77	66	46	25

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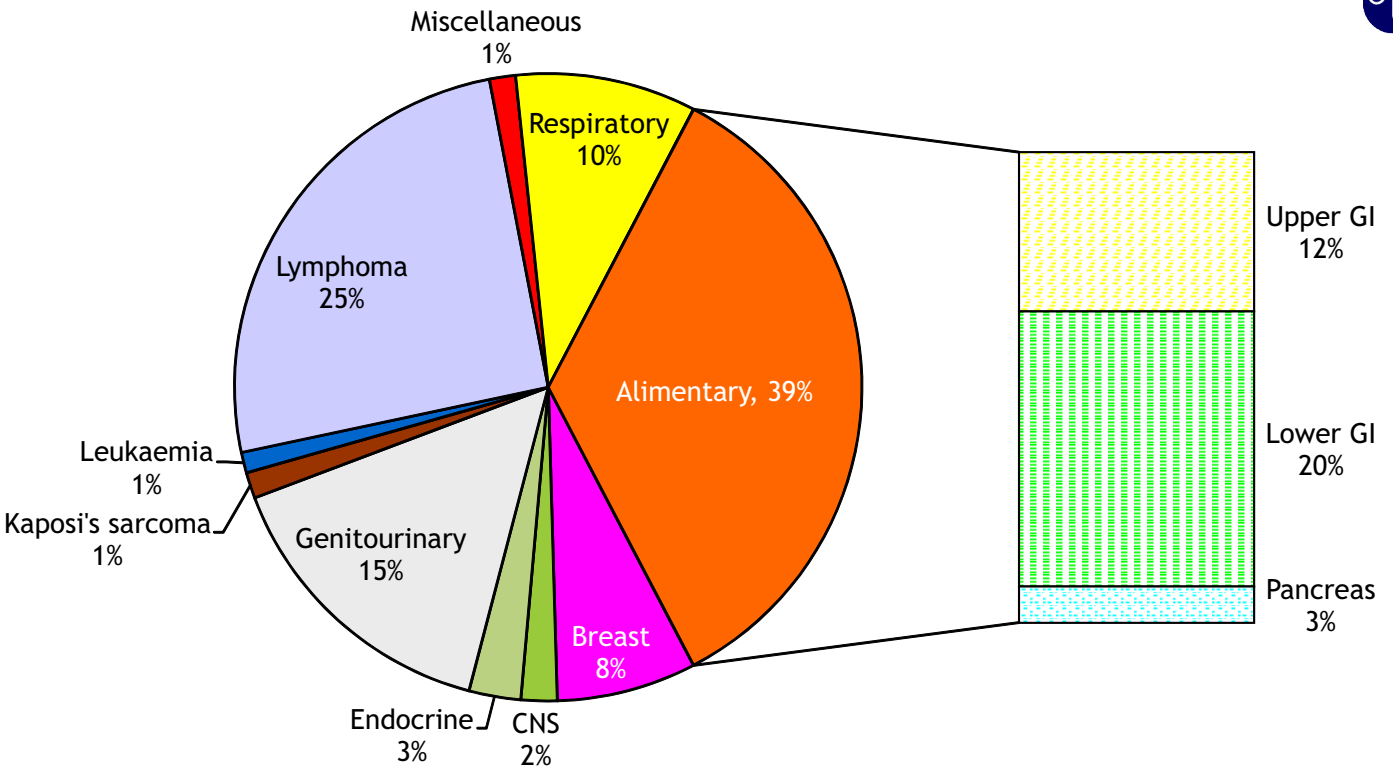
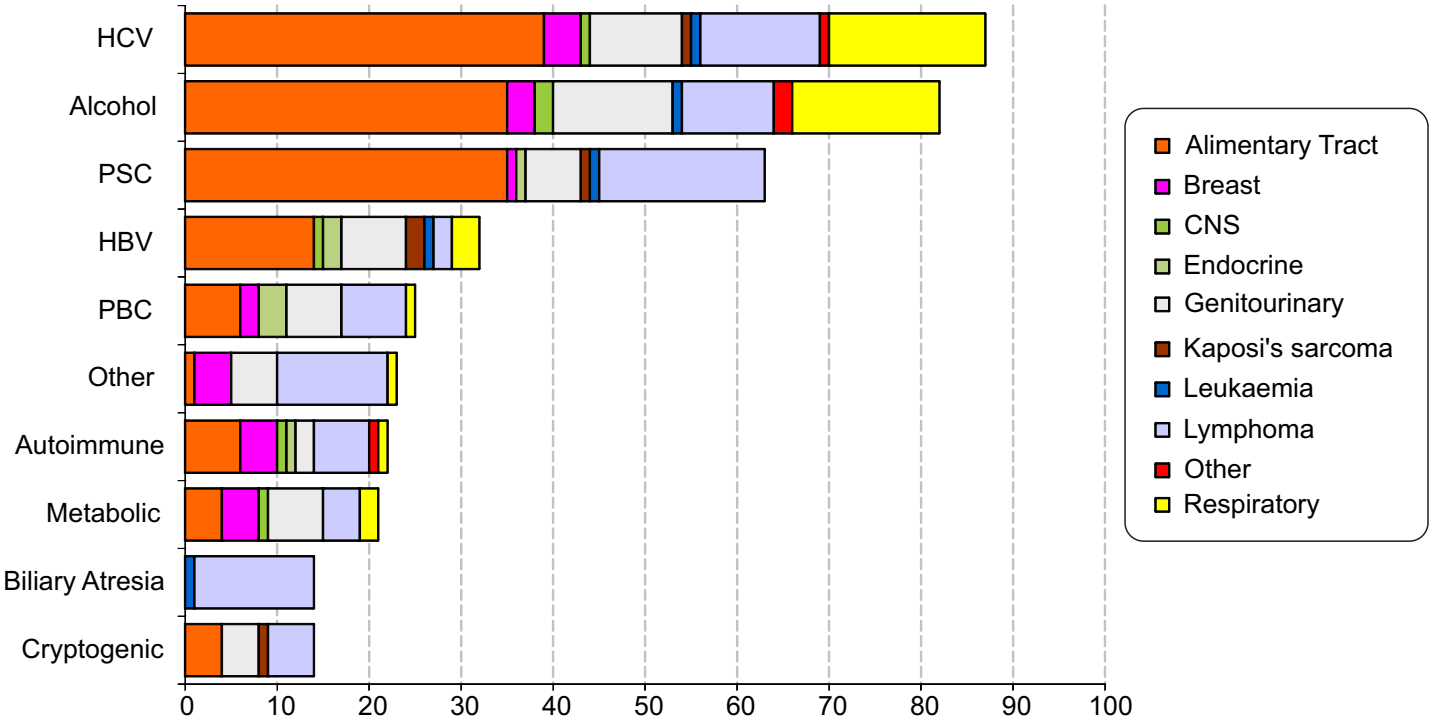
De Novo Non - Skin Cancer
n = 351/4800 (7%)



Pre Transplant Liver Disease and De Novo Non - Skin Cancer
n = 351/4800 pts (7%)



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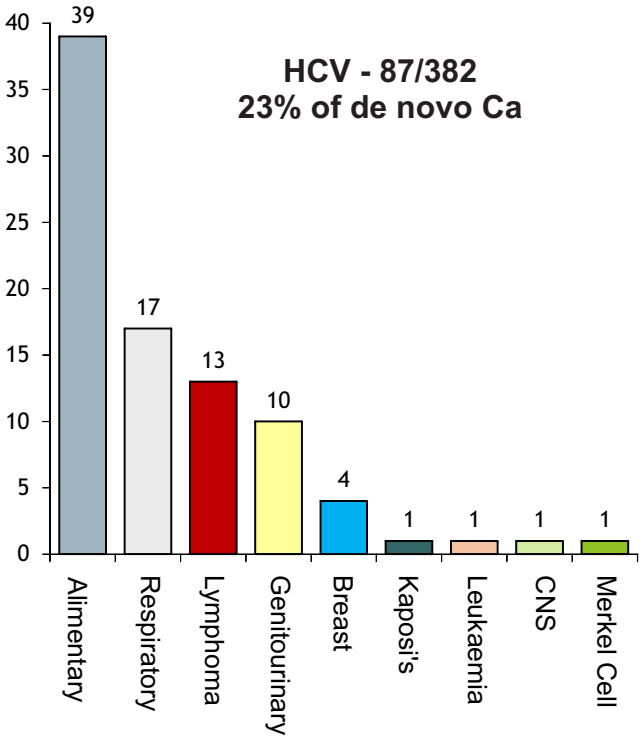
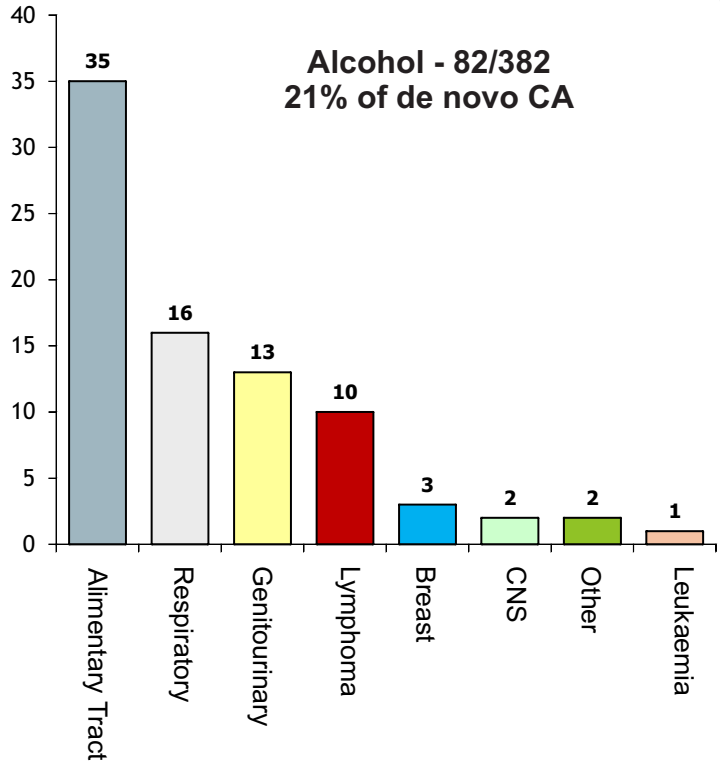
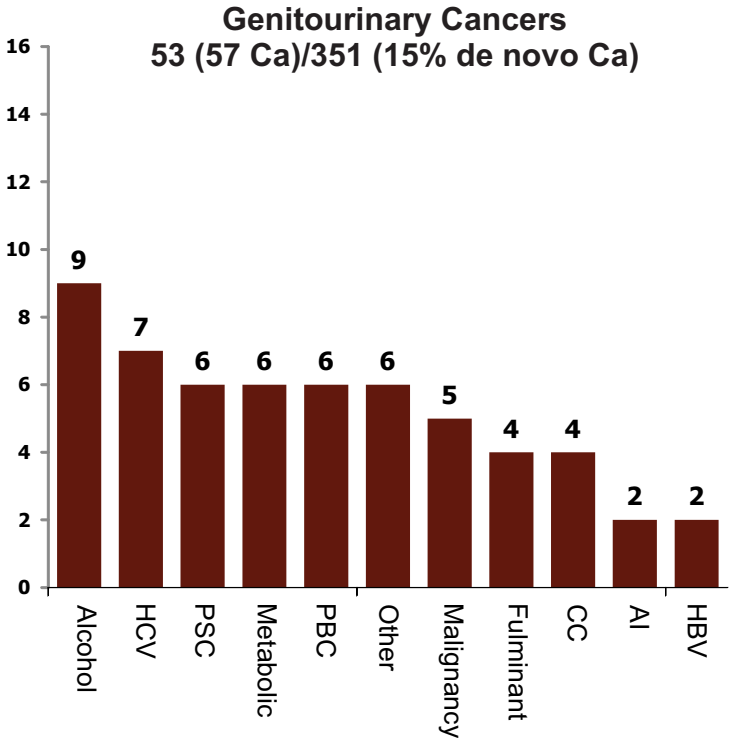
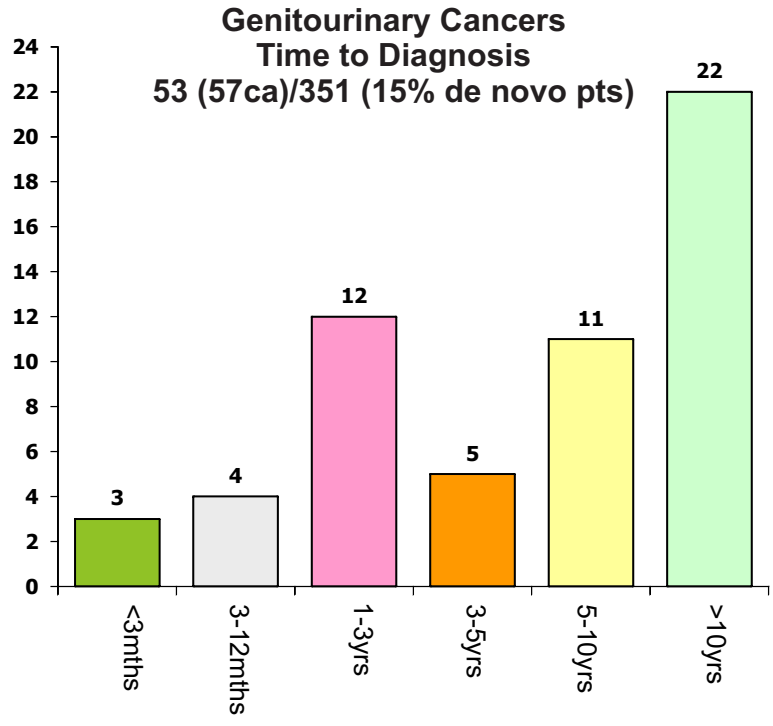
Pre Transplant Primary Disease and De Novo Non - Skin Cancer n = 323 (352 Ca)/4506 pts (7%)





Pre Transplant Primary Liver Disease and De Novo Non - Skin Cancer n = 351 (382 Ca)/4800 pts (7%)





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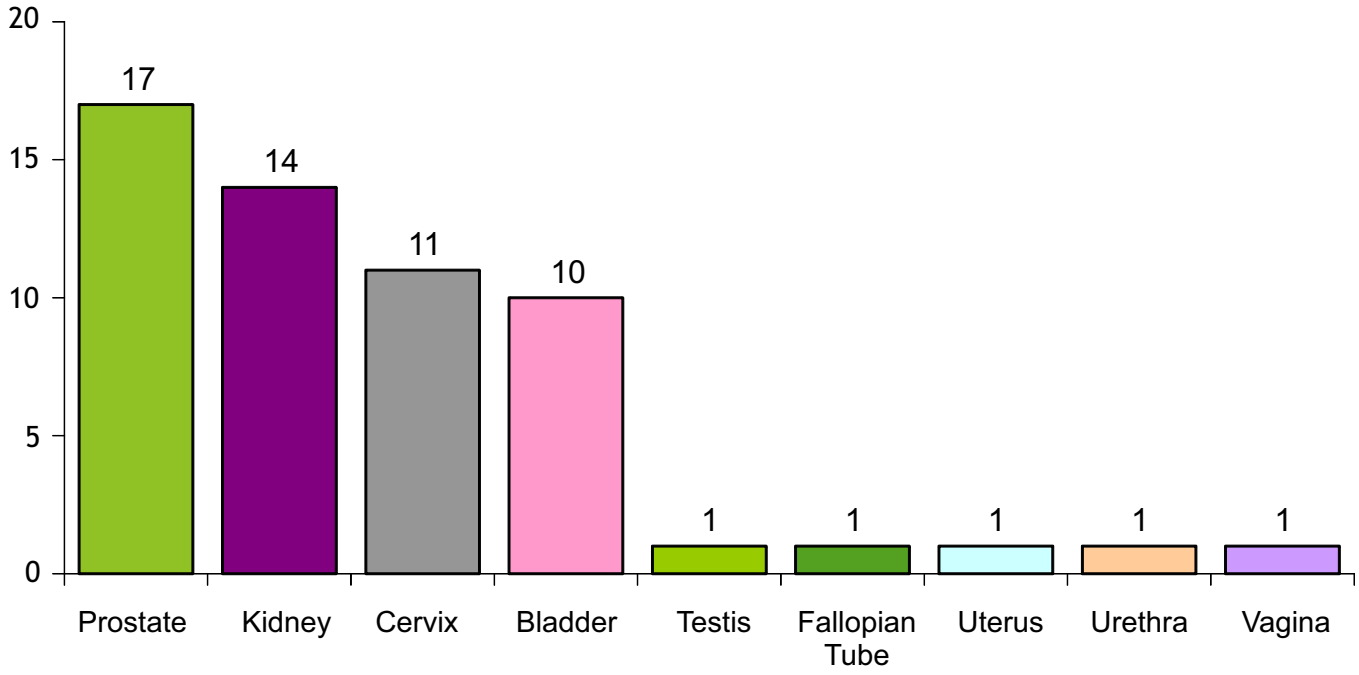
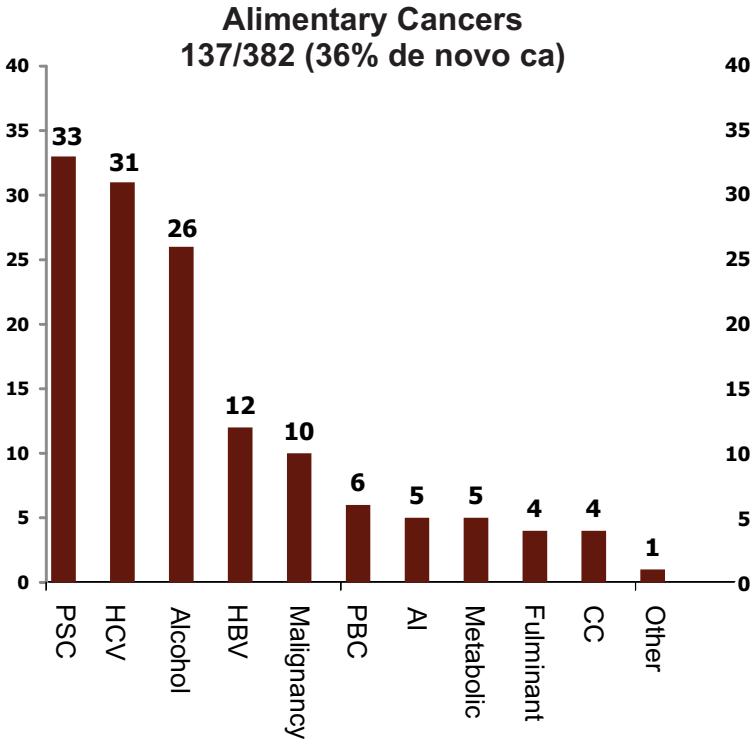
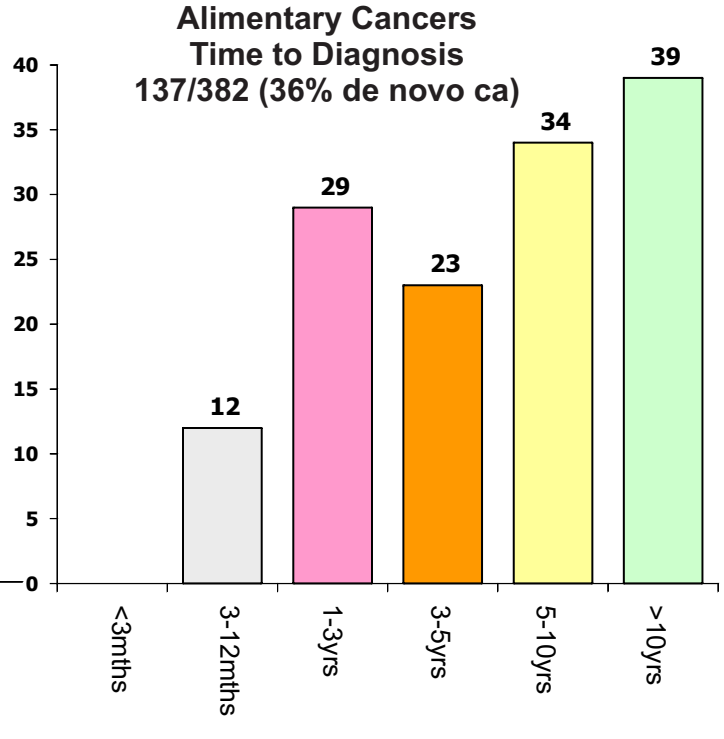
De Novo Non - Skin Cancer Genitourinary Tract Incidence n = 57/382 cancers (15%)



Pre Transplant Primary Disease and De Novo Non - Skin Cancer n = 351 (382 Ca)/4800 pts (7%)





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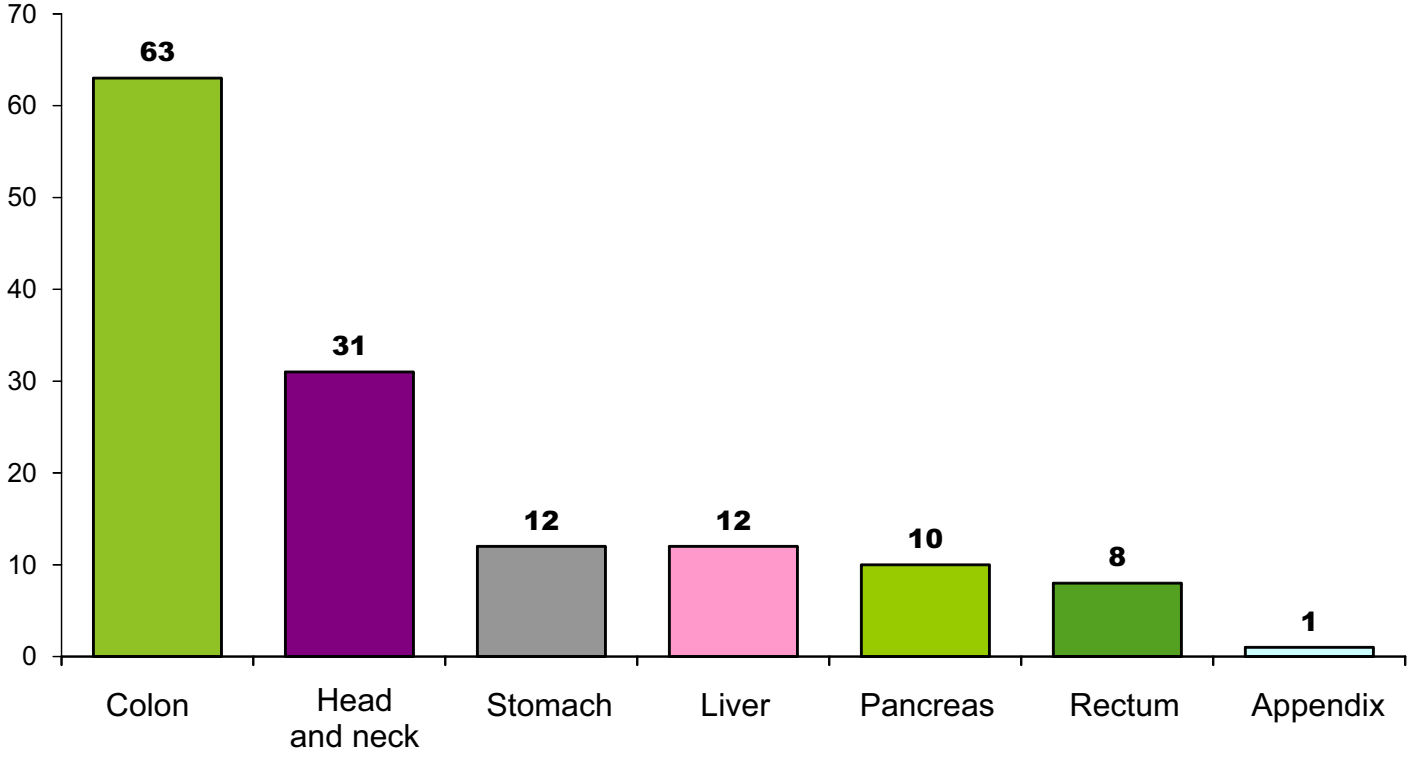
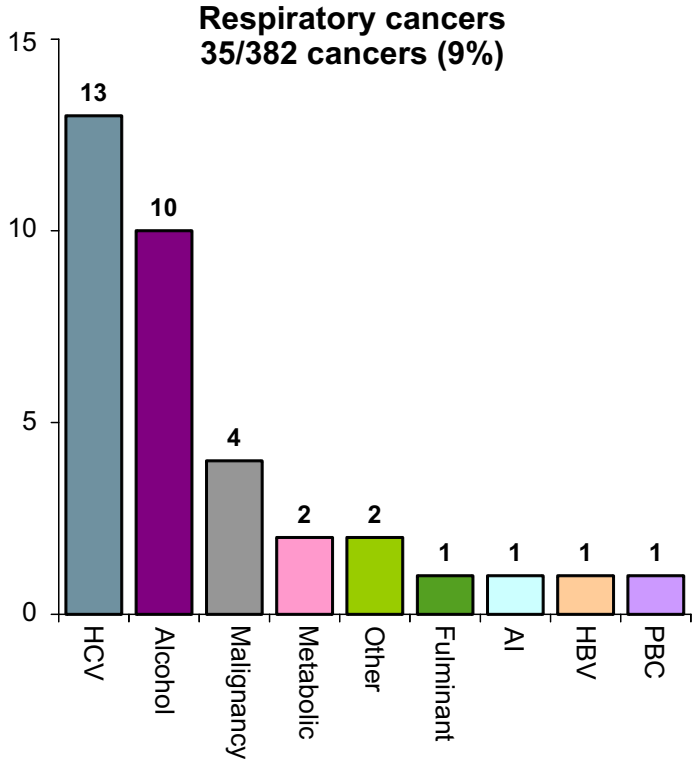
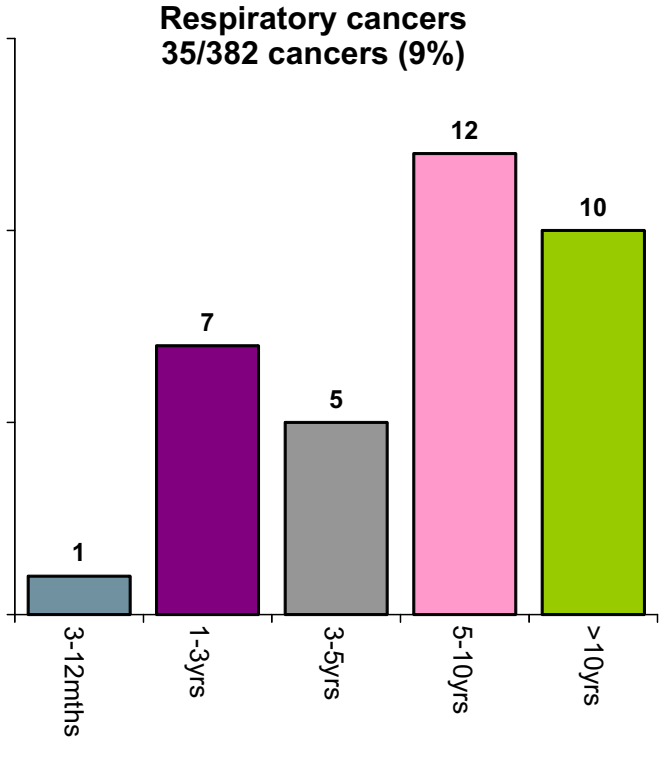
De Novo Non - Skin Cancer Alimentary Tract Incidence n = 137/382 cancers (36%)



De Novo Non Skin Cancer Respiratory Cancer Incidence





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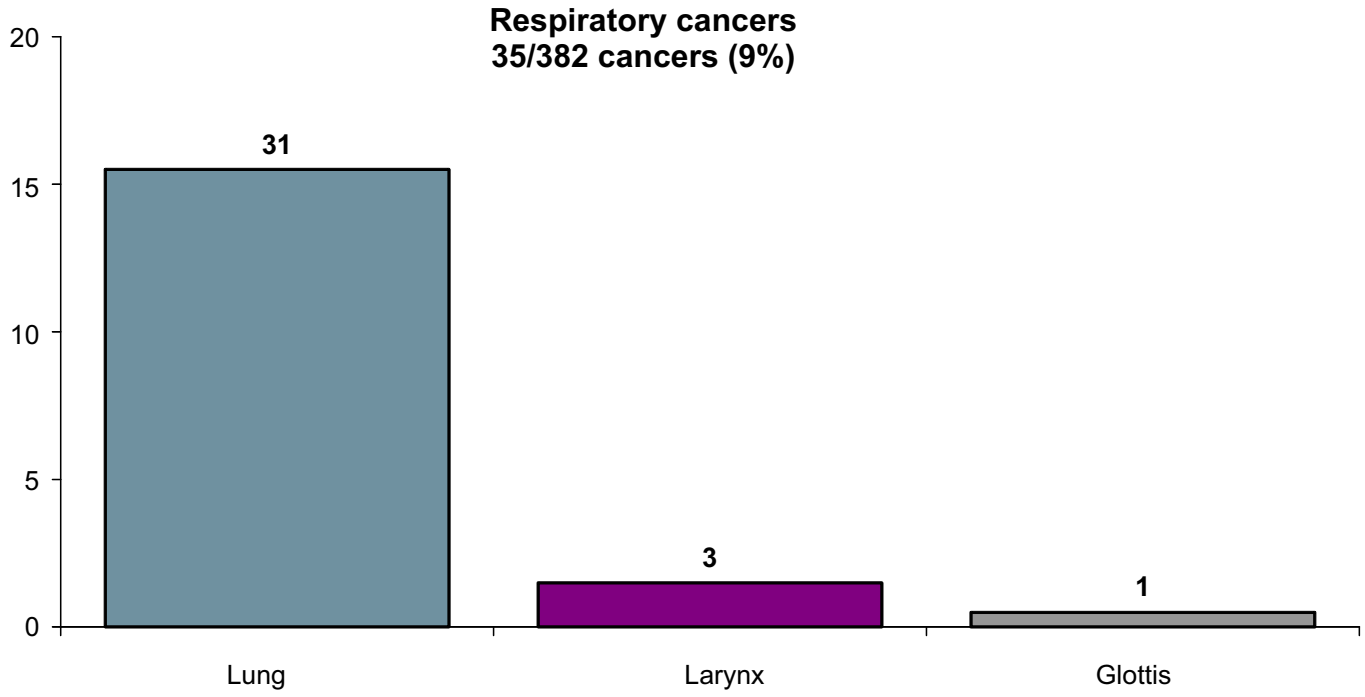
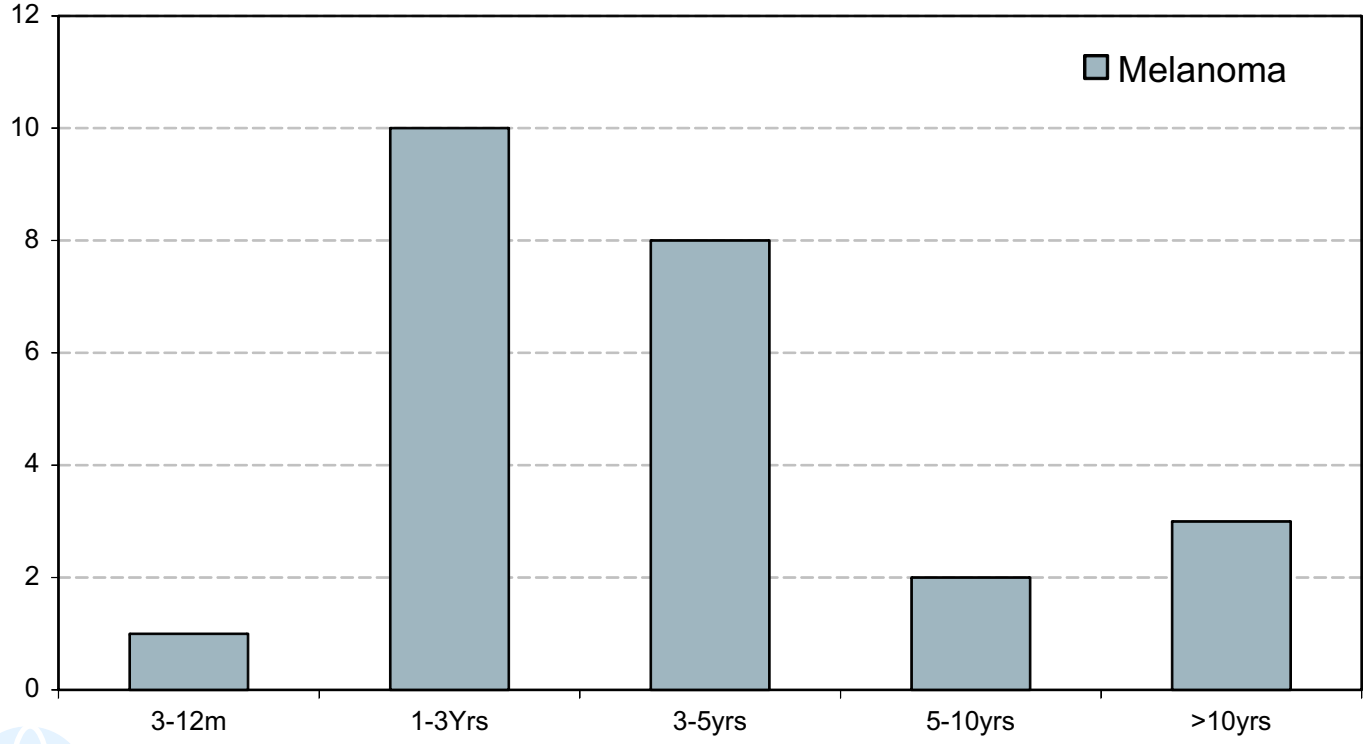
De Novo Non Skin Cancer
Respiratory Cancer Incidence



Time to Melanoma Skin Cancer Development Post Tx.
n =4800
37 (0.8% of all pts)



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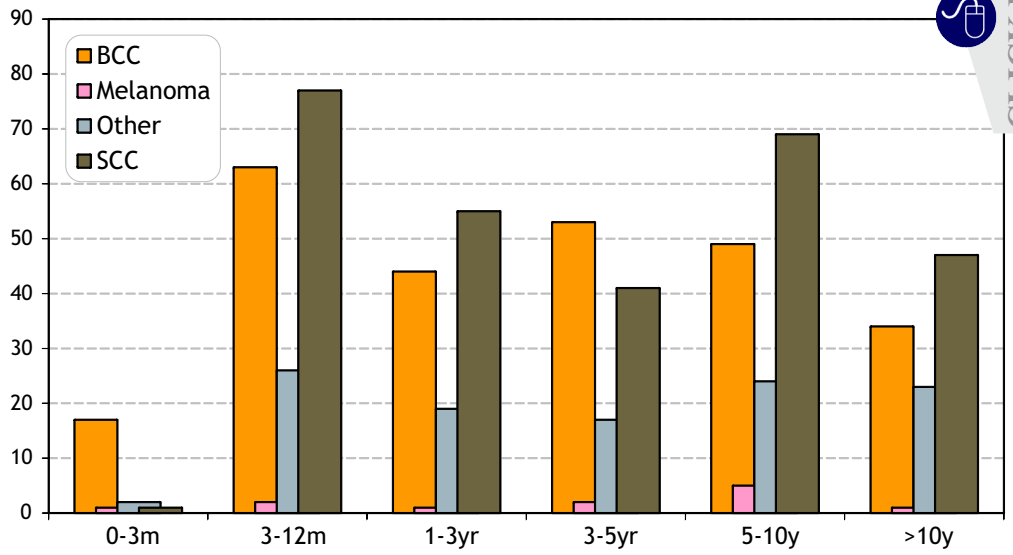
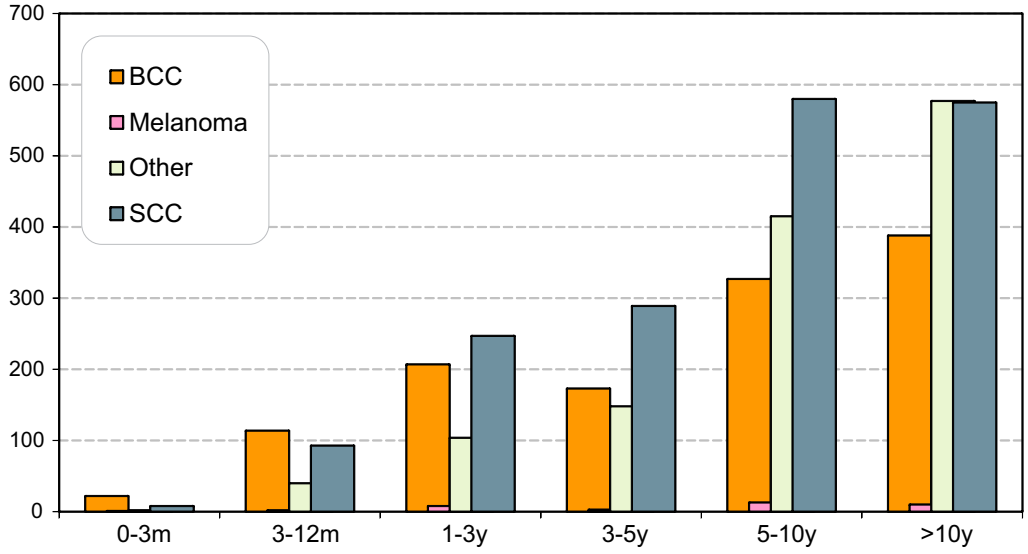
Time to 1st Skin Cancer Development
673/4800
(14% of all pts)

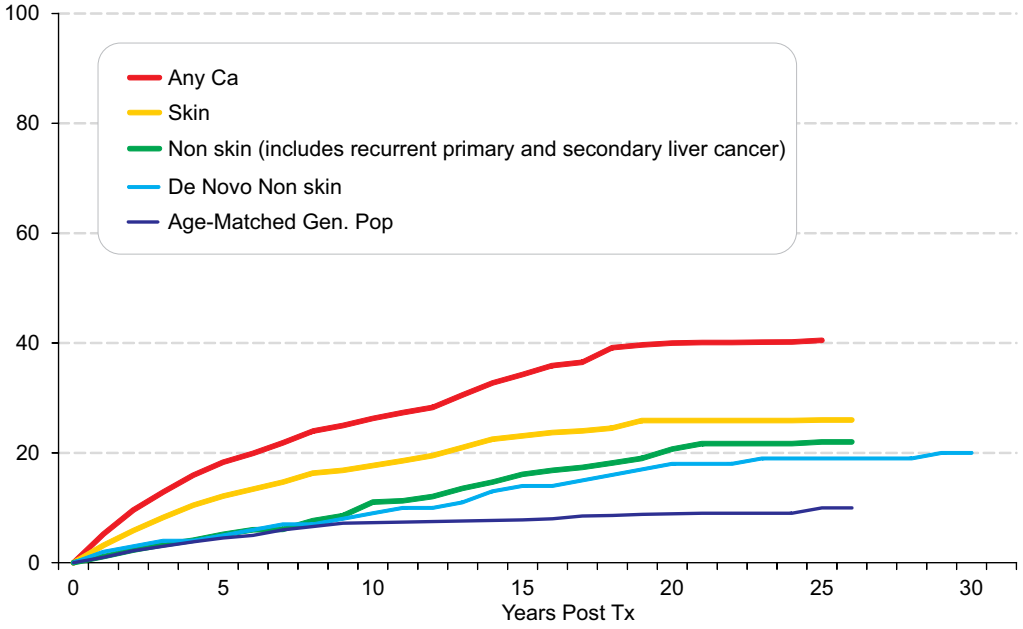


Time to Multiple Skin Cancer Development
324/677*/4800
(7% of all pts)



677 pts developed skin cancer post Tx. 324 have multiple skin cancer types.

Cumulative Risk of Diagnosis of Cancer Following Liver Tx. 1985-2015
Patients at Risk (4800)



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Appendix I

Liver Transplant Units of Australia and New Zealand

Australian National Liver Transplant Unit
Royal Prince Alfred Hospital
Missenden Road
CAMPERDOWN NSW 2050
Email: 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

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Appendix II

ANZLTR PRIMARY Diagnosis
Metabolic disorders by Age Group

Primary Diagnosis	Age group		Total
	Child	Adult	
α -1 Antitrypsin deficiency	39	51	**90**
Crigler-Najjar	10	1	**11**
Familial amyloid polyneuropathy	0	35	**35**
Glycogen storage disease	4	6	**10**
Haemochromatosis	3	29	**32**
Homozygous Hypercholesterolemia	7	2	**9**
Idiopathic copper toxicosis	1	0	**1**
Indian childhood cirrhosis	1	0	**1**
Other*	13	7	**20**
Primary hyperoxaluria	9	8	**17**
Tyrosinemia	5	0	**5**
Urea cycle disorders**	20	4	**24**
Wilsons disease	8	30	**38**
Total	**120**	**173**	**293**

* *Maple syrup urine disease 4*
Amyloidosis 2
Bile acid Transport disorder 2
Protein C deficiency 2
Propionic acidemia 3
Methylmalonic acidemia 2
Familial immunodeficiency
Mitochondrial disease
Porphyria 3

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

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Appendix III

ANZLTR PRIMARY Diagnosis - Other by Age Group

Primary Diagnosis	Age group		Total
	Child	Adult	
Alagille syndrome	31	7	**38**
Alagille non-syndromic	2	0	**2**
Benign liver tumour - Adenomatosis	0	2	**2**
Benign liver tumour - Hemangioma	0	4	**4**
Caroli's disease / congenital hepatic fibrosis	2	21	**23**
Choledocal cyst	2	2	**4**
Cholestatic disease-Other	4	10	**14**
Chronic Budd Chiari	1	32	**33**
Congenital biliary fibrosis	0	2	**2**
Ductopenia	1	3	**4**
Granulomatous hepatitis / sarcoidosis	0	4	**4**
Histiocytosis X	5	1	**6**
Liver Trauma	0	1	**1**
Neonatal hepatitis	4	0	**4**
Nodular regenerative hyperplasia	0	6	**6**
Polycystic Liver disease	0	22	**22**
Polycystic liver and kidney disease	2	15	**17**
Progressive familial intrahepatic cholestasis(PFIC)	22	5	**27**
Secondary biliary cirrhosis	3	16	**19**
Secondary biliary cirrhosis - Hepatolithiasis	0	4	**4**
Secondary biliary cirrhosis - Cystic fibrosis	13	21	**34**
Other - specify[#]	15	26	**41**
Total	107	204	**311**

*Vanishing bile duct syndrome*
Haemangiotelangiectasia
Veno-occlusive disease
Chronic Active Hepatitis A
Non-cirrhotic portal hypertension
Kassabach-Merritt syndrome
Arterial-venous malformation
Hereditary haemorrhagic telengectasia / OWRD
Oriental cholangio hepatitis
COACH syndrome
Biliary sclerosis
Cornelia De Lange Syndrome
Hepatic Lymphangiomatosis

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Appendix IV

ANZLTR PRIMARY Diagnosis
Fulminant Hepatic Failure by Age Group

Primary Diagnosis	Age group		Total
	Children	Adult	
Acute - Budd Chiari	0	2	**2**
Acute - Wilson's	8	17	**25**
Acute - α-1 -AAT	2	0	**2**
Acute Autoimmune hepatitis	0	8	**8**
Acute Unknown / unspecified	47	95	**142**
Acute - Paracetamol	4	18	**22**
Acute - Other drugs	3	26	**29**
Acute Herbs / mushrooms	1	11	**12**
Acute - Hepatitis A	1	3	**4**
Acute - Hepatitis B	0	66	**66**
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	5	**7**
Subacute Autoimmune hepatitis	2	18	**20**
Subacute - Drug / Herbs	1	15	**16**
Subacute - Unknown / unspecified	5	32	**37**
Subacute - Hepatitis A	0	2	**2**
Subacute - Hepatitis B	0	20	**20**
Subacute - Non A-G	0	4	**4**
Total	**90**	**369**	**459**

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Appendix V

ANZLTR Causes of Patient death

Graft failure - other	Age group		Total
	Children	Adult	
Vascular thrombosis	8	16	24
Hepatic artery	*4*	*9*	*13*
Portal vein	*2*	*7*	*9*
Hepatic vein	*2*	*-*	*2*
Non thrombotic infarction	3	-	3
Primary non function	4	18	22
Massive haemorrhagic necrosis	4	0	4
Recurrent disease *(ALD, PSC, CAH:AI)*	-	22	22
De novo Hep C	-	2	2
Biliary Complications	3	12	15
Other *(PNC, immune hepatitis, outflow obstruction)*	8	17	25
TOTAL	30	87	117

Miscellaneous	Children	Adult	
Multiorgan failure	10	88	98
Renal Failure	1	36	37
Graft vs Host disease	-	6	6
Social *(accident, suicide,non-compliance, Rx withdrawn)*	1	18	19
Sudden death *(cause unknown)*	3	27	30
Other *(Hyperkalaemia,motor neurone disease diabetes complications, drug reaction, progression FAP essential thrombocythemia)*	3	35	38
TOTAL	18	210	228