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AUSTRALIA & NEW ZEALAND

LIVER TRANSPLANT REGISTRY

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

DATA TO 31-12-2013

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MANAGEMENT COMMITTEE

FUNDING

ANZLTR is funded by the Australian Organ and Tissue Authority.

CITATION

The suggested citation for this report is as follows:

ANZLT Registry Report 2014
Australia and New Zealand Liver Transplant Registry
Brisbane, QLD, AUSTRALIA
Editors: S.V. Lynch, G.A. Balderson

STATISTICAL METHODS

Kaplan-Meier survival curves have been produced using IBM SPSS® for Windows™ Release 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 25th Report of the Australia and New Zealand Liver Transplant Registry (ANZLTR). This report contains data to the 31st December 2013 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 2013, 4586 orthotopic liver transplants (OLT) were performed in Australia and New Zealand on 4244 patients, 3488 adult patients [82%] and 756 children (< 16 years) [18%]. The median age of all recipients was 47.9 years. The ages ranged from 24 days to 73.1 years. There is a significant difference in gender distribution between children (M=47%) and adults (M=65%)

6. Two hundred and sixty-four new patients were transplanted in 2013 compared with 246 in 2012.

7. The trend to increasing age of adult recipients in recent years continued and the overall adult median age is now 50.8 years. The median age of new adult recipients in 2010-13 was 54.0 years.

8-9. In 2013,16 more transplants were performed than in 2012 [284 vs 268]. Split grafts continue to make a significant contribution to the total number of paediatric transplants performed providing 22 of 46 [48%] grafts in 2013 and 219 of 858 [26%] overall. In children, other reduced size grafts have been used 379 [44%] cases including 67 living donor grafts. One child has been treated with liver cell implantation. Of adult patients, 266 have received reduced size grafts - 223 split liver grafts (including 1 as auxiliary graft), 29 other reduced size grafts (1 as auxiliary graft) and 14 living donor grafts. Including two domino transplant of a whole liver has been performed.

10-11. Overall, chronic viral hepatitis (CVH) is the most common primary indication for liver transplantation. In children biliary atresia (BA) is the most common primary disease. In adults chronic hepatitis C [CVH : HCV] is the primary disease in 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), Fulminant Hepatic Failure (Appendix IV).

12-15. The number of patients transplanted for non alcoholic fatty liver disease [NAFLD/NASH] continued to increase with 14 new patients transplanted in 2013 bringing the total to 95. 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 2010-13 compared with the previous eras, the number with a primary diagnosis of hepatocellular carcinoma [HCC] is higher at 13% with the majority of these patients having 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 2013 was 47%.

16. Overall 1 year patient survival of all patients is 89% at 1 year, 81% at 5 years and 73% 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 (60-65 and >65 years) had poorer longer term outcomes.

18-19. Patient survival in 2000-04 cohort shows 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 2010-13 cohort was 92% for all patients [92% for children, 92% 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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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 76% 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-one percent of all deaths occurred within 6 months of transplant. Early graft failure was due to poor or no early graft function. By 1 year malignancy and graft failure from recurrent disease or chronic rejection cause most deaths. 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 an increase in the number of cadaveric donors in 2013 with 279 grafts transplanted from deceased donors. The number of livers split to produce two transplantable grafts was 21 in 2013. Eleven liver grafts donated after cardiac death were transplanted. The number of people on the waiting list at 31 December 2013 was lower then the number on the waiting list at 31 December 2012.

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

36. Eighty-two patients [67 children, 15 adults] have now received a living donor graft with 5 performed in 2013. Seventy-six were transplanted as a primary graft, 5 as a second and 1 as a third graft. The median age of the donors was 33.8 years with a range of 20.1 to 54.5 years. Two adult grafts were domino whole liver graft.

37. Waiting list activity for 2013 shows the number of patients listed for transplantation continued to increase with 164 remaining on the waiting list at 31 December 2013. Patient delistings due to death, becoming too ill or tumour [HCC] progression accounted for 10% of all delistings while 284 [52%] were transplanted. Forty-eight patients were listed as urgent in 2013 [19 with initial listing as Category 1 and 29 Category 2]. Fourteen [74%] of Category 1 and 26 [89%] of Category 2 patients had a positive outcome.

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38-39. Median waiting times tended to be higher in 2013 in some blood groups. Blood group O 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 857 (20%) patients were transplanted who had a liver malignancy – 336 (8%) as a primary diagnosis and 521 (12%) as a secondary diagnosis or incidental tumour, with Hepatocellular Carcinoma being the most common. Post transplant 119 (14%) of these patients developed a recurrent cancer whilst in 118 (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 Cholangiocarinoma had significantly poorer survival.

46-51. Three hundred and thirty nine de novo non-skin types of cancer developed in 331 (8%) recipients. Twenty four 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 (121), Lymphoma (84) and Genitourinary (42).

The incidence of de novo non-skin cancers appears to be related to the type of pre-transplant underlying disease. Most notable is the incidence of de novo non-skin malignancy in patients with underlying Primary Sclerosing Cholangitis and HCV, both being statistically significant ($p<0.0001$).

51-52 Six hundred and ten patients (19%) developed 4055 skin cancers with 293 (5% of all pts) having multiple skin cancers and 30 developed Melanoma.

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

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Section 1

Demographic Data

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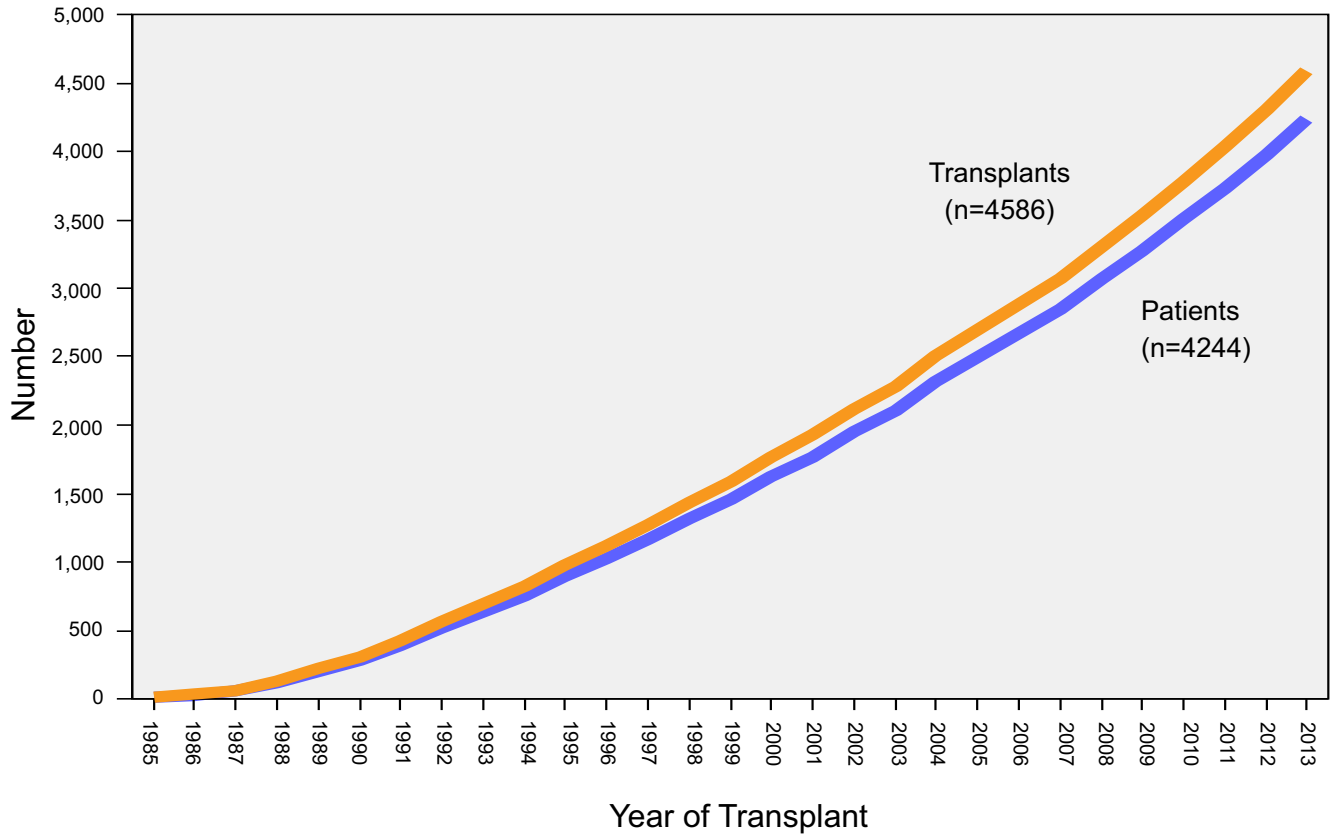
Cumulative Number of Patients & Transplants



Summary Statistics - Age and Gender

ALL PATIENTS TRANSPLANTED

	Children [<16y]	**Adults**	**Total**
Patients	756	3488	4244
Age			
Mean ± SD	4.5 ± 4.5y	48.7 ± 11.6y	40.8 ± 20.0y
Median	2.4y	50.8y	47.9y
Range	24d -15.9y	16.0 - 73.1y	24d - 73.1y
Gender			
Female	399 (53%)	1210 (35%)	1609 (38%)
Male	357 (47%)	2278 (65%)	2635 (62%)
Surviving	607 (80%)	2451 (70%)	3058 (72%)

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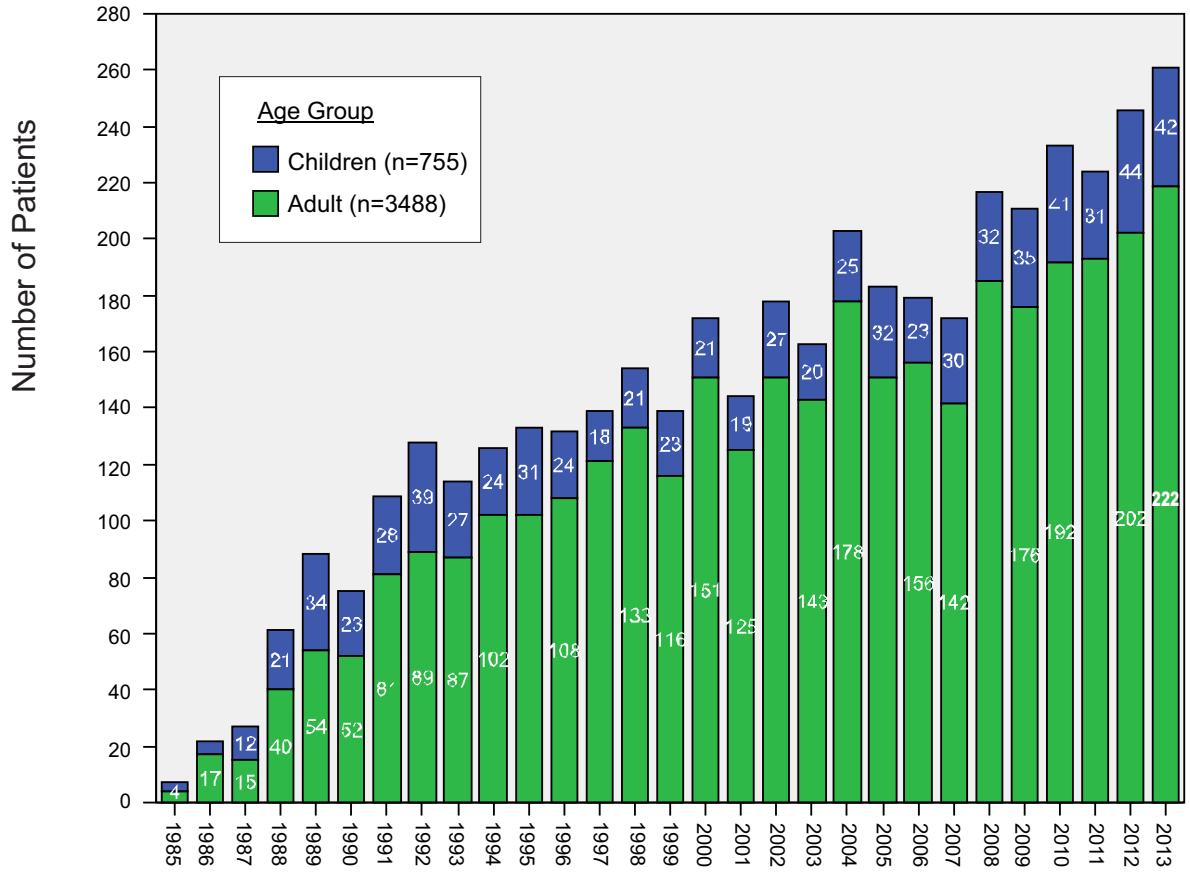
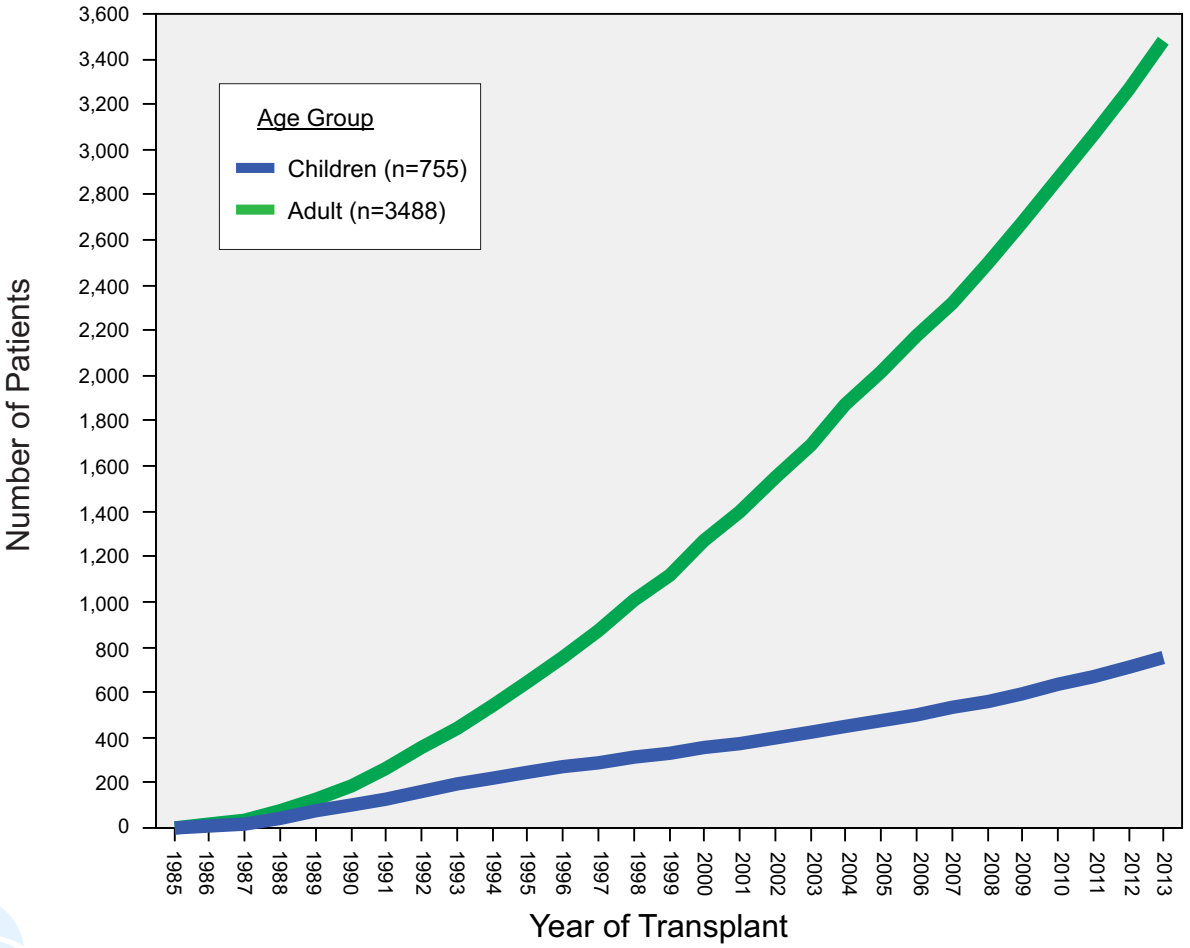
Number of New Patients Transplanted by Year



Cumulative Number of New Patients Transplanted



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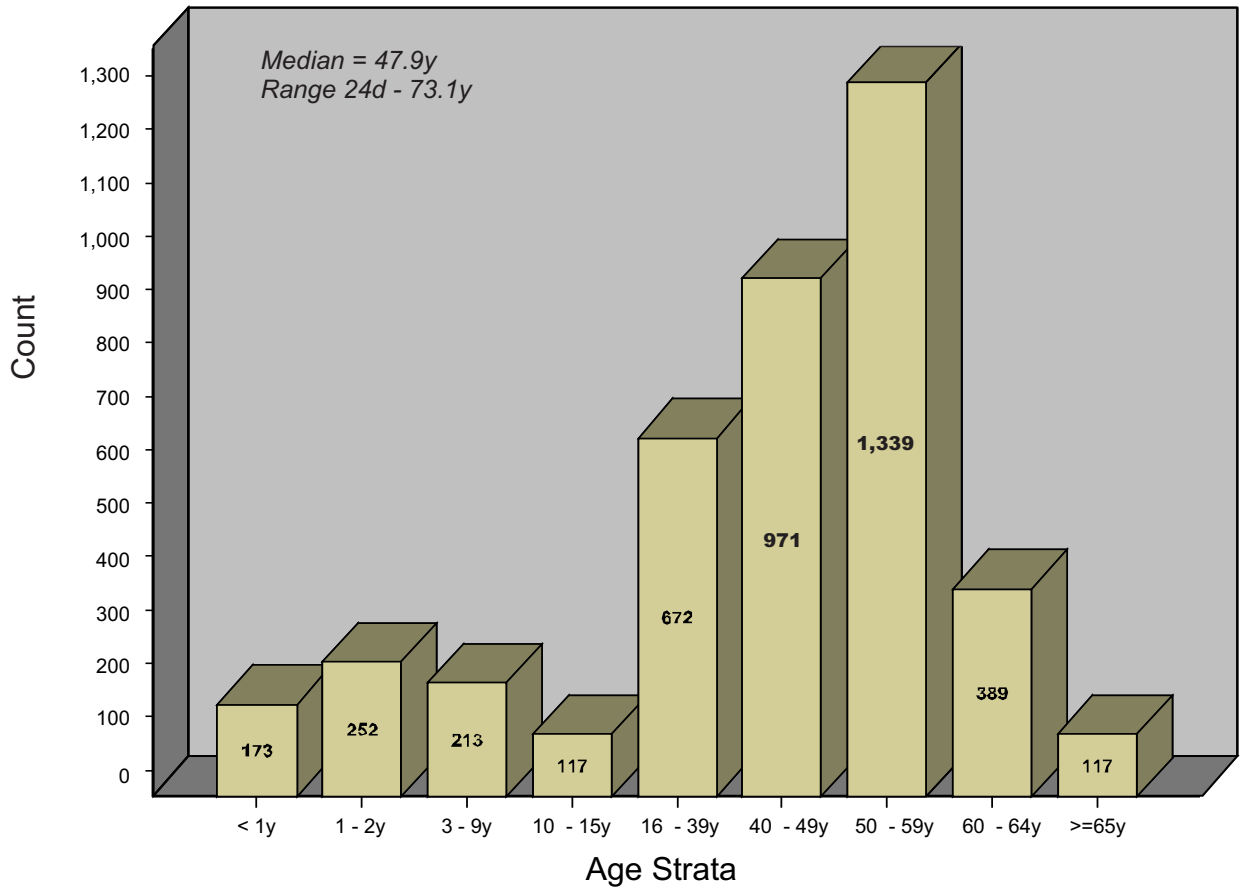
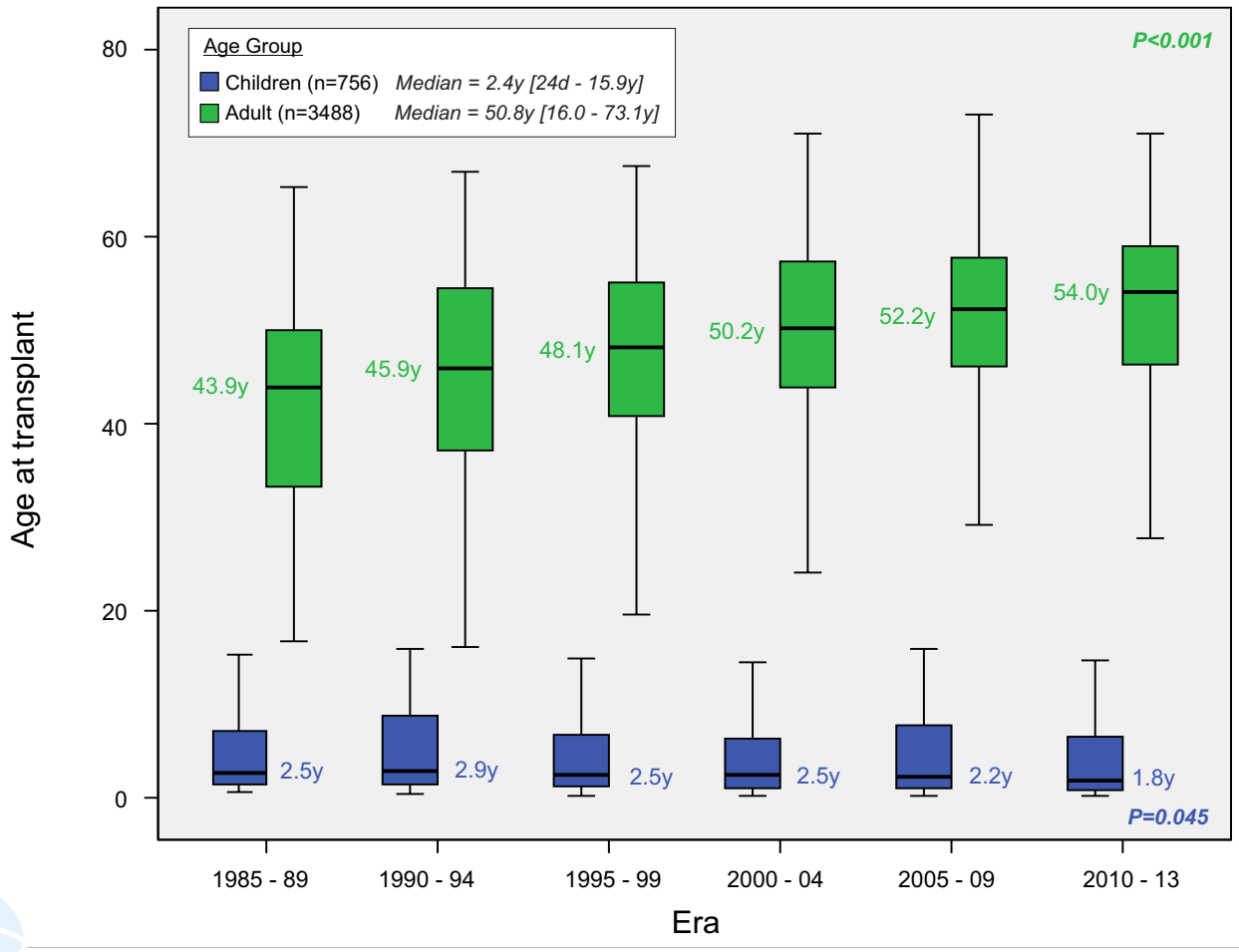
Number of Recipients By Age at Primary Transplant N=4244



Age at Primary Transplant by Era



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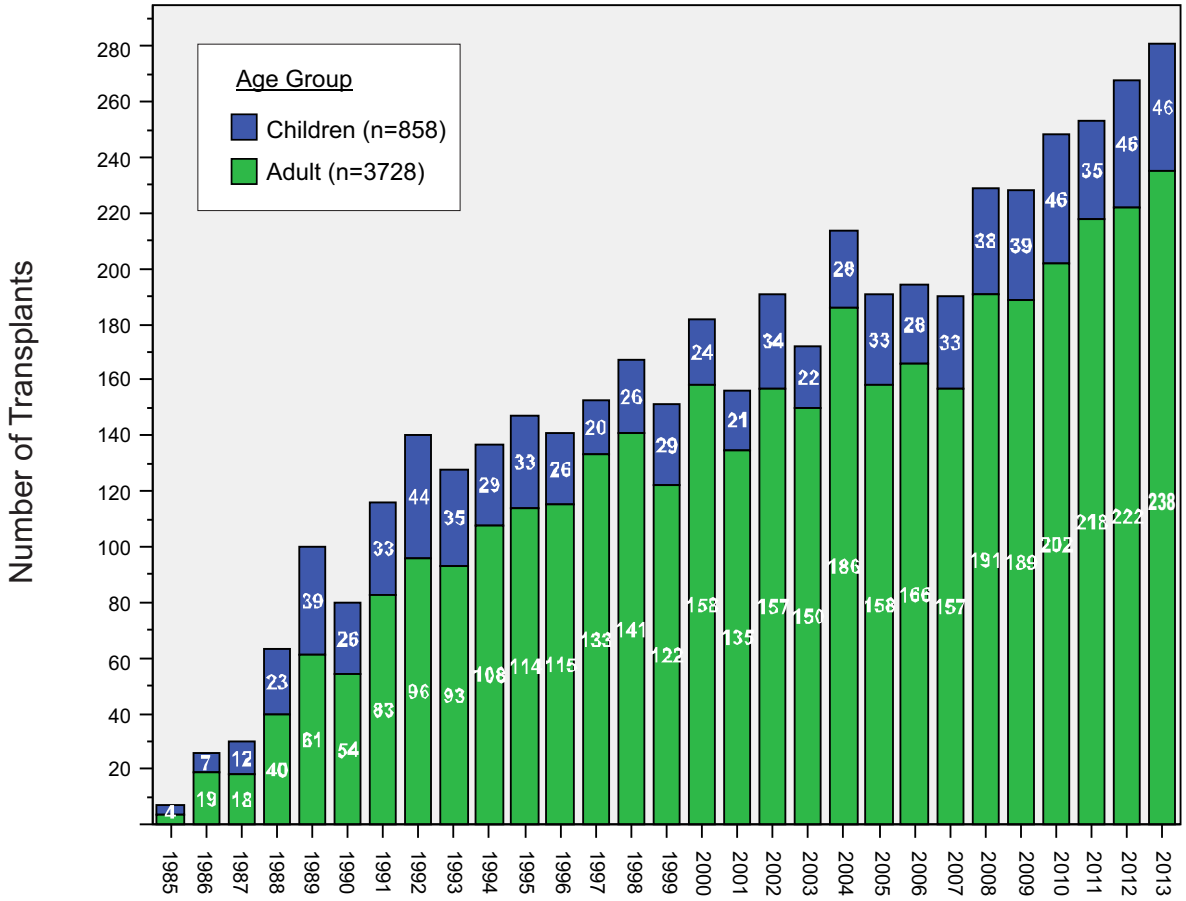
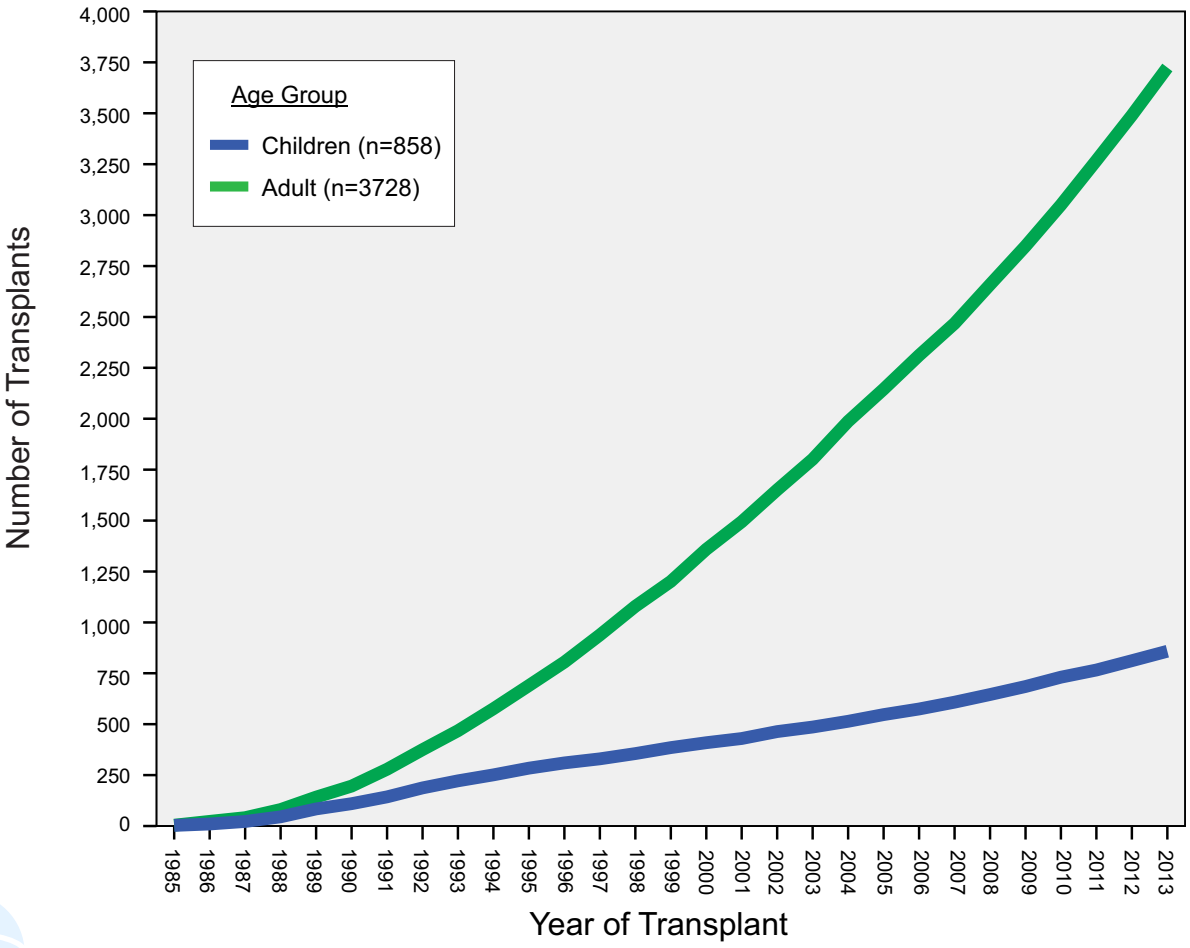
Number of Transplants by Year

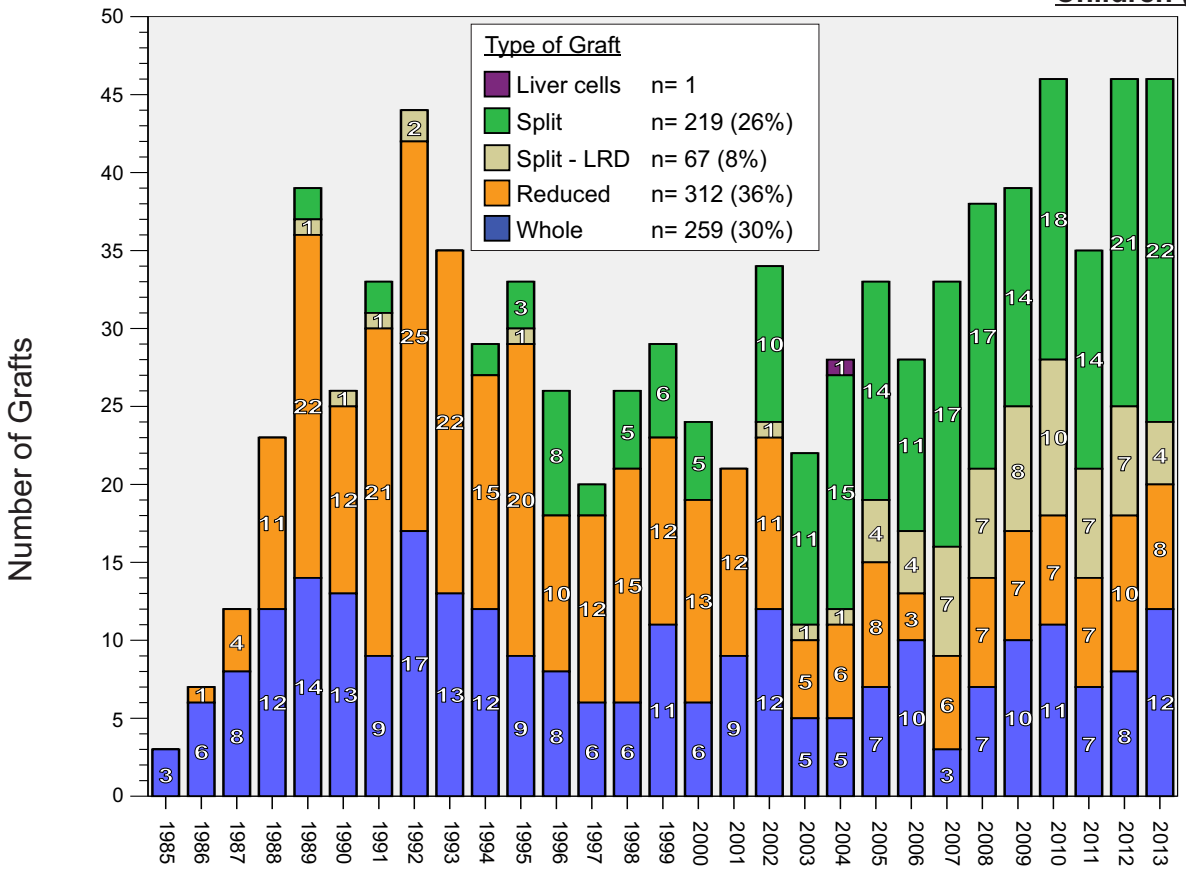


Cumulative Number of Transplants

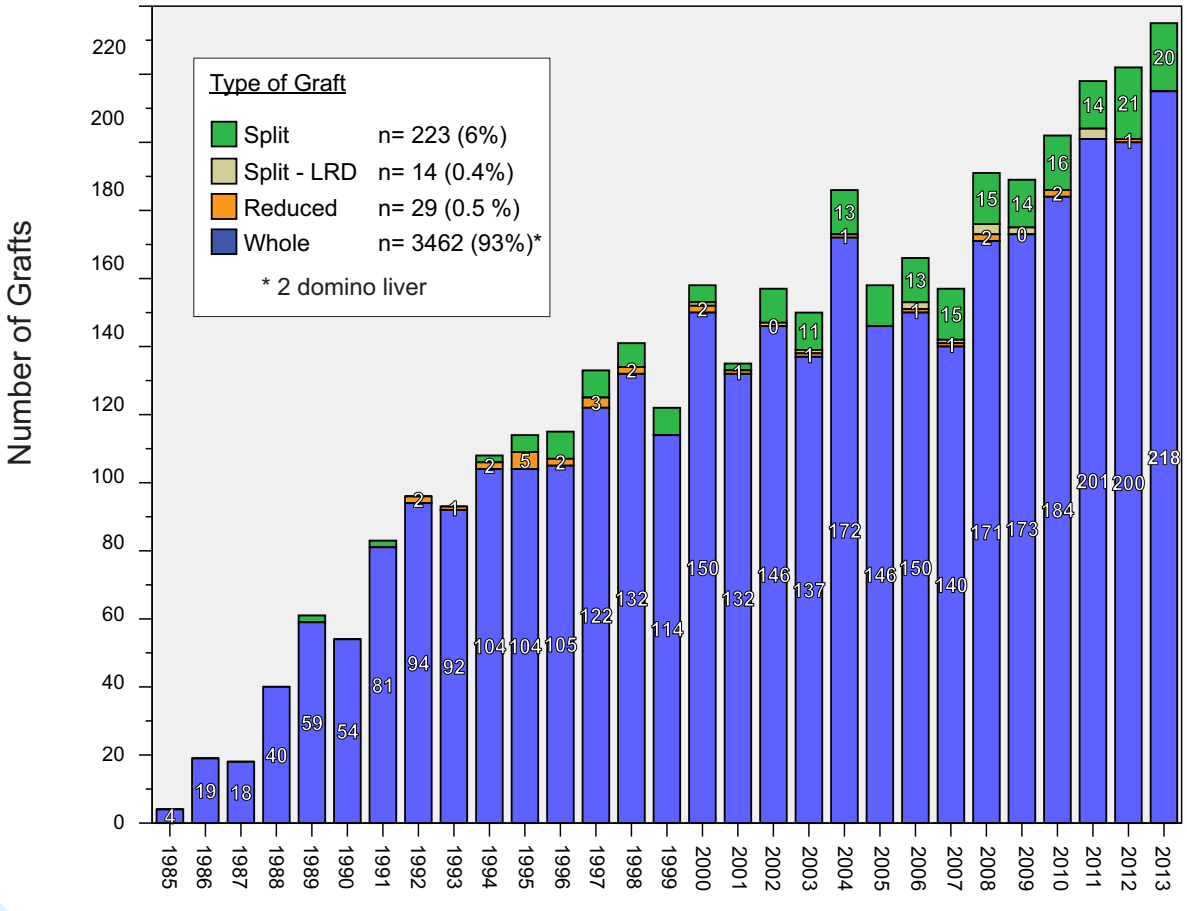


Type of Graft by Year
Split vs Reduced vs Whole

Children (n = 858)



Adults (n = 3728)



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Section 2

Primary Diagnosis

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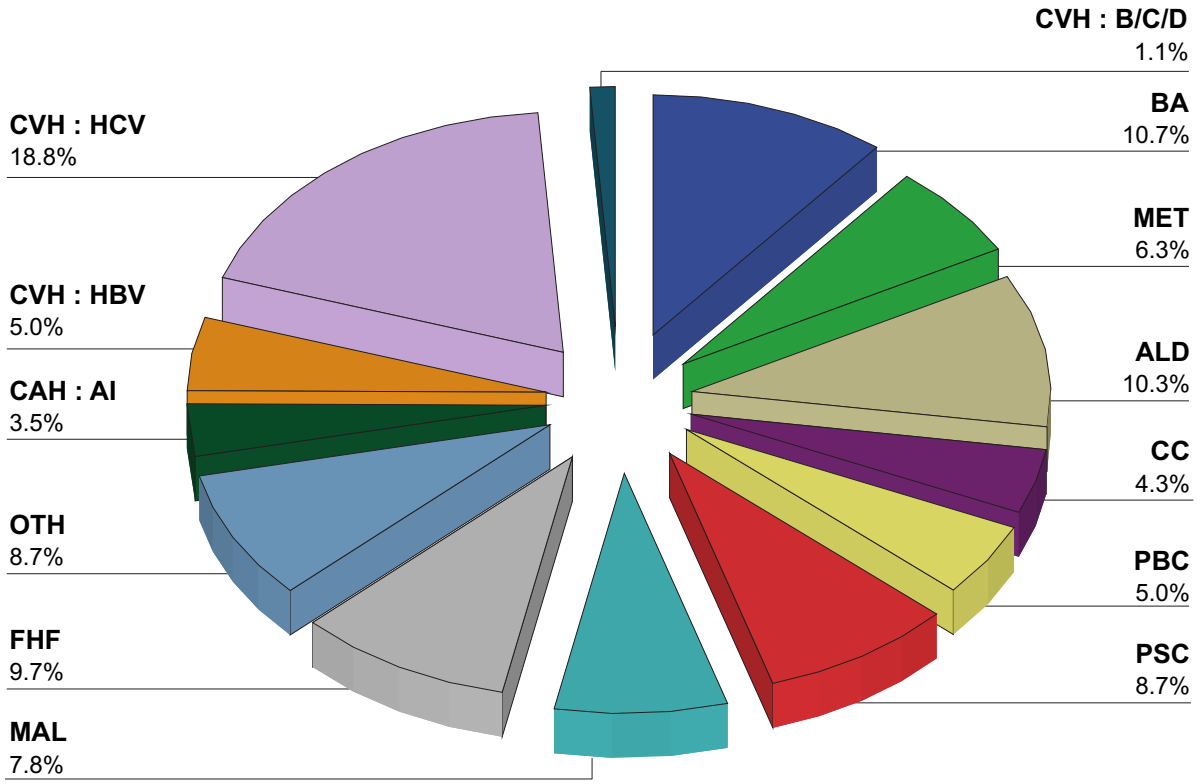
Primary Diseases of All Recipients



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*
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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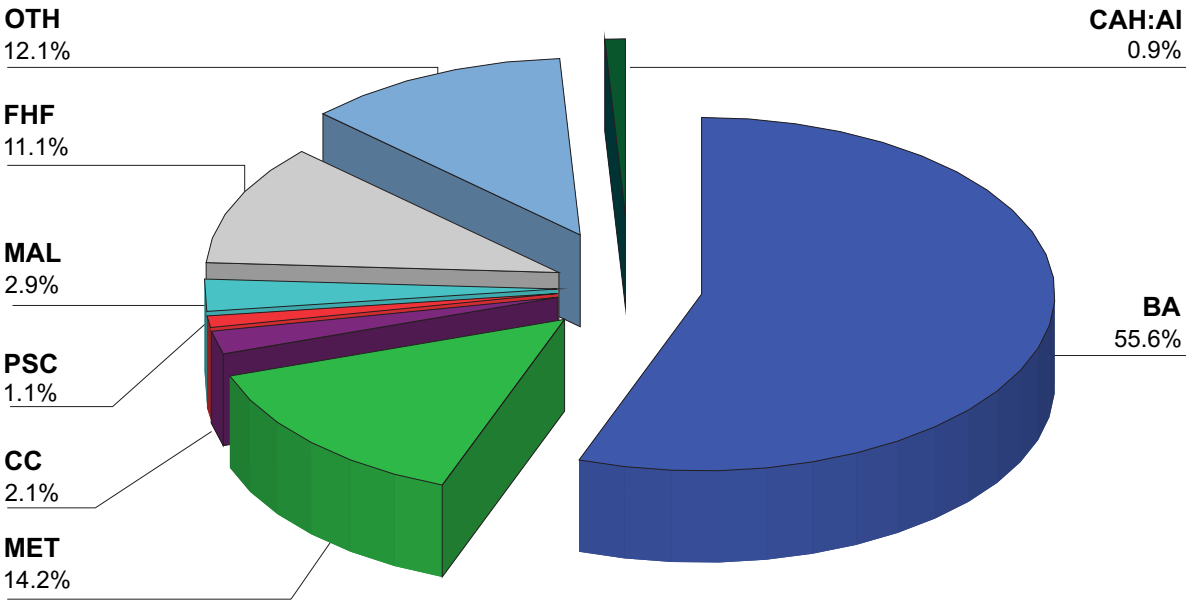
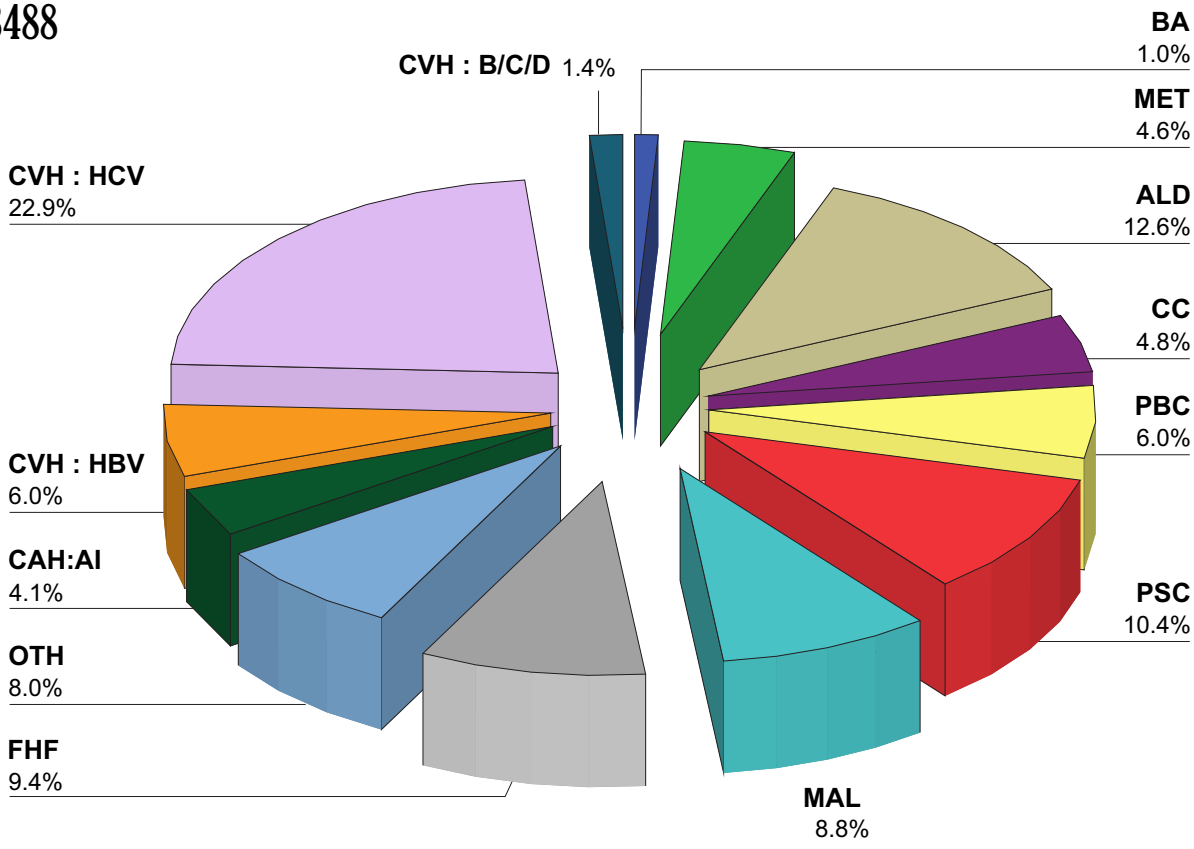
Primary Diseases of Children
n =755



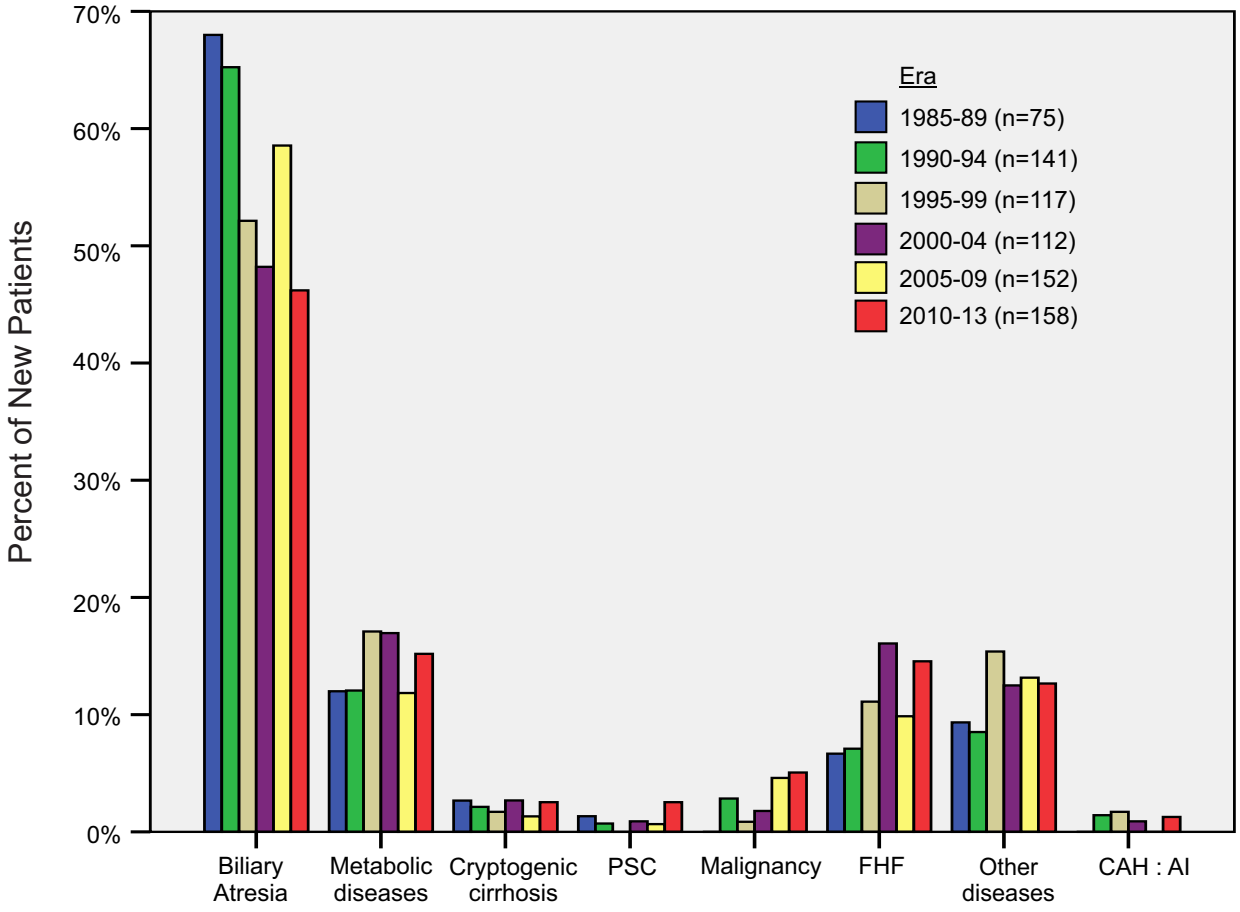
Primary Diseases of Adult Recipients
n = 3488



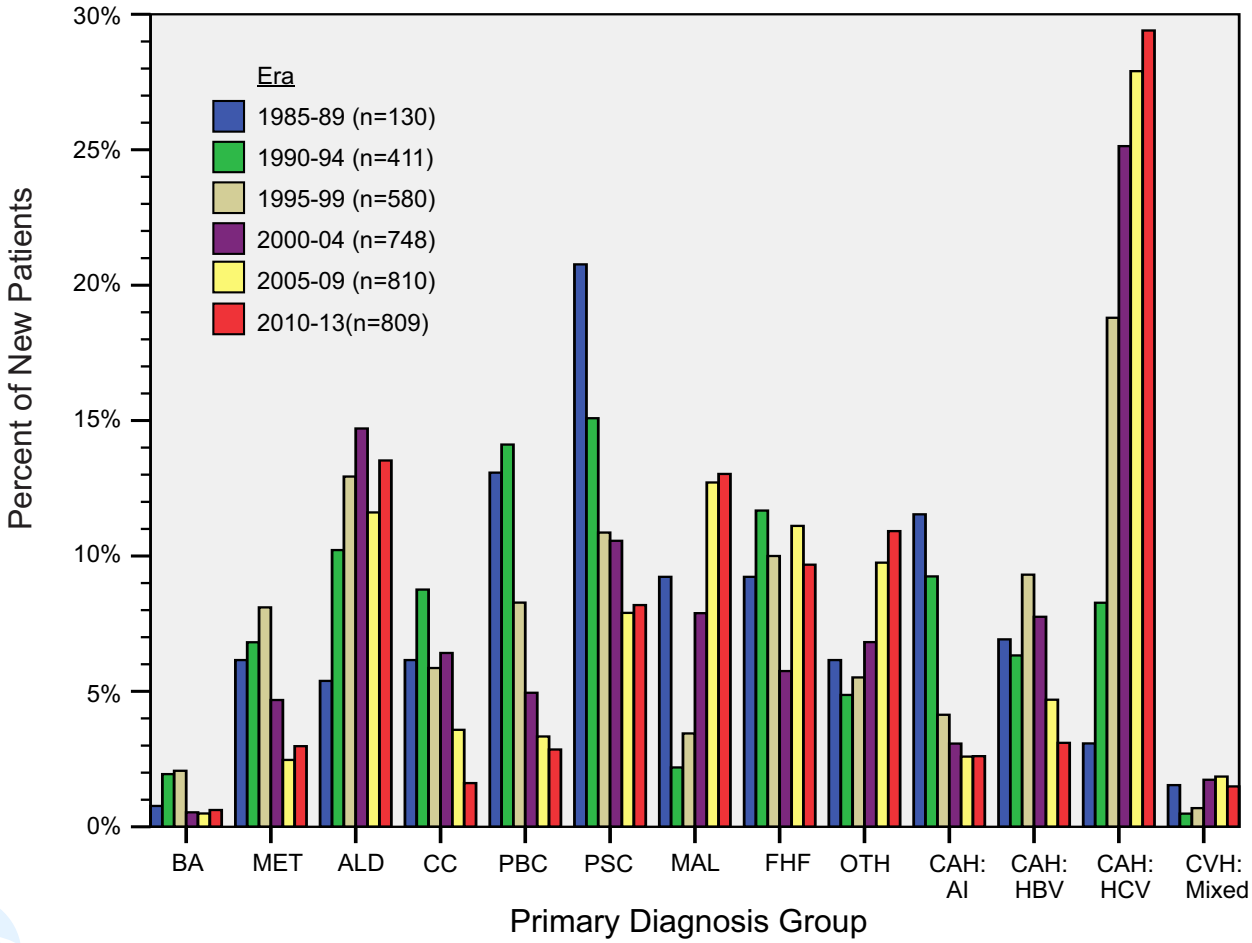
Diagnosis Group

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=755)



Adults (n = 3488)



Adult Primary Diagnosis by Era

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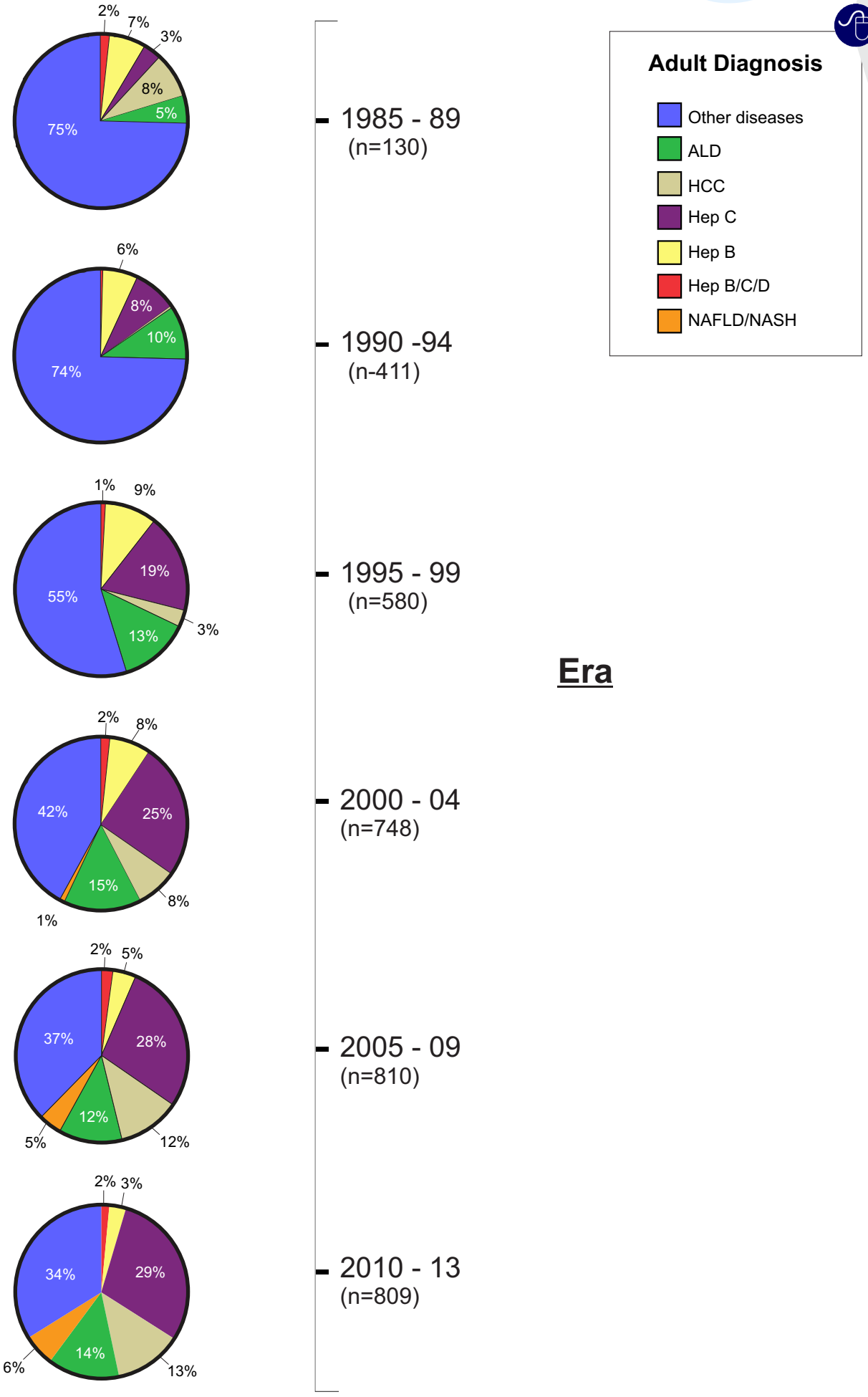

Adult Primary Diagnosis by Year

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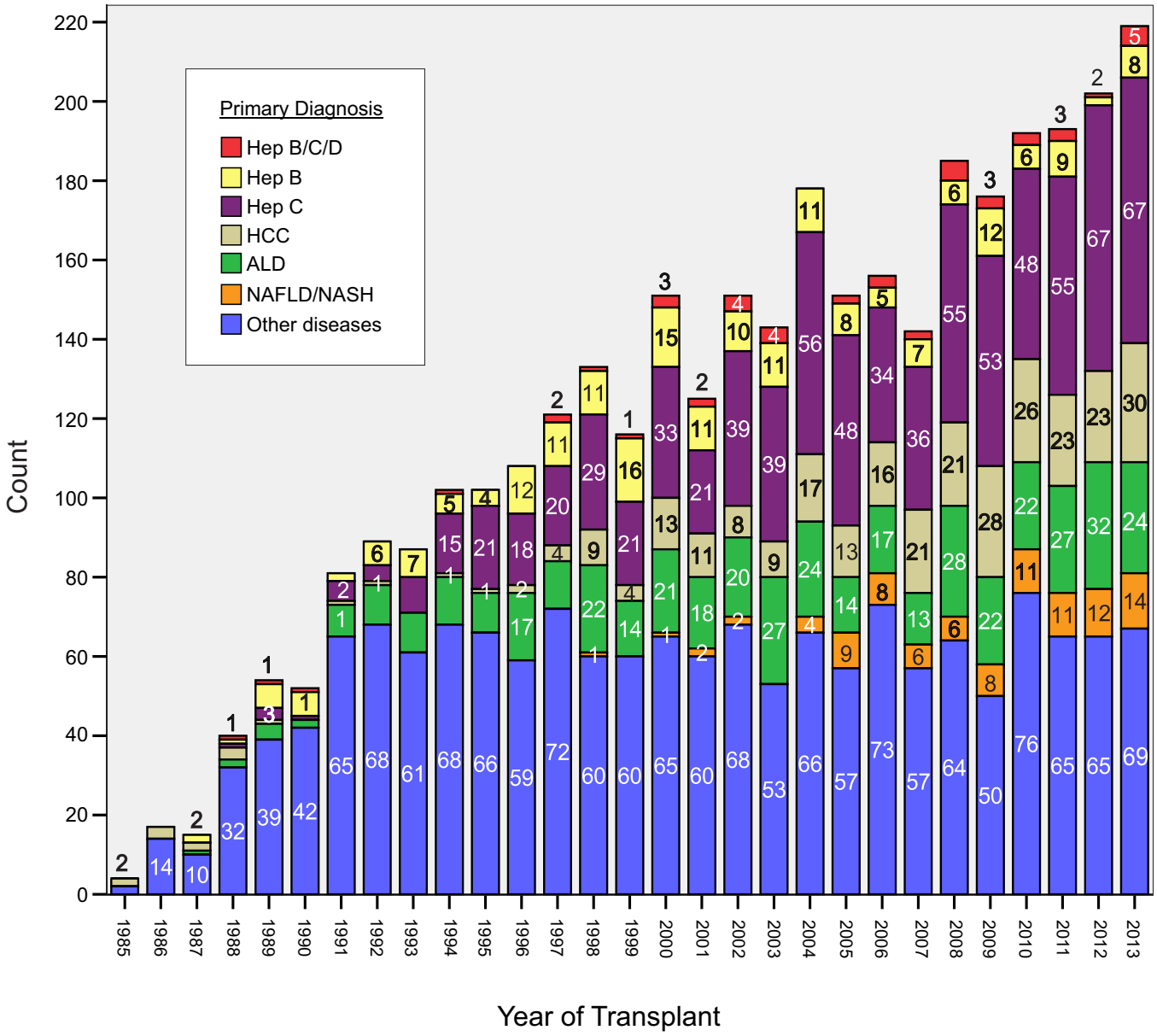

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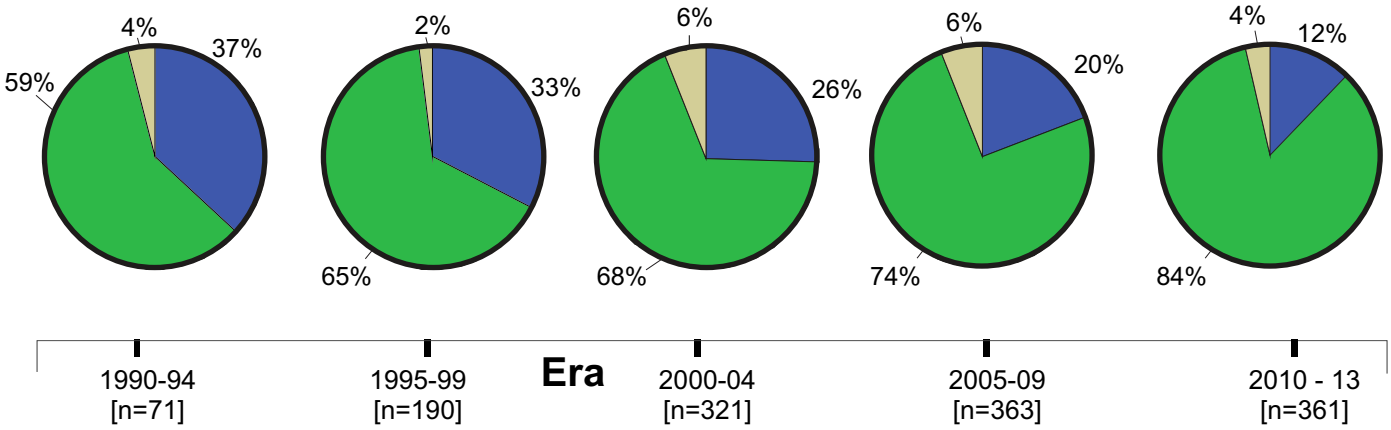
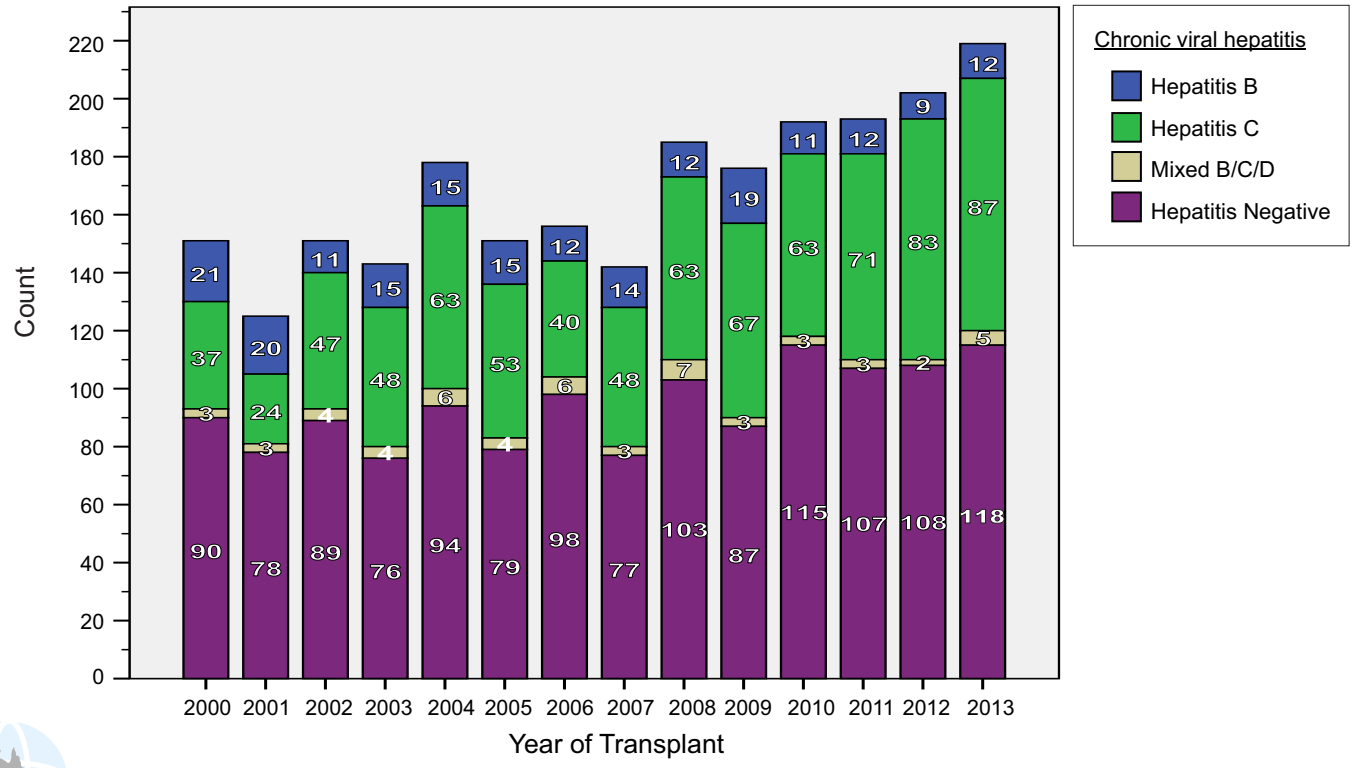
Chronic Viral Hepatitis as Primary or Secondary Diagnosis in Adult Patients

Primary Diagnosis	n =	Secondary / Tertiary diagnosis: Hepatitis C	Hepatitis B	Hepatitis B,C	HCC	NAFLD	ALD
Hepatitis C	798		7		232	4	210
Hepatitis B	210	3			78		6
Hepatitis BD/BC/BCD	48				8		7
HCC + cirrhosis	293	140	81	7		9	54
ALD	438	19	3		57	8	
NAFLD	95		2		17		5
Other	1606	14	7		55	3	22
TOTAL	3488						

Type of Chronic Viral Hepatitis in Adult Patients



Hepatitis diagnosis



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Section 3

Patient Survival

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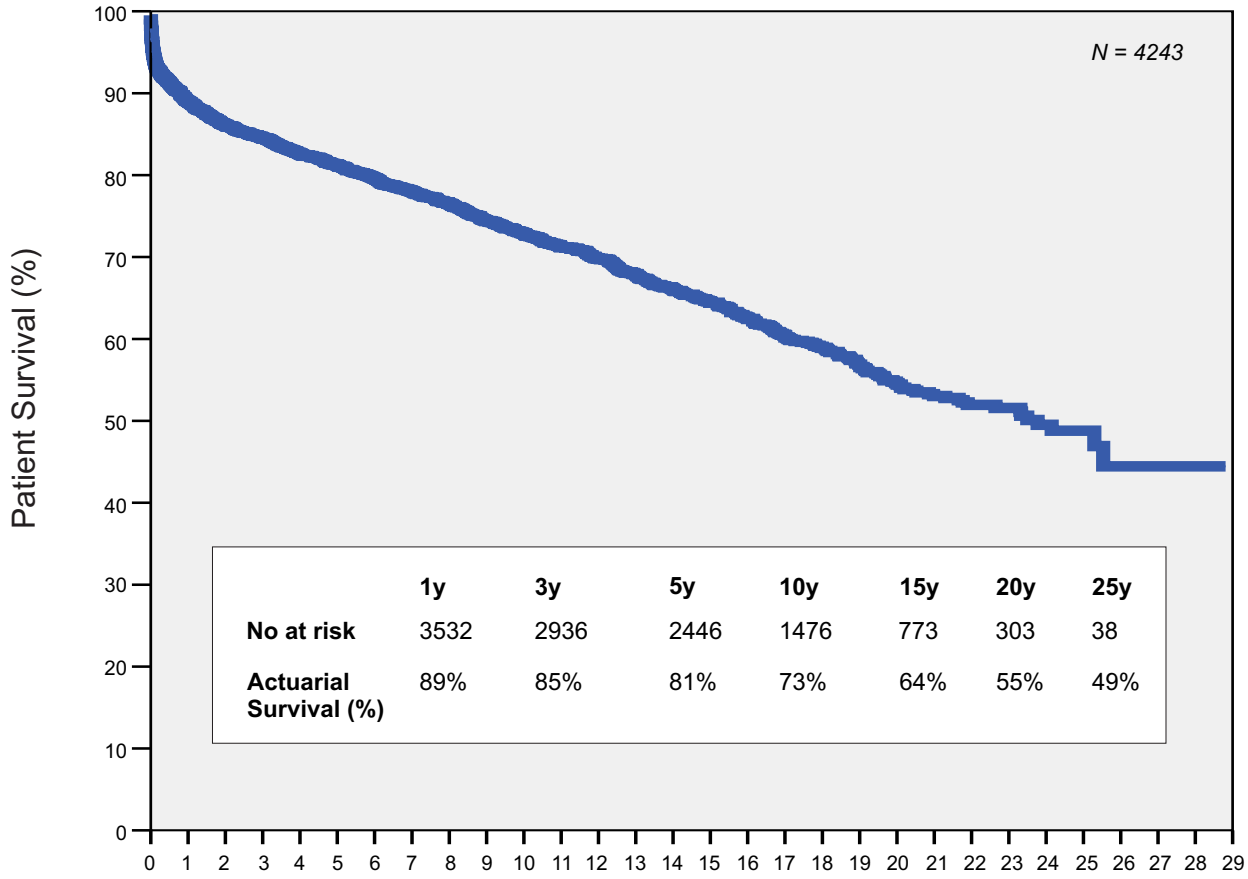
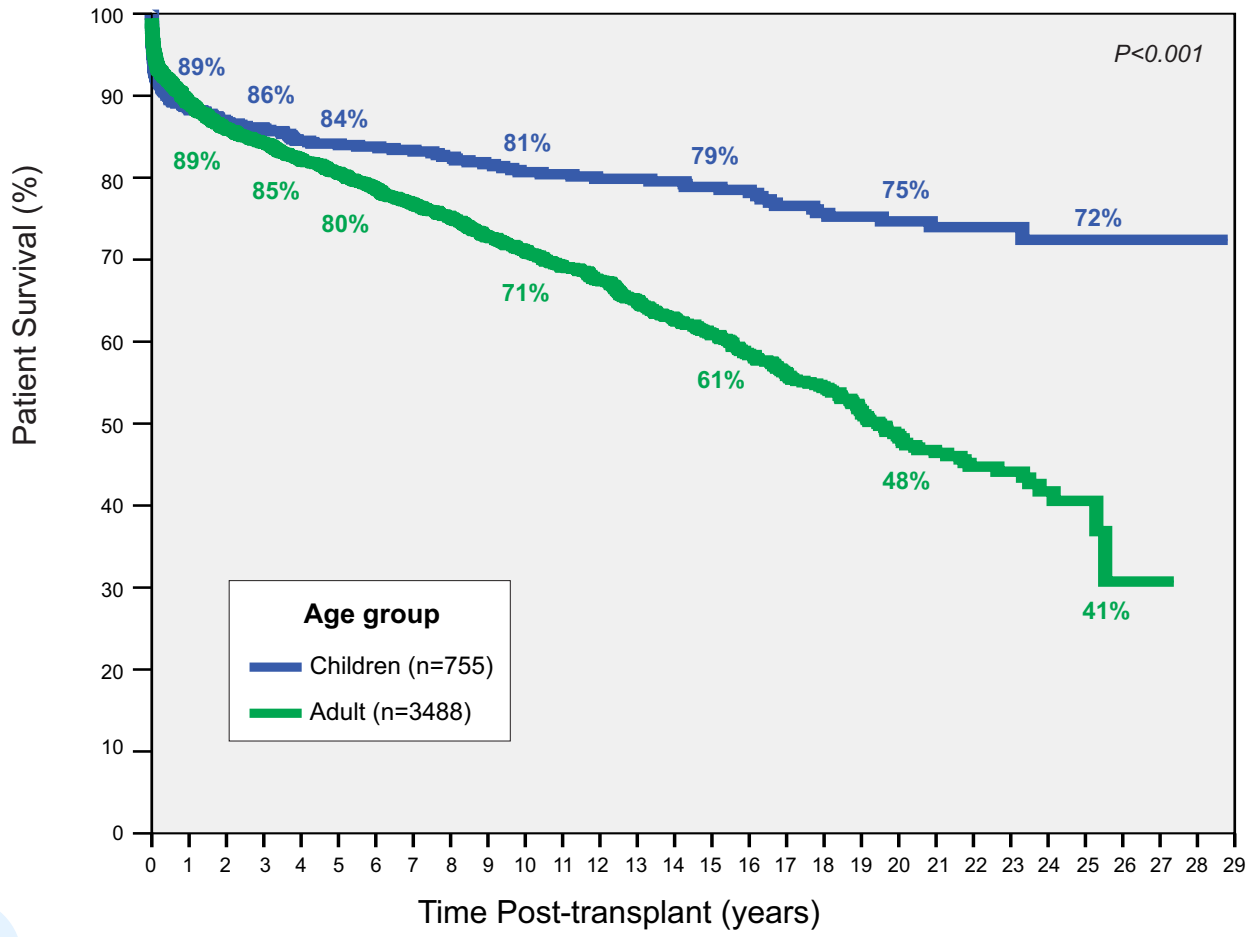
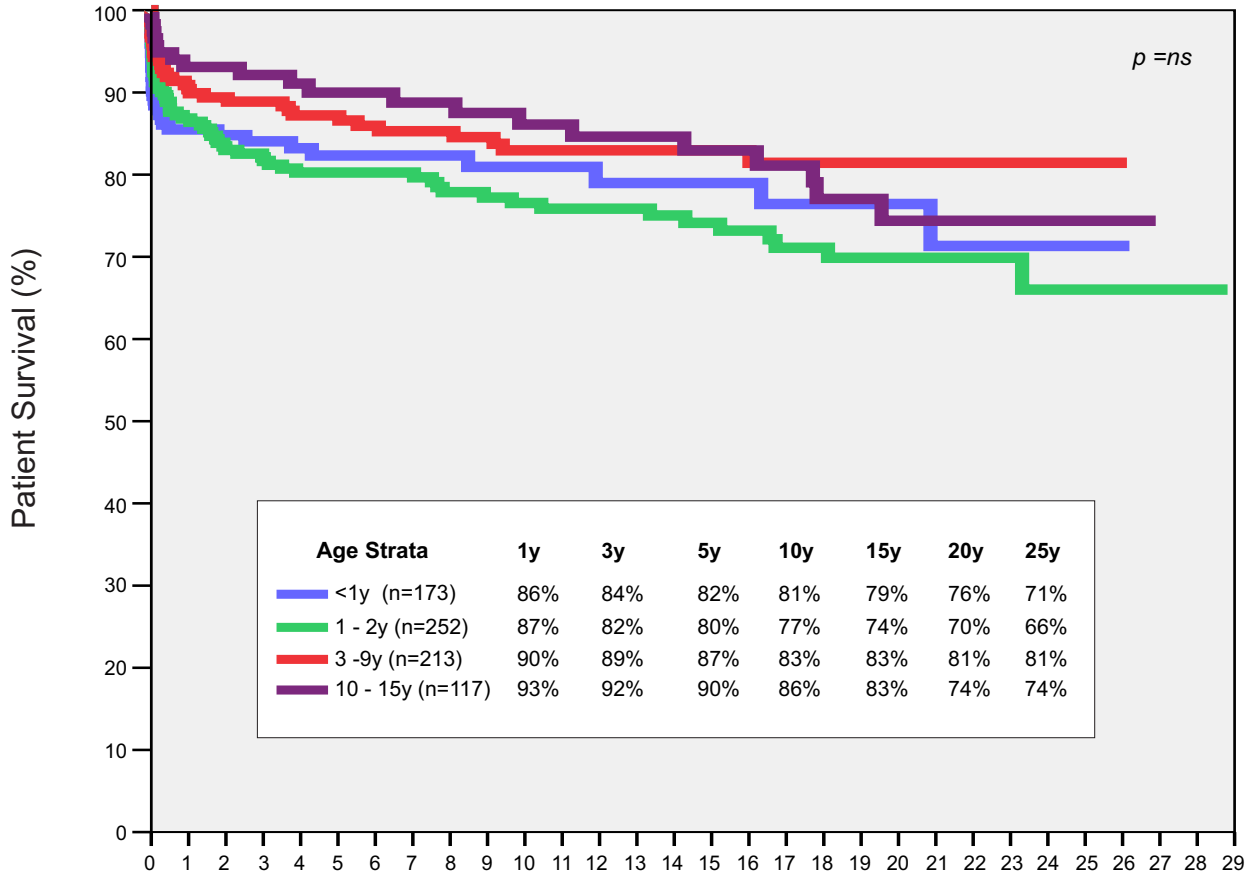
Patient Survival Post Transplant



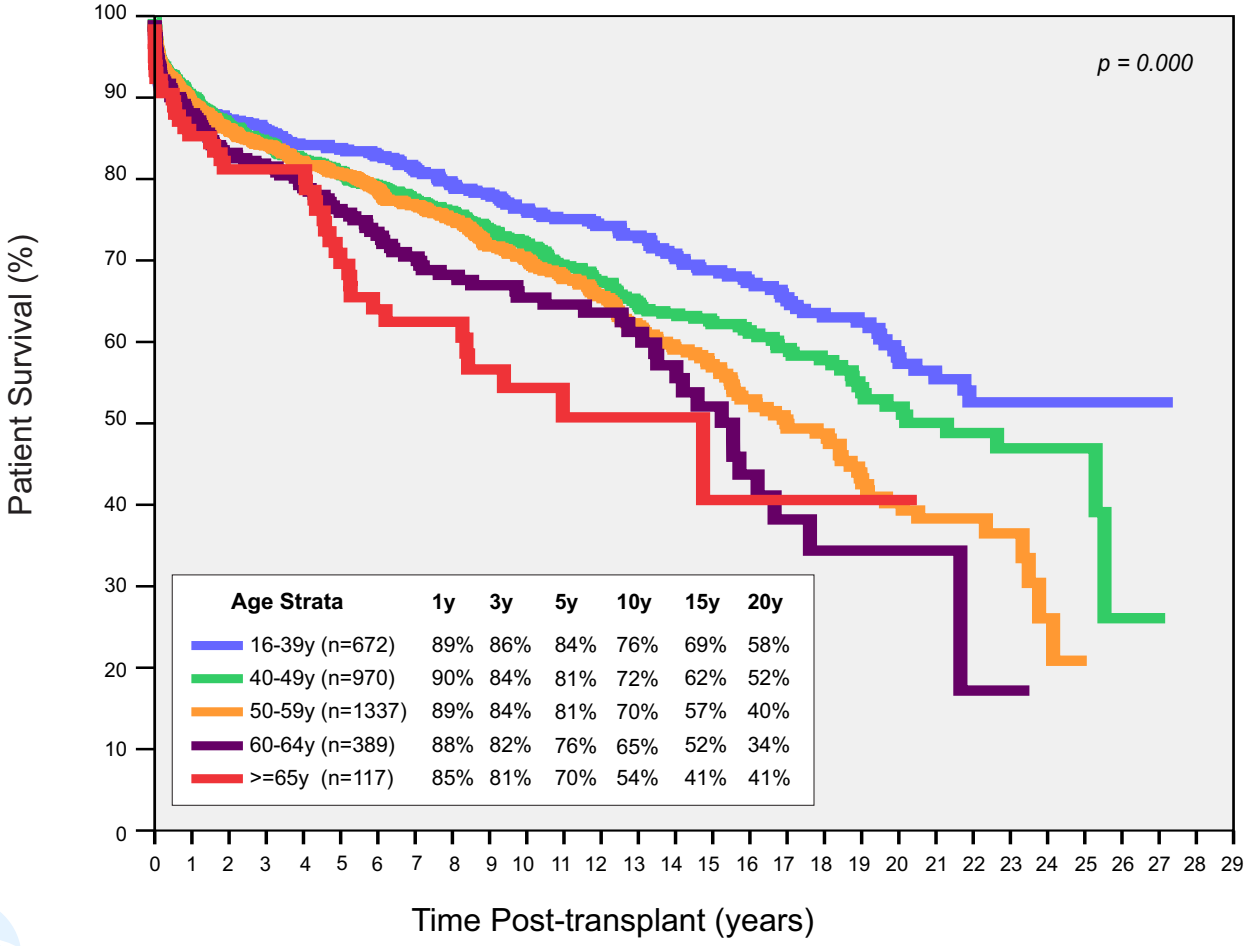
	1y	3y	5y	10y	15y	20y	25y
No at risk	3532	2936	2446	1476	773	303	38
Actuarial Survival (%)	89%	85%	81%	73%	64%	55%	49%



Children n= 755



Adults n = 3488



All Patient Survival by Year of Transplant

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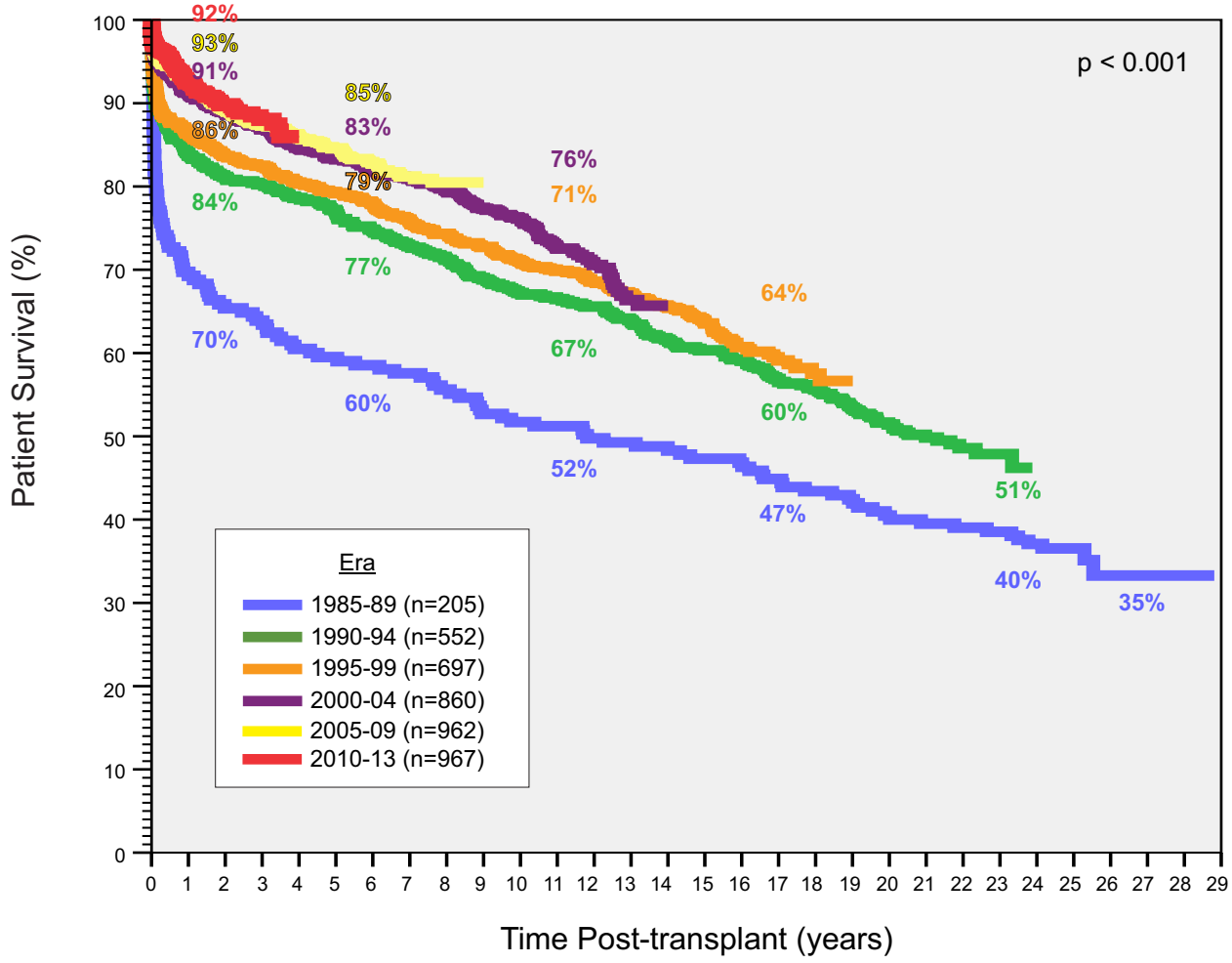

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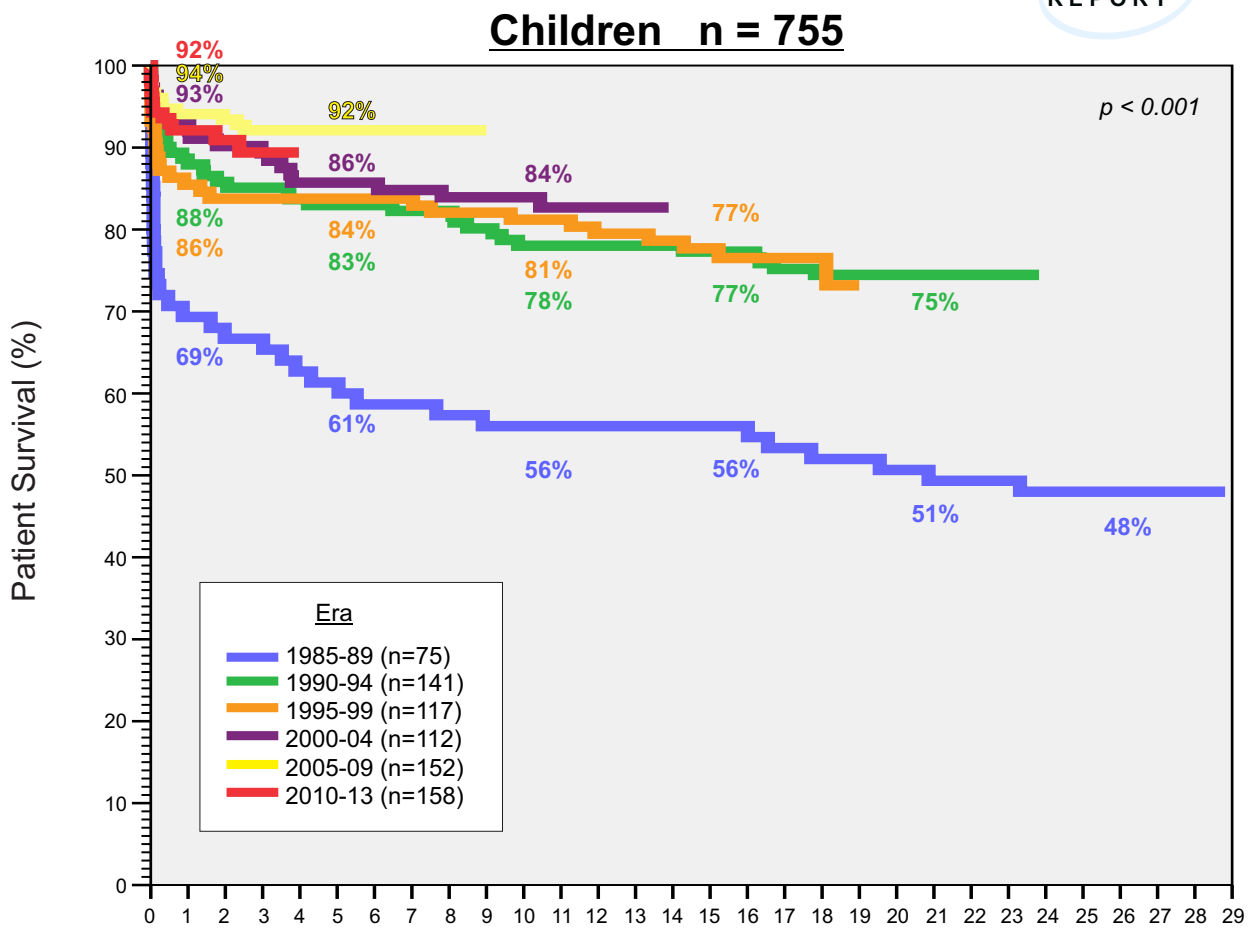
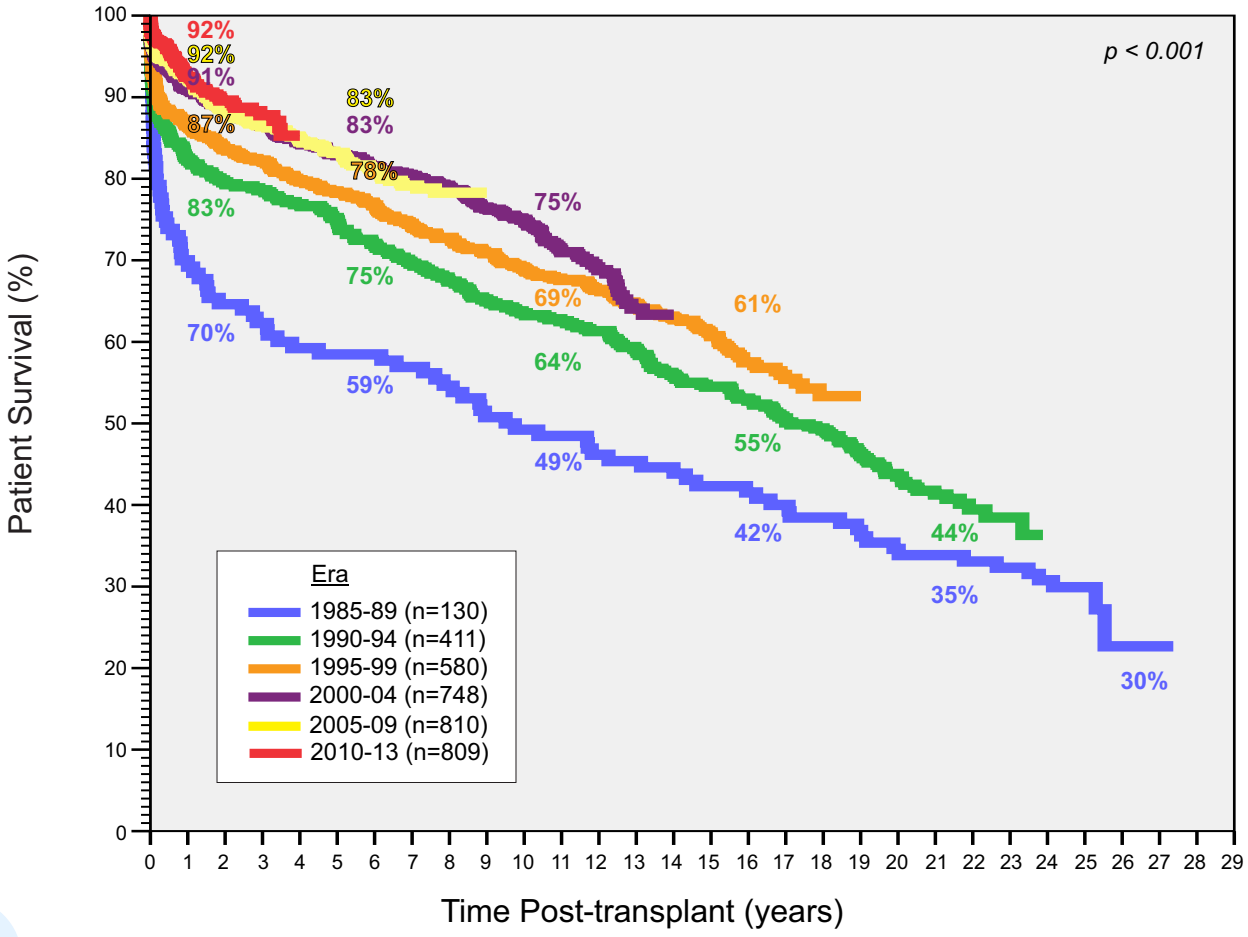
Patient Survival - Children



Patient Survival - Adults



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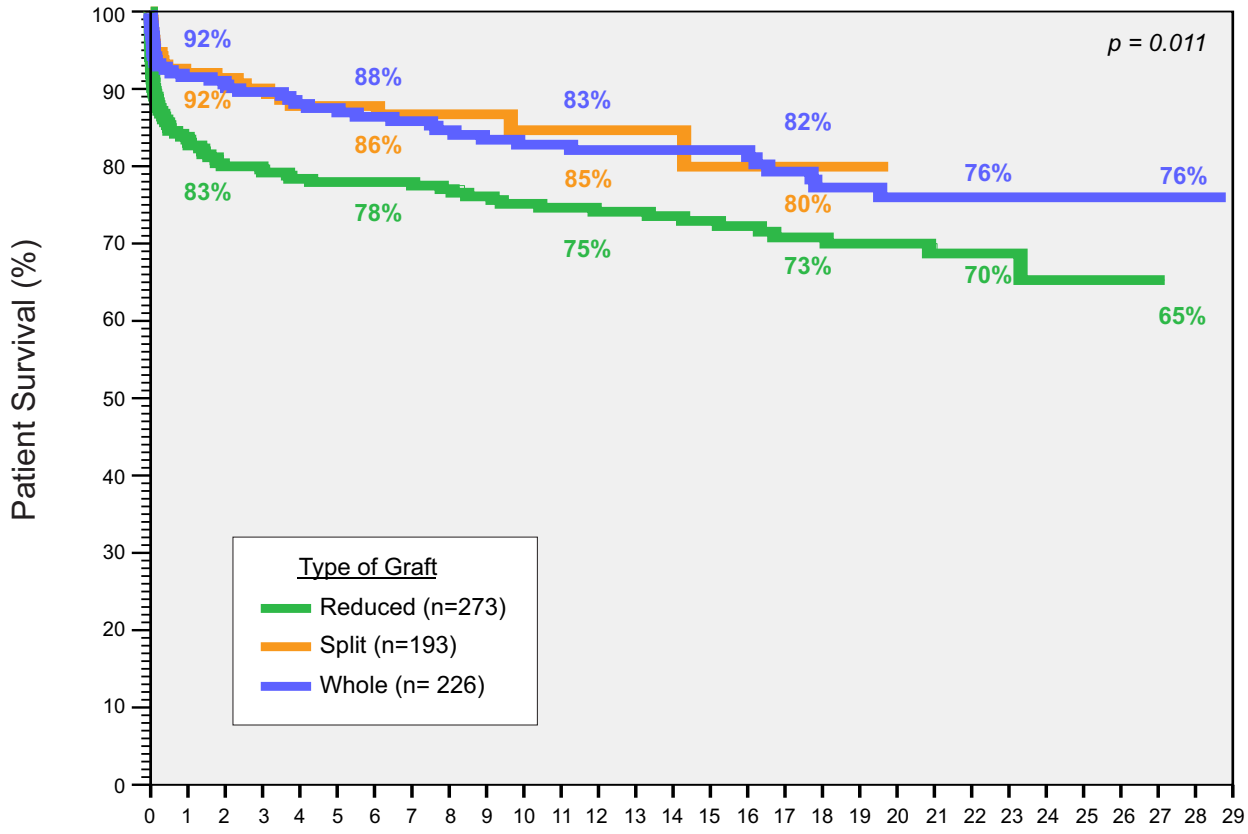
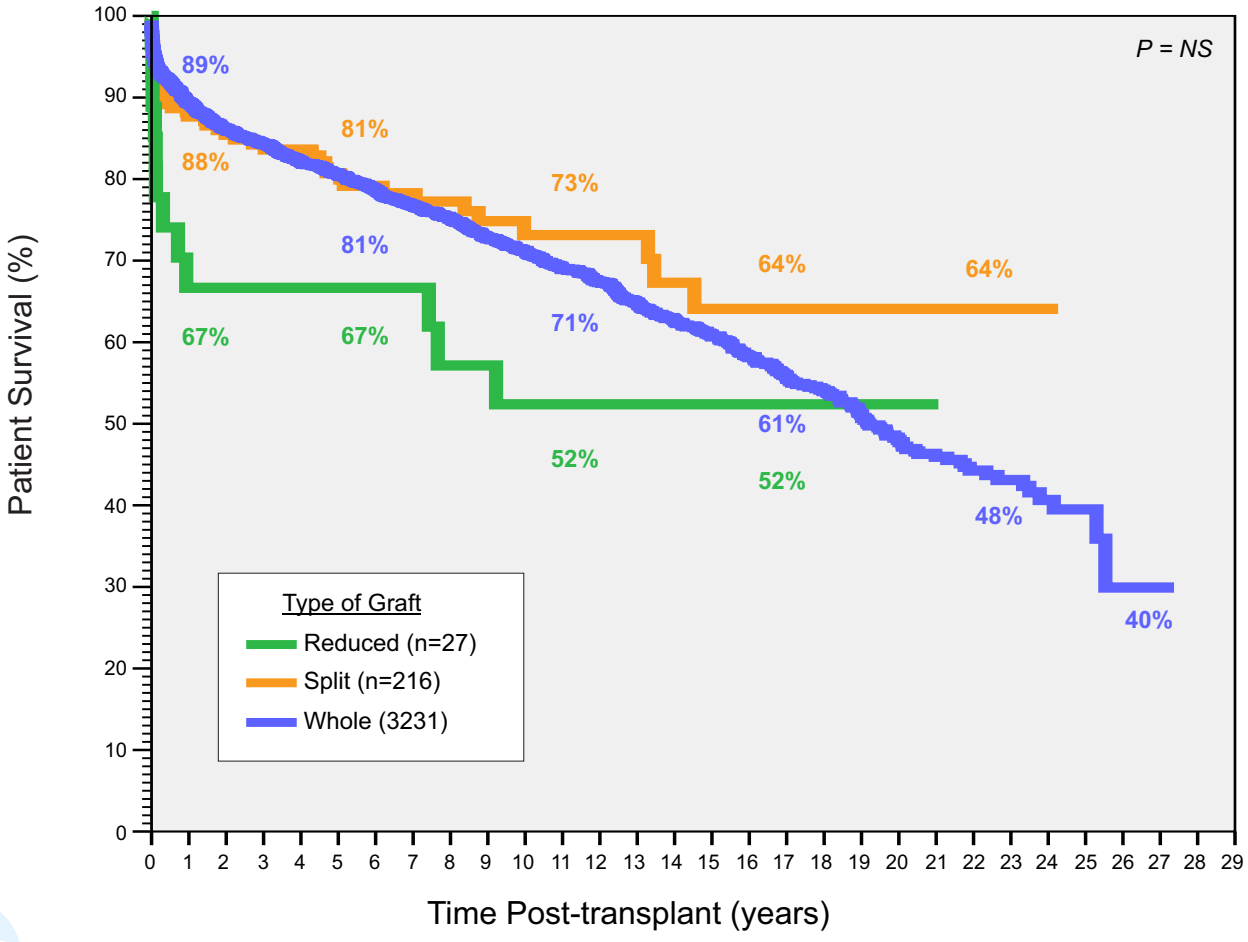
Patient Survival by Type of Primary Graft [Deceased donors]

Children - n = 692



Adults - n = 3474



Patient Survival by Weight - Children

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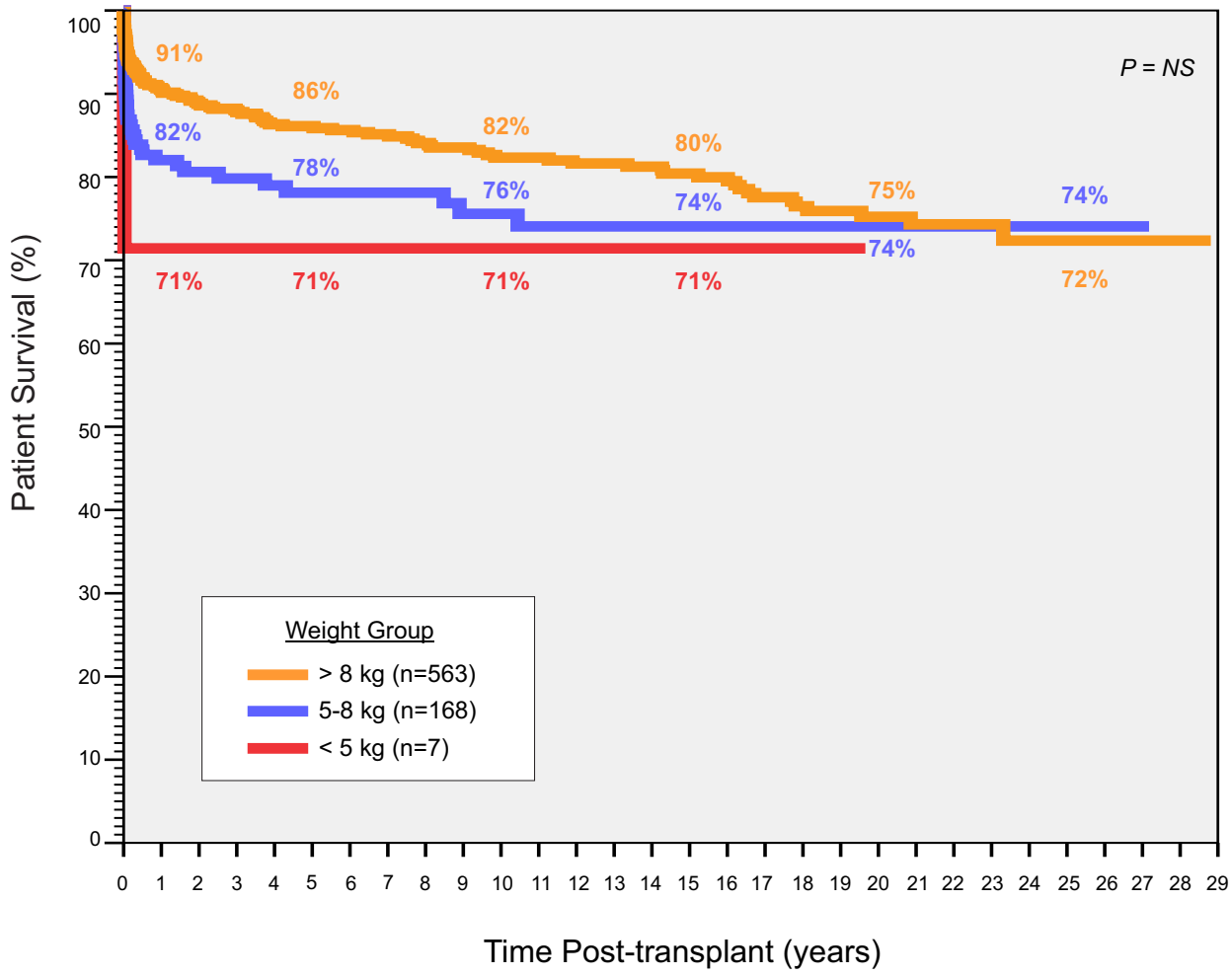
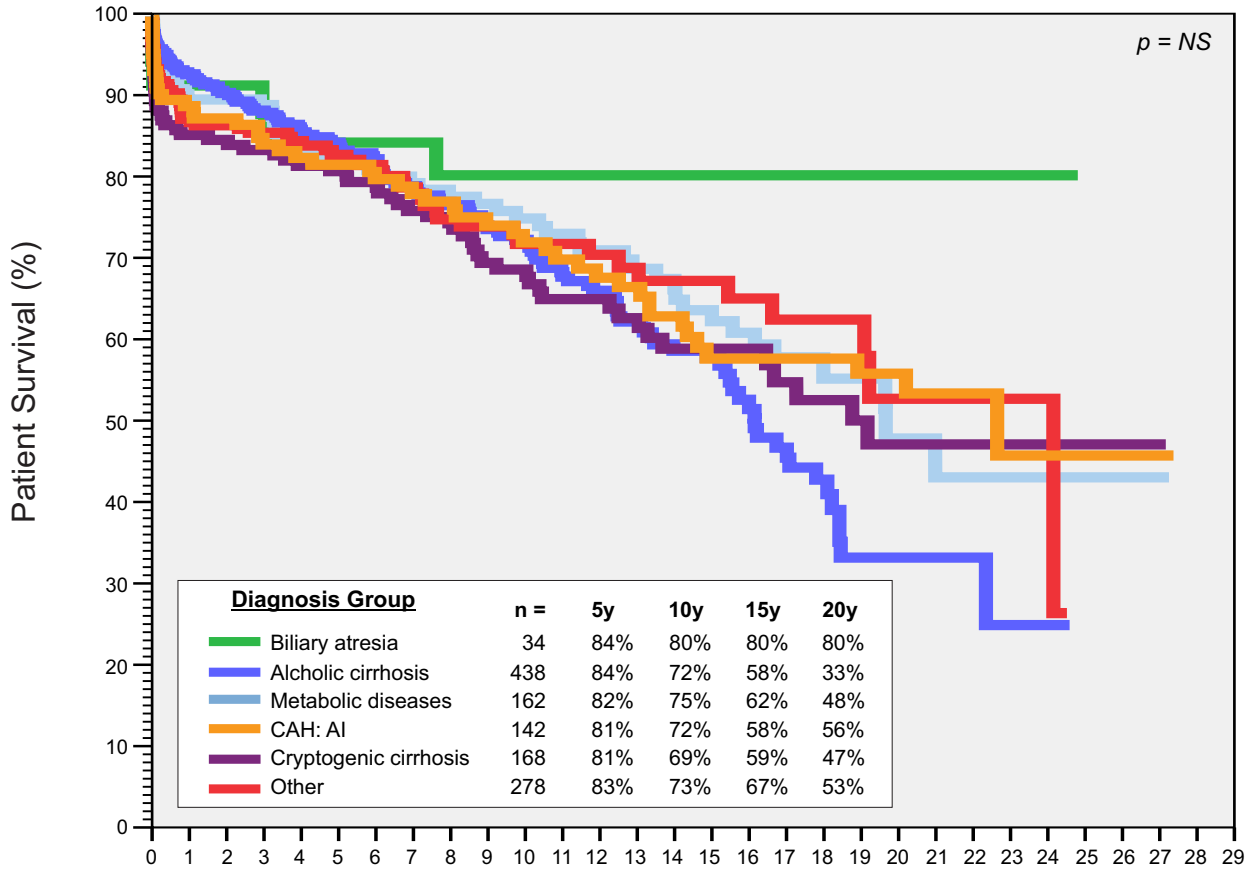
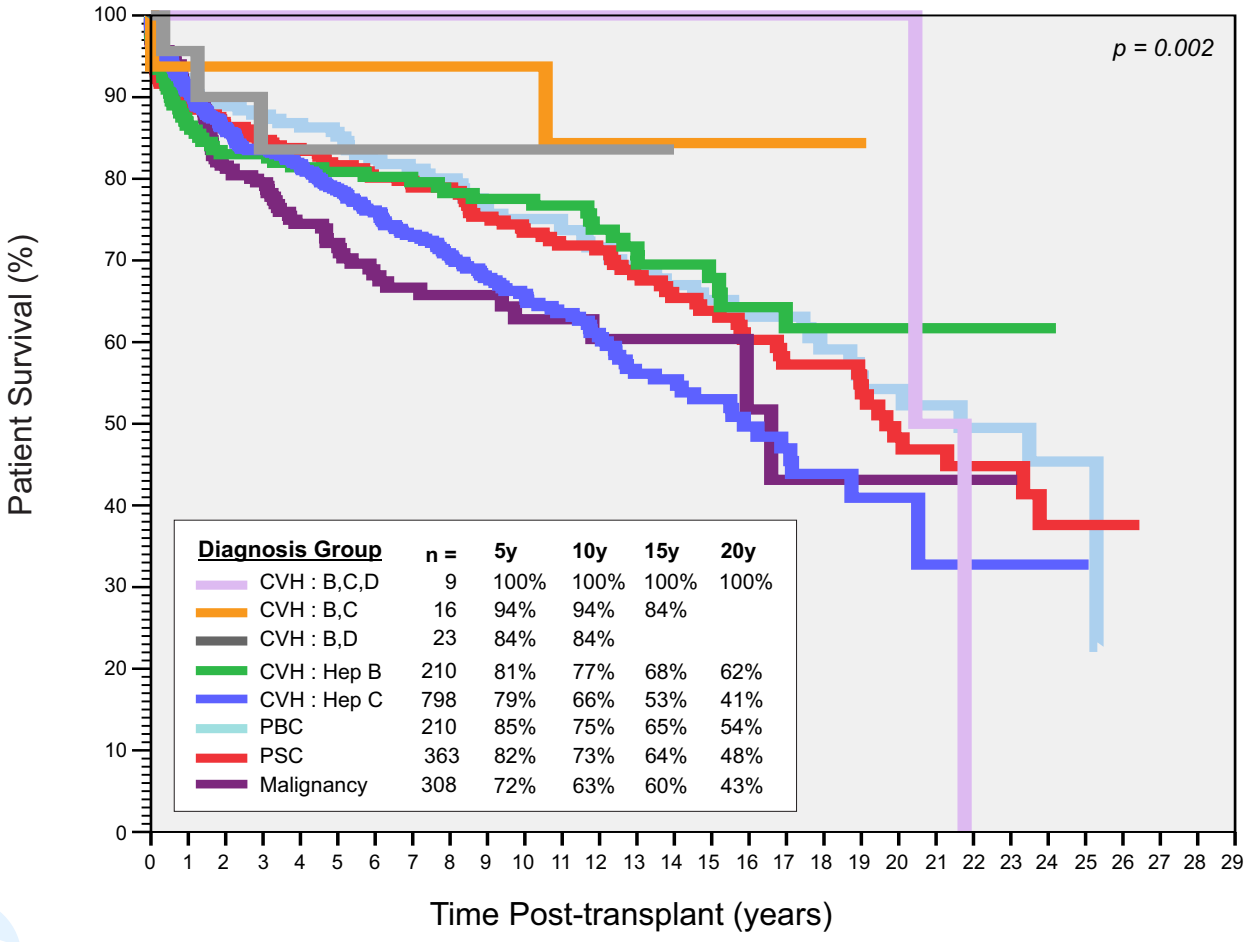


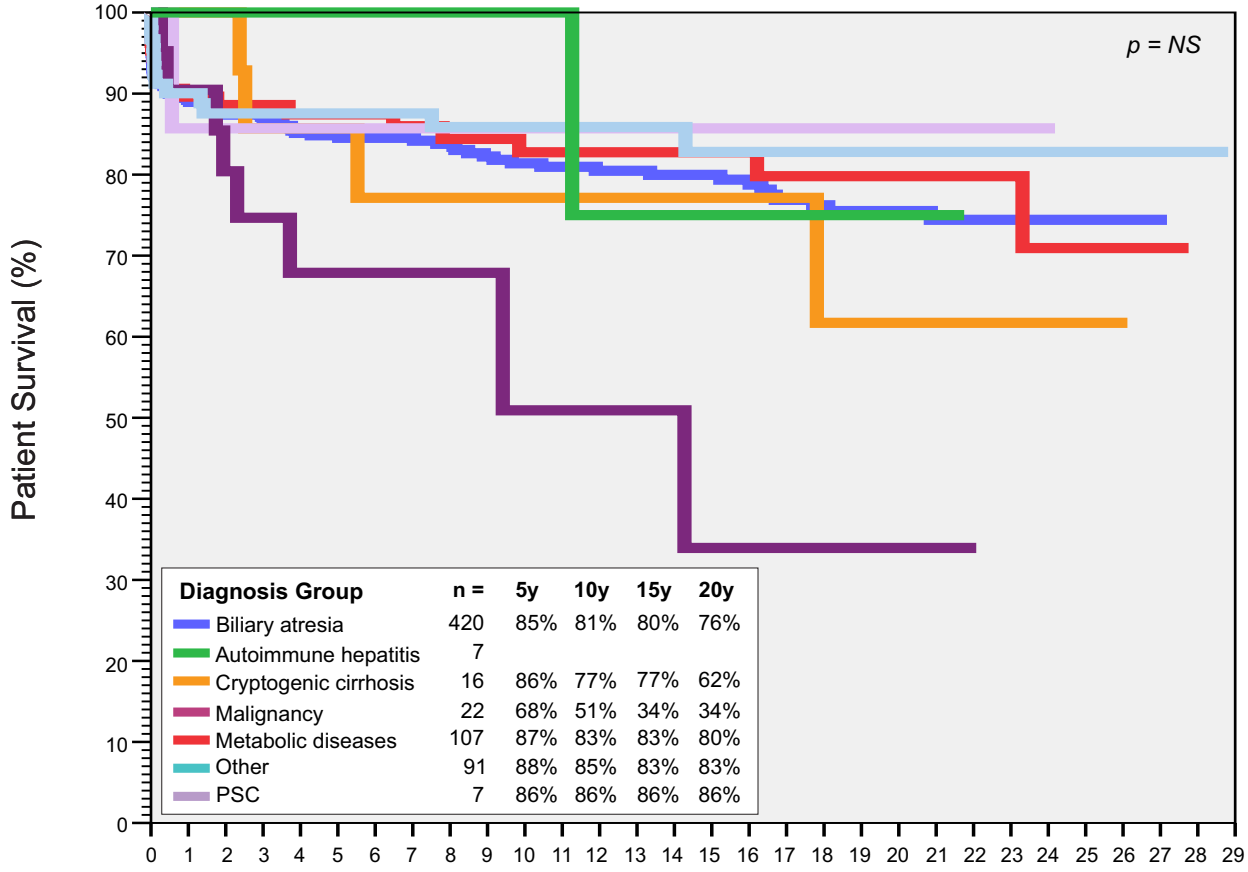
(1) Adults [excluding FHF] - n=1222



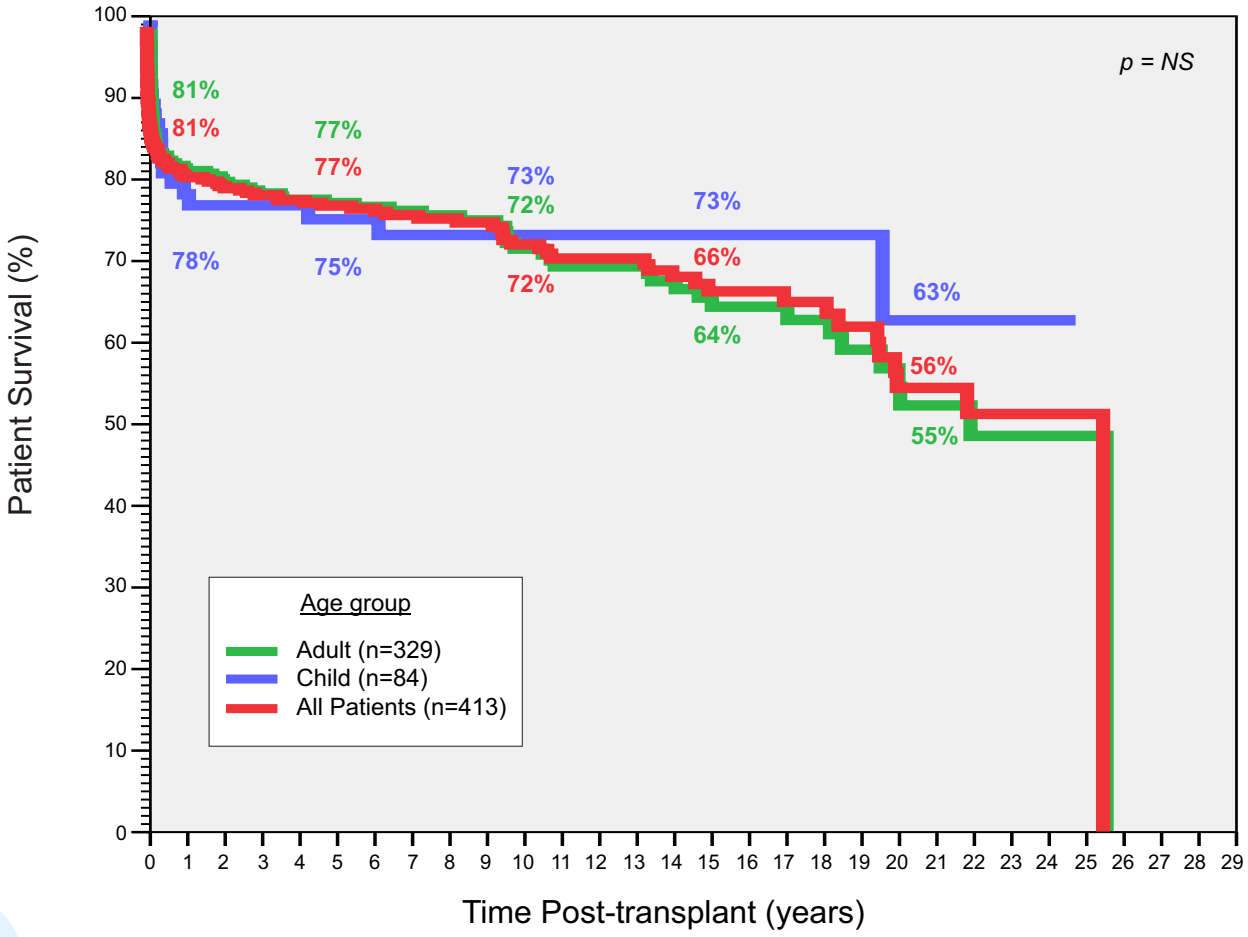
(2) Adults [excluding FHF] - n = 1937

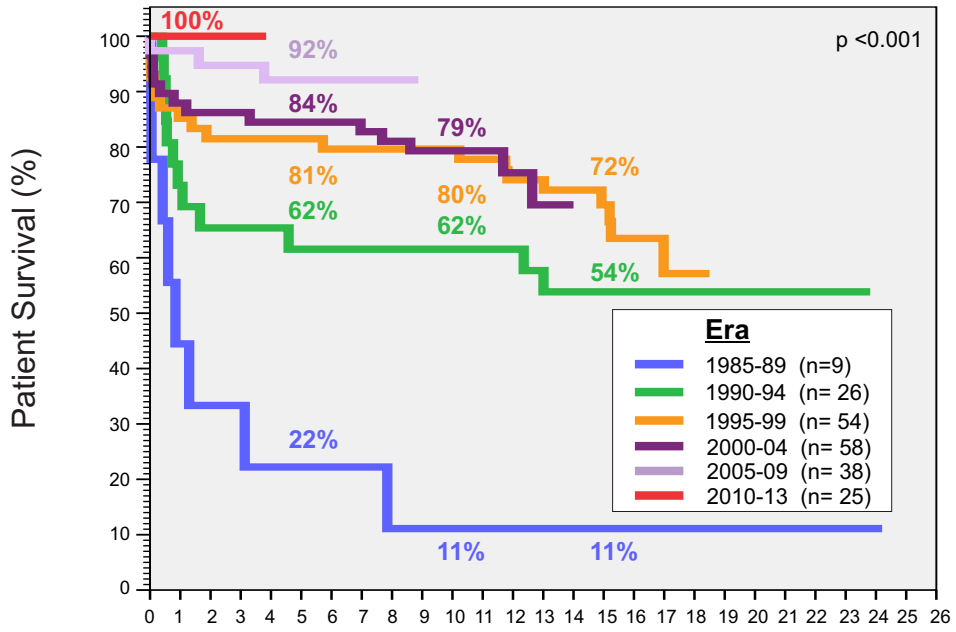


(3) Paediatric recipients [excluding FHF] - n= 671

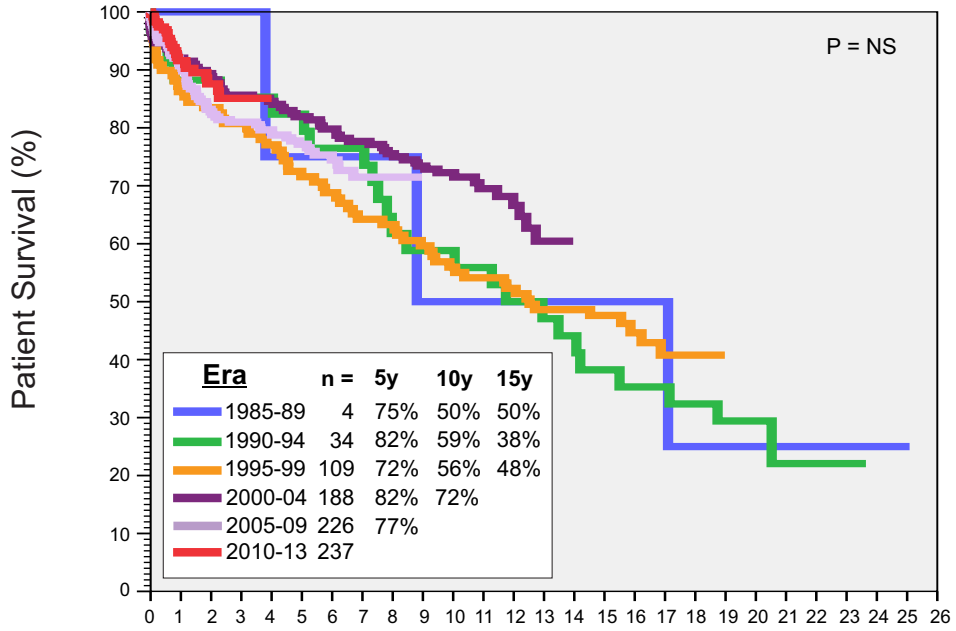


(4) Fulminant hepatic failure n = 413

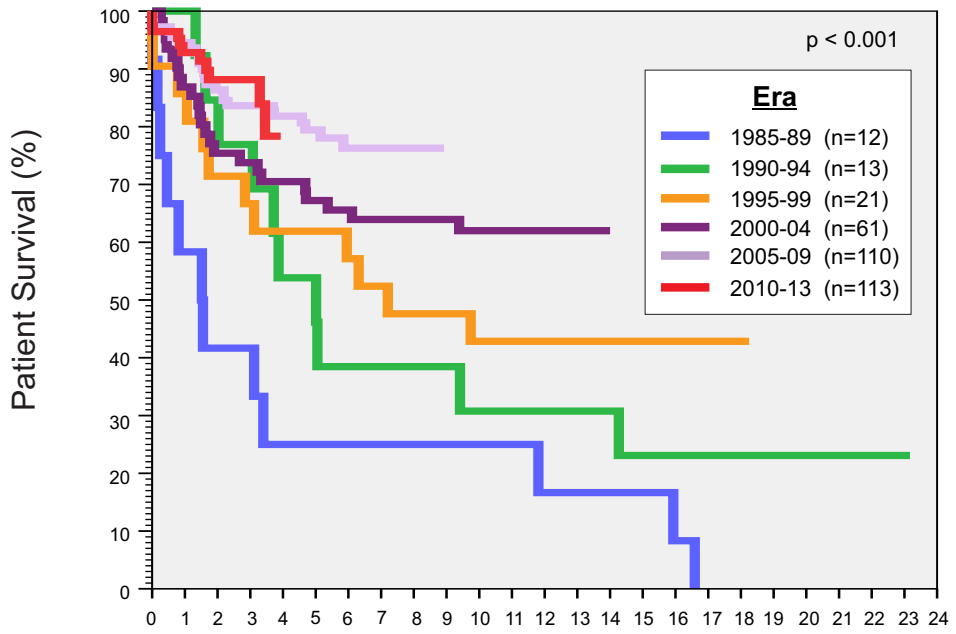




Adults CVH: Hepatitis B
n = 210



Adults CVH: Hepatitis C
n = 798



Malignancy
Adults and Children
n=330

Adults (n = 308)
Children (n=22)

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Section 4

Graft Outcome

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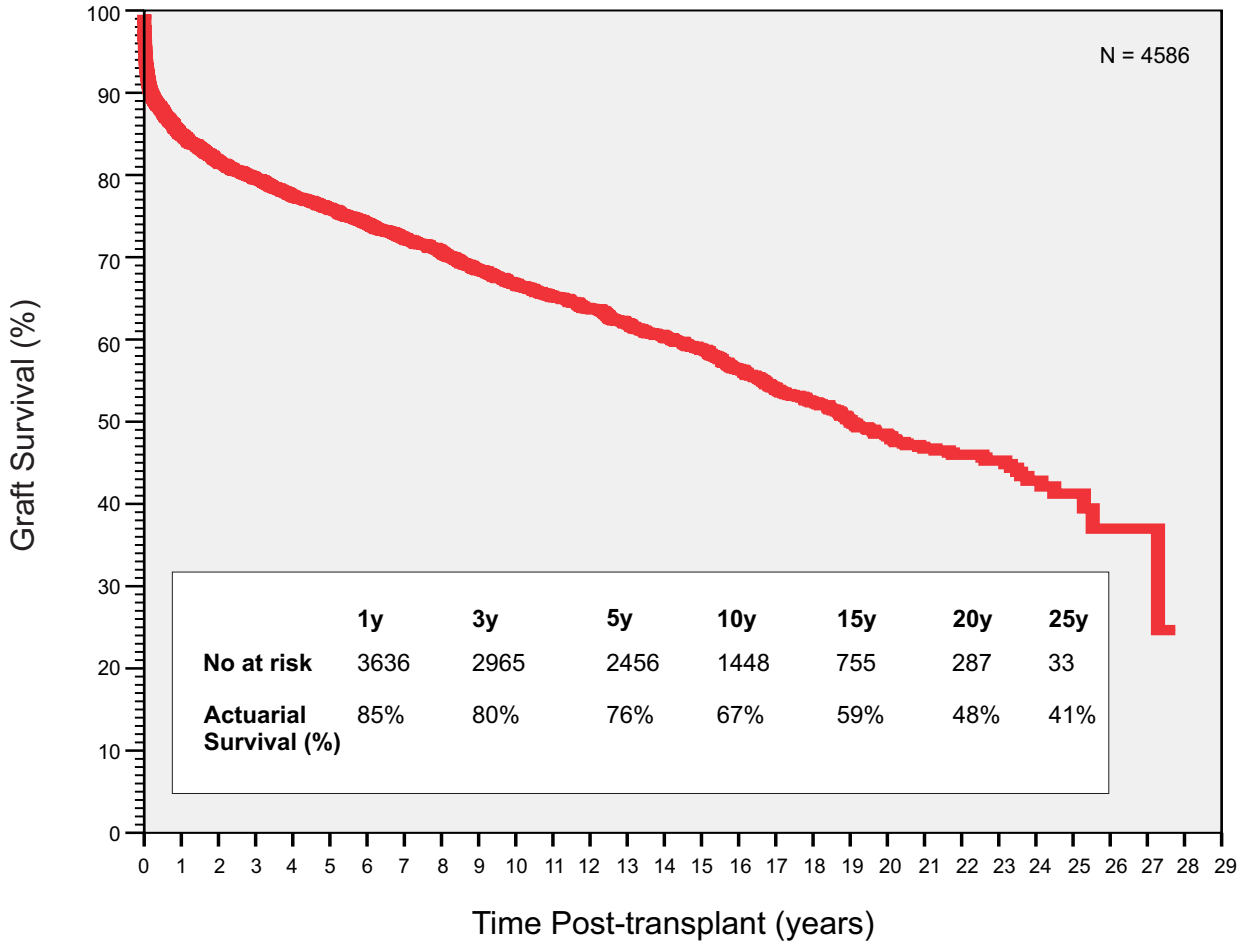
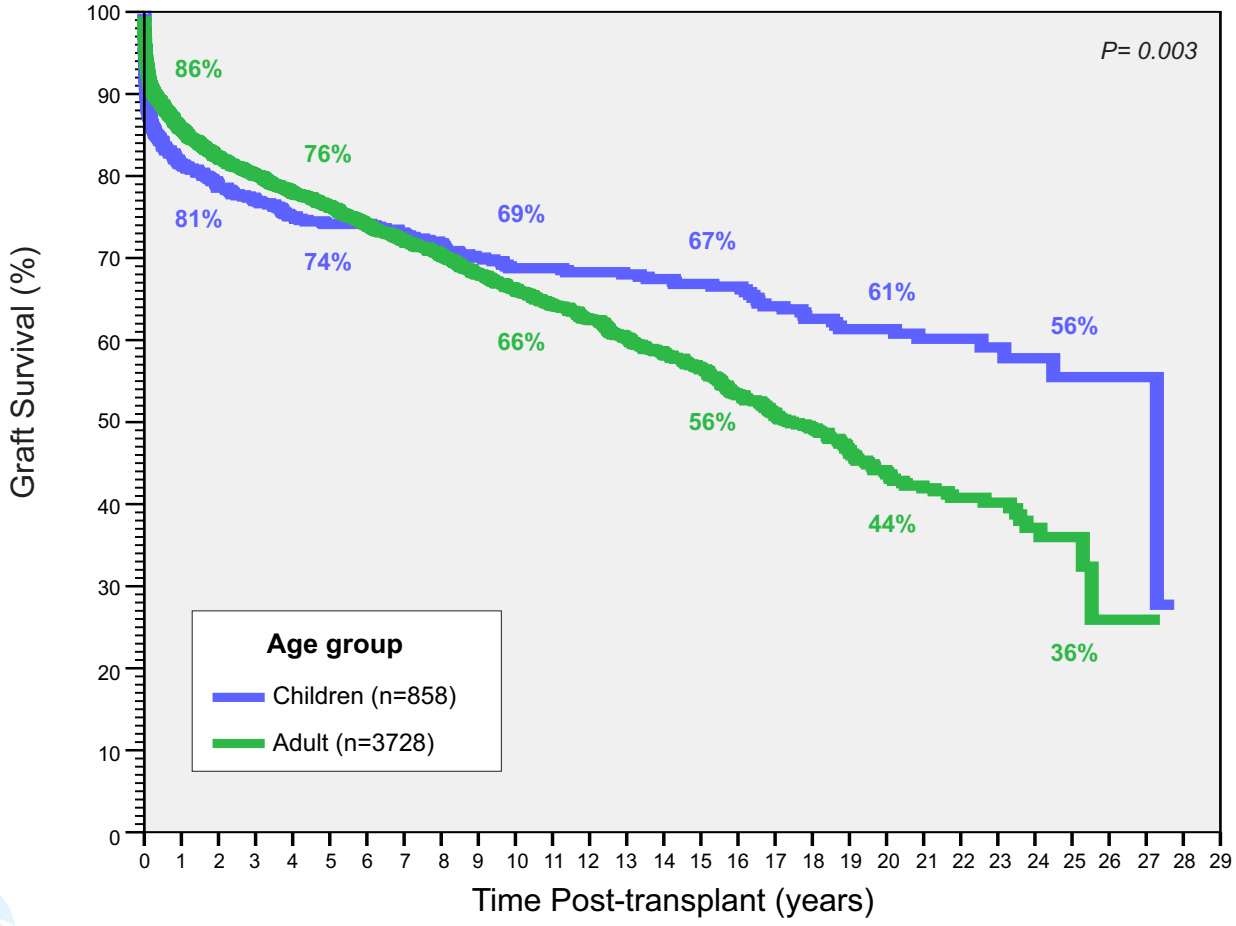
Graft Survival - All Grafts

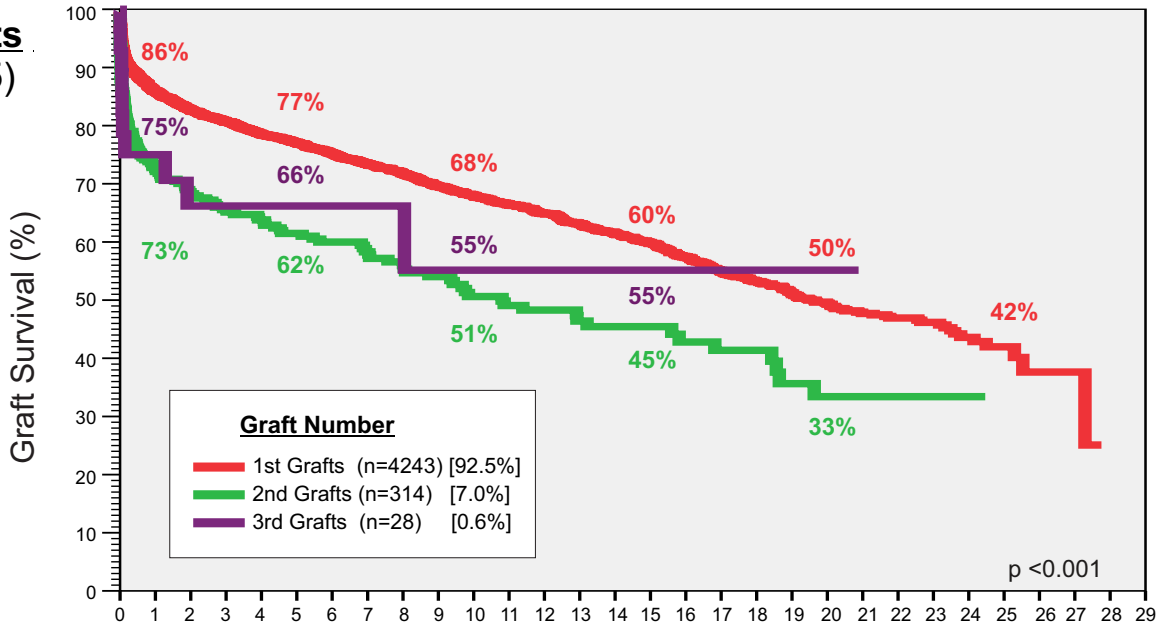


	1y	3y	5y	10y	15y	20y	25y
No at risk	3636	2965	2456	1448	755	287	33
Actuarial Survival (%)	85%	80%	76%	67%	59%	48%	41%

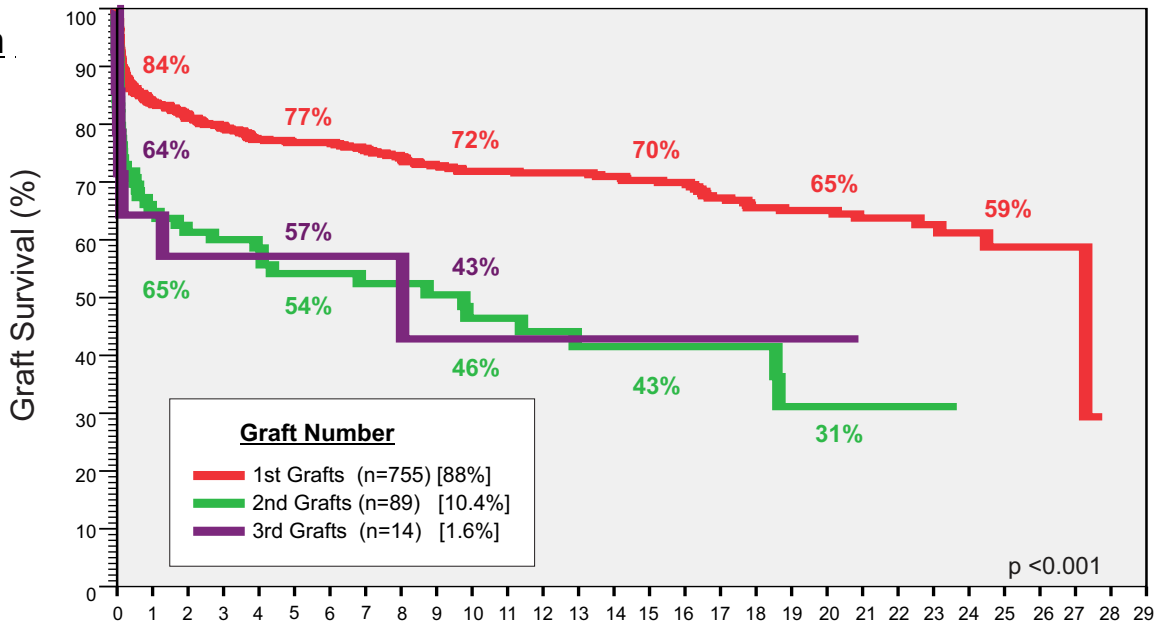
Graft Survival by Age Group



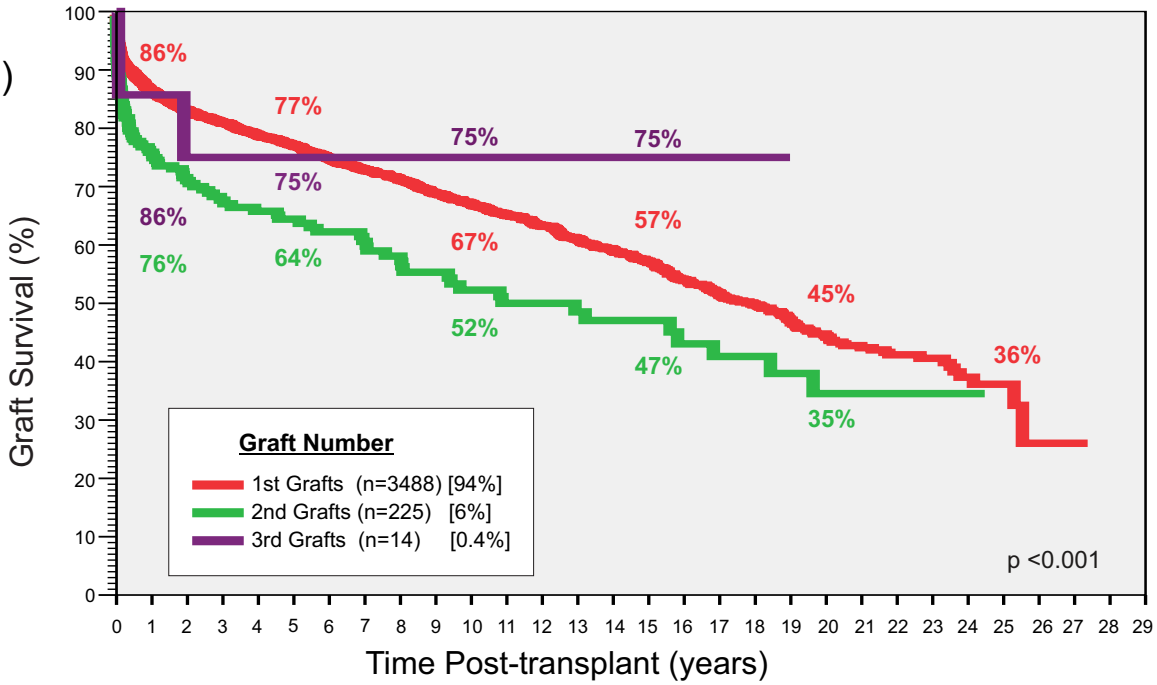
All Grafts
(n= 4585)



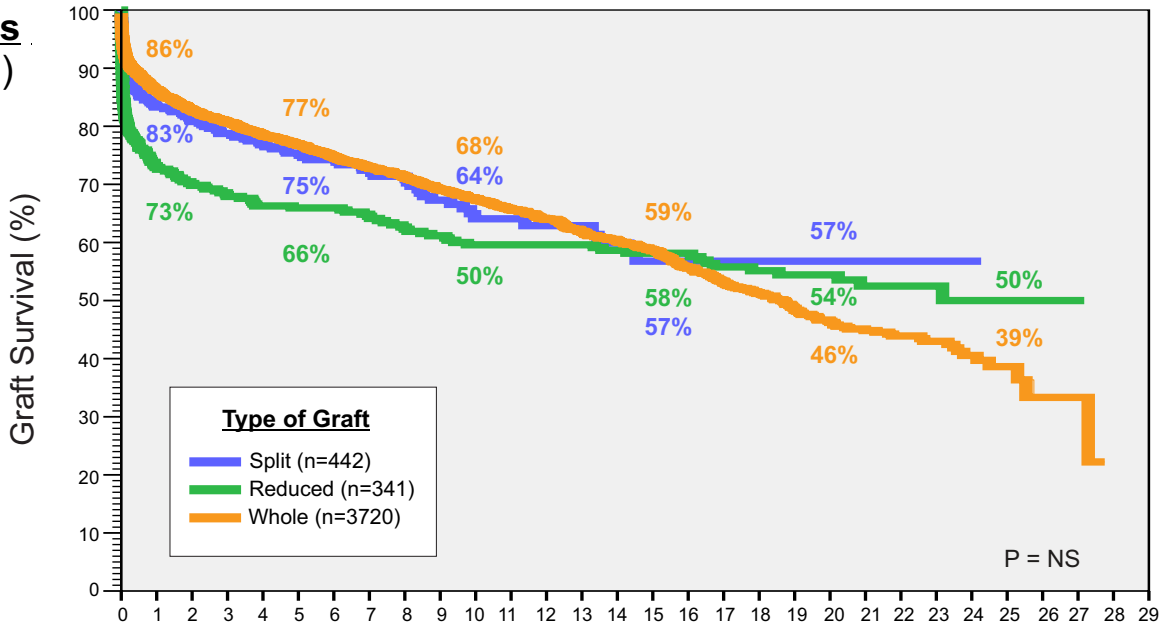
Children
(n= 858)



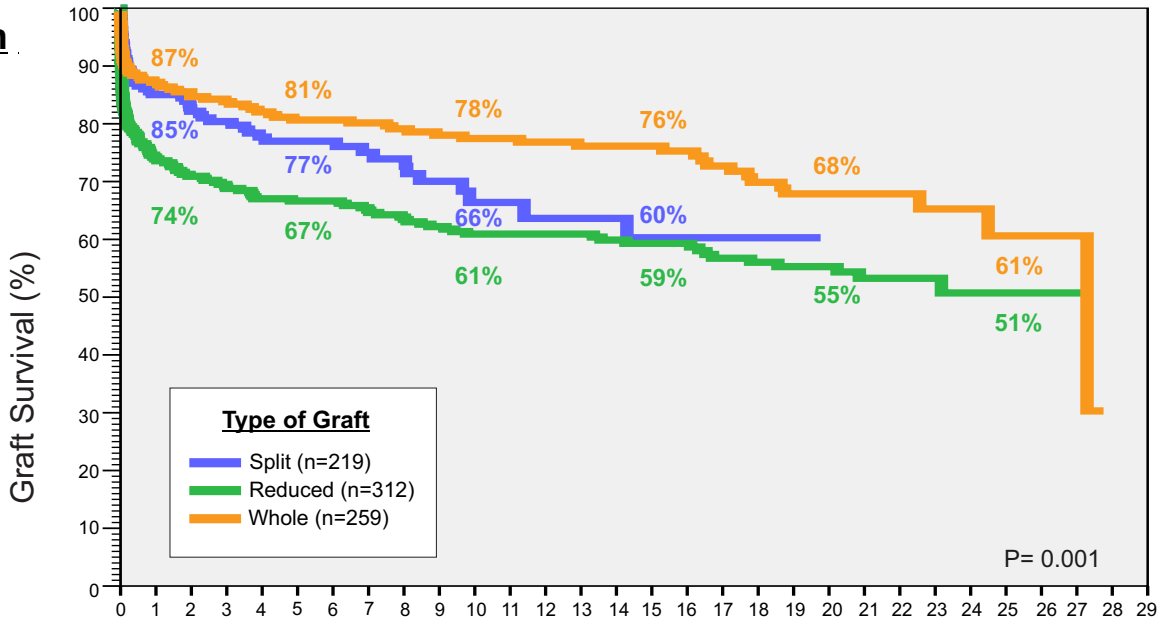
Adult
(n= 3727)



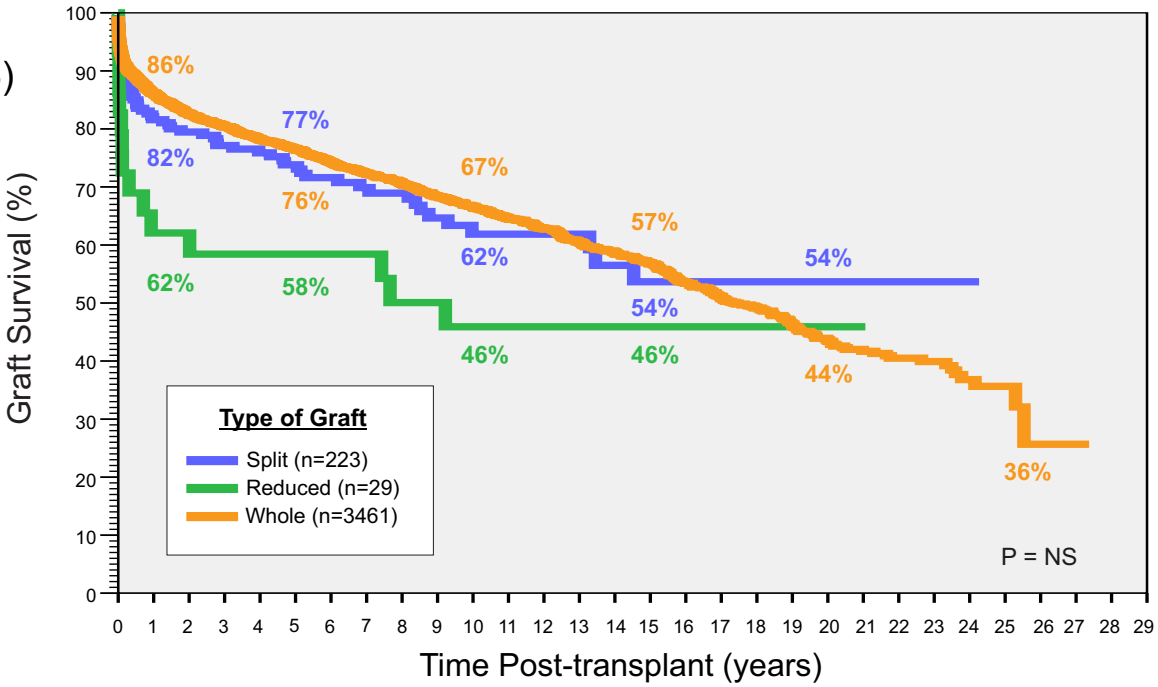
All Grafts
(n= 4503)



Children
(n= 790)



Adult
(n= 3713)



Time Post-transplant (years)

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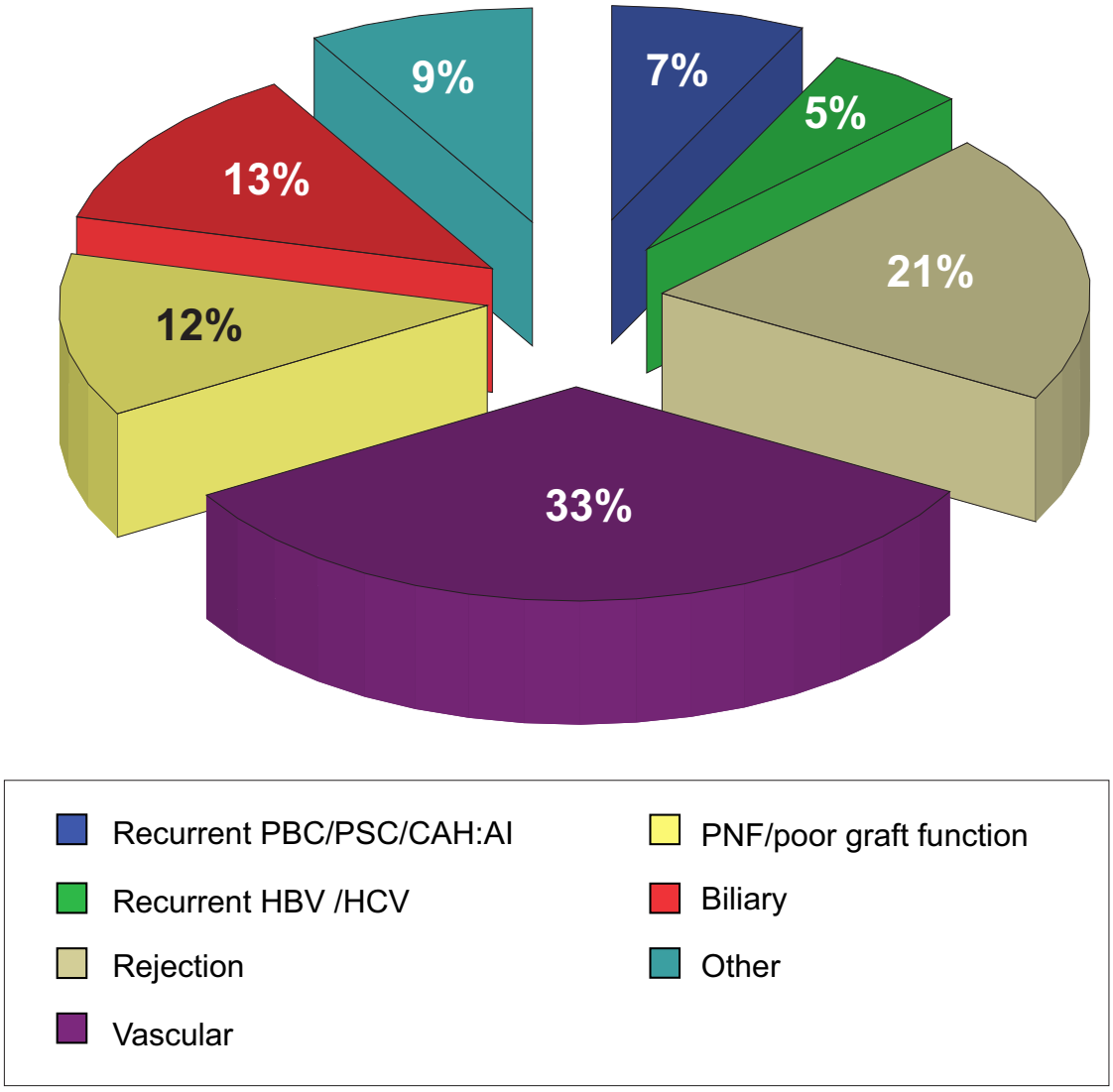
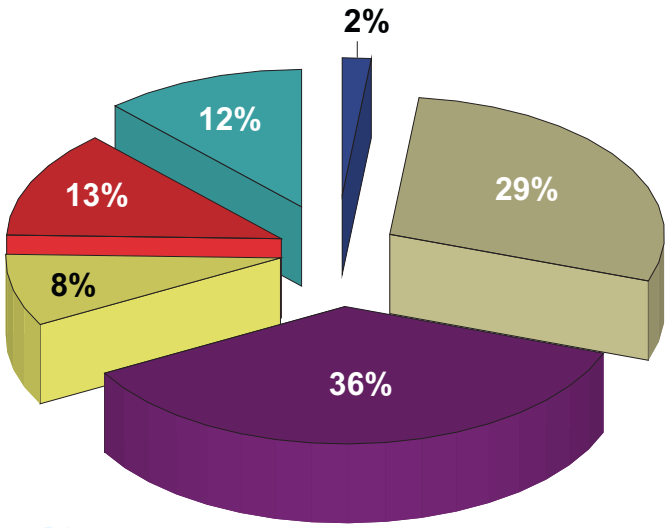
Indication for Retransplantation

n = 341 *(313 2nd grafts, 28 3rd grafts)*

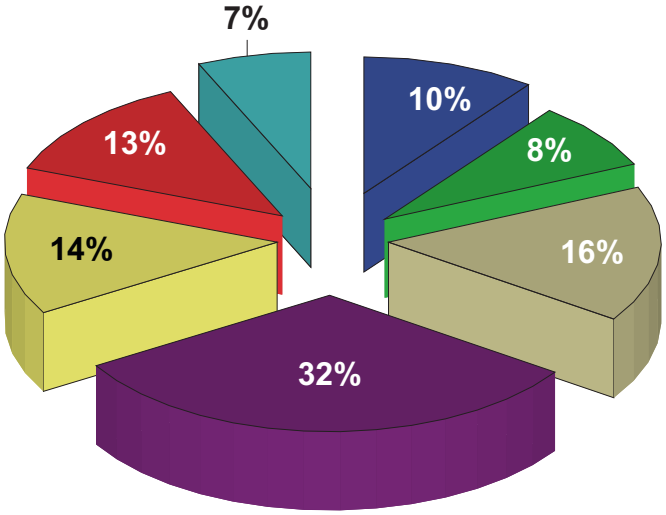


Age Group

Children
(n= 118)



Adults
(n= 223)



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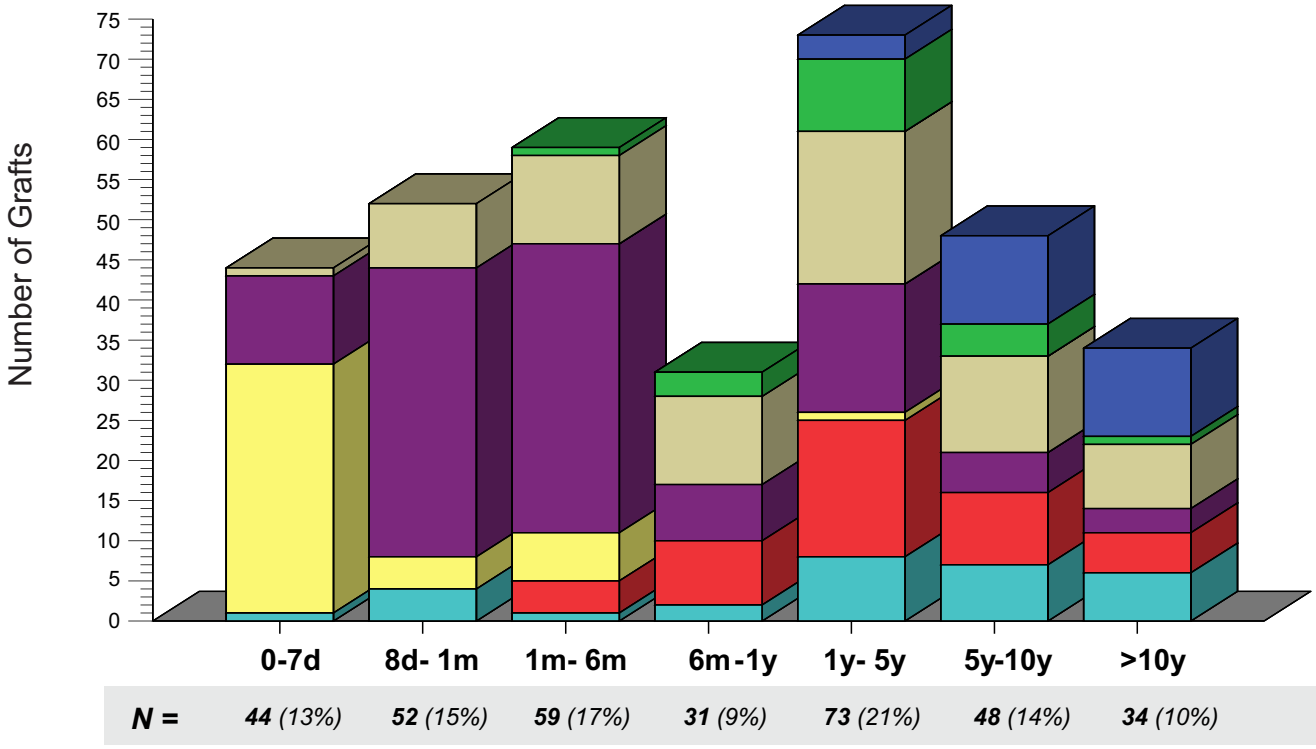
Indication for Retransplantation

n = 341 *(313 2nd grafts, 28 3rd grafts)*

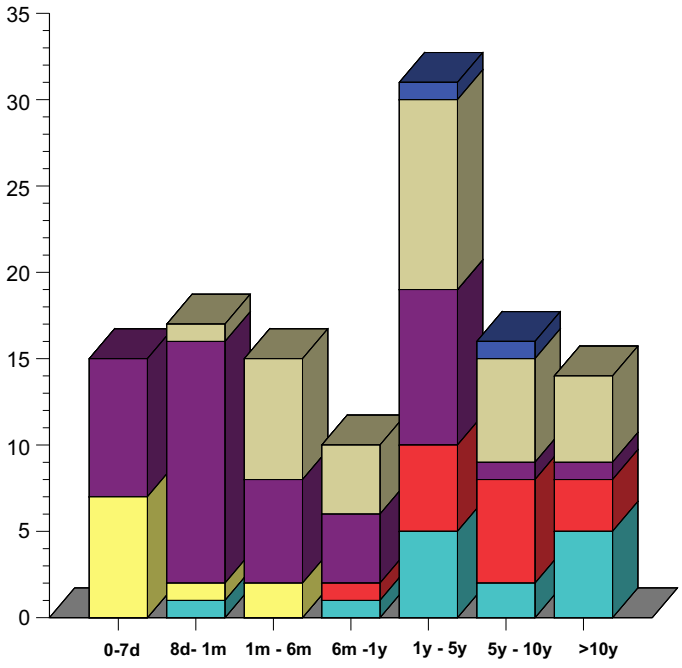


	0-7d	8d- 1m	1m- 6m	6m -1y	1y- 5y	5y-10y	>10y
N =	**44** (13%)	**52** (15%)	**59** (17%)	**31** (9%)	**73** (21%)	**48** (14%)	**34** (10%)

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

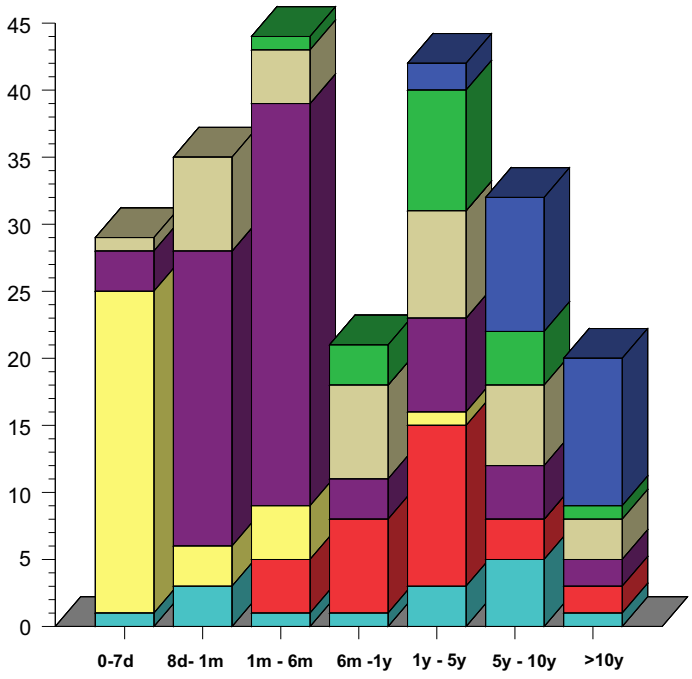
Recurrent HBV /HCV | Vascular | Biliary

Children (n=118)



	0-7d	8d- 1m	1m - 6m	6m -1y	1y - 5y	5y - 10y	>10y
N =	**15** (13%)	**17** (14%)	**15** (13%)	**10** (8%)	**31** (26%)	**16** (14%)	**14** (12%)

Adults (n=223)



	0-7d	8d- 1m	1m - 6m	6m -1y	1y - 5y	5y - 10y	>10y
N =	**29** (13%)	**35** (16%)	**44** (20%)	**21** (9%)	**42** (19%)	**32** (14%)	**20** (9%)

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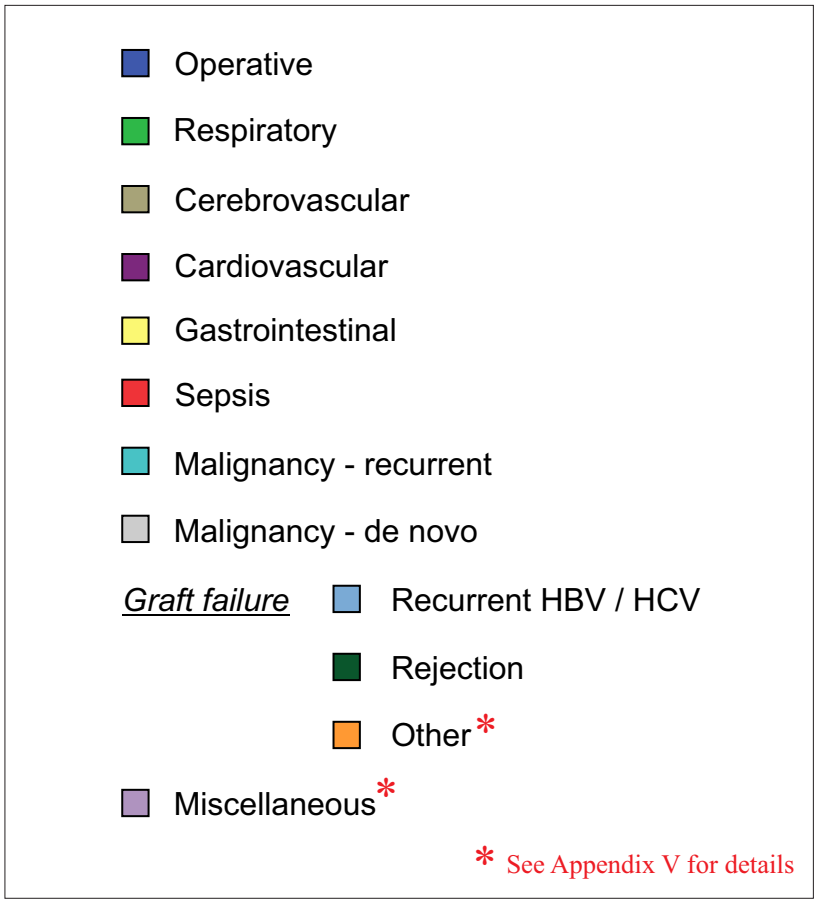
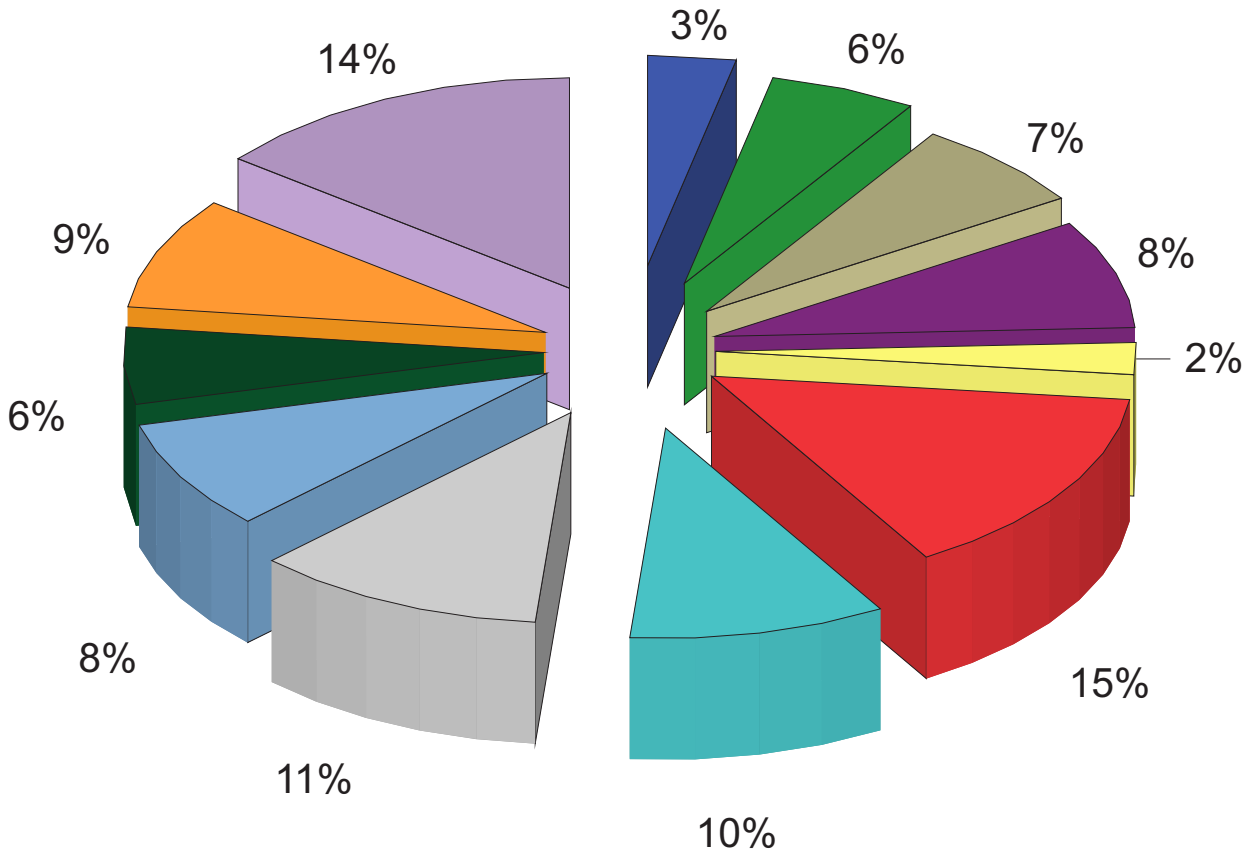
Section 5

Cause of Patient Death

All Patients n = 1185





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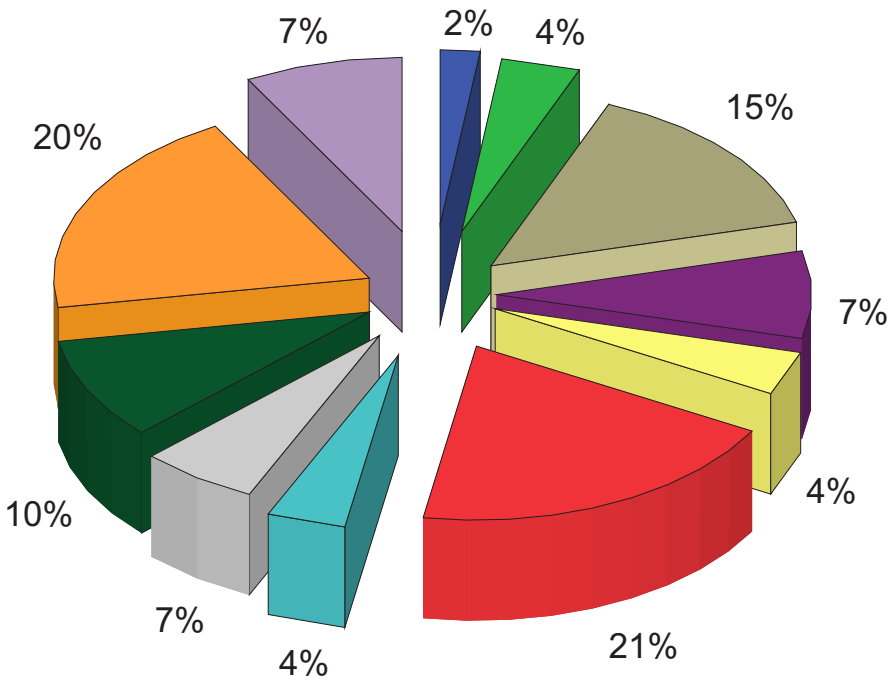
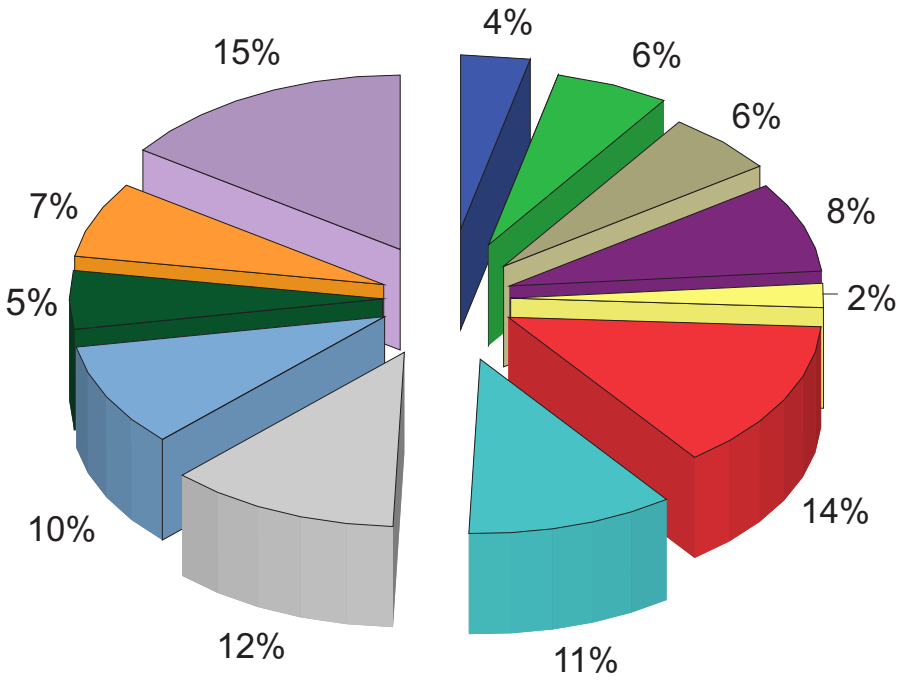
Causes of Death in Children
n =148



Causes of Death in Adult
n = 1037



- 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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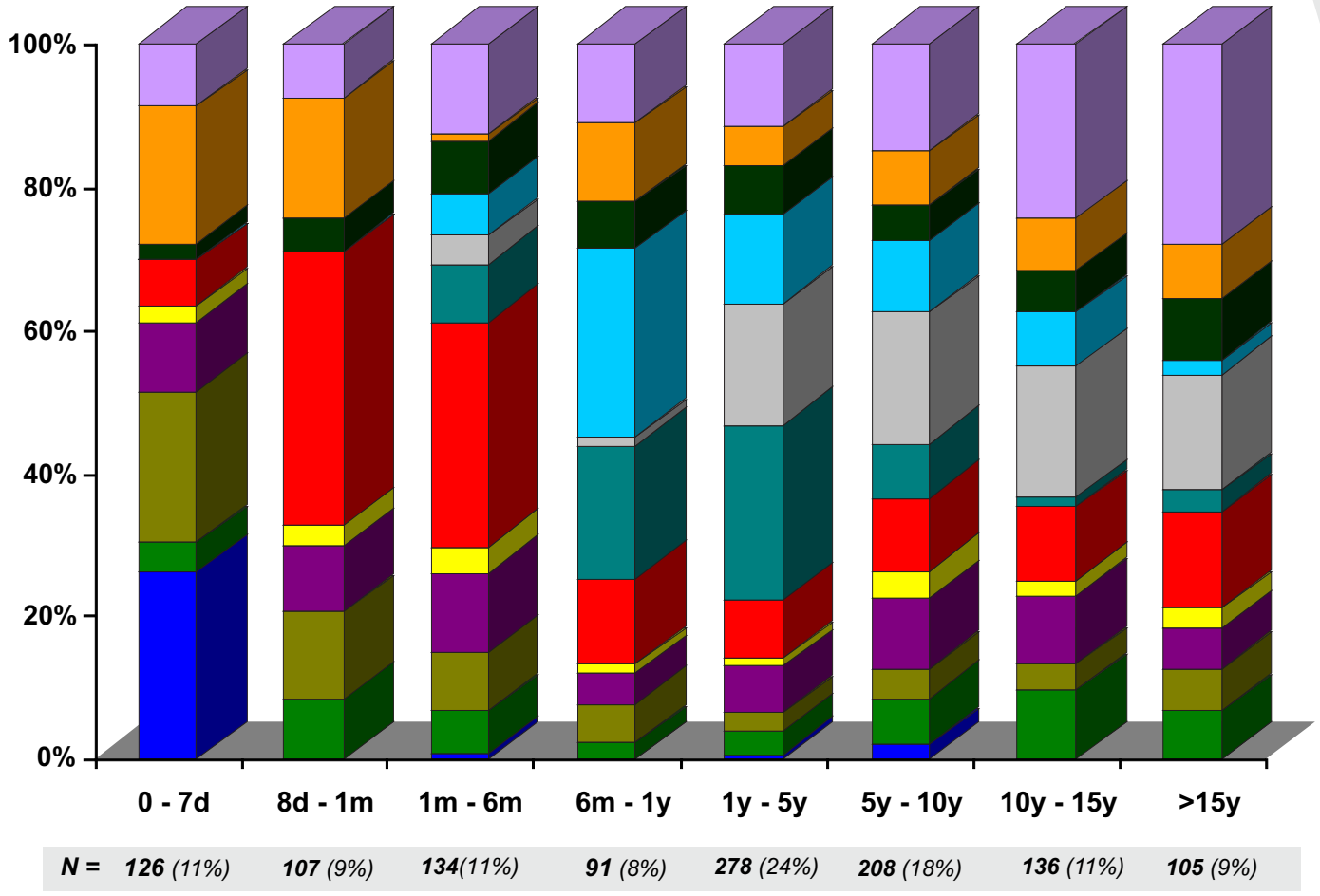
Cause of Death by Time Post Transplant



N =	126 (11%)	107 (9%)	134(11%)	91 (8%)	278 (24%)	208 (18%)	136 (11%)	105 (9%)

- 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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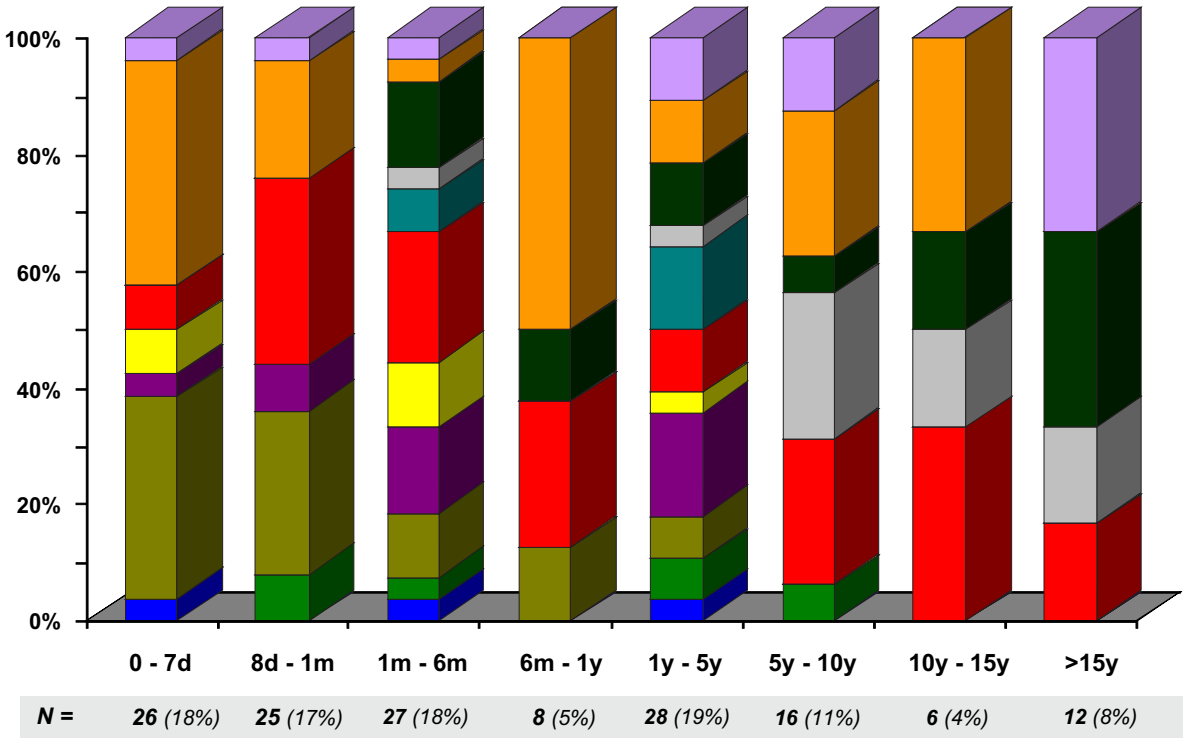
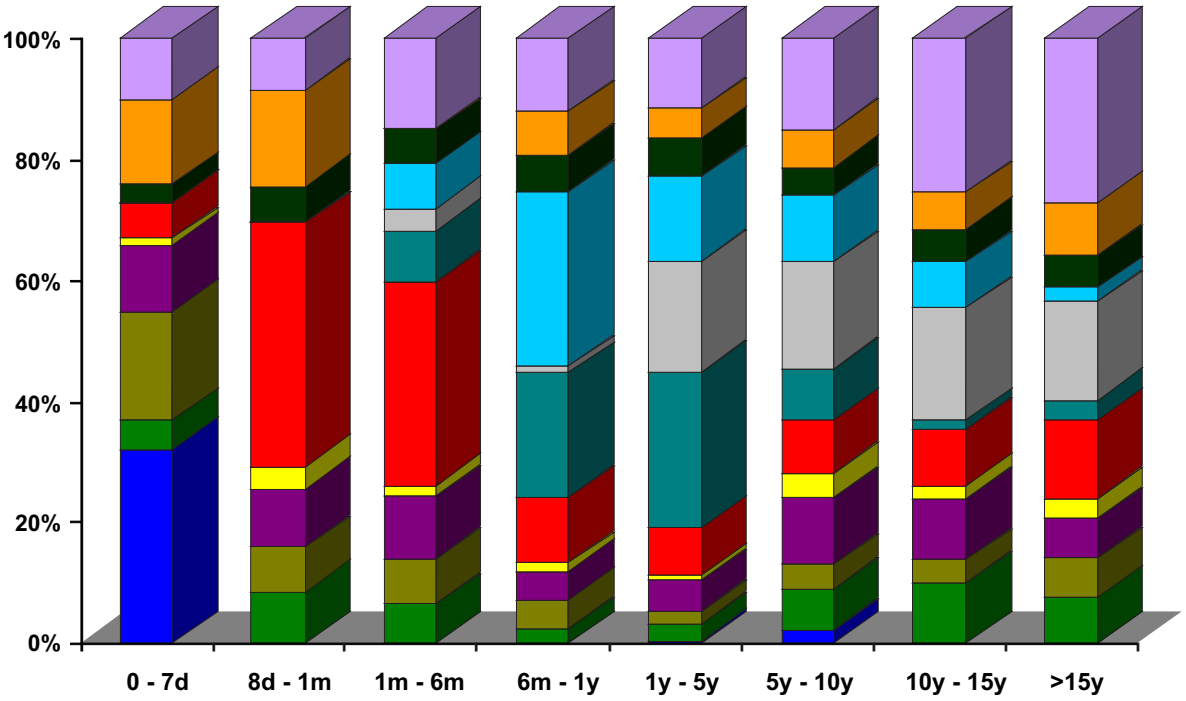
Cause of Death by Time Post Transplant Children (n=148)



N =	0 - 7d	8d - 1m	1m - 6m	6m - 1y	1y - 5y	5y - 10y	10y - 15y	>15y
	26 (18%)	25 (17%)	27 (18%)	8 (5%)	28 (19%)	16 (11%)	6 (4%)	12 (8%)

Cause of Death by Time Post Transplant Adult (n=1037)



N =	0 - 7d	8d - 1m	1m - 6m	6m - 1y	1y - 5y	5y - 10y	10y - 15y	>15y
	106 (10%)	82 (8%)	107 (10%)	83 (8%)	250 (24%)	192 (19%)	130 (12%)	93 (9%)

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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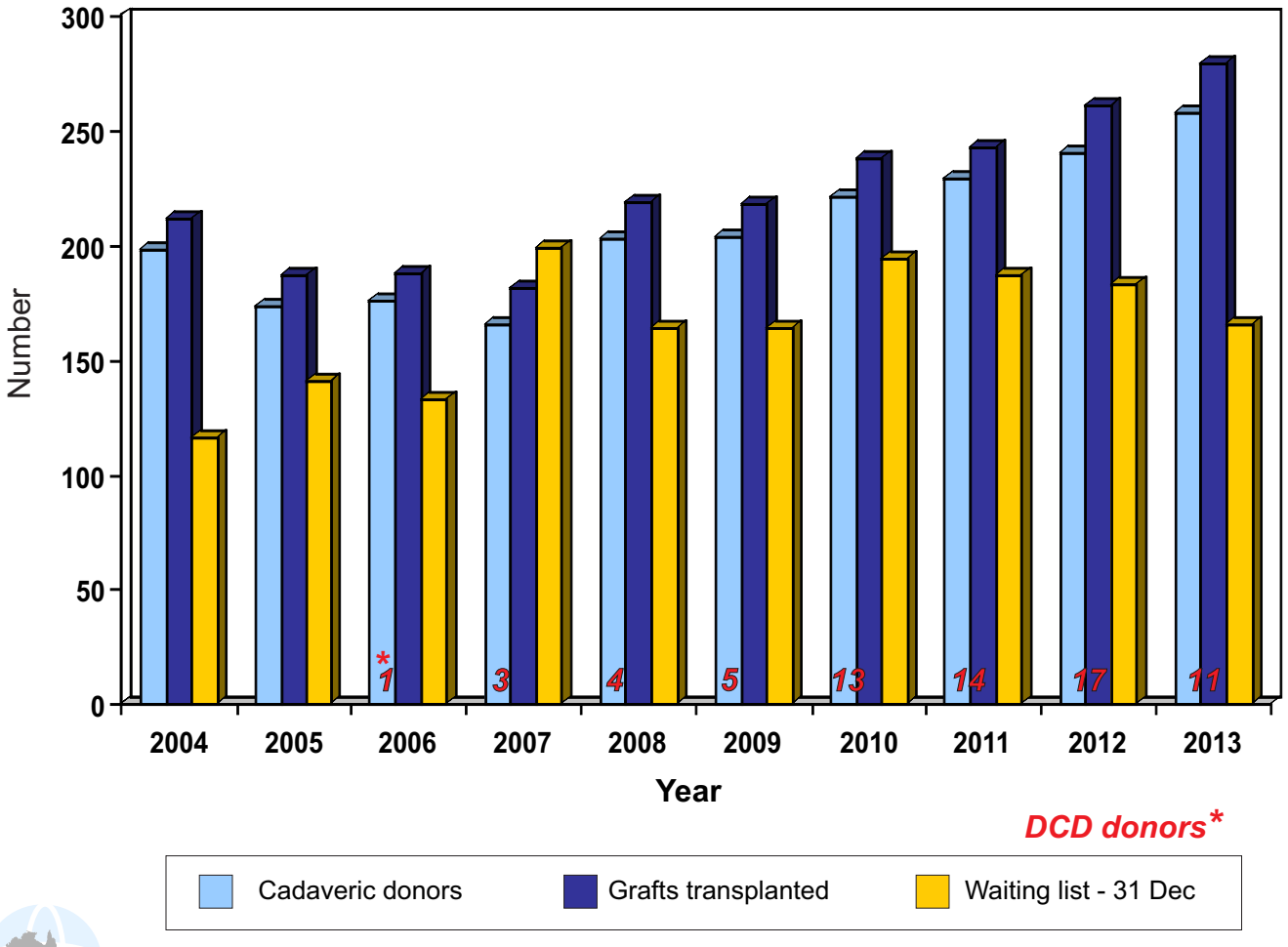
Deceased Donation by Year

	QLD	NSW/ACT	VIC/TAS	SA/NT	WA	NZ	TOTAL
2004	30	49/4	35/1	26/1	17	35	198
2005	24	36/8	38/2	17/3	25	21	174
2006	28	34/3	39/6	25	17	24	176
2007	25	36/1	36	19/2	15	32	166
2008	33	40/3	41/5	31/1	25	23	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

Grafts from deceased donors



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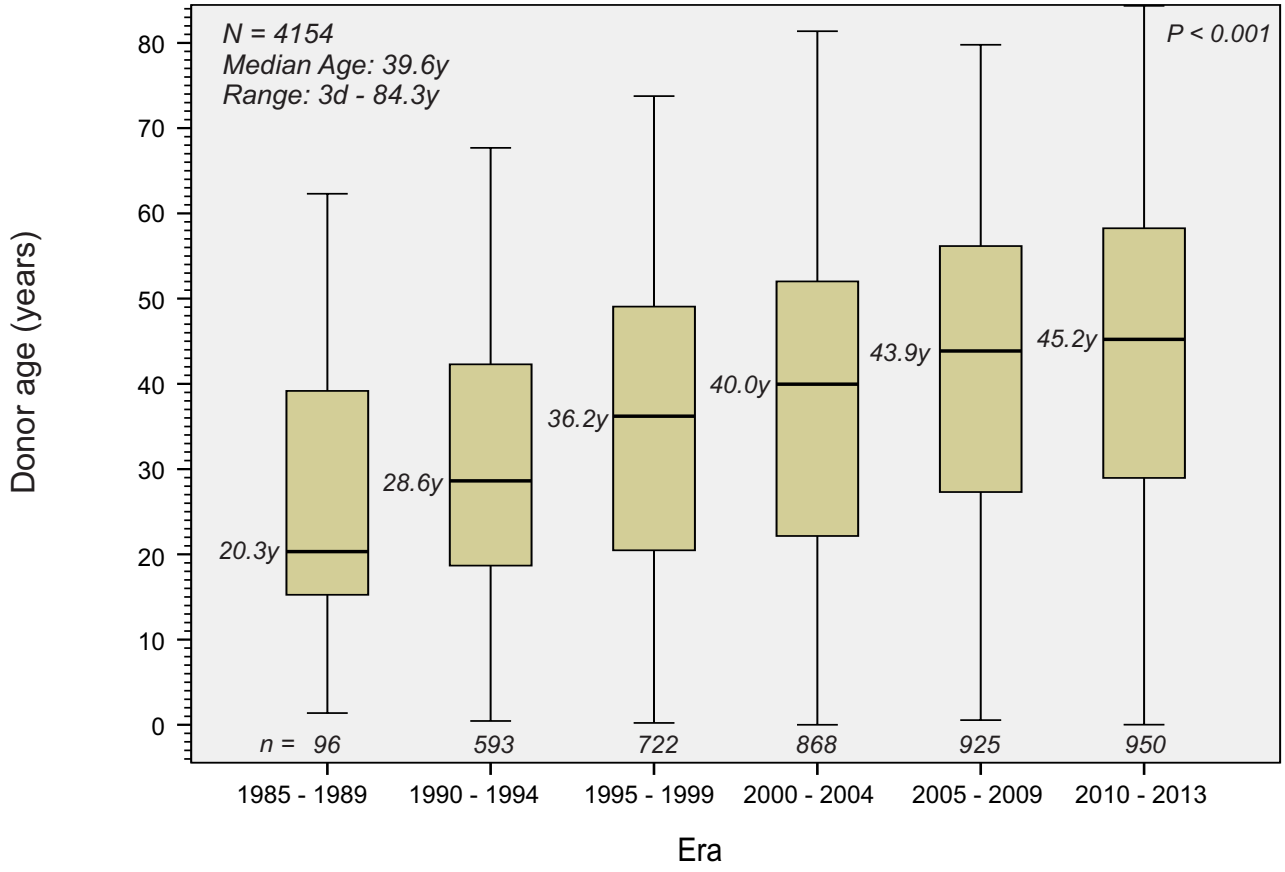
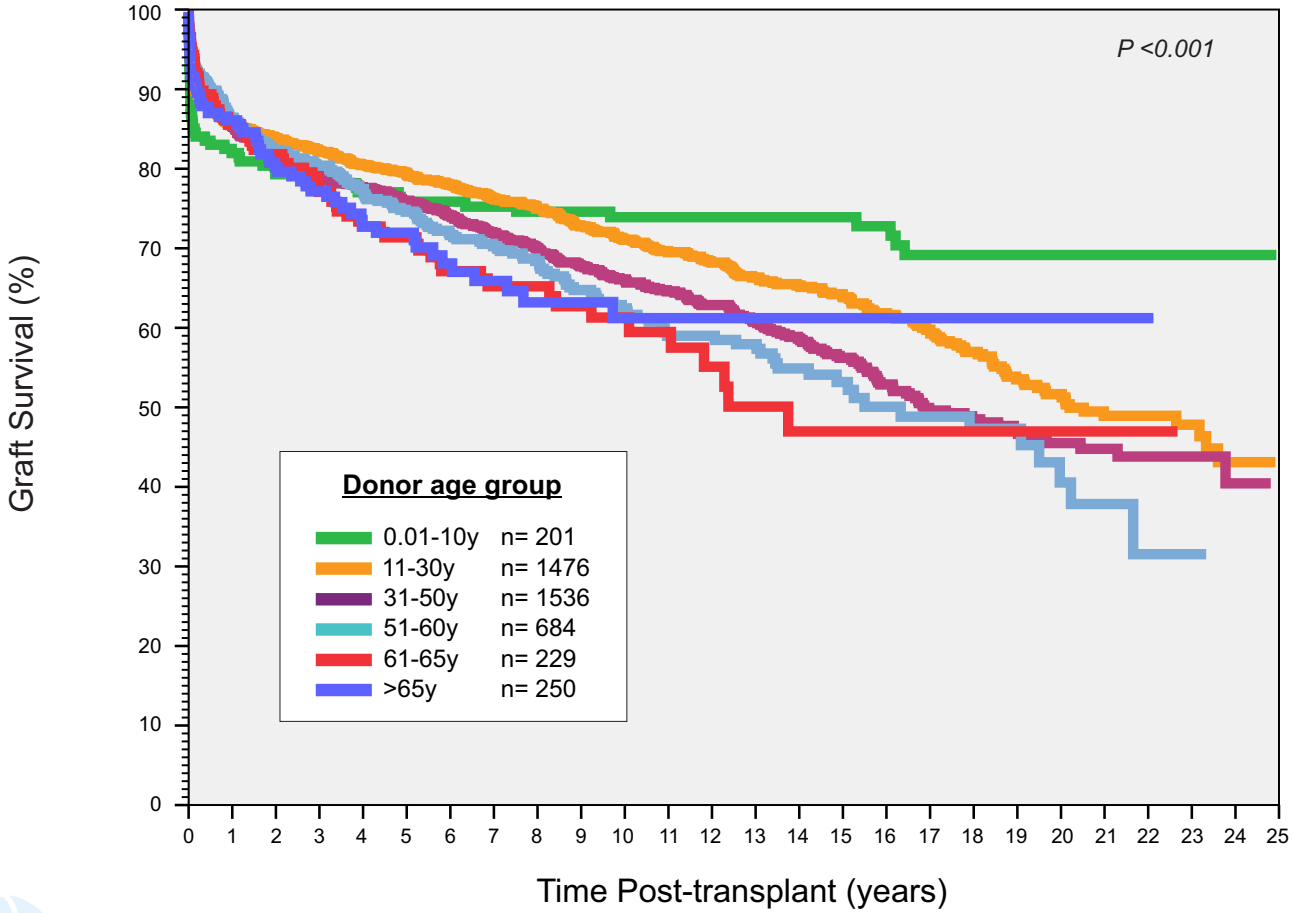
Donor Age by Era
N = 4154



Graft Survival by Donor Age
N = 4376



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Section 7

Living Donor Transplantation

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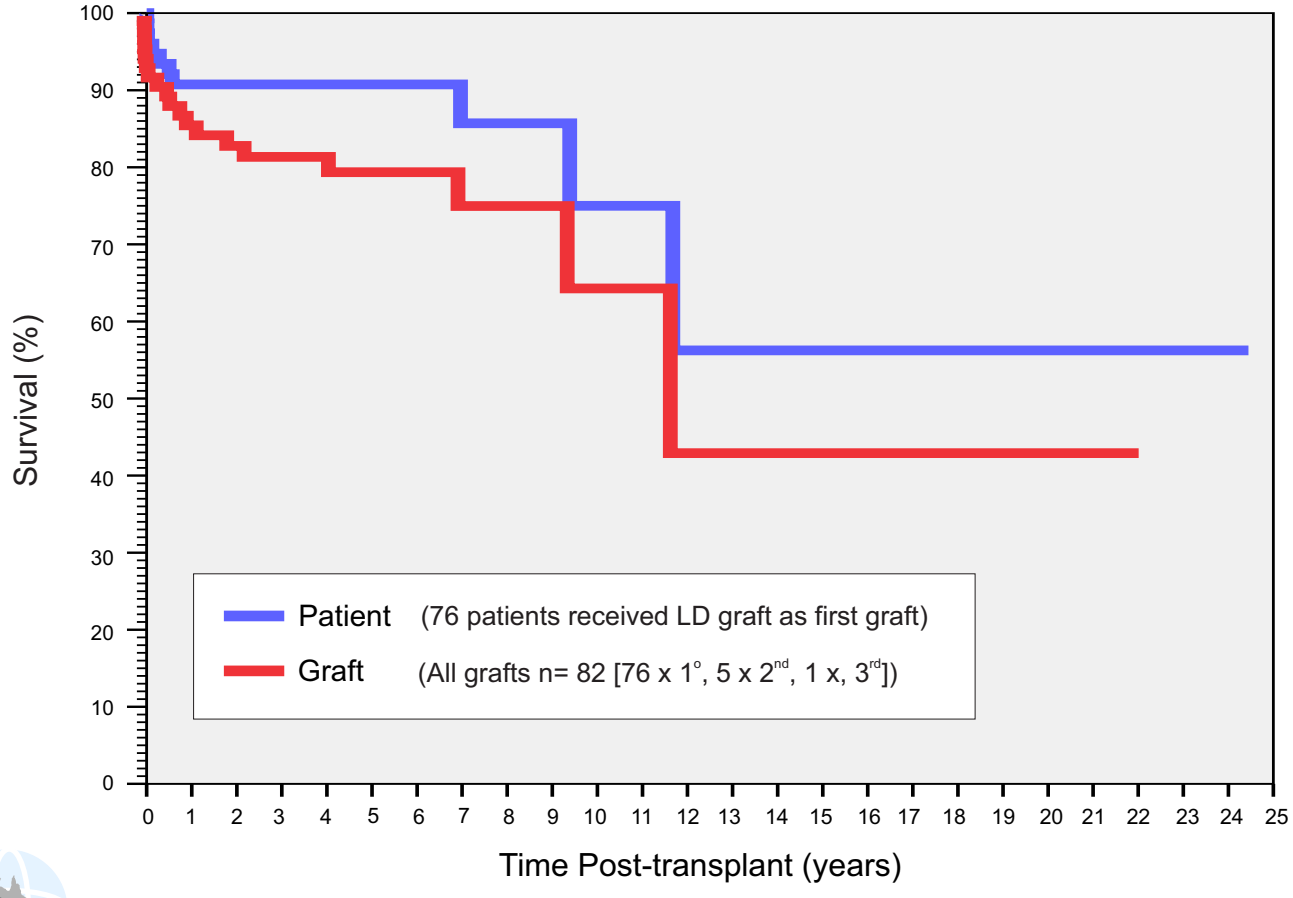
Living Donor Transplantation
N = 82

	Recipient Age Group		
	Child [n=67]	Adult [n=15]*	All [n=82]
Donor gender	-	-	-
Male	40	9	49
Female	27	6	33
Donor age	-	-	-
Median	35y	30.4y	33.4y
Range	20.1 - 54.5y	22.8 - 54.3y	20.1 - 54.5y
Donor relationship	-	-	-
Mother	15	-	15
Father	32	-	32
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	6	1	7
Cousin	3	-	3
Spouse	-	1	1

* *2 x whole liver domino transplant*



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Section 8

Waiting List

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Waiting List Activity
[Data 1/1/08 - 31/12/13]

Activity	2009	2010	2011	2012	2013				
Listed at 1 January	169	175	194	192	186	-	TOTAL 2013	Adult	Paediatric
New listings	335	335	336	351	-	360			
TOTAL	**504**	**510**	**530**	**543**	**186**	**360**	**546**	**475**	**71**
	OUTCOME					OUTCOME			
Transplant	**228 [46%]**	**248 [49%]**	**253 [49%]**	**268 [50%]**	**114**	**170**	**284 [52%]**	**238 [51%]**	**46 [63%]**
Delisted	**101 [20%]**	**68 [13%]**	**85 [13%]**	**89[13%]**	**36**	**62**	**98 [18%]**	**92 [20%]**	**6 [8%]**
Died on list	32	12	17	29	7	19	26	23	3
Too sick	17 } 14%	12 } 8%	17 } 8%	16 } 8%	1	10	11 [10%]	10 } 10%	1 } 6%
Tumour progression	8	12	20	10	4	12	16	16	-
Improved	18	16	12	17	14	10	24	22	2
Other	26	12*	19*	17*	10	11	21*	21	0
Still listed at 31 Dec	*175 [34%]*	*194 [38%]*	*192 [36%]*	*186 [34%]*	*36*	*128*	**164 [30%]**	*145*	*19*

[* Patient declined, Malignancy, Drug Use, Infection, Further investigations, Medical]

Outcome of Initial Urgent Listing

OUTCOME	CATEGORY 1						
	2009 (n=17)	2010 (n=19)	2011 (n=15)	2012 (n=16)	2013 N=19	2013 Adult n=12	2013 Paediatric n=7
TRANSPLANTED	9 } 65%	13 } 74%	12 } 80%	11 } 81%	11 } 74%	7	4
IMPROVED	2	1	-	2	3	2	1
DIED / TOO SICK	6	5	3	3	5	3	2
OTHER TREATMENT	-	-	-	-	-	-	-

OUTCOME	CATEGORY 2						
	2009 (n=21)	2010 (n=30)	2011 (n=28)	2012 (n=19)	2013 N=29	2013 Adult n=10	2013 Paediatric n=19
TRANSPLANTED	18 } 90%	23 } 93%	22 } 86%	14 } 89%	22 } 89%	8	14
IMPROVED	1	5	2	3	4	0	4*
DIED / TOO SICK	2	1 / 1	3	1	2	1	1
OTHER TREATMENT	-	-	1 active 31/12/11	1 active 31/12/12	1 active 31/12/13	1 active 31/12/13	-

[*4 temporary listing chronic patients; all later transplanted]

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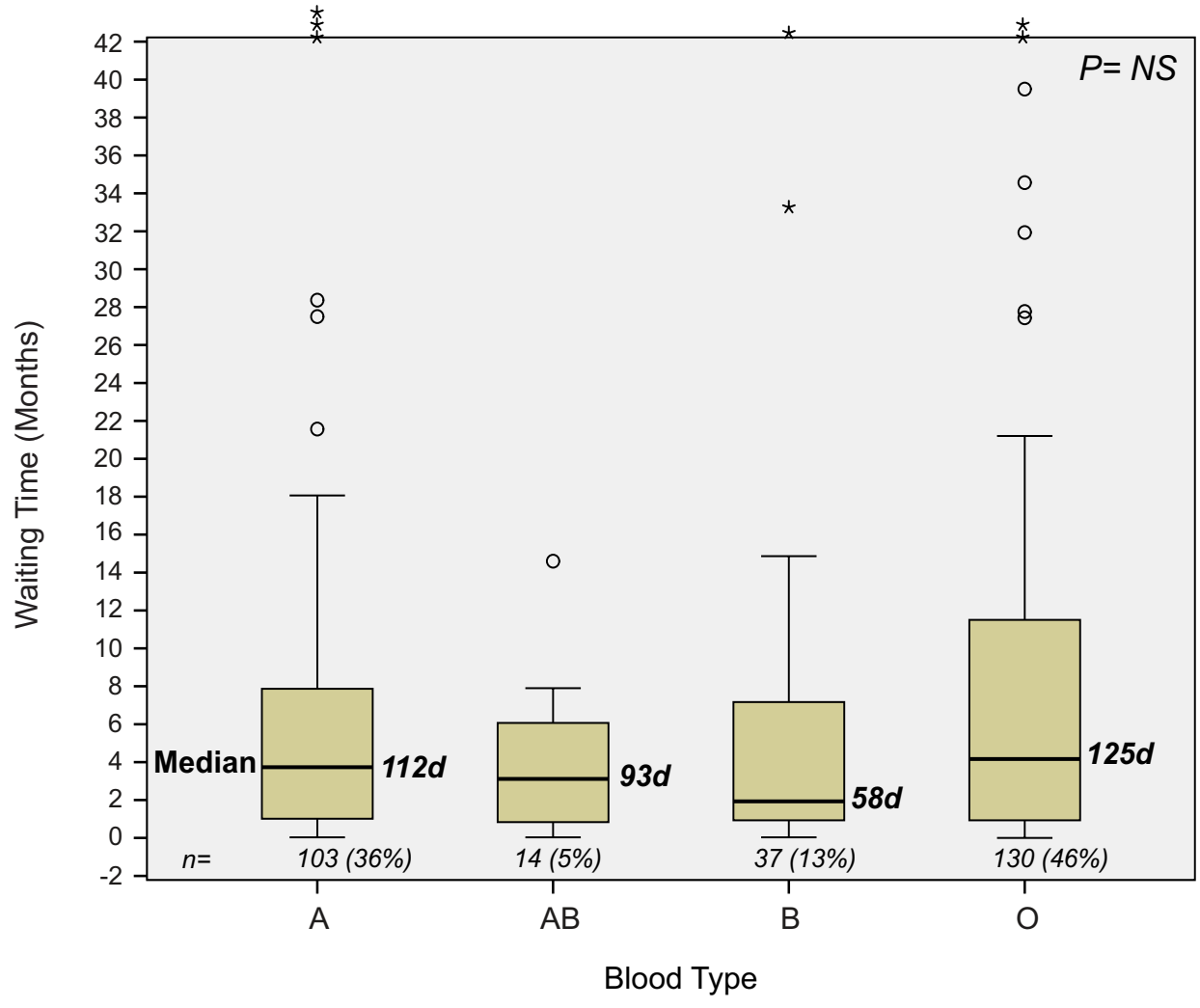
Outcome by Blood Group

	Blood Group				
	A	O	B	AB	TOTAL
n=	188 (35%)*	249 (46%)	83 (15%)	25 (5%)	545
Not transplanted	85	119	46	11	261
Transplanted	103 (55%)**	130 (52%)	37 (45%)	14 (56%)	284

* *% of total number listed*

** *% of blood group*

Waiting Time to Transplant 2013



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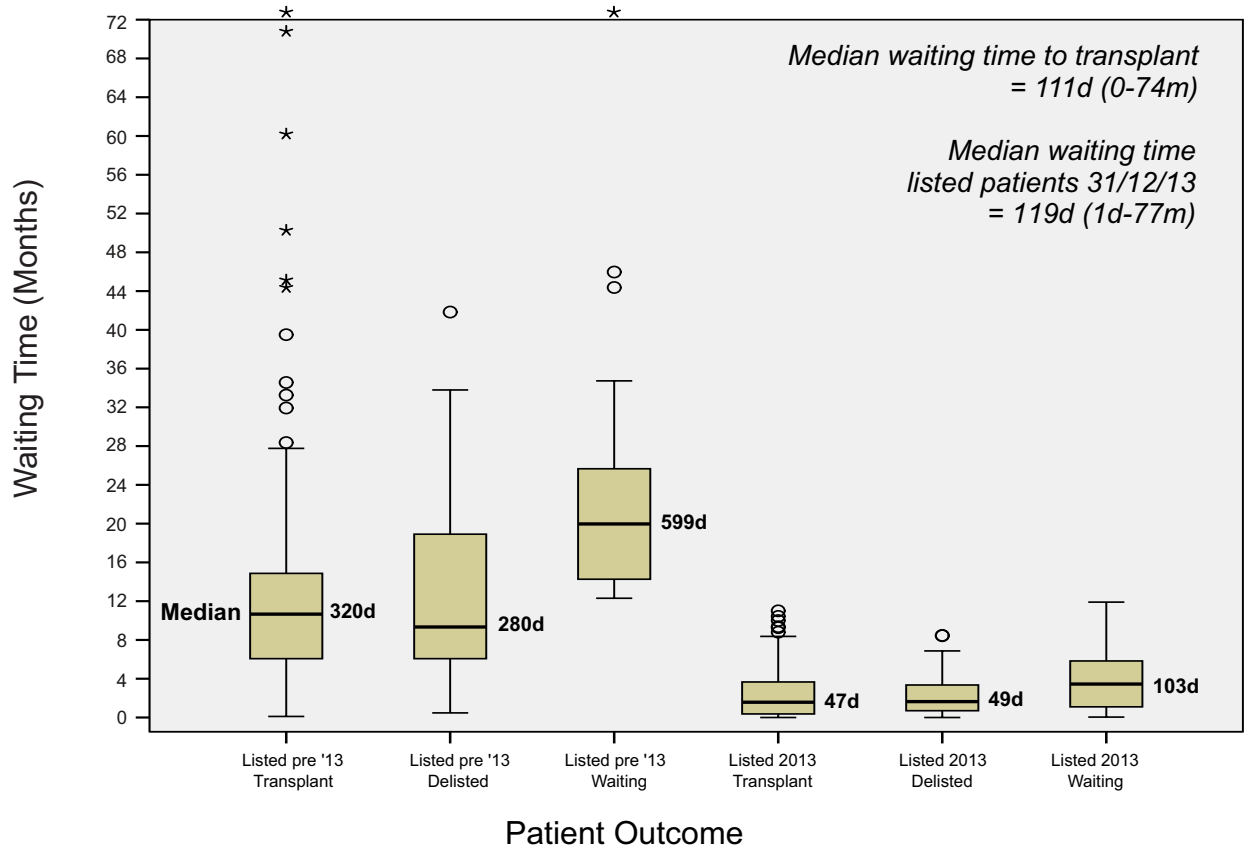
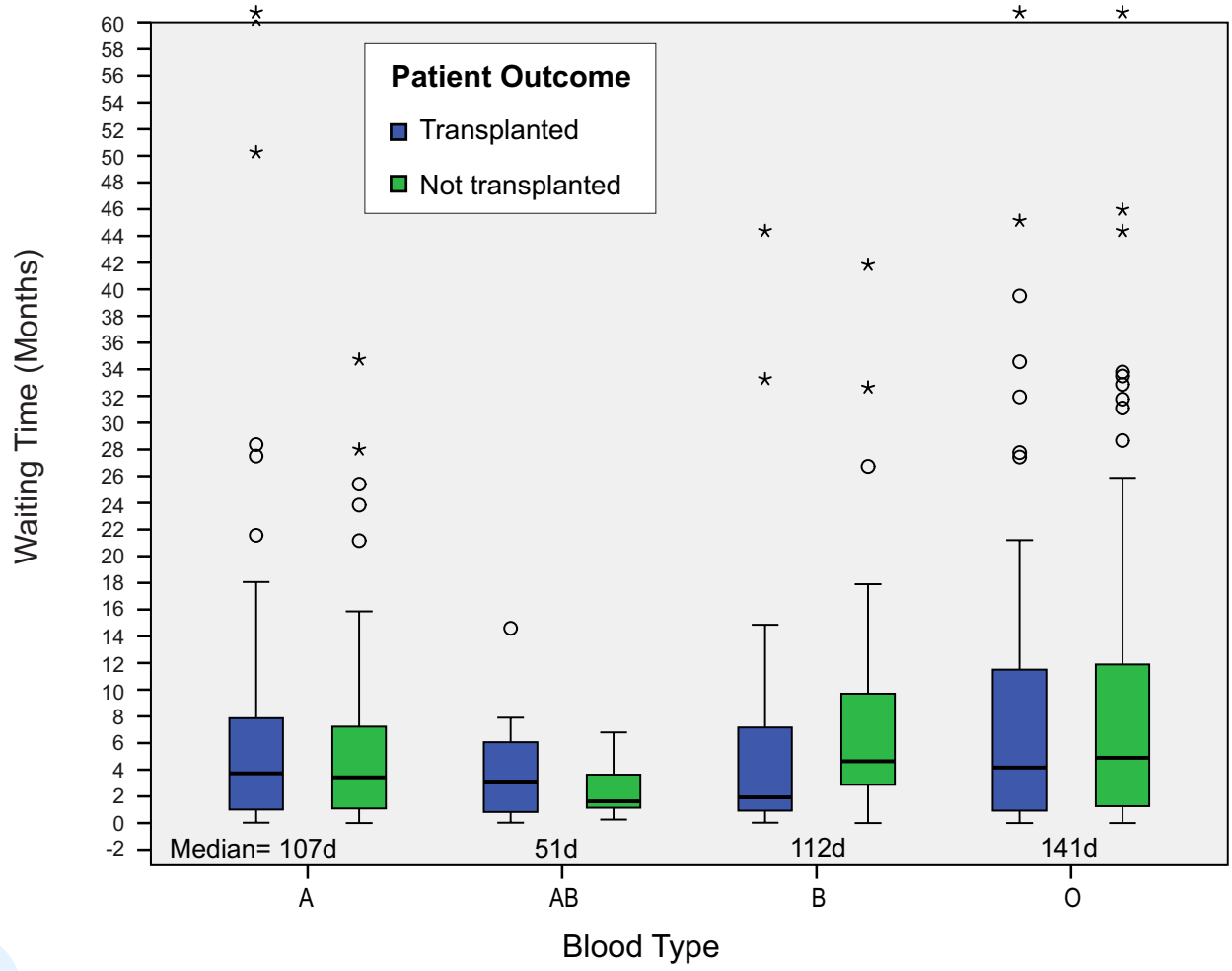
Waiting Time by Outcome



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 = 4244

At Tx	Total number pts. transplanted = 4244
Liver Cancer as indication for Transplant	336 (8%)
Liver Ca as a Secondary Diagnosis	521 (12%) 523 Ca
Total	858* (20%)
Post Tx	
Recurrent Liver Ca	118 (3% of all pts, 14% pts with Ca at Tx)
De Novo Ca	303 (7%) 329 Ca
Skin Ca	616 (14%)
Total	1038 (24%)
Multiple Ca types	204 (5% of all pts)
Pre-Tx cancer developed de novo non skin cancer	184 (4% of pts with Ca at Tx)
Transferred from Donor	2
Developed non skin Ca < 90days	9

Data to 31/12/2013

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

Liver Cancer as Primary Diagnosis
n = 336/4244

TYPE OF CA	No	DIED	DIED OF THIS CA
HEPATOCELLULAR CA	298	68	36 (51%)
HEPATOBLASTOMA	20	6	4 (67%)
FIBROLAMELLAR	6	5	2 (40%)
CARCINOID	4	4	4 (100%)
EPITHELOID HAEMANGIOENDOTHELIOMA	3	0	0
CHOLANGIOCARCINOMA	2	1	1 (50%)
ANGIOSARCOMA	1	1	1 (100%)
GASTRINOMA	1	1	1 (100%)
PANCREATIC ISLET CELL	1	1	1 (100%)
TOTALS	**336 (8% of pts)**	**87 (26% of those with PCa)**	**50 (15% of those with PCa)**

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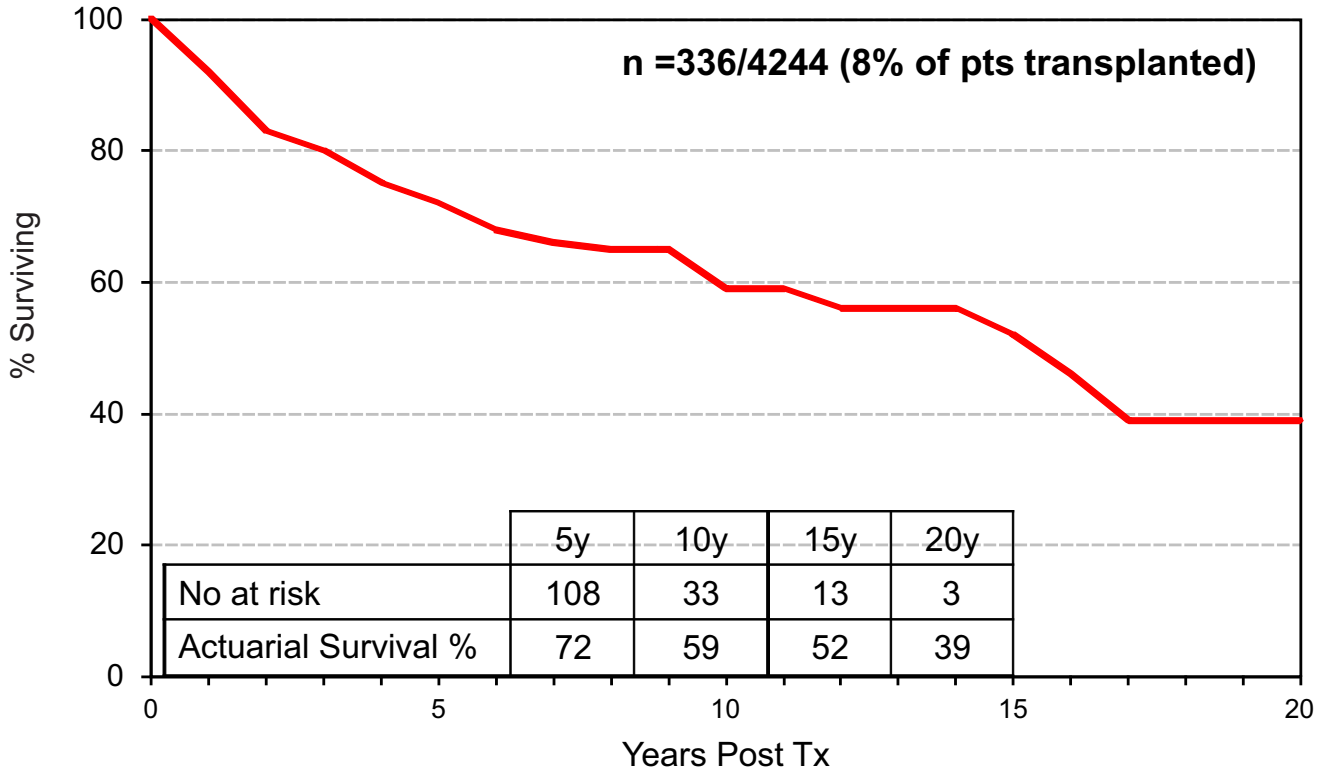
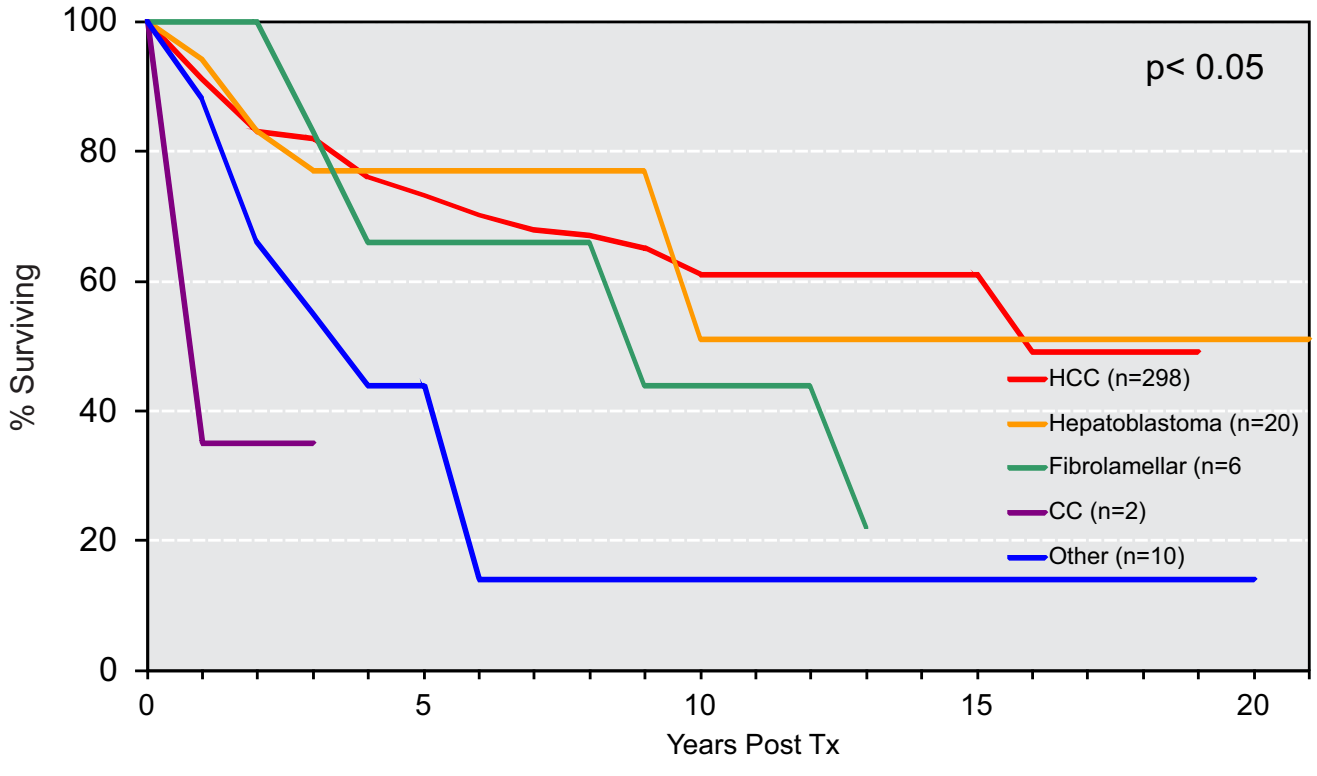
Overall Survival
Primary Liver Cancer
n = 336/4244 (8% of pts transplanted)



	5y	10y	15y	20y
No at risk	108	33	13	3
Actuarial Survival %	72	59	52	39

Overall Survival
Primary Liver Cancer
n = 336/4244 (8%)



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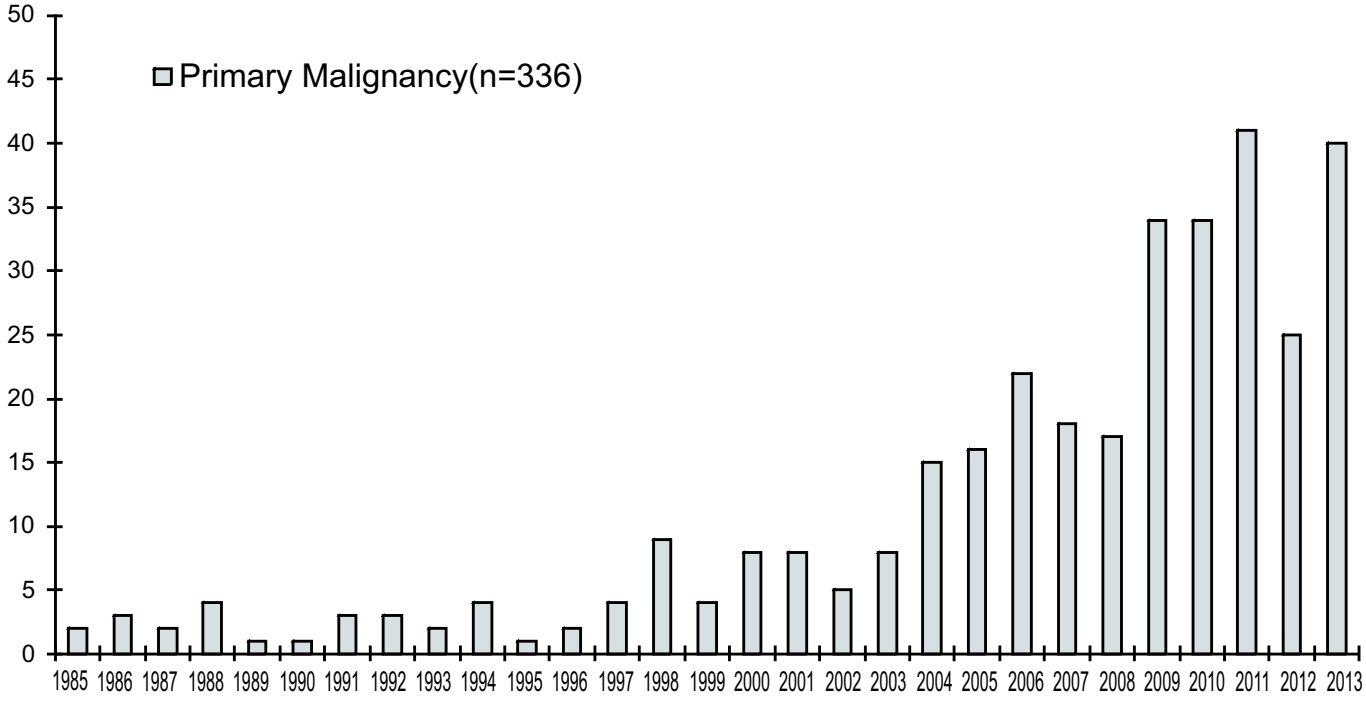
Primary Liver Cancer
Actuarial Survival Summary
n =336/4244

		1yr	5yr	10yr	15yr	20yr
HCC (n=297)	n	238	96	26	6	1
	%	91	73	61	61	49
Hepatoblastoma (n=20)	n	16	7	3	2	1
	%	94	77	51	51	51
Other (n=10)	n	9	4	2	1	1
	%	88	44	14	14	14
Fibrolamellar (n=6)	n	6	4	4	2	
	%	100	66	66	11	
CC (n=2)	n	1	0			
	%	100				

Primary Liver Cancer Incidence
n = 336/4244



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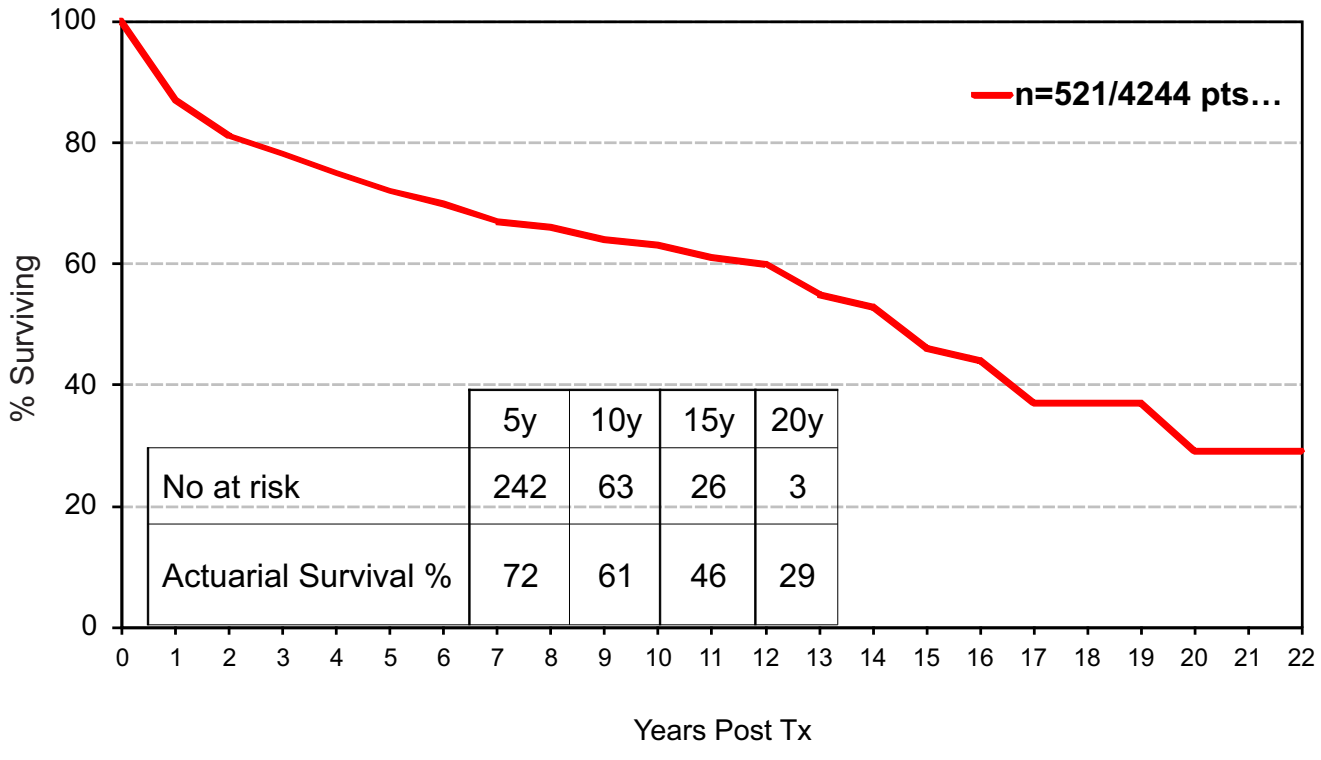
Liver Cancer as a Secondary Diagnosis
n = 521/4244

	No	Died	Died of This Cancer
HEPATOCELLULAR CA*	472	133	37(28%)
CHOLANGIO CA	37	29	16(56%)
FIBROLAMELLAR	4	0	0
HEPATOBLASTOMA*	3	1	0
OTHER	7	5	2
Total	**523* in 521 pts (12%)**	**168 (32% of pts with SCa)**	**55 (11% of pts with SCa)**

*** 2 patients had 2 secondary cancers**

Overall Survival
Liver Cancer as a Secondary Diagnosis



	5y	10y	15y	20y
No at risk	242	63	26	3
Actuarial Survival %	72	61	46	29

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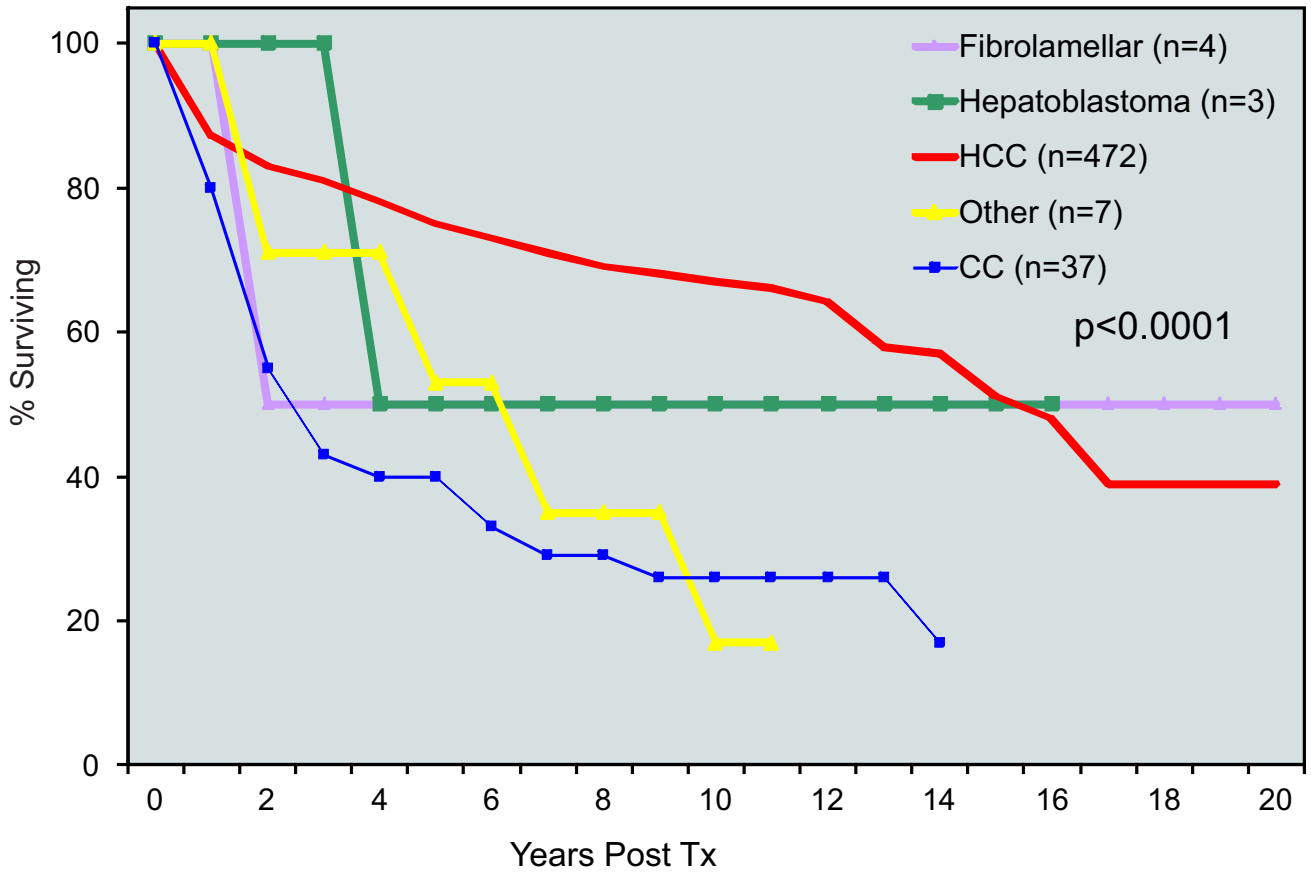
Liver Cancer as a Secondary Diagnosis
n =521/ 4244 (12%)



Secondary Liver Cancer
Actuarial Survival Summary
n =521/ 4244 (12%)

		1yr	5yr	10yr	15yr
CC (n=37)	n	30	13	5	2
	%	80	40	26	0.8
HCC (n=470)	n	376	225	101	15
	%	87	75	67	48
Hepatoblastoma (n=3)	n	3	2	2	1
	%	66	66	66	66
Fibrolamellar (n=4)	n	4	4	2	1
	%	100	53	50	50
Other (n=7)	n	7	3	2	0
	%	100	50	17	0

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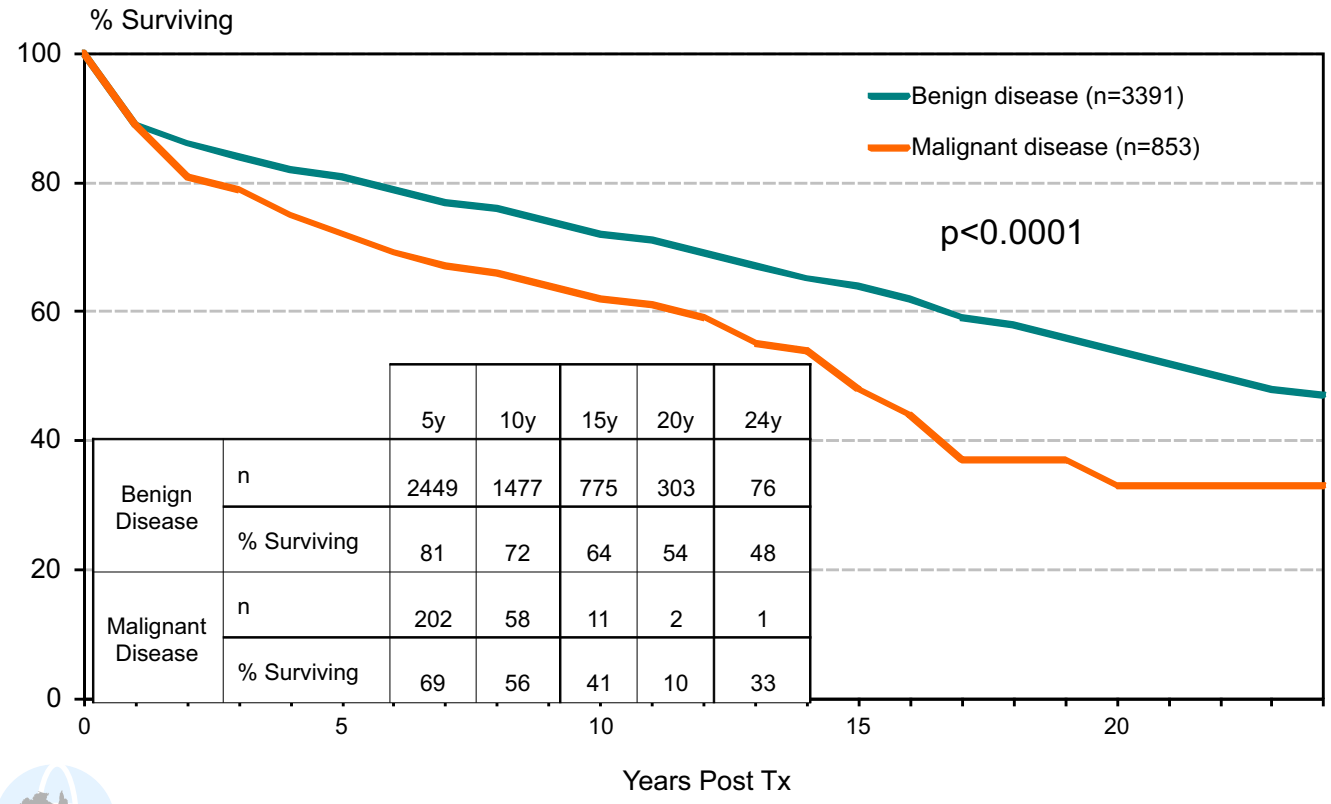
Liver Cancer (Primary or Secondary Diagnosis) n = 853/4244

TYPE OF CA	No.	DIED	DIED OF THIS CA
HEPATOCELLULAR CA*	769	203	74 (37%)
CHOLANGIOCARCINOMA*	39	29	17 (55%)
HEPATOBLASTOMA*	23	6	4 (25%)
FIBROLAMELLAR	10	5	2 (40%)
CARCINOID	4	4	4 (100%)
ADENOCARCINOMA	5	3	1 (25%)
EPITHELOID HAEMANGIOENDOTHELIOMA	4	0	0 0
ANGIOSARCOMA	2	2	2 (100%)
GASTRINOMA	1	1	1 (100%)
PANCREATIC ISLET CELL	1	1	1 (100%)
TOTALS	**858* Ca in 853 pts (20% of pts)**	**254 (30%of those with Ca)**	**106 (12% of those with Ca at Tx)**

*** 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 = 4244



		5y	10y	15y	20y	24y
Benign Disease	n	2449	1477	775	303	76
	% Surviving	81	72	64	54	48
Malignant Disease	n	202	58	11	2	1
	% Surviving	69	56	41	10	33

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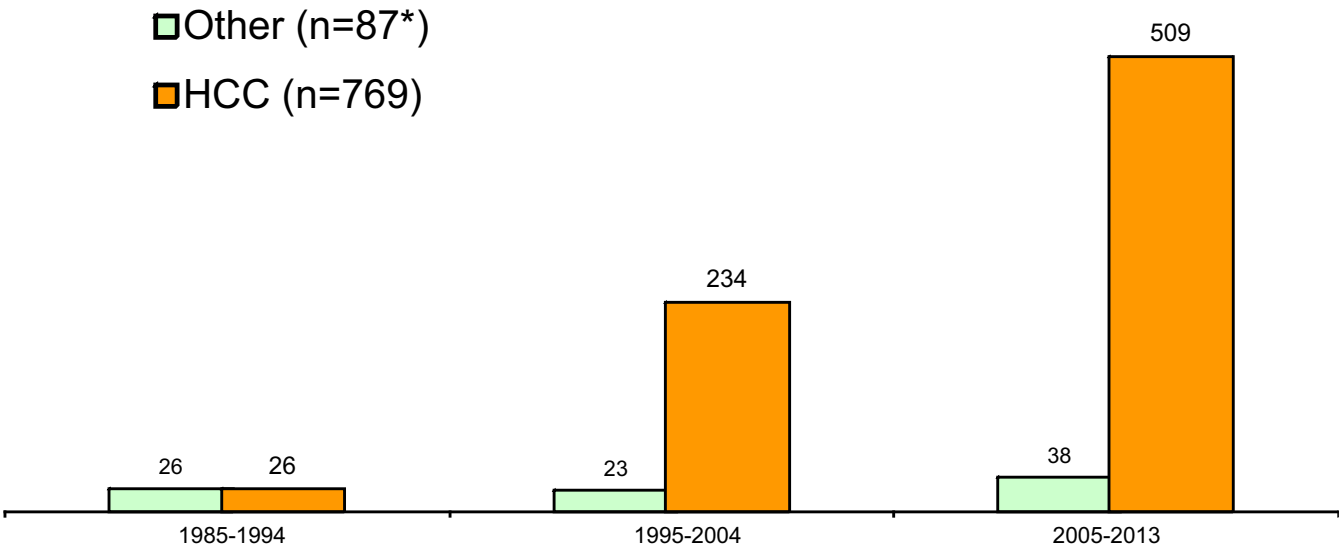
Liver Cancer at Transplantation
n = 853/4244 (20%)



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

De Novo Non Skin Cancer
n = 303/4244

	No	Male	Female	Age of pts (yrs)	Time to diagnosis (mths)	Died of This Cancer
Alimentary*	121	91	30	12.6 – 83 (m 57)	3 – 275(m 49)	57 (44%)
Lymphoma*	84	52	32	1– 70 (m 42)	1 – 217 (m 5.35)	31 (37%)
Genitourinary*	42	29	13	21 – 75 (m 59)	2 – 231 (m 25)	4 (10%)
Breast	25	-	25	30 – 74 (m 54)	11 – 241 (m 79)	10 (36%)
Respiratory	29	23	6	29 – 75(m 58)	7 – 212(m 39)	23 (79%)
Kaposi's	5	4	1	32 – 65 (m 51)	2 – 48 (m 16)	0
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%)
Leukaemia	3	1	2	3 – 50 (m 30)	16 – 44 (m 30)	0
Miscellaneous	4	2	2	62 – 73 (m 65)	60– 234 (m 87)	1(25%)
Total	***329 ca in 303 pts**	**211**	**118**	**1 – 83 (m 42)**	**1 – 207 (m 55)**	**135 (40% of pts with Ca)**

*** 25 patients had more than 1de novo malignancies**

Time to diagnosis - m=median -

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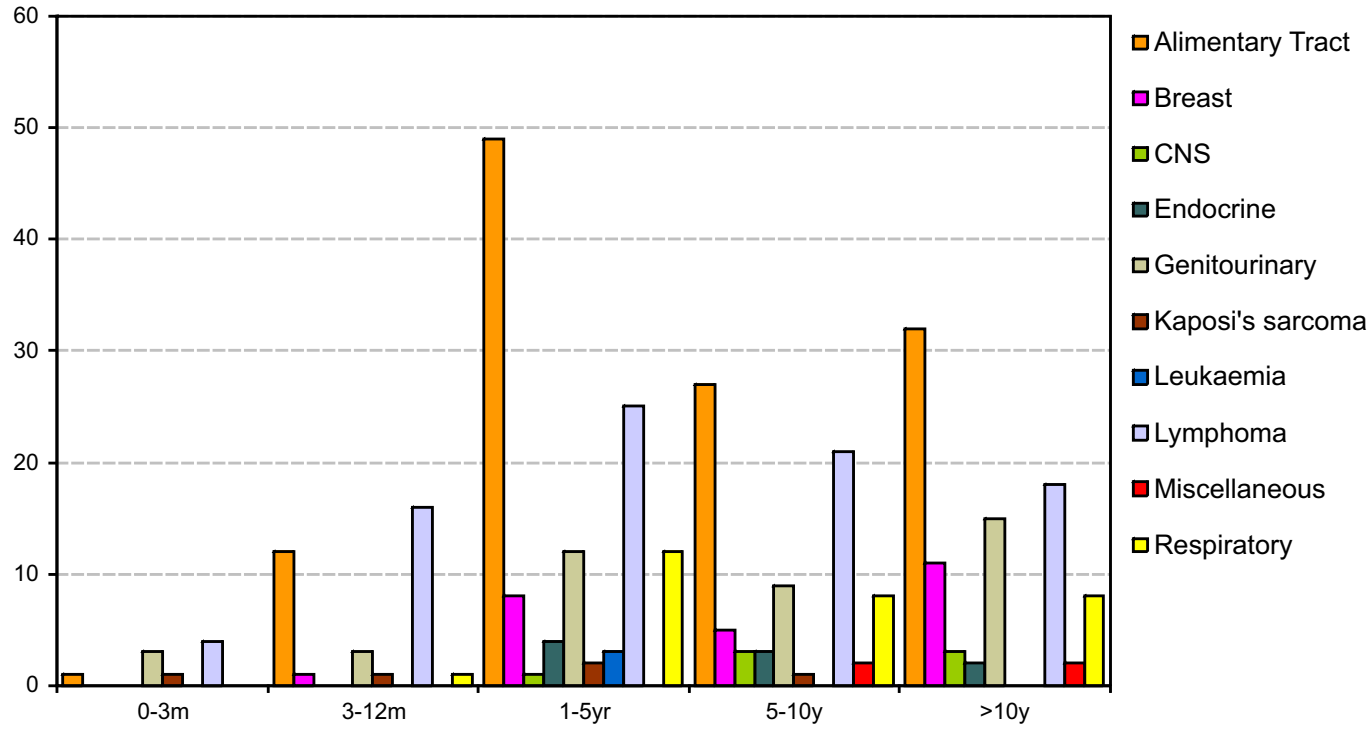
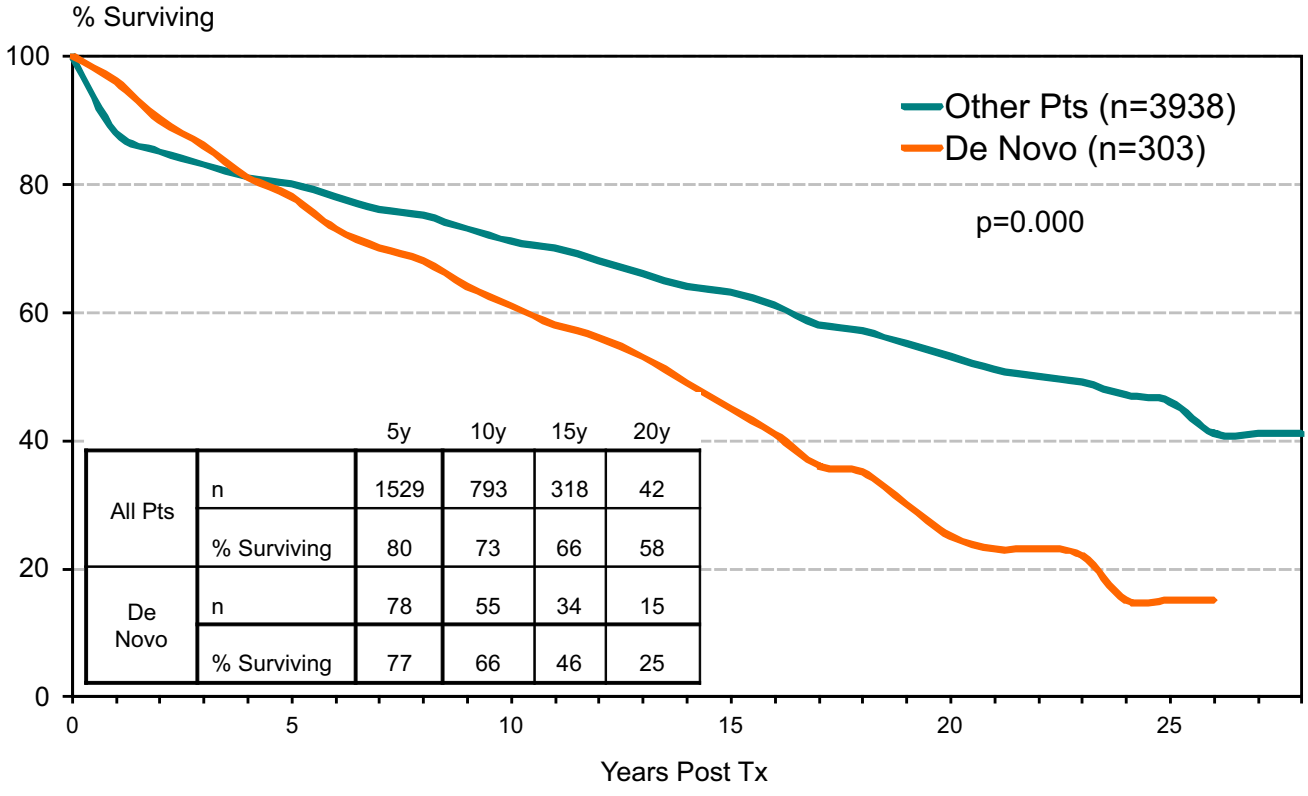
Time to De Novo Non Skin Cancer
n = 4244
329 cancers in 303 pts (7% of all pts)



De Novo Non Skin Cancer vs All Patients
n = 4244



		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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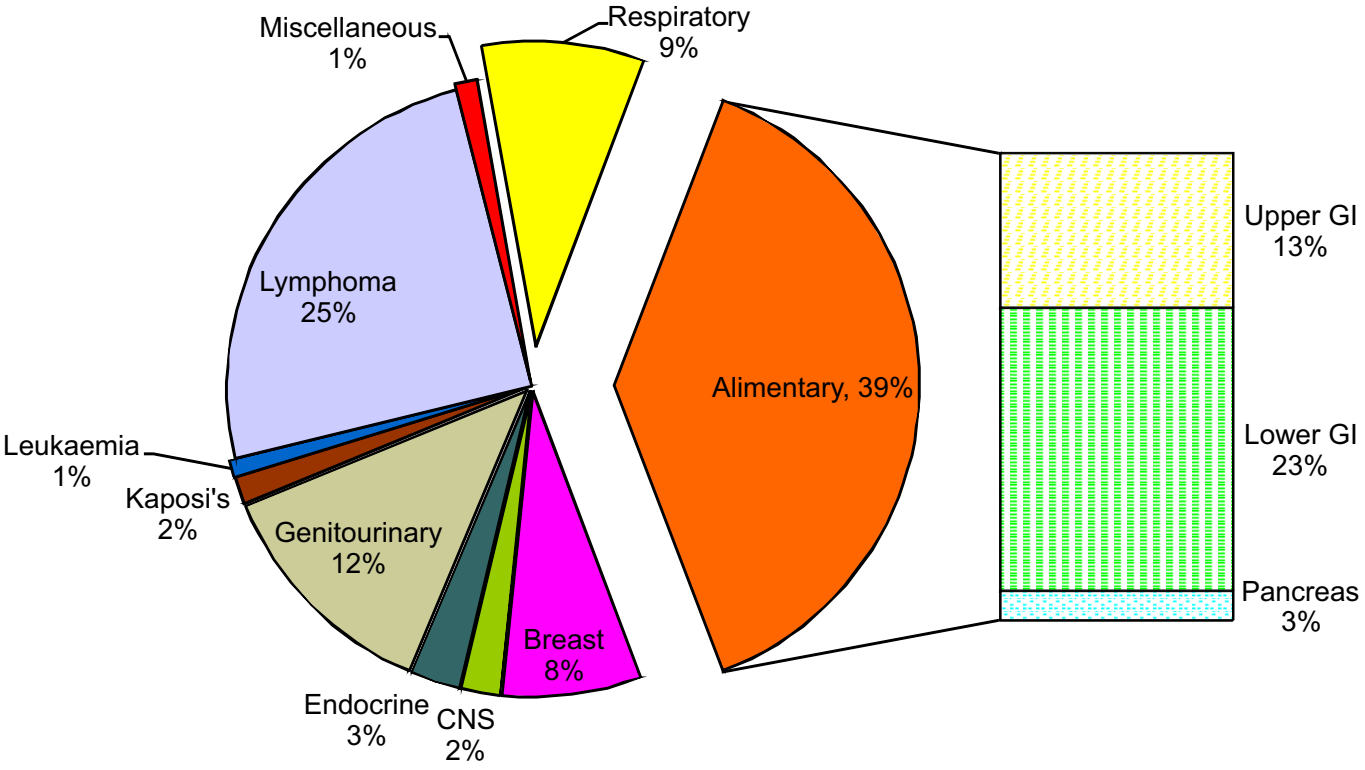
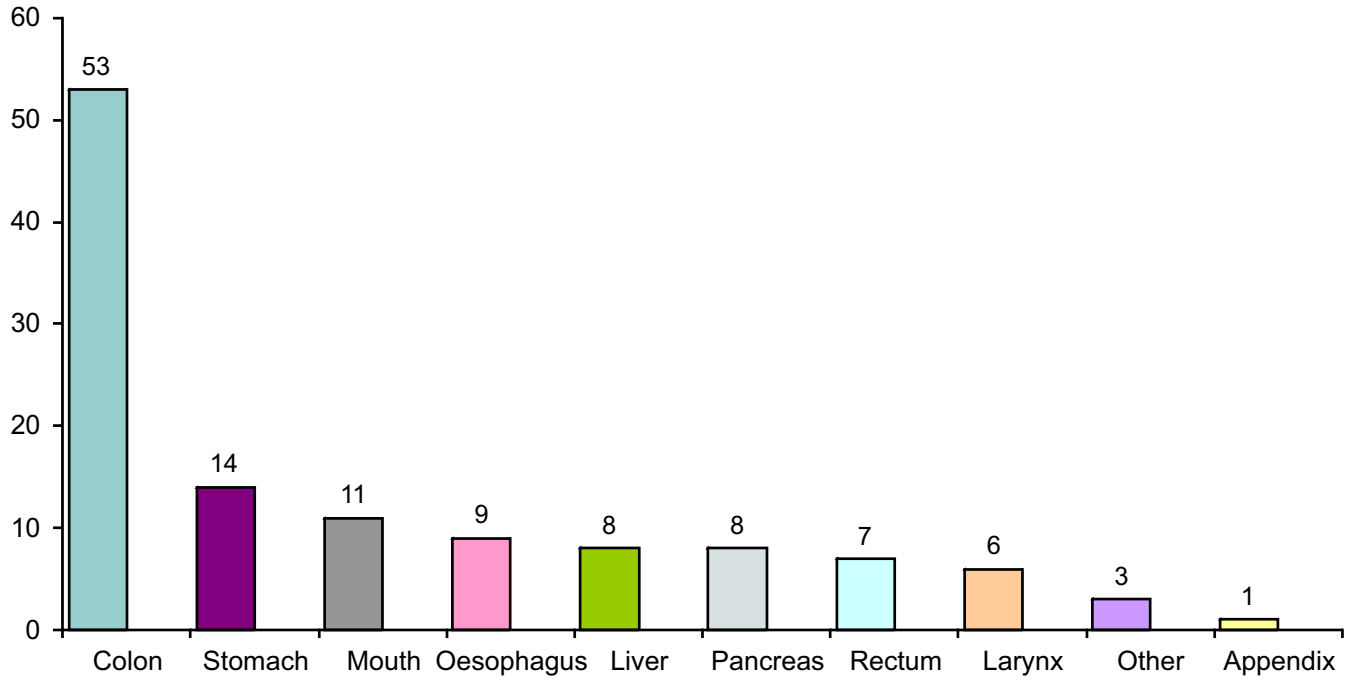
De Novo Non Skin Cancer
n = 303/4244 (7%)



De Novo Non Skin Cancer
Alimentary Tract Incidence
n = 121/329 cancers (36%)



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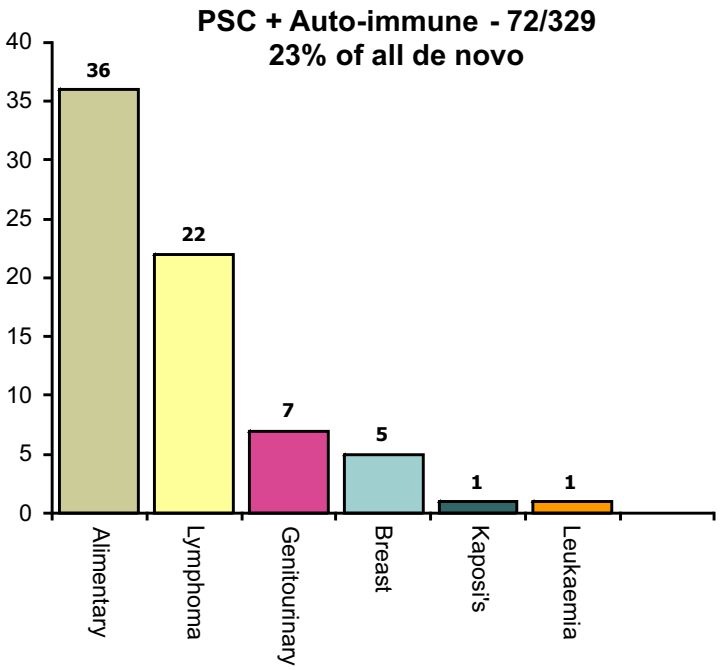
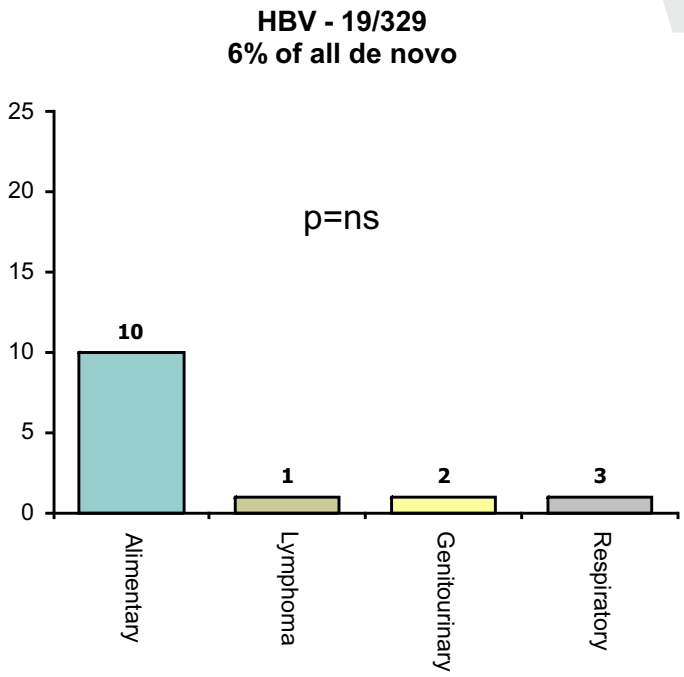
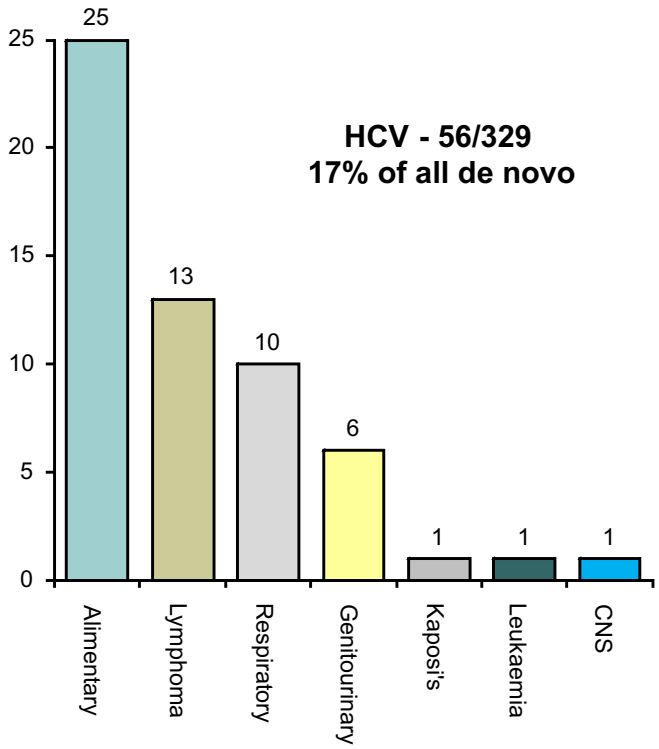
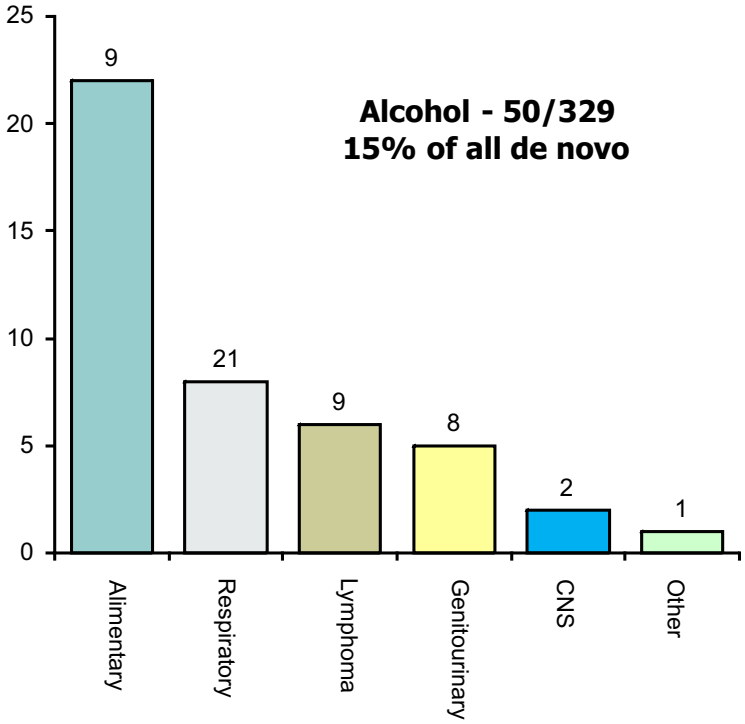
Pre Transplant Liver Disease and De Novo Non Skin Cancer n = 303/4244 (7%)



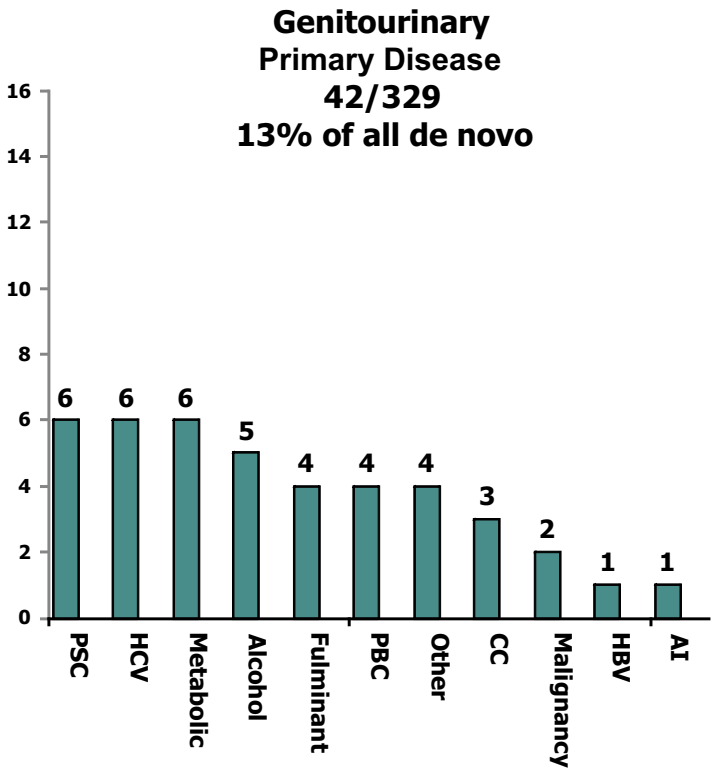


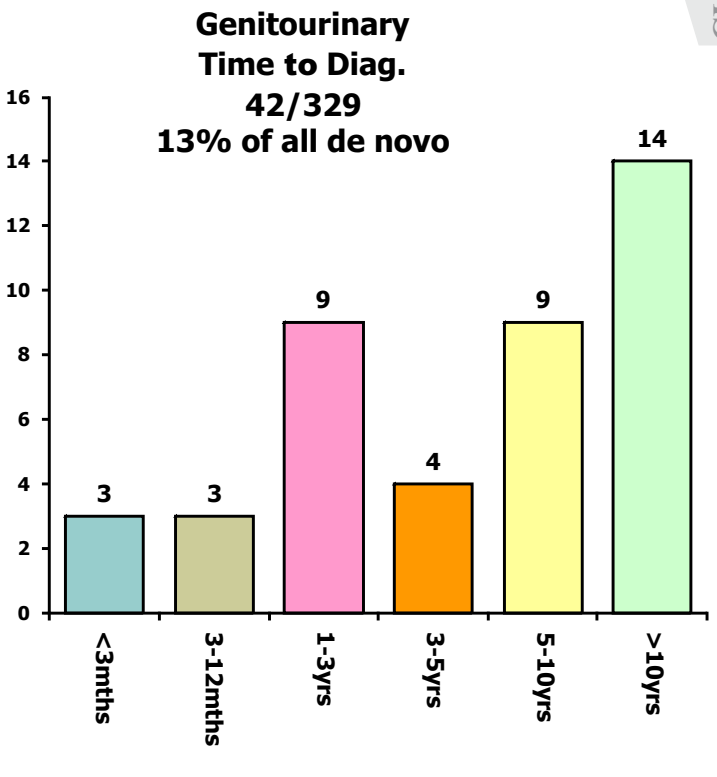
Pre Transplant Liver Disease and De Novo Non Skin Cancer n = 309/3980 (7%)



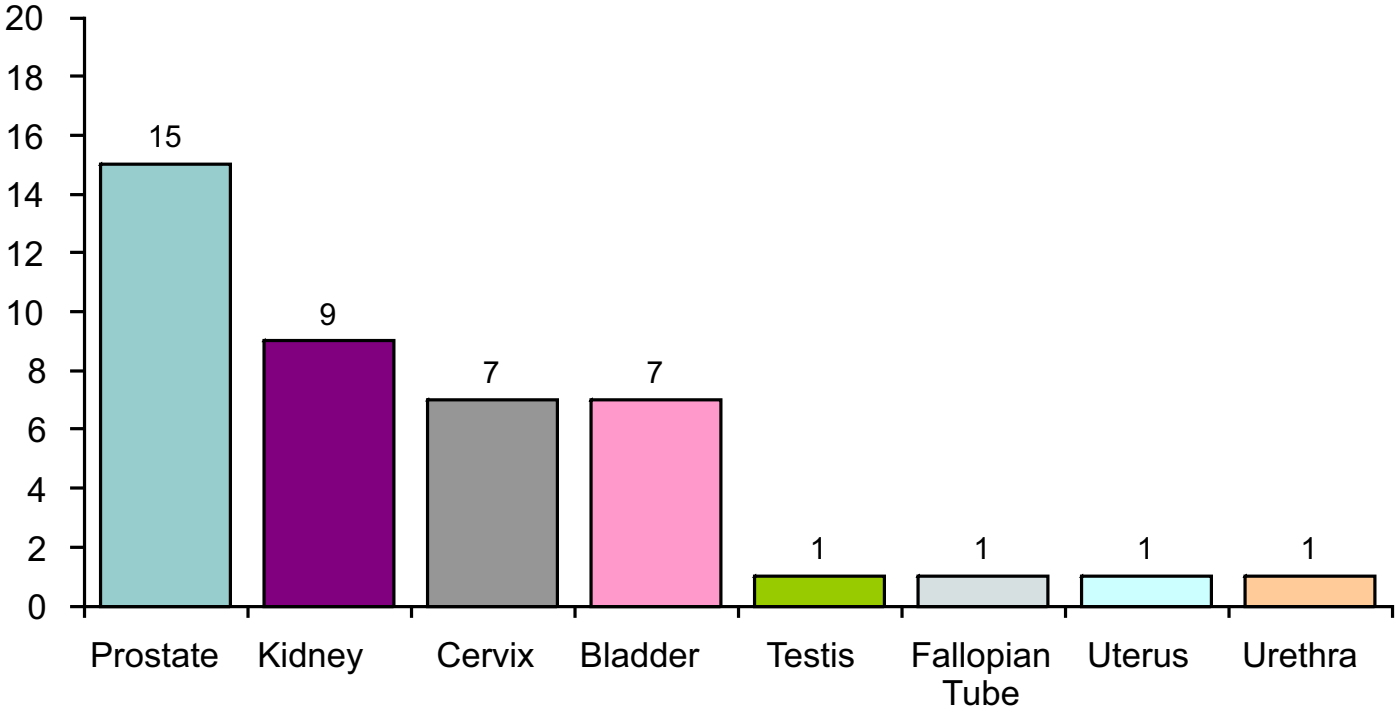


Pre Transplant Liver Disease and De Novo Non Skin Cancer
n = 303/4244 pts (8%)





De Novo Non Skin Cancer
Genitourinary Tract Incidence
n = 42/329 cancers (13%)



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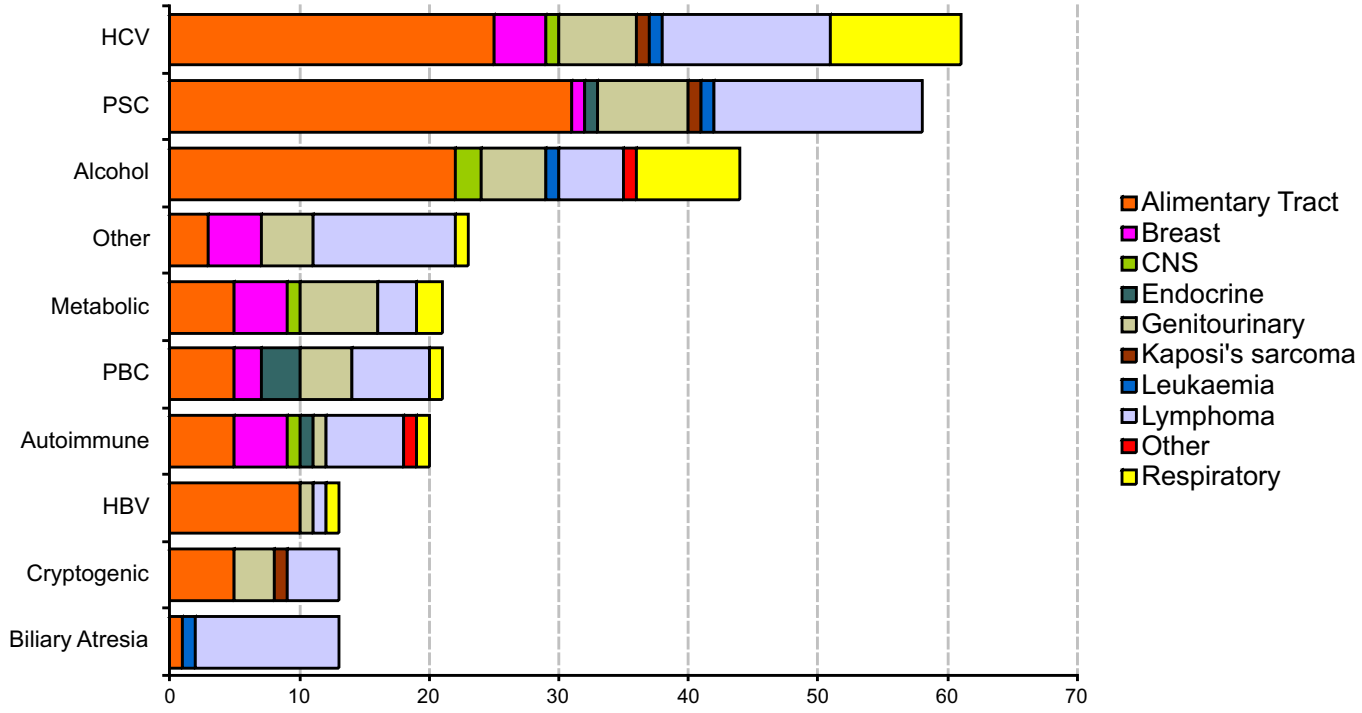
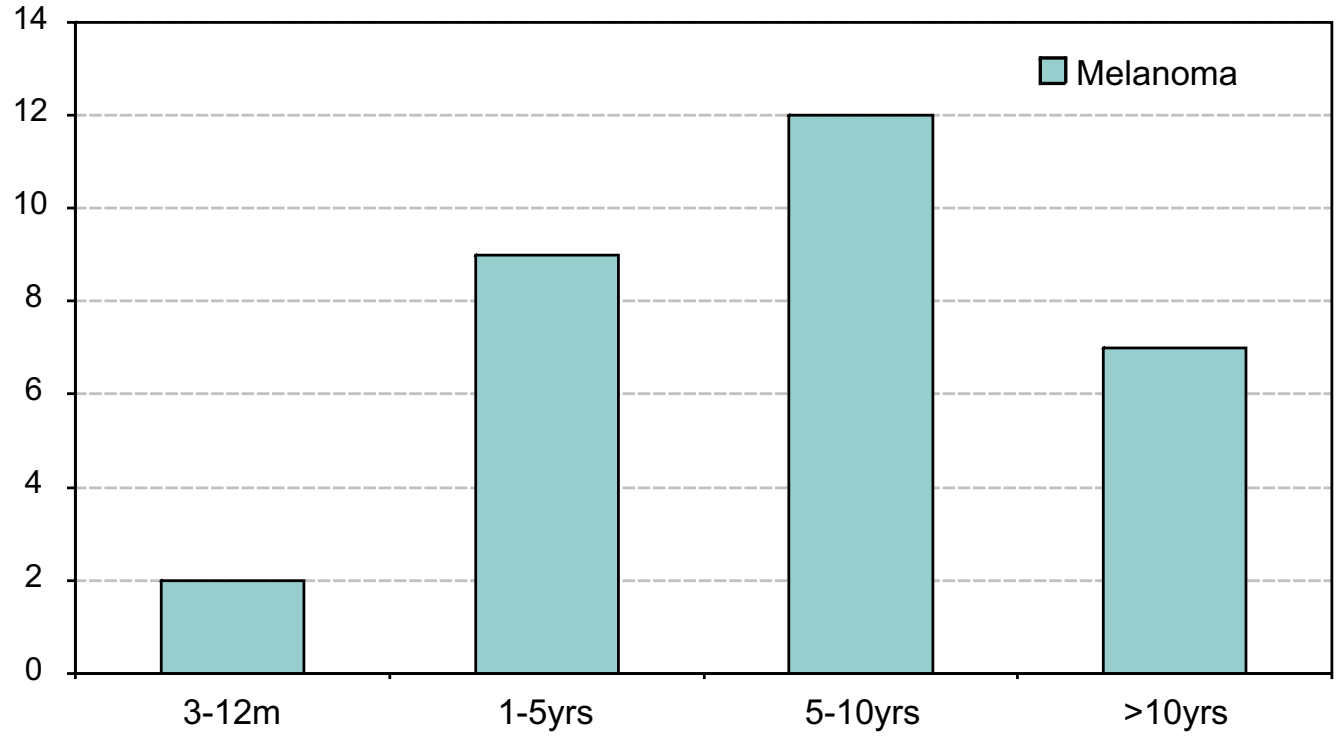
Pre Transplant Liver Disease and De Novo Non Skin Cancer n = 303/4244 pts (7%)



Time to Melanoma Skin Cancer Development Post Tx. n =4244 30 (0.7% of all pts)



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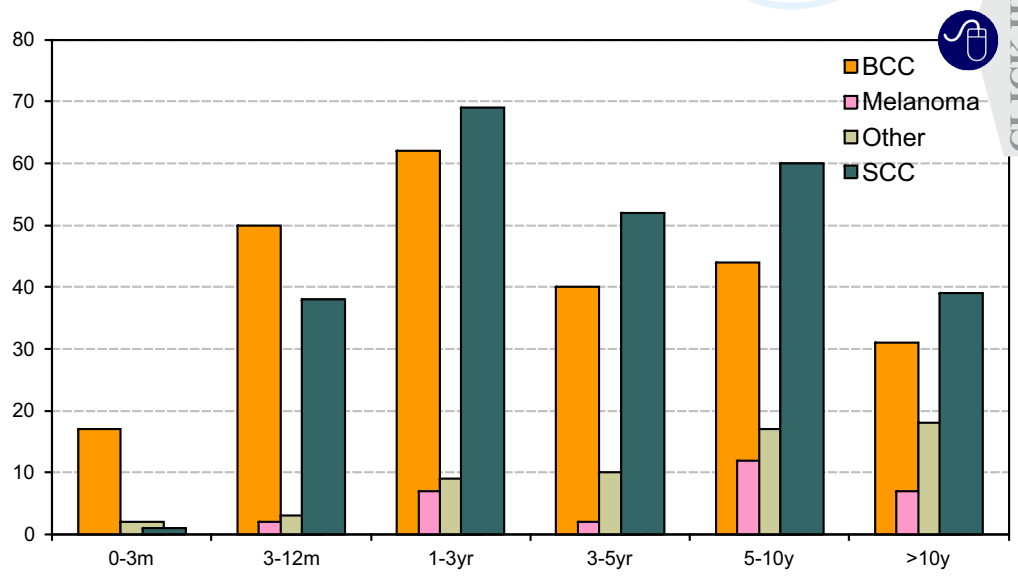
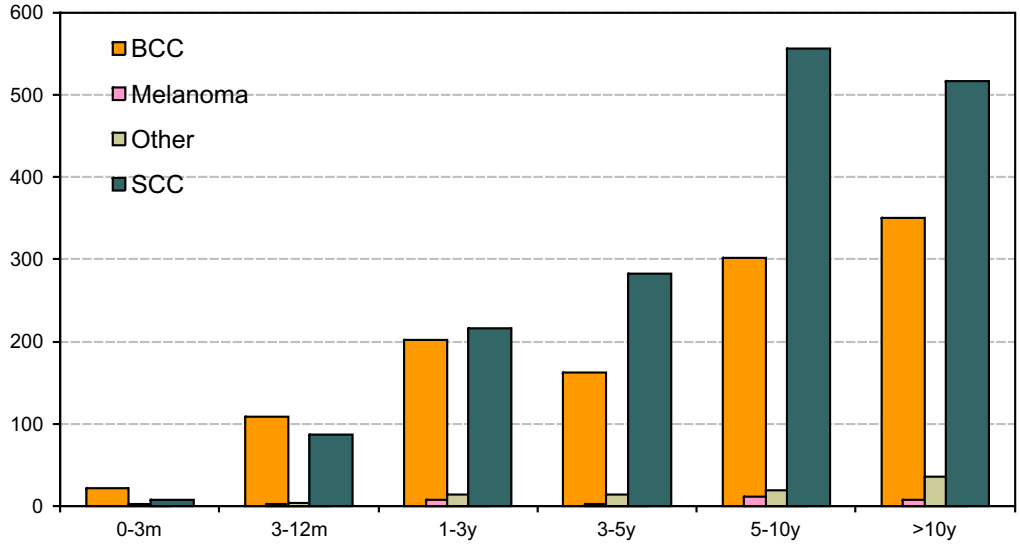
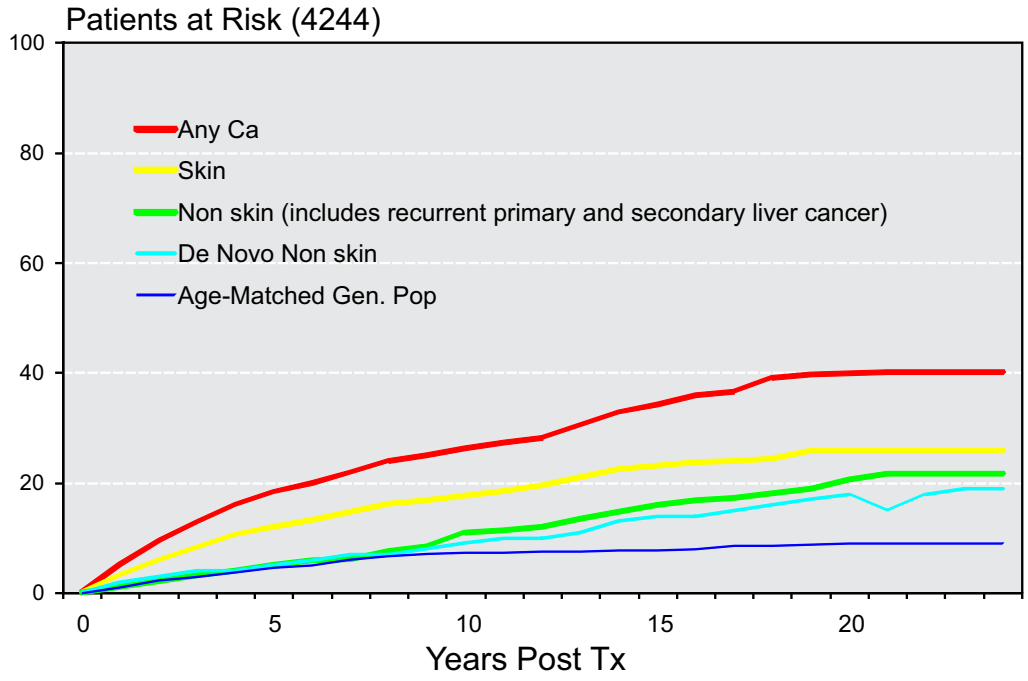
Time to lst Skin Cancer Development
n=4244
616 (14% of all pts)



Time to Multiple Skin Cancer Development
n=4244
204 (5% of all pts)



Cumulative Risk of Diagnosis of Cancer Following Liver Tx. 1985-2013



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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.sswahs.nsw.gov.au/Gastro/LiverTransplant/default.htm

and

The Children's Hospital at Westmead
Hawkesbury Road
WESTMEAD NSW 2145

Victorian Liver Transplantation Unit
The Austin Hospital
Studley Road
HEIDELBERG VIC 3084
http://www.austin.org.au/Content.aspx?topicID=397

and

The Royal Children's Hospital
Flemington Road
PARKVILLE VIC 3052

Queensland Liver Transplant Service
Princess Alexandra Hospital
Ipswich Road
WOOLLOONGABBA QLD 4102

and

The Royal Children's Hospital
Bowen Bridge Road
HERSTON QLD 4029

South Australian Liver Transplant Unit
Flinders Medical Centre
Flinders Drive
BEDFORD PARK SA 5042
http://www.flinders.sa.gov.au/flinders_centre_for_digestive_health/

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

New Zealand Liver Transplant Unit
Auckland City Hospital
Park Road
Auckland
New Zealand
Http://www.nzliver.org/

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Appendix II

ANZLTR PRIMARY Diagnosis
Metabolic disorders by Age Group

Primary Diagnosis	Age group		Total
	Child	Adult	
α -1 Antitrypsin deficiency	37	48	**85**
Crigler-Najjar	9	1	**10**
Familial amyloid polyneuropathy	0	34	**34**
Glycogen storage disease	2	5	**7**
Haemochromatosis	3	29	**32**
Homozygous Hypercholesterolemia	5	2	**7**
Idiopathic copper toxicosis	1	0	**1**
Indian childhood cirrhosis	1	0	**1**
Other*	14	3	**17**
Primary hyperoxaluria	8	6	**14**
Tyrosinemia	4	0	**4**
Urea cycle disorders**	18	4	**22**
Wilsons disease	8	28	**36**
Total	**110**	**160**	**270**

* *Bile acid synthesis disorder*
Protein C deficiency
Methylmalonic acidemia
Familial immunodeficiency
Mitochondrial disease
Amyloidosis
Maple syrup urine disease
Porphyria
Propionic acidemia

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

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Appendix III

ANZLTR PRIMARY Diagnosis - Other by Age Group

Primary Diagnosis	Age group		Total
	Child	Adult	
Alagille syndrome	27	8	**35**
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	3	19	**22**
Choledocal cyst	2	2	**4**
Cholestatic disease-Other	2	8	**10**
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	95	**95**
Polycystic Liver disease	0	21	**21**
Polycystic liver and kidney disease	1	10	**11**
Progressive familial intrahepatic cholestasis(PFIC)	20	5	**25**
Secondary biliary cirrhosis	3	11	**14**
Secondary biliary cirrhosis - Hepatolithiasis	0	4	**4**
Secondary biliary cirrhosis - Cystic fibrosis	11	17	**28**
Other - specify#	10	25	**35**
Total	91	278	**369**

*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	15	**23**
Acute - α-1 -AAT	2	0	**2**
Acute Autoimmune hepatitis	0	6	**6**
Acute Unknown / unspecified	43	91	**134**
Acute - Paracetamol	3	15	**18**
Acute - Other drugs	3	23	**26**
Acute Herbs / mushrooms	0	6	**6**
Acute - Hepatitis A	0	3	**3**
Acute - Hepatitis B	0	57	**57**
Acute - Non A-G	13	17	**30**
Acute - Hepatitis E	0	1	**1**
Acute - Post liver resection/trauma	1	2	**3**
Subacute - Budd Chiari	1	2	**3**
Subacute - Wilson's	2	4	**6**
Subacute Autoimmune hepatitis	1	15	**16**
Subacute - Drug / Herbs	1	15	**16**
Subacute - Unknown / unspecified	5	31	**36**
Subacute - Hepatitis A	0	2	**2**
Subacute - Hepatitis B	0	19	**19**
Subacute - Non A-G	0	4	**4**
Total	**84**	**329**	**413**

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Appendix V

ANZLTR Causes of Patient death

Graft failure - other	Age group		Total
	Children	Adult	
Vascular thrombosis	8	15	23
Hepatic artery *Portal vein* *Hepatic vein*	*4* *2* *2*	*9* *6* *-*	*13* *8* *2*
Non thrombotic infarction	3	-	3
Primary non function	4	17	21
Massive haemorrhagic necrosis	4	0	4
Recurrent disease *(ALD, PSC, CAH:AI)*	-	17	17
De novo Hep C	-	2	2
Biliary Complications	3	12	15
Other *(PNC, immune hepatitis, outflow obstruction)*	7	12	19
TOTAL	29	75	104

Miscellaneous	Children	Adult	
Multiorgan failure	5	48	53
Renal Failure	1	31	32
Graft vs Host disease	-	7	7
Social *(accident, suicide,non-compliance, Rx withdrawn)*	1	16	17
Sudden death *(cause unknown)*	2	24	26
Other *(Hyperkalaemia,motor neurone disease diabetes complications, drug reaction, progression FAP essential thrombocythemia)*	2	26	28
TOTAL	11	152	163